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DEVELOPMENT AND *IN VITRO* CHARACTERIZATION OF ACETOHYDROXAMIC ACID FLOATING MICROBALLOONS

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ABSTRACT

In the present work, floating microballoons of Acetohydroxamic acid using Eudragit RS 100, Eudragit S 100, HPMC K4M, Ethylcellulose as polymers were formulated to deliver Acetohydroxamic acid via oral route. The results of this investigation indicate that, solvent evaporation method can be successfully employed to formulate Acetohydroxamic acid microballoons. The in-vitro release studies demonstrated that microballoons of Acetohydroxamic acid prepared using Eudragit RS 100 along with Eudragit S 100 in 1:1 ratio (formulation F5) shown maximum amount of drug release, hence it is considered as the optimized formulation. The in vitro release kinetics revealed that the optimized formulation (AHF5) release the drug in zero order manner based on the regression values of kinetic models.

KEY WORDS

Acetohydroxamic acid, Floating microballoons, Solvent evaporation method, Gastric residence time, Floating, Gastroretentive drug delivery systems.

INTRODUCTION:

Microballoons are gastro retentive drug-delivery systems with non-effervescent approach. Microballoons (Hollow microsphere) are in strict sense, empty particles of spherical shape without core. These microballoons are characteristically free flowing powders comprising of proteins or synthetic polymers, ideally having a size less than 200 micrometer. Microballoons are considered as one of the most favourable buoyant systems with the unique advantages of multiple unit systems as well as better floating properties, because of central hollow space inside the microsphere. The drug, acetohydroxamic acid (AHA) inhibits cytoplasmof bacteria, which plays an important role in the chemotactic motility of H. pylori. As AHA is a small molecule (molecular mass, 75.07), it can permeate intact bacterial cells and effectively inhibit the urease activity of H. pylori. Freely diffusible AHA inhibits over 95% of urease activity after 10 min (10, 11). Floating microballoons can greatly improve the pharmacotherapy of stomach through local drug release. Thus, eradicating Helicobacter pylori from sub-mucosal tissue of the stomach are useful in the treatment of peptic ulcers, chronic gastritis, gastrooesophageal reflux diseases etc. Thus, Floating microballoons of acetohydroxamic acid were formulated for treatment of Helicobacter pylori infection.

MATERIALS AND METHODS

Acetohydroxamic acid, Eudragit RS 100, Eudragit S 100, HPMC K4M, Ethylcellulose, Ethanol, Dichloromethane chemicals of Laboratory grade from SD Fine chemicals Pvt Ltd were used.

A. Formulation Development

i) Preliminary studies for screening of polymers:

Preliminary trials of floating microballoons were performed and the excipients which are suitable for the

preparation of floating microballoons were selected based on percentage yield, buoyancy and entrapment efficiency. Based on preliminary trials different polymers such as Eudragit RS 100, Eudragit S 100, Ethyl cellulose and HPMC K4M in different ratios alone or in combinations were selected to formulate floating microballoons.

ii) Solubility studies:

The equilibrium solubility of Acetohydroxamic Acid was measured in 0.1M hydrochloric acid (pH of 1.2), phosphate buffer of pH 6.8, distilled water and pH 7.4 respectively in order to determine its solubility. Excess amounts of the drug were added to 50 ml-stoppered conical flasks (n=3). The flasks were shaken mechanically at 37°C±0.5°C for 24, hrs in a horizontal shaker (HS 501 Digital, IKA-Labortechnik, and Staufen, Germany). After 2, days of equilibrium, aliquots were withdrawn and filtered (0.22 µm pore syringe filter). Then, the filtered samples were diluted with an appropriate amount of dissolution medium and assayed by UV-spectrophotometer at 299nm for Acetohydroxamic acid.

B. Drug-Excipient Compatibility study:

i) Differential scanning calorimetry

The physicochemical compatibilities of the drug and the excipients were tested by differential scanning calorimetric (DSC) analysis. DSC thermograms of the drug alone, drug-excipient physical mixture and optimized formulation were derived from DSC (Perkin-Elmer,4000). The instrument was calibrated with an indium standard. The samples (2-4 mg) were heated (20-300 °C) at a constant scanning speed (10 °C/min) in sealed aluminum pans, using nitrogen purged gas.

ii) FTIR spectroscopy:

Compatibility studies were carried out to know the possible interactions between Acetohydroxamic acid and excipients used in the formulation. Physical mixtures of drug and excipients were prepared to study the compatibility. Drug-polymer compatibility studies were carried out using FTIR spectrophotometer (Schimadzu) by KBr pellet technique. IR spectrum of pure drug and polymers were seen in between 4000-400 cm-1.

C. Formulation Method

Formulation of floating microballoons:

The floating microballoons were formulated by solvent evaporation method. (Senthilkumaran K *et al.,* 2011; Chouhan M *et al.,* 2013). A Schematic representation of method followed in the preparation of floating microballoons is shown in the Figure 1.

