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Preparation and evaluation of montelukast sodium chewable tablets using modified karaya gum

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ABSTRACT

Montelukast sodium is an anti asthmatic drug. It mainly prevents leukotriene mediated effect associated with asthma and allergic arthritis. It also relieves symptoms of seasonal allergies. Asthma and seasonal allergies are more prevalent in children and swallowing an intact tablet is a major problem in this population. In addition, patients with asthma need fast and immediate action of tablet and avoidance of water is also desirable. Hence the main objective of this study is to improve the palatability by formulating montelukast sodium as chewable tablet to avert the problem of swallowing and to provide rapid onset of action, thus improving patient compliance and it also shows increase in bioavailability. In this study montelukast sodium chewable tablets were prepared by wet granulation method using different concentrations of xanthan gum, karaya gum, modified karaya gum as diluent and sodium starch glycolate (SSG) as disintegrant. The tablets were evaluated for various parameters and the results were found to be satisfactory and within specifications. F12 was selected as optimized formulation containing modified karaya gum 30% and SSG 4%, as it showed complete drug release in 90 minutes. Comparison studies were performed for optimized and marketed formulations and difference (f_1) and similarity factors (f_2) values were found to be 3.82 and 75.12 respectively. The optimized formulation was subjected to stability studies for three months as per ICH guidelines and showed good physical stability with insignificant changes in physical appearance and quality control tests.

Key words: Asthma, allergic arthritis, bioavailability, diluent, palatability, disintegrant.

INTRODUCTION

An oral dosage form is the most popular and preferred pharmaceutical dosage forms due to its ease of administration and also its processing is economical.[1, 2] However, in some patients, oral dosage forms are not necessarily a convenient dosage form due to difficulty in swallowing. Conversely, many patients cannot tolerate the taste of drugs when formulated as liquid dosage forms, thus leading to poor patient compliance. Recent developments are concentrating on oral dosage forms which provide good palatability and ease of administration especially for children or elderly patients. In such cases, fast disintegrating, sublingual, chewable, sustained release and colon targeted tablets serve as good options of the oral tablets. Amongst these, chewable tablets improve the compliance in pediatric and geriatric patients. [3]

Chewable tablets disintegrate slowly when chewed or allowed to dissolve in the mouth for local action. Chewable tablets are especially useful in tablet formulations for children and are commonly employed in the preparation of multiple vitamin tablets. [4] The drug chosen for the present study is montelukast sodium because of its application in asthma condition.

Montelukast sodium is a potent, orally active and selective leukotriene receptor antagonist that acts by inhibiting physiological actions of the cysteinyl leukotrienes. It is used in prophylaxis as well as treatment of asthma, exercise-

induced bronchospasm, allergic rhinitis and urticaria to relieve the symptoms of seasonal allergies. [5] Asthma and seasonal allergies are more prevalent in children who may have problem in swallowing a tablet intact. Faster onset of action of drug is needed for asthma patients and also avoidance of water while medication is desirable. Hence to prevent the problem of swallowing and to provide rapid onset of action, in this study, chewable tablets of montelukast sodium were formulated. These advantages in terms of increased bioavailability, patient compliance, averting the problems of swallowing in pediatrics and geriatric patients and rapid onset of action make these tablets accepted dosage form in the present market.

In this study, montelukast sodium chewable tablets were formulated using xanthan gum, karaya gum, modified karaya gum as diluent; hyroxy propyl cellulose (HPC) as binder and sodium starch glycolate (SSG) as disintegrant. Xanthan gum is a linear, high molecular weight extracellular heteropolysaccharide, produced commercially by viscous fermentation of gram negative bacterium *Xanthomonas campesteris*. [6] Karaya gum is the dried extrudate obtained from *Sterculia urens* and other related species of sterculia. [7] Modified karaya gum is obtained by heating gum karaya for 2 hours at 120^0C. [8, 9] Modified form of gum karaya has low viscosity and less swellability when compared to the parent gum karaya. [10] Hydroxy propyl cellulose is primarily used in oral products as a binder, film-coating agent and extended release matrix polymer. Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations. [11] Disintegration occurs by rapid uptake of water followed by rapid and enormous swelling.

Hence based on benefits and demand for the chewable tablets in the current market, an attempt was made in the development of an economical method for the preparation of the montelukast sodium chewable tablets which could be applicable for industry.

MATERIALS AND METHODS

Materials

Montelukast sodium and hydroxyl propyl cellulose were obtained as a gift sample from Micro labs, Bangalore, mannitol was purchased from Universal laboratories, karaya gum from Yarrow Chem. Products, aspartame was purchased from Himedia laboratories, magnesium stearate and vanillin were obtained from S D Fine chemicals Ltd. All reagents used were of analytical grade.

PREFORMULATION STUDIES:

Drug-excipients compatibility with FTIR

Identification of pure drug and the excipients was performed using infrared spectroscopy. FT-IR spectroscopy (Shimadzu Corporation, Tokyo, Japan) by KBr pellet method. The powder was compressed under 10 tons pressure in a hydraulic press to form a transparent pellet. The pellet was scanned from 4000 to 400 cm^{-1} and the resultant spectrum was compared for any spectral changes. They were observed for the presence of characteristic peaks for the respective functional group in the compound.

