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Preparation and *In Vitro* Evaluation of Ranitidine Floating Microspheres in The Treatment of Gastrointestinal Infections

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ABSTRACT

Introduction: Ranitidine hydrochloride, a member of the H2-receptor antagonist class, is widely employed in treating gastrointestinal conditions like ulcers, gastroesophageal reflux disease (GERD) and Zollinger-Ellison syndrome by reducing gastric acid production. Microspheres, designed for extended drug delivery and enhanced bioavailability, were formulated and evaluated in this study. **Aim:** To develop ranitidine hydrochloride microspheres capable of prolonging drug delivery and improving bioavailability. **Methods:** The inotropic gelation method was utilized to prepare alginate microspheres incorporating polymers such as ethyl cellulose, sodium carboxymethyl cellulose, HPMC, and carbopol®. The resulting drug-loaded microspheres exhibited spherical rigidity after cross-linking with a 10% w/v calcium chloride solution. Evaluation parameters including Fourier transform infra-red (FTIR) analysis, precompression characteristics, percentage yield, swelling index, and drug content were determined. **Results:** The FTIR results obtained, showed there was no incompatibility among the excipients and the active pharmaceutical ingredient. The Scanning electron microscopy (SEM) obtained, indicated the presence of spherical particles present in the formulation. The pre-compression evaluation showed that the angle of repose ranged from 4.85 ± 0.02 to 7.22 ± 0.06o for batched F4 and F1 respectively, while the Carr's index ranged from 73.5 ± 2.47 % to 87.00 ± 3.53 % for batches F-7 and F-1 respectively. The percentage yield ranged from 73.5 ± 2.47 % to 87.00 ± 3.53 % for batches F-7 and F-1 respectively. *In vitro* drug release studies revealed sustained drug release over 4 hours, with a maximum release of 69.50 ± 1.77 % observed for batch F-1. **Conclusion:** Overall, the optimised formulated ranitidine hydrochloride microsphere (F-1) demonstrated prolonged and controlled release characteristics, indicating its potential

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use in controlled drug delivery applications in the treatment of gastro-intestinal infections.

Keywords: Ranitidine Hydrochloride, Drug Delivery, Microspheres, Formulation, Ulcer.

INTRODUCTION

The process of gastric emptying for certain dosage forms can vary significantly, particularly those with prolonged stomach residence compared to conventional ones [1]. When designing controlled-release dosage forms, multiple factors need consideration to ensure optimal absorption and bioavailability. For instance, challenges arise in targeting specific areas within the gastrointestinal tract (GIT) effectively. The absorption of a drug is directly linked to its contact time with the small intestine mucosa [2]. Controlled-release formulations aim to release drugs at a predetermined rate, maintaining desired drug concentrations over specific time intervals while minimizing side effects [3]. Gastric retentive systems are tailored to prolong retention within the GIT, thereby extending drug exposure in the gastric region and enhancing absorption potential [4]. Various methods, such as floating drug delivery systems (FDDS), are utilized to prolong gastric retention [5].

Floating microspheres offer several advantages that render them appealing for drug delivery purposes [6]. Firstly, they facilitate sustained drug release, thereby enhancing therapeutic outcomes. Secondly, their versatility allows for easy formulation with various drugs to cater to specific requirements. Thirdly, they enable straightforward administration without necessitating high dosages. Lastly, they boast stability and prolonged storage capabilities [7].

Functionally, floating microspheres operate by encapsulating the drug within a polymer matrix, shielded by a membrane [7]. This matrix facilitates controlled drug release over time, while the membrane prevents rapid release. Designed to be buoyant, these microspheres float in gastric fluid, prolonging their residence time in the stomach. This prolonged contact enhances drug absorption and bioavailability by extending interaction with the stomach lining. Additionally, floating microspheres can shield the drug from stomach degradation [8,9].

The development and assessment of floating microspheres containing ranitidine hydrochloride are essential for pharmaceutical research [10]. Gastro retentive systems, particularly floating microspheres, offer a viable approach to prolong drug residence time in the stomach, thereby enhancing drug absorption and therapeutic effectiveness. Despite the proven success of floating microspheres with other drugs, their application to ranitidine hydrochloride remains largely unexplored, highlighting a gap in current pharmaceutical research [11].

MATERIALS AND METHODS

Ranitidine (RAN/4/2010/00680F), was purchased from Emzor Pharmaceuticals Ltd, Lagos. Sodium alginate, ethyl cellulose, sodium carboxyl methyl cellulose (Na-CMC), were purchased from (Sigma Aldrich, Kosher, USA). Methanol was obtained from (Astron Chemicals, Ahmedabad), Glycerin and sodium hydroxide were provided from (Mingtai Chemical Taiwan), Calcium chloride was obtained from (Evonik, Germany), Hydroxy propyl methyl cellulose (HPMC) were obtained from (DFE Pharma, UK), Sorbitol was obtained from (TCI, USA). Distilled water was obtained from (UNN Water Resources Management Laboratories Ltd; UNN, Enugu State, Nigeria).

