FORMULATION AND EVALUATION OF IMMEDIATE RELEASE TABLETS OF MONTELUKAST SODIUM

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ABSTRACT

Oral drug delivery has been known for decades as the most widely used route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. Montelukast is a leukotriene receptor antagonist used for the maintenance treatment of asthma, chronic asthmatic attacks and to relieve symptoms of seasonal allergies. Its biological half life is 2.5 – 5.5 hrs thereby decreasing bioavailability up to 64%. In order to improve bioavailability, immediate release tablets were developed. In the present work the immediate release tablets of Montelukast sodium were prepared by direct compression method. Crosspovidone (5, 7.5, 10 w/w), crosscarmellose sodium (5, 7.5, 10 w/w) and sodium starch glycolate (5, 7.5, 10 w/w) were used as super disintegrants in different Concentrations. The blend of all formulations were evaluated for various precompression parameters like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio and were found to be satisfactory. The drug excipients compatibility studies were performed using FTIR technique. The tablets were evaluated for various parameters like weight variation, thickness, hardness and friability. All the results were within acceptable IP limits. Among all the formulations sodium starch glycolate (7.5%) was found to disintegrate within 20 sec. The in vitro performance of optimised formulation F8 showed 98.75% 0f the drug release within first 60 min.

KEYWORDS: Montelukast sodium, sodium starch glycolate, superdisintegrants, direct compression, immediate release.

INTRODUCTION

Oral drug delivery is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Oral route is considered most natural, uncomplicated, convenient and safe due to its ease of administration, patient acceptance and cost effective manufacturing process. For many drug substances conventional immediate release formulations provide clinically effective therapy while maintaining the required balance of pharmacokinetic and pharmacodynamic profiles with an acceptable level of safety to the patient. Oral route of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly patient compliance. The most popular solid dosage forms are tablets and capsules. But the important drawback of these dosage forms is the difficulty to swallow Oral dosage form is the most popular route for drug therapy. Over 80% of the drugs formulated to produce systemic effects in the United States are produced as oral dosage forms. Compared to other oral dosage forms, tablets are the manufacturer's dosage form of choice because of their relatively low cost of manufacture, package. [1, 2]

Current technologies in oral drug delivery [3, 4]

Over the last 3 decades, many novel oral therapeutic systems have been invented along with the appreciable development of drug delivery technology. Although these advanced DDS are manufactured or fabricated in traditional pharmaceutical formulations ,such as tablets, capsules ,sachets, suspensions, emulsions and solutions they are superior to the conventional oral dosage forms in terms of their therapeutic efficacies ,toxicities and stabilities.

Based on the desired therapeutic objectivies, oral DDS may be assorted into three categories.

1. Immediate release preparations,
2. Controlled release preparations and
3. Targeted release preparations.

(a) Immediate release preparations

These preparations are primarily intended to achieve faster onset of action for drugs such as analgesics, antipyretics and coronary vasodilators. Other advantages include enhanced oral bioavailability through transmucosal delivery and pregastric absorption, convenience in drug administration to elderly and bedridden.

Conventional IR formulations include fast disintegrating tablets and granules that use effervescent mixtures such as sodium carbonate (or sodium bicarbonate) and citric acid (or tartaric acid), and super disintegrants, such as sodium starch glycolate, crosscarmellose sodium and cross povidone .Current technologies in fast –dispersing dosage forms include modified tabletting systems, floss or shear form technology, which employs of centrifugal force and controlled temperature and freeze drying.

(b) Controlled –released preparations

The currently employed CR technologies for oral drug delivery are diffusion controlled systems: solvent activated systems and chemically controlled systems. Diffusion-controlled systems include monolithic and reservoir devices in which diffusion of the drug is the rate limiting step, respectively, through a polymer matrix or a polymer membrane. Solvent-activated systems may be either osmotically controlled or controlled by polymer swelling. Chemically controlled release drugs via polymeric degradation (surface or bulk matrix erosion) or cleavage of drug from a polymer chain.

c) Targeted release preparations

Site specific oral drug delivery requires spatial placement of a drug delivery device at a desired site within the GIT tract. Although it is virtually possible to localize a device within each part of GI tract, the attainment of site-specific delivery in the oral cavity and the rectum is relatively easier than the stomach and the small and large instestine. The later requires consideration of both longitudinal and transverse aspects of GI constraints.

Immediate Release Drug Delivery System [5, 6]

Immediate release drug delivery system is a conventional type of drug delivery. It is designed to disintegrate and release their medicaments with no special rate controlling features. These are the dosage forms in which ≥85% of labeled amount dissolves with in 30min. However for immediate release tablets, tablet disintegrants play an important role in ensuring that the tablet matrix break up on contact with fluid in the stomach to allow the release the active drug which then become available in whole or in part, for absorption from GIT.

