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Formulation and evaluation of ofloxacin mucoadhesive buccal tablets

K. Suryateja, c. Shalini*, ramya sri. S

Department of pharmaceutics, arya college of pharmacy, sangareddy, telangana, india.
Surapharma labs, dilsukhnagar, hyderabad, telangana-500060, india.

Address of correspondence: c. Shalini

ABSTRACT

In the present work, the mucoadhesive tablets of ofloxacin were prepared by using different concentrations of sodium alginate and pectin as a binder. The formulation was prepared by wet granulation method. The compatibility studies of drug and excipient were performed by ft- ir spectroscopy. After examining the flow properties of the powder blends the results were found to be within prescribed limits and indicated good flowing property, hence it was subjected to compression. The tablets were evaluated for post-compression parameters like weight variation, hardness, thickness, friability, drug content uniformity, surface ph, *in-vitro* studies like swelling, mucoadhesive strength and drug release. In dissolution studies f3 formulation was considered as optimised formulation. The *in vitro* drug release of all formulations exhibits complete release of ofloxacin with followed by higuchi mechanism.
All the evaluation parameters given the positive result and comply with the standards. The results indicated that the mucoadhesive buccal tablets of ofloxacin may be good choice to bypass the extensive hepatic first pass metabolism with an improvement in bioavailability of ofloxacin through buccal mucosa.

Keywords: ofloxacin, sodium alginate, pectin and buccal tablets.

INTRODUCTION

Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of dosing .problems such as first pass metabolism and drug degradation in the git environment can be circumvented by administering the drug via buccal route. Moreover, the oral cavity is easily accessible for self medication and be promptly terminated in case of toxicity by removing the dosage form from buccal cavity. It is also possible to administer drugs to patients who cannot be dosed orally via this route successful buccal drug delivery using buccal adhesive system requires at least three of the following (a) a bioadhesive to retain the system in the oral cavity and maximize the intimacy of contact with mucosa (b) a vehicle the release the drug at an appropriate rate under the conditions prevailing in the mouth and (c) strategies for overcoming the low permeability of the oral mucosa. Buccal adhesive drug delivery stem promote the residence time and act as controlled release dosage forms.

The use of many hydrophilic macromolecular drugs as potential therapeutic agents is their in adequate and erratic oral absorption. However, therapeutic potential of these compounds lies in our ability to design and

achieve effective and stable delivery systems. Based on our current understanding, it can be said that many drugs can not be delivered effectively through the conventional oral route.

The main reasons for the poor bio-availability of many drugs through conventional oral route are:

- ✓ Pre-systemic clearance of drugs.
- ✓ The sensitivity of drugs to the gastric acidic environment which leads to gastric irritation. Limitations associated with gastro intestinal tract like variable absorption characteristics.

Buccal mucosa composed of several layers of different cells. The epithelium is similar to stratified squamous epithelia found in rest of the at least one of which is biological nature are held together by means of interfacial forces.[1]

Buccal drug delivery is a type of bioadhesive drug delivery especially it is a mucoadhesive drug delivery system is adhered to buccal mucosa.

- ➢ The term bioadhesion is commonly defined as an adhesion between two materials where at least one of the materials is of biological origin. In the case of bioadhesive drug delivery systems, bioadhesion often refers to the adhesion between the excipients of the formulation (i.e. The inactive media) and the biological tissue.
- ➢ The term mucoadhesion can be considered to refer to a sub group of bioadhesion and, more specifically, to the case when the formulation interacts with the mucous layer that covers a mucosal tissue.

The mucosal layer lines a number of regions of the body including gastrointestinal tract, urogenital tract, airway, ear, nose and eye. Hence mucoadhesive drug delivery system includes the following:

1. Buccal delivery system
2. Oral delivery system
3. Ocular delivery system
4. Vaginal delivery system
5. Rectal delivery system
6. Nasal delivery system[2]

Overview of the oral mucosa structure the oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer18, 19 can be seen in figure 1. The epithelium of the buccal mucosa is about 40- 50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer. The epithelial cells increase in size and become flatter as they travel from the basal layers to the superficial layers. The turnover time for the buccal epithelium has been estimated at 5-6 days[3], and this is probably representative of the oral mucosa as a whole. The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 μm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingivae measure at about 100-200 μm. The composition of the epithelium also varies depending on the site in the oral cavity. The mucosae of areas subject to mechanical stress (the gingivae and hard palate) are keratinized similar to the epidermis. The mucosae of the soft palate, the sublingual, and the buccal regions, however, are not keratinized[4]. The keratinized epithelia contain neutral lipids like ceramides and acylceramides which have been associated with the barrier function. These epithelia are relatively impermeable to water. In contrast, nonkeratinized epithelia, such as the floor of the mouth and the buccal epithelia, do not contain acylceramides and only have small amounts of ceramide [5-7]. They also contain small amounts of neutral but polar lipids, mainly cholesterol sulfate and glucosyl ceramides. These epithelia have been found to be considerably more permeable to water than keratinized epithelia.