Preformulation Studies

Some of the pre-formulation studies carried out in this research include: drug identification, compatibility of the drugs/excipients and formular development. Drug-excipient compatibility study (FTIR spectroscopy) Infra-red spectra of pure drug, and other excipients were obtained by (Shimadzu 8400S Japan) FTIR spectrometer. The samples were previously ground and mixed thoroughly with potassium bromide, an infra-red transparent matrix at 1:5 (sample: KRr) ratio respectively. The KBr discs were prepared by compressing the powders at a pressure of 5 tons for 5 minutes in a hydraulic press. The scans were obtained at a resolution of 4 cm-1 from 4000 to 400 cm-1.

Method of Preparation

Orifice inotropic gelation method was used for the preparation of ranitidine microspheres using polymers such as ethyl cellulose (EC), Na-CMC, hydroxypropyl methyl cellulose (HPMC) and sodium alginate. A homogenous polymser solution was prepared by dissolving Sodium alginate (1g) and the polymers (1g) in purified water (32 ml). Then ranitidine (1g), the active substance was added to the polymer solution and stirred thoroughly to form a viscous dispersion. A 10 % w/v calcium chloride solution was prepared which has been

used as a cross linking agent. The prepared dispersion was then manually added drop wise into calcium chloride (10% w/v) solution (40 ml) with the help of a syringe having a needle of size no.18. The calcium chloride solution having the droplets was then allowed to stay for 15 minutes for the curing reaction to take place and produce spherical rigid drug loaded spheres. The spheres obtained after the reaction were then collected and washed repeatedly with acetone. After washing, it is required to dry the spheres properly at 45°C for 6 hours.

Table 1. Composition of formulations

Ingredients (g)/Batches	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
Ranitidine	1	1	1	1	1	1	1	1	1
Sodium alginate	1	1	0.8	1	0.8	1	0.8	1	0.8
Ethyl cellulose	1	0.2	1	-	-	-	-	-	-
Na-CMC	-	-	-	1	0.2	1	-	-	-
HPMC	-	-	-	-	-	-	1	0.2	1
Acetone (ml)	30	30	30	30	30	30	30	30	30
$Cacl_2$	10	10	10	10	10	10	10	10	10

Yield Analysis of the Recovered Microspheres

The relative yield was calculated based on the amount of microspheres of each formulation obtained relative to the amount of solid materials used in the dispersed phase. The percentage yield was calculated according to the following equation [12]:

Yield (%) = actual weight of microspheres/total weight of drug and polymer x 100 (1)

Pre-compression Evaluation of Powder Blend

Angle of Repose

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. A plastic funnel in ring-supported by a retort stand. A sheet of paper was placed below the funnel assembly. A sheet of fibre board was placed below the funnel orifice making sure it fits tightly. A given quantity of the microsphere (30 g) was transferred into the funnel. The fibre sheet was drawn away and the timer simultaneously started. The timer was stopped when all of the powder had passed through the funnel. The height of the heap was measured using a graduated ruler. A pencil was used to outline the base of the contour. The angle of the conical heap so formed was determined from equation 2. The powder was returned to the funnel and the experiment was repeated thrice.

$\tan \theta$ = height of powderheap,(h)/radius of powder heap,(r) (2)

Bulk Density

This is the ratio between given mass of powder and its bulk volume. A weighed quantity of the microsphere (30.0 g) was placed in a 100-ml graduated cylinder. The cylinder was gently dropped onto a wooden surface three times from a height of one inch at 2 sec intervals. The volume assumed after the treatment was taken as the bulk volume. The experiment was repeated thrice.

Bulk density (g/ml) = mass/bulk volume (3)

Tapped Density

This is the ratio between given mass of powder and its bulk volume. A weighed quantity (30.0 g) of the powder was placed in a 100-ml graduated cylinder. The cylinder was tapped up to 500 times on the wooden surface or to a constant volume. The final volume attained represents the tapped volume. The experiment was repeated thrice.

Tapped density (g/ml) = mass/tapped volume (4)

Carr's Index

This is used to access the flowability of a powder. The Carr's compressibility index (CI %) was calculated from the poured (bulk density) and tapped densities. CI was calculated using the following equation.

Carr' s index = Tapped density -bulk density/Tapped density x 100 (5)

Hausner's Ratio

The Hausner's ratio (HR), defined as the ratio of tapped to bulk densities. It is a common technique widely used to describe the packing behavior of powders when they are subjected to tapping.

