IJPSR (2021), Volume 12, Issue 4 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 April 2020; received in revised form, 29 July 2020; accepted, 16 August 2020; published 01 April 2021

FORMULATION AND EVALUATION OF GASTRORETENTIVE METRONIDAZOLE TABLETS USING *BRACHYSTEGIA EURYCOMA* GUM

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Keywords:

Total buoyancy time, Gastroretentive tablets, Swelling index, Metronidazole, Floating lag time

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ABSTRACT: This study was conducted to evaluate gastroretentive metronidazole tablets formulated using *Brachystegia eurycoma* gum as a matrix. The gum was isolated from powdered dried *Brachystegia eurycoma* seeds. Gastroretentive metronidazole tablets were produced by direct compression technique using *Brachystegia eurycoma* gum, sodium carboxymethylcellulose, or their combination as the matrix. Sodium bicarbonate was used as a gas generating agent. The tablets were evaluated based on hardness, friability, weight uniformity, drug content, swelling studies, buoyancy lag time, and total buoyancy time. Hardness ranged from 4.57 ± 0.053 to 11.81 ± 0.90 Kgf. None of the tablets deviated from the mean tablet weight by more than ± 5%. The friability of the tablets was within 0.28 to 1.00% except for formulation MF1 that was 1.93%. Drug content was between 91.51% and 109.53%. The buoyancy lag time was between 2.35 and 20.15 min, and tablets from all the formulations maintained a total buoyancy time of above 12 h. Eighty percent (80%) of metronidazole was released from formulations MF1 to MF5 after 6, 9, 7, 5, and 12 h, respectively. The kinetics of release was by first order and Higuchi model, whereas the mechanism of release was by diffusion for formulations MF1 to MF3 and by non Fickian diffusion for formulations MF5 to MF6. Tablets from the optimized formulation, MF2 was stable after storage for one year at room temperature. Gastroretentive metronidazole tablets formulated using *Brachystegia eurycoma* gum as matrix showed good post compression properties on evaluation, especially buoyancy lag time, total buoyancy time, and *in-vitro* release.

INTRODUCTION: When drugs are administered, they disintegrate and release their contents into the gastrointestinal tract, from where they are absorbed into the systemic circulation to exert their pharmacological effects.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(4).2076-84

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(4).2076-84

Gastric emptying of dosage forms is a highly variable process, and this, coupled with a very fast gastrointestinal transit, may lead to incomplete drug release from the dosage form into the absorption window resulting in decreased efficacy of the administered dose [1-3].

Having the capacity to extend and control emptying time is an important feature of dosage forms that can reside in the stomach for a longer time than conventional dosage forms [1]. Gastroretentive systems can stay in the gastric region for a long period and thereby, extending the gastric

residence of the drugs markedly. Extension of gastric retention time results in an increase in bio-availability, a decrease in drug waste, and an increase in the solubility of drugs that are less soluble in a high pH environment [4, 5]. It is also useful in the local drug delivery to the stomach and proximal small intestine [6]. Controlled gastric retention of solid dosage forms can be accomplished using the mechanism of mucoadhesion, floatation, sedimentation, expansion, modified shape systems, or by giving of pharmacological agents that delay gastric emptying [4-8]. Floating dosage forms, also called hydrodynamic systems have a bulk density that is lower than that of gastric fluids, and therefore, they float or are buoyant in gastric fluid, but they do not affect the gastric emptying rate. They can be in the form of capsules or tablets [1, 9].

Floating dosage forms are usually composed of the drug dispersed in a gel forming polymer and carbon dioxide generating agents (calcium carbonate, sodium carbonate and citric acid). When the dosage form absorbs water in the stomach, the polymer gels and carbon dioxide is generated and trapped within the gel resulting in reduced bulk density. Polymer hydration and gelation are enhanced when the particles of the drug and excipients are relatively fine [9]. Helicobacter pylori infection is the main cause of gastritis, gastro-duodenal ulcers, gastric adeno-carcinoma, and mucosa-associated tissue lymphoma [10]. First-line seven-day triple therapy regimens involve the use of a twice-daily standard dose of a proton pump inhibitor (PPI), amoxicillin 1 g twice daily, and either clarithromycin 500 mg twice daily or metronidazole 400 mg twice daily. In penicillin allergy, PPI, metronidazole, and clarithromycin are used [11].

Metronidazole is a nitroimidazole anti-infective agent that is used in the treatment of amoebiasis, trichomoniasis, giardiasis, and many other parasitic diseases. It is a white, pale yellow to a brownish cream crystalline substance that has a melting point of 159-163 °C. At a temperature of 20 °C, its solubility in water is 1 g/100 ml; in ethyl alcohol, 0.5 g/100 ml and in chloroform, 0.4 g/100 ml. It is slightly soluble in ether and soluble in dilute acids [12, 13]. *Brachystegia eurycoma* is one of the plants in the family Caesalpiniaceae, phylum spermatophyte, and order Fabaceae.

