Introduction

Theophylline is well known used in asthma. Its therapeutic range is narrow, blood level concentration between 10-20 micrograms. Due to its toxicity and easily to be eliminated from blood circulation, to control the release rate and reduce the frequency of administration, it is necessary to prepare in controlled release dosage form. From several reports, the methods of production are spray drying techniques (Takeuchi, H. et al 1989), direct compression (Young, S. and Horng, Y., 1989), matrix tablet (Shah, A.C., 1989, Timmins et al 1992), membrane coated tablet (Marini et al 1991), Pelletization (Mario, A. et al 1983).

This experiment performed by wet granulation using Sodium alginate as hydrophilic polymer. (Alginate forms gel in water but it is insoluble at pH less than 3, Boylan, 1986). The release rate of tablet affected by gel formation and erosion of matrix. The release profile will show the release rate at different pH in term of diffusion constant and erosion constant. The pH relate to viscosity will be discussed. The releasing pattern of theophylline at different pH will be shown.

Materials and method

Sodium alginate (Seco, Lot. No. 7/6, Germany), Theophylline (Fluka, Germany) 200 mg were used as matrix and active ingredient respectively.

By wet granulation method with 10% PVP K-30 as binder and absolute alcohol as granulating liquid. The tablets were made using single punch tablet machine (Yeo Heng, Bangkok) with the ratio of drug/matrix was 1:1, 1:2 and 1:3 respectively. The tablets were 1/2 inch diameter and controlled hardness between 5-7 kg. The percent friability was less than 0.4. The weight variations were in acceptable range.
Viscosity studies. Using Oswald viscometer (A.H. Thomas Co., PA., USA) to determine viscosity at different pH.

Dissolution studies  The drug release test of the tablets was carried out according to the USP apparatus II in the simulated gastric fluid (pH 1.2), Phosphate buffer pH 4.5, 6.5 and intestinal fluid pH 7.5 without enzymes. The dissolution medium was controlled at 37°C and stirred constantly at 50 rpm (Hanson, USA). Samples of tablets equivalent to 200 mg theophylline were taken for dissolution test. The concentration of theophylline was determined spectrophotometrically at 275 nm. (Beckman DU-64, USA) All experiments were performed in triplicate and the mean was presented.

Results and discussion

The release pattern of formulation in different drug-polymer matrix in simulated intestinal fluid (SIF) and simulated gastric fluid (SGF) showed in Figure 1 and 2. We found that the polymer matrix can sustain the drug release in longer than 12 hours at pH 1.2. The polymer matrix is intact. It started by the penetration of water into tablet. The drug dissolved and diffused from the intact matrix. In SIF, the ratio 1:2 is the best formulation for 12 hours complete release but the ratio 1:3 releasing time is longer than 12 hours. The percent release correlated with time by constant rate. From an observation, the matrix eroded outer part of the barrier and at the same time the water penetrated the matrix and formed gel. The gel eroded while releasing drug. Gel forming will block the drug with no diffusion and control the rate of water permeate. When the gel eroded and dissolved, water permeated into inner core to form newer gel to control the release till it dissolved completely.