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Original Research Article

Formulation and evaluation of mucoadhesive microballons of nizatidine for peptic ulcer

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ABSTRACT

The mucoadhesive microballons were prepared by using combination of polymer-polymer complexation (PAA-PVP) using solvent diffusion method. Mucoadhesive microballons is one of dosage forms which make available the prospectto increase the bioavailability of drug. The prepared delivery system managing the discharge rate of nizatidine between therapeutic absorption by extended the gastric emptying time. The delivery systems make certain accessibility of drug content at the assimilation site for the preferred period of time, also the possibility of enhancing the bioavailability and control the release of nizatidine show evidence of absorption by prolonging the gastric emptying time of the dosage form.

***Keywords*:** Peptic ulcer, mucoadhesive microballons, nizatidine

INTRODUCTION

A peptic ulcer is a specific area of stomach or intestinal mucosa, which caused by the digestive action of gastric juice or upper small intestinal secretions. The peptic ulcers majority regularly location is within a few centimeters of the pylorus. It is also occur beside the lesser curvature of the antral end of the stomach. But rarely, sometimes at lower end of the esophagus where stomach juices frequently reflux.

The peptic ulcer mainly caused by various parameters i.e. high acid and peptic content,

irritation with poor blood supply, poor secretion of mucus and infection generated by bacterial infection of H. pylori. One of type of peptic ulcer called a marginal ulcer may develop due to a surgical opening at stomach and jejunum section of the small intestine. The typical cause of peptic ulceration is an imbalance of factor as rate of secretion of gastric juice and the degree of protection afforded by gastroduodenal mucosal barrier. The neutralization of the gastric acid by duodenal juices should be important for management of acid attack at GIT. Commonly all areas are normally expose to gastric juice with mucous glands at lower part of esophagus. The mucous cell coating of the stomach mucosa present at mucous neck cells of the gastric glands. The deep pyloric glands secrete more mucus also at upper duodenum for secretion of highly alkaline mucus. The specific causes of peptic ulcer in the human being bacterial infection by H. pylori, which break down the gastroduodenal mucosal barrier and stimulates gastric acid secretion. The mucosal membrane protects the stomach and internal organs of excess secretion of gastric acid secretion. This may facilitate the bacteria Helicobacter pylori to penetrate the barrier and cause internal infections. So, peptic ulcer caused with both gastric acid and bacteria for the expansion of the disorder [1]. Diagnosis of ulcer due to symptoms is most common feature depends on ulcer location and patient age [2]. Peptic ulcer can be diagnosed specifically by direct visualization of endoscopy or radiology or by detection of H. pylori tests. The histology of tissue, culture process of biopsy, detection of presence of urea with ammonia was confirmed by endoscopic tests. The presence of H. pylori in serum, urea breathe test and stool antigen test comes under non-endoscopic test [3]**.**

The present work was done with nizatidine as API, which is a valuable inhibitor of histamine blocking agent at the site of H_2 receptors of body. The drug nizatidine reduces stomach acid production by inhibiting the action of histamine on stomach cells present on gastric basolateral membrane of parietal cells. The effective inhibition action produced the reduction of basal and nocturnal gastric acid secretions. Nizatidine is approximately fully absorbed after oral administration and in 1 to 3 h peak plasma absorption was reached. Absorption is increased by the presence of food and decreased by 10 % in the presence of antacids such as aluminum hydroxide gel and magnesium silicate. It is partially metabolized by the liver, but does not inhibit the hepatic mixed function oxidase system. Three metabolites have been identified, nizatidine N-2–oxide, nizatidine S-oxide and N-2–mono des methyl nizatidine (60 %

activity of nizatidine). Nizatidine is widely distributed throughout the body and has been detected in breast milk (0.1 % of the administered dose). 90 % of an administered dose is excreted in urine, partly by active tubular secretion, with 60 % as the unchanged drug.

Hence, the main ambition of the current study was to intend nizatidine microballoons to raise its gastric residence time in the stomach. This may consequently enhance its bioavailability and increase patient compliance. *Ex-vivo* (*in-vitro*) and *in vivo* evaluation of the prepared dosage forms were performed for justified the effect of formulation.

MATERIALS AND METHODS

The drug nizatidine was generously supplied as a gift sample from Dr. Reddy Lab, Hydrabad, India. PAA was procured from Himedia Laboratories Pvt. Ltd, Mumbai, India. PVP, span 80, and n-hexane were procured from CDH Pvt. Ltd. Mumbai, India.

Preparation of mucoadhesive microballoons

Microballoons were prepared by solvent dispersion method using soya oil as the continuous phase. The drug (100 mg) and polymer in different proportions from 1:1 to 1:5 drug to polymer ratio (PAA-PVP; 1:1) were weighed and dissolved into a mixture of absolute ethanol and water (7:3) at room temperature. The above organic phase was then mixed in the soya oil containing Span 80 (1.5 % v/v) with 500rpm agitation using mechanical stirrer (Heidolph PZP-2000, Germany). The prepared microballons were gradually hardened with a time of drying period and collected by washed three times with n-hexane and dried at room temperature [4-5].