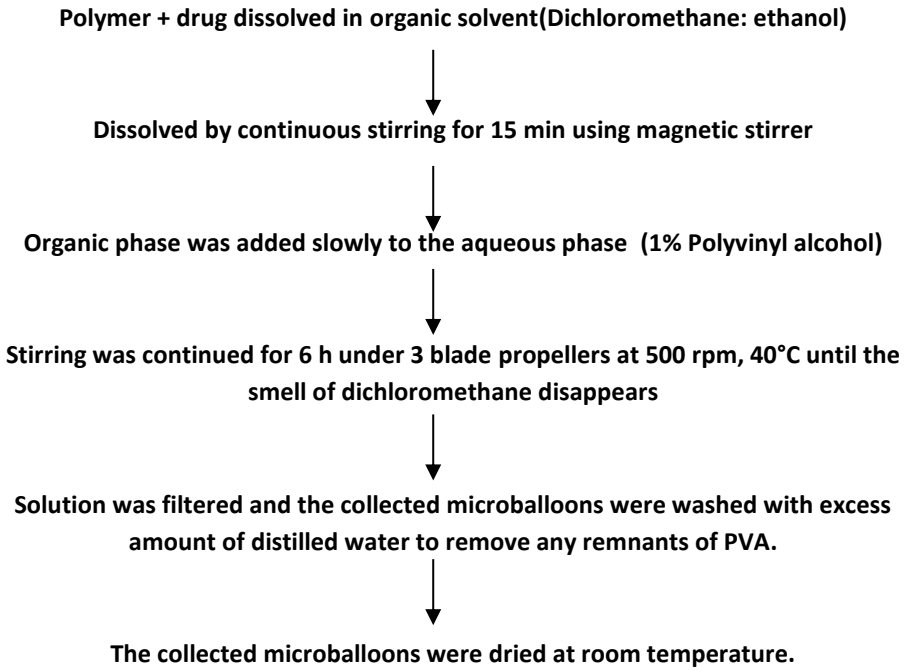

Figure: 1 A Schematic representation of method followed in the preparation of floating microballoons by solvent evaporation technique.

Floating microballoons of Acetohydroxamic Acid were successfully formulated by solvent evaporation technique. All the possible experimental trials were successfully carried out and were further evaluated.

Table 1: Composition of floating microballoons of acetohydroxamic acid

S. No	Materials	AH F1	AH F2	AH F3	AH F4	AH F5	AH F6	AH F7	AH F8	AH F9	AHF 10	AHF 11	AHF 12	AHF 13	AHF 14	AHF 15
1	Drug (mg)	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
2	Eudragit RS 100	250	250	250	500	500	500	250	250	500	500	NA	NA	NA	NA	NA
3	Eudragit S 100	250	500	750	250	500	750	750	750	500	500	NA	NA	NA	NA	NA
4	HPMC K4M	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	250	250	250	500	500
5	Ethylcellulose	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	250	500	750	250	500
6	Ethanol	15	15	15	15	15	15	20	10	20	10	15	15	15	15	15
7	Dichloromethane	15	15	15	15	15	15	10	20	10	20	15	15	15	15	15
Ratio of Drug to Polymer		1:1:1	1:1:2	1:1:3	1:2:1	1:2:2	1:2:3	1:1:3	1:1:3	1:2:2	1:2:2	1:1:1	1:1:2	1:1:3	1:2:1	1:2:2
Ratio of Solvent		1:1	1:1	1:1	1:1	1:1	1:1	2:1	1:2	2:1	1:2	1:1	1:1	1:1	1:1	1:1

D. Evaluation Methods

i) Micromeritic properties

Microballoons are evaluated by their micromeritic properties such as particle shape and size, bulk density, tapped density, Hausner's ratio and flow properties which is determined by carr's index and angle of repose.

ii) Particle size measurement

Particle size of prepared microballoons was measured using an optical microscope, and the mean particle size was calculated by measuring 100 particles with the help of a caliberated ocular micrometer (Patel T *et al.,* 2013).

iii) Scanning electron microscope (SEM)

The surface morphology and surface characteristics of best formulation were carried out by Scanning Electron Microscope (SEM). Microballoons were scanned and examined under Electron Microscope connected with fine coat, Ion sputter. The sample was loaded on copper sample holder and sputter coated with carbon followed by gold (Gadad A *et al.,* 2011).

iv) Tapped density

Tapped density and compressibility index are calculated by measuring the change in volume using a bulk density apparatus; angle of repose is determined by fixed funnel method.

The compressibility/carr's index was calculated using following formula:

$$I = V_b - V_t / V_b \times 100$$

Where, V_b is the bulk volume and V_t is the tapped volume. The value given below 15% indicates a powder with usually give rise to good flow characteristics, whereas above 25% indicate poor flow ability. Angle of repose of the micro balloons are determined by the fixed funnel method.

v) Percentage yield

The prepared microballoons of all batches were accurately weighed. The weight of prepared microballoons was divided by the total amount of all the excipients and drug used in the preparation of the microballoons, which give the total percentage yield of floating microballoons (Gadad A *et al.,* 2011). It was calculated by using following formula,

Percentage yield =

Actual yield of product/Total weight of excipients and drug

vi) Entrapment efficiency

The amount of entrapped drug in the microballoons was calculated based on the total drug content and the unentrapped drug of the floating microballoons. The unentrapped drug was determined by taking one dose equivalent of floating microballoons and washed with 0.1N HCl to remove the free drug on the surface. The drug content of microballoons was determined by dispersing 50 mg formulation (accurately weighed) in 10 ml 0.1 N HCl, followed by agitation with a magnetic stirrer for 12 h to dissolve the polymer and to extract

the drug. Both the solutions of unentrapped drug and total drug were filtered through a whatman filter, the drug concentration was determined spectrophotometrically at 299nm by making desired dilution with 0.1N HCl (Gadad A *et al.,* 2011). Percentage entrapment efficiency was calculated as follows

% Entrapment efficiency = (Total drug content – unentrapped drug) *100/ Total drug content

***vii) In vitro* buoyancy:**

Microballoons were spread over the surface of a USP dissolution apparatus type II filled with 900 ml of 0.1 N HCl. The medium was agitated with a paddle rotating at 50 rpm for 12 h. The floating and the settled portions of microballoons were recovered separately. The microballoons were dried and weighed. Buoyancy percentage was calculated as the ratio of the mass of the microballoons that remained floating and the total mass of the microballoons (Mastiholimath VS *et al.,* 2008).

