Chapter 4

Conversion of the prepared compound into surfactant
4.1 Introduction to surfactant

Surfactants are having wide array of pharmaceutical applications. Day by day demand of surfactants is increasing drastically due to its recent prevalence in developing formulations. Owing to the higher water solubility of one of the most widely used surfactant (sodium lauryl sulphate), interest have recently arisen to synthesize a compound bearing quinazoline nucleus with lauryl group. Synthesized compound when analyzed by QSAR exhibits the low water solubility which is a major impediment in achieving low MIC values. Thus only few compounds having higher antibacterial activity were transformed into surfactant. These synthesized compounds can be further screened for antimicrobial activity. The synthesized surfactant was further evaluated for physicochemical properties like surface tension, cloud point, foaming height, wetting time and emulsification power which was used to improve the stability of the whole system.

4.2 Experimental Work

4.2.1 Development of QD surfactant

On the basis of antibacterial activity, we emphasized on the synthesis of new compounds such as QD-6 and QD-7 with improved water solubility. However due to the poor yield and lack of knowledge regarding the synthesis of QD-7, QD-6 were selected for further synthesis. Additionally the structure of compound was determined by TLC, IR, Mass and NMR.
A solution of compound QD-6 (0.01M) and Sodium Lauryl Sulphate (0.01 mole) were refluxed 12 hrs in boiling Ethanol (20ml) in the presence of potassium hydroxide (Scheme 2). Then mixtures were concentrated on water bath and finally recrystallized by ethanol. Yield: 45%; UV λmax: 245 nm; Rf: 0.77 (Pet.ether: ethyl acetate: methanol); Mpt: 160°C

![Scheme 2: Synthesis of surfactant](image)

### 4.2.2 Determination of physical properties

#### 4.2.2.1 Surface tension

Surface tension was measured using Stalgmometer with 0.1 % (w/v) aqueous solution of surfactant at room temperature (25°C) [1].

#### 4.2.2.2 Cloud point

This can be envisaged by gradually heating 0.1 % (w/v) solution in a controlled temperature bath and recording the time at which the clear or nearly clear solutions became definitely turbid. The reproducibility of this
temperature was checked by cooling the solutions until they become clear again {2}.

4.2.2.3 Wetting time

Wetting time was determined by immersing a sample of cotton fabric in a 0.1 % (w/v) aqueous solution of surfactant {3}. So, they can find a wide application in textile industry

4.2.2.4 Foaming properties

This method follows traditional method in which a 25 ml solution 0.1% (w/v) was shaken vigorously for 10 seconds in a 100 ml glass stopper, graduated cylinder, at 25°C. The solution was allowed to stand for 30 seconds, and the foam height was measured {4}.

4.2.2.5 Emulsification stability

10 ml of a 0.1% (w/v) aqueous solution of surfactant and 5 ml of liquid paraffin at 40°C was prepared for Emulsification stability. The emulsifying property was determined by the time it took for an aqueous volume separating from the emulsion layer to reach 9 ml. counting from the moment the shaking was stopped {5}.

4.2.2.6 Determination of Critical Micelle Concentration (CMC)

The critical micelle concentration of surfactant was determined by plotting surface tension values against the concentration of each surfactant.
4.3 Biological activity

The antimicrobial activities of some synthesized compounds were determined in vitro using the Cup plate method [6]. Different species of Gram positive and Gram negative bacteria were used for screening antibacterial activity. The compound in question was dissolved in Dimethyl Formamide (DMF) and different concentrations were chosen (10-250 μg/ml). Fresh broth culture of Gram positive and Gram negative bacteria were used to inoculated uniform Agar plates. The discs were incubated at 28°C for 24 h. The formed zones of inhibition was measured in mm scale.

4.4 Result and Discussion

Prior to this study () various related wok was done to improve the antimicrobial activity of a compound by introducing new molecular parameter such as heteroatoms [7], chemical functions [8–11], aromatics [12] or non aromatic cyclic substituents [13]. In our study attempts were made to synthesize a whole system wich acts as a drug as well as surfactant.

4.4.1 Physicochemical properties

The investigation of the surface active properties of the compound has been done in the neutral medium (pH 7.3), at a concentration of 0.1 % (w/v) and 25°C. These types of surfactants are especially interesting
because they are not the most common. Therefore the traditional procedure was used to follow up the properties.