Brachystegia eurycoma seed flour forms a gel with water and produces a gummy texture when used in soups, thereby making it desirable for the eating of garri and pounded yam [14]. In Nigeria, the Igbos calls it achi, while it is called akalado or eku by Yorubas, akpakpa, or apaupan by the Ijaw and okwen by the Edos [15]. *Brachystegia eurycoma* seed gum compares favorably with commercial gums used in the food industry [14]. It has been used as a binding agent in tablet formulation [16] and as a suspending agent in metronidazole suspensions [17]. *Brachystegia eurycoma* gum egg albumen mixture was applied in the formulation of modified release metronidazole tablets [18]. The objective of this study was to formulate gastro-retentive tablets of metronidazole to be used in the treatment of peptic ulcers caused by Helicobacter pylori using *Brachystegia eurycoma* gum (BEG) and Sodium carboxymethylcellulose (NaCMC) as swellable polymers for their floating and drug release retardant properties. The formulated tablets were to be evaluated for floating lag time, total buoyancy time, swelling behaviour, and *in-vitro* drug release.

MATERIALS AND METHODS:

Materials: Metronidazole (BDH Chemicals Poole, England), sodium bicarbonate (Loba Chemie, Mumbai, India), microcrystalline cellulose (Avicel-PH 101) (FMC Biopolymer, Philadelphia, USA), sodium carboxymethylcellulose (BDH Chemicals Ltd Poole England), acetone (Guangxing Guanghua Chemical, China) and magnesium stearate (Kem Light Chemicals Ltd, Mumbai, India). All reagents used were of analytical quality.

Method:

Isolation of *Brachystegia eurycoma* Gum: *Brachystegia eurycoma* seeds were bought from the Ogbete market in Enugu, Enugu State, Nigeria. The seeds were boiled, dehusked, dried, and milled. Two hundred grams of the *Brachystegia eurycoma* seeds powder was macerated in 1 liter of distilled water for 24 h. It was filtered using a muslin bag, and to the filtrate was added an equal volume of acetone to precipitate the gum. The gum was washed twice with 100 ml of acetone each and dried in an oven at 40 ^{o}C for 6 h. The gum was stored in a dry, tightly covered container until used.

Preparation of Metronidazole Excipients Mix: Metronidazole powder and other excipients for the

floating tablets formulation were mixed according to the formula in **Table 1.** Metronidazole was weighed, transferred, and triturated in a mortar. *Brachystegia eurycoma* gum (BEG) was added and they were triturated together. Sodium bicarbonate was added as the gas generating agent, while microcrystalline cellulose was added as a directly compressible filler. They were properly triturated and mixed.

TABLE 1: COMPOSITION OF THE METRONIDAZOLE FLOATING TABLETS

Ingredients	MF1	MF2	MF3	MF4	MF5
Metronidazole (mg)	400	400	400	400	400
Brachystegia eurycoma gum (mg)	130	195	97.5	-	-
NaCMC (mg)	-	-	97.5	130	195
Microcrystalline cellulose (mg)	73.5	8.5	8.5	73.5	8.5
Sodium bicarbonate (mg)	40	40	40	40	40
Magnesium stearate (mg)	6.5	6.5	6.5	6.5	6.5
Total (mg)	650	650	650	650	650

Evaluation of the Metronidazole Excipients Mix: The blend of metronidazole powder, BEG, and other excipients were subjected to micro-meristics analysis.

Bulk Density: Ten grams of the metronidazole-excipient mix was weighed and transferred into a 25 ml measuring cylinder. The volume was recorded as the bulk volume. The bulk density was calculated using equation 1.

Bulk density = (Weight of powder mix (g) / (Bulk volume of the powder mix (ml)) 1

Tapped Volume: The measuring cylinder containing the metronidazole powder-mix was tapped 100 times, and the new volume was recorded as the tapped volume. The Tapped density was calculated using equation 2.

Tapped Volume= (Weight of the powder-mix (g) / (Tapped volume of the powder-mix (ml)) 2

Carr's Index: This was calculated using equation 3.

Carr's Index= (Tapped density) / (Bulk density). . ……3

Hausner's Ratio: This was calculated using equation 4.