% Buoyancy = Qf *100/ (Qf + Qs)

Where Qf and Qs are the weight of the floating and the settled microballoons respectively.

viii) Drug content:

Drug contentof each formulation equivalent to unit dose (250mg) was determined by spectrophotometrically. Each formulation was taken and finely powdered in glass mortor and dissolved in solution of 0.1 N HCl for 6 hours. Solution was then filtered and absorbance was noted at 299 nm.

***ix) In vitro* release study:**

The drug release study was carried out using USP dissolution apparatus type XXIII basket type dissolution apparatus at 37 ± 0.5 ºC and at 50 rpm using 900 ml of 0.1N HCl (pH 1.2) as a dissolution medium. 5 ml of sample solution was withdrawn at predetermined time intervals up to 12h and the samples were filtered through whatman filter paper, diluted suitably and analyzed spectrophotometrically with UV-Visible spectrophotometer at a maximum absorbance wavelength of 299nm. Equal amount of fresh dissolution medium was replaced immediately after withdrawal of the test sample (Dhoka MV *et al.,* 2010). The dissolution studies were performed and the average percentage drug release was calculated.

x) Drug release kinetic studies:

The mechanism of release was determined by fitting the release data to the various kinetic equations such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas and finding the R^2 values of the release profile corresponding to each model (Nagabandi VK *et al.,* 2013). using PCP Disso v3 software.

xi) Stability studies:

Microballoons were hermetically sealed in glass bottles and stored for 3 months at 4±0.5°C, room temperature and 40±1°C and 75% RH as per ICH guidelines. After every month, one bottle was used for evaluation. The microballoons were evaluated for physical appearance, drug content and percentage of drug release after12 hr.

RESULTS AND DISCUSSIONS:

i) Solubility studies

Saturation Solubility of pure drug was determined in different solvents by and the values obtained are given in the Table 3 and shown in figure 2. From the results obtained it was observed that the drug is very freely soluble in distilled water. Solubility was found to be comparatively lesser in 0.1N HCl and the solubility is increased with increase in pH.

Table 2: Saturation solubility studies of acetohydroxamic acid

Solvent	Solubility (mg/ml)			
	1	2	3	Average
Double distilled water	1022	1023	1020	1021.7
0.1N HCl	330	353	345	342.7
pH 6.8 phosphate buffer	650	675	682	669.0
pH 7.4 phosphate buffer	1123	1124	1138	1128.3

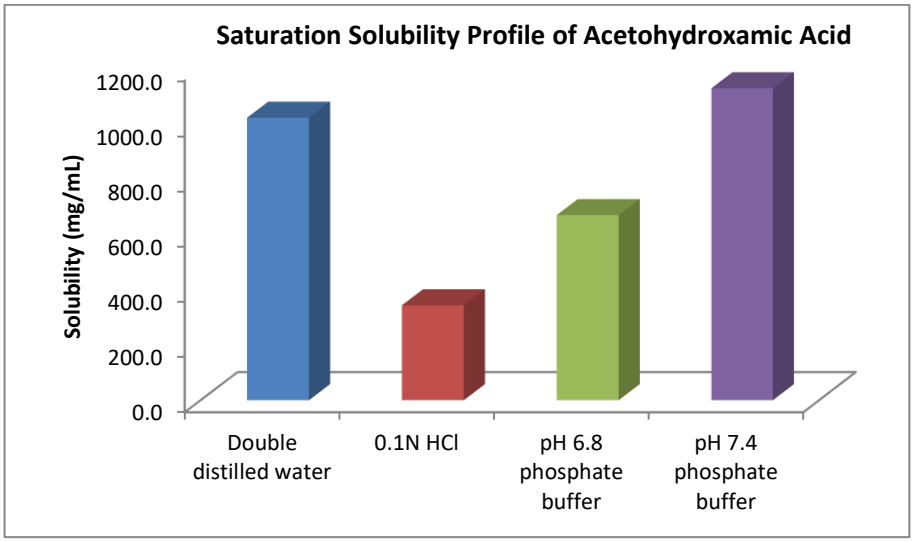

Figure 2: Saturation Solubility Profile

ii) Drug-Excipient Compatibility study

DSC thermogram of pure drug is shown in figure---. Endothermic peak was observed at 78.3°C indicates the drug melting point for pure drug. The shift in the endothermic peak of drug was very less in physical mixture of microballoons, which indicates that the drug and polymers used were compatible with one another.

