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Evaluation of Ciprofloxacin Floating-Bioadhesive Tablet Formulated with Okra Gum as Multifunctional Polymer

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Abstract

Floating drug delivery systems and bioadhesive drug delivery systems are gastroretentive systems for increasing gastric residence time to obtain improved drug bioavailability. This study was to evaluate the floating and bioadhesive characteristics of Ciprofloxacin tablets formulated with *Abelmoschus esculentus* gum (okra gum).Okra gum was extracted and granules were prepared using the extracted Okra gum as well as sodium alginate and HPMC at concentrations of 2.5, 5 and 10 % w/w. Ciprofloxacin floating bioadhesive (CFB) tablets were evaluated for hardness, friability, *in vitro* buoyancy test, *ex vivo* bioadhesion test and drug release profiles. The floating lag time (FLT) and total floating time (TFT) for CFB tablets formulated with 10% w/w okra gum were 5.7 minutes and 8 hours respectively while the bioadhesive force was 1.324 N. Formulations of ciprofloxacin tablets containing admixtures of okra gum and sodium alginate or HPMC resulted in significant decrease ($p < 0.05$) in the floating lag times (≤ 3.1 minutes) and significant increase ($p < 0.05$) in total floating times (> 12 h). The bioadhesive force for CFB tablets containing admixtures of okra gum and sodium alginate or HPMC gave higher values in the range of 1.766 – 2.207 N. The *in vitro* release profiles for CFB tablets formulated with okra gum alone did not show sustained release below 10 % w/w. Batches FB10 and FB11 containing admixtures showed sustained release with maximum release of 86% at maximum time of 9 h. The dissolution profiles of tablets from batches F10 and F11 compared favourably with the profile for the commercial brand of floating ciprofloxacin tablet, MF. From the study Okra gum has shown to possess good floating and bioadhesive properties and may be utilized in the formulation gastro-retentive dosage form of ciprofloxacin which can possibly be harnessed as a targeted site-specific delivery system in the eradication of *Helicobacter pylori* in gastric ulcer disease as well as in the treatment of *Salmonella typhi* induced enteric fever.

1 Introduction

Floating drug delivery systems (FDDS) and bioadhesive drug delivery systems (BDDS) are gastroretentive systems for increasing gastric residence time to obtain improved drug bioavailability local or systemic effects[1].

Floating drug delivery systems achieves gastric retention by floating as a result of density of dosage form lesser than that of gastric fluid, resulting in increased bioavailability. Bioadhesive drug delivery utilizes mucoadhesive properties of some polymers for site specific targeting of drug for prolonged periods of time[2].

Floating dosage forms required sufficiently high levels of fluids in the stomach to stay afloat and work efficiently and are meant to remain floating on the gastric fluid when the stomach is full after a meal but buoyancy may decrease and tablet may be expelled through the pylorus into the small intestine. Thus the buoyancy of an FDDS in the stomach may be limited to only 3 – 4 hours. Also they are not suitable for drugs with solubility and

or stability challenges, drugs that may irritate the gastric mucosa and drugs that exhibit instability within the acid environment of the stomach.

In the case of bioadhesive drug delivery system, the tablet may be forced out of the stomach mucosa wall when stomach contents are mixing around due to peristalsis[3].

A current trend in gastroretentive drug delivery system is a combination of two approaches, so as to maximize the benefits inherent in each of them and minimize failures. Below are some possible combinations: Swellable and floating, Bioadhesive and swelling, Bioadhesive and high density, Floating and bioadhesive and Floating pulsatile systems[4].

The combined floating - bioadhesive dosage form (FBDF**)** avoids disadvantages of the single or individual gastroretentive drug delivery system, decreases the frequency of drug administration, increases the desired residence of drug at the site of action, mainly in the stomach, minimizes cost of treatment as well as side effects and improves patient adherence[5,6]. Therefore, a combined floating – bioadhesive system would surmount the disadvantages of floating and bioadhesive systems thereby improving bioavailability and ultimately improve therapeutic effect.

In recent times, researchers have harnessed this combined floating-bioadhesive system to improve drug delivery using natural gums such as cashew gum[7], tamarind gum[8], and guar gum[9]. Hence the aim of this study was to evaluate okra gum as a multifunctional polymer in floating-bioadhesive drug delivery.

The model drug ciprofloxacin was chosen because it is predominantly absorbed from stomach and the proximal part of the small intestine, has a short elimination half-life of 3 -4 hours, is rapidly absorbed orally, shows 60 to 70% oral bioavailability and it is administered twice or thrice daily due to its elimination half-life. This delivery system can be harnessed in the treatment of enteric fever caused by *Salmonella typhi*, eradication of *Helicobacter pylori* in peptic ulcer disease etc.

2 Materials and Methods

2.1 Extraction of Abelmoschus esculentus (Okra) gum

The fresh okra fruits (pods) were washed with water, chopped into smaller sizes, blended using a kitchen blender and soaked in water for 2 hour, boiled for 30 minutes and left to stand for 1 hour to allow for complete release of the mucilage into the water. The mucilage was then passed through a muslin cloth to remove the marc and then precipitated with acetone in a ratio of 1:1 (volume of acetone to volume of filtrate). The precipitated mucilage was then separated, dried in an oven at 45ºC, pulverised with mortar and pestle, passed through a 200 µm sieve and stored in an air-tight container.