Characterization of mucoadhesive microballoons

Shape and surface morphology

Scanning electron microscopy (SEM, JealJX 840-A, Tokyo, Japan) was performed to characterize the surface of formed mucoadhesive microballons. A double adhesive tape fixed to an aluminum stub frivolously sprinkling with powder then layered with gold film using reduced pressure. This film acts as a conducting medium on which a stream of electron was allowed to flow and then photograph was taken with scanning electron microscope [6-10].

Flow properties

Flow properties were determined in terms of Carr's index (Ic) and Hausner's ratio (HR) using the following equations:

$HR = \rho t / \rho b$

$Ic = \rho t - \rho b / \rho t$

Where, ρt = tapped density

ρb = bulk density

The angle of repose (θ) of the microballons, which measures the resistance to particle flow, was determined by the fixed funnel method, using the following equation:

$\tan \theta = 2H/D$

Where, 2H/D is the surface area of the free-standing height of the heap that formed after making the microballons flow from the glass funnel [6-10]. The result was showed in Table 1.

Particle sizeanalysis

Microballons were studied microscopically for their size and size distribution using optical microscopic method. A compound microscope fitted with a calibrated ocular micrometer and a stage micrometer slide was used to count at least 100 particles (Olympus NWF 10x; Educational Scientific Stores, India) [6-10].

Percentage yield of microballoons

The prepared mucoadhesive microballoons were weighed after drying [6-8]. The percent yield of microballons were calculated with following formulae

% yield= (Total weight of microballons / Total weight of drug polymer ratio) x100

Drug entrapment efficiency

For determination drug entrapment efficiency500mg of microballons containing a drug were taken, crushed by trituration and suspended in a minimal amount of dichloromethane (10ml) for dissolving the coat shell of the microballons. The suspension was suitably diluted with 0.1N hydrochloric acid buffer (100 ml) for 1hr and filtered to separate the shell fragments. Then Drug entrapment efficiency was analyzed after suitable dilution by spectrophotometrically with a UV-detector (Shimadzu, UV-1800) at λ_{max} 228 nm [6-7]. The drug entrapment efficiency was calculated as follows:

$$\text{Drug entrapment efficiency} = \frac{\text{Calculated drug concentration} \times 100}{\text{Theoretical drug content}}$$

Degree of swelling of microballons

For estimating the degree of swelling 1gm of microsphere were suspended in 5 ml of simulated gastric fluid USP (pH 1.2). The particle size was monitored by microscopy technique every 1 hour using an optical microscope (Labomed CX RIII). The increase in particle size of the microballons was noted for up to 8 h [12-14].

The formula used for calculation of degree of swelling is given below

$$\alpha = [\omega_g - \omega_0]/\omega_0$$

Where α = degree of swelling,

ω_0 = initial weight of microballons

ω_g = final weight of microballons

In vitro wash-off test for microballons

The mucoadhesive properties of the microballons were evaluated by *in vitro* wash-off test. For this 1 cm piece of rat stomach mucosa was tied onto a glass slide using thread. About 100 microballons was spread onto the wet, rinsed, tissue specimen, and the prepared slide was hung onto the groves of a USP tablet disintegrating test apparatus. Apparatus was functioned to provide up and down movements to tissue specimen in replicated gastric fluid USP having pH 1.2 containing beaker. At the end of 1 h, 5 h and 10 h intervals and the number of microballons still adhering onto the tissue was measured. The phase contrast microscope was used for study of mucoadhesion nature of microballons. The opical microscopic image showed the floppy part of surface of microballons after the wetting nature of microballons (Figure 3).

In vitro drug release studies

In vitro drug release studies of nizatidine microballons was carred out using a modified USP XXIV dissolution apparatus type I (basket mesh # 120, equals 125 μm) (DA-6DR USP standards; Veego-Scientific) in 0.1 mol/l hydrochloric acid (pH 1.2) as the dissolution fluid (900 ml). The content was rotated at 100 rpm and thermostatically controlled at 37±0.5°C. The withdrawn samples (5 ml) were analyzed spectrophotometrically with a UV-detector (Shimadzu, UV-1800) at λ_{max} 228 nm. All experiments were performed in triplicate. To sink condition of dissolution media was maintained by replenished the volume with same amount of fresh dissolution fluid each time [6-7].

In vivo antisecretory and ulcer protective activity of optimized mucoadhesive microballons formulation

To assess the i*n vivo* antisecretory and ulcer protective activity of optimized (F5) mucoadhesive microballons formulation, the albino rats (body weight approx.100 ± 20 g; with no prior drug treatment) were used. Albinorats were divided into three group having six rats in each group. They were fasted for 24 h before drug treatment. The

animals were deprived of food and water during the experiment.

Group I animals were administered absolute alcohol per oral (p. o.) at the dose of 2 ml /kg. The groups II were administered 10 ml solution of plain drugs (equivalent to 10 mg/kg nizatidine hydrochloride) 30 min before oral dose of absolute alcohol (2 ml/kg). The group III were administered 10 ml suspension of optimized microballons formulation (F5) (equivalent to 10 mg/kg nizatidine hydrochloride) 30 min before oral dose of absolute alcohol (2 ml/kg).

After 4 h of pyloric-ligation the animals of each group were sacrifice by decapitation.

The abdomen of sacrificed animal was incised and entire stomach was cut and removed from the body of the animal after tied the cardiac end (oesophageal end) of the stomach. The A cut was given to the pyloric region just above the knot and the contents of the stomach were collected in a graduated centrifuge tube and the stomach was opened along the greater curvature. Stomach mucosa was washed with 1ml-distilled water and the washing was added to the gastric juice.

