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Formulation and Evaluation of Buccal Tablets Atenolol

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ABSTRACT

Atenolol is a β-adrenergic antagonist with half-life of 6-8 hours and having poor bioavailability of 46-60%. It is widely used in the treatment of myocardial infraction and congestive heart failure.The objective of the present work is to formulate and characterize buccal tablets of Atenolol using different mucoadhesive polymers that provides direct entry of drug into the systemic circulation, thus avoiding the hepatic first pass effect, to evaluate the pre and post compression parameters, *In-vitro* studies, to carry out stability studies as per ICH guidelines, to predict the drug release mechanism and statistical analysis of the results.

Key words: Atenolol, Carbapol 934P, Guar gum, Carboxy methyl cellulose sodium, HPMC, Lactose, Talc and Magnesium Stearate.

Introduction

The oral route is by far the most popular route of drug administration. Oral administration is also best with inherent physiological constraints such as chemical degradation during passage through the mucosa and subsequently the liver [1-4]. The duration of a drug after oral administration is mainly a function of drug-related properties such as rate of absorption and clearance as well as residence time of the delivery system at the absorption site. Most sustained release drug delivery systems developed thus far are aimed at slowing the apparent absorption rate by reducing during release rate from the dosage form[5-8]. The residence time of most sustained/controlled release dosage forms is primarily determined by gastric emptying and intestinal motility. Gastric emptying is influenced by factors such as autonomic and hormonal activity, and volume, composition, viscosity, osmolality, pH, caloric value, temperature of stomach contents as well as by many drugs. It is generally assumed that the desirable site of absorption is the proximal and mid small intestine, the transit time of most delivery systems in which only 2-3 hrs long. Consequently, a sustained is release formulation of about 12-hrs duration or longer can only be achieved by slowing gastric emptying [9-11]. Several approaches have been proposed for prolongation of GI transit time. These include flotation tablets and capsule, unfolding of stratified medication sheet, bio adhesive polymers, and certain fatty acids. Drug can be absorbed from the oral cavity through the oral mucosa either sublingually (under the tongue) or buccally (between the cheek and gingiva). In general, rapid absorption from these routes is observed because of the thin mucous membrane and rich blood supply, for highly hydrophilic drugs (log p < 2), which also suffer from extensive pre systemic elimination and require a rapid onset of action, sublingual or oral administration may offer advantages over oral administration[12-14].

MATERIALS AND METHODS

Atenolol were obtained from Yarrow chem.products, Mumbai. Carbapol 934P, Guar gum, Carboxy methyl cellulose sodium, HPMC, Lactose, Talc and Magnesium Stearate were obtained from Central drug house Pvt. Ltd, New Delhi.

FORMULATION OF BUCCAL TABLETS OF ATENOLOL

The tablets were prepared by direct compressionmethod, using different polymers in varying concentrations asshownin Table 4. The buccal tablets were prepared usingcarbopol 934p,Guar gum and SodiumCMC as mucoadhesive polymers. The drug and polymer was taken in the ratios of 1:0.5, 1:1, 1:1.5, and 1:2for different formulations and HPMC was taken in a constant weight for all formulations. The required quantities of drug and polymer were mixed in mortar and pestle and passed through the sieve no. #20. The granules obtained were compressed into tablets by rotary tablet punching machine[47].

A total of 12 batches of tablet formulations were prepared.

Formulation details of Buccal Tablets of Atenolol

S.NO	INGREDIENTS	FORMULATIONS (Qty. in mg)											
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
1	Atenolol	25	25	25	25	25	25	25	25	25	25	25	25
2	Carbopol 934P	12.5	25	37.5	50	X	X	X	X	X	X	X	X
3	Guar gum	X	X	X	X	12.5	25	37.5	50	X	X	X	X
4	Sodium CMC	X	X	X	X	X	X	X	X	12.5	25	37.5	50
5	HPMC K-100	20	20	20	20	20	20	20	20	20	20	20	20
6	Lactose	62.5	50	37.5	25	62.5	50	37.5	25	62.5	50	37.5	25
7	Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
	Total tablet weight	125	125	125	125	125	125	125	125	125	125	125	125

CHARACTERIZATION OF PREPARED BUCCAL TABLET FORMUALTIONS

Pre compression parameters of prepared granules.