*2.2 Preparation of Ciprofloxacin granule***s**

Ciprofloxacin granules were prepared using the wet granulation technique. Nine batches of granules were prepared using okra gum, sodium alginate and HPMC at concentrations of 2.5%, 5% and 10% ^{W}/w for each of the polymers used. Two extra batches of granules were prepared using admixtures of 5% ^{W}/w okra gum with 5% ^{W}/w sodium alginate and 5% ^{W}/w okra gum with 5% ^{W}/w HPMC giving a total of eleven (11) batches (Table 2.1).

2.3 Evaluation of prepared granules

The prepared granules were evaluated for micromeritic properties such as bulk and tapped densities[10], angle of repose[11], Carr's index and Hausner ratio using established procedures[12].

2.3.1 Bulk and tapped densities*:-*

A 20g quantity of granules from each batch was weighed and packed into a 50 ml graduated cylinder. The granules were carefully levelled without compacting and the unsettled apparent volume (V_0) was read and recorded as the bulk volume. Thereafter, the cylinder was tapped and the volume obtained after hundred taps (100 taps) was recorded as the final tapped volume (V_f). The process was done in triplicate and then the bulk density and tapped density in g/ml were calculated using Equations 1.1 and 1.2.

$$Bulk\ density = \frac{M}{V_0} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.1$$

Where, M = mass of the powder, V_0= bulk or unsettled apparent volume of the powder

$$Tapped\ density = \frac{M}{V_f} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.2$$

Where, M = mass of the powder, V_f= final tapped volume of the powder

2.3.2 Angle of repose

A sample of each set of granules (20 g) was allowed to fall freely from a funnel clamped to a retort stand at a height of 7.5 cm from a horizontal surface. The diameter and the height of the pile formed by the granules were measured using a meter rule. The angle of repose was calculated using Equation 1.3.

$$Angle\ of\ repose\ (\theta) = tan - 1 \left(\frac{h}{r}\right) \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.3$$

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

2.3.3 Carr's compressibility index and Hausner ratio*:-*

Calculated from bulk and tapped densities using Equations 1.4 and 1.5.

$$Carr's\ index\ (\%) = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} * 100\ Eqn\ 1.4a$$

$$Carr's\ index\ (\%) = \frac{V_{0-V_f}}{V_0} * 100 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.4b$$

$$Hausner\ ratio = \frac{Tapped\ density}{Bulk\ density} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.5a$$

$$Hausner\ ratio = {}^{V_0}\!/_{V_f} \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.5b$$

Where V_0 = unsettled apparent volume,

V_f = final tapped volume

2.4 Formulation of ciprofloxacin floating – bioadhesive tablets

Ciprofloxacin granules were compressed to tablets after addition of 1% ^{w}/w of talc and 1% ^{w}/w of magnesium stearate using a single punch tablet machine (Manesty Machine Ltd, B3B Liverpool, England) at 35 arbitrary units on the load scale.

The compressed tablets were collected, dedusted and stored in a labelled air tight container. The compositions of ciprofloxacin floating-bioadhesive tablets are shown in Table 1.

Table 1: Compositions of Ciprofloxacin floating bioadhesive tablets

Composition (mg)	**FB1**	**FB2**	**FB3**	**FB4**	**FB5**	**FB6**	**FB7**	**FB8**	**FB9**	**FB10**	**FB11**
Ciprofloxacin	250	250	250	250	250	250	250	250	250	250	250
Okra gum	15	30	60	-	-	-	-	-	-	30	30
Sodium alginate	-	-	-	15	30	60	-	-	-	30	-
HPMC	-	-	-	-	-	-	15	30	60	-	30
Sodium Bicarbonate	100	100	100	100	100	100	100	100	100	100	100
Citric acid	76	76	76	76	76	76	76	76	76	76	76
PVP K30	30	30	30	30	30	30	30	30	30	30	30
Magnesium stearate	6	6	6	6	6	6	6		6	6	6
Talc	6	6	6	6	6	6	6	6	6	6	6
Lactose	117	102	72	117	102	72	117	102	72	72	72
Total	600	600	600	600	600	600	600	600	600	600	600

FB1 - FB3 (Okra gum 2.5%, 5% and 10%), FB4 - FB6 (Sodium alginate 2.5%, 5% and 10%) FB7 - FB9 (HPMC 2.5%, 5% and 10%), FB10 (Okra gum 5% + Sodium alginate 5%) and FB11 (Okra gum 5% + HPMC 5%)

2.5 Evaluation of tablets

The compressed floating – bioadhesive tablets of ciprofloxacin were evaluated for weight uniformity, hardness and friability using standard methods for conventional tablets[13]. Tablets were also evaluated for *in vitro* dissolution test, *in vitro* buoyancy test and *ex vivo* bioadhesion test.

2.5.1 Weight uniformity

In order to carry out this test, twenty (20) tablets were randomly selected from each batch of tablets and weighed individually. The average weights as well as percentage deviations were computed. The tablets meet the USP test if not more than 2 tablets are outside the percentage limits and if no tablets differs by more than 2 times the percentage limit.

2.5.2 Tablets tensile strength (Ts) Determination

The thickness (***t***), diameter (***D***) and the crushing load of each of 10 tablets selected at random were determined using Veego Digital Tablet Hardness Test Apparatus (Veego Instruments Corporation Mumbai -400099 India. Model NO: VDIGITAB – 1. Sr. NO: 04-1112). Mean thickness value (***t***) and crushing load (***P***) were obtained and used to calculate the tensile strength (***Ts***).

