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FORMULATION AND IN VITRO EVALUATION OF BUCCAL TABLETS OF FLUVASTATIN BY DIRECT COMPRESSION METHOD

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ABSTRACT

Buccal drug delivery has been considered as an alternative to oral dosing for compounds subjected to degradation in the gastrointestinal tract or to hepatic first pass metabolism. An attempt has been made to develop buccoadhesive tablets comprising of drug containing bio adhesive layer and drug free backing layer to release the drug for extended period of time with reduction in dosing frequency. Various formulations of Fluvastatin buccal tablets were prepared by direct compression method using bio adhesive polymers like Carbopol 976 P, Xanthum gum and Chitosan. Buccal drug delivery system prolong the residence time of dosage form at the site and thus contribute to improved and/or better therapeutic performance of the drug. The maximum bio adhesive strength was observed in tablets formulated with Carbopol 976 P.

KEYWORDS: Buccal, Fluvastatin, Carbopol 976 P, Xanthan gum, Chitosan.

INTRODUCTION

Oral administration of pharmaceutical compositions has some drawbacks. For instance, it is difficult to keep the medicament at the desired location so that it can be absorbed, distributed and metabolized easily. Accordingly, there has been much interest in the use of the mucosal lining of body cavities. Regions in the oral cavity where effective drug delivery can be achieved are buccal, sublingual, palatal and gingival. Buccal and sublingual sectors are the most commonly used routes for drug delivery and they may be used for the treatment of local or systemic diseases. The permeability of the oral mucosa is probably related to the physical characteristics of the tissues. The buccal mucosa offers many advantages because of its smooth and relatively immobile surface and its suit ability for the placement of controlled-

release system which is well accepted by patients. The buccal mucosa is a useful route for the treatment of either local or systemic therapies overcoming the drawbacks of conventional administration routes. The buccal mucosa is relatively permeable, robust in comparison to the other mucosal tissues and is more tolerant to potential allergens which have a reduced tendency to irreversible irritation or damage. So, it has been largely investigate as a potential site for controlled drug delivery in various chronic systemic therapies. However, salivary production and composition may contribute to chemical modification of certain drugs. Moreover; involuntary swallowing can result in drug loss from the site of absorption. Furthermore, constant salivary scavenging within the oral cavity makes it very difficult for dosage forms to be retained for an extended period of time in order to facilitate absorption in this site. The relatively small absorption area and the barrier property of the buccal mucosa contribute to the inherent limitations of this delivery route. Both the buccal and sublingual membranes offer advantages over other routes for administration. For example, drugs administered through the buccal and sublingual routes have a rapid onset of action and improved bioavailability of certain drugs. These routes can bypass the first-pass effect and exposure of the drugs to the gastrointestinal fluids. Additional advantages include easy access to the membrane sites so that the delivery system can be applied, localized, and removed easily. Further, there is good potential for prolonged delivery through the mucosal membrane within the oral mucosal cavity. The palatal mucosa is intermediate in thickness and keratinized thus lessening its permeability. All of these epithelia are coated with a layer of mucus. Bio adhesive polymer can significantly improve the performance of many drugs, as they are having prolonged contact time with these tissues. These patient compliance controlled drug delivery products have improved drug bioavailability at suitable cost. Drug selection for oral trans mucosal delivery is limited by the physicochemical properties of the drugs themselves. To be delivered transmucosally, drugs must have unique physicochemical properties, i.e. a proper balance between solubility and lipophilicity. Generally only a few milligrams of drug can cross the oral mucosa, even if the drug has a favorable profile for oral mucosal delivery. Since the early 1980s there has been renewed interest in the use of bio adhesive polymers to prolong contact time in the various mucosal routes of drug administration. The ability to maintain a delivery system at a particular location for an extended period of time has great appeal for both local as well as systemic drug bioavailability. Drug absorption through a mucosal surface is efficient because mucosal surfaces are usually rich in blood supply, providing rapid drug transport to the systemic circulation and avoiding degradation by gastrointestinal enzymes and first pass hepatic

