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Formulation and evaluation of mucoadhesive buccal tablets of metoprolol succinate

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Abstract
Buccaladhesive tablets that are prepared in the present investigation consist of usage of natural polymers which can prolong the drug release period of time. The drugs that are selected are of beta blockers which have short bioavailability and have greater need at the particular hour. The selection of buccaladhesive form to bypass first pass metabolism and degradation that occurs due to liver. These are adhesive forms which stay at the particular location and releases the drug due to swell in the polymer. Therefore all these advantages made the buccaladhesive system better when compared to other forms.
In this particular investigation the polymers that are selected are studied for viscosity at different concentrations, at different temperature conditions, different climatic conditions and also for stability. Different tests were performed which gives information regarding the nature of polymer. The formulations are planned by taking different concentrations of drug and polymers in varying concentrations from high to low. Based on this drug release is calculated and compared with that of the synthetic polymers. Natural polymers are named as NBA01, NBA02, NBA03 and NBA04.
The drug release is based upon swelling index and quantity of polymer. High viscosity is imparted with high concentration of polymer and vice versa. The optimized formulation is selected basing upon the maximum duration of drug release; this is further studied for stability followed by *in vivo* studies.

Keywords: metoprolol succinate, natural polymers, buccaladhesive tablets

1. Introduction
The development of the dosage form took place not by chance but by need. The developed dosage form should meet the needs of the patient and act efficiently, stable and economical and releases the drug to the desired location with least side effects [1]. Earlier there were conventional dosage forms that were prepared but recently they were replaced with NDDS, these generated positive outputs by increasing the life of the drug. Now NDDS is not just theory, extensive work is going on in all possible ways where it can be suitable and advantageous, one among them is buccal adhesive drug delivery system [2, 3, 4].
The exceptional features of oral mucosa make it a feasible site for sustained release delivery systems, which could maintain a steady release of drug in the systemic circulation [5]. Various delivery approaches have been developed to deliver drugs into the oral cavity for either local or systemic action. These include mouthwashes, lozenges, gels, chewing gums, lollipops, films, patches, tablets and some specialized transmucosal devices [6].
In the present work, natural polymers were taken and studied for suitability as bio adhesive polymers, using these polymers buccaladhesive formulations were prepared, compared among natural polymers for various parameters and optimized formulations were studied for *in vivo*.

2. Materials and Methods
Metoprolol succinate was procured from MSN laboratories

Grewia gum [7, 8]
Synonyms: *Chadara* Forsk, *Sasali* Adans
Kingdom: Plantae
Order: Malvales
Family: Sparrmanniaceae
Subfamily: Grewiodeae
Genus: Grewia L.

Grewia polysaccharide gum is procured by eradication from the inner stem bark of the plant *Grewia damine.*
Hakea gum [9, 10, 11]
Kingdom: Plantae
Order: Proteales
Family: Proteaceae
Subfamily: Hakea
Genus: Grewia L.

Dulce gum [12, 13, 14]
Kingdom: Plantae
Order: Fabales
Family: Fabaceae
Genus: Pithecellobium

Aegle Marmelos gum [15, 16, 17]
Kingdom: Plantae
Order: Sapindales
Family: Rutaceae
Genus: Aegle

3. Collection and extraction of natural buccadhesive materials [18, 19].

The bark of *G. Damine*, dried gummy exudates of *H. Laurina*, seeds of Aegle Marmelos for *A. Marmelos* and *P. Dulce* were collected from in and around areas of Andhra Pradesh. Several approaches were tried for eradication of the gum from the inner stem bark of the shrub, dried gummy exudates and dried seeds. The dried and pulverized inner stem bark of the *G. Damine* shrub, dried gummy exudate of *H. Laurina and* dried seeds of *A. Marmelos* and *P. Dulce* are dissipated in dematerialized water using an impeller. The fibrous material from the dispersed mucilage is removed by tightening through a muslin cloth. Further the mucilage is centrifuged before extraction of the gum with 96% ethanol. The extracted gum is redispersed in water and re extracted to get a gum which is then dried in an oven at 50°C for 8h. The gum can be further purified by treatment with 0.1M sodium hydroxide or hydrochloric acid or with sodium chloride followed by extraction with 96% ethanol. It must be noted that treatment of the natural material with dilute alkali, dilute acid, or electrolytes could result in modification of the parent material with consequent variations in the physicochemical properties of the resultant material. The gum obtained from *G. Damine* is coded as NBA01 (Natural Buccaladhesive Material 01), for *H. Laurina* is coded as NBA02 (Natural Buccaladhesive Material 02), *A. Marmelos* is coded as NBA03 (Natural Buccaladhesive Material 03) and *P. Dulce* is coded as NBA04 (Natural Buccaladhesive Material 04)

4. Characterisation of buccaladhesive polymers

The buccaladhesive polymers were characterized for phytochemical constituents, pH, swelling index, melting point, particle size, derived properties, flow properties, moisture content, solubility studies and microbiological properties. Data shown in tables 2-7.

