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Research Article

DESIGN AND INVITRO EVALUATION OF MONTELUKAST SODIUM EFFERVESCENT FLOATING TABLETS

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A B S T R A C T

The aim of present research work is to develop an ideal floating drug delivery system using montelukast sodium to increase the gastric residence time in stomach and to assess the *in-vitro* quality control tests for prepared tablet formulation. Materials and Methods: In this study montelukast sodium tablets were prepared using xanthan gum, guar gum, karaya gum as polymers, sodium bicarbonate as gas releasing agents, citric acid as acidifying agents, and magnesium stearate as flow promoters and SMCC HD 90 as a diluent. The direct compression method was used by using a rotary compression machine. Before compression, granular material was evaluated for precompression parameters such as angle of repose, bulk density, tapped density, carr's index and hausner's ratio. After punching, tablets were evaluated for weight variation, friability, hardness, drug content, floating lag time, buoyancy, and cumulative percent drug release. The formulations were optimized for different concentrations of guar gum, karaya gum, and xanthan gum and their formulations. Optimized formulations were subjected to stability studies and characterization by FTIR. Results and Discussion: All prepared tablets showed good *in-vitro* buoyancy for >9 to>24hours. Optimized formulation showed cumulative percent drug release of 99.8±0.14 %, buoyancy lag time 39.06±0.03sec and duration of buoyancy >24±0.3. Release kinetics of optimized formulation showed zero order with non-fickian diffusion. Conclusion: Out of all nine formulations, F3 has 40mg of xanthan gum and was considered as best formulation based on buoyancy, swelling studies and drug release mechanism corresponds to zero order and non-fickian diffusion.

INTRODUCTION

The aim of the present work was to formulate and evaluate the gastro retentive drug delivery system (Floating tablet) of Montelukast sodium using combination of polymersto increase their retention in stomach, which ultimately results in the increase of bioavailability along with extended duration of action resulting in possible reductionin dose, less side effects, low overall cost of therapy and hence better patient compliance. The current research was aimed to formulate, evaluate, and optimize gastro retentive formulations of Montelukast sodium using a combination of natural polymers such as guar gum and xanthan gum. Montelukast sodium is a leukotriene receptor antagonist (LTRA) administered as oral tablets at high doses 2-3 times per day. Hence in the present investigation, it is aimed to develop effervescent floating tablets of montelukast sodium to reduce frequency of dosing, achieve maximum gastric residence time and to improve drug availability [1,2,3].

Mechanism of Floating Systems

Various attempts have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include: 1) Introducing floating dosage forms (gas generating systems or swelling or expanding systems), 2) Mucoadhesive systems, 3) High-density systems,4) Modified shape systems, 5) Gastric-emptying delaying devices and 6) Co-administration of gastric emptying delaying drugs. Among these the floating dosage forms are the most used dosage forms [4,22,23]. Floating dots have been made to retain the dosage form in the stomach as a way of increasing the retention time. These attempts include: 1) Introducing floating dosage forms (gas generating systems or swelling or expanding systems), 2) Mucoadhesive systems, drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of the drug,

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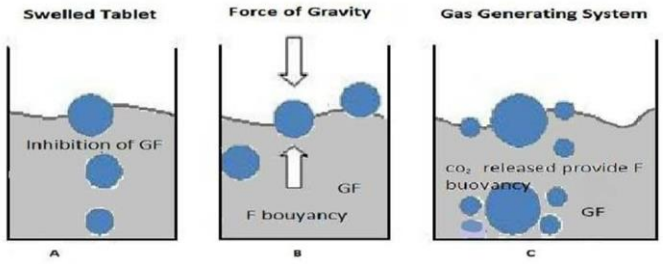
the residual system is eliminated from the stomach [5]. This results in an increased gastric retentive time (GRT) and control of the fluctuations in the plasma drug concentrations. To measure the floating force kinetics, a novel apparatus for determination of resultant weight has been reported in the literature. The apparatus operates by measuring continuously the force equivalent to F as a function of time that is required to maintain the submerged objects [17]. The apparatus helps in optimizing FDDS with respect to stability and durability of floating forces produced to prevent the drawbacks of unforeseeable intragastric buoyancy capability variations.

F= F buoyancy-F gravity= (Df – Ds) gV

Where F=total vertical force, D_f =fluid density, D_s =object density, V=volume, g=acceleration due to gravity



MATERIALS AND METHODS

Formulation and Evaluation of Montelukast Sodium Effervescent Tablets

Montelukast sodium was kindly supplied as a gift sample from Sri Krishna pharmaceuticals limited, Hyderabad, India. Xanthan gum, Guar gum and Karaya gum were supplied by Research lab fine industries, Mumbai, India and SMCC HD90 was supplied by SD fine chem Ltd, Hyderabad, India. Sodium bicarbonate and Citric acidwere supplied by Merck specialities Pvt Ltd, Mumbai, India. Magnesium stearate supplied by SD fine chem Ltd, Hyderabad, India. All chemicals were of analytical grade and distilled water was used throughout the experimental studies.

