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Research Article

DEVELOPMENT AND EVALUATION OF MUCOADHESIVE BUCCAL TABLETS OF SALBUTAMOL SULPHATE

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ABSTRACT
Prime object of present study was to develop and evaluate mucoadhesive tablets of Salbutamol Sulphate by non aqueous granulation of polymers HPMC K-4M (Hydroxypropyl Methyl Cellulose) and Chitosan in different ratios (1:1. 1:2 & 2:1). The tablets were evaluated for weight variation, hardness, thickness, drug content uniformity, mucoadhesion and swelling index. Swelling index of batches containing more HPMC K-4M was greater than that of containing less HPMC K-4M. In vitro bioadhesive strength studies showed that tablets containing more HPMC K-4M were excellent in bioadhesive nature. The in-vitro drug release was studied in phosphate buffer (pH 6.8). And all batches were subjected to release kinetics model fitting.

KEYWORDS: Mucoadhesive, Salbutamol sulphate, Buccal tablet, HPMC, Swelling index, Bioadhesive

INTRODUCTION

Salbutamol sulphate is widely used as a bronchodialator, tocolytic and adrenergic β-agonist. It is a moderately selective (β-2) receptor agonist similar in structure to terbutaline, is widely used as a bronchodialator to manage asthma & other chronic obstructive airway disease. The R-isomer - levabuterol is responsible for bronchodialation while the S-isomer increase bronchial reactivity.
Salbutamol sulphate is a β-2 adrenergic agonist. It stimulates β-2 adrenergic receptor in the lungs results in relaxation of bronchial smooth muscle. It is believed that salbutamol sulphate increases cAMP production by activating adenylate cyclase and the action of salbutamol sulphate are mediated by cAMP. Increase intracellular cAMP increase the activity of cAMP dependent protein kinase, which inhibits the phosphorylation of myosin & lowers intracellular calcium concentration. A lowered intracellular calcium concentration leads to a smooth muscle relaxation.
The doses forms of salbutamol sulphate are also available as oral solution, syrups, tablet and injection etc. But there are several reasons to select this drug for a mucoadhesive buccal tablet, which is a type of controlled release dosage form -

- It is readily absorbed from the gastro-intestinal tract
- Because of first pass metabolism its oral bioavailability is 50%.
- Small doses, suitable half-life and good solubility,

Successful buccal drug delivery using buccal adhesive system requires at least three of the following (a) a bioadhesive to retain the system in the oral cavity and maximize the intimacy of contact with mucosa (b) a vehicle the release the drug at an appropriate rate under the conditions prevailing in the mouth and (c) strategies for overcoming the low permeability of the oral mucosa. Buccal adhesive drug delivery stem promote the residence time and act as controlled release dosage forms[1,9].

MATERIALS AND METHODS

Salbutamol sulphate was a gift sample from Pharmasynth Formulation Ltd. Haridwar (PFL) and HPMC K4M & Chitosan were also gift sample from Pharmasynth Formulation Ltd. Haridwar (PFL).

Preparation of mucoadhesive tablet

Buccal mucoadhesive matrix tablet each containing 10mg of Salbutamol sulphate were prepared by non-aqueous granulation method (using isopropyl alcohol). Polymers were sieved in different ratios and then Salbutamol sulphate was mixed in that mixtures, then granulation was done with isopropyl alcohol, that damp mass was passes through 16 no. sieve, dried in air and lubricant such as magnesium stearate, talc and diluents such as microcrystalline cellulose, aerosil were mixed and then compress 110mg tablet using 16-station rotary compression machine, to a hardness of 4-6 kg/cm^2 with 6.0 mm punch[6,7,8]. All the prepared tablets were evaluated for friability, hardness, and weight variation and disintegration time. Disintegration time was determined using phosphate buffer pH 6.8 as a test fluid.