metabolism. Hyperlipidemia is a major cause of atherosclerosis and its associated disorders like coronary heart diseases, ischemic cerebrovascular diseases etc. Recognition of hypercholestermia as a risk factor has led to the development of drugs that reduces cholesterol levels. Statins are the most effective antihyperlipidemic agents. Statins act as competitive inhibitors of HMG-CoA reductase which catalyzes the step of cholesterol synthesis. Statins also reduces the triglycerides levels caused by elevated VLDL levels. All the statins are subjected to extensive first past metabolism by liver and gut wall enzymes, resulting in low systemic availability of the parent compound. Fluvastatin is also administered in its active form as a sodium salt and is almost completely absorbed, but 50-80% of the absorbed drug undergoes first pass metabolism whereby it is converted to its inactive metabolites which have a very short elimination half-life.

MATERIALS AND METHODS

Drug: Fluvastatin. Polymers like carbopol, chitosan and xantham gum. Excipients like Talc, Magnesium Stearate, and MCC etc. brought from the commercial labs.

Method: direct compression method

Step 1: Weigh all the ingredients in required quantity

Step 2: Transfer all ingredients into a mortar, triturate for 10minutes until to get fine powder and sieve the material.

Step 3: then transfer the material into blender for proper distribution of drug in blend for 10minutes.

Step 4: then addition of lubricant, mix well.

Step 5: Perform the micromeritic properties (Precompression studies).

Step 6: Compression.

Table 1: Formulation chart of buccal tablets (Total weight of tablet is 200mg).

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Fluvastatin	40	40	40	40	40	40	40	40	40
Chitosan	30			40			50		
Carbopal 976 p	30			40			50		
Xanthan Gum	30			40			50		
TALC	2	2	2	2	2	2	2	2	2
Magnesium stearate	4	4	4	4	4	4	4	4	4
MCC	124	114	104	124	114	104	124	114	104
Total (Mg)	200	200	200	200	200	200	200	200	200

RESULTS

Determination of λmax

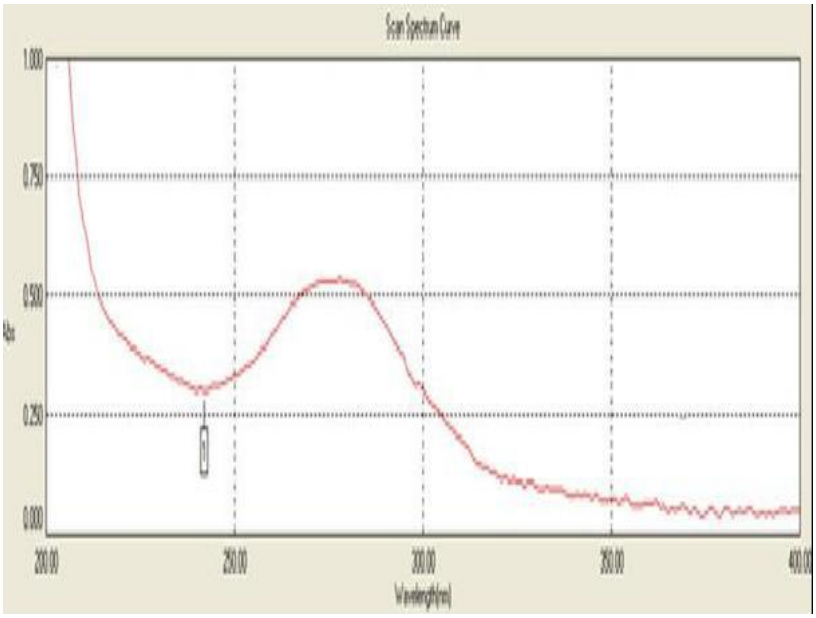

Figure shows UV Spectrum of fluvastatin.

