UNIVERSITI TEKNOLOGI MARA

SOLUBILITY ENHANCEMENT MECHANISM OF LOVASTATIN USING ARGININE AS CO-SOLUTE

NUR FARAHANI BINTI ZOLKIFLEE

Thesis submitted in fulfillment
of the requirements for the degree of
Master of Science
(Pharmaceutics)

Faculty of Pharmacy

April 2019

ABSTRACT

Lovastatin (LVS) is one of the cholesterol lowering drugs categorised as Class II Biopharmaceutics Classification System (BCS). LVS exhibits low aqueous solubility and bioavailability thus presenting a great challenge to formulators. Though various studies have been conducted to enhance its solubility however, very few actually describe this phenomenon in terms of thermodynamics and solute-solvent interaction. Arginine (ARG), an amino acid, has been reported to enhance the solubility of wheat protein gluten that is extremely insoluble through hydrogen bonding and π electron-cation interaction. Hence, the purpose of this study was to explore the feasibility of ARG as a solubility enhancer for LVS. It also aimed to describe the solute-solvent and solute-cosolute interactions, as well as thermodynamics parameters that bolstered the solubility of LVS in the presence of ARG. The water solubility of LVS at different concentrations of ARG (0.01-0.8 mol dm^{-3}) was determined. These solutions were subjected to conductometric, volumetric, viscometric, acoustic and refractometric measurements at temperatures (T) of 298.15, 303.15 and 308.15 K. Furthermore, ultraviolet-visible (UV) spectrophotometric data were collected to complement thermophysical findings. A significant solubility enhancement of LVS in the presence of ARG as a co-solute was observed. Thermodynamic parameters obtained suggested a high degree of solute-solvent interactions and formation of complexation of LVS and ARG which was confirmed by spectral results. Though strong solute-solute interactions were detected in the LVS-ARG system, however solute-solvent interactions dominated. Based on results of the maximum molecular interaction and polarizability of the LVS-ARG system, it could be concluded that solute-solvent interaction was associated with the water structure disruption followed by solvation.

ACKNOWLEDGEMENT

Firstly, Alhamdulillah thanks to Allah for giving me the opportunity to embark on my master studies and for completing this challenging journey successfully. My gratitude and thanks go to my supervisor Dr Meor Mohd Redzuan Meor Mohd Affandi for continuous support of my research motivation and sharing his immense knowledge. His guidance during our meetings has helped me in all the time of research and writing of this thesis.

I wish to express my thanks to Prof Dato' Dr Abu Bakar Abdul Majeed, my co-supervisor for his guidance and suggestions. His help has made the completion of this thesis possible. I also would like to thank my Plant Design supervisor Dr Azilah binti Ajit for her splendid recommendation letter and helpful advice before I decided to begin this journey.

My appreciation goes to my lab mates Kak Zura and Kak Hanim and also to the science officers of Faculty of Pharmacy who provided assistance during experimental works. Special thanks to my former colleagues in FKKSA for the continuous moral support and academic discussions even if we are not working in the same area of study anymore.

Finally, this thesis is dedicated to my parents for the vision and determination to educate me. Thank you for always having my back.

TABLE OF CONTENTS