Cationic Surfactants: Synthesis, Characterization, Micellization, Biological Behaviour and Drug Interaction

Thesis Submitted to the Department of Chemistry, Quaid-i-Azam University, Islamabad, in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

In

Inorganic/Analytical Chemistry

By

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DECLARATION

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To

My Parents,

My Daughter

&

My Husband

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List of Abbreviations

Asc Ac = Ascorbic acid

CMC = Critical micelle concentration

DMSO = Dimethylsulfoxide

EO = Ethylene oxide

FT-IR = Fourier transformed infrared

G = Gibb's free energy

H = Enthalpy

K_b = Binding constant

K = Kelvin

NMR = Nuclear magnetic resonance

NAPLs = Non-aqueous phase liquids

PEG = Polyethylene glycol

PAHs = Polycyclic aromatic hydrocarbons

S = Entropy

SANS = Small angle neutron scattering

SDS = Sodium dodecyl sulfate

SD = Standard deviation

TCE = Trichloroethylene

UV = Ultraviolet

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Summaira Fayyaz

ABSTRACT

In this study, by condensation reactions twenty three new amphiphilic surfactants were made. Out of them, 14 were *n*-alkyl pyridinium bromides and 9 were *n*-alkyl quinolinium bromides. All synthesized amphiphiles were characterized and identified by "NMR (^{1}H, ^{13}C)"and "FT-IR" spectroscopic techniques. Using "conductometry and UV/visible spectroscopic methods" the "micellization process" of all surfactants was studied in detail. Throughout this study ethanol was selected as solvent to study the "micellization process". The critical micellization concentration (CMC) values for all *n*-alkyl pyridinium bromides were noted to be very low, ranging from 0.27 to 0.42 mM and for *n*-alkyl quinolinium bromides it was found 0.38-0.51 mM.In all these "surfactants" the CMC value was found to be inversely proportional to the alkyl chain length. The "temperature effect" on the CMC and thermodynamics of micelle formation were thoroughly studied in the range of "298-318 K". Thermodynamic parameters (ΔG, ΔH and ΔS) of the "micellization process" of these surfactants were calculated. ΔG showed a negative value and ΔH was found to be positive indicating that the process of micellization was spontaneous and endothermic in nature. Biological activities like antibacterial, antifungal and antioxidant activitities of these amphiphiles were also explored. All compounds were found to be significantly bactericidal against different bacterial strains and fungicidal against different strains of fungi.

These surfactants were also assessed for their potential use in a drug delivery system. For this purpose, the interactions of these surfactants with drugs (Flurbiprofen and Ketoprofen) were studied using UV- visible spectroscopic methods. It was found that both kinds of surfactants, (n-alkyl pyridinium and n-alkyl quinolinium based surfactants) bind well with the selected drugs. The "binding constant (K_b)" and "number of drug molecules incorporated per micelle (n)" were computed. Estimations of "K_b" and "n" indicated a solid collaboration of chosen drugs with the combined surfactants. A negative estimation of "Gibb's free energy (ΔG)" of the binding demonstrated the immediacy of medication surfactant associations.

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Chapter-1

Introduction

1.1 Surfactants

Surfactants are called “surface active agents” [1]. They are also termed as amphiphiles because of their amphiphilic (dual) nature. They have both hydrophilic and hydrophobic parts integrated in one molecule. Usually its “hydrophilic head group” shows affinity towards water and other polar solvents and a hydrophobic tail hates water or polar solvents. Surfactants have a tendency “to decrease the surface tension (or interfacial tension) between two liquids or between a liquid and a solid”.

“Surfactants” are used in a variety of products oscillating from pharmaceuticals to laundry detergents to motor oils and cleansing supplies. They are used as wetting agents, emulsifiers and dispersants. Besides all this, they are also applied in highly advanced industrial techniques like magnetic recording, micro-electronics and biotechnology [2-4].

1.1.1 Surfactants and Surface Tension

Surfactant molecules are adsorbed at surfaces or accumulated at interfaces. This way they lower the interfacial free energy. “The minimum amount of work required to create an interface is called the interfacial free energy and it is related to the surface or interfacial tension”. The “surface or interfacial tension, γ is the “amount of work W” required to generate “a unit area ΔA” of an interface.

$$W = \gamma . \Delta A \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

Or

$$\gamma = W/ \Delta A \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

The above equations make it clear that the “surface tension is directly proportional to the amount of work and inversely proportional to the area of the interface”.

Surfactants have the capability of being adsorbed to existing interfaces and thus decreasing “the interfacial free energy by lowering the surface or interfacial tension between the two phases” [5-9].

1.2 Classification of Surfactants

Surfactants are commonly classified into four groups as; anionic, cationic, zwitter- ionic and non-ionic [10], depending upon "the nature of the hydrophilic head group". Tails of surfactants are the same, mostly comprising of a hydrocarbon chain that can be aliphatic (branched, linear) or aromatic.

1.2.1 Non-ionic Surfactants

Non-ionic surfactants have no charge on their head group. They are the most widely used surfactants and are reckoned as the most diverse type of surfactants respecting their structure, composition and surface properties [11]. Triton X-100, spans and tweens are non-ionic surfactants. Their structures are shown in figures 1.1-1.3.

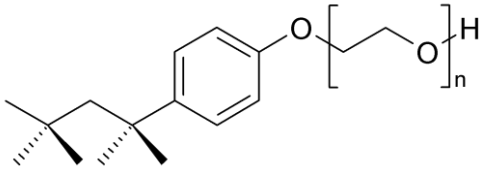


Figure 1.1: Structure of Triton X-100 [11]

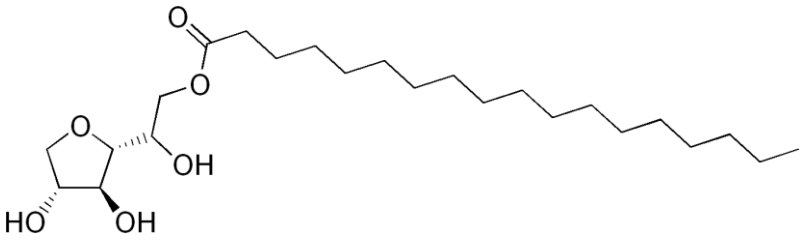


Figure 1.2: Structure of Span 60 [11]

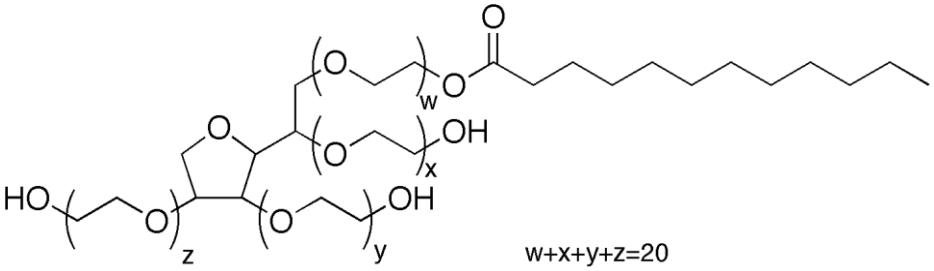


Figure 1.3: Structure of Tween 20 [11]

1.2.2 Anionic Surfactants

They have anionic functional head groups, such as phosphate, sulfonate, carboxylates and sulphates. Examples of anionic surfactants are ammonium lauryl sulphate, dioctyl sodium sulfosuccinate (DOSS), and perfluoro octane sulfonate (PFOS) etc. These are the most common surfactants. Many of these are used in emulsion polymerization. Figures 1.4-1.6 show the structures of these surfactants [12].

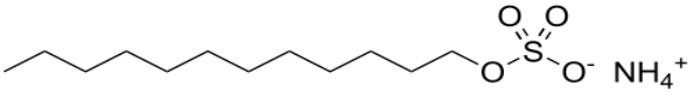


Figure 1.4: Structure of Ammonium lauryl sulphate [12]

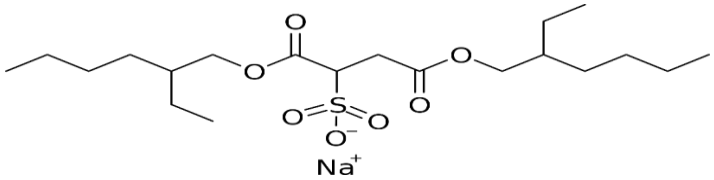


Figure 1.5: Structure of Dioctyl sodium sulfosuccinate [12]

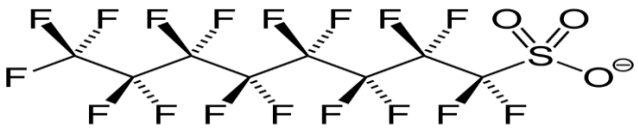
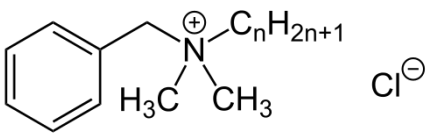


Figure 1.6: Structure of Perfluoro octane sulfonate [12]

1.2.3 Cationic Surfactants

They have a head group which is positively charged. These surfactants are used in cosmetics, textile industry and corrosion inhibition. Additionally they have potent antimicrobial activities [12]. "Cetylpyridinium chloride (CPC), Benzethonium chloride (BZT), Benzalkonium chloride (BAC)", are examples of cationic surfactants and their structures are shown in figures 1.7-1.9.



n = 8, 10, 12, 14, 16, 18

Figure 1.7: Structure of Benzalkonium chloride [12]

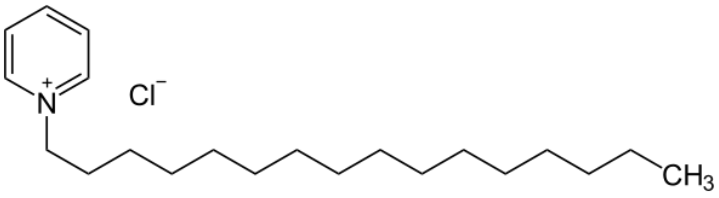


Figure 1.8: Structure of Cetylpyridinium chloride [12]

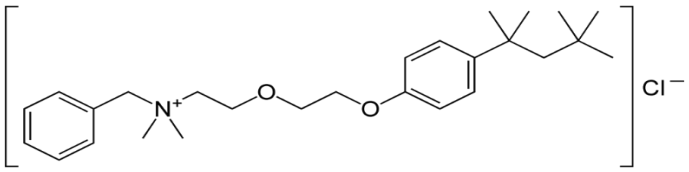


Figure 1.9: Structure of Benzethonium chloride [12]

1.2.4 Zwitter- Ionic Surfactants

They are also known as amphoteric surfactants because they carry both positively and negatively charged groups in the same molecule. Their anionic part may vary and the cationic part is based on primary, secondary, tertiary amines or quarternary ammonium cations. Zwitterionic surfactants are pH dependent surfactants [13]. Examples are lecithin, myristamine oxide, and sodium lauroamphoacetate. Figures 1.10 - 1.12 represent the structures of the mentioned surfactants.

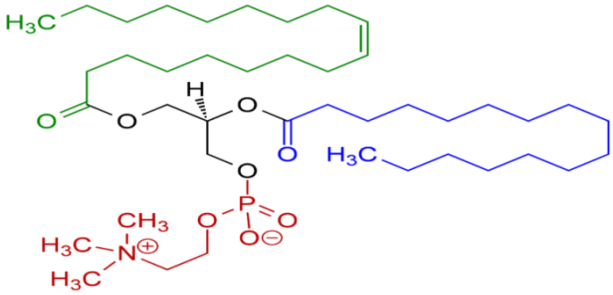


Figure 1.10: Structure of Lecithin [13]

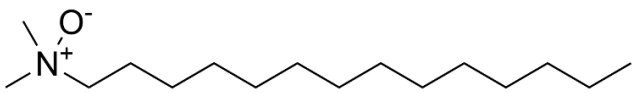


Figure 1.11: Structure of Myristamine oxide [13]

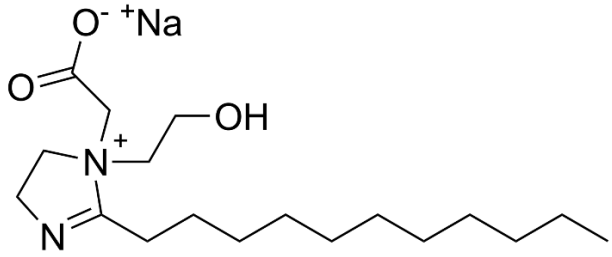


Figure 1.12: Structure of Sodium lauroamphoacetate [13]

1.3 Micelles and Micellization

Because of their dual nature, when surfactants are dissolved in water, they are forced to build the special structures in the aqueous medium. The surfactant molecules become self-aggregated in the form of a cluster at an air-water or oil-water interface. They keep their hydrophilic head bunches within the watery stage and permit the hydrophobic hydrocarbon chains to elude into the vapour or oil stages, as shown in Figure 1.13.

This cluster arrangement of amassed surfactant molecules is named ‘‘micellization’’and such totals are called as ‘‘micelles’’. The method of micellization, could be a result of adjustment between amphiphile and dissolvable [2].

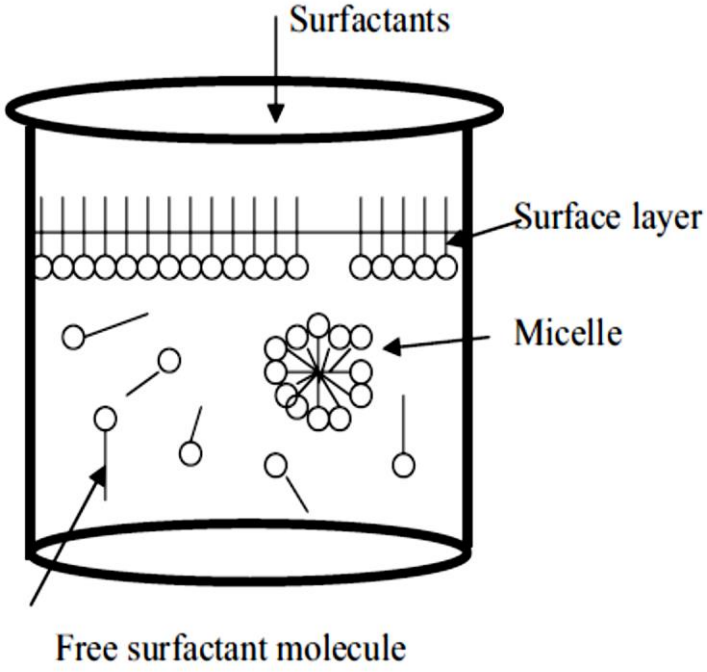


Figure 1.13: Micelle formation

1.3.1 Critical Micelle Concentration

"The least sum of surfactant particles to create a micelle is called the critical micelle concentration (CMC)" [14]. On its CMC estimation, usage and properties of a surfactant strongly lay and can be affected by various parts like the concoction idea of the surfactant molecule, temperature, dissolvable, included substances, pH, ionic strength and so forth [14, 15]. Micelles remain in an enthusiastic off set with surfactant monomers past the CMC and may have unmistakable shapes and sizes.

At the CMC estimation, a few physical properties (e.g. electrical conductivity, surface pressure, etc.) suddenly alter their values in surfactant arrangements, as schematically appeared in Figure 1.14. However, the CMC may be a limit concentration run, not a settled esteem.

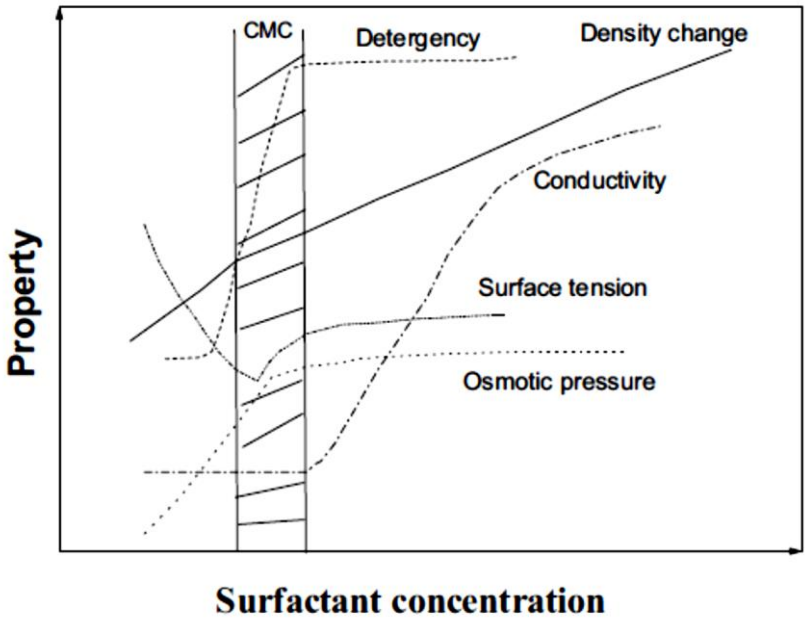


Figure 1.14 Critical micelle concentration at various physicochemical properties [16].

1.3.2 Energetics of Micellization

This circumstance of micelle formation is enthusiastically more positive than complete solubilisation. The solid adsorption of such particles comes about within the arrangement of an orientated monomolecular layer at the surface or interface. This surface action may be an energetic marvel, since the ultimate state of a surface or interface speaks to adjust between the propensity towards the adsorption and the inclination towards the total blending due to thermal movement of the particles. The surface tension is thus lowered due to the tendency of surfactants to pack into an interface, which causes an increase in the interface. Expansion of a

surfactant diminishes the interfacial tension between two fluids adequately. Hence it favours emulsification [17]. The driving force of micelle formation is the increment in entropy, which is caused by the discharge of well-organised water molecules from the water hating portion of the amphiphile (the hydrophobic impact) [18]. The micelle arrangement is restricted by the repulsion between hydrophilic parts of the surfactants, and by their affinity for water. This is also an entropic effect, since diminishing in entropy will emerge from constraining the surfactant molecules together. The competition between these two entropic effects administers whether the system phase-separates or the molecules instead form small clusters, like dimers. Micelles are found in between these two states where neither of the effects are strong enough to completely dominate the behaviour. Micelle formation is affected by all of these energy changes. Micelle formation does not occur below the critical micelle concentration (CMC), as the free unites have high entropy of mixing, which is not countered by the energy of having water around the entire surfactant [1, 2 and19].

1.3.3 Shapes of Micelles

Micelles can have different shapes such as spherical, cylindrical and bilayer shapes as shown in Figure 1.15. The main factor which governs the shape of a micelle is the volume ratio between the hydrophilic head and the hydrophobic tail [20]. When there is a large difference between the head group and the tail of a surfactant and the head group has a much larger volume, spherical micelles are formed. And when there is a smaller difference, cylindrical micelles are formed and at no difference bilayers are formed.

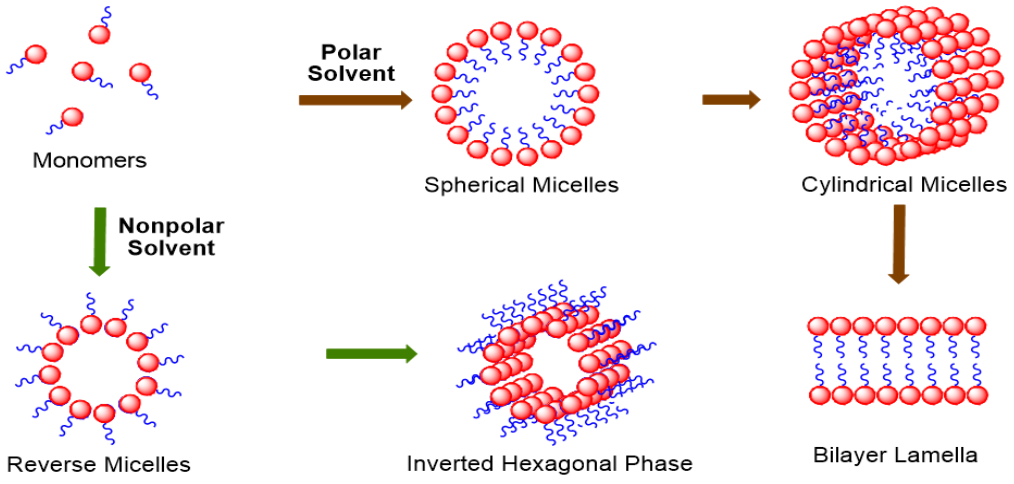


Figure 1.15 shapes of Micelles [21]

A spherical micelle is the simplest form of aggregate for self-assembled micellar structures. The surfactant monomers aggregate in such a manner that the hydrophobic portion is partitioned from the solvent and it forms a spherical core where the hydrophilic part shields the core from the aqueous solution. Considering the spherical micelles, these have an ideal aggregation number, "N_{agg}" where all the micelles have minimal free energy [22]. Within the case of having an accumulation number smaller than the ideal aggregation number, the hydrophobic portion will be in contact with water. In the opposite event, if the aggregation number is greater than the optimal aggregation number, the head groups will be stuffed as well near together and subsequently repel each other. Spherical micelles are therefore found to be moderately mono disperse and with a structure harsh to changes in concentrations over CMC [23, 24].

For cylindrical micelles, no optimal aggregation number is observed where the molecules have a minimal free energy. This is due to end-cap effects, as the molecules at the ends are forced to pack into hemispheres. These molecules will therefore have a head group area larger than the optimal. The molecules distant from the cylinder ends are energetically independent of the cylinder length and the only limiting factor preventing the formation of extremely long cylinders is the increase in entropy arising from adding more surfactant molecules to the cylindrical micelles. The hemispherical end-caps favour the growth, as merging two micelles would reduce the energy of the end-caps. Cylindrical micelles are therefore found to be polydisperse in length and the length is sensitive to changes in the concentration above CMC [23, 24].

Micelle shapes can be affected by external factors like temperature and pH of the solution. These external factors may change the optimal head group area of the amphiphilic molecule. Increased salinity strongly affects the head group areas of ionic surfactants, as the optimal head group area will decrease with increasing electrolyte concentration. Viably, charge screening will debilitate the repugnance between the head bunches. Ideal head bunch zones of non-ionic surfactants are influenced by temperature as a head group region is found to diminish with expanding temperature [19, 23 and 24].

1.3.4 Atomic Organization in Micelles

According to the customary portrayal of a micelle, the hydrocarbon chain is all-trans and coordinated radially internal, in polar solvents as appeared in Figure 1.15. Clearly, all chain ends were situated at the focal point of the micelle which brought about abnormally high

thickness that was not genuinely fitting. An interphase model was acquainted with portray the atomic course of action in micelles that thought about both chain congruity and steric imperative [25-27]. The interphase model is upheld by little edge neutron dispersing (SANS) and NMR tests instead of the outspread chain or oil bead models. The interphase model deduced confused alkyl chains close to the micelle surface and considerably more arranged chains close to the center of the micelle. With the fast advancement in computational science, a more unequivocal micellar structure was investigated utilizing sub-atomic unique recreations [28-30]. The outspread thickness appropriations from the micelle place for hydrocarbon chains, the head gathering and water were obviously exhibited [27].

1.3.5 Micellar Solubilization

The dissolvability of water insoluble substances is expanded by surfactant arrangements, for example, cleansers and bile salts, referred to as ahead of schedule as in nineteenth century [31]. It was until the 1930s, when the solubilization wonders by surfactants were legitimized utilizing the speculation of the development of colloidal particles or micelles [32]. It was seen that at the grouping of surfactant over the basic micelle fixation esteem, the solubilization of trans-azobenzene in arrangements of cetylpyridinium salts had happened [33]. Numerous examinations have been done on micellar solubilization of drugs [34-40].

Numerous variables had been discovered to have the option to influence solubilization limits of micelles, for example, hydrocarbon chain length and headgroup of surfactants, extremity and hydrophobicity of the solubilizate (drug), temperature, pH, ionic quality, and so on. A more drawn out hydrocarbon chain length of surfactants normally delivers a higher solubilization limit. The more nonpolar the solute, the more critical is the solubilization. For instance, polysorbate 20, 40, 60 and 80 had disintegrated a progression of medications and the solubilization was expanded with expanding the alkyl chain length of surfactants [35, 37 and 41]. At the point when the alkyl chain length of surfactants was settled, the water adoring head bundle could likewise impact the solubilization limit and the inclination relied upon the solute properties. In a consider, a plan of surfactants with same hydrocarbon chain length, was used to solubilize hydrocarbon and nonpolar mixes and it was discovered that the solubilizing forces of the surfactants were in the request for anionic < cationic < non-ionic.

In another examination for polar solutes, when solubilized in the layer of the micelles, the outcomes were fairly unique. Furosemide, a diuretic, was solubilized in anionic SDS (sodium dodecyl sulfate) micelles, non-ionic polysorbate 80 micelles and PEG (polyethylene glycol) polymers and watched the positioning request of the solubilization ability to be SDS >

polysorbate 80>PEG. With raised temperatures, the micellar solubilization limit would typically increment [42, 43] with certain exemptions, e.g., benzocaine in polysorbate frameworks had lower solubilization power at higher temperatures [44].

1.3.6 Area of medications inside the Micelles

Micelles may solubilize water-insoluble medications in a run of microenvironments, from the hydrophobic focus to the amphiphilic surface (palisade). Unquestionably then the micellar solubilization instrument must be fundamentally identified with the zone of sedate inside the micellar get-togethers. The little size of these totals brings about a more noteworthy surface-to-volume proportion. Accordingly, the surface region must be considered in any mechanical picture of micellar solubilization. Numerous spectroscopic procedures, including fluorescence extinguishing [45, 46] UV-obvious spectroscopy [47, 48] little edge X-beam diffraction [49] NMR [50, 51] EPR [46, 52] and circuitous strategies dependent on thermodynamic examination [53] have been utilized to test the locus of medication solubilization in micelles.

1.3.7 Micelles, Plasma Membranes and Drugs

Every cell in the human body, no matter where it exists, in the skin, muscles, heart, brain or in any other organ, it is separated by a membrane. These membranes are structurally a bilayer of phospholipids in which protein molecules are imbedded. In this phospholipid bilayer, polar heads are oriented towards the aqueous medium and nonpolar tails are pointed inwards. These cell membranes or more precisely plasma membranes not only separate each cell from the other but also govern the transportation of different molecules across the cells. As the inside core of the phospholipid bilayer consists of nonpolar hydrophobic tails, it is highly hydrophobic in nature and molecules crossing this should also be nonpolar and hydrophobic [54].

A bilayer of cationic surfactants having a polar head bunch and a nonpolar tail include an incredible auxiliary similitude with the plasma membrane as shown in Figure 1.16. Like membranes, micelles have a polar, hydrophilic or lipophobic external part and a nonpolar, hydrophobic or lipophilic region inside the micelle. This similitude empowers the micelles to cross these membranes with ease.

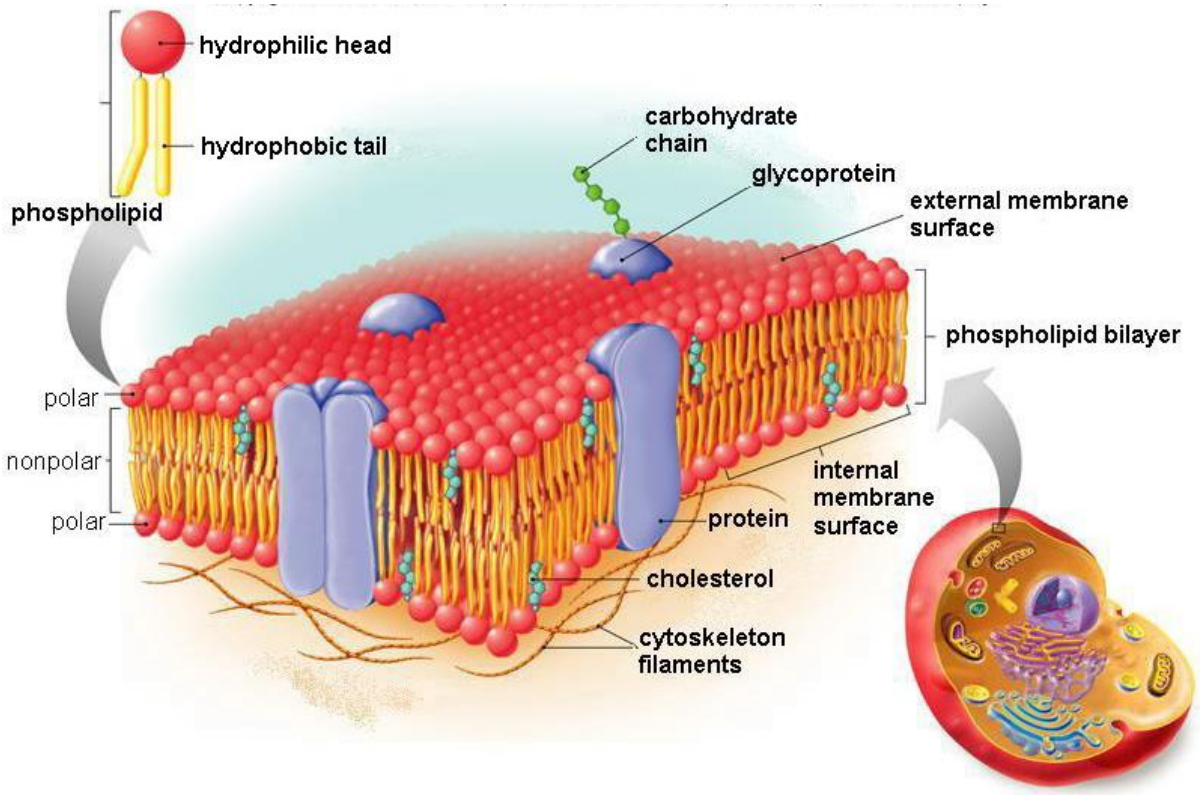


Figure 1.16: Structure of a Plasma Membrane [55].

Thus, every molecule crossing the bio membranes should have a hydrophobic character. The efficiency of drugs heavily depends on their tendency to pass through these membranes and to reach at the point of action. Molecules of drugs should have lipophilic nature; they should be able to have affinity for the hydrophobic inner core of membranes. Drug molecules not only have polar character to have high solubility, they must also have lipophilic nature to cross membranes and show high permeability. If a drug lacks in hydrophobic or lipophilic affinity, they can cross plasma membranes by attaching or encapsulating themselves in micelles [56].

1.4 Drug Conveyance and Micelles

The usage of micelles in drug conveyance frameworks is, among the most prepared lipid-based quiet transport systems. The soonest drug use of micelles as solubilization specialists was the utilization of cleanser to solubilize cresols in planning of the Saponated Solutions of Cresol, U.S.P. what's more, Lysol, B.P. toward the finish of nineteenth century [35]. Surfactants, as emulsifying specialists, had been applied in drugs considerably before [57].

It was not until the 1950s that the drug utilizations of micellar solubilization had gotten orderly consideration [35] and turned out to be widely concentrated thereafter. In the current

drug market, numerous items use micelles as medication conveyance frameworks. For outlines: against malignancy quiet paclitaxel/Taxol® (Bristol-Myers Squibb) occupations, Cremorphor EL micelles as the significant movement vehicles through IV implantation. Dutasteride/Avodart® (Glaxo SmithKline) was planned into gelatine case that could frame blended micelles of mono and diglycerides of caprylic/capric corrosive upon oral organization. There are numerous focal points of micelles as a medication conveyance specialist instead of basic solubilization of medications. Micelles are typically thermodynamically stable [58] and they may make sure about some instable medications from substance debasement when the receptive useful gatherings of the medications are canvassed in the focal point of a micelle [59]. A couple of polymeric micelles have tumor focussing capacity through "enhanced permeation and retention" (EPR) sway [60]. Micelles could likewise assume a significant function in numerous lipid-based conveyance frameworks, for example, "self-emulsifying drug delivery systems" (SEDDS). Emulsions or miniature emulsions are shaped by weakening SEDDS with watery liquids in the GI lot. The edibility of the lipid segment is believed to be basic in the medication delivery and assimilation in light of the fact that inedible lipids, for example, paraffin oil, frequently hinder the medication retention by keeping the medication inside the lipophilic store [61]. The lipid absorption, principally through lipolysis, will hydrolyse fatty substances to mono-or diglycerides and unsaturated fats that structure blended micelles in with phospholipids and bile salts [62, 63]. The medications solubilized in the blended micelles are promptly consumed on account of the more noteworthy surface/volume proportion and the fast exchange pace of the monomers and out of the micelles. The amount of the medication that could be solubilized in the blended micelles would be essential in steady maintenance.

1.5 Applications of Surfactants

Surfactants are very useful compounds and have wide spread applications. Surfactants are not only being used as detergents and soaps but they are being utilized in many important areas like; gene and drug delivery systems, medicines and personal care products, petroleum processing, oil recovery, food items, pesticides, corrosion inhibition and many others [10, 64-71].

1.5.1 Surfactants in Medicines and Personal Care Products

Cationic surfactants like quarternary ammonium salts, alkyl polyglucosides and alkyl pyridinium salts have viable germicidal and antimicrobial action [10, 64-66]. Individual items

like shampoos and other skin agreeable items sold as normal items comprise numerous surfactants which do not come from characteristic sources however got from common sources [66]. Numerous beautifying agent's plans comprise of emulsion details for capacity purposes. Great skin-item interactions are provided by good cosmetic details and these lines encourage great entrance of dynamic fixings into the skin layers [66-68].

1.5.2 Surfactants in Foods

Surfactants are an extremely basic piece of some prevalent nourishment things like dessert which is 40–50% air (by volume) that is a partially solidified froth. Various surfactants are utilized as emulsifiers and stabilizers during various phases of frozen yogurt development [69]. Surfactants are utilized as a covering in the amalgamation of various edibles like chocolate and sugar-panned ice cream parlour things to create a tastefully appealing splendour [70]. They are additionally added to make a scattering of the covering particles, which at that point takes into consideration legitimate wetting and bond over the sweet surface. Surfactants are utilized to build the delightfulness of the dessert by shaping an emulsion between the fat and mouth spit, which limits the waxy mouth′s feel. Margarine and mayonnaise are additionally instances of emulsions [71].

1.5.3 Surfactants in Lung Disease

Surfactant substitution treatment can likewise be utilized to treat different types of lung sickness, for example, "meconium aspiration disorder", "neonatal pneumonia" and "innate diaphragmatic hernia" [72]. Surfactants used in lungs disorder commonly comprise of "phospholipids and proteins" [73, 74]. They are a fundamental agent to provide a low surface strain at the alveolar air-fluid interface. At the point when there is a lack of surfactant, the high surface strain of the dainty fluid layer covering the respiratory epithelium of the lungs would cause an alveolar breakdown toward the finish of termination. Similarly, a decreased surface strain keeps alveolar spaces small. It neutralizes alveolar development during the inspiration and supports the alveolar withdrawal during expiration. The lung surfactant framework likewise shields the lung from damage and disease brought about by inward breath of particles and smaller scale living beings [72, 74].

1.5.4 Surfactants in Pesticides

Pesticides are exceptionally significant in yield insurance incorporate herbicides, fungicides and bug sprays. A key in the definition of pesticides is item dependability and item

proficiency. The current pattern in pesticides is towards the items that are progressively viable, innocuous to client, having less effect on the earth, increasingly helpful to utilize and redesigned viability of the applied item. Science and innovation is being used to streamline the physical properties of the items to keep up/improve item executions [75]. On account of showered pesticides, colloid and interface innovation impact all parts of utilization. Sprinkle globules influence the outside of leaves and set up a store from which the "pesticide" moves into the leaf or interfaces the "bug". The shower design is affected by the apparatus ramble, the physical properties of the sprinkle fluid and the improvement of sprayer "vehicle". Outer factors, for example, temperature, dampness, wind, daylight and precipitation likewise assume jobs in adequacy [75]. "Ethoxylated alcohols, alkylphenols, sorbitan and alkylamines" are examples of common surfactants, utilized in pesticide plans. Organosilicone surfactants have begun to show up in commercial splash application items. They show decreased "surface strains", for improved "leaf wetting" and a low special "surface weight" for sprinkling "drop upkeep" on leaves [76].

1.5.5 Surfactants as Wetting Specialist

Surfactants decrease interfacial strains by testimony at a strong surface and afterward modifying the capacity of "water or oil" to wet the ideal "strong surface". At the point when the kept "surfactant area" is with the end goal that its "hydrophobic tail bunches" are found away from the "surface" then there will be a result in which there will be a lessening in "water-wetting" and an upsurge in "oil-wetting". Likewise, if the situating is so that the polar head bunch is far away from the surface, there will be an ascent in "water-wetting". Furthermore, due to the dual nature of surfactant molecules, definite structural features can disturb the stuffing of surfactant molecules and afterwards influence the surface wettability.

Surfactants lessen the interfacial pressure by adsorbing at a "strong surface", and adjust "the size of water or oil to wet the surface". At where the "adsorbed surfactant setting is with the end goal that its hydrophobic tail congregations point away from the surface, the outcome is a lessening in water-wetting and an expansion in oil-wetting". Subsequently, if the way is with the end goal that the "polar head gathering" is away from the surface, at that point there will be an "expansion in water-wetting. By the by the double thought of surfactant iotas, unambiguous supporting capacities can affect the squeezing of surfactant particles and consequently impact shallow wettability".

.A few researches have revealed that wettability moves from oil-wetting to water-wetting due to surfactant depositions [77, 78]. An event of surfactant prompted wettability modification

can be found in the handling of swelling clays, for instance, montmorillonite, with a cationic surfactant, so as to generate organophilic mud for the use in non-watery boring muds [79, 80]. This adsorption behaviour and wettability can be transformed by varying hydrophobic tail assemblies. Some supplementary parts of the hydrophobic tails like extended versus direct hydrophobic tails, [81] polar assemblies [82] and tail lengths [83] likewise influence adsorption and wettability. Wetting properties of oils are enhanced by changing the concentrations of the surface active agents [84]. Temperature can similarly regulate wettability by manipulating any of the surfactant or the surfactant–surface adsorption features [83, 85].

1.5.6 Detergency

Detergency is the demonstration of "surface active agent that causes or supports in the expulsion of earth or stains from fabrics or strong surfaces through the act of official at interfaces and decreasing the effort alluring to impact the evacuation [86]". The "wetting operators" that rapidly "diffuse and adsorb" at reasonable interfaces" are ordinarily the handiest cleansers.

Soap is a superficial dynamic unsaturated fat salt, encompassing eight carbon molecules [86]. Since a long time in the past, they have been used as cleansers. Precisely, they have been created by the "saponification of glyceride oils and fats with NaOH or KOH", giving glycerol as by item. They are amazing cleansers; anyway they are impacted by the pH and the hardness of water causing cleanser filth. Notwithstanding the way that the demonstration of chemical designers will compensate for this issue, cleaning agents have been from an overall perspective displaced by the built cleansers. The majority of the surfactant assemblings are needed to those materials that are mixed into business chemical plans. "Alkyl sulfates, alkyl–aryl sulfonates and non-ionic polyethylene oxide subsidiaries" despite everything record for most of surfactant manufactures [86].

Not all "surfactants" are reasonable chemicals. For them to be estimated as an OK chemical, it must be a good wetting operator, having the "capacity to eliminate earth and mud into the washing fluid, being a conventional solubilizing master of wetting specialists". The object to be cleaned could be a hard "surface like plates, high thickness plastics, or a material like cotton, produced strands or an aspect of the body like skin or hair". The earth may have unpredictable engineered courses of action and atomic sizes. In perspective cleanser actions are restricted in degree. For instance, in cleanser defining a distinction is seen between soaking of "hard surfaces (for example glass and metal) and delicate surfaces (for example

textiles)". On account of hard surfaces, the equilibrium will in general be set up quickly and for delicate surfaces, dynamic impacts may cause troubles. For particular cleanser applications, the circumstance is much increasingly confused, since the execution will in general be made as a decision by criteria which are not just identified with soil expulsion. Surface active materials that enough adsorb at the solid/water and soil/water interfaces are the best engineered mixes. Adsorption at the air/water interface with the ensuing bringing down of the surface weight and foaming are not fundamentally models of detergency [86].

The best cleansers are commonly consisting of surfactant micelles. Therefore, micelles are considered to be a necessary piece of the detergency mechanism. In any case, presently it is realized that cleanser activities are reliant on the accumulation of monomeric surfactants. The improvement of micelles is discretionary to the cleaning method, and the crucial limit of the surfactant micelles emits an impression of being giving a flexibly to restocking un-related surfactant adsorbed from arrangement, and for solubilizing grease and oils. The manufactured highlights of surfactant particles that are associated with incredible chemical exercises, lead to micelle plans as a battling methodology.

At last, cleansers cannot work independent from anyone else in reasonable circumstances. Therefore various added substances are utilized. The matter of cleanser added substances is tremendous. Regular added substances incorporate developers, brighteners, the anti-redeposition specialists and co-surfactants [86].

1.5.7 Surfactants in Oil Recovery

Surfactants are also being utilized in process of oil recovery from rocks due to their amphiphilic nature. For the recovery of residual oil from the pores present on rock structures the capillary forces control the residual oil in the rocks and are responsible for secondary or enhanced (tertiary) oil recovery processes. In chief, oil recuperation from underground repositories, the hair like powers portrayed by the pores, are in charge of holding a significant part of the oil (leftover oil) in parts of the pore structure in the sand or rock. These are similar powers that are planned to defeat in optional or upgraded (tertiary) oil recuperation forms [87-90].

The similar oil and water immersions rely on the conveyance of aperture sizes in the stone. If the stone is essentially "water wetting", the tinier pores will all in all have more water and less oil than greater pores [91]. One by and large endeavours to diminish the capillary forces constraining the oil or potentially change the consistency of the uprooting liquid so as to adjust the viscous powers being exerted to bring oil out of the holes. For the most part, it is

required to diminish the interfacial pressure for this reason. This is practiced by adding an appropriate surfactant to diminish the interfacial pressure to minor values [89, 92]. In specific structures, the extension of a fourth part to an "oil/water/surfactant system can make the interfacial strain drop to near zero characteristics", letting unconstrained emulsification to extremely little drop sizes (micro emulsions) [93]. Micro emulsions have some exceptional possibilities, and can have significant applications in zones, for example, upgraded oil recuperation, soil and spring remediation, nourishments, pharmaceuticals, beautifying agents, herbicides and pesticides [89, 92, 94-96].

1.5.8 Soil Remediation by Surfactants

The pollution of groundwater by "non-aqueous phase liquids (NAPLs)" is a matter of worry all over the world. Common NAPLs such as "trichloroethylene (TCE)", and "1, 1, 1-trichloroethane (TCA)" can without much of a stretch enter through the "subsurface and get hard to dispose of in light of the fact that they have appropriately higher solubilities". With respect to drinking water standards, it is a cause of concern because NAPLs have low biodegradability [97]. So, they can remain inside the soil for a longer time and represent a long-haul danger to groundwater standards [98]. The utilization of surfactants to expel NAPLs from polluted groundwater has been under significant assessment and "field testing" throughout ongoing decades, particularly for thick "non-aqueous phase liquids", for example, "chlorinated solvents" [99, 100] in light of the fact that they are generally dangerous to remediate.

According to surfactant selection criteria [100], the methods applied to attain the dislocation, solubilization, and flushing of the NAPLs are derived from surfactant-based improved oil recapture methods [101,102]. With a respectable "surfactant" detailing dependent on great stage conduct, up to 99.9% of the "NAPLs" can be recollected from a soil [100]. There are different sorts of bio surfactants, some of which have been utilized in improved oil recuperation, and just as in expulsion of metal contaminants, for example, zinc and copper.

"The components of disintegration, surfactant-related complexation, and ionic trade" are involved in the "expulsion of substantial metals and radionuclides" from the earth [103]. To eliminate "oil and diesel oil" from earth, "Microfoams" of natural and concoction surfactants are utilized. The utilization of "microfoams" has been examined as an option in contrast to the utilization of surfactant arrangements, since they have the "benefit of improving the contact with the polluted condition because of their surface properties" [104]. As a proficient

adsorbent, coal squander initiated by “rhamnolipid biosurfactants” is utilized for the adsorption of cadmium from fluid arrangement [105]. Biodegradation of “polycyclic aromatic hydrocarbons (PAHs)” is encouraged by biosurfactants. The evacuation of PAHs in the slime is improved by “immunizing indigenous biosurfactant-creating microorganism *Pseudomonas aeruginosa* S5 in coking wastewater”. It fills in as an “in-site remediation innovation” [106]. The impacts of “surfactants on the physiology of miniature creatures” run from hindrance of development because of surfactant harmfulness to incitement of development brought about by the utilization of “surfactants as a co-substrate”. The most significant impact of surfactants on the communications among soil and poison is incitement of mass vehicle of the toxin from the dirt to the fluid stage. This can be brought about by three distinct instruments: “emulsification of fluid poison, micellar solubilisation, and encouraged vehicle” [107].

1.6 Surfactant Toxicity and Persistence

The utilization of surfactants is broadly regarded as secure and threat free. Regionally, the utilization of enterprise surfactants could be very huge which should not be prolonged to conditions in which they input floor waters, due to the fact that surfactants are extensively poisonous to aquatic existence [108]. It is essential to apprehend the environmental issues and risks associated with any huge extent surfactants which turned into as soon as expected to be three million tonnes in 1995 [109]. Surfactant consumption in industry will possibly enlarge as new applications are found. Therefore its miles important to take important measures to cope with this hassle [110-112].

The toxicity and persistence of surfactants can be fairly predicted for diverse environmental situations [108,109]. The toxicity is dependent greatly upon the chemical nature and structure of surfactants. A growth in the length of hydrophobic alkyl chain group usually enhances toxicity, whereas “increasing ethylene oxide (EO) numbers with the same hydrophobic group decreases toxicity” [113]. These inclinations can be understood by considering the “toxicity mechanism of surfactants, called membrane disruption and protein denaturation, as a function of the surface-active properties of surface active agents” [108]. This is the way that, poisonousness of the surfactants can be adjusted by altering the framework. To decrease the natural and wellbeing hazards related with surfactants it is important to comprehend the ecological destiny and outcomes of these synthetic mixes, both in standard applications and in spontaneous deliveries. It is necessary to make provisions that surfactants left in the back are not a danger for surroundings. The environmental issues, springing up due to the delivery

of surfactants through the subsurface need to be dealt as a fragment of the development of this era [113]. In order to understand the surfactant biodegradation, a few not unusual issues ought to be considered, consisting of mechanisms for debasing the alkyl chains which might be part of all marketable surfactants and poisonousness of surfactants is likewise almost expectable, with the goal that it is probably going to reach at tolerably thorough choices at the natural insurance of mixes [108]. Similarly as with other colloidal classes, ceaseless investigation is attractive to know the wellness perils related with them. As far as it is concerned about a safe and sustainable world, there is need to manage the usage of all chemicals as well as surfactants with special protocols that can lead to safer and better utilization of items. It is needed to develop newer, greener and better surfactants with minimum possible toxicity and minimum possible negative impact on the environment. It is highly necessary if we want to provide a liveable and breathable planet to our future generations.

1.7 n-Alkylpyridinium and n-Alkylquinolinium Surfactants

Alkyl pyridinium surfactants are a significant class of cationic amphiphilic micelles. They have been generally utilized in pharmacological applications and are utilized to avoid the commencement and amassing of cariogenic dental plaque and gum disease and furthermore as sporicidal and decontaminants in microbiological processes [114]. The pyridinium salts have demonstrated critical antimicrobial movement against different microorganisms. These are utilized to wound recuperating and in the treatment of urological contaminations [115,116]. Cetylpyridinium chloride displays an incredible calming movement as well as represses the action of a few grid metalloproteinase proteins which are an explanation of inflammation [115,117]. Numerous pyridine subsidiaries have diverse conzcoction and pharmacological structures which give them different organic properties like enemy of malignant growth, hostile to viral, mitigating and antituberculostatic movement [115]. The pyridinium based surfactants have been known for their wide extent of employments for instance “erosion hindrance, material taking care of, oil recovery, emulsion polymerization, use in cosmetics items and mineral lightness”. In particular, organic usages of pyridinium salts consolidate their “use, as meds, quality conveyance operator, DNA extraction and antimicrobial properties” [118].

Like *n*-Alkyl pyridinium surfactants, *n*-Alkyl quinolinium surfactants are also of great interest and importance. Quinolinium based surfactants are not well explored but being

similar in nature and structure, it is expected that quinolinium based surfactants will also have excellent amphiphilic properties. Quinolinium based Gemini surfactants have been studied and reported with admirable antimicrobial activity. Therefore, these surfactants are also an exciting field for further research and exploration [113-118].

1.8 Aims and Objectives

n-Alkylpyridinium and *n*-Alkylquinolinium surfactants are non-toxic in nature. They have a potential to be explored for their biological applications. This study was focused on the following aims and objectives.

- To synthesize and characterize new cationic surfactants
- To study the micellization behaviour of *n*-alkyl pyridinium surfactants in ethanol.
- To study the biological activities of synthesised surfactants.
- To study the association behaviour of the chosen medications with the synthesised mixes.

1.9 Plan of Work

- New amphiphilic compounds were planned to synthesise by one pot synthetic method.
- They were planned to characterize by IR and NMR (^{1}H, ^{13}C) spectroscopic methods.
- It was planned to determine the CMC values of these amphiphiles by using conductometric method.
- The conductometric results of the CMC values obtained were planned to verify by utilizing another technique that is UV visible spectroscopic method.
- To study the thermodynamics of micellization process, it was planned to determine the CMC values of all the synthesized surfactants, by using conductometric method.
- To find the usefulness of all the synthesized amphiphiles, it was planned to find their biological activities.
- To study their drug carrying capacity, they were planned to interact with the selected drugs Ketoprofen and Flurbiprofen by employing the UV visible spectroscopic method.

Chapter-2

Materials and Methods

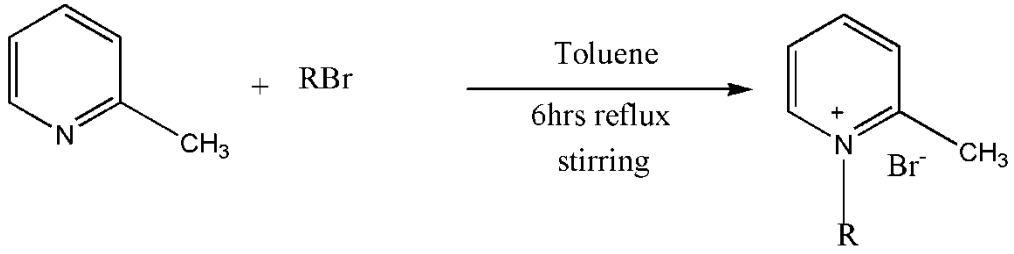
2.1 Materials

Throughout this research, all "chemicals and reagents" used were obtained from "Sigma Aldrich, USA" and were "analytical grade". All chemicals were utilized as received, without any further purification or treatment. The chemicals used were alkyl bromides (hexyl to pentadecyl), 2-methylpyridine, 3-methylpyridine, 4-methylquinoline, ethanol, toluene, ketoprofen and flurbiprofen. Solvents were purchased from Merck, Germany and used after drying by reported methods [10].

2.2 Synthesis

2.2.1 Synthesis of n-Alkyl-2-methylpyridinium bromides

To synthesise compounds a6 - a12, a14 and a15 with different alkyl chain lengths, varying from hexyl to pentadecyl (excluding tridecyl), equimolar quantities (10 mM) of 2-methylpyridine and the respective alkyl bromides were added in 50 mL of dry toluene in a 250 mL round bottom flask and refluxed for 6 hrs. Afterwards, reaction mixture was passed through a Whatman filter paper and evaporated using a rotary evaporator. Brownish yellow coloured viscous oily liquids were obtained after rotary evaporation.



R = C_6H_{13}, C_7H_{15}, C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$, $C_{11}H_{23}$, $C_{12}H_{25}$, $C_{14}H_{29}$, $C_{15}H_{31}$

2.2.1.1 n-Hexyl-2-methylpyridinium bromide (a6)

Amounts of reagents used: 1.62 ml (10mM) (2-methyl pyridine) and 2.84 ml (10mM) bromohexane. Yield: 76%.

FT-IR (cm^{-1}): "1300 (C-N), 1634 (C=N), 1590 (C=C), 1465 (-CH_2), 3023 (CH-Aromatic), 1145 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "8.4 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =3.0Hz), 9.45 (1H, H^3,t ,^3J [^1H, ^{1}H] =6.0Hz), 8.3 (1H, H^4, t, ^3J [^{1}H,^{1}H] =3.0Hz), 9.43 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.68(3H, H^6, s), 4.75 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.1-1.3 (8H, H^{8-11} , m), 0.83 (3H, H^{12}, t, ^3J [^{1}H, ^{1}H] =6.0Hz) " .

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.3 (C3), 128.2 (C4), 145.3 (C5), 20.74 (C6), 58.4(C7), 22.34-31.15 (C8-C11), 13.9(C12)".

2.2.1.2 n-Heptyl-2-methylpyridinium bromide (a7)

Amounts of reagents used: 1.62 ml (10mM) (2 methyl pyridine) and 3.13 ml (10mM) bromoheptane Yield: 74%.

FT-IR (cm^{-1}): "1302 (C-N), 1632 (C=N), 1578 (C=C), 1466 (-CH_2), 3016 (CH-Aromatic), 1146 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ -ppm): "8.02 (1H,H^2 ,d, ^3J [^1H, ^{1}H] =9.0Hz), 7.99 (1H, H^3, t,^3J [^1H, ^{1}H] =6.0Hz), 8.3 (1H, H^4, t, ^3J [^{1}H,^{1}H] =9.0Hz), 9.40 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.94 (3H, H^6, s), 4.75(2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.1-1.4 (10H, H^{8-12} , m), 0.84 (3H, H^{13}, t, ^3J [^{1}H, ^{1}H] =6.0Hz) ".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.3(C3), 130.4 (C4), 145.3(C5), 20.7 (C6), 58.4(C7), 22.4-31.4 (C8-C12) 14.0 (C13)".

2.2.1.3 n-Octyl-2-methylpyridinium bromide (a8)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 3.30 ml (10 mM) bromoctane. Yield: 76%.

FT-IR (cm^{-1}): "1300 (C-N), 1632 (C=N), 1575 (C=C), 1464 (-CH_2), 3039(CH-Aromatic), 1141 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ -ppm): "8.42 (1H,H^2 ,d, ^3J [^{1}H, ^{1}H] =9.0Hz), 7.91 (1H, H^3, t,^3J [^{1}H, ^{1}H] =6.0Hz), 8.36 (1H, H^4, t, ^3J [^{1}H,^{1}H] =9.0Hz), 9.34 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.94 (3H, H^6, s), 4.70 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.1-1.87 (12H, H^{8-13} , m), 0.79 (3H, H^{14}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.1(C3), 130.4 (C4), 147.3(C5), 20.6 (C6), 58.3(C7), 22.4-31.5 (C8-C13) 13.9 (C14)".

2.2.1.4 n-Nonyl-2-methylpyridinium bromide (a9)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 3.80 ml (10 mM) bromononane. Yield: 77%.

FT-IR (cm^{-1}): "1309 (C-N), 1634 (C=N), 1590 (C=C), 1465 (-CH_2), 3023(CH-Aromatic), 1145 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ - ppm): "8.02 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =9.0Hz), 7.90 (1H, H^3, t,^3J [^1H, ^{1}H] =6.0Hz), 8.37 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 9.47 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.91 (3H, H^6, s), 4.74 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.1-1.89 (14H, H^{8-14} , m), 0.80 (3H, H^{15}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.3(C2), 146.3(C3), 130.5 (C4), 145.3(C5), 20.74 (C6), 58.3(C7), 22.5-34.1 (C8-C14) 14.03 (C15)".

2.2.1.5 n-Decyl-2-methylpyridinium bromide (a10)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 4.14 ml (10 mM) bromodecane. Yield: 75%.

FT-IR (cm^{-1}): "1300 (C-N), 1630 (C=N), 1574 (C=C), 1465 (-CH_2), 3023 (CH-Aromatic), 1141 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ-ppm): "8.41 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.93 (1H, H^3, t,^3J [^1H, ^{1}H] =9.0Hz), 8.38 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 9.39 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.92 (3H, H^6, s), 4.74 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.1-1.92 (16H, H^{8-15} , m), 0.83 (3H, H^{16}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.3(C3), 130.4 (C4), 145.3(C5), 20.73 (C6), 58.4(C7), 22.5-31.7 (C8-C15) 14.07 (C16)".

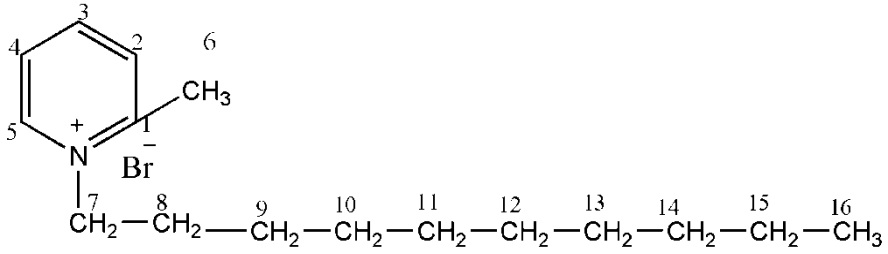


Figure 2.1: Structure of a10

2.2.1.6 n-Undecyl-2-methylpyridinium bromide (a11)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 4.50 ml (10 mM) bromoundecane. Yield: 78%.

FT-IR (cm^{-1}): "1303 (C-N), 1629 (C=N), 1575 (C=C), 1462 (-CH_2), 3050 (CH-Aromatic), 1172 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$!, δ -ppm): "8.40 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =6.0Hz), 7.95 (1H, H^3, t,^3J [^1H, ^{1}H] =9.0Hz), 8.00 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 9.59 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.97 (3H, H^6, s), 4.83 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.2-1.96 (18H, H^{8-16} , m), 0.82 (3H, H^{17}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.3(C2), 146.5(C3), 130.3 (C4), 145.2 (C5), 20.73 (C6), 58.4(C7), 22.65-34.15 (C8-C16) 14.01 (C17)".

2.2.1.7 n-Dodecyl-2-methylpyridinium bromide (a12)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 4.79 ml (10 mM) bromododecane. Yield: 76%.

FT-IR (cm^{-1}): "1307 (C-N), 1629 (C=N), 1573 (C=C), 1462 (-CH_2), 3043 (CH-Aromatic), 1170 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "8.41 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =9.0Hz), 7.93 (1H, H^3, t,^3J [^1H, ^{1}H] =6.0Hz), 8.02 (1H, H^4, t, ^3J [^{1}H,^{1}H] =9.0Hz), 9.58 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.90 (3H, H^6, s), 4.88 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0Hz), 1.2-1.98 (20H, H^{8-17} , m), 0.82 (3H, H^{18}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.3(C3), 130.4 (C4), 145.3 (C5), 20.74 (C6), 58.4(C7), 22.65-34.0 (C8-C17) 14.0 (C18)".

2.2.1.8 n-Tetradecyl-2-methylpyridinium bromide (a14)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 5.94 ml (10 mM) bromotetradecane. Yield: 77%.

FT-IR (cm^{-1}): "1309 (C-N), 1629 (C=N), 1573 (C=C), 1463 (-CH_2), 3043 (CH-Aromatic), 1168 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "7.86 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =9.0Hz), 7.97 (1H, H^3, t,^3J [^1H, ^{1}H] =6.0Hz), 8.33 (1H, H^4, t, ^3J [^{1}H,^{1}H] =9.0Hz), 9.72 (IH, H^5 , d, ^3J [^{1}H,^{1}H]

=5.4Hz), 2.97 (3H, H^6, s), 4.91 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.2-1.91 (24H, H^{8-19} , m), 0.87 (3H, H^{20}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ -ppm)": "154.2(C1), 126.4(C2), 146.6(C3), 130.1 (C4), 145.1 (C5), 20.86 (C6), 58.6(C7), 22.70-34.01 (C8-C19) 14.13 (C20)".

2.2.1.9 n-Pentadecyl-2-methylpyridinium bromide (a15)

Amounts of reagents used: 1.62 ml (10 mM) (2 methyl pyridine) and 5.78 ml (10 mM) bromopentdecane. Yield: 75%.

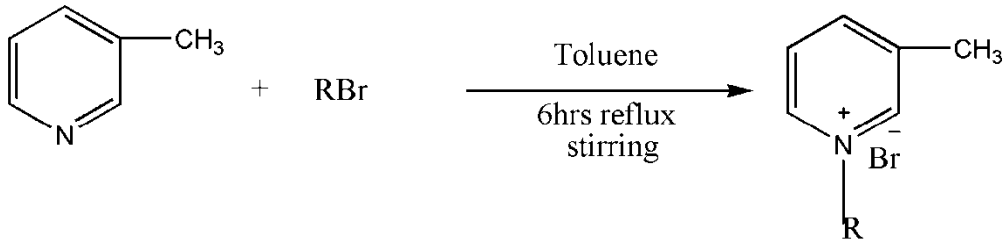
FT-IR (cm^{-1}): "1204 (C-N), 1635 (C=N), 1590 (C=C), 1466 (-CH_2), 3022 (CH-Aromatic), 1165 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "8.41 (1H,H^2 ,d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.91 (1H, H^3, t,^3J [^1H, ^{1}H] =9.0Hz), 8.36 (1H, H^4, t, ^3J [^{1}H,^{1}H] =9.0Hz), 9.66 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.98 (3H, H^6, s), 4.84 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =9.0 Hz), 1.2-1.90 (26H, H^{8-20} , m), 0.86 (3H, H^{21}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "154.2(C1), 126.4(C2), 146.8 (C3), 130.02 (C4), 144.9 (C5), 20.82 (C6), 58.4 (C7), 22.80-34.1 (C8-C20) 14.14 (C21)".

2.2.2 Synthesis of n-Alkyl-3-methylpyridinium bromides

Five *n*-alkyl-3-methylpyridinium surfactants (b6, b8, b10, b12, b14) were synthesized according to the procedure given above with alkyl chains of six, eight, ten, twelve and fourteen carbon atoms. The compounds obtained were oily liquids with a colour varying from yellow to brownish yellow.



R = C_6H_{13}, C_8H_{17}, $C_{10}H_{21}$, $C_{12}H_{25}$, $C_{14}H_{29}$

2.2.2.1 n-Hexyl-3-methylpyridinium bromide (b6)

Amounts of reagents used: 1.12 ml (10 mM) (3 methyl pyridine) and 1.42 ml (10 mM) bromohexane. Yield: 78%.

FT-IR (cm^{-1}): "1206 (C-N), 1633 (C=N), 1590 (C=C), 1465 (-CH_2), 3013 (CH-Aromatic), 1154 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "9.0 (1H,H^1 ,s,), 8.0 (1H, H^3, d,^3J [^1H, ^{1}H] =7.5Hz), 8.5 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 8.9 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.64(3H, H^6, s), 4.68(2H, H^7, t, ^3J [^{1}H, ^{1}H] =5.7 Hz), 1.33-2.12 (8H, H^{8-11} , m), 0.90 (3H, H^{12}, t, ^3J [^{1}H, ^{1}H] =6.6Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "145.6(C1), 139.1(C2), 142.0 (C3), 127.7 (C4), 143.9 (C5), 25.7 (C6), 61.1(C7), 18.2-31.4 (C8-C11), 14.1 (C12)".

2.2.2.2 n-Octyl-3-methylpyridinium bromide (b8)

Amounts of reagents used: 1.12 ml (10 mM) (3 methyl pyridine) and 1.65 ml (10 mM) bromoctane. Yield: 79%.

FT-IR (cm^{-1}): "1206 (C-N), 1632 (C=N), 1590 (C=C), 1464 (-CH_2), 3014(CH-Aromatic), 1152 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ -ppm): "9.09 (1H,H^1 ,s,), 8.05 (1H, H^3, d,^3J [^1H, ^{1}H] =7.5Hz), 8.5 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 8.9 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.64 (3H, H^6, s), 4.68 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =5.7 Hz), 1.33-2.12 (12H, H^{8-13} , m), 0.90 (3H, H^{14}, t, ^3J [^{1}H, ^{1}H] =6.6Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "145.6(C1), 139.5(C2), 142.0(C3), 127.7 (C4), 144.2(C5), 25.7(C6), 61.4(C7), 18.4-31.6 (C8-C13), 14.1 (C14)".

2.2.2.3 n-Decyl-3-methylpyridinium bromide (b10)

Amounts of reagents used: 1.12 ml (10 mM) (3 methyl pyridine) and 2.07 ml (10 mM) bromodecane. Yield: 79%.

FT-IR (cm^{-1}): "1204 (C-N), 1632 (C=N), 1590 (C=C), 1465 (-CH_2), 3020 (CH-Aromatic), 1173 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ -ppm): "9.37 (1H,H^1 ,s,), 8.03 (1H, H^3, d,^3J [^1H, ^{1}H] =7.5Hz), 9.20 (1H, H^4, t, ^3J [^{1}H,^{1}H] =6.0Hz), 8.24 (IH, H^5 , d, ^3J [^{1}H,^{1}H] =6.0Hz), 2.61 (3H, H^6, s), 4.86 (2H, H^7, t, ^3J [^{1}H, ^{1}H] =5.7 Hz), 1.31-2.42 (16H, H^{8-15} , m), 0.82 (3H, H^{16}, t, ^3J [^{1}H, ^{1}H] =6.6Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ -ppm)": "145.6(C1), 139.6(C2), 142.3(C3), 127.9 (C4), 144.5 (C5), 22.6(C6), 61.8(C7), 18.6-31.9 (C8-C15), 14.1 (C16)".