Mechanism of drug release [7, 8]

On exposure to aqueous fluids, hydrophilic matrices take up water and the polymer starts hydrating to from a gel layer. Drug release is controlled by diffusion barriers/by erosions. An initial burst of soluble drug may occur due to surface leaching when a matrix containing a

swellable glassy polymer comes in to contact with an aqueous medium, there is an abrupt change from a glassy to rubbery state associate with swelling process with time, water infiltration deep in to a case increasing the thickness by the gel layer. The outer layer become fully hydrated and starts dissolving or eroding. When water reaches the centre of the system and the concentration of drug falls below the solubility value, the release rate of the drug begins to reduce. At the same time an increase in thickness of the barrier layer with time increases the diffusion path length, reducing the rate of drug release.

Desired Criteria for Immediate Release Drug Delivery System [9, 10]

Immediate release dosage form should-In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.

- ✓ In the case of liquid dosage form it should be compatible with taste masking.
- ✓ Be portable without fragility concern.
- ✓ Have a pleasing mouth feel.
- ✓ It should not leave minimal or no residue in the mouth after oral administration.
- ✓ Exhibit low sensivity to environmental condition as humidity and temperature.
- ✓ Be manufactured using conventional processing and packaging equipment at low cost.

Advantages of Immediate Release Drug Delivery System [11, 12]

An immediate release pharmaceutical preparation offers:

- ✓ Improved compliance/added convenience.
- ✓ Improved stability.
- ✓ Suitable for controlled/sustained release actives.
- ✓ Allows high drug loading.
- ✓ Ability to provide advantages of liquid medication in the form of solid preparation.
- ✓ Adaptable and amenable to existing processing and packaging machinery
- ✓ Cost- effective.
- ✓ Release the drug immediately.
- ✓ More flexibility for adjusting the dose
- ✓ It can be prepared with minimum dose of drug.
- ✓ There is no dose dumping problem.
- ✓ Immediate release drug delivery systems used in both initial stage and final stage of disease.
- ✓ At the particular site of action the drug is released from the system

Super Disintegrants [13, 14]

A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the breakup of the compacted mass when it is put into a fluid environment.

ADVANTAGES

a. Effective in lower concentrations.

b. Less effect on compressibility and flowability.

c. More effective intragranularly.

Mechanism of superdisintegrants [15, 16, 17]

The tablet breaks to primary particles by one or more of the mechanisms listed below.

a) Because of heat of wetting (air expansion)

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

b) Swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

c) Porosity and capillary action (Wicking)

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

d) Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

e) Due to deformation

During tablet compression, disintegranted particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

f) Due to release of gases

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

Conventional Technique Used in the Preparation Of Immediate Release Tablets.
* Tablet molding technique
* Direct compression technique
* Wet granulation technique
* Mass extrusion technique

i)   Tablet Molding [16]

In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydroalcoholic solvent and is molded in to tablet using compression pressure lower than used in conventional tablets compression.The

solvent is then removed by air- drying. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic Van Scoik incorporated drug containing discrete particles, which were formed by spray congealing a molten mixture of hydrogenated cottonseed oil,sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

ii) Direct Compression Method [17]

The term "direct compression" is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required. Amongst the techniques used to prepare tablets, direct compression is the most advanced technology. It involves only blending and compression, thus offering advantage particularly in terms of speedy production, as it requires fewer unit operations, less machinery, reduced number of personnel and considerably less processing time along with increased   product stability.

iii) Granulation [18, 19]

Granulation may be defined as a size enlargement process which converts small particles into physically stronger & larger agglomerates. The objective of granulation is to improve powder flow and handling, decrease dustiness, and prevent segregation of the constituents of the product. Granulation method can be broadly classified into two types.

(i) Wet granulation and

(ii) Dry granulations

Ideal characteristics of granules:

The ideal characteristics of granules include spherical shape, smaller particle size distribution with sufficient fines to fill void spaces between granules, adequate moisture (between 1-2%), good flow, good compressibility and sufficient hardness. The effectiveness of granulation depends on the following properties:

- ✓ Particle size of the drug and excipients
- ✓ Type of binder (strong or weak)
- ✓ Volume of binder (less or more)

- ✓ Wet massing time (less or more)

- ✓ Amount of shear applied

- ✓ Drying rate (Hydrate formation and polymorphism)

iv) Mass - Extrusion [20]