Differential scanning calorimetry (DSC)

DSC analysis was performed using Shimadzu DSC-60, Japan, differential scanning calorimeter (DSC). 3-5 mg samples were weighed and placed in a closed, hermetically sealed sample pans with a pin hole. Thermograms were obtained by heating the sample at a constant rate 10^0C /min. A dry purge of nitrogen gas (50 ml/min) was used for all runs. Samples were heated from 0^0C to 350^0C. The melting point, heat of fusion, disappearance of the crystalline sharp peak of the drug and appearance of any new peak and peak shape were noted.

Flow property related studies

Preparation of mixed blend of drug and excipients **[12]**

Required quantity of each ingredient was taken for each specified formulation and all the ingredients were subjected to grinding to a required degree of fineness which is then passed through sieve no 60. The granules were prepared by blending powder using water as granulating agent and the wet mass was screened using sieve no. 18. The obtained granules were dried and subjected to precompression tests.

Angle of Repose

The frictional forces in granules can be measured by the angle of repose (q). The angle of repose of the prepared granules was measured by using the fixed funnel method. Specified quantity of the granules was taken and poured into the funnel, which automatically forms the heap. The formed heap's diameter and height were measured. Then the angle of repose of the granules was measured by using below mentioned formula,

$$\mathbf{q = Tan^{-1} (h/r)}$$

Where h and r are the height and radius of the granules heap

Determination of Bulk Density and Tap Density
Apparent bulk density (rb) was determined by pouring the granules into a graduated cylinder. The bulk volume (Vb) and weight of the granules (M) was measured. From this the bulk density (ρb) was calculated using the formula.

ρb = M/Vb

The measuring cylinder containing a known mass of granules was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the granules was measured. The tapped density (**ρ**t) was calculated as

ρt = M/Vt

Compressibility Index
The simplest way of measuring the free flow of granules is by compressibility. It is an indication of the ease with which a material can be induced to flow and is given by compressibility index (I), which is calculated as

I = (ρt - ρo/ρt) ´100

Where, **ρ**t = tapped density
ρo = initial bulk density

Hausner ratio is an indirect assessment of ease of granules flow. It is calculated by the following formula

Hausner ratio = ρt / ρd

Where, **ρ**t = tapped density
ρo = bulk density

PREPARATION OF MONTELUKAST SODIUM CHEWABLE TABLETS:
General procedure: [13] All ingredients, according to different formulations given in Table.1 were triturated individually in a mortar and passed through #60 sieve. Then, required quantities of all the ingredients except magnesium stearate were weighed for a batch size of 100 tablets and mixed uniformly in a geometrical ratio. Purified water was added drop wise to the dry blend of powders and mixed thoroughly to form a wet mass, which was then passed through sieve no.16 The granules were dried in a hot air oven for 30 min and passed through sieve no.18. Finally magnesium stearate was added as lubricant. The granules were compressed to tablets containing 5 mg of montelukast sodium using 11.9 mm convex round punches on a Rimek-1 ten station rotary tablet machine. Total weight of tablet was kept as 500 mg± 5%.

Optimization of gum was carried out in the formulations F1 to F9; amongst them 150mg modified karaya gum was found to be optimized. Hence 150 mg modified karaya gum formulation was selected and further evaluated to study the effect of different concentration of disintegrant in formulations F10 to F12 and final optimized formulation was reported.

Table 1: Formulations of montelukast sodium chewable tablets

Ingredients (mg)	Formulations											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Drug	5	5	5	5	5	5	5	5	5	5	5	5
Mannitol	317.5	292.5	267.5	317.5	292.5	267.5	317.5	292.5	267.5	307.5	302.5	297.5
LMH	50	25	-	50	25	-	50	25	-	-	-	-
XG	50	100	150	-	-	-	-	-	-	-	-	-
KG	-	-	-	50	100	150	-	-	-	-	-	-
MKG	-	-	-	-	-	-	50	100	150	150	150	150
HPC	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Starch	50	50	50	50	50	50	50	50	50	-	-	-
SSG	-	-	-	-	-	-	-	-	-	10	15	20
Aspartame	5	5	5	5	5	5	5	5	5	5	5	5
Vanillin	5	5	5	5	5	5	5	5	5	5	5	5
Water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs	Qs
Mg. St	5	5	5	5	5	5	5	5	5	5	5	5
Total (mg)	500	500	500	500	500	500	500	500	500	500	500	500

LMH = Lactose monohydrate, XG = Xanthan gum, KG = Karaya gum MKG = Modified karaya gum, Mg. St = Magnesium stearate.

EVALUATION OF CHEWABLE TABLETS [14]

Weight Variation Test

Twenty tablets were selected at random, individually weighed and the average weight was calculated. The uniformity of weight was determined according to I.P. Specifications. As per I.P not more than two of individual weights should deviate from the average weight by more than 5% and none should deviate more than twice that percentage.

Thickness and Diameter

The thickness and diameter of the tablets were measured using vernier caliper. 10 tablets were selected from each batch and results were expressed as mean values ±SD.

Hardness Test

Tablet requires a certain amount of strength or hardness and resistance of friability to withstand mechanical shocks of handling during manufacture, packing and shipping. The Monsanto hardness tester was used for the measurement of hardness of the prepared chewable tablets. Three tablets were selected from each batch for testing and results were expressed in Kg/cm^2.

Friability Test

It was done in a Roche friabilator apparatus where the tablets were subjected to the combined effects of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Pre weighed samples of 20 tablets were placed in the friabilator, which was operated for 100 revolutions. The tablets were reweighed. Conventional compressed tablets lose less than 0.5 to 1.0% of their weight which is generally considered acceptable.

