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Research Article

FORMULATION AND EVALUATION OF FLOATING TABLETS OF SALBUTAMOL SULPHATE

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Abstract: Salbutamol plasma half-life is 1.6 hours and need to administer frequently for better therapeutic activity. To overcome these problems it is required to deliver the single dose for a prolonged period of time. Salbutamol shows maximum solubility at acidic pH hence required to deliver the drug in the stomach is beneficial. The objective of the present work to develop sustained release floating tablets of the Salbutamol sulphate, which were designed to extend the gastric residence time and prolongs the drug release after oral administration. Different polymers such as HPMC K15, HPMC K100M, were used in order to get the desired sustained release profile over prolonged period of time. The release and floating property was depends on the polymer type and polymer proportion. The formulation prepared with HPMC K100M has more floating time then the formulation prepared with the HPMC K15 and HPMC K4M. The retardation of the polymer is in the following order HPMC K100M> HPMC K 15 M > HPMC K4M . FTIR study shows that there is no drug polymer interaction. This study has gives the preliminary idea about the development of floating drug delivery systems of Salbutamol sulphate with the use of gas generating agent.

Key words: Floating tablet, Salbutamol sulphate, *in vitro* bouncy, gastric residence time, HPMC polymer

1. INTRODUCTION:

Salbutamol sulfate is one of the widely used drug for the treatment of bronchial asthma, chronic bronchitis and emphysema[1]. The drug undergoes extensive first-pass metabolism and thus requires frequent administrations by oral route[2]. Salbutamol sulphate has a site-specific absorption in stomach and upper part of small intestine[3]. Reported oral bioavailability of salbutamol sulphate is ~ 40 %; due to extensive metabolism via intestinal sulphonation, first pass metabolism in liver & also degradation in colon[4]. The metabolism is due to extensive sulphonation in gut as compared to liver[5]. The half life of Salbutamol sulphate is about 1.6 hrs[6]. The relatively short term acting injectables and aerosol dosage forms of Salbutamol sulphate are recommended for instant relief in severe asthmatic attacks. Salbutamol sulphate is available in the form of aerosols. The recommended dose in adults and children is 2– 3 inhalations every 4–6 h. More frequent administration is not recommended. A gastroretentive drug delivery system may be advantageous over conventional oral dosage forms and inhalers due to its ability to maintain prolonged therapeutic concentrations in the systemic circulation. Asthma being a chronic disease, and as most of the patients suffer from nocturnal attacks[8], there is need for drug delivery systems which maintains therapeutic concentrations for long duration.

Floating drug delivery systems (FDDS) were first described by Davis in 1968. These systems were used to prolong the gastric residence time of drug delivery systems[7]. They remain buoyant in the stomach for prolonged period of time without affecting the gastric emptying rate of other contents[9]. FDDS is suitable for drugs with an absorption window in the stomach or the upper small intestine[10], for drugs which act locally in the stomach[11] and for drugs that are poorly soluble or unstable in the intestinal fluid[12]. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability[13]. FDDS or hydrodynamically balanced systems have a bulk density lower than gastric fluid and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. Based on the mechanism of buoyancy, two distinctly different technologies, *i.e.* non-effervescent and effervescent systems, have been used in the development of FDDS. The effervescent system uses matrices prepared with swellable polymers and effervescent components *e.g.* sodium bicarbonate and citric acid or stearic acid. In non-effervescent FDDS, the drug mixes with a gelforming hydrocolloid, which swells in contact with gastric fluid after oral administration to maintain a relatively stable shape and a bulk density of less than unity within the outer gelatinous barrier. The air trapped by the swollen polymer confers buoyancy to these dosage forms[14,15].The aim was to

increase bioavailability of Salbutamol sulphate and to study the effect of polymer, HPMC K4M, HPMC K15M, HPMC K 100M and Stearic acid on drug release profile.

2. MATERIALS AND METHODS

2.1 MATERIALS:

Salbutamol sulphate was obtained as a gift sample from Bari pharmaceuticals Lab, HPMC K15M,HPMC K4M, HPMC K100M, Sodium bicarbonate, Magnesium stearate, talc, Microcrystalline cellulose was obtained from Bari scientific traders. All other materials used are of analytical grade.

2.2 METHODOLOGY

1. Preformulation study

Preformulation studies were primarily performed to investigate the physicochemical properties of drug and to establish it

A) Selection of drug and other ingredients

Salbutamol sulphate which is Anti asthamatic agent was selected as model drug based on its physico-chemical, biological properties and also based on its suitability for gastro retentive drug delivery. HPMC K4M, HPMC K15M, HPMC K100M were selected as gastro retentive polymers.

Microcrystalline cellulose was selected as diluent and magnesium stearate, talc were selected for lubrication of formulati

B) Compatibility study

Fourier Transform Infrared (FTIR) spectrophotometer was used for analysis of samples to interpret the interact Sodium bicarbonate.

C) Solubility study of salbutamol sulphate

The solubility of drug was studied in solvents like 0.1 N HCl and distilled water. A 100 mg of drug was taken and solubilized in 100 ml of solvents separately and the solubility was observed. Then a suitable medium was selected depending upon the solubility results.