Calibration curve of fluvastatin

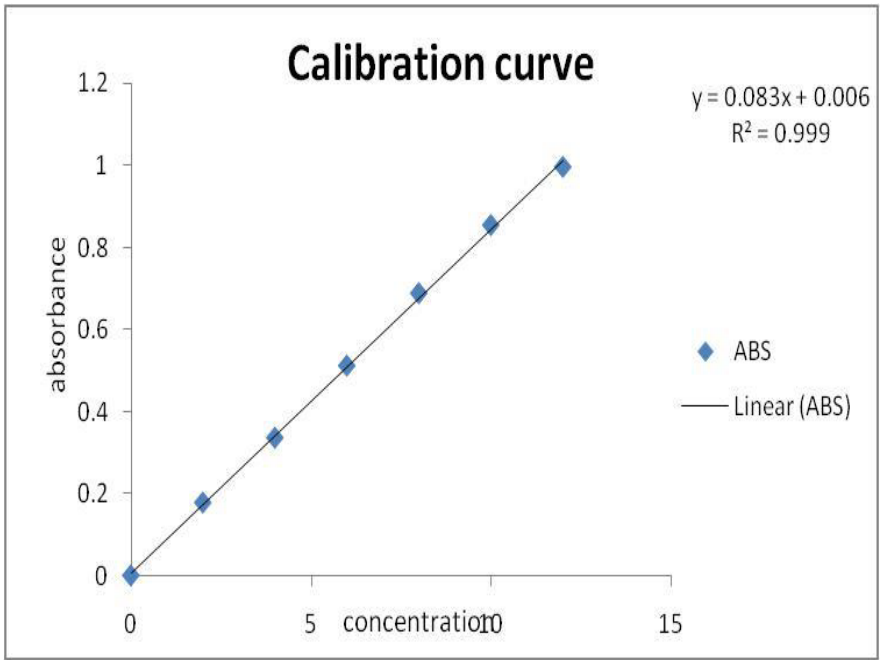

Figure shows Standard graph of Fluvastatin in Phosphate buffer pH6.8.

DISCUSSION

The calibration curve for fluvastatin was constructed and has given R2 values of 0.999.

Evaluation of precompression parameters of Fluvastatin

S:No	FORMULATION	BULK DENSITY	TAPPED DENSITY	CARR'S INDEX	ANGLE OF REPOSE	HAUSNER'S EQUATION
1	F1	0.256	0.281	8.896	23.11	1.097
2	F2	0.269	0.298	9.731	22.84	1.107
3	F3	0.248	0.293	15.35	23.61	1.181
4	F4	0.257	0.299	14.04	24.50	1.163
5	F5	0.227	0.271	16.23	23.46	1.193
6	F6	0.251	0.298	15.77	22.14	1.187
7	F7	0.264	0.320	17.5	23.36	1.212
8	F8	0.225	0.260	13.46	21.85	1.155
9	F9	0.274	0.321	14.64	21.22	1.17

DISCUSSION

The results of pre compress in on parameters evaluation indicate that the all formulations are giving satisfactory values indicating all blends are suitable for direct compression method of tablet manufacturer.

Drug – Excipient compatibility studies

The compatibility between the drug and polymer was compared by FT-IR spectra. The position of peak in FT-IR spectra of pure Fluvastatin is compared with those in FT-IR spectra of Fluvastatin plus excipients.

Hence, it can be concluded that drug can be used with the selected polymer without causing instability in the formulation. The data obtained is shown in fig 2 & 3. The spectra are reported in Figures below.