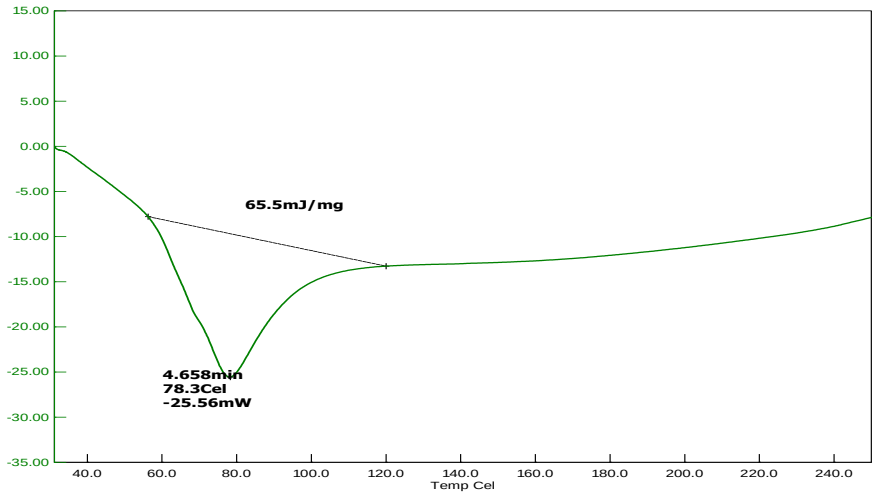

Figure 3: DSC thermogram of pure drug

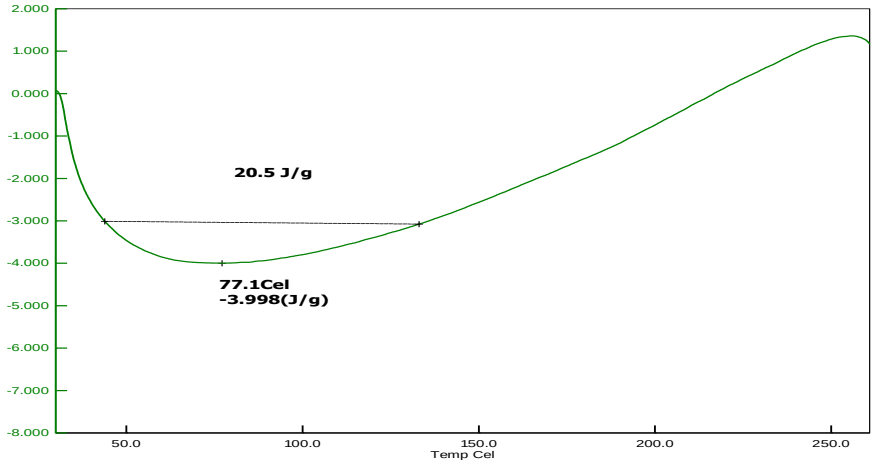

Figure 4: DSC thermogram of physical mixture

The drug-excipient compatibility study was done by Fourier transform infrared (FT-IR) spectroscopy study. The prominent peaks of Acetohydroxamic acid pure drug (Fig. 5) were shown at 3184.25cm^{-1} (due to –N-H), 1536.44cm^{-1} (due to C=O),1490cm^{-1} (due to –C-H) and1073 cm^{-1}. These prominent peaks of drug were also observed in the IR spectrum of optimized formulation of drug (Fig. 6) with various excipients, which indicates that, the drug was not interacted with the polymers used in the study which confirms the stability of the drug.

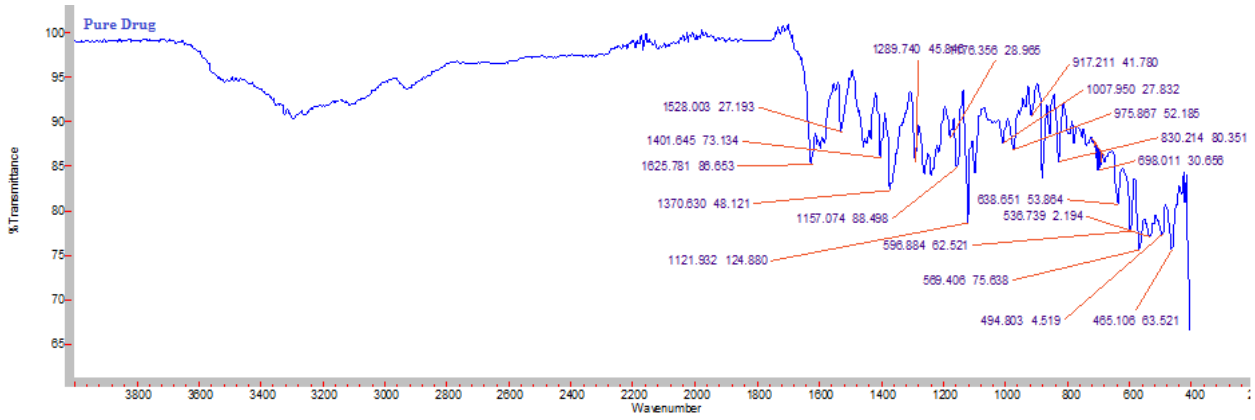

Figure 5: FTIR of Pure Drug

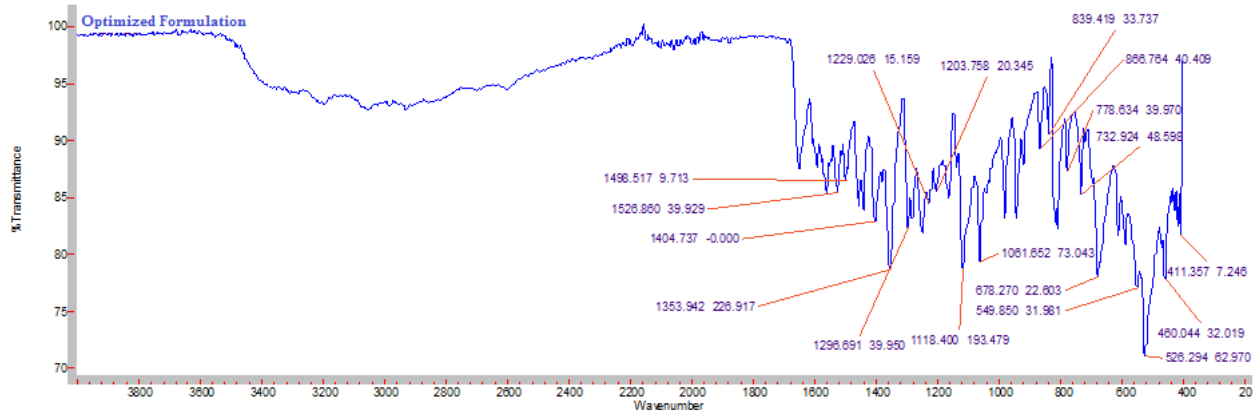

Figure 6: FTIR of Optimized formulation

iii) Percentage yield

The floating microballoons were prepared and percentage yield was calculated for all the formulations. The results of % yield is shown in the table 3. The percentage yield was in the range of 60-90 % for all the formulations. It was found to be less than 70% yield with ethyl cellulose and HPMC K4M and for optimized formulation the yield was around 80 %.

