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Original Article

GASTRORETENTIVE NIZATIDINE LOADING MICROBALLOONS FOR TREATMENT OF PEPTIC ULCER

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ABSTRACT

Objective: The aim of the present work was to formulate a controlled release dosage form of water soluble drug such as Nizatidine to increase its gastric retention in the stomach and consequently, enhance its absorption and improve its bioavailability.

Methods: Microballoons were prepared by emulsion non solvent evaporation method using ethyl cellulose 7 CP in different ratios. The prepared microballoons were evaluated for yield percentage, entrapment efficiency, *in vitro* buoyancy and *in vitro* dissolution.

Results: Results showed that as drug to polymer ratio increased from 1:1 to 1:5 yield percentage, entrapment efficiency, *in vitro* buoyancy increased from 70.4+1.5 to87.2+1.8, from 71.5+2.1 to 90.2+2.6 and from 82.1+3.2 to 93.2+2.6, respectively, while the amount of drug released decreased from 88.1+2.1 to 68.9+1.8. When stirring rate increased from 800 rpm to 1600 rpm, the three parameters decreased from 93.2+2.7 to 81.5, from 96.4+3.5 to 82.6+1.7 and from 97+5.4 to 88.2+4.1, respectively, while the amount released increased from 63.1+2.6 to 73.8+1.2. When Span 80 concentrations increased from 0.1% to 2% the three parameters decreased from 95.2+2.6, to 81.6+3.2, from 97.6+1.8 to 82.4+1.8 and from 97.3+5.2 to 89.1+4.6, respectively, and the amount released percentage increased from 61.2+2.6 to 76.1+1.6. All drug release showed Higuchi diffusion models. The increase in the mean T_{max} and the decrease in the mean C_{max} of microballoons compared to the plain drug indicate a sustained release of microballoons and reflects a high improvement in its bioavailability.

Conclusion: It is evident from this study that microballoons are promising gastric prolonging the delivery system for nizatidine and have good stability.

Keywords: Microballoons, Gastro retentive system, Nizatidine, Buoyancy.

INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve and maintain the desired drug concentration [1]. As the numbers of drugs have increased new techniques are required to develop orally active therapy, thus gastro retentive dosage forms which prolong the residence time of drugs in the stomach and improve their bioavailability have been developed. Microballoons are gastro retentive dosage based on non effervescent approach. They are low density system that has sufficient buoyancy to float over the gastric contents and remain in the stomach for prolonged period [2].

Nizatidine is a histamine H2 receptor antagonist that inhibits stomach acid secretion and commonly used in the treatment of peptic ulcer and gastro esophageal reflux. Nizatidine has short biological half life (1-2 h) and susceptible to metabolism by colonic bacteria [3, 4].

So, the main goal of the present study was to design Nizatidine microballoons to increase its gastric residence time in the stomach, consequently enhance its bioavailability and increase patient compliance. In vitro and in vivo evaluation of the prepared dosage forms were performed. The formula which combined excellent floating behavior, yield, entrapment and sustained drug release was chosen for *in vivo* investigation in rabbits to determine its pharmacokinetics parameters.

MATERIALS AND METHODS

Nizatidine was kindly supplied by Saudi Pharmaceutical industries & Medical Appliances Corporation (SPIMACO), AL-Qassim city, KSA. Ethylcellulose 7 CP was kindly supplied by Egyptian International pharmaceutical industrial company, all other solvents and chemicals were of analytical grade.

Preparation of microballoons

Microballoons were prepared by emulsion non solvent evaporation method using mineral oil as the continuous phase. The drug (50 mg) and polymer in different proportions from 1:1 to 1:5 drug to polymer ratio were weighed and dissolved into a mixture of absolute ethanol and methylene chloride (1:1) at room temperature. The above organic phase was then emulsified in the mineral oil containing different concentrations of Span 80 with vigorous agitation using mechanical stirrer (Heidolph PZP-2000, Germany). After 5 min, 60 ml of n-hexane (non solvent) were added to the emulsion at a rate of 1 ml/min. stirring was maintained until all the organic phase was evaporated. Then, microballoons were separated by filtration and washed with two portions of n-hexane (100 ml) each. The washed microballoons were dried at room temperature over night.