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking. Montelukast sodium (ML) is an orally active leucotriene receptor antagonist used for the treatment of asthma. It blocks the action of leukotriene D4 on the cysteinyl leukotriene receptor CysLT1 in the lungs and bronchial tubes by binding to it . The cysteinyl leukotrienes (LTC4, LTD4, LTE4) are products of arachidonic acid metabolism and are released from various cells, including mast cells and eosinophils. [21, 22, 23]

These eicosanoids bind to cysteinyl leukotriene receptors (CysLT) found in the human airway. Cysteinyl leukotrienes and leukotriene receptor occupation have been correlated with the pathophysiology of asthma, including airway edema, smooth muscle contraction, and altered cellular activity associated with the inflammatory process, which contribute to the signs and symptoms of asthma. Montelukast is an orally active compound that binds with high affinity and selectivity to the CysLT1 receptor (in preference to other pharmacologically important airway receptors, such as the prostanoid, cholinergic, or β-adrenergic receptor). It inhibits physiologic actions of LTD4 at the CysLT1 receptor without any agonist activity. It is freely soluble in ethanol, methanol and water and practically insoluble in acetonitrile and its bioavailability is 63% Montelukast is rapidly absorbed following oral administration.

The main objective of the present study is to formulate the immediate release tablets of Montelukast sodium which will improve the biological half-life as well as bioavailability of montelukast. This makes montelukast as a suitable candidate for incorporation in immediate release dosage form and was used as a model drug. So in order to improve stability, patient compliance and to reduce dose dumping. Monteukast was formulated as an immediate release drug delivery system by using super disintegrates like sodium starch glycolate, crosspovidone, cross carmellose sodium.

MATERIALS AND METHODS

Materials

Montelukast sodium was a gift sample received from Hetero Drugs Pvt Ltd, Hyderabad. Micro crystalline cellulose USP – NF (Avicel PH 101) was received from FMC biopolymer, crosscarmellose sodium, povidone K-30 were purchased from BASF Germany. All other chemicals and reagents used were of analytical grade and were used as received.

Determination of drug solubility [24]

An excess amount of drug was taken and dissolved in measured amount of distilled water in a glass vial to get saturated solution. from this the supernatant was filtered to separate the undissolved drug particles and diluted sutably and then the concentration was measured in U.V. spectrophotometer. The concentration of drug was assessed after 24hrs.

Drug excipient compatibility studies by FTIR [25, 26]

The spectrum analysis of pure drug and physical mixture of drug and different excipients used in the formulation of tablets was studied by FTIR. FTIR spectra was recorded by preparing potassium bromide (KBr) disks. These disks were prepared by mixing few mg of sample with potassium bromide by compacting in a hydrostatic press under vaccuum at $6-8$ tonns pressure. The resultant disc was mounted in a suitable holder in IR spectrophotometer and IR spectrum was recorded from 4000 cm^{-1} to 500cm^{-1} in a scan time of 12 minutes. The resulatnt spectrum was compared for any spectral changes. They were observed for the presence of characteristic peaks for the respective functional group in the compound.

Preparation of calibration curve of Montelukast

It was prepared by using 0.5% SLS solution. Standard solution was prepared by dissolving 25mg of drug in 25ml of 0.5% SLS solution to give a concentration of 1mg/ml (1000μg/ml). From the stock solution different concentrations of 5,10,15,20 & 25μg/ml were prepared. Finally the absorbance was measured at 342nm.

Bulk density [25]

Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.15 g powder blend introduced into a dry 100 ml cylinder, without compacting. The powder was carefully levelled without compacting and the unsettled apparent volume, Vo, was read. The bulk density was calculated using the following formula.

$\rho_b = M / V_o$

Where ρ_b = Apparent bulk density

                         M = Weight of sample

                         V = Apparent volume of powder

Tapped density [26]

After carrying out the procedure as given in the measurement of bulk density the cylinder containing the sample was tapped 500 times initially followed by an additional taps of 750 times until difference between succeeding measurement is less than 2% and then tapped volume, V_f was measured, to the nearest graduated unit. The tapped density was calculated, in gm per ml, using the following formula.

$\rho_{tap} = M / V_f$

Where ρ_{tap} = Tapped density

                         M = Weight of sample

                         V_f = Tapped volume of powder

Carr's index (%) [25]

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

Compressibility index $= [(\rho_{tap} - \rho_b) / \rho_{tap}] / \times 100$

Where ρ_b = Bulk density

                 ρ_{tap} = Tapped density

Hausner's ratio [26]

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's ratio=Tapped density (ρ_t) / Bulk density (ρ_b)

Where ρ_t tapped density and ρ_b is bulk density. Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones, between 1.25 to 1.5 showing moderate flow properties and more than 1.5 poor flow.