D) Construction of standard graph of salbutamol salphate

Calibration curve of Salbutamol sulphate was plotted in 0.1N HCl which was selected from solubility study. Salbutamol sulphate was estimated spectrophotometrically at λ_{max} of 276nm.

a) Preparation of 0.1N HCl:

8.5 ml of concentrated HCl was taken in 1000 ml volumetric flask and diluted with distilled water up to mark.

b) Preparation of standard solution:

First stock solution of Salbutamol sulphate was prepared by dissolving 100 mg in 100 ml of 0.1N HCl, so as to get a solution of 1000 µg/ml concentration. Then second stock solution was prepared by diluting 10 ml of stock solution to 100 ml with 0.1N HCl, so as to get a solution of 100 µg/ml. Accurately measured aliquot portions of second stock solution, like 5 ml, 10 ml, 15 ml, 20ml, 25 ml, were transferred in to 10 ml volumetric flasks and were diluted up to the mark with 0.1N HCl. Absorbance of each solution was measured at λ_{max} of 276 nm using 0.1N HCl as the blank, by UV-spectrophotometric method. A graph of concentration of drug versus absorbance was plotted.

E) Characterization of powder mixture

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many process variables involved in mixing and all these can affect the characteristics of blends produced. The following properties of powder blend were determined to ascertain the flow property.

a) Angle of repose:

It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ, is in equilibrium with the gravitational force.

The fixed funnel method was employed to measure the angle of repose. A funnel was secured with its tip at a given height (h) above a graph paper that is placed on a flat horizontal surface. The blend was carefully poured through the funnel until the apex of the conical pile just touches the tip of the funnel. The radius (r) of the base of the conical pile was measured. The angle of repose (θ) was calculated using the following formula:

$$\tan \theta = h/r$$

Where, θ = angle of repose
h = height in cm
r = radius in cm

Table 1: Pharmacopeial specifications for angle of repose

Angle of repose (θ)	Type of flow
< 25	Excellent
25 – 30	Good
30 – 40	Passable
> 40	Very poor

b) Bulk density:

Density is defined as the weight per unit volume. Bulk density, ρ_b is defined as the mass of

powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together.

The fixed amount of powder blend was introduced into a dry 10 ml cylinder, without compacting. The powder was carefully leveled without compacting and the unsettled apparent volume V_0 was read. The bulk density was calculated using the formula:

$$\rho_b = M / V_0$$

Where, ρ_b = Apparent bulk density
M = Mass of sample
V_0= Apparent volume of powder

c) Tapped density:

It is the ratio of total mass of powder to tapped volume of powder. The volume was measured by tapping the powder for 500 times. Then taping was done for 750 times and the volume was noted. If the difference between the two volumes is more than 2%, continued for 1250 times. Tapping was continued until the difference between volumes is <2% and V_f was measured to the nearest graduated unit. The tapped density was calculated in gm per ml using the formula:

$$\rho_{tap} = M / V_f$$

Where ρ_{tap} = Taped density
M = Weight of powder
V_f = Tapped volume of powder

d) Measure of powder compressibility:

The Compressibility Index (Carr's Index) is a measure of flow of a powder to be compressed. It is determined from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is. As such, it is a measure of the relative importance of interparticulate interactions. In a free flowing powder, such interactions are generally less significant and the bulk, tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticle interactions and a greater difference between the bulk and tapped densities will be observed. These differences are reflected in the Compressibility Index which is calculated using the following formula:

$$\text{Carr's Index} = [(\rho_{tap} - \rho_b) / \rho_{tap}] \times 100$$

Where, ρ_b = bulk density
ρ_{tap} = tapped density

Table 2: Pharmacopeial specifications for Carr's Index

Carr's Index	Type of flow
5-15	Excellent
12 – 16	Good
18 – 21	Fair
> 23	Poor

3. Evaluation of floating tablets

A) Characterization of tablets for physicochemical parameters

The prepared Salbutamol sulphate floating tablets were evaluated for their physicochemical parameters like weight variation, hardness, friability and drug content.

a) Weight variation:

To study the weight variation, ten tablets from each formulation were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity. The percent deviation was calculated using the following formula:

2. Formulation

Floating tablets preparation

Salbutamol sulphate was mixed manually in polybags with gastro retentive polymers separately as per formulae and MCC was added as diluent and sodium bicarbonate, added as effervescent agents (Table 3) and mixed for 10 mins. The blend was lubricated with magnesium stearate for 3-5mins and talc was added as glidant. The mixed blend was then compressed into tablets by direct compression method using 8 mm punches on a sixteen station rotary tablet punching machine.

$$\% \text{ deviation} = \frac{\text{(Individual wt. – Average wt.) X100}}{\text{Average wt.}}$$

The average weight of tablets in each formulation was calculated and presented with standard deviation.