iv) Entrapment Efficiency

The entrapment Efficiency of floating microballoons of Acetohydroxamic Acid was calculated and the results are depicted in the table 3. The entrapment efficiency was in the range of 60-90 % for all the formulations and was found to be 89.6%for optimized formulation. The entrapment efficiency was low with formulations prepared with ethylcellulose and HPMC K4M. There was no effect of solvent ratio was observed in the % Entrapment Efficiency.

***v)In vitro* Buoyancy**

The percentage buoyancy was calculated for all the formulations and it was found that all the formulations were able to float on the dissolution medium (0.1N HCl) over a period of 12h. Even after 12h of agitation of the dissolution medium, the microballoons continued to float without any apparent gelation. The high buoyancy of the microballoons is mainly due to the presence of

pores and cavities which were formed during solvent evaporation. The percentage buoyancy was slightly less with formulations prepared with ethylcellulose and HPMC K4M and decreased as the concentration of the polymers increased. This is because of high viscosity of the polymer solution which in turn is the reason for the less formation of pores and cavities in microballoons during solvent evaporation.The results of *in vitro* buoyancy studies are shown in table 3. The percentage buoyancy was in the range of 60-90 % for all the formulations and was found to be 85.5% for optimized formulation.

vi) Drug content:

Drug content of all the prepared formulations was found to be within the acceptable range of 90.0 - 110.0%. Values obtained are given below

Table 3: Physico chemical properties of prepared microballoons

Formulation Code	% Yield	%EE	%Buoyancy	Drug content (%)
AHF1	85.2	82.5	75.8	98.8
AHF2	84.6	92.1	82.5	98.9
AHF3	83.7	93.4	83.1	97.8
AHF4	75.9	91.5	86.5	100.2
AHF5	79.7	89.6	85.5	100.3
AHF6	82.1	92.7	85.6	99.8
AHF7	82.5	93.7	85.4	99.6
AHF8	83.4	86.5	82.4	100.2
AHF9	82.4	94.5	78.3	101.2
AHF10	75.4	92.6	79.5	100.5
AHF11	69.8	68.9	65.4	99.8
AHF12	65.4	64.5	64.5	99.7
AHF13	64.2	62.4	63.2	99.7
AHF14	63.2	61.2	62.4	98.9
AHF15	61.4	60.2	61.5	97.8

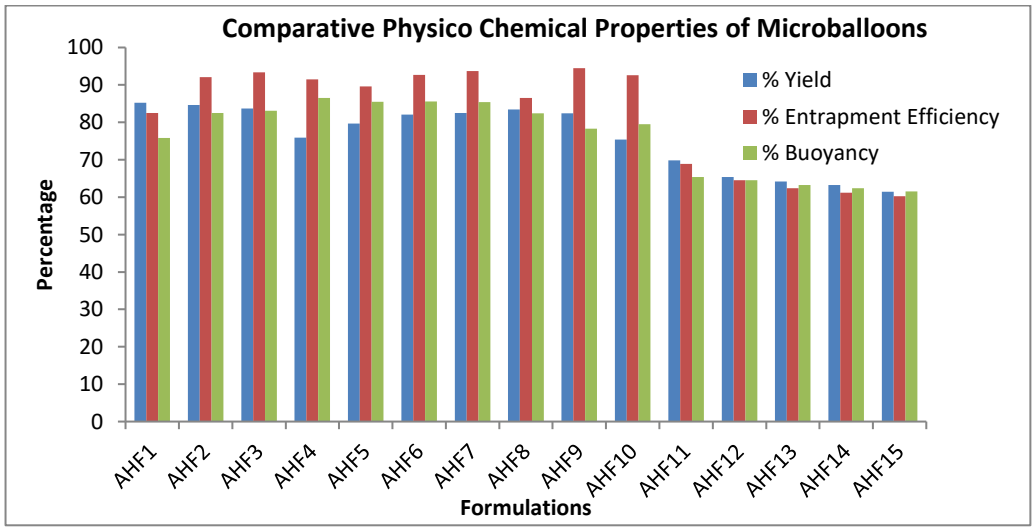

Figure 7: Comparative physic chemical properties of microballoons

vi) Particle size measurement

The particle size was measured using caliberated optical microscope and the average particle size of floating microballoons was found to be in the range of 120-180µm as shown in the table 4. It was observed that, on increasing the polymer amount, the average particle size increased. This may be due to diminished shearing efficiency at higher concentration of the polymer (higher viscosity).

vii) Scanning electron microscope (SEM)

The surface morphology of the floating microballoons was studied using scanning electron microscope (SEM). The surface morphology of optimized formulation (AHF5) was shown in the figure 8. From the SEM

micrographs it is apparent that the acetohydroxamic acid loaded microballoons were predominately spherical in appearance. The surface was observed to be smooth, dense and less porous, whereas the internal core was highly porous and irregular with numerous depressions that are expression of evaporation of water, ethanol and dichloromethane (Fig. 8). The less porous outer surface and highly porous internal surface supported controlled release of drug from the microballoons and good buoyancy

