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EFFECT OF POLYMERS ON MUCOADHESIVE STRENGTH FORBUCCOADHESIVE COMPACTS OF SALBUTAMOL SUPLHATE

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ABSTRACT

The mechanism of mucoadhesion involves the interpretation of the mucus with other molecules strengthened by the formation of secondary chemical bonds between them. Several literatures showed that sophisticated instruments are required for measurement of mucoadhesive force. This work was undertaken to measure and compare the bioadhesive strength of buccoadhesive compacts by using different polymers such as HPMC 4KM, Carbopol 934P and Carbopol 974P is simple, rapid, economic, accurate, reproducible method. Bioadhesive strength is carried out by using pig buccal mucosa and 1%(w/v) colloidal solution of sodium alginate as a model mucosal membrane. Buccoadhesive compacts(BC's) of Salbutamol sulphate in different drug concentrations (4mg and 8mg) were prepared by direct compression method using polymers like carbopol 934P, Carbopol 974P and hydroxyl propyl methyl cellulose 4KM(HPMC 4KM) the ratios of 1:0, 1:1, 1:2 and 0:1 used as test samples for comparison of bioadhesive strength of different polymers and mucosa. Compatibility studies are also carried out by using FT-IR. From the experimental data, the buccoadhesive compacts of salbutamol sulphate will stay long time when the fixed to buccal mucosa because of more bioadhesive strength.

KEYWORDS: Salbutamol sulphate, polymers, buccoadhesive compacts, bioadhesive strength.

INTRODUCTION

In recent years, considerable interest has shown in the use of mucoadhesive dosage forms with regard to enhancing the local and systemic administration of peptides and other poorly absorbed drugs from the gastrointestinal tract. Longer and Robinson defined the term "bioadhesion" as the "attachment of a synthetic or natural macromolecule to mucus and/or an epithelial surface" [1]. The general definition of adherence of a polymeric material to biological surfaces (bioadhesives) or to the mucosal tissue (mucoadhesives) still holds[2].

Bioadhesiveness is the vital for optimizing performance for the tablet containing excipients which has this property. There are many many methods and instruments to measure the bioadhesive strength and reports the same[3].

Salbutamol sulphate is a β2-adrenergic agonists. It reverses branchospasm and reduces airways resistance. Salbutamol sulphate causes dilatation of large airways as shown by increased specific airways conductance and forced expiratory volume. It also improves small airways functioning as reflected in FEF 25 and FEF75 of vital capacity. Salbutamol is available in market as tablet, pressurized aerosol, and rotocaps for inhalation, nebulizer solution and syrup[4]. Salbutamol suphate is given orally 6-16mg in devided doses: slow I.V. injection, equivalent of 250µg of salbutamol: by I.V. infusion, the equivalent of 3-20µg of salbutamol/min[5].

Buccoadhesive delivery system has several advantages over conventional dosage forms. It significantly reduces dose, maintains constant blood levels for longer time, offers greater bioavailability and avoids first pass metabolism and large fractions of the drug goes in to systemic circulation[6].

Hence in the present work is to measure the bioadhesive strength and bioadhesive force of buccoadhesive compacts containing different polymers such as HPMC 4KM, Carbopol 934P and Carbopol 974P by using pig buccal mucosa and 1%(w/w) colloidal solution of sodium alginate as a model mucosal membrane and compatibility study by using FT-IR.

MATERIALS AND METHODS:

Salbutamol sulphate I.P was obtained as gift sample from Kemwell Pvt Ltd- Bangalore, Carbopol 934P obtained as gift sample from B.P.R.L-Bangalore, HPMC-4KM, gift sample obtained by B.P.R.L-Bangalore,

Carbopol 974P gift sample obtained by Dr. Reddy's Laborataries-Hydarabad. Lactose, Magnesium stearate, Sodium hydroxide, Potassium di hydrogen ortho phosphate, Sodium chloride, Potassium chloride, Magnesium chloride, Sodium bicarbonate, Sodium di hydrogen ortho phosphate, Glucose, Sodium alginate and calcium chloride-Analytical grade. The reagents required for the present experimental work are Phosphate buffer pH 6.6[7], Tyrode solution and 1% (w/v) [8] & sodium alginate solution[9].