The formulated tablets were evaluated for weight variation, hardness and friability according to pharmacopeial protocol. Tablets of each formulation were ground in a mortar to make powder. An accurately weighted amount of the powder, equivalent to 10mg of the drug was pored into 100ml volumetric flask. The powder was dissolved in phosphate buffer (pH 6.8) using a magnetic stirrer for 25±2 minutes. After filtration solution was assayed spectrophotometrically (Double Beam UV Visible Spectrophotometer, Shimadzu 1700 series) for Salbutamol sulphate at 278nm, against phosphate buffer (pH 6.8) blank. The drug content was calculated from the standard calibration curve of drug in pH 6.8 buffer. The bioadhesive strength of the tablet estimated using a modified physical balance[2]. Porcine pouch was used as model membrane for measurement of bioadhesive strength and phosphate buffer pH 6.8 as a moistening fluid. The weight required to detach the tablet from the mucosal surface was taken as the measure of bioadhesive strength[4,9].

The water absorbing capacity of tablets was calculated by gravimetry. The swelling rate of the bioadhesive tablet was evaluated by using 1% agar gel plate. The average weight of the tablet was calculated (W_1). The tablets were placed on gel surface in a petri dish at 37±1^0. Tablets were removed at different time intervals (0.5, 1.0, 2.0, 3.0, 4.0 hrs.) wiped with filter paper and reweighed (W_2). The swelling index was calculated by the formula[3].

$$\textbf{Swelling index} = (W_2 - W_1)/W_1$$

The drug release rate was determined using USP type III dissolution apparatus. The tablet was placed in dissolution vessel containing 900 ml of phosphate buffer (pH 6.8) at 37±1^{0}C and the paddle was stirred at 30rpm. At the interval of 30 minutes 5 ml of samples were withdrawn up to 5 hours and same volume of samples was compensated with fresh dissolution media and assayed spectrophotometrically at 278nm using double beam spectrophotometer (Shimadzu 1700). All samples were analyzed in triplicate.

Kinetics of drugs release

Dissolution data of the prepared formulations of Solbutamol was fitted to various mathematical models (zero-order, first order and Higuchi) in order to describe the kinetics of drug release[5].

RESULTS AND DISCCUSSION

The various physical parameters for the tablets were found as follow-

The hardness of the tablets containing HMPC K-4M & Chitosan in ratio 1:1, 1:2 & 2:1 were found to be 5.0 kg/cm^2, 3.0kg/cm^2 & 5.2kg/cm^2 respectively. On the basis of results their hardness was in order of HC-1>HC-3>HC-2 showing that as the ratio of HPMC in tablets was increased the hardness of tablet also increased and when the ratio of Chitosan was doubled as compare to HPMC, showed minimum hardness of 3.0kg. The thickness of the tablets were found to be 3.1, 3.2, and 3.2 mm and the friability of the tablets were found in the range of 0.40 – 0.70%. The drug content of the tablets of batches HC-1, HC-2, HC-3 was found in the range of 100±5%. The surface pH of tablets of batches HC-1, HC-2 and HC-3 was found to be 6.02, 5.65 and 6.8 respectively.

The swelling index of buccal adhesive tablets for a period of 4-hr is shown in figure-1. The tablets containing HPMC K-4M & Chitosan in the ratio of 1:1, 1:2, 2:1 showed swelling rate as 0.267, 0.305 and 0.241 respectively.

The bioadhesive strength was measured in the sense of adhesion between a polymer and mucus. The observed bioadhesive strength of the tablets batches HC-1, HC-2 & HC-3, in the order of HC-3<HC-1<HC-2. It showed that HPMC K4M was more responsible for bioadhesion as compared to chitosan.