Preparation of standard graph of montelukast sodium in 0.1N Hydrochloricacid

8.3 ml of concentrated hydrochloric acid was taken and dissolved in distilled water upto 1000 ml to get 0.1N HCl.

Preparation of Montelukast Sodium Stock Solution

50 mg of drug was takenand dissolved in 50 ml of 0.1N HCl to make final concentration of 1000 µg/ml. From this stock solution, take 5 ml and diluted to 50 ml with 0.1N HCl to get 100 µg/ml, further dilution was done taking 1ml, 2ml,3ml, 4ml and 5ml making up to 10 ml to get a working standard solution of 1, 2, 3, 4and 5 µg/ml. These solutions was scanned in double beam UV spectrophotometer (Lab India UV 3200) between 200-400 nm and the λmax was found to be 268nm.

Preparation of Floating Effervescent Tablets of Montelukast Sodium

In the present study montelukast sodium floating effervescent tablets were prepared using the Direct Compression technique. The excipients used were SMCC HD90 is a free-flowing diluent. xanthan gum,Guar gum and karaya gum were used as swelling and rate-controlling polymers. sodium bicarbonate as gas releasing agent. Citric acid isused as acidifying agent and magnesium stearate was used as lubricant in various proportions. Based on preparations availability in the market the tablet weight was fixed [8].

All the ingredients and montelukast sodium were weighed accurately and mixed in the ascending order of their weights and passed through sieve no 20 to get uniform mixing. Then talc and magnesium stearate were added and punched by using a 16 station rotary tablet compression machine with flat 8mm punches. The total weight ofthe tablet was made upto 200mg.

Table 1 Formulation of Effervescent floating tablets of montelukast sodium

Formulation Code	Drug (mg)	SMCC HD90	Xanthan gum (mg)	Guar gum (mg)	Karaya gum (mg)	Sodium bicarbonate (mg)	Citric acid (mg)	Magnesium stearate (mg)	Total weight (mg)
F1	10.4	66.6	20	-	-	50	50	3	200
F2	10.4	56.6	30	-	-	50	50	3	200
F3	10.4	46.6	40	-	-	50	50	3	200
F4	10.4	66.6	-	20	-	50	50	3	200
F5	10.4	56.6	-	30	-	50	50	3	200
F6	10.4	46.6	-	40	-	50	50	3	200
F7	10.4	66.6	-	-	20	50	50	3	200
F8	10.4	56.6	-	-	30	50	50	3	200
F9	10.4	46.6	-	-	40	50	50	3	200

Each tablet contains 10.4mg of montelukast sodium.

Evaluation of Montelukast Sodium Effervescent Tablets

Evaluation of blends

The flow properties of the powder were very important in handling and processing operations. Hence the following micromeritic properties were studied on the montelukast sodium powder formulations.

Angle of repose (θ)

It is described as the maximum possible angle among the surface piles of powder to horizontal plane[16].

$$\theta = \tan^{-1}(h/r)$$

Where θ is repose angle, h is height in cm, r is radius in cm.

The angle of repose was analyzed by means of conventional fixed funnel processes.100 gm of the drug powders had flown through the funnel which was fixed to the standat a fixed height (h). Then the height and radius of the powders bed was noted.

Bulk density (D_b)

This is defined as the ratio of mass of the granule to the volume of powders bulk. It was determined by placing 100 gm of powder material into the measuring cylinder and noted the initial volume of the powder. This is called a bulk volume. Through this bulk volume, bulk density was calculated by using the following formula [15,10].

$D_b = M/V_b$

Where M is powder mass, V_b is powders bulk volume, D_b is the bulk density of powders.

Tapped density (D_t)

It is defined as the ratio of mass of total powders to the tapped volume of powders. This was determined by tapping the 100 gm of powder for 750 times and noted the volume using tap density tester USP (Bulk density apparatus, Secor, India). The tapping is further continued till the difference between two

successive volumes is <2%and is expressed in gm/ml, given by [4,6,15].

Dt=M/Vt

Where M is powder mass, Vt is powders tapped volume.

Carr's Index (Compressibility percentage)

It can be calculated from bulk and tapped density which shows powder flowproperties and is expressed as

I = Dt-Db / Dt X100

Where Dt is tapped density of the powders and Db is the bulk density of the powders [19,25].

Hausner's Ratio

It is an indirect index of ease of powders and is calculated from the bulk and tapped density of montelukast powder formulation,expressed as [17,22].