Hausner's ratio = (Tapped density - bulk density) / (Tapped density) × 100% 4

Preparation of the Floating Tablets: Magnesium stearate was added to the metronidazole-excipients mix and mixed lightly. The powder-mix was directly compressed into tablets using a CJD 316 sixteen station rotary tablet press (Clit Jemkay Engs. Pvt, Ltd. Ahmedabad, India) fitted with 13 mm punches.

Evaluation of Floating Tablets: Thickness, Diameter, and Hardness: Six tablets chosen at random from each of the formulations were inserted individually into the tablet chamber of a digital tablet hardness test apparatus (DIGITAB model, Veego instruments, Mumbai, India). The hardness, thickness, and diameter values were displayed and recorded.

Weight Variation: Twenty tablets were selected at random and weighed individually. The average weight of the tablets and the weight deviation of each tablet from the mean were calculated and recorded.

Friability: From each of the formulations, ten tablets were chosen at random and weighed together. They were placed in the drum of friabilator (Veego digital friabilator, Veego Instruments, Mumbai, India), and the drum was rotated at 25 rpm for 4 min. The tablets were removed from the drum, dusted, and re-weighed. The friability (%) for all the formulations were calculated respectively using equation 5.

% Friability = (Initial weight-final weight) / (initial weight) × 100 5

Drug Content: From each of the formulations, ten tablets were chosen at random and triturated. Powder equivalent to 100 mg of metronidazole was weighed and transferred to a 100 ml volumetric flask. A small quantity of 0.1N HCl was added and it was then shaken for 5 min. More quantity of 0.1N HCl was added to make the volume up to 100 ml. The flask was shaken for 15 min and the content filtered through Whatman filter paper.

The filtrate was diluted adequately, and the absorbance of the resultant solution was measured spectrophotometrically at 275 nm using UV/Visible spectrophotometer (Agilent Technologies, Malaysia) against 0.1N HCl blank to determine the drug content.

Swelling Studies: The swelling behavior was evaluated using a method earlier used by some researchers [19, 20]. The floating metronidazole tablets were weighed, and their weights were recorded as the initial weights (W_i). Petri dishes were weighed (W_1), and a tablet was put in each of them. Thirty milliliters of distilled water was measured and transferred into each of the Petri dishes containing the tablets. At intervals of 1, 3, and 9 h, respectively, the water in the Petri dish was mopped up using absorbent paper. Each Petri dish containing the already swollen tablet was weighed (W_2). The final weight of the tablets (W_f) was calculated from equation 6.

$$\text{Final weight of tablet } (W_f) = W_2 - W_1 \quad \ldots 6$$

The swelling index was calculated using equation 7.

$$\text{Swelling index} = (Wf\text{-}Wi)/Wi \times 100 \quad \ldots . 7$$

Where W_f = final weight of the tablet and W_i = initial weight of the tablet.

***In-vitro* Buoyancy Studies:** A 100 ml beaker was filled to the 100 ml mark with 0.1N HCl, and one tablet from one of the metronidazole tablet formulations was gently dropped into it. The time taken for the tablet to rise to the top was recorded as the floating lag time. The duration of time the tablet remained afloat was recorded as the total floating or buoyancy time. This was repeated in triplicate for all the metronidazole tablet formulations.

***In-vitro* Dissolution Studies:** The USP apparatus I was used to performing the in vitro dissolution test. The dissolution chamber of the apparatus was filled with 900 ml of 0.1N HCl maintained at 37 ± 0.5 ºC as the dissolution medium. One of the gastro-retentive metronidazole tablets was placed in the basket of the dissolution chamber and rotated at 100 rpm. Five milliliters samples were withdrawn and replaced with a freshly preheated medium at given time intervals (0.5, 1, 2, 3, 4, 5, 6, and 7 h). The samples were filtered and diluted. The samples were analyzed using the UV/visible spectrophotometer (Agilent Technologies, Malaysia) at a wavelength of 275 nm. The percentage of drug released was calculated using the equation obtained from the calibration curve.

Kinetic Modeling of Drug Release: The release kinetics of metronidazole from formulations MF1 to MF5 in 0.1 N HCl were determined by applying for zero order, first order, Higuchi, and Hixson - Crowell's cuberoot law 21-25 to the cumulative drug release using equations 8 to11.

The drug release mechanism was obtained by fitting the first 60% drug release data into the Korsmeyer - Peppas model 26, 27 as in equations 12 and 13.

Zero Order Model:

$$C = K_0 t \ldots \ldots \ldots \quad \ldots 8$$

C = % Release, K0 = Zero order rate constant expressed in units of concentration/time (t).