Table 4: Pharmacopoeial specifications for tablet weight variation

Average weight of tablets (mg) (I.P)	Average weight of tablets (mg) (U.S.P)	Maximum percentage deviation allowed
Less than 80	Less than 130	10
80 – 250	130 – 324	7.5
More than 250	More than 324	5

Table 3: Formulation composition of Salbutamol sulphate floating tablets

Weight in mg									
Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Salbutamol sulphate	9.6	9.6	9.6	9.6	9.6	9.6	9.6	9.6	9.6
HPMC K15M	50	100	150	-	-	-	-	-	-
HPMC K4M	-	-	-	50	100	150	-	-	-
HPMC K100M	-	-	-	-	-	-	50	100	150
Sodium bicarbonate	15	15	15	15	15	15	15	15	15
Magnesium stearate	5	5	5	5	5	5	5	5	5
PVP K30	31.2	31.2	31.2	31.2	31.2	31.2	31.2	31.2	31.2
Talc	5	5	5	5	5	5	5	5	5
Microcrystalline cellulose	134.2	84.2	34.2	134.2	84.2	34.2	134.2	84.2	34.2
Total weight in mg	250	250	250	250	250	250	250	250	250

b) Tablet Thickness:

Tablet thickness is an important characteristic in reproducing appearance. Ten tablets were taken from each formulation and their thickness was recorded using digital vernier calipers. The average thickness of tablets in each formulation was calculated and presented with standard deviation.

c) Tablet Hardness:

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness was determined using Monsanto hardness tester and the average was calculated and represented with standard deviation.

d) Friability:

It is a measure of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Pre weighed tablets (10 tablets) were placed in the friabilator which was allowed to revolve for 4 minutes. This device consists of a plastic chamber that is set to revolve around 100 rpm for 4 minutes dropping the tablets at a distance of 6 inches with each revolution. At the end of test, tablets were reweighed. The loss in the weight of tablets is the measure of friability and is expressed in percentage as:

$$F (\%) = (W_o\text{-}W) X100/W_0$$

Where, W_o is the weight of the tablets before the test and

W is the weight of the tablets after test.

Pharmacopoeial limits of % friability allowed for tablets are 0.5-1.0%.

e) Assay of Salbutamol sulphate:

Twenty tablets were taken from each formulation and powdered separately. Then the powder equivalent to one average tablet weight was taken and allowed to dissolve in 250 ml of 0.1N HCl on a rotary shaker overnight. Then the solution was centrifuged and the supernatant was collected. The absorbance of supernatant was measured after dilution using a UV-Visible Spectrophotometer at λ_{max} of 276 nm.

B) In vitro floating lag time

The in vitro buoyancy was determined by floating lag time. The tablets were placed in a 100 ml beaker containing 0.1N HCl. The media was kept in stagnant condition and the temperature was maintained at 37^o C. The time required for the tablet to rise to the surface and float was determined as floating lag time.

C) In vitro floating duration time

The floating capacity of the tablets was determined using USP Dissolution apparatus II containing 900ml of simulated gastric fluid. The time interval between introduction of the tablet in to the dissolution medium and its buoyancy to the dissolution medium was taken as buoyancy lag time and for which time the tablet constantly floats on the surface of the medium was observed visually and taken as floating duration.

D) In vitro drug release

The release of Salbutamol sulphate from floating tablets was determined by using Dissolution type 2 test apparatus. The dissolution test was performed using 900ml 0.1N HCl solution at 37 ± 0.5^{o}C temperature and at 50 rpm. At specified time intervals, samples of 5 ml were withdrawn from the dissolution medium and that amount was replaced with fresh medium to maintain the volume constant. The samples were filtered and diluted to a suitable concentration with 0.1 N HCl. The absorbances of the diluted samples

were measured at 276nm for Salbutamol sulphate by using UV-Visible double beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from standard curve.

Release kinetics

Data of the in vitro drug release was fitted into different equations to explain the release kinetics of Salbutamol sulphate from floating tablets. The kinetic equations used were zero-order and first-order.

a) Zero – order release kinetics:

It defines a linear relationship between the fractions of drug released versus time

$$Q = Kt$$

Where Q is the fraction of drug released at time t

K is the zero order release rate constant

A plot of the fraction of drug released against time will be linear if the release obeys zero order release kinetics.

b) First- order release kinetics:

Wagner assuming that the exposed surface area of a formulation decreased exponentially with time during dissolution process suggested that drug release from most slow release formulations could be described adequately by apparent first- order kinetics. The equation used to describe first- order release kinetics is

$$\ln (1-Q) = -k_1 t$$

Where, Q is the fraction of drug released at time t and k_1 is the first order release rate constant.

Thus a plot of the logarithm of the fraction of drug remained against time will be linear if the release obeys first order release kinetics.

Models of drug release mechanism

The drug release data of floating tablets was fitted in to different mechanism models like Higuchi model, Korsmeyer-Peppas model and Hixson-Crowell model to interpret the drug release mechanism from tablets.

a) Higuchi (Diffusion) model:

It defines a linear dependence of the active fraction released per unit of surface (Q) on the square root of time.

$$Q = k_2 t^{1/2}$$

Where, k_2 is the release rate constant.

A plot of the fraction of drug released against square rot of time will be linear if the release obeys Higuchi equation. This equation describes drug release as a diffusion process based on the Fick's law and square root time dependent.

b) Korsmeyer – Peppas model:

A plot of the fraction of logarithm of % drug released against logarithm of time will be linear if the release obeys Korsmeyer - Peppas equation.

$$\text{Log } Q = \log k_3 + n \log t$$

Where, k_3 is the release rate constant, n is diffusional exponent

4. RESULTS AND DISCUSSION

1. Preformulation study

Preformulation studies were primarily performed to investigate the physicochemical properties of drug and to establish its compatibility with polymers and other excipients.

