Solubility Enhancement of Drugs with Aid of Surfactants: Research Done Since Last Two Decades

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Abstract: This review aims to explore the past work done on the solubility enhancement of drugs using surfactants. Surfactants play an important part in many routes of interest in both essential and practical science. The most vital function of surfactant is the formation of micelle in solution, which has specific significance in medicine because of their ability to improve the solubility of poorly water-soluble drugs, which need high doses to extend therapeutic plasma levels after oral administration. Poor water solubility is the major issue met with the formulation development of new chemical objects. A drug taken by the patient should present in the solution form at the site of absorption. The use of surfactants to elevate the dissolution of poorly soluble drugs has been employed. Surfactants can reduce surface tension and improve the dissolution of lipophilic drugs in the aqueous medium. When the levels of surfactants surpass their critical micelle concentration it deceives the drugs within the micelles. The authors collected sufficient literature on work done on the solubility enhancement of drugs using surfactants and presented in this paper. The authors conclude that this quick reference will be helpful for researchers in finding the literature on solubility enhancement of drugs using surfactants on a single click.

Keywords: Surfactants, solubility, absorption, drugs, literature,
INTRODUCTION

Solubility is a property of dissolution of a solute in a solvent which produces a homogenous system and is one of the most essential parameters to attain the necessary concentration of drug in systemic circulation for necessary therapeutic response. Solubility is the vital parameter for achieving the drug in blood for therapeutic actions. The poor water solubility of lipophilic drugs for oral absorption (BCS Class II drugs) is a major issue for formulation developer. Numerous practices are used for the improvement of the solubility of poorly water-soluble drugs, among them the following approaches are widely used.

- Physical and chemical alterations of the drug
- Other means like particle size reduction, salt formation, crystal engineering, solid dispersion, complexation, and surfactants.

2. Solubility enhancement by surfactants

Surfactants are also known as Interface Active Agents or Surface Active Agents are compounds that lower the surface tension (or interfacial tension) between two liquids, between a gas and a liquid, or between a liquid and a solid. These surfactants may act as a detergent, wetting agents, emulsifiers, foaming agents, and dispersants.

2.1. Classification of surfactants based on charge

The Classification of surfactants based on the charge is illustrated in table 1.

<table>
<thead>
<tr>
<th>Type of surfactant</th>
<th>Charge</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cationic</td>
<td>Positive</td>
<td>Benzalkonium chloride, Cetylpyridinium chloride, and Cetrimide</td>
</tr>
<tr>
<td>Anionic</td>
<td>Negative</td>
<td>Soaps; Sodium lauryl sulphate, detergents</td>
</tr>
<tr>
<td>Non-Ionic</td>
<td>No charge</td>
<td>Sorbitan esters (SPANS) like SPAN 20, 40, 60, 65, 80, and 85; Polysorbates (Tweens) like Tween 20, 40, 60, 65, 80, and 85; Poly Ethylene Glycols</td>
</tr>
<tr>
<td>Amphoteric (Ampholytes) (Zwitterionic)</td>
<td>Both Positive and Negative</td>
<td>Lecithin</td>
</tr>
</tbody>
</table>

The past attempts made on increasing the solubility of drugs using surfactants are illustrated in table 2.