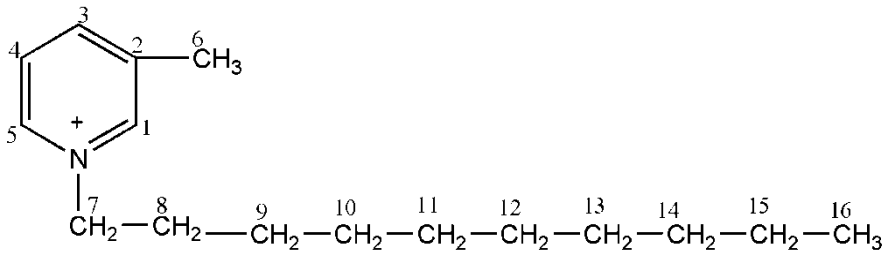


Figure 2.2: Structure of b10

2.2.2.4 n-Dodecyl-3-methylpyridinium bromide (b12)

Amounts of reagents used: 1.12 ml (10 mM) (3 methyl pyridine) and 2.39 ml (10 mM) bromododecane. Yield: 77%.

FT-IR (cm^{-1}): "1206 (C-N), 1632 (C=N), 1504 (C=C), 1465 (-CH_2), 3025 (CH-Aromatic), 1175 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ - **ppm):** "9.37 (1H,H^1 s,), 8.02 (1H, H^3, d, $^3J^1$H, ^{1}H =7.5Hz), 9.19 (1H,H^4, t, $^3J^1$H,^{1}H=6.0Hz), 8.25 (IH, , H^5, d $^3J^1$H,^{1}H =6.0Hz), 2.60 (3H, s, H^6), 4.86(2H, t, H^7, $^3J^1$H, ^{1}H=6.0 Hz), 1.23-2.03 (20H, m, H^{8-17}), 0.80 (3H, t, H^{18}, $^3J^1$H, ^{1}H =6.0Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ-ppm)": "145.6(C1), 139.6(C2), 142.2(C3), 127.9(C4), 144.4(C5), 22.6 (C6), 62.0(C7), 18.6-31.8 (C8-C17), 14.1 (C18)".

2.2.2 .5 n-Tetradecyl-3-methylpyridinium bromide (b14)

Amounts of reagents used: 1.12 ml (10 mM) (3 methyl pyridine) and 2.97 ml (10 mM) bromotetradecane. Yield: 76%.

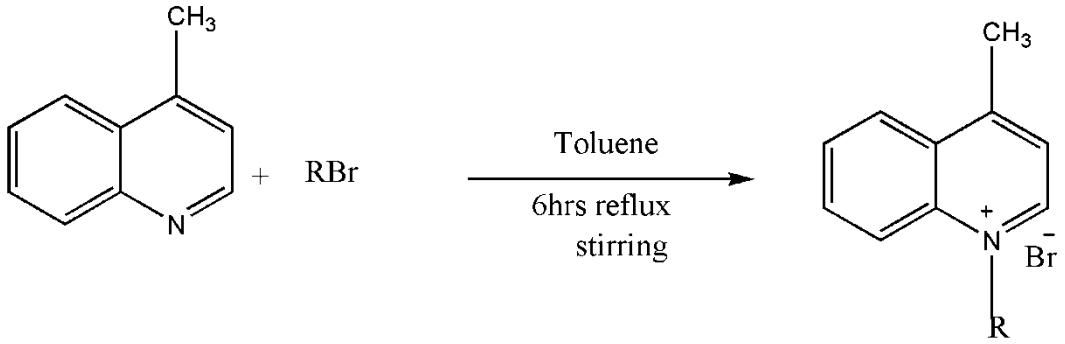
FT-IR (cm^{-1}): "1201 (C-N), 1633 (C=N), 1594 (C=C), 1465 (-CH_2), 3021 (CH-Aromatic), 1145 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ-ppm): "9.35 (1H,H^1 s,), 8.05 (1H, H^3, d, $^3J^1$H, ^{1}H =7.5Hz), 8.22 (1H,H^4, t, $^3J^1$H,^{1}H=6.0Hz), 8.30 (IH, d , H^5, $^3J^1$H,^{1}H =5.4Hz), 2.65 (3H, s, H^6), 4.93(2H, t, H^7, $^3J^1$H, ^{1}H=5.7 Hz), 1.19-2.05 (24H, H^{8-19} m,), 0.87 (3H, H^{20}, t, $^3J^1$H, ^{1}H =6.6Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ-ppm)": "145.6(C1), 139.6(C2), 142.2(C3), 127.8(C4), 144.5(C5), 26.1(C6), 62.4(C7), 27.75-34.1 (C8-C19), 22.67 (C20)".

2.2.3 Synthesis of n-Alkyl-4-methylqunolinium bromides

To synthesize nine *n*-alkyl-4-methylquinolinium bromide surfactants, (c6-c12, c14 and c15) 4-methylquinoline was reacted with different alkyl bromides according to the same procedure as detailed in section 2.2.1. The compounds obtained were dark brown coloured oily viscous liquids.



R = C_6H_{13}, C_7H_{15}, C_8H_{17}, C_9H_{19}, $C_{10}H_{21}$, $C_{11}H_{23}$, $C_{12}H_{25}$, $C_{14}H_{29}$, $C_{15}H_{31}$

2.2.3.1 n-Hexyl-4-methylqunolinium bromide (c6)

Amounts of reagents used: 1.86 ml (10 mM) (4 methyl quinoline) and 2.84 ml (10 mM) bromohexane. Yield: 73%.

FT-IR (cm^{-1}): "1244 (C-N), 1690 (C=N), 1595 (C=C), 1456 (-CH_2), 3029 (CH-Aromatic), 1165 (-CH_3)"

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "8.77 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =6.0Hz), 8.30 (1H, H^2, d,^3J [^1H, ^{1}H] =9.0Hz), 7.24(1H, H^5, d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.5 (IH, H^6 , t, ^3J [^{1}H,^{1}H] =9.0Hz), 7.7(1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 7.9 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =6.0 Hz), 2.94 (3H, H^{10} s), 5.22 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.2-1.28 (8H, H^{12-15} , m), 0.78 (3H, H^{16}, t, ^3J [^{1}H, ^{1}H] =3.0Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ -ppm)": "145.3(C1), 129.2(C2), 157.8.0 (C3), 126.8 (C4), 123.4 (C5), 126.5 (C6), 128.2(C7), 118.7 (C8), 136.9 (C9), 22.3 (C10), 57.8 (C11), 18.79-31.22 (C12-C15), 13.9 (C16)".

2.2.3.2 n-Heptyl-4-methylqunolinium bromide (c7)

Amounts of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 3.13 ml (10 mM) bromoheptane Yield: 75%.

FT-IR (cm^{-1}): "1244 (C-N), 1602 (C=N), 1531 (C=C), 1460 (-CH_2), 3028 (CH-Aromatic), 1168 (-CH_3)"

^{1}H NMR (300MHz, $CDCl_3$, δ -ppm): "10.12 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =6.0Hz), 8.71 (1H, H^2, d,^3J [^1H, ^{1}H] =6.0Hz), 7.22 (1H, H^5, d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.52(IH, H^6 , t, ^3J [^{1}H,^{1}H] =3.0Hz), 7.66(1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 7.96 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =6.0 Hz), 2.93 (3H,H^{10} s), 5.23(2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.20-1.26 (10H, H^{12-16} , m), 0.78 (3H, H^{17}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "146.9(C1), 129.1(C2), 157.9 (C3), 126.5 (C4), 123.3 (C5), 126.8 (C6), 128.2(C7), 118.8 (C8), 136.9 (C9), 22.4 (C10), 57.8 (C11), 18.74-31.46 (C12-C16), 13.9 (C17)".

2.2.3.3 n-Octyl-4-methylqunolinium bromide (c8)

Amount of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 3.30 ml (10 mM) bromoctane. Yield: 79%.

FT-IR (cm^{-1}): "1245 (C-N), 1612 (C=N), 1532 (C=C), 1465 (-CH_2), 3016 (CH-Aromatic), 1148 (-CH_3)".

^{1}H NMR (300MHz, "$CDCl_3$", δ -ppm): "9.98 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =6.0Hz), 8.21 (1H, H^2, d,^3J [^1H, ^{1}H] =9.0Hz), 7.16 (1H, H^5, d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.45 (IH, H^6 , t, ^3J [^{1}H,^{1}H] =6.0Hz), 7.58 (1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 7.87 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =3.0 Hz), 2.86 (3H,H^{10} s), 5.15 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.0-1.93 (12H, H^{12-17} , m), 0.74 (3H, H^{18}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ -ppm)": "146.3(C1), 129.2(C2), 158.0 (C3), 126.6 (C4), 123.2 (C5), 126.8 (C6), 128.1(C7), 118.8 (C8), 136.8 (C9), 22.4 (C10), 57.8 (C11), 18.78-31.56 (C12-C17), 13.9 (C18)".

2.2.3.4 n-Nonyl-4-methylqunolinium bromide (c9)

Amounts of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 3.80 ml (10 mM) bromononane. Yield: 75%.

FT-IR (cm^{-1}): "1256 (C-N), 1628 (C=N), 1534 (C=C), 1464 (-CH_2), 3018 (CH-Aromatic), 1145 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ - ppm): "10.04 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =6.0Hz), 8.69 (1H, H^2, d,^3J [^1H, ^{1}H] =6.0Hz), 7.22 (1H, H^5, d, ^3J [^{1}H,^{1}H] =6.0Hz), 7.50 (IH, H^6 , t, ^3J [^{1}H,^{1}H]

=3.0Hz), 7.63 (1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 7.93 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =6.0 Hz), 2.63 (3H,H^{10} s), 5.19 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.1-1.70 (14H, H^{12-18} , m), 0.78 (3H, H^{19}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

"**^{13}C NMR** (75.5 MHz $CDCl_3$, δ -ppm)": "149.0(C1), 129.3(C2), 157.9 (C3), 126.8 (C4), 123.3 (C5), 126.8 (C6), 128.1(C7), 118.8 (C8), 136.8 (C9), 22.5 (C10), 57.8 (C11), 20.44-34.14 (C12-C18), 18.8 (C19)".

2.2.3.5 n-Decyl-4-methylqunolinium bromide (c10)

Amount of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 4.14 ml (10 mM) bromodecane. Yield: 74%.

FT-IR (cm^{-1}): "1261 (C-N), 1604 (C=N), 1531 (C=C), 1462 (-CH_2), 3018 (CH-Aromatic), 1168 (-CH_3)".

^{1}H NMR (300MHz, $CDCl_3$, δ-ppm): "8.75 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =3.0Hz), 8.10 (1H, H^2, d,^3J [^1H, ^{1}H] =6.0Hz), 7.10 (1H, H^5, d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.53 (IH, H^6 , t, ^3J [^{1}H,^{1}H] =6.0Hz), 7.68 (1H, H^7, t, ^3J [^1H, ^{1}H] =6.0Hz), 7.94 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =6.0Hz), 2.24 (3H,H^{10} s), 5.39 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=12.0 Hz), 1.91-1.85 (16H, H^{12-19} , m), 0.86 (3H, H^{20}, t, ^3J [^{1}H, ^{1}H] =9.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "149.4(C1), 129.1(C2), 157.8 (C3), 126.6 (C4), 123.4 (C5), 126.8 (C6), 128.2(C7), 118.8 (C8), 136.9(C9), 22.6(C10), 57.8 (C11), 22.63-34.13 (C12-C19), 14.1 (C20)".

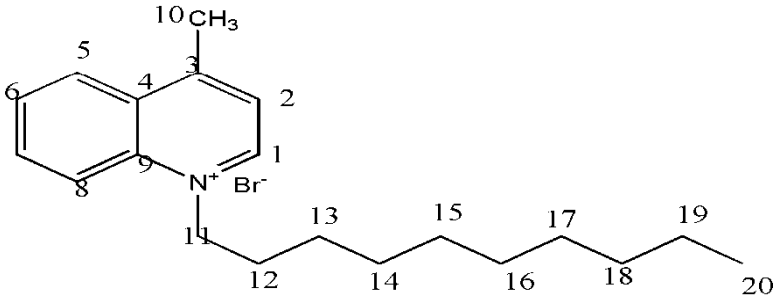


Figure 2.3: Structure of c10

2.2.3.6 n-Undecyl-4-methylqunolinium bromide (c11)

Amounts of reagents used: 1.86 ml (10 mM) (4-methyl Quinoline) and 4.50 ml (10 mM) bromoundecane. Yield: 78%.

FT-IR (cm^{-1}): "1207 (C-N), 1610 (C=N), 1531 (C=C), 1462 (-CH_2), 3088 (CH-Aromatic), 1165 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "10.30 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =6.0Hz), 9.00 (1H, H^2, d,^3J [^1H, ^{1}H] =5.4Hz), 7.92 (1H, H^5, d, ^3J [^{1}H,^{1}H] =6.0Hz), 7.80 (IH, H^6 , t, ^3J [^{1}H,^{1}H] =6.0Hz), 8.22 (1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 8.37 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =3.0Hz), 2.02 (3H, H^{10} s), 5.29 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.2-1.5 (18H, H^{12-20} , m), 0.82 (3H, H^{21}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "149.5(C1), 129.4(C2), 157.8 (C3), 124.7 (C4), 123.4 (C5), 126.8 (C6), 128.2(C7), 118.8 (C8), 136.9(C9), 22.6(C10), 57.8 (C11), 20.22-31.85 (C12-C20), 14.1 (C21)".

2.2.3.7 n-Dodecyl-4-methylqunolinium bromide (c12)

Amounts of reagents used: 1.86 ml (10 mM) (4- methyl Quinoline) and 4.79 ml (10 mM) bromododecane. Yield: 79%.

FT-IR (cm^{-1}): "1208 (C-N), 1608 (C=N), 1531 (C=C), 1462 (-CH_2), 3018 (CH-Aromatic), 1165 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "10.12 (1H,H^1 ,d, ^3J [^1H, ^{1}H] =3.0Hz), 8.34 (1H, H^2, d,^3J [^1H, ^{1}H] =3.0Hz), 7.27 (1H, H^5, d, ^3J [^{1}H,^{1}H] =3.0Hz), 7.55 (IH, H^6 , t, ^3J [^{1}H,^{1}H] =3.0Hz), 7.68 (1H, H^7, t, ^3J [^1H, ^{1}H] =3.0Hz), 7.93 (1H, H^8, d, ^3J [^{1}H, ^{1}H] =6.0 Hz), 2.69 (3H,H^{10} s), 5.22 (2H, H^{11}, t ,$^3J^1$H, ^{1}H=6.0 Hz), 1.1-2.0 (20H, H^{12-21} , m), 0.82 (3H, H^{22}, t, ^3J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "149.2(C1), 129.4(C2), 157.9 (C3), 126.8 (C4), 123.0 (C5), 126.9 (C6), 128.2(C7), 118.8 (C8), 136.9(C9), 22.6(C10), 57.8 (C11), 18.90-31.83 (C12-C21), 14.09 (C22)".

2.2.3.8 n-Tetradecyl-4-methylqunolinium bromide (c14)

Amounst of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 5.94 ml (10 mM) bromotetradecane. Yield: 74%.

FT-IR (cm^{-1}): "1212 (C-N), 1612 (C=N), 1533 (C=C), 1492 (-CH_2), 3010 (CH-Aromatic), 1168 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "10.29 (1H,H^1 ,d, ^{3}J [^{1}H, ^{1}H] =6.0Hz), 8.35 (1H, H^2, d,^{3}J [^{1}H, ^{1}H] =9.0Hz), 6.98 (1H, H^5, d, ^{3}J [^{1}H,^{1}H] =9.0Hz), 7.63 (IH, H^6 , t, ^{3}J [^{1}H,^{1}H] =6.0Hz), 7.76 (1H, H^7, t, ^{3}J [^{1}H, ^{1}H] =9.0Hz), 7.94 (1H, H^8, d, ^{3}J [^{1}H, ^{1}H] =6.0Hz), 2.79 (3H,H^{10} s), 5.24 (2H, H^{11}, t ,$^{3}J^{1}$H, ^{1}H=6.0 Hz), 1.1-2.04 (24H, H^{12-23} , m), 0.82 (3H, H^{24}, t, ^{3}J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "149.5(C1), 129.4(C2), 157.8 (C3), 126.8 (C4), 123.4 (C5), 127.4 (C6), 127.5(C7), 118.9 (C8), 136.9(C9), 26.5(C10), 57.8 (C11), 26.5-34.01 (C12-C23), 14.1 (C24)".

2.2.3.9 n-Pentadecyl-4-methylqunolinium bromide (c15)

Amounts of reagents used: 1.86 ml (10 mM) (4 methyl Quinoline) and 5.78 ml (10 mM) bromopentdecane. Yield: 76%.

FT-IR (cm^{-1}): "1202 (C-N), 1612 (C=N), 1587 (C=C), 1467 (-CH_2), 3012 (CH-Aromatic), 1168 (-CH_3)".

^{1}H NMR (300 MHz, $CDCl_3$, δ -ppm): "10.22 (1H,H^1 ,d, ^{3}J [^{1}H, ^{1}H] =6.0Hz), 8.34 (1H, H^2, d,^{3}J [^{1}H, ^{1}H] =3.0Hz), 7.28 (1H, H^5, d, ^{3}J [^{1}H,^{1}H] =6.0Hz), 7.96 (IH, H^6 , t, ^{3}J [^{1}H,^{1}H] =6.0Hz), 7.98 (1H, H^7, t, ^{3}J [^{1}H, ^{1}H] =6.0Hz), 8.01 (1H, H^8, d, ^{3}J [^{1}H, ^{1}H] =6.0 Hz), 2.99 (3H,H^{10} s), 5.27 (2H, H^{11}, t ,$^{3}J^{1}$H, ^{1}H=6.0 Hz), 1.1-2.05 (26H, H^{12-24} , m), 0.82 (3H, H^{25}, t, ^{3}J [^{1}H, ^{1}H] =6.0Hz)".

^{13}C NMR (75.5 MHz $CDCl_3$, δ -ppm): "149.4(C1), 129.4(C2), 157.8 (C3), 126.8(C4), 123.4 (C5), 127.2(C6), 128.8(C7), 118.9(C8), 136.9(C9), 26.4(C10), 57.8(C11), 26.49-34.06(C12-C24), 14.1 (C25)".

2.3 Instrumentation

2.3.1 NMR Spectroscopy

The molecular structures of the synthesized compounds were determined using "nuclear magnetic resonance (NMR) spectroscopy". Proton NMR spectroscopy (^{1}H NMR) is used to obtain information about hydrogen nuclei in the molecules of a substance, in order to determine the structure of its molecules. For the confirmation of carbon nuclei in a molecule carbon NMR (^{13}C NMR) spectroscopy is utilized. A Bruker AV 300 MHz spectrometer was used to record NMR spectra at "300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C using $CDCl_3$ as a solvent".

2.3.2 FT-IR Spectroscopy

Infra-red spectroscopy helps to detect various functional groups in a molecule which gives different vibration bands. The presence of a particular functional group can be easily testified in a molecule. Fourier transformed infra-red (FT-IR) spectroscopic method was utilized for the confirmation of different functional groups of the synthesized compounds. A "Thermo-Nicolet-6700 FT-IR spectrophotometer" was used in the range of "400–4000 cm^{-1}". The FT-IR data supported the results obtained by NMR spectroscopy [119].

2.3.3 UV-Visible Spectroscopy

A computer controlled double beam Shimadzu 1601 Ultraviolet (UV) visible spectrophotometer was used during the entire study. Cells used for the measurements of electronic absorption spectra were made of quartz with a path length of 1.0 cm. Critical micelle concentrations (CMC) of the surfactants were measured from this UV-Visible data. Drug-surfactant interactions of all surfactants with the selected drugs, Ketoprofen and Flurbiprofen were also studied by using UV-Visible spectroscopy.

2.3.4 Conductometry

The specific conductivity was measured with an "Inolab Cond-720 conductometer" with a cell constant of "0.471 μScm^{-1}". The measured conductivity values have the accuracy ± 0.5 %. A thermostated circulating water bath with a precision of ± 0.1 K was used to keep the temperature constant. Prior to the conductivity measurements, the solutions were thermostated for at least 15 minutes.

2.4 Drug-Surfactant Interaction Studies

Spectroscopic methods were utilized to study drug-surfactant interactions. For this task, solutions of the chosen medications (Ketoprofen and Flurbiprofen), standard stock solutions of all the mixes were made in ethanol and in appropriate concentrations and then diluted for further studies. Concentration of Ketoprofen ranges from 0.32-0.41 mM and that of Flurbiprofen from 0.29-0.43 mM. Surfactant solutions in both pre micellar and post micellar states were interacted with the drugs. Concentration of surfactant solutions were gradually increased from pre-micellar to post-micellar level. Solutions of compounds of a, b and c series range from "0.48mM to 0.26mM and 0.5mM to 0.24 mM and 0.6mM to 0.28 mM respectively". Same amounts of compound and medication were mixed for all synthesised mixes, and UV-Visible spectra were obtained [120-122].

2.5 Experiment for Antibacterial Activity

Four bacterial strains were selected to test the antimicrobial activities of these surfactants. "Two Gram-positive bacteria ((*Bacillus subtilis* (ATCC 6051) and *Staphylococcus aureus* (ATCC 6538)) and two Gram-negative bacteria [(*Escherichia coli* (ATCC 15224) and *Enterobacter aerogenes* (ATCC13048)]" were among the selected bacterial strains. The method used to determine bactericidal activity was "the agar well-diffusion method" [123]. Broth culture (0.75 mL) containing ca. 10^6 colony forming units (CFU) per mL of the test strain was added to 75 mL of nutrient agar medium at 45 °C, mixed well, and then poured into a 14 cm sterile petri plate. The media was permitted to solidify, and a sterilized metallic borer was used to create 8 mm wells. Afterwards 100 µL of DMSO solution of the test sample at 1.0 mg mL^{-1} was added to the respective wells. The negative control used was DMSO and positive controls were the standard antibacterial drugs "Kanamycin sulphate (1 mg mL^{-1}) and Streptomycin sulphate (1 mg mL^{-1})". In triplicate, plates of each bacterial strain were set up and were hatched vigorously at 37°C for 24 hrs. The action was dictated by estimating the breadth of zone indicating total hindrance (mm). 2.5 % was the normal relative standard deviation of the outcomes.

2.6 Experiment for Antifungal Activity

To assess the fungicidal activity of the synthesised surfactants against different fungal strains, three fungal strains, "*Aspergillus niger, Aspergillus flavus, and Aspergillus fumigates"* were selected for this study. Sabouraud's dextrose agar was used as media for antifungal assay. The fungal strains were inoculated separately in a Sabouraud's dextrose broth for 6 hours and the suspensions were established to give approximately 10^5 CFU/mL.

The agar well dispersion strategy was actualized to survey antifungal action [124]. Sabouraud's dextrose agar (SDA) was used for contagious societies. The way of life medium was immunized with the parasitic strains independently suspended in Sabouraud's dextrose stock. Eight mm measurement wells were punctured into the agar and loaded up with mixes and dissolvable spaces (liquor and n-hexane). A standard anti-microbial Terbinafine focus (1 mg/ml) was utilized as certain control and parasitic plates were hatched at 37 °C for 3 days. The widths of the watched restraint zone were estimated.

2.7 Experiment for Antioxidant Activity

For the blended surfactants, the antioxidant activity was assessed by the β-carotene strategy following the detailed technique [125, 126] with minor alterations. An aliquot (50 µL) of the β-carotene chloroform arrangement (20 mg/mL) was moved into a flagon containing 40 µL

of linoleic corrosive, 1.0 mL of chloroform, and 530 µL of Tween 40 and afterward blended. The chloroform was dissipated utilizing an oxygenator. After the dissipation, oxygenated refined water (around 100 mL) was added to acquire an absorbance of 0.65 ± 0.5 units at 470 nm. An aliquot (0.4 mL) of a Trolox arrangement (200 mg/L) or weakened organic product extricate (200 mg/L) was added to 5 mL of the β-carotene arrangement and brooded in a water shower at 40 °C. The estimations were made after 2 min and 120 min at an absorbance of 470 nm utilizing a spectrophotometer. The antioxidant action was determined as the percent hindrance comparative with the control [126].

Chapter 3

Results and Discussion

3.1. Physical Properties of the Synthesized Compounds

All these surfactants are oily liquids which are soluble in most of the organic solvents and in an aqueous medium as well. Physicochemical properties are summed up in Table 3.1.

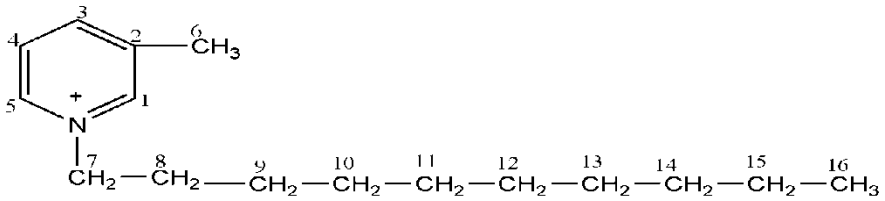
Table 3.1: Physicochemical properties of the surfactants

Compound code	Molecular formula	Molecular mass (g/mol)	Colour	CMC at 298.16 K (mM)
a6	$C_{12}H_{20}NBr$	257.9	Yellow	0.42
a7	$C_{13}H_{22}NBr$	271.9	Yellow	0.41
a8	$C_{14}H_{24}NBr$	285.9	Brownish Yellow	0.40
a9	$C_{15}H_{26}NBr$	299.9	Brownish Yellow	0.38
a10	$C_{16}H_{28}NBr$	313.9	Brownish Yellow	0.36
a11	$C_{17}H_{30}NBr$	327.9	Brownish Yellow	0.35
a12	$C_{18}H_{32}NBr$	341.9	Brownish Yellow	0.34
a14	$C_{20}H_{36}NBr$	369.9	Brownish Yellow	0.32
a15	$C_{21}H_{38}NBr$	383.9	Brownish Yellow	0.30
b6	$C_{12}H_{20}NBr$	257.9	Yellow	0.41
b8	$C_{14}H_{24}NBr$	285.9	Yellow	0.35
b10	$C_{16}H_{28}NBr$	313.9	Brownish Yellow	0.31
b12	$C_{18}H_{32}NBr$	341.9	Brownish Yellow	0.29
b14	$C_{20}H_{36}NBr$	369.9	Brownish Yellow	0.27
c6	$C_{16}H_{22}NBr$	307.9	Greyish Black	0.51
c7	$C_{17}H_{24}NBr$	321.9	Greyish Black	0.49
c8	$C_{18}H_{26}NBr$	335.9	Greyish Black	0.48
c9	$C_{19}H_{28}NBr$	349.9	Greyish Black	0.46
c10	$C_{20}H_{30}NBr$	363.9	Greyish Black	0.45
c11	$C_{21}H_{32}NBr$	377.9	Greyish Black	0.43
c12	$C_{22}H_{34}NBr$	391.9	Greyish Black	0.42
c14	$C_{24}H_{38}NBr$	419.9	Greyish Black	0.40
c15	$C_{25}H_{40}NBr$	433.9	Greyish Black	0.38

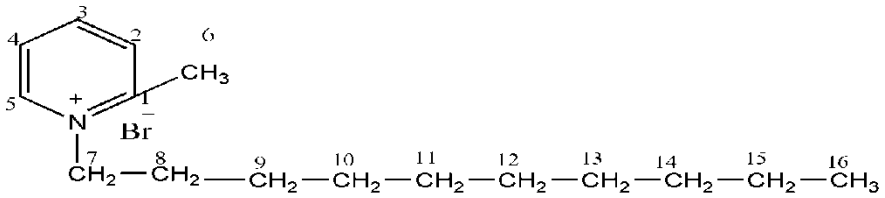
3.2 Structural Analysis

Structures of the compounds were confirmed using different spectroscopic methods like FT-IR and ^{1}H and ^{13}C NMR, spectroscopy.

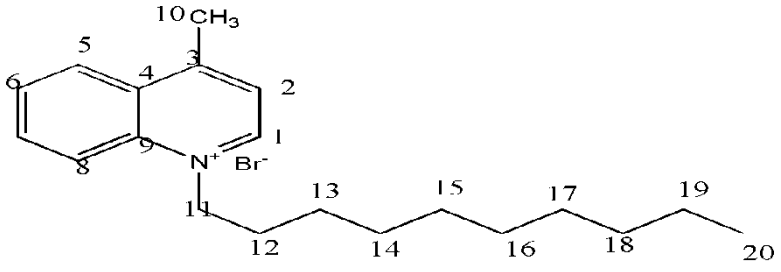
Numbering of protons and carbon atoms present in all the synthesized surfactants is done according to the representative structures of compounds a10, b10 and c10 which are shown in Scheme 1. The remaining structures are the same with a varying chain length.



***n*- Decyl-3-methyl pyridinium bromide (b10)**



***n*- Decyl-2- methyl pyridinium bromide (a10)**



***n*- Decyl -4-methyl quinolinium bromide (c10)**

Scheme.1: Numbering of carbon atoms present in b10, a10, and c10.

3.2.1 (FT-IR) Spectroscopy

Infrared spectra of all the synthesized compounds helped to determine their structural information and formation. The absorptions of each types of bonds (C-N, C=N, C=C, CH_3, CH_2 and C-H aromatic) were found in certain vibrational infrared region of the spectra. The pinnacles that showed up in FT-IR spectra of blended mixes are appointed to their individual bonds as per writing [119].

C-N vibrates at lower frequency i.e., at 1201-1309 cm $^{-1}$ than that of C=N at 1602-1690 cm $^{-1}$ because stronger bonds have larger force constants and vibrates at higher frequencies than weaker bonds. Force constants for double bonds are twice than those of single bonds [119].

Table 3.2: FT-IR data of synthesised amphiphiles

S. No.	Sample code	ν (cm^{-1})					
		C-N	C=N	C=C	CH_2	-CH (aromatic)	-CH_3
1	a6	1300	1634	1590	1465	3023	1145
2	a7	1302	1632	1578	1466	3016	1146
3	a8	1300	1630	1575	1464	3039	1141
4	a9	1309	1634	1590	1465	3023	1145
5	a10	1300	1630	1574	1465	3048	1141
6	a11	1303	1629	1575	1462	3050	1172
7	a12	1307	1629	1573	1462	3043	1170
8	a14	1309	1629	1573	1463	3043	1168
9	a15	1204	1635	1590	1466	3022	1165
10	b6	1206	1633	1590	1465	3013	1154
11	b8	1206	1632	1590	1464	3014	1152
12	b10	1204	1632	1590	1465	3020	1173
13	b12	1206	1632	1504	1465	3025	1175
14	b14	1201	1633	1594	1465	3021	1145
15	c6	1244	1690	1595	1456	3029	1165
16	c7	1244	1602	1531	1460	3028	1168
17	c8	1245	1612	1532	1465	3016	1148
18	c9	1256	1628	1534	1464	3018	1145
18	c10	1261	1604	1531	1462	3018	1168
20	c11	1207	1610	1531	1462	3088	1165
21	c12	1208	1608	1531	1462	3018	1165
22	c14	1212	1612	1533	1492	3010	1168
23	c15	1202	1612	1587	1467	3012	1168

Characteristic bands, around 1201-1309 cm^{-1} for C-N bond confirm the alkyl chain attachment with the pyridine ring. All relevant and significant peaks appeared in the infra-red spectra of these compounds, compounds a6-a15, b6 to b14 and c6 to c15 are given in the Table 3.2. FT-IR spectra of compound a10 and b10 are given in Figures 3.1 and 3.2 respectively. These absorption frequencies are in accordance with those present in the literature [119].

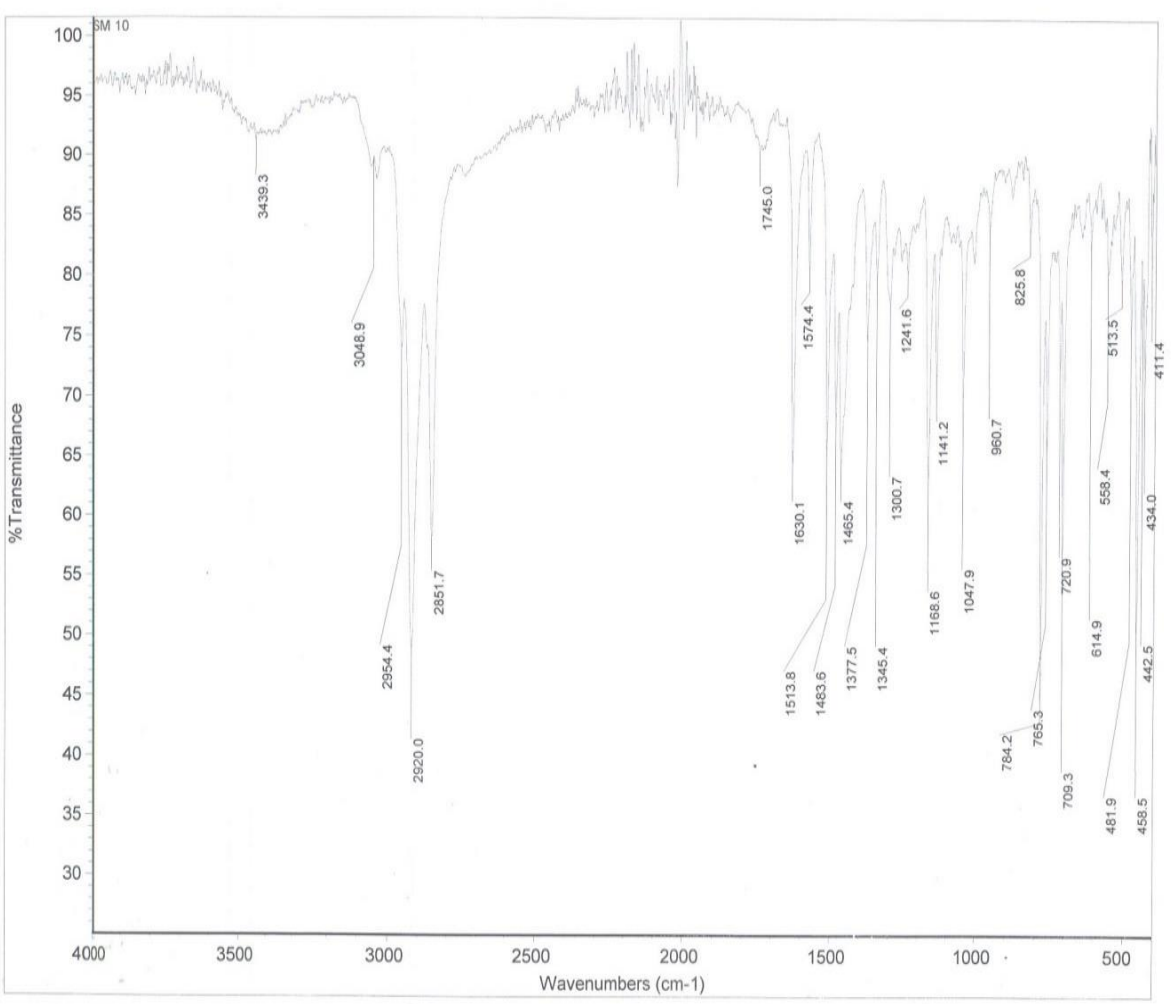


Figure 3.1: FT-IR Spectrum of compound a10

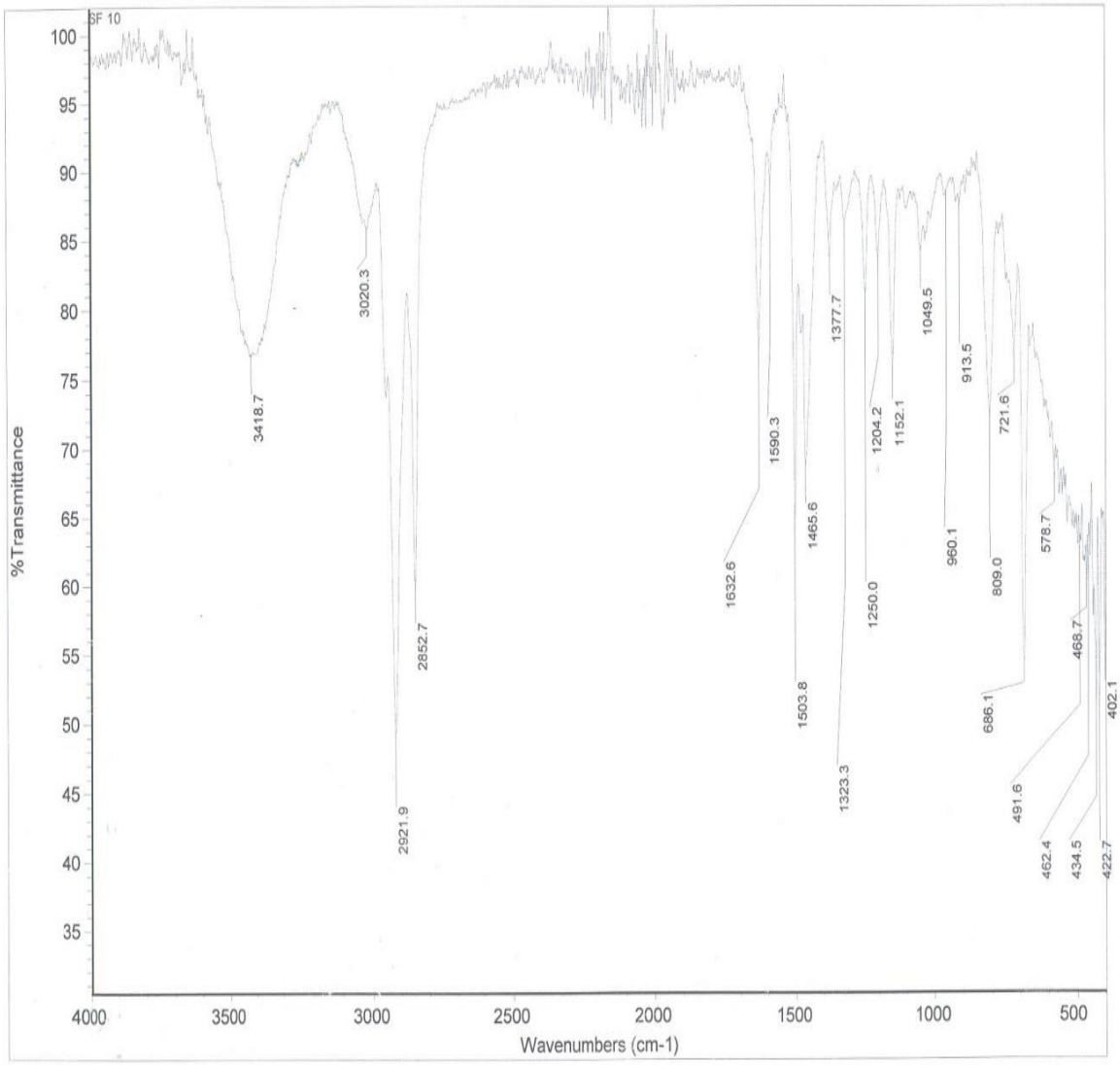


Figure 3.2: FT-IR Spectrum of compound b10

3.2.2 *Structural analysis by NMR*

"^{1}H and ^{13}C NMR" spectroscopic strategies were likewise used to affirm the organization and synthesis of these mixes. Chemical shift values are given in ppm and the multiplicities of signals in ^{1}H NMR are given with chemical shifts; (s = singlet, d = doublet, t = triplet and m

= multiplit). The data of ^{1}H NMR of all the synthesized compounds of a and b series, recorded in $CDCl_3$ is given in Tables 3.3

Table No. 3.3: ^{1}H NMR data of compounds of Series a and b

S. No.	Comp	CH(2) (d)	CH(3) (t)	CH(4) (t)	CH(5) (d)	CH(6) (s)	N-CH_2 (t)	$(CH_2)n$ (m)	CH_3 (t)
1	a 6	8.4	9.45	8.30	9.43	2.68	4.75	1.1-1.3	0.83
2	a 7	8.02	7.99	8.31	9.40	2.94	4.75	1.1-1.4	0.84
3	a 8	8.42	7.91	8.36	9.34	2.94	4.70	1.1-1.87	0.79
4	a9	8.02	7.90	8.37	9.47	2.91	4.74	1.1-1.89	0.80
5	a 10	8.41	7.93	8.38	9.39	2.92	4.74	1.1-1.92	0.83
6	a 11	8.40	7.95	8.00	9.59	2.97	4.83	1.2-1.96	0.82
7	a 12	8.41	7.93	8.02	9.58	2.90	4.88	1.2-1.98	0.82
8	a 14	7.86	7.97	8.33	9.72	2.97	4.91	1.2-1.91	0.87
9	a 15	8.41	7.91	8.36	9.66	2.98	4.84	1.2-1.90	0.86
10	b 6	9.00	8.00	8.5	8.90	2.64	4.68	1.33-2.12	0.90
11	b 8	9.09	8.05	8.9	8.50	2.65	4.69	1.31-2.13	0.90
12	b 10	9.37	8.03	9.2	8.24	2.61	4.86	1.31-2.42	0.82
13	b 12	9.37	8.02	9.19	8.25	2.60	4.86	1.23-2.03	0.80
14	b 14	9.35	8.05	8.22	8.30	2.65	4.93	1.19-2.05	0.87

The synthesized mixes of a and b arrangement were fundamentally affirmed by observing the “signals of protons” at “position seven” in the items which are moved to “higher situations” after the development of these mixes. In compounds of series a, these positions were shifted from 3.39 to 4.75 a6, 4.75 a7, 4.70 a8, 4.74 a9, 4.74 a10, 4.83 a11, 4.75 a12, 4.91 a14 and 4.89 a15. In compounds of series b such shifting occurred from 3.39 to 4.68 b6, 4.69 b8, 4.86 b10, 4.86 b12 and 4.93 b14.

^{1}H NMR data of compounds of series c (c6-c12, c14 andc15) is shown in Table 3.4.

Table No. 3.4: ^{1}H NMR data of compounds c6-c12, c14 andc15

S. No.	Code	CH(1) (d)	CH(2) (d)	CH(5) (d)	CH(6) (t)	CH(7) (t)	CH(8) (d)	CH(10) (s)	N-CH_2 (t)	(CH_2)n (m)	CH_3 (t)
1	c 6	8.77	8.30	7.24	7.50	7.70	7.90	2.94	5.22	1.2-1.28	0.78
2	c 7	10.12	8.71	7.22	7.52	7.66	7.96	2.93	5.23	0.8-1.26	0.78
3	c 8	9.98	8.21	7.16	7.45	7.58	7.87	2.86	5.15	1.0-1.9	0.74
4	c 9	10.04	8.69	7.22	7.50	7.63	7.93	2.63	5.19	1.1-1.7	0.78
5	c 10	8.75	8.10	7.10	7.53	7.68	7.94	2.24	5.39	1.9-1.85	0.86
6	c 11	10.30	9.00	7.92	7.80	8.22	8.37	2.02	5.29	1.2-1.5	0.82
7	c 12	10.12	8.34	7.27	7.55	7.66	7.93	2.69	5.22	1.1-2.0	0.82
8	c 14	10.29	8.35	6.98	7.63	7.76	7.94	2.79	5.24	1.1-2.04	0.82
9	c 15	10.22	8.34	7.28	7.96	7.98	8.01	2.99	5.27	1.1-2.05	0.82

In compounds of series c, formation of compounds was confirmed by significant shift in signals of proton at position eleven in the products. These signals were moved downfield after the synthesis of compounds from "3.39 to 5.22 c6, 5.23 c7, 5.15 c8, 5.19 c9, 5.39 c10, 5.29 c11, 5.22 c12, 5.24 c14 and 5.27 c15".

In all the compounds aryl protons have greater chemical shift values i.e., 7 - 8 they were deshielded by diamagnetic anisotropy of the ring [119]. It is anisotropic effect that gives CH_3 protons, attached to the ring, the greater chemical shift value of 2.02-2.99. These protons lie in the deshielding region of the anisotropic field. The CH_3 protons far away from the ring, i.e, in the chain are found shielded, with lower chemical shift values of 0.74- 0.90.

Protons at C5 of compounds series a, are near to electropositive nitrogen atom and are more deshielded than other, that's why has greater chemical shift values than other aryl protons.

^{13}C NMR spectra of all the synthesized compounds of series a b and c, confirm their formation.

In compounds of series a and b, confirmation of compound formation was made by observing the signals of carbon at position seven which were advanced in the products. For compounds of series a, these signals were shifted from 33.71 to 58.4 a6, 58.4 a7, 58.3 a8, 58.3 a9, 58.4 a10, 58.4 a11, 58.4 a12, 58.6 a14 and 58.4 a15. Similarly, in compounds of series b, these

signals were shifted from 33.71 to 61.1 b6, 61.4 b8, 61.8 b10, 61.8 b12 and 62.4 b14. Structural confirmation of series c compounds was obtained by observing shift in signals of carbon at position eleven in the products. These signals have shown downfield shift i.e., from 33.71 to -57.8 c6-c15.

The data for "^{13}C NMR" of all the synthesised compounds is given in Table 3.5 and 3.6.

Table No. 3.5: ^{13}C NMR data of compounds of Series a and b.

S. No.	Code	C1	C2	C3	C4	C5	C6	N-CH_2	$(CH_2)n$	CH_3
1	a6	154.2	126.4	146.3	128.2	145.3	20.7	58.4	22.3-31.1	13.9
2	a7	154.2	126.4	146.3	130.4	145.3	20.7	58.4	22.4-31.4	14.0
3	a8	154.2	126.4	146.1	130.4	147.3	20.6	58.3	22.4-31.5	13.9
4	a9	154.2	126.3	146.3	130.5	145.3	20.7	58.3	22.5-34.1	14.0
5	a10	154.2	126.4	146.3	130.4	145.3	20.7	58.4	22.5-31.7	14.0
6	a11	154.2	126.3	146.5	130.3	145.2	20.7	58.4	22.6-34.1	14.0
7	a12	154.2	126.4	146.3	130.4	145.3	20.7	58.4	22.6-34.0	14.0
8	a14	154.2	126.46	146.63	130.19	145.16	20.86	58.60	22.7-34.01	14.13
9	a15	154.2	126.42	146.88	130.02	144.96	20.82	58.4	22.7-34.1	14.14
10	b 6	145.6	139.1	142.0	127.7	143.9	25.7	61.1	18.2-31.4	14.1
11	b 8	145.6	139.5	142.0	127.7	144.2	25.7	61.4	18.4-31.6	14.1
12	b 10	145.6	139.6	142.3	127.9	144.5	22.6	61.8	18.6-31.9	14.1
13	b 12	145.6	139.6	142.2	127.9	144.4	22.6	61.8	18.6-31.8	14.1
14	b 14	145.6	139.6	142.2	127.8	144.5	26.1	62.4	25.7-34.1	22.6

Table No. 3.6: ^{13}C NMR data of compounds of Series c

S. No.	Code	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	N-CH_2	$(CH_2)n$	CH_3
1	c 6	145.3	129.2	157.8	126.8	123.4	126.5	128.2	118.7	136.9	22.3	57.8	18.7-31.2	13.9
2	c 7	146.9	129.1	157.9	126.5	123.3	126.8	128.2	118.8	136.9	22.4	57.8	18.7-31.4	13.9
3	c 8	146.3	129.2	158.0	126.6	123.2	126.8	128.1	118.8	136.8	22.4	57.8	18.7-31.5	13.9
4	c 9	149.0	129.3	157.9	126.8	123.3	126.8	128.1	118.8	136.8	22.5	57.8	20.4-34.1	18.8
5	c 10	149.4	129.1	157.8	126.6	123.4	126.8	128.2	118.8	136.9	22.6	57.8	22.6-34.1	14.1
6	c 11	149.5	129.4	157.8	124.7	123.4	126.8	128.2	118.8	136.9	22.6	57.8	20.2-31.8	14.1
7	c 12	149.2	129.4	157.9	126.8	123.3	126.9	128.2	118.8	136.9	22.6	57.8	18.9-31.8	14.09
8	c 14	149.5	129.4	157.8	126.8	123.4	127.4	127.5	118.9	136.9	26.5	57.8	26.5-34.0	14.1
9	c 15	149.4	129.4	157.8	126.8	123.4	127.2	128.8	118.9	136.9	26.4	57.8	26.4-34.0	14.1

To find out whether these surfactants are stable or not, ^{1}H-NMR and ^{13}C-NMR spectra were recorded in benzene and methanol and found to be stable. The spectra were exactly same as in $CDCl_3$. ^{1}H-NMR and ^{13}C-NMR spectra for compound a10 and b10 are given in Figures 3.3, 3.4, 3.5 and 3.6 respectively.

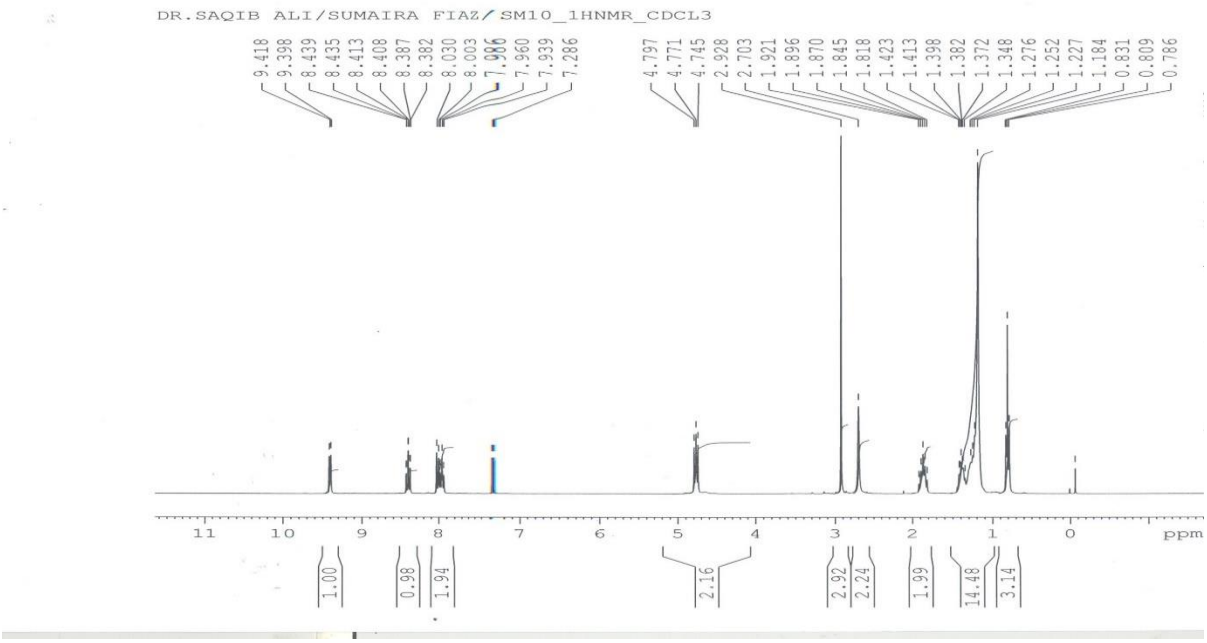


Figure 3.3: ^{1}H NMR Spectra of a10

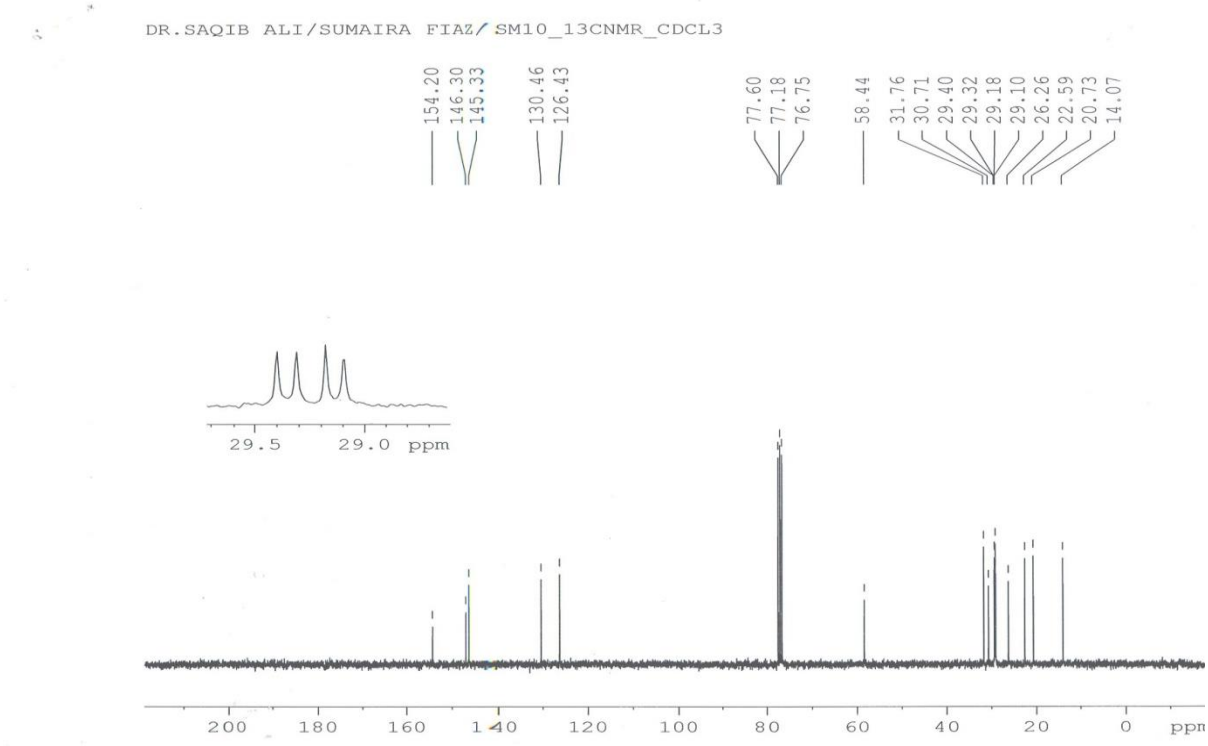


Figure 3.4: ^{13}C NMR Spectrum of a10.

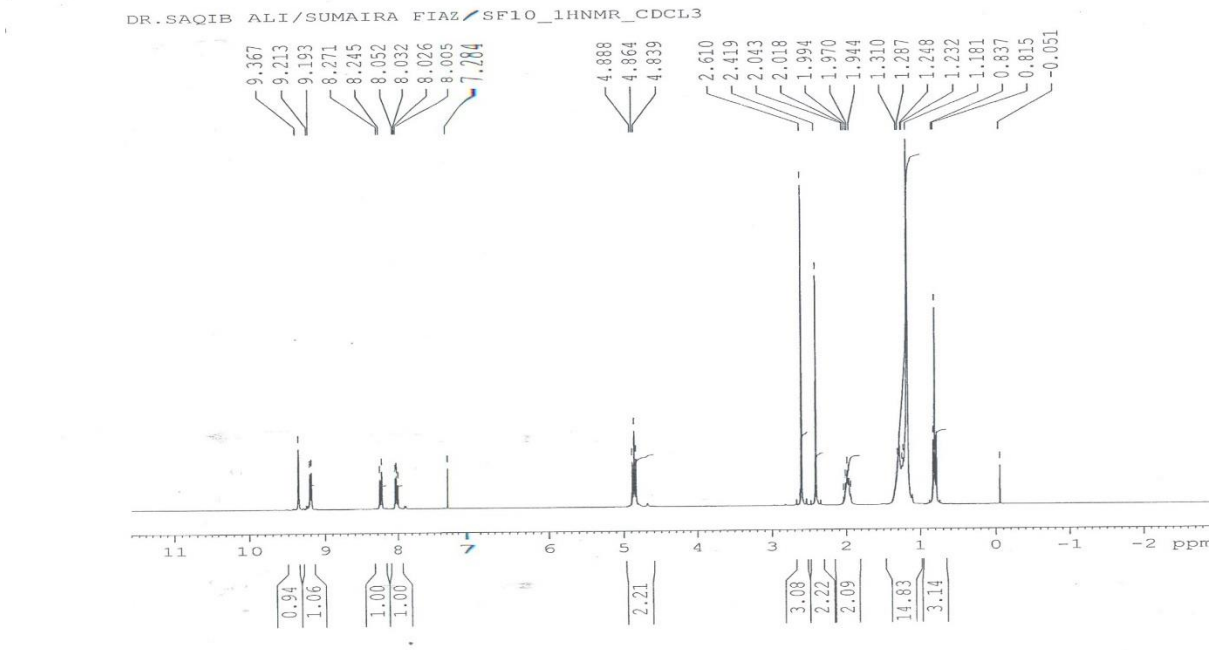


Figure 3.5: ^{1}H NMR Spectrum of b10.

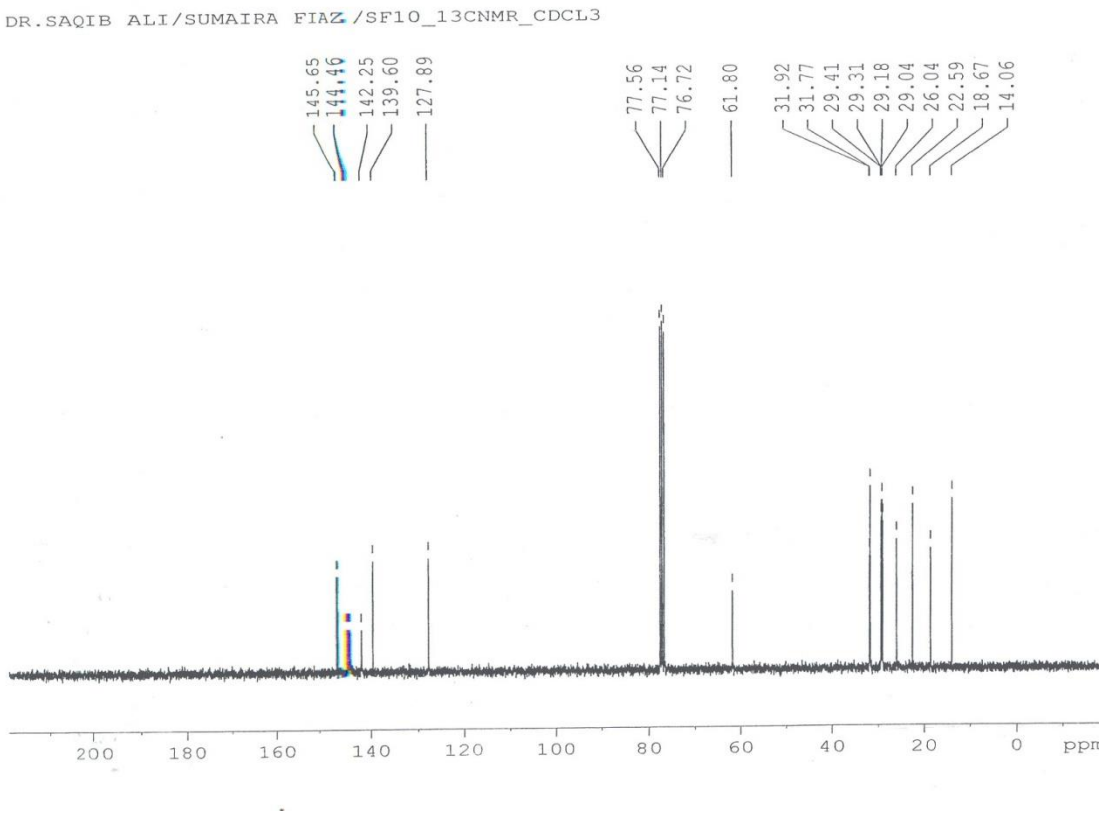


Figure 3.6: ^{13}C NMR Spectrum of b10.

3.3 CMC studies

One of the most important and fundamental parameters to be assessed for a surfactant is its Critical Micelle Concentration (CMC).The efficiency of surfactant directly depends on its CMC. It is the minimum amount of a surface-active material (surfactant) required to attain the highest surface tension.

A lower value of CMC is always desired because it accounts for a minor amount of surfactant required for effective emulsification, solubilization and dispersion of micelles at interfaces. Lower CMC values will help to perform as better wetting agent and more useful detergent. For utilization of surfactants as drug carriers, a lower CMC value is always a matter of interest and a quality that is highly demanded for such exploration and successful application of amphiphiles in this field [127-130].

UV-Visible spectroscopic methods along with conductometric methods were used to determine the CMC of all synthesised compounds. In the conductometric method, a "0.01 M KCl solution" was used for the calibration of the conductometer cell with a "cell constant of 0.47μS/cm".

"Standard solutions" of compounds of series a and b were made in the range of 0.50 mM to 0.20 mM and for series c in range from 0.60mM to 0.30mM in "ethanol and their conductivity was measured at 298 K". Conductivity of these solutions was plotted as a function of concentration. It was observed in the graphs that the conductivity is linearly correlated to the surfactant concentration, in both the pre and post micellar regions, being the slope in premicellar region greater than that in the post micellar region.

CMC values were obtained from the intersecting point in each graph [131-133]. Figure 3.7 shows the plots of specific conductivity against the concentration of the compounds of series, plots of series b and c are given in appendixes A3 and A4 respectively.

CMC values obtained for series a, at 298 K ranges from a6, 0.42mM to a15, 0.30mM. For b series a, b6, 0.41mM to b14, 0.27 mM and for series c, c6, 0.51mM to c15, 0.38mM.

CMC values obtained from conductometric method for all compounds of series were verified by UV- visible spectroscopic method. For this purpose, first of all λ-max values of all the compounds of series a, b and c were determined from the "plot of absorption versus wavelength and then absorptions of solutions of all the compounds of series a, b and c used in conductivity measurements were recorded at their respective λ-max values". The λ-max values for series a and b compounds were 266 and 267 nm and that of series c was 239 nm.

When recorded absorbance values of all compounds of series a, b and c (at their respective λ-max) were plotted against concentration of the surfactants, an intonation point was seen in each chart, affirming the beginning of micellization.

Figure 3.8 shows the absorbance versus concentration plot for mixes of series a and appendixes A1 and A2 speaks to the plots of absorbance versus concentration charts of series b and c mixes. The decided CMC values for all series mixes by spectroscopic and conductometric strategies are in acceptable understanding.

The gotten CMC values for mixes of series a and b are lower than the detailed estimations of 0.824 and 0.798 mmolL-1 for hexadecylpyridinium bromide in water at 303 K [133] which could be credited to the unsubstituted idea of the pyridinium ring [134].

The CMC values observed for series c compounds are greater than those of series a and b due to structural difference as CMC values depends on structure of compounds [14, 15]. CMC of c series compounds are lower than those of same reported compounds [135]. This difference is attributed to solvent effect.

Similar compounds have reported CMC values in water and here that of series c compounds are obtained in ethanol. Change in solvent of surfactant either increase or decrease its CMC value depending on the hydrophobic and hydrophilic interaction of surfactant. Ability of water to make hydrogen bonding with surfactant and increase in dielectric constant due to water, cause surfactant monomers to stabilize and disfavours the micellization at low concentration. [135]

Moreover, while comparing CMC values of series a and b, which only differ by position of methyl group attachment, it can be observed that compounds of series a (*n*-alkyl-2-methlpyridinium bromides) have a little higher CMC values than series b (*n*-alkyl-2-methlpyridinium bromides). The reason behind this small difference is the steric hindrance due to the position of methyl group. At carbon number-2, methyl group provides more steric hindrance then at carbon number-3. Therefore, CMC value for compounds of series a, is higher [134].

For compounds of series a, plots of Conductivity *v s* concentration and that of Absorbance *v s* concentration are shown in Figures 3.7 and 3.8 respectively.