MATERIALS AND METHODS

Ofloxacin provided by sura labs, dilsukhnagar, hyderabad. Sodium alginate from panchi chemicals pvt ltd, mumbai. Pectin from alkem labs pvt, ltd, mumbai. Lactose from sd fine chem.ltd. Mumbai. Magnesium stearate from sd fine chemicals, mumbai. Talc from qualigens fine chemicals, mumbai.aspartame from sd fine chemicals, mumbai. Ethyl cellulose from alkem labs pvt, ltd, mumbai.

Methodology

Preformulation studies

Analytical method used in the determination of ofloxacin

Preparation of ph 6.8 phosphate buffer:

Preparation of 0.2 m sodium hydroxide solution: accurately weighed 8 g of sodium hydroxide pellets were dissolved in 1000 ml of distilled water and mixed.

Dissolved 6.805 g of potassium dihydrogen orthophosphate in to 800ml of purified water and mixed. Added 112ml of 0.2m naoh solution in to this solution, diluted to volume with purified water. Then adjusted the ph of this solution to 6.8 with 0.2m naoh solution.

Preparation of ph 7.4 phosphate buffer: accurately measured 250 ml of 0.2m potassium dihydrogen ortho phosphate and 195.5 ml of 0.2m naoh was taken into the 1000 ml volumetric flask. Volume was made up to 1000 ml with distilled water.

Preparation of standard graph in phosphate buffer ph 6.8

100 mg of pure drug was dissolved in small amount of methanol (5-10 ml), allowed to shake for few minutes and then the volume was made up to 100ml with phosphate buffer ph 6.8, from this primary stock (1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer ph 6.8. From this secondary stock 1, 2, 3, 4, 5 ml was taken separately and made up to 10 ml with phosphate buffer ph 6.8 to produce 10, 20, 30, 40, 50 µg/ml respectively. The absorbance was measured at 292 nm using a uv spectrophotometer. Standard calibration curve values were shown in table 7. The standard calibration curve of ofloxacin in phosphate buffer ph 6.8 was shown in fig 1.

Preparation of standard graph in phosphate buffer ph 7.4

100 mg of drug was dissolved in small amount of phosphate buffer and make the volume up to 100ml with phosphate buffer ph 7.4, from this primary stock(1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer ph 7.4. From this secondary stock 1, 2, 3, 4, 5 ml were taken separately and made up to 10 ml with phosphate buffer ph 7.4, to produce 10, 20, 30, 40, 50 µg/ml respectively. The absorbance was measured at 294 nm using a uv spectrophotometer. Standard calibration curve values were shown in table 8. The standard calibration curve of ofloxacin in phosphate buffer ph 7.4 was shown in fig 2.

Solubility studies

The solubility of ofloxacin in phosphate buffer solution ph 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (ph 6.8). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2µm whattman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 292 nm using a uv spectrophotometer.

The standard curves for ofloxacin were established in phosphate buffers (ph 6.8) and from the slope of the straight line the solubility of ofloxacin was calculated. The studies were repeated in triplicate (n = 3), and mean was calculated.

Evaluation of pre-compression blend:

The quality of tablet, once formulated, by rule is generally dictated by the quality of physicochemical properties of blends. There are many formulations and process variables involved in mixing and all these can affect the characterization of blends produced. Prior to compression, granules were evaluated for their characteristic parameter such as tapped density, bulk density, carr's index, angle of repose, hausner's ratio. Compressibility index was calculated from the bulk and tapped density using a digital tap density apparatus. The various characteristics of blends tested are as given below:

Angle of repose:

The angle of repose of granules was determined by the funnel method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the granules. The granules were allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\tan\theta = h/r$$

Where, θ = angle of repose
h = height of the cone
r = radius of the cone base

The relationship between the angle of repose and flowability is as follows:

Table 1: angle of repose values

s.no	angle of repose	flowability
1.	<25	excellent
2.	25-30	good
3.	30-40	passable
4.	>40	poor flow

Bulk density:

Density is defined as weight per unit volume. Bulk density ρb, is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles

to adhere together. Bulk density is very important in the size of containers needed for handling, shipping and storage of raw material and blend. It is also important in size blending equipment. 30 gm of powder blend introduced into a dry 100 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume v_0, was read. The bulk density was calculated using the formula:

$$\rho b = m/v_0$$

Where, ρb= apparent bulk density.
m=weight of the sample.
v=apparent volume of powder.