Hausner ratio= tapped density/bulk density (6)

Swelling Index

The weight of the microspheres was taken and then dispersed in phosphate buffer (pH 7.2) for 12 hours. The excess liquid was removed using blotting paper and the weight of the swollen microspheres taken. The swelling index was calculated thus:

Swelling index = Weight of swollen microsphers-weight of dried microsphers/weight of swollen microspheres (7)

Drug Content

A 1 gm quantity of sample was taken and dissolved in 100 ml distilled water in a beaker. After 6 hours, the sample was filtered and suitable dilution was done. Then the absorbance of the solution is measured at 313 nm and drug content was calculated.

Dissolution Study

The 500 ml of distilled water was placed in the dissolution apparatus (USP apparatus type-II paddle method) was assembled. The sample was then placed in the vessel and the apparatus was operated for 4 hrs at 50 rpm. The definite time interval, 5 ml was withdrawn from the vessel and another 5 ml of the blank was added to the vessel. The withdrawn fluid is then filtered and suitable dilution was done. Samples are then analyzed under UV Spectrophotometer at 313 nm.

Morphology of the Ranitidine Microspheres

The morphology of the obtained microspheres was examined by a light microscope (Zeiss, Me 63 C, West Germany) with varied magnification powers. One drop of the freshly prepared microsphere suspension was poured onto a slide and sealed with a cover glass. Photomicrographs were captured using Samsung digital camera [13]. The morphology, size uniformity and aggregation or coalescence of the microspheres were studied.

Data Analysis

All the measurements were repeated at least thrice and the data obtained analyzed by Student t-test and One-Way Analysis of Variance (ANOVA). Statistical analysis was performed using Statistical Product and Services Solution software (SPSS, version 22.0 Inc., Chicago IL, USA) and Excel Microsoft Office version 2012. The results were presented as mean ± SD, and statistical differences between means considered significant at ($p < 0.05$).

RESULTS AND DISCUSSION

Organoleptic Properties of the Drug (Drug Identification)

Table 2 showed the organoleptic properties of ranitidine. The drug had a choking smell. The colour of the drug was white, had a bitter taste and the texture was fine powder.

Table 2. Organoleptic properties of the drug Property

	Ranitidine
Odour	Choking
Colour	White
Taste	Bitter
Texture	Fine powder

FTIR Compatibility Studies

FTIR Spectroscopy (drug- excipient compatibility studies)

Figure 1: shows the characteristic peaks of ranitidine at 3819.7, 3211.5, 2590.9, 1880.6 and 1347.4 cm-1 corresponding to -OH, -NH single bond stretch, C-H single bong stretch, nitriles, C=O, C=C and C=N and C-O, C-N, C-C single bond stretch respectively.

Figure 2: shows the characteristics peaks of ethyl cellulose at 3925.2, 3245.2, 2582.1, 1997.8 and 1468.4 cm-1 corresponding to O-H, N-H single bond stretch, C-H single bond stretch, carbenes triple bond, C=O, C=C double bond and C-C, C-O single bond respectively. According to Mayavansh et al, the spectrum of EC showed characteristic peaks at 3390 and a band at 1636 cm-1 corresponding to the stretching and bending modes of the surface hydroxyls. The peak at 2905

cm-1 belongs to the asymmetrically stretching vibration of C-H in a pyramid ring and the broad absorption peak at 1059 cm-1 is attributed to the C-O of cellulose [14].

Figure 3: shows the characteristic peaks of sodium carboxymethyl cellulose at 3852.3, 3169.1, 2554.2, 1993.8 and 1495.6 cm-1 corresponding to O-H, N-H single bond stretch, C-H single bond stretch, nitriles and carbenes triple bond, C=O, C=C double bond and C-O, C-C single bond respectively. According to Oth et al (2020), the spectrum of Na-CMC showed characteristic peaks at 3700 cm-1 indicating the presence of –OH stretching bond. The strong bonds at 1093, 459 and 798 cm-1 were associated to the asymmetric and symmetric Si-O—Si stretching vibration bonding [15].

Figure 4: shows the characteristic peaks of HPMC at 3675.0, 3269.4, 2434.3, 1900.5 and 1428.8 corresponding to –O-H, single bond stretch, C-H single bond stretch, nitriles and carbenes triple bond, C=O C=C double bond, C-O, C-C single bond respectively. According to Chaudheri et al; the spectrum of starch showed characteristics peaks at 3448 for –OH stretching, 2930 for –CH stretching, 1646 for C-O bending associated with OH group, and 1381 cm-1 associated with –CH symmetric bending [16].

Figure 5: shows the characteristic peaks of calcium chloride at 3900.1, 3143.6, 2427.5, 1873.9 and 1454.0 corresponding to –OH, -NH single bond stretch, -CH single bond stretch, C=O, C=C and C -O, C-C single bond respectively. According to Alagusundaram et al, the twin peaks at 1577 and 1466 cm-1 were attributed to asymmetric carbohydrate (-COO) stretching vibration and symmetric carbohydrate vibration respectively, while peaks at 2917 and 2850 cm-1 were attributed to the –CH stretching vibration [17].

