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INVESTIGATION OF THE SOLID DISPERSION OF AQUEOUS INSOLUBLE DRUG (GRISEOFULVIN) WITH POLYETHYLENE GLYCOL (PEGs) BY THE MEANS OF NMR SPECTROSCOPY

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ABSTRACT

Poorly water-soluble drugs are associated with slow drug absorption leading eventually to inadequate and variable bioavailability. Nowadays, there are many approaches that have been developed to improve the solubility of drugs. Some of the examples are increasing the total surface area of the drug (surfactant), modification of crystal form of the drug, and the inclusion and complexation of the drug substance with the excipient. The incorporation of drugs into hydrophilic carrier has frequently been reported to increase the dissolution rate of poorly soluble drugs, often leading to improved drug bioavailability. Polyethylene glycols (PEGs) are water-soluble liquids or waxy solids used in cosmetic and pharmaceutical preparations and in the manufacturing of emulsifying or wetting agents and lubricants. Polyethylene glycol 400 (PEG 400) is a good example of a commonly used inert cosolvent that has wide application across several therapeutic areas for both oral and parenteral administration. PEGs can form a complex with aqueous insoluble drugs and interact well with water molecules; therefore in this study it could act as hydrotropic agent to enhance the solubility of aqueous insoluble griseofulvin. However, the molecular mechanism of hydrotropic solubilization has not yet been elucidated completely and studies have shown that hydrotropy differs from the micellar solubilization of hydrophobic substances in water by surfactant molecules. Therefore, the solid dispersion of aqueos insoluble griseofulvin with different concentrations of PEGS was done by the means of NMR spectroscopy to detect any chemical shifts, conformational changes and also more importantly to detect any increase in griseofulvin solubility and dissolution rate.

CHAPTER 1

INTRODUCTION

1.1. BACKGROUND OF THE STUDY

Poorly water-soluble drugs are associated with slow drug absorption leading eventually to inadequate and variable bioavailability (Serajuddin et al., 1990). Horter and Dressman (1997) defined a poorly water-soluble drug as the one whose dissolution in the gastrointestinal fluid (GI) under ordinary conditions takes a longer time than its transition through the absorption sites in the GI tract. Therefore, most formulation strategies for such drugs are targeted at enhancing their dissolution rate and/or solubility in vivo by achieving their fine dispersion at absorption level. Although salt formation, particle size reduction, and others have commonly been used to increase dissolution rates of drugs, there are practical limitations with these techniques and the desired bioavailability enhancement may not always be achieved (Wadke et al.,1989; Serajuddin, 1999). Solid dispersion systems in which the drug is dispersed in solid water-soluble matrices either molecularly or as fine particles have also shown promising results in increasing bioavailability of poorly water-soluble drugs (Chiou and Riegelman, 1971; Ford, 1986).