RESULTS

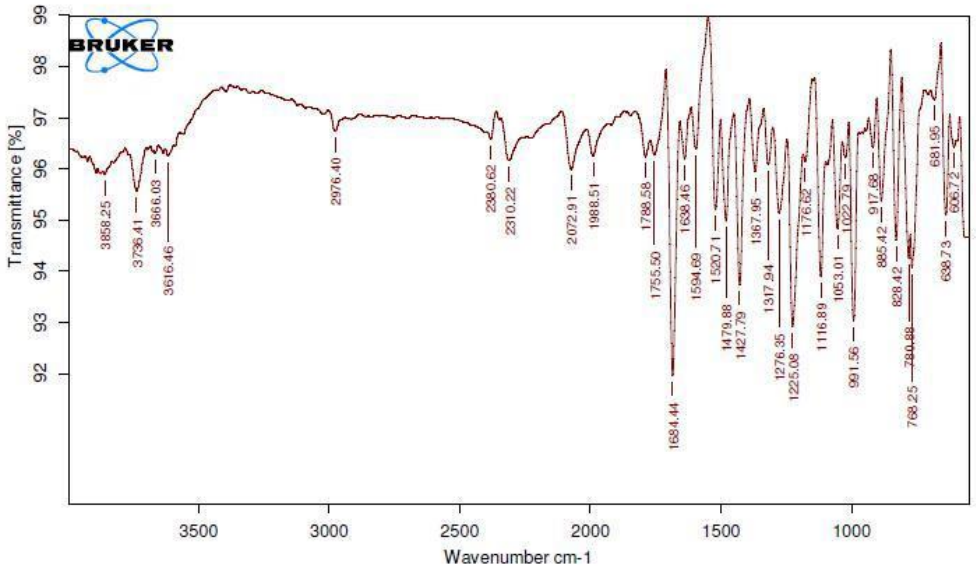

Figure shows FT-IR Spectra of pure drug Fluvastatin.

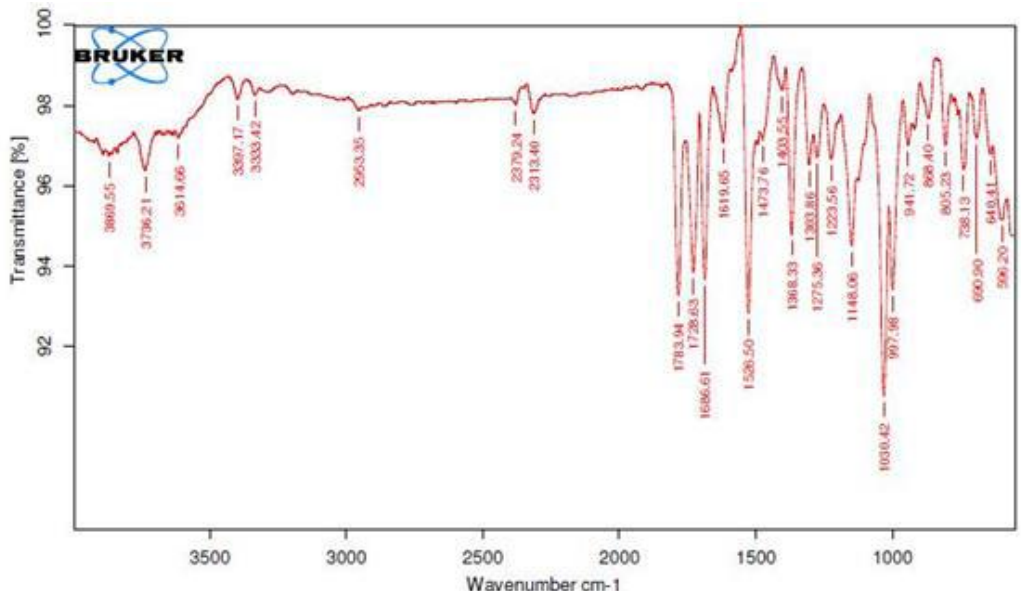

Figure shows FT-IR Spectra of optimized formula (F6).

DISCUSSION

The FT IR studies indicate that the important peaks (1694.4 cm-1(amide), 1594.59cm-1 (N-H bonds) curve) not changed indicating that there is no drug interaction with the excipients used in the formulation.