Hausner's ratio = Dt /Db

Where Dt is powders tapped density and Db is powders bulk density.

Determination of Physical Properties of Tablets

The tablets from each formulation were subjected to the following tests.

Appearance The general appearance of the tablet, and overall elegance and visual identity is very much needed for consumer acceptance [12,25].

Tablet thickness and diameter: Thickness and diameter of the tablet is a very important characteristic in reproducing appearance. Some filling equipment utilizes the counting mechanism to get uniform thickness. Randomly 10 tablets were taken from each formulation and the thickness and diameter was determined with a vernier calipers (Mitutoyo, Japan). The size of the tablet should be dimensionally described, monitored, and controlled [9,11,16].

Weight variation

A group of 20 tablets were taken from each formulation randomly selected and weighed using an electronic balance (Mettler-Toledo, Switzerland) and the average weight of the tablets was determined. The individual tablet weights were compared with average weight [10,13].

Hardness of tablets

Strength of the tablet is defined as tensile strength (N: Newton). The crushing load on a tablet is defined as the force necessary to fracture a tablet into 2 halves by applying compression. The hardness of the tablet was measured by tablet hardness tester (Monsanto hardness tester, India) [14,19].

Friability

It is a measurement of the mechanical strength of a tablet. The friability is determined to evaluate the effects of rubbing and shocks which may frequently cause tablet to damage, cap, or rupture. For this purpose, Friabilator (Rochefriabilator Analab, India) is used. A pre-weighed group of 20 tablets was charged in the fabrilator and subjected to 100 revolutions (USP). The dusted tablets were then reweighed. Compressed tablets must not drop more than 1% of their weight [21].
The friability (F) is expressed by

F= W initial-W final / W initial x100

Drug content

20 tablets were randomly selected and weighed. The average weight was noted. Tablets were crushed in a mortar pestle, powder equivalent to 10mg of montelukast sodium was taken, shaken, and diluted with 0.1N HCl containing 0.5 % w/v of sodiumlauryl sulphate (SLS) in 100 ml volumetric flask. Filter the solution and to the necessarydilutions using 0.1NHCl along with 0.5% w/v of SLS to get 5 µg/ml of montelukast sodium. Measure the absorbance of the resulting solution at 268 nm against a blank solution containing all the components except drug and analyzed using a double beamUV spectrophotometer (Lab India UV 3200) [12,18].

Swelling index

The swelling behaviour of the tablets was determined in triplicate, tablets were weighed individually and placed in a glass beaker, containing 200 ml of 0.1 N HCl containing 0.5% SLS, placed in a water bath at 37 ºC ± 0.5 ºC. At fixed time intervals, the tablets were removed, and the excess surface liquid was carefully removed using tissue paper. The swollen tablets were then re-weighed. The percentage swelling Index (SI) was calculated using the formula [24].
(SI%) =Wfinal -WInitial/Wfinal x100

Buoyancy Lag Time

The floating lag time (FLT) is determined by taking three tablets randomly and placingthem in a beaker containing 200 mL of 0.1 N HCl containing 0.5% SLS with a temperature maintained at 37±0.5 ºC using a water bath. The time required for the tablet to rise from the bottom of the beaker to the surface and float was determined [8].

Duration of Buoyancy

The total floating duration, that is, the time during which the tablet remains buoyant, was recorded to be the Floating Lag Time (FLT) and the duration of time in which the tablet constantly floated is called Total floating time [8,20].

Cumulative percentage in vitro drug release

In vitro dissolution apparatus type II was used (Lab India DS8000) for *in vitro* drug release of montelukast sodium. 900ml of 0.1 N HCl along with 0.5% SLS was used as a dissolution medium and the paddle was rotated at 50rpm for 30min,1hr, 2hr, 3hr, 4hr,5hr,6hr,7hr,8hr,9hr,10hr,11hr,12hr and 24hr. 10ml of the sample from eachbasket was withdrawn at predetermined time intervals and the same 10 ml was replaced with fresh dissolution fluid as medium to maintain the sink conditions. Thecollected samples at different intervals were analysed at 268nm using a double beam UV spectrophotometer (Lab India UV 3200) [19,23].

Application of Release Rate Kinetics to Dissolution Data

The *in vitro* dissolution data of optimised formulation F6 was subjected to examine kinetics of drug release rate by plotting the release rates of drug at different time intervals in Zero order, First order, Higuchi and Korsemeyer Peppas plot.

