Available Online through
www.ijpbs.com

International Journal of Pharmacy and Biological Sciences (eISSN: 2230-7605)
IJPBS |Volume 1| Issue 3 |JULY-SEPT |2011|240-245

DESIGN AND IN-VITRO EVALUATION OF MUCO- ADHESIVE BUCCAL TABLETS OF SALBUTAMOL SULPHATE

B.Srinivas [1], Chandan Mohanty [2], Pritosh Pattanaik [1], Ravi Naik [1], Chandan Brahma[3]*
[1] Pratishta Institute of Pharmaceutical Sciences, Durajpally, Suryapet, Andhra Pradesh India
[2]Deevena College of pharmacy, Chivemla, Suryapet-508213, Andhra Pradesh, India
[3]Vikas College of Pharmacy, Suryapet, Andhra Pradesh, India
*Corresponding Author Email: balususrinivas03@yahoo.co.in

Research Article

RECEIVED ON 31-07-2011 ACCEPTED ON 15-08-2011

ABSTRACT

In the present investigation an attempt has been made to design efficacious and prolonged release mucoadhesive tablet of salbutamol sulphate using various polymers to avoid the first pass metabolism to reduce dossing frequency and to improve patient compliance. Mucoadhesive buccal tablet of salbutamol sulphate were fabricated with objective of avoiding first pass metabolism and to improve its bioavailability with reduction in dosing frequency. The mucoadhesive polymers used in the formulations were Carbopol 934P, Methocel K4M, and Chitosan. Tablets were prepared by direct compression method using polymers in different ratios. The formulations are characterised for swelling index, in-vitro bioadhesion strength and in-vitro release studies. The best mucoadgesieve performance and in-vitro drug release profile were exhibited by the tablet containing Chitosan and Methocel K4M in ratio of 1:1. It was observed that the optimised formulation follows Hixson Crowel release kinetics.

KEYWORDS: Buccal delivery, Chitosan, Salbutamol sulphate, Mucoadhesive, Bioadhesive strength.

Introduction

Buccal delivery of drugs provides an attractive alternate to the oral route drug administration, particularly in disadvantages associated with the latter mode of dosing. Problems such as first pass metabolism and drug degradation in the harsh gastrointestinal environment can be circumvented by administering drug via buccal route. Moreover the oral cavity is easily accesible for self medication and can be promptly in case of toxicity just by removing the dosage form from buccal cavity. It is also possible to administer drug to who cannot be dosed orally via this route. [1-4]Salbutamol sulphate is widely used as bronchodilator, tocolytic and adrenergic β-agonist. It is widely used as bronchodilator to manage asthma and othere chronic obstractive airway disease. The R-isomer – levabuterol is responsible for bronchodilation. While the S-isomer increase the brancheal reactivity.

Salbutamol sulphate is β-2 adrenergic agonist. It stimulate β-2 reseptors in lungs results in relaxation of smooth muscle,. It is believed that salbutamol sulphate increases cAMP production by activating adenalite cyclase and the action is mediated by cAMP. Increase intracellular cAMP increase the activity of cAMP dependant protienkinase which inhibit phosphorilation of myocin and lowetr inttracellular calcium concentration. A lower concentration of calcium leads to smooth muscle relaxation.

The doses forms of salbutamol sulphate are also available as oral solution, syrup, tablet and injection etc. But as it is rapidly absorbed from gastrointestinal tract, oral bioavailability is 50% because it undergo first pass metabolism this drug is selected for muccoadeive buccal tablet.

MATERIALS AND METHODS:

Salbutamol sulphate was obtained from Dr. Reddy's lab Hyd, Carbapol934P, HPMC-K-4M were used. Chitosan was obtained from Unichem Labs ltd, Mumbai.