Each stomach was examined by 10X magnification glass and the ulcers were graded using the following scoring system.

0 = normal mucosa

0.5 = red colouration

1.0 = spot ulcers.

1.5 = haemorrhagic streaks

2.0 = ulcers> 3 but <5

2.5 = ulcers > 5

The gastric contents were centrifuged at 3000 rpm for 10 min and 1ml of the supernatant was diluted to 9 ml of distilled water. The solution was titrated against 0.01N sodium hydroxide using Topfer's reagent till the solution turns to orange colour. The volume of sodium hydroxide required to neutralize the acid corresponding to the total acidity, was determined from the optimized formulation. Acidity (mEq/l/100g) and ulcer index can be expressed as:

$$\text{Acidity} = \frac{\text{Volume of sodium hydroxide} \times \text{normality} \times 1}{0.1}$$

$$\text{Ulcer Index} = \frac{10}{X} \qquad \text{Where } X = \frac{\text{Total Mucosal Area}}{\text{Total Ulcerated Area}}$$

The acidity and ulcer index of control (absolute alcohol induce), optimized mucoadhesive microballons formulation (F5) treated animals are reported in Table 6 and graphically shown in Figure 5.

Stability Studies

The stability study of the drug-loaded PAA-PVP microballons (F5) was done after selection by *in-vitro* drug release study.

Degradation of drug from frormulation is probably take place during high temperature and humidity. Hence the prepared mucoadhesive microballons were subjected to accelerated stability testing [15-16].

Effect of storage on particles size and structural integrity of PAA-PVP microballons

The change in structural integrity and particles size of the optimized PAA-PVP microballons (F5) stored at 4±1 °C, 28±1 °C and 45±1 °C temperatures was determined separately using optical microscopy method (Erma, Japan) after a definite period of time of i.e. 15, 30, 45 and 60 days. The observations are reported in Table 7 and in Figure 7.

Effect of storage on residual drug content

The residual drug content determination of mucoadhesive microballons formulation was stored in amber colored glass vials. After 15, 30 and 45 days the microballons formulation were dissolved in 3ml dichloromethane and filter through polycarbonate membrane (200 nm) (Millipore, USA). Than after suitable dilution with SIF (pH 1.2) the drug content determined spectrophotometrically (Shimdazu 1800, Japan). The observations are recorded in Table 8 and shown in Figure 8.

Table 1. Flow properties of mucoadhesive microballons

No.	Code	Drug:Polymer	Angle pf repose (Ɵ)	Carr's Index (%)	Hausner's ratio
1	F1	1:1	22.5±0.103	14.06±0.026	1.16±0.014
2	F2	1:2	24.5±0.102	14.43±0.038	1.16±0.015
3	F3	1:1	26.5±0.112	15.64±0.015	1.19±0.013
4	F4	1:2	29.5±0.198	15.87±0.019	1.21±0.012
5	F5	1:1	28.5±0.176	13.47±0.041	1.12±0.013

Mean ±SD

Table 2. Particle size of mucoadhesive microballons

No.	Code	Drug:Polymer	dmean (µm)
1	F1	1:1	361.45±0.540
2	F2	1:2	371.95±0.378
3	F3	1:3	381.17±0.435
4	F4	1:4	381.86±0.532
5	F5	1:5	383.24±0.435

Mean ±SD

Table 3. Percentage yield of mucoadhesive microballons

No.	Code	Drug:Polymer	Theoratical yield (gm)	Practical yield (gm)	Percentage yield (%)
1	F1	1:1	2	1.646	94.62±0.04
2	F2	1:2	3	2.564	94.23±0.11
3	F3	1:3	4	3.769	91.04±0.02
4	F4	1:4	5	4.552	85.47±0.04
5	F5	1:5	6	5.677	82.30±0.17

Mean ±SD

Table 4. Other parameters of mucoadhesive microballons

No.	Code	Drug:Polymer	Encapsulation efficiency (%)	Swelling rate (%)	% Mucoadhesion
1	F1	1:1	85.62± 0.02	42.5 ± 1.15	75.63 ± 0.018
2	F2	1:2	83.72± 0.03	55.9 ± 2.48	81.64 ± 0.110
3	F3	1:3	90.45± 0.02	58.9 ± 2.48	83.64 ± 0.111
4	F4	1:4	93.51± 0.01	59.9 ± 2.48	86.69 ± 0.198
5	F5	1:5	91.23± 0.04	61.5 ± 0.76	88.64 ± 0.198