First Order Model:

$$\text{Log } Cr = \text{Log}C0 - K1\ t/2.303 \ldots \ldots \ldots \ldots . 9$$

Cr = % Remaining, C0 = Initial concentration of drug, K1 = First Order constant, t = Time

Higuchi's Square root Law Model:

$$Q = KHt\ ½ \ldots \ldots \ldots \ldots \ldots . 10$$

Q = % Released, KH = Constant reflecting design variables of the system, t = Time

Hixson - Crowell's Cuberoot Law Model:

$$[(100 - f)/100]1/3 = 1 - KHCt \ldots .. \ldots \ldots . 11$$

f = % Released, KHC = Rate constant, t = Time

Korsmeyer - Peppas Model:

$$Mt/M\infty = Ktn \ldots . . 12$$

$$\text{Log } Mt/M = \log K + n \log t \ldots \ldots \ldots . 13$$

Where Mt / M∞ are the fraction of drug released at time t, k is the rate constant and n is the release exponent. The n value is used to characterize different release mechanisms for cylindrical shaped matrices.

Drug Excipients Compatibility Studies: This was done using Fourier transform infrared spectroscopy (FTIR). FTIR spectra for the pure drug and optimized formulation (MF2) were recorded using the Shimadzu-IR Affinity 1 Spectrophotometer (Shimadzu, Japan).

The IR spectrum of the samples was prepared using potassium bromide (spectroscopic grade) discs by means of hydraulic pellet press at a pressure of seven to ten tons.

Stability Studies: The optimized formulation, MF2 was stored in an airtight container at room temperature (25 ± 3 ºC for one year. Samples were collected at 3 months interval for a year and analyzed for buoyancy and *in-vitro* dissolution.

RESULTS AND DISCUSSION:

Yield of Gum: The yield of *Brachystegia eurycoma* gum was 63.66 ± 1.05%. The yield of the gum was high, and this may result in the gum been cost-effective and affordable.

Evaluation of the Metronidazole Excipients mix: The results in **Table 2** showed the bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio values for the metronidazole-excipients mix used for the different formulations.

Angle of Repose: The result in Table 2 showed that Formulations MF1 and MF2 showed good flow while MF3 showed passable flow. Powder-mix for formulations MF1 and MF2 can flow easily from the hopper to the die of the tableting machine. This will ensure even fill with the die resulting in tablets with uniform weight. For MF3, the addition of a glidant such as Aerosil® or talc to the formulation may improve flow [28].

Formulations MF4 and MF5 had poor flow properties. The use of a vibrator or an auger may profit flow, resulting in tablets with uniform weights.

Carr's Index: This ranged from 27.45 ± 1.70 to 32.41 ± 1.60, which showed that the powder mix for all the formulations had poor flow properties.

Hausner's Ratio: Powders with values that are smaller than 1.25 show good flow, while those with values above 1.25 show poor flow. The values for all the formulations as shown in **Table 2** were greater than 1.25 but below 1.5.

This shows that the flow properties could be improved by the addition of a glidant. Alternatively, a vibrator or an auger could be used to assist flow from the hopper to the die of the tableting machine.

TABLE 2: MICROMERITICS OF METRONIDAZOLE EXCIPIENTS MIX

Formulation	Angle of Repose (^{o})	Carr's index (%)	Hausner's Ratio	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)
MF1	28.81 ± 00	32.41 ± 1.60	1.48 ± 0.03	0.56 ± 0.00	0.82 ± 0.02
MF2	28.81 ± 00	27.45 ± 1.70	1.38 ± 0.03	0.59 ± 0.00	0.81 ± 0.02
MF3	35.71 ± 3.47	31.43 ± 0.00	1.46 ± 0.00	0.57 ± 0.00	0.83 ± 0.00
MF4	40.69 ± 0.88	28.43 ± 1.13	1.40 ± 0.02	0.55 ± 0.01	0.77 ± 0.00
MF5	43.02 ± 3.78	32.06 ± 1.10	1.47 ± 0.02	0.57 ± 0.01	0.83 ± 0.00

Evaluation of Floating Tablets:

Thickness, Diameter and Hardness: As shown in **Table 3**, the tablets' thickness and diameter did not deviate from the accepted limits.

The hardness value for the formulations ranged from 4.57 ± 0.53 to 11.81 ± 0.90 and they were all within the acceptable limits.

Weight Variation: None of the evaluated tablets deviated from the average weight by up to 5%. As shown in Table 3, the weight of the tablets ranged from 646.92 to 654.25 g. British Pharmacopoeia specifies that not more than two of the individual weights should deviate from the average weight by more than ± 5 %, and none should deviate by more than ± 10 % [12].

Friability: As shown in Table 3, tablets from all the formulations except MF1 (1.93%) had friability values below 1%. This shows that the tablets (except those of MF1) will be capable of withstanding the shock of abrasion that might arise as a result of further processing or during transportation.