Tapped density:

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped using a suitable mechanical tapped density tester that provides a fixed drop of 14±2 mm at a nominal rate of 300 drops per minute. The cylinder was tapped 500 times initially followed by an additional tap of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, v_f was measured, to the nearest graduated unit. The tapped density was calculated, in gm per ml, using the formula:

$$\rho_{tap} = m/v_f$$

Where, ρ_{tap}= tapped density.
m = weight of the sample.
v_f = tapped volume of the powder.

Carr's index:

The compressibility index (carr's index) is a measure of the propensity of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is measure of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are generally less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions, and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the compressibility index which is calculated using the following formula:

$$\text{carr's index} = [(\rho_{tap}-\rho b)]/\rho_{tap}]\times 100$$

where, ρb= bulk density
ρ_{tab}= tapped density

Table 2: carr's index values

s.no	carr's index	flowability
1.	5-12	free flowing
2.	13-16	good
3.	18-21	fair to passable
4.	23-35	poor
5.	33-38	very poor
6.	>40	extremely poor

Hausner's ratio:

It is the ratio of tapped density to the bulk density. Hausner's found that this ratio was related to interparticle friction and, as such, could be used to predict powder flow properties. Generally a value less than 1.25 indicates good flow properties, which is equivalent to 20% of carr's index.

$$\text{Hausner's ratio} = \rho_{tap}/\rho b$$

Where, ρ_{tap} = tapped density.
ρb = bulk density.

Table 3: hausner's ratio values

s.no	Hausner's ratio	flowability
1.	0-1.2	free flowing
2.	1.2-1.6	cohesive powder

Preparation of tablets:

1. The ingredients were weighed.
2. All the ingredients except magnesium stearate, sodium alginate, pectin, pvp k90 and ipa were sieved and hand mixed together.
3. Then pvp k 90 was dissolved in sufficient quantity of ipa was added slowly in small quantities to the previous blend and it was hand mixed thoroughly.
4. The wet mass was air dried to remove the ipa.
5. The dried mass was then passed through sieve no. 30 to obtain granules.
6. The granular mixture was then compacted using a 10 station punching machine using 9mm punch tooling with an average weight of 500mg per tablet.

Table 4: formulation chart

Ingredients (mg)	Formulation codes							
	F1	F2	F3	F4	F5	F6	F7	F8
Ofloxacin	200	200	200	200	200	200	200	200
Sodium alginate	50	100	150	200	-	-	-	-
Pectin	-	-	-	-	50	100	150	200
Lactose	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s	Q.s
Magnesium stearate	8	8	8	8	8	8	8	8
Talc	9	9	9	9	9	9	9	9
Aspartame	10	10	10	10	10	10	10	10
Backing layer ethyl cellulose	50	50	50	50	50	50	50	50
Total weight	500	500	500	500	500	500	500	500

Evaluation of buccal tablets:

Physicochemical characterization of tablets:

The prepared ofloxacin buccal tablets were studied for their physicochemical properties like weight variation, hardness, thickness, friability and drug content.

Weight variation:

The weight variation test is done by taking 20 tablets randomly and weighed accurately. The composite weight divided by 20 provides an average weight of tablet. Not more than two of the individual weight deviates from the average weight by 10 % and none should deviate by more than twice that percentage. The weight variation test would be a satisfactory method of determining the drug content uniformity.
The percent deviation was calculated using the following formula:

% deviation = (individual weight – average weight / average weight) x 100

The average weight of tablets in each formulation was calculated and presented with standard deviation

.

Table 5: pharmacopoeial specifications for tablet weight variation

average weight of tablets (mg)	maximum % of difference allowed
80 or less	10
More than 80 but less than 250	7.5
250 or more	5

Tablet thickness:

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter were measured using vernier calipers.

Tablet hardness:

This test is used to check the hardness of a tablet, which may undergo chipping or breakage during storage, transportation and handling. In these five tablets will select at random and the hardness of each tablet will measure with monsanto hardness tester. The hardness is usually measured in terms of kg/cm^2.