Preparation of buccoadhesive compacts of Salbutamol sulphate

Buccoadhesive compacts were prepared by direct compression method. All the ingredients were passed through #100 and were blended in mortar for uniform mixing. Blending was done separately for core, peripheral and backing layers. The blended powder of core layer was compressed using 7mm flat faced tablet punches. The core layer was then removed, placed in the center of a 10mm die cavity filled with ingredients of peripheral layer and was compressed. Then the upper punch was raised and ingredients of backing layer was added and finally compressed to a pressure of 14 units.

In the present work, 16 formulations (F_1 to F_{16}) Buccoadhesive compacts of Salbutamol sulphate in two different concentrations (4mg and 8mg / compact) were prepared using variable concentrations of Carbopol-HPMC 4KM (1:0, 1:1, 1:2 and 0:1).

Table No. 01. Composition of buccoadhesive compacts of Salbutamol sulphate (F_1-F_{16})

Ingredients	Formulations															
	Carbopol-934P								Carbopol-974P							
	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	F_{10}	F_{11}	F_{12}	F_{13}	F_{14}	F_{15}	F_{16}
Core layer																
Salbutamol sulphate	4	4	4	4	8	8	8	8	4	4	4	4	8	8	8	8
Lactose	16	16	16	16	16	16	16	16	16	16	16	16	16	16	16	16
Carbopol	20	10	6.7	0	20	10	6.7	0	20	10	6.7	0	20	10	6.7	0
HPMC 4KM	0	10	13.3	20	0	10	13.3	20	0	10	13.3	20	0	10	13.3	20
Peripheral layer																
Carbopol	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40
HPMC 4KM	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40	40
Backing layer																
Magnesium stearate	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Carbopol	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1
HPMC 4KM	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1	12.1
Colour agent	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

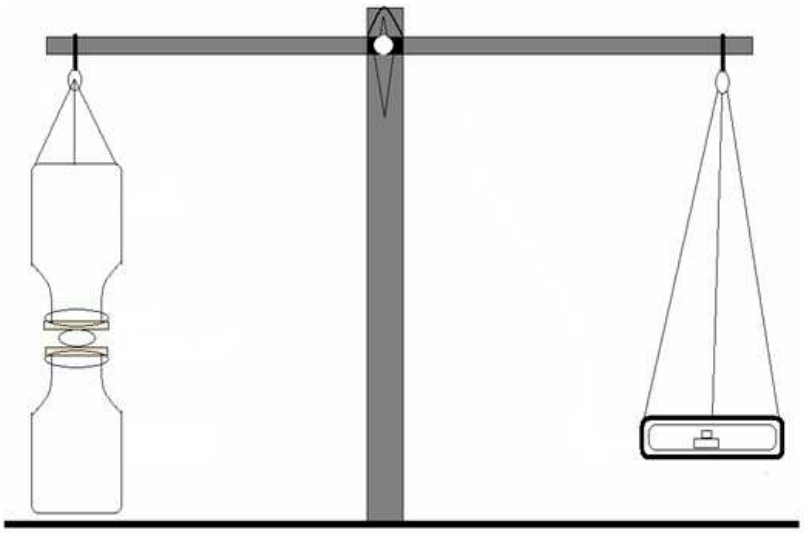
EVALUATION

a. *In vitro* bioadhesion studies[9-14]

The apparatus used for *In vitro* bioadhesion studies is shown in Figure-01. *In vitro* bioadhesion studies were carried out using pig buccal mucosa and modified two armed balance. The beaker on one side of the balance was counter balanced by using suitable weights on the other side. The BC was fixed to the tissue holder with cyanoacrylate adhesive. A circular piece of pig buccal mucosa was fixed to the tissue holder with cynoacrylate adhesive and was immersed in tyrode solution and the temperature was maintained at 37±1˚C. Then the BC was placed on the buccal mucosa by using a preload of 50gms and kept it aside for 5 min to facilitate adhesion bonding. After preloading time, the preload was removed and the water was allowed to flow into the beaker kept on the other side of the balance at the flow rate of 1 drop/sec until the BC detaches from the buccal mucosa. The weight required to detach the BC from the buccal mucosa was measured. Similarly *In vitro* biadhesion studies was also carried out using 1%(w/v) colloidal solution of sodium alginate as a model mucosal membrane. The weight required to detach the BC from the buccal mucosa was measured. The force of adhesion was calculated using the following formula.

