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Effect of Different Polymer Concentration on Bio-Adhesion of Antihypertensive Bio-Adhesive Layer

Aadesh Kumar
Assistant Professor,
Deptt.of Pharmaeutical Sciences,
Kumaun University Block Road,
Bhimtal Nainital,
Uttarakhand

Tanuj Joshi
Assistant Professor,
Deptt.of Pharmaeutical Sciences,
Kumaun University Block Road,
Bhimtal Nainital,
Uttarakhand

Govind Rajpal
Teaching Personnel,
Roorkee College of Pharmacy,
Roorkee, Uttarakhand

Abstract

The term bioadhesion refers to any bond formed between two biological surfaces or a bond between a biological and a synthetic surface. Bio-adhesive system layer will adhere on gastric mucus which can provide significant of gastro-retentive system. Gastric retention will provide advantages such as the delivery of drugs with narrow absorption windows in the small intestinal region. Also, longer residence time in the stomach could be advantageous for local action in the upper part of the small intestine, for example treatment of peptic ulcer disease. Furthermore, improved bioavailability is expected for drugs that are absorbed readily upon release in the GI tract Nifedipine- (anti-hypertensive drug) which is primarily absorbed from stomach and required more than three times a day but by using bio-adhesive layer it can be retain on stomach for more absorption and will reduce the frequency of dosing. The aim of study was to formulate and optimize the bio-adhesive gastro-retentive system of anti-hypertensive drug Nifidipine and To study the effect of different polymer concentration on Bio-adhesion.

Keywords : Carbopol 934P, HPMC, Bio-Adhesive, Nifidipine, Gastro-Retentive,

Introduction

The term bioadhesion refers to any bond formed between two biological surfaces or a bond between a biological and a synthetic surface. In case of bioadhesive drug delivery, the term bioadhesion is used to describe the adhesion between polymers, either synthetic or natural and soft tissues or the gastrointestinal mucosa. Generally speaking, bioadhesion is a term which broadly includes adhesive interactions with any biological or biologically derived substance, and mucoadhesion is used when the bond is formed with a mucosal surface. For drug delivery purpose, the term bioadhesion implies attachment of a drug carrier system to a specific biological location. The biological surface can be epithelial tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion. Bioadhesion can be modeled after a bacterial attachment to tissue surfaces, and mucoadhesion can be modeled after the adherance of mucus on epithelial tissue.[1]

Adhesion can be defined as the bond produced by contact between a pressure sensitive adhesive and a surface. In biological systems, four types of bioadhesion could be distinguished.[2]

1. Adhesion of a normal cell on another normal cell.
2. Adhesion of a cell with a foreign substance.
3. Adhesion of a normal cell to a pathological cell.
4. Adhesion of an adhesive to a biological substance.

For drug delivery purpose, the term bioadhesion implies attachment of a drug carrier system to a specific biological location. The biological surface can be epithelial tissue. If adhesive attachment is to a mucus coat, the phenomenon is referred to as mucoadhesion. Bioadhesion can be modeled after a bacterial attachment to tissue surfaces, and mucoadhesion can be modeled after the adherance of mucus on epithelial tissue.[4]

Mechanism of Bioadhesion[3]

For Bioadhesion to occur, three stages are involved-

Stage-1

An intimate contact between a Bioadhesive and a membrane either from a good wetting of the Bioadhesive and a membrane or from the swelling of bioadhesive.

Stage-2

Penetration of the bio-adhesive into the service of the tissue takes place.