Drug Content: This ranged from 91.51% to 109.53%, as shown in **Table 3**. The values were within acceptable limits.

TABLE 3: POST COMPRESSION EVALUATION PARAMETERS OF METRONIDAZOLE FLOATING TABLETS

Formulation	Thickness (mm)	Diameter (mm)	Hardness (N)	Friability (%)	Weight (g)	Drug Content (%)
MF1	4.11 ± 0.04	13.06 ± 0.03	4.57 ± 0.53	1.93	648.74 ± 1.23	95.62
MF2	4.17 ± 0.06	13.07 ± 0.02	4.91 ± 0.71	1.00	646.92 ± 1.15	91.51
MF3	3.87 ± 0.04	13.02 ± 0.05	7.25 ± 1.29	0.38	651.37 ± 1.44	109.53
MF4	3.77 ± 0.05	13.02 ± 0.05	11.81 ± 0.90	0.28	654.21 ± 1.99	107.63
MF5	38.3 ± 0.04	13.00 ± 0.04	11.65 ± 0.14	0.28	654.25 ± 1.46	104.82

Buoyancy Lag time and Total Floating time: Fig. 1 showed the tablets before and during the floating period.

FIG. 1: BUOYANCY STUDIES; (A) TABLETS AT START OF STUDY (B) TABLETS AFTER 0.5 H (C) TABLETS AFTER 15 H

As shown in **Table 4**, the floating lag time for the different formulations ranged from 2.35 min to 20.15 min. It shows that the tablets will float early enough to avoid being evacuated during gastric emptying.

The tablets from all the formulations floated for more than 12 h, which shows that they will remain afloat long enough to allow the complete release of the drug into the gastrum.

TABLE 4: THE FLOATING BEHAVIOR OF THE FLOATING METRONIDAZOLE TABLETS

Formulation	Floating Lag time (min)	Total Floating or Buoyancy time (hour)
MF1	3.05	> 12
MF2	2.35	> 12
MF3	5.00	> 12
MF4	20.15	> 12
MF5	13.40	> 12

Swelling Behaviour of the Floating Tablets: From **Fig. 2**, it is shown that the tablets absorbed water and gelled. They gained more than 300% of their normal weight within the first hour. The extent of swelling by tablets from formulations MF1 and MF2 that contained BEG were less than those that contained NaCMC or their combination (MF3 to MF5). Tablets from all the formulations maintained their geometric integrity (shape) after ten hours of study.

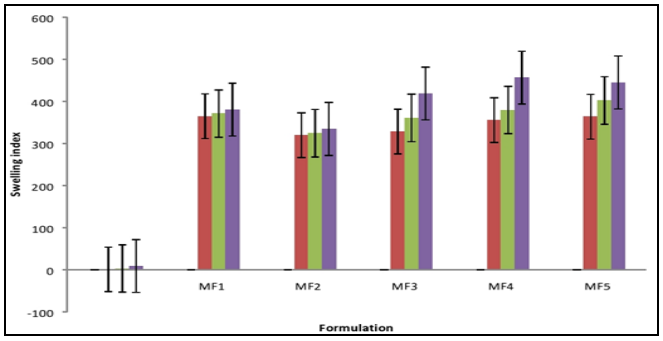

FIG. 2: SWELLING BEHAVIOR OF THE FLOATING TABLETS. Key: swelling index **AT - 1 H; - 3 H; - 9 H**

***In-vitro* Dissolution Studies:** The results in **Fig. 3** showed that 80% of metronidazole was released from formulations MF1 to MF5 at 6, 9, 7, 5 and 12 h, respectively. This showed that formulations MF2, MF3 and MF5 could be used successfully to sustain the release of metronidazole from the floating tablets.

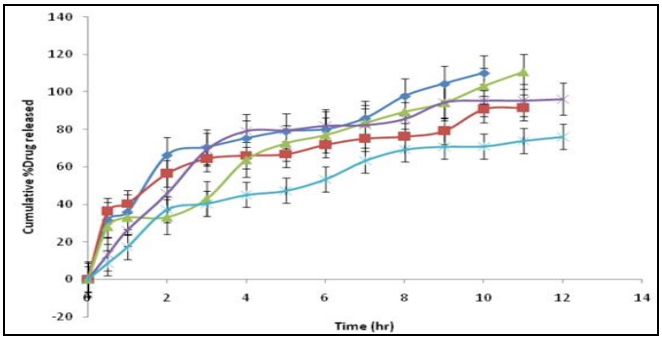

FIG. 3: *IN-VITRO* DRUG RELEASE PROFILE OF THE FLOATING TABLET FORMULATIONS. Key: - MF1 (20% BEG); - MF2 (30% BEG); - MF3 (15% BEG + 15% NACMC); - MF4 (20% NACMC);-MF5 (30% NACMC)

Kinetic Modeling of Drug Release: The results of the kinetics of the release of metronidazole from the different floating tablet formulations as shown in **Table 5** showed that they were dominantly released by a combination of first-order and Higuchi model, though other models may have contributed too.