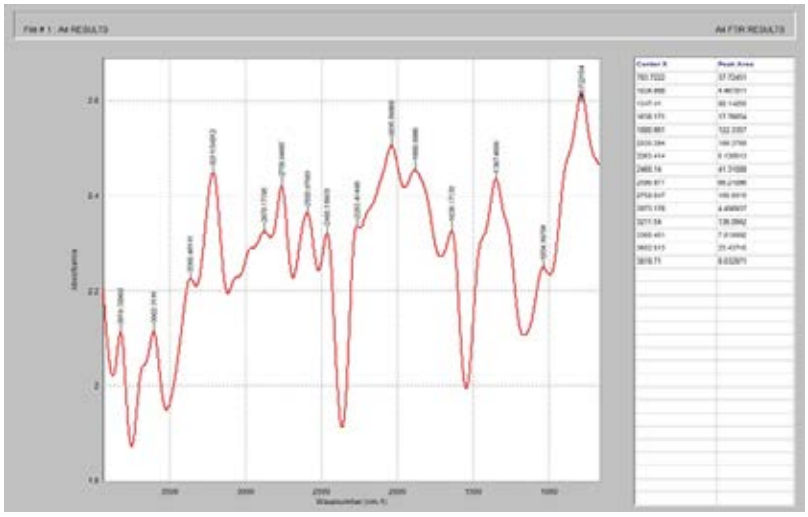

Figure 1. FTIR spectrum of Ranitidine.

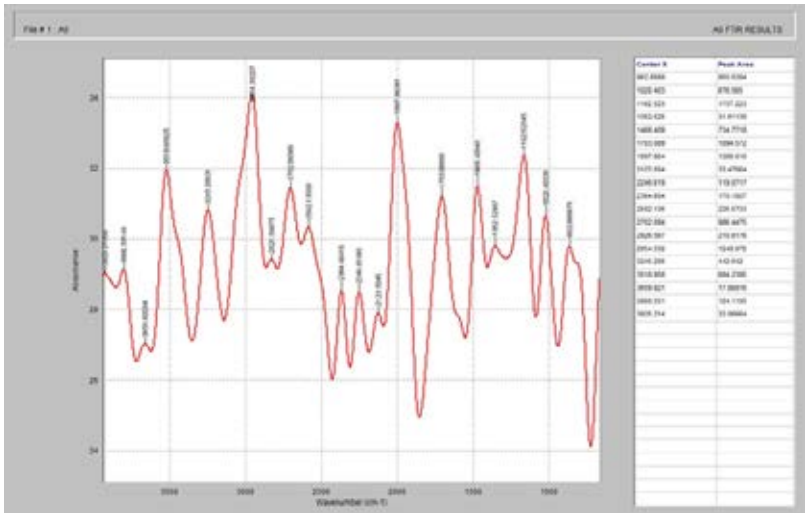

Figure 2. FTIR spectrum of ethyl cellulose.

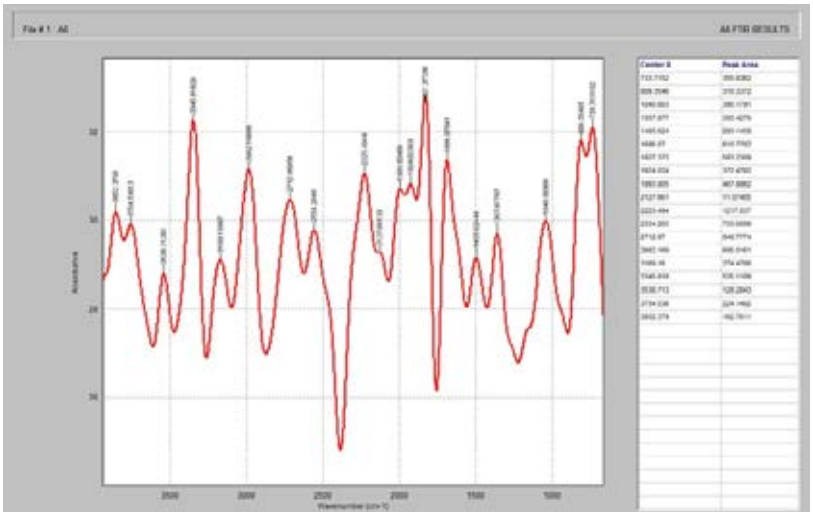

Figure 3. FTIR spectrum of carboxymethyl cellulose.