Table 1: Formulation of Buccal adhesive Tablets of Metoprolol Succinate prepared by using Natural Polymers

S. No	Ingredients (mg/tablet)	Formulation Code																
		MNF 1	MN F 2	MN F 3	MN F 4	MN F 5	MN F 6	MNF 7	MN F 8	MN F 9	MN F 10	MN F 11	MN F 12	MN F 13	MN F 14	MNF 15		MN F 16
1.	Metoprolol	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
2.	NBA-01	25	50	75	100	-	-	-	-	-	-	-	-	-	-	-	-	-
3.	NBA-02	-	-	-		25	50	75	100	-	-	-	-	---	-	-		-
4.	NBA-03	-	-	-	-	-	-			25	50	75	100	-	-	-	-	
5.	NBA-04	-	-	-	-	-	-	-	-	-	-	-	-	25	50	75		100
6.	Mannitol	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
7.	Ethyl Cellulose	5	10	15	20	5	10	15	20	5	10	15	20	5	10	15	30	20
8.	DCP	100	70	40	10	100	70	40	10	100	70	40	10	100	70	40	75	10
9.	Magnesium Stearate	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
10.	Talc	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Total(mg)		200	200	200	200	200	200	200	200	200	200	200	200	200	200	200		200

5. Compatability Studies

The presence of incompatibility between drug and other excipients were evaluated by performing drug – polymer interaction studies. The interaction study done by using Infrared spectroscopy and Differential Scanning Calorimetry. The IR spectra and DSC spectra of pure drug Metoprolol, Natural Buccal Adhesive Polymers (NBA01, NBA02, NBA03, NBA 04) and drug polymer blends were taken and compared for studying the presence of incompatibility between drug and polymer.

Interaction study by FTIR

IR spectroscopy studies were carried out using Perkin Elmer model 2000 by KBr pellet method. The IR spectrum was recorded from the range of 4000 to 400 cm^{-1} and peaks obtained were identified. FTIR spectrums are shown in figs 3 to 8 and interpretations of spectral data are presented in table 9.

Interaction study by DSC

Differential scanning colorimetric analysis were performed to characterize the drug–polymer compatibility. The DSC thermograms of pure drug (Metoprolol Succinate, polymers (NBA01, NBA02, NBA03, NBA04) and drug-polymer blends were recorded in a DSC analyzer Model DSC-50 Shimadzu. DSC spectrums were shown in figs. 9 to 10 and interpretations of spectrums are presented.

6. Evaluation of tablets

Tablets that are prepared (table1) and are studied for Weight variation, Hardness, Thickness, friability and disintegration time in water, 0.1N HC1 and phosphate buffer of pH 7.4.
Weight variation was tested by using Balance in comparison with average weight of tablets. Hardness of the tablets was tested by using a Monsanto hardness tester. Thickness was tested by using Vernier calipers. Friability of the tablets was determined in a Roche Friabilator. Disintigration times were determined in a Thermionic tablet disintegration test machine. Post compression parameters were tabulated in tables 10, 11.
The prepared tablets were studied for swelling index, the swelling ability of the polymer shows impact on the drug release hence it has to be studied. Similarly buccaladhesive strength was expressed in newtons, this helps to know how strong the bond exists between the buccal mucosa and the prepared tablets. The data were shown in table 12.

7. Drug release study

Release of drug from the tablets was studied in pH 6.8, pH 1.2 for Metoprolol (900ml) as prescribed in USP. One tablet containing 50 mg of metoprolol, was taken maintaining a paddle speed of 100 rpm and a temperature of 37 ± 0.5°C. Samples were withdrawn through a filter at different time intervals, suitably diluted and studied for drug release using a Shimadzu UV double beam Spectrophotometer. Drug release experiments were conducted in triplicates. The drug release data were shown in fig.11

8. Analysis of release data

The drug release data were fitted to Zero-order [20], first order [21], Higuchi [22] and Peppas [23] equations to determine the corresponding release rate and mechanism of drug release from the Buccaladhesive tablets prepared. Relationship was studied among the release rate constant and the concentration of polymer used; this was followed by studying the impact of Ethyl cellulose on drug release. Graphs were plotted for all the formulations and were shown in fig. 12.

Results

Table 2: List of phytochemical constituents identified

Tests	Results			
	NBA01	NBA02	NBA03	NBA04
Alkaloids	–	–	-	-
Carbohydrates	+	+	+	+
Flavonoids	-	–	-	-
Tannins	-	-	-	-
– Absence	+ Presence			

Table 3: Swelling Index of NBA01, NBA02, NBA03 and NBA04

Parameter	Result			
	NBA01	NBA02	NBA03	NBA04
Swelling index (after 3hr)				
At, Distilled water	15.09 ± 0.34	18.24 ± 34.3	23.12 ± 0.47	12.16 ± 0.26
pH – 1.2	13.33 ± 0.28	15.92 ± 28.2	18.23 ± 0.35	10.76 ± 0.35
pH – 6.8	14.12 ± 0.29	17.29 ± 29.1	22.12 ± 0.32	11.14 ± 0.23

Table 4: Particle size distribution of NBA01 and NBA02 gums powder

Size range (µm)	Number of Particles			
	NBA01	NBA02	NBA03	NBA04
0-30	20	21	28	16
30-60	40	43	45	42
60-90	230	226	221	228
90-120	180	177	156	141
>120	30	25	19	12

Table 5: Characterization of NBA01, NBA02, NBA03 and NBA04

Property	Results Obtained			
	NBA01	NBA02	NBA03	NBA04
Tapped density(gm/cc)	0.702±0.02	0.715±0.36	0.615±0.14	0.74±0.22
Bulk density (gm/cc)	0.632±0.04	0.618±0.02	0.623±0.15	0.603±0.66
Bulkiness (cc/gm)	1.58±0.04	1.60±0.45	1.51±0.66	1.56±0.81
Angle of repose(^{0})	28.20±1.28	26.12±0.66	27.33±0.51	25.60±0.33
Compressibility index (%)	10.45±1.34	9.33±0.25	10.51±0.61	10.37±0.47
Hausner's ratio	1.2±1.54	1.1±0.56	1.02±0.42	1.3±0.51
Moisture content	14.96±1.12	12.12±0.56	12.32±0.15	11.47±0.33