The mechanism of release metronidazole from formulations MF4 and MF5 was by non-Fickian diffusion ($0.45 < n < 0.89$), *i.e.*, through diffusion and erosion of matrix, but the mechanism for formulations MF1 to MF3 was by diffusion since their n value was less than 0.45 [20, 29].

TABLE 5: KINETICS OF RELEASE OF THE FLOATING TABLETS

		MF1	MF2	MF3	MF4	MF5
Zero order	R^2	0.555	0.187	0.837	0.544	0.781
	K	12.97	10.18	11.30	10.48	7.738
First order	R^2	0.830	0.908	0.957	0.954	0.971
	K	0.345	0.180	0.283	0.274	0.113
Higuchi model	R^2	0.954	0.866	0.973	0.929	0.978
	K	35.38	29.43	31.64	31.28	22.73
Hixon-Crowell	R^2	0.799	0.733	0.776	0.891	0.918
Model	K	-0.113	-0.054	-0.095	-0.064	-0.036
Korsmeyer-Peppas	N	0.409	0.212	0.350	0.458	0.492
	R^2	0.954	0.544	0.513	0.634	0.626
	K	0.379	0.560	0.378	0.367	0.313

Drug Excipients Compatibility Studies: The FTIR spectrum of metronidazole as shown in **Fig. 4**, showed peaks at 1042.18 (C - OH stretching vibration), 1302.93 (C - C stretching), 1459.68 (NO stretching vibration), 1672.45 (C - O stretching, 2893.93 (C - H stretching), 3338.08 (N - H stretching vibration), 3633.98 (O - H stretching). There were no changes in the major peaks of metronidazole in the presence of *Brachystegia eurycoma* gum as shown in **Fig. 5,** and this signifies that they are compatible.