Stage-3

Inter penetration of the chains of the bioadhesive with mucous takes place. Low chemical bounds can then settle

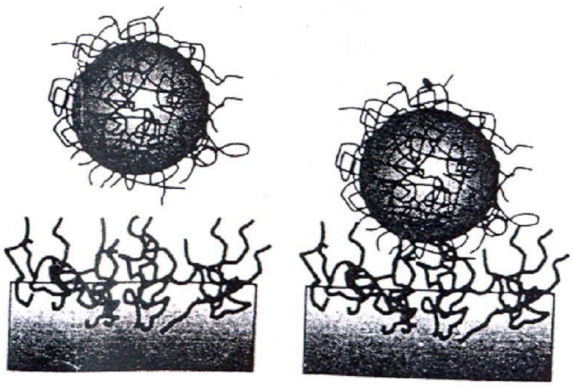

Fig.No.01. Interpenetration of Bio-Adhesive and Mucous Polymer Chain

The bonding between the mucus and the biological substance occurs chiefly through both physical and chemical interactions results from enlargement of the adhesive material and chemical bonds due to electro static interaction, hydrophobic interactions, hydrogen bonding and dispersion forces.

In fact the buoyant dosage unit enhances gastric residence time (GRT) without affecting the intrinsic rate of emptying. Unfortunately floating devices administered in a single unit form (Hydrodynamically balanced system) HBS are unreliable in prolonging the GRT owing to their 'all- or-nothing' emptying process and, thus they may causes high variability in bioavailability and local irritation due to large amount of drug delivered at a particular site of the gastrointestinal tract.[7]

The term "hypertension" literally means an abnormally raised arterial blood pressure. There are many conditions which elevate arterial pressure, includingprimary renal disease, pheochromocytoma, hyperthyroidism, hyperaldosteronism and coarctation of aorta, leading to secondary hypertension. In about 80 to 85 per cent of patients of hypertension, no specific cause is evident, and such a condition is labeled as primary or essential hypertension.[5] Most antihypertensive drugs can effectively reduce mildly elevated blood pressure, but their use is associated with many side effects. Thus the decision whether to use a drug to control borderline or mild hypertension is made on the basis of the benefit: risk ratio.[6]

Aim of Study

The aim of present research is to study the effect of different polymer concentration on Bio-adhesion of Antihypertensive Bio-adhesive layerThe objective was to formulate and optimize the bio-adhesive gastro-retentive system. Bio-adhesive system layer will adhere on gastro mucus which can provide the significant of gastro-retentive system.

Materials and Methods

Materials

Nifidipine was procured from M/s Hi-Media Lab, Carbopol 934P and HPMC E15 were procured from Lobachem. All other ingredients used were of analytical grade.

Formulation of Bio-Adhesive Layer

1) Nifedipine 1000mg was dissolve in 15 to 20ml of ethanol.
2) Different Amount of Carbopol 934P for particular preparation was mixed in 20 to 30ml of ethanol with constant string with the help of glass rod and to this different amount of HPMC was added as required for preparation.
3) Solution of Nifedipine prepared in fist step was added to the mixture of Carbopol and HPMC with constant string with the help of glass rod.
4) Mixture of all ingredients was poured in a Petri-dish.
5) Kept the preparation of two day at room temperature.

In-vitro Mucoadhesivity Test[4]

The mucoadhesive property of bio-adhesive layer was evaluated in-vitro by modified physical balance for mucoadhesion. Pieces of mucosa (5cm×6cm) were mounted onto glass slides. About 2cm×3cm of bio-adhesive layer were attached at one arm of physical balance that was mounted above the mucosa. Modified physical balance was balance by adding water in required arm of before made them contract. Both layer and mucosa were wet with the help 0.1N HCl and made them in contract for 5minute. Water was added to the opposite arm until layer was removed.

A preload of 10 mg is placed on the slide for 5 min (preload time) After the completion of preload time, preload is removed from the glass slide and water is then added in the plastic bottle in left side arm by peristaltic pump at a constant rate of 100 drops per min. The addition of water is stopped when mucoadhesive dosage form is detached from the goat or rat stomach mucosa. The weight of water required to detach mucoadhesive dosage form from stomach mucosa is noted as mucoadhesive strength in grams.

$$\text{Force of adhesion (N)} = \frac{\text{Mucoadhesive Strength}}{1000} \times 9.81$$

Bond strength (N/m^2) = Force of adhesion (N)/ Surface area of tablet (m^2)

Tensile Strength

Taking a piece of about 4cm×5cm and fixed it between two rings of same diameter of about 3cm or less so that a weight of 10 gm can be put on it. 0.1N HCl was pouring at the layer, after five minute 10 gm weight was placed on it and the time at which layer brake was noted for each preparation.