Characterization of Montelukast Sodium Effervescent Floating Tablets

Fourier Transform Infrared Spectroscopy (FT-IR) Studies

A composite group of tablets were crushed in a mortar and placed in the path (beam) of IR radiation of the ATR facility

for drug characterization. Scan the standard montelukast sodium from 400 to 4000 cm^{-1} and 1 cm^{-1} resolution using (Bruker alpha FT-IR/ATR, Lab India) FT-IR with ATR facility. Compare this spectrum of montelukast sodium effervescent floating formulation with pure drug montelukast sodium [7,13].

RESULTS AND DISCUSSIONS

Standard graph of montelukast sodium in 0.1N HCl

Montelukast sodium has maximum absorbance at 268nm. The standard graph of montelukast sodium in 0.1NHCl containing 0.5% SLS was plotted by taking the concentration range from 1µg/ml to 10µg/ml. The calibration curve for montelukast sodium in 0.1N hydrochloric acid was linear from 1µg/ml to 10µg/ml with R^2>0.999.

Table 2 Standard graph of montelukast sodium in 0.1NHCl

Concentration(µg/ml)	Absorbance
1	0.109
2	0.216
4	0.435
6	0.686
8	0.873
10	1.074

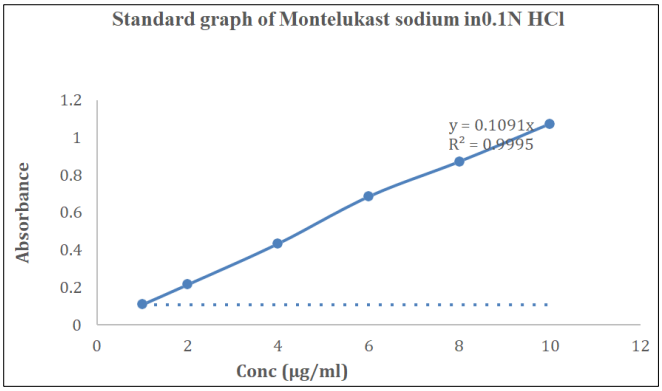


Figure 2 Standard graph of montelukast sodium in 0.1NHCl

Evaluation of Montelukast Sodium Effervescent Tablets

Evaluation of blend

The micromeritic properties of montelukast sodium powders formulation are essential in handling operations because the uniformity of the dose and ease of filling the powders into the container is determined by its flow properties. The powders flow properties can be accessed from Carr's index, Hausner's ratio and angle of repose. Results for powders formulations were represented in Table 3. Results indicate angle of repose ≤31.7±0.14° assuring that the flow properties were good for all the formulations. Apart from this, Carr's index and Hausner's ratio were ≤15.3±0.15 % and ≤ 1.18±0.15 respectively for all the nine formulations and showed good mixing, flowability and compressibility.

Table 3 Pre compression parameters of Powder formulations (F1 to F9) (n=3,mean ±SD)

Formulation Code	Angle of repose (°)	Bulk Density (g/cc)	Tapped Density (g/cc)	Compressibility index (%)	Hausner's ratio
F1	30.2±0.15	0.22±0.12	0.25±0.31	13.6±0.03	1.13±0.03
F2	31.3±0.13	0.26±0.07	0.29±0.33	11.5±0.21	1.12±0.24
F3	30.3±0.13	0.22±0.15	0.26±0.29	13.6±0.13	1.18±0.15
F4	31.2±0.11	0.30±0.16	0.34±0.11	13.7±0.02	1.13±0.05
F5	30.7±0.10	0.26±0.12	0.30±0.13	15.3±0.15	1.15±0.22
F6	30.3±0.13	0.25±0.01	0.29±0.12	12±0.06	1.16±0.15
F7	30.6±0.15	0.25±0.13	0.28±0.13	12±0.04	1.14±0.17
F8	31.7±0.14	0.30±0.22	0.34±0.11	13.3±0.16	1.13±0.19
F9	30.6±0.16	0.25±0.11	0.28±0.13	10.6±0.12	1.12±0.21

Evaluation of prepared montelukast sodium effervescent tablets

The prepared tablets from each formulation are white, circular, odorless which were analyzed for thickness, diameter, weight variation, hardness, friability, buoyancy lag time, duration of buoyancy, swelling index, *in vitro* dissolution, and drug content showed in tables-4.3 and table-4.4**.** The diameter and thickness of all the tablet formulations were almost uniform. The average weight of the tablet in all formulations ranged from 200±0.09 mg to 206 ±0.02 mg. All the tablets formulated in this study met the USP needs for weight variation (USP 31) and in all the formulations had<2% deviation**.** Thehardness of the tablets ranged from 3.9±0.02 to 4.2±0.07 kg/cm^2 which indicated good mechanical strength during compression. The percentage friability for all nine formulations ranged from 0.15±0.01 to 0.37±0.11 demonstrating the friability was within the acceptable limits (USP 31), indicating that the tablets are not brittle and canhandle without difficulty.