A) Compatibility:

The infrared spctra of pure drug and mixture of polymers and excipients were studied by FT IR spectroscopy using the KBR. Here spectral changes in the mixture are the basis for the determination of compatibility. The obtained spectrums of different formulation combinations were shown below.

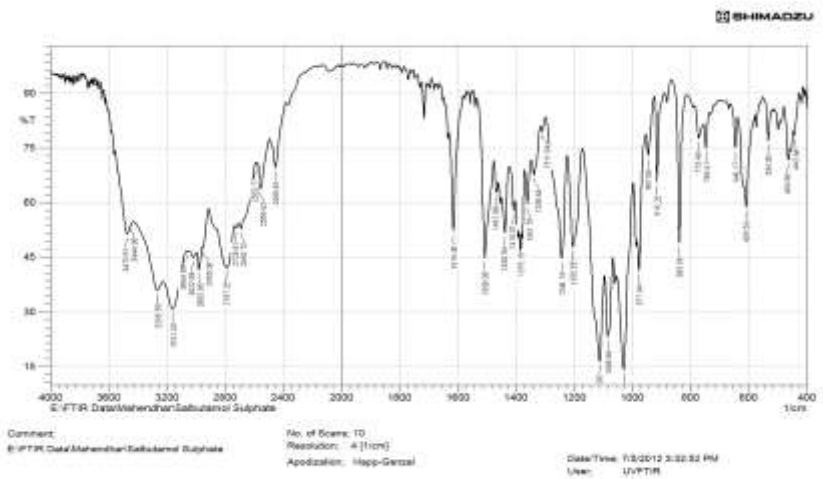

Figure 1: IR spectrum of pure salbutamol sulphate

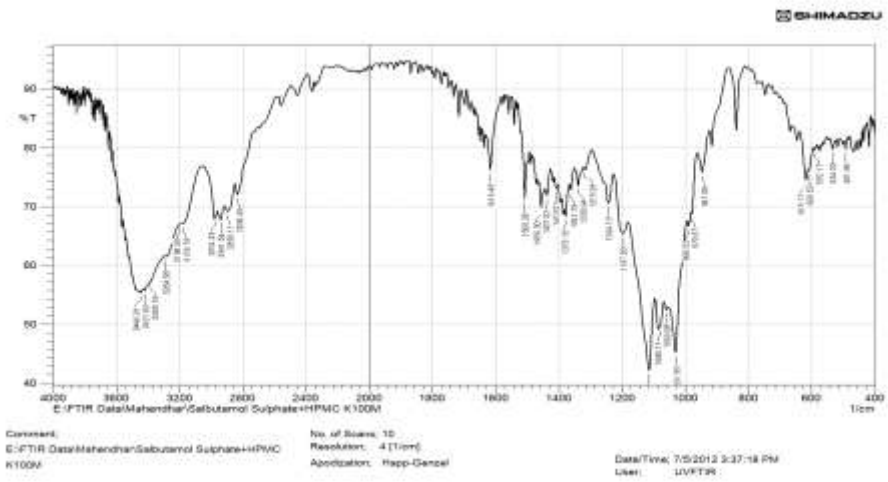

Figure 2: IR spectrum of physical mixture containing salbutamol salpate + HPMC K100M

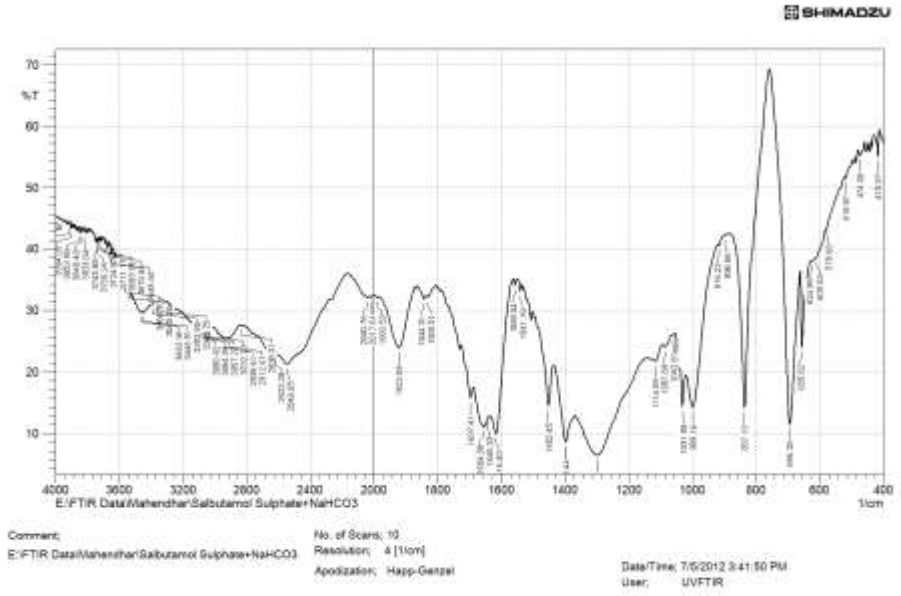

Figure 3: IR spectrum of physical mixture containing salbutamol salpate +$NaHCO_3$

Standard calibration curve for Salbutamol sulphate:

Initially the pure Salbutamol sulphate was scanned in between UV-range such as 250-350 nm.The maximum absorbance for salbutamol sulpate was found at 276nm. A standard concentration of salbutamol sulphate in the range of 5-25 µg/ml was prepared in 0.1N HCl and the absorbance were measured at 276nm.