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Drug Entrapment Efficiency[9]

2×3cm of bio-adhesive layer was weighted accurately and drug was extracted from bio-adhesive layer by digesting for 24 hours in 10 ml of 6.8 pH phosphate buffer solution. During this period the suspension was agitated. After 24 hrs the suspension was centrifuged at 2000 rpm for about 3 minutes. The supernatant obtained was assayed spectrophotometrically for drug contents.

The drug entrapment efficiency (DEE) was determined as:

$$DEE = (Pc / Tc) \times 100$$

Pc is practical content,
Tc is the theoretical content.
All the experimental units were analyzed in triplicate (n=3).

Thickness

Thickness of each layer was measured with the help of Vanier calipers meter.

Results and Discussion

The Bio-adhesive layer of Nifidipine was prepared by wet mixing process as per formula given in (table-1).

Table-1: Composition of Bio-Adhesive Layer

Formulation No.	HPMC E15 (in mg)	CARBOPOL (in mg)	DRUG (in mg)
F1	100	1500	1000
F2	400	1500	1000
F3	600	1500	1000
F4	800	1500	1000
F5	1000	1500	1000
F6	600	2000	1000
F7	600	3000	1000
F8	-	1500	1000
F9	600	-	1000
F10	400	400	1000
F11	100	200	1000
F12	200	600	1000
F13	600	300	1000
F14	600	200	1000
F15	600	1500	1000
F16	1500	1500	1000

Evaluation of the Study

Production Yield

Production yield was found to be good between 88 to 95% but best result was found 95% of preparation F5 in which the concentration of both polymer CP and HPMC was high 1000mg and 1500mg respectably.

Release Profile

Good release was found in preparation (F6 from 0.13 to 91.56) and F7 (from 2.77 to 85.20) among all sixteen preparations.

Mucoadhesivity test

Formulations F1, F2, F3, F6 and F7 in contain high amount of cabopol 934P results high mucoadhesive strength to retain on mucous as compare to other preparations.

Tensile Strength

Formulations F6, F7 and F16 show high tenstile strength as compare to rest of preparation to maintain their structure.

Drug entrapment Efficiency

Good entrapment was found between 74 to 97% of bio-adhesive layers but highest entrapment was found of preparation F7 and F16 that was 97%.

Thickness

All the prepared layer was found 1.5 to 2 mm thick and uniformity was throughout of the layer.

Comparison of Different Polymer Concentration on Bio- Adhesion

Table No. 02. Effect of Cp on Bio-Adhesion and Release

Formulation code	Amount of cp(w/w)	Bioadhesion	Cumulative amount of drug release (%)at at 12th hour
F1	0.038	215	8.42
F2	0.13	220	7.02
F3	0.19	237	16.98
F4	0.24	110	1.05
F5	0.28	50	0.973
F6	0.166	230	91.56
F7	0.130	220	92.8