Preparation of mucoadhesive tablets:

Mucoadhesive tablets of salbutamol sulphate were prepared by direct compression technique using different grades of polymer with varying concentrations.(**Table-1**). The tablets were prepared using carbopol 934P, HPMC-K4M as primary polymers and Chitosan used as secondary polymer as a penetration enhancer.[5-6]. The effect of secondary polymer on drug release mucoadhesion was studied. The tablets were compressed using 8mm flat faced punch on a single stroke punching machine.[7-8]

Table 1: Composition of buccoadhesive tablets

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8
Salbutamol sulphate	10	10	10	10	10	10	10	10
Chitosan	90	60	120	90	60	120	90	60
Carbopol	90	120	60	-	-	-	-	-
HPMC K-4M	-	-	-	90	120	60	-	-
Magnesium stearete	01	01	01	01	01	01	01	01

Determination of physicochemical parameters:

Twenty tablets were weighed individually and and checked for the weight variation. Thickness was measured using vernier callipers. Five tablets of each formulation were taken and amount of drug present in each tablet was determined. The surface pH of tablet was determined in order to investigate the possibility of any irritation in the oral cavity. The tablets were kept in contact with stimulated saliva fluid for two hours and pH was noted by bringing the electrode in contact with surface of the formulations. Bio adhesive strength of the tablets were measured in a modified physical balance using methods discoursed by Gupta et al.[9] Sheep buccal mucosa was used as model mucosal membrane and stimulated saliva fluid as moistening fluid.(**Figure-1**)

Fig.1. Developed balance for determination of bioadhesive strength

Swelling studies:

The swelling properties of the tablets were evaluated by determination of percentage swelling. Each tablet was weighed (W1) and immersed in simulated saliva fluid at pH 6-8 for predetermined time, then the tablets were

wiped off to remove excess of surface water by using filter paper and weighed(W2).[10-13]

% Swelling= (w2)-(W1) / (W1)×100

In-vitro release studies:

In-vitro release studies of salbutamol sulphate bioadhesive tablet were determined using USP Dissolution Testing Apparatus-II (Paddel type). The dissolution test was performed by using 500ml of 6.8 phosphate buffer, at 37±0.5°c at 50 rpm. Aliquot (5ml) of the solution was collected from the dissolution apparatus hourly for 8 hours and were replaced with fresh dissolution medium. Aliquot were withdrawn at one hour interval from a zone midway between the surface of the dissolution medium and the top of the rotating paddle not less than 1cm apart from the vessel wall.[11-12] The aliquots were filtered, and the absorbance was measured at 283nm spectrophotometrically.

RESULT AND DISCUSSION:

The average weight of tablet was found to be 189mg to 193mg with the maximum percentage deviation of ±0.265 for all the formulation. The tablets showed thickness in the range of 1.20 to 1.50mm (±0.34).

The percentage drug content of all the formulation was found to be 91 to 97%(±0.75). Thus the entire tablet complies with that of the standard. Surface pH of the formulation was found to be 5.9 to 6.4. these result reveals that all the the formulation provide an acceptable pH in the range of salivery pH (5.5 to 7.0). It was also observed that they did not provide any local irritation to the mucosal surface. **Table 2** shows the mucoadhesive strength, swelling index and percentage matrix erosion of different formulation. The strength of the formulation (tablet) was depend on the property of mucoadhesive polymers, which adher to the mucosal surface and also the concentration of polymers used. The buccal tablets were prepared by using Carbopol 934P, and HPMC K-4M as primary polymers. Chitosan was used as the secondary polymer. The buccal tablets containing polymers in various ratios were evaluated for bioadhesive strength, swelling index and drug release in order to obtain an optimised formulation. In the trial 190mg was set as a target weight of single tablet. The polymers in the concentration of 80% to achieve 8hrs bioadhesion. The decrease in the polymer concentration result in decreasing bioadhesion time. The primary and secondary polymers are in the ratios of 1:1, 1:2, 1:3 were used for preparing tablets.