Angle of repose [25]

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 pored 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 θ = h/r

Where; θ = Angle of repose

       h = Height of the cone

       r = Radius of the cone base

Preparation of immediate release tablets of Montelukast sodium

All ingredients were triturated individually in a mortar and passed through #60 mesh sieve. Then required quantity of montelukast sodium, crosspovidone, crosscarmellose sodium, sodium starch glycolate and microcrystalline cellulose were weighed for a batch size of 50 tablets and mixed uniformly in a mortar. Finally lactose monohydrate was added as a lubricant. This uniformly mixed blend was compressed into tablets containing 10mg drug using 10mm flat face surface punches by direct compression method. Total weight of the tablet was kept 180mg. (Table 1)

Evaluation of Tablets

Tablet thickness [29]

The thickness in millimetres (mm) was measured individually for 10 pre weighed Tablets by using micrometer (screw gauge). The average thickness and standard deviation were reported.

Weight variation [30]

Twenty Tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of three batches were calculated. It passes the test for weight variation, if not more than two of the individual Tablet weights deviate from the

average weight by more than the allowed percentage deviation and none deviate by more than twice the percentage shown. It was calculated on an electronic weighing balance.

Tablet hardness [30]

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 condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of 6 Tablets was determined using Monsanto hardness tester and the average is calculated and presented with standard deviation.

Friability [31]

The friability values of the Tablets were determined using a Roche-type friabilator. Accurately weighed six Tablets were placed in Roche friabilator and rotated at 25rpm for 4 min. The Tablets were then dusted and re-weighed to determine the loss in weight. Friability was then calculated as percent weight loss from the original Tablets.

Percentage friability was calculated using the following equation.

Friability = ([w_O − w] /w_O) × 100

Range: 0.5-1.0

Where; w_O = weight of the Tablet at time zero before revolution.

        w = weight of the Tablet after 100 revolutions.

In-Vitro Disintegration test [31]

The disintegration time was measured using disintegration apparatus. One Tablet was placed in each tube of the basket. The basket with bottom surface made of a stainless steel screen (mesh no. 10) was immersed in water bath at 37 ± 2^0C. The time required for complete disintegration of the Tablet in each tube was determined using stop watch. The range is 30sec to 1min.

Dissolution test

Dissolution test was performed by using USPXXIV dissolution test apparatus. 900ml of 0.5%SLS was used as dissolution medium. The stirrer was adjusted to rotate at 50 rpm and temperature was maintained at 37±0.5°C throughout the experiment. One tablet was used in each test. 5ml of samples were withdrawn by means of syringe fitted with pre filter at known intervals of time and analysed for drug release by measuring the absorbance at 342nm. The

volume withdrawn at each time intervak was replacd with fresh dissolution medium of same quantity.

RESULTS AND DISCUSSION

Solubility

These tests were performed as per procedure and it was found that it is freely soluble in water and methanol and insoluble in acetonitrile.

Drug-excipient compatibility study

Compatibility studies were performed using FTIR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied by making a KBr disc. The characteristic absorption peaks of montelukast sodium were obtained at different wave numbers in different samples. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. This indicates that the drug is compatible with the formulation components. The spectra for all formulations are shown below. [Fig. 1-4 & Table 2]

Preparation of calibration curve for Montelukast sodium

Standard solutions in the range of 5 to 25µg/ml were prepared and absorption values were recorded at 342 nm against the reference. From this data, the standard curve of montelukast sodium was obtained by plotting absorbance on Y-axis against concentration on X-axis. (Fig. 5)

Precompression parameters

Formulation of granules is the key factor in the production of tablet dosage form involving immediate release of drug. Granules ready for compression containing drug and various excipients were subjected for pre-compression parameters (Micromeritic properties) to study their flow properties, and to achieve uniformity of tablet weight. The results of all the pre-compressional parameters are given below. [Table 3]. Precompression parameters like angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio were conducted for all the formulation. The two most important attributes for the direct compression formula are good flow and good compressibility. A comparison of the bulk density and tapped density can give a measure of the relative importance of this interaction in a given powder; such a comparison is often used as an index of the ability of the powder to flow. The angle of repose gives important information about the flow characteristics of the

Powder mixture. The angle of repose conducted for all the formulations are within the range of 17.2±0.04 to 22.4±0.02. The bulk density and Tapped density conducted are within the range of 0.53±0.01 to 0.58±0.05 and 0.60±0.01 to 0.72±0.01 respectively. The carr's index is found to be within the range of 6.03±4.3 to 26.11±1.8 The Hausner's ratio is found to be within the range of 1.09±0.04 to 1.15±0.03. The results revealed that all the formulations had shown good pre-compressional properties showing better flowability.