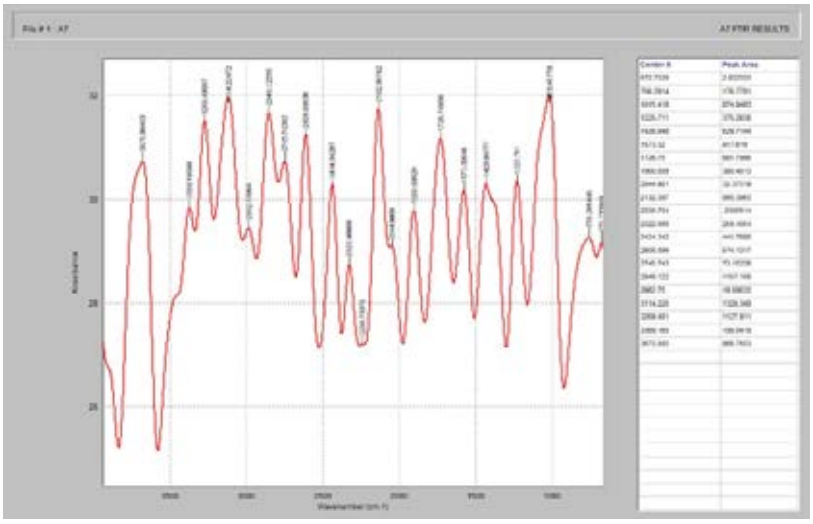

Figure 4. FTIR spectrum of HPMC.

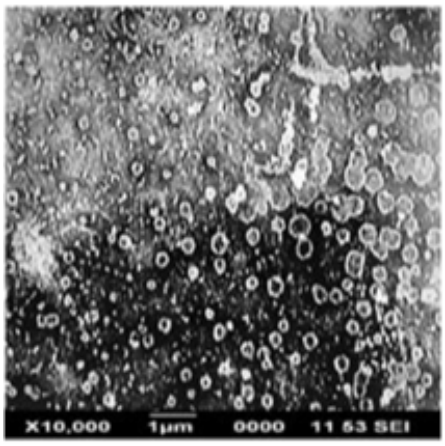

Figure 5. SEM for Batch F3.

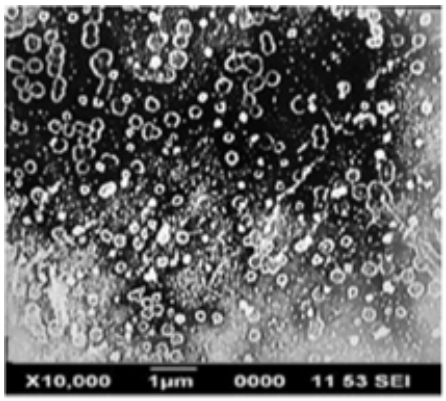

Figure 6. SEM for batch F5.

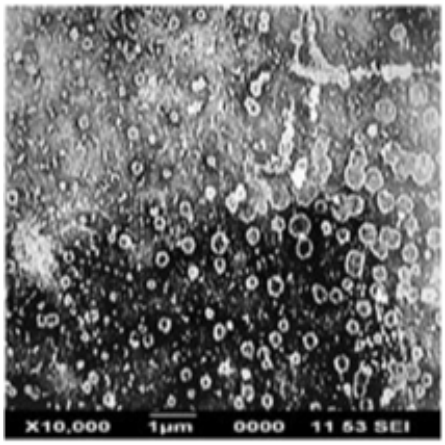

Figure 7. SEM for batch F9.

Post Compression Evaluation

Angle of Repose

The angle of repose is a characteristic of the internal function or cohesion of the particles. If a powder is non-cohesive, the angle of repose will be high, but if a powder is cohesive, the angle of repose will be low. The angle of repose of the formulations ranged from 3.525 ± 0.02 for batch F-5 to 9.415 ± 0.36 for batch F-3.

Bulk density

Bulk density was used to measure the flow properties of the powder. It is a function of the particle size and particle size distribution. It has a direct relationship with the flow characteristics of a powder. The bulk density of the formulations ranged from 0.507 ± 0.00 to 0.625 ± 0.01 for batches F-5 and F-7 respectively.

Tapped density

Tapped density is a function of particle size and size distribution. It ranged from 0.502 ± 0.00 to 0.627 ± 0.02 for batches F4 and F6 respectively.

Carrs Index

This is affected by particle size and particle size distribution. According to BP specifications, excellent free flowing granules range from 5-15%, while good free flowing granules range from 12-16%. Very poor fluid cohesive powders have C.I of > 38%, while powders with C.I. > 40% indicates very poor flow. From the results obtained, it ranged from 13.04 ± 0.01 to 13.90 ± 0.03 for batches F-7 and F-1 respectively.

Hausners ratio

It has a direct relationship between he tapped and bulk density. According to specifications, excellent free flowing granules range from 1.00 ± 1.11, while good free flowing granules range from 1.12 to 1.18. Very poor fluid cohesive powders have H.R. of 1.6 to 1.59. It ranged from 1.095 ± 0.05 to 1.138 ± 0.01 for batches F-3 and F-7 respectively.