Friability:

The friability test will carried out in roche friabilator. Ten tablets weighed (w initial) initially and put in a rotating apparatus drum. Then, they are subjected to fall from 6 inches in height. After completion of 100 rotations, the tablets again weighed (w final). The percent loss in weight or friability (f) calculated by the formula given below.

$$\text{friability (\%)} = \frac{\text{initial weight of 10 tablets} - \text{final weight of 10 tablets}}{\text{initial weight of 10 tablets}} \times 100$$

$$F\ (\%) = [wo\text{-}w/w_o]\ x100$$

Where, w_0 is the initial weight of the tablets before the test and
W is the final weight of the tablets after test.

Assay:

six tablets of each formulation were taken and amount of drug present in each tablet was determined. Powder equivalent to one tablet was taken and added in 100ml of ph 6.8 phosphate buffer followed by stirring for 10 minutes. The solution was filtered through a 0.45µm pvdf membrane filter, diluted suitably and the absorbance of resultant solution was measured by using uv-visible spectrophotometer at 292 nm using ph6.8 phosphate buffer.

In vitro release studies:

In vitro drug release was performed on buccal tablets using usp rotating paddle apparatus (lab india dissolution tester ds8000). The dissolution medium consisted of 500 ml of phosphate buffer ph 6.8. The experiment was performed at 37±0.5 °c, with a rotation speed of 50 rpm. Buccal tablet was attached to the glass slide with instant adhesive (cyanoacrylate adhesive). The slide was placed at the bottom of the dissolution vessel. Samples (5 ml) were withdrawn at predetermined time intervals and the equivalent amount was replaced with fresh medium. The samples were filtered through whatman filter (0.45 µm) paper and analyzed by uv spectrophotometer at 292 nm.

Swelling index

The, previously weighed (w1), tablets were placed individually in a petri-dish containing 10ml of distilled water. The weight of the tablet (w2) after 30min was noted down after wiping the excess water from the tablet using a filter paper. The swelling index was calculated using the formula

$$\text{swelling index} = \frac{w2 - w1 \quad x100}{w1}$$

Mucoadhesion strength:

The apparatus used for testing bioadhesion was assembled in the laboratory mucoadhesion strength of the tablet was measured on a modified physical balance employing the method described by gupta et al using sheep buccal mucosa as model mucosal membrane. A double beam physical balance was taken, the left pan was removed. To left arm of balance a thick thread of suitable length was hanged. To the bottom side of thread a glass vial of 30 ml capacity with uniform surface was tied. A clean 500 ml glass beaker was placed below hanging glass vial within which was placed another glass beaker of 100 ml capacity in inverted position. The temperature control system involves placing thermometer in 500 ml beaker and intermittently adding hot ph 6.8 in 500 ml beaker containing ph 6.8 the balance was so adjusted that right hand-side was exactly 5 g heavier than the left.

Surface ph:

the surface ph of the buccal tablet was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline ph may irritate the buccal mucosa, we sought to keep the surface ph as close to neutral as possible. Was used to determine the surface ph of the tablet. A combined glass electrode was used for this purpose. The tablet was allowed to swell by keeping it in contact with 1 ml of phosphate buffer (ph 6.8) for 2 h at room temperature. The ph was identified by bringing the

electrode into contact with the tablet surface and allowing the surface to equilibrate for 1 min.

Moisture absorption:

agar (5% m/v) was dissolved in hot water. It was transferred into petri dishes and allowed to solidify. Six buccal tablets from each formulation were placed in a vacuum oven overnight prior to the study to remove moisture, if any, and laminated on one side with a water impermeable backing membrane. They were then placed on the surface of the agar and incubated at 37°c for one hour. Then the tablets were removed and weighed and the percentage of moisture absorption was calculated by using following formula:

$$\% \text{ moisture absorption} = \frac{\text{final weight} - \text{initial weight}}{\text{initial weight}} \times 100$$

Drug-excipient compatibility studies

Fourier transform infrared spectroscopic studies

a fourier transform – infra red spectrophotometer was used to study the non-thermal analysis of drug-excipient (binary mixture of drug: excipient 1:1 ratio) compatibility. The spectrum of each sample was recorded over the 450-4000 cm^{-1}. Pure drug of ofloxacin with physical mixture (excipients) compatibility studies were performed.

RESULTS AND DISCUSSION

Solubility studies:

Table 6: solubility studies

S.no	Medium	Amount present (µg/ml)
1	Phosphate ph 6.8 buffer	95.14
2	Phosphate ph 7.4 buffer	92.03

Saturation solubility of ofloxacin in various buffers were studied and shown in the table 6. The results revealed that the solubility of the ofloxacin was increased from ph 6.8 to 7.4. The solubility of the ofloxacin in phosphate buffer ph 6.8 is 95.14µg/ml and it was selected as the suitable media for the release studies because the ph of the phosphate buffer ph 6.8 is nearer to that of buccal mucosa ph.