Evaluation of tablets

All the formulations were evaluated for various parameters like hardness, friability, disintegration time. Weight variation and in vitro release values are given. The hardness of the tablets was found to be 2.4 $\pm$ 0.10 to 2.6 $\pm$ 0.057 kg/cm^{2}and friability was found to be below 1% indicating good mechanical resistance. The thickness of the tablets was found to be 2.5±0.1 to3.5±0.5. All the tablets passed weight variation test, as percentage weight variation was within the pharmacopoeia limits i.e.±7.5%. Batch F8 was selected as optimized batch containing sodium starch glycolate as superdisintegrant in 7.5% concentration. It was shown less disintegration time of 20 seconds. It was observed that less disintegration time was observed when SSG was used as superdisintegrant, may be due to swelling at faster rate upon contact with water and elimination of lump formation after disintegration when compared with Crosspovidone and croscarmellose sodium. [Table 4].

In-vitro dissolution study

The dissolution study on formulation no: F1 to F9 were carried out using 900 ml of dissolution medium 0.5%SLS .The rapid *In-Vitro* dissolution was shown in the formulation F8 containing Sodium Starch Glycolate (7.5%) High dissolution resulted due to faster break down & rapid disintegration of tablet.By this study an important conclusion can be drawn that addition of superdisintegrants technique has improved the dissolution profile of the water soluble drugs besides the disintegration time.[Table 5].

Table 1: Formulations of Montelukast tablets containing different superdisintegrants.

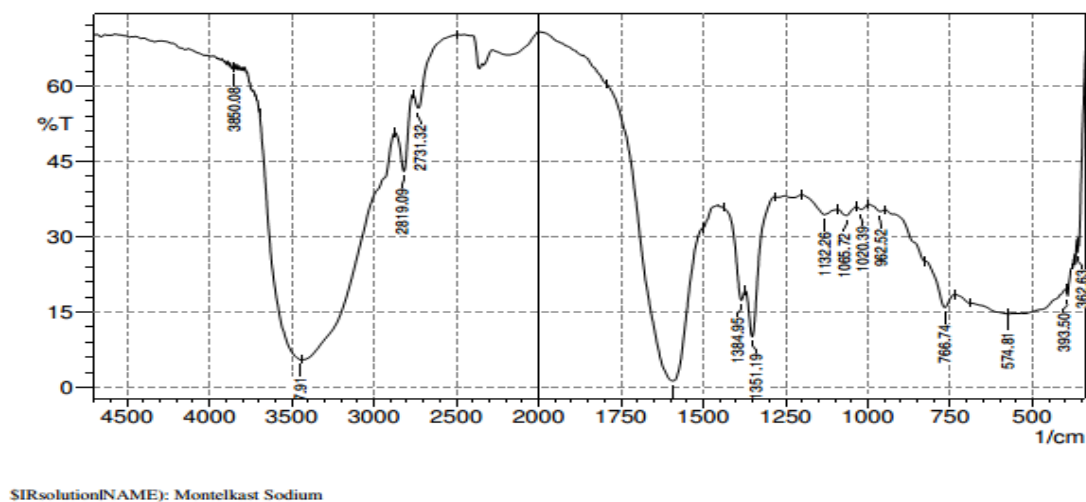| Materials	F1	F2	F3	F4	F5	F6	F7	F8	F9
Montelukast sodium(mg)	10	10	10	10	10	10	10	10	10
Microcrystalline cellulose(mg)	111	106	102	111	106	102	111	106	102
Lactose monohydrate(mg)	50	50	50	50	50	50	50	50	50
Cross providone (mg)	9	13.5	18	-	-	-	-	-	-
Cross cormellose sodium (mg)	-	-	-	9	13.5	18	-	-	-
Sodium starch glycolate (mg)	- 180	- 180	- 180	- 180	- 180	- 180	9 180	13.5 180	18 180