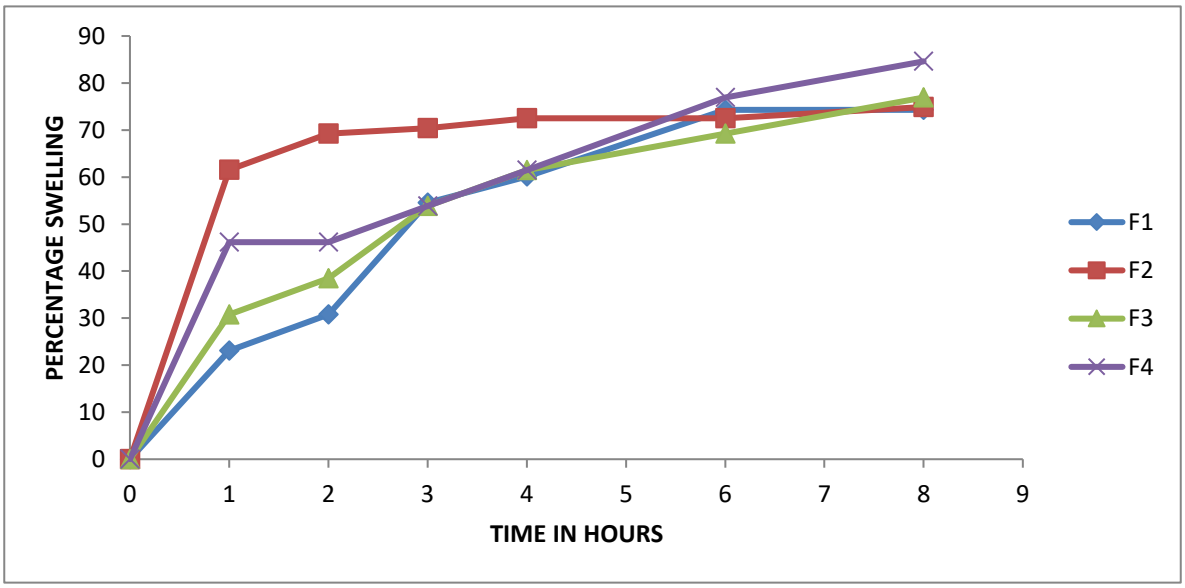
S.NO	FORMULATION CODE	BULK DENSITY* (g/ml)	TAPPED DENSITY* (g/ml)	HAUSNER'S RATIO*	CARR'S INDEX* (%)	ANGLE OF REPOSE* (θ)
1	F1	0.351±0.002	0.412±0.002	1.17±0.002	14.5±0.11	$21^0 73' \pm 0.115$
2	F2	0.356±0.002	0.418±0.002	1.17±0.002	14.3±0.15	$22^0 06' \pm 0.642$
3	F3	0.285±0.002	0.312±0.002	1.09±0.002	8.8±0.20	$17^0 93' \pm 0.550$
4	F4	0.302±0.002	0.351±0.002	1.15±0.002	13.4±0.11	$16^0 56' \pm 1.155$
5	F5	0.276±0.002	0.313±0.002	1.13±0.011	11.7±0.10	$21^0 6' \pm 0.818$
6	F6	0.417±0.002	0.473±0.002	1.14±0.015	11.8±0.05	$21^0 \pm 0.346$
7	F7	0.445±0.002	0.474±0.002	1.05±0.011	6.2±0.15	$21^0 13' \pm 1.601$
8	F8	0.305±0.002	0.351±0.002	1.12±0.020	13.0±0.20	$20^0 63' \pm 4.215$
9	F9	0.338±0.002	0.394±0.002	1.12±0.011	14.3±0.15	$19^0 53' \pm 1.172$
10	F10	0.356±0.002	0.418±0.002	1.17±0.011	14.6±0.15	$22^0 4' \pm 0.692$
11	F11	0.356±0.002	0.418±0.002	1.15±0.011	14.7±0.05	$22^0 06' \pm 0.642$
12	F12	0.351±0.002	0.412±0.002	1.15±0.011	14.6±0.05	$21^0 73' \pm 0.115$

*Average of three determinations

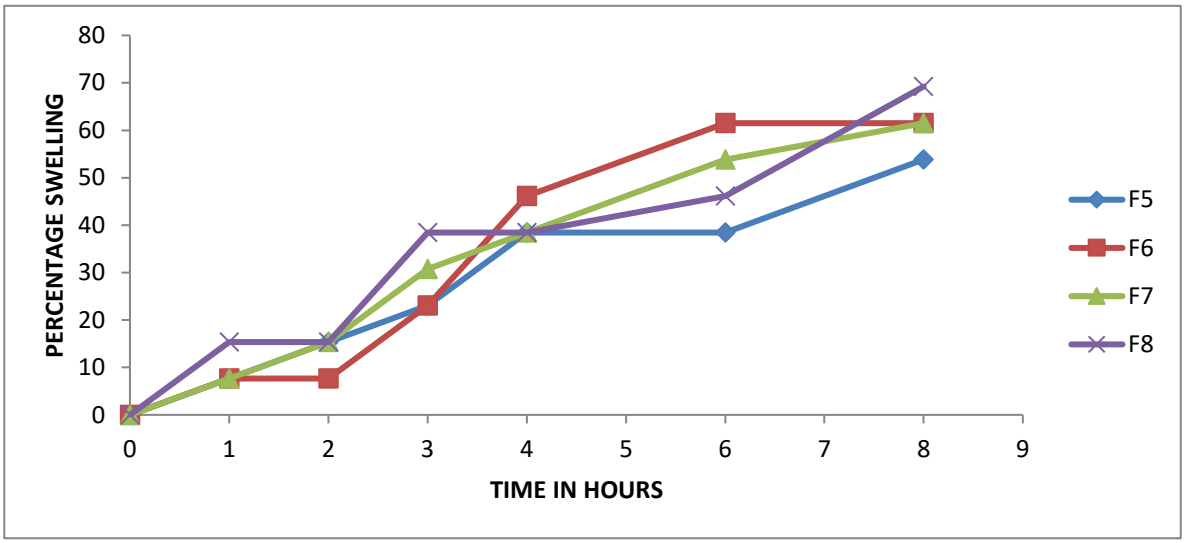
Post compression parameters for prepared tablets.