Table 3. Flow properties of microspheres (mean ± SD)

Formulation code	Angle of repose (°)	Bulk density (g/ml)	Tapped density (g/ml)	Carr's Index (%)	Hausners ratio
F-1	7.220 ± 0.06	0.530 ± 0.01	0.545 ± 0.00	13.90 ± 0.03	1.291 ± 0.18
F-2	3.657 ± 0.11	0.537 ± 0.02	0.602 ± 0.00	13.75 ± 0.02	1.056 ± 0.01
F-3	9.415 ± 0.36	0.511 ± 0.01	0.616 ± 0.01	14.55 ± 0.02	1.095 ± 0.05
F-4	4.855 ± 0.02	0.444 ± 0.02	0.502± 0.00	14.90 ± 0.02	1.035 ± 0.01
F-5	3.525 ± 0.02	0.507 ± 0.00	0.594 ± 0.01	15.05 ± 0.01	1.173 ± 0.05
F-6	4.491 ± 0.01	0.592 ± 0.01	0.627 ± 0.02	12.75 ± 0.01	1.154 ± 0.00
F-7	5.045 ± 0.02	0.625 ± 0.01	0.618 ± 0.00	13.04 ± 0.01	1.139 ± 0.01
F-8	6.627 ± 0.16	0.507 ± 0.00	0.628 ± 0.02	13.00 ± 0.01	1.265 ± 0.07
F-9	6.845 ± 0.03	0.623 ± 0.01	0.633 ± 0.01	13.89 ± 0.01	1.360 ± 0.03

Percentage Yield of the Ranitidine Hydrochloride Microspheres

The yield of different microspheres varied from 83.00 ± 3.53 to 73.50 ± 2.47 for batches F-9 and F-7 respectively, when the drug polymer ratio was changed from 1:1 to 0.8. According Jemini et al, the reduction in the percentage yield with increasing drug/polymer ratio may be due to the loss of smallest and lightest particles during filtration and washing processes [18].

Table 4. The percentage yield of ranitidine hydrochloride microspheres (mean ± SD)

Formulation code	Yield (%) ± SD
F-1	87.00 ± 3.53
F-2	82.5 ± 1.76
F-3	77.00 ± 0.70
F-4	81.00 ± 4.24
F-5	77.00 ± 1.41
F-6	83.00 ± 2.12
F-7	73.5 ± 2.47
F-8	84.00 ± 0.70
F-9	83.00 ± 2.21

Swelling Index and Drug Content of Ranitidine Hydrochloride Microspheres

The swelling index is used to determine the amount of phosphate buffer absorbed by the microspheres after dissolving them in the buffer. From the result obtained, it ranged from 62.50 ± 0.35 to 82.50 ± 1.06 for batches F-1 and F-9 respectively.

The drug content was determined for the 9 formulations. It was found to be between 24.50 ± 2.47 % to 41.00 ± 4.24 % for F-1 and F-9 respectively. This depicts that the formulation F9 containing polymer Carbopol gave the highest drug content, while formulation F-1 that didn't contain any polymer gave the least drug content.

Table 5. Swelling index and Drug content of ranitidine hydrochloride microspheres (mean ± SD)

Formulation code	Swelling index (%)	Drug content (%)
F-1	62.50 ± 0.35	24.50 ± 2.47
F-2	67.50 ± 1.77	30.50 ± 3.18
F-3	71.00 ± 0.71	28.00 ± 0.00
F-4	76.00 ± 1.41	31.00 ± 2.83
F-5	77.50 ± 3.89	28.50 ± 1.77
F-6	78.50 ± 3.18	29.00 ± 0.71
F-7	76.50 ± 4.60	34.00 ± 1.71
F-8	80.50 ± 0.35	30.50 ± 0.35
F-9	82.50 ± 1.06	41.50 ± 4.24

In Vitro Release Study

The release study of ranitidine hydrochloride microspheres were done for 4 hours in phosphate buffer (pH 7.4). The microspheres formed demonstrated controlled release of the drug. From the results obtained, formulation 1 gave the highest drug release of 69.50%, while formulation 9 having HPMC gave the lowest release of 39.75%. The microspheres could be said to provide a better carrier system for controlled drug delivery.

Table 6. Drug release profile of ranitidine hydrochloride microspheres (mean ± SD)