Characterization of microballoons

Particle size analysis

Particle size of microballoons was determined with optical microscope (Seizz MC 63 C-Germany) under regular polarized light and mean particle size was calculated (n=3) with the help of a calibrated oculo meter [5].

Yield of microballoons

The prepared microballoons were collected and weighed. The measured weight was divided by total amount of non-volatile components, which were used for the preparation of microballoons

% yield= (actual weight of product/total weight of excipient and drug) x100 [6, 7].

In vitro buoyancy

Microballoons (equivalent to 300 mg) were dispersed in 900 ml of 0.1 N hydrochloric acid solution (pH 1.2) containing Tween 20 (0.02 w/v %) at 37 ^{o}C to simulate gastric fluids. The mixture was stirred with a paddle at 50 rpm using dissolution apparatus (Type PTW II, Pharma test, Germany) and after 12 hr, the layer of buoyant microballoons was pipetted and separated by filtration. The buoyant microballoons were dried overnight at room temperature. The weight was measured and buoyancy was determined by the weight ratio of the buoyant microballoons to the amount dispersed at the beginning of experiment [8, 9].

Entrapment efficiency

Microballoons were dissolved in a minimum amount of methanol and drug was extracted into suitable aqueous media (0.1N hydrochloric acid) by evaporating methanol. The solution was filtered through what man filter paper, diluted suitably and analyzed for drug content spectrophotometrically at 315 nm (UV-Spectrophotometer Shimadzu UV-1201, Japan) using 0.1N hydrochloric acid as a blank [10, 11].

***In vitro* drug release study**

This study was carried out for all batches in dissolution test apparatus USP type II. Medium used was 900 ml of 0.1N HCl pH 1.2. Microballoons equivalent to 50 mg nizatidine was taken for the dissolution studies. The tests were carried out for 12 h at 50 rpm and 37±1 °C. Five ml of the aliquot was withdrawn hourly; filtered and equal volume of fresh medium was replenished to the dissolution vessel to maintain sink condition. The solution was analyzed for the drug content spectrophotometrically at 315 nm against 0.1N hydrochloric acid as a blank. Three trials were carried out for all batches and the average SE (standard error of mean) values were calculated [12, 13].

Stability study

Selected formulations were placed in a screw capped glass containers and stored at ambient room temperature 25+1 ° C, in refrigerator at 4+1 ° C and in oven at 50+1 ° C, for a period of 3 mo. The *in vitro* release amount of nizatidine and other characters was determined monthly [14].

***In vivo* study**

HPLC condition

HPLC (Waters Instrument, Germany) with the reverse phase C18 column was used. The UV detector was set at 239 nm. The mobile phase consisted of 0.01M di hydrogen phosphate adjusted to pH 3.5 and acetonitrile in a ratio of 63:37 V/V. The eluent was passed through the column at a flow rate of 1.5 ml/minute [15].

Preparation of standard calibration curve

Stock solution of nizatidine was prepared at a concentration of 100µg/ml using the mobile phase. Standard solutions containing 2, 4, 6, 8, 10, 12, 14, 16 µg were prepared by diluting the stock with the mobile phase and analyzed using 20 µl (10 µg/ml) amlodipine as internal standard [16]. Standard calibration curve was established in plasma by adding 100 µl aliquot of each of the above dilutions to 100 µl blank plasma. The spiked plasma samples were processed as described below.