Table 5**. Standard values of salbutamol sulphate**

s.no	Concentration µg/ml	Absorbance at 276 nm
0	0	0
1	5	0.150
2	10	0.282
3	15	0.405
4	20	0.496
5	25	0.664

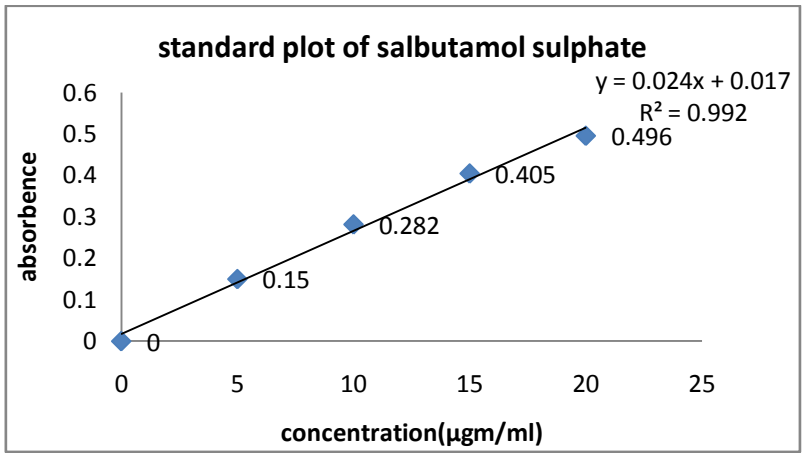

Figure 4. Standard curve of Salbutamol sulphate in 0.1N HCl

EXPERIMENTAL RESULTS

Table : 6 pre compression flow properties of salbutamol sulphate blend

FORMULATION CODE	ANGLE OF REPOSE(Θ)	BULK DENSITY (gm/cm^3)	TAPPED DENSITY (gm/cm^3)	CARRS INDEX(%)	HAUSNERS RATIO
F1	25.1±0.03	0.52±0.04	0.68±0.01	16.1±0.03	1.29±0.04
F2	27.5±0.02	0.57±0.02	0.67±0.02	20.8±0.03	1.26±0.04
F3	26.1±0.01	0.58±0.01	0.73±0.01	21.1±0.02	1.32±0.01
F4	27.5±0.04	0.57±0.03	0.67±0.01	21.6±0.02	1.30±0.02
F5	29.7±0.02	0.55±0.02	0.73±0.02	24.7±0.04	1.22±0.05
F6	28.0±0.01	0.57±0.01	0.69±0.01	17.6±0.05	1.24±0.04
F7	26.0±0.02	0.55±0.01	0.73±0.03	17.6±0.01	1.24±0.01
F8	26.1±0.01	0.53±0.02	0.72±0.02	25.8±0.04	1.85±0.05
F9	25.1±0.03	0.56±0.03	0.71±0.02	21.1±0.04	1.27±0.04

Table: 7 Evaluation data of salbutamol sulphate floating tablets

Formulation	Avg. Weight (Mean±S.D) (n=20)	Thickness(mm)	Hardness (Kg/cm$^{2)}$ (n=3)	Friability (n=20)	% Drug content (n=3)	Floating lag time
F1	253.4±0.48	3.0±0.01	5±0.57	0.21	100.2±0.68	22 mins
F2	250.6±0.74	3.1±0.02	4.5±0.62	0.46	99.89±0.58	19 mins
F3	251.7±0.62	3.2±0.02	5.5±0.47	0.39	98.94±0.72	11mins
F4	249.4±0.47	2.8±0.02	5±0.72	0.42	99.80±0.46	28mins
F5	250.2±0.23	2.9±0.02	4.5±0.48	0.26	99.54±0.62	18 mins
F6	249.9±0.32	3.0±0.01	6±0.68	0.54	99.49±0.47	16 mins
F7	251.1±0.54	3.0±0.02	5±0.38	0.49	100.24±0.53	20 mins
F8	252.8±0.37	2.9±0.01	5.5±0.48	0.29	99.68±0.71	17 mins
F9	250.8±0.29	2.3±0.02	4.5±0.68	0.37	100.12±0.49	13 mins

In-vitro buoyancy studies

In vitro buoyancy study was evaluated for the selected formulations . The tablets were dropped into 100 ml of 0.1 N HCl taken in 250 ml of beaker. The tablets were observed for the floating time. Digital photographs were taken at initial, 3 hours, 6 hours and 12 hours. The tablets prepared with HPMC K15 floats up to 11hours in the media. HPMC K100M remain floats for about 12 hours and more.

Formulation development of Salbutamol sulphate floating tablets with HPMC K15M .

The Floating tablets of Salbutamol Sulpate were prepared by using different concentrations of the HPMC K15M . The drug and HPMC K15 were directly mixed uniformly, and then the above blend was pre lubricated with talc and finally lubricated with magnesium state .Various physicochemical properties were studied.