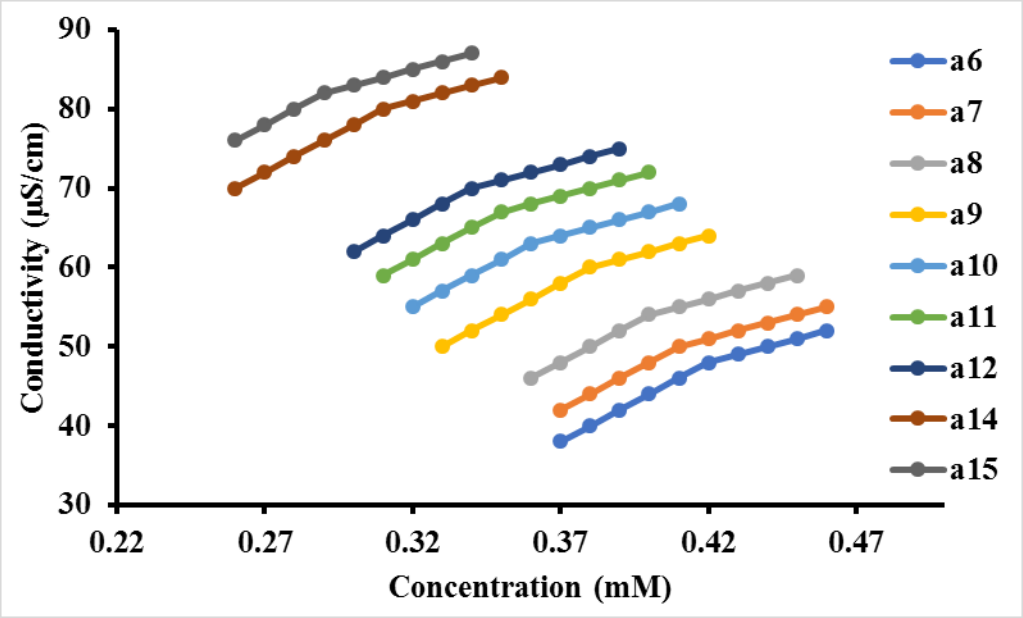


Figure 3.7: Conductivity *v s* concentration plots for series a (a6 - a12, a14 and a15)

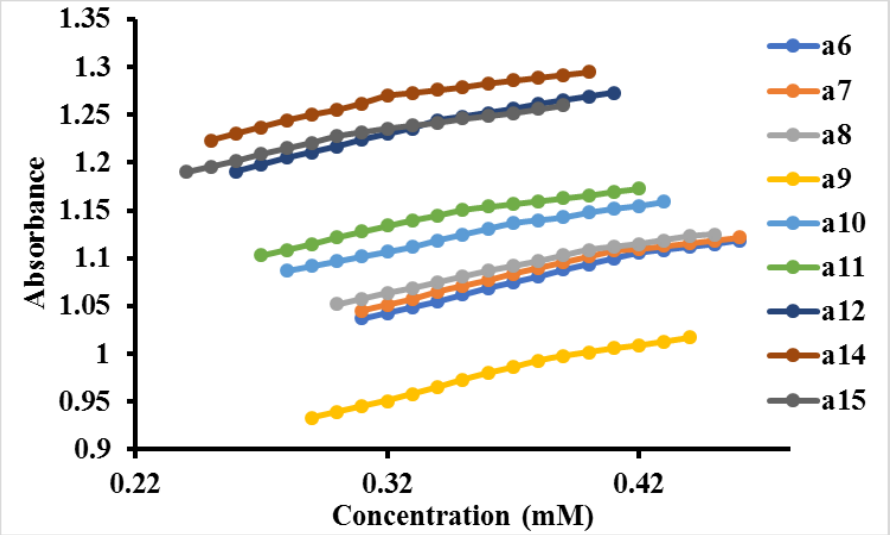


Figure 3.8: Absorbance *v s* concentration plots for series a (a6 - a12, a14 and a15)

3.3.1 Effect of temperature on CMC

Temperature is an important factor which affects CMC values. CMC variations over a range of temperatures exhibit a complex attitude. Initially CMC decreases on an increase in temperature, but this is not the sole happening. After decreasing to a minimum, it drastically starts to rise on elevating the temperature. Let's have a thorough and deep insight of such behaviour of CMC depending on the variation of the temperature [10].

In Figure 3.9, CMC values are plotted against temperature for all compounds of series a (a6-a12, a14 and a15), when temperature is increased, CMC values, at first, decline and then rise.

Similar observations are recorded for series b and c as well but plots are given in appendixes A5 and A6 accordingly. Similar observations are exhibited for the micellization behaviour of many other surfactants of similar nature like octyltrimethyl-ammonium bromide [136], polysorbates [15], imidazolium ionic liquids [137] and cationic Gemini surfactants [138]. These compounds have formed U shaped graphs when CMC was plotted versus temperature. An increase in temperature has affected CMC in two opposite directions. The early reduction of CMC values at raised temperatures is because of a diminishing in collaborations between the head gathering of surfactants and dissolvable particles which favours the cycle of micellization. So micellization takes place at lower concentrations due to less probability of hydrogen bonding. Whereas the upsurge in the values of CMC with further rise in temperature is due to a breakdown of solvent structures surrounding the hydrophobic group which disfavours the micellization at low concentrations. So, a large number of molecules begin to form aggregates, micellization occurs at high concentrations resulting in increased CMC values [14]. In Figure 3.10, the variation in CMC values of compound a6 is given. The dependence of CMC values for rest of the synthesized compounds at different temperatures is shown in appendixes A7 to A14 for compounds a7 to a15, for the series b in appendixes A5 to A19 and for series c, in appendixes A20 to A28.

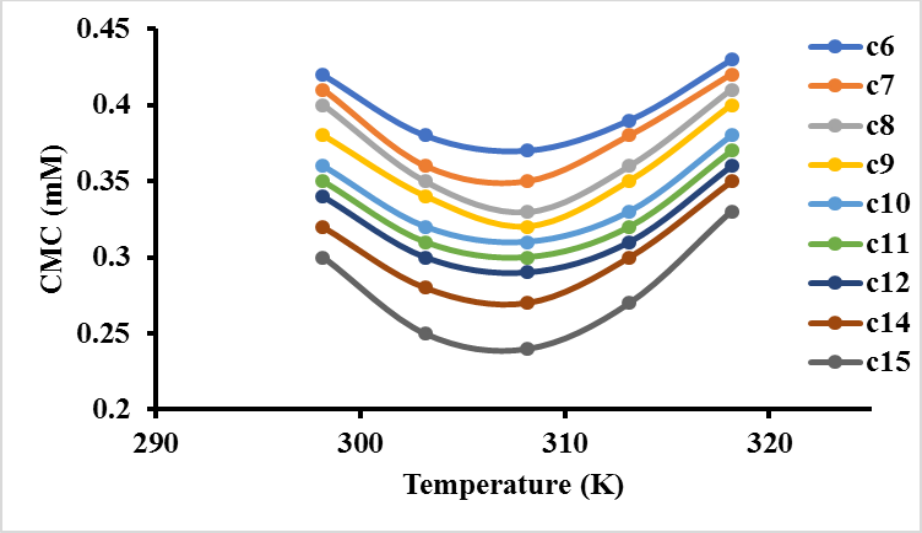


Figure 3.9: Variation of CMC values as a function of temperature for series a (a6 - a12, a14 and a15)

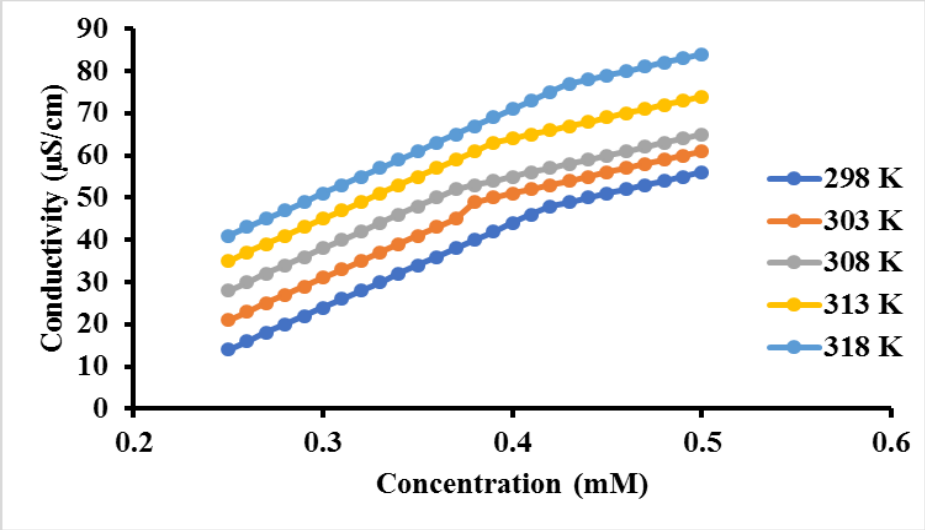


Figure 3.10: CMC of compound a6 at different temperatures

3.3.2 Effect of hydrophobic tail group on CMC

Generally, in the series of surfactants which differ only by a -CH_2- group in the hydrophobic chain, CMC reduces with the growth of the length of the alkyl chain. The reason may be that the addition of a CH_2-group enhances the hydrophobic nature of the alkyl chain which attributes the dehydration/desolvation of the alkyl chain, causing a decrease of the CMC value [14].

Experimentally, it was also observed that CMC values decreased by increasing the chain length of all compounds of three series under investigation. For example, at room temperature, the CMC value for compound b6 is 0.41mM for b8, it is 0.35 mM for b10, it 0.31mM, for b12, it is 0.29 mM and for b14, it is 0.27 mM. An increase of the hydrocarbon chain length has the inclination to enhance the hydrophobic contact between the counter ion and the micellar core, so micellization takes place at a lower concentration [28]. The Stauff–Kleven's equation was also followed by these results [20] as given in the equation:

$$\log CMC = A - Bn_c \qquad (1)$$

where

A and B are constants for a predefined homologous arrangement at a predetermined temperature, and nc is the quantity of carbon molecules in the alkyl chain. The consistent A fluctuates with synthetic sythesis hydrophilic gatherings, while the steady B, administers the impact of every extra CH_2 bunch on the CMC.

Figures 3.11 to 3.13 are the logarithmic plots of the CMC values in mM, against the alkyl chain length (the number of carbon atoms) at room temperature. Similar observations were

also observed for compounds **a6** - a15 and c6 - c15. These results are also in agreement with earlier literature reports for the pyridinium based surfactants [133].

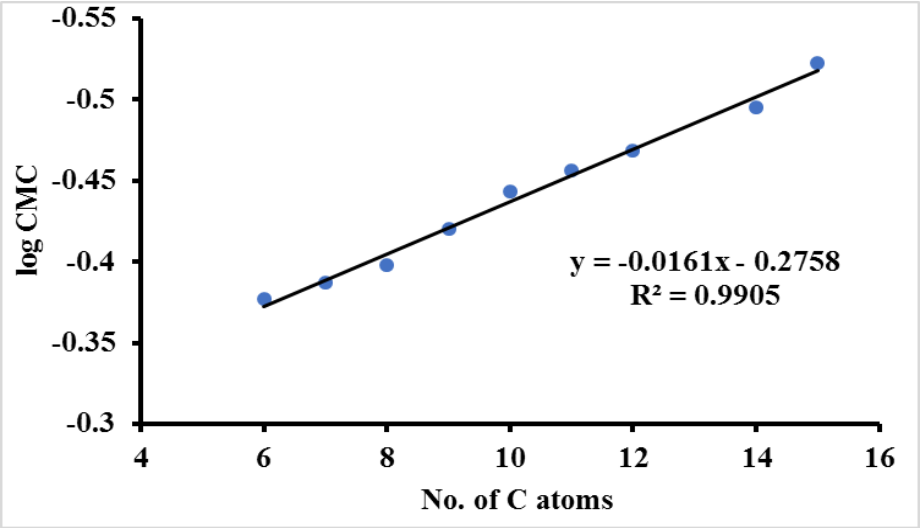


Figure 3.11: log CMC *v s* number of C-atoms in hydrophobic chain of series a (a6-a12, a14 and a15)

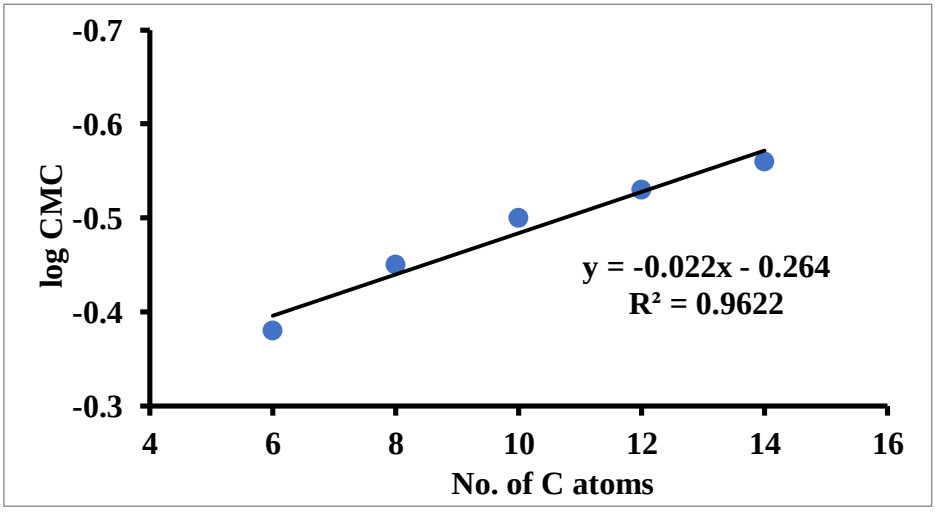


Figure 3.12: log CMC *v s* number of C-atoms in hydrophobic chain of series b (b6, b8, b10, b12 and b14)

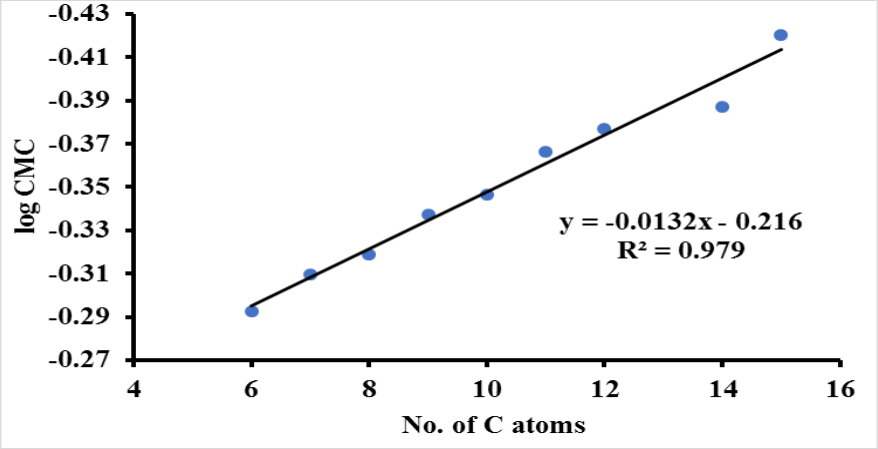


Figure 3.13: log CMC *v s* number of C-atoms in hydrophobic chain of series c (c6-c12, c14 and c15)

3.4 Thermodynamic Parameters

CMC is dependent on the temperature. The temperature dependence of CMC was used to elaborate thermodynamic indicators like "Gibbs free energy (ΔG)", "entropy (ΔS)" and "enthalpy (ΔH)". Equation given below (equation 2) was utilized to calculate Gibbs free energy [37]:

$$\Delta G = (2 - \beta)\, RT \ln X_{CMC} \qquad (2)$$

where β = degree of dissociation

R= general gas constant (8.314 J/mol K)

T = absolute temperature

X_{CMC} = mole fraction of CMC value

$\beta = S_2 / S_1$

β in equation 2, is "the ratio between slopes of areas of conductivity concentration plots before and after micelle formation".

The "ΔH", enthalpy of micellization was determined using the equation 3 [37]:

$$\Delta H = -2.3(2 - \beta)RT^2[\partial(\log X_{CMC})/\partial T] \qquad (3)$$

The entropy "ΔS" of micelle formation was determined from equation 4 [37]:

$$\Delta S = (\Delta H - \Delta G)/T \qquad (4)$$

The thermodynamic parameters, calculated for micelle formation of series b are given in Table 3.7, and results of series a and c are given in appendixes B1 and B2 respectively. These

values are in accordance with the formerly calculated values for similar compounds [10, 139]. The values of Gibb's free energy, enthalpy and entropy are presenting a direct relation with the increasing length of the alkyl chain, attached to the N-atom of the pyridine ring.

It was demonstrated that the cycle of micelle arrangement was unconstrained by finding the negative worth of "ΔG". Moreover, values of ΔG decrease further on an increase of the temperature. It shows that higher temperatures are not suitable for micellization because at elevated temperatures there is more disturbance among the solvent molecules which makes micelle formation difficult and extra energy is needed to retain micelles surfactant molecules.

Both "enthalpy (ΔH)" and "entropy (ΔS)" have positive qualities. "The positive estimations of enthalpy (ΔH) and entropy (ΔS) represent the endothermic idea of the cycle and increment in the assertion of the framework".

The reason for the positive value of entropy is that of initially, when surfactant molecules are added to the solvent, the ethanol molecules surround the surfactant molecules and that might improve the orderness of the system. However, throughout the micelle formation, the surfactant molecules will relocate and re-organise themselves in the solution and will repel surrounding solvent molecules. This will result in the more disordered state of the system. Additionally, the bigger the alkyl chains, the more a reason for relocation of surfactant molecules.

Therefore, an increase of the chain length gives higher entropy value. This is because, rise in the alkyl chain length grounds enhancement in hydrophobic character of the molecule and increase in the hydrophobicity causes an increase in the stability of the micelle structure [140].

"The positive assessments of the entropy of the micellization of *n*-alkyl-3-methylpyridinium bromides in ethanol" could similarly be explained dependent on the "plan of ice sheet of the ethanol iotas" around the amphiphilic molecules that would improve the system's structure, yet during "micellization measure i.e., the ejection of surfactant molecules from the course of action will blast the cold mass achieving the extension in the entropy of the structure [10]"

.

Table 3.7: Thermodynamic data of (series b) compounds

	Temperature	*CMC*	*XCMC*	*LnXCMC*	*ΔG(J/mol)*	*ΔH(J/mol)*	*ΔS(J/mol.K)*
b6							
1	298.16	0.41	0.0000194	-10.85203	-40351.68	25281.94	220.12
2	303.16	0.37	0.0000163	-11.02434	-41679.81	24069.35	216.87
3	308.16	0.36	0.0000156	-11.06823	-42535.91	24809.84	218.54
4	313.16	0.38	0.0000170	-10.98229	-42890.43	25683.43	218.97
5	318.16	0.43	0.0000203	-10.80488	-42871.31	26510.12	221.55
b8							
1	298.16	0.35	0.0000203	-10.8048	-40176.36	15521.299	186.80
2	303.16	0.31	0.0000180	-10.92513	-41304.73	16046.234	189.17
3	308.16	0.30	0.0000175	-10.9533	-42094.22	16579.898	190.40
4	313.16	0.32	0.0000187	-10.8869	-42518.21	17122.291	190.44
5	318.6	0.36	0.0000200	-10.81977	-42732.90	17673.400	189.88
b10							
1	298.16	0.31	0.000018	-10.9251	-40623.38	17738.62	195.74
2	303.16	0.27	0.0000156	-11.0682	-41845.63	18338.47	198.52
3	308.16	0.26	0.0000152	-11.0942	-42635.71	18948.45	199.84
4	313.16	0.28	0.0000163	-11.0243	-43054.50	19568.33	199.97
5	318.16	0.33	0.0000191	-10.8658	-43113.03	20198.18	198.99
b12							
1	298.16	0.29	0.0000168	-10.9941	-40879.94	19955.95	204.03
2	303.16	0.25	0.0000145	-11.1413	-42122.23	20636.87	207.01
3	308.16	0.24	0.0000140	-11.1764	-42951.80	21317.01	208.55
4	313.16	0.26	0.0000152	-11.0942	-43327.49	22014.37	208.65
5	318.16	0.31	0.0000180	-10.9251	-43348.44	22722.96	207.66
b14							
1	298.16	0.27	0.0000156	-11.0682	-41155.47	25499.27	223.55
2	303.16	0.23	0.0000133	-11.2277	-42448.66	26361.67	226.97
3	308.16	0.21	0.0000124	-11.2978	-43418.16	27238.40	229.28
4	313.16	0.24	0.0000140	-11.1765	-43648.90	28129.47	229.20
5	318.16	0.29	0.0000170	-10.9823	-43575.27	29034.89	228.21

3.5 Biological Studies

Different biological applications of all these compounds where studied using different standard operating procedures. Antimicrobial, antifungal and anti-oxidant activities of these compounds were explored to find their potential as biologically active compounds.

3.5.1 Antibacterial Activities

Antibacterial activities of all synthesised compounds were examined against four bacterial strains. The standard antibiotics used were Kanamycin sulphate and Streptomycin sulphate. Antibacterial movement of a compound is viewed as huge if "the zone of restraint is over 20 mm". On the off chance that it is "18-20 mm, it is acceptable. 15–17 mm is viewed as low and under 11-14 mm is considered as irrelevant [141]".

All mixes have displayed antibacterial movement against chosen bacterial strains. In this investigation, mixes b6 and b8 have indicated critical movement against *Enterobacter aerogenes*. While compound b6 was additionally delegated altogether bactericidal against *Bacillus subtilis* and *Escherichia coli.*

The compounds with larger alkyl chains having 10, 12 and 14 carbon atoms in the hydrophobic chains, are more effective against all four bacterial strains studied as compared to compounds with smaller alkyl chains [10]. Besides, "compound b6 was discovered to be proficient against *Escherichia coli* and the chain length didn't influence antimicrobial movement against *Bacillus subtilis*". This information had not given any pattern about the antimicrobial viability identified with the chain length of the examined surfactants.

"Adsorptive capacities, hydrophobicity of alkyl chain, surface action and electron thickness of nitrogen particle are the key causes behind bactericidal exercises of both pyridinium and quinolinium surfactants. The conjunction of a hydrophilic nitrogen iota and a hydrophobic chain in a similar particle may be the plausible explanation behind the antimicrobial exercises [142]". Every one of these highlights together finance the antibacterial conduct of these surfactants. Contrasting the antimicrobial exercises of these mixes with "n-alkylimidazolium bromides with equivalent chain length, similar to n-hexyl-3-methyl imidazolium bromide and n-octyl-3-methyl imidazolium bromide", it was discovered that pyridinium surfactants are preferred anti-toxins over imidazolium ionic fluids [143].

Results of series b against all bacterial strains are given in Table 3.8 and results of the remaining compounds are given in appendixes B3.

Table 3.8: Antibacterial activity data of (series b) compounds

Average Zone of Inhibition in mm				
Compounds	***Enterobacter aerogenes*(-)**	***Escherichia coli* (-)**	***Staphylococcus aureus* (+)**	***Bacillus subtilis* (+)**
b6	21	28	7	25
b8	21	11	6	12
b10	18	27	10	25
b12	32	25	39	27
b14	31	27	38	23
Kanamycin Sulfate	22	30	16	34
Streptomycin Sulfate	12	13	0	10

3.5.2 Antifungal Activities

Percent inhibition in the direct growth of a fungal strain was used as measure to estimate the antifungal activities of the compounds. Results of antifungal activities for the series b are given in Table 3.9. The rest of the results are given in Appendixes B4.

All synthesized compounds were exceedingly active against tested fungal strains and showed good results. The hydrophilic part of the surfactant molecules is attached through an intermolecular hydrogen bonding on the surface membrane of the fungus. Surfactants have a potential to work as antifungal agents, because they target the extra cytoplasmic region and thus do not need to enter the cells, thereby avoiding most cellular pump-based resistance mechanisms. The role of the alkyl chain and chain length is still not well understood [144].

Table 3.9: Antifungal activity data of (series b) compounds

Antifungal activity (% inhibition in linear growth)				
S. No.	**Sample code**	***Aspergillus niger***	***Aspergillus flavus***	***Aspergillus fumigates***
1	b 6	21 ± 1.09	33±0.49	41±2.00
2	b 8	31±1.00	47±1.00	61±2.78
3	b 10	20±0.75	29±0.89	33±0.94
4	b 12	43±1.97	48±0.49	61±4.00
5	b 14	39±1.00	52±2.35	67±3.39
	Terbinafine	96.5±0.75	89.5±0.75	94.0±.0.00

3.5.3 Antioxidant Activities

The role of these surfactants as antioxidant agents was explored and estimated by a relevancy between sample and control in terms of percent inhibition. Results of series b are given in Table 3.10 and the results of the other two series are given as appendixes B5.

Our results of antioxidant activities are based on the postulate that an antioxidant having surface-active qualities would have a better tendency to limit oxidation of lipids in emulsions because amphiphile molecules gather at the oil-water interface.

Consequently, the antioxidant would play a role of protector for the fatty molecules enclosed in the micelle [145]. Moreover, antioxidants that are lipophilic in nature are more efficient in systems of larger surface area, like in micelles, membranes or emulsions [146].

That's why such antioxidants would have better attraction for the oil-water boundaries and, thus, would inhibit lipid oxidation in a more efficient way. These results open possible new areas of usage for these surfactant antioxidants in the different fields like food materials, therapeutics, or cosmetics industries.

Table 3.10 Antioxidant activity data of (series b) compounds

Antioxidant activity (% inhibition)						
S. No.	**Sample code**	**Amount per 10 Ml**				
		5 mg	**4mg**	**3mg**	**2mg**	**1mg**
1	b 6	24.1±1.00	17.1±1.90	13.5±0.95	10.5±0.35	82±0.19
2	b 8	31.5±1.35	29±0.49	21±0.31	19±0.39	13.0±0.18
3	b 10	39.2±2.50	30±1.00	26±1.00	23±1.00	20±0.18
4	b 12	31.2±0.97	30±2.10	27±1.31	20±0.28	15.3±0.21
5	b 14	40±2.00	37±3.09	31±1.00	27±1.00	20±0.29
	Ascorbic acid	80.5±2.00	70.5±3.50	58±3.00	49.5±0.50	42.5±3.50

3.6 Drug Surfactant Interactions

As surfactants have an incredible potential to be investigated as a medication transporter, it is essential to consider drug-surfactants association in detail. The importance of micelles in drug delivery system is due to their nontoxic nature and amphiphilic nature. Being hydrophobic at the inside and hydrophilic at the interface, they possess a remarkable resemblance with plasma membrane structures. They are lipid bilayers and micelles can easily cross these membranes, in this way micelles can carry loaded drugs to a target. Drugs which normally cannot pass through this barrier, can cross in a very efficient way. That's

why micelles are a natural choice to explore their role as a modern drug delivery system. Such explorations and investigations may lead to the successful discovery of efficient drug carriers which will help to release drugs in a better, controlled, skillful and desirable way.

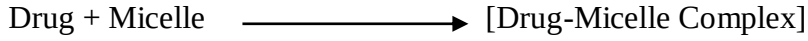
Moreover, micelles can solubilize drugs of both kinds polar and nonpolar. Polar drugs are normally attracted and attached in polar parts of an amphiphile while nonpolar drugs interact with nonpolar hydrophobic areas. In this way, these micelles will also provide an added facility to solubilize the drugs which are insoluble in water and will enhance the availability of such drugs which are difficult to administrate otherwise [147-150].

Additionally micelles have low thickness, little total size, straightforward infiltration and long shell life. “The solubilization configuration” is impacted by the “charge on surfactant” and “structure of the medicine”. More hydrophobic of surfactants gives greater proclivity to the hydrophobic medication [151]. Cationic surfactants micelles are more like layer since they give both hydrophobic and electrostatic collaborations [152].

Because of their incredible solubilizing power, surfactants are used to solubilize the medications that can't be utilized in light of their high and uncontrolled harmfulness [151]. The expansion or diminishing in absorbance at micellar fixation is because of the capacity of medication atoms to go into the micelle. The expansion in absorbance is because of the way that in spite of the fact that drug particles are inside the micelles however their chromophores are as yet arranged close to the surface, consequently they assimilate light more well than in mass arrangement [153]. The decline in absorbance shows that the medication particles are caught inside the micellar center.

The CMC of surfactants are influenced by the communication with the medications. Micelles are reasonable transporters on the grounds that hydrophobic medications are fused in hydrophobic center of micelles [154].

Drug surfactant interactions generally hinge on the charge of drug molecule [147]. Contingent on the “charge, drug atoms ordinarily cooperate with the head gatherings of surfactant particles with inverse charge”. Whereas drug molecules which are neutral can infiltrate through the hydrophobic inside, being non-polar in nature [148,151]. Over all, such interactions result in a drug-micelle complex formation and then the drug is released at the target area and in a controlled mechanism [149,150].



At premicellar fixations, drug – surfactant totals are shaped and at postmicellar focuses, these totals burst to monnomers which are then appended to micelles. The hydrophobic cooperation happens in the micellar center and electrostatic association just brings the medication and surfactant close enough for the activity of hydrophobic communication [155].

Micelles decline the reactions of the medications and increment their availibity at the site of activity. Low CMC estimations of surfactants are significant on the grounds that here medications stay in the micelles because of more noteworthy connection, so decrease in bioavailibity of medication to organic framework happens. On the off chance that high CMC estimation of surfactant is utilized for drug organization, at that point on weakening, CMC will blast and medication will be hastened before to play out its activity in the framework [156]. Medications are typified in micellar framework by concoction formation or by physical entanglement. The destabilization of micelles happens by change of hydrophobic square with the hydrophilic one, along these lines micelles will toss the stacked medications to the site of activity [157].

3.6.1 Selected Drugs

Drugs chosen for investigating their interaction with the micelles of the synthesized surfactants were Ketoprofen and Flurbiprofen which are “nonsteroidal anti-inflammatory drugs (NSAID)”. The reason of selection of these medications was that they are poorly soluble in water. The encapsulation of these drugs in micelles may improve their solubility and may help to lead towards better administration of these drugs with improved efficacy. [158,159].

3.6.1.1 Ketoprofen

Ketoprofen belongs to the “propionic acid class of nonsteroidal anti-inflammatory drugs (NSAID)”. It has active pain-relieving and antipyretic effects against moderate to severe pains. It is a mode of action to inhibit the production of prostaglandin in the body. It is administrated for treatments of severe toothaches due to inflammation, severe rheumatoid arthritis, osteoarthritis, and nerve pains like sciatica, postherpetic neuralgia. It can be taken orally or in the form of a cream, ointment, liquid, spray, or gel [160-162]. Generally it is better in efficacy when compared to ibuprofen or diclofenac [163]. A general structure of Ketoprofen is given in Figure 3. 14.

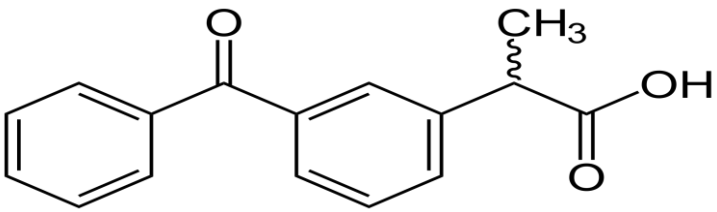


Figure: 3.14: Structure of Ketoprofen

3.6.1.2 Flurbiprofen

Flurbiprofen is also a NSAID belonging to the phenylalkanoic acid family. It is an effective pre and post-operative analgesic [158]. It is also used as analgesic to treat severe pain in cancer patients. Flurbiprofen binds itself with "human serum albumin (HAS). In the blood serum its amount in free structure is tiny. Furthermore, to ease torment it is important to have its sufficient sum in the blood serum, because of malignancy when inoculated in blood. It is important to lessen its affiliation to accomplish this objective [159]. So, a proper drug delivery is very important to enhance its efficacy. Structure of Flurbiprofen is given in Figure 3.15.

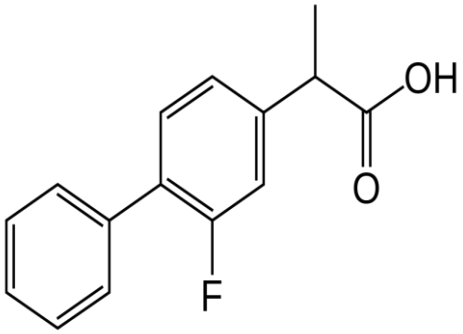


Figure 3.15: Structure of Flurbiprofen.

Due to the amphiphilic nature and the physiological negative charge of NSAIDs, our methodology depends on the possibility that these medications can go about as solid restricting counterions and structure catanionic totals with long-chain cationic surfactants.

Chauhan et al. [164] built up a strategy to expand the conveyance of an anionic medication from contact focal points using a long-chain cationic surfactant [164].

3.6.2 Study of Drug Surfactant interaction by UV-Visible Spectroscopy

The drug-surfactant interaction was explored using UV-visible spectroscopic methods [149,150]. The gotten information was additionally used to process "binding constants (K_b)" and "the amount of medication atoms (n) joined to every micelle". The medication surfactant communication was determined by watching the change in the "absorption conduct of the medication" on expansion of "the surfactant in different concentrations"

Absorption of drug Ketoprofen at its λ_{max} was recorded in ethanol as shown in Figure 3.16. And absorption of drug Ketoprofen at different concentrations of compound a6 was also recorded in ethanol shown in Figure 3.17. Change in λ_{max} in absorption spectra of Ketoprofen was observed by the adition of compound a6. These changes in absorption maxima due to the presence of varying concentrations of compound a6 are clearly visible in Figure 3.16. In absence of compound a6, λ_{max} of drug was 254 nm and in presence of compound a6, it is shifted from 254 nm to 259nm. There is shift of 5nm (bathochromic effect).This upfielded shift shows the electrostatic interaction of drug the Ketoprofen with compound a6. Within the sight of "differing convergence of compound a6", at the "fixed centralization of medication", there was "increment in absorbance (hyperchromic impact) along with red shift (bathochromic impact)".The appearance of new peak at 259 nm confirms the Ketoprofen-compound a6 adduct or complex formation [165]. This electronic coupling between drug and compound a6 is also called as drug aggregation [166].

Drug molecules aggregate either in parallel or head to tail faishon. If the absorption band of drug is red shifted, then drug molecule will be aggregated in head to tail fashion and if blue shifted, then it will be in parallel fashion. In the absorption band of Ketoprofen with a6, it is red shifted so the drug Ketoprofen is aggregated in head to tail fashion [166, 167].

It is expected that the medication will cling to micelles at "different zones. ie. the micellar core, stern layer or the surfactant solvent interface because solubilization is dynamic process [165]".

With increase in concentration of compound a6 from 0.36mM to 0.48mM, hyperchromic effect was obtained in absorption spectra of drug. This expansion intensity of bands was because of the addition of Ketoprofen in the micellar inside however chromophores are situated at the dissolvable micelle interface, so assimilate all the more light, because of increment in nearby convergence of chromophores [166]. As the stength of the surfactant

arrangement is dynamically expanded, solvophobic or hydrophobic contacts of alkyl bunches with the polar dissolvable begin to heighten. This condition propels aliphatic alkyl chains of the surfactants to connect with of Ketoprofen at the situation of the fragrant gatherings. As the alkyl fastens begin to connect with aryl gatherings of the medication, contrarily charged gatherings of the medication begin getting free which causes an expansion of the absorption [168-171].

A similar behaviour was also observed for the interaction of Ketoprofen with all newly synthesized compounds with an almost similar pattern. The compounds of series a and series b differ by a position of methyl group attached to the aromatic ring. This difference has no significant effect on the interaction of the surfactant molecule with the drug. There is no difference in the interaction of a6 or b6, a8 or b8 with Ketoprofen. Likewise, based surfactants have also successfully shown the interactions with the drug and have followed the same pattern.

To study the interaction of series c compounds with both drugs (Flurbiprofen and Ketoprofen), the absorption spectra of both drugs at their λ_{max} (254nm and 246nm) were taken in absence of compounds and in presence of compounds. The absorption spectra of drugs were also recorded at varying concentrations of compounds from 0.60mM (postmicellar concentration) to 0.44mM (premicellar concentration). There was no shift in the λ_{max} of both drugs upon the addition of compounds, suggesting no complex formation at the beginning. But there was decrease in the intensity of absorption bands of drugs (hypochromic effect) at the varying concentration of compounds. This characteristic spectral behaviour confirms the drug surfactant interactions.

There is a difference in the interaction pattern of pyridinium and quinolinium surfactants with Ketoprofen. The reason accounting for such trend is due to a structural change in quinolinium bromides, although the charge distribution around the positively charged nitrogen atom is the same. The descending behaviour in absorbance (hypochromic effect provides a clue for the interaction of Ketoprofen with pre and post micellar concentrations of quinolinium surfactants. This decrease in absorbance indicates an encapsulation of drug molecules inside the micelle core. Plots for the rest of the compounds of series a, b and c with Ketoprofen are given in the appendixes from A29 - A64.

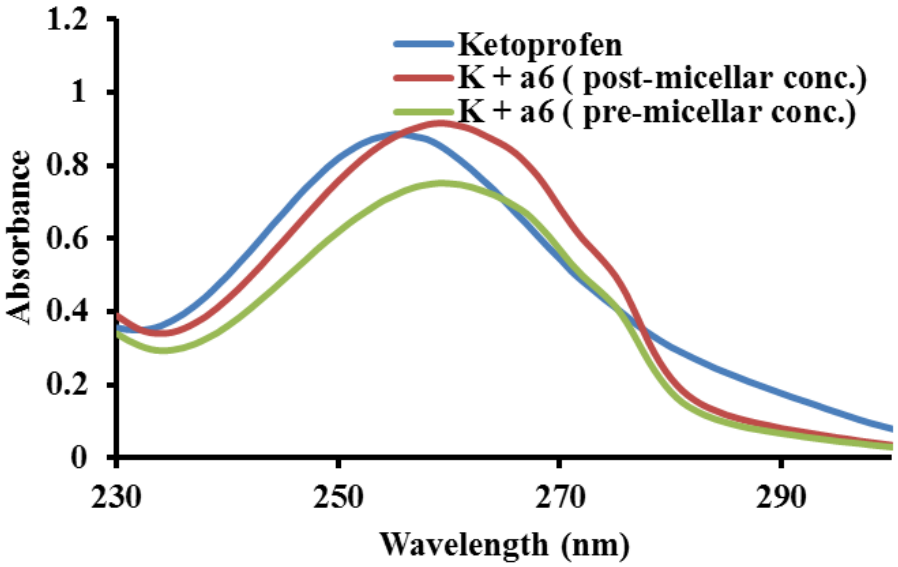


Figure 3.16: Absorption spectra of Ketoprofen, without and with pre-micellar and post-micellar region of compound a6.

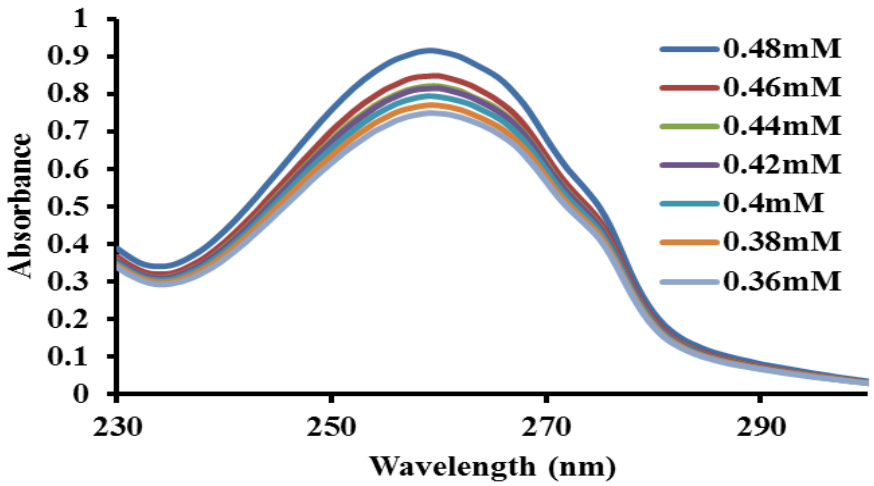


Figure 3.17: With different concentrations of compound a6, absorption spectra of Ketoprofen

The UV-visible absorption spectra of the interaction between Flurbiprofen and compound a6 have been given in Figures 3.18 and 3.19 which represents that the absorption decreases with its interaction with pre and post micellar concentrations along with the shift of its λ_{max} (bathochromic effect) indicating the encapsulation of drugs in the micelles.

Absorption of drug Flurbiprofen was recorded in ethanol at its λ_{max} (246nm), shown in Figure 3.18. By the addition of compound a6, change in λ_{max} of drug was noted. It was shifted from 246 nm to 257nm (bathochromic effect).

This move in the "wavelength of maximum absorbance of medication by the introduction of compound a6 is the sign of making of medication surfactant complex [165]". This 11nm shift of drug in varying concentration of compound a6 from 0.48mM to 0.34mM also indicates the electronic coupling between drug and compound a6. Flurbiprofen is aggregated in head to tail fashion [166, 167]. Once shift has occurred further increase in concentration, decrease the intensity of absorption bands in the spectra. This decrease in absorbance of Flurbiprofen with increase in a6 concentration shows the hypochromic effect, suggesting the burriel of chromophore in the interior of micelles, here the encapsulation of drug Flurbiprofen has taken place in the micellar core of the compound a6 [166].

Such behaviour is shown by all other compounds. Graphs of the interactions of all other compounds of series a, b and c with Flurbiprofen are given in appendixes A65- A102.

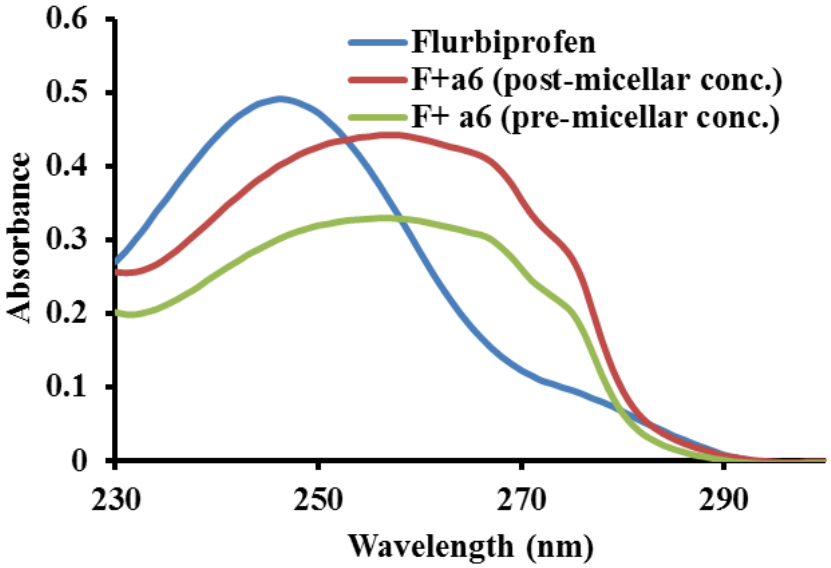


Figure 3.18: Absorption spectra of Flurbiprofen, without and with pre-micellar and post-micellar region of compound a6.

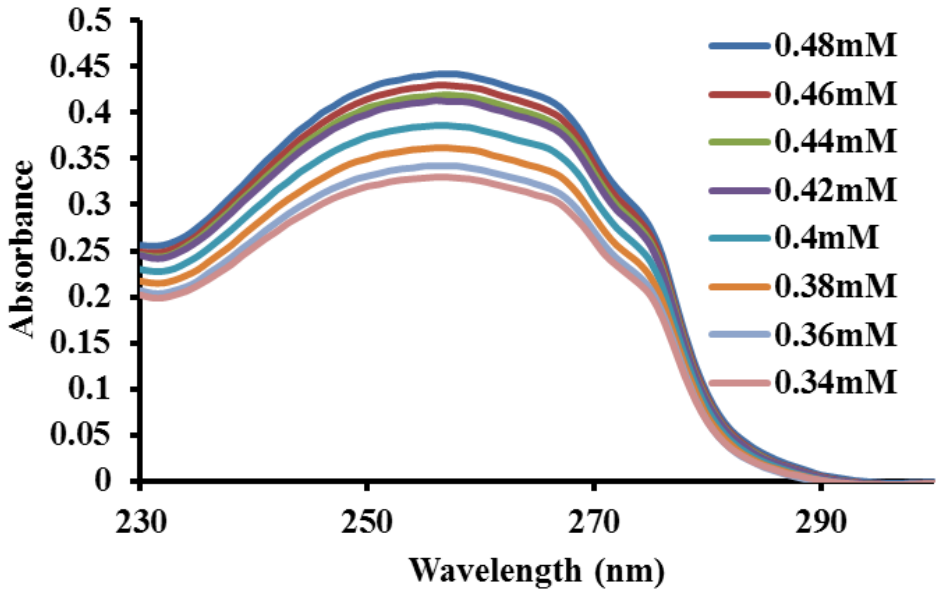


Figure 3.19: With different concentrations of compound a6, absorption spectra of Flurbiprofen.

The central method of activity for NSAIDs is hindrance of the cyclooxygenase proteins, COX-1 and COX-2. Accessible proof proposes that the pain relieving and mitigating properties of NSAIDs emerge from their restraint of the COX-2 isoform [172].

UV spectroscopic investigations have indicated that the locus of solubilization for Ketoprofen was discovered to be towards the charged outside of the micelles, in the Stern layer, though Flurbiprofen was found to solubilize more in the micellar inside for mixes of an and b arrangement.

The associations of NSAIDs with cationic layer impersonates have been examined utilizing test strategies for indomethacin with dihexadecyldimethylammonium bromide [173]; for piroxicam, meloxicam, and tenoxicam with cetyltrimethylammonium bromide (CTAB) [150]; and for diclofenac with little unilamellar vesicles [174].

The associations of NSAIDs with lipid films have likewise been concentrated by atomic elements reproductions [175]. The utilization of surfactant micelles as NSAID conveys has been examined utilizing ibuprofen in anionic micelles [176], naproxen and diclofenac in cationic micelles [177], indomethacin in both anionic and cationic micellar congregations [178].

Different procedures that have been utilized to examine segment coefficients for NSAIDs in surfactant-based frameworks incorporate biopartitioning micellar chromatography [179], fluorescence anisotropy [180] and spectrophotometry [181]

Spectrophotometric procedure when contrasted with different strategies incorporate its moderately ease, effortlessness, and generally speaking unwavering quality.

3.6.2.1 Binding constant of Medication-Surfactant Complex

The "Kawamura equation" was used to investigate the "interaction of drug molecules with the micelle systems" [182] given as equation (6).

$$\text{“}1/\Delta A = 1/ K_b\, \Delta A\infty(C_a+C_s^{mo})+1/\Delta A\infty\text{”} \quad (6)$$

where

$\Delta A = A - A^o$

A = absorbance of drug in the presence of surfactant

A^o = absorbance of drug in the absence of surfactant

C_a =drug concentration

Cs^{mo} = Cs-CMC^o.

CMC^o= CMC of surfactant in solvent

C_s = total surfactant concentration.

$\Delta A\infty = A_b - A^o$.

A_b = absorbance of surfactant bound drug.

The interaction of compound a6 with Ketoprofen follows a straightline pattern as shown in Figure 3.20.

The rest of the compounds of all three series follow this trend (Appendixes A103-A119).

From the plot of "1/ΔA versus 1/(Cs^{mo} + Ca)" it was calculated, the "binding constant (K_b) and Gibb's free energy (ΔG) " for the "interaction of Ketoprofen and all compounds". Table 3.11 depicts the data for the interaction of all compounds with the drug Ketoprofen.

Association parameters of all compounds series of a, b and c are shown in Table 3.11.

CMC of all compounds of series is known and from varying concentration and known CMC, all required parameters of association are calculated by using equation (6).

Table 3.11: Association parameters of all the compounds of (series a, b and c) with Ketoprofen at their different concentrations

S. No.	Cs	$(CMC)10^{-3}$	Cs^{mo}	$(Ca)10^{-3}$	$(Cs^{mo}+Ca)10^{-3}$	$(1/ Cs^{mo} + Ca)10^{3}$	ΔA	1/ΔA
a6								
1	0.48	0.42	0.06	0.34	0.40	2500.00	-0.026	-38.46
2	0.46	0.42	0.04	0.34	0.38	2631.57	-0.091	-10.98
3	0.44	0.42	0.02	0.34	0.36	2777.77	-0.116	-8.62
4	0.42	0.42	0.00	0.34	0.34	2941.17	-0.123	-8.13
5	0.40	0.42	-0.02	0.34	0.32	3125.00	-0.143	-6.99
6	0.38	0.42	-0.04	0.34	0.30	3333.33	-0.162	-6.17
7	0.36	0.42	-0.06	0.34	0.28	3571.42	-0.184	-5.43
a7								
1	0.48	0.41	0.07	0.33	0.40	2500.00	0.023	83.33
2	0.46	0.41	0.05	0.33	0.38	2631.57	0.012	-66.66
3	0.44	0.41	0.03	0.33	0.36	2777.77	-0.006	-38.46
4	0.42	0.41	0.01	0.33	0.34	2941.17	-0.041	-24.39
5	0.40	0.41	-0.01	0.33	0.32	3125.00	-0.085	-11.76
6	0.38	0.41	-0.03	0.33	0.30	3333.33	-0.119	-8.40
7	0.36	0.41	-0.05	0.33	0.28	3571.42	-0.129	-7.75
8	0.34	0.41	-0.03	0.33	0.26	3846.15	-0.143	-6.99
a8								
1	0.48	0.40	0.08	0.33	0.41	2439.02	0.027	37.03
2	0.46	0.40	0.06	0.33	0.39	2564.10	0.013	76.92
3	0.44	0.40	0.04	0.33	0.37	2702.70	-0.009	-111.1
4	0.42	0.40	0.02	0.33	0.35	2857.14	-0.024	-41.66
5	0.40	0.40	0.00	0.33	0.33	3030.30	-0.070	-14.28
6	0.38	0.40	-0.02	0.33	0.31	3225.80	-0.081	-12.34
7	0.36	0.40	-0.04	0.33	0.29	3448.27	-0.097	-10.09
8	0.34	0.40	-0.06	0.33	0.27	3703.70	-0.107	-9.34
a9								
1	0.46	0.38	0.08	0.34	0.42	2380.95	-0.033	-30.30
2	0.44	0.38	0.06	0.34	0.40	2500.00	-0.049	-20.40
3	0.42	0.38	0.04	0.34	0.38	2631.57	-0.051	-19.60
4	0.40	0.38	0.02	0.34	0.36	2777.77	-0.069	-14.49

5	0.38	0.38	0.00	0.34	0.34	2941.17	-0.090	-11.11
6	0.36	0.38	-0.02	0.34	0.32	3125.00	-0.112	-8.92
7	0.34	0.38	-0.04	0.34	0.30	3333.33	-0.129	-7.75
8	0.32	0.38	-0.06	0.34	0.28	3571.42	-0.146	-6.84
a10								
1	0.44	0.36	0.08	0.35	0.43	2325.58	0.288	3.47
2	0.42	0.36	0.06	0.35	0.41	2439.02	0.265	3.77
3	0.40	0.36	0.04	0.35	0.39	2564.10	0.175	5.71
4	0.38	0.36	0.02	0.35	0.37	2702.70	0.171	5.84
5	0.36	0.36	0.00	0.35	0.35	2857.14	0.161	6.21
6	0.34	0.36	-0.02	0.35	0.33	3030.30	0.153	6.53
7	0.32	0.36	-0.04	0.35	0.31	3225.80	0.149	6.71
8	0.30	0.36	-0.06	0.35	0.29	3448.27	0.083	12.04
a11								
1	0.44	0.35	0.09	0.34	0.43	2325.58	-0.007	-142.8
2	0.42	0.35	0.07	0.34	0.41	2439.02	-0.030	-33.33
3	0.40	0.35	0.05	0.34	0.39	2564.10	-0.060	-16.66
4	0.38	0.35	0.03	0.34	0.37	2702.70	-0.081	-12.34
5	0.36	0.35	0.01	0.34	0.35	2857.14	-0.154	-6.49
6	0.34	0.35	-0.01	0.34	0.33	3030.30	-0.164	-6.09
7	0.32	0.35	-0.03	0.34	0.31	3225.80	-0.206	-4.85
8	0.30	0.35	-0.05	0.34	0.29	3448.27	-0.223	-4.48
a12								
1	0.44	0.34	0.10	0.35	0.45	2222.22	0.224	4.46
2	0.42	0.34	0.08	0.35	0.43	2325.58	0.203	4.92
3	0.40	0.34	0.06	0.35	0.41	2439.02	0.164	6.09
4	0.38	0.34	0.04	0.35	0.39	2564.10	0.136	7.35
5	0.36	0.34	0.02	0.35	0.37	2702.70	0.106	9.43
6	0.34	0.34	0.00	0.35	0.35	2857.14	0.078	12.82
7	0.32	0.34	-0.02	0.35	0.33	3030.30	0.047	21.27
8	0.30	0.34	-0.04	0.35	0.31	3225.80	0.019	52.61
a14								
1	0.42	0.32	0.10	0.35	0.45	2222.22	-0.076	-13.15
2	0.40	0.32	0.08	0.35	0.43	2325.58	-0.106	-9.43
3	0.38	0.32	0.06	0.35	0.41	2439.02	-0.132	-6.13

4	0.36	0.32	0.04	0.35	0.39	2564.10	-0.163	-5.64
5	0.34	0.32	0.02	0.35	0.37	2702.70	-0.177	-5.61
6	0.32	0.32	0.00	0.35	0.35	2857.14	-0.178	-5.37
7	0.30	0.32	-0.02	0.35	0.33	3030.30	-0.186	-4.97
8	0.28	0.32	-0.04	0.35	0.31	3225.80	-0.201	-4.44
a15								
1	0.40	0.30	0.10	0.32	0.42	2380.95	0.023	-43.47
2	0.38	0.30	0.08	0.32	0.40	2500.00	0.01	100.00
3	0.36	0.30	0.06	0.32	0.38	2631.57	-0.01	-100.0
4	0.34	0.30	0.04	0.32	0.36	2777.77	-0.02	-50.00
5	0.32	0.30	0.02	0.32	0.34	2941.17	-0.03	-33.33
6	0.30	0.30	0.00	0.32	0.32	3125.00	-0.05	-20.00
7	0.28	0.30	-0.02	0.32	0.30	3333.33	-0.06	-16.66
8	0.26	0.30	-0.04	0.32	0.28	3571.42	-0.07	-14.28
b6								
1	0.50	0.41	0.09	0.32	0.41	2439.08	0.099	10.10
2	0.48	0.41	0.07	0.32	0.39	2564.10	0.081	12.34
3	0.46	0.41	0.05	0.32	0.37	2702.70	0.061	16.39
4	0.44	0.41	0.03	0.32	0.35	2857.14	0.046	21.73
5	0.42	0.41	0.01	0.32	0.33	3030.30	0.002	50.00
6	0.40	0.41	-0.01	0.32	0.30	3225.80	-0.032	-31.25
7	0.38	0.41	-0.03	0.32	0.29	3448.27	-0.042	-23.80
8	0.36	0.41	-0.05	0.32	0.27	3703.70	-0.056	-17.95
b8								
1	0.42	0.35	0.07	0.32	0.39	2564.10	0.124	8.06
2	0.40	0.35	0.05	0.32	0.37	2702.70	0.103	9.70
3	0.38	0.35	0.03	0.32	0.35	2857.14	0.084	11.90
4	0.36	0.35	0.01	0.32	0.33	3030.30	0.048	20.83
5	0.34	0.35	-0.01	0.32	0.31	3225.80	0.005	50.00
6	0.32	0.35	-0.03	0.32	0.29	3448.27	-0.023	-43.47
7	0.30	0.35	-0.05	0.32	0.27	3703.70	-0.033	-30.30
8	0.28	0.35	-0.07	0.32	0.25	4000.00	-0.042	-23.80
b10								
1	0.40	0.31	0.09	0.33	0.42	2380.95	0.025	40.00
2	0.38	0.31	0.07	0.33	0.40	2500.00	0.002	500

3	0.36	0.31	0.05	0.33	0.38	2631.57	0.001	1000
4	0.34	0.31	0.03	0.33	0.36	27777.77	-0.007	-142.8
5	0.32	0.31	0.01	0.33	0.34	2941.17	-0.028	-35.71
6	0.30	0.31	-0.01	0.33	0.32	3125.00	-0.029	-34.48
7	0.28	0.31	-0.03	0.33	0.30	3333.33	-0.032	-31.25
8	0.26	0.31	-0.05	0.33	0.28	3571.42	-0.078	-12.82
b12								
1	0.38	0.29	0.09	0.34	0.43	2325.58	-0.122	-8.196
2	0.36	0.29	0.07	0.34	0.41	2439.02	-0.132	-7.57
3	0.34	0.29	0.05	0.34	0.39	2564.1	-0.133	-7.51
4	0.32	0.29	0.03	0.34	0.37	2702.70	-0.142	-7.04
5	0.30	0.29	0.01	0.34	0.35	2857.14	-0.159	-6.28
6	0.28	0.29	-0.01	0.34	0.33	3030.30	-0.162	-6.17
7	0.26	0.29	-0.03	0.34	0.31	3225.50	-0.181	-5.52
8	0.24	0.29	-0.05	0.34	0.29	3448.27		
b14								
1	0.36	0.27	0.09	0.31	0.40	2500.00	-0.185	-5.405
2	0.34	0.27	0.07	0.31	0.38	2631.57	-0.185	-5.405
3	0.32	0.27	0.05	0.31	0.36	27777.77	-0.187	-5.347
4	0.30	0.27	0.03	0.31	0.34	2941.17	-0.190	-5.263
5	0.28	0.27	0.01	0.31	0.32	3125.00	-0.190	-5.263
6	0.26	0.27	-0.01	0.31	0.30	3333.33	-0.191	-5.235
7	0.24	0.27	-0.03	0.31	0.28	3571.42	-0.204	-4.901
8	0.22	0.27	-0.05	0.31	0.26	3846.15		
c6								
1	0.60	0.51	0.09	0.41	0.50	2000.00	-0.425	-2.35
2	0.58	0.51	0.07	0.41	0.48	2083.33	-0.438	-2.28
3	0.56	0.51	0.05	0.41	0.46	2173.91	-0.475	-2.10
4	0.54	0.51	0.03	0.41	0.44	2272.72	-0.490	-2.04
5	0.52	0.51	0.01	0.41	0.42	2380.95	-0.524	-1.90
6	0.50	0.51	-0.01	0.41	0.4	2500.00	-0.541	-1.84
7	0.48	0.51	-0.03	0.41	0.38	2631.57	-0.575	-1.73
8	0.46	0.51	-0.05	0.41	0.36	2777.77	-0.595	-1.68
c7								
1	0.58	0.49	0.09	0.41	0.50	2000.00	-0.215	-4.65

2	0.56	0.49	0.07	0.41	0.48	2083.33	-0.216	-4.63
3	0.54	0.49	0.05	0.41	0.46	2173.91	-0.216	-4.62
4	0.52	0.49	0.03	0.41	0.44	2272.72	-0.216	-4.62
5	0.50	0.49	0.01	0.41	0.42	2380.95	-0.217	-4.60
6	0.48	0.49	-0.01	0.41	0.4	2500.00	-0.217	-4.60
7	0.46	0.49	-0.03	0.41	0.38	2631.57	-0.219	-4.56
8	0.44	0.49	-0.05	0.41	0.36	2777.77	-0.220	-4.54
c8								
1	0.56	0.48	0.08	0.41	0.49	2040.82	-0.217	-4.60
2	0.54	0.48	0.06	0.41	0.47	2127.66	-0.218	-4.58
3	0.52	0.48	0.04	0.41	0.45	2222.22	-0.218	-4.58
4	0.50	0.48	0.02	0.41	0.43	2325.58	-0.219	-4.56
5	0.48	0.48	0.00	0.41	0.41	2439.02	-0.219	-4.56
6	0.46	0.48	-0.02	0.41	0.39	2564.1	-0.219	-4.56
7	0.44	0.48	-0.04	0.41	0.37	2702.70	-0.219	-4.56
8	0.42	0.48	-0.06	0.41	0.35	2857.14	0.220	-4.54
c9								
1	0.54	0.46	0.08	0.41	0.49	2040.82	-0.218	-4.58
2	0.52	0.46	0.06	0.41	0.47	2127.66	-0.218	-4.58
3	0.50	0.46	0.04	0.41	0.45	2222.22	-0.218	-4.58
4	0.48	0.46	0.02	0.41	0.43	2325.58	-0.219	-4.56
5	0.46	0.46	0.00	0.41	0.41	2439.02	-0.219	-4.56
6	0.44	0.46	-0.02	0.41	0.39	2564.1	-0.220	-4.54
7	0.42	0.46	-0.04	0.41	0.37	2702.70	-0.220	-4.54
8	0.40	0.46	-0.06	0.41	0.35	2857.14	0.221	-4.52
c10								
1	0.52	0.45	0.07	0.41	0.48	2083.33	-0.219	-4.56
2	0.50	0.45	0.05	0.41	0.46	2173.91	-0.220	-4.54
3	0.48	0.45	0.03	0.41	0.44	2272.73	-0.220	-4.54
4	0.46	0.45	0.01	0.41	0.42	2380.95	-0.221	-4.52
5	0.44	0.45	-0.01	0.41	0.40	2500.00	-0.221	-4.52
6	0.42	0.45	-0.03	0.41	0.38	2631.57	-0.222	-4.50
7	0.40	0.45	-0.05	0.41	0.36	27777.77	-0.222	-4.50
8	0.38	0.45	-0.07	0.41	0.34	2941.17	-0.223	-4.48
c11								

1	0.50	0.43	0.07	0.41	0.48	2083.33	-0.095	-10.52
2	0.48	0.43	0.05	0.41	0.46	2173.91	-0.095	-10.52
3	0.46	0.43	0.03	0.41	0.44	2272.73	-0.095	-10.52
4	0.44	0.43	0.01	0.41	0.42	2380.95	-0.096	-10.41
5	0.42	0.43	-0.01	0.41	0.40	2500.00	-0.096	-10.41
6	0.40	0.43	-0.03	0.41	0.38	2631.57	-0.096	-10.41
7	0.38	0.43	-0.05	0.41	0.36	27777.77	-0.097	-10.30
8	0.36	0.43	-0.07	0.41	0.34	2941.17	-0.098	-10.20
c12								
1	0.50	0.42	0.08	0.41	0.49	2040.82	-0.096	-10.41
2	0.48	0.42	0.06	0.41	0.47	2127.66	-0.097	-10.30
3	0.46	0.42	0.04	0.41	0.45	2222.22	-0.097	-10.30
4	0.44	0.42	0.02	0.41	0.43	2325.58	-0.097	-10.30
5	0.42	0.42	0.00	0.41	0.41	2439.02	-0.098	-10.20
6	0.40	0.42	-0.02	0.41	0.39	2564.1	-0.098	-10.20
7	0.38	0.42	-0.04	0.41	0.37	2702.70	-0.098	-10.20
8	0.36	0.42	-0.06	0.41	0.35	2857.14	-0.099	-10.10
c14								
1	0.46	0.42	0.06	0.41	0.47	2127.66	-0.215	-4.65
2	0.44	0.42	0.04	0.41	0.45	2222.22	-0.216	-4.62
3	0.42	0.42	0.02	0.41	0.43	2325.58	-0.216	-4.62
4	0.40	0.42	0.00	0.41	0.41	2439.02	-0.217	-4.60
5	0.38	0.42	-0.02	0.41	0.39	2564.1	-0.218	-4.58
6	0.36	0.42	-0.04	0.41	0.37	2702.70	-0.219	-4.56
7	0.34	0.42	-0.06	0.41	0.35	2857.14	-0.220	-4.54
8	0.32	0.42	-0.04	0.41	0.33	3030.30	-0.221	-4.52
c15								
1	0.44	0.41	0.06	0.41	0.47	2127.66	-0.216	-4.62
2	0.42	0.41	0.04	0.41	0.45	2222.22	-0.216	-4.62
3	0.40	0.41	0.02	0.41	0.43	2325.58	-0.218	-4.58
4	0.38	0.41	0.00	0.41	0.41	2439.02	-0.219	-4.56
5	0.36	0.41	-0.02	0.41	0.39	2564.1	-0.219	-4.56
6	0.34	0.41	-0.04	0.41	0.37	2702.70	-0.219	-4.56
7	0.32	0.41	-0.06	0.41	0.35	2857.14	-0.220	-4.54
8	0.30	0.41	-0.04	0.41	0.33	3030.30	-0.221	-4.52

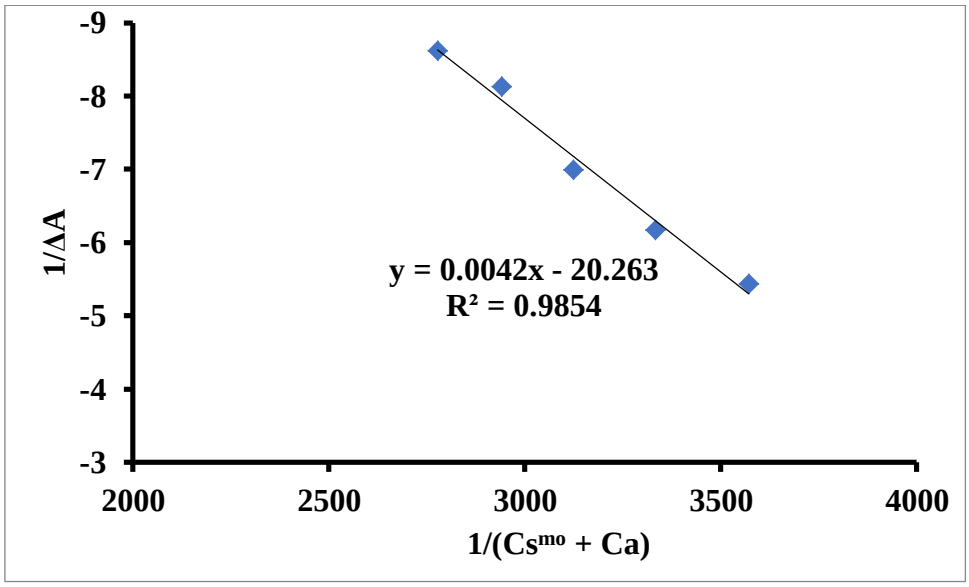


Figure 3.20: Graph of "1/ΔA versus 1/ (Cs^{mo} + Ca)" of a6 + Ketoprofen.

The interaction of all newly synthesized compounds with Flurbiprofen also followed a straight-line pattern as shown in Figure 3.21, the interaction of Flurbiprofen with compound a6. Plots for all other compounds are incorporated in appendixes from A120 - A138. Similarly, Table B6 shows the data for the interaction of all compounds with the drug Flurbiprofen.