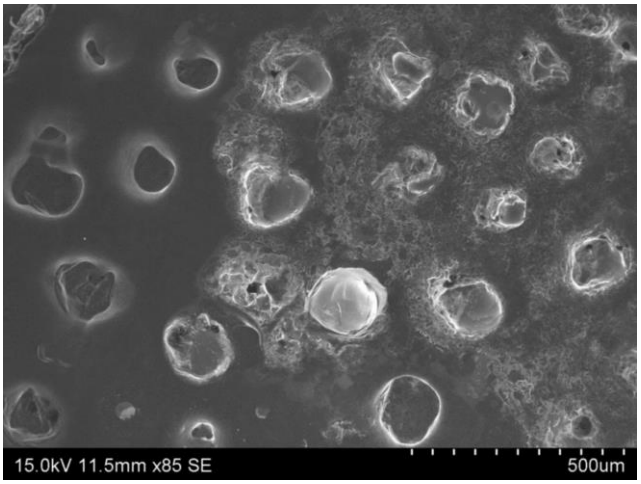

Figure 8: Scanning electron micrographs of floating microballoons

viii) Tapped density & Bulk density

The measured tapped density bulk density, compressibility index and angle of repose are within the limits which indicates good flow properties of microballoons.

Table 4. Observations of in vitro evaluation parameters of floating microballoons

Formulation	Mean Particle Size (µm)**	Bulk Density*	Tapped Density*	Compressibility Index*	Angle of Repose*
AHF1	135.35±2.35	0.72± 0.11	0.65± 0.02	9.72± 1.21	15.2± 1.2
AHF2	145.35±3.36	0.74± 0.21	0.64± 0.04	13.51± 1.25	16.1± 1.4
AHF3	157.45±5.21	0.76± 0.13	0.67± 0.05	11.84± 2.21	17.2± 1.5
AHF4	146.38±1.36	0.8± 0.12	0.69± 0.06	13.75± 1.24	15.4± 1.4
AHF5	158.29±3.56	0.76± 0.22	0.65± 0.02	14.47± 1.34	15.6± 2.1
AHF6	129.45±5.36	0.76± 0.12	0.64± 0.04	15.79± 1.21	19.8± 3.4
AHF7	148.35±3.67	0.79± 0.02	0.65± 0.02	17.72± 2.35	15.7± 3.5
AHF8	153.26±5.67	0.72± 0.03	0.68± 0.05	5.56± 1.25	15.5± 2.5
AHF9	138.37±2.48	0.71± 0.04	0.67± 0.01	5.63± 1.20	15.3± 2.3
AHF10	135.31±2.46	0.76± 0.04	0.68± 0.02	10.53± 2.12	15.7± 1.2
AHF11	125.37±2.45	0.75± 0.05	0.69± 0.04	8.00± 1.26	15.6± 1.1
AHF12	129.39±2.46	0.74± 0.12	0.66± 0.02	10.81± 2.21	16.2± 1.3
AHF13	164.35±2.55	0.76± 0.02	0.67± 0.01	11.84± 2.15	16.8± 1.2
AHF14	172.35±3.56	0.77± 0.03	0.69± 0.02	10.39± 1.26	15.9± 2.3
AHF15	129.35±3.26	0.81± 0.05	0.67± 0.05	17.28± 3.21	15.9± 2.2

*** All values represent Mean ± SD; n=3**

**** All values represent Mean ± SD; n=100**

ix) *In vitro* drug release study

Dissolution studies of all the formulations were carried out using USP dissolution apparatus XXIII basket type dissolution apparatus. The dissolution profiles were compared among different formulations. The cumulative percentage drug release was decreased with increase in the polymer concentration. Based on the results of *in vitro* drug release studies it was found that

AH F5 has shown 100% drug release for 12hr sustained manner with zero order kinetics. The results of the *in vitro* drug release studies are shown in the table 5 and the dissolution profile in the figure 4 to 6. The *in vitro* release kinetics revealed that the optimized formulation (AHF5) release the drug in zero order manner based on the regression values. Observed R^2 values, n values of the optimized formulation are shown in the table 6.