Standard graph in phosphate buffer ph 6.8 (λ max 292 nm)

Standard graph of ofloxacin was plotted as per the procedure in experimental method and its linearity is shown in table 7 and fig 1**.** The standard graph of ofloxacin showed good linearity with r^2 of 0.999, which indicates that it obeys "beer- lamberts" law.

Table 7: standard graph values of ofloxacin in ph 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
10	0.135
20	0.264
30	0.384
40	0.498
50	0.641

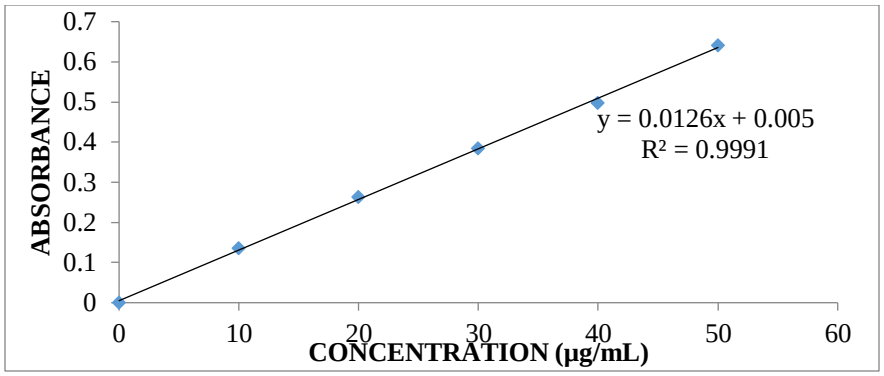

Fig 1: standard graph of ofloxacin in ph 6.8 phosphate buffer

Standard graph in phosphate buffer ph 7.4 (λ max 294 nm)

Standard graph of ofloxacin was plotted as per the procedure in experimental method and its linearity is shown in table 8 and fig 2. The standard graph of ofloxacin showed good linearity with r^2 of 0.997, which indicates that it obeys "beer- lamberts" law.

Table 8: standard graph values of ofloxacin in ph 7.4 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
10	0.121
20	0.229
30	0.344
40	0.471
50	0.551

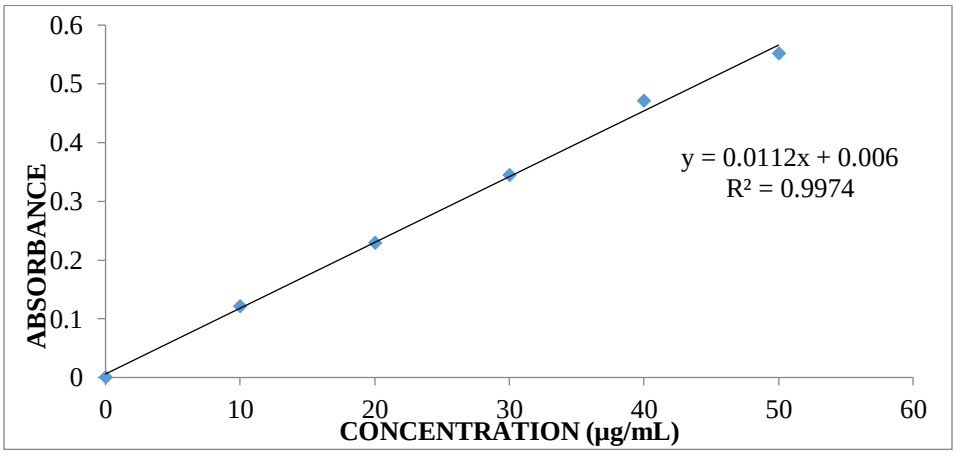

Fig 2: standard graph of ofloxacin in ph 7.4 phosphate buffer

Evaluation:

Characterization of pre-compression blend:

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.355±0.05 to 0.625 ±0.1 (gm/cm^3) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.409±0.07 to 0.833 ±0.1 showing the powder has good flow properties. The compressibility index of all the formulations was found to be below 25.00 which show that the powder has good flow properties. All the formulations has shown the hausner's ratio below 1.33 indicating the powder has good flow properties.