S.NO	FORMULATION CODE	WEIGHT VARIATION* (mg)	FRIABILITY* (%)	HARDNESS* (kg/cm^2)	THICKNESS* (mm)	PERCENTAGE DRUG CONTENT*
1	F1	130±4.588	0.77±0.015	4.5±0	4.16±0.258	97.6±0.69
2	F2	130±4.588	0.73±0.015	4.16±0.057	4.16±0.258	99.0±1.00
3	F3	128±4.104	0.81±0.010	5.93±0.115	6.01±0.040	99.0±1.00
4	F4	130±4.588	0.38±0.015	5.73±0.115	6.03±0.051	99.3±1.15
5	F5	130±4.588	0.77±0.017	4.0±0.1	6.0±0.1	97.3±1.15
6	F6	128.5±3.663	0.38±0.011	4.16±0.057	6.16±0.0516	96.8±2.11
7	F7	129±4.472	0.38±0.005	4.06±0.115	6.01±0.040	97.0±0.92
8	F8	127±4.702	0.37±0.011	4.13±0.057	6.56±0.081	97.3±1.66
9	F9	128±4.104	0.78±0.020	5.43±0.057	6.35±0.054	98.6±1.15
10	F10	128±4.104	0.77±0.015	5.53±0.0115	6.5±0	97.7±1.61
11	F11	128±4.104	0.76±0.005	5.26±0.115	6.36±0.0516	97.2±0.69
12	F12	128±4.104	0.77±0.005	5.73±0.115	5.75±0.273	97.7±1.61

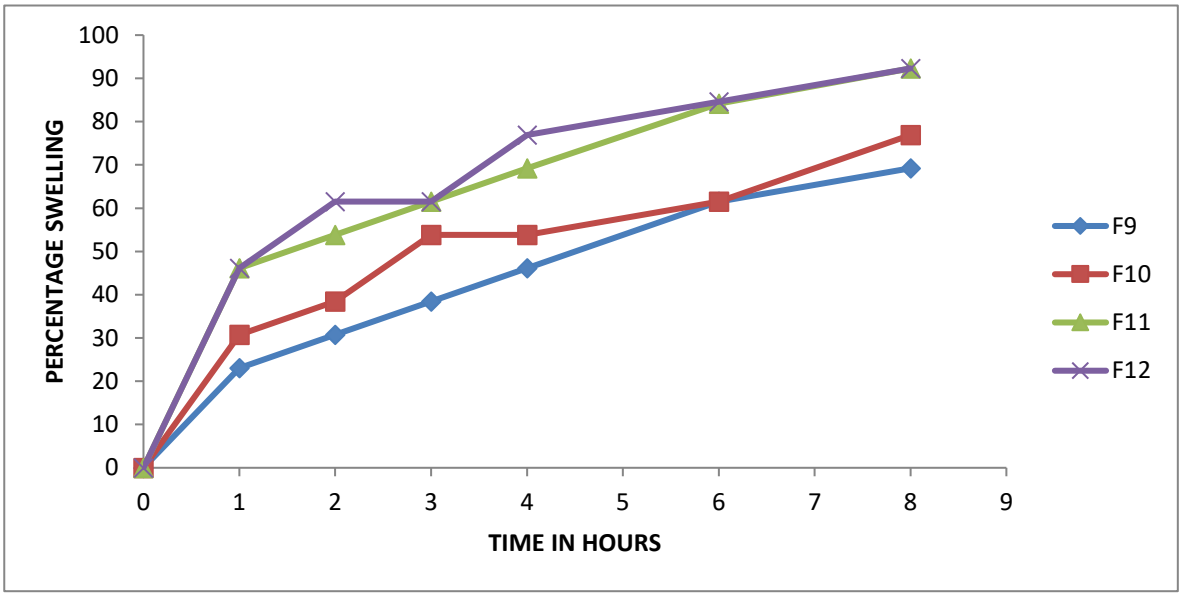
*Average of three determinations



Graph showing swelling study of formulations F1 to F4.