Drug content: Twenty tablets were randomly selected and average weight was calculated. Tablets were powdered in a glass mortar. Powder equivalent to 5 mg of drug was weighed and dissolved in 100 ml of 0.5% w/v sodium lauryl sulphate solution. This solution was filtered and drug content was analyzed spectrophotometrically at 342 nm. [15, 16]

Content uniformity: The content uniformity test is employed to ensure that every tablet contains the amount of drug substance intended with little variation among tablets within a batch. The test involves individually determining the amount of active ingredient in each of 10 tablets using the analytical method specified in the individual monograph.

***In vitro* disintegration test:** Disintegration time of tablets was carried out in a tablet disintegration test apparatus, using 1000 ml of 0.5% w/v sodium lauryl sulphate solution at 37±0.5º C.

***In vitro* drug release**: *In vitro* drug release of montelukast sodium chewable tablets was determined using USP Dissolution Apparatus II (Paddle type) (Electrolab TDT-08L). The dissolution test was performed using 900 ml 0.5% w/v sodium lauryl sulphate solution at 37°C ± 0.5°C. The speed of rotation of paddle was set at 50 rpm. 5 ml samples were withdrawn at every 10 min interval and same volume was replaced with fresh media. Percentage drug release was determined by UV spectrophotometer (ELICO-164 double beam spectrophotometer, India) at 342 nm against blank.

Modification of dissolution conditions for chewable tablets

In principle, the test procedure employed for chewable tablets should be the same as that of regular tablets. This concept is based on possibility if swallowing the dosage form without proper chewing, but because of the non-disintegrating nature of the dosage form, there may be a necessity to alter test conditions (e.g. increase the agitation rate) and specifications (e.g. increase the test duration). The rotating basket (USP Apparatus I) with the addition of glass beads may also provide more "intensive" agitation for *in vitro* dissolution testing of chewable tablets. This modification was employed for the dissolution of optimized formulation in order to simulate the conditions of the mouth while chewing.

Similarity and Difference Factors

A model independent approach was used to estimate the dissimilarity factor (f_1) and similarity factor (f_2) to compare the dissolution profile of optimized formulation with marketed formulation. [17]

The following equations were used for calculating f_1 and f_2.

$$f_1 = \{[\Sigma_{t=1}^{n} |R_t - T_t|] / [\Sigma_{t=1}^{n} R_t]\} \times 100$$

The similarity factor (f_2) is given by the following equation:

$f_2 = 50 \times \log \{[1 + (1/n) \Sigma_{t=1}^{n} (R_t - T_t)^2]^{-0.5} \times 100\}$

Where n = no of time points, the Rt = dissolution value of the reference batch at time t, the Tt=dissolution value of the test batch at the same time point.

Accelerated Stability Studies

Stability studies were carried out for optimized formulation, according to "international conference on Harmonization" (ICH) guidelines in Zone III. The best formulation F12 was wrapped in aluminum foil and placed in an amber colored bottle and kept at 40°C /75% RH in stability chamber (Oswald, Mumbai) for 3 months. At an interval of 30 days, the tablets were withdrawn, evaluated for physical properties and *in vitro* drug release.

RESULTS

Chewable tablet was formulated by using xanthan gum, karaya gum, modified karaya gum and mannitol as diluents, HPC as binder, sodium starch glycolate as disintegrant, aspartame as sweetener, vanillin as flavor and magnesium stearate as lubricant. The tablets were prepared by wet granulation using water as a granulating agent because tablets produced by direct compression do not possess the required hardness of chewable tablets. The physico-chemical properties of the prepared chewable tablets were confirmed to the required specifications.

Flow Properties Results of flow properties are found to be, Angle of repose (θ) = 22.34±0.82 to 24.97±0.87; Bulk density (gm/cm^3) = 0.476±0.017 to 0.586±0.015; Tapped density (gm/cm^3) = 0.587±0.010 to 0.682±0.003; Compressibility index (I) =1.126±0.004 to 1.134±0.021;Hausners ratio = 8.24±0.947 to 11.89±0.562. These values indicate that the prepared powder blend exhibited good flow properties and were found to be within the compendial limits of Indian Pharmacopoeia.

***In Vitro* Evaluation of chewable Tablets**

All the formulations were evaluated for various parameters like hardness, friability, drug content, disintegration time and *in vitro* drug release studies. The hardness of the tablets was found to be 5 to 6 kg/cm^2 (limits 4-8) and friability was found to be 0.21± to 0.36 (limits 0.5-1%), these values indicate good mechanical resistance where as thickness of the tablets was found to be 4.4± to 4.5 (limits ± 5% deviation). All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeial limits i.e. ±10%. The drug content was found to be 98.01±1.23 to 101.05±1.56 % and content uniformity 98.12±1.56 to 101.34±2.35 (limits 85-115%), indicating the uniform distribution of drug in the tablets.