Table 6: Solubility studies of gums

Solvents used	Solubility of Natural Mucoadhesive Materials			
	NBA01	NBA02	NBA03	NBA04
Cold Water	-	-	-	-
Hot water	+	+	+	+
Ethanol	-	-	-	-
Methanol	-	-	-	-
Ethyl acetate	-	-	-	-
n-Hexane	-	-	-	-

Soluble – (+); Insoluble – (−)

Table 7: Microbial load of gums

Parameter	Result	General specification
Microbial limits		
1. Total aerobic microbial count	NBA01-20 CFU/g	Not more than 100CFU/g
	NBA02-16 CFU/g	Not more than 100CFU/g
	NBA02-14CFU/g	Not more than 100CFU/g
	NBA02-17 CFU/g	Not more than 100CFU/g
2. Total fungal count	NBA01-30 CFU/g	Not more than 100CFU/g
	NBA02-28 CFU/g	Not more than 100CFU/g
	NBA03-29 CFU/g	Not more than 100CFU/g
	NBA04-23 CFU/g	Not more than 100CFU/g
3.Pathogens		
a. *Staphy. aureus*	NBA01,NBA02,NBA03,NBA0-Abs/gm	a.Shall be absent/g
b. *Pseudo. aeruginosa*	NBA01,NBA02,NBA03,NBA0-Abs/gm	b. Shall be absent/g
c. *E. coli*	NBA01,NBA02,NBA03,NBA0-Abs/gm	c. Shall be absent/g
d. *Salmonella*	NBA01,NBA02,NBA03,NBA0-Abs/gm	d. Shall be absent/g

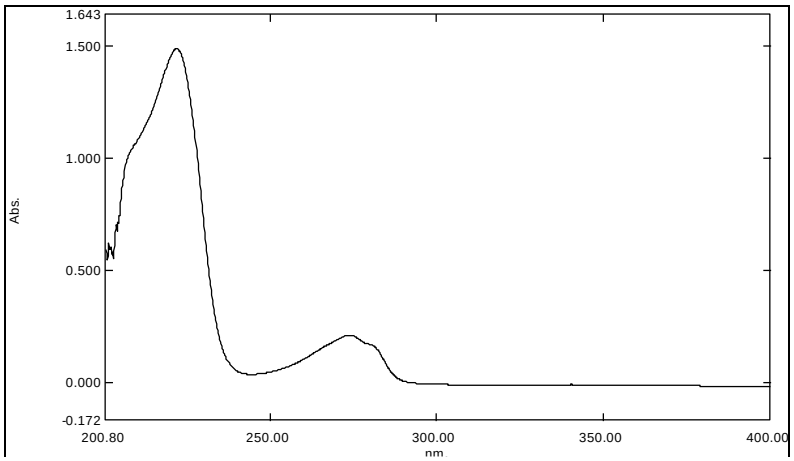

Fig 1: Scanning of Metoprolol at 274nm

Table 8: Results for standard calibration curve of pure drug

Metoprolol	
Concentration in µg/ml	**Absorbance at 274nm in pH6.8**
0	0
2	0.054
4	0.109
6	0.163
8	0.214
10	0.277
12	0.327