2.5.3 Tablets friability test:-

Ten (10) tablets were selected at random and weighed. The tablets were placed in the drum of a friabulator (Erweka friabulator) and subjected to cascading and free falling stress for 4 min at 25 rpm. The tablets were removed from the friabulator, dedusted and reweighed. The difference between the initial weight and final weight expressed in percentage was taken as percentage weight loss (friability percentage).

2.5.4 Content uniformity test

Ten tablets were randomly selected from each batch, weighed and powdered. Powder equivalent to the average weight of the tablet was accurately weighed and transferred into a 100 ml volumetric flask to dissolve in a suitable quantity of 0.1 N HCl and made up to 100ml. The solution was filtered and 2 ml of filtrate was transferred to a 100 ml volumetric flask containing

0.1 N HCl; the volume was made up to volume. The absorbance of the resulting solution was measured by UV spectrophotometry at 276nm[14]

2.5.5 Ciprofloxacin analysis (Calibration curve)

A standard calibration curve of ciprofloxacin was prepared as follows: 1mg of ciprofloxacin was weighed and dissolved in 0.1N hydrochloric acid (HCL) and made up to 8ml volume, to give a stock concentration of 0.125 mg/ml. Serial dilutions were made from the stock concentration to give solution of 3.9, 7.8, 15.6, 31.2 and 62.5 µg/ml. The absorbances of these standard solutions were measured at a wavelength of 276 nm using ultraviolet – visible spectrophotometer (PG Instrument, USA). The tests were done in triplicate and mean values recorded. A plot of mean absorbance against concentrations was done to obtain the calibration curve. The same procedure was used to compute the amount of ciprofloxacin released into the dissolution medium at various time intervals.

2.5.6 In vitro dissolution studies

In vitro dissolution tests were performed in triplicate using dissolution tester (Erweka apparatus – type: DT, Nr: 56263, Heusenstamm, Germany), USP dissolution apparatus 1 rotating at 100 rpm in 900 ml of 0.1 N HCl at 37 ± 0.5ºC. Aliquot of dissolution medium equal to 5 ml was withdrawn at specified time intervals and same volume of fresh dissolution medium was replaced. The withdrawn media were properly diluted and the concentration of ciprofloxacin was determined using UV Spectrophotometer (PG Instrument, USA) at a wave length of 276 nm by using the regression equation from the standard calibration curve

2.5.7 In vitro buoyancy test

One tablet from each batch was placed in a beaker containing 900 ml of 0.1 N HCl and the time lag taken for tablet to rise to the surface and float was recorded as floating lag time (FLT), while the duration of floating on the surface without rupturing was recorded as total floating time, TFT[15, 16].

2.5.8 Ex vivo Bioadhesion test

A 50 ml burette was clamped on to a retort stand and a plastic stage clamped at an angle of 30º below the burette. A freshly excised rat ileum of about 4 cm was pinned onto the stage; one tablet was weighed and placed on the exposed mucus surface. Normal saline was allowed to flow from the burette at a rate of 10 ml/min. The weight of fluid that detached the tablet was recorded and used to compute the bioadhesive force using the equation below[17].

$$F = \frac{W}{10^5} * g \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots Eqn\ 1.6$$

Where F = bioadhesive force in Newton (N), W = mass applied (g) and g = acceleration due to gravity (981 cm / s^2)

3 Results and Discussions

3.1 Micromeritic properties of granules

The bulk and tapped densities for the different batches of ciprofloxacin granule were similar with only slight variations in the values. There were no significant differences in the densities of granules prepared with the test gum (okra gum), batches FB1- FB3 and those of sodium alginate (FB4- FB6), HPMC (FB7 – FB9) and the admixtures of okra gum/sodium alginate (FB10) and okra gum/HPMC (FB11). The slight variations observed were not statistically significant.

The relatively close bulk and tapped density values shows that the interparticulate interactions are less significant and granules are free flowing. This is reflected in the compressibility index and the Hausner ratio as revealed in Table 2 with Compressibility Index and the Hausner ratio values in the range of 10.16 – 13.79 and 1.11 – 1.16 respectively, which are also indicative of good flow properties[18]. These observations were further corroborated by the angle of repose values which were in the range of 31.24 – 34.52^0, indicative of good flow also. Angle of repose is not an intrinsic property of the powder but very much depends on the method used to form the cone (heap) of powder.

3.2 Results of ciprofloxacin tablet evaluation

3.2.1 Weight uniformity

All the batches complied with the weight uniformity test because for each batch, no individual tablet deviated from their respective mean values by more than ± 5%. This will help to ensure that uniformity of dosage form is achieved because the active ingredient, ciprofloxacin, forms a greater part of the tablet, unlike in cases of potent drugs administered in low doses where the excipients form the greater part of the tablet (Table 3)

3.2.2 Content uniformity

All the batches complied with the test because the individual contents fell within the official range of 85 – 115%. The values obtained were in the range of 95 – 105% (Table 3). According to the European Pharmacopoeia (Ph. Eur), a batch fails to comply if more than one individual content is outside the range of 85 – 115% or if one is outside the limit 75 – 125% of the average content[19].