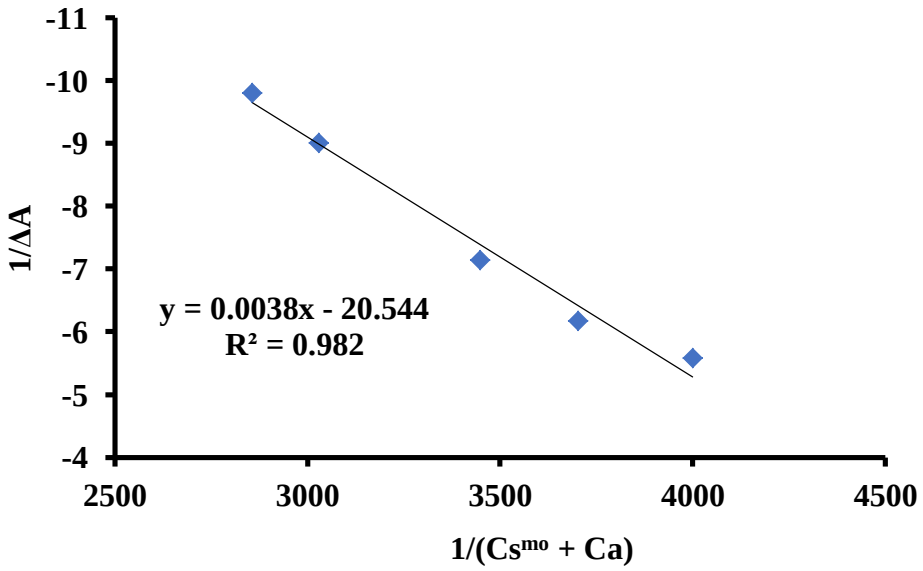


Figure 3.21: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a6 + Flurbiprofen.

3.6.2.2 Per Micelle number of Drug Molecules attached (n)

The "number of drug molecules attached per micelle" was determined by using equations 7-9:

$$n = \frac{Cm}{M} \qquad (7)$$

$$M = \frac{Cs - CMC}{N} \qquad (8)$$

$$Cm = \frac{A^{\circ} - A}{\epsilon^{\circ} - \epsilon m} \qquad (9)$$

where

"ϵ^{o} is calculated from A^{o} and ϵ_m from A_m"

n = number of drug molecules per micelle

C_m= concentration of drug solubilized in micelle in (mol/dm^3)

M= micelle concentration (mol/dm^3)

C_s= concentration of surfactant in (mol/dm^3)

N = aggregation number of surfactant

A^{o} = absorbance of drug in the absence of surfactant

A = absorbance of drug in the presence of surfactant

ϵ^{o} and ϵ_m = absorptivities at A^{o} and A_m respectively

A_m = the value of absorbance where it becomes almost constant.

In case of Ketoprofen and Flurbiprofen, the number of drug molecules attached (n) with all the surfactants are presented in Table 3.12 and in appendix B7. Table 3.13 and B8 represent the values of "binding constants (K_b) and Gibb's free energy of binding (ΔG) for all surfactant–drug complexes". The "negative value of ΔG" presented a "spontaneous nature of interaction between surfactant and drug [183]".

Table 3.12: Parameters obtained from drug Ketoprofen association with all series

Compounds	A	Am	A◦	E◦×10^5	Em×10^5	Cm×10^{-6}	M×10^{-6}	(n)
Series a								
a6	0.770	0.860	0.866	2.54	1.79	1.28	1.2	1.06
a7	0.627	0.685	0.653	1.97	1.42	0.47	1.4	0.33
a8	0.630	0.681	0.654	1.98	1.41	0.42	1.6	0.26
a 9	0.698	0.734	0.767	2.25	1.59	1.04	1.6	0.65
a10	1.081	1.198	0.910	2.60	2.70	1.71	1.6	1.06
a11	0.722	0.879	0.886	2.60	1.99	2.66	1.8	1.48
a12	1.016	1.134	0.910	2.60	2.50	10.00	2.0	5.0
a14	0.733	0.834	0.910	2.60	1.98	2.52	2.0	1.26
a15	0.529	0.589	0.566	1.76	1.47	1.27	2.0	0.63
Series b								
b6	0.534	0.665	0.566	1.76	1.33	0.744	1.698	0.46
b8	0.561	0.690	0.566	1.76	1.64	0.416	2.590	0.16
b10	0.760	0.792	0.767	2.32	1.98	1.75	1.8	0.97
b12	0.658	0.695	0.817	2.40	1.82	2.77	1.8	1.53
b14	0.475	0.525	0.566	1.76	1.45	2.84	1.8	1.57
Series c								
c6	0.881	0.980	1.405	3.42	1.63	2.72	1.8	1.65
c7	1.189	1.190	1.405	3.42	2.05	1.57	1.8	0.87
c8	1.186	1.188	1.405	3.42	2.12	1.67	1.6	1.04
c 9	1.186	1.187	1.405	3.42	2.19	1.78	1.6	1.11
c10	1.185	1.186	1.405	3.42	2.28	1.92	1.4	1.37
c11	1.309	1.310	1.405	3.42	2.62	1.19	1.4	0.85
c12	1.308	1.309	1.405	3.42	2.61	1.20	1.6	0.75
c14	1.189	1.190	1.405	3.42	2.58	2.55	1.2	2.12
c15	1.187	1.189	1.405	3.42	2.70	3.02	1.2	2.52

Table 3.13: Obtained esteems of Binding constants and Gibb's free energy of all the compounds of (series a, b and c) with Ketoprofen.

S. No.	Compounds	K_b (dm^3/mol)	ln K_b	ΔG (KJ/mol)
1	a6	5065	8.530	-21.145
2	a7	5345	8.584	-21.279
3	a8	6447	8.771	-21.743
4	a9	4210	8.345	-20.687
5	a10	968.7	6.876	-17.044
6	a11	5051	8.524	-21.138
7	a12	1832	7.513	-18.624
8	a14	6065	8.710	-21.592
9	a15	3769	8.234	-20.413
10	b6	2111	7.650	-17.370
11	b8	2317	7.750	-17.600
12	b10	4055	8.307	-20.594
13	b12	5185	8.553	-21.203
14	b14	4419	8.393	-20.807
15	c6	5416	8.597	-21.399
16	c7	79600	11.284	-27.973
17	c8	6450	8.771	-21.744
18	c 9	4210	8.345	-20.687
19	c10	968.7	6.876	-17.044
20	c11	5051	8.527	-21.138
21	c12	1831	7.513	-18.624
22	c14	6065	8.710	-21.592
23	c15	3769	8.234	-20.413

Conclusions

Cationic surfactants are an exciting class of compounds which are valuable due to their enormous applications. Herein, three series of cationic surfactants are reported with alkyl chain lengths varying from hexyl to pentadecyl. Out of these, two series were based on *n*-alkyl pyridinium bromides and one series was based on *n*-alkyl quinolinium bromides. Important single step, one-pot based synthesis of these surfactants is demonstrated which is comparatively easier and cheaper. The confirmation of the desired product formation was obtained using techniques like "NMR (^{1}H, ^{13}C) and the FT-IR spectroscopy".

These surfactants have shown an excellent micelle formation behaviour and a very small value of CMC. CMC values were measured using conductometric methods and the results were further verified by "UV–visible spectroscopic measurements". "The micellization" was supported by the expansion of the quantity of carbon iotas in the solvophobic chains. The "micellization cycle was unconstrained and endothermic in nature".

These surfactants have also shown considerable biological activities. All surfactants have indicated sensible antibacterial exercises, when their bactericidal action was tried against four selected bacterial strains. The presence of hydrophobic alkyl chains, the surface action of the surfactant, the adsorption proficiencies, along with the positively charged nitrogen atom are the features which account for antibacterial activities of these surfactants. These surfactants have also shown notable antifungal activities. The hydrophilic portion of the amphiphilic molecule can attach with cell membranes of the fungus and may lead to cell wall distraction and the eventual death of the fungi. They have also shown some antioxidant activities as well. Overall, the synthesized compounds are of significant biological importance.

These compounds are also likely candidates for drug delivery systems because they have shown excellent interactions with the selected drugs Ketoprofen and Flurbiprofen. During the drug interaction studies, it was found that there is a well-established and proven electrostatic interaction between drugs and the studied compounds. The Kawamura equation was employed to calculate binding constants and the values of the binding constants were further used to calculate Gibbs's free energies. The high values of the binding constants, no of drug molecules attached per micelle (n) and the negative values of Gibbs's free energy have indicated strong and spontaneous interactions between drugs and surfactant molecules.

Future Planning

Writing reviews of these mixes and their CMC conclusions have indicated that no endeavors have been made to get their CMC esteems in nonaqueous solvents. Thus, studies ought to be done to feature the concealed parts of their micellization cycle in such solvents. Amphiphilic micelles being nontoxic in nature and having very small CMC values are paving a way for modern drug carrying vehicles. This work has demonstrated some extensive and really interesting results that can lead us to develop a surfactant-based drug delivery system especially for those drugs which are insoluble in aqueous medium. In future this work can provide some fruitful basic support to progress for a conclusive useful product for humanity.

In this work we have explained in detail the interaction mechanism of three series of surfactants with Ketoprofen and Flurbiprofen which are water insoluble drugs. This project may be extended to other drugs and surfactants and the results obtained will be helpful to get knowledge about usefulness of both drugs and surfactants.

In future, interaction such surfactants as a drug delivery vehicle with other drugs like tryptophan, diclofenac sodium and anticancer drugs cyclohexanone carboxylates, uracil derivatives can give us a detailed and useful insight about more efficient use of these drugs.

Results obtained have given us clue about interactions of drugs with biomembranes, that's why the interactions of drugs with real biomembranes could be done under physiological conditions. Computer aided drug designing and human friendly surfactants should be searched out. In brain diseases and disorder, crossing the blood brain barrier (BBB) and enhancing the targeted intracellular delivery are important areas for future research in drug delivery systems. Nanotechnology is opening up new avenues for drug delivery vehicles.

In future we need to study drug release mechanism of such surfactants and their interactions with blood and proteins to find out the pathways of interactions of these surfactants with human body and different tissues, all possible effects, side effects, and their release from human body to develop a practical and applicable drug carrier mechanism. Based on these drug-surfactant interactions studies, interaction of different insoluable dyes can be easily studied using simple techniques like UV-visible spectroscopy and conductometry.

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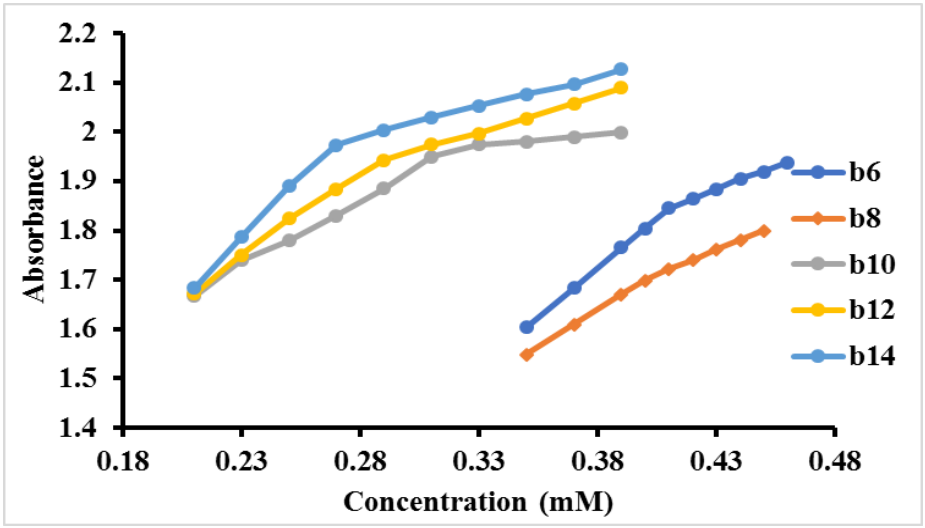
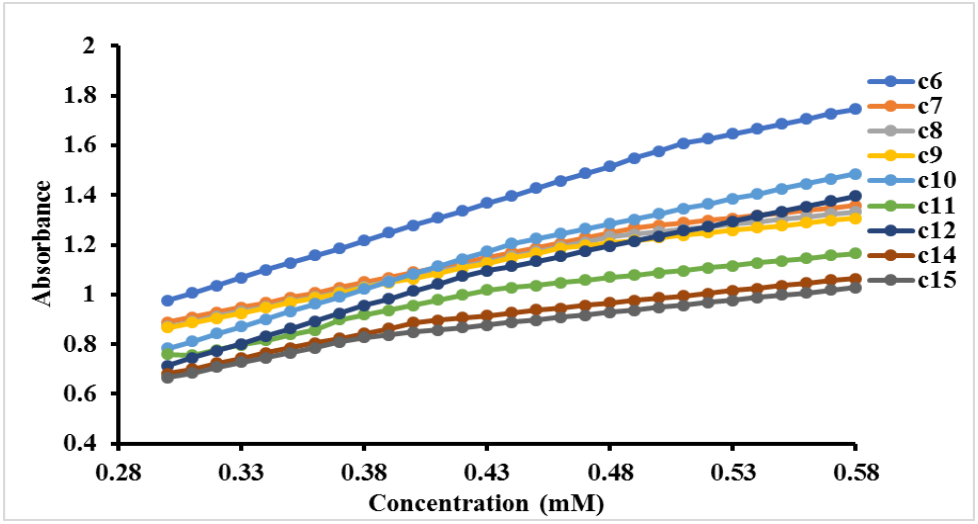
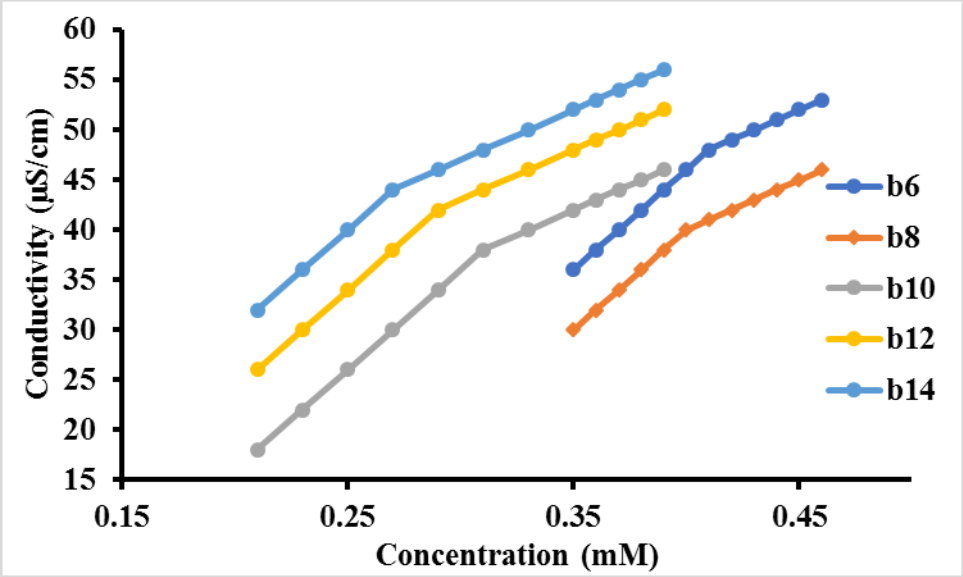
Appendixes-A



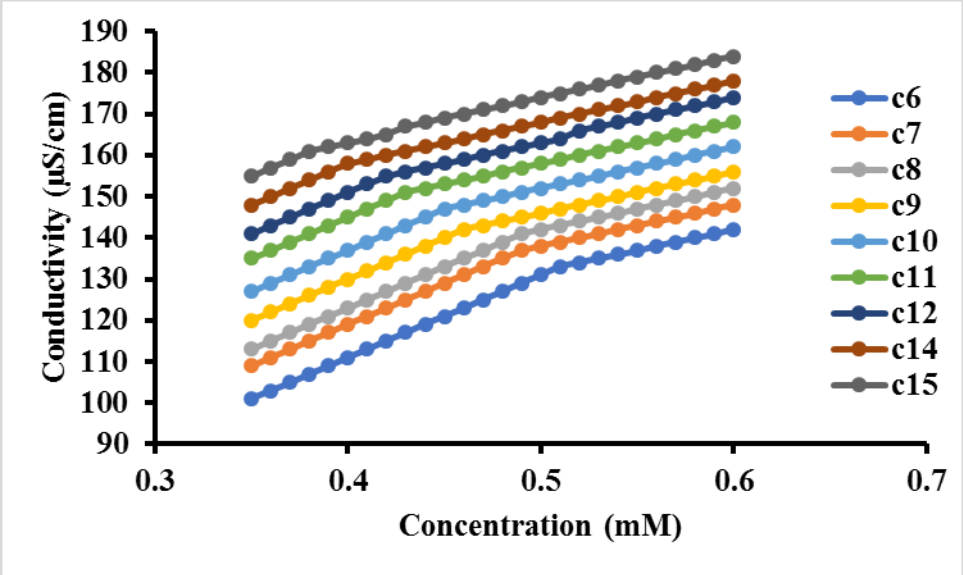
A1: Absorbance *v s* concentration plots for series b (b6, b8, b10, b12 and b14)



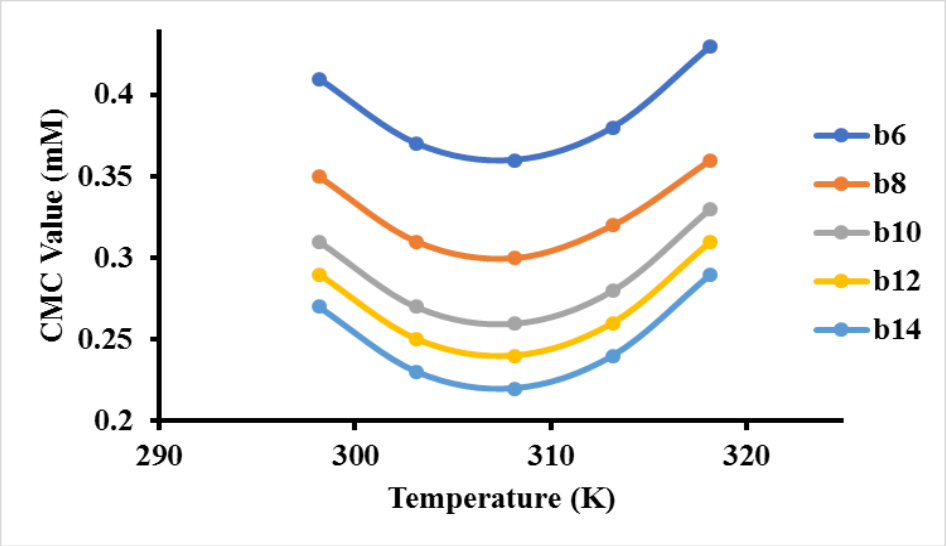
A2: Absorbance *v s* concentration plots for series c (c6-c12, c14 and c15)



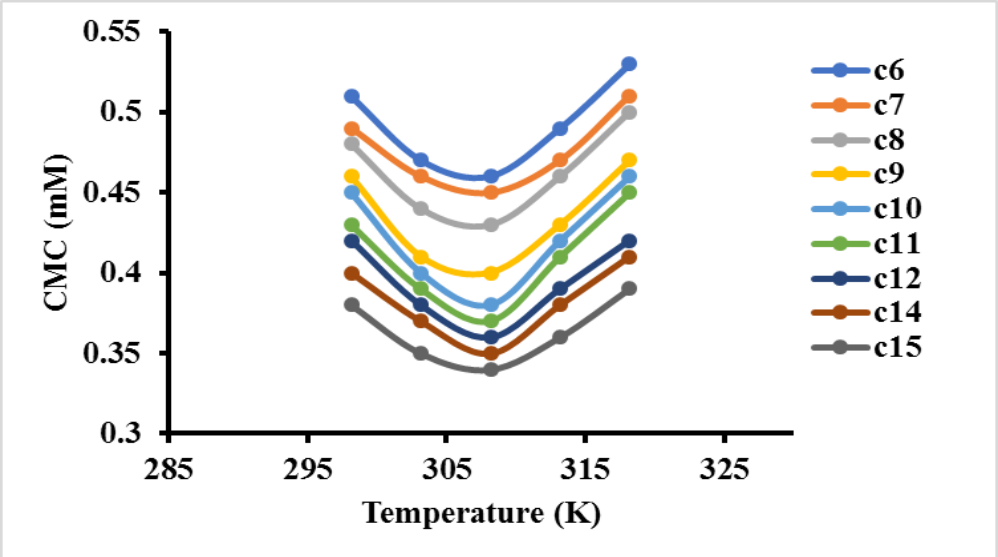
A3: Conductivity *v s* concentration plots for series b (b6, b8, b10, b12 and b14)



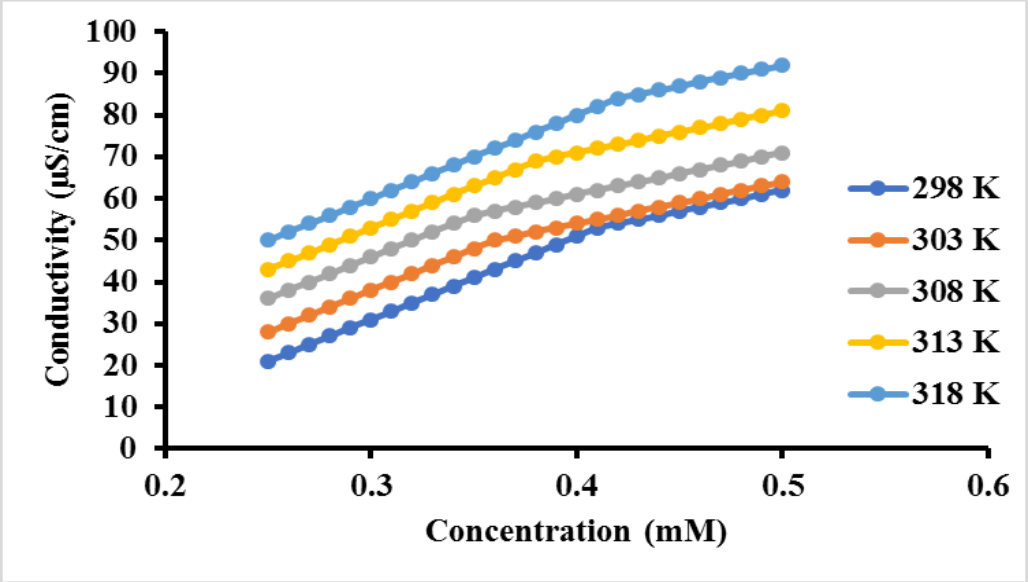
A4: Conductivity *v s* concentration plots for series c (c6 – c12, c14 and c15)



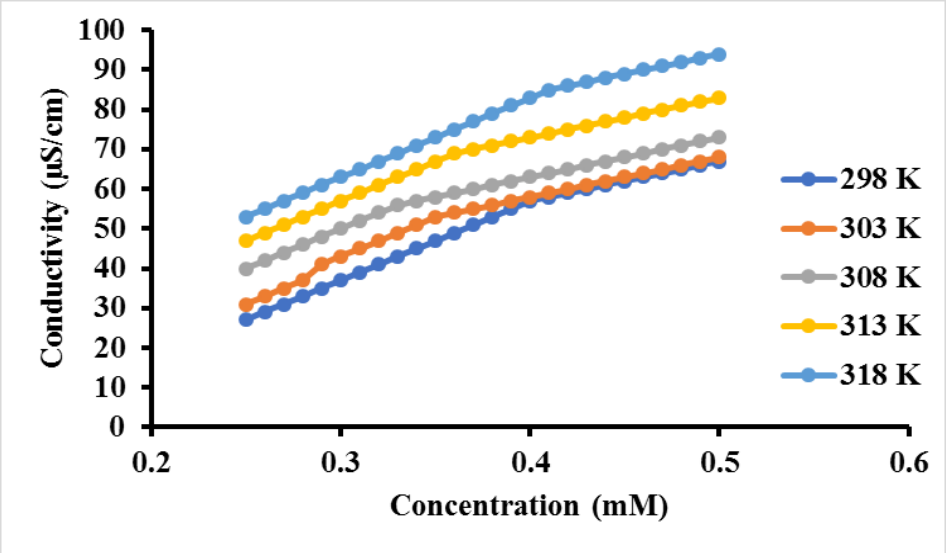
A5: Variation of CMC values as a function of temperature for series b (b6, b8, b10, b12 and b14)



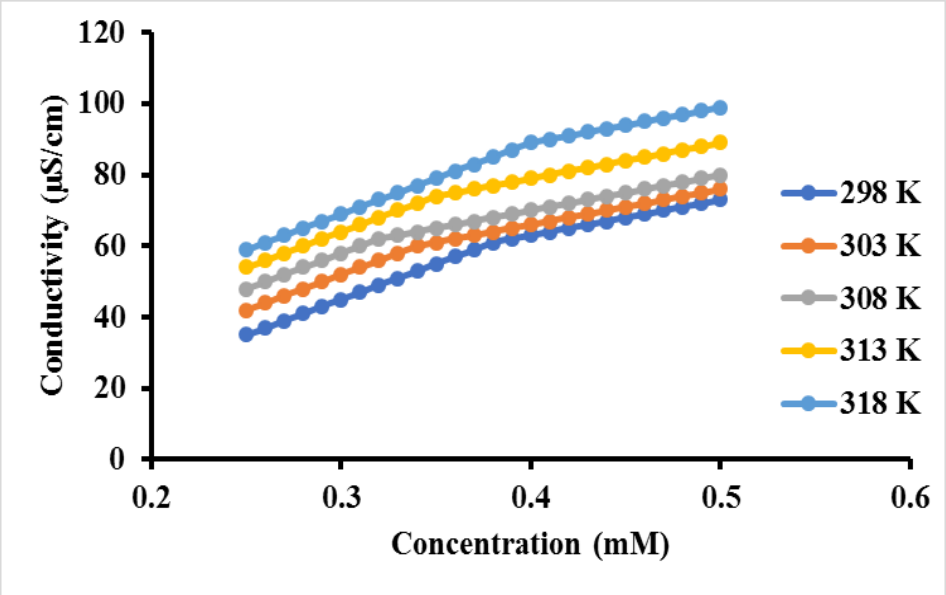
A6: Variation of CMC values as a function of temperature for series c (c6-c12, c14 and c15)



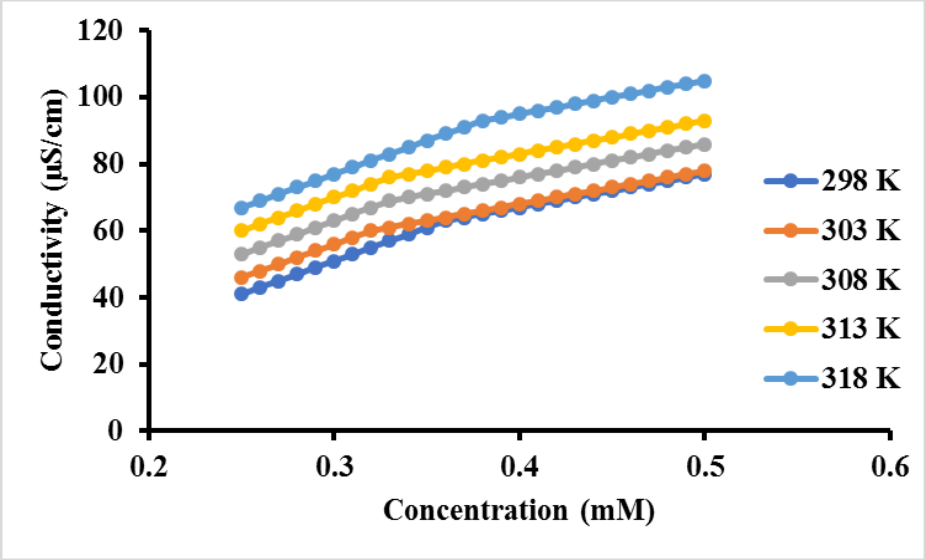
A7: CMC of compound a7 at different temperatures



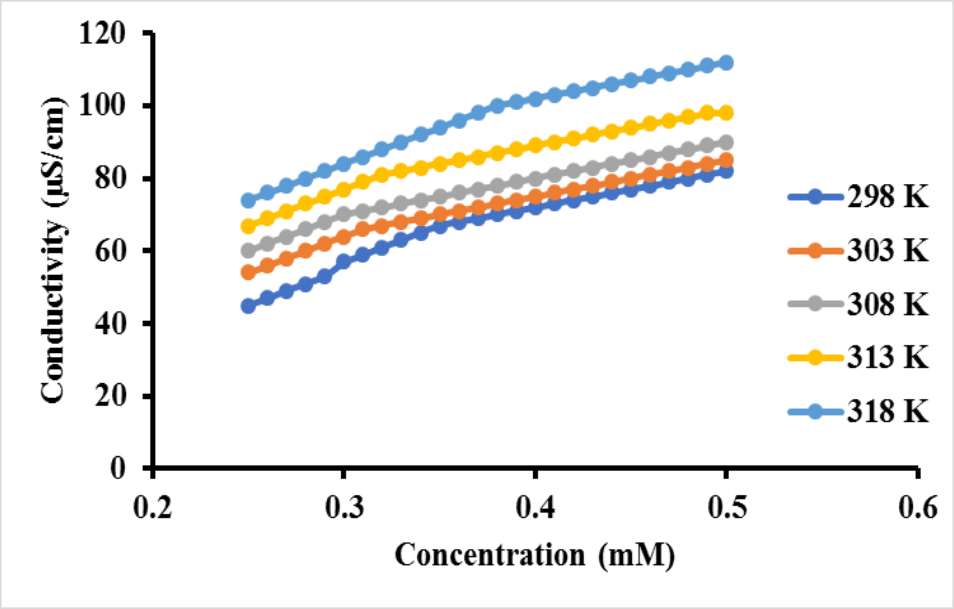
A8: CMC of compound a8 at different temperatures



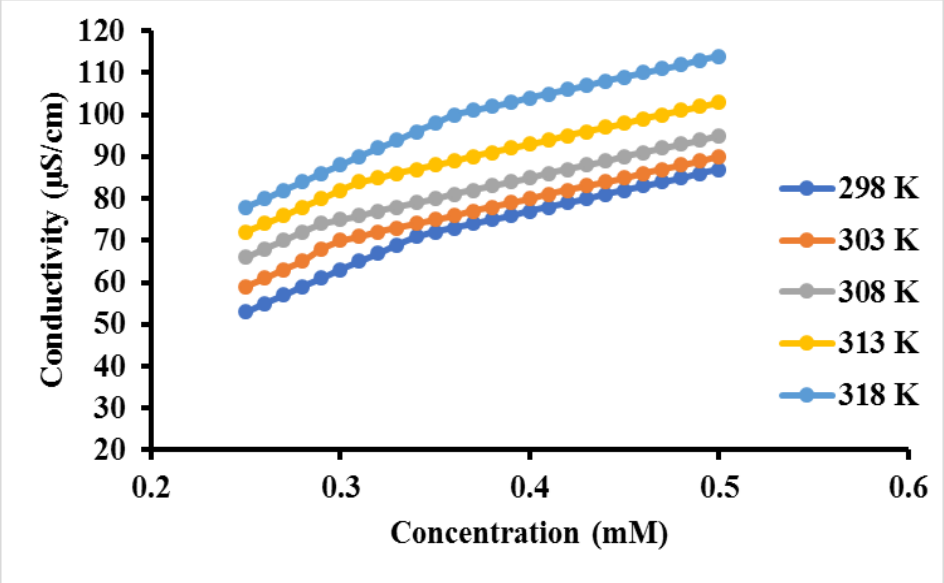
A9: CMC of compound a9 at different temperatures



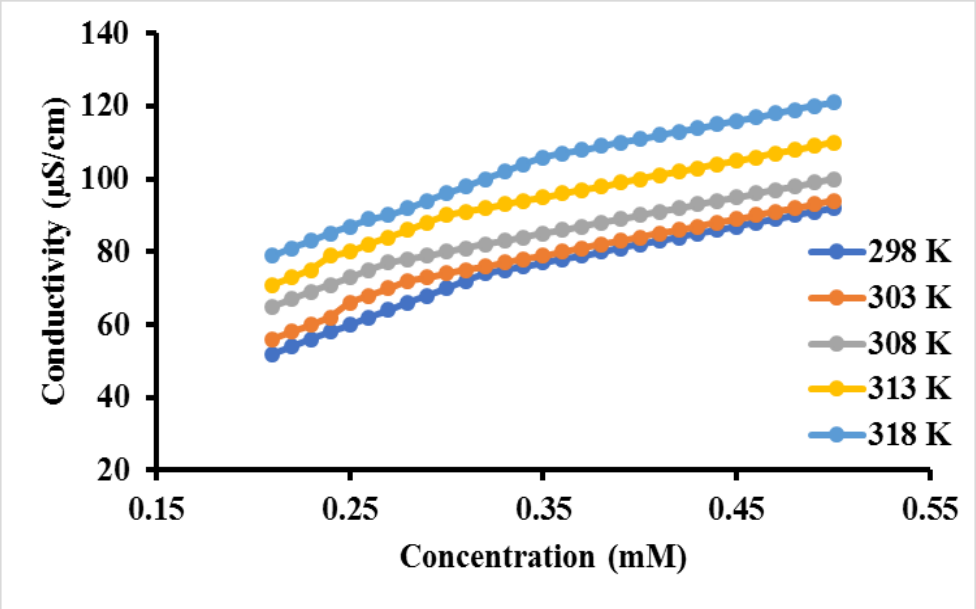
A10: CMC of compound a10 at different temperatures



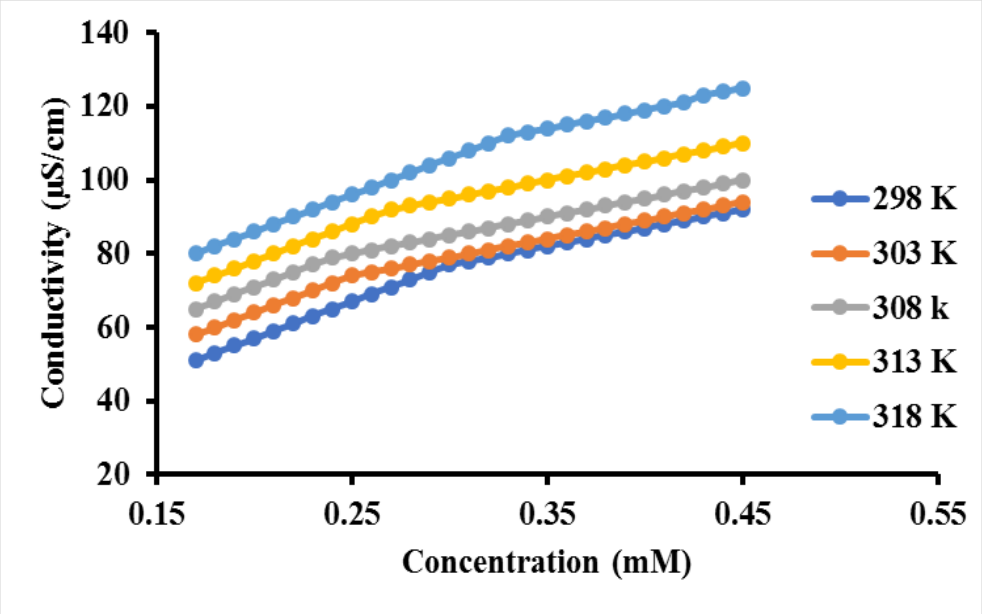
A11: CMC of compound a11 at different temperatures



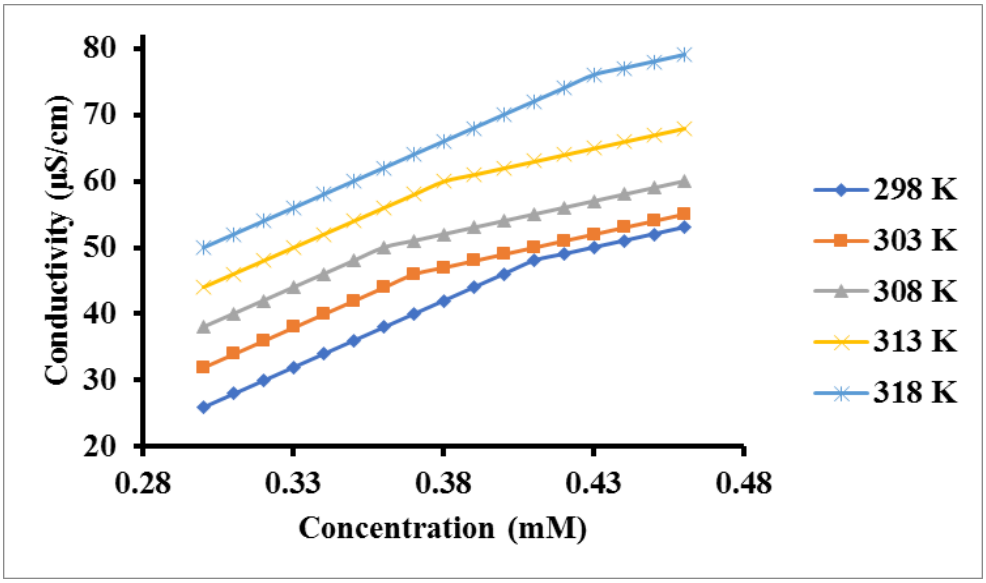
A12: CMC of compound a12 at different temperatures



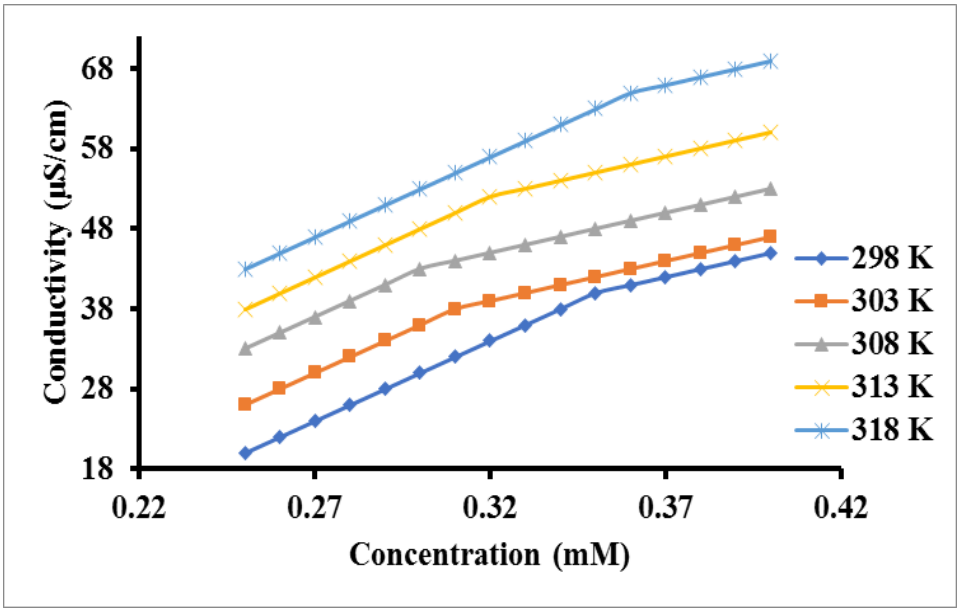
A13: CMC of compound a14 at different temperatures



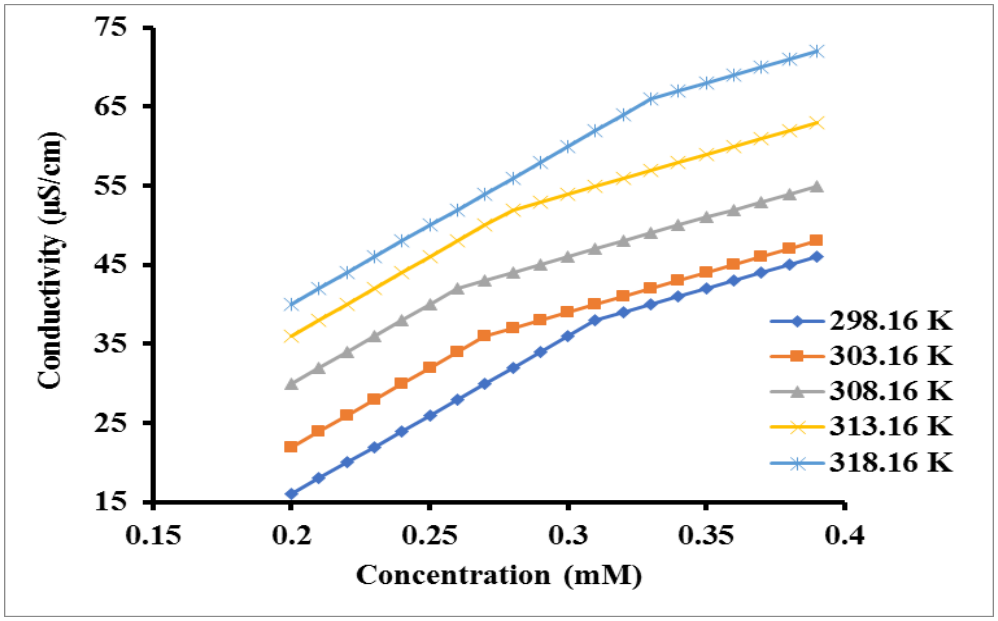
A14: CMC of compound a15 at different temperatures



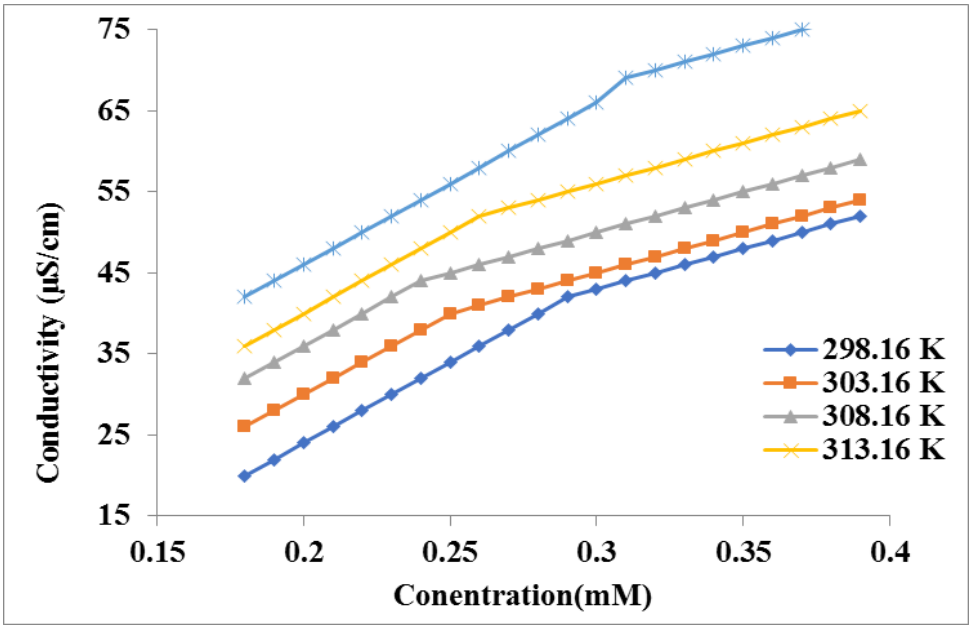
A15: CMC of compound b6 at different temperatures



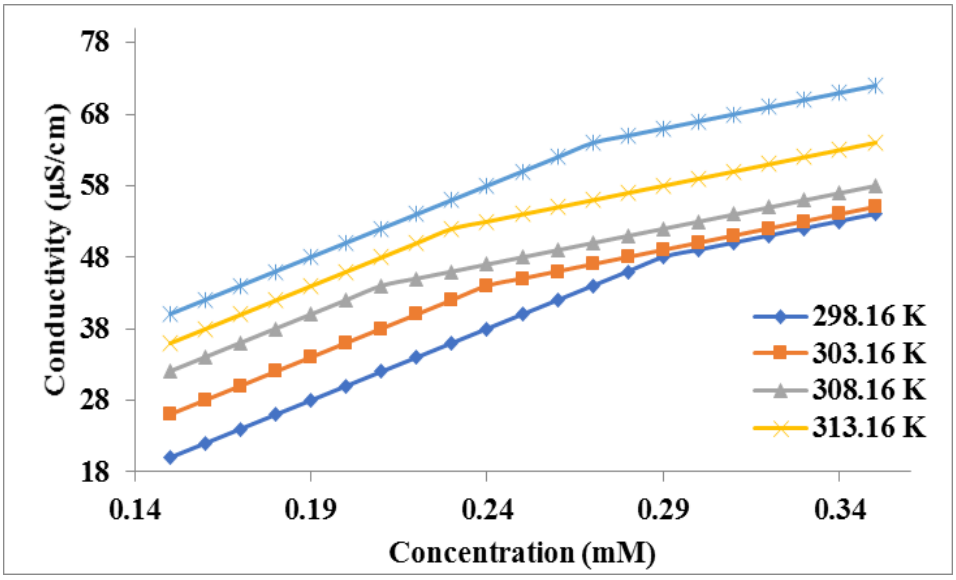
A16: CMC of compound b8 at different temperatures



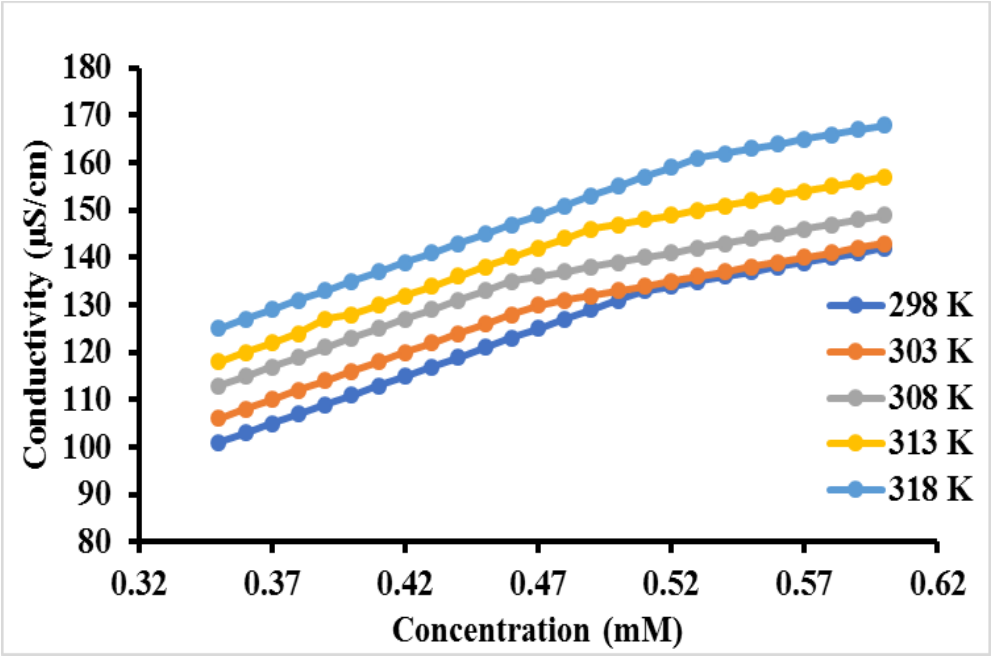
A17: CMC of compound b10 at different temperatures



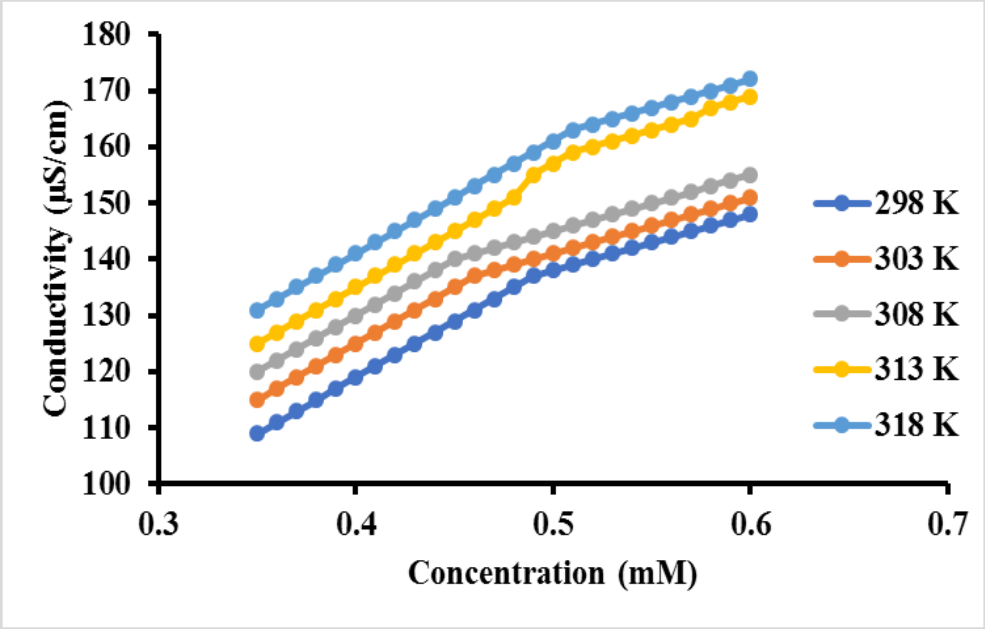
A18: CMC of compound b12 at different temperatures



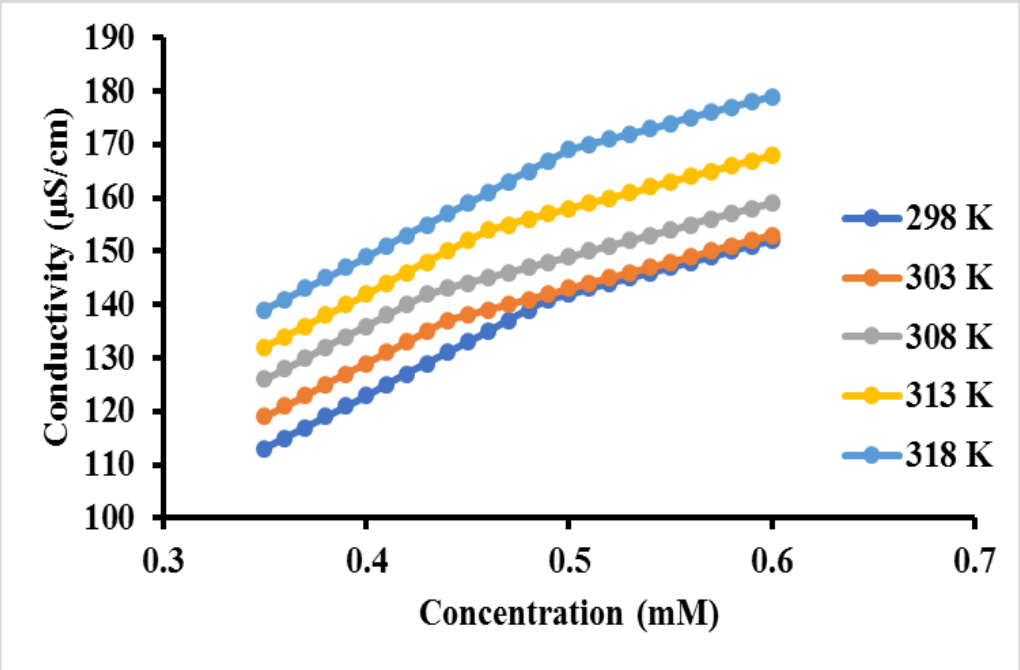
A19: CMC of compound b14 at different temperatures



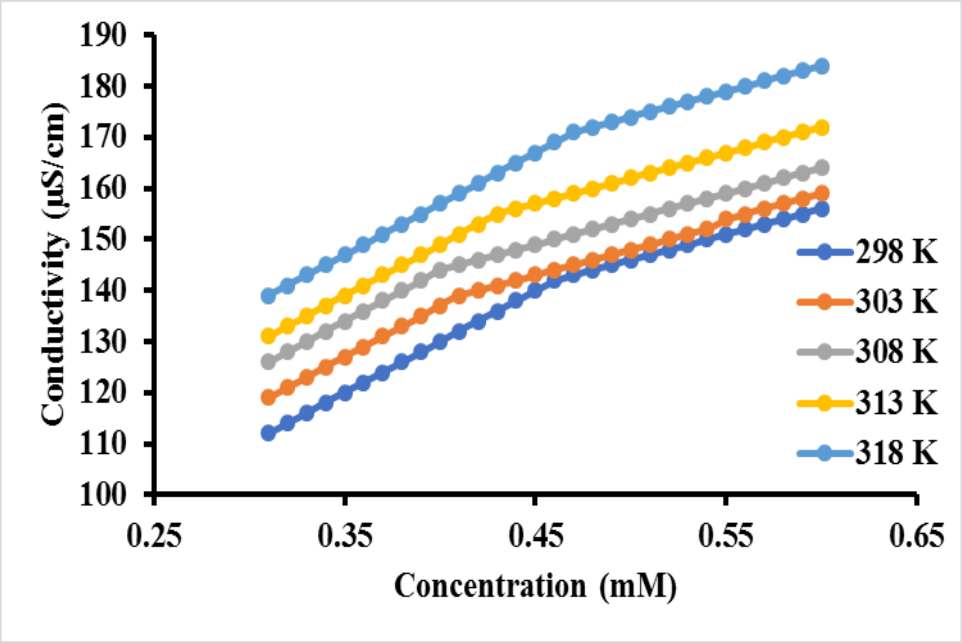
A20: CMC of compound c6 at different temperatures



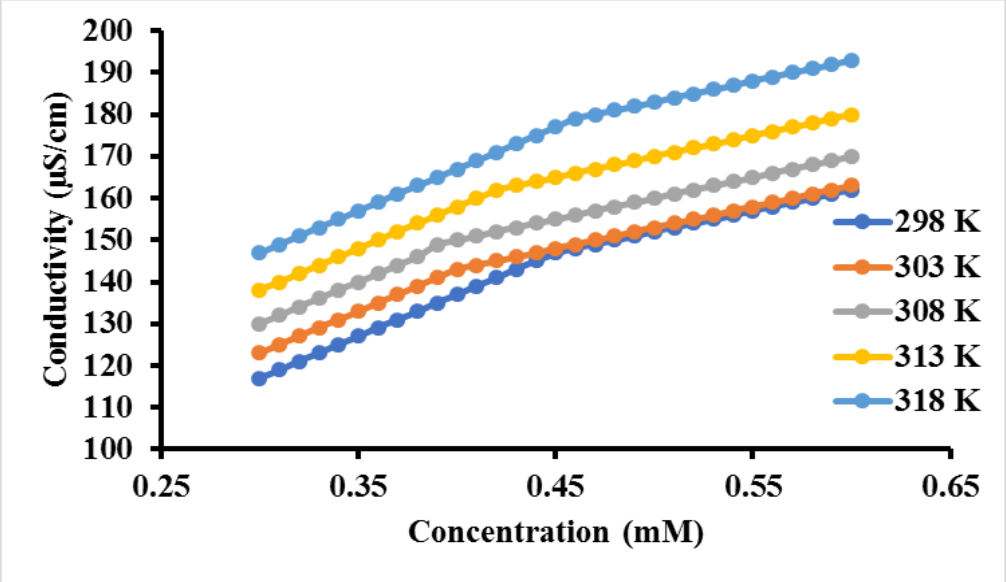
A21: CMC of compound c7 at different temperatures



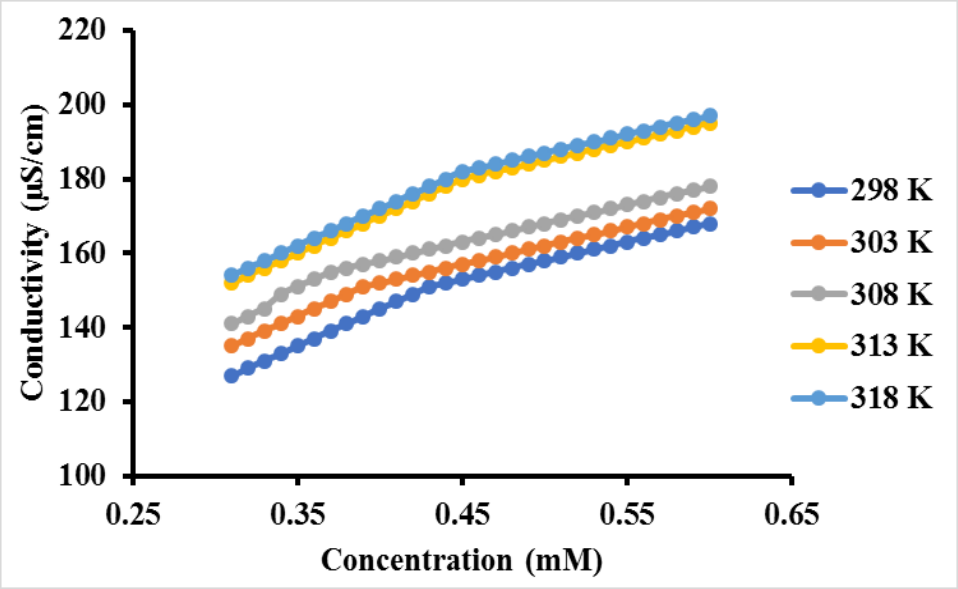
A22: CMC of compound c8 at different temperatures



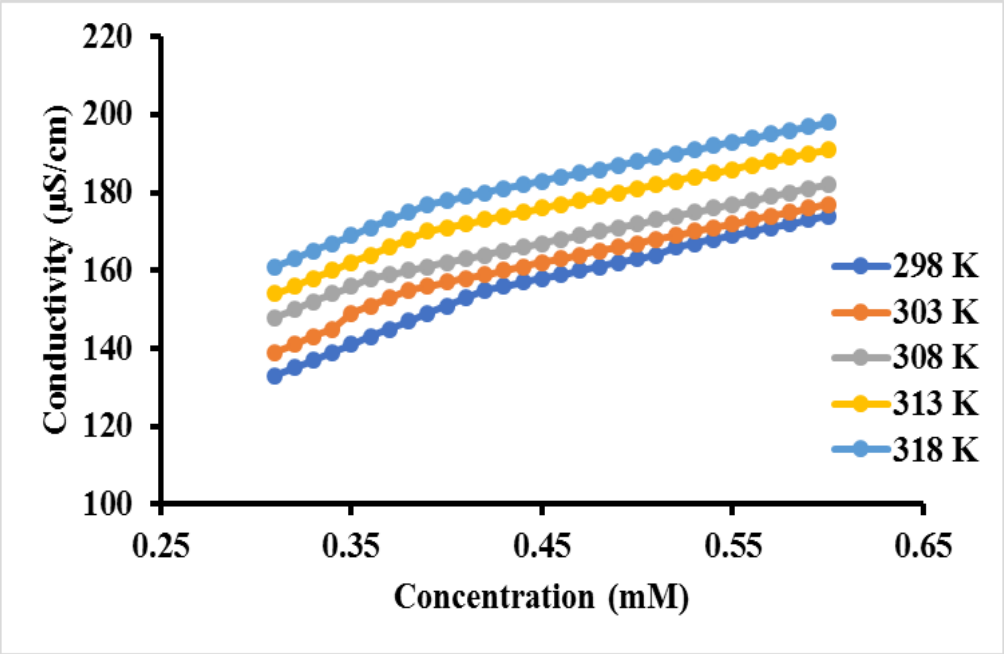
A23: CMC of compound c9 at different temperatures



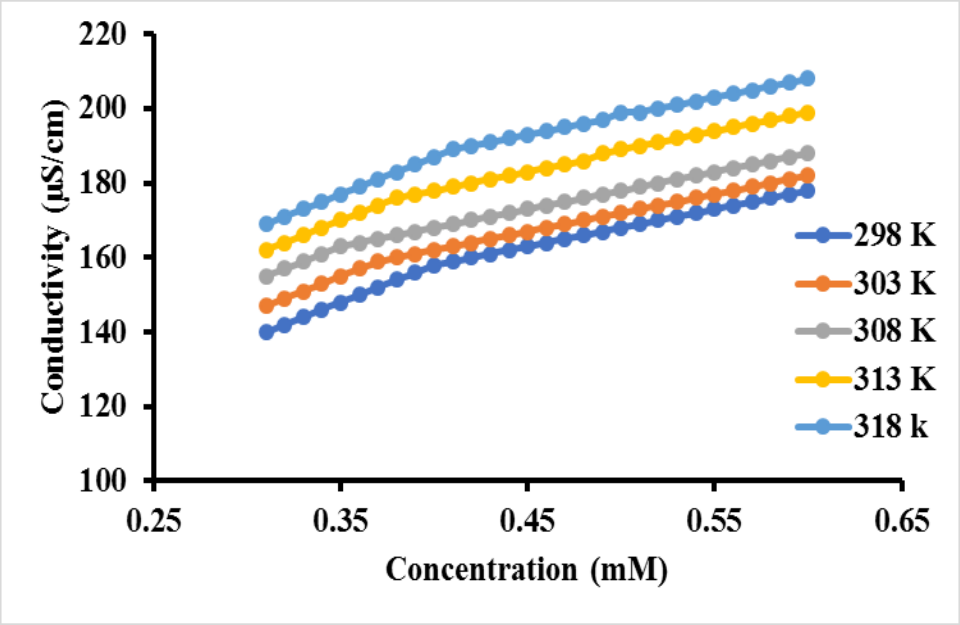
A24: CMC of compound c10 at different temperatures



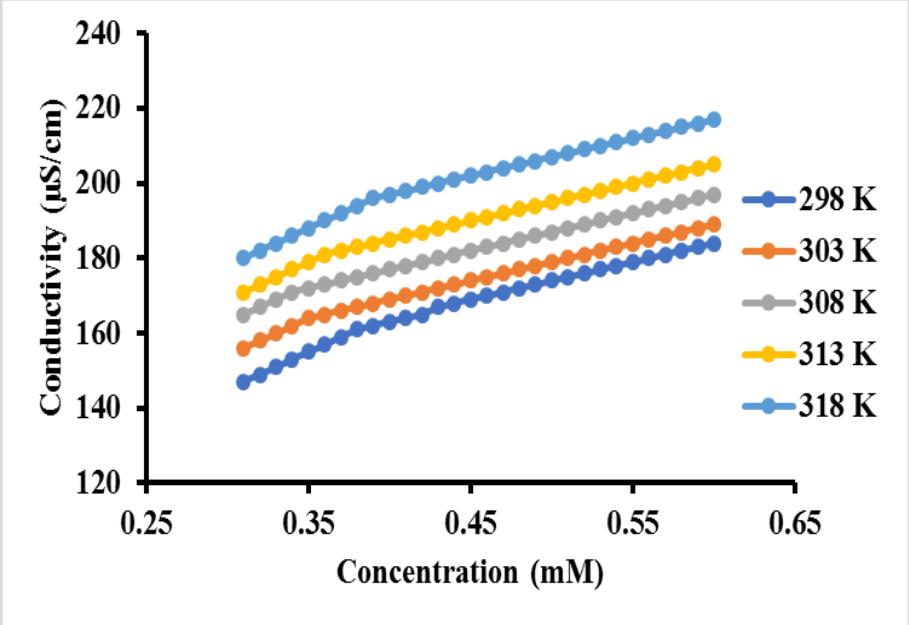
A25: CMC of compound c11 at different temperatures



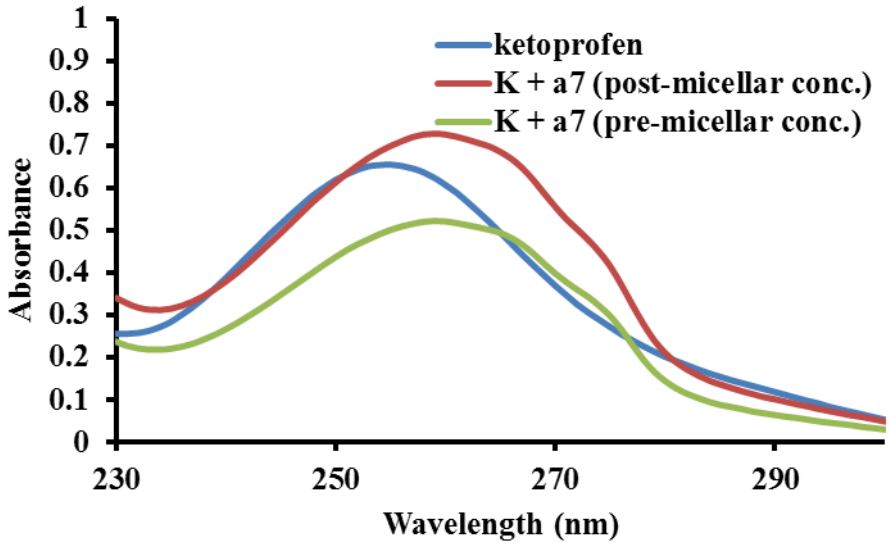
A26: CMC of compound c12 at different temperatures



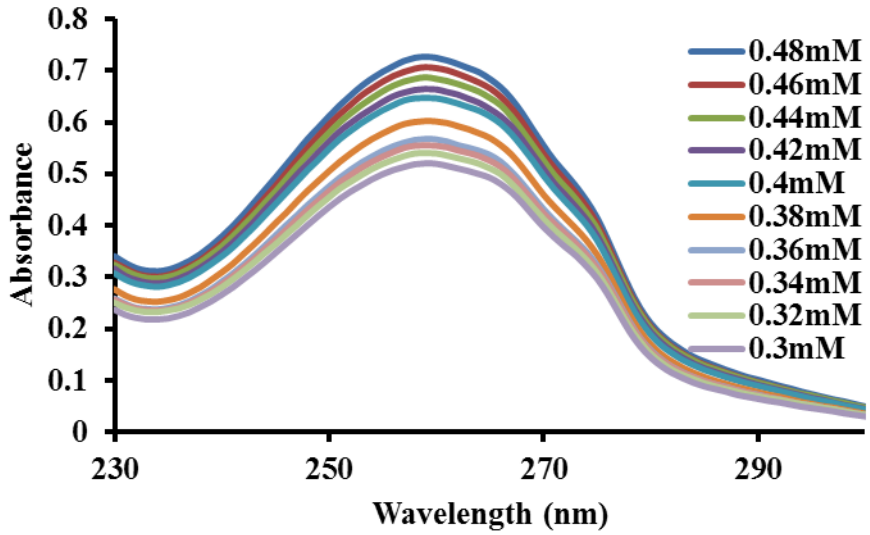
A27: CMC of compound c14 at different temperatures



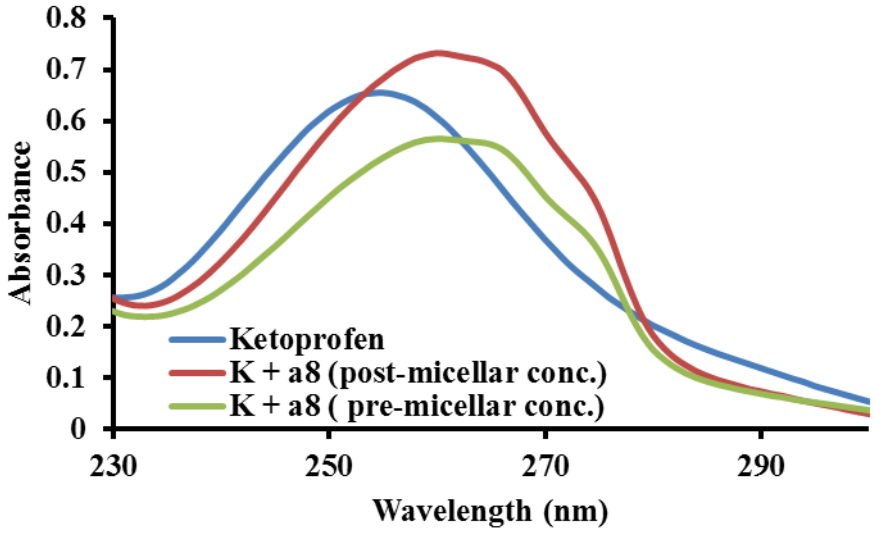
A28: CMC of compound c15 at different temperatures



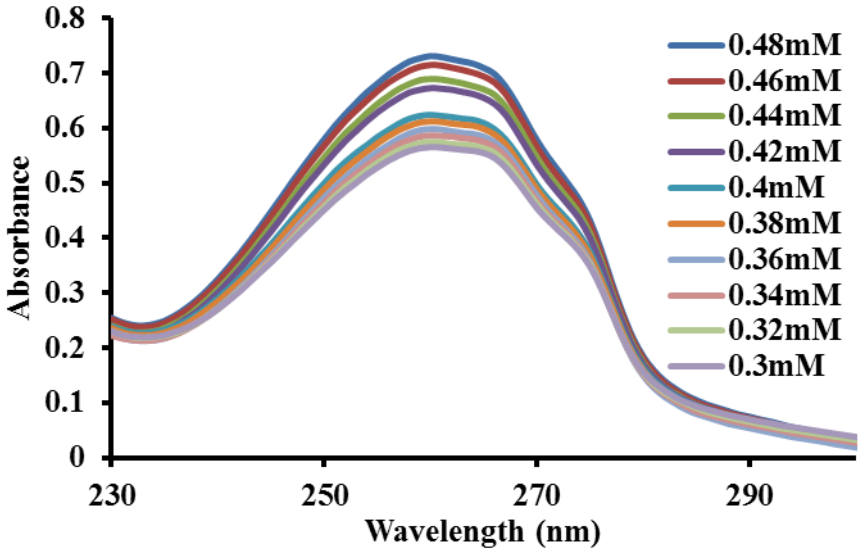
A29: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a7.