Sample preparation

100 µl of 10 % perchloric acid and 20 µl of internal standard were added to 100 µl of the spiked plasma and the unknown plasma was shacked vigorously for 1 minute, then 2 ml of diethyl ether was added. The mixture was centrifuged at 4000 rpm and 4 ° C. 2 ml of supernatant was taken and dried at 40 ° C in vacuum oven. The residue then reconstituted in minimal amount of the mobile phase and injected into the column [17].

Experimental design

White male rabbits (weighing 1.5-2 kg) were used for the *in vivo* study. Animals were housed in the standardized conditions at the animal house of the Faculty of Pharmacy, Zagazig University, Egypt. All animals were acclimatized and kept under constant temperature (25±2 °C). All animal procedures were performed in accordance to the approved protocol for use of experimental animals set by the standing committee on animal care of the Faculty of Pharmacy, Zagazig University, Egypt. Animals were divided into three groups' three rabbits each. The study was designed as a single oral dose. All groups received an equivalent of 5 mg nizatidine/kg body weight of rabbits (determined by trials). Group 1 received nizatidine alone, group 2 received microballoons (1:5, 1200 rpm, 1% Span 80) and group 3 was control. One hard gelatin capsule was administered to each rabbit through a stomach tube with the aid of distilled water. Blood samples (about 1 ml) were withdrawn from the sinus orbital into EDTA tubes at 0.5, 1, 2, 4, 6, 8, 10, 12 and 24 h after each administration. The blood samples were centrifuged immediately at 3000 rpm for 10 min and the plasma samples were stored at-20±0.5°C for subsequent assay.

Kinetic analysis of the data

The data of drug release from microballoons were subjected to theoretical analysis to determine the order of kinetic release according to the following equations:

- Zero order kinetic. Ct = Co–Kt.
- First order kinetic. Log Ct = log Co-Kt/2.303.
- Diffusion control model. $Q/A=2\ Co\ (A/\pi)^{½}t^{½}$ [18].

Statistical analysis of the data

Experimental results were expressed as mean±SE (standard error). One-way analysis of variance (ANOVA) was applied to check significant differences. Differences were considered to be statistically significant at $p< 0.05$ [17, 19, 20].

RESULTS AND DISCUSSION

Good resolved, spherical microballoons with the smooth surface was obtained as shown in fig. 1

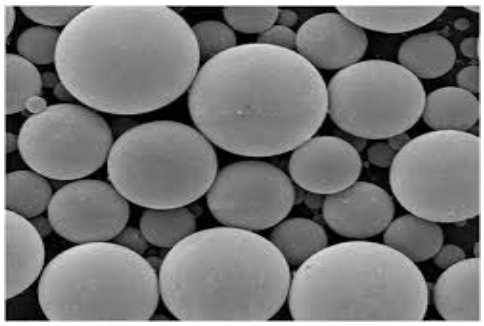

Fig. 1: Photomicrograph of microballoons (1:5, 1% Span80, 1200 rpm)

Effect of drug: polymer ratio

As drug to polymer ratio increased from 1:1 to 1:5, the mean diameter, yield percentage, percent entrapment and buoyancy percentage of the microballoons increased significantly ($P<0.05$) from 230 µm+1.9 to 324 µm+2.6, from 70.4%+1.5 to 87.2%+1.8, from 71.5%+2.1 to 90.2%+2.6 and from 82.1+3.2% to 93.2+3.6%, respectively (table 1). The diameter of nizatidine microballoons increased significantly **(**$p< 0.05$**)** with increasing drug to polymer ratio. This is in a good agreement with Najmuddin *et al.*, 2010 (21)who found that the mean particle size of microballoons of ketoprofen prepared from ES100 and EL100 increased from 123.33±15.27 to 192.33±27.5 for ES100 and increased from 102.33±21.12 to 156.66±27.53 for EL100, when drug to polymer ratio increased from 1:1 to 1:3.