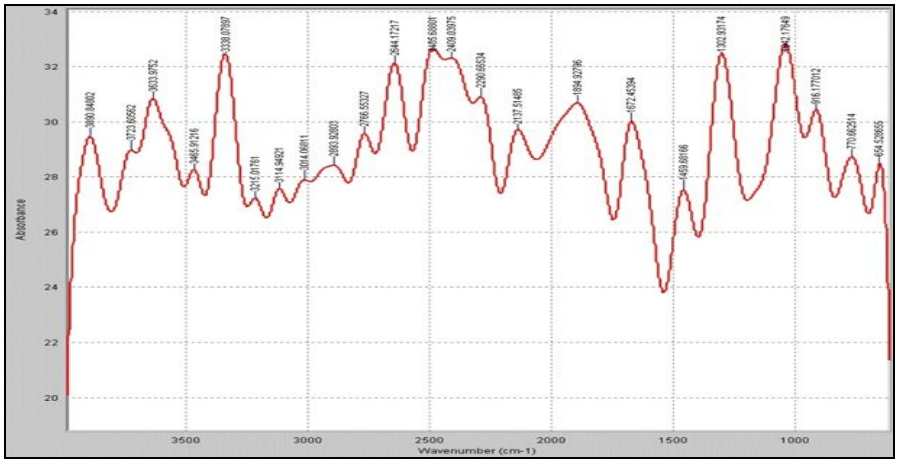

FIG. 4: FTIR SPECTRUM OF METRONIDAZOLE

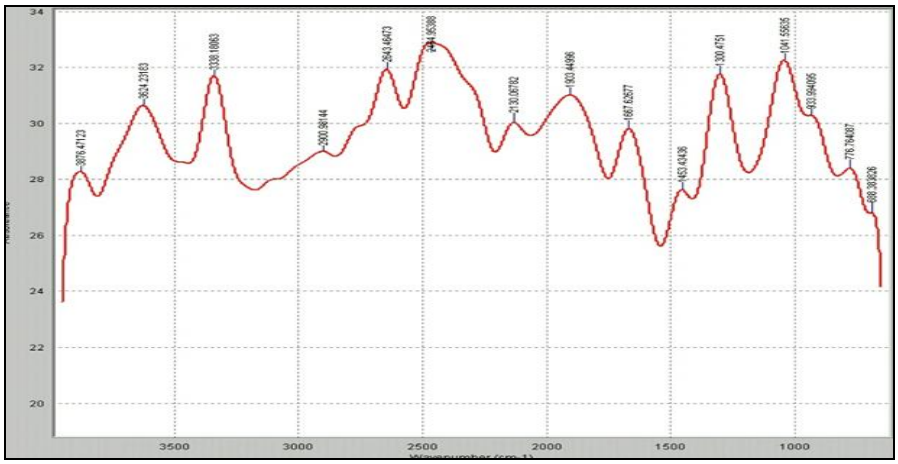

FIG. 5: FTIR OF METRONIDAZOLE + BEG

Stability Studies: The results of the *in-vitro* dissolution studies after 4, 8, and 12 months are shown in **Fig. 6** indicated that there were no major changes in the drug release pattern. There were no major changes in buoyancy lag time (2.35 - 5.00 min), and total buoyancy time was still above 12 h.

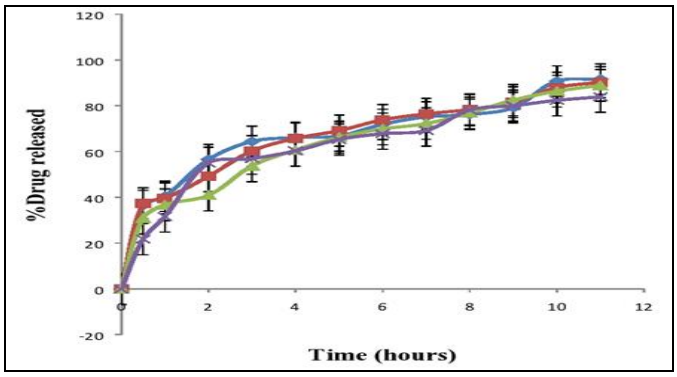

FIG. 6: % DRUG RELEASED FOR THE OPTIMIZED FORMULATION MF2 AT 0, 4, 8 AND 12 MONTHS. KEY: - 0 month; – 4 months, - 8 months; - 12 months

CONCLUSION: The study showed that *Brachystegia eurycoma* gum could be used alone or in combination with sodium carboxymethylcellulose to produce gastro-retentive metronidazole tablets that stayed afloat for over 12 h. Higher concentrations of the gum (30%w/w) were used to produce floating tablets that sustained the release of metronidazole from the matrix more than lower concentrations (20%w/w).

ACKNOWLEDGEMENT: The authors are grateful to the Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmacy, Delta State University, Abraka, Nigeria, for providing its laboratory for use during the research.

CONFLICTS OF INTEREST: No conflict of interest.

REFERENCES:

1. Akpabio EI, Effiong DE, Uwah TO and Sunday NI: Formulation and *in-vitro* evaluation of theophylline hydrochloride effervescent floating tablets: effect of polymer concentration on tablet buoyancy. International J Pharmacy and Pharmaceutical Scienc 2019; 12(1): 59-65.
2. Babu AK and Ramana MV: Development and in vivo evaluation of gastroretentive floating tablets of anti-