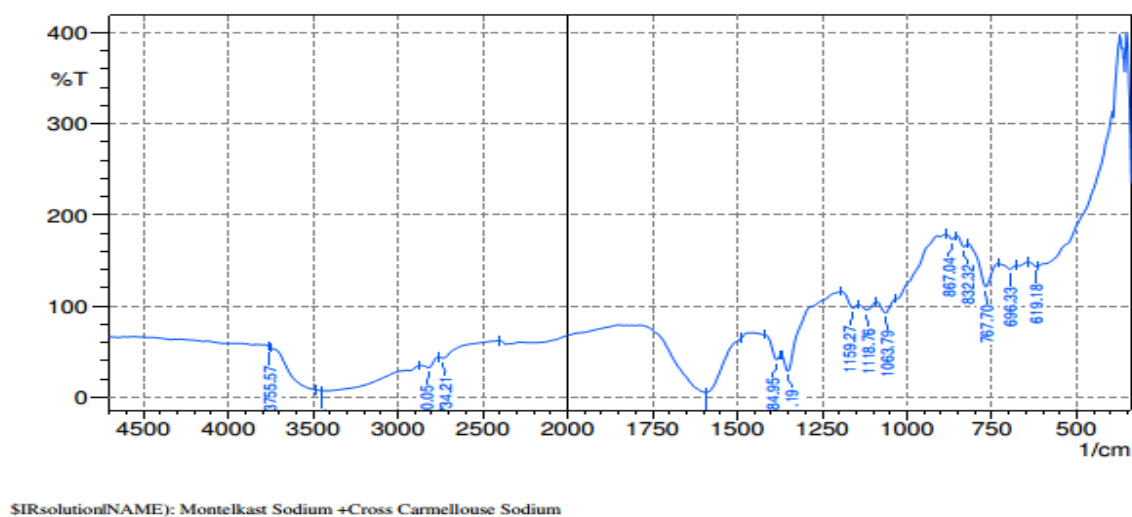**Figure 1: FTIR spectra of Pure Montelukast Sodium.**

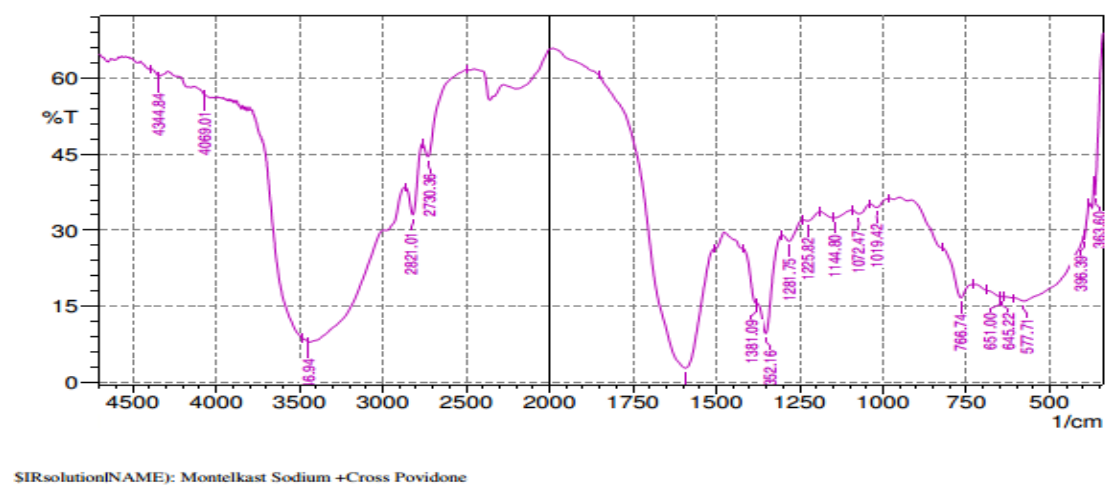**Figure 2: FTIR spectra of Pure Montelukast Sodium+Cross carmellose Sodium**

Figure 3: FTIR spectra of Pure Montelukast Sodium+Cross povidone.

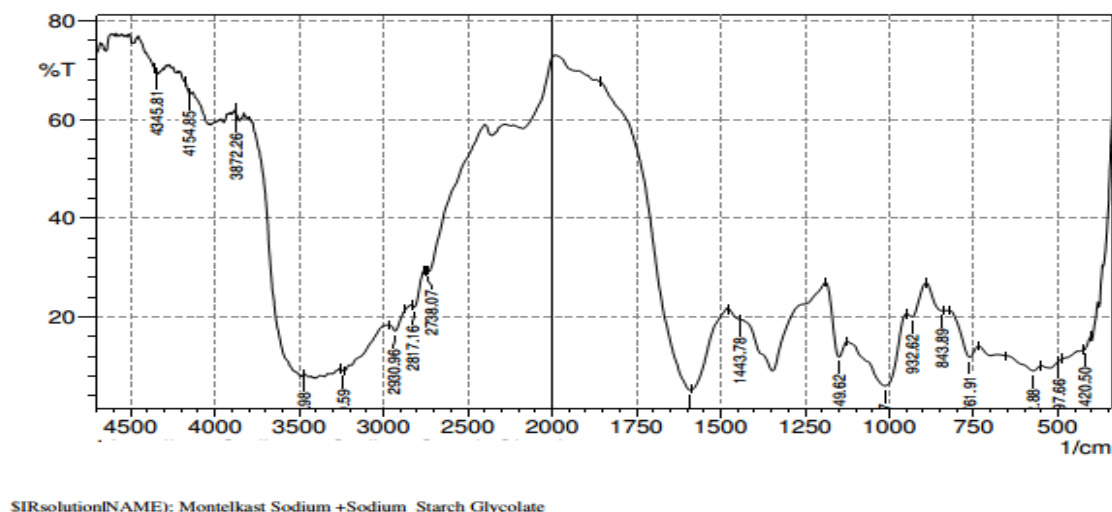SIRsolutionINAME): Montelkast Sodium +Sodium Starch Glycolate