Time (mins)/ Batch	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
15	2.35 ± 0.25	2.10 ± 0.35	2.55 ± 0.35	2.55 ± 0.18	2.55 ± 0.18	2.35 ± 0.25	2.40 ± 0.07	2.65 ± 0.46	2.15 ± 0.25
30	7.60 ± 0.57	8.10 ± 0.07	7.80 ± 0.42	7.7 ± 0.14	7.65 ± 0.18	8.00 ± 0.35	7.95 ± 0.04	7.90 ± 0.35	8.20 ± 0.14
60	17.25 ± 1.59	7.80 ± 2.97	17.85 ± 2.02	15.10 ± 0.70	9.00 ± 4.24	7.77 ± 2.89	16.45 ± 1.03	17.55 ± 1.80	11.65 ± 0.11
90	35.20 ± 0.57	14.90 ± 0.07	35.00 ± 0.71	27.05± 2.16	19.85 ± 2.93	15.85 ± 0.81	36.50 ± 1.06	26.25± 1.59	15.40 ± 0.49
120	47.80 ± 0.57	13.65 ± 3.08	43.00 ± 1.41	35.65 ± 0.25	27.00 ± 6.36	18.20 ± 0.14	36.50 ± 2.12	33.75 ± 1.59	17.60 ± 0.28
150	51.00 ± 2.83	20.85± 0.60	50.00 ± 2.12	39.75 ± 0.18	29.75 ± 7.25	19.75 ± 0.04	51.25 ± 0.88	42.30 ± 2.62	19.70 ± 0.07
180	57.00 ± 4.95	23.45 ± 0.32	55.00 ± 2.47	48.70 ± 1.20	37.85 ± 6.47	24.00 ± 0.28	57.40 ± 0.42	51.20 ± 0.85	25.73 ± 0.88
210	64.00 ± 2.83	25.35 ± 0.46	65.00 ± 3.53	54.60 ± 0.99	41.35 ± 9.90	25.90 ± 0.42	62.20 ± 0.14	58.35 ± 0.25	33.05 ± 1.73
240	69.50 ± 1.77	29.95 ± 0.17	62.50 ± 1.06	62.40 ± 1.70	45.00 ± 9.98	29.40 ± 3.04	64.75 ± 1.94	64.75 ± 3.36	39.75 ± 0.53

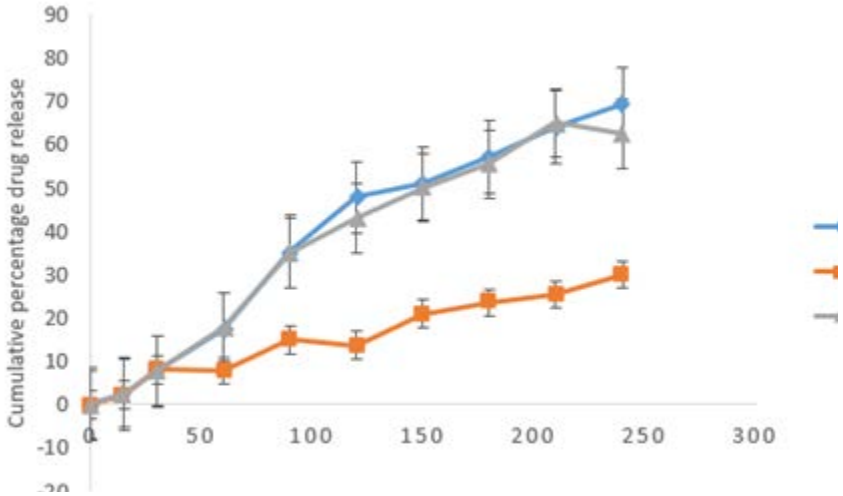

Figure 8. Cumulative percentage drug release of batches F-1 to F-3.

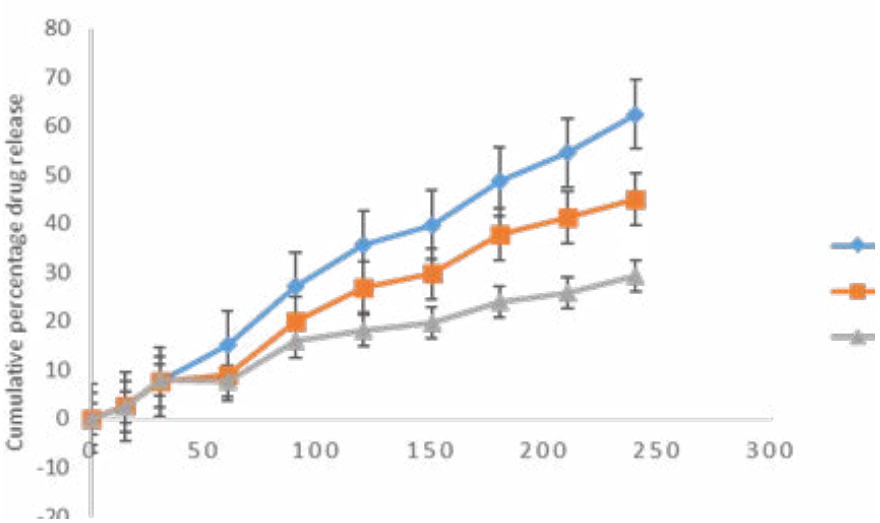

Figure 9. Cumulative percentage drug release of batches F-4 to F-6.