All the formulations were checked for drug content uniformity. The uniformity of drug results was good among various batches of tablets and the percent of drug content forall formulations was found to be greater than 98.56±0.08. The results also indicated acceptable and uniform dispersion of drugs in all tablet formulations shown in Table 4.

Table 4 Post Compression evaluation parameters (n=3, mean ±SD)

Formulation code	Weight variation(mg)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)
F1	205±0.17	4.0±0.11	0.15±0.01	99.08±0.21
F2	206±0.02	4.1±0.08	0.19±0.10	99.41±0.21
F3	200±0.09	4.1±0.11	0.35±0.12	99.23±0.09
F4	201±0.02	3.9±0.07	0.33±0.01	98.94±0.07
F5	202±0.12	4.0±0.03	0.32±0.08	98.56±0.08
F6	203±0.13	3.9±0.08	0.17±0.01	100.84±0.15
F7	204±0.04	4.1±0.01	0.37±0.11	99.23±0.13
F8	203±0.11	3.9±0.02	0.37±0.08	100.24±0.13
F9	205±0.02	4.2±0.07	0.35±0.07	99.37±0.17

In-vitro buoyancy studies were performed to evaluate the duration of buoyancy and buoyancy lag time in the presence of various rate-controlling polymers. The duration of buoyancy varied from >9±0.03hr to >24±0.04hr and buoyancy lag time varied from39.06±0.03sec to >120±0.03 sec for all the nine formulations. F3 formulation exhibited a short buoyancy lag time of 39.06±0.03 sec as well as a high swelling index of 28.97±0.12. Xanthan gum is a natural, swellable, sustainable polymer having zero order drug release. When this natural xanthan gum is present along with sodium bicarbonate and citric acid, upon influx into the stomach, carbon dioxide is released, causing the formulation to float in the stomach, thereby improving the bioavailability of the drug with substantial benefits, further drug wastage was reduced. *In vitro* buoyancystudy data is shown in Table 5.

Swelling index

The hydration ability of the formulation may have a significant result on tablet buoyancy and release kinetics. The swelling behavior of a tablet depends on the swellable polymers present in the formula. The formulations F1, F2, and F3 have 20mg,

30mg, 40mg of xanthan gum. An increase in the concentration of xanthan gum showed an increase in the viscosity of the gel layer and an increase in the time for water to reach the inner core of the tablet. F1 to F3 formulations showed swelling indices of 20.1±0.03, 22.06±0.12, and 28.97±0.12 respectively. Formulations F4, F5 and F6 showed swelling indices of 17.1±0.13, 18.6±0.14 and 18.9±0.05 respectively. Formulations F7, F8, and F9 showed swelling indices of 16.2±0.12, 18.3±0.11 and 19.4±0.0.6, respectively. The formulation F3 showed the highest swelling index (28.97±0.12) among all nine formulations and contained 40mg of xanthan gum per tablet. It is observed that as the percentage of xanthan gum in formulation is increasedthe swelling rate of formulations increased as shown in Table 5.

Table 5 In vitro buoyancy studies and swelling index of Montelukast Effervescent floating tablets (n=3, mean ± SD)

Formulation code	Buoyancy lag time(sec)	Duration of buoyancy (hr)	Swelling Index (%)
F_1	50±0.13	21±0.23	20.1±0.03
F_2	43±0.03	23±.21	22.06±0.12
F_3	39.06±0.03	>24±0.20	28.97±0.12
F_4	66±0.21	>9±0.03	17.1±0.13
F_5	80±0.04	>10±0.12	18.6±0.14
F_6	120±0.03	>12±0.03	18.9±0.05
F_7	90±0.13	>24±0.04	16.2±0.12
F_8	85±0.08	>24±0.03	18..3±0.11
F_9	75±0.08	>24±0.02	19.4±0.06

In vitro Dissolution Studies

In vitro dissolution studies of all the floating effervescent tablet formulations of montelukast were carried out in 900mlin 0.1NHClcontaining 0.5% SLS for up to 24hrs.At different time intervals, cumulative percent drug release was calculated. The *in vitro*drug release data of all formulations from F1 to F9 was tabulated in Table 4.5. The percent cumulative drug release verse time in hours was plotted and was shown in Fig. 3