Table 5: % Drug Release Data of Microballoons

Time (Hr)	% Drug Release														
	AHF1	AHF2	AHF3	AHF4	AHF5	AHF 6	AHF7	AHF8	AHF9	AHF1 0	AHF 11	AHF 12	AHF 13	AHF 14	AHF 15
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	25.6 ±1.1	20.2 ±3.3	15.8 ±3.4	20.5 ±2.6	4.6± 5.2	4.2± 2.3	15.7 ±2.8	15.8 ±3.7	4.8± 2.4	5.2± 2.8	5.6± 2.8	4.5± 2.7	3.5± 3.2	5.8± 2.4	4.9± 3.4
1	42.9 ±5.2	35.6 ±4.4	25.9 ±4.2	35.9 ±3.8	8.5± 3.6	7.5± 3.9	24.6 ±3.5	25.6 ±3.9	8.8± 1.2	10.2 ±2.7	9.5± 6.4	8.5± 2.7	5.5± 1.6	10.2 ±2.4	9.2± 2.1
2	62.5 ±4.2	52.1 ±0.5	45.9 ±3.7	55.5 ±3.8	17.5 ±6.3	12.5 ±3.9	42.5 ±6.4	45.5 ±3.9	18.2 ±2.3	20.2 ±2.5	15.5 ±5.8	12.5 ±3.7	10.2 ±2.4	15.5 ±3.7	13.2 ±2.8
3	85.9 ±4.3	64.8 ±5.6	59.7 ±6.4	65.6 ±4.5	25.6 ±3.8	20.2 ±4.6	58.7 ±5.6	60.2 ±3.8	26.5 ±2.3	26.7 ±3.7	20.5 ±5.7	15.5 ±3.9	12.5 ±2.9	22.2 ±3.8	16.5 ±2.7
4	99.6 ±3.5	75.2 ±7.5	67.9 ±3.9	75.9 ±5.6	34.5 ±3.9	30.2 ±2.8	65.6 ±5.6	66.4 ±4.6	35.6 ±2.8	36.5 ±0.8	26.9 ±3.7	20.2 ±2.8	15.9 ±2.7	26.5 ±3.8	21.2 ±1.2
6	100. 2±2. 6	85.9 ±5.6	75.9 ±4.3	87.9 ±6.3	52.6 ±6.9	45.5 ±1.5	72.5 ±5.8	73.5 ±5.9	53.6 ±3.7	56.3 ±4.6	39.5 ±5.7	35.4 ±3.7	25.6 ±3.7	41.2 ±2.9	36.5 ±2.7
8	100. 1±3. 5	100. 2±3. 8	87.6 ±7.2	99.5 ±3.9	65.8 ±7.2	55.6 ±4.5	85.6 ±6.7	86.5 ±2.9	66.5 ±3.8	65.6 ±6.7	45.5 ±2.7	40.2 ±2.9	35.6 ±2.9	46.5 ±3.7	41.2 ±4.3
10	100. 3±0. 4	100. 1±4. 5	100. 2±3. 9	100. 2±6. 7	82.6 ±6.7	65.4 ±5.7	99.5 ±6.9	100. 2±2. 7	83.6 ±3.8	86.8 ±4.9	67.5 ±2.8	55.5 ±3.7	45.6 ±3.7	68.5 ±2.6	56.8 ±4.7
12	100. 2±0. 5	100. 2±3. 6	100. 1±3. 8	100. 2±6. 8	100. 1±3. 8	72.5 ±5.6	100. 1±5. 8	100. 1±3. 8	100. 1±2. 7	100. 3±5. 7	72.5 ±2.6	65.2 ±2.9	56.5 ±3.7	73.5 ±2.4	66.5 ±4.8