3.2.3 Hardness

There is no official pharmacopoeial specification for tablet hardness, but a tablet should not be too hard or too soft, some literatures have suggested a range of 4 – 8 kg others 5 – 10 kg as an acceptable hardness limit for uncoated tablets. The hardness values obtained from this study showed that only batches FB6, FB8, FB9 and MF had values above 10 kg (Table 3). Batch MF which is a commercial brand already in the market has a mean hardness value of 24.5 kg; this could be due to the

size and shape of the tablet, being a caplet with average weight of 1.4560 g. This tablet is not meant to disintegrate since it is a sustained release floating dosage form and if the level of hardness does not affect other parameters especially the dissolution and release profile then it could well be accepted.

Table 2: Micromeritic properties of Ciprofloxacin granules

Formulation batches	Angle of repose (^{0}) ±SD	Flow rate g/s ±SD	Bulk density g/cm^3 ± SD	Tapped density g/cm^3 ± SD	Carr'sIndex % ± SD	Hausner Ratio ± SD
FB1	31.94 ± 1.14	1.59 ± 0.49	0.50 ± 0.02	0.56 ± 0.02	10.71	1.12
FB2	33.44 ± 1.28	1.92 ± 0.60	0.49 ± 0.03	0.55 ± 0.03	10.90	1.12
FB3	34.52 ± 1.08	2.22 ± 0.31	0.51 ± 0.02	0.58 ± 0.03	12.06	1.14
FB4	33.79 ± 1.91	1.77 ± 0.64	0.48 ± 0.03	0.54 ± 0.01	11.11	1.13
FB5	32.25 ± 0.72	2.04 ± 0.23	0.48 ± 0.01	0.54 ± 0.01	11.11	1.13
FB6	31.72 ± 0.43	2.24 ± 0.18	0.50 ± 0.00	0.58 ± 0.02	13.79	1.16
FB7	32.22 ± 0.35	2.04 ± 0.10	0.51 ± 0.01	0.57 ± 0.01	10.52	1.11
FB8	31.96 ± 0.17	2.31 ± 0.02	0.56 ± 0.02	0.65 ± 0.02	13.84	1.16
FB9	33.44 ± 0.43	2.16 ± 0.02	0.53 ± 0.01	0.59 ± 0.02	10.16	1.11
FB10	31.24 ± 0.20	2.00 ± 0.10	0.50 ± 0.01	0.56 ± 0.02	10.71	1.12
FB11	32.20 ± 1.10	1.98 ± 0.50	0.51 ± 0.00	0.57 ± 0.03	10.52	1.11

Table 3: Physicochemical properties of ciprofloxacin tablets

Formulation batches	Weight variation (g) ±SD	Drug content (%) ±SD	Hardness (KgF) ±SD	Tensile Strength (MN/m^2) ± SD	Friability (%) ± SD
FB1	0.5985 ± 0.01	98.42 ± 0.25	4.55 ± 0.48	0.067 ± 0.01	0.68 ± 0.02
FB2	0.5998 ± 0.01	99.78 ± 0.50	7.20 ± 0.51	0.104 ± 0.05	1.59 ± 0.01
FB3	0.6018 ± 0.01	99.90 ± 0.77	8.41 ± 0.39	0.076 ± 0.02	0.50 ± 0.01
FB4	0.5981 ± 0.01	100.05 ± 0.15	6.43 ± 0.40	0.093 ± 0.05	0.56 ± 0.02
FB5	0.6005 ± 0.01	95.50 ± 0.91	6.52 ± 0.35	0.089 ± 0.00	1.00 ± 0.01
FB6	0.6045 ± 0.02	99.25 ± 0.95	11.57 ± 0.93	0.162 ± 0.02	0.57 ± 0.02
FB7	0.6046 ± 0.01	99.95 ± 0.95	6.60 ± 0.42	0.091 ± 0.03	1.00 ± 0.04
FB8	0.5997 ± 0.01	105.50 ± 0.13	12.23 ± 0.64	0.173 ± 0.04	0.45 ± 0.01
FB9	0.60316 ±0.01	98.33 ± 0.85	12.85 ± 0.21	0.070 ± 0.01	0.48 ± 0.01
FB10	0.5990 ± 0.00	101.15 ± 0.15	8.14 ± 0.50	0.117 ± 0.05	0.59 ± 0.03
FB11	0.6010 ± 0.00	99.35 ± 0.66	8.500 ± 0.33	0.117 ± 0.10	0.60 ± 0.02
MF	1.4560 ± 0.02	100.42 ± 0.88	24.468 ± 0.63	0.100 ± 0.00	0.082±0.01

MF = Market formulation (Ciprofloxacin floating tablet 1g)

Measuring the hardness of a tablet is not a reliable indicator for tablet strength as some formulations when compressed into very hard tablets tend to 'cap' or lose their crown portions on attrition. Such tablets tend to powder, chip and fragment[20].

3.2.4 Friability

All the batches had good percentage friability values except FB2 with friability value of 1.59% (Table 3) which is above the pharmacopoeial limit of 1%. This could be as a result of internal factors like the moisture content of tablet granules and finished tablets in this batch.

3.2.5 Tensile strength

At the compression load of 35 arbitrary units on the load scale, the tensile strength values for tablets from batch FB6 (10 % sodium alginate polymer batch) and FB8 (5% HPMC) were higher than other batches. These values were higher than those of tablets from corresponding concentrations for batches produced using okra gum ($p < 0.05$), as shown in Table 3. The higher the tensile strength value, the higher the degree of plastic deformation which also leads to a greater area of contact for inter-particle bonding to form the tablets[21, 22].