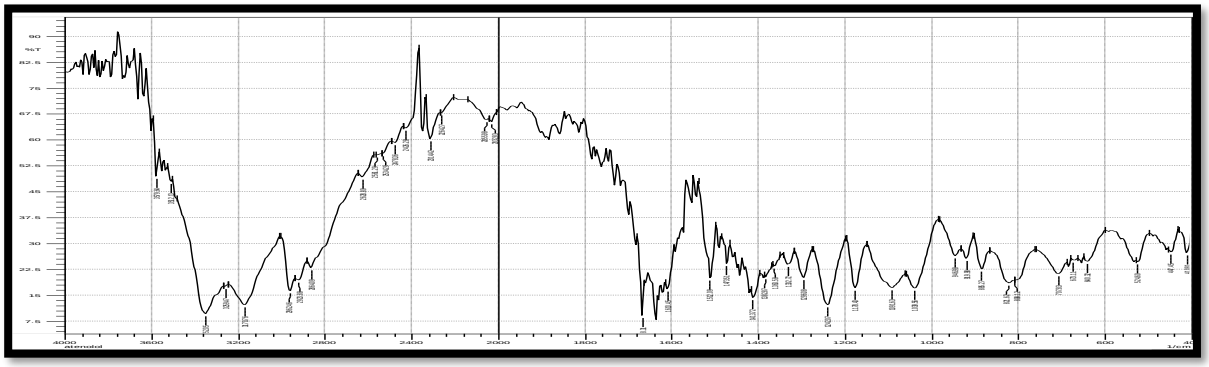


Graph showing swelling study of formulations F5 to F8.

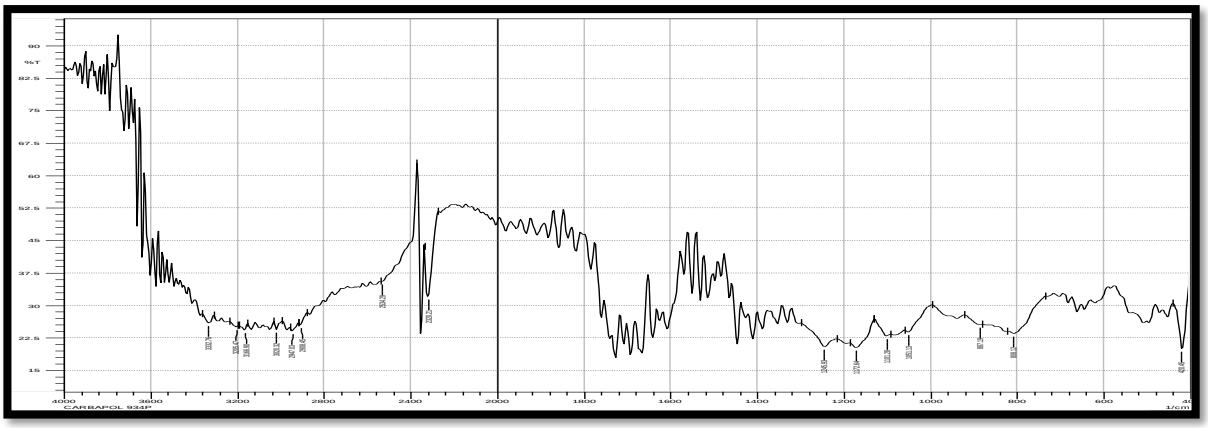


Graph showing swelling study of formulations F9 to F12.