Post compression parameters Evaluation

S. NO. Variation	Formulations	Weight (mm)	Thickness	Hardness (kg/cm2)	Friability	%Drug content (%w/w) (mg)
1	F1	198.34	2.93	3.87	0.42	97.52
2	F2	198.38	2.93	3.90	0.87	98.52
3	F3	198.34	2.93	3.85	0.51	96.66
4	F4	198.65	2.85	3.89	0.65	95.11
5	F5	198.63	2.90	3.88	0.81	96.52
6	F6	199.96	2.84	3.89	0.12	99.52
7	F7	199.30	2.90	3.93	0.77	98.63
8	F8	197.25	2.44	3.97	0.65	97.33
9	F9	199.50	2.90	3.75	0.52	98.74

Swelling Studies

Formulation Code	5 hour	10hour
F1	37.2	53.8
F2	38.98	59.4
F3	42.6	64.5
F4	33.4	50.35
F5	35	53.8
F6	39.13	60.3
F7	17.7	28.3
F8	18.7	30.7
F9	21.3	36.2

DISCUSSION

The swelling study results indicates that all formulation have sufficient swelling character concentration is essential for good mucoadhesive property as more will be the swelling greater will be exposure of the formulation to the biological surface more will be the mucoadhesion.

In vitro Dissolution Studies

Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	27.3	34.49	29.28	40.23	38.45	24.98	30.9	27.6	26.15
2	35.12	38.18	40.02	52.45	45.24	35.32	38.23	36.89	34.52
3	47.23	47.42	49.83	63.2	54.3	47.32	47.1	45.73	41.87
4	55.15	53.98	61.6	71.32	63.05	53.4	55.38	59.43	55.21
5	67.26	65.23	73.83	83.76	75.29	65.12	69.2	71.28	68.81
6	85.23	69.13	79.12	90.1	80.45	75.22	81.16	80.84	76.93
7	98.98	74.47	86.68	96.9	86.45	84.18	98.23	87.68	91.23
8	84.32	91.42	98.85		93.01	92.72	99.48	97.52	
9		101.2	100.02			99.8		98.38	
10	99.9								

DISCUSSION

The formulations(F1,F2,F3) prepared by using chitosan in concentration of 30mg,40mg and 50mg respectively were subjected to in vitro dissolution studies. The increasing concentration of chitosan controls the drug release in comparison to least concentration but could not control he burst release after 9 hours.

The formulations (F7,F8,F9) containing xanthan gum in the concentration of 30mg,40mg and 50 mg respectively control the drug release up to 7 hours, 8 hours and 8 hours respectively and indicating not suitable for better sustaining of drug release.

Among formulations (F4, F5, F6) containing carbopol940p in it was observed that as the concentration increased, the drug release was well controlled. F6 formulation was observed to give highest sustaining of drug release (up to 10 hours) among all formulations.