The tensile strength values for batches FB9 (okra gum / sodium alginate) and FB10 (okra gum / HPMC) was greater than batches FB1- FB3 (okra gum alone). This means that the combination of polymers led to a higher degree of plastic deformation of the granules. All the batches of ciprofloxacin showed adequate mechanical strength from the results of hardness, friability and tensile strength tests.

3.2.6 Floating and Bioadhesive properties of ciprofloxacin tablets

Tablets prepared to use okra gum all floated within 15 minutes with average floating lag times of 11.3 min for batch FB1 (2.5% ^{w}/w), 9 min for FB2 (5% ^{w}/w) and 5.7 min for FB3 (10% ^{w}/w) but batch FB1 and FB2 lost their integrity and disintegrated within 6 hr, resulting in a total floating time of 4 and 5 hr respectively while FB3 was sustained with total floating time of 8 hr (Table 4). Ideally, floating systems should float a few minutes after contact with the gastric fluid to prevent the dosage forms transiting into the small intestine. Therefore, floating formulations can be optimized to obtain the shortest lag time, good matrix integrity and floating duration of more than 8 hours to prolong the gastro retention time[23].

Formulations FB10 and FB11 containing admixtures of okra gum / sodium alginate and okra gum / HPMC respectively resulted in significant decrease ($p < 0.05$) in the floating lag times (≤ 3.1 minutes) and significant increase ($p < 0.05$) in total floating times (> 12 h). The combination of okra gum with the other polymers significantly improved the buoyancy capability of the tablets. Batch FB6 (10% ^{w}/w sodium alginate) had the average fastest FLT of 1.1 min and an average TFT of above 12 hr while batch MF had the longest TFT of above 18 hr as well as the longest FLT of 13.6 min (Table 4), probably due to the high hardness value of 24.5 KgF (see Table 3). Compression force strongly affect the lag time of floating systems, tablets compressed at higher pressure were found to be less porous with high density preventing the tablets to float[24, 25].

The bioadhesive strengths of tablets produced with sodium alginate were greater than the corresponding concentrations of those produced with the test gum, okra gum ($p < 0.05$). Tablets produced with HPMC also showed slightly higher bioadhesive strengths than those of okra gum but these variations were not statistically significant ($p > 0.05$). Batches with the combination of okra gum and either sodium alginate or HPMC had significantly better bioadhesive strengths ($p < 0.05$) than those in which okra gum was used alone (Table 4). Batch MF had good floating property but poor bioadhesive property. From the result of the floating and bioadhesive tests, it could be observed that for tablets produced with okra gum, batch FB3 had sufficiently good floating as well as bioadhesive properties (Tables 4 and Fig 1a & 1b)

3.2.7 Dissolution profiles of tablets

The dissolution profiles of tablets formulated with okra gum as a release retardant revealed that okra gum was not able to sustain the release of ciprofloxacin at concentrations of 2.5% w/w (Batch FB1) and 5% w/w (Batch FB2), but at 10% w/w (Batch FB3), release was sustained for up to 8 hr (Fig 2). The dissolution profile of Batch FB2 (5% w/w okra gum) was significantly improved ($p < 0.05$) with sufficient retardation when combined with 5% w/w sodium alginate (Batch FB10) or 5% w/w HPMC (Batch FB11) as shown in Fig 3

The dissolution profiles of tablets from batches F10 (Okra gum 5% w/w + Sodium alginate 5% w/w) and F11 (Okra gum 5% w/w + HPMC 5% w/w) compared favourably with the profile for the commercial brand of floating ciprofloxacin tablet, MF as seen in Fig 4. The commercial brand of floating ciprofloxacin tablet, MF showed superior dissolution profile over FB2 (5 %w/w Okra gum) and FB3 (10 %w/w Okra gum) as revealed in Fig 5.

3.2.8 Drug release kinetics

The data obtained from *in vitro* release studies were fitted into various release models, namely; zero order, first order, Higuchi square root and Korsmeyer- Peppas model to predict or determine the kinetic and mechanism of release of ciprofloxacin. Table 5 gives the regression coefficients (R^2) for all the batches under the various release models as well as the diffusion or release exponent 'n' values estimated from the linear regression of the Korsmeyer- Peppas plot. The kinetic model that fits the release data is the one with highest R^2 values[26, 27].

Drug release from Ciprofloxacin floating- bioadhesive tablets for Batches FB1-FB11 followed first order release kinetics but Batch MF followed Higuchi model with R^2 value of 0.9950. First order kinetics can be used to describe the drug dissolved in pharmaceutical dosage forms such as those containing water soluble drugs in porous materials[28].

The diffusion or release exponent 'n' value is used to characterize different release mechanisms, when first 60% drug release data is fitted into Korsmeyer–Peppas model. Fickian diffusion occurs if n = 0.45, Anomalous (non-Fickian) diffusion

refers to a combination of both diffusion and erosion controlled rate release (0.45 < n < 0.89).