Mean ±SD

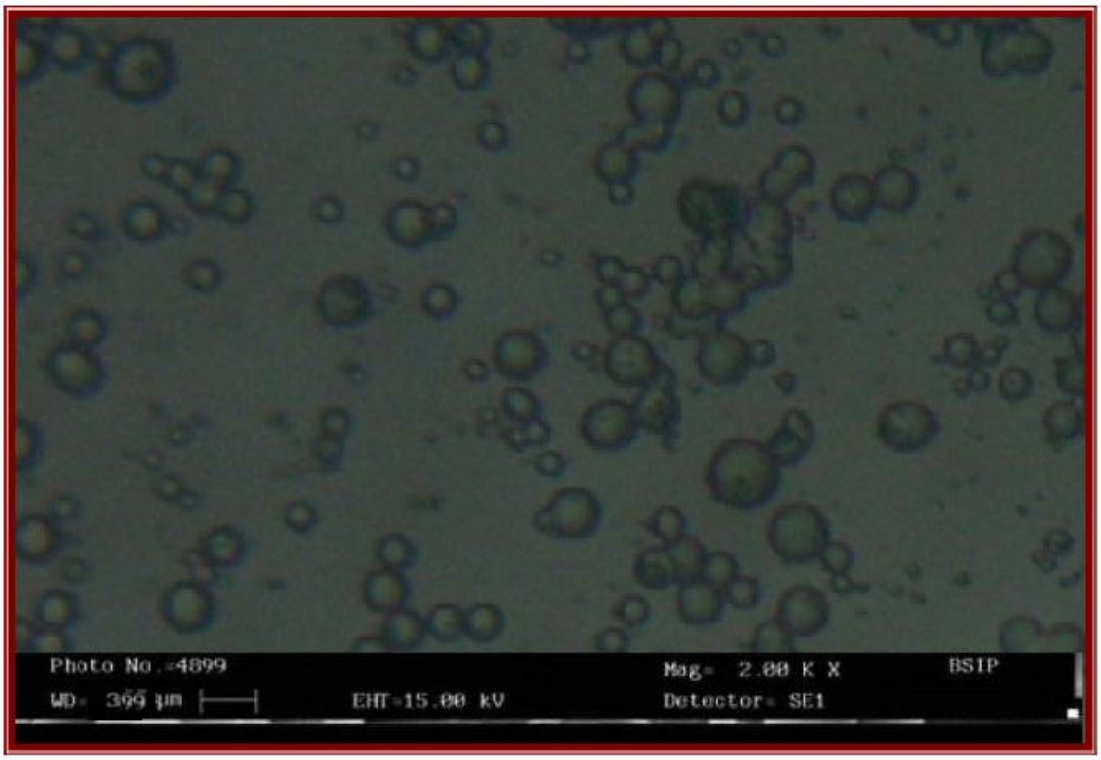

Figure 1. SEM photomicrograph of PAA-PVP microballons (100X).

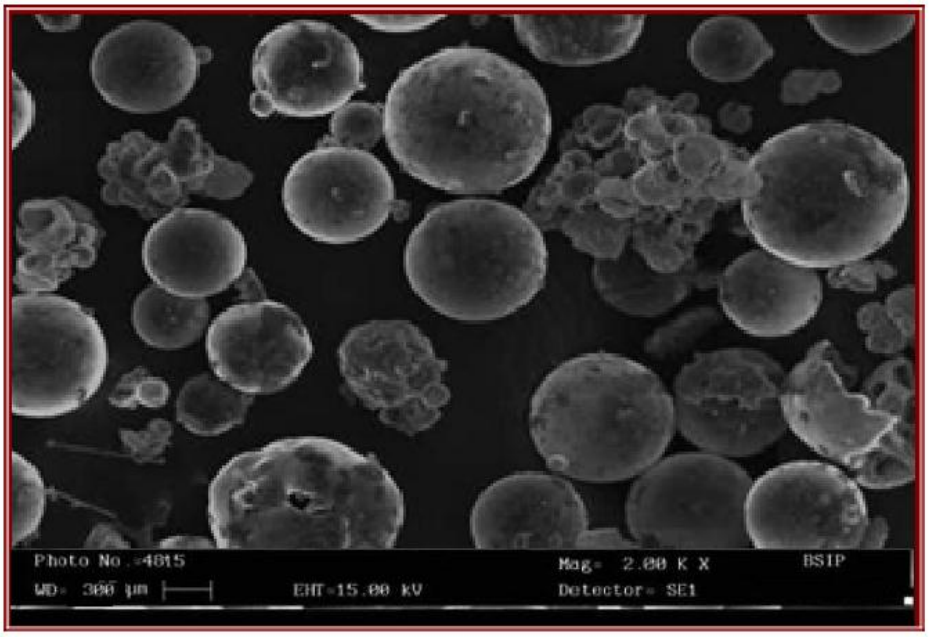

Figure 2. SEM photomicrograph of PAA-PVP microballons (650X).

