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Research Article

ENHANCEMENT OF SOLUBLIZATION OF IBUPROFEN USING SUCROSE LAURATE

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ABSTRACT

The objective of this paper was to investigate solubility of a poorly-soluble drug (ibuprofen) using sucrose monolaurate. Sucrose laurate was used in this research in different concentrations ranging from 2 to 20% to solubilize ibuprofen. Ibuprofen was analyzed using UV-Visible Spectrophotometer at wave length of 222 nm. The results showed that sucrose laurate in the concentration of 20% gave the best solubility of ibuprofen up to 45 mg/ml. Also the low critical micelle concentration of sucrose laurate favors the solubility of this poorly soluble drug. As a conclusion, this research sucrose laurate can be successfully used for enhancing solubility and hence, the bioavailability of ibuprofen for pediatric administration.

Keywords: Ibuprofen, solubilization, Sucrose laurate, Micellar solublization, Pharmaceutical applications

INTRODUCTION

The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro-intestinal fluids often cause insufficient bioavailability [1-3]. This may be achieved by incorporating the drug in a hydrophilic carrier material obtaining products called solid dispersions [4]. The mechanisms involved in solubility and dissolution rate enhancement include transformation of unstable modifications into more stable ones or even into the amorphous state, reduction of particle size possibly to the molecular level as well as enhancement of wettability and solubility of the drug by the carrier material [5]. However, if a solid dispersion represents a thermodynamically unstable system, it is prone to convert into a more stable state [6].

Ibuprofen is one of the drugs that are classified under non-steroidal anti-inflammatory drugs (NSAIDs) and was used in many research works [7-24]. It acts by inhibiting isoforms of cyclo-oxygenase 1 and 2. NSAIDS are usually poorly soluble in water and it has usually associated with problem on gastrointestinal tract such as ulceration, bleeding and perforation [25]. Ibuprofen is NSAIDs with antipyretic, analgesic and anti-inflammatory properties. They are effective for the treatment of inflammatory disorder and painful condition such as headache, gout, osteoarthritis and also to treat mild to moderate pain of dysmenorrhoea. It must be absorbed into the bloodstream through the wall of the gut but unfortunately less than 1mg of ibuprofen dissolves in 1ml of water (<1mg/1ml).

Oral bioavailability of a drug depends on its solubility and/or dissolution rate, and dissolution may be the rate-determining step for the onset of therapeutic activity. Therefore, poorly aqueous soluble drugs are usually characterized by a low bioavailability due to less absorption, which is a major concern of pharmaceutical industries worldwide [26]. Various techniques available to improve drug solubility as well as drug dissolution of poorly aqueous soluble drugs include micronization, formation of inclusion complexes with cyclodextrins, formation of amorphous drugs, formation solid dispersions of drugs using various hydrophilic carriers, and formation of micelles by using surface active agents [27].

There are many types of chemicals that can be used as safe surfactants such as alkylbenzenesulfonates, alcohol ethoxylates, sulfates, ethersulfates and sucrose esters [28, 30]. Sucrose esters are the safest surfactants in pharmaceutical applications [31, 32].Compared to other non-ionic surfactant, they have many advantages, include mildness; lack of color, odor and taste; rapid biodegradation following use; no toxicity concerns (ethylene oxide free); and in many applications, they require a lower usage rate than do other surfactants [33, 34].

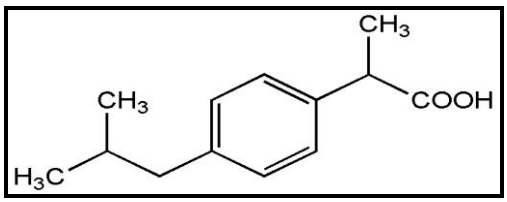

Fig. 1: Structure of Ibuprofen ($C_{13}H_{18}O_2$) (Carvalho et al., 2006) [35]

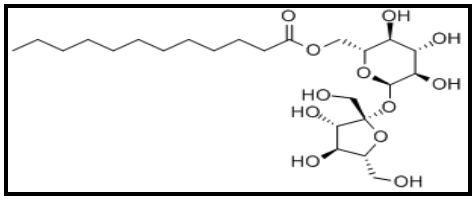

Fig. 2: Chemical structure of sucrose laurate(Adapted from Youan et al., 2003) [35]