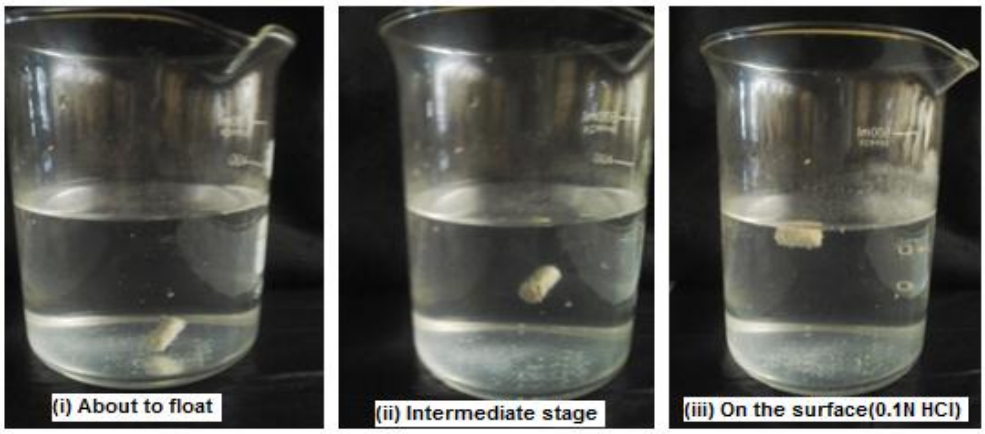

Fig. 1a: Photographs showing *in vitro* buoyancy characteristics of Ciprofloxacin floating bioadhesive tablet (CFBT) formulated with okra gum (Batch FB3, 10% w/w Okra gum)

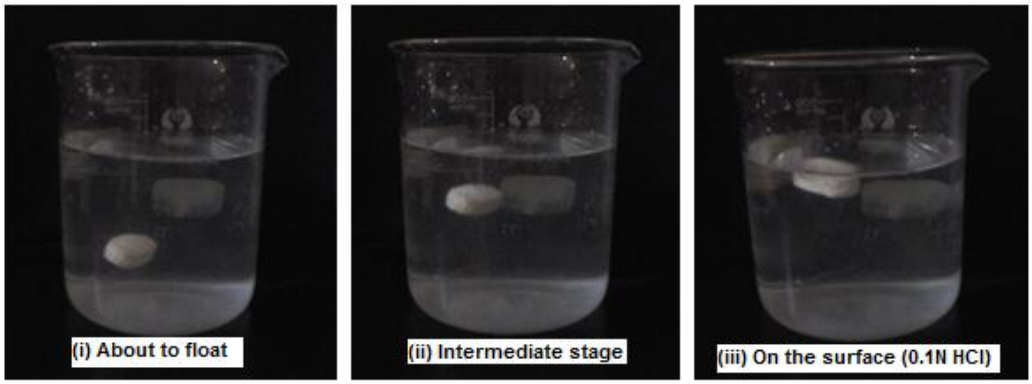

Fig. 1b: Photographs showing *in vitro* buoyancy characteristics of commercially available Ciprofloxacin floating tablet (Batch MF)

Table 4: Floating and Bioadhesive properties of Ciprofloxacin FBT

Formulation Batches	Floating Lag Time (FLT) (min) ±SD	TotalFloatingTime (TFT) (hr)	Bioadhesive strength (N)
FB1	11.3 ± 1.00	4	0.88 ± 0.02
FB2	9.0 ± 0.57	5	1.03 ± 0.01
FB3	5.7 ± 0.76	8	1.32 ± 0.02
FB4	7.5 ± 0.50	10	1.72 ± 0.04
FB5	1.2 ± 0.28	> 12	1.91 ± 0.01
FB6	1.1 ± 0.36	> 12	2.25 ± 0.03
FB7	9.3 ± 0.36	11	0.98 ± 0.03
FB8	10.3 ± 0.17	> 12	1.07 ± 0.03
FB9	7.0 ± 1.60	>12	1.47 ± 0.14
FB10	2.0 ± 0.57	>12	2.20 ± 0.12
FB11	3.1 ± 0.55	>12	1.77 ± 0.02
MF	13.6 ± 9.38	> 18	1.03 ± 0.15

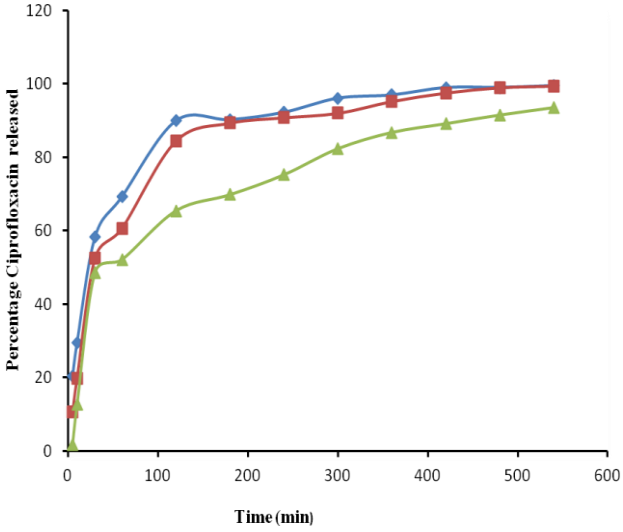

Fig 2:- Drug release profiles of Ciprofloxacin floating bioadhesive tablets prepared using Okra gum (FB1 – 2.5 %w/w —♦—, FB2 – 5 %w/w —■—, FB3 – 10 %w/w —▲—)