Disintegration time

The disintegration time of F7 to F9 containing modified karaya gum decreased as the proportion of the gum increased. Whereas, the disintegration time for F1 to F6 containing karaya gum and xanthan gum increased with increase in their concentration as shown in Figure.1

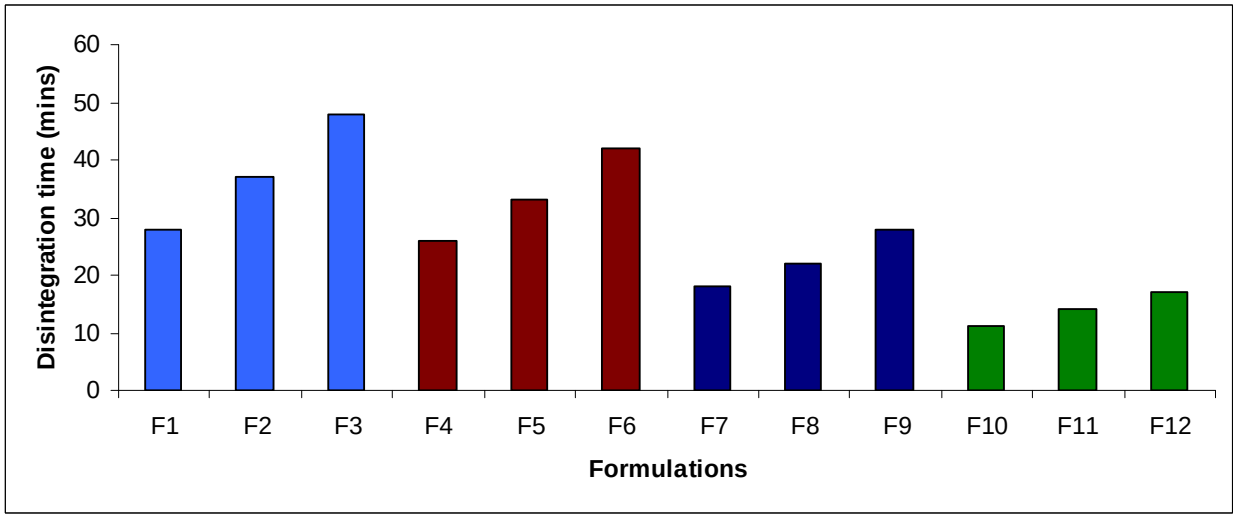


Figure 1: Disintegration time of formulations

***In-vitro* Drug Release Studies**

Xanthan gum and karaya gum were added in formulations F1, F2, F3, F4, F5, and F6 in 10%, 20% and 30% concentrations. The *in vitro* drug release after 90 min in F3 and F6 formulations was found to be 68% and 50%. Increase in the concentration of gum retarded the drug release for upto 3 hours. Modified karaya gum was added as a diluent in the formulations F7, F8 and F9 in 10%, 20% and 30% concentrations respectively. Employment of 30% modified karaya gum in F9, resulted in 100% release of the drug invitro within 90 min, as depicted in Table2

Table 2.Cumulative percentage drug release of different formulations

S No.	Time (min)	Cumulative percentage drug released								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	10	25.76±2.12	20.36±1.96	18.72±1.29	17.31±2.28	15.11±1.36	12.16±1.27	23.46±0.95	27.86±1.37	31.61±2.34
3	20	31.16±2.43	25.76±1.78	21.42±1.32	20.52±1.13	19.24±2.81	16.88±1.29	31.66±2.43	33.66±1.46	38.36±1.28
4	30	37.46±2.52	32.96±1.57	28.17±2.87	26.99±2.14	24.33±2.74	20.14±1.42	46.06±2.75	40.11±2.31	45.11±1.53
5	40	45.56±1.98	38.36±2.53	33.12±2.47	31.19±2.48	28.86±1.47	25.06±1.57	44.71±1.24	47.86±1.21	51.56±1.39
6	50	56.36±1.87	45.56±2.12	42.12±2.93	39.45±1.26	33.64±1.09	30.36±1.74	49.11±2.12	53.06±2.53	59.76±1.23
7	60	67.16±3.46	53.21±2.91	46.62±2.27	45.11±2.63	39.96±1.33	36.60±2.59	59.56±2.54	62.71±2.11	69.61±1.99
8	60	73.46±2.13	58.61±2.71	54.27±1.32	51.23±2.31	46.54±2.53	42.26±1.22	67.11±2.98	70.36±1.78	75.91±2.13
9	70	78.86±2.74	67.61±2.32	59.67±1.73	58.55±2.56	50.16±2.81	45.76±1.34	80.16±1.92	79.81±1.05	88.86±1.82
10	90	86.51±1.85	77.96±1.39	68.22±2.53	67.49±2.21	55.86±3.03	50.53±1.48	91.41±1.28	89.16±1.19	100.01±1.33
11	100	-	-	-	-	-	-	99.86±0.79	99.16±1.84	98.31±2.51

Values are expressed as Mean ±SD, n=6

Hence based on the results of disintegration test and dissolution test performed on formulations F1 to F9, the formulation F9 containing modified karaya gum at 30% concentration was selected and to this formulation effect of disintegrant at different concentration was studied and final optimized chewable tablet formulation was reported. Dissolution studies were conducted on formulation F10, F11 and F12 (containing modified karaya gum and different concentrations of SSG) Figure 2, clearly shows that formulation (F12) containing SSG in 4% concentration has 100% drug release in 90 min where as drug release for other formulations F 10 and F11 were found to be 71%, 72% respectively. Thus, formulation F12 was selected as final optimized formulation. Finally, percentage of the diluents and disintegrant were optimized and the chewable tablet was prepared by wet granulation technique that was able to release the drug within 90 min. The final optimized formula contained the diluents (modified karaya gum and mannitol) 30% and 60% respectively, 2.5% binder (HPC), 4% disintegrant SSG, 1% sweetener (aspartame), 1% flavor (vanillin) and 1% lubricant (magnesium stearate).