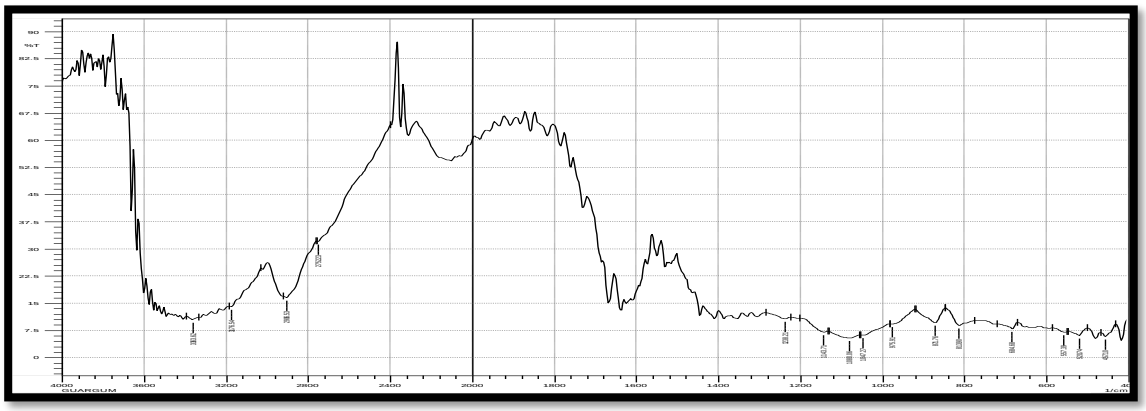
Drug - excipient compatibility studies



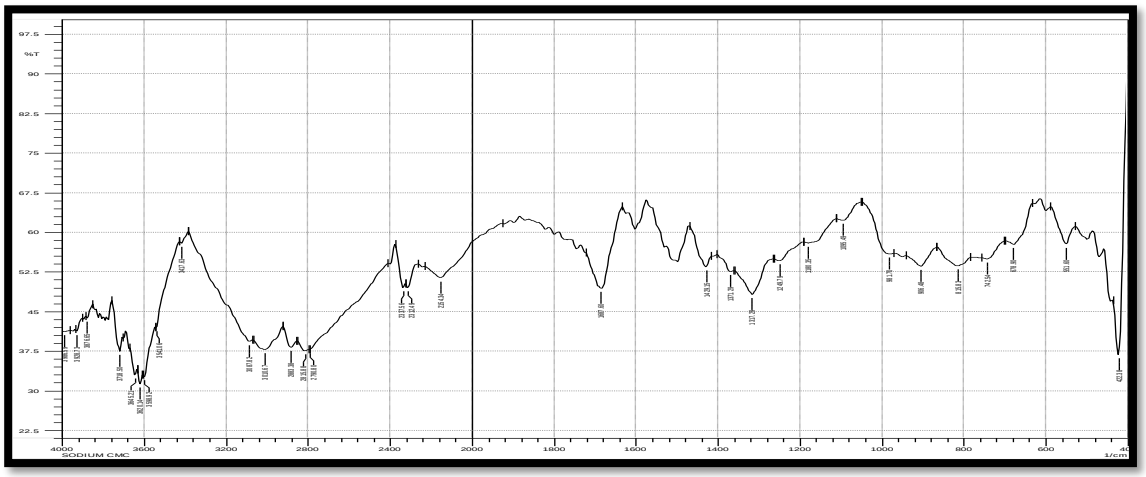
FTIR Spectrum of Atenolol.



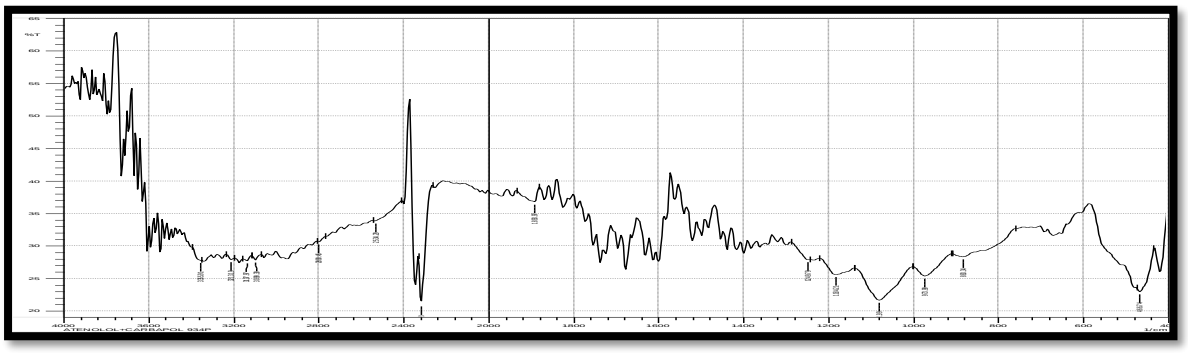
FTIR Spectrum of Carbopol 934P.



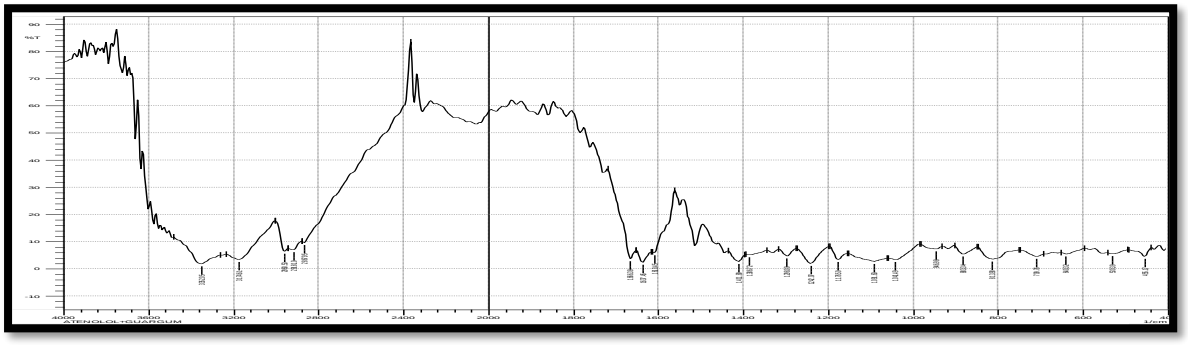
FTIR Spectrum of Guargum.