Table 9: physical properties of pre-compression blend

Formulation code	Angle of repose (ɵ)	Bulk density (gm/cm^3)	Tapped Density (gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	26.90±1.2	0.410±0.01	0.480±0.02	14.58	1.17
F2	29.89±1.4	0.390±0.04	0.462±0.01	15.58	1.18
F3	28.97±1.5	0.355±0.05	0.409±0.07	13.20	1.15
F4	23.2 ±0.2	0.555 ±0.1	0.714 ±0.1	22.22	1.285
F5	25.2 ±0.1	0.384 ±0.4	0.434 ±0.3	11.53	1.130
F6	27.1 ±0.1	0.416 ±0.2	0.476 ±0.3	12.50	1.142
F7	24.4 ±0.4	0.476 ±0.3	0.526 ±0.2	9.52	1.105
F8	28.3 ±0.4	0.625 ±0.1	0.833 ±0.1	25.00	1.333

Evaluation of buccal tablets:

Physical evaluation of ofloxacin buccal tablets:

The results of the weight variation, hardness, thickness, friability and drug content of the tablets are given in table 10. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 4.0 to 4.9 kg/cm^2 and the friability values were less than 0.53 % indicating that the buccal tablets were compact and hard. The thickness of the tablets ranged from 5.01 – 5.97 mm. All the formulations satisfied the content of the drug as they contained 96.34-99.21 % of ofloxacin. Thus all the physical attributes of the prepared tablets were found to be practically within control limits.

Table 10: physical evaluation of ofloxacin buccal tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Content uniformity (%)
F1	500.14	5.36	4.3	0.53	96.34
F2	498.96	5.14	4.1	0.43	99.14
F3	499.39	5.01	4.0	0.34	97.34
F4	500.24	5.97	4.6	0.25	99.12
F5	497.35	5.34	4.8	0.41	98.41
F6	499.12	5.11	4.2	0.39	97.39
F7	500.24	5.92	4.9	0.32	99.21
F8	496.92	5.17	4.6	0.28	98.27

Swelling index

Table 11: swelling index and mucoadhesive strength (g)

S.no.	Formulations	Swelling Index (%)	Mucoadhesive Strength(g)
1	F1	1.65	15.36±2.30
2	F2	2.15	16.10±0.11

3	F3	3.99	24.16±1.80
4	F4	2.82	17.29±3.06
5	F5	1.34	18.30±1.96
6	F6	2.69	19.14±2.39
7	F7	3.10	20.29±0.55
8	F8	3.24	21.43±1.27

Swelling index is an important parameter in judging the mucoadhesion property, at least in the initial stages, since water uptake is important for the polymers to uncoil and interact with the mucin.

The swelling indices of the ofloxacin buccal tablets reveals that while the buccal tablet formulations are all made of different materials, the extent of swelling differs based on the individual tablet composition.

The swelling indices of the first two formulations are quite low because of the fact that they started to disintegrate and lose mass soon after placing them upon the petri-dish. The formulations containing higher levels of the polymers sodium alginate displayed the highest swelling index.

In vitro release studies:

In vitro drug release studies were conducted in phosphate buffer ph 6.8 and the studies revealed that the release of ofloxacin from different formulations varies with characteristics and composition of matrix forming polymers.

Table 12: *in vitro* dissolution data for formulations f1 – f9

Time (h)	Cumulative percente of drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
0.5	38.15	32.26	28.02	23.13	42.14	40.71	33.62	25.17
1	46.97	41.00	36.19	28.50	57.97	50.18	34.49	30.98
2	59.30	53.14	48.22	32.14	64.53	56.44	43.98	37.24
3	63.09	59.36	55.99	40.62	72.44	61.47	50.73	43.19
4	71.20	69.80	64.17	47.86	88.09	75.90	57.49	50.37
5	82.14	76.16	73.43	56.11	98.94	83.19	65.74	61.21
6	96.11	86.21	87.58	70.43		97.34	71.52	67.07
7		97.36	93.04	73.27			85.16	82.43
8			98.49	88.92			94.30	90.49

From the dissolution studies observed total eight formulation are prepared. The formulations prepared with sodium alginate in different concentrations. The formulation f3 was maximum drug released 98.49 % in 8 h. Concentration of polymer increased the drug release was decreased.

The formulation was prepared with pectin the drug release was observed, the formulation f7 was showed 94.30 % maximum drug release in 8 hours.

Among all formulations f3 was showed maximum drug release in 8 hrs. So formulation f3 was selected as optimised formulation.

Table 13: moisture absorption, surface ph of selected formulations

Formulation code	Moisture absorption	Surface ph
F3	98	5.7
F7	95	6.1

The moisture absorption studies give important information of the relative moisture absorption capacities of polymers and it also give information regarding whether the formulations maintain the integrity or not. Among the selected formulations f3 formulation shown good moisture absorption.

