UNIVERSITI TEKNOLOGI MARA

FORMULATION AND EVALUATION OF AN ISOCRATIC MIXTURE LIQUID SELF-NANOEMULSIFYING SYSTEM TO IMPROVE LIPOPHILIC DRUG DELIVERY THROUGH GASTROINTESTINAL TRACT

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Self-nanoemulsifying drug delivery system (SNEDDS) is an isocratic mixture of oil, surfactant and co-surfactant which spontaneously emulsifies in water under gentle agitation. SNEDDS has been reported to increase the absorption rate and enhance the plasma concentration of poorly water-soluble compounds. The rate limiting dissolution step is avoided by presenting the compound in solution. In addition, SNEDDS deliver the compound as fine emulsion giving a large surface area for diffusion. It is released by lipid digestion. Solubilisation of drug in the core micelles is important to maintain the compound in solution. The solubility of the compound in oils and several formulations was examined to determine the dose loading potential. This study was performed to evaluate self-nanoemulsification as a potential delivery system to improve the bioavailability of drugs. The ternary phase diagram was used in this study to screen potential surfactants and co-surfactants for SNEDDS formulations. Various combinations of surfactants and co-surfactants were evaluated on their self-emulsifying properties. Combinations of surfactants and co-surfactants that showed good self emulsifying properties were selected for subsequent evaluations. Combinations of more than two or three surfactants and co-surfactants provided good self-emulsifying properties. The combination of polyoxyethylene sorbitan mono-oleate (T80) / oleyl polyoxylglycerides (OP) (2:1), caprylic capric triglycerides (CCT) / ethoxylated castor oil (ECO) (2:1) and olive oil (OO) showed the best emulsifying property. The best performing isocratic mixture of SNEDDS was selected and loaded with ubiquinone as the model of drug at different percentages, up to 25% w/w. An additive (α-tocopherol) was loaded into the formulation combined with ubiquinone to prevent crystallization of SNEDDS and improved solubilisation capacity of ubiquinone. A simple analytical method of determining ubiquinone in rat plasma was also developed by direct injection into the HPLC. Under these conditions the method had a mean recovery of 99.5%, while within-day and between-day coefficients of variation and percentages of error were less than 5%. The limit of quantification was 0.189μg/ml. Finally, *in vivo* studies were done to study the bioavailability of ubiquinone in the rat plasma. The SNEDDS formulations achieved a higher rate and longer extent of absorption compared with the self microemulsifying drug delivery system (SMEDDS) and oil-based formulations under fasting condition. Moreover, the 90% confidence interval of the logarithmic transformed AUC values of SNEDDS over those of SMEDDS was between 1.3 and 1.7. Meanwhile, SNEDDS over oil suspension was between 2.2 and 3.6 whereas SMEDDS over oil suspension was between 1.5 and 2.3. This demonstrated the potential use of SNEDDS to enhance bioavailability of hydrophilic compounds.

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TABLE OF CONTENTS