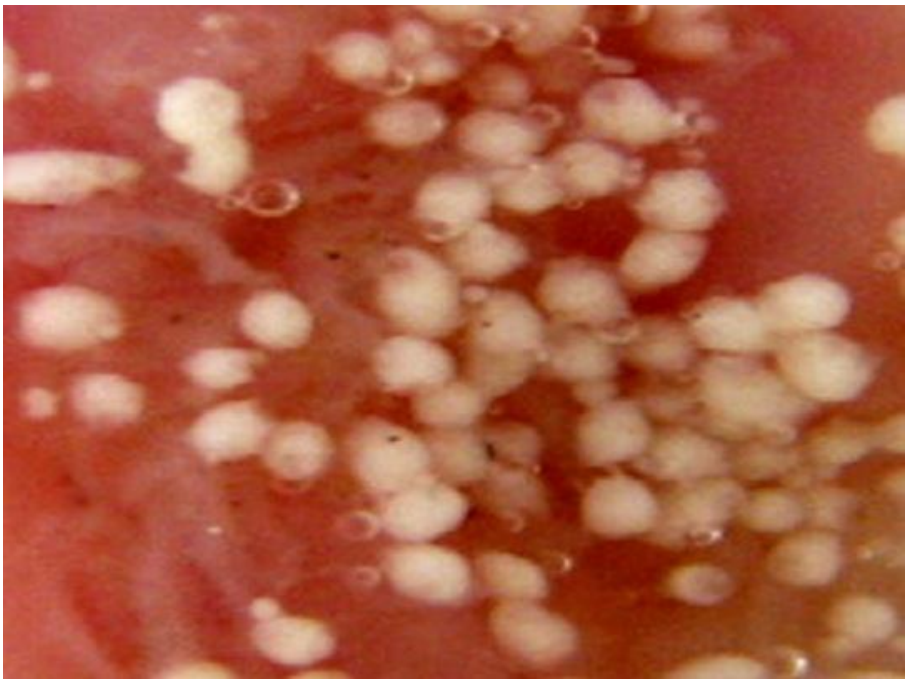

Figure 3. *In vitro* wash-off test of Nizatidin loaded mucoadhesive microballons after 10 h (Phase contrast microscope)

Table 5. *In vitro* drug release studies of mucoadhesive microballons

Time	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	4.71	3.39	0.781	0.571	0.322
2	13.21	10.39	3.45	2.45	1.23
3	18.68	16.5	13.23	10.23	4.67
4	35.67	29.34	21.27	16.46	11.34
5	45.27	37.56	26.56	22.34	18.45
6	53.25	49.54	38.34	31.45	26.56
7	66.34	58.45	48.34	41.78	38.78
8	76.54	72.23	58.34	52.04	49.87
9	88.74	84.46	69.87	63.34	59.03
10	95.37	91.61	81.26	79.67	71.23
11	98.12	96.01	91.36	90.23	81.23
12	99.99	99.34	99.21	99.01	89.17

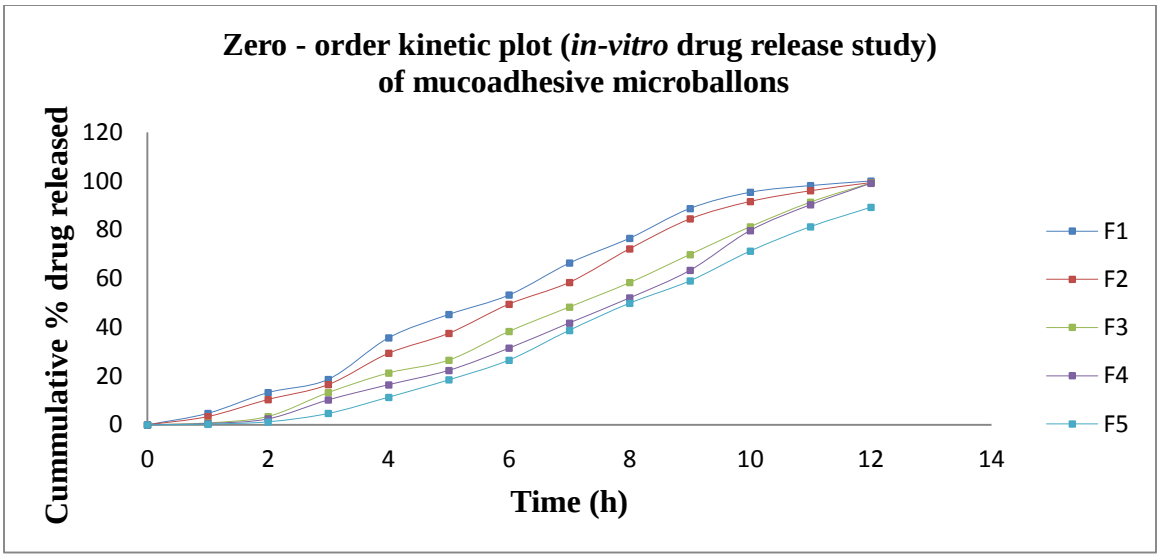

Figure 4. Zero order release kinetic studies of mucoadhesive microballons

RESULTS

The scanning electron photomicrograph (SEM) of optimized formulation reveals that the microsballons were spherical, discrete with smooth texture. The photomicrographs are shown in Figure 1-2.

The flow properties of prepared mucoadhesive microballons followed good to excellent flow properties during the filling in capsular form. The result was showed in Table 1. The average particle size of optimized formulation F1 – F5, was found to be 361.45±0.540 µm with 383.24±0.435. The result was showed in Table 2. The percentage yield of mucoadhesive microballons were varied due to addition of more amount of polymer from 94.62±0.04 to 82.30±0.17 %. The result indicated that, it will decrease due more time and speed for mixing. The result was shown in Table 3.

The drug entrapment efficiency was varied from 83.72± 0.03 to 93.51± 0.01. The swelling rate percentage 42.5 ± 1.15 to 61.5 ± 0.76 and percent mucoadhesion 75.63 ± 0.018 to 88.64 ± 0.198 % were increased due to more amount of polymer use during formulation of microballons. The result was showed in Table 4 and Figure 3. *In vitro* nizatidine release from optimized microballons (F1 – F4)were Carried out in SGF (pH 1.2by dissolution paddle apparatus type-II specified in the U.S.P. XXIII. Nearly

linear relationship between the % cumulative release of Nizatidine and time (h) was obtained for the 12 h. The result suggested that the microballons formulation follows a diffusion controlled drug release mechanism. The observations are recorded in Table 5 and graphically shown in Figure 4. The kinetic study of *in vitro* release interpretate that, the drug was retarded at the site of action i.e. peptic part of GIT for treatment of peptic ulcer by nizatidine hydrochloride.