All of the Salbutamol floating tablets with HPMC K15M (F-1 to F-3) were evaluated for various physicochemical parameters such as weight variation, hardness, thickness, friability and drug content. The Hardness of the tablets was found in the range of 4.5-5.5 kg/cm^2 for tablets prepared (F-1, F2 &F-3). Friability of below 1% clearly indicates the good mechanical strength of the prepared tablets. Assay of the prepared tablets was found in the range of 98- 100 % clearly indicating the good content uniformity. In vitro buoyancy study in 100 ml of the 0.1 N HCl shows that the prepared tablets were floated to the surface of the medium. This clearly indicates the good floating property.

***In-vitro* drug release studies of Salbutamol sulphate floating tablets prepared with HPMC K15M.**

In vitro dissolution studies were conducted in 900ml of 0.1 N HCl using USP-II apparatus. The results indicated that as the polymer concentration of HPMC K15 increases the drug release rate was retarded. All the formulation shows good floating properties. F-1 formulation containing 50mg retards the drug only for 7hours. F-2 formulation containing 100 mg of the HPMC K15 retarded the drug release for about 9hours, F-3 formulation containing 150mg and of HPMC K15 retards the drug for 11hours.

The dissolution data of all formulations were fitted to various kinetic models such as zero-order, first-order, and Higuchi, and Peppas models. Table 11 describes the *in vitro* drug release kinetic of Salbutamol sulphate floating tablets. The results of in vitro dissolution of the prepared Salbutamol sulphate floating tablets were summarized in the table 11. Figure 19 shows the plots of the cumulative % release vs time profile of the prepared tablets.

Table 8. Cumulative percentage drug release and release kinetics of formulations prepared with HPMC K15.

Time	F1	F2	F3
1	35.5	30.8	25.3
2	53.9	49.2	33.2
3	67.9	58.9	48.4
4	75.3	68.3	52.3
5	82.5	71.4	56.2
6	91.5	82.4	63.6
7	102	89.4	74.2
8		94.5	82.6
9		101.4	89.3
10			94.6
11			103

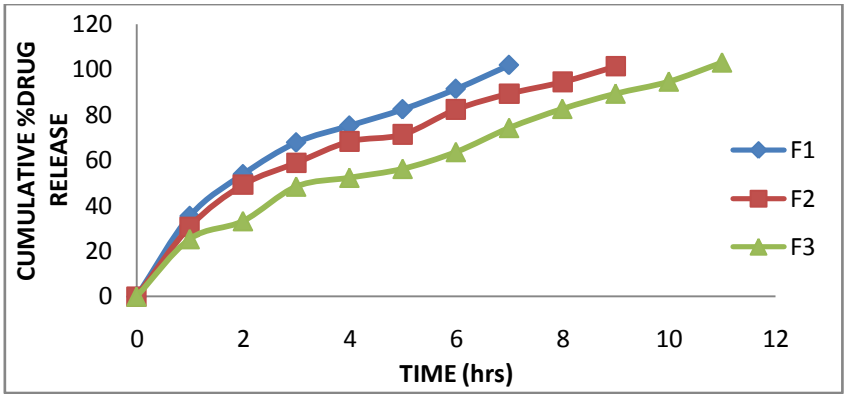

Figure : 5 Dissolution profile of salbutamol sulphate with HPMCK15M

Formulation development of Salbutamol sulphate floating tablets prepared with HPMC K4M

The Floating tablets of Salbutamol Sulpate were prepared by using different concentrations of the HPMC K4M . The drug and HPMC K4M were directly mixed uniformly, and then the above blend was pre lubricated with talc and finally lubricated with magnesium state .Various physicochemical properties were studied.

Good physicochemical properties were observed in the prepared formulations with a hardness of 5-6 kg/cm^2 and a friability of less than 1 %. This clearly indicates that the prepared tablets were having good strength .The drug content of the tablet was found in the 98.6%-105% clearly indicates the good content uniformity of the drug in the prepared tablets. In vitro buoyancy study shows that the prepared tablets were floated in less than 1min .

In vitro drug release studies of Salbutamol sulphate floating tablets prepared with HPMC K4M.

In vitro dissolution studies showed that the drug release was extended from 6-8 hours . In F4 Only 105 % of the drug was released in 6 hours in the formulation F-6 which contains 150 mg of the polymer .The drug release was mainly depends on the polymer proportion, as the polymer proportion was increased the drug release was retarded.

The drug release kinetics study reveals that the formulations follow zero order release. This clearly indicates that release was not depending on the concentration. The correlation coefficient of the Higuchi model was observed between 0.982-0.995 is clearly indicates the diffusion Mechanism .Peppas release exponent clearly indicates the drug release follows non fickion diffusssion mechanism.