HPMC K-4M and Chitosan in 1:1 ratio has been selected as optimum concentration magnesium stearate was selected as a lubricant. The in-vitro release of salbutamol sulphate from mucoadhesive tablet was found vary according to the types and ratio of the matrix forming polymers used. The release of the salbutamol sulphate was decreased with increase in concentration of carbopol and HPMC K-4M. The percentage of drug released from the formulation F1, F2,and F3 (**Fig: 2**)was found to be 60.20%, 45.34%, 62.45%,respectively containing different concentration of Chitosan in combination with Carbopol 934P. The possible reason for reduction in the total release of the drug may be due to the interaction between the two oppositively charged bioadhesive polymers i.e. cationic Chitosan and Carbopol 934P. It may be expected that inter polymer complex between carboxylic group of Chitosan will be formed and the dissolution rate retarded by complex formation which leads to decrease dissolution.[14] It was observed that, decrease the concentration of polymers HPMC the release of the drug from the formulation is faster. Formulation F7 to F8 released their content before the designated time period and

hence were discarded from study. Formulation F4 shown statistically significant percentage release and was selected for further studies. Increase the concentration of Chitosan showed an increased percentage.

Table 2. Bioadhesive strength and Swelling index of various mucoadhesive Salbutamol sulphte tablets.

Formulation code	Bioadhesive strength	Swelling index
F1	18.10 ±0.45	196±3.05
F2	25.7±1.21	150±5.29
F3	18.2±1.22	200±12.58
F4	23.39±1.80	145.2±5
F5	20,6±0.20	136.7±11.48
F6	17.5±0.50	193±10.14
F7	18.29±0.8	130±15.27
F8	16.9±0.65	105±7.63

Fig.2. Release profile of the formulations F1, F2, and F3

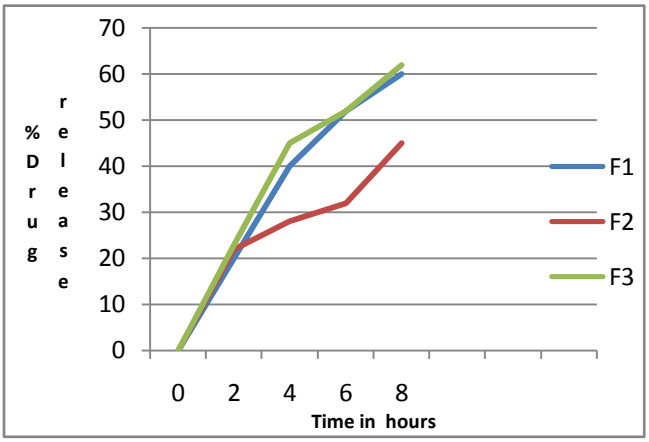
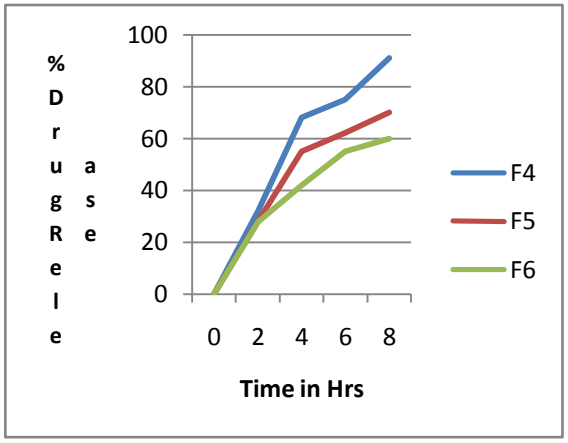


Fig.3. Release profile of the formulation F4, F5, and F6.



Bioadhesion study:

The highest bond strength was possessed by the formulation F2 containing Chitosan and Carbopol 934P in the ratio of 1:2. Decrease the content of the Carbopol 934P resulted in decreased adhesion force. Increasing the bond strength of F8 was followed by bath F6 which were composed of Chitosan: HPMC K-4M in the ratio of 2:1.

Swelling index:

Swelling index was determined with respect to time. The swelling index of the tablet was increased with increasing concentration of Chitosan. The polymer absorbed large volumes of water rapidly and swells to its maximum hydrated size without dissolving in aqueous media.

