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Research Article

DEVELOPMENT AND EVALUATION OF MUCOADHESIVE BUCCAL TABLETS OF SALBUTAMOL SULPHATE

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ABSTRACT

Mucoadhesive tablets of salbutamol sulphate were prepared by non aqueous granulation of polymers HPMC K-4M (Hydroxypropyl Methyl Cellulose) & EC (Ethyl Cellulose) 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 contain less HPMC K-4M. In vitro bioadhesive strength studies showed that tablets containing more HPMC K-4M were great bioadhesive in nature. The maximum in-vitro release observed in formulation HE-1. (1:1 ratio) and the kinetics studies shows that release follows peppas model.

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 -

1. It is readily absorbed from the gastro-intestinal tract
2. Its oral bioavailability is 50%.
3. It is subject to first pass metabolism in the liver and due to this dosage form, its bioavailability is reaches to 100%
4. 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].

MATERIALS AND METHODS

Salbutamol sulphate was a gift sample from Pharmasynth Formulation Ltd. Haridwar (PFL) and HPMC K4M, Ethylcellulose, Polyvinyl pyrrolidone k-30 & Sodium alginate 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 are sieved in different ratios and then salbutamol sulphate is mixed in this mixtures, then granulation is done with isopropyl alcohol, this damp mass pass through 16 no. sieve, dry then in air and lubricant such as magnesium stearate, talc & diluents such as Microcrystalline cellulose, Aerosil are mixed and then compress it with 16-station rotary compression machine into 110mg tablet, to a hardness of 4-6 kg/cm^2 using 6mm punch. All the prepared tablets were evaluated for friability, hardness, weight variation and disintegration time. Disintegration time was determined by 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 min. after filtration the solution was assayed spectrophotometrically (UV Visible Spectrophotometer, Sumarzu 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.

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, was placed in an incubator 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.

Swelling index = $(W_2 - W_1)/W_1$[3]

The drug release rate was determined using USP dissolution apparatus. The tablet 110 mg was glued in the center of a 9 cm diameter glass disc. The dissolution media was phosphate buffer pH 6.8 maintained at 37±1^0 and stirred at 30rpm. Samples (5ml)

withdrawn at suitable time interval, were compensated with fresh dissolution media and assayed spectrophotometrically at 278nm. Samples were analyzed in triplicate. To examine the release kinetics of Salbutamol sulphate from the prepared buccoahesive tablet, the results were analyzed by employing the Peppas and Sahin equation[4], $M/M\alpha = Kt^n$, where $M_1/M\alpha$ is fractional drug released at a time t. value of n was calculated to determine Fickian /Non-Fickian release characteristics of the drug. (table.1)

RESULTS

The various physical parameters for the tablets are found as follow:

The hardness of the tablets containing HMPC K-4M & EC in ratio 1:1, 1:2 & 2:1 was observed as 5.0 kg/cm^2, 3.0kg/cm^2 & 5.2kg/cm^2 respectively. The thickness of the tablets were found as 3.1, 3.2, &3.2 mm & the friability of the tablets were found in the range in the range of 0.40 – 0.70%. The drug content of the tablets were found as in formulation HE-1, HE-2, HE-3 in the range of 100±5%. The surface pH of tablets of batches HE-1,HE-2 and HE-3 were as 6.02, 5.65 and 6.8 respectively.

The swelling index of buccal adhesive tablets for a period of 4-hr is shown in fig.1 The tablets containing HPMC K-4M & EC at the ratio of 1:1, 1:2, 2:1 showed swelling rate as 0.267, 0.238 and 0.305 respectively.

The bioadhesive strength was measure of adhesion between a polymer and mucus. The bioadhesive strength of the tablets batches HE-1, HE-2 & HE-3, in the order of HE-3<HE-1<HE-2.

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

DISCUSSION

Among the physical parameters tablets contain HPMC K-4M & EC in ratio 1:1, 1:2 & 2:1 shows hardness in orders 2:1>1:1>1:2, means that as the ratio of HPMC in tablets increases the hardness of tablet also increase and when the ratio of EC is double as compare to HPMC, shows minimum hardness of 3.0kg.

The friability of the tablets of formulation batches HE-1, HE-2 and HE-3 were as 0.45, 068 and 0.41% suggest that as the ratio of HPMC K-4M & EC in ratio 1:1, 1:2 &2:1, were not vary so much.