Table 9. Cumulative percentage drug release of formulations prepared with HPMC K4M

TIME	F4	F5	F6
1	50.4	42.6	25.9
2	64.3	56.2	44.2
3	72.6	64.4	50.2
4	84.2	72.4	62.2
5	94.6	90.6	77.8
6	105	94.2	92.5
7		98.6	96.8
8			101.6

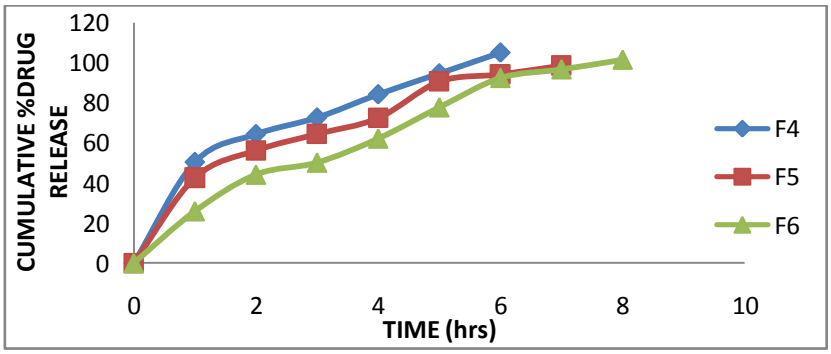

Figure 6. Cumulative percentage drug release profiles of formulations prepared with HPMC K4M

Formulation development of Salbutamol sulphate floating tablets prepared with HPMC K100M

The formulation of Salbutamol sulphate tablets were prepared with concentration of polymers. The individual formulations F7, F8, F9 containing 50 mg 100mg 150 mg of polymer proportion was selected and equal proportion of all other Excipients were incorporated in the tablets formulation as mentioned in table 6. The tablets were prepared with equal proportion of all other Excipients . The tablets were compressed with 8mm round flat-faced punch.

The prepared tablets were evaluated for various physicochemical parameters such as weight variation, hardness, thickness, friability and drug content. Good physicochemical properties were observed with a drug content of 99.68 -100.24 %.

In vitro drug release studies of Salbutamol sulphate floating tablets prepared with HPMC K 100 M

In-vitro dissolution study shows that the drug release was retarded more in the combination of polymer used when compared with the individual formulation ie F-7 and F-9.

Table 10.Cumulative percentage drug release and release kinetics of formulations prepared with HPMC K100M

Time	F7	F8	F9
1	41.1	27.8	24.3
2	62.2	35.2	29.8
3	71.9	57.9	45.4
4	75.1	61	53.2
5	78.6	72.4	64.6
6	80.5	78.6	68.4
7	84.6	80.8	73.9
8	90.2	89.4	78.6
9	104	92.9	91.5
10		96.8	93.1
11		102	94.6
12			96.6

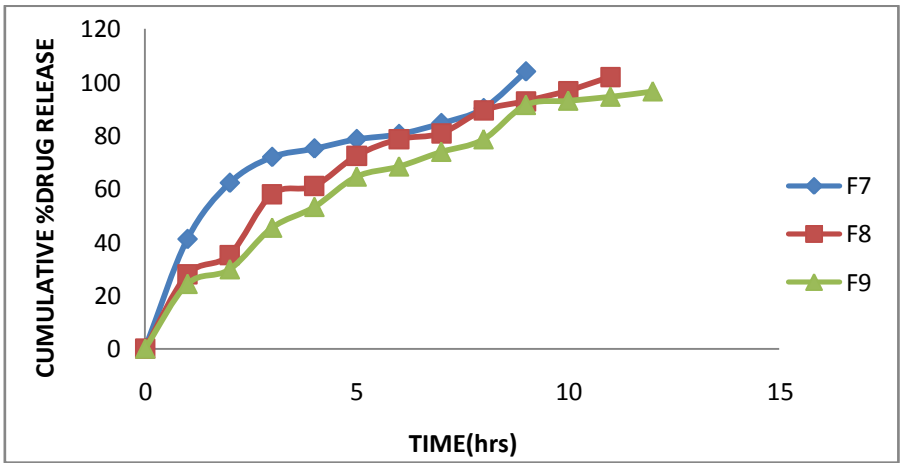

Figure 7. Cumulative percentage drug release profiles of formulations prepared with HPMC K100

Table :11 Release kinetics for the optimized formulation F9

FORMULATION	ZERO ORDER		FIRST ORDER		HIGUCHI		PEPPAS		
F9	R^2	K_0	R^2	K_1	R^2	K_H	R^2	n	K_P
	0.947	8.124	0.945	-0.113	0.962	26.94	0.977	0.537	1.355