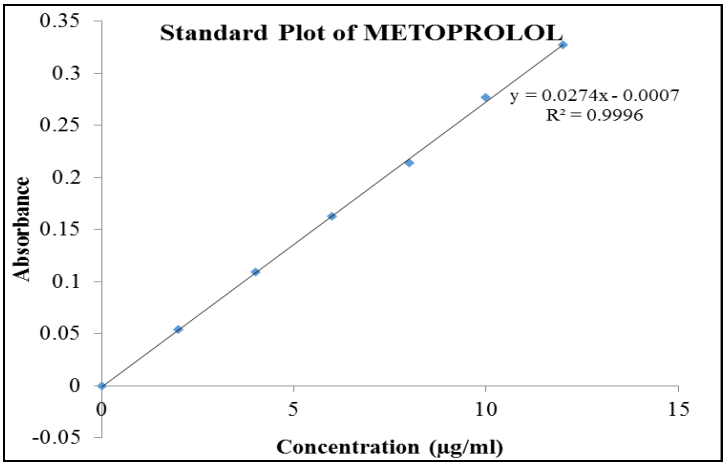

Fig 2: Standard calibration plot of Metoprolol in pH 6.8

Drug polymer interaction study

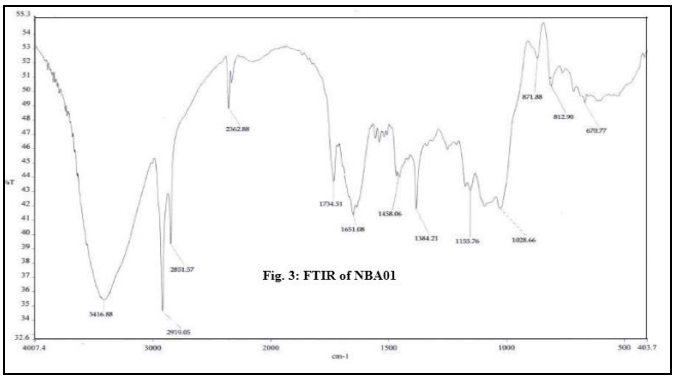

Fig 3: FTIR of NBA01

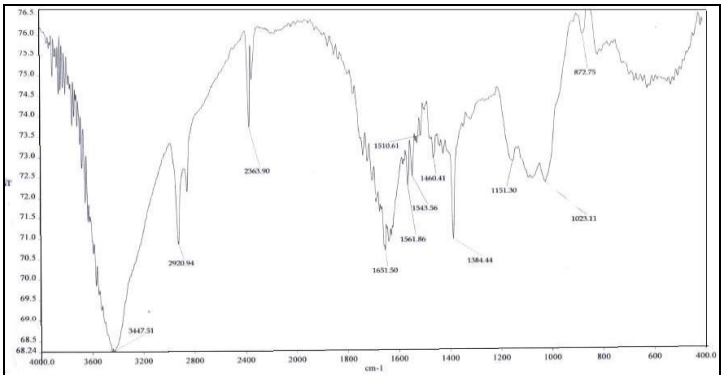

Fig 4: FTIR of NBA02

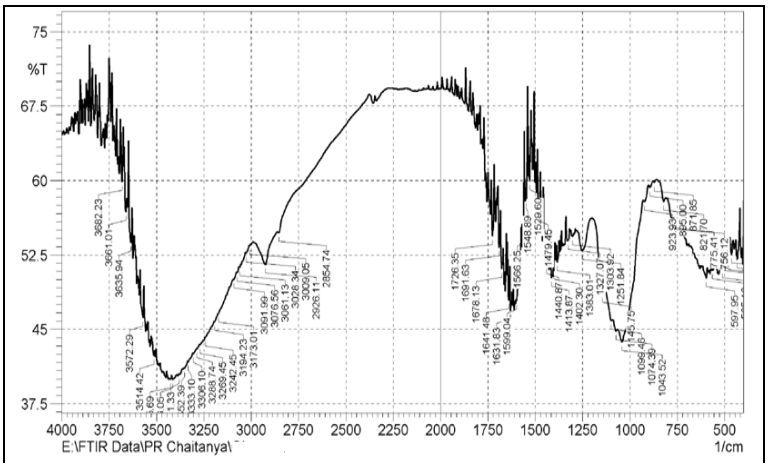

Fig 5: FTIR of NBA03

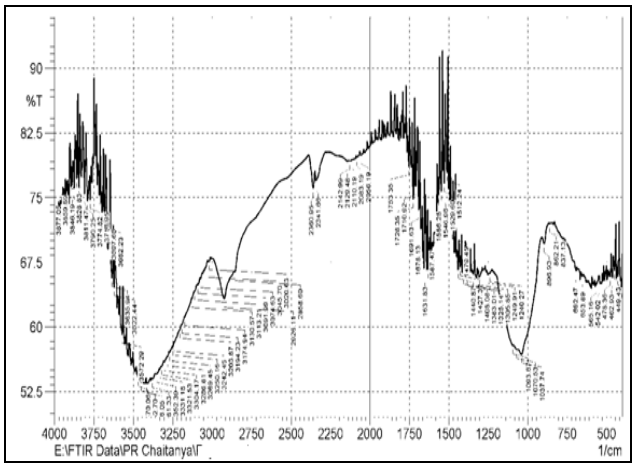

Fig 6: FTIR of NBA04

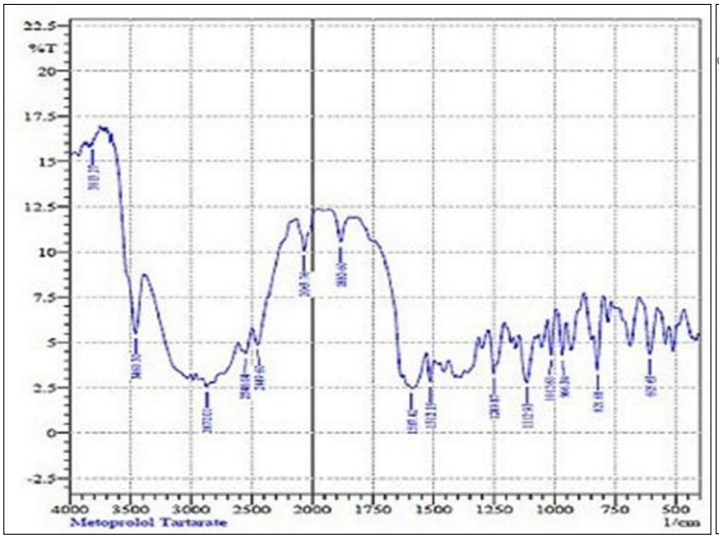

Fig 7: IR of Pure Metoprolol Succinate

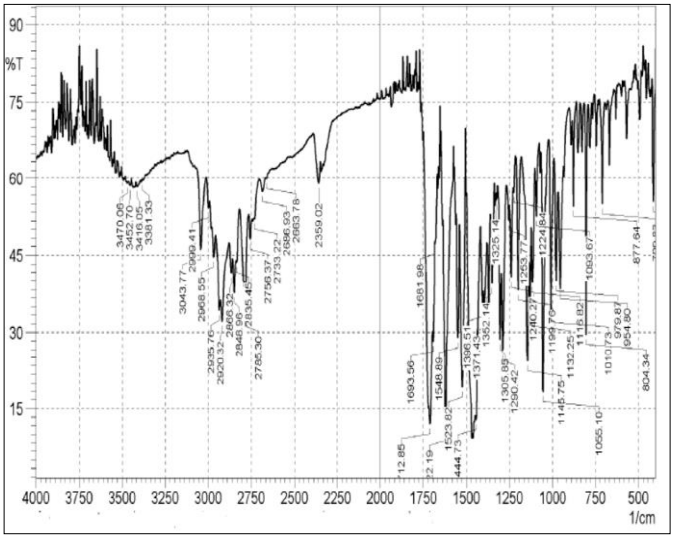

Fig 8: IR of MNF1

Table 9: IR spectral data of NBA01, NBA02, NBA03, NBA04, MNF1.