$$\text{Force of adhesion (N)} = \frac{\text{Mucoadhesive strength X 9.81}}{100}$$

Fig No-1: Modified apparatus for *in-vitro* Bioadhesion test.



FTIR Studies:

IR spectra for drug, and powdered tablets were recorded in a Fourier transform infrared spectrophotometer (FTIR 1615, Perkin Elmer, USA) with KBr pellets.

RESULTS AND DISCUSSION

***In vitro* Bioadhesive Strength Determination Studies:**

In vitro bioadhesion studies were carried out using bioadhesion apparatus with pig buccal mucosa. The results of bioadhesive strengths and bioadhesive forces of salbutamol sulphate BCs are given in Table-02 and are graphically represented in Figure-02 and Figure-03. The bioadhesive strength and bioadhesive forces of salbutamol suphate (4mg) BCs containing carbopol 934P is in the following order, F2>F3>F4>F1. The bioadhesive strength and bioadhesive forces of salbutamol suphate (8mg) BCs containing carbopol 934P is in the following order, F6>F7>F8>F5. The bioadhesive strength and bioadhesive forces of salbutamol sulphate (4mg) BCs containing carbopol 974P is in the following order, F10>F11>F12>F9. The bioadhesive strength and bioadhesive forces of salbutamol sulphate (8mg) BCs containing carbopol 974P is in the following order, F14>F15>F16>F13. The maximum bioadhesive strength was observed in BCs containing Carbopols and HPMC in the ratio 1:1 followed by 1:2, 0:1 and 1:0. It was also seen that the bioadhesive strength did not changed significantly altered as the drug concentration increased from 4mg to 8mg/BC.

BCs with Carbopol 974P showed lesser bioadhesive strength when compared to BCs of corbopol 934P.

Similarly *in vitro* bioadhesion studies were also carried out using 1%(w/v) colloidal solution of sodium alginate as a model mucosal membrane. The results obtained are in the similar order, but 1%(w/v) colloidal solution of sodium alginate exhibited greater bioadhesive strength compared to the pig buccal mucosa.

Table No.2 *in-vivo* bioadhesive strength data of salbutamol sulphate (F1-F16).

Sl. No	Formulation No	*In vitro* bioadhesive strength in gram			
		Pig buccal mucosa		1% Sodium alginate solution	
		Mean ± SD*	Mucoadhesion force (N)	Mean ± SD*	Mucoadhesion force (N)
1.	F_1	40.00 ± 0.0	3.924	181.67 ± 2.4	17.822
2.	F_2	65.00 ± 4.0	6.377	293.33 ± 6.2	28.776
3.	F_3	51.67 ± 2.4	5.069	246.67 ± 4.7	48.865
4.	F_4	46.67 ± 2.4	4.578	216.67 ± 4.7	21.255
5.	F_5	38.33 ± 2.4	3.760	185.00 ± 4.1	18.149
6.	F_6	61.67 ± 2.4	6.050	291.67 ± 2.4	28.613

7.	**F_7**	48.33 ± 2.4	4.741	261.67 ± 2.4	25.670
8.	**F_8**	41.67 ± 2.4	4.088	230.00 ± 4.1	22.563
9.	**F_9**	30.00 ± 0.0	2.943	143.33 ± 2.4	14.061
10.	**F_{10}**	51.67 ± 2.4	5.069	245.00 ± 8.2	24.035
11.	**F_{11}**	40.00 ± 0.0	3.924	215.00 ± 4.1	21.092
12.	**F_{12}**	36.70 ± 2.4	3.600	181.67 ± 2.4	17.822
13.	**F_{13}**	30.00 ± 0.0	2.943	148.33 ± 2.4	14.511
14.	**F_{14}**	48.33 ± 2.4	4.741	246.67 ±10.3	24.198
15.	**F_{15}**	38.33 ± 2.4	3.760	216.67 ± 2.4	21.255
16.	**F_{16}**	35.00 ± 0.0	3.434	186.67 ± 2.4	18.312

Figure No. 02. Bioadhesive strength of formulations(F_1-F_{16}).