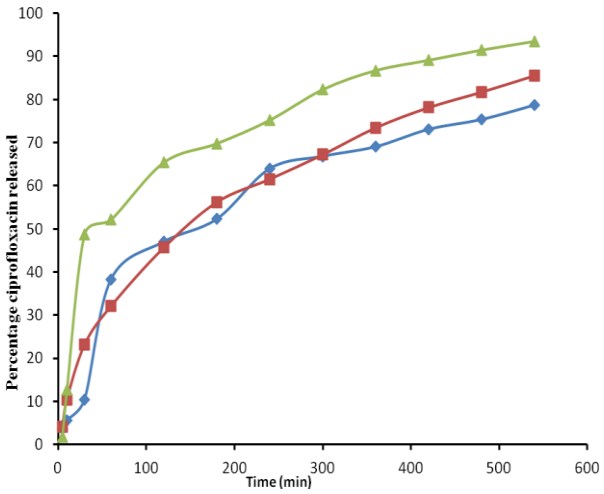

Fig 3: Drug release profiles of Ciprofloxacin floating bioadhesive tablets comparing Okra gum and its admixtures. (FB10 —♦— Okra gum 5% w/w + Sodium alginate 5% w/w and FB11 —■— Okra gum 5% w/w + HPMC 5% w/w and FB3 —▲— Okra gum 10% w/w)

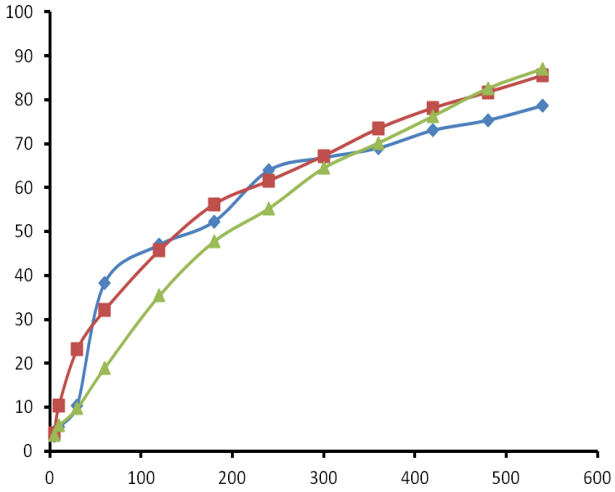

Fig 4: Drug release profiles of Ciprofloxacin floating bioadhesive tablets (FB10 —♦— Okra gum 5% w/w + Sodium alginate 5% w/w, FB11 —■— Okra gum 5% w/w + HPMC 5% w/w) and MF —▲—

Case-II transport is indicated by n =0.89, while n > 0.89 indicates Super case-II transport. Case II relaxation or super case II transport refers to the erosion of the polymeric chain[29]. The release mechanism for all the batches of ciprofloxacin tablets was by non-Fickian diffusion (0.45 < n < 0.89) as shown in Table 5.

3.2.9 Results of evaluation of drug- excipient interaction:-

The FTIR spectra of pure ciprofloxacin powder and admixture of ciprofloxacin and test gum (okra gum) are shown in Fig 6 and 7. The spectrum of pure ciprofloxacin showed major infra red (IR) bands in the functional group region around 2700 – 3500 cm^{-1} (which represents N–H stretch, O–H stretch and C–H stretch) and 1600 – 1800 cm^{-1} (which represents C=C, C=O and C=N stretches)[30].

The spectrum of physical admixture of ciprofloxacin and okra gum showed the major bands as seen in the spectrum of ciprofloxacin but with weak intensity. The spectrum of formulated tablet (Fig 8), showed that there were no interactions between ciprofloxacin and the excipients used in the formulation since there was no appearance of a new peak, and**/**or disappearance of original drug or excipient peak which would be indicative of drug - excipient interaction.respectively. While Fig 7 represents the FTIR spectrum of formulation FB3 containing 10% w/w of okra gum.

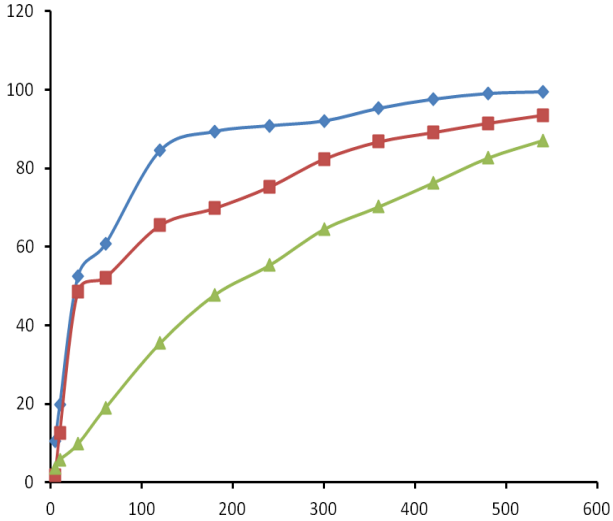

Fig 5: Drug release profiles of Ciprofloxacin floating bioadhesive tablets prepared using Okra gum (FB2 – 5 %w/w —♦—, FB3 – 10 %w/w —■—) and MF —▲—

4 Conclusions

From the study Okra gum has shown to be a well hydrated multifunctional polymer with good floating and bioadhesive properties and can possibly be used alone or in combination with sodium alginate and HPMC in the formulation of ciprofloxacin gastro-retentive dosage form.

Ciprofloxacin floating – bioadhesive drug delivery system can possibly be harnessed as a targeted site-specific (stomach-specific) delivery system in the eradication of *Helicobacter pylori* in gastric ulcer disease as well as in the treatment of *Salmonella typhi* induced enteric fever.

5 Conflict of interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

6 Author's contributions

ALALOR carried out literature review and experimental work of the present study. IWUAGWU was responsible for statistical

work and manuscript proofing. UHUMWANGHO carried out discussion of the present study. All authors read and approved the final manuscript.