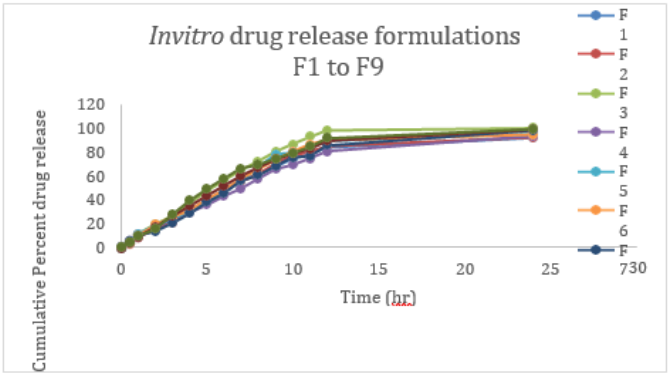


Figure 3 *In vitro* drug release studies

Formulations F1, F2 and F3 had xanthan gum as 20mg, 30mg and 40mg, while formulations F4, F5 and F6 were prepared by using guar gum 20mg, 30mg and 40mgand formulations F7, F8 and F9 were prepared by using Karaya gum as 20mg, 30mgin each formulation. Cumulative percent release for 24 h for F1 to F9 ranges from 91.8±0.36 to 99.8±0.14. Among all nine formulations, F3showed the maximum percentage of drug release 99.8±0.14% within 24 hours. As the concentration of xanthan gum increases in formulations showed greater release for prolonged periods at higher rates. Hence F3 formulation containing xanthan gum as 60 mg was optimized formulation.

Application of Release Rate Kinetics to Dissolution Data

From the *in vitro* dissolution studies, the optimized formulation F3 was further tested for the mechanism of drug release kinetics. The data were fitted into Zero order, first order, Higuchi, and Kors Meyer Peppas mathematical models to study the drug releasemechanism.

Table 6 Cumulative percent drug release of formulations F1 to F9 (n=3, mean ± SD)

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	3.2± 0.13	3.56±0. 09	4.23±0. 03	5.22± 0.12	5.24± 0.08	4.22± 0.13	5.86± 0.11	4.32± 0.14	4.08± 0.12
1	9.58± 0.10	9.13±0. 04	11.31± 0.04	10.45± 0.14	11.52± 0.12	10.19± 0.11	10.21± 0.13	9.05± 0.15	9.56± 0.05
2	14.87± 0.08	14.84± 0.03	19.42± 0.02	16.87± 0.13	18.42± 0.13	18.95± 0.16	13.55± 0.14	17.32± 0.02	15.24± 0.08
3	23.85± 0.03	21.07± 0.02	26.34± 0.09	23.61± 0.08	24.09± 0.15	25.58± 0.15	20.53± 0.16	26.47± 0.03	27.62± 0.11
4	31.45± 0.09	30.42± 0.09	36.93± 0.11	29.42± 0.10	30.47± 0.12	31.09± 0.11	28.41± 0.08	34.51± 0.15	39.07± 0.12
5	38.13± 0.12	39.57± 0.13	47.22± 0.12	35.57± 0.13	39.53± 0.09	40.56± 0.08	37.93± 0.06	43.42± 0.12	48.86± 0.15
6	48.42± 0.11	47.12± 0.15	56.23± 0.09	42.84± 0.09	46.32± 0.11	48.31± 0.03	45.22± 0.11	51.73± 0.11	57.54± 0.16
7	55.06± 0.09	55.07± 0.04	64.74± 0.14	49.43± 0.15	55.67± 0.12	57.76± 0.04	55.92± 0.12	60.14± 0.13	66.32± 0.06
8	62.14± 0.06	61.46± 0.09	72.23± 0.15	57.52± 0.17	67.09± 0.11	65.53± 0.11	60.43± 0.14	66.95± 0.08	69.21± 0.09
9	67.45± 0.05	70.45± 0.16	80.21± 0.08	65.74± 0.12	78.08± 0.17	73.67± 0.11	68.52± 0.12	73.52± 0.09	74.53± 0.11
10	74.21± 0.03	77.21± 0.14	86.53± 0.05	69.15± 0.15	79.56± 0.13	80.42± 0.02	75.32± 0.13	78.63± 0.12	79.22± 0.12
11	78.42± 0.11	80.43± 0.07	92.62± 0.03	74.53± 0.11	83.54± 0.14	86.57± 0.08	76.78± 0.14	82.64± 0.15	84.21± 0.16
12	83.67± 0.10	85.12± 0.08	98.21± 0.12	80.51± 0.07	89.43± 0.09	90.06± 0.12	85.42± 0.06	89.31± 0.13	91.45± 0.14
24	91.8± 0.36	92.3± 0.16	99.8± 0.14	93.4± 0.12	95.1± 0.13	94.6± 0.13	98.1± 0.05	98.75± 0.11	99.07± 0.08

The drug release mechanism was inferred to be zero order and non- Fickian diffusion in the sense that drug release was independent of the concentration of drug, and the mechanism of drug release in F3 is swelling or relaxation of the polymer chain.