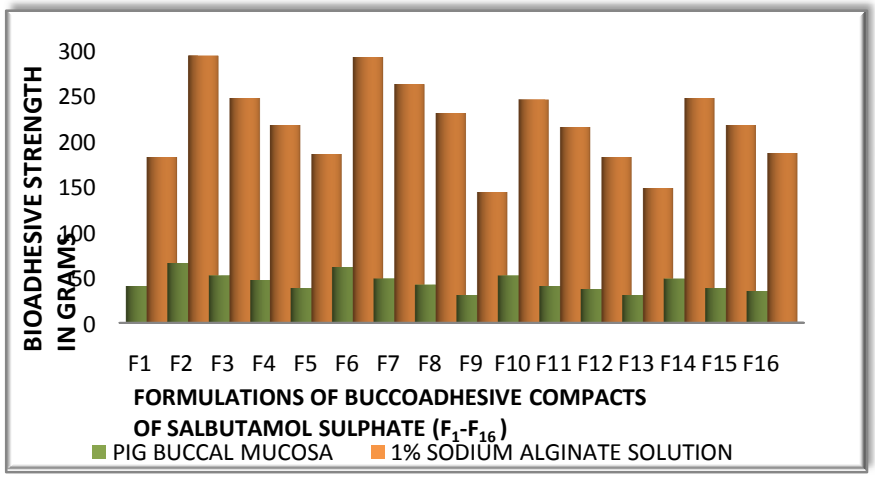
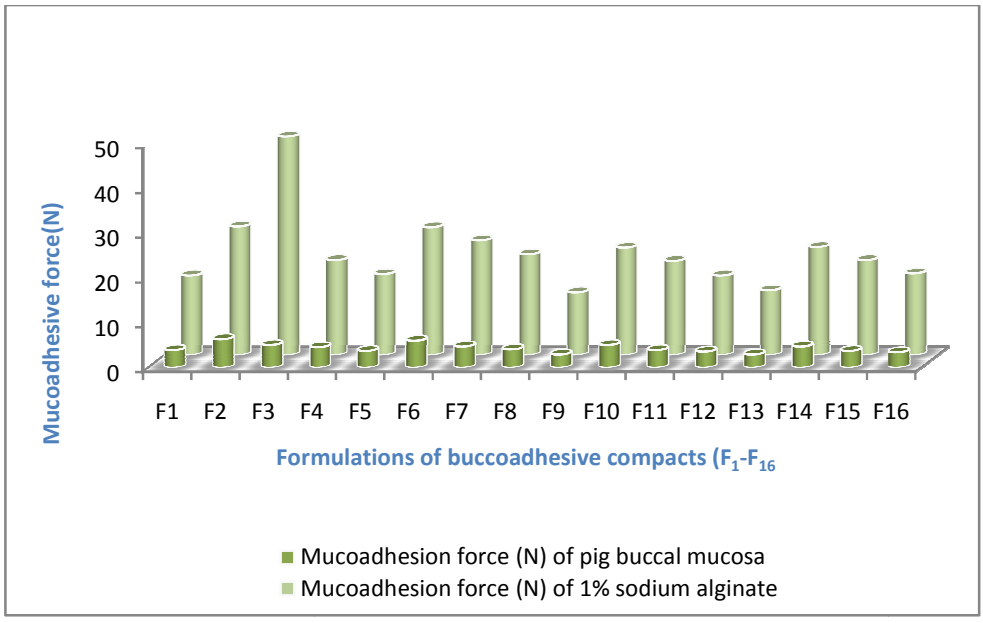


Figure No. 03. Bioadhesive Force(M) of formulations(F_1-F_{16}).