Wave Number in cm^{-1}	Characteristic bands
NBA01	
3416.5	OH
2919.05	CH-Strech
1757.57	C=O
1651.08	C=C
1364.21	CH-bend
1155.76	C-O alcohol
NBA02	
3447.51	OH
2920.9	CH
1651.50	C=C
1384	CH-bend
1154.30	C-O alcohol
NBA03	
3551.06	OH
3306.10	NH
3078.56	=C-H
1569.04	C=C
1440.87	CH-bend
1145.75	C-O alcohol
NBA04	
3563.08	-OH
3026.43	=C-H
1651.43	C=C
1093.81	C-O alcohol
METOPROLOL PURE DRUG	
3426.43	NH
2962.36	CH
3328.63	OH
1126.38	C-O-C
1556.3	C=C
MNF1	
3452.70	OH
3043.77	=C-H
2920.32	CH
1694.35	C=C
1145.75	C-O

9. Interaction by DSC

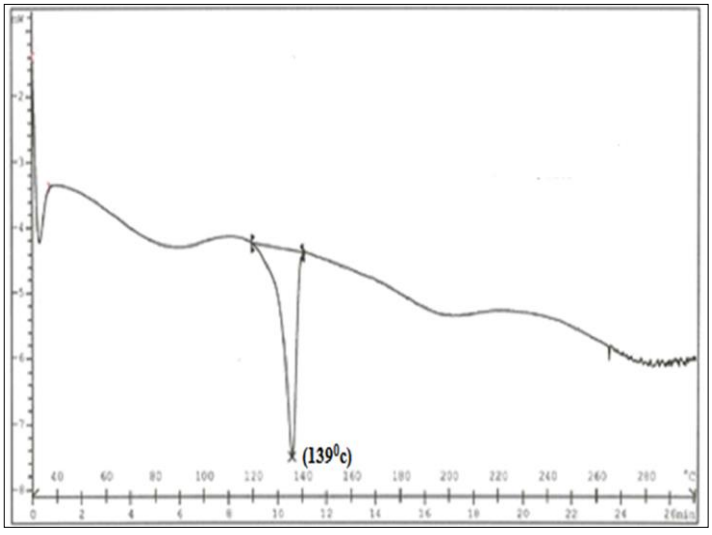

Fig 9: DSC of Metoprolol pure drug

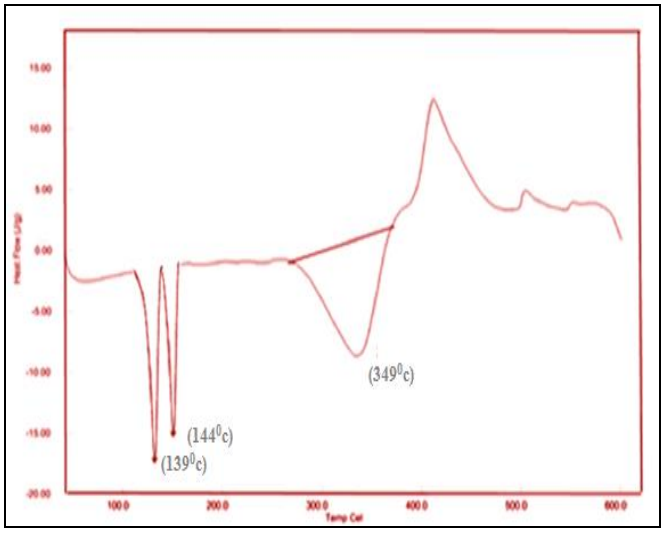

Fig 10: DSC of MNF01

Table 10: Evaluation of granules containing metoprolol using natural polymers

Formulation	Bulk density (gm/mL) ± SD*	Tapped density (gm/mL) ± SD*	Compressibility index (%)± SD*	Hausner's ratio± SD*	Angle of repose (°)± SD*
MNF01	0.56±0.23	0.63±0.28	12.63±0.16	1.12±0.06	24.60±0.36
MNF02	0.59±0.49	0.68±0.19	11.92±0.14	1.15±0.03	22.34±0.21
MNF03	0.51±0.12	0.62±0.36	13.31±0.13	1.18±0.02	29.23±0.52
MNF04	0.48±0.15	0.52±0.14	12.01±0.18	1.08±0.05	25.35±0.47
MNF05	0.49±0.06	0.55±0.28	14.32±0.12	1.12±0.02	22.42±0.35
MNF06	0.45±0.11	0.53±0.17	13.85±0.11	1.17±0.03	22.24±0.24
MNF07	0.48±0.18	0.56±0.39	15.87±0.14	1.16±0.06	26.40±0.39
MNF08	0.49±0.22	0.53±0.18	14.85±0.13	1.08±0.03	23.42±0.54
MNF09	0.47±0.19	0.52±0.16	13.43±0.15	1.10±0.04	22.43±0.81
MNF10	0.46±0.12	0.53±0.12	11.62±0.16	1.15±0.06	23.55±0.29
MNF11	0.49±0.15	0.55±0.28	15.10±0.12	1.12±0.05	22.64±0.11
MNF12	0.42±0.37	0.48±0.13	13.04±0.17	1.14±0.08	23.35±0.54
MNF13	0.53±0.21	0.59±0.26	12.23±0.14	1.11±0.04	26.41±0.33
MNF14	0.51±0.39	0.58±0.39	14.36±0.16	1.13±0.02	23.35±0.73
MNF15	0.49±0.14	0.52±0.21	13.33±0.13	1.06±0.07	22.43±0.14
MNF16	0.59±0.32	0.64±0.21	15.69±0.14	1.08±0.03	23.46±0.24