Table – 1: Kinetic Studies

Kinetic model		Batches		
		HE-1	HE-2	HE-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
Peppas	R	0.9979	0.9980	0.9964
	SSQ	54	69	85
	K	16.3363	14.0995	16.7077
Hixcrow	R	0.9738	0.9712	0.9776
	SSQ	456	514	427
	K	-0.0874	-0.0838	-0.0910

SSQ = Residual Sum of Square

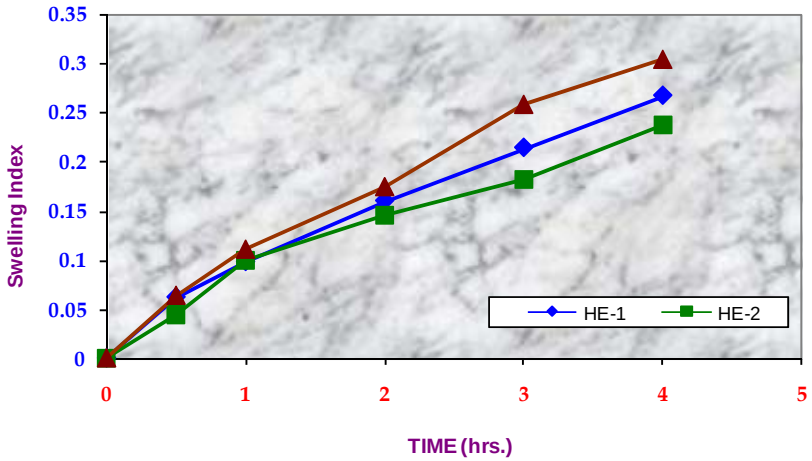

Fig. 1: Swelling index profile of buccal adhesive tablets of salbutamol sulphate

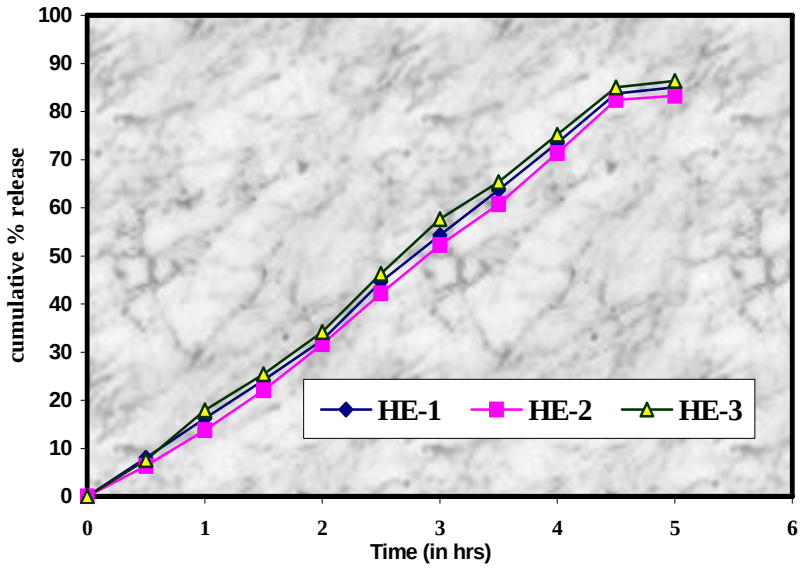

Fig. 2: In-vitro release of salbutamole Sulphate from buccal adhesive tablets containing HPMC K-4M & EC

The swelling index is the water absorbing capacity of the tablets, it was observed in formulation HE-3, which had the polymer ratio 2:1, shows that HPMC had more water absorbing capacity.

In vitro bioadhesion studies show that tablet containing HPMC K-4M & EC (2:1 ratio) has maximum bioadhesive strength, it means HPMC K-4M has more bioadhesive property than EC.

An ideal controlled release system should release the drug immediately to attain the required therapeutic level, at a faster rate and maintain the therapeutic level for longer period of time. The release of drug from tablets varied with the type and ratios of polymers used. The release of salbutamol sulphate from tablets, containing HPMC K-4M & EC at different ratio were near about same, it means in those formulation polymer ratios had not significant effect on drug release.

REFERENCES

1. Varshosaz, J. & Dehghan, Z., Eur. J. Pharm. Biopharm, 2002, 54, 135.
2. Gupta, A., Garg, S. & Khar, R.K., Indian drugs, 1992, 30, 152.
3. Machida, H., Masuda, H., Fujiyana, N., Ito, S., Iwata, M. & Nagal, T., Chem. Pharm. Bull., 1979, 29, 93.
4. Pramod Kumar, T.M., Desai, K.G.H., Development & evaluation of novel Buccaladhesive core-in-cup tablets of proparanolol hydrocheloride Indian J. Pharm. Sci., 2006, 66 (4): 438-443.
5. Peppas, N.A. & Sahlin, J.J., Int. J. Pharm., 1989, 57, 169.
6. Kaur, G., Tiwari, A.K., Jain, S., & Saini, M., Chitosan based Buccoadhesive tablets of pentazocine HCl: in-vitro & in-situ kinetics, Indian J. Pharm. Sci., 2005, 67(6): 743-747.
7. Balatripura Sundari, G., & Chowdary, K.P.R., Design & Evaluation of Mucoadhesive controlled release oral tablets of glipizide, Indian J. Pharm. Sci., 2003, 65(6): 591-594.
8. Thombre, A.G., Denoto, A.R. & Gibbes, D.C., J. controlled release, 1999, 60, 333.
9. Lenaerats, V. & Gury, R., Bioadhesive drug delivery systems, 1990, p.p. 25-42, & 65-72.
10. Nagai, T., & Konishi, R. Buccal / gingival drug delivery system, J, control, Rel., 1987 (6), p. 353.
11. Zaho, K., & Singh, J. control release, 1999, 62, 359.