FTIR Studies:

From FT-IR spectra it may be concluded that there is no chemical interaction between the drug and polymer.

Figure No. 04: FT-IR spectra of pure Salbutamol Sulphate.

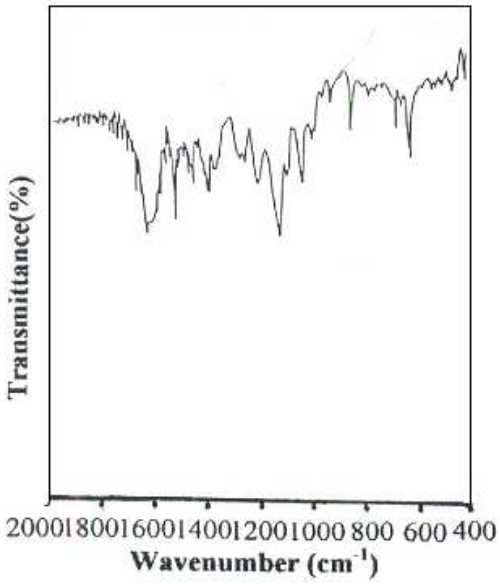


Figure No. 05: FT-IR spectra of pure Carbopol 934P.

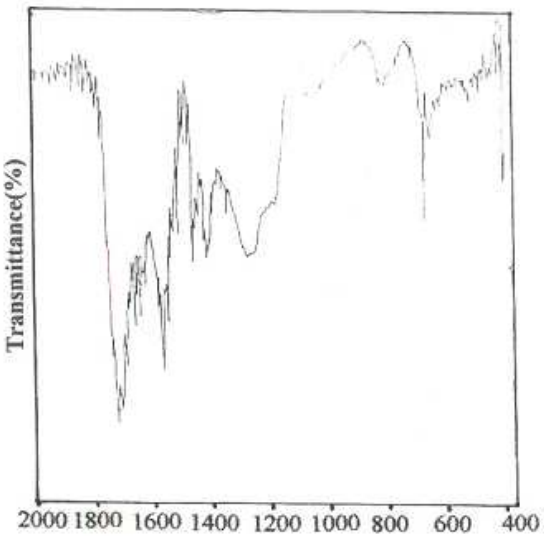


Figure No. 06: FT-IR spectra of pure Carbopol 974P.

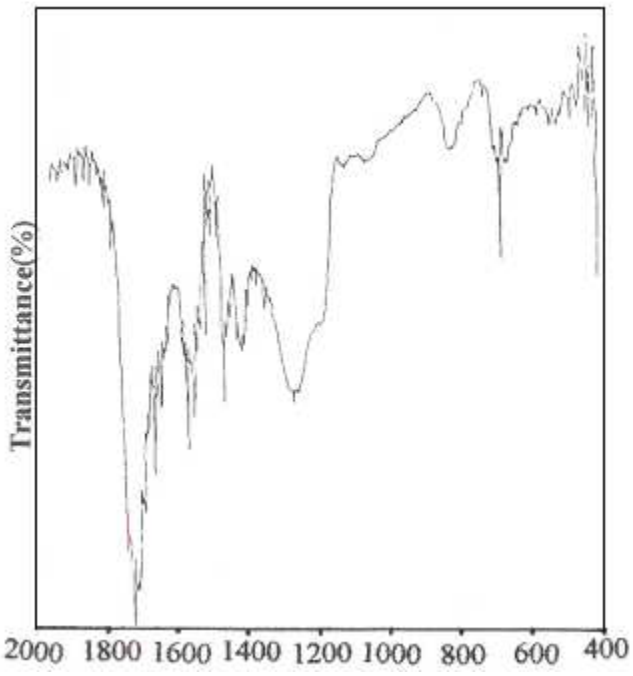


Figure No. 07: FT-IR spectra of pure HPMC 4KM.