Table 11: Post Compression Parametrs of Metoprolol using natural polymers

Formulation Code	Weight (mg) ±SD* (n=20)	Friability (%)±SD* (n=10)	Hardness (Kg/Cm^2) ±SD* (n=3)	Thickness (mm) ±SD* (n=3)	Drug Content (%)±SD (n=10)
MNF1	200.0± 1.42	0.32 ± 0.02	4.50 ± 0.14	3.5± 0.03	97.85 ± 0.09
MNF2	199.0± 0.68	0.48± 0.16	5.20 ± 0.30	3.4± 0.02	96.53 ± 0.07
MNF3	200.0± 1.02	0.22 ± 0.09	4.90 ± 0.19	3.4± 0.01	96.12 ± 0.15
MNF4	198.0± 1.18	0.47 ± 0.12	5.00 ± 0.33	3.5± 0.04	97.02 ± 0.06
MNF5	199.0± 0.79	0.39 ± 0.12	4.50 ± 0.21	3.4± 0.02	97.53 ± 0.12
MNF6	201.0± 0.63	0.49 ± 0.27	5.10 ± 0.15	3.5± 0.04	96.98 ± 0.11
MNF7	198.0± 0.49	0.61 ± 0.15	5.00 ± 0.34	3.5± 0.02	99.34 ± 0.45
MNF8	199.0± 0.33	0.17 ± 0.09	5.00 ± 0.27	3.4± 0.03	97.45 ± 0.57
MNF9	200.0± 0.60	0.65 ± 0.07	4.50 ± 0.18	3.5± 0.01	98.78 ± 0.28
MNF10	201.0± 0.81	0.32 ± 0.16	4.65 ± 0.43	3.4± 0.05	95.36 ± 0.27
MNF11	200.0± 0.45	0.48 ± 0.11	4.50 ± 0.47	3.3± 0.02	96.28 ± 0.16
MNF12	201.0± 1.33	0.25 ± 0.16	4.50 ± 0.34	3.5± 0.06	96.57 ± 0.19
MNF13	200.0± 0.59	0.39 ± 0.02	4.32 ± 0.61	3.5± 0.02	91.81 ± 0.21
MNF14	200.0± 0.75	0.75 ± 0.42	4.21 ± 0.22	3.4± 0.03	92.33 ± 0.25
MNF15	201.0± 0.12	0.31 ± 0.16	4.49 ± 0.27	3.5± 0.01	96.27 ± 0.41
MNF16	200.0± 0.45	0.16 ± 0.02	5.21 ± 0.44	3.5± 0.04	92.15 ± 0.09

Table 12: Swelling index of buccaladhesive tablets of Metoprolol using natural polymers

F. Code	Swelling index				
	30 min	60 min	120 min	180 min	240 min
MNF01	0.22±0.02	0.49±0.02	0.92±0.03	1.00±0.03	0.85±0.03
MNF02	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	0.94±0.02
MNF03	0.12±0.01	0.29±0.01	0.62±0.01	0.67±0.01	1.2±0.02
MNF04	0.19±0.02	0.35±0.01	0.72±0.02	0.77±0.03	1.3±0.04
MNF05	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	0.54±0.02
MNF06	0.12±0.02	0.27±0.02	0.64±0.03	0.78±0.03	0.85±0.03
MNF07	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	0.94±0.02
MNF08	0.12±0.01	0.29±0.01	0.62±0.01	0.67±0.01	1.02 ±0.02
MNF09	0.19±0.02	0.35±0.01	0.72±0.02	0.77±0.03	0.81±0.04
MNF10	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	0.94±0.02
MNF11	0.12±0.01	0.29±0.01	0.62±0.01	0.67±0.01	1.01 ±0.02
MNF12	0.19±0.02	0.35±0.01	0.72±0.02	0.77±0.03	1.2±0.04
MNF13	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	0.84±0.02
MNF14	0.12±0.01	0.29±0.01	0.62±0.01	0.67±0.01	0.91±0.02
MNF15	0.19±0.02	0.35±0.01	0.72±0.02	0.77±0.03	1.01±0.04
MNF16	0.07±0.01	0.20±0.01	0.40±0.01	0.49±0.00	1.3±0.02

