Release adjustment of a drug combination using pellets within an erodible matrix system

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ABSTRACT

Purpose: To adjust the release of drugs of different solubility (propranolol HCl and carbamazepine) as drug combination using pellets within an erodible matrix tablets system.
Methods: Sugar cores loaded with 40% propranolol HCl were coated with 10% ethylcellulose 10 cP in a fluidized bed coater. Tablets were prepared by direct compression of blends containing propranolol HCl coated pellets and carbamazepine (drug loading 17.5% w/w for each drug) and the following excipients: hydroxypropylmethylcellulose (HPMC) as a matrix-forming polymer (30% w/w), magnesium stearate (1 % w/w) and lactose (q.s. to achieve tablet weight 600 mg). Drug release was performed in a USP paddle apparatus in phospate buffer pH 6.8.
Results: Using pellets within matrix tables approach, an almost similar release of propranolol HCl and carbamazepine (f2 = 68.3) was obtained. Typical sigmoidal release of highly soluble drug was improved into linear release. Release of propranolol HCl was affected by the ethylcellulose pellet coating and viscosity of HPMC as polymer matrix while that of carbamazepine was affected by the carbamazepine particle size and HPMC. This knowledge facilitates formulation of drug combination of different solubilities. Drug release of soluble drugs can be adjusted by its permeability of the coating, while that of the poorly soluble drug can be adjusted by increasing erosion rate of matrix.
Conclusion: Compression of coated pellets of propranolol HCl and carbamazepine powder as model drugs in the outer matrix was an effective method for adjustable release of propranolol HCl and carbamazepine as drug combinations in matrix tablet system.

Keywords: Release, drug combination, pellets, matrix tablet

1. Introduction

Various diseases such as cancer, acquired immune deficiency syndrome (AIDS), tuberculosis, diabetes (Type 2), heart diseases, or central nervous system (CNS) disorders require medical treatment with more than one drug. Drug combination therapy for the treatment of a disease offers some advantages including increased convenience for physician and patient, improved compliance and low cost of production, storage and transport. One of the manufacturing challenges regarding product formulation issues of drug combination could be due to the different solubility of the drugs which will give different release profile. Several publications have reported the effect of drug solubility on the release from hydrophilic, monolithic matrices. Higher drug solubility generally leads to faster release because of their high diffusional driving force. As drug solubility declined, there was an increased contribution of erosion on drug release from hydrophilic matrix systems (Viriden, 2011b; Zuleger, 2002; Ford et al., 1987; Zueleger and Lippold, 2001).