Table 5: R^2 Values for Different Release Models

Formulation Batches	Zero Order	First Order	Higuchi model	Korsmeyer - Peppas	
			R^2		n
FB1	0.6368	0.9708	0.8174	0.9133	0.4504
FB2	0.6657	0.9692	0.8401	0.8952	0.4490
FB3	0.7484	0.9685	0.8902	0.7977	0.6626
FB4	0.8498	0.9797	0.9600	0.9571	0.4511
FB5	0.8501	0.9794	0.9614	0.9774	0.4518
FB6	0.8637	0.9727	0.9627	0.9641	0.5056
FB7	0.8296	0.9698	0.9419	0.9505	0.4523
FB8	0.8857	0.9874	0.9798	0.9795	0.4578
FB9	0.9031	0.9902	0.9866	0.9873	0.4669
FB10	0.8346	0.9450	0.9494	0.9521	0.6847
FB11	0.9043	0.9921	0.9895	0.9635	0.5943
MF	0.9626	0.9943	*0.9950	0.9936	0.7013

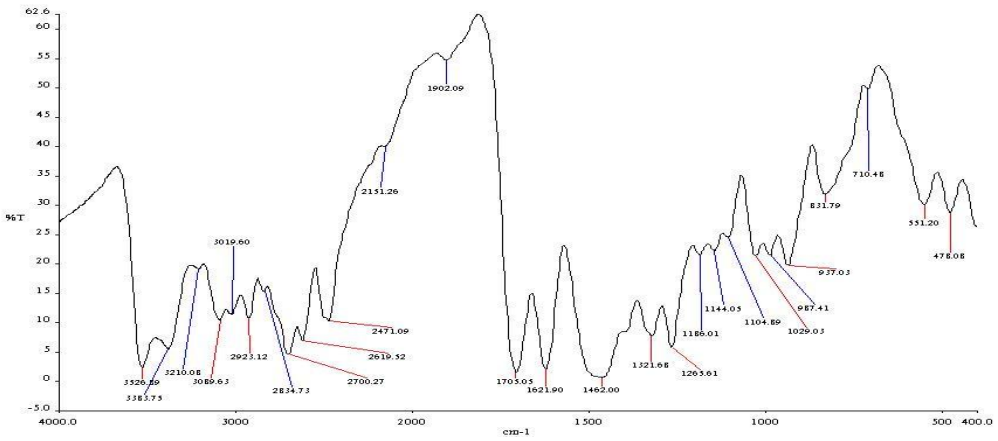

Fig 6: FTIR Spectrum of Pure Ciprofloxacin powder

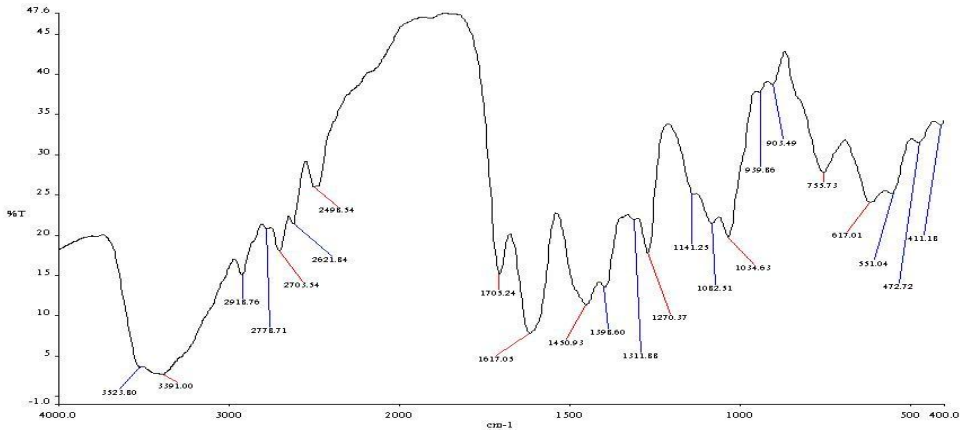

Fig 7: FTIR Spectrum of Admixture of Ciprofloxacin and Okra gum

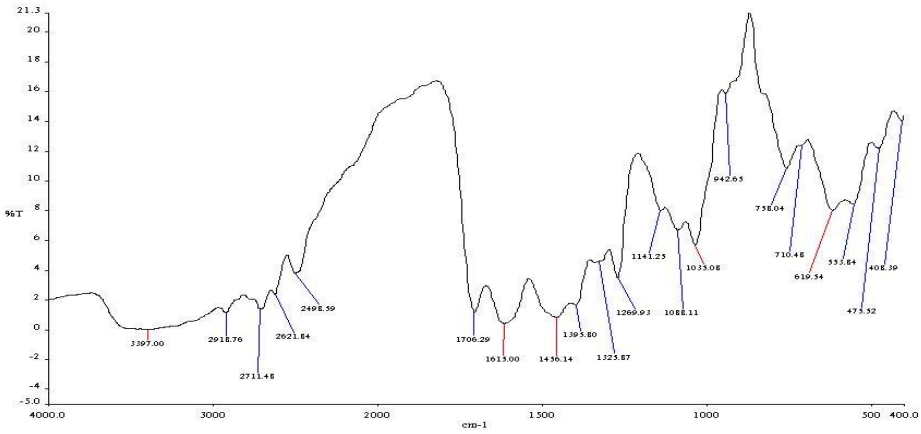

Fig 8: FTIR Spectrum of Formulation FB3 (10% w/w Okra gum)

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