The surface ph of the buccal tablets was determined in order to investigate the possibility of any side

effects. As an acidic or alkaline ph may cause irritation to the buccal mucosa, it was determined to keep the surface ph as close to neutral as possible. The surface ph of the selected formulations was found to be 5.7 to 6.1 and the ph was near to the neutral. These results suggested that the polymeric blend identified was suitable for oral application and formulations were not irritant to the buccal mucosa.

Release kinetics:

data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of ofloxacin release from buccal tablets. The data was fitted into various kinetic models such as zero, first order kinetics; higuchi and korsmeyer peppas mechanisms and the results were shown in below table.

Table 14: release kinetics and correlation coefficients (r^2)

Cumulative (%) release q	Time (t)	root (t)	log(%) release	log (t)	log (%) remain	release rate (cumulative % release / t)	1/cum% release	Peppas log q/100	% drug remaining	Q01/3	Qt1/3
0	0	0			2.000				100	4.642	4.642
28.02	0.5	0.707	1.447	-0.301	1.857	56.040	0.0357	-0.553	71.98	4.642	4.160
36.19	1	1.000	1.559	0.000	1.805	36.190	0.0276	-0.441	63.81	4.642	3.996
48.22	2	1.414	1.683	0.301	1.714	24.110	0.0207	-0.317	51.78	4.642	3.727
55.99	3	1.732	1.748	0.477	1.644	18.663	0.0179	-0.252	44.01	4.642	3.531
64.17	4	2.000	1.807	0.602	1.554	16.043	0.0156	-0.193	35.83	4.642	3.297
73.43	5	2.236	1.866	0.699	1.424	14.686	0.0136	-0.134	26.57	4.642	2.984
87.58	6	2.449	1.942	0.778	1.094	14.597	0.0114	-0.058	12.42	4.642	2.316
93.04	7	2.646	1.969	0.845	0.843	13.291	0.0107	-0.031	6.96	4.642	1.909
98.49	8	2.828	1.993	0.903	0.179	12.311	0.0102	-0.007	1.51	4.642	1.147

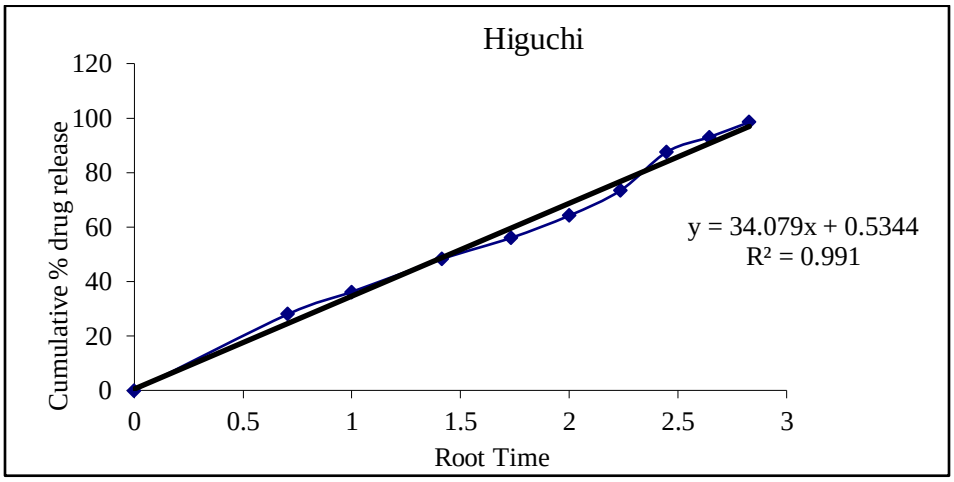

Fig 3: higuchi plot of optimized formulation

this formulation was following higuchi release mechanism with regression value of 0.991.

Drug – excipient compatibility studies by physical observation:

Ofloxacin was mixed with various proportions of excipients showed no color change at the end of two months, proving no drug-excipient interactions.

Ftir

Ftir spectra of the drug and the optimized formulation were recorded. The ftir spectra of pure ofloxacin drug, drug with polymers (1:1) shown in the below figures respectively. The major peaks which are present in pure drug ofloxacin are also present in the physical mixture, which indicates that there is no interaction

between drug and the polymers, which confirms the stability of the drug.