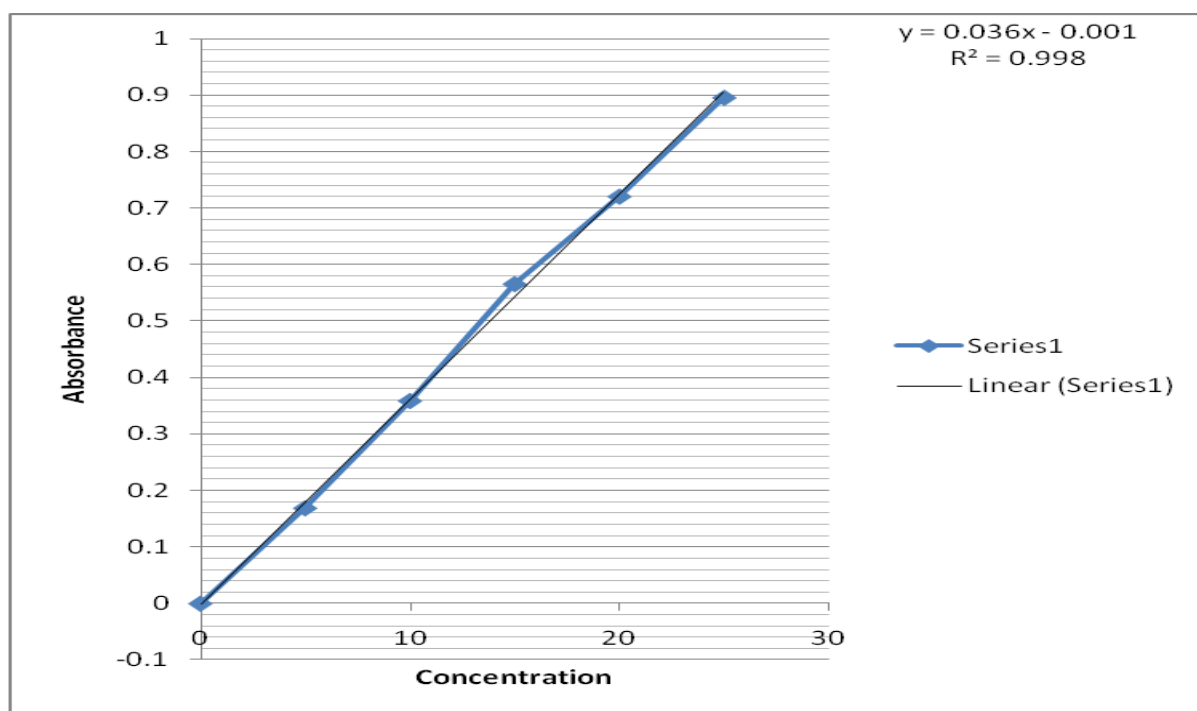**Figure 4: FTIR spectra of Pure Montelukast Sodium+Sodium starch glycolate.**

Figure 5: Calibration curve of Montelukast in 0.5% SLS solution at 342nm.

Table 2: IR interpretation of pure drug and other superdisintegrants.

Functional Group Present	Standard wave Range cm $^{-1}$	Pure drug cm $^{-1}$	Cross carmellose sodium cm $^{-1}$	Cross povidone cm $^{-1}$	Sodium starch glycolate cm $^{-1}$
C – Cl (Aliphatic)	800 – 600	794.70	773.70	775.41	792.70
C – S (Aliphatic)	700 – 600	669.32	694.90	669.81	669.32
C =N (Aromatic)	1600 -1430	1496.81	1436.81	1496.81	1492.81
C = O (Aliphatic)	1870 -1660	1685	1635.89	1683.61	1684.61
C = C (Aromatic)	1645 – 1600	1606	1610	1613.82	1602.82
C – H (Aliphatic)	2960 – 2850	2937	2932	2934.60	2936.60

Table 3: Preformulation studies of blend of all formulations.