This is also in a good agreement with Gadad *et al.*, 2011 [22], who found that the mean particle size of microballoons of captopril prepared from ES100 and ethylcellulose increased from 57.66±7.27 to 93.20±9.63 for ES100 and from 62.46±6.58 to 85.52±6.32 for ethylcellulose, when drug to polymer ratio increased from 1:1 to 1:4. The increase in particle size with increasing drug to polymer ratio could be ascribed to the increase in viscosity of the medium with increasing polymer concentration resulting in enhanced interfacial tension and diminishing shearing efficiency, this result in formation of larger particles [21, 23, 24]. An increase in drug to polymer ratio from 1:1 to 1:5, lead to a significant increase in entrapment efficiency, yield percentage and floating percentage. These results are in a good agreement with that mentioned by Najmuddin *et al.*,

2010(21), who prepared microballoons of ketoprofen by emulsion solvent diffusion method using ES100, and EL100. They found that, the entrapment efficiency, the yield percentage and the floating percentage increased from 61.07±0.98 to 81.7±2.02, from 62.4±0.72 to 89.45±1.5, and from 80.66±2.08 to 91.66±1.52, respectively, with increasing the concentration of ES100, and EL100. This is in a good agreement with Gadad *et al.*, 2011[22] who prepared floating microspheres of captopril using ES100 and found that with increasing drug to polymer ratio from1:1 to 1:4, entrapment efficiency increased from 76.72±2.57 to 90.9±1.07. Patil et al., 2009 [25] also found that, with increasing ethylcellulose concentration the yield percentage increased from 69.7±0.02 to 76.93±0.02. This could be ascribed to the fact that an increase in polymer concentration leads to an increase in the viscosity of the medium and consequently, the formation of larger particles which leads to an increase in the three parameter [11, 21, 25].

Table 1: Effect of drug to polymer ratio on nizatidine microballoons

Drug: polymer	Mean diameter µm+SE	% Yield+SE	% Entrapment+SE	% Buoyancy+SE
1:1	230+1.9	70.4+1.5	71.5+2.1	82.1+3.2
1:2	254+2.3	75.8+1.9	77.1+1.5	86.5+4.1
1:3	280+1.5	79.5+2.6	82.1+0.9	90.6+3.6
1:4	300+3.2	84.1+2.6	84.6+1.5	92.2+5.0
1:5	324+2.6	87.2+1.8	90.2+2.6	93.2+3.6

Mean+SE, (n=3).

Effect of stirring rate

As stirring rate increased from 800 rpm to 1600 rpm, the mean diameter, yield percentage, percent entrapment and buoyancy percentage of the microballoons decreased significantly (P <0.05)from 369 µm+3.4 to 260 µm+2.6, from 93.2%+2.6 to 81.5%+1.9, from 96.4%+3.5 to 82.6%+1.7 and from 97.0%+4.6 to 88.2%+5.4, respectively (Table2). The diameter of microballoons significantly decreased (p< 0.05) with increasing stirring rate from 800 to 1600 rpm. This may be attributed to the fact that the polymer solution under higher stirring rates subjected to higher shear force which led to the splitting of the polymer solution into smaller droplets [26, 27]. This is in a good agreement with Mazumder et al., 2010 [28], who found that as the stirring speed of all formulation increased from 800 rpm to 1200 rpm, a significant decrease in particle size was observed for ethylcellulose and ethylcellulose in combination with ERS100 microballoons. This is also in a good agreement with Nath *et al.*, 2010 [29], who found that when the stirring speed was increased from 600 to 1000 rpm, particle size of salbutamol sulphate loaded ethylcellulose microballoons significantly decreased from 397±2.4 to 271±1.8 (p< 0.05).

It was found that increasing the stirring rate lead to a significant decrease in the three parameters which could be ascribed to the decrease in particle size with the increase in stirring rate [20] and this leads to:

1. A significant reduction in entrapment efficiency as smaller particles will entrap less amount of the drug [30].

2. A significant reduction in floating percentage as smaller the microballoons, the floating ability will be less, while larger the size, floating ability will be more [25].