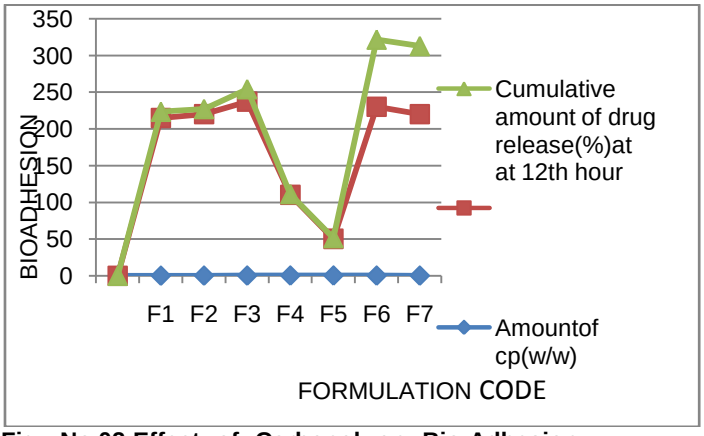
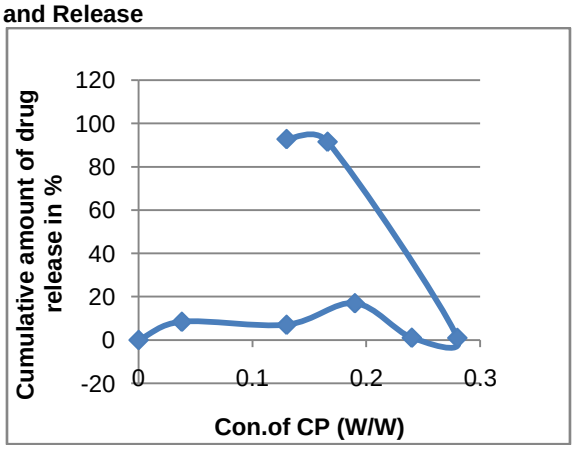


Fig. No.02:Effect of Carbopol on Bio-Adhesion and Release



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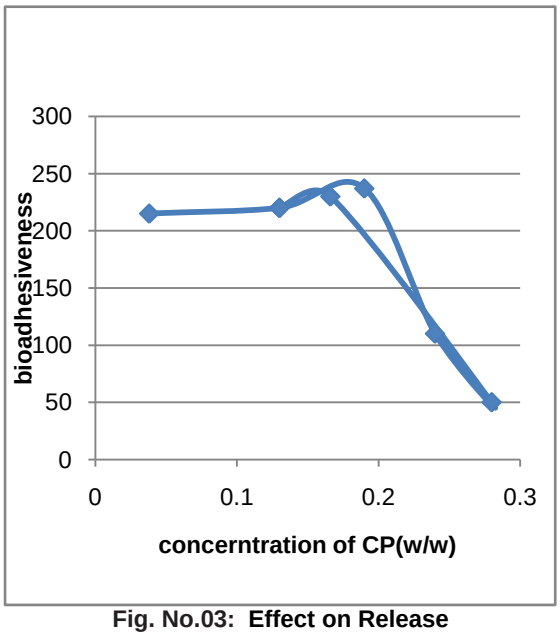


Fig. No.03: Effect on Release

Fig.No.04: Effect on Bioadhesion

Table No. 03 Effect of HPMC on Bio-Adhesion and Release

Formulation code	Con. (w/w) of HPMC	Bioadhesion	Cumulative amount of drug release at 12th hour
F9	0	10	1.56
F14	0.1	28	60.07
F13	0.15	20	56.07
F10	0.22	10	22.19
F12	0.33	00	90.04
F15	0.48	30	97.85
F6	0.55	230	91.56
F7	0.65	220	85.2