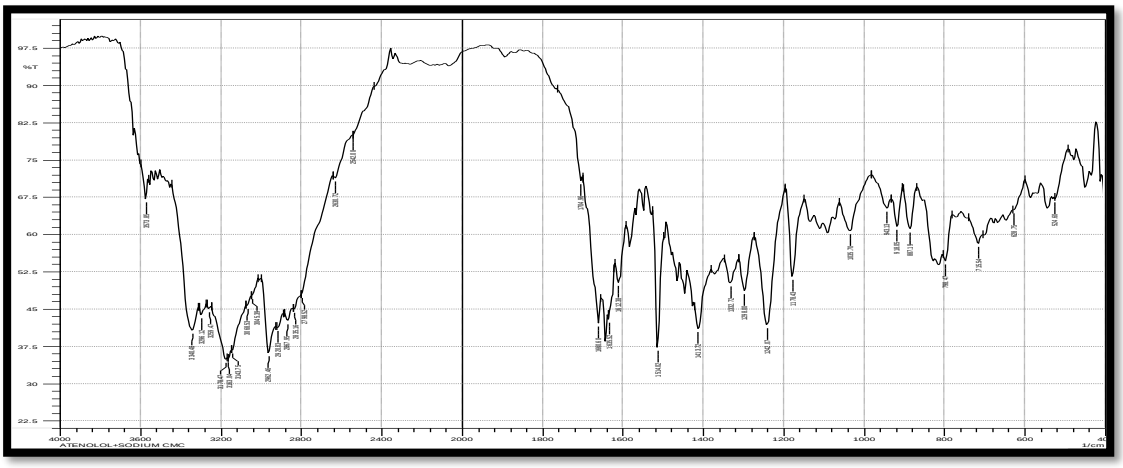
FTIR Spectrum of Sodium CMC.



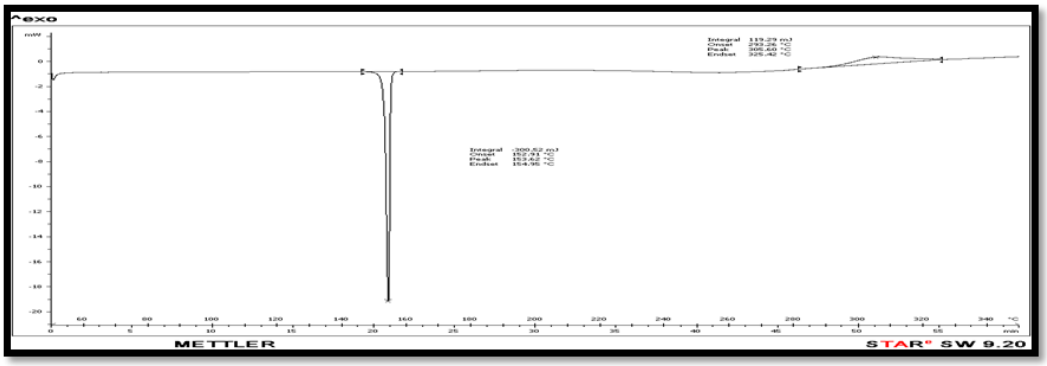
FTIR Spectrum of physical mixture of Atenolol with Carbopol 934P.



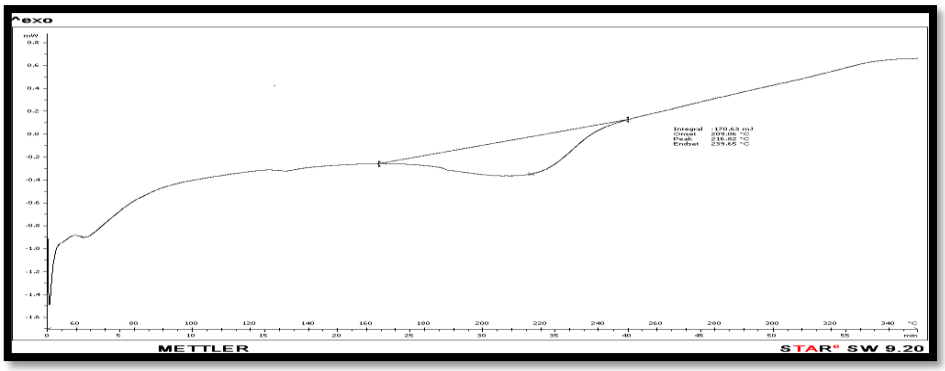
FTIR Spectrum of physical mixture of Atenolol with Guargum.