The *in-vivo* antisecretory and ulcer protective activity of optimized microballons formulation (F5) was observed in pylorous-ligated rats. In present study group I of animals confirmed for acute ulcers produced by oral administration of absolute alcohol (2 ml/kg) and used for determination of volume of gastric juice, free acidity, total acidity and ulcer index (Figure 5).

The animals of group II, administered 10 ml plain drug solution (equivalent to 10 mg/kg nizatidine hydrochloride) 30 min prior oral dose of absolute alcohol (2 ml/kg). The result was found to have reduced the 34.09 % volume of gastric juice. The total acidity was reduced from 163.4 ±1.3 to 101.3±1.9 mEq /l. The free acidity was recorded 39.5±0.6 mEq /l and ulcer index reduced from 3.01 ± 0.25 to 1.94 ± 0.19.

The animal of group III administered 10 ml suspension of optimized microballons formulation (F5) (equivalent to 10 mg/kg nizatidine hydrochloride) 30 min prior oral dose of absolute alcohol (2 ml/kg) were found to have reduced the 56.81 % volume of gastric juice. The total acidity was reduced from 163.4 ±1.3 to 58.9±1.3 mEq /l. The free acidity was registered 19.4±0.2 mEq /l and ulcer index reduced from 3.01 ± 0.25 to 1.94 ± 0.19.Stability studies were carried out with optimized mucoadhesive microballons formulation F5, which was stored for a period of 60 days at 4±1 °C, 28±1 °C and 45±1 °C. The particle size of formulation was determined by optical microscopy using a calibrated ocular micrometer. The particle size of the mucoadhesive microballons was found to increase at 28±1 °C, which may be attributed to the aggregation of mucoadhesive microballons at higher temperature at 45±1 °C. The mucoadhesive microballons aggregated and a change in spherical shape to ellipsoidal shape with irregular mucoadhesive cavity of mucoadhesive microballons was observed i.e. these mucoadhesive microballons were unstable at higher temperature like 45±1°C. The observation are recorded in Table 7 and graphically shown in Figure 6.The selected optimized mucoadhesive microballons formulation (F5) was stored at 4±1 °C, 28±1 °C and at 45±1 °C and the residual drug content of the formulation was determined

after 15, 30 and 45 days. It was observed that the formulation stored at 4±1 °C and 28±1 °C was quite stable as fewer drugs was degraded on storage for 45 days while it was quite unstable at 45±1 °C for 45 days. The observation are recorded in Table 8 and graphically shown in Figure 7. Therefore it is clear from this study that the optimized microballons formulation (F5) able to protects gastric mucosa from ulceration for a longer period of time.

Table 6. Data for ulcer protective activities of optimized microballonsformulation (F5)

No	Formulation code(s)	Dose	Volume of gastric juice (ml/100g)	pH	Acidity (mEq/l/100g)		Ulcer index (mm)
					Free	Total	
1	Control (absolute alcohol)	(2 ml/kg)	4.4 ± 0.3	2.1±0.4	70.1±0.9	163.4±1.3	3.01±0.25
2	Plain drug solution	(Equivalent to 10mg/kg nizatidine hydrochloride)	2.9±0.5	3.9±0.2	39.5±0.6	101.3±1.9	1.94±0.19
3	Microballons formulation (F5)	(Equivalent to 10mg/kg nizatidine hydrochloride)	1.9±0. 2	4.1±0.4	19.4±0.2	58.9±1.3	0.51±0.08