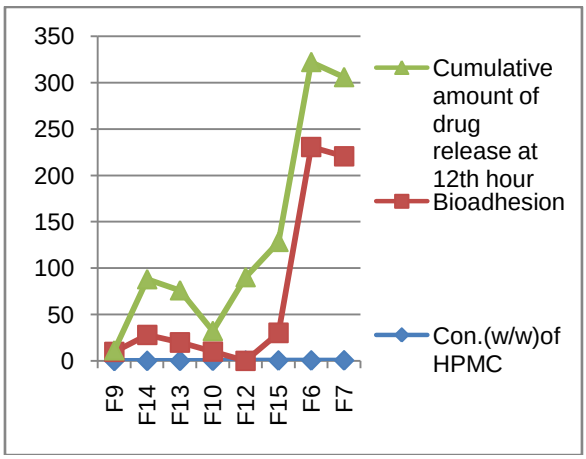


Fig. No.05: Effect of HPMC on Bio-Adhesion and Release

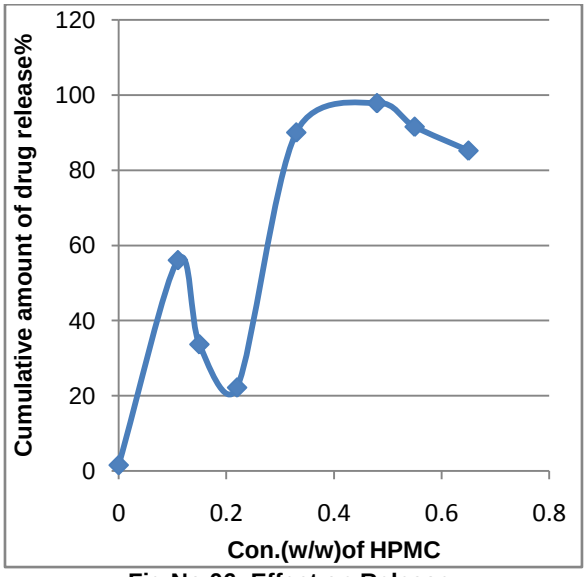
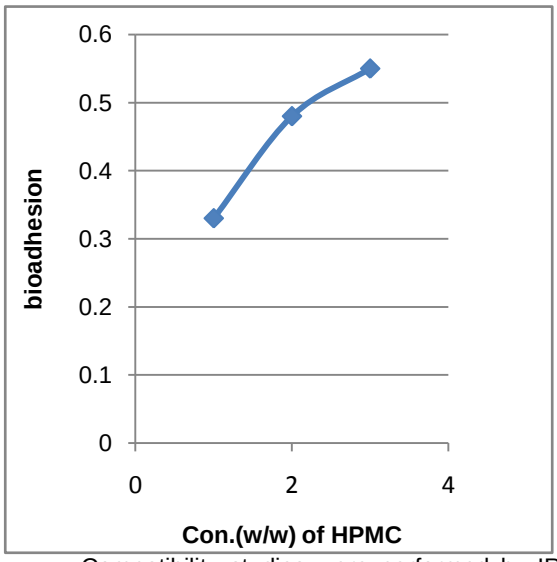


Fig.No.06: Effect on Release

Fig.No.07: Effect on Bioadhesion

Compatibility studies



Compatibility studies were performed by IR Spectroscopy of Nifidipine with Carbopol and HPMC.

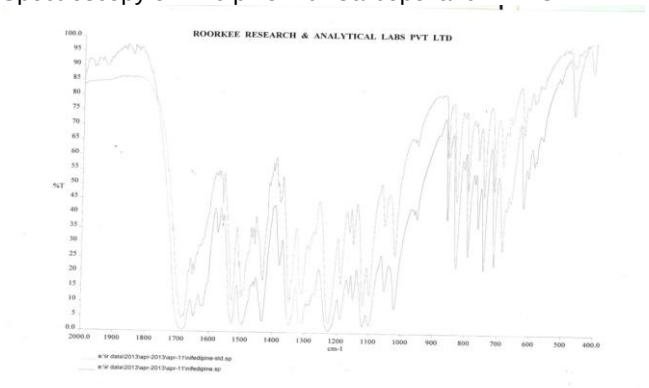


Fig.No.08: IR Spectra of Nifedipine as Sample With IP Reference Spectra

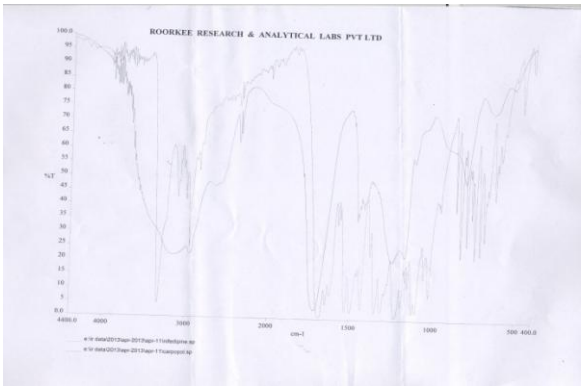


Fig. No.09: IR Spectra of Carbopol 934P and Nifedipine.