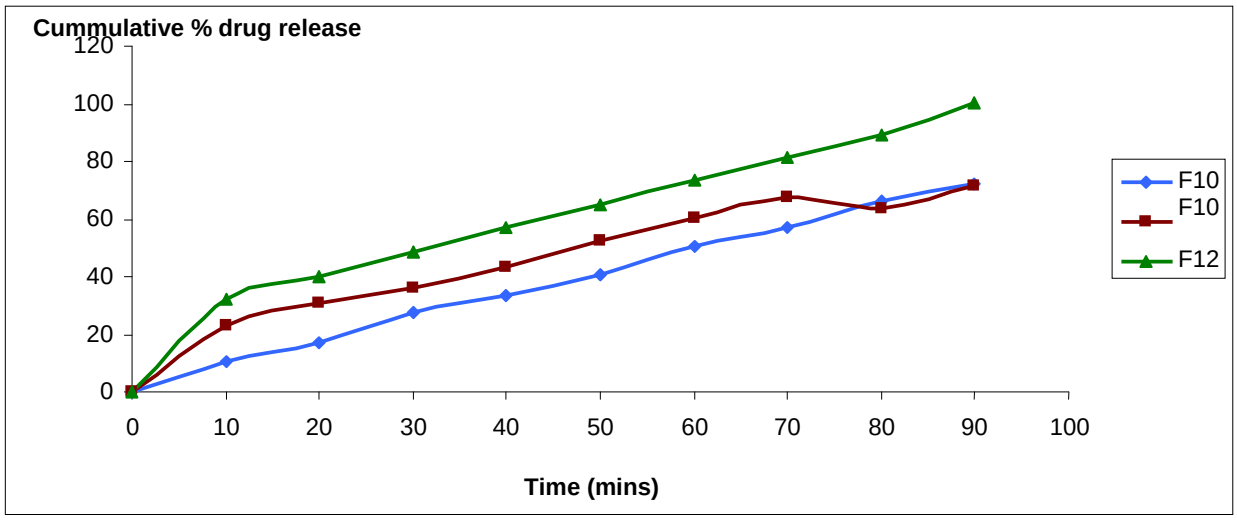


Figure 2: Dissolution profile of montelukast sodium tablets with SSG

Modification of dissolution conditions of chewable tablets

This test was performed on optimized formula F12 by using rotating basket (USP Apparatus 1) by the addition of glass beads with all the other test conditions remaining the same. Glass beads were added to provide more "intensive" agitation for *in vitro* dissolution testing of chewable tablets. The results were compared to those with paddle apparatus and basket apparatus without glass beads. From the Figure 3, the cummulative % drug release at 90 mins was found to be 100% in USP II apparatus, 89% in USP I with beads and 80.5% in USP I without beads.

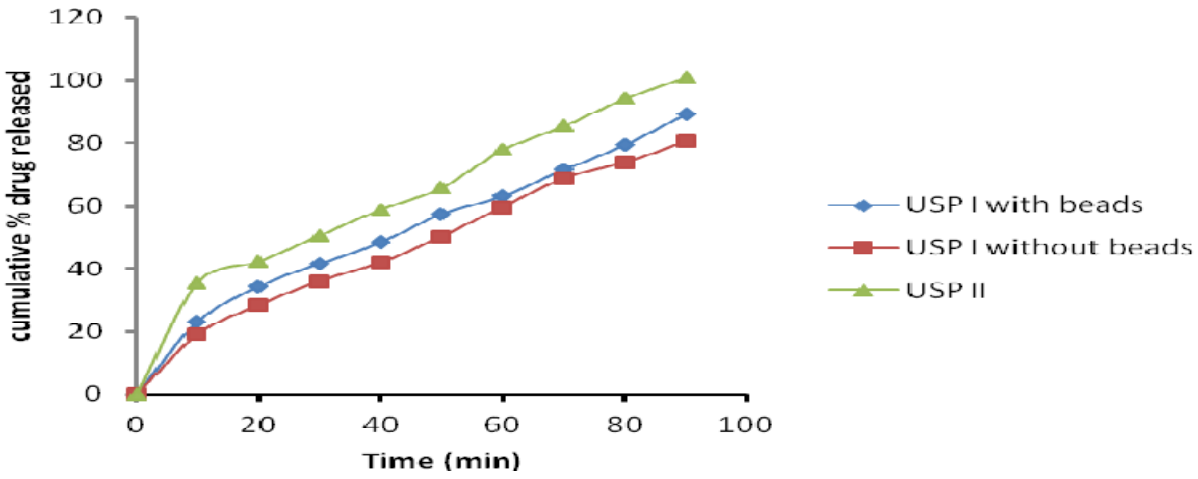
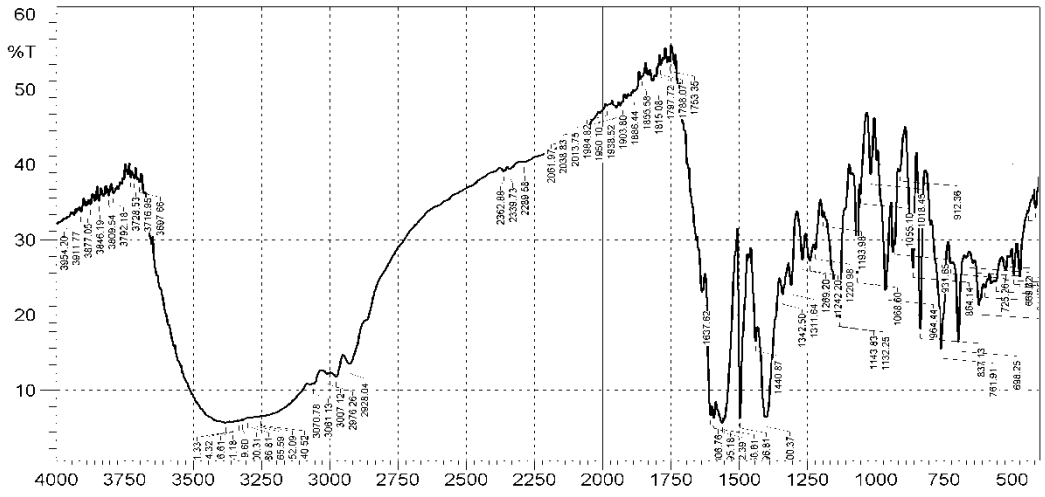