*****All values are expressed as mean ±SD (*n* = 5).

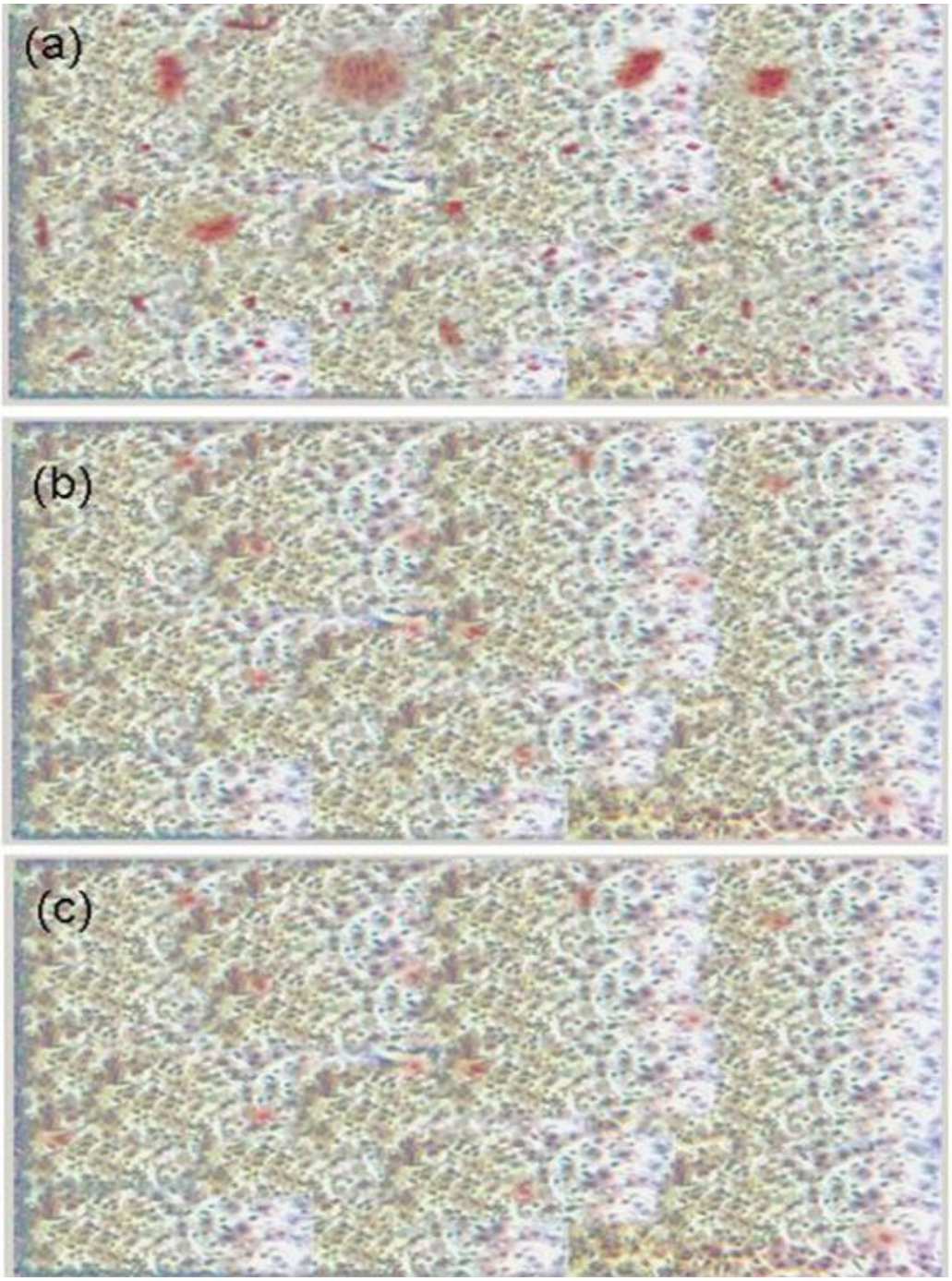

Figure 5. *In vivo* antisecretary and ulcer protective effect of optimized microballons formulation (F5) in absolute alcohol induce rats (Gastric mucosa of albino rat after 4 h administration with (a) Absolute alcohol (2ml/kg); (b) Administered plain drug solution; (c) Administered optimized microsballons formulation.

Table 7. Effect of particles size and structural integrity of optimized PAA-PVP microballons formulation stored at different temperature

No	Formulations code (s)	Storage Temperature	Particles size (µm)					Particles shape after 60days
			Initial	15 days	30 days	45 days	60 days	
1	F5	4±1°C	109.3±2.3	110.2 ±1.4	112.4 ±1.1	113.1 ±2.3	114.3 ±1.4	Spherical
		28±1°C	109.3±2.3	112.3 ±2.1	113.4 ±1.7	115.3 ±1.2	116.5 ±1.6	Nearly Spherical
		45±1°C	109.3±2.3	116.2 ±1.6	129.3 ±1.2	143.4 ±1.7	159.3 ±2.2	Ellipsoidal

Mean SD ± (n=3)

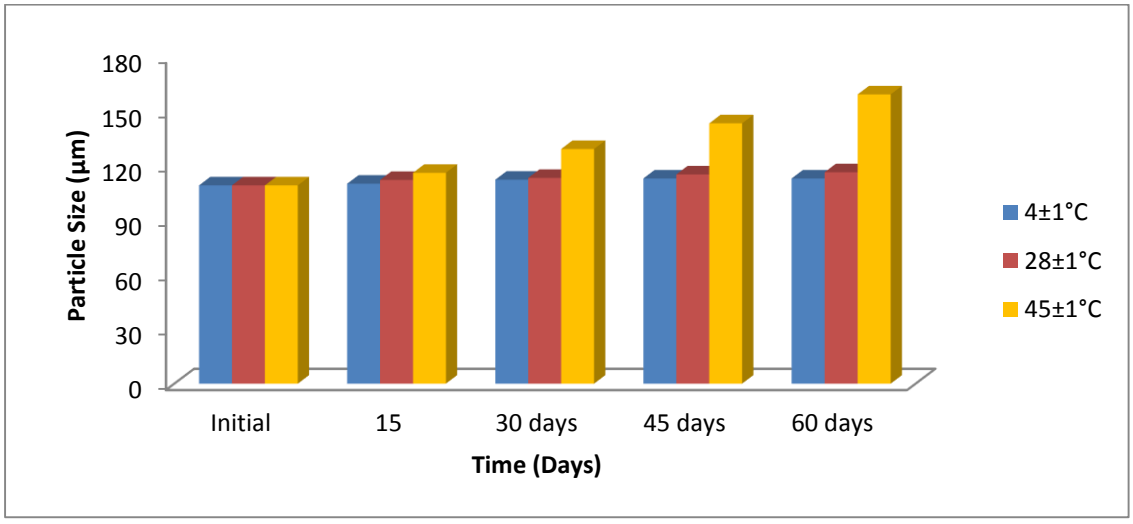

Figure 6. Effect of storage temperature on particle size of optimized mucoadhesive microballons formulation (F5)