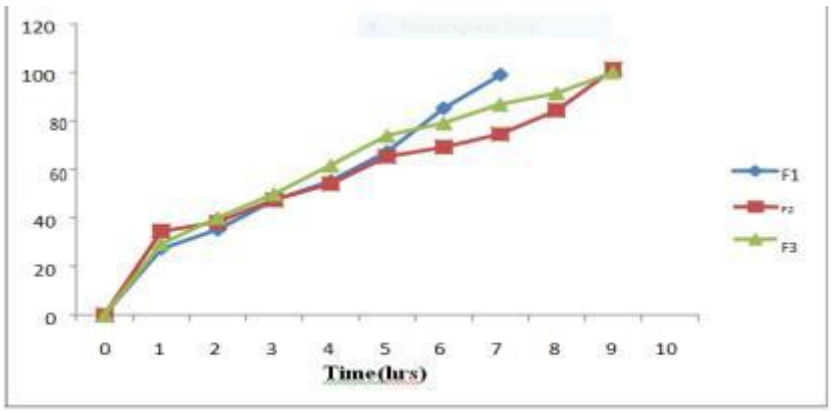

Figure:10 percentage drug release of Formulations F1-F3

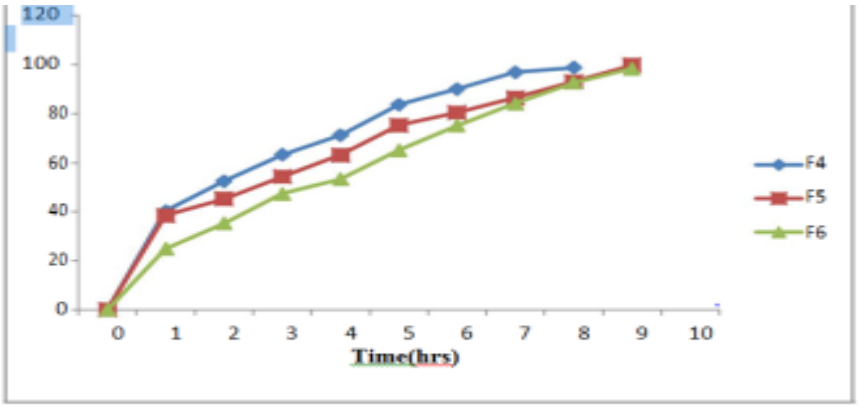

Figure shows percentage drug release of Formulations F4-F6

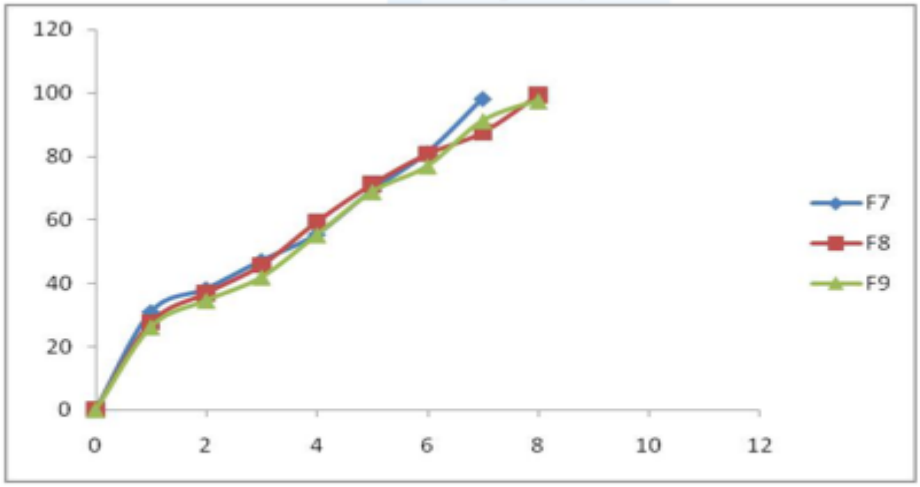

Figure shows percentage drug release of Formulations F7-F9

Drug release kinetics studies

Zero order kinetics

Time Log Release	√t Drug	% of drug	Log % of Remind Release	Drug	Log % of Drug Remind
1	0	1	24.98	1.397	75.02	1.875
2	0.30	1.41	35.32	1.547	64.68	1.810
3	0.477	1.73	47.32	1.675	52.68	1.721
4	0.602	2	53.4	1.727	46.6	1.668
5	0.698	2.23	65.12	1.813	34.88	1.542
6	0.77	2.44	75.22	1.876	34.78	1.541
7	0.84	2.64	84.18	1.925	15.82	1.199
8	0.90	2.82	92.72	1.967	7.28	0.862
9	0.95	3	98.38	1.992	1.62	0.209
10	1	3.16	99.9	1.999	0.1	-1

CONCLUSION

The main objective of the present study was to formulate and evaluate the buccal tablets of Fluvastatin Carbopol, Chitosan and Xanthan gum were selected as buccoadhesive polymers on the basis of their matrix forming properties and mucoadhesiveness. The prepared tablets were evaluated for various parameters such as compatibility studies, drug content, weight variation, hardness, thickness, friability, swelling studies, microenvironment pH, in vitro drug release studies, in vitro mucoadhesion strength and Release rate kinetics. The following conclusions were drawn from the results.