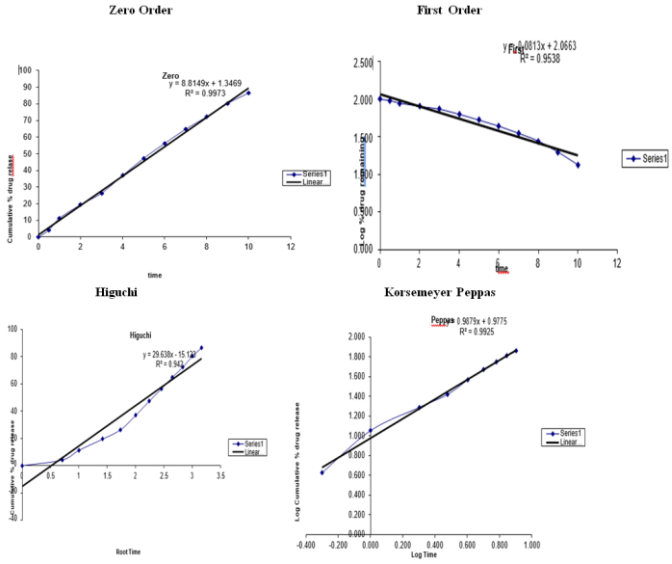


Figure 4 Release kinetic models of optimized formulation F3

Table 7 Mathematical Kinetic Model Applied To *In Vitro* Release Data of F6

Formulation Code	Zero order	First order	Higuchi kinetics	Korsmeyer peppas	
F3	R2	R2	R2	N	R2
	0.9973	0.9538	0.9420	0.98	0.9925

Characterization of Montelukast Sodium Effervescent floating Tablets

Fourier Transform Infrared Spectroscopy (FT-IR) Studies

FTIR spectra of montelukast sodium effervescent floating tablets and montelukast sodiumpure drug were shown in Figure 4.5. The significant all peaks of montelukast sodium were present in the entire spectrum obtained between drug and excipients. The FTIR spectra showed that there are no significant changes in chemical integrity of drug formulation.

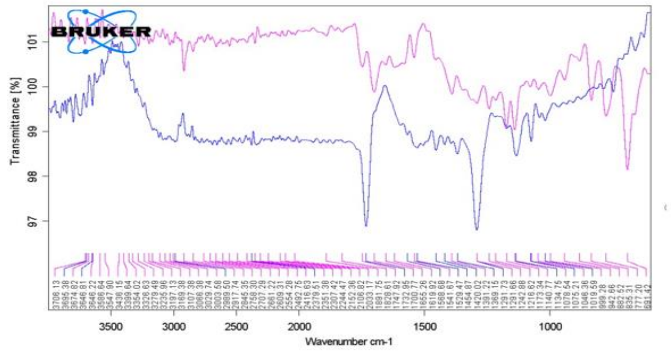


Figure 5 FTIR spectra of a) Montelukast sodium effervescent floating tablet formulation b) montelukast sodium pure drug

DISCUSSION

Montelukast sodium was kindly supplied as a gift sample from Sri krishna pharmaceuticals limited, Hyderabad, India. Xanthan gum, Guar gum and Karaya gum were supplied by Research lab fine industries, Mumbai, India and SMCC HD90 was supplied by SD fine chem Ltd, Hyderabad, India. Sodium bicarbonate and Citric acidwere supplied by Merck specialties Pvt Ltd, Mumbai, India. Magnesium stearate supplied by SD fine chem Ltd, Hyderabad, India. All chemicals were of analytical grade and distilled water was used throughout the experimental studies.

In the current study floating Montelukast sodium effervescent tablets were prepared using SMCC HD90, xanthan gum as swelling and rate-controlling polymers, sodium bicarbonate as gas releasing agent, citric acids acidifying agent, magnesium stearate as lubricants. Direct compression technique was employed, and tablet weight was fixedas 200mg.

All the ingredients and Montelukast sodium were weighed accurately and mixed in the ascending order of their weights then passed through sieve no 20 to get uniform sizedpowders. Then magnesium stearate was added to the previous powder formulations and punched by using a 16station rotary tablet compression machine with flat 8mm punches.

The micromeritic properties of Montelukast sodium powder formulation can be accessed from Carr's index, Hausner's ratio and angle of repose. Results indicate angle of repose ≤31.7±0.14° assuring that the flow properties were good for all the formulations. Apart from this, Carr's index and Hausner's ratio were ≤15.3±0.15 % and ≤1.18±0.15 respectively for all the nine formulations and showed good mixing, flowability and compressibility.

