Development and In vitro Evaluation of Sustained Release Matrix Tablets of Theophylline using Hydrophilic Polymer as Release Retardant


ABSTRACT: In the present investigation, an attempt has been made to increase therapeutic efficacy, reduce frequency of administration and improve patient compliance by developing sustained release matrix tablets of theophylline. Sustained release matrix tablets of theophylline were developed by using drug and different concentrations of polymer such as 10, 20, 30, 40 and 50%. Hydroxypropylmethylcellulose (HPMC) was used as a matrix material and microcrystalline cellulose as diluent. All the lubricated formulations were compressed using 10 mm flat faced punches. Compressed tablets were evaluated for uniformity of weight, drug content, friability, hardness, thickness, in vitro dissolution and swelling index. All the formulations were found to be within pharmacopoeial standards. Among the different formulations, F1 showed sustained release of drug for 12 h with 84.23% release. The effect of release modifier (PEG 6000) on in vitro drug release was also studied. Thus, HPMC can be used as an effective matrix former, to extend the release of theophylline.

KEYWORDS: Matrix tablets, Theophylline, HPMC, in vitro, PEG 6000.

Introduction

The goal of any drug delivery system is to deliver a therapeutic amount of drug to the proper site in the body and to maintain a desired concentration (Longer, 1990). The development of oral controlled release dosage forms has attracted much attention in the recent years and hydrophilic matrix tablets are among the most widely used of the numerous controlled releases dosage forms (Fan, 1989 and Heller, 1987). Hydroxypropylmethylcellulose (HPMC) is hydrophilic cellulose ether widely used as excipients in controlled release preparation, due to their release behavior of the drug (Alderman, 1984 and Wan, 1991). When these formulations meet water there is a rapid hydration of the macromolecules in the solid liquid interface, followed by a formation of a viscous layer (Veiga, 1997). The matrix system produced as a result of this process can pass along the gastrointestinal tract without breaking up, releasing the drug progressively (Wan, 1993). Theophylline, an asthmatic drug is based on the relaxation of bronchi. This drug has a great variability in clearance (elimination t½ 3-4 h, adults 6-12 h) and a narrow therapeutic range (7.5-20 µg/ml). Once or twice daily administration of controlled release preparations in patients with chronic obstructive pulmonary disease (COPD) is recommended for better patient compliance (Sreenivasa Rao, 2001). Hence, in the present investigation, an attempt has been made to fabricate a controlled release dosage form of theophylline using HPMC as matrix material with other commonly used tablet excipient. The in vitro release studies were conducted for all the formulations and an attempt has been made to study the drug release kinetics from the formulations.

Experimental Materials

Theophylline anhydrous was procured from Sigma, USA. The polymer hydroxypropylmethylcellulose (K15M) was obtained as a gift sample from Colorcon Asia Pvt Ltd, Verna, Goa. Microcrystalline cellulose NF (Avicel pH 102) was obtained as gift sample from Signet chemical corporation, Mumbai. All other chemicals and reagents used in the study were of analytical grade.

Preparation of SR matrix tablets

Sustained release tablets of theophylline were prepared by using drug and different polymer concentration such as 5, 10, 15, 20, and 25%w/w of tablet by wet granulation technique as shown in Table 1. HPMC was used as a matrix forming material, while microcrystalline cellulose (Avicel pH102) was used as a diluent. Talc and magnesium stearate was used as lubricant. All the ingredients were passed through sieve no 100. Required quantities of drug, polymer and diluents were mixed thoroughly and sufficient quantity of granulating agent (isopropanol and water in the