- From the FT-IR spectra it was observed that similar characteristic peaks appear with minor differences (within limit) for the drug and its formulations. Hence it may be concluded that there was no chemical interaction between the drug and excipients used.
- All the formulations passes test for weight variation, content uniformity and showed acceptable results with respect to drug content and percentage friability.
- Swelling index was calculated with respect to time. Swelling index increased as the weight gain by the tablets increased proportionally with rate of hydration. The swelling indices of tablets with Carbopol and Chitosan increased with increasing amounts of Carbopol. Maximum swelling was seen with formulations (F3, F6, F2) containing Chitosan and Carbopol, the values increased with increasing amounts of Carbopol.
- Analysis of drug release mechanism showed that the drug release followed non-Fickian diffusion and the best fit model was found to be 1st order.
- Tablets containing Chitosan showed least adhesion force than tablet of all other formulations, which is due to low viscosity. These observations indicate that the bio adhesive strength of Carbopol is much more than Chitosan.
- After all the evaluation tests formulation coded F6 was selected for stability studies and the results revealed no significant change in % drug content and physical characters. Stability studies indicated that the selected formulation was stable.
- Based on the results of evaluation tests and stability tests formulation F6 was concluded as best formulation for buccal drug delivery system.

REFERENCES

1. R. Khanna, S.P. Agarwal, Alka Ahuja., Muccoadhesive Buccal Drug Delivery: A Potential alternative to Conventional Therapy. Indian Pharm. Sci., 1998; 60(1): 1-11.

2. Ahuja. A, Khar. R. K, Ali. J., Muccoadhesive Drug Delivery Systems. Drug Dev. Ind. Pharm., 1997; 23(5): 489-515.
3. Hans. E, Junginger., Bio adhesive polymer Systems for peptide delivery. Acta Pharm. Technol, 1990; 36(3): 110-126.
4. Mortazavi S.A, Carpenter B.G, Smart J.D., An investigation of the rheological behaviour of the mucoadhesive/ mucosal inter phase. Int. J. Pharm., 1992; 83; 221-225.
5. MortazaviS.A, Smart J.D., Factors influencing Gel-Strengthening at the mucoadhesive mucus Interface. Int. Pharm. Pharmacol., 1994; 46: 86-90.
6. Madsen.F, Eberth, Smart.J.D. A rheological examination of the mucoadhesive/mucus interactions-The effect of mucoadhesive type and concentrations. J. Contr. Rel., 1998; 50: 167178.
7. Rajesh. B, Gandhi, Robinson. R.J. Bio adhesion in Drug Delivery. Indian J. Pharm. Sci., 1998; 50(1): 145-152.
8. Mathiowtiz. E, Chickering. D, Jucob. S. J, Santoss. C, Bio adhesive drug delivery systems. Encyclopedia of Pharmaceutical technology. Marcel Decker: New York, 1992; 9.
9. Ponchel. G, Touchard. F, Duchene. D, Peppas. N., MortazaviS.A, Carpenter B.G, Smart J.D., Bio adhesive analysis of controlled release system- I Fracture and interpretation analysis in poly (acrylic acid)- containing system. J. Contr. Rel., 1987; 5: 129-141.
10. Mortazavi. S.A, Carpenter. B.G, Smart. J. D, A comparative study on the role played by mucus Glycoproteins in the rheological behaviour of mucoadhesive/mucosal Interphase. Int. J. Pharm., 1993; 94: 195-201.