Figure 3: Comparison of cumulative percentage drug release of optimized formulation using modified dissolution apparatus

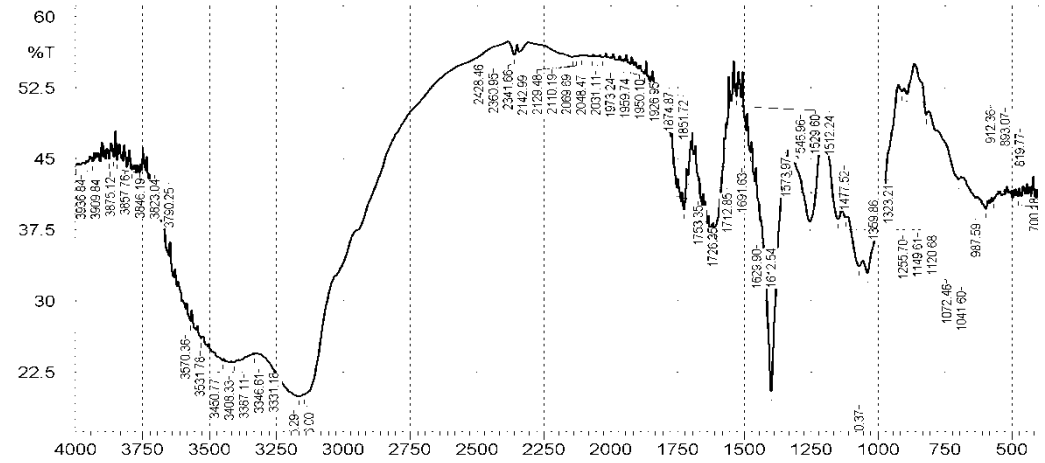
DRUG-EXCIPIENTS COMPATIBILITY STUDIES:

Fourier Transforms Infrared Spectroscopy analysis

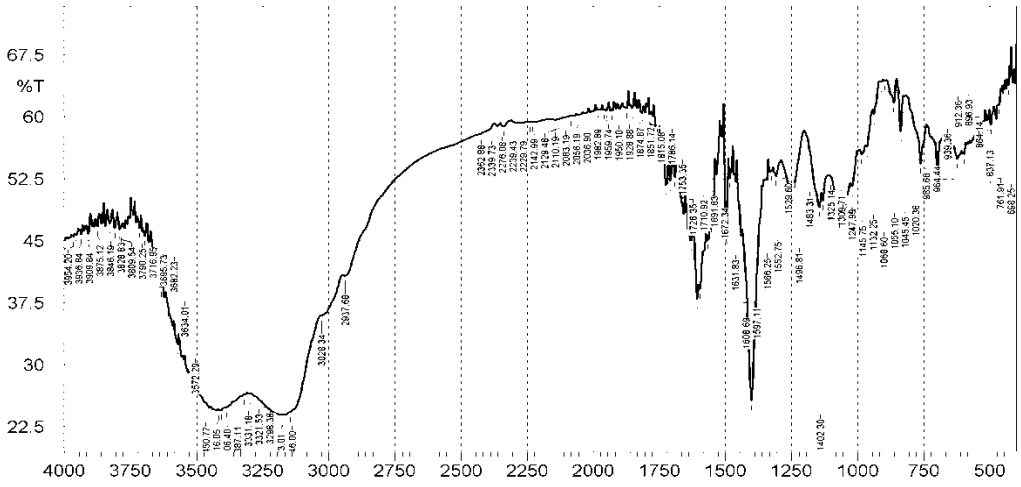
FTIR spectra of pure montelukast sodium, modified karaya gum alone and blend of gum with drug were studied. Figure.4-6 shows the FTIR spectra of pure montelukast sodium, modified karaya gum and F12.