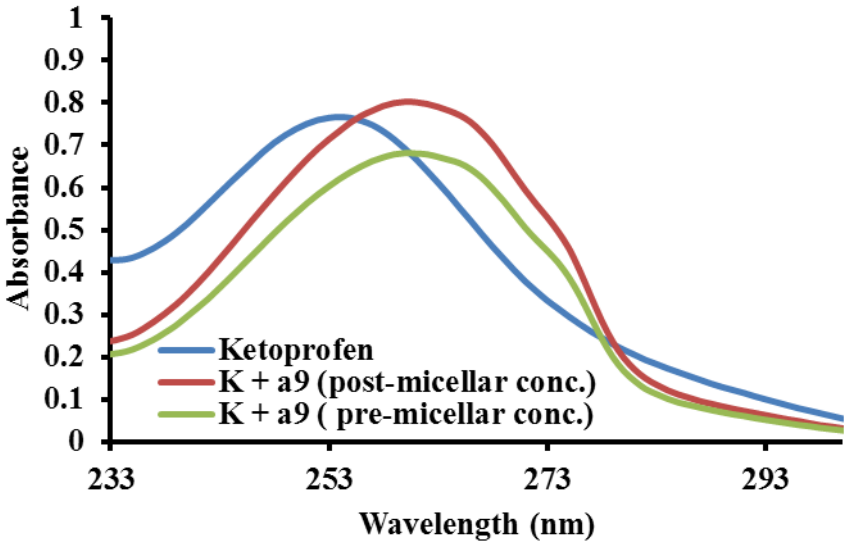
A30: With different concentrations of compound a7, absorption spectra of drug Ketoprofen.



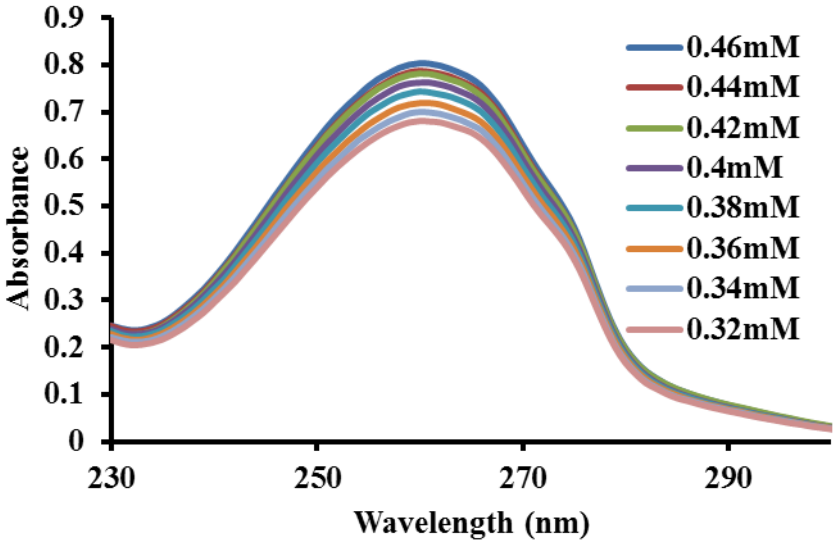
A31: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a8.



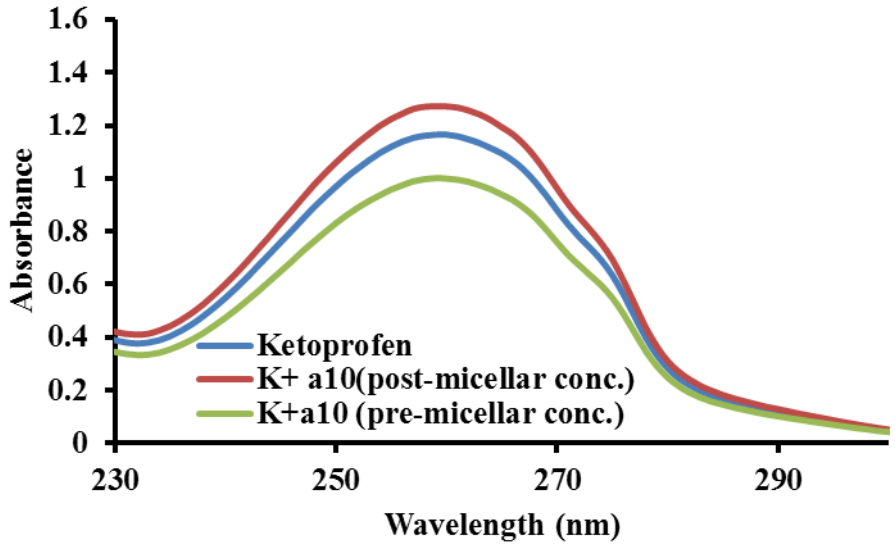
A32: With different concentrations of compound a8, absorption spectra of drug Ketoprofen.



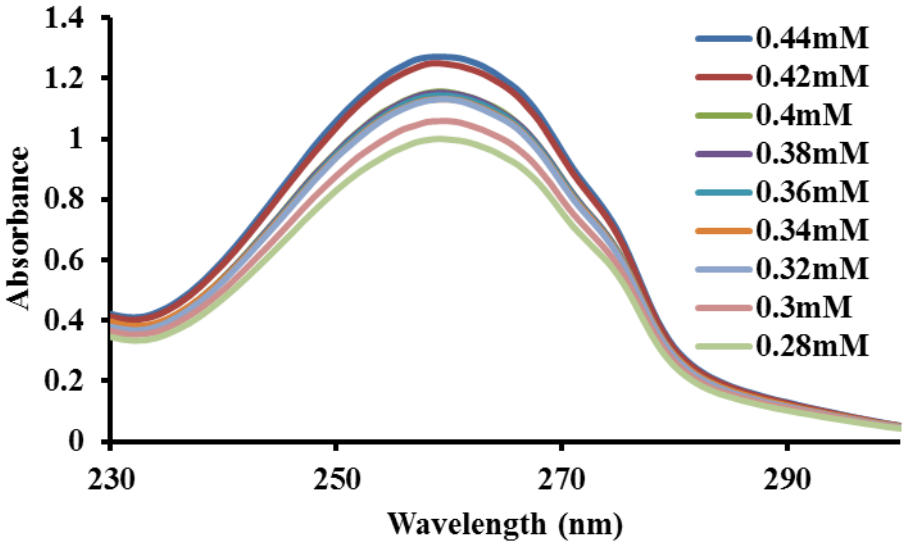
A33: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a9.



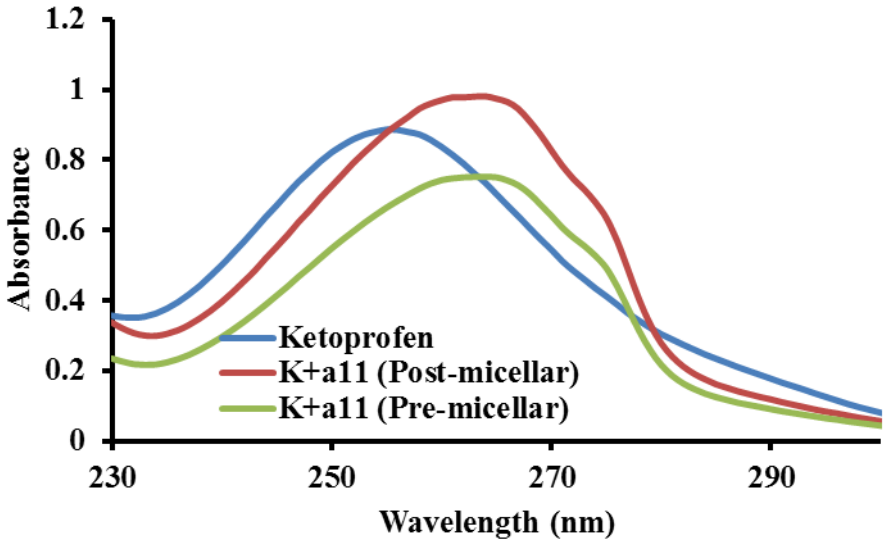
A34: With different concentrations of compound a9, absorption spectra of drug Ketoprofen.



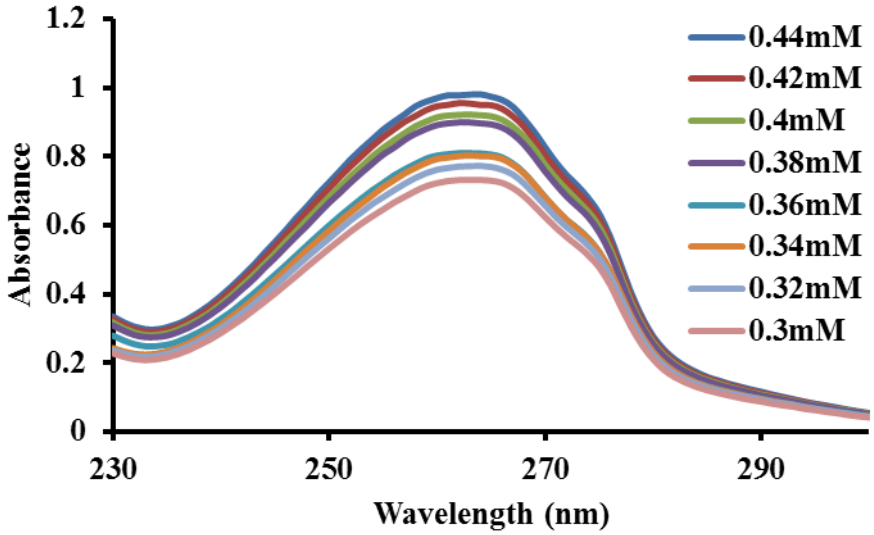
A35: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a10.



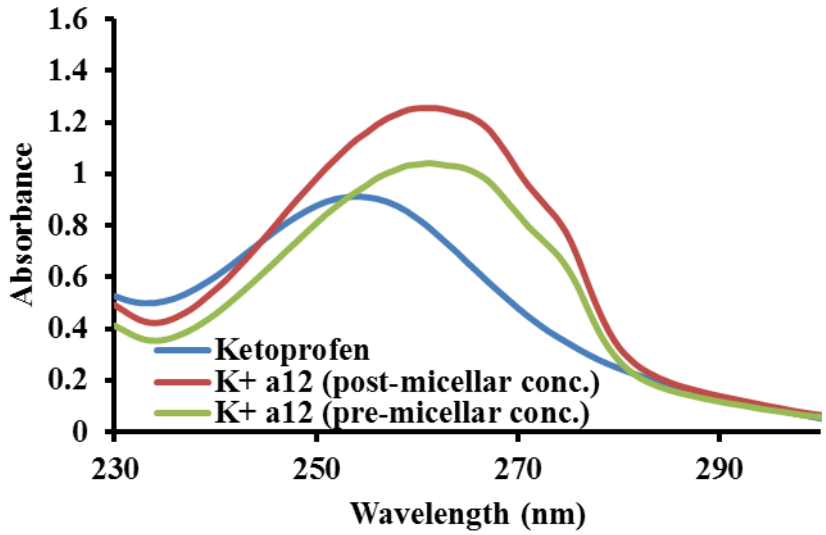
A36: With different concentrations of compound a10, absorption spectra of drug Ketoprofen.



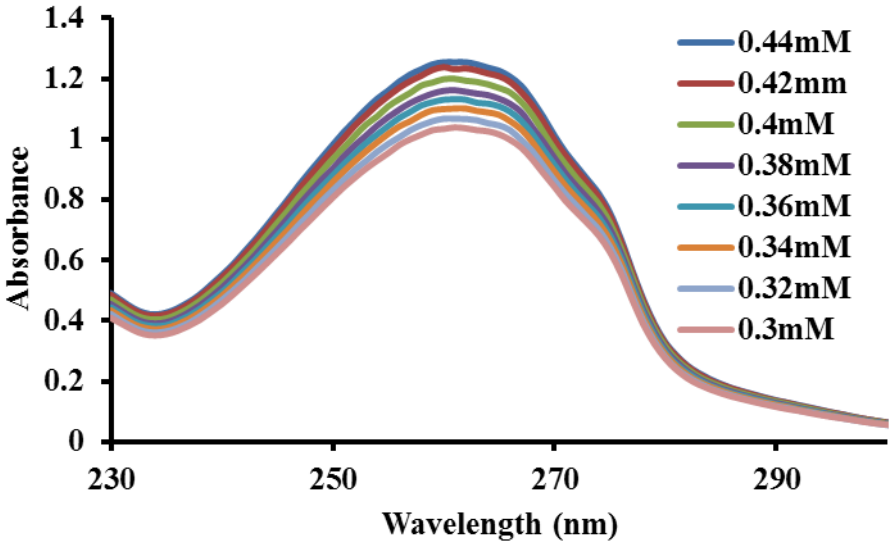
A37: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a11.



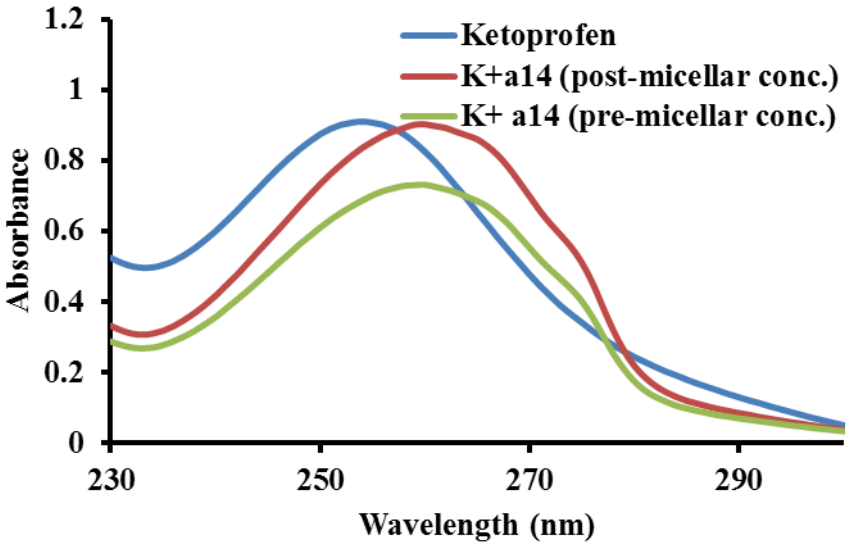
A38: With different concentrations of compound a11, absorption spectra of drug Ketoprofen.



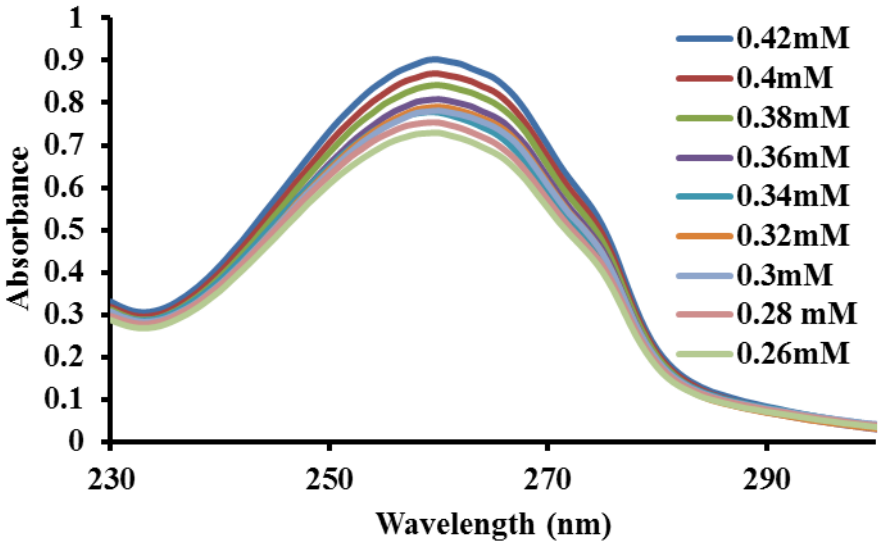
A39: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a12.



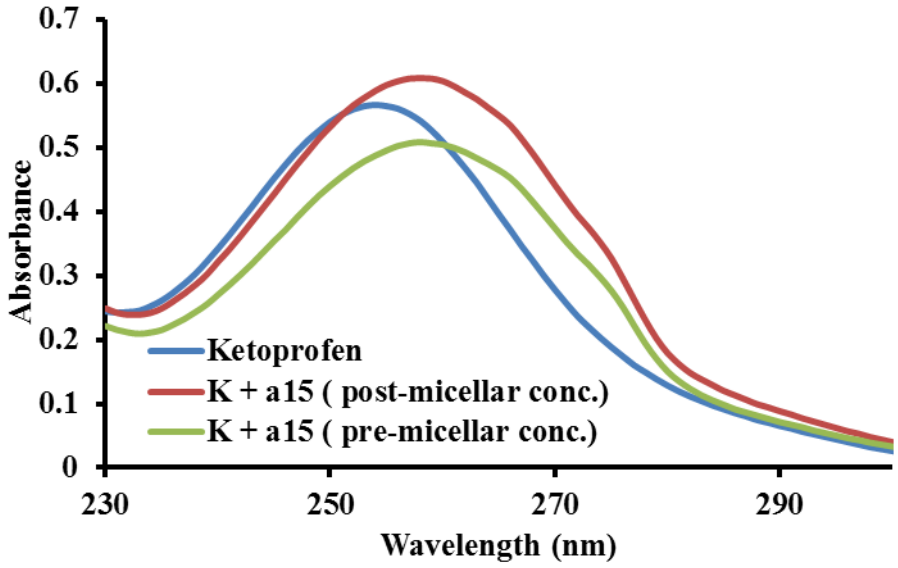
A40: With different concentrations of compound a12, absorption spectra of drug Ketoprofen.



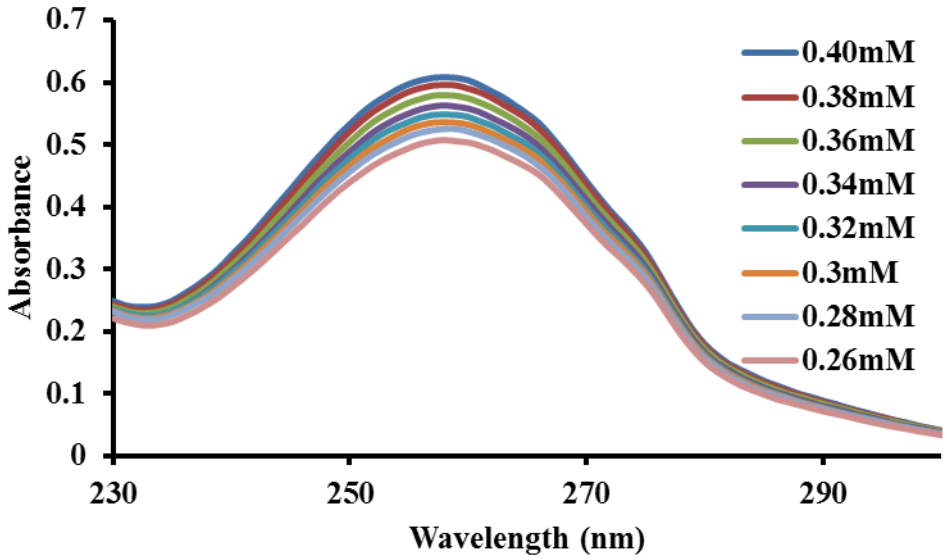
A41: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a14.



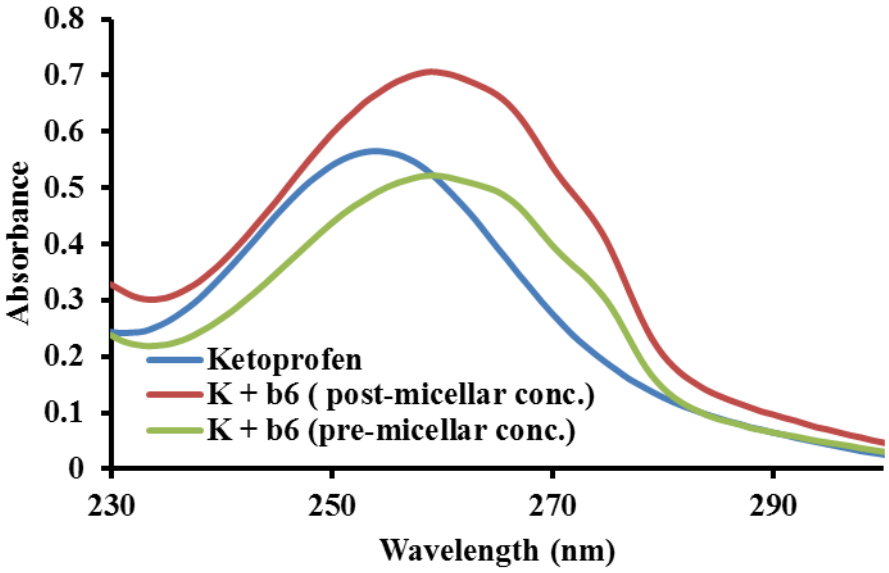
A42: With different concentrations of compound a14, absorption spectra of drug Ketoprofen.



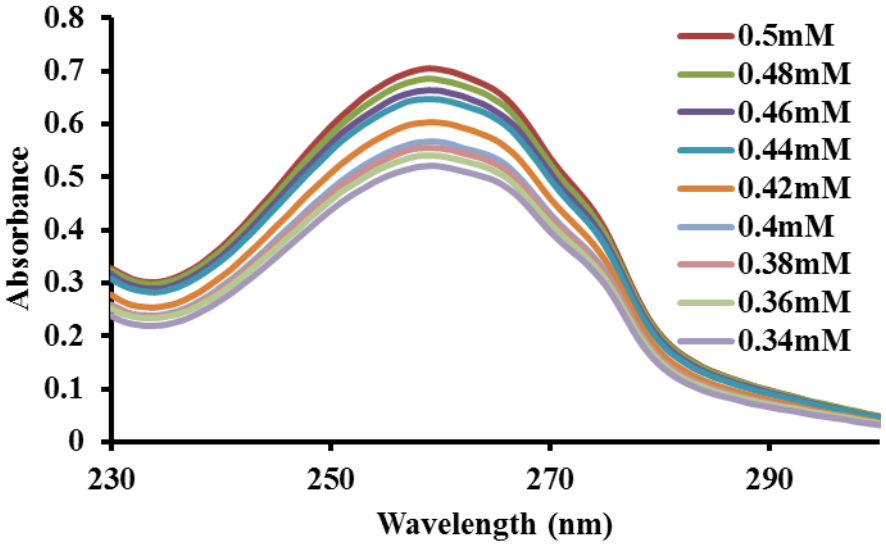
A43: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound a15.



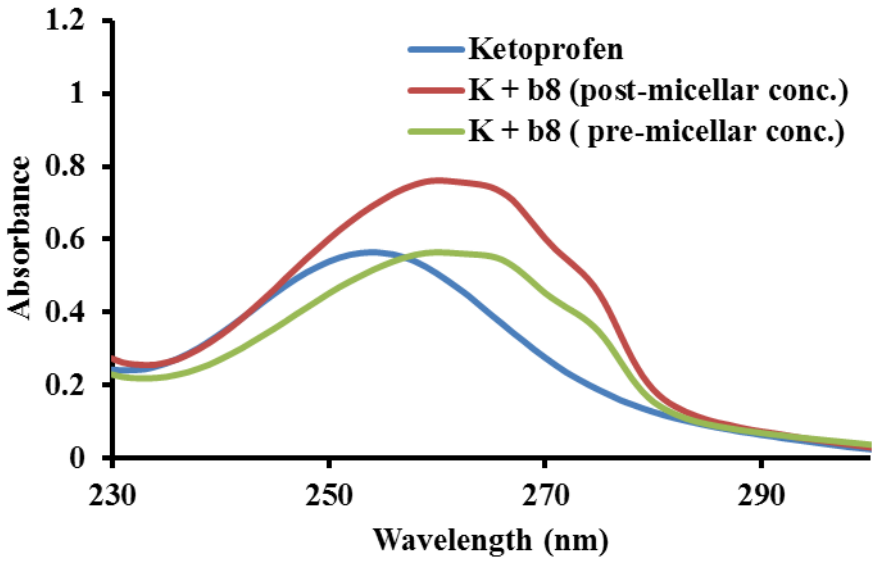
A44: With different concentrations of compound a15, absorption spectra of drug Ketoprofen



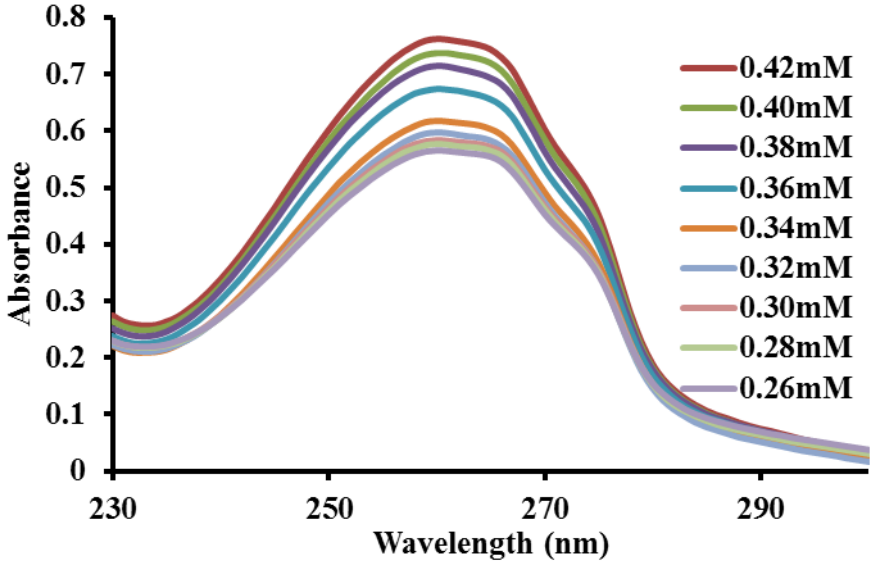
A45: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound b6.



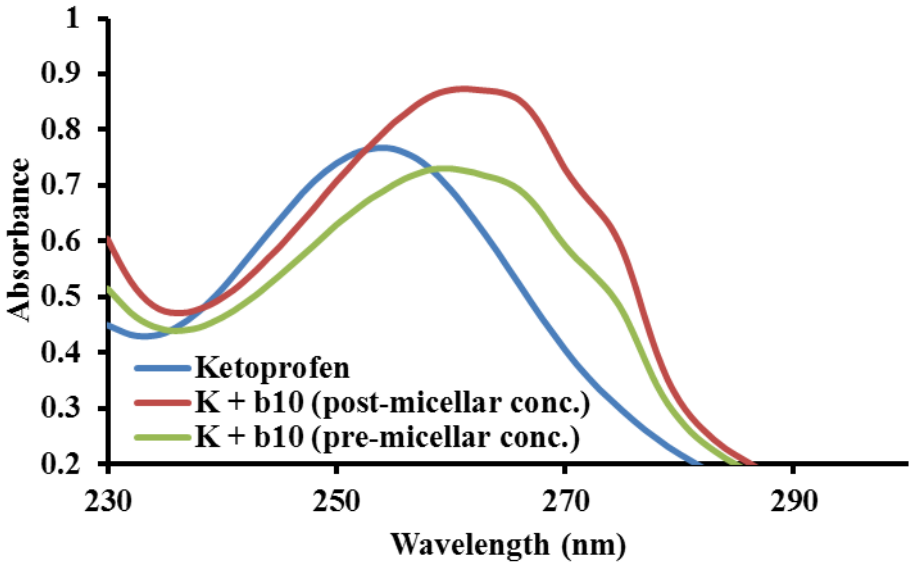
A46: With different concentrations of compound b6, absorption spectra of drug Ketoprofen.



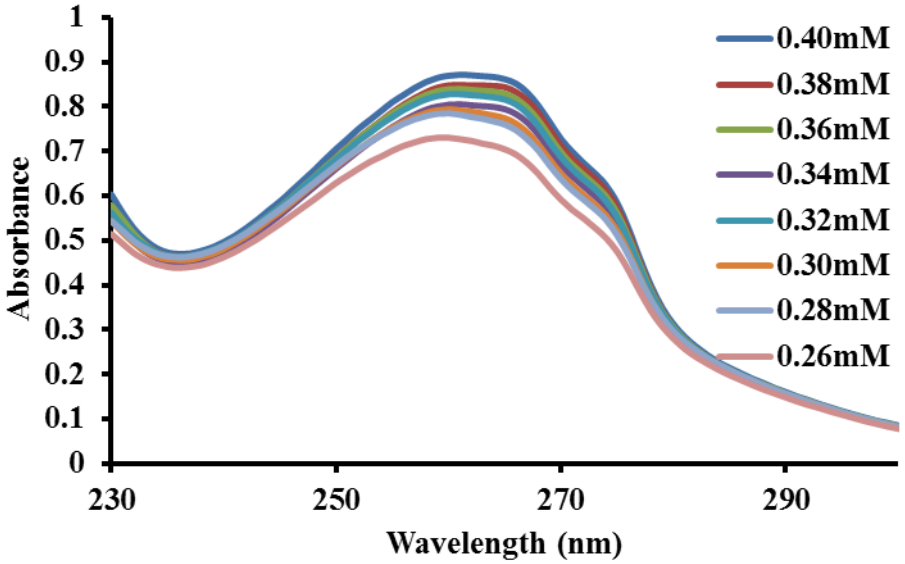
A47: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound b8.



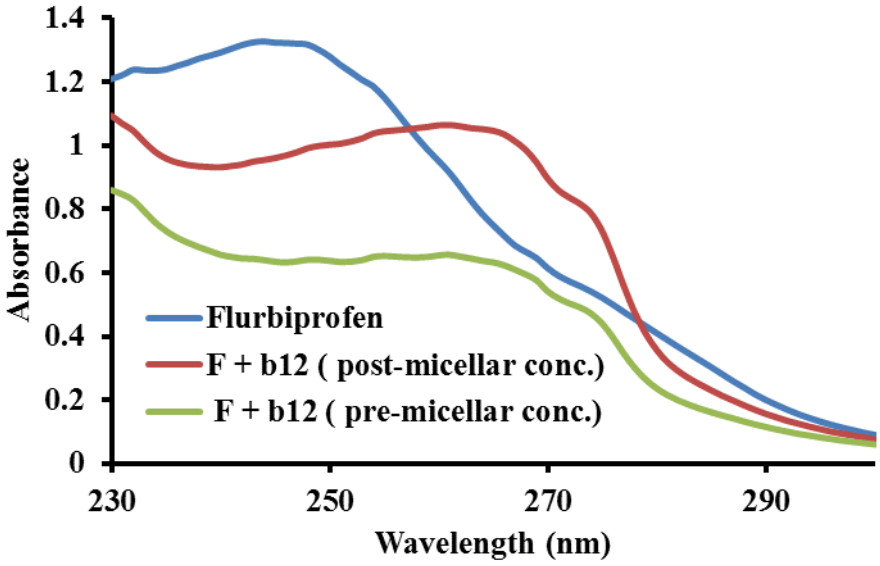
A48: With different concentrations of compound b8, absorption spectra of drug Ketoprofen.



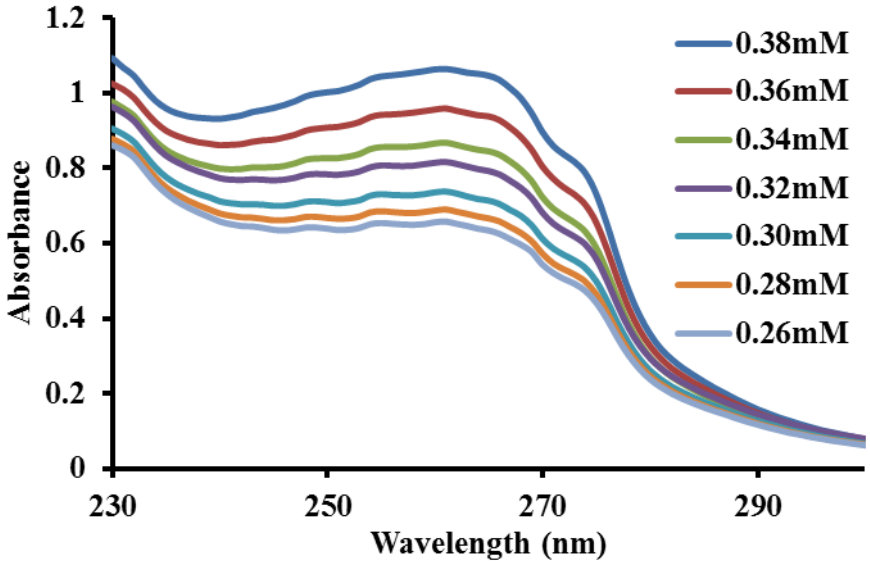
A49: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound b10.



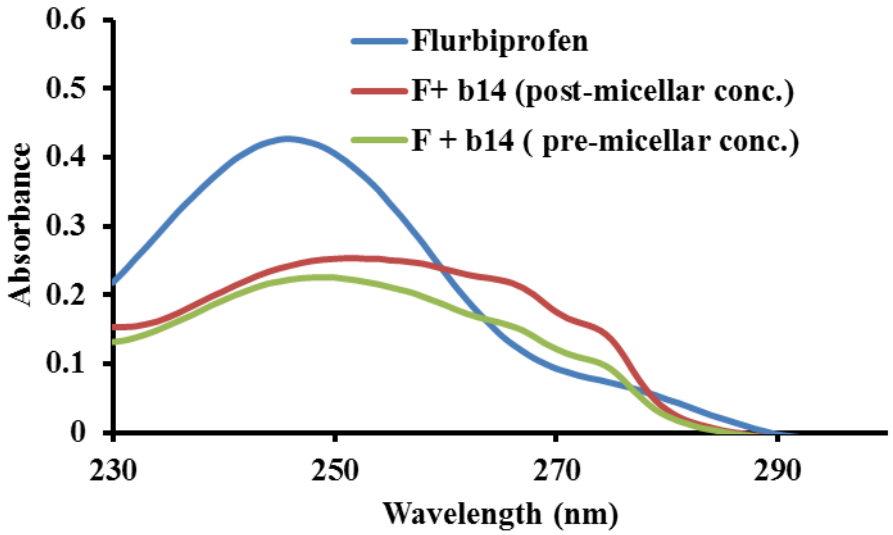
A50: With different concentrations of compound b10, absorption spectra of drug Ketoprofen.



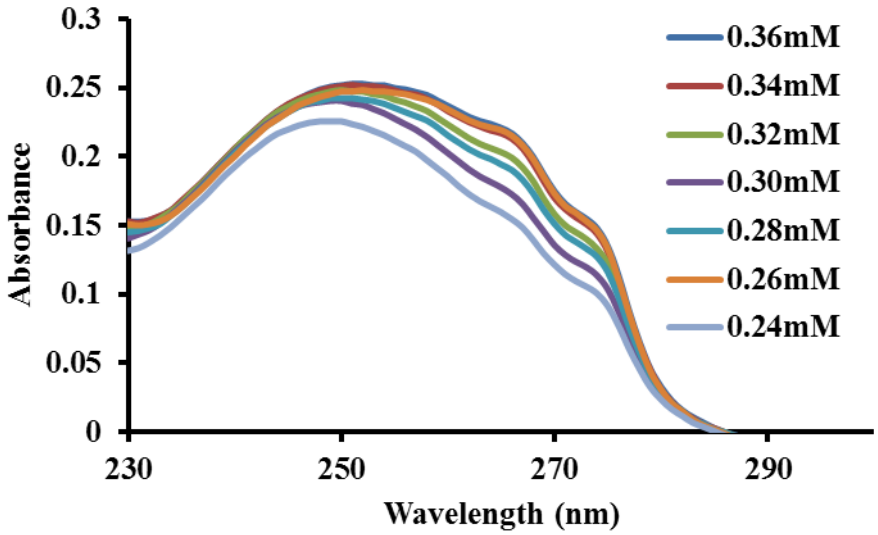
A51: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound b12.



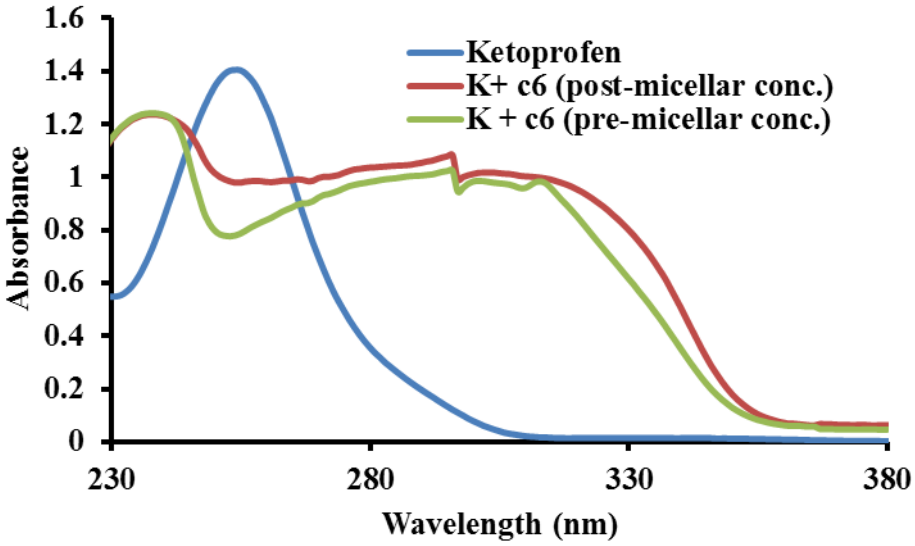
A52: With different concentrations of compound b12, absorption spectra of drug Ketoprofen.



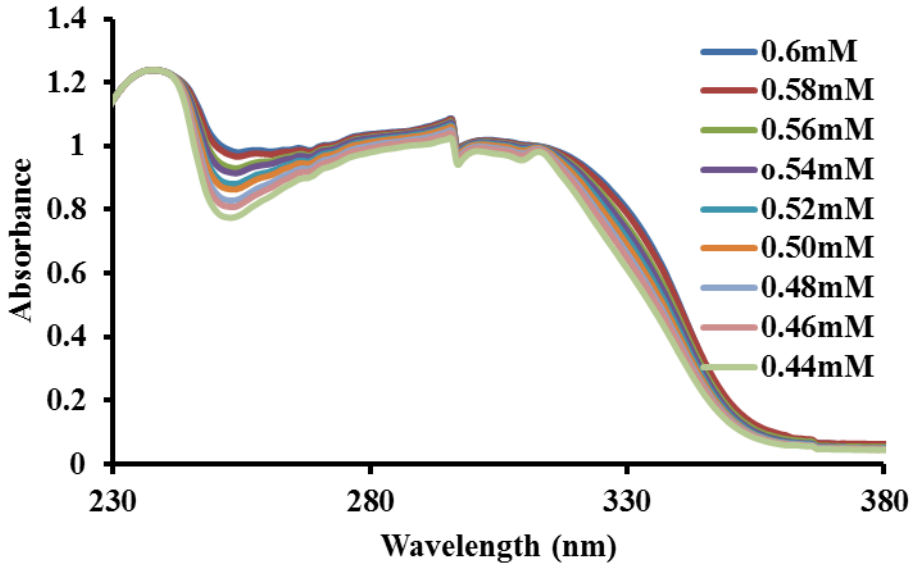
A53: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound b14.



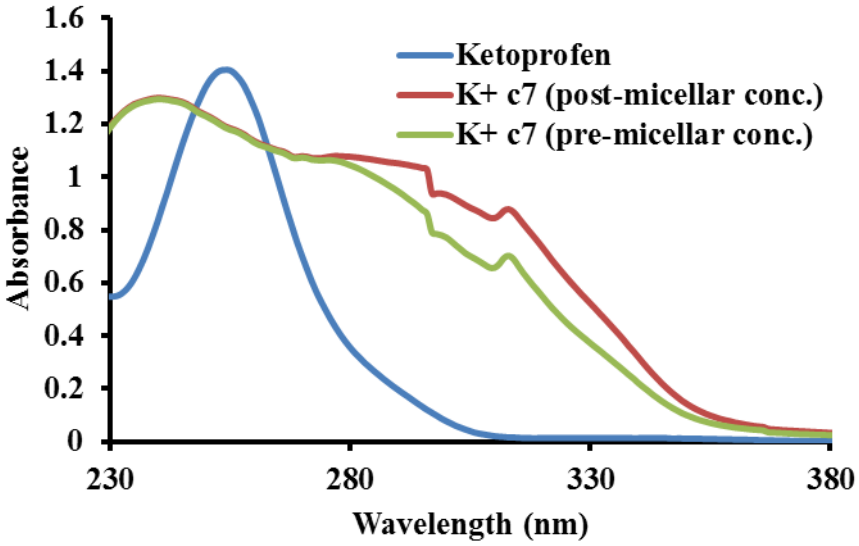
A54: With different concentrations of compound b14, absorption spectra of drug Ketoprofen.



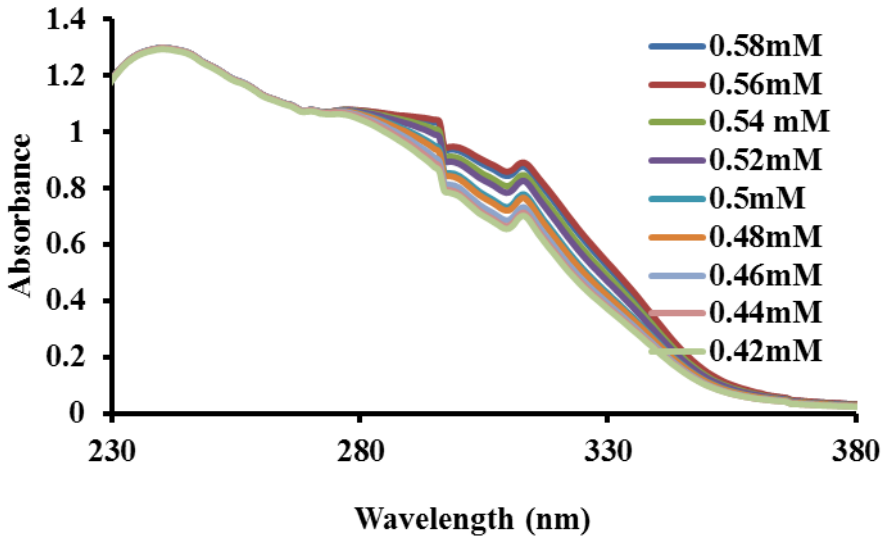
A55: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c6.



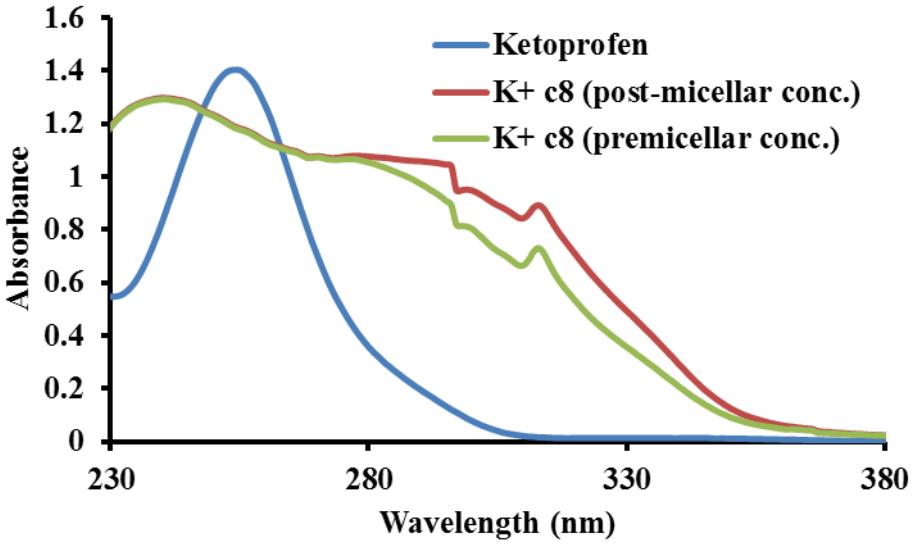
A56: With different concentrations of compound c6, absorption spectra of drug Ketoprofen.



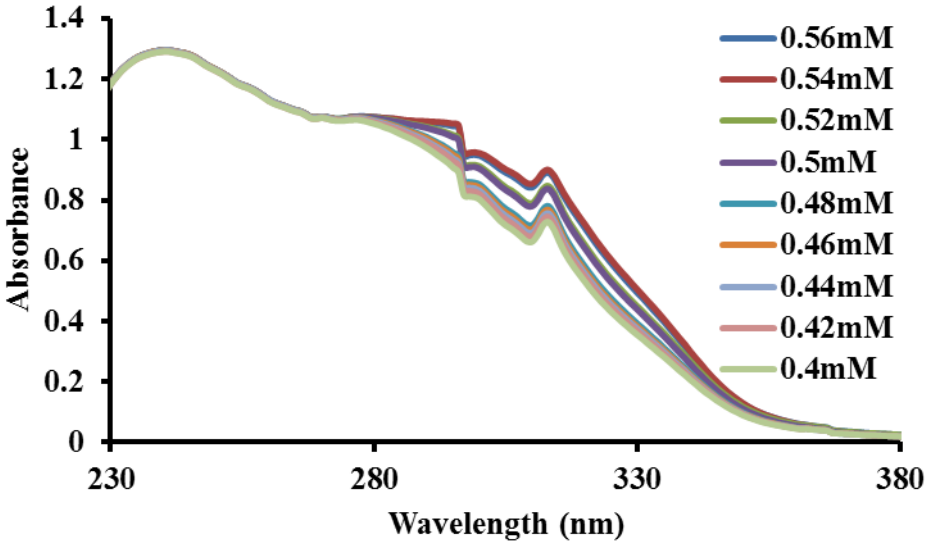
A57: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c7.



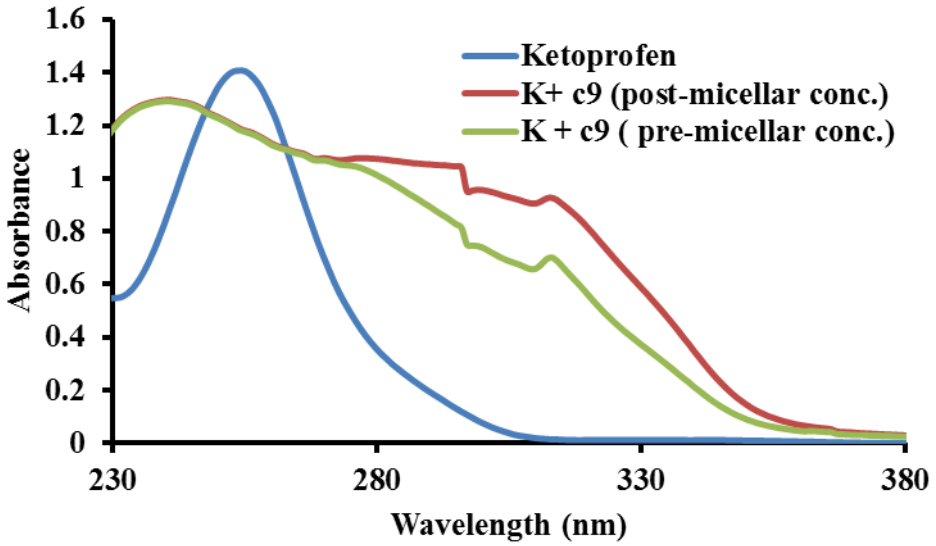
A58: With different concentrations of compound c7, absorption spectra of drug Ketoprofen.



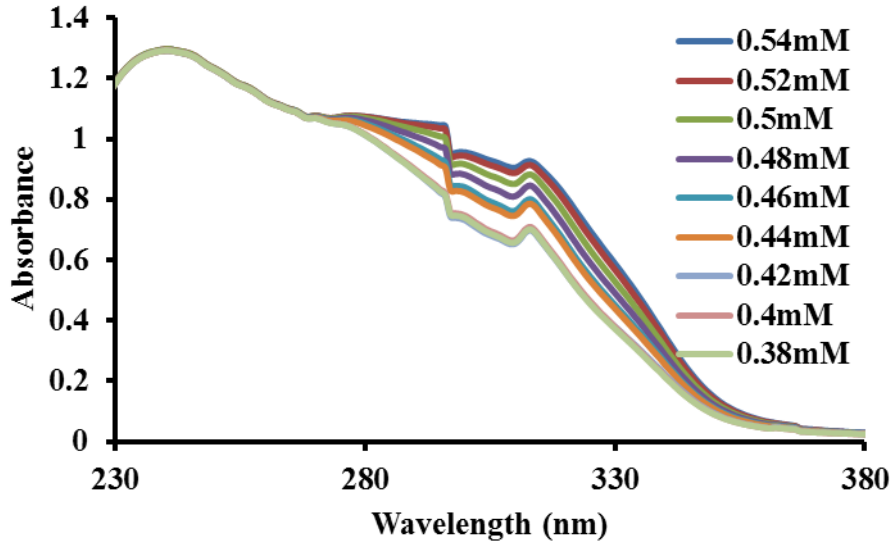
A59: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c8.



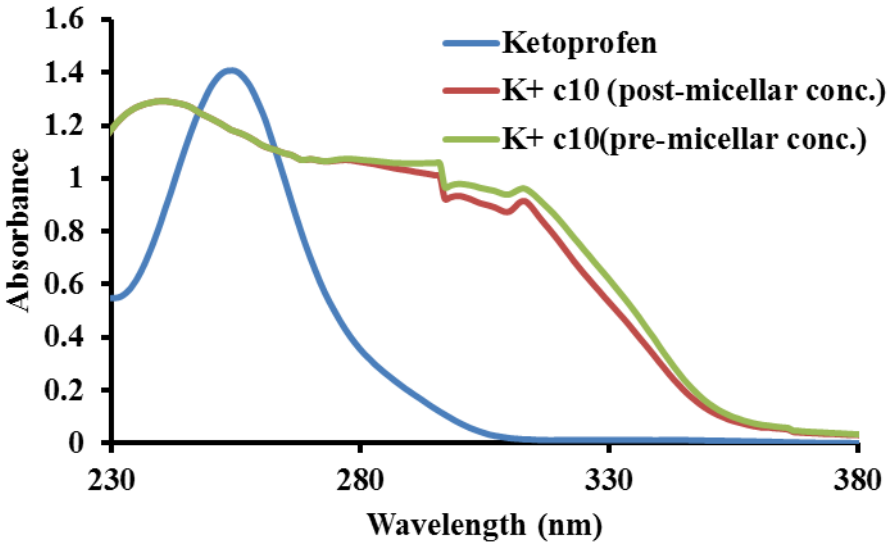
A60: With different concentrations of compound c8, absorption spectra of drug Ketoprofen.



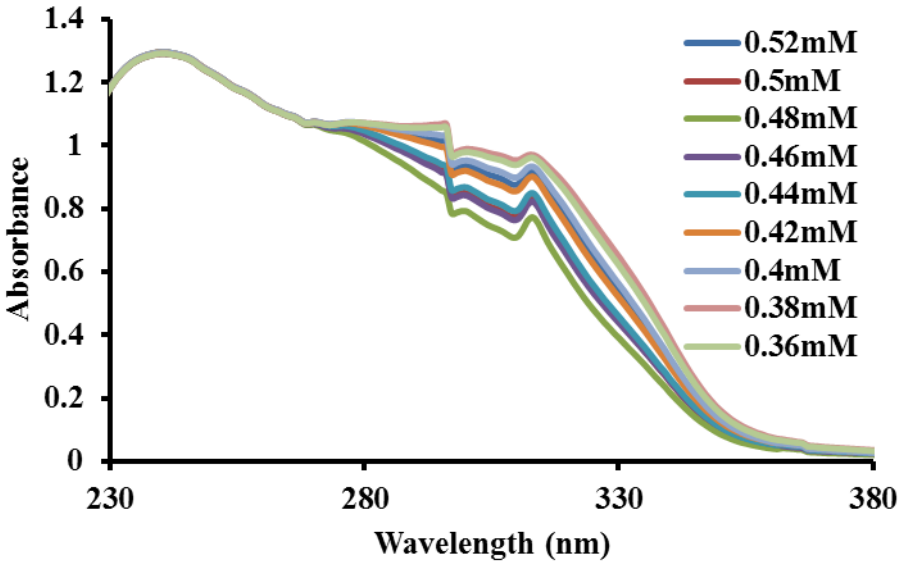
A61: Absorption spectra of drug Ketoprofen, without and with pre-micellar and post-micellar region of compound c9.



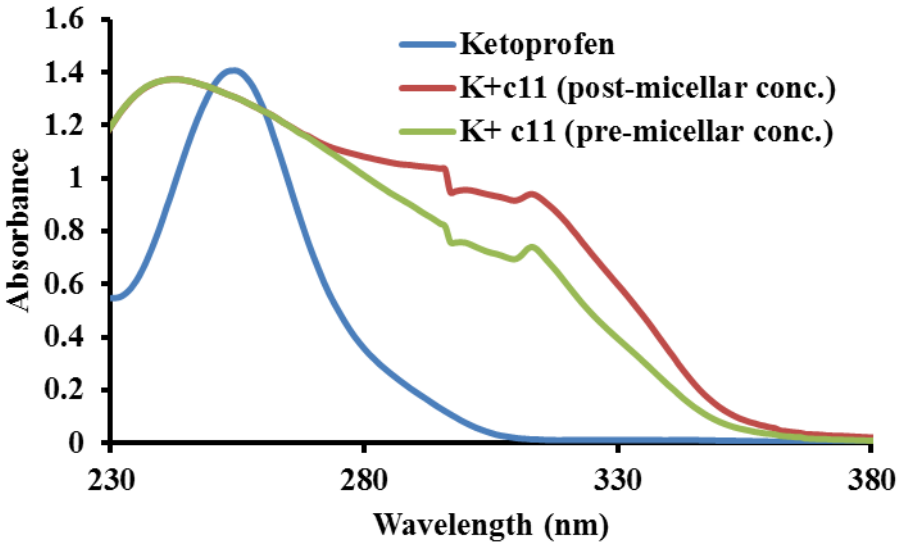
A62: With different concentrations of compound c9, absorption spectra of drug Ketoprofen.



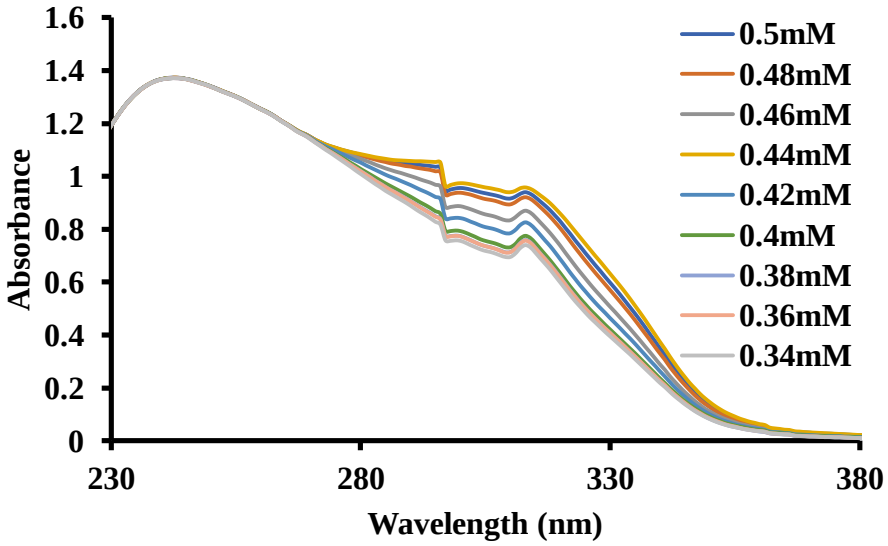
A63: Absorption spectra of drug Ketoprofen, without and with pre- micellar and post-micellar region of compound c10.



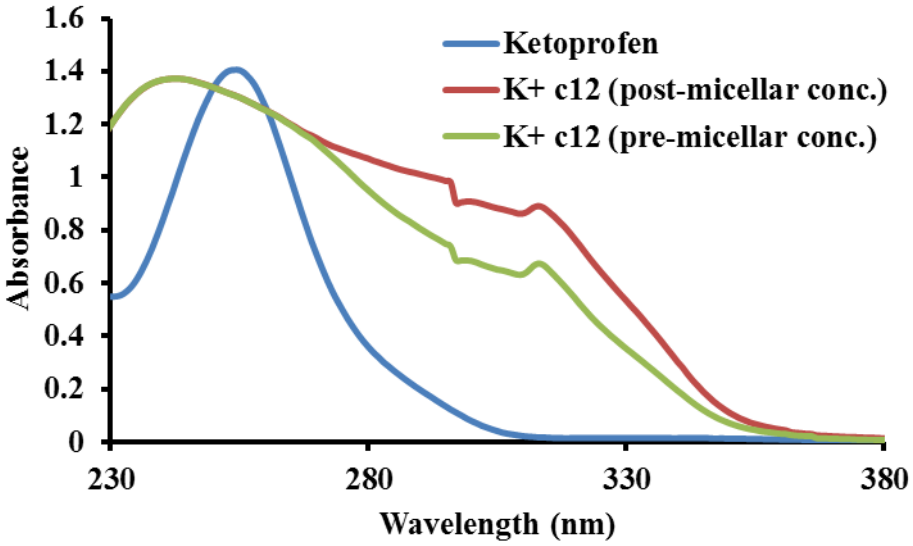
A64: With different concentrations of compound c10, absorption spectra of drug Ketoprofen.



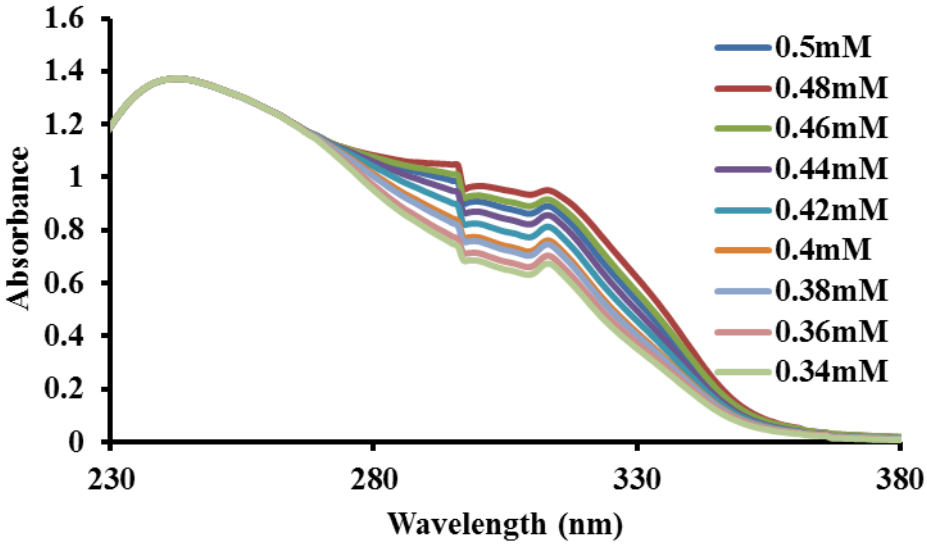
A65: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c11.



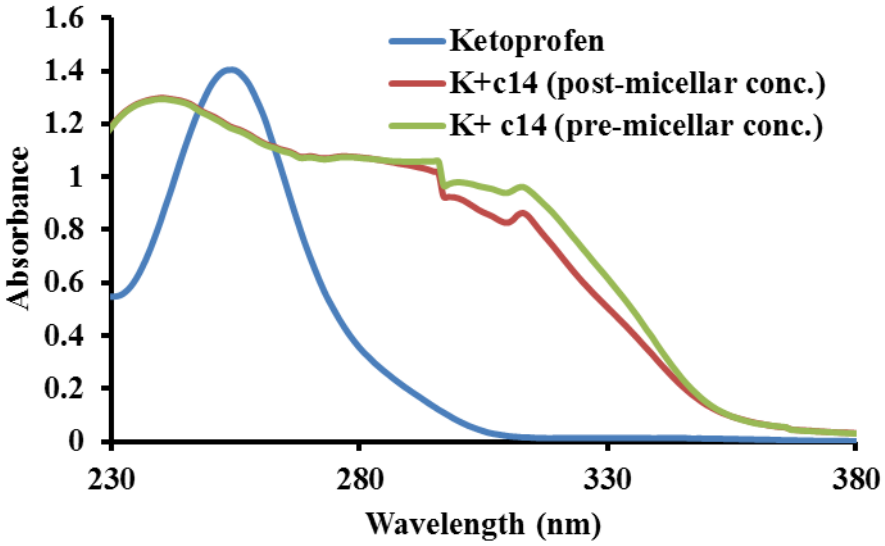
A66: With different concentrations of compound c11, absorption spectra of drug Ketoprofen.