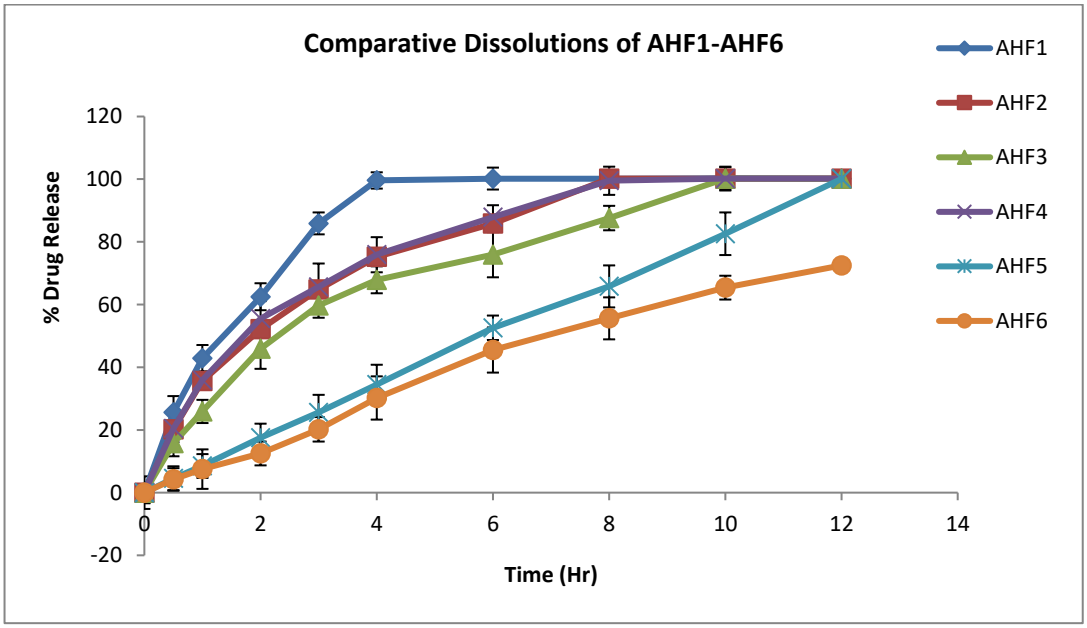

Figure 9: *In vitro* dissolution data for formulations AH1-AH6

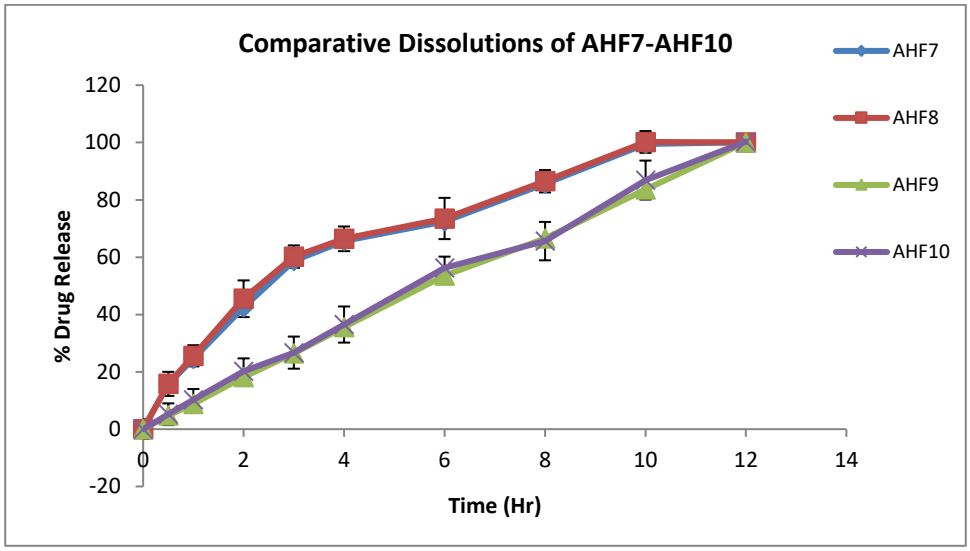

Figure 10: *In vitro* dissolution data for formulations AH7-AH10

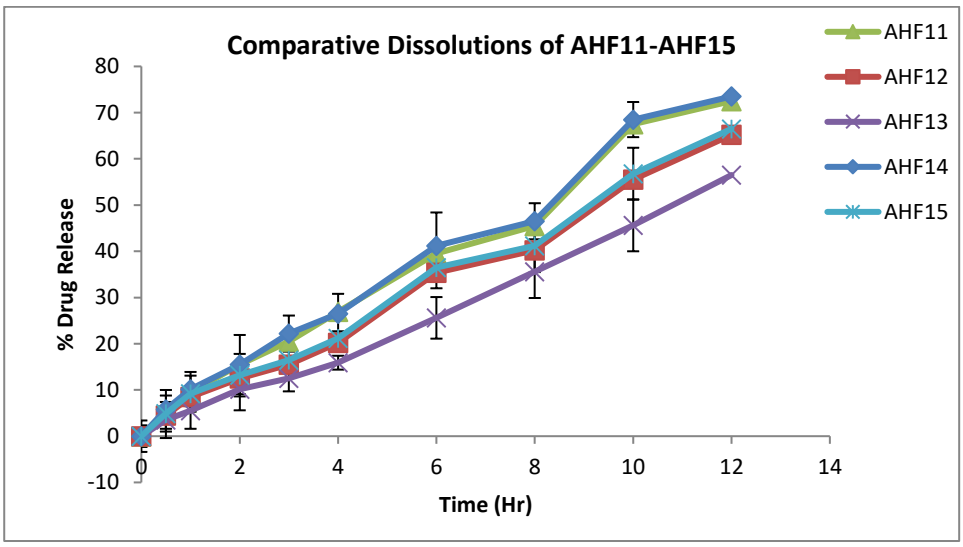

Figure 11: *In vitro* dissolution data for formulations AH11-AH15

x) Release Kinetics of Floating Microballoons

The *in vitro* release kinetics revealed that the optimized formulation (AHF5) releases the drug in zero order manner based on the regression values. Observed R^2 values, n values and the relative plots of the optimized formulation are shown in the Table-6.

Table 6: Drug release kinetics of floating microballoons

Formulation	Release Kinetics Parameters				
	Zero Order	First Order	Higuchi Model	Karse-Meyer Peppas	Hixon –Crowell
AHF1	0.791	0.994	0.92	0.909	0.983
AHF2	0.902	0.996	0.981	0.979	0.994
AHF3	0.935	0.995	0.991	0.987	0.992
AHF4	0.895	0.997	0.978	0.977	0.994
AHF5	0.999	0.986	0.964	0.999	0.989
AHF6	0.993	0.996	0.927	0.995	0.997
AHF7	0.944	0.993	0.991	0.989	0.992
AHF8	0.938	0.993	0.991	0.987	0.99
AHF9	0.999	0.981	0.967	0.999	0.99
AHF10	0.998	0.989	0.968	0.998	0.989

AHF11	0.994	0.986	0.964	0.993	0.99
AHF12	0.996	0.987	0.958	0.995	0.991
AHF13	0.997	0.998	0.949	0.998	0.991
AHF14	0.994	0.986	0.965	0.993	0.99
AHF15	0.902	0.996	0.981	0.979	0.994

xi) Stability studies

It was observed that the optimized formulation was found to be stable at storage conditions for three months

Formulation AHF5	Storage conditions								
	Physical change			Drug content (%)			% Cumulative Drug Release after 12 hrs		
	4±0.5°C	Room Temp	40±1°C	4±0.5°C	Room Temp	40±1°C	4±0.5°C	Room Temp	40±1°C
Initial	No	No	No	100.3	99.8	99.7	100.1±3.8	100.1±3.8	100.1±3.8
After 1 month	No	No	No	100.3	99.8	99.7	100.1±3.8	100.1±3.8	100.1±2.6
After 2 months	No	No	No	100	99.4	99.2	100±3.8	100±2.8	100
After 3months	No	No	No	99.8	99.2	99.0	100±1.8	100	99.9±3.8

CONCLUSION

In the present work, hollow floating microballoons of Acetohydroxamic acid were prepared by the solvent evaporation technique using different concentrations of polymers like Eudragit RS 100, Eudragit S 100, HPMC K4M, Ethylcellulose dispersed in ethyl alcohol and dichloromethane as a solvent system. Prepared floating microballoons showed significant floating ability, good buoyancy, and sustained drug release. In vitro drug release of microballoons was influenced by polymers concentration. From the percentage loading efficiency and in vitro drug release studies, it was observed that F5 formulation exhibits greater drug loading efficiency and sustained release behaviour. On fixing the in vitro drug release data of optimized formulation to various kinetic models, it was found that it exhibits the zero order of kinetics. Thus, Acetohydroxamic acid loaded floating microballoons can prove to be potential pharmaceutical dosage form for prolonging the gastric retention time of dosage form.

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