Formulation	Bulk density (gm/cm^3)	Tapped density(gm/cm^3)	Angle of repose(θ)	Carr'sIndex (%)	*H*ausner's ratio
F1	0.53±0.005	0.68±0.07	22.4±0.02	13.26±0.06	1.28±0.03
F2	0.57±0.005	0.67±0.01	21.2±0.04	10.86±0.01	1.15±0.03
F3	0.54±0.02	0.65±0.02	19.7±0.06	12.7±0.02	1.21±0.03
F4	0.58±0.015	0.65±0.01	18.8±0.03	11.3±0.04	1.20±0.01
F5	0.53±0.007	0.72±0.01	17.2±0.04	8.88±0.03	1.29±0.08
F6	0.54±0.005	0.66±0.01	19.2±0.05	9.09±0.08	1.25±0.13
F7	0.53±0.01	0.61±0.01	19.8±0.6	12.0±0.02	1.15±0.04
F8	0.57±0.03	0.62±0.005	17.6±0.04	10.86±0.05	1.16±0.02
F9	0.57±0.01	0.60±0.01	17.2±006	12.5±0.04	1.09±0.04
	n=3±SD	n=3±SD	n=3±SD	n=3±SD	n=3±SD

Table 4: Evaluation of tablets.

Formulation	Thickness (mm)	Hardness(kg /cm2)	Friability (%)	Weight variation (mg)	Disintegration time(sec)
F1	3.5±O.1	3.7±0.1	0.35±0.03	178±0.02	40±0.4
F2	3.2±0.3	3.4±0.3	0.92±0.05	180±0.01	62±0.3
F3	3.1±0.1	4.3±0.5	0.65±0.02	175 ±0.05	58±1.8
F4	3.3±0.5	3.6 ±0.2	0.63±0.01	179±1.0	49±2.3
F5	2.8±0.2	3.4±0.4	0.60±0.03	174±2.0	23.5±2.2
F6	3.2±0.1	3.8±0.6	0.96±0.02	178±0.05	37±3.0
F7	3.3±0.3	3.7±0.2	0.64±0.06	175±1.0	22.5±1.5
F8	2.6±0.2	3.2±0.1	0.75±0.03	180±0.07	20±1.8
F9	2.8±0.1	3.1±0.1	0.92±0.02	176±0.09	48±1.6

Table 5: Cumulative percentage drug release of F1 to F9.

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	19.26 ±0.75	25.85 ±1.00	28.09± 0.84	24.54± 0.96	27.13± 0.39	30.64± 0.83	28.32± 0.91	32.94± 1.02	33.46± 1.02
10	28.67 ±0.60	34.30 ±0.86	46.23± 0.98	33.23± 0.96	36.34± 0.96	41.83± 0.94	37.54± 0.93	40.03± 1.32	46.23± 1.13
15	47.39 ±0.62	56.73 ±0.88	57.85± 0.71	49.88± 0.89	58.85± 0.83	57.79± 0.25	56.98± 0.93	59.53± 1.06	58.50± 1.16
20	58.82 ±0.85	60.51 ±0.84	68.53± 0.97	57.45± 0.87	64.04± 0.36	67.30± 0.67	63.53± 0.98	66.80± 1.23	67.01± 1.42
30	63.86 ±0.55	69.24 ±0.86	77.89± 0.05	62.50± 0.64	70.95± 0.35	73.83± 0.68	70.91± 0.86	72.62± 1.48	74.92± 1.13
45	71.21 ±0.74	78.87 ±0.72	87.24± 0.06	70.65± 0.56	79.34± 0.86	82.38± 0.39	78.77± 0.93	80.15± 1.36	83.08± 1.12
60	82.56 ±0.82	89.50 ±1.67	91.41± 0.76	79.81± 0.78	90.41± 0.84	96.69± 0.31	89.16± 0.94	98.79± 1.24	87.6±1. 69

mean±S.D, n = 3

CONCLUSION

Montelukast sodium is a leukotrine receptor antagonist used for the maintanance tratement of asthma and to relieve symptoms of seasonal allergies. As conditions like asthma requires quick releif the immediate release tablets of montelukast were prepared by using various superdisintegrats. Totally nine formulations were prepared by using different superdisintegrants by direct compression method. All the formulations were subjected for both precompression as well as post compression studies and the results found to be satisfactory. The F8 formulation was considered as an optimised formulation due to its less disintegration time and maximum cumulative percentage drug release of 98.79% at 60th min when compared with other formulations.

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