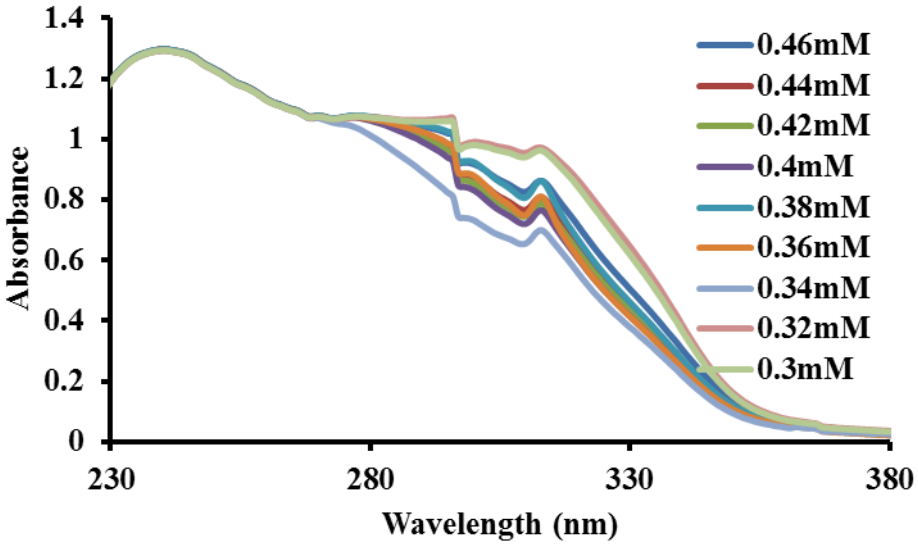
A67: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c12.



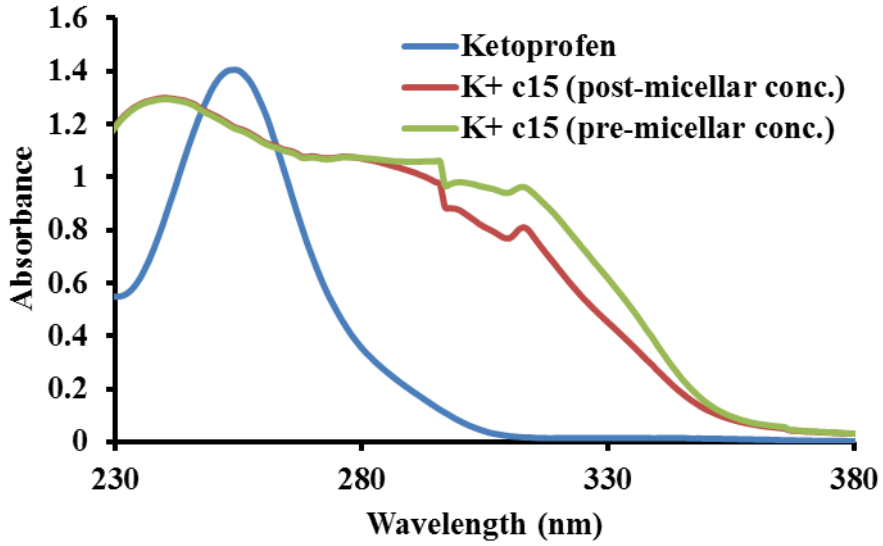
A68: With different concentrations of compound c12, absorption spectra of drug Ketoprofen.



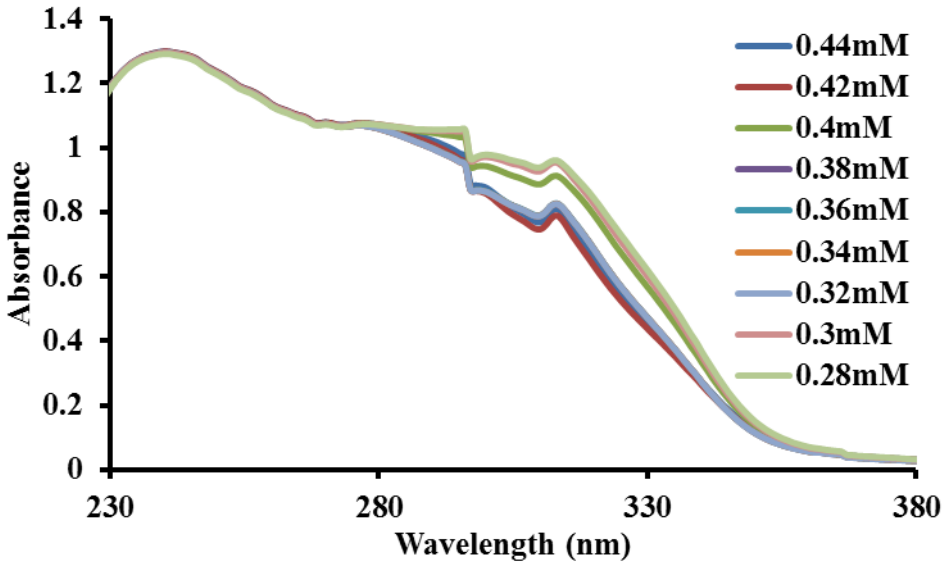
A69: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c14.



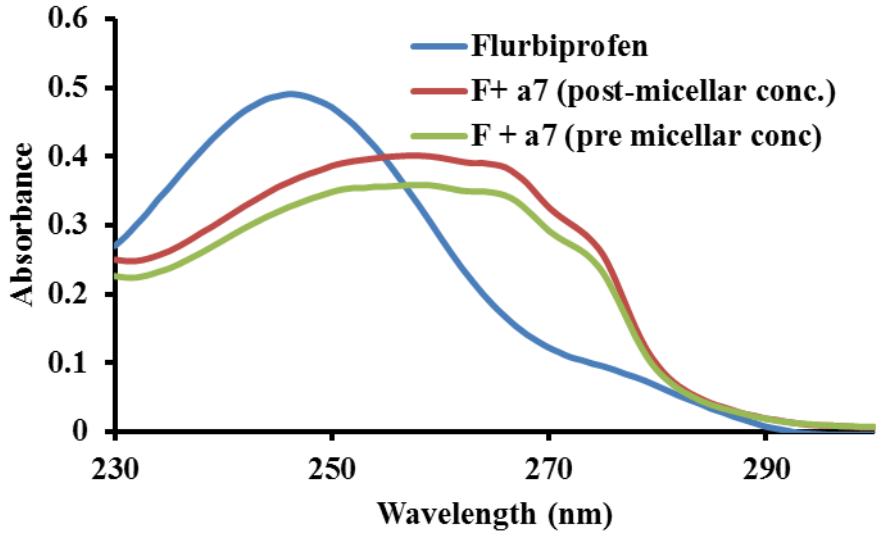
A70: With different concentrations of compound c14, absorption spectra of drug Ketoprofen



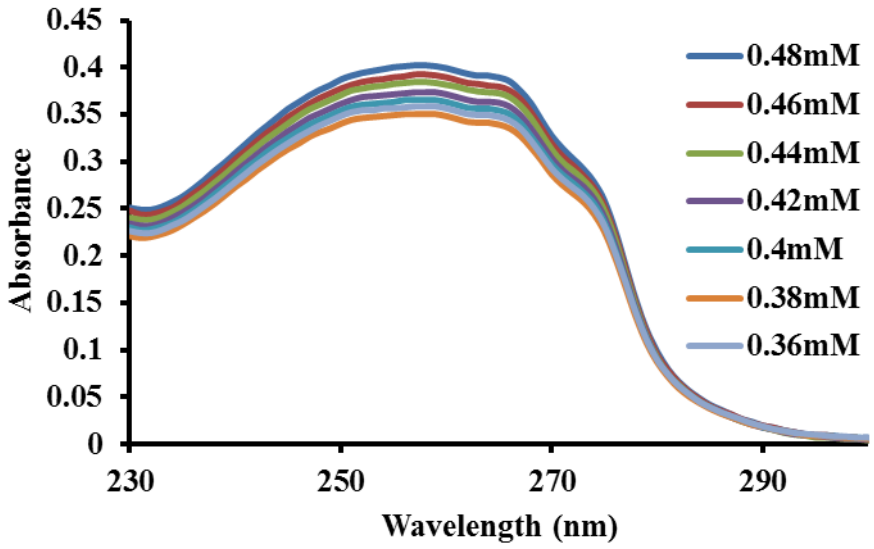
A71: Absorption spectra of drug Ketoprofen without and with pre-micellar and post-micellar region of compound c15.



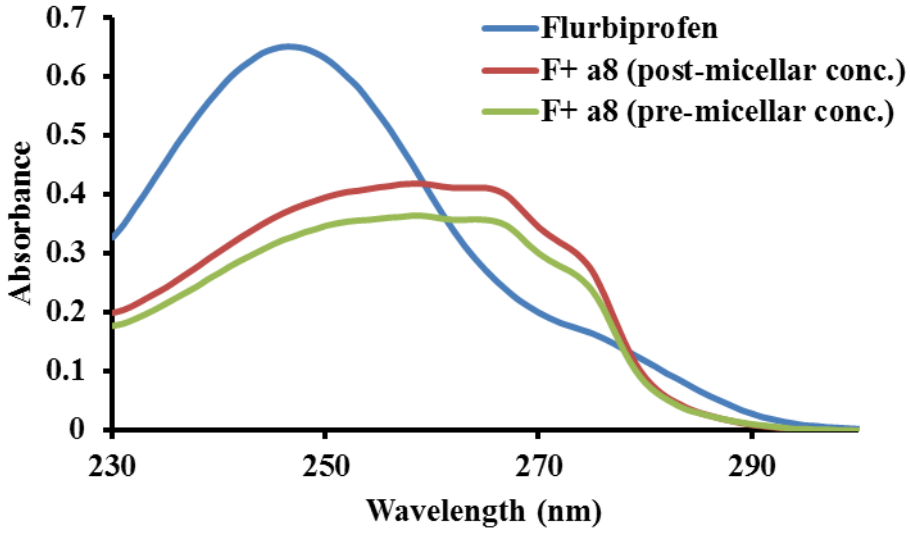
A 72: With different concentrations of compound c15, absorption spectra of drug Ketoprofen.



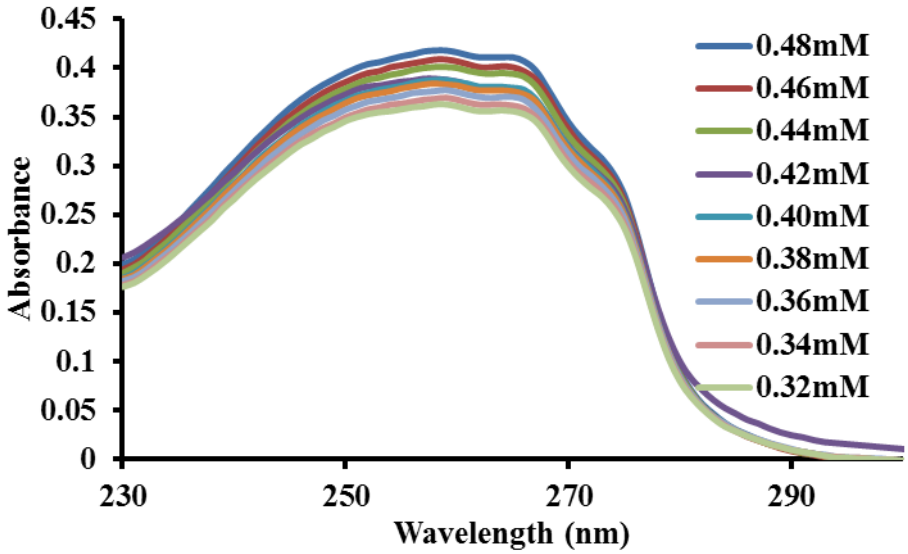
A73: Absorption spectra of drug Flurbiprofen without and with premicellar and post-micellar region of compound a7



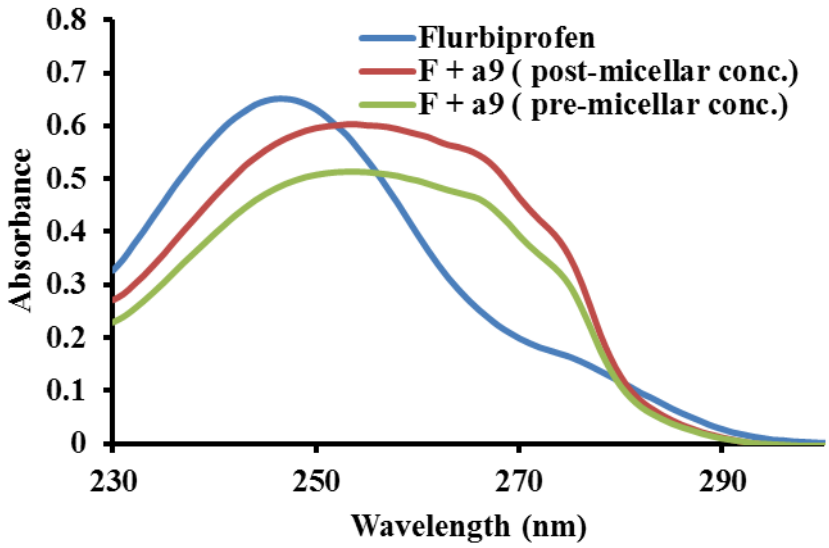
A74: With different concentrations of compound a7, absorption spectra of drug Flurbiprofen.



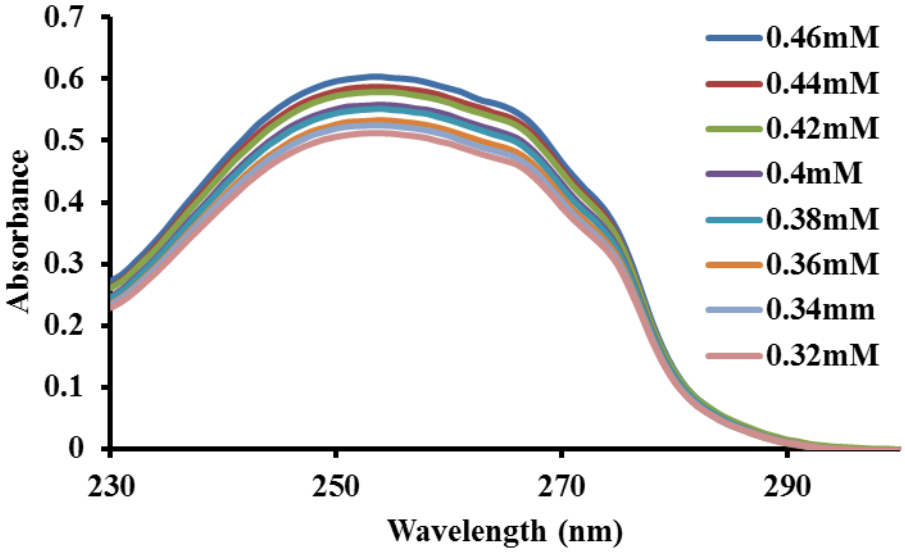
A75: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a8.



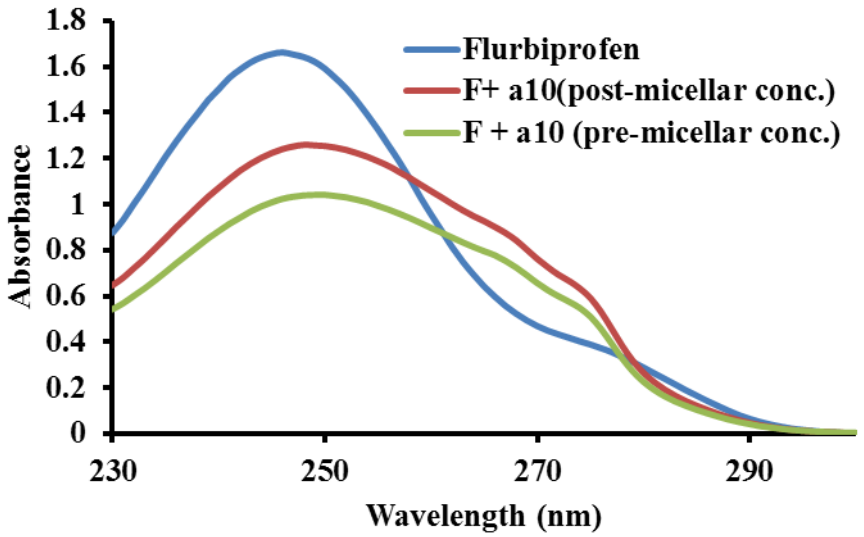
A76: With different concentrations of compound a8, absorption spectra of drug Flurbiprofen.



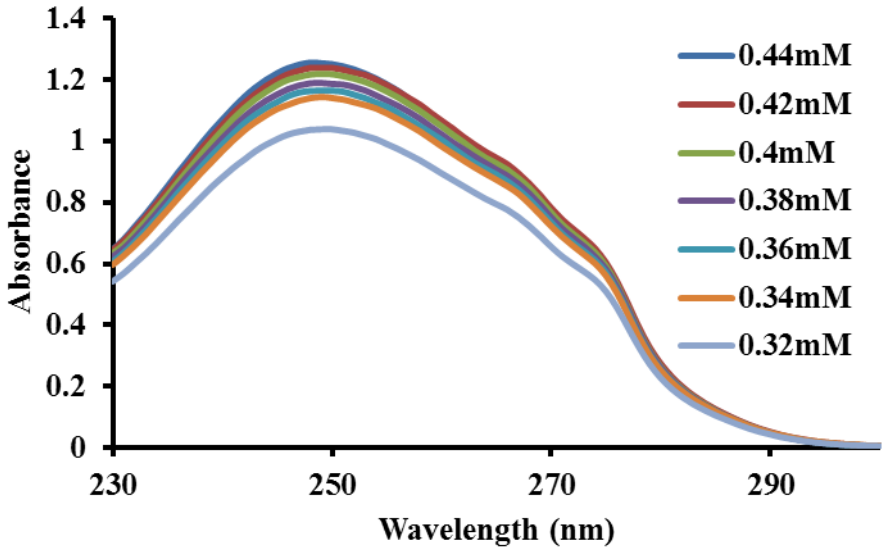
A77: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a9.



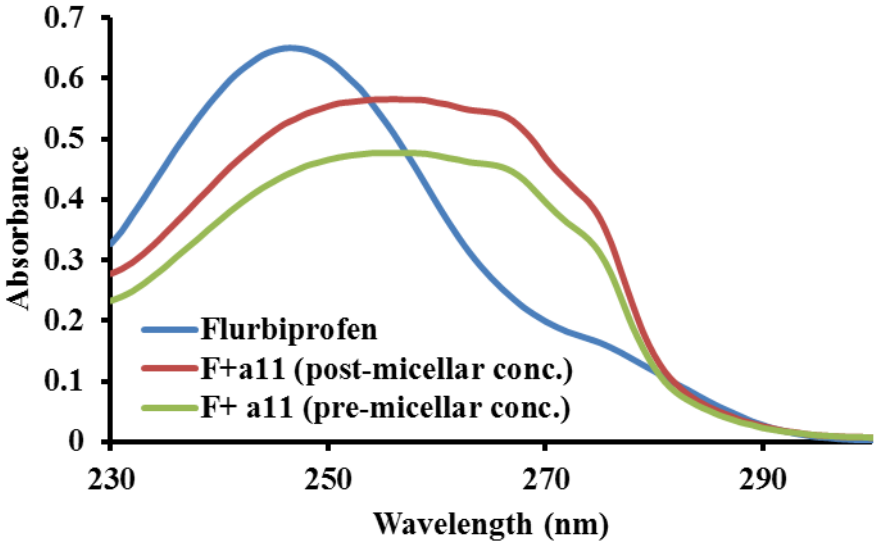
A78: With different concentrations of compound a9, absorption spectra of drug Flurbiprofen.



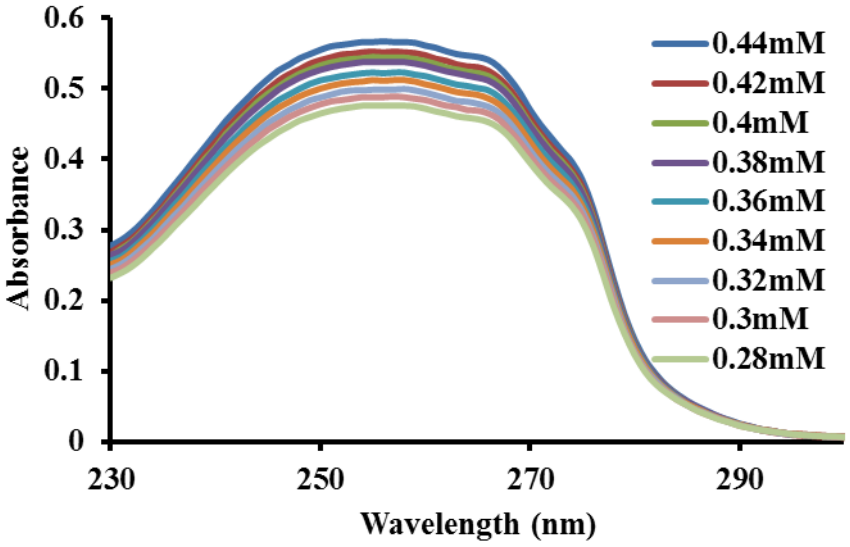
A79: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a10.



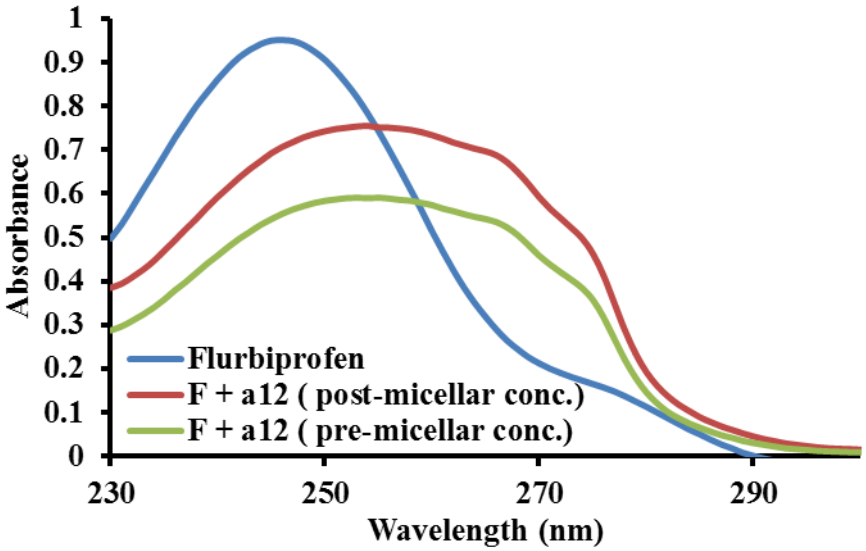
A80: With different concentrations of compound a10, absorption spectra of drug Flurbiprofen.



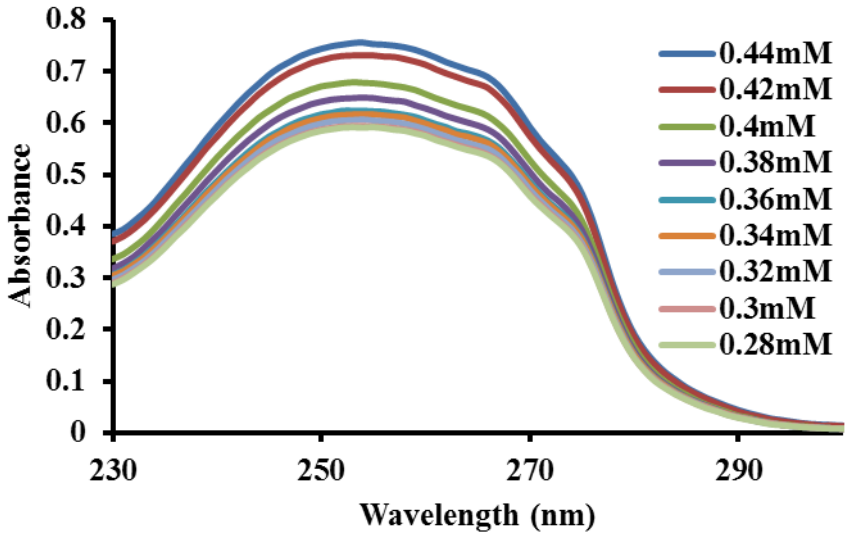
A81: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a11.



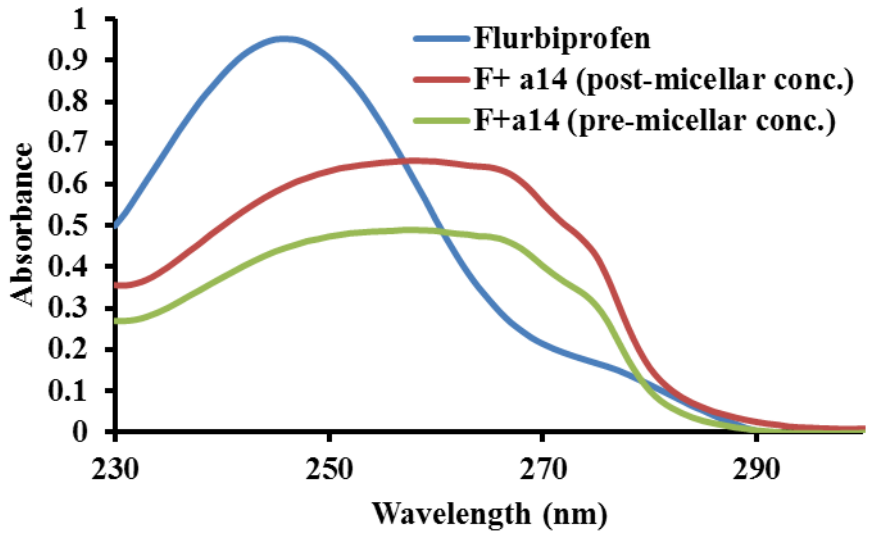
A82: With different concentrations of compound a11, absorption spectra of drug Flurbiprofen.



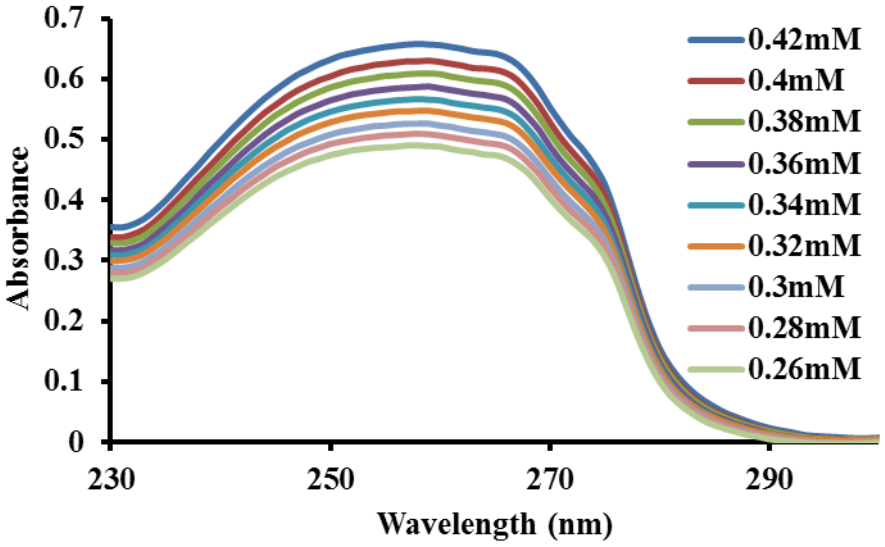
A83: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a12.



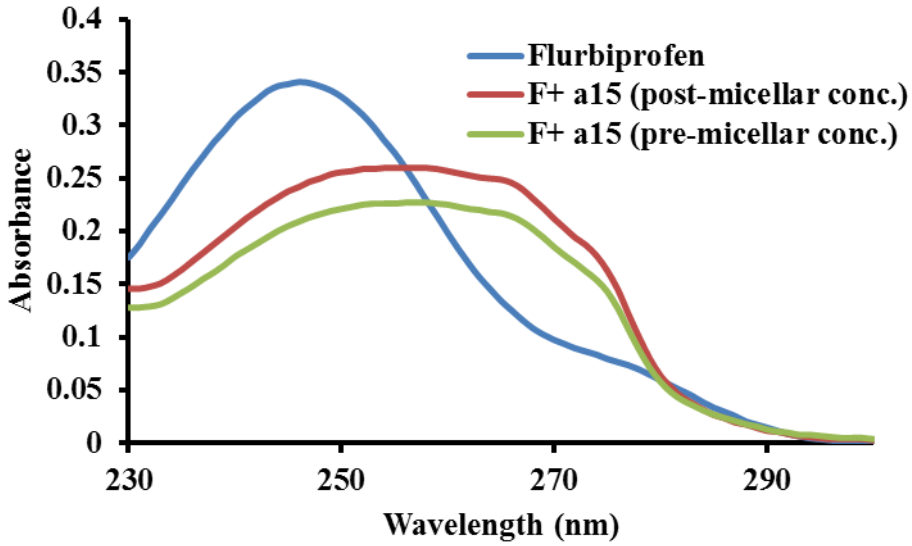
A84: With different concentrations of compound a12, absorption spectra of drug Flurbiprofen.



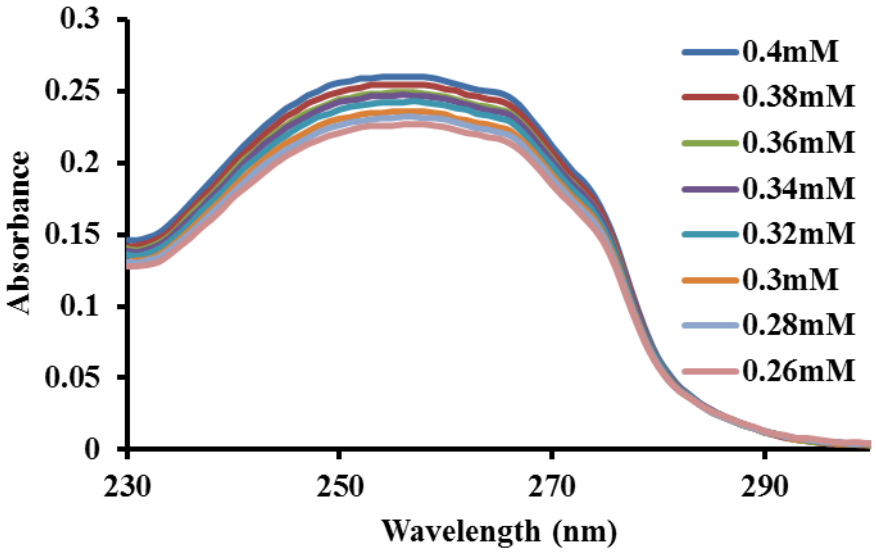
A85: Absorption spectra of drug Flurbiprofen without and with premicellar and post-micellar region of compound a14.



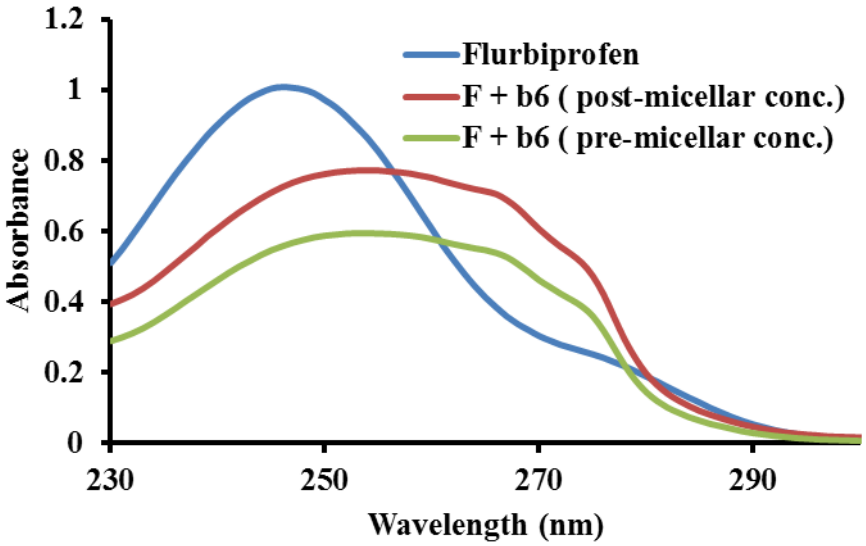
A86: With different concentrations of compound a14, absorption spectra of drug Flurbiprofen



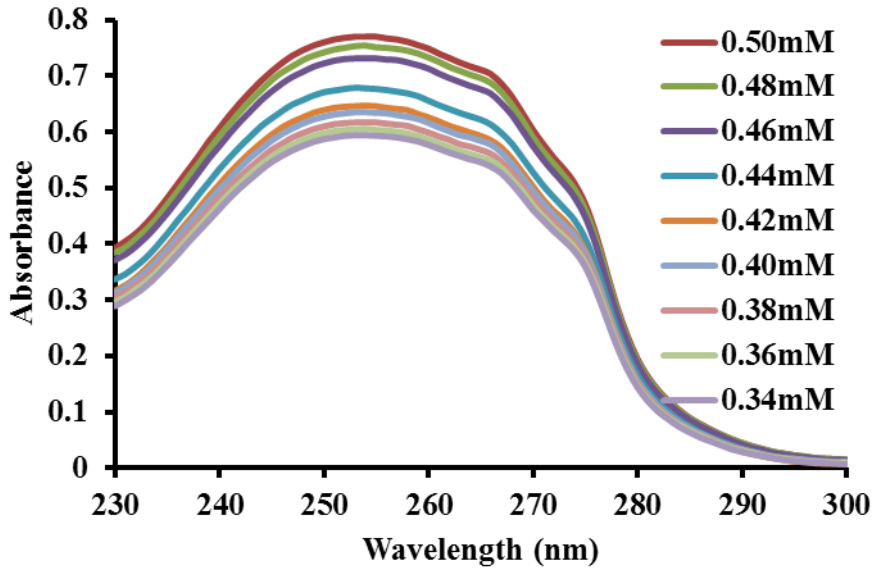
A87: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound a15.



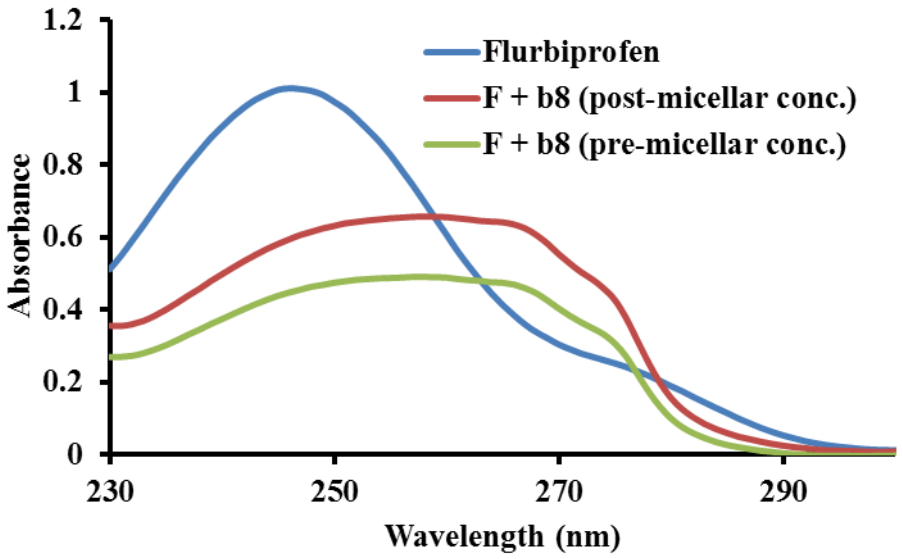
A88: With different concentrations of compound a15, absorption spectra of drug Flurbiprofen.



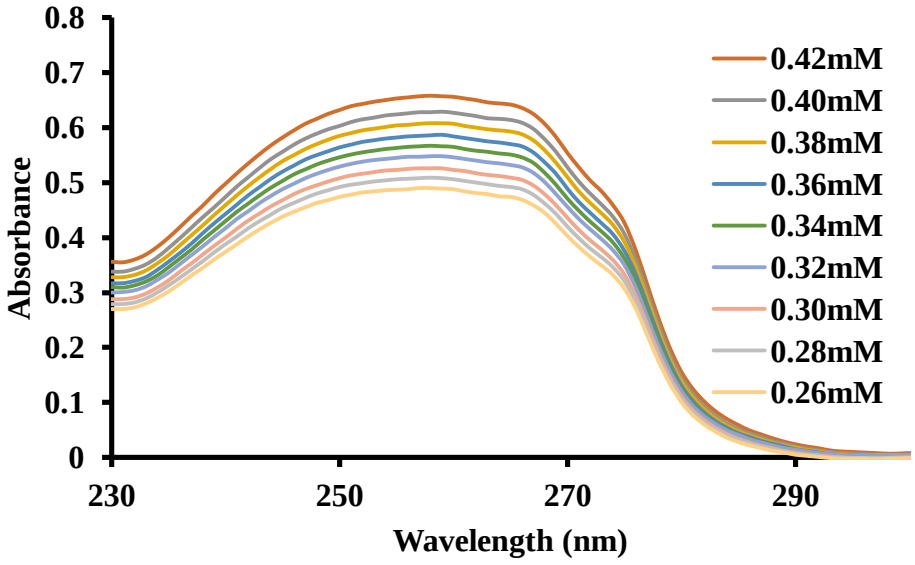
A89: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound b6.



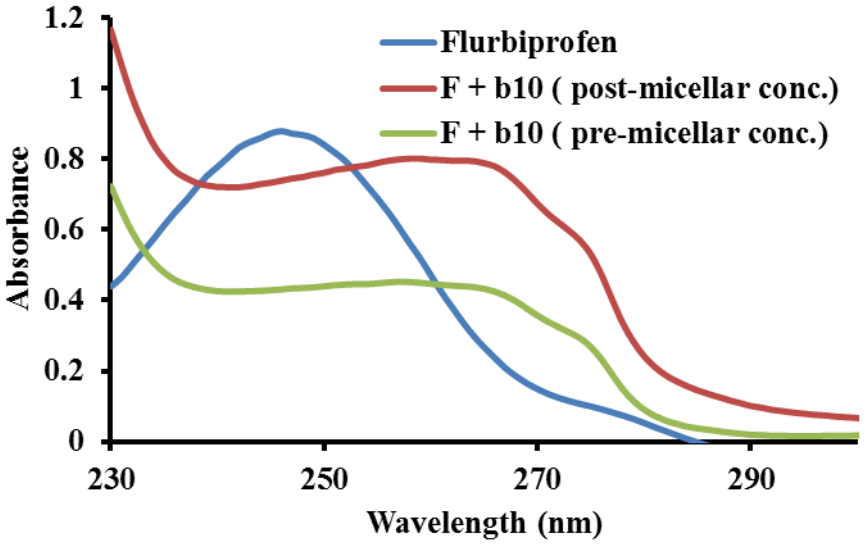
A90: With different concentrations of compound b6, absorption spectra of drug Flurbiprofen.



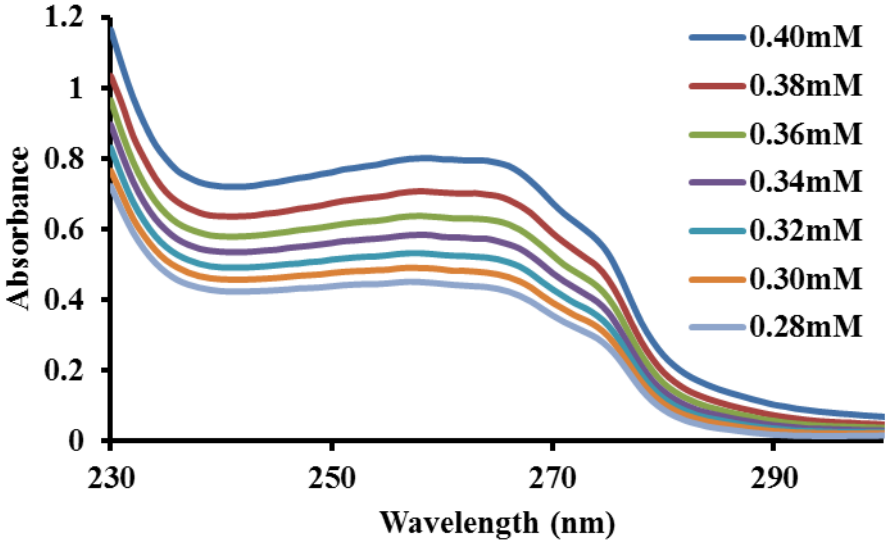
A91: Absorption spectra of drug Flurbiprofen without and with premicellar and post-micellar region of compound b8.



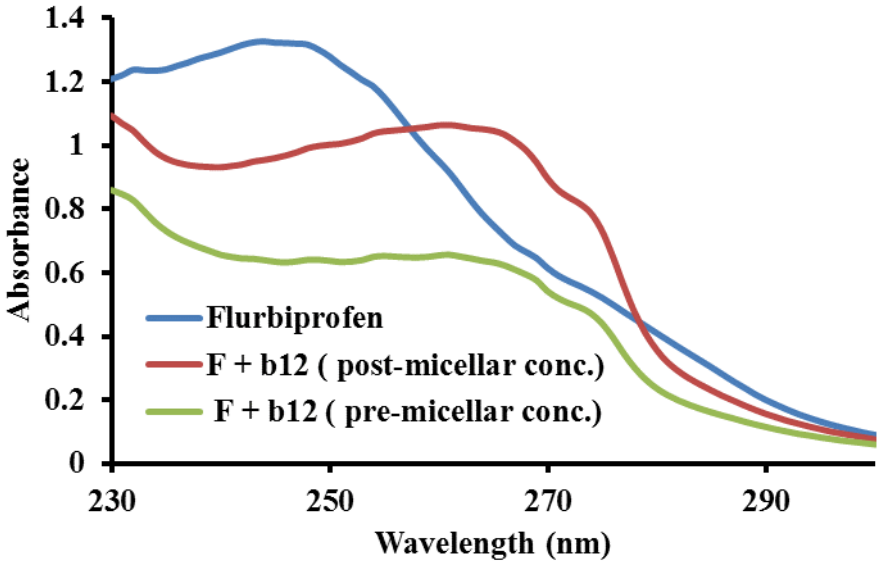
A92: With different concentrations of compound b8, absorption spectra of drug Flurbiprofen.



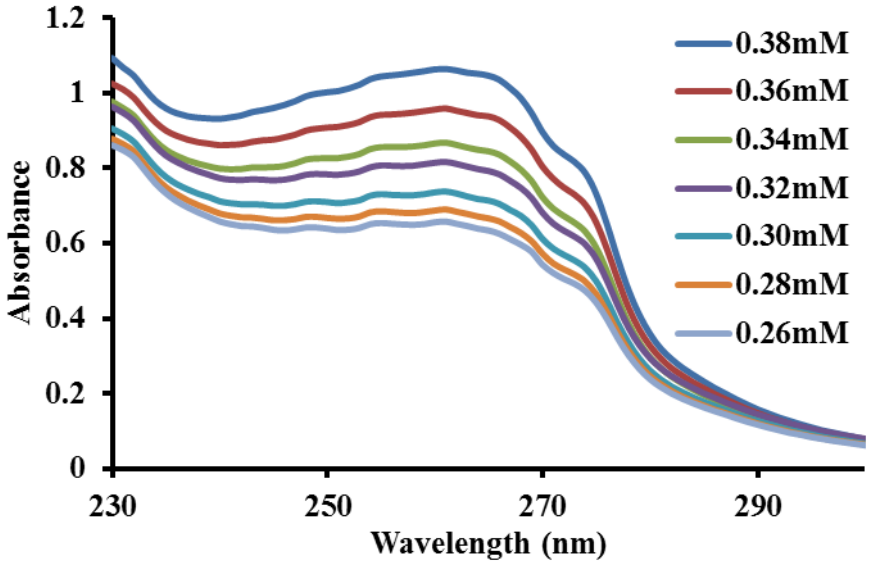
A93: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound b10.



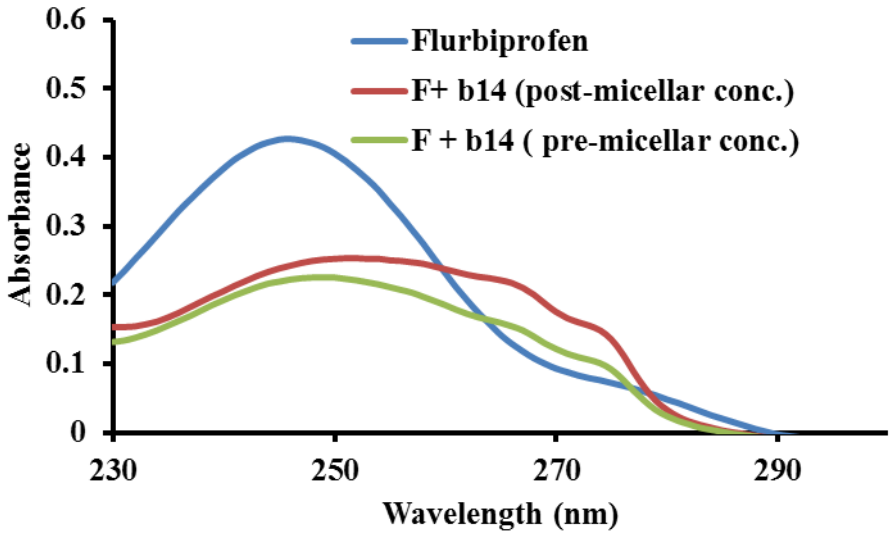
A94: With different concentrations of compound b10, absorption spectra of drug Flurbiprofen.



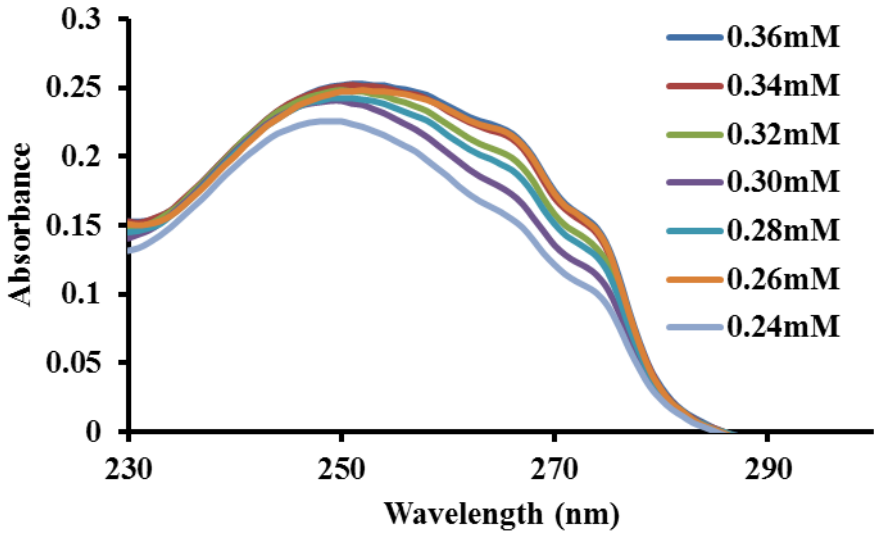
A95: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound b12.



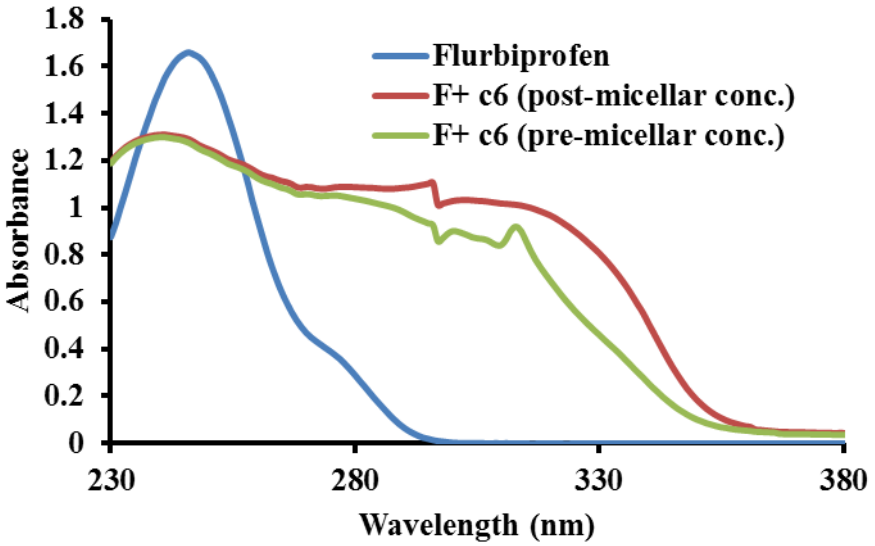
A96: With different concentrations of compound b12, absorption spectra of drug Flurbiprofen.



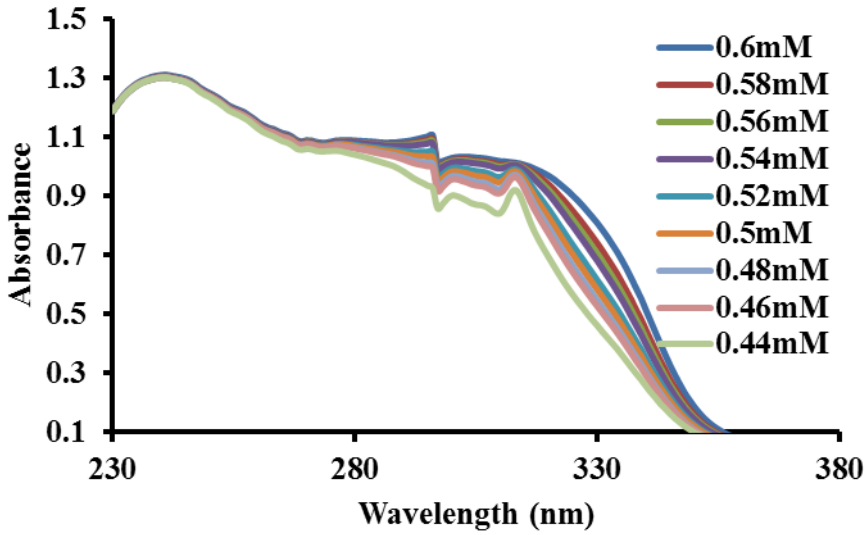
A97: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound b14.



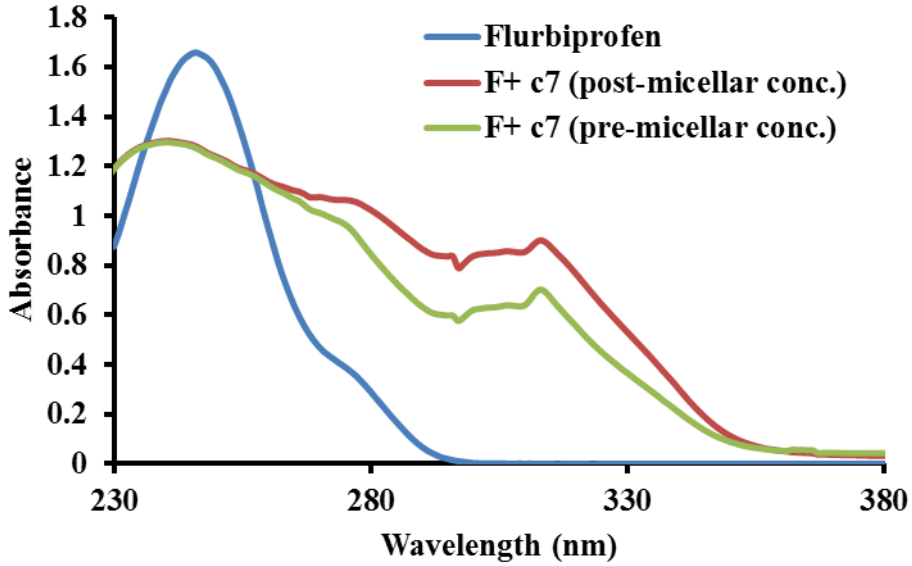
A98: With different concentrations of compound b14, absorption spectra of drug Flurbiprofen.



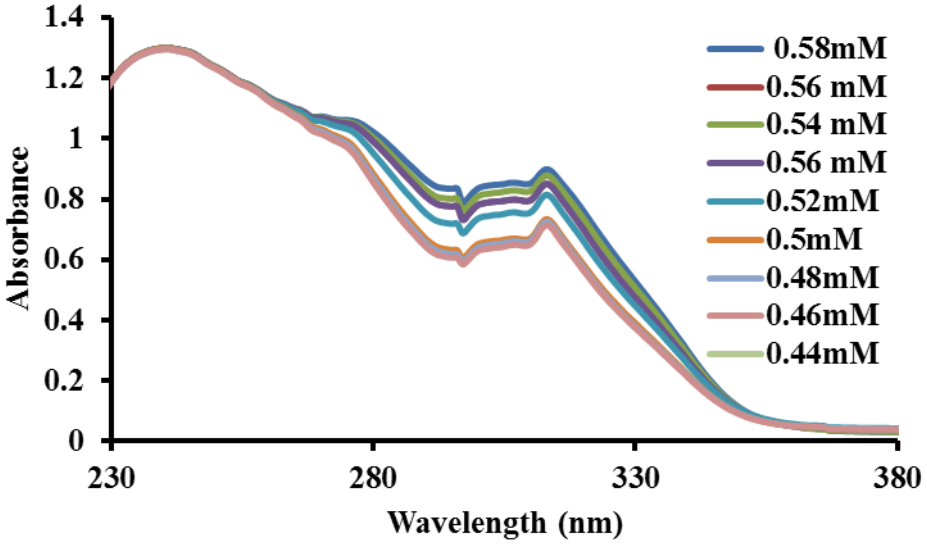
A99: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c6.



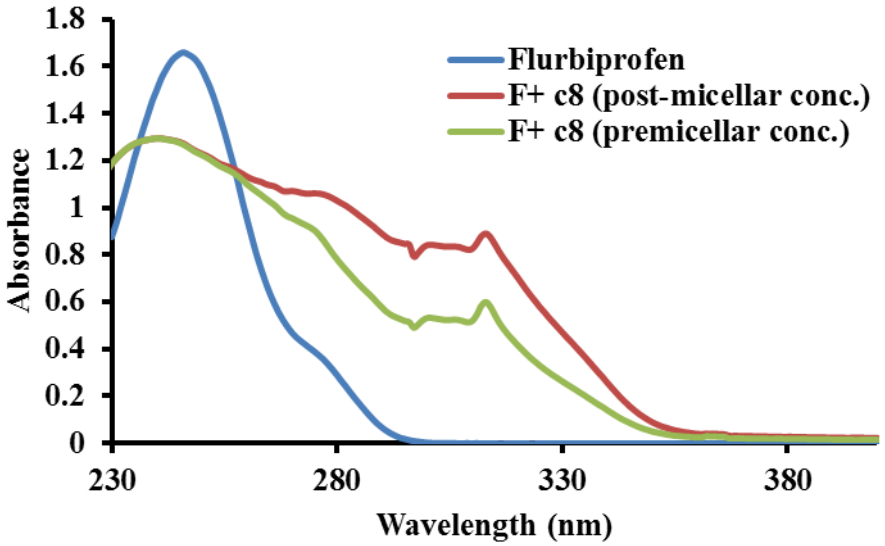
A100: With different concentrations of compound c6, absorption spectra of drug Flurbiprofen



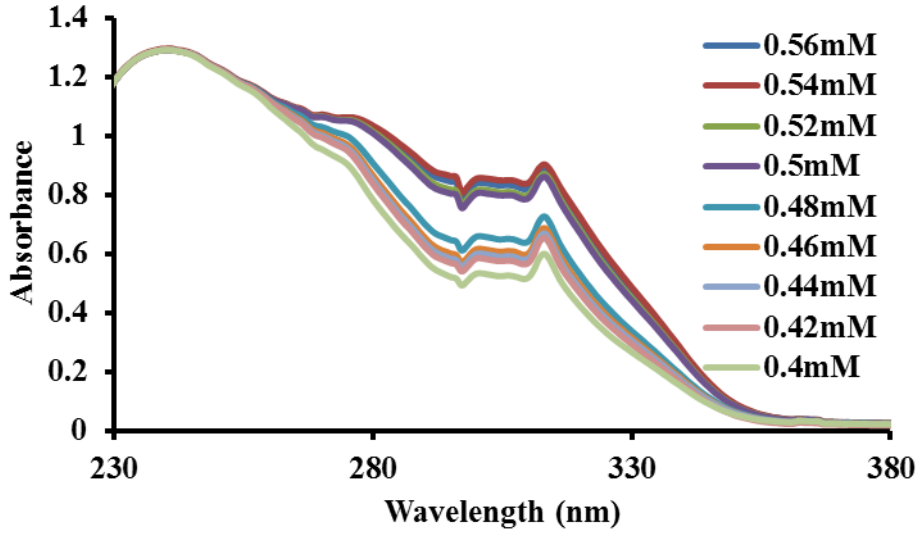
A101: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c7.



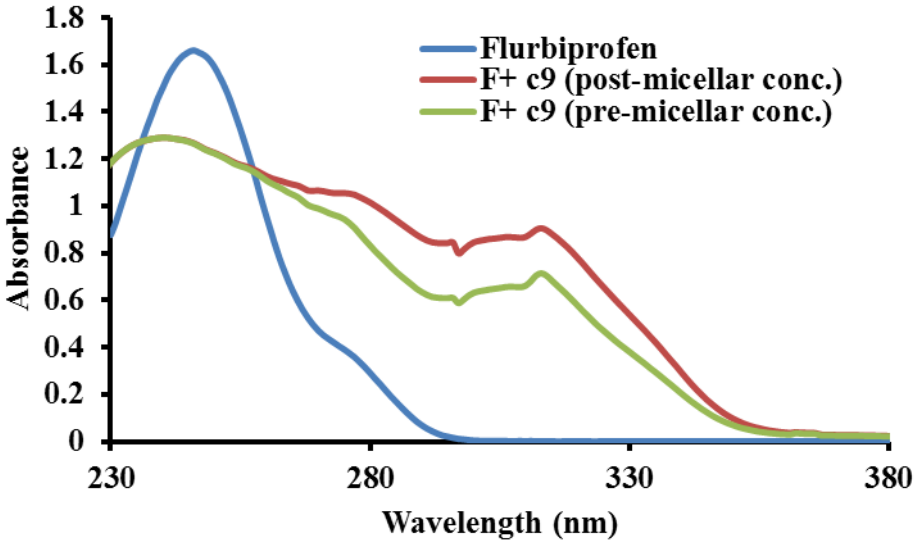
A102: With different concentrations of compound c7, absorption spectra of drug Flurbiprofen



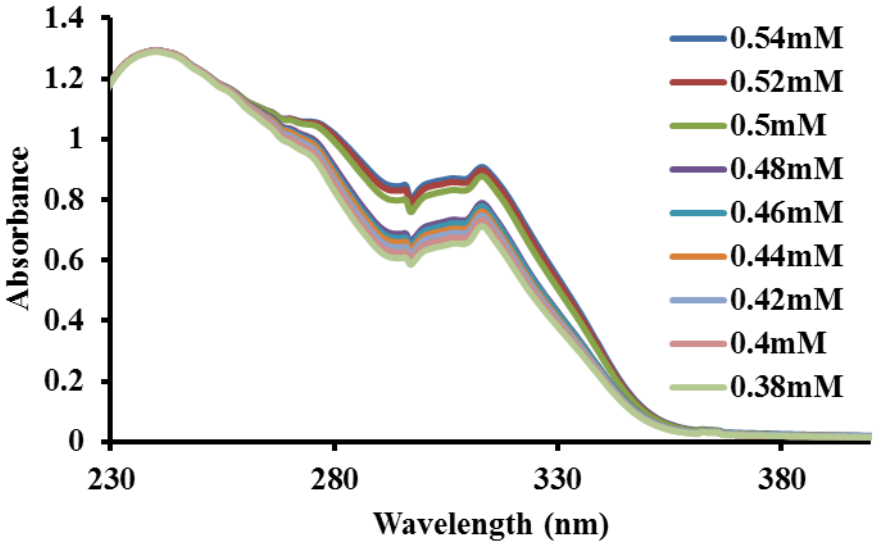
A103: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c8.



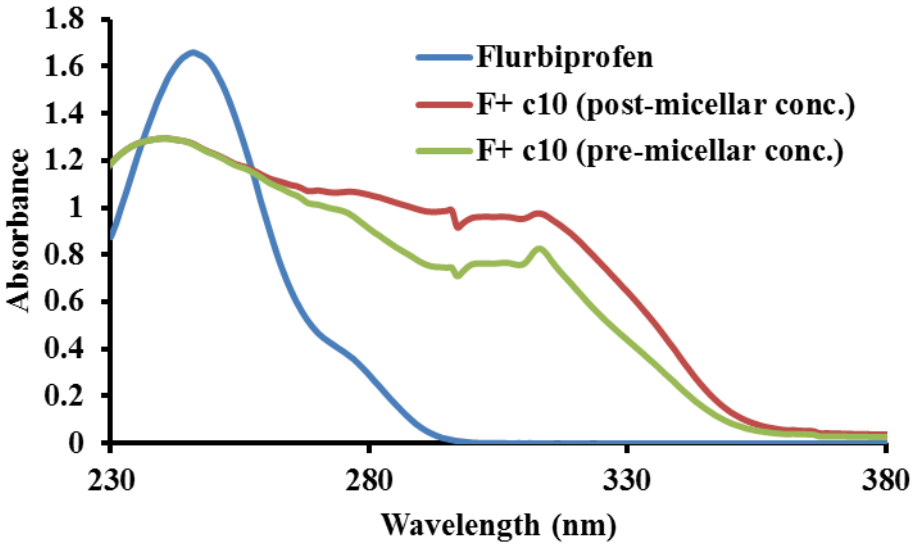
A104: With different concentrations of compound c8, absorption spectra of drug Flurbiprofen.



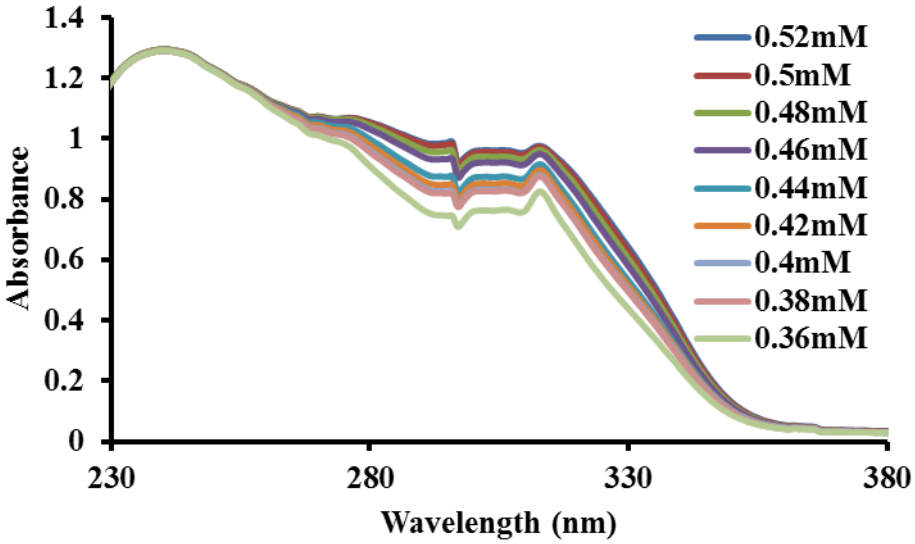
A105: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c9.



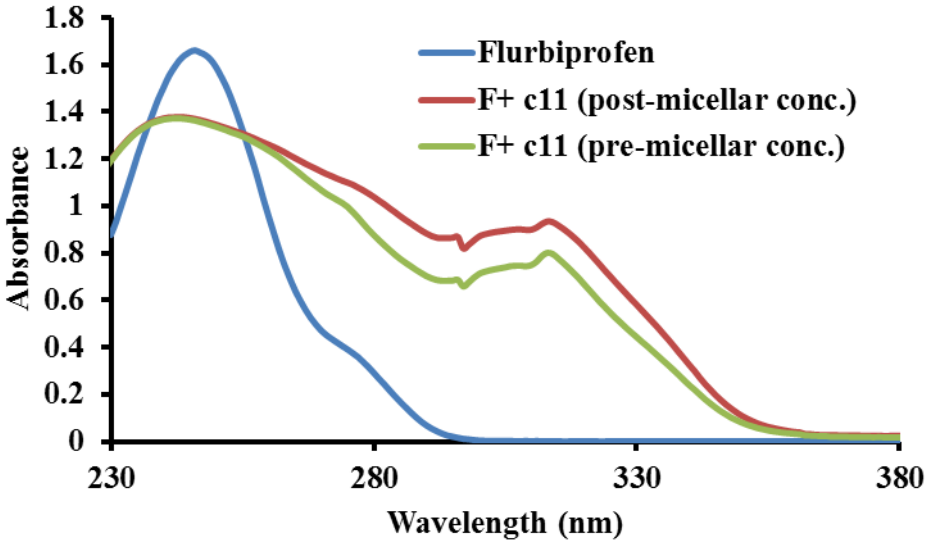
A106: With different concentrations of compound c9, absorption spectra of drug Flurbiprofen.