3. A significant reduction in yield percentage.

When the stirring speed was too slow, the diffusion rate of the solvent decreased due to the formation of larger droplets. The subsequent hardening may decrease the yield of microballoons due to their sticking to the vessel and coalescing into aggregates.

When the stirring speed was too fast, solidification of the polymer occurred before the formation of spherical microballoons due to higher rate of diffusion e. g., too fast solidification may result in a fiber like structure.

From previous results, it can be concluded that the decrease in the yield percentage was mainly due to aggregates at lower stirring speed and fiber like structure at higher stirring speed [26]. This is in a good agreement with that found by Mazumder *et al.*, 2010 [28], who found that when stirring speed was increased from 1000 to 1200 rpm, the entrapment efficiency of stavudine decreased.

Table 2: Effect of stirring rate on nizatidine microballoons (1:5, 1% Span80)

Stirring rate(rpm)	Mean diameter µm+SE	% Yield+SE	% Entrapment+SE	% Buoyancy+SE
800	369+3.4	93.2+2.6	96.4+3.5	97.0+4.6
1200	324+2.6	87.2+1.8	90.2+2.6	93.2+3.6
1600	260+2.6	81.5+1.9	82.6+1.7	88.2+5.4

Mean+SE, (n=3).

Effect of span 80 concentration

As the concentration of Span80 increased from 0.1% to 2%, the mean diameter, yield percentage, percent entrapment and buoyancy percentage of the microballoons decreased significantly (P<0.05) from 390 µm+5.1 to 290 µm+4.6, from 95.2%+3.6 to 81.6%+2.8, from 97.6%+3.4 to 82.4%+2.4 and from 97.3%+5.6 to 89.1%+1.9, respectively (Table3). The diameter of microballoons significantly decreased as the concentration of Span 80 increased. Increasing the surfactant concentration produces smaller and more stable droplets, thereby reducing the fusion of smaller droplets to form larger droplets or aggregates [26]. This result is in a good agreement with Al-Helw *et al.*, 1998 [31] who found that increasing of Span 80 concentration from 0.1% to 4% leads to a reduction in particle size of chitosan microballoons from 390 to 297 µm. Also Mazmuder *et al.*, 2009 [32], who found that as the concentration of Tween 80 increased, the mean particle size decreased significantly. This also in a good agreement with Jain *et al.*, 2004 [33], who found that the mean diameter of albendazole microballoons prepared from ERLP significantly decreased from 152.6±2.8 to 132.7±1.3, when emulsifier concentration increased from 0.5 to 1.25. An increase in Span 80 concentrations from 0.1% to 2%, results in a significant decrease in the three parameters.

The decrease in entrapment efficiency could be attributed to the fact that, at low surfactant concentration, the surface of microballoons is smooth and intact, while increasing surfactant concentration results in a brittle surface, which leads to a drug loss during washing with n-hexane [34]. The floating ability of microballoons decreased with increasing surfactant concentration and this may be due to the easy penetration of the simulated gastric fluid solution through the porous brittle surface [35].

Nepal *et al.*, 2007 [26], found that with increasing surfactant concentration, the size of microballoons significantly decreased. An increase in the surfactant concentration produced smaller and more stable droplets, thereby reducing the fusion of smaller droplets to form larger droplets or aggregates. Ultimately small sized microballoons were generated and this lead to entrapment of less amount of the drug, the floating ability decreased and the loss of the smallest and lightest particles during filtration occurred. This is in a good agreement with Mazmuder *et al.*, 2009 [32], who found that as the concentration of Tween 80 increased, percentage yield and percentage entrapment efficiency decreased significantly.

Table 3: Effect of Span80 concentration on nizatidine microballoons characters (1:5, 1200 rpm)

Span 80 concentration (%)	Mean diameter µm+SE	% Yield+SE	%Entrapment+SE	%Buoyancy+SE
0.1	390+5.1	95.2+3.6	97.6+3.4	97.3+5.6
0.6	372+4.1	92.5+2.9	93.1+5.6	95.6+3.8
1	324+1.6	87.2+1.8	90.2+2.6	93.2+3.6
2	290+4.6	81.6+2.8	82.4+2.4	89.1+1.9

Mean+SE, (n=3).