(a)



(b)



(c)

Figure 4: FTIR spectra of a) montelukast sodium b) modified karaya gum c) optimized formulation, F12

FTIR studies revealed characteristic absorption peaks of pure drug montelukast sodium. FTIR spectra of pure drug has a broad peak at 3300 cm^{-1} indicating a tertiary -OH groups and a peak near 1700 cm^{-1} shows -COOH. The aromatic C-H peaks are also observed between 2900-3000 cm^{-1} as shown in fig 4 (a). In figure 4 (c) characteristic absorption peaks were observed in the same range of pure drug peak which was similar to the previous literature reports indicating that there is no functional alteration of drug and excipients in F12. [18]

Differential scanning calorimetry

DSC analysis was performed for pure drug, modified karaya gum and optimized formulation F12 and respective DSC thermograms were recorded. Figure 5 is the stacked DSC thermogram in which topmost curve indicates the thermogram of pure drug, middle curve indicates the thermogram of modified thermogram and bottom curve indicates thermogram of the formulation F12. The DSC thermograms of pure drug montelukast sodium (topmost curve) exhibited very sharp endothermic peak at 139.8°C corresponding to its melting point. Thus, it signifies the presence of the drug in its pure form. The thermogram of modified karaya gum (middle curve) exhibited a peak at 125°C which corresponds to its melting point. The DSC thermogram of the drug (bottom most curve) in F12 formulation does not show profound shift in peaks indicating compatibility which is similar to previous literature reports. [19]

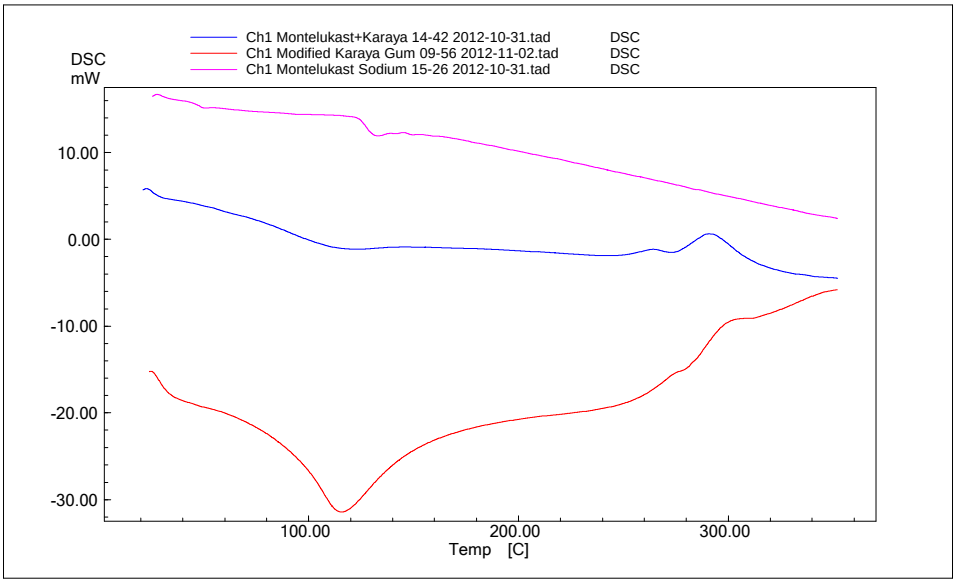


Figure 5: Stacked graph containing DSC thermograms of montelukast sodium, modified karaya gum and F12

Comparison of optimized formulations with marketed MONTAIR-5

The optimized formulation F12 was compared with the marketed tablet for disintegration time, drug content, hardness and friability**.** Results are shown in table 3. *In vitro* drug release of optimized formulation F12 and marketed formulation were performed and the percentage release was found to be 100.23 and 100.12% respectively in 90 mins.

Table 3: Comparison of optimized formulation with marketed formulation

Parameters	Marketed formulation (MONTAIR -5)	Optimized formulation
Hardness (kg/cm2)	6.1±0.19	6.0±0.32
Friability (%)	0.22±0.39	0.24±0.14
Disintegration time (sec)	20±1.10	21±0.51
Drug content (%)	100.06±1.23	99.57±1.61

Figure 6 depicts the comparison of *in vitro* dissolution of optimized formulation with marketed formulation. The difference (f_1) and similarity factors (f_2) were calculated for *in vitro* drug release of optimized and marketed formulation and values were found to be 3.82 and 75.12 respectively.

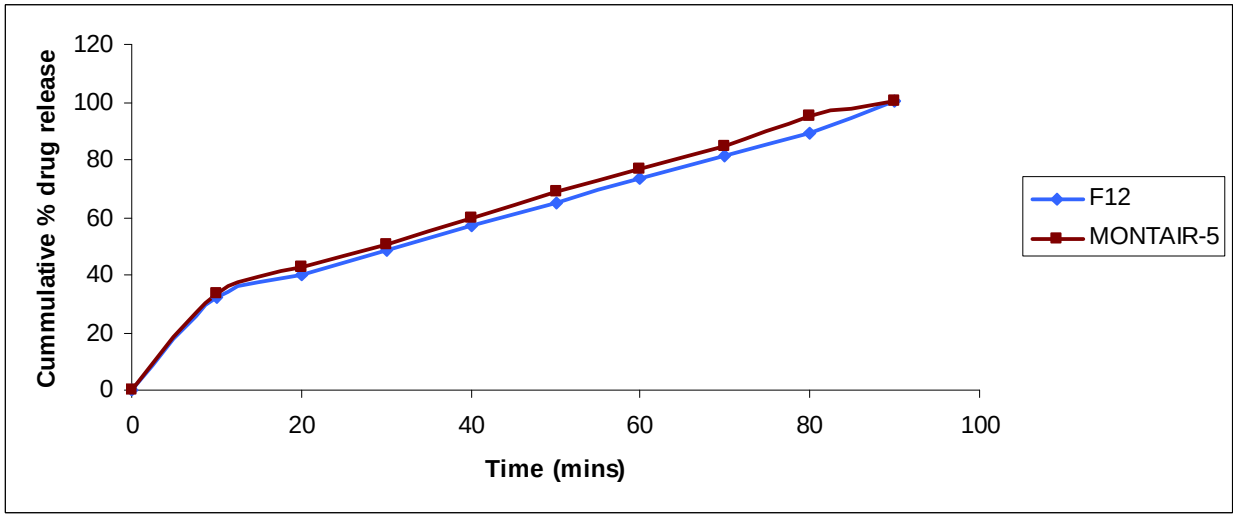


Figure 6: *In vitro* drug release of formulation (F12) with marketed formulation (MONTAIR-5).