The *in-vitro* drug release studies were performed in dissolution apparatus USP type III. The result showed that drug release from tablets was up to 4.5 hrs and in between 4.5 to 5.0 hrs no significant increase was observed. The cumulative % drug release from tablets batches HC-1, HC-2 & HC-3 at 4.5 hrs were 85.02%, 83.27%, and 86.33% respectively. (Figure 2)

All release kinetic models were applied on the formulation HC-1, HC-2 & HC-3. The best-fit model was found to be zero order for all formulation. (Table-1)

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Table 1: Kinetic Studies

Kinetic model		Batches		
		HC-1	**HC-2**	**HC-3**
Zero	R	0.9964	0.9952	0.9964
	SSQ	56	78	60
	K	17.8162	17.2527	18.293
Ist	R	0.95	0.9469	0.9526
	SSQ	958	994	954
	K	-0.3307	-0.3112	-0.3479
Matrix	R	0.9191	0.9093	0.9246
	SSQ	1414	1550	1365
	K	32.5819	31.4368	33.5226
Hixcrow	R	0.9738	0.9712	0.9776
	SSQ	456	514	427
	K	-0.0874	-0.0838	-0.0910

SSQ = Residual Sum of Square

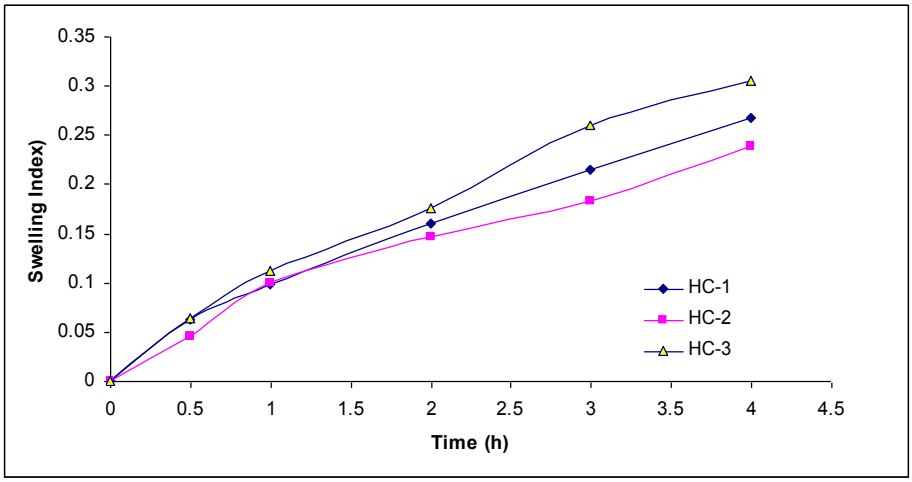

Figure 1: Swelling index profile of buccal adhesive tablets of Salbutamol Sulphate

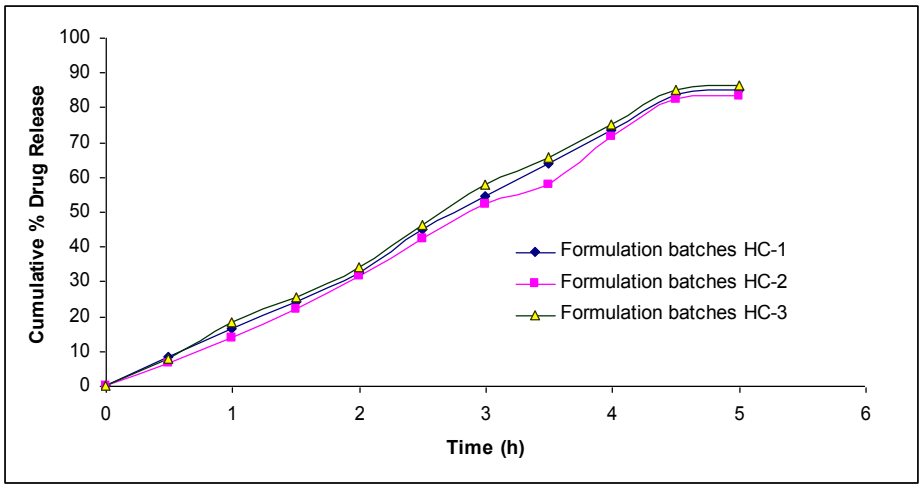

Figure 2: Swelling index profile of buccal adhesive tablets of Salbutamol Sulphate

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