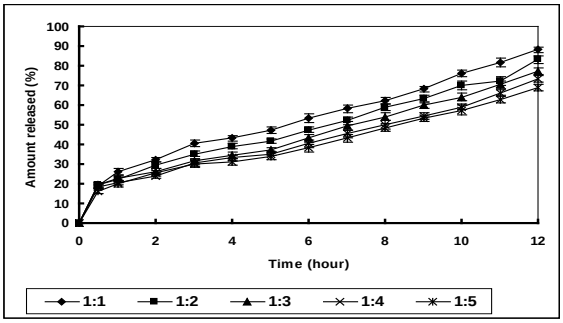

Fig. 2: Effect of drug to polymer ratio on the amount of nizatidine released percentage. The data represent the mean+SE of three determinations

In vitro drug release study

Amount of nizatidine released from microballoons was found to be decreased significantly (P<0.05) from 88.1%+1.6 to 68.9%+2.1 after 12 h when the drug to polymer ratio increased from 1:1 to 1:5. on the other hand, the amount of nizatidine released increased from 63.1%+1.2 to 73.8%+1.8 and from 61.2%+2.6 to 76.1%+1.8, when stirring rate increased from 800 to 1600 rpm and Span80 concentration increased from 0.1% to 2%, respectively (fig. 2, 3 and 4). Results showed that as drug to polymer ratio increased from 1:1 to 1:5, the amount of drug released slightly but significantly decreased. This is in a good a agreement with that mentioned by Najmuddin *et al.*, 2010 [21], who found that the amount of ketoprofen released significantly decreased with increasing the concentration of either ES100 or EL100 and he ascribed this to the fact that the increase in ES100 and EL100 concentration leads to the increased density of polymer matrix into the microballoons, which result in an increased diffusional path length. This may decrease the overall drug release from polymer matrix. Furthermore, smaller microballoons are formed at lower polymer concentration and have larger surface area exposed to the dissolution medium. The amount of nizatidine released increased with increasing stirring rates from 800 to 1600 rpm. This could be ascribed to the formation of smaller particle size microballoons at the higher stirring rates [26]. Smaller particles have larger surface area exposed to the dissolution medium and hence, higher dissolution rate. This is in a good agreement with that mentioned by Khidr *et al.*, 1995 [30], who found that an increase of stirring speed from 600 to 1000 during preparation of cellulose propionate microballoons enhanced the dissolution rate of meclophenamate Na from these microspheres. And also with Mazumder *et al.*, 2010 [28], who found that the release rate of stavudine increased significantly with the increase of stirring speed, this for ethylcellulose or in combination with ERS100 microballoons. It is clear from the results that, as the concentration of the emulsifier increased, the amount of drug released significantly increased. This may be explained by two mechanisms; the first is that at higher concentration of the emulsifier, the formed microballoons were more porous than those made at lower concentration [34, 36]. The second mechanism is that the increase in surfactant concentration results in the formation of smaller and more stable droplets, thereby reducing the fusion of smaller droplets to form larger droplets or aggregates [26]. This leads to an increase in dissolution rate as the smaller microspheres have larger surface area which exposed to the dissolution medium. This is also in a good agreement with Mazumder *et al.*, 2009 [32], who found that the release rate of chlorpheniramine maleate from etylcellulose and cellulose acetate microballoons increased significantly as the concentration of surfactant increased.