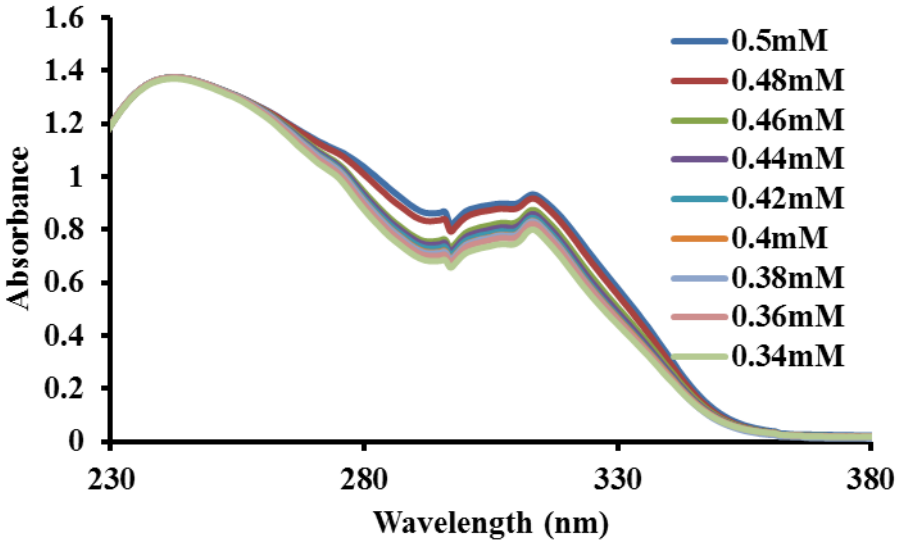
A107: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c10.



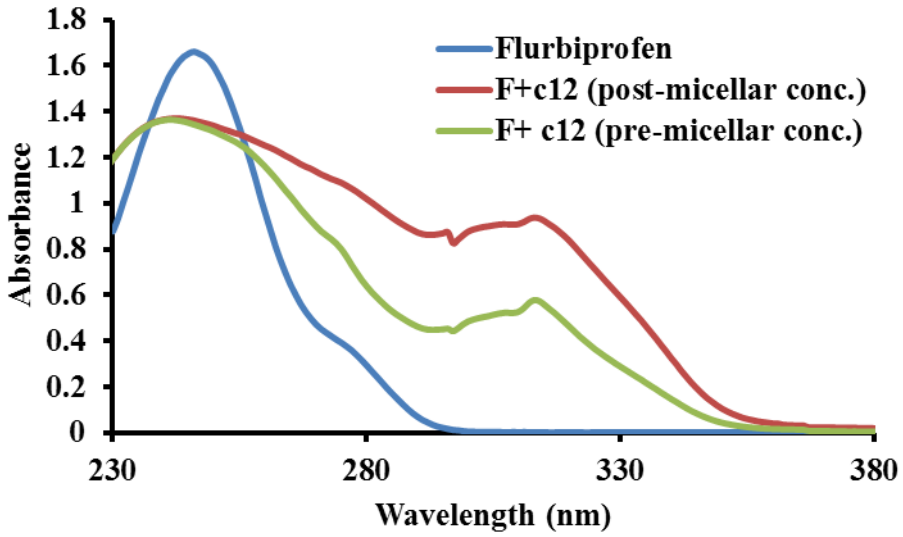
A 108: With different concentrations of compound c10, absorption spectra of drug Flurbiprofen.



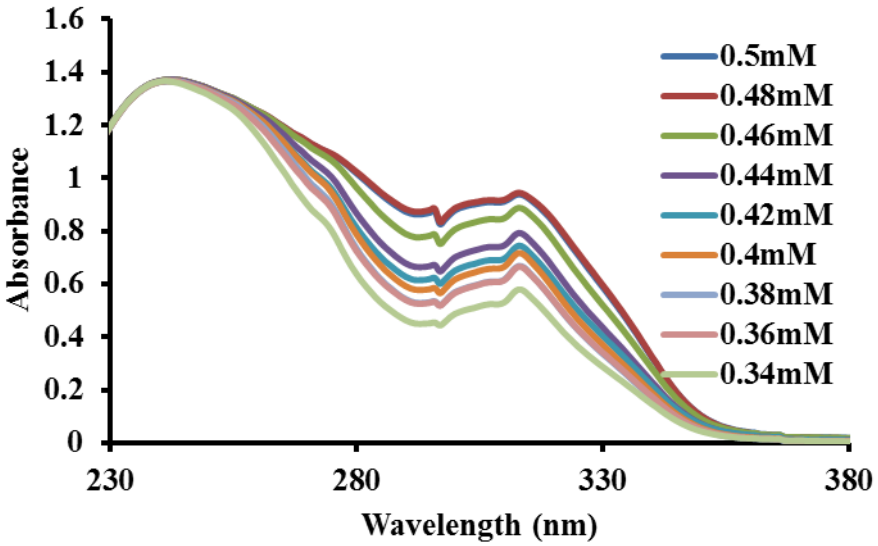
A109: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c11.



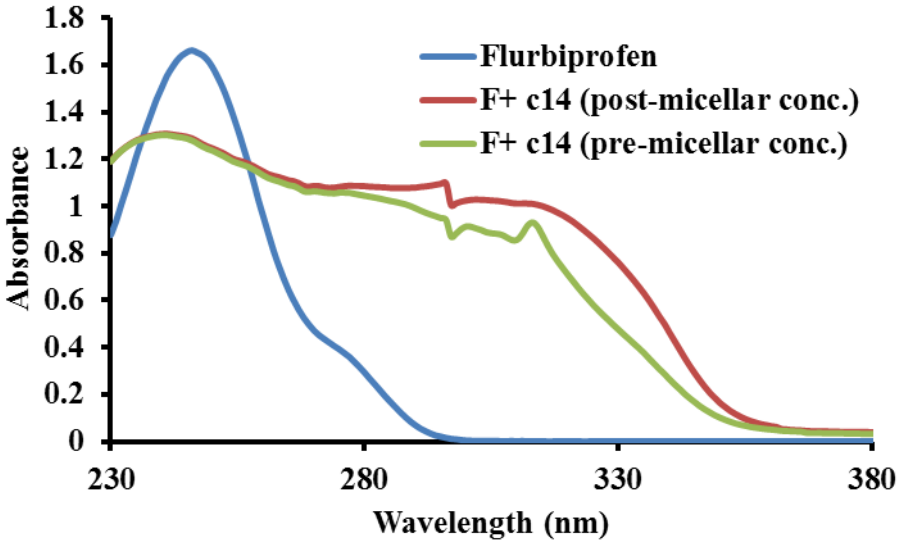
A110: With different concentrations of compound c11, absorption spectra of drug Flurbiprofen.



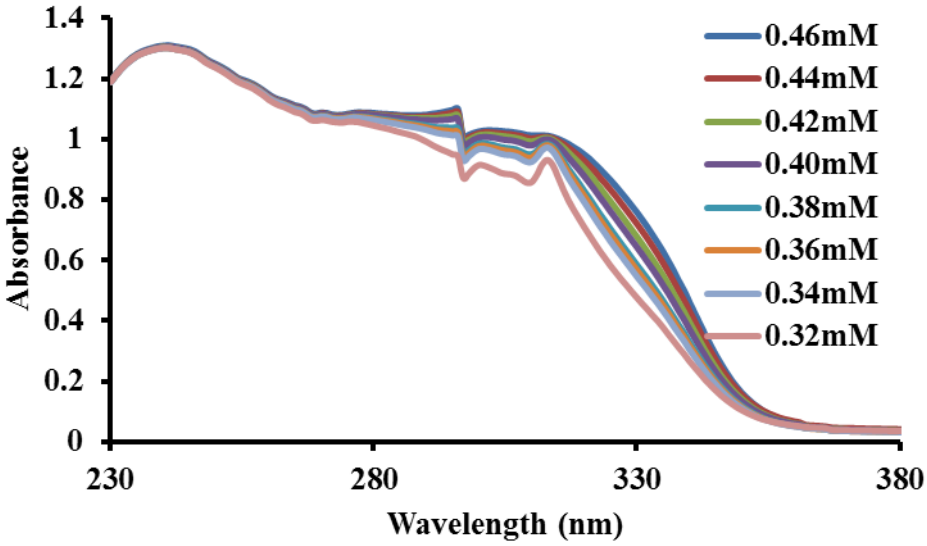
A111: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c12.



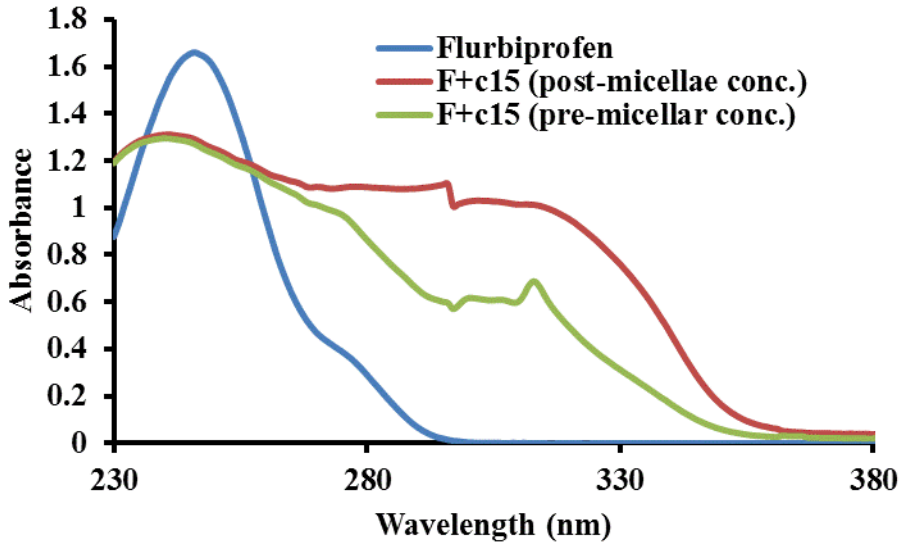
A112: With different concentrations of compound c12, absorption spectra of drug Flurbiprofen.



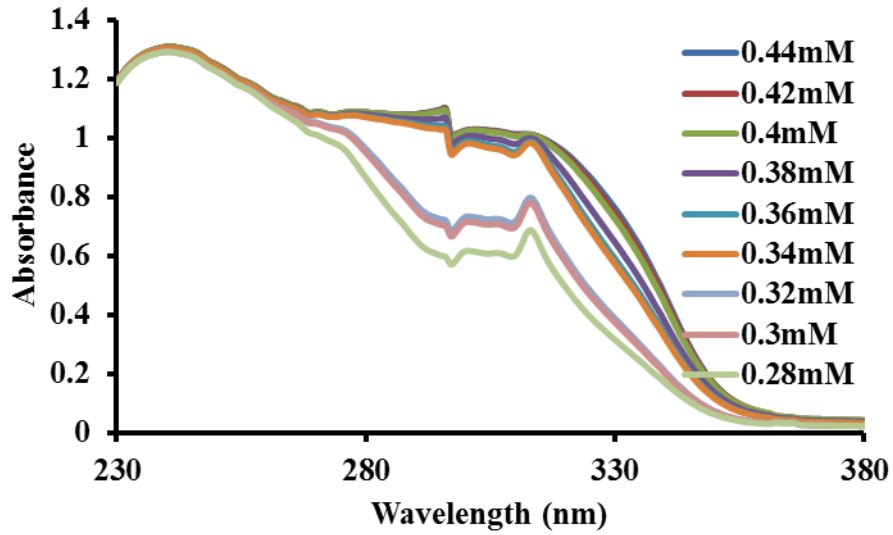
A113: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c14



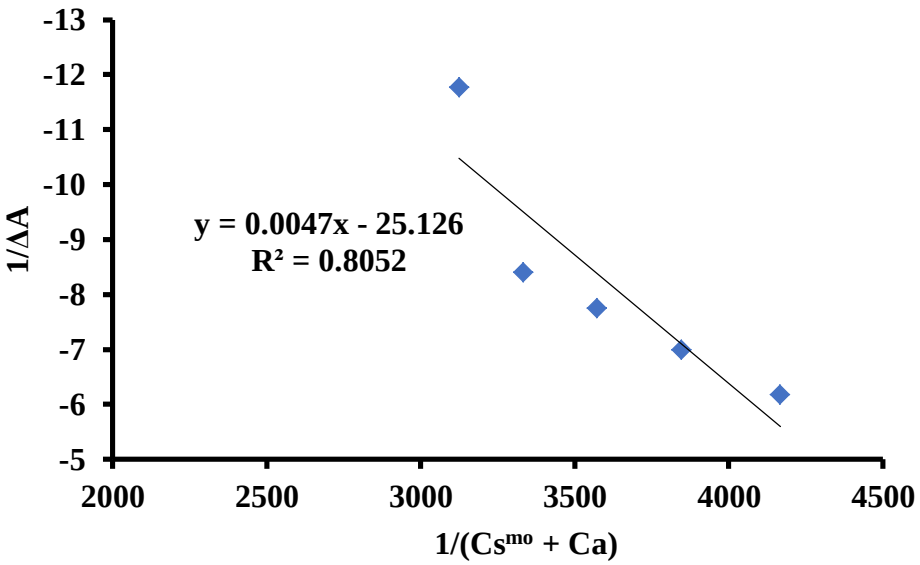
A114: With different concentrations of compound c14, absorption spectra of drug Flurbiprofen.



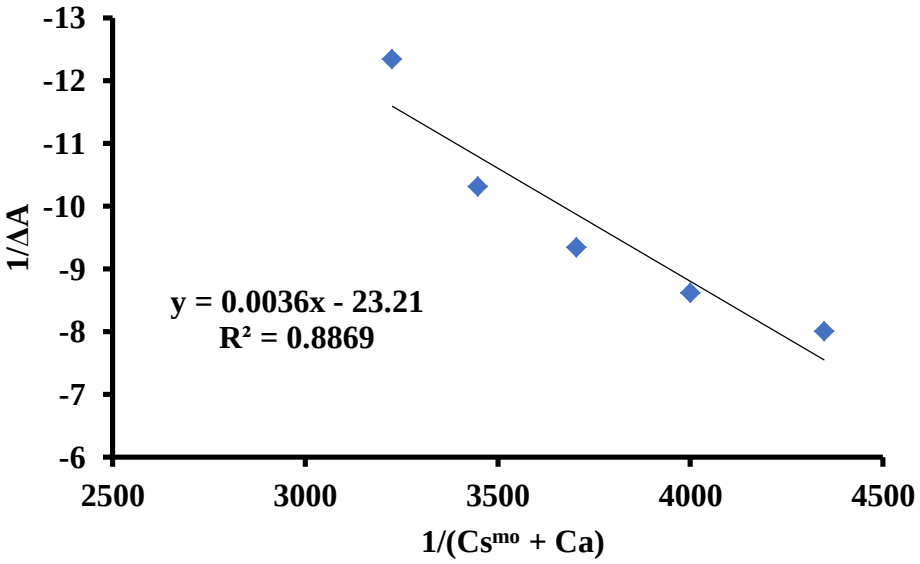
A115: Absorption spectra of drug Flurbiprofen without and with pre-micellar and post-micellar region of compound c15



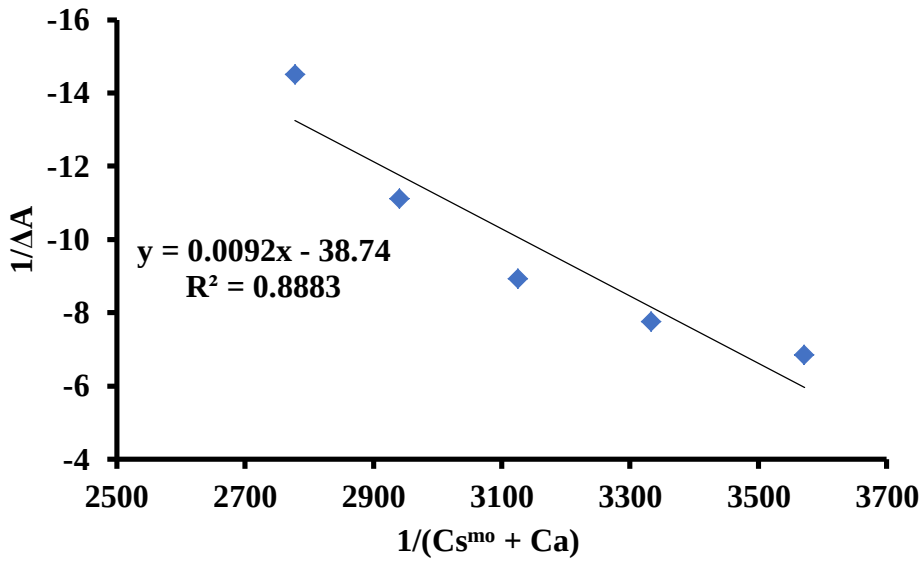
A116: With different concentrations of compound c15, absorption spectra of drug Flurbiprofen.



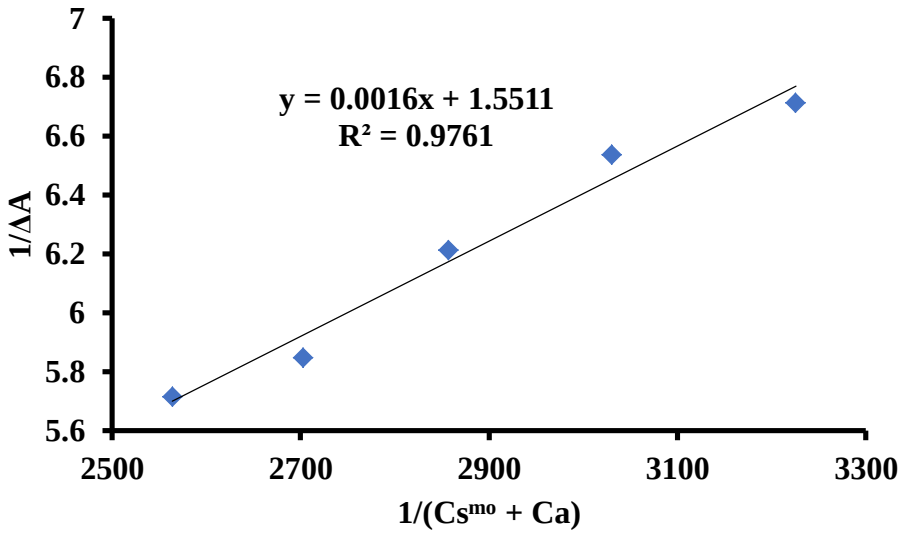
A117: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a7 + Ketoprofen.



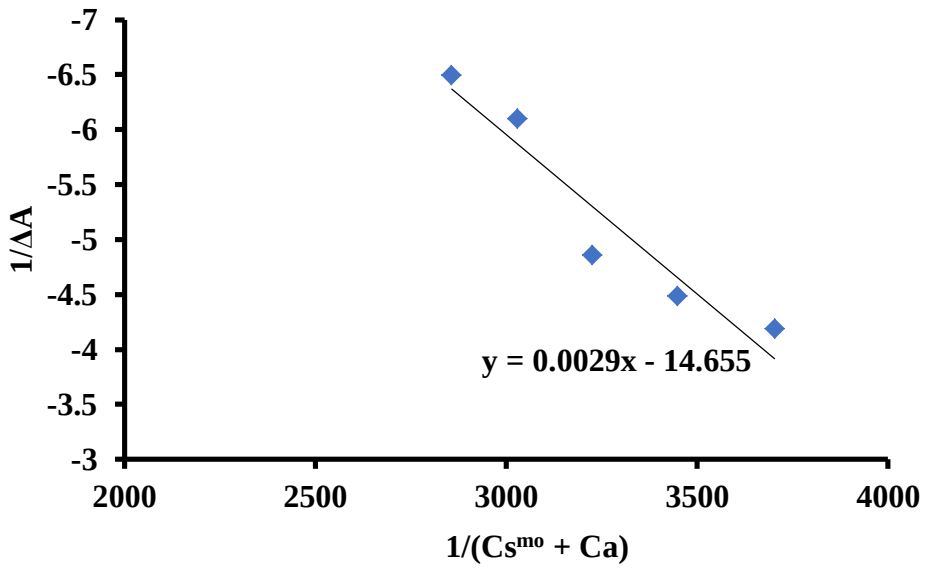
A118: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a8 + Ketoprofen.



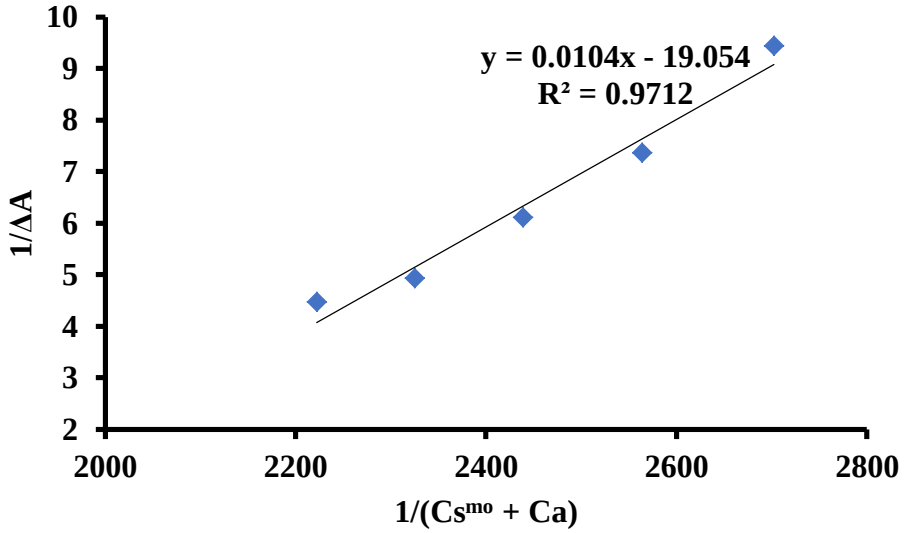
A119: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" + Ketoprofen.



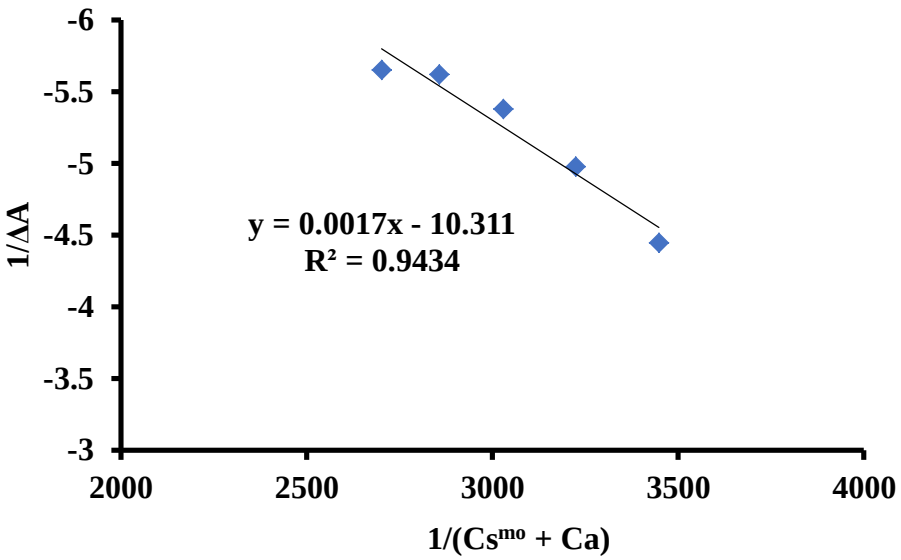
A120: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a10 + Ketoprofen.



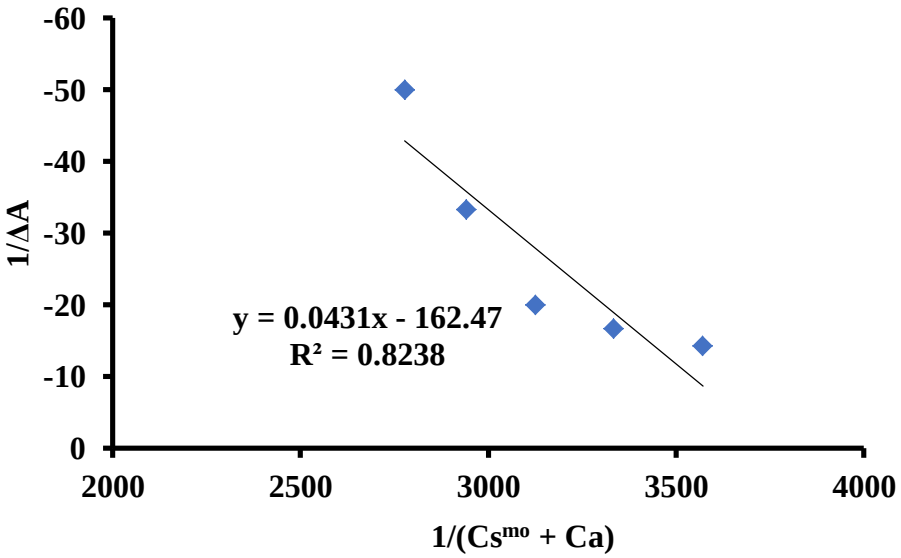
A121: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a11+ Ketoprofen.



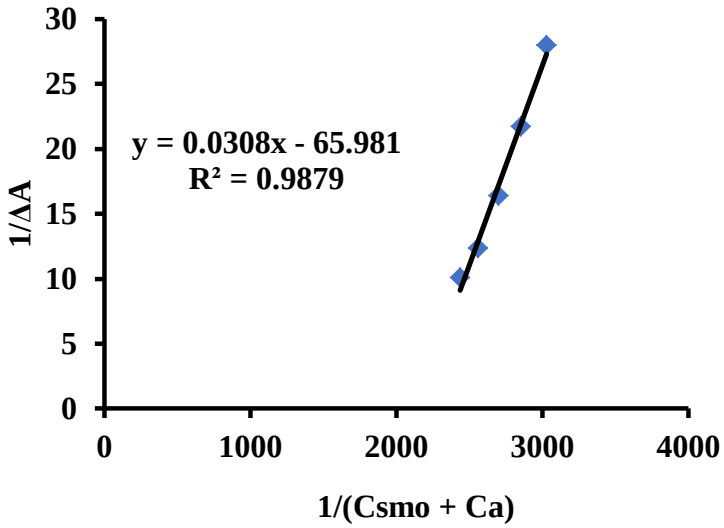
A122: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a12 + Ketoprofen.



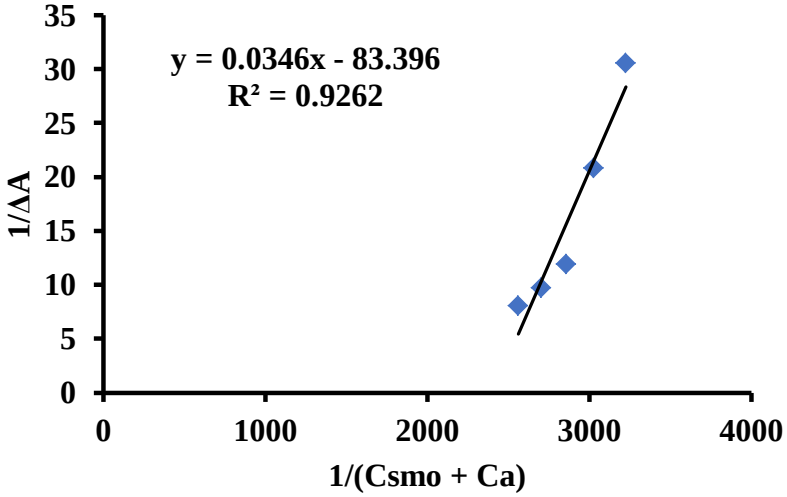
A123: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a14 + Ketoprofen.



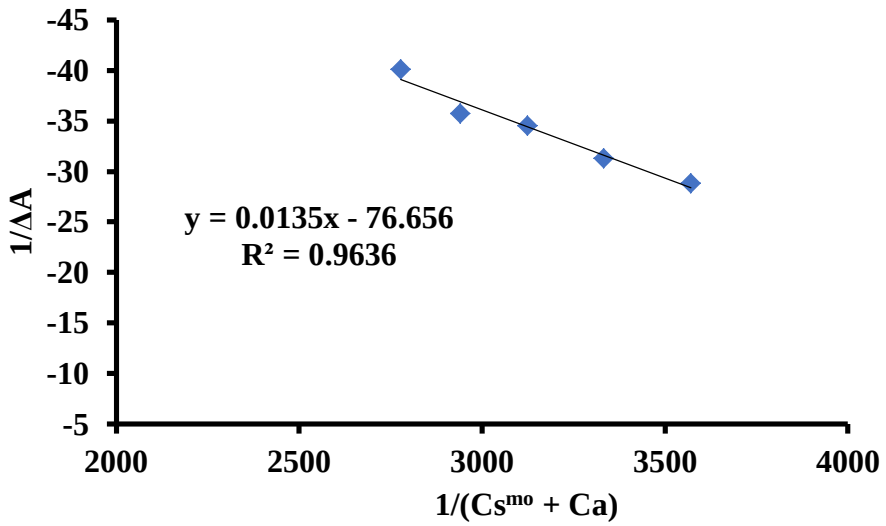
A124: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a15 + Ketoprofen.



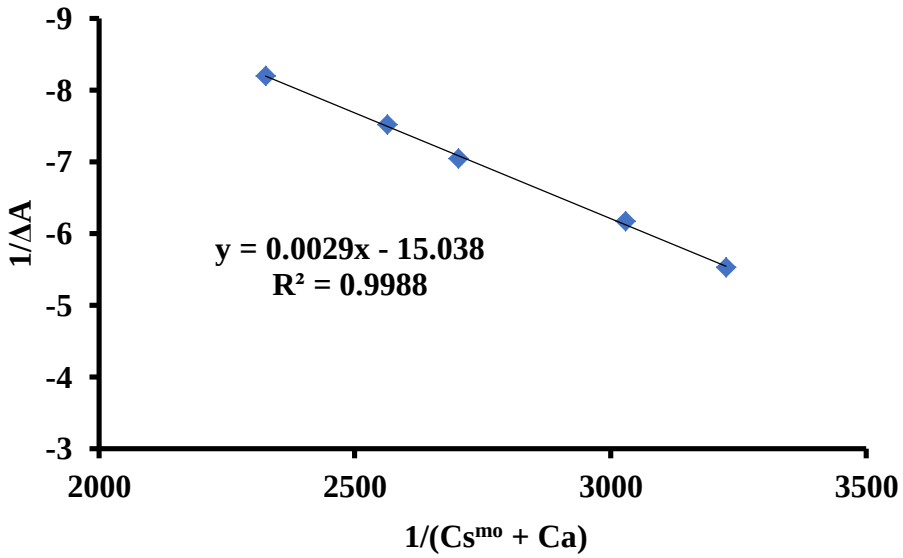
A125: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b6 + Ketoprofen.



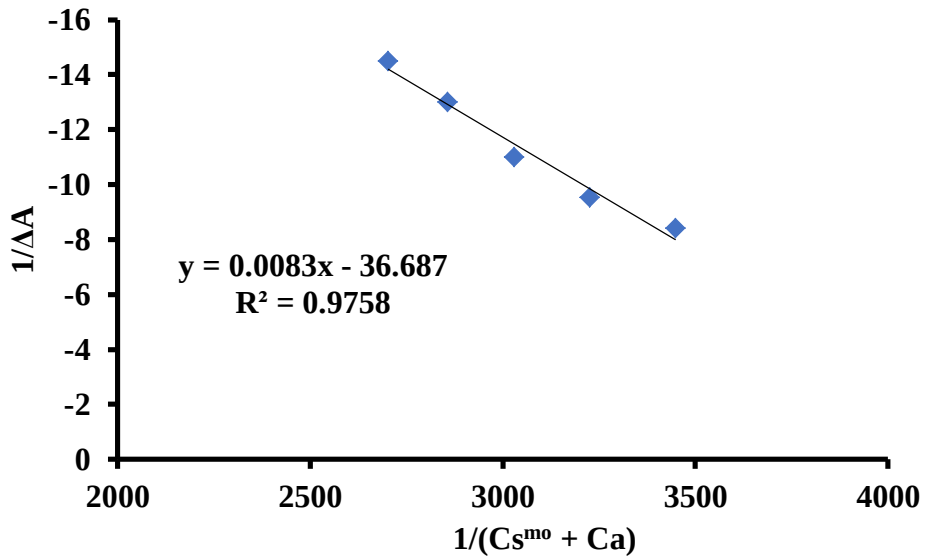
A126: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b8 + Ketoprofen.



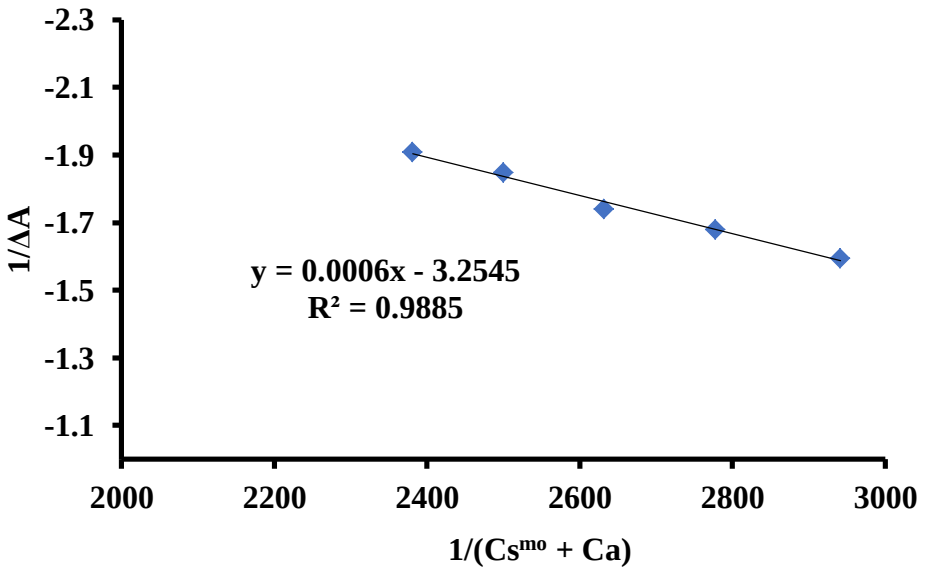
A127: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b10 + Ketoprofen.



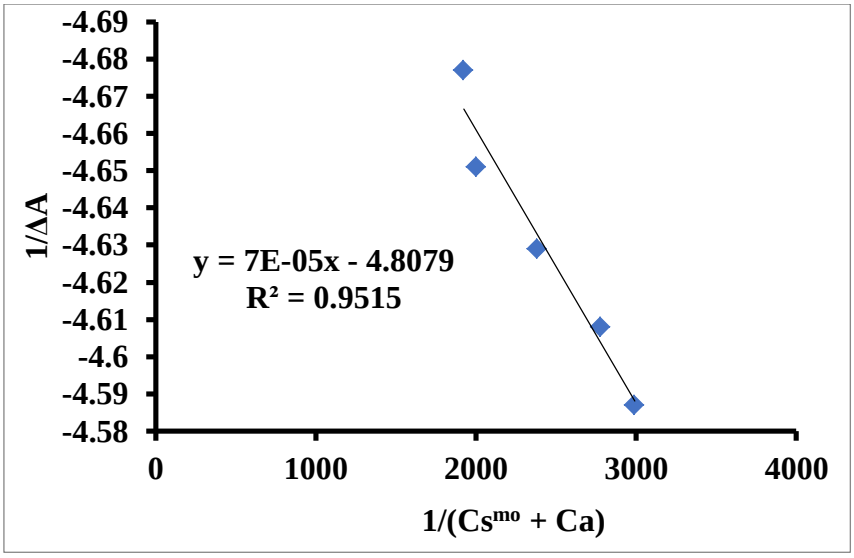
A128: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b12 + Ketoprofen.



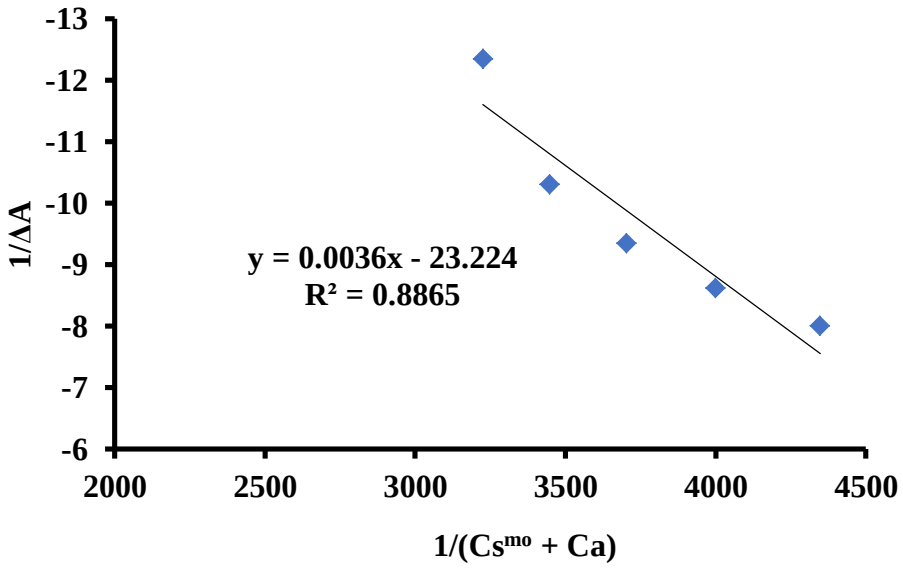
A129: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b14 + Ketoprofen.



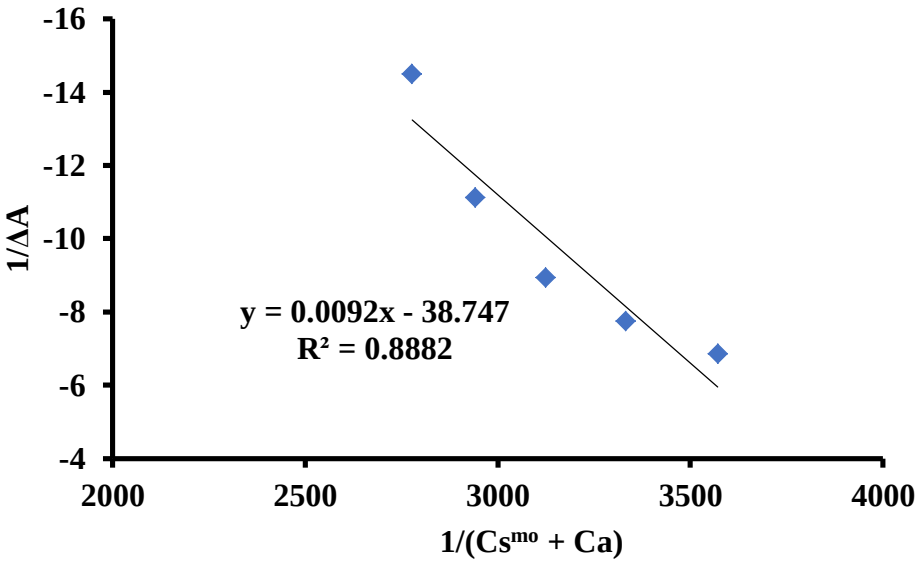
A130: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c6 + Ketoprofen.



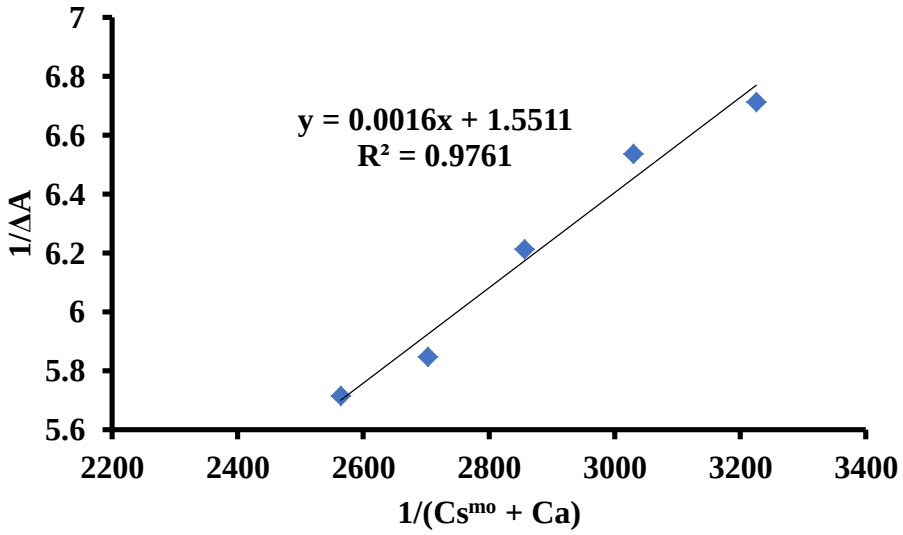
A131: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c7 + Ketoprofen.



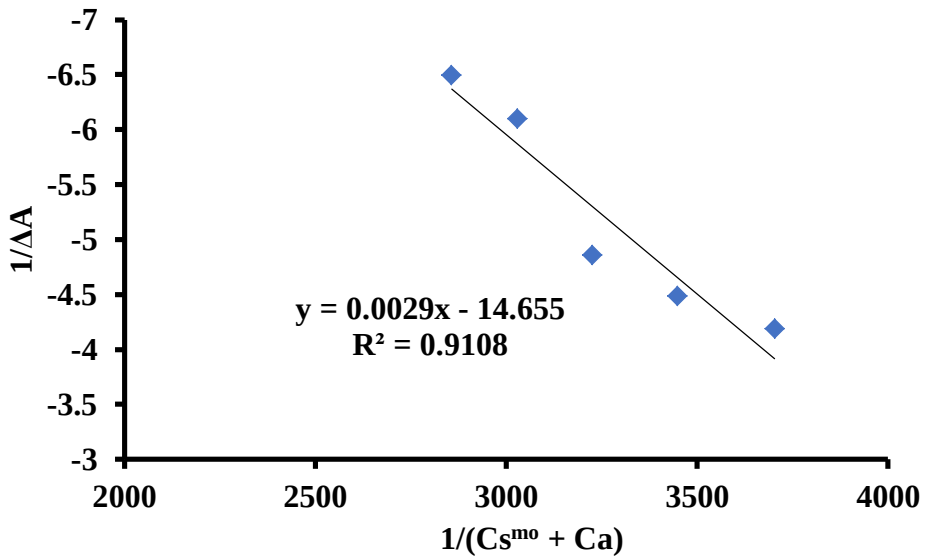
A132: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" + Ketoprofen.



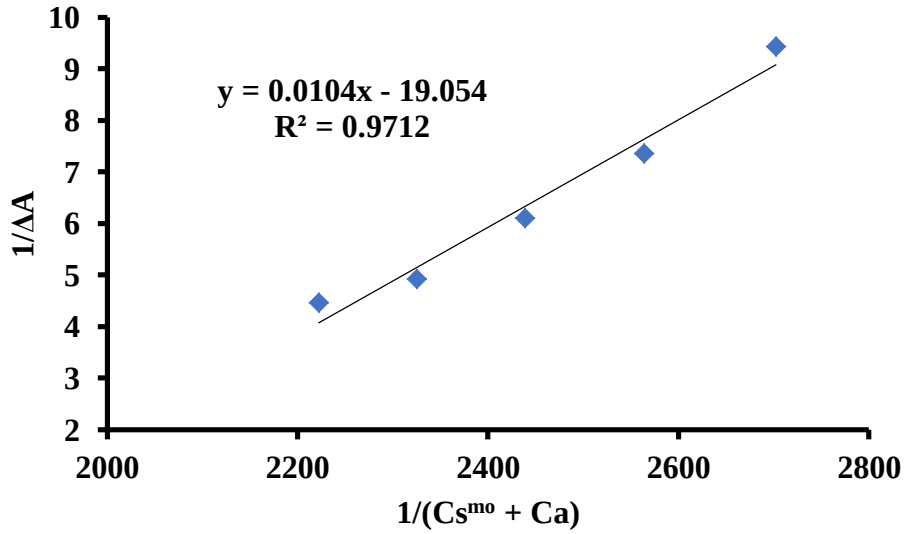
A133: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c9 + Ketoprofen.



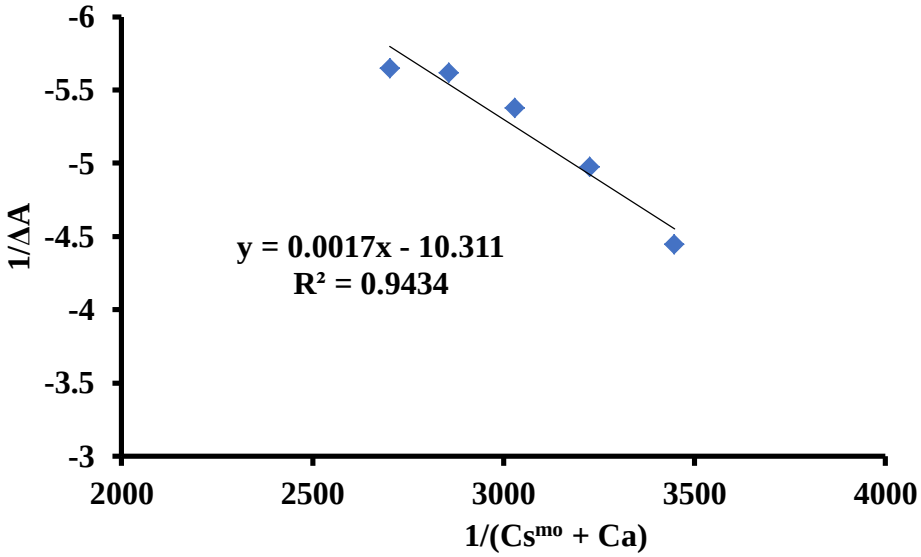
A134: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c10+ Ketoprofen.



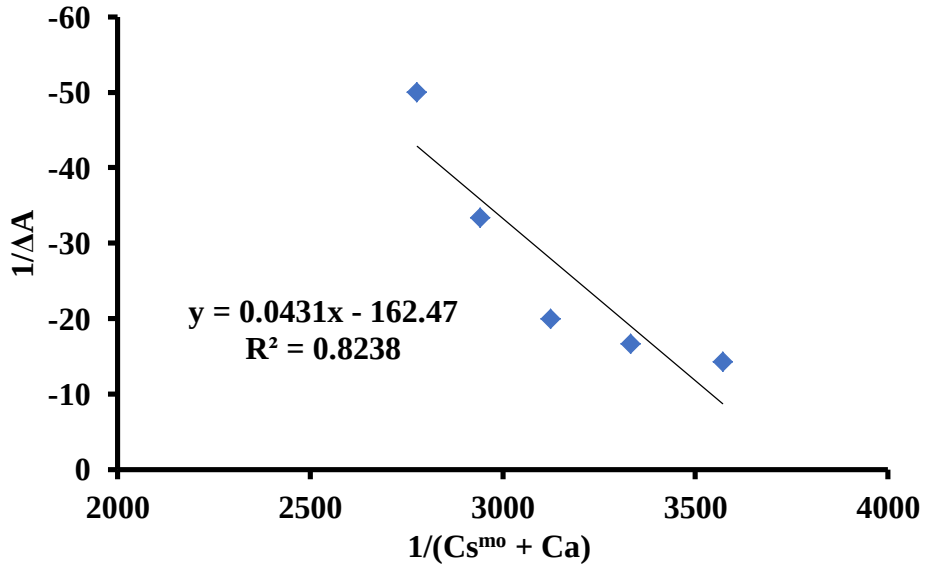
A135: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c11 + Ketoprofen.



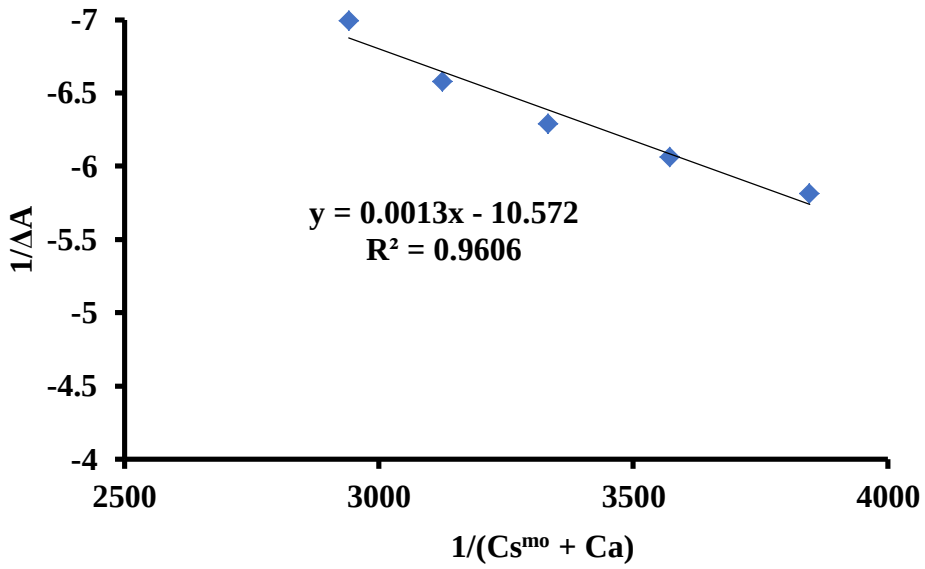
A136: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c12 + Ketoprofen.



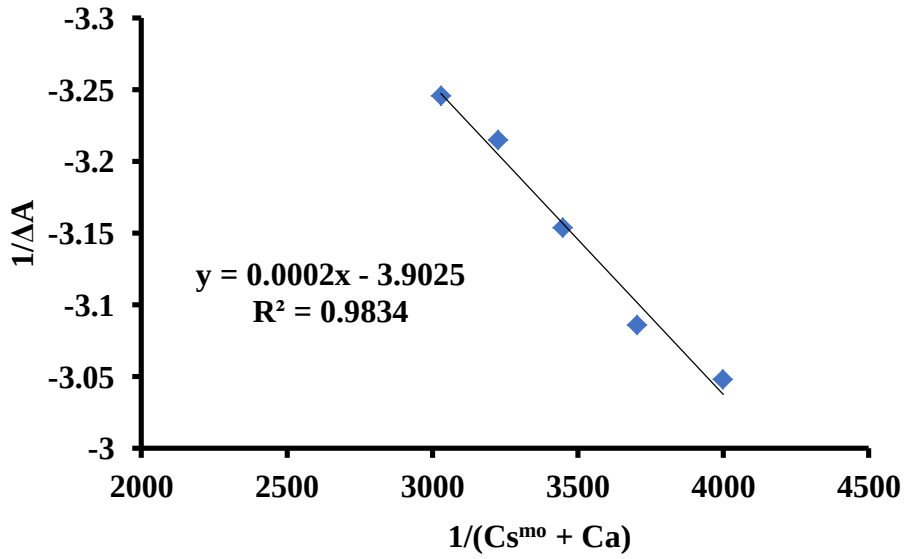
A137: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c14 + Ketoprofen.



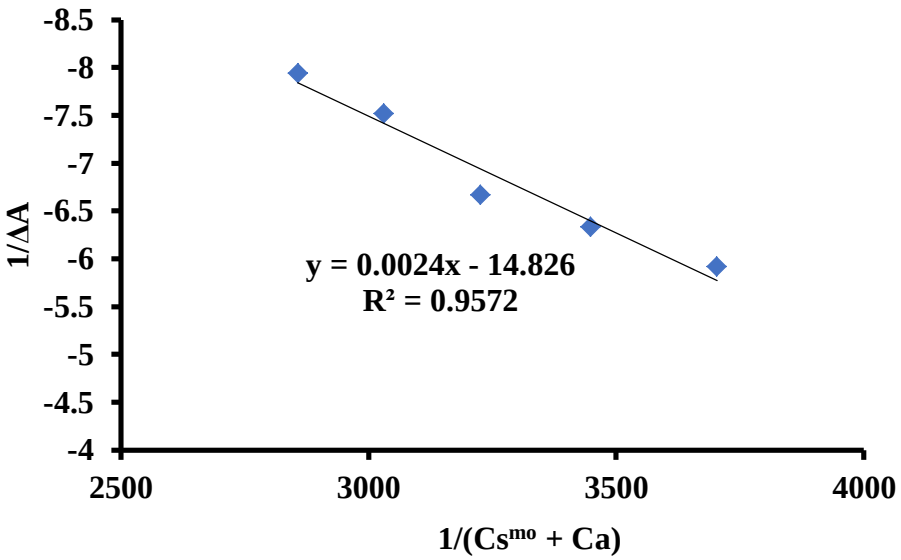
A138: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c15 + Ketoprofen.



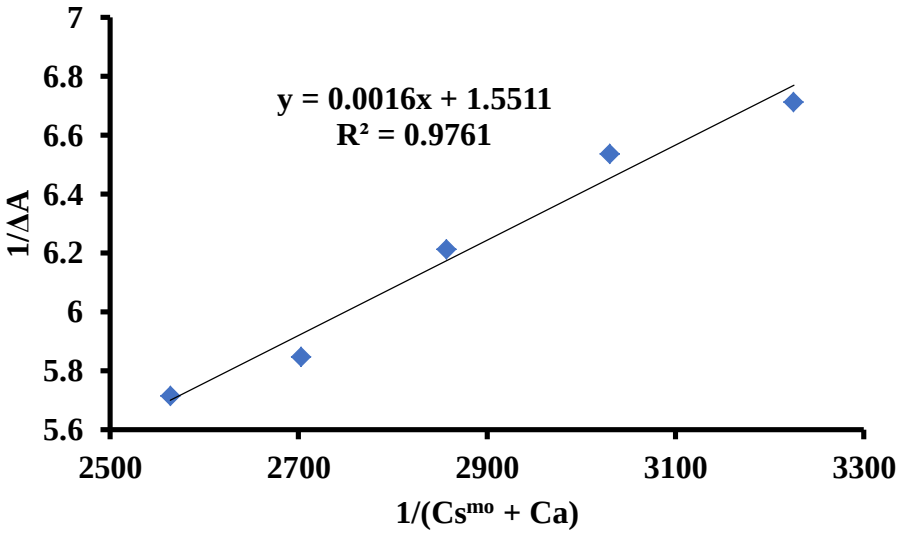
A139: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a7 + Flurbiprofen.



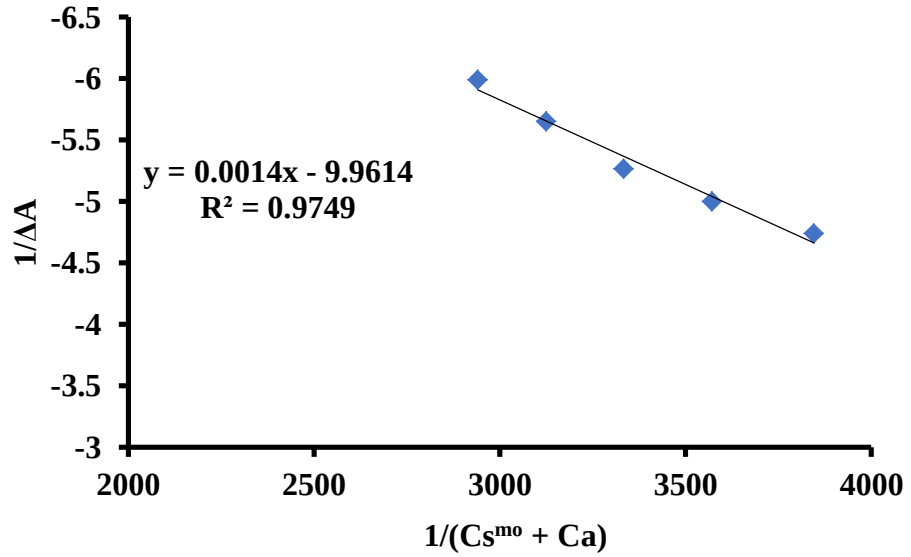
A140: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a8 + Flurbiprofen.



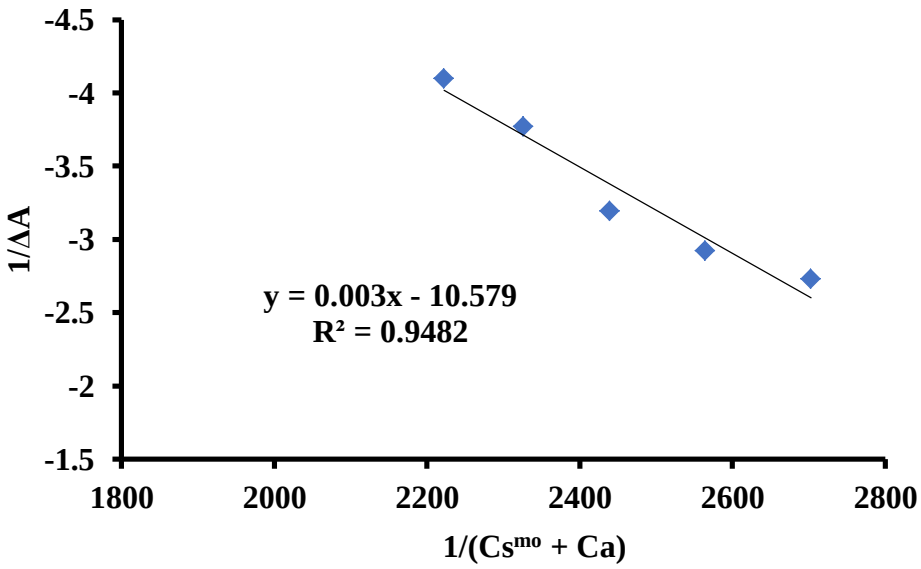
A141: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a9 + Flurbiprofen.



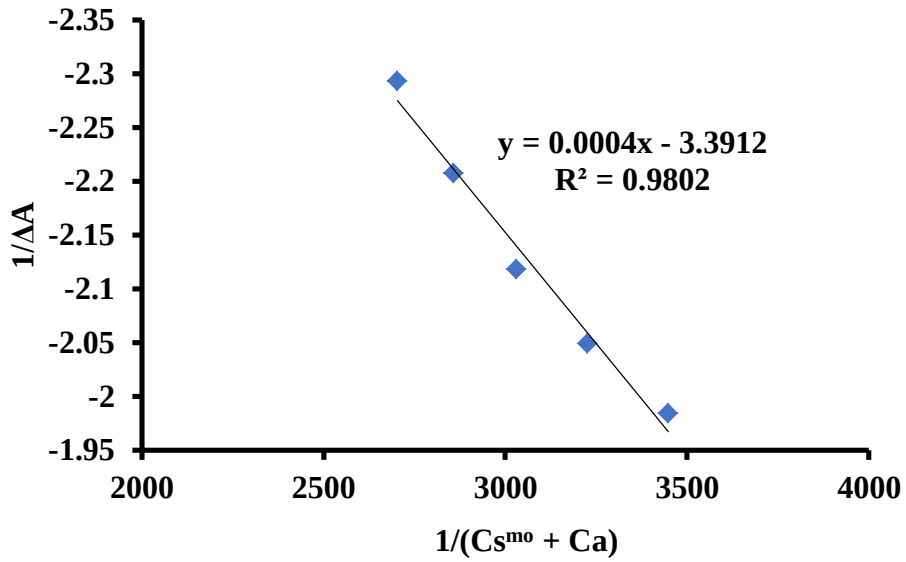
A142: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a10 + Flurbiprofen.



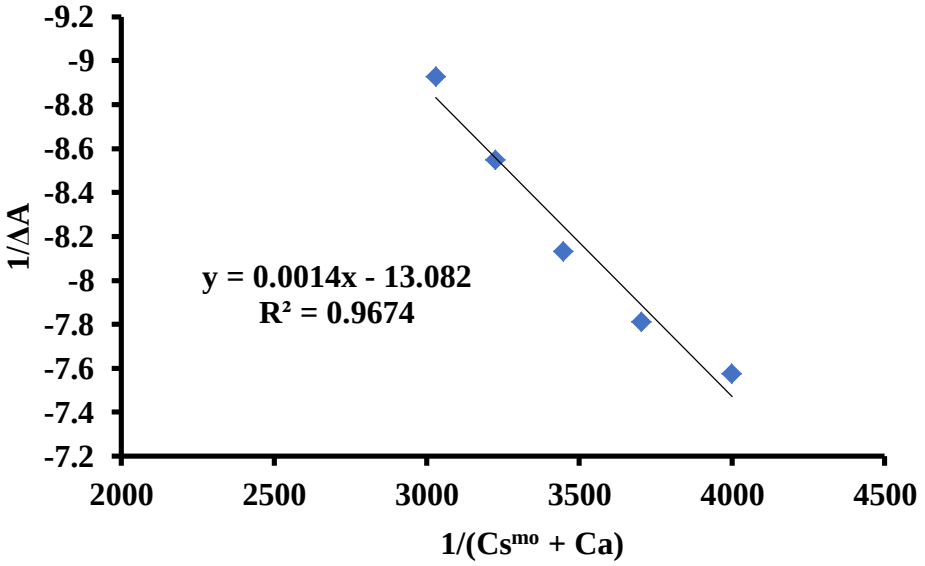
A143: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a11 + Flurbiprofen.



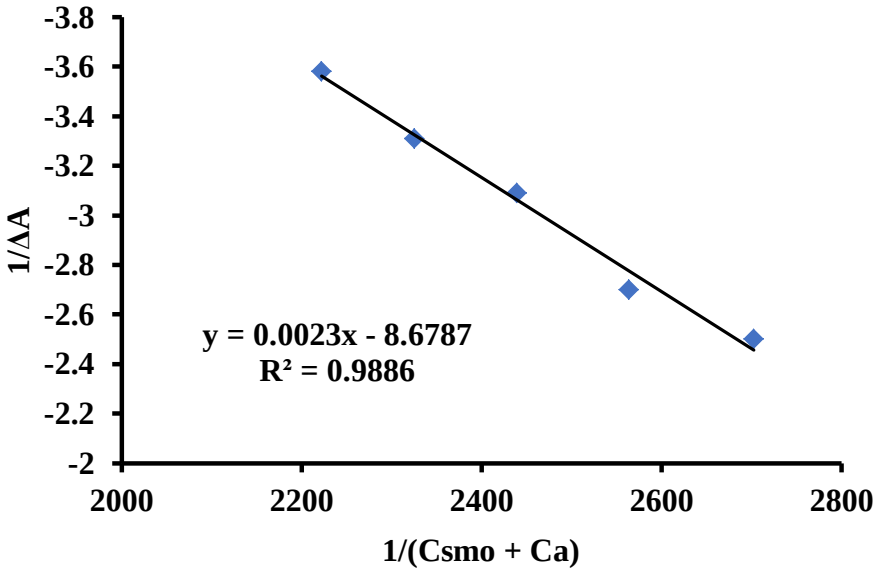
A144: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a12 + Flurbiprofen.



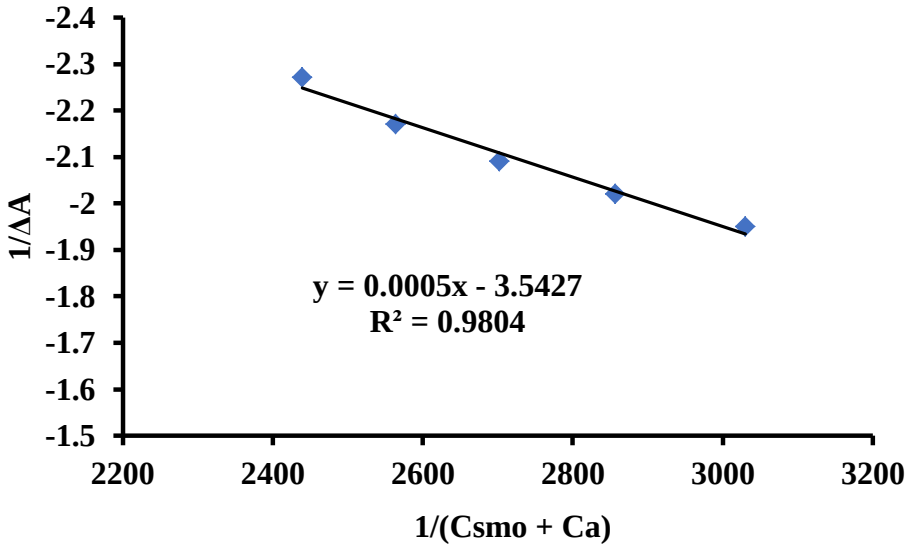
A145: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a14 + Flurbiprofen.



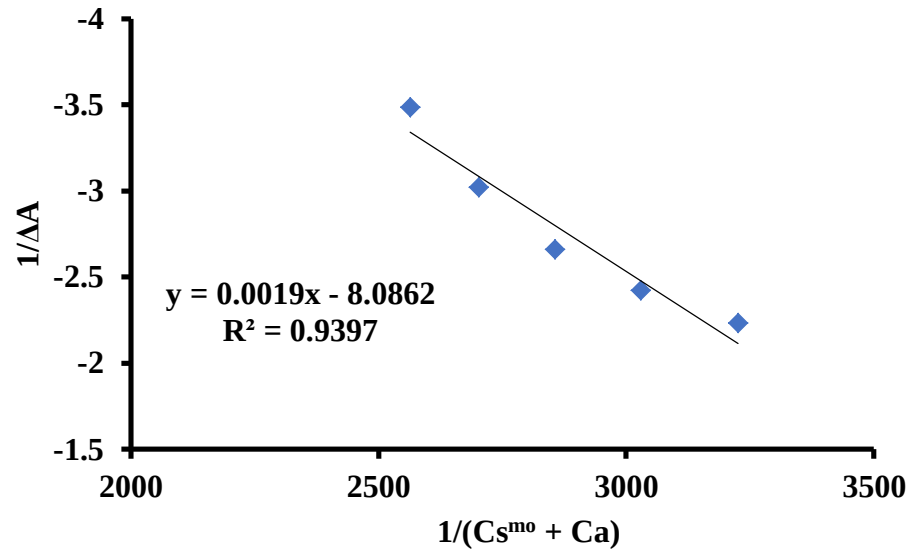
A146: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of a15 + Flurbiprofen.