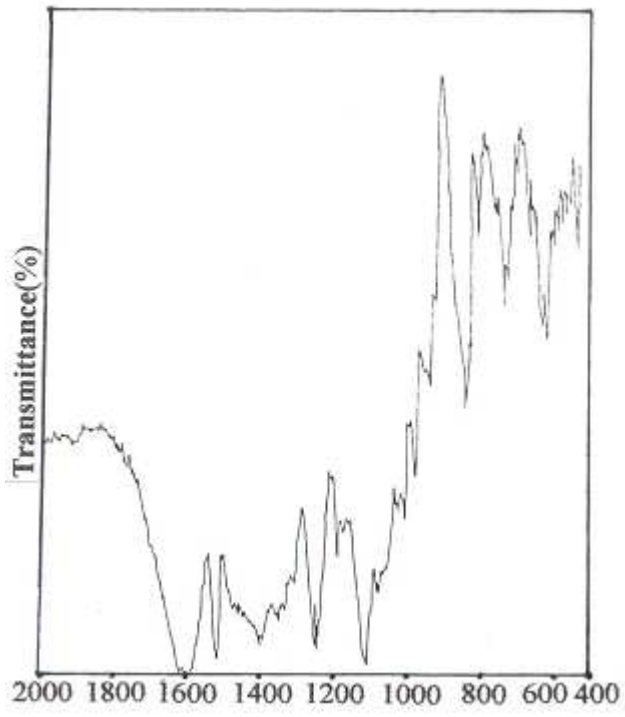
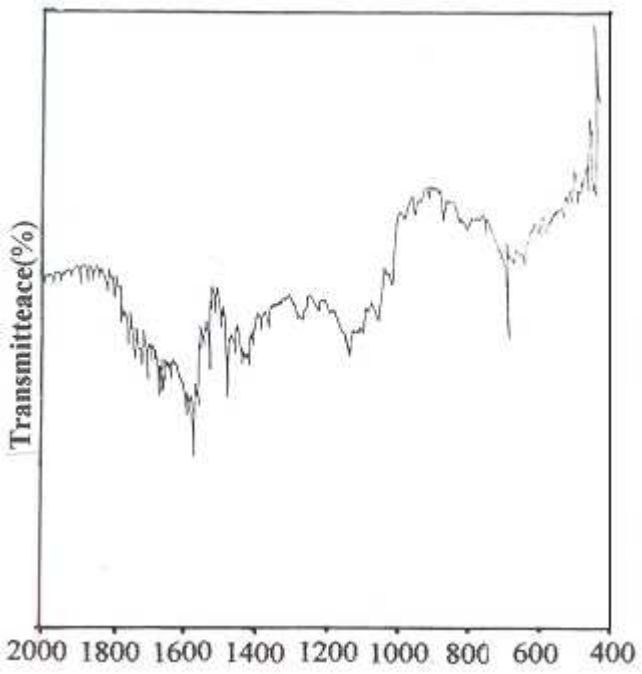


Figure No. 08: FT-IR spectra of pure Formulation F_6



Conclusion

Buccoadhesive compacts(BC's) of Salbutamol sulphate in different concentrations (4mg and 8mg) were prepared by direct compression method using polymers like Carbopol 934P (CP-934P) and carbopol 974P (CP-974P) and Hydroxyl propyl methyl cellulose 4KM(HPMC 4KM) the ratios of 1:0, 1:1, 1:2 and 0:1. The compacts were evaluated for *In vitro* bioadhesive strength and compatibility studies. The bioadhesive strength and bioadhesive forces obtained from Buccoadhesive compacts (BC's) of Salbutamol sulphate in different concentrations (4mg and 8mg) are in the similar order. Maximum bioadhesive strength and bioadhesive force was observed in compacts formulated with a combination of carbopol-HPMC 4KM (1:1). Formulations containing CP-934P exhibited higher bioadhesive strength and bioadhesive force as compared with CP-974P. From FT-IR spectra it may be concluded that there is no chemical interaction between the drug and polymer. From the results of the present experimental work it may be concluded that buccoadhesive compacts of Salbutamol sulphate can be

developed and bioadhesion measurement method is reproducible, accurate and precise. The method is sensitive and can be applied for the compacts containing mucoadhesive polymers.

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