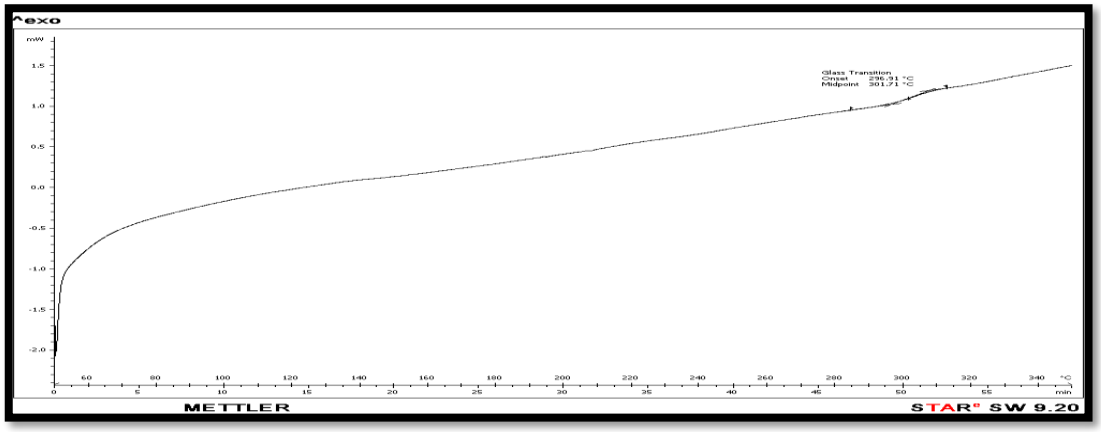
FTIR Spectrum of physical mixture of Atenolol with Sodium CMC.



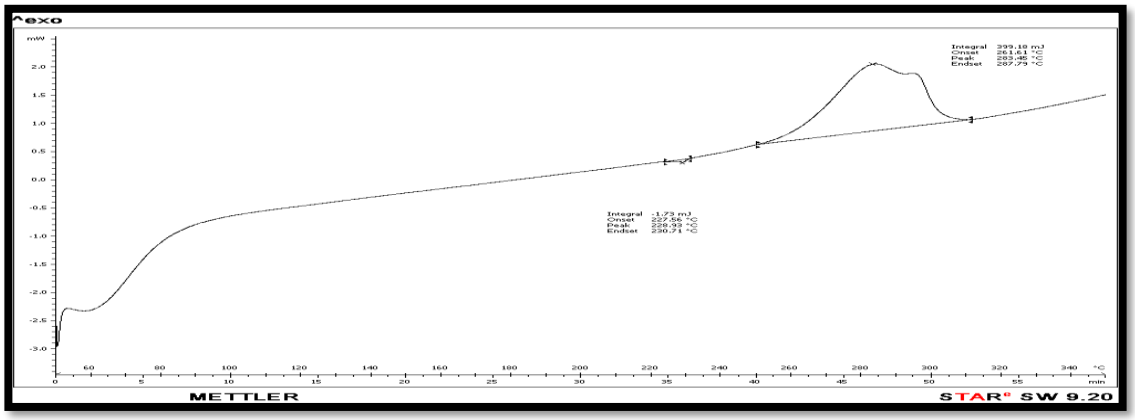
DSC Thermogram of Atenolol.



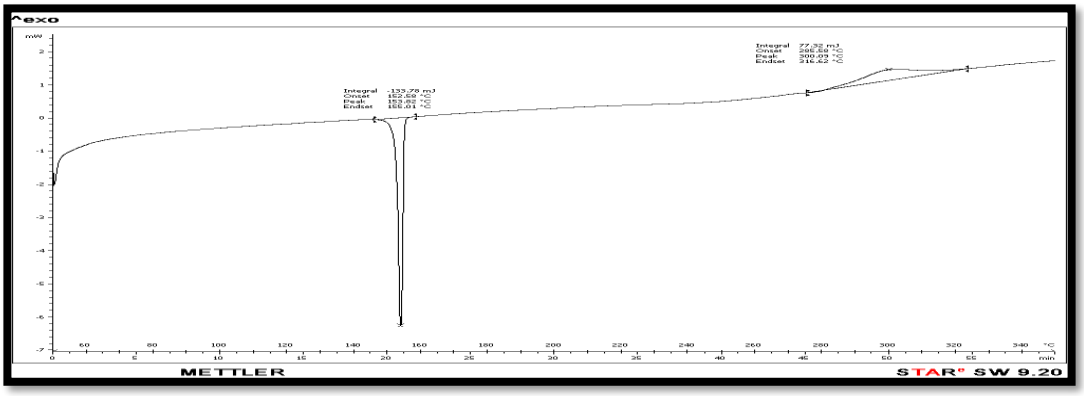
DSC Thermogram of Carbopol 934P.