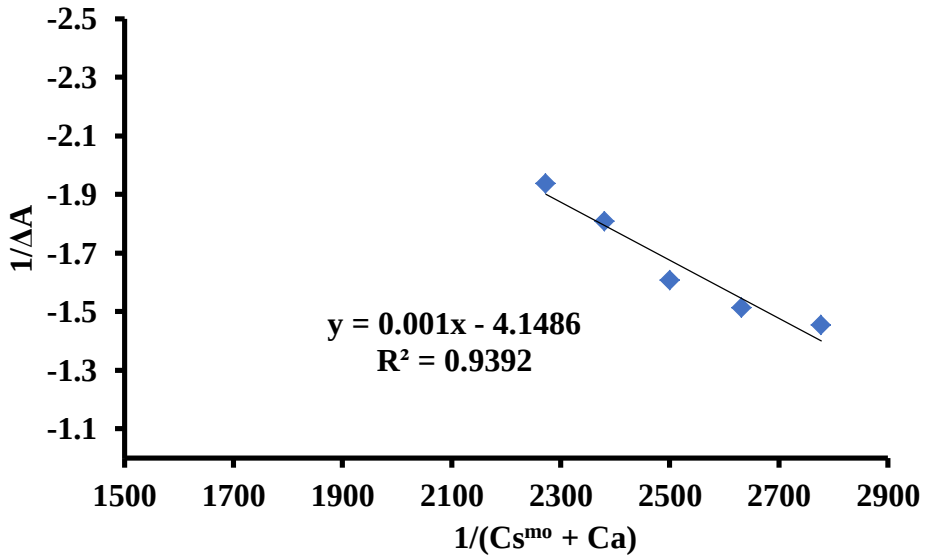
A147: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b6 + Flurbiprofen.



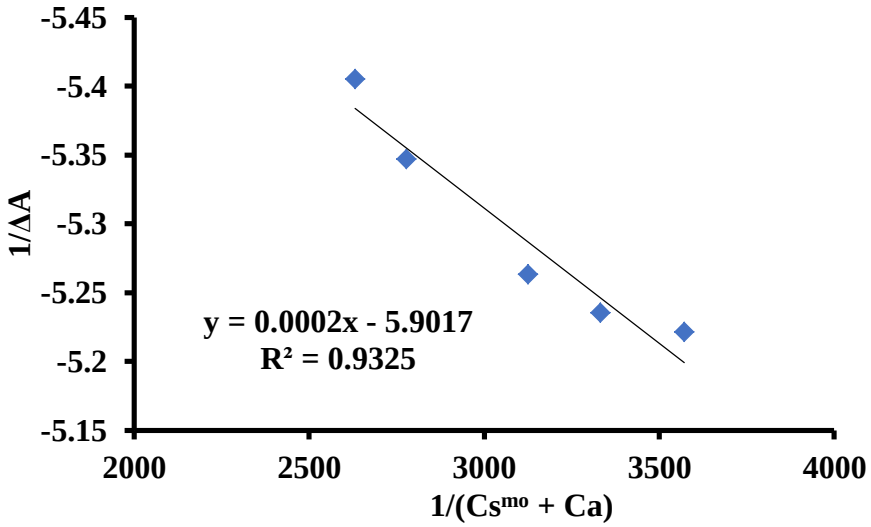
A148: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b8+ Flurbiprofen.



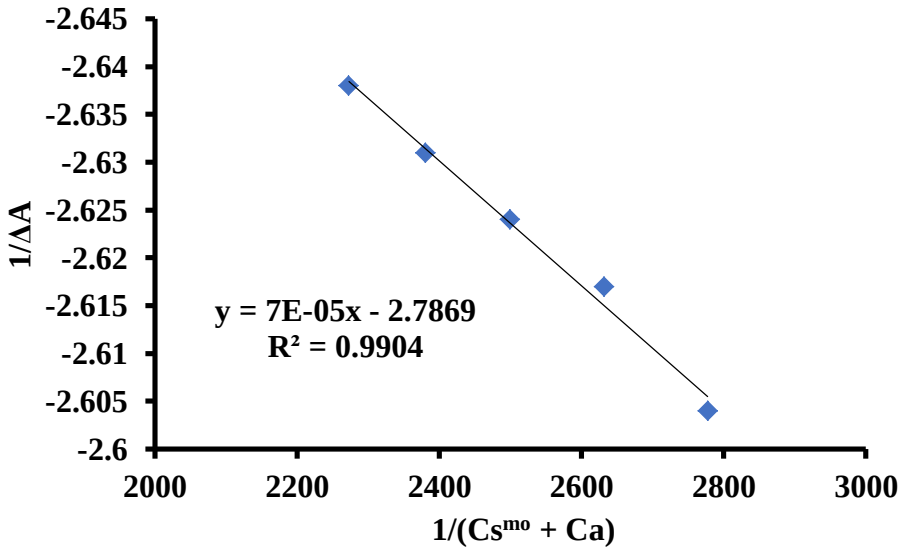
A149: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b10+ Flurbiprofen.



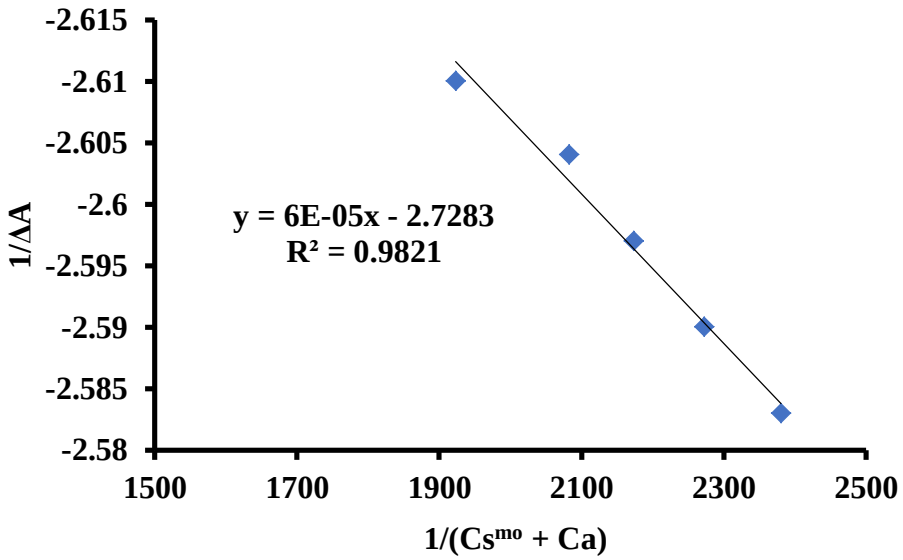
A150: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b12+ Flurbiprofen.



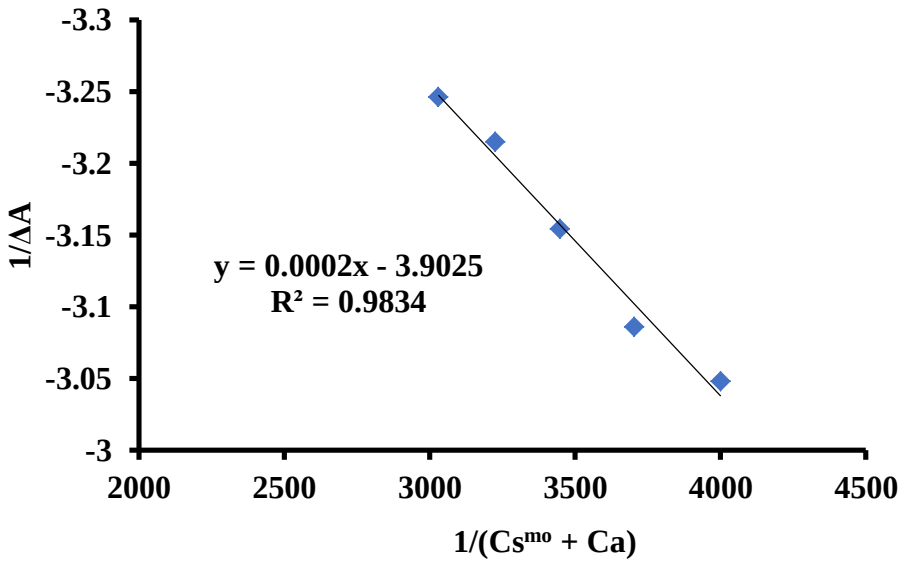
A151: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of b14+ Flurbiprofen.



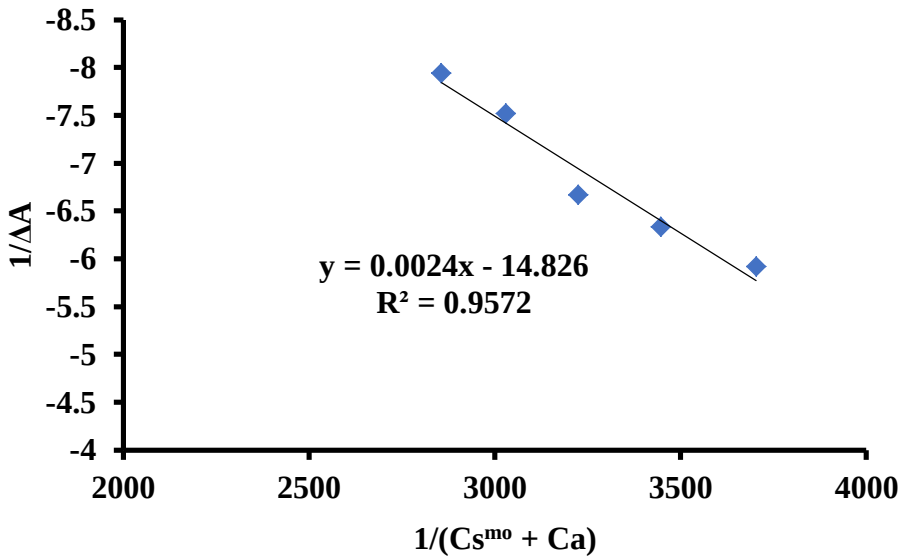
A152: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c6+ Flurbiprofen.



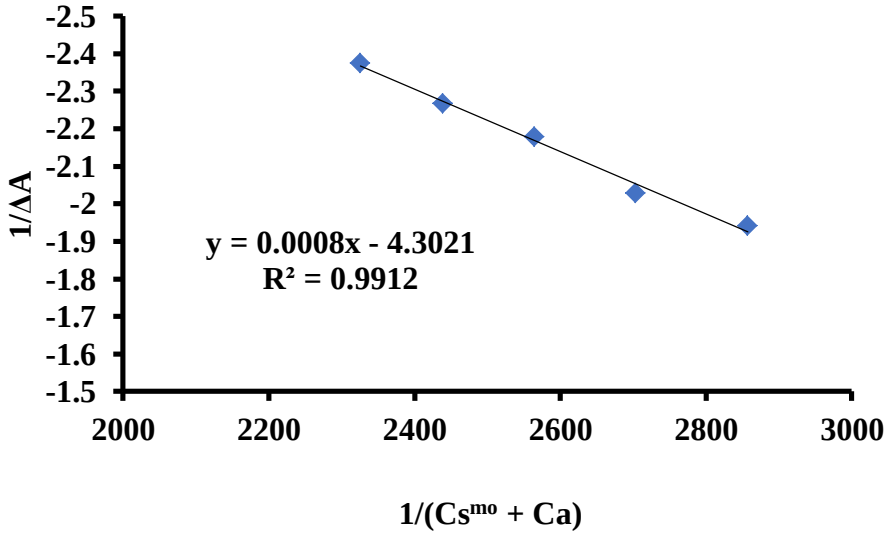
A153: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c7+ Flurbiprofen.



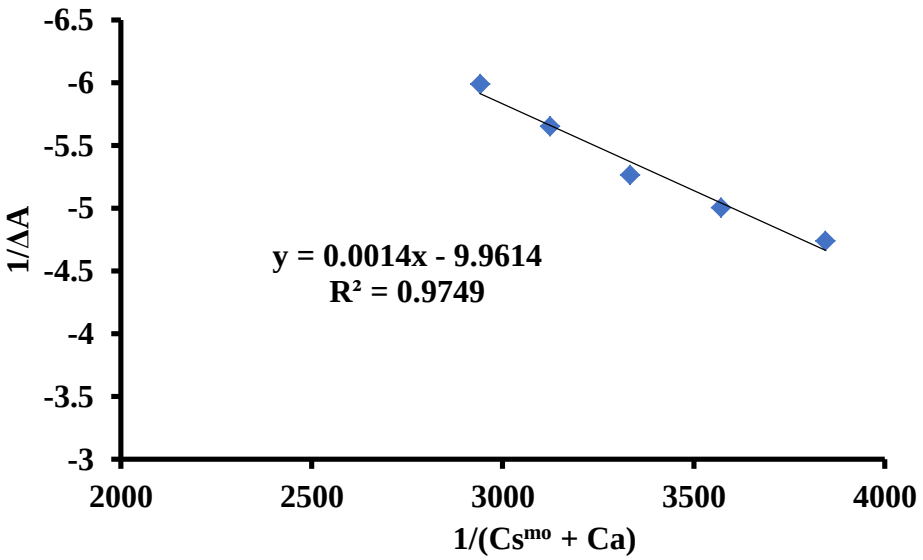
A154: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c8+ Flurbiprofen.



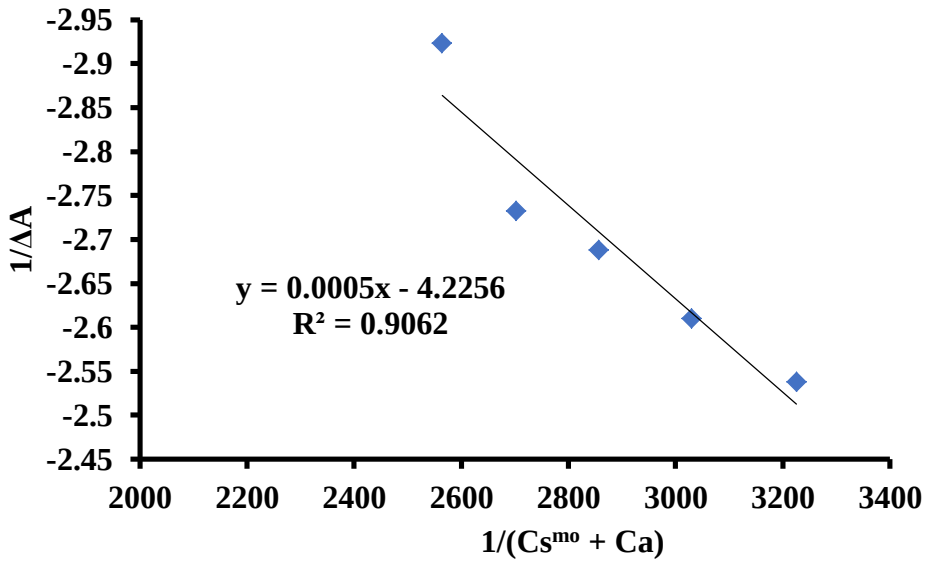
A155: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c9+ Flurbiprofen.



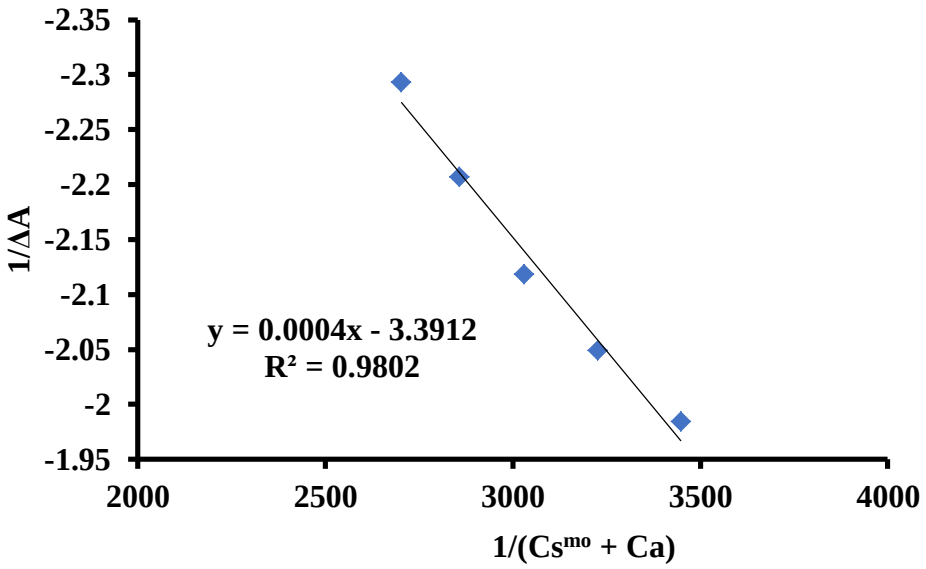
A156: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c10+ Flurbiprofen.



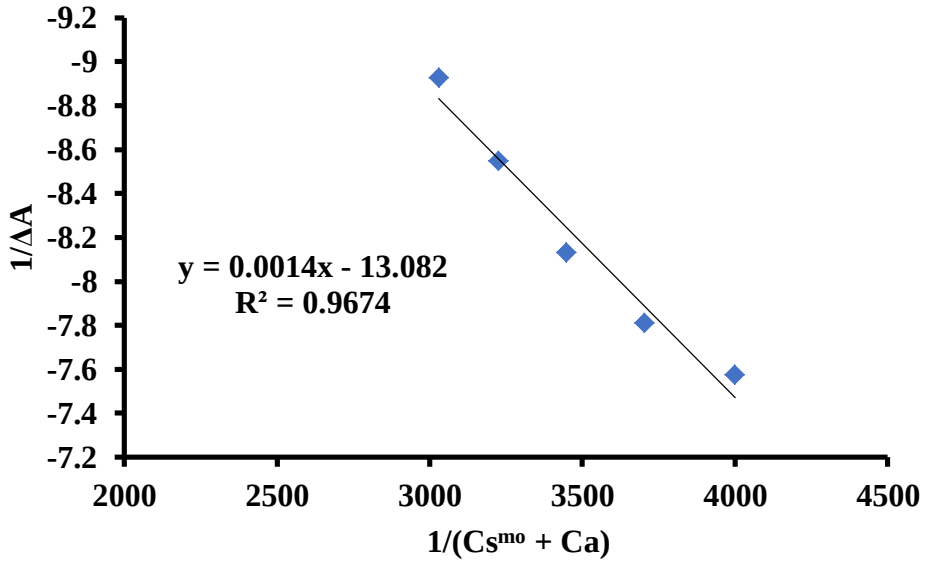
A157: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c11+ Flurbiprofen.



A158: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c12 + Flurbiprofen.



A159: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c14 + Flurbiprofen.



A160: Graph of "1/ΔA versus 1/(Cs^{mo} + Ca)" of c15 + Flurbiprofen.

Appendixes B1: Thermodynamic data of the compounds of (series a)

S. No.	Temperature	CMC	XCMC	Ln XCMC	ΔG (J/mol)	ΔH(J/mol)	ΔS(J/mol. K)
a6							
1	298.16	0.42	0.0000194	-10.8520	-39351.68	25281.94	120.12
2	303.16	0.38	0.0000164	-11.0243	-40679.81	24069.35	116.87
3	308.16	0.37	0.0000156	-11.0682	-41535.91	24809.84	118.54
4	313.16	0.39	0.0000150	-10.9822	-42890.43	25683.43	118.97
5	318.16	0.43	0.0000243	-10.8048	-43871.31	26510.12	121.55
a7							
1	298.16	0.41	0.0000203	-11.8048	-38176.36	25521.299	146.80
2	303.16	0.36	0.0000180	-11.9251	-37304.73	26046.234	149.17
3	308.16	0.35	0.0000175	-12.9533	-42094.22	26579.898	140.40
4	313.16	0.38	0.0000187	-11.8869	-43518.21	27122.291	150.44
5	318.16	0.42	0.0000187	-11.8869	-44518.21	27122.291	140.44
a8							
1	298.16	0.40	0.0000184	-10.9251	-42623.38	27738.62	175.74
2	303.16	0.35	0.0000156	-11.0682	-43845.63	28338.47	188.52
3	308.16	0.33	0.0000152	-11.0942	-44635.71	28948.45	199.84
4	313.16	0.36	0.0000163	-11.0243	-45054.50	29568.33	199.97
5	318.16	0.41	0.0000191	-10.8658	-46113.03	23198.18	198.99
a9							
1	298.16	0.38	0.0000167	-10.9941	-45879.94	29955.95	214.03
2	303.16	0.34	0.0000135	-11.1413	-46122.23	30636.87	217.01
3	308.16	0.32	0.0000150	-11.1764	-47951.80	31317.01	218.55
4	313.16	0.35	0.0000162	-11.0942	-48327.49	32014.37	218.65
5	318.16	0.40	0.0000190	-10.9251	-49348.44	32722.96	217.66
a10							
1	298.16	0.36	0.0000157	-11.0682	-49155.47	35499.27	243.55
2	303.16	0.32	0.0000134	-11.2277	-52448.66	36361.67	246.97
3	308.16	0.31	0.0000125	-11.2978	-53418.16	37238.40	249.28
4	313.16	0.33	0.0000142	-11.1765	-53648.90	38129.47	249.20
5	318.16	0.38	0.0000171	-10.9823	-53575.27	39034.89	248.21
a11							
1	298.16	0.35	0.0000156	-11.0682	-41155.47	55499.27	253.55
2	303.16	0.31	0.0000143	-11.2277	-45448.66	56361.67	256.97
3	308.16	0.30	0.0000144	-11.2978	-46418.16	57238.40	259.28
4	313.16	0.32	0.0000145	-11.1765	-47648.90	58129.47	259.20
5	318.16	0.37	0.0000173	-10.9823	-49575.27	59034.89	258.21
a12							
1	298.16	0.34	0.0000156	-11.0682	-51155.47	65499.27	273.55
2	303.16	0.30	0.0000133	-11.2277	-52448.66	66361.67	276.97
3	308.16	0.29	0.0000124	-11.2978	-53418.16	67238.40	279.28
4	313.16	0.31	0.0000140	-11.1765	-53648.90	68129.47	279.20
5	318.16	0.36	0.0000170	-10.9823	-53575.27	69034.89	278.21
a14							
1	298.16	0.32	0.0000156	-11.0682	-61155.47	75499.27	283.55
2	303.16	0.28	0.0000133	-11.2277	-62448.66	76361.67	286.97
3	308.16	0.27	0.0000124	-11.2978	-63418.16	77238.40	289.28
4	313.16	0.30	0.0000140	-11.1765	-63648.90	78129.47	289.20
5	318.16	0.35	0.0000170	-10.9823	-63575.27	79034.89	288.21
a15							
1	298.16	0.30	0.0000156	-11.0682	-71155.47	85499.27	293.55
2	303.16	0.25	0.0000133	-11.2277	-72448.66	86361.67	296.97
3	308.16	0.24	0.0000124	-11.2978	-73418.16	87238.40	299.28
4	313.16	0.27	0.0000140	-11.1765	-73648.90	88129.47	299.20
5	318.16	0.33	0.0000170	-10.9823	-73575.27	89034.89	298.21

B2: Thermodynamic data of the compounds of (series c)

S. No.	Temperature	CMC	XCMC	Ln XCMC	ΔG(J/mol)	ΔH(J/mol)	ΔS(J/mol. K)
c6							
1	298.16	0.51	0.0000195	-10.85203	-50351.68	45281.94	320.12
2	303.16	0.47	0.0000164	-11.02434	-51679.81	44069.35	316.87
3	308.16	0.46	0.0000157	-11.06823	-52535.91	44809.84	318.54
4	313.16	0.49	0.0000177	-10.98229	-52890.43	45683.43	318.97
5	318.16	0.53	0.0000208	-10.80488	-52871.31	46510.12	321.55
c7							
1	298.16	0.49	0.0000203	-10.804889	-60176.36	55521.299	486.80
2	303.16	0.46	0.0000180	-10.92513	-61304.73	56046.234	489.17
3	308.16	0.45	0.0000175	-10.95330	-62094.22	56579.898	490.40
4	313.16	0.47	0.0000187	-10.88698	-62518.21	57122.291	490.44
5	318.16	0.51	0.0000187	-10.88698	-62518.21	57122.291	490.44
c8							
1	298.16	0.48	0.000018	-10.9251	-70623.38	67738.62	595.74
2	303.16	0.44	0.0000156	-11.0682	-71845.63	68338.47	598.52
3	308.16	0.43	0.0000152	-11.0942	-72635.71	68948.45	599.84
4	313.16	0.46	0.0000163	-11.0243	-73054.50	69568.33	599.97
5	318.16	0.50	0.0000191	-10.8658	-73113.03	60198.18	598.99
c9							
1	298.16	0.46	0.0000168	-10.9941	-80879.94	79955.95	604.03
2	303.16	0.41	0.0000145	-11.1413	-82122.23	70636.87	607.01
3	308.16	0.40	0.0000140	-11.1764	-82951.80	71317.01	608.55
4	313.16	0.43	0.0000152	-11.0942	-83327.49	72014.37	608.65
5	318.16	0.47	0.0000180	-10.9251	-83348.44	72722.96	607.66
c10							
1	298.16	0.45	0.0000156	-11.0682	-91155.47	85499.27	523.55
2	303.16	0.40	0.0000133	-11.2277	-92448.66	86361.67	526.97
3	308.16	0.38	0.0000124	-11.2978	-93418.16	87238.40	529.28
4	313.16	0.42	0.0000140	-11.1765	-93648.90	88129.47	529.20
5	318.16	0.46	0.0000170	-10.9823	-93575.27	89034.89	528.21
c11							
1	298.16	0.43	0.0000156	-11.0682	-101155.4	95499.27	623.55
2	303.16	0.39	0.0000133	-11.2277	-112448.6	96361.67	626.97
3	308.16	0.37	0.0000124	-11.2978	-113418.1	97238.40	629.28
4	313.16	0.41	0.0000140	-11.1765	-113648.9	98129.47	629.20
5	318.16	0.45	0.0000170	-10.9823	-113575.2	99034.89	628.21
c12							
1	298.16	0.42	0.0000156	-11.0682	-141155.4	105499.27	723.55
2	303.16	0.38	0.0000133	-11.2277	-142448.6	106361.67	726.97
3	308.16	0.36	0.0000124	-11.2978	-143418.1	107238.40	729.28
4	313.16	0.39	0.0000140	-11.1765	-143648.9	108129.47	729.20
5	318.16	0.43	0.0000170	-10.9823	-143575.2	129034.89	728.21
c14							
1	298.16	0.40	0.0000156	-11.0682	-141155.4	125499.27	823.55
2	303.16	0.37	0.0000133	-11.2277	-142448.6	126361.67	826.97
3	308.16	0.35	0.0000124	-11.2978	-143418.1	227238.40	829.28
4	313.16	0.38	0.0000140	-11.1765	-143648.9	228129.47	829.20
5	318.16	0.41	0.0000170	-10.9823	-143575.2	229034.89	828.21
c15							
1	298.16	0.38	0.0000156	-11.0682	-141155.4	225499.27	923.55
2	303.16	0.35	0.0000133	-11.2277	-142448.6	226361.67	926.97
3	308.16	0.34	0.0000124	-11.2978	-243418.1	227238.40	929.28
4	313.16	0.36	0.0000140	-11.1765	-343648.9	228129.47	929.20
5	318.16	0.39	0.0000170	-10.9823	-443575.2	229034.89	928.21

B3: Antibacterial activity data of the compounds of (series a and c)

Average Zone of Inhibition in mm					
S. No	**Compounds**	***Enterobacter aerogenes* (-)**	***Escherichia coli* (-)**	***Staphylococcus aureus* (+)**	***Bacillus subtilis* (+)**
Series a					
1	a6	4	5.5	13.5	9
2	a7	7	4.9	11.25	7
3	a8	2	7.25	14.78	3
4	a9	1.9	8	10	9
5	a10	3	4.0	8.0	12
6	a11	11	8.0	14	16
7	a12	13	9.5	12	13
8	a14	1.8	2	6	6
9	a15	6	1	9	5.49
Series c					
10	c6	14	13	14.5	7
11	c7	17	14	17	15
12	c8	3	9.3	12	4
13	c9	1	9	15	2
14	c10	14	7	12.5	7
15	c11	17	15	13.	15
16	c12	16.35	13	9.5	18
17	c14	12	8	10.5	13
18	c15	16	7	15	9
19	Kanamycin Sulfate	22	30	16	34
20	Streptomycin Sulfate	12	13	0	10
21	Clarithromycin	27	29.5	41	35

B4: Antifungal activity data of the compounds of (series a and c)

Antifungal activity (% inhibition in linear growth)				
S. No.	**Sample code**	***Aspergillus niger***	***Aspergillus flavus***	***Aspergillus fumigates***
Series a				
1	a6	28.5±2.50	52.0±1.00	62.5±4.50
2	a7	25.3 ±1.00	57.0±2.15	64.7±2.81
3	a8	31.7±1.09	53.01±1.99	61.92±1.88
4	a9	38.9±2.41	59.00±3.21	55.62±2.35
5	a10	44.0±1.00	47.0±2.00	59.0±2.00
6	a11	24.5±1.50	56.5±1.50	54.5±4.50
7	a12	23.5±2.50	44.0±3.00	44.5±2.50
8	a14	48.0±1.00	71.5±1.50	67.0±1.00
9	a15	53.0± 2.75	67.98±3.05	69.35±3.47
Series c				
10	c6	46.5±5.50	62.0±0.00	72.5±1.50
11	c7	48.31±3.71	63.00±1.99	67.32±3.09
12	c8	44.65±3.82	45.75±2.43	59.54±2.99
13	c9	55.62±2.79	49.21±2.51	41.25±1.49
14	c10	64.0±3.00	35.5±2.50	39.0±2.00
15	c11	32.5±3.50	57.0±2.00	47.0±1.00
16	c12	40.0±2.00	54.5±1.50	39.5±6.50
17	c14	58.5±2.50	65.0±2.00	57.5±2.50
18	c15	52.5±2.500	59.5±4.50	63.0±4.00
	Terbinafine	96.5±0.75	89.5±0.75	94.0±.0.00

B5: Antioxidant Activity data of the compounds of (series a and c)

Antioxidant activity (% inhibition)						
S. No.	Sample code	Amount per 10 mL				
		5 mg	4mg	3mg	2mg	1mg
Series a						
1	a6	56.5±1.50	32±1.00	13.5±2.50	10±1.00	7.5±0.50
2	a7	42.0±0.99	21.25±1	16±0.98	11.4±1.7	9.23±0.35
3	a8	39.0±1.21	27± 0.75	13±0.51	11.9±1.29	11.2±0.72
4	a9	37.2±1.31	20.2±0.75	19±0.62	16.7±1.2	11.9±0.58
5	a10	29.5±0.50	23.5±1.50	20.5±2.50	16±2.00	13±2.00
6	a11	20.5±0.00	19±1.00	18.5±0.50	17±0.00	13±1.00
7	a12	33±4.00	26±1.00	16±1.00	13±1.00	9.5±0.50
8	a14	39.5±1.50	31±1.00	22.5±1.50	16.5±1.50	10.5±0.50
9	a15					
Series c						
10	c6	66.5±1.50	53.5±1.50	48.5±0.50	36±1.00	26±3.00
11	c7	68.1±1.25	43.2±0.90	40.9±0.71	34.25±1.0	24 ±1.98
12	c8	65.3±1.00	43.8±1.00	51±1.25	33.9±0.98	27.1±1.09
13	c9	45.1± 1.0	50.1±2.09	47±1.00	35.2±0.91	24.2±1.00
14	c10	67±1.00	52±1.00	48±0.00	36.5±0.50	25±0.00
15	c11	22.5±1.00	20.5±1.50	20±1.00	15.5±1.50	16±0.00
16	c12	20±1.50	16.5±1.50	13±0.00	12±1.00	10.5±0.50
17	c14	25±1.50	21.5±2.50	19±2.00	17.5±1.50	17±0.00
18	c15	41±1.00	33±2.00	29±0.00	27.5±1.50	24.5±3.50
	Ascorbic acid	80.5±2.00	70.5±3.50	58±3.00	49.5±0.50	42.5±3.50

B6: Association parameters of all the compounds of (series a, b and c) with Flurbiprofen at their different concentrations

S. No.	Cs	(CMC)10^{-3}	Cs^{mo}	(Ca)10^{-3}	(Cs^{mo}+Ca)10^{-3}	1/ Cs^{mo} + Ca	ΔA	1/ΔA
a6								
1	0.48	0.42	0.06	0.31	0.37	2702.70	-0.091	-10.98
2	0.46	0.42	0.04	0.31	0.35	2857.14	-0.102	-9.80
3	0.44	0.42	0.02	0.31	0.33	3030.30	-0.111	-9.00
4	0.42	0.42	0.00	0.31	0.31	3225.80	-0.117	-8.54
5	0.40	0.42	-0.02	0.31	0.29	3448.27	-0.140	-7.14
6	0.38	0.42	-0.04	0.31	0.27	3703.70	-0.162	-6.17
7	0.36	0.42	-0.06	0.31	0.25	4000.00	-0.179	-5.58
a7								
1	0.48	0.41	0.07	0.31	0.38	2631.57	-0.128	-7.81
2	0.46	0.41	0.05	0.31	0.36	2777.71	-0.138	-7.24
3	0.44	0.41	0.03	0.31	0.34	2941.17	-0.143	-6.99
4	0.42	0.41	0.01	0.31	0.32	3125.00	-0.152	-6.57
5	0.40	0.41	-0.01	0.31	0.30	3333.33	-0.159	-6.28
6	0.38	0.41	-0.03	0.31	0.28	3571.42	-0.165	-6.06
7	0.36	0.41	-0.05	0.31	0.26	3846.15	-0.172	-5.81
8	0.34	0.41	-0.07	0.31	0.24			
a8								
1	0.48	0.40	0.08	0.33	0.41	2439.02	-0.282	-3.54
2	0.46	0.40	0.06	0.33	0.39	2564.10	-0.290	-3.44
3	0.44	0.40	0.04	0.33	0.37	2702.70	-0.297	-3.36
4	0.42	0.40	0.02	0.33	0.35	2857.14	-0.301	-3.32
5	0.40	0.40	0.00	0.33	0.33	3030.30	-0.308	-3.24
6	0.38	0.40	-0.02	0.33	0.31	3225.80	-0.311	-3.21
7	0.36	0.40	-0.04	0.33	0.29	3448.27	-0.317	-3.15
8	0.34	0.40	-0.06	0.33	0.27	3703.70	-0.324	-3.04
a9								
1	0.46	0.38	0.08	0.33	0.41	2439.02	-0.083	-12.04
2	0.44	0.38	0.06	0.33	0.39	2564.10	-0.100	-10.00
3	0.42	0.38	0.04	0.33	0.37	2702.70	-0.106	-9.43
4	0.40	0.38	0.02	0.33	0.35	2857.14	-0.126	-7.93
5	0.38	0.38	0.00	0.33	0.33	3030.30	-0.133	-7.51
6	0.36	0.38	-0.02	0.33	0.31	3225.80	-0.150	-6.66
7	0.34	0.38	-0.04	0.33	0.29	3448.27	-0.158	-6.32
8	0.32	0.38	-0.06	0.33	0.27	3703.70	-0.169	-5.91
a10								
1	0.44	0.36	0.08	0.43	0.51	1960.78	-0.421	-2.37
2	0.42	0.36	0.06	0.43	0.49	2040.82	-0.441	-2.26
3	0.40	0.36	0.04	0.43	0.47	2127.66	-0.459	-2.17
4	0.38	0.36	0.02	0.43	0.45	2222.22	-0.493	-2.02

5	0.36	0.36	0.00	0.43	0.43	2325.58	-0.515	-1.94
6	0.34	0.36	-0.02	0.43	0.41	2439.02	-0.541	-1.84
7	0.32	0.36	-0.04	0.43	0.39	2564.10	-0.638	-1.56
8	0.30	0.36	-0.06	0.43	0.37	2702.70		
a11								
1	0.44	0.35	0.07	0.33	0.42	2380.95	-0.125	-8.00
2	0.42	0.35	0.05	0.33	0.40	2500.00	-0.138	-7.24
3	0.40	0.35	0.03	0.33	0.38	2631.57	-0.147	-6.80
4	0.38	0.35	0.01	0.33	0.36	2777.71	-0.152	-6.57
5	0.36	0.35	-0.01	0.33	0.34	2941.17	-0.167	-5.98
6	0.34	0.35	-0.03	0.33	0.32	3125.00	-0.177	-5.64
7	0.32	0.35	-0.05	0.33	0.30	3333.33	-0.190	-5.26
8	0.30	0.35	-0.05	0.33	0.28	3571.42	-0.200	-5.00
a12								
1	0.44	0.34	0.10	0.34	0.45	2222.22	-0.244	-4.09
2	0.42	0.34	0.08	0.34	0.43	2325.58	-0.265	-3.77
3	0.40	0.34	0.06	0.34	0.41	2439.02	-0.313	-3.19
4	0.38	0.34	0.04	0.34	0.39	2564.10	-0.342	-2.92
5	0.36	0.34	0.02	0.34	0.37	2702.70	-0.366	-2.73
6	0.34	0.34	0.00	0.34	0.35	2857.14	-0.372	-2.68
7	0.32	0.34	-0.02	0.34	0.33	3030.30	-0.383	-2.61
8	0.30	0.34	-0.04	0.34	0.31	3225.80	-0.394	-2.53
a14								
1	0.42	0.32	0.10	0.35	0.45	2222.22	-0.356	-2.80
2	0.40	0.32	0.08	0.35	0.43	2325.58	-0.382	-2.61
3	0.38	0.32	0.06	0.35	0.41	2439.02	0.401	-2.49
4	0.36	0.32	0.04	0.35	0.39	2564.10	-0.420	-2.38
5	0.34	0.32	0.02	0.35	0.37	2702.70	-0.436	-2.29
6	0.32	0.32	0.00	0.35	0.35	2857.14	-0.453	-2.20
7	0.30	0.32	-0.02	0.35	0.33	3030.30	-0.472	-2.11
8	0.28	0.32	-0.04	0.35	0.31	3225.80	-0.488	-2.04
a15								
1	0.40	0.30	0.10	0.29	0.39	2564.10	-0.099	-10.10
2	0.38	0.30	0.08	0.29	0.37	2702.70	-0.105	-9.52
3	0.36	0.30	0.06	0.29	0.35	2857.14	-0.110	-9.09
4	0.34	0.30	0.04	0.29	0.33	3030.30	-0.112	-8.92
5	0.32	0.30	0.02	0.29	0.31	3225.80	-0.117	-8.54
6	0.30	0.30	0.00	0.29	0.29	3448.27	-0.123	-8.13
7	0.28	0.30	-0.02	0.29	0.27	3703.70	-0.128	-7.81
8	0.26	0.30	-0.04	0.29	0.25	4000.00	-0.132	-7.57
b6								
1	0.50	0.41	0.09	0.35	0.44	2272	-0.18	-5.49
2	0.48	0.41	0.07	0.35	0.42	2380	-0.20	-4.92
3	0.46	0.41	0.05	0.35	0.40	2500	-0.22	-4.54
4	0.44	0.41	0.03	0.35	0.38	2631	-0.23	-4.34
5	0.42	0.41	0.01	0.35	0.36	2777	-0.25	-4.00

6	0.40	0.41	-0.01	0.35	0.34	2941	-0.27	-3.70
7	0.38	0.41	-0.03	0.35	0.32	3125	-0.28	-3.50
8	0.36	0.41	-0.05	0.35	0.30	3333	-0.29	-3.44
b8								
1	0.42	0.35	0.07	0.35	0.42	2380	-0.118	-8.47
2	0.40	0.35	0.05	0.35	0.40	2500	-0.143	-6.99
3	0.38	0.35	0.03	0.35	0.38	2631	-0.164	-6.09
4	0.36	0.35	0.01	0.35	0.36	2777	-0.185	-5.40
5	0.34	0.35	-0.01	0.35	0.34	2941	-0.209	-4.78
6	0.32	0.35	-0.03	0.35	0.32	3125	-0.233	-4.29
7	0.30	0.35	-0.05	0.35	0.30	3333	-0.255	-3.92
8	0.28	0.35	-0.07	0.35	0.28	3571	-0.273	-3.66
b10								
1	0.40	0.31	0.09	0.34	0.43	2325.58	-0.140	-7.14
2	0.38	0.31	0.07	0.34	0.41	2439.02	-0.220	-4.54
3	0.36	0.31	0.05	0.34	0.39	2564.10	-0.287	-3.48
4	0.34	0.31	0.03	0.34	0.37	2702.70	-0.331	-3.02
5	0.32	0.31	0.01	0.34	0.35	2857.14	-0.376	-2.65
6	0.30	0.31	-0.01	0.34	0.33	3030.30	-0.413	-2.42
7	0.28	0.31	-0.03	0.34	0.31	3225.80	-0.448	-2.23
8	0.26	0.31	-0.05	0.34	0.29			
b12								
1	0.38	0.29	0.09	0.39	0.48	2083.33	-0.354	-2.82
2	0.36	0.29	0.07	0.39	0.46	2173.91	-0.440	-2.27
3	0.34	0.29	0.05	0.39	0.44	2272.72	-0.516	-1.93
4	0.32	0.29	0.03	0.39	0.42	2380.95	-0.553	-1.80
5	0.30	0.29	0.01	0.39	0.40	2500.00	-0.622	-1.60
6	0.28	0.29	-0.01	0.39	0.38	2631.57	-0.661	-1.51
7	0.26	0.29	-0.03	0.39	0.36	2777.77	-0.688	-1.45
8	0.24	0.29	-0.05	0.39	0.34	2941.17		
b14								
1	0.36	0.27	0.09	0.31	0.40	2500.00	-0.185	-5.40
2	0.34	0.27	0.07	0.31	0.38	2631.57	-0.185	-5.40
3	0.32	0.27	0.05	0.31	0.36	2777.77	-0.187	-5.34
4	0.30	0.27	0.03	0.31	0.34	2941.17	-0.190	-5.26
5	0.28	0.27	0.01	0.31	0.32	3125.00	-0.190	-5.26
6	0.26	0.27	-0.01	0.31	0.30	3333.33	-0.191	-5.23
7	0.24	0.27	-0.03	0.31	0.28	3571.42	-0.204	-4.90
8	0.22	0.27	-0.05	0.31	0.26	3846.15		
c6								
1	0.60	0.51	0.09	0.43	0.52	1923.07	-0.369	-2.71
2	0.58	0.51	0.07	0.43	0.50	2000.00	-0.374	-2.67
3	0.56	0.51	0.05	0.43	0.48	2083.33	-0.376	-2.65
4	0.54	0.51	0.03	0.43	0.46	2173.91	-0.377	-2.65
5	0.52	0.51	0.01	0.43	0.44	2272.72	-0.379	-2.63
6	0.50	0.51	-0.01	0.43	0.42	2380.95	-0.380	-2.63

7	0.48	0.51	-0.03	0.43	0.40	2500.00	-0.381	-2.62
8	0.46	0.51	-0.05	0.43	0.38	2631.57	-0.382	-2.61
c7								
1	0.58	0.49	0.09	0.43	0.52	1923.07	-0.383	-2.61
2	0.56	0.49	0.07	0.43	0.50	2000.00	-0.384	-2.60
3	0.54	0.49	0.05	0.43	0.48	2083.33	-0.384	-2.60
4	0.52	0.49	0.03	0.43	0.46	2173.91	-0.385	-2.59
5	0.50	0.49	0.01	0.43	0.44	2272.72	-0.386	-2.59
6	0.48	0.49	-0.01	0.43	0.42	2380.95	-0.387	-2.58
7	0.46	0.49	-0.03	0.43	0.40	2500.00	-0.387	-2.58
8	0.44	0.49	-0.05	0.43	0.38	2631.57	-0.388	-2.57
c8								
1	0.56	0.48	0.08	0.43	0.51	1960.78	-0.391	-2.55
2	0.54	0.48	0.06	0.43	0.49	2040.81	-0.391	-2.55
3	0.52	0.48	0.04	0.43	0.47	2127.65	-0.391	-2.55
4	0.50	0.48	0.02	0.43	0.45	2222.22	-0.392	-2.55
5	0.48	0.48	0.00	0.43	0.43	2325.58	-0.392	-2.55
6	0.46	0.48	-0.02	0.43	0.41	2439.02	-0.393	-2.54
7	0.44	0.48	-0.04	0.43	0.39	2564.10	-0.395	-2.53
8	0.42	0.48	-0.06	0.43	0.37	2702.70	-0.396	-2.52
c9								
1	0.54	0.46	0.08	0.43	0.51	1960.78	-0.392	-2.55
2	0.52	0.46	0.06	0.43	0.49	2040.81	-0.392	-2.55
3	0.50	0.46	0.04	0.43	0.47	2127.65	-0.392	-2.55
4	0.48	0.46	0.02	0.43	0.45	2222.22	-0.393	-2.54
5	0.46	0.46	0.00	0.43	0.43	2325.58	-0.393	-2.54
6	0.44	0.46	-0.02	0.43	0.41	2439.02	-0.394	-2.53
7	0.42	0.46	-0.04	0.43	0.39	2564.10	-0.395	-2.53
8	0.40	0.46	-0.06	0.43	0.37	2702.70	-0.396	-2.52
c10								
1	0.52	0.45	0.07	0.43	0.50	2000.00	-0.390	-2.56
2	0.50	0.45	0.05	0.43	0.48	2083.33	-0.391	-2.55
3	0.48	0.45	0.03	0.43	0.46	2173.91	-0.391	-2.55
4	0.46	0.45	0.01	0.43	0.44	2272.72	-0.392	-2.55
5	0.44	0.45	-0.01	0.43	0.42	2380.95	-0.393	-2.54
6	0.42	0.45	-0.03	0.43	0.40	2500.00	-0.393	-2.54
7	0.40	0.45	-0.05	0.43	0.38	2631.57	-0.394	-2.53
8	0.38	0.45	-0.03	0.43	0.36	2777.77	-0.395	-2.53
c11								
1	0.50	0.43	0.07	0.43	0.50	2000.00	-0.293	-3.41
2	0.48	0.43	0.05	0.43	0.48	2083.33	-0.294	-3.40
3	0.46	0.43	0.03	0.43	0.46	2173.91	-0.295	-3.38
4	0.44	0.43	0.01	0.43	0.44	2272.72	-0.296	-3.37
5	0.42	0.43	-0.01	0.43	0.42	2380.95	-0.296	-3.37
6	0.40	0.43	-0.03	0.43	0.40	2500.00	-0.296	-3.36
7	0.38	0.43	-0.05	0.43	0.38	2631.57	-0.297	-3.35

8	0.36	0.43	-0.03	0.43	0.36	2777.77	-0.298	-3.35
c12								
1	0.50	0.42	0.08	0.43	0.51	1960.78	-0.299	-3.34
2	0.48	0.42	0.06	0.43	0.49	2040.81	-0.300	-3.33
3	0.46	0.42	0.04	0.43	0.47	2127.65	-0.300	-3.33
4	0.44	0.42	0.02	0.43	0.45	2222.22	-0.301	-3.32
5	0.42	0.42	0.00	0.43	0.43	2325.58	-0.302	-3.31
6	0.40	0.42	-0.02	0.43	0.41	2439.02	-0.303	-3.30
7	0.38	0.42	-0.04	0.43	0.39	2564.10	-0.305	-3.27
8	0.36	0.42	-0.06	0.43	0.37	2702.70	-0.308	-3.24
c14								
1	0.46	0.40	0.06	0.43	0.49	2040.81	-0.371	-2.69
2	0.44	0.40	0.04	0.43	0.47	2127.65	-0.375	-2.66
3	0.42	0.40	0.02	0.43	0.45	2222.22	-0.377	-2.65
4	0.40	0.40	0.00	0.43	0.43	2325.58	-0.378	-2.64
5	0.38	0.40	-0.02	0.43	0.41	2439.02	-0.379	-2.63
6	0.36	0.40	-0.04	0.43	0.39	2564.10	-0.380	-2.63
7	0.34	0.40	-0.06	0.43	0.37	2702.70	-0.381	-2.62
8	0.32	0.40	-0.08	0.43	0.35	2857.14	-0.383	-2.61
c15								
1	0.44	0.38	0.06	0.43	0.49	2040.81	-0.371	-2.69
2	0.42	0.38	0.04	0.43	0.47	2127.65	-0.374	-2.67
3	0.40	0.38	0.02	0.43	0.45	2222.22	-0.375	-2.66
4	0.38	0.38	0.00	0.43	0.43	2325.58	-0.378	-2.64
5	0.36	0.38	-0.02	0.43	0.41	2439.02	-0.379	-2.63
6	0.34	0.38	-0.04	0.43	0.39	2564.10	-0.380	-2.55
7	0.32	0.38	-0.06	0.43	0.37	2702.70	-0.391	-2.55
8	0.30	0.38	-0.08	0.43	0.35	2857.14	-0.392	-2.54

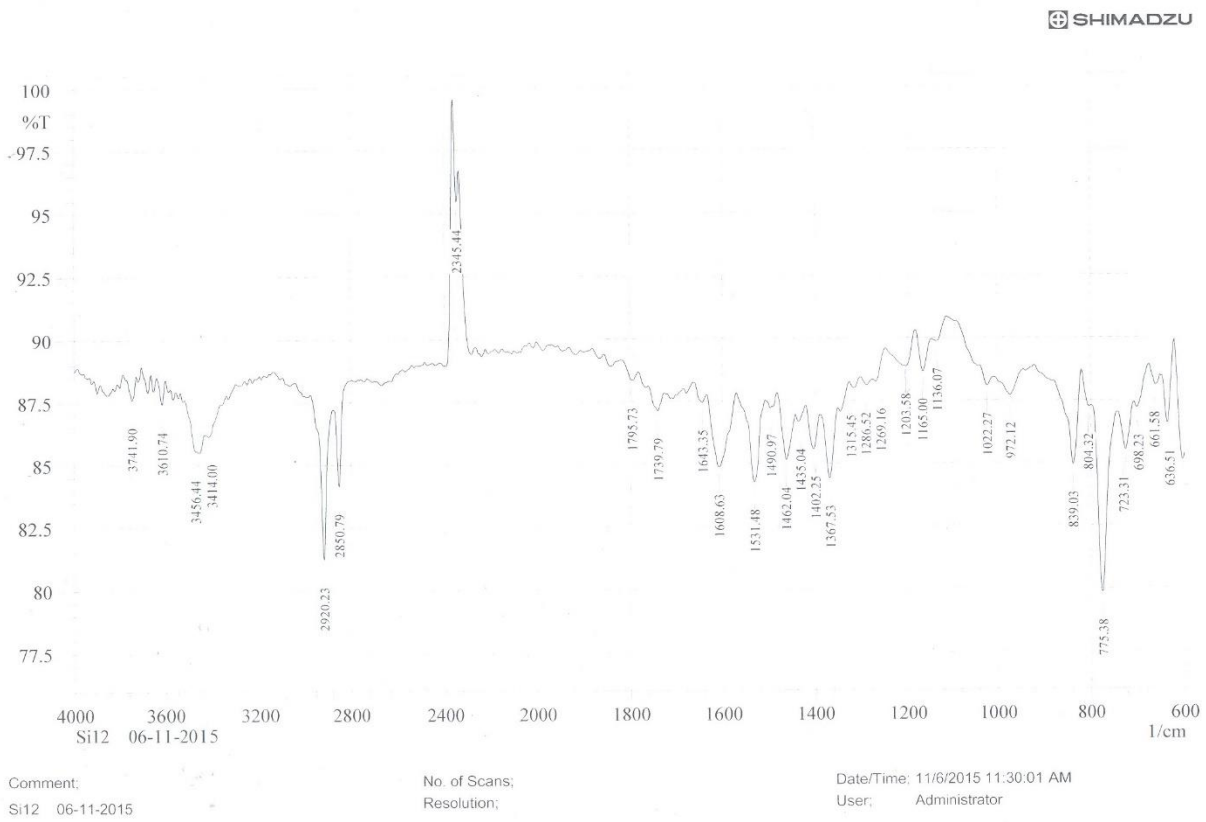
B7: Parameters obtained from drug Flurbiprofen association with all the compounds of (series a, b and c)

Compounds	**A**	**Am**	**A◦**	**E◦×10^{5}**	**Em×10^{5}**	**Cm×10^{-6}**	**M×10^{-6}**	**(n)**
a6	0.380	0.400	0.491	1.58	0.83	1.48	1.2	1.23
a7	0.339	0.363	0.491	1.58	0.75	1.83	1.4	1.30
a8	0.349	0.368	0.650	1.96	0.76	2.52	1.6	1.50
a9	0.524	0.567	0.650	1.96	1.23	1.72	1.6	1.07
a10	1.168	1.240	1.661	3.86	2.81	4.72	1.6	2.95
a11	0.483	0.525	0.650	1.96	1.19	2.15	1.8	1.19
a12	0.585	0.707	0.951	2.71	1.60	3.29	2.0	1.64
a14	0.515	0.595	0.951	2.71	1.41	3.35	2.0	1.67
a15	0.224	0.242	0.341	1.17	0.60	2.05	2.0	1.02
b6	0.596	0.724	1.009	2.80	1.44	3.054	1.698	1.79
b8	0.515	0.596	1.009	2.80	1.41	3.570	2.590	1.38
b10	0.503	0.739	0.879	2.58	0.73	2.04	1.8	1.13
b12	0.700	0.968	1.322	3.38	2.54	7.32	1.8	4.0
b14	0.237	0.242	0.427	1.37	0.67	2.68	1.8	1.49
c6	1.282	1.292	1.661	3.86	2.15	2.21	1.8	1.23
c7	1.275	1.278	1.661	3.86	2.20	2.32	1.8	1.29
c8	1.269	1.270	1.661	3.86	2.26	2.45	1.6	1.53
c 9	1.269	1.268	1.661	3.86	2.34	2.58	1.6	1.61
c10	1.269	1.271	1.661	3.86	2.44	2.76	1.4	1.97
c11	1.365	1.368	1.661	3.86	2.73	2.62	1.4	1.87
c12	1.360	1.362	1.661	3.86	2.72	2.64	1.6	1.65
c14	1.284	1.290	1.661	3.86	2.80	2.56	1.2	2.96
c15	1.286	1.290	1.661	3.86	2.93	4.02	1.2	3.35

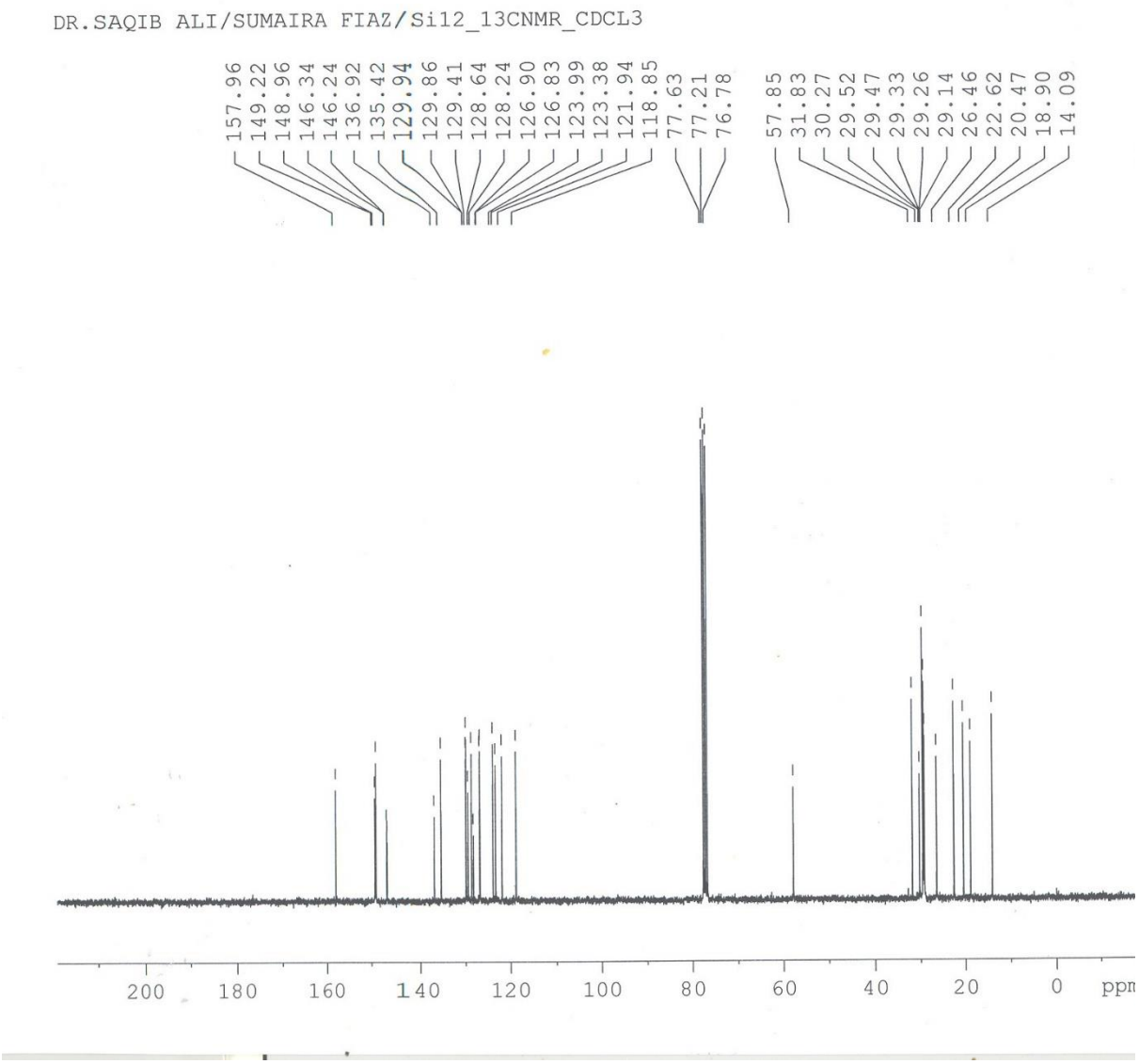
B8: Obtained esteems of Binding constants and Gibb's free energy of the compounds of (series a, b and c) with Flurbiprofen.

S. No.	Compound	K_b (dm^3/mol)	ln K_b	ΔG (KJ/mol)
1	a6	5406	8.595	-21.306
2	a7	8130	9.003	-22.318
3	a8	19500	9.878	-24.486
4	a9	6175	8.728	-21.636
5	a10	968.7	6.876	-17.044
6	a11	7114	8.869	-24.738
7	a12	3523	8.167	-20.245
8	a14	8475	6.742	-16.713
9	a15	9342	9.142	-22.663
10	b6	3671	8.210	-18.650
11	b8	6726	8.810	-20.010
12	b10	4252	8.355	-20.711
13	b12	4140	8.328	-20.646
14	b14	3012	8.010	-19.856
15	c6	39714	10.589	-26.250
16	c7	45333	10.721	-26.578
17	c8	19500	9.878	-24.486
18	c 9	6175	8.728	-21.637
19	c10	5375	8.589	-21.292
20	c11	7114	8.869	-21.987
21	c12	8440	9.040	-22.411
22	c14	8475	9.044	-22.421
23	c15	9342	9.142	-22.663

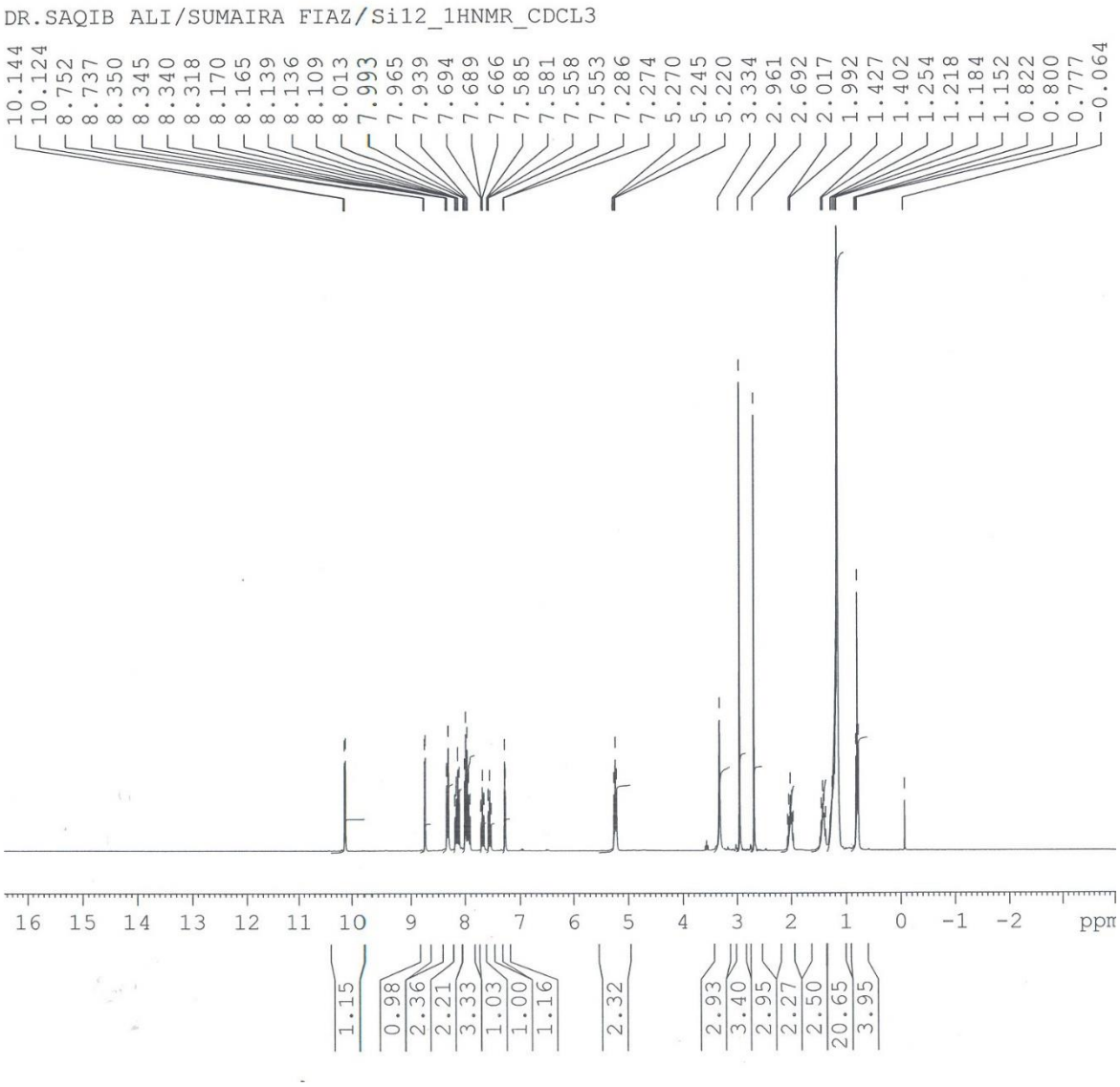
Appendixes-C



C1: IR Spectrum of c12



C2: ^{1}H NMR Spectrum of c12



C3: ^{13}C NMR Spectrum of c12

List of Publications

The following research articles have been published from this work;

1. **Summaira Fayyaz,** Saqib Ali, Nasir Khalid, Afzal Shah, Faizan Ullah, One Pot Synthesis and Properties of Cationic Surfactants: *n*-Alkyl-3-Methylpyridinium Bromide, Journal of Surfactants and Detergents, 2016, 19, 841-848.

2. **Summaira Fayyaz,** Rabia Talat. Saqib Ali, Nasir Khalid, Afzal Shah, Faizan Ullah, Synthesis, characterization, micellization behavior of cationic surfactants: *n*-Alkyl-3-methylpyridinium bromide and their study of interaction with drugs (Flurbiprofen and Ketoprofen) using UV- visible Spectroscopy, Journal of Surfactants and Detergents 2019, 22, 625-632.

3. Rabia Talat, **Summaira Fayyaz,** Saqib Ali, Nasir Khalid, Ali Haider, Afzal Shah,Faizan Ullah, Designing of new cationic surfactant based micellar systems as drug carriers: an investigation in to the drug cell membrane interactions, Journal of Dispersion Science and Technology, 2019, 40, 958-968.

4. **Summaira Fayyaz**, Rabia Talat, Saqib Ali, Nasir Khalid, Afzal Shah, Faizan Ullah, Ali Haider, Synthesis of 2-Methylpyridinium Based Surfactants: Characterization and Potential Application as Drug Carrier Systems, Proceedings of the Pakistan Academy of Sciences: A. Physical and Computational Sciences, 2019, 56, 31-50.