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Original Article

DEVELOPMENT OF LIQUISOLID FORMULATION FOR IMPROVED SUSTAINED RELEASE OF PROPRANOLOL HYDROCHLORIDE

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ABSTRACT

Objective: The aim of this study was to develop a liquisolid formulation of propranolol hydrochloride to obtain an improved sustained release profile by varying the ratio of liquid vehicles.

Methods: In this study, propranolol hydrochloride (PPH) was dispersed in the combination of propylene glycol and polysorbate 80, as the liquid vehicles, with different ratios. Eudragit® RL and Aerosil® were used as carrier and coating materials, respectively, to produce a dry and free-flowing powder. In addition, HPMC was used to amplify the retardation effect. The prepared formulations were evaluated for its physicochemical properties, including loss on drying, flow rate, angle of repose calculation, drug content analysis, FT-IR spectroscopy, as well as dissolution studies. The obtained dissolution profiles were subsequently fitted to the mathematical model in order to determine the drug kinetics.

Results: The results show that all formulations performed dry and free-flowing granules containing PPH in the range of 7-9%. Furthermore, all the prepared formulations were able to sustain the drug release for a total of 8 h in two different dissolution media, namely simulated gastric fluid and simulated intestinal fluid. F4 containing propylene glycol and polysorbate 80 (1:2) possessed the lowest drug release rate. It was also obtained that F1 and F3 followed first-order kinetics while F2, F4, and F5 complied with the Higuchi model.

Conclusion: Overall, there was no difference in all the dissolution profiles based on the calculation of the difference and similarities factor.

Keywords: Liquisolid granules, Propranolol hydrochloride, Sustained release

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INTRODUCTION

During the last decades, conventional dosage forms are rapidly replaced by novel drug delivery systems. Sustained release dosage forms have become one of the most favourable in modern therapeutics [1]. Sustained release drug delivery system is an alternative to maintain therapeutic dose in the systemic after a single application. This can be a solution to optimize the efficacy and safety of the treatment, also reduce the frequency of drug consumption resulting in improving patient compliance [2]. The candidate drug that is able to be formulated into sustained release dosage form must possess some of the criteria, including having a short half-life, high-frequent usage of drugs, and low dose drugs, which are preferred [3]. There are several methods that can be utilised to sustain the drug release, including the incorporation of drugs into hydrophobic materials, coating with swelling polymers, and encapsulating the drug molecule with certain polymers [4].

Liquisolid technology is a novel and promising method to produce a free-flowing and compressible dry powder using simple physical mixing of carrier and coating materials incorporated into a non-volatile liquid containing drugs [5]. The type of liquid used in this system is mainly non-volatile liquid, water-miscible with high boiling temperatures, such as propylene glycol, polyethylene glycols, glycerine, or polysorbate [5]. The drug powder is incorporated in the liquid resulting in liquid medication, either a drug solution or a drug suspension. After the carrier powder is saturated with the liquid medication, a liquid layer formed on the particle surface is adsorbed by the coating material. Consequently, a dry, free-flowing, and compressible powder is obtained [6]. This technology is initially used in the purpose of improving drug solubility of poorly water-soluble drugs by using water-soluble polymer [7–9]. However, this method has been developed and the same principle was utilised to prepare sustained release formulation using hydrophobic polymers [5, 10]. This method is preferred due to its simplicity, versatility, and low cost [2].

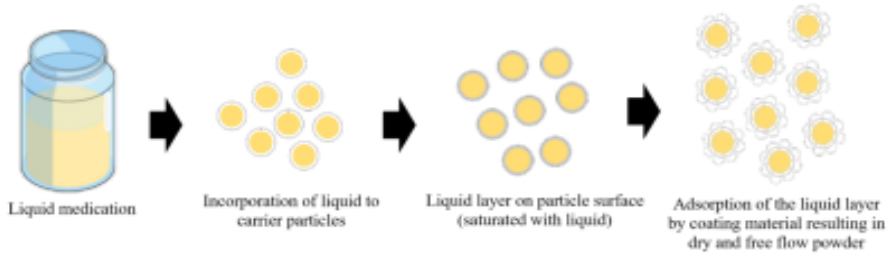

Fig. 1: Schematic representation of liquisolid system

Propranolol, in the form of hydrochloride salt, is a suitable drug for sustained release formulation. It is one of the β-blocker anti-hypertension drugs with a dose of 40 mg twice daily [11]. Propranolol is classified in the Biopharmaceutical Classification System (BCS) Class I with high solubility and high permeability which lead to fast elimination out the body. Additionally, it has low