ijlpr 2020; doi 10.22376/ijpbs/lpr.2020.10.5.P11-16

International Journal of Lifescience and Pharma Research

Review Article

Pharmaceutics for novel drug Formulations

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 plays 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,

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Recieved On 15 May 2020
Revised On 26 June 2020
Accepted On 05 August 2020
Published On 07 December 2020

Funding This research did not receive any specific grant from any funding agencies in the public, commercial or not for profit sectors.

Citation Ramyasree Jwalapuram, Hindustan Abdul Ahad, Chinthaguinjala Haranath, Reshma Thadipatri, Chenga Venkata Hima Varshitha, Yedire Bharath Kumar , A desktop reference to the solubility enhancement of drugs with the aid of surfactants..(2020).Int. J. Life Sci. Pharma Res.11(5), P11-16 http://dx.doi.org/10.22376/ijpbs/lpr.2020.10.5.P11-16

1. 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[1]. 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. Many approaches implemented to elevate solubility of such drugs viz., micronization, chemical alteration, modifying the pH, solid dispersion, complexation, co-solvency, surfactants, etc. Low aqueous solubility is the main reason that occurred during the formulation development of New Chemical Entities (NCE's) and also for the Generic development[2]. More than 40% of NCE's determined in the pharma firms are practically aqueous insoluble. Solubility is the most vital challenge during formulation development to scientists. A drug taken by the patient should present in the solution form at the site of absorption[3]. Enhanced solubility is desired in formulations like mouth dissolving tablets, solid dispersions for faster onset of action[4]. Solubility enhancement using surfactants has to gain attraction for formulations for their ease of use, simplicity, effective in small concentrations, compatibility with a wide range of drugs[5, 6], and negligible issues in animal and human subjects when the dosage form is given. The present work highlights the drugs which were tried for their solubility enhancement using surfactants, which helps the researchers for a quick look into the past work done in the last 20 years.

2. METHODOLOGY

Numerous practices are used for the improvement of the solubility of poorly water-soluble drugs, among them the following approaches are widely used[7].

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

2.1. 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.

2.2. Classification of surfactants based on charge

The Classification of surfactants[8] based on the charge is illustrated in table 1.

Table 1: Classification of surfactants

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

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

Table 2: Drugs and surfactants used for solubility enhancement

Drug	Surfactant	Reference
Nicotine	Tween 80	[9]Haq *et al*., 2020
Paclitaxel	Span 20 and Tween 80	[10]Khan *et al*., 2020
Emamectin Benzoate	Polyvinylpyrrolidone K30 (PVP-K30)	[11]Huang *et al*., 2019
Silymarin-laden	PVP-K30 and Polyethylene glycol (PEG- 6000)	[12]Ali *et al*., 2019
Levodropropizine	Hydroxypropyl-beta-cyclodextrin (HP-beta-CD)	[13]Yousaf *et al*., 2019
Eprosartan Mesylate	Hydroxypropyl methylcellulose (HPMC) and polysorbate 80	[14]Yousaf *et al*., 2018
Atazanavir Sulfate	Tween 80	[15] Sundar *et al*., 2018
Cefuroxime	PVP-K30 and PEG 4000	[16]Gorajana *et al*., 2015
Cilostazol	Eudragit-L100 and Eudragit-S100	[17]Park *et al*., 2015
Megestrol acetate	HPMC, PVP-K30	[18]Ha *et al*., 2015
Tacrolimus	Capryol PGMC (propylene glycol monocaprylate)	[19]Seo *et al*., 2015
Tadalafil	PEG-4000, Tween80 and Span80	[20]Obeidat *et al*., 2014
Efavirenz	PEG-8000, PVP-K30, Tween 80	[21]Koh *et al*., 2013
Carvedilol	PVP-K30 and Tween 80	[22]Lee *et al*., 2013
Carvedilol	PVP	[23]Marasini *et al*. 2013
Sulfathiazole	PVP-K29/32, sodium lauryl sulphate (SLS)	[24]Dave *et al*., 2013
Meloxicam	PVP	[25]Noolkar *et al*., 2013
Simvastatin	HPMC and SodiumDodecylSulfate (SDS)	[26]Luo *et al*., 2013
Desloratadine	Poloxamer 188 and poloxamer 407	[27]Kolasinac *et al*., 2012
Flurbiprofen	sodium carboxymethyl cellulose (Na-CMC) and HP-□-CD	[28]Kang *et al*., 2012
Telmisartan	Poloxamer 407, PEG 6000	[29]Patel, *et al*., 2012

Benfotiamine	PVP-K30 and HPMC E4	[30]Patel *et al*., 2012
Indomethacin	SLS	[31]Dave *et al*., 2012
Valsartan	HPMC and SLS	[32]Yan *et al*., 2012
Lacidipine	PVP-K29 and K32	[33]Mukharya *et al*., 2012
Repaglinide	PVP-K30	[34]Yin *et al*., 2012
Efavirenz	PEG	[35]Madhavi *et al*., 2011
Sirolimus	PVP-K30	[36]Kim *et al*., 2011
Allopurinol	PVP-K30 and PVP-K90, PEG-4000 and PEG-6000	[37]Samy *et al*., 2010
Itraconazole	PVP, poloxamer	[38]Park *et al*., 2010
Simvastatin	PEG and PVP	[39]Silva *et al*., 2010
Tacrolimus	HP-beta-CD and Dioctyl sulfosuccinate (DOSS)	[40]Joe *et al*., 2010
Ezetimibe	Pluronic 188	[41]Sancheti *et al*., 2009
Atorvastatin calcium	HPMC	[42] Zhang *et al*., 2009
Meloxicam	Poloxamer 188	[43]Ghareeb *et al*., 2009
Ibuprofen	HPMC and poloxamer	[44]Park *et al*., 2009
Ibuprofen	Poloxamer 407	[45]Newa *et al.,* 2008
Rofecoxib	Poloxamer 188	[46]Shah *et al*., 2007
Simvastatin	HP-beta-CD	[47]Jun *et al*., 2007
Lovastatin	PEG-4000 and PVP-K30	[48]Patel *et al*., 2007
Meloxicam	PVP-K30	[49]El-Badry *et al.,* 2006
Ibuprofen	Poloxamer 188	[50] Yong CS et al., 2005
Carbamazepine	PVP-K30	[51]Sethia and Squillante, 2004
Fenofibrate	PEG	[52]Law *et al*., 2003

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–solute and solute–solvent 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[53, 54], hydrophobic polymer[55], and hydrophilic–hydrophobic polymers[56]. 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[57, 58]. 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[59]. Non-ionic surfactant tween 80 was seen as not a decent solvent for the amphoteric 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) [60]. 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 phosphate (CP) at various pH, it was discovered that cationic surfactant CTAB and non-ionic surfactant tween 80 were appropriate for improving the dissolvability of CP, while the anionic surfactants SDS and sodium taurocholate were found as solvency retardants[61, 62].

4. CONCLUSION

The authors conclude from this paper that solubility is the main aspect of drug absorption and action. Among the various approaches in enhancing the solubility addition of surfactants is an economical and easy and effective approach in enhancing drug solubility. This article gives a quick reference to the research on the literature on past work done on solubility enhancement using surfactants in this paper.

5. AUTHORS CONTRIBUTION STATEMENT

All authors involved in the development of theory performed the computations and verified the manuscript.

6. CONFLICT OF INTEREST

Conflict of interest declared none

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