4.4.1.1 Surface tension

The surface tension of prepared compound is shown in Table 4.1. This compound has low surface activity due to electrostatic repulsion between ions in molecule.

4.4.1.2 Cloud point

An understanding of the property called cloud point is a very important factor. This property can be used in various applications of surfactants in aqueous system. The cloud point of the prepared surfactant is less than 100°C because of presence of long alkyl chain. Its hydrophobicity increase with increase in the alkyl chain.

4.4.1.3 Wetting time

For the prepared compound, at all points of the investigation, the synthesized surfactant was efficient wetting agent.

4.4.1.4 Foam power

Foam power was also investigated for surfactant and is generally rated as foamy. The foam height of the prepared surfactant was measured. A low foaming height has an application in the dyeing industry {15}.

4.4.1.5 Emulsion stability

Studies are still being carried out on the use of surfactant in emulsion formation which is of immense importance to technological development. It was proven that the emulsifying stability of the prepared surfactant
containing heterocyclic nucleus exhibit moderate emulsifying properties. The results might lead to the application of the surfactant of choice in the manufacturing of cosmetics.

Table 4.1 Physical properties of Surfactant

<table>
<thead>
<tr>
<th>PHYSICAL PROPERTIES</th>
<th>VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>White crystal</td>
</tr>
<tr>
<td>pH</td>
<td>7.3</td>
</tr>
<tr>
<td>CMC</td>
<td>0.4 %</td>
</tr>
<tr>
<td>Surface Tension (0.3%)</td>
<td>27 (dyne/cm)</td>
</tr>
<tr>
<td>Foam Height (0.1%)</td>
<td>3 cm</td>
</tr>
<tr>
<td>Emulsion Stability (0.1%)</td>
<td>25 min</td>
</tr>
<tr>
<td>Wetting Time</td>
<td>10 sec</td>
</tr>
<tr>
<td>Cloud point</td>
<td>60°C</td>
</tr>
<tr>
<td>Log P</td>
<td>3.12</td>
</tr>
</tbody>
</table>

4.4.1.6 Critical Micelle Concentration

The surface tension decreases from its original value to a lower constant one, which is attained at the CMC. The value of CMC for drug was found to be 0.4 % (Fig. 4.1). Hydrophobic group is an important driving force in micellization. Increase in hydrophobicity, decrease in CMC value. The number of carbon atoms was found to be a determining factor in the values of CMC {16}. 
Figure 4.1 Effect of varying the concentration of drug on the surface tension

4.5 Biological activity

Most of the antibiotics act by specific mechanism by showing interefereance in the metabolic processes of micro organism. By keeping this in view we here synthesized a compound which acts through specific mechanism. Structure activity relationship of the designed compound is basically depends on two factors.

The presence of heterocyclic moiety and the length of aliphatic chain regulate the anti-microbial activity of synthesized product. Among the two factors Carbon chain length plays a greater role by exhibibiting absorption at the interface of cell membrane, which is responsible for the decrease in permeability of cell leading to altered biological process and cause cell death.
Table 4.2 Zone of inhibition with different microbes

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>Zone of Inhibition (mm)*</th>
<th>Ciprofloxacin</th>
<th>DMF</th>
</tr>
</thead>
<tbody>
<tr>
<td>S.aureus 6571</td>
<td>25</td>
<td>25</td>
<td>----</td>
</tr>
<tr>
<td>B.subtilis ATCC 6051</td>
<td>21</td>
<td>26</td>
<td>----</td>
</tr>
<tr>
<td>S.dysenteriae K12</td>
<td>29</td>
<td>29</td>
<td>----</td>
</tr>
<tr>
<td>E.coli 6</td>
<td>20</td>
<td>22</td>
<td>----</td>
</tr>
</tbody>
</table>

*Conc: 125µg/ml

![Graph showing activity of compound for different microbes](image)

Figure 4.2 Activity of compound for different microbes
4.6 Conclusion

Our previous work lead to the conclusion that prepared surfactant constituting hydrophilic (sulfate ion) and hydrophobic (long alkyl chain) properties in a single framework, demonstrates good emulsifying or surface active properties which can be used as a topical agent as well as anti-bacterial formulations.
4.7 References