Stability Studies:[20]

The stability of optimized formulation F12 was known by performing stability studies for three months at accelerated conditions of 40±2^{0}C/75±5% RH. The tablets were observed for physical and chemical changes. Results are shown in Table 4. Figure 9 shows the similarity in dissolution profiles of the optimized formulation F12 performed during stability studies.

Table 4: Physico chemical properties of F12 during acclerated stability studies

Parameters	Time in months			
	0 (Initial)	**1st month**	**2nd month**	**3rd month**
Hardness (kg/cm^2)	6.0±0.32	6.0±0.11	5.9±0.13	5.9±0.95
Disintegration time (min)	21±0.51	21±0.673	21±0.710	20±0.639
Drug content (%)	99.57±1.61	100.14±0.83 No change	99.97±0.19	100.20±1.20
Color and appearance	No change		No change	No change

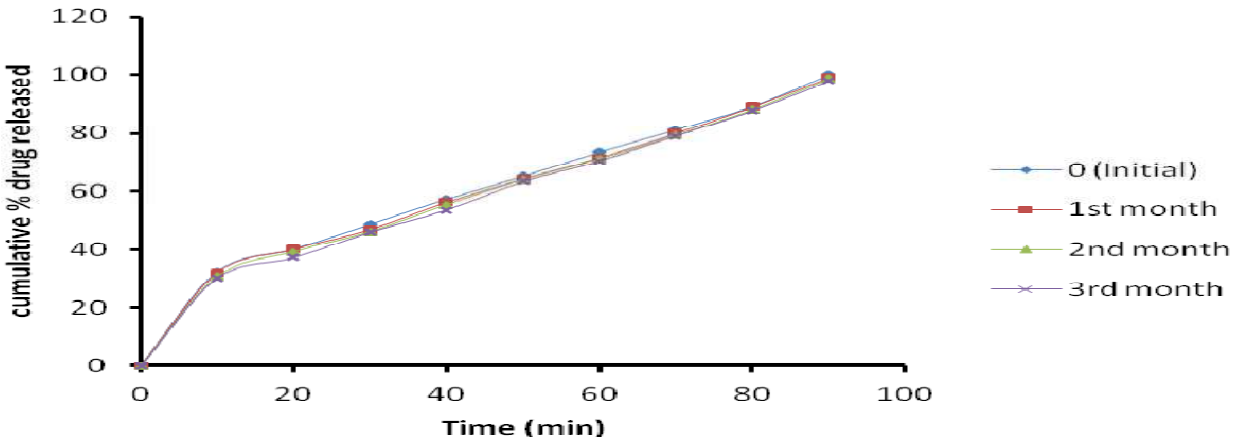


Figure 7: *In vitro* drug release studies of F12 during acclerated stability studies

DISCUSSION

Natural gums were selected to formulate the tablets as these gums are biodegradable in human body, non-toxic, [21] safe, cost-effective and have regulatory acceptance. All the formulations were evaluated for release studies. From the results it can be concluded that the formulation F12 has shown complete drug release in 90 mins. A significantly higher rate and extent of drug release was observed with the formulation containing modified karaya gum which is due to its excellent erodible properties with less swellable nature and low viscosity. [22] Drug release from xanthan gum and karaya gum was less owing to its high viscosity and swelling nature of the gums.

Sodium starch glycolate in higher concentrations (4%) absorbs water more rapidly, resulting in swelling which leads to rapid disintegration of tablets. Hence based on the results of *in vitro* drug release and disintegration studies, SSG in 4% with modified karaya gum in 30 % concentration was reported as final optimized formulation.

The drug excipient compatibility studies revealed from FTIR and DSC infers that no change was observed in the characteristics of drug during the formulation development and compression.

Upon comparison of *in vitro* dissolution profiles of optimized formula with marketed product it was found that the release profiles of the optimized formulation was similar to that of the marketed formulation and was within limits of the acceptance criteria i.e, similarity factor (f_2) is 50-100 and difference factor (f_1) is 0-15.

The optimized formulation F12 was subjected to stability studies for 3 months. At the interval of 30 days the tablets were withdrawn and evaluated for hardness, thickness, weight variation, friability**.** No significant changes were found in these parameters compared to the initial data. Drug release profiles were not affected by exposing to temperature and the specified humidity conditions.

CONCLUSION

Simple and economical method was implemented for the preparation of chewable tablets of montelukast sodium using xanthan gum, karaya gum and modified karaya gum as diluent and sodium starch glycolate as disintegrant. The formula F12 was optimized as it showed acceptable results in terms of disintegration time and *in vitro* drug release. This formula has shown similar results in comparison with a marketed product. It also showed physical stability when stored at 40°C under 75% RH for 3 months.

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