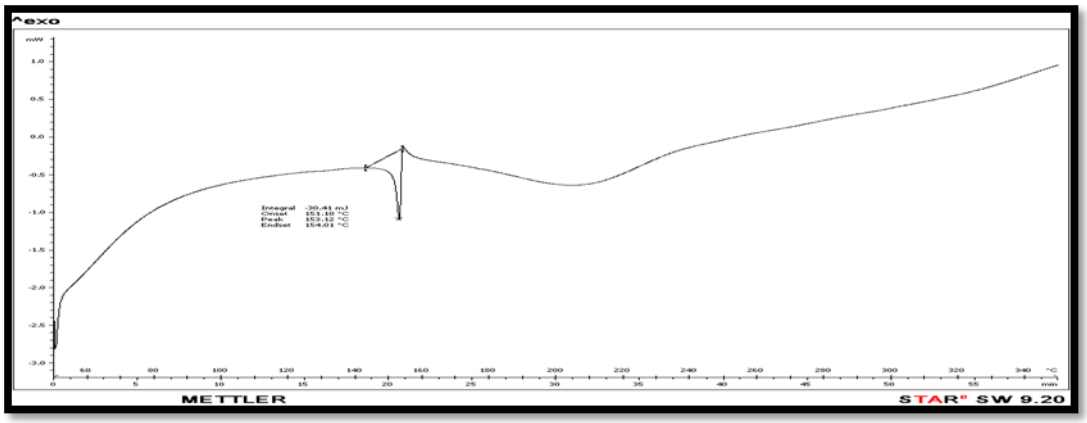
DSC Thermogram of Guargum.



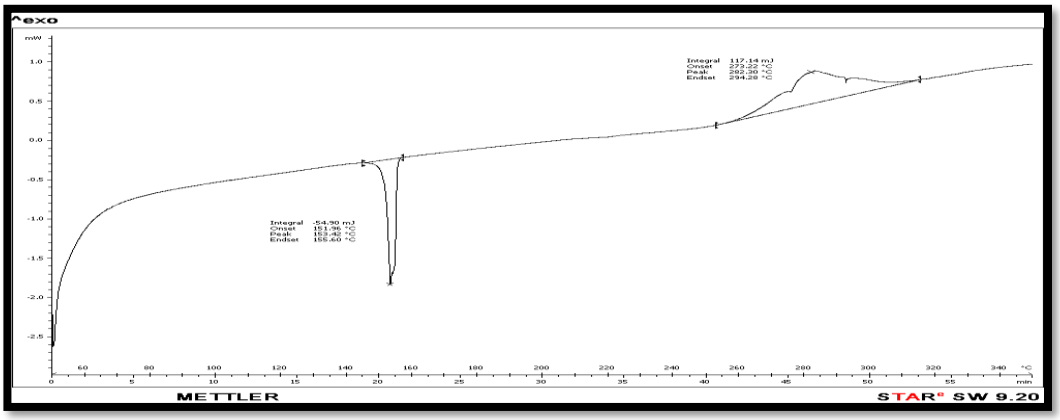
DSC Thermogram of SodiumCMC.



DSC Thermogram of physical mixture of Atenolol with Carbopol 934P.



DSC Thermogram of physical mixture of Atenolol with Guargum.



DSC Thermogram of physical mixture of Atenolol with SodiumCMC.

CONCLUSION

The present study was aimed at an attempt to develop bioadhesive drug delivery system for Atenolol. The main interest in such a dosage form was to avoid extensive first pass metabolism and for prolonged effect, thereby providing increased therapeutic action.Mucoadhesive formulations in the form of sustained release tablets were developed to a satisfactory level in terms of drug release, bioadhesive performance, physicochemical properties and surface pH. *In-vitro* drug release studies revealed that the drug was sustained over a period of 8 hours and *In-vitro* permeation studies were found to be maximum for a period of 24 hours. Buccal delivery of Atenolol is found to be a promising route for controlling the hypertension. They are found to be more advantageous in comparison to the conventional drug delivery systems containing Atenolol. The formulations of bioadhesive polymers Carbopol 934P and SodiumCMC are found to be more suitable for the bioadhesion than guar gum. The results guaranteed the achievement of therapeutic concentration in the action site, the decrease of drug side effects and the improvement of patient compliance. Thus a stable, safe and effective buccoadhesive tablet of atenolol can be formulated successfully. The scale up of the same needs to be studied in future.

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