There was no disappearance of any characteristics peak in the ftir spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

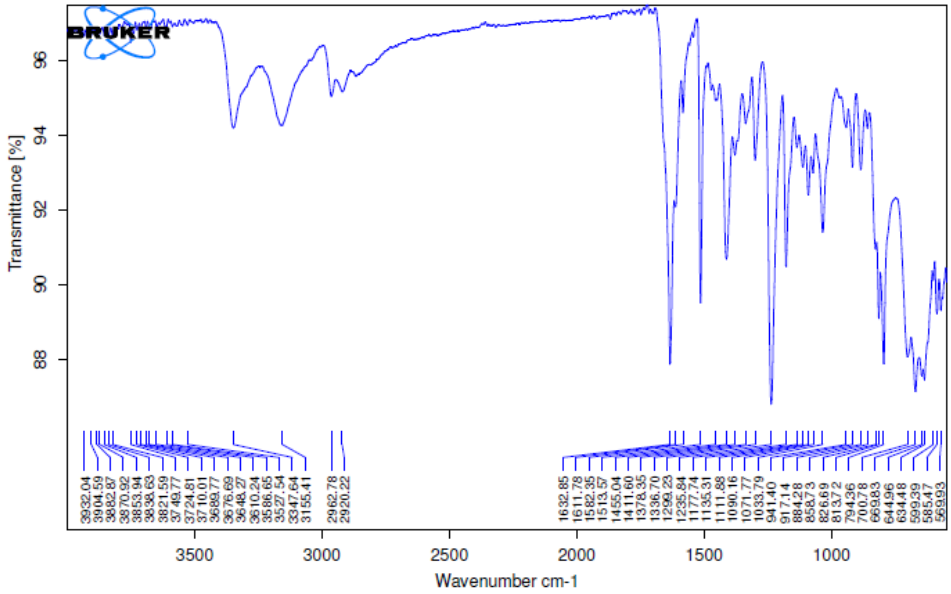

Fig 4: ftir peak of pure drug ofloxacin

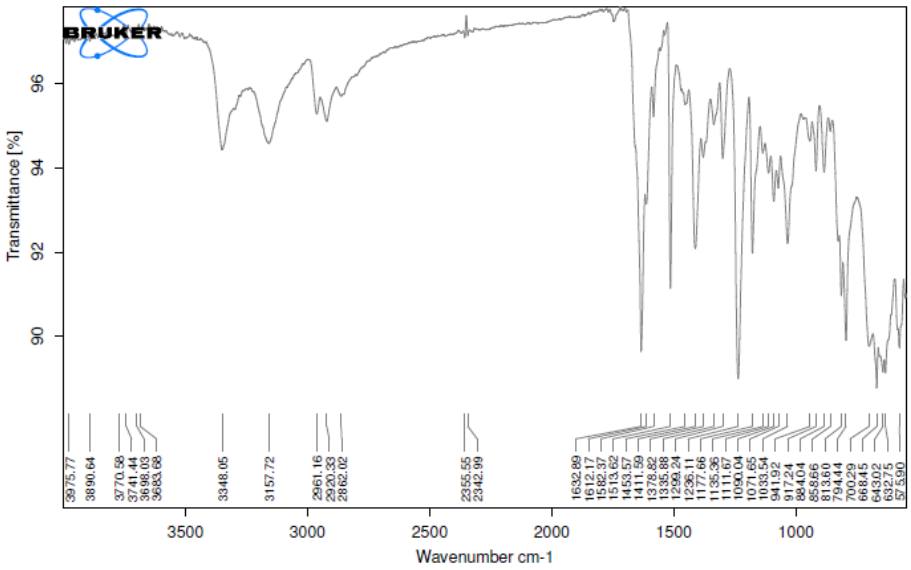

Fig 5: ftir peak of optimised formulation

CONCLUSION

The outcomes of this study indicate that mucoadhesive tablets of ofloxacin with controlled drug release can be successfully prepared by wet granulation method using sodium alginate and pectin as mucoadhesive polymers. The prepared mucoadhesive buccal tablets subjected to infrared spectrum study suggested that there was no drug -polymer interaction. All the prepared tablets were in acceptable range of weight variation, hardness, thickness, friability and drug content as per pharmacopoeial specification. The surface ph of prepared buccal tablets was in the range of salivary ph, suggested that prepared tablets could be used without risk of mucosal irritation. The buccal tablets showed good swelling property maintaining the

integrity of formulation which is required for bioadhesion. The *in-vitro* release of ofloxacin was extended for 8 h. Formulations f3 batch shows good *in- vitro* drug release 98.49%. All the tablets showed good mucoadhesive strength.

By consideration of all above parameters, it that sodium alginate appears to be suitable for use as a release retardant in the manufacture of buccal tablets because of its good swelling, good flow rate and suitability for mucoadhesion formulations. From the dissolution study, it was concluded that sodium alginate can be used as an excipient for preparing mucoadhesive buccal tablets.

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