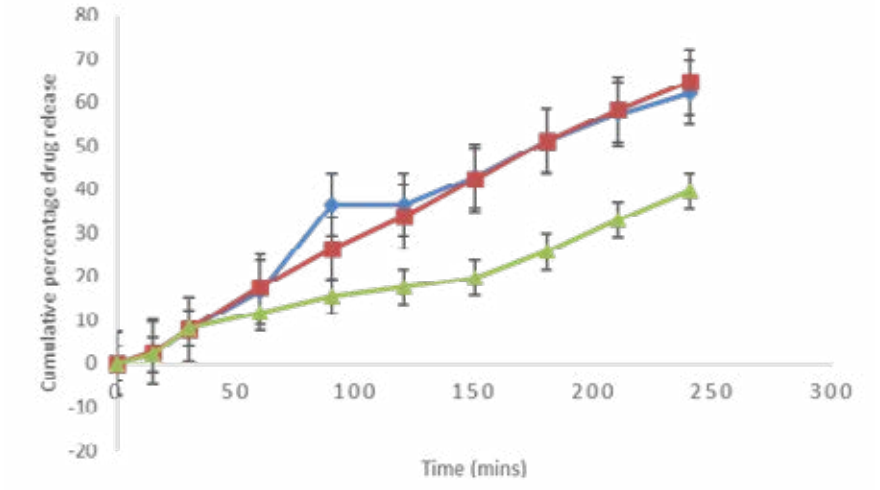

Figure 10. Cumulative percentage drug release of batches F-7 to F-9.

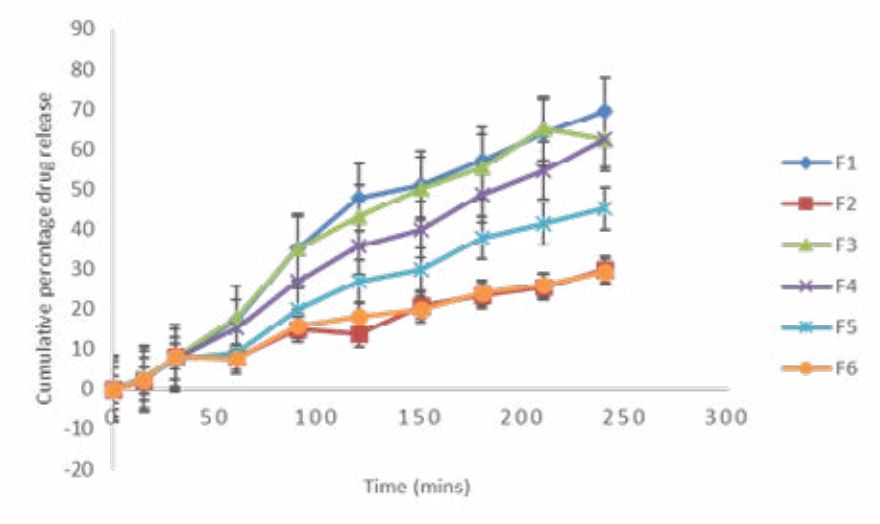

Figure 11. Cumulative percentage drug release of batches F-1 to F-6.

Morphology of the Ranitidine Hydrochloride Microspheres

The morphology of the obtained microspheres was examined by a light microscope (Zeiss, Me 63 C, West Germany) with varied magnification powers (Figs. 5-7).

Results obtained showed the presence of spherical shapes of different shapes and sizes. The smoothness of the ranitidine hydrochloride floating microspheres was increased by increasing the polymer concentration. The ranitidine hydrochloride microspheres with HPMC contained smooth surface and smaller in size compared to the microspheres with ethyl cellulose.

Table 7. Determination of maximum wavelength of ranitidine

Concentration (µg/ml)	Absorbance
0.0	0.0
1.0	0.107
2.0	0.200
3.0	0.283
4.0	0.371
5.0	0.456
6.0	0.539

Table 8. Determination of calibration curve of ranitidine in pH 6.8 at 315 nm

Concentration (µg/ml)	Absorbance
0.0	0.0
6	0.160
10	0.289
15	0.450
20	0.590
25	0.720
30	0.870

CONCLUSION/RECOMMENDATION

Overall, the optimised formulated ranitidine hydrochloride microsphere (F-1) demonstrated prolonged and controlled release characteristics, indicating its potential use in controlled drug delivery applications in the treatment of gastro-intestinal infections. In vivo studies is recommended on the formulated microspheres.

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ABBREVIATIONS

GIT: Gastrointestinal Tract; FDDS: Floating Drug Delivery Systems; RAN: Ranitidine; Na-CMC: Sodium Carboxylmethyl Cellulose; FTIR: Fourier Transform Infrared; EC: Ethyl Cellulose; HPMC: Hydroxypropyl Methyl Cellulose; C.I: Carr's Index; H.R: Hausner's Ration.

AUTHOR CONTRIBUTIONS

Ezegbe Chekwube Andrew: Conceptualization

Nwankwo Emmanuel Chinedu: Methodology

Okafor Pauline: Investigation

Onunkwo Godswill: Funding acquisition, Project administration

Ezegbe Chekwube Andrew: Supervision

Odo Benjamin: Writing – original draft

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CONFLICTS OF INTEREST

Authors declare that they have no competing interests.

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