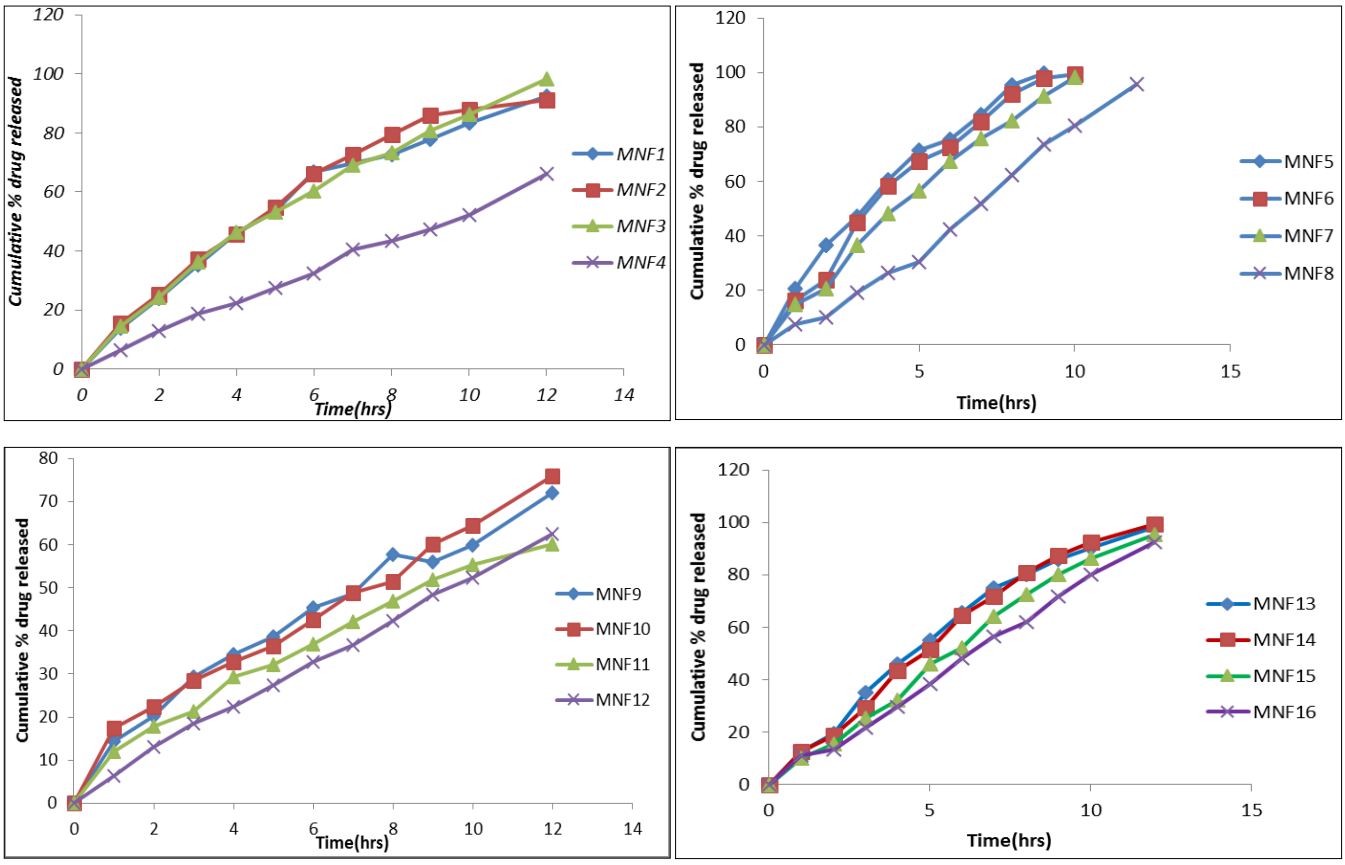

Fig 11: Drug release profiles from MNF1-MNF16

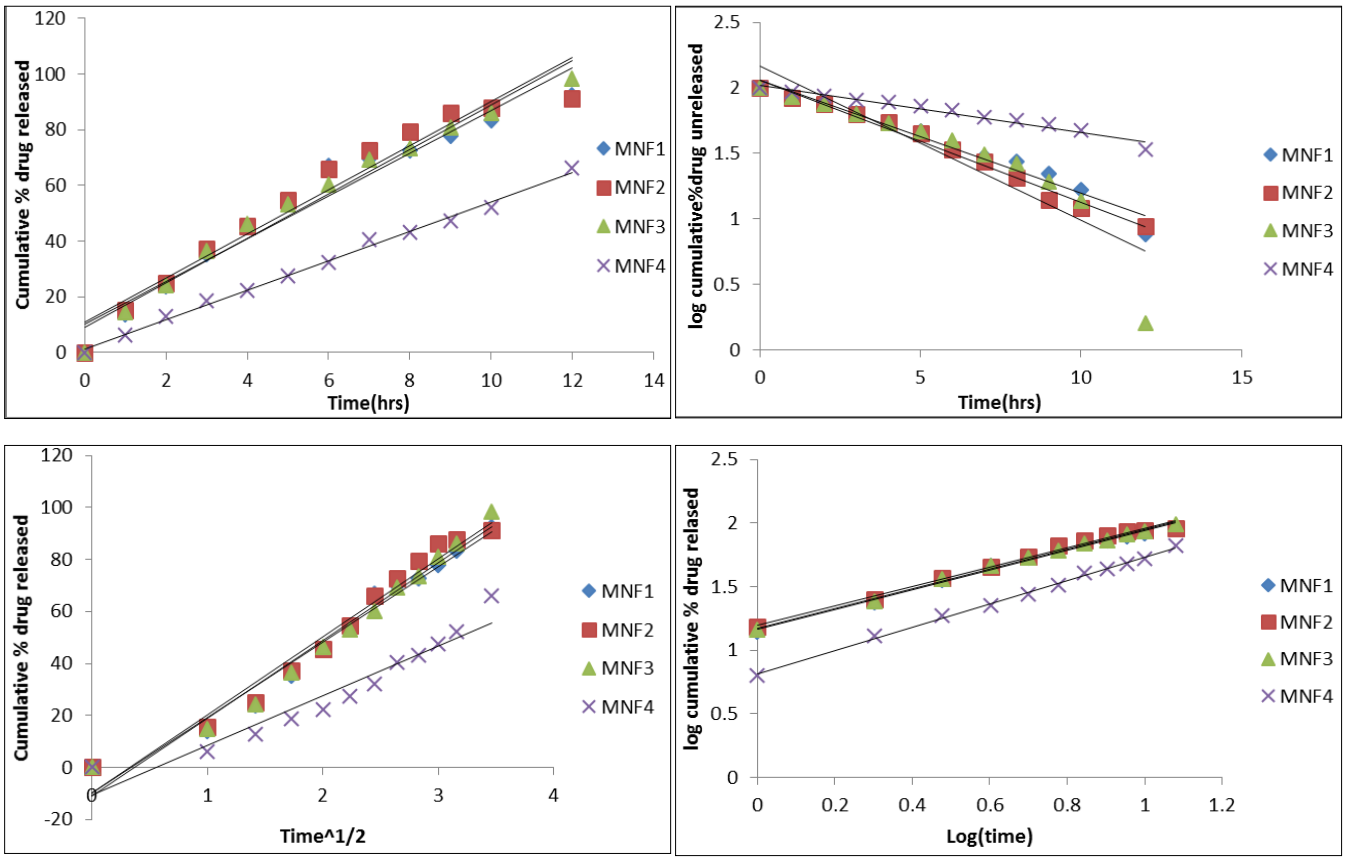

Fig 12: Kinetics plots for formulations MNF1-MNF4

Table 13: Correlation coefficients for MNF1-MNF4

Formulation	Correlation coefficient			
	Zero order	First order	Higuchi	Peppas
MNF1	0.9740	0.9612	0.9794	0.9328
MNF2	0.9873	0.9542	0.9766	0.9293
MNF3	0.9796	0.8344	0.9792	0.9389
MNF4	0.9969	0.9725	0.9377	0.9652

Table 14: Release Characteristics formulations MNF1-MNF4

Formulation	Drug(1):Polymer concentration	K1 (hr-1)	Ko (mg/hr)	'n' in Peppa's equation
MNF1	0.5	0.170	8.27	0.754
MNF2	1.0	0.190	7.97	0.761
MNF3	1.5	0.164	7.73	0.774
MNF4	2.0	0.07	7.6	0.879

10. Discussion

During the study we are using natural polymers hence before they are been used in the study, it is required to know how they are been extracted, percentage yield and followed by characterization of gums

Different extraction techniques were tried and out of which best method was selected and used during the study. The yield that was obtained for 4 gums were different. It was observed that NBA01, NBA02, NBA03 and NBA04 are 26%w/w, 35%w/w, 38%w/w, 42%w/w respectively.

Characterization of gums helps in knowing the phytochemical constituents and nature of the hydrocolloid. The gums that were selected NBA01, NBA02, NBA03, NBA04 were of polysaccharide in nature. They were confirmed by testing them by using stains where the gum was turned pink which confirms the presence of hydrocolloid, and the other test was hot water test, it was observed that gum swells when it was in contact.

In order to know the nature of the gums that were extracted, pH plays a major role. The extracted gums were taken and immersed in pH meter found that all were within the basic range or nearer to neutral.

The drug release from the buccaladhesive tablet depends on the swelling index of the gums; hence it was shown how the gums swell in contact with different buffers. Swelling nature was found high with both pH 6.8buffer and water.

For the gums to have good flow properties they should maintain particle size and shape, here particle distribution was studied and from this we can know the range of particles that were available.

Similarly in order to know the properties of powder gums, derived properties were studied. The values that were obtained and were within the range and shown.

Solubility studies were performed on these gums, by taking different solvents of varying polarities. Since the property of gum was drastically affected by microbes, hence the gums were studied for the presence of microbes, even during the study and after storage also.

FTIR and DSC studies were done in order to know the nature of functional groups present in these gums. Similarly the gums were studied for DSC in order to know the compatability of gums.