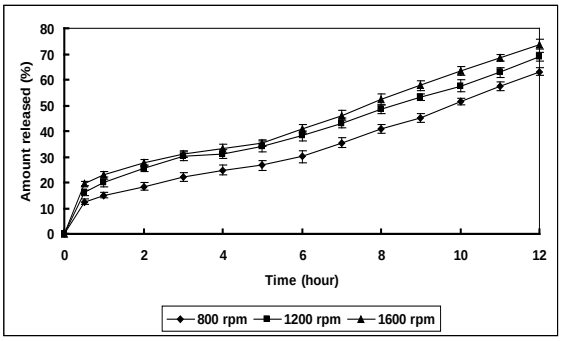

Fig. 3: Effect of drug to polymer ratio on the amount of nizatidine released percentage. The data represent the mean+SE of three determinations

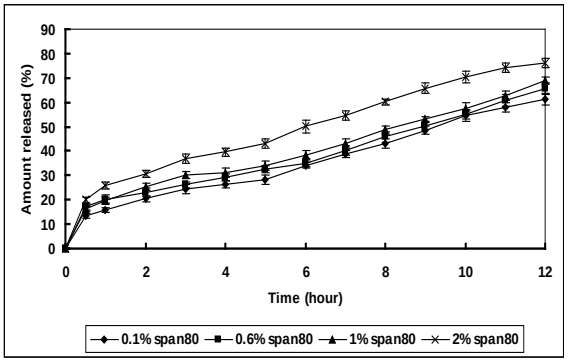

Fig. 4: Effect of Span 80 concentration on amount of nizatidine released percentage (1:5, 1200 rpm). The data represent the mean+SE of three determinations

Stability study

All selected formulae showed high stability under the stored conditions (data not shown).

***In vivo* study**

Fig. 5 shows the chromatogram of rabbit plasma containing nizatidine and amlodipine as an internal standard. It can be noticed that, a typical and well resolved peaks are obtained for plasma, nizatidine and internal standard. The retention times of nizatidine and amlodipine are 6 and 3.5 min, respectively.

The standard calibration curves for nizatidine in rabbit plasma ranging from 2-20 µg/ml were prepared by plotting peak area ratio against drug concentration. The data for calibration curves are shown in fig. 5. It can be observed that, a good linearity is obtained with a good correlation coefficient (R) of 0.9942. The mean equation obtained for the calibration curve was;

$$Y= 0.9792X-0.3794$$

Where, Y represents the peak area ratio of nizatidine to amlodipine and X represents the concentration of nizatidine in plasma (µg/ml).

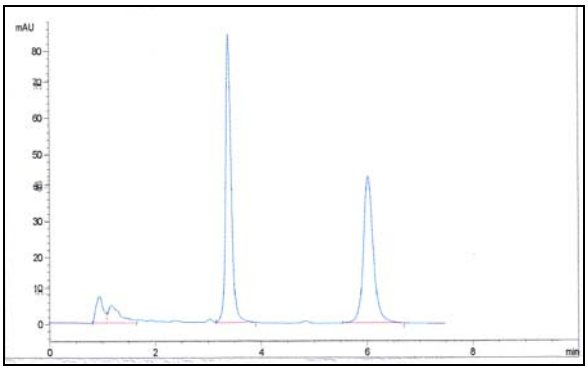

Fig. 5: Typical HPLC chromatogram of nizatidine and amlodipine

The mean plasma concentrations as a function of time for nizatidine after oral administration of plain nizatidine and nizatidine microballoons are illustrated in fig. 7. From the obtained results, it is evident that, there is a significant difference between the mean plasma concentrations after oral administration of microballoons at all time intervals compared to the plain drug. Also, there was a noticeable difference in the T_{max} between the plain drug and microballoons.