Table 8. Percent residual drug content in optimized mucoadhesive microballons formulation (F5)

No.	Time in days	% Residual drug content		
		4±1°C	**28±1°C**	**45±1°C**
1	Initial	100	100	100
2	15	98.3 ± 1.2	96.8 ± 2.7	92.2 ± 2.2
3	30	96.2 ± 2.5	93.2 ± 2.3	86.4 ± 2.6
4	45	92.2 ± 2.3	84.7 ± 2.1	78.4 ± 2.9
5	60	91.1± 1.3	81.6 ± 1.1	74.2 ± 2.1

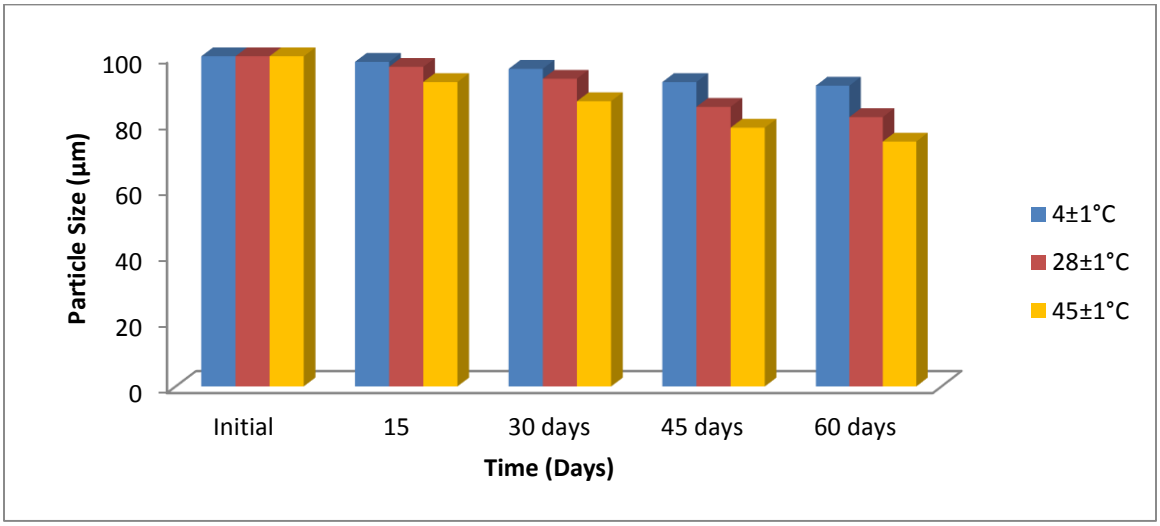

Figure 7. Percent residual drug content in optimized mucoadhesive microballons formulation (F5) stored at different temperatures.

DISCUSSION

The PAA-PVP mucoadhesive microballons were prepared with interpolymeric complexation process. The solvent was evaoporated for the preparation of microballons. The microballons characterize with a various number of parameters. The scanning electron photomicrograph (SEM) exposed spherical, discrete with smooth texture of microballons. The flow properties of prepared mucoadhesive microballons followed good to excellent with maximum percentage yield of mucoadhesive microballons. The drug entrapment efficiency was varied from 83.72± 0.03 to 93.51± 0.01. The swelling rate percentage and percent mucoadhesion were improved with suitable amount of polymer for formulation of microballons. The *in vitro* nizatidine release from optimized microballons was carried out in SGF (pH 1.2 by dissolution paddle apparatus type-II specified in the U.S.P. XXIII. The result suggested that the microballons formulation follows a diffusion controlled drug release mechanism and retarded at the site of action i.e. peptic part of GIT for treatment of peptic ulcer by nizatidine hydrochloride. The *in-vivo* antisecretory and ulcer protective activity of optimized microballons formulation (F5) was observed in pylorous-ligated rats. The stability studies of particle size of the mucoadhesive microballons was found to increase. This may be recognized to the aggregation of mucoadhesive microballons at higher temperature. Therefore it is clear from this study that the optimized microballons formulation (F5) able to protects gastric mucosa from ulceration for a longer period of time.

CONCLUSION

Oral route of drug administration is vastly accepted owing to advantages over other route of administration like ease of administration, patient compliance and flexibility in formulation, etc. Oral dosage forms advancement are continue in immediate release dosage form to site specific drug delivery. Mucoadhesive microballons is one of oral dosage forms, which make available the prospect to increase the bioavailability of drug. In present study mucoadhesive microballons of nizatiine an antiulcer drug was prepared by using combination of PAA-PVP polymer-polymer complexation by using solvent diffusion method. The prepared mucoadhesive microballons maintained the

therapeutic absorption windows of nizatidine by controlling discharge rate through extended the gastric emptying time. The delivery system offered the possibility of enhancing the bioavailability and controls the release of nizatidine show evidence of absorption window by prolonging the gastric emptying time of the dosage form.

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