psychotic drug risperidone. International J of Pharm and Pharmaceutical Sciences 2016; 8(11): 43-52.
3. Thapa PP and Jeong SH: Effects of formulation and process variables on gastroretentive floating tablets with a high-dose soluble drug and experimental design approach. Pharmaceutics 2018; 10(161): 1-25.
4. Kumar VV, Gladiola BD, Chetty CM and Ugandar RE: Formulation and evaluation of gastroretentive drug delivery system of zanamivir using different polymers. J of Biomed and Pharmaceutical Research 2019; 8(4): 41-47.
5. Mishra SK and Gupta MK: Characterization and evaluation of nizatidine floating microspheres based drug delivery system for anti-ulcer activity. International J of Pharma Sciences and Research 2019; 10(10): 4557-67.
6. Kane SY and Momin M: Design and optimization of expandable gastroretentive patch of metronidazole for Helicobacter pylori infection management. International of Pharma Sciences and Research 2019; 10(11): 5216-23.
7. Patel MB, Shaikh F, Patel V and Surti NI: Controlled-release effervescent floating matrix tablets of metformin using combination of polymers. International Journal of Pharmacyand Pharma Sciences 2016; 8(11): 114-119.
8. Amrit K, Mina B, Sajan M, Suguna T and Sowmya C: Formulation and evaluation of sustained release floating tablets of valsartan. Worl J of Pha Res 2017; 6(2): 579-93.
9. Sonia N, John WI, Kumaran J, Aparna P and Jaghatha T: A review on floating drug delivery system. World Journal of Pharmaceutical and Medical Resear 2018; 4(5): 275-81.
10. Sheila E and Crowe MD: Helicobacter pylori infection. The New England J of Medicine 2019; 380: 1158-65.
11. MIMS Gastroenterology Clinic: Treatment Regimens for Eradication of H. pylori (PHE Guideline); updated on the 28 February 2019. https://www.mims.co.uk/treatment-regimens-eradication-h-pylori-phe-guidlines/gi-tract / article / 882106 (accessed August 18, 2019).
12. Alalor CA, Agbamu E and Okafo SE: Evaluation of mucoadhesive microspheres of metronidazole formulated using ionic gelation technique. Scholars Academic Journal of Pharmacy 2018; 7(12): 480-87.
13. British Pharmacopoeia. Stationary Office London, UK; 2014.
14. Irondi EA and Akindahunsi AA: Methanol extracts of *Brachystegia eurycoma* and *Detarium microcarpum* seeds flours inhibit some key enzymes linked to the pathology and complications of type 2 diabetes *in-vitro*. Food Science and Human Wellness 2015; 4(4): 162-68.
15. Igbe I and Okhuarobo A: Expanding the insights into the usefulness of *Brachystegia eurycoma* Harms: A review of its nutritional and medicinal values. Journal of Intercultural Ethnopharmacology 2018; 7(1): 1-13.
16. Olayemi O and Jacob O: Preliminary evaluation of *Brachystegia eurycoma* seed mucilage as tablet binder. Intern J of Pharma Rese and Innovation 2011; 3: 1-6.
17. Uhumwangho MU and Ileje IL: Preliminary evaluation of the suspending properties of *Brachystegia eurycoma* gum on metronidazole suspension. International Current Pharmaceutical Journal 2014; 3(11): 328-30.
18. Uzondu AL, Nwadike KN and Okoye EI: Application of Brachystegia eurycoma gumegg albumen mixture in the formulation of modified release metronidazole tablets. Interna J of Pharma Scie and Dru Res 2014; 6(2): 109-13.
19. Pandey S, Shah RR, Gupta A and Arul B: Design and evaluation of buccoadhesive controlled release formulations of prochlorperazine maleate. International J of Pharmacy and Pharma Sciences 2016; 8(1): 375-79.
20. Okafo SE and Chukwu A: Formulation and evaluation of diclofenac matrix tablets containing a hydrophilic polymer, Sida acuta gum. World Journal of Pharmaceutical Research 2017; 6(7): 36-47.
21. Paul B, Adimoolam S and Qureshi MJ: Formulation and in-vitro evaluation of mmetronidazole loaded HPMC K15M mucoadhesive microcapsules for H. pylori infection using 32 – full factorial designs. Inter J of Pharmaceutical Sciencesand Research 2019; 10(2): 555-67.
22. Selvaraj GJ, Balasubramanian A and Ramalingam K: Application of novel natural mucoadhesive polymer in the development of pentoxifylline mucoadhesive tablets. Inte J of Applied Pharmaceutics 2019; 11(6): 37-41.
23. Aboueisha YA, Gad S, Khalil WF, Ahmed EA and Ghorab MM: Effect of ethyl cellulose content on release profile and pharmacodynamics of fenoprofen microparticles. Indian J of Pharma Education and Research 2019; 53(3): 446-56.
24. Higuchi T: Mechanism of sustained action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. Journal of Pharmaceutical Sciences 1963; 52: 1145-49.
25. Hixson AW and Crowell JH: Dependence of reaction velocity upon surface and agitation. Industrial & Engineering Chemistry 1931; 23(8): 923-19.
26. Korsmeyer RW, Gurny R, Doelker E, Buri P and Peppas NA: Mechanisms of solute release from porous hydrophilic polymers. International Journal of Pharmaceutics 1983; 15: 25-35.
27. Siepmann J and Peppas NA: Modeling of drug release from delivery systems based on Hydroxy-propyl-methylcellulose (HPMC). Advanced Drug Delivery and Review 2001; 48: 139-57.
28. Wells JI and Aulton ME: Preformulation. In Aulton ME, editor. Pharmaceutics, The science of dosage form design. Edinburgh: Churchill Livingstone; 1999; 223-53.
29. Ariania L, Silvia S and Hayun: Formulation of diclofenac sodium sustained release tablet using coprocessed excipients of crosslinked amylase xanthan gum as matrix. International Journal of Pharmacy and Pharmaceutical Sciences 2016; 8(6): 151-55.

How to cite this article:
Okafo SE, Alalor CA and Ordu JI: Formulation and evaluation of gastroretentive metronidazole tablets using *Brachystegia eurycoma* gum. Int J Pharm Sci & Res 2021; 12(4): 2076-84. doi: 10.13040/IJPSR.0975-8232.12(4).2076-84.