MATERIALS AND METHODS

Ibuprofen and sucrose laurate were supplied by Sigma Bhd. Sdn. Other chemical were of analytical reagent. Distilled and sterilized water was used to prepare all solutions. Surfactant solutions were prepared by dilution of sucrose laurate stock solution (20% w/v) at the following concentration: 0.07815, 0.15625, 0.3125, 0.625, 1.25, 2.5, 5, 10, and 20% w/v. The surface tension of surfactant solutions were determined using Du Nouy ring method at room temperature [36] which measures the force required to detach a platinum ring from a surface. The maximum force needed to pull the ring through the inter phase is expressed as surface tension, mN/m. The ring was cleaned carefully with chromic acid and several times of water is appropriated to minimized errors.Excess amounts of Ibuprofen (more than 200mg/5 ml) were added to aqueous solutions of increasing sucrose laurate solution concentration (8 solutions). Each sample was centrifuged at 5000 rpm for 5 minutes to get clear solution. The supernatant was diluted as to be accurately detected by the UV-Vis spectrophotometer. The standard solution for solubility measurement was prepared by dissolving ibuprofen in sodium hydroxide solution. A standard linear graph is obtained from ibuprofen standard sample in the concentration 1 x 10^{-6}, 1 x 10^{-5}, 1 x 10^{-4}, 1 x 10^{-3}, 0.01, 0.1, and 1% w/v. The solutions were prepared from the stock solution using 25 ml volumetric flask. The ibuprofen adsorption was determined using UV-Visible Spectrophotometer at 222 nm.

RESULTS AND DISCUSSON

The aqueous solubility of an active pharmaceutical ingredient is a main criterion since it determines the dissolution, absorption and

thus the efficacy of the drug in the human body [36]. In this research, solubilization of ibuprofen was improved using sucrose laurate as surfactant. Contacts between drug particles and water are reduced and the drug becomes more soluble in water. This phenomenon facilitates the administration of drugs in pediatric therapy. It is also a convenient method for some people who cannot swallow solid dosage forms of this drug as tablets or capsules [28]. The results showed that the relationship between concentration of sucrose laurate surfactant and absorbance of ibuprofen is directly proportional to each other. In other word, when the concentration of the surfactant increased. This is because at higher concentration the surfactant forming micelles are formed and held the ibuprofen molecule together thus increases its solubility. This experimental method using a sucrose ester surfactant provides an option tool to improve the release of poorly soluble drugs in aqueous solution. The proposed method of solubility improvement is simple, safe for human. Thus, solubilization technique by sucrose esters proved its efficiency and safety for the formulation of ibuprofen in liquid dosage form.

Table 1: Surface tension for different concentration of sucrose laurate

Concentration of sucrose laurate (% w/v)	Surface tension (mN/m)
0	68.0 ± 0.01[a]
0.07815	37.3± 0.03[b]
0.15625	36.2±0.05[c]
0.3125	35.0±0.03[d]
0.625	35.0±0.06[d]
1.25	35.0±0.02[d]
2.5	34.5±0.01[e]
5.0	34.0±0.05[e]
10.0	33.0±0.03[f]
20.0	32.5±0.04[g]

[a-g]Means within a column with same subscript are not significantly different at (P < 0.05).

Values are means of triplicate measurements.

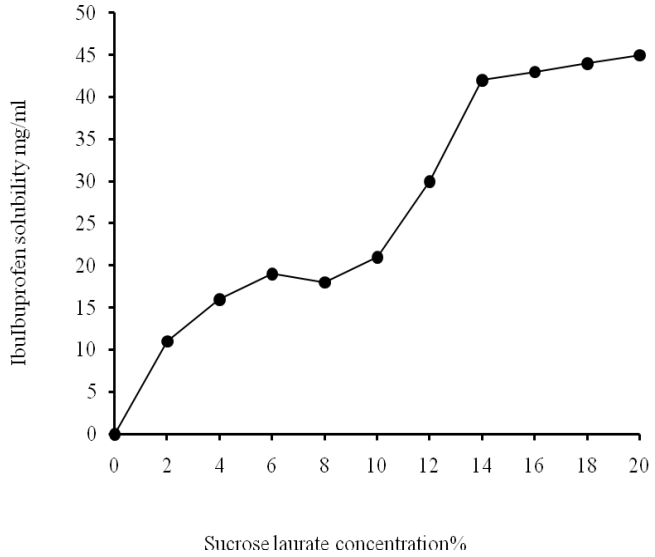

Fig. 3: Solubility of Ibuprofen in different concentrations of sucrose laurate

CONCLUSION

The application of micelles in drug delivery is used to minimize drug degradation, drug loss, prevent harmful side effects and increase drug bioavailability. The low toxicity of non-ionic surfactants makes them particularly interesting for solubilization and drug delivery purposes. Sucrose laurate is preferred than other non-ionic surfactants because it is it has a high value of HLB (Hydrophil Lipophil Balance) of 15 and less toxic. Based on the results obtained, it can be concluded that solubility of ibuprofen can be improved using sucrose esters as surfactants. The finding of this research suggested that sucrose laurate can be successfully used for enhancing solubility and hence, the bioavailability of ibuprofen for pediatric administration.

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