Table 1: Classification of surfactants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Surfactant</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine</td>
<td>Tween 80</td>
<td>¹Haq et al., 2020</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Span 20 and Tween 80</td>
<td>²Khan et al., 2020</td>
</tr>
<tr>
<td>Emanemtine Benzoate</td>
<td>Polyvinylpyrrolidone K30 (PVP-K30)</td>
<td>³Huang et al., 2019</td>
</tr>
<tr>
<td>Silymarin-laden</td>
<td>PVP-K30 and Polyethylene glycol (PEG-6000)</td>
<td>⁴Ali et al., 2019</td>
</tr>
<tr>
<td>Levodropropazine</td>
<td>Hydroxypropyl-beta-cyclodextrin (HP-beta-CD)</td>
<td>⁵Yousaf et al., 2019</td>
</tr>
<tr>
<td>Eprosartan Myelate</td>
<td>Hydroxypropyl methylcellulose (HPMC) and polysorbate 80</td>
<td>⁶Yousaf et al., 2018</td>
</tr>
<tr>
<td>Atazanavir</td>
<td>Sulfate Tween 80</td>
<td>⁷Sundar et al., 2018</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>PVP-K30 and PEG 4000</td>
<td>⁸Gorajana et al., 2015</td>
</tr>
<tr>
<td>Cilostazol</td>
<td>Eudragit-L100 and Eudragit-S100</td>
<td>⁹Park et al., 2015</td>
</tr>
<tr>
<td>Megestrol acetate</td>
<td>HPMC, PVP-K30</td>
<td>¹⁰Ha et al., 2015</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Capryol PGMC (propylene glycol monocaprylate)</td>
<td>¹¹Seo et al., 2015</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>PEG-4000, Tween80 and Span80</td>
<td>¹²Obeidat et al., 2014</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>PEG-8000, PVP-K30, Tween 80</td>
<td>¹³Koh et al., 2013</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>PVP-K30 and Tween 80</td>
<td>¹⁴Lee et al., 2013</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>PVP</td>
<td>¹⁵Marasini et al. 2013</td>
</tr>
<tr>
<td>Sulfathiazole</td>
<td>PVP-K29/32, sodium lauryl sulphate (SLS)</td>
<td>¹⁶Dave et al., 2013</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>PVP</td>
<td>¹⁷Noolkar et al., 2013</td>
</tr>
<tr>
<td>Simvastatin</td>
<td>HPMC and Sodium Dodecyl Sulfate (SDS)</td>
<td>¹⁸Luo et al., 2013</td>
</tr>
<tr>
<td>Desloratadine</td>
<td>Poloxamer 188 and poloxamer 407</td>
<td>¹⁹Kolasinac et al., 2012</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>sodium carboxymethyl cellulose (Na-CMC) and HP-β-CD</td>
<td>²⁰Kang et al., 2012</td>
</tr>
<tr>
<td>Telmisartan</td>
<td>Poloxamer 407, PEG 6000</td>
<td>²¹Patel et al., 2012</td>
</tr>
</tbody>
</table>
3. DISCUSSION

Surfactants have both a hydrophilic and a hydrophobic portion and are generally classified as anionic, cationic, or nonionic. Surfactants are chemical agents that change the characteristics of solution interfaces. They elevate the solubility and diminishes the interfacial tension. The hike in total aqueous solubility that occurs in a surfactant system is always related to a decrease in interfacial tension. Since the solubility of a drug molecule in water is likely to be contingent on numerous varied structural factors and properties viz., size, shape, hydrophobicity of substituent groups, and their effect on the water structure, degree of ionization and another solute–solvent and solute–solution interactions. The relative solubility increase by various surfactants was found to vary with the nature of the drug. The impacts of surfactant on the medication discharge rate have been broadly examined. Large numbers of the researchers worried about the surfactant impacts on discharge rate from various matrices especially from the hydrophilic polymers, hydrophobic polymer, and hydrophilic–hydrophobic polymers. In an examination of the impact of stretching on surfactant properties of sulfosuccinates, it was accounted for that if the micelles are little enough the materials are as yet thought to be solvent because the structures are beneath the size that influences lucidity. It was additionally detailed that deflocculating is one of the components that quicken the discharge rate of the somewhat solvent medications. It was discovered that low molecular weight surfactants decrease the surface tension and increase the pace of disintegration, whereas higher molecular weight surfactant decreases the disintegration. Surfactants are known to solubilize inadequately solvent medications at a fixation over the Critical Micelle Concentration (CMC) as revealed previously. Non-ionic surfactant tween 80 was seen as not a decent solvent for the amphoterically inadequately dissolvable drugs, while ionic surfactants sodium dodecyl sulfate (SDS) was seen as much better dissolvable when contrasted with the cationic surfactant cetyl trimethyl ammonium bromide (CTAB). Exceptionally high dissolvability of drugs SDS shows that the non-polar piece of the atom solubilizes into the micellar inside, while the positively charged gatherings are in the external center, diminishing the appalling powers of the head gatherings of the surfactant particles, along these lines diminishing CMC, expanding the conglomeration number and volume of micelles and expanding solubilization. Much lower dissolvability in CTAB demonstrated that the direction of solubilized atoms is with the end goal that the negatively charged gatherings don’t partake in solubilization. It was accounted for the evaluation of solubilization attributes of various surfactants for carvedilol solubilization. It was accounted for the evaluation of solubilization of various surfactants for carvedilol solubilization.
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