The mean pharmacokinetic parameters of plain nizatidine and nizatidine microballoons represented by the value of C_{max} (µg/ml), T_{max} (hr), $t_{1/2}$ (hr) and AUC_{0-24} (µg. hr. ml^{-1}) are summarized in table 4. From the obtained data, it is observed that, the absorption of plain nizatidine was rapid and reached its peak plasma concentration in (1.5±0.08 h), whereas, the mean T_{max} for microballoons was 3.6±0.12 h. The mean peak plasma concentrations (C_{max}) were 1.489±0.07 µg/ml for microballoons and 2.125±0.11 µg/ml for plain drug. The mean AUC_{0-24} was found to be 10.375±0.34 µg. hr. ml^{-1} for microballoons compared to 10.111±0.51µg. hr. ml^{-1} for plain drug. From the obtained results, it is evident that, there is a significant difference between the mean plasma concentrations after oral administration of nizatidine microballoons at all time intervals compared to the plain drug. Also, there was a noticeable difference in the T_{max} between the drug and microballoons. The increase in the mean T_{max} and the decrease in the mean C_{max} of microballoons compared to the plain drug indicate a sustained release of microballoons and reflect a high improvement in its bioavailability. These results are in accordance with those of Ofokansi and Adikwu 2007 [37], who found that, the bioavailability as well as the time to attain peak plasma level for cefuroxime sodium was generally higher from the microspheres in comparison with that of the control.

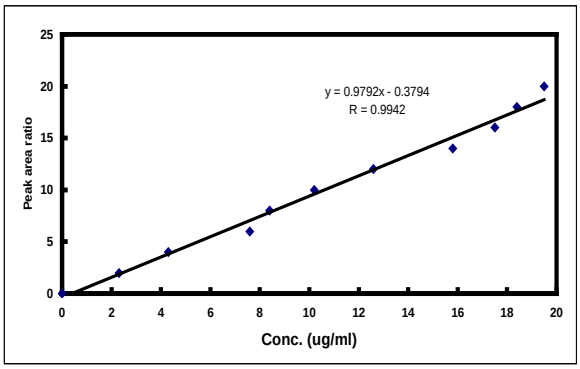

Fig. 6: Standard calibration curve of nizatidine in rabbit plasma using amlodipine as an internal standard

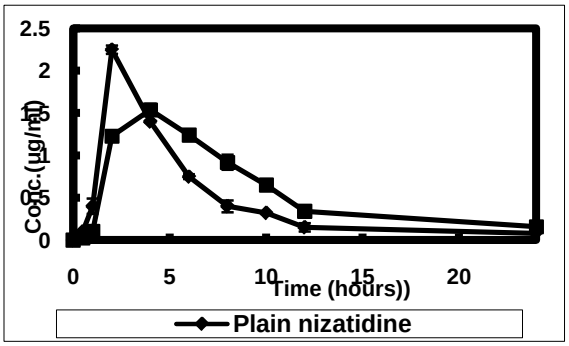

Fig. 7: Plasma levels of plain nizatidine and nizatidine microballoons. The data represent the mean+SE of three determinations

Table 4: Pharmacokinetics parameters after oral administration of plain nizatidine and nizatidine microballoons

Formulae	C_{max} (µg/ml)	T_{max} (h)	$t_{1/2}$ (h)	AUC_{0-24} (µg. h. ml^{-1})
Plain nizatidine	2.125±0.11	1.5±0.08	3.8±0.05	10.111±0.51
Nizatidine microballoons	1.489±0.07	3.6±0.12	5.9±0.22	10.375±0.34

Values are expressed as mean+SE; Cmax, the maximum peak plasma concentrations of nizatidine; Tmax, time of maximum concentration; t1/2, half life time; AUC0-24, area under plasma level-time curve over 24 h.

CONCLUSION

Microballoons promises to be a potential approach for increased gastric residence time, enhanced bioavailability and controlled delivery of various therapeutic agents. The present study reported the development of nizatidine loaded microballoons using ethylcellulose polymer. All prepared formulae remained buoyant for more than 12 h and released nizatidine in a controlled manner over 12 h; thus, they may reduce the frequency of dosing thereby, minimize side effects, prolong residence time in stomach and increase the efficiency of the drug.

CONFLICT OF INTERESTS

Declare none

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