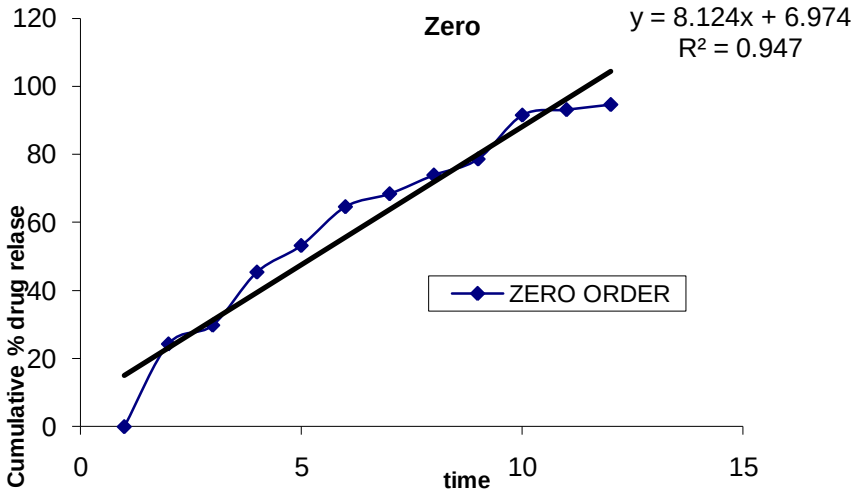

Figure : 8. Zero order Release plot of optimized formulation F9

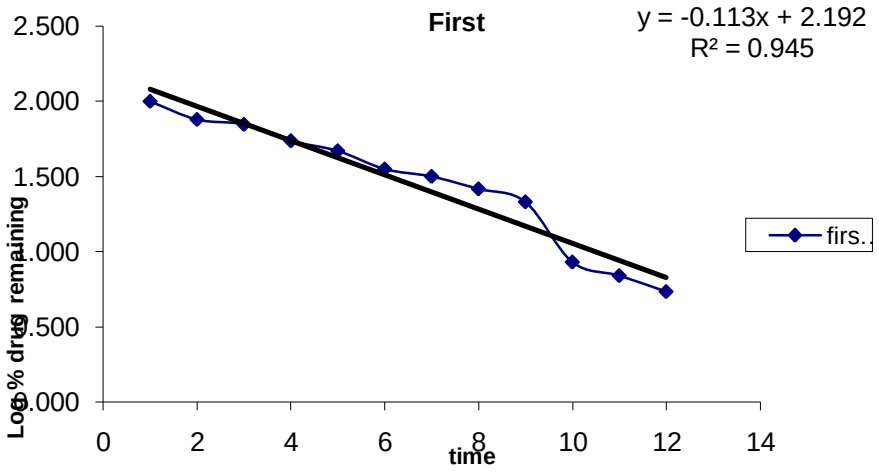

Figure :9. First order Release plot of optimized formulation F

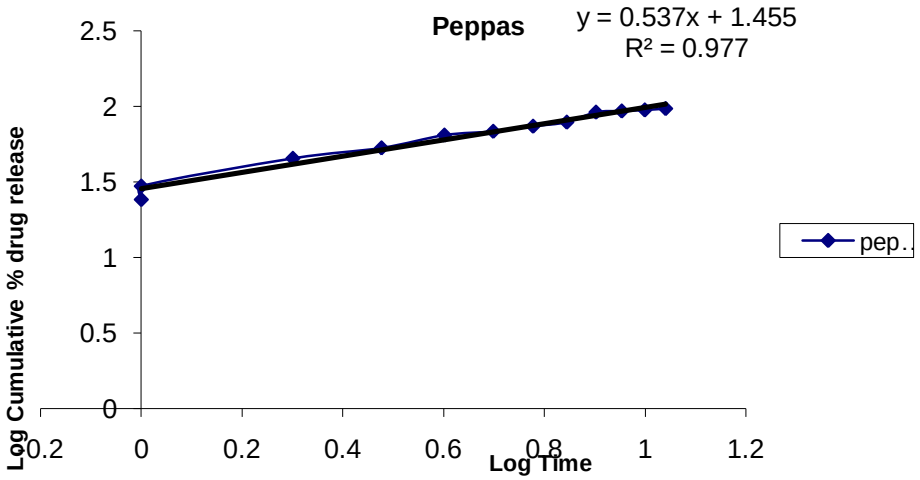

Figure :10 Korse meyer- Peppasorder Release plot of optimized formulation F9

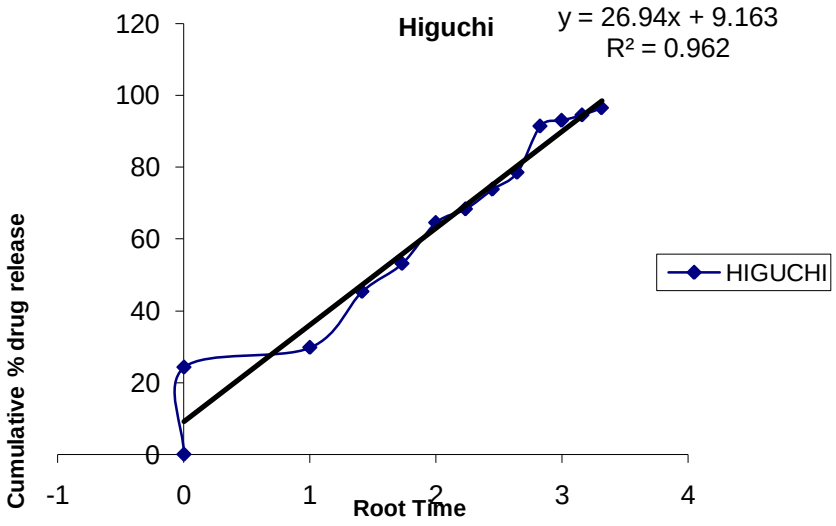

Fig -11 Higuchis plot of optimized formulation F9

5. CONCLUSION

Floating tablets of salbutamol salpate were prepared to increase gastric residence time there by improves its bioavailability and to over come the limitations of conventional approaches of Gastric retention.

By observing drug release rate from each formulation, The drug release retarding order of polymers is HPMC K100M>HPMC K15M>HPMC K4M.

Among all these formulations HPMC K 100M shown better in retarding the release of the drug release. Hence it was concluded that F9 formulation optimized for better drug release.

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