The uptake of water by HPMC is a slower process compared with Chitosan. HPMC is a hydrophilic polymer which swells slowly to form a gel which then dissolves in the presence of water.The gelling property of this polymer will provide the binding strength to oppose bursting effect of Chitosan. Hence the integrity of tablet was maintained further period of time until most of HPMC was dissolved.

Assessment of duration of bioadhesion:

The duration of bioadhesion decreased with decreasing concentration of HPMC. The duration of bioadhesion of the formulated bioadhesion tablet were determined and found to be around 8hours except the formulation F5 and F8. Less duration of bioadhesion of F5 and F8 may be due to lesser quantity of Chitosan which might be insufficient to maintain the integrity of the formulations.

CONCLUSION:

The present work was aimed to develop the mucoadhesive drug delivery system of salbutamol sulphate with prolonged effect and to avoid the first pass metabolism. From the study it was observed that formulation F4 (**Fig:3**)was best in terms of drug release, bioadhesive performance and physicochemical properties.

Therefore it can be concluded that stable formulation could be developed by incorporating Chitosan and HPMC K-4M in the ratio 7:1 for sustained release of salbutamol sulphate from mucoadhesive tablet with adequate bioadhesiveness and swelling properties without the risk of mucosal damage.

REFERENCES:

1. Harris D and Robinson JR. Drug delivery via the mucous membrane of oral cavity. J Pharm Sci. 1992;81:1-10.
2. Tocker G. A method to study the kinetic of oral mucosal drug absorption for solution. Chem. Pharm. Bill. 1998;40:679-683.
3. Junginger H E, Hoogestrate JA and Verhof JC. Recent advances in buccal drug delvary and absorption in-vitro and in-vivo studies. J.Control. Rel. 1999;62:149-159.
4. Shojael H. Buccal mucosa as route systemic drug delivary –A review.J. Pharm. Sci.1998;15-30.
5. Tripati KD .Essential of Medical Pharmacology,7th ed; Jaypee publisher Ltd.Delhi.2008;pp:639.
6. Miyazaki S and Nayakama A . The use of chitin and chitosan as drug carriers. Chem. Pharm. Bull. 1981; 29:3067-3069.
7. Nakhat PD and Babla IB. Design and characterization of buccoadhesive tablets of promethazine hydrochloride. Indian drugs.2007;47:520-5-7.
8. Ramna M, Nagda V and Himaja MB .Design and evaluation of mucoadhesive buccal drug delivary systems containing metaprolol tartarate. Ind. J. Pharm. Sci. 2007;65:515-518.
9. Gupta A, Garg S Khar RK. Mucoadhesive buccal drug delivary system. A-review. Indian drugs 1992;29:586-593.
10. Owens TS , Dansereav RJ and Sakr A . Development and evaluation of extended release bioadhesive sodium fluoride tablets. Int. J. Pharm.2005;288:109-122.

11. Heller J, Washington DC and penhale DG. Use of bioerodible polymers in self – relugated drug delivary systems. 76th vol, Controlled Release Technology,Pharmaceutical applications,Washington DC,1997; PP281-282,

12. Kamath KR AND Park K .Mucosal adhesive preparation, Encyclopedia of Pharmaceutical Technology, Marcel Dekker, New York .1994;pp 133-163.

13. Smart JD,Kellaway IW and Worthington HE. An in-vitro investigation of mucosal-adhesive materials for use in controlled drug delivary. J. Pharm. Pharmacol. 1984;36:295-299.

14. Jain NK, Khar RK, Ahuja A and Ali J. Controlled and Novel Drug delivery. 1st ed. CBS Publishers, NewDelhi.1997;pp355-37.

Address for the Correspondence:
B.Srinivas *
Department of Pharmaceutics
Pratishta Institute of Pharmaceutical Sciences,
Durajpally,
Suryapet-508214, Andhra Pradesh, India
Telephone No-08684-200285,
Mobile-09502086044
E-mail: balususrinivas03@yahoo.co.in