After the completion of preformulation studies, the natural buccal adhesive polymers were taken and made into formulations by varying ratios of drug and polymer. MNF1-MNF4 formulations using NBA01 as polymer, followed by MNF5-MNF8, MNF9-MNF12 and MNF13-MNF16, using NBA02, NBA03 and NBA04.

In order to access the flow properties of the formulated powders or granules, they were studied for precompression parameters. The results were noted in the tables the values that were obtained were within the range of limits.

After the formulations were prepared they were evaluated for post compression parameters, which include weight variation, Hardness, friability, drug content. The data was given in the table. The results obtained were within the limits.

Swelling index tests were performed on the prepared formulations, during the study it was observed that higher the concentration of the polymer higher was the swelling rate, different ratios of drug and polymer were prepared during the study, in all the cases the drug release was retarded by increasing the percentage of gum.SI were done for all the formulations and that were given in the tables.

Release Kinetics

These studies were performed in order to know whether the drug release was depended on concentration of the polymer or not, followed by the mathematical confirmation of the data obtained during the in vitro studies. It was clearly seen from the data that all the formulations followed Zero order drug release. This was confirmed by the regression coefficient values obtained.

Release kinetics were studied for all the formulations using Higuchi and Peppas, the n value that was obtained from the peppas reveals whether the drug release was following fick's law or not, whether the drug was diffusion controlled or eroded when it comes in contact with water.

Stability Studies

All the prepared formulations were tested for the stability studies, it was seen that the nature of the tablet prepared by NBA01 was not altered throughout the study.

11. Conclusion

The formulation of buccaladhesive tablets consists of active ingredient along with an buccal adhesive polymer which can allow the drug to stay in the buccal region for prolonged period of time. Since the formulation stays in the buccal region, it is mandatory to add an agent such as mannitol, which can mask the taste of the drug. In this present investigation Metprolol succinate was selected. In this study 4 natural polymers were selected and named as NBA01, NBA02, NBA03, NBA04 were selected. All these were used and MNF1-MNF16 for (METOPROLOL natural polymer) NBA01 was used for MNF1-MNF4, NBA02 used forMNF5-MNF8, NBA03 used for MNF9-MNF12, NBA04 for MNF13-MNF16. Formulations were prepared by varying concentration of drug and polymer starting from low concentration of polymer to high concentration of polymer.

Several formulations were prepared; it was clearly observed that the formulations prepared by using NBA01 was most suited for Metoprolol.

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