The prepared tablets from each formulation are white, circular, odorless which were analyzed for thickness, diameter, weight variation, hardness, friability, buoyancy lag time, duration of buoyancy, swelling index, *in vitro* dissolution, and drug content. The diameter and thickness of all the tablet formulations were almost uniform. The average weight of the tablet in all formulations ranged from 200±0.06 mg to 206 ±0.02mg. All the tablets formulated in this study met the USP needs for weight variation (USP 31) and in all the formulations were within the pharmacopeial limits**.** The hardness of the tablets ranged from 3.9±0.02 to 4.2±0.07kg/cm^2 which indicated good mechanical strength during compression. The percentage friability for all nine formulations ranged from 0.15±0.01 to 0.37±0.11 demonstrating the friability was within the acceptable limits (USP 31).

All the formulations were checked for drug content uniformity. The uniformity of drug results was good among various batches of tablets and the percentage of drug content for all formulations was found to be greater than 98.56±0.08. The results also indicated acceptable and uniform dispersion of drugs in all tablet formulations. *In vitro* buoyancystudies were performed. The duration of buoyancy varied from >9±0.03hr to >24±0.04hr and buoyancy lag time varied from 39.06±0.03sec to >120±0.03 sec for all the nine formulations. F3 formulation exhibited a short buoyancy lag time of 39.06±0.03 sec as well as a high swelling index of 28.97±0.12. Xanthan gum is a natural, swellable, sustainable polymer having zero order drug release. When this natural xanthan gum is present along with sodium bicarbonate and citric acid, upon influx into the stomach, carbon dioxide is released, causing the formulation to float in the stomach, thereby improving the bioavailability of the drug with substantial benefits,further drug wastage was reduced.

The swelling behavior of a tablet depends on the swellable polymers present in the formula. The swelling behavior of a

tablet depends on the swellable polymers presentin the formula. The formulations F1, F2, and F3 have 20mg, 30mg, 40mg of xanthan gum. An increase in the concentration of xanthan gum showed an increase in the viscosity of the gel layer and an increase in the time for water to reach the inner core of the tablet. F1 to F3 formulations showed swelling indices of 20.1±0.03, 22.06±0.12, and 28.97±0.12 respectively. Formulations F4, F5 and F6 showed swelling indices of 17.1±0.13, 18.6±0.14 and 18.9±0.05 respectively. Formulations F7, F8, and F9 showed swelling indices of 16.2±0.12, 18.3±0.11 and 19.4±0.0.6, respectively. The formulation F3 showed the highest swelling index (28.97±0.12) among all nine formulations and contained 40mg of xanthan gum per tablet. It is observed that as thepercentage of xanthan gum in formulation increases the swelling rate of formulations increased. *In vitro* dissolution studies of montelukast sodium tablets were carried out in 0.1NHCl containing 0.5% SLS in 900ml for up to 24h. At fixed time intervals, cumulative percent drug release was calculated. The percent cumulative drug release verse time in hours was plotted. F1, F2 and F3 had xanthan gum at 20mg, 30mg and 40mg, while F4, F5 and F6 were prepared by using Guar gum 20mg, 30mg and 40mg and F7, F8 and F9 were prepared by using karaya gum as 20mg, 30mg and 40mg each in each formulation respectively. Cumulative percent release for 24 h for F1 to F9 ranges from 91.8±0.36 to 99.8±0.14. Among all nine formulations, F3 showed the maximum percentage of drug release 99.8±0.14% within 24 hours. As the concentration of xanthan gum increases in formulations showed greater release for prolonged periods at higher rates. Hence F3 formulation containing xanthan gum as 40 mg was optimized formulation.

From the *in vitro* dissolution studies, the optimized formulation F3 dissolution data wasused for the mechanism of drug release kinetics. The data were fitted into Zero order, first order, Higuchi and Korsmeyer Peppas models to study the drug release mechanisms. The drug release mechanism was found to be zero order and Non- Fickian diffusion in the sense that drug release was independent of the concentrationof drug, and the mechanism of drug release in F3 is swelling or relaxation of the polymer chain.

The FTIR spectra showed that there are no significant changes in chemical integrity of drug formulation.

CONCLUSION

Montelukast sodium effervescent floating tablets were prepared using SMCC HD90 and xanthan gum as polymers in various proportions. Direct compression method wasused. The results of present research showed that the tablet containing montelukast sodium alone cannot effectively maintain its release rates for 24hrs. In the present studythis problem can be minimized by using xanthan gum in various proportions, which helps in increasing the viscosity of the dissolution fluid, thereby prolonging the release of the drug at higher release rates for 24 hours. Among all nine formulations, the F3 formulation containing 40 mg of xanthan gum was considered the best formulation based on buoyancy and swelling studies. From the present study, it was concluded that the formulation F3 has shown high swelling or relaxation of polymers. The drug release mechanisms of F3 formulation correspond to zero order and non-fickian diffusion behavior.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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