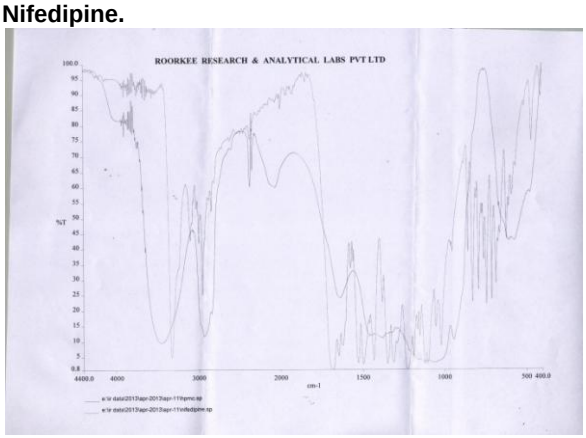


Fig. No.10: IR Spectra of HPMC and Nifidipine.

Conclusion

Bio-adhesive layers of nifedipine were prepared in different concentration of carbopol 934P and Hydroxymethylcellulose by simple mixing and pouring method, ethanol as a solvent. Pieces of 2×3cm of bio-adhesive layer were taken for evaluation.

Prepared layers were found to be uniform in thickness and smooth at optimum concentration ratio of polymer. In absent or lower concentration of HPMC, layer was formed with less bio adhesiveness and released rate, also at lower concentration of CP layer were formed with very less bioadhesivess and tenstile strength but as the concentration of HPMC and CP was increases, release of nifedipine also increases as in preparation F7 (1:5) but further increase in concentration of both, decrease the release of nifedipine and bioadhesiveness.

By observation of tables and graph it was found that as the concentration of CP increase mucoadhesion was increase but not proportional so longer. At a higher concentration of CP, decrease in mucoadhesion and release can be observed. Drug release was found increase and mucoadhsion was decrease with increase in the concentration of HPMC. Release of drug from layer was depend up on concentration of both polymer, release was decreased with increase concentration of CP but it was found that as the concentration of CP increase, mucoadhesion was increase, but not proportional so longer. At certain higher concentration of CP, decrease in mucoadhesion indicating entracross-linking and release. In research work we found that bioadhesive layer of nifedipine can be formed by taken polymer CP and HPMC. Good Bioadhesion and release of drug were depending upon a proper combination of polymer.

Copatiblity studies assumed that Nifidipine is compatible with both CP and HPMC polymer.

Reference

1. Sultana S, Talegaonkar S, Bhatnager A, (2012), Asian journal of pharmaceutics,;1(4): 295-298
2. Pandya NB, Jivani RR and Jivani NP (2012), International journal of pharmaceutical formulation and analysis; 3(1): 37-44.
3. Shinde S, Tadwee I, Shahi S, (2012), International journal of pharmaceutical research & allied sciences;1(1): 01-13.
4. Pratima NA , Tiwari S, Kamble S, (2012), International journal of research in pharmacy and science; 2(3):32-59
5. Tripathi K.D. Essentials of medical pharmacology. Jaypee brothers medical publiseshers (P)Ltd, New Delhi,4th edition pp. 512-554.
6. Goodman and Gilman's The Pharmacological Basis of Therapeutics, Academic Press, New York, 1990 8th edition. Page no. 774.
7. Yadav VK., Kumar B, Prajapati SK, Shafaat K, (2011), International Journal of drug Delivery. 3: 357-370.
8. Gaba P, Singh S, Gaba M, Gupta GD, (2011), Saudi Pharmaceutical Journal.; 19: 143–152.
9. Gurnany E, Singhai P, Soni A, Jain R, Jain SK, Jain A. (2011), Journal of pharmacy research;4(6): 1899-1908.
10. Hwang SJ, Park H, Park K. (1998), Crit Rev Their Drug Carrier Sys; 15: 243-84.
11. Flavia CC, Marcos LB, Raul CE, Maria PD, (2010), Brazilian Journal of Pharmaceutical Sciences,46: 01-05.