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RELEASE ADJUSTMENT OF DRUG COMBINATIONS WITH DIFFERENT DRUG SOLUBILITY FROM MULTILAYERED PELLET SYSTEMS

A. Y. Chaerunisaa, A. Dashevskiy, R. Bodmeier
College of Pharmacy, Freie Universität Berlin, Berlin, Germany

ABSTRACT

Purpose: To control the release of two drugs of different solubility from multilayered pellets coated with ethylcellulose (EC):HPC blends.

Methods: Model drugs with different solubility (propranolol HCl, diprophylline, theophylline, and caffeine) were layered onto sugar cores (Suglets® 710-850µm) using 20% HPMC (Methocel®E5) as the binder to achieve a 15% weight gain in a fluidized bed coater (Aeromatic Strea-1). Drug-layered pellets (D_1) were coated with EC: HPC (ratio 65:35 to 80:20) in a fluidized bed coater (Mini Glatt®) to achieve coating levels of 10%w/w as first coating (C_1). For multilayer pellets, carbamazepine, theophylline or caffeine as second drug layer (D_2) were layered onto coated D_1 pellets. Multilayer drug-loaded cores were coated with EC : HPC (ratio 60:40 to 75:25) as second coating C_2. The drug release was performed in a USP paddle apparatus.

Results: Due to different solubilities of the two drugs, the same drug release profile could not be achieved from the same pellets with the same polymeric coating. Therefore, drug with high solubility (D_1) was coated by less permeable coating (C_1) consecutively layered with low soluble drug (D_2) and coated with more permeable coating (C_2). The permeability of first and second coating were adjusted with the HPC content and coating level. Based on experimental data, an applicability map of drug combinations with coating parameters (amount of HPC and coating level) for first and second coating were elaborated in order to achieve the desired release of D_1 and D_2. The correlation between solubility of D_1/D_2 to release of D_1 /D_2 follows pareto law (exponential). Different combinations of drug loading in multilayer pellets showed that higher drug loading ratio of D_1/D_2 gave an increase in release ratio of D_1/D_2.

Conclusion: Release of drug combinations from multilayer pellets with desired release could be adjusted and predicted by changing HPC content and coating level of each coating.

Keywords: Drug combination, release, coating, pellets

INTRODUCTION

Oral dosage forms can be in the form of tablets, capsules and pellets. Pellets, in turn, can be filled in to hard gelatin capsules or compressed as tablets. Coated pellets are frequently used for oral controlled drug delivery and offered