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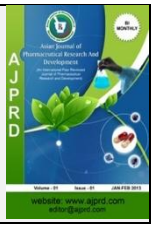

Open Access Research Article

Formulation and Evaluation of Montelukast Sodium Oral Dissolving Film

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A B S T R A C T

The preliminary batches were planned for the formulation and development of placebos of fast dissolving film by using solvent casting method. Total 10 formulations were prepared by using concentration of polymer i.e pullulan in different proportion. In formulations F5 to F6 various concentration of pullulan were incorporated as well as in other formulation trails taken with different concentration of different natural i.e Sodium alginate, SSG and synthetic i.e HPMC, eudragit to find out best suitable polymer for the film formation. Among all formulations, formulation F5 was found to be satisfactory. The placebos were evaluated for various parameters such as physical appearance, weight variation, thickness, surface pH and disintegration time. F5 formulation came out with best result after various evaluations and so it was further prepared by incorporating Montelukast Sodium API. This formulation was then evaluated for various parameters along with assay, content uniformity and dissolution. The results obtained from the F5 formulation complied with the specifications given for ODF. A batch to batch was also observed after obtaining the results. Further, various batches were prepared with various concentration of PEG-400 and evaluated. It was observed that the batch with the higher concentrations of PEG-400 retarded release of drug from formulation. In vitro release studies showed that the formulation F5 match with the required dissolution profile, the drug release retarded in F1, F2 and F3 formulations due to different concentration of polymer and plasticizer, which did not match with the required dissolution profile. The in vitro release of formulation F5 was found to be most promising as it was in accordance required dissolution profile.

Key Words: fast dissolving film, Montelukast Sodium, Sodium alginate, SSG.

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INTRODUCTION

Drug administration through oral cavity offers several advantages. The oral mucosa is easily accessible and therefore makes uncomplicated application of dosage forms. Moreover, the oral mucosa can withstand against local stress and damage and the cellular recovery process is fast after such incidents.[1] Active substances can be given locally to treat several oral diseases like bacterial and fungal infections, periodontal disease etc. Drug permeation through mucosal endothelium provides systemic action. Various dosage forms and devices i.e. buccal patches, mechatronic delivery devices and buccoadhesive discs have been developed for systemic drug absorption.[2]

The above mentioned advantages of drug delivery through oral cavity offers new alternatives in the administration of the drugs to special age group like children and the elderly candidates. These patients need special drug administration requirements as they face difficulty to swallow solid dosage forms such tablets and capsules.

Poor taste of drug is also a cause of the refusal and spat out of the medications. Furthermore, the paediatric population is a very diverse group as it is divided into six different groups: preterm new-born infants, term new-born infants, infants/toddlers, pre-school children, school children and adolescents. As such, there are considerable differences in the acceptability and appropriateness of different dosage forms for the different age groups. Therefor for such age-groups solid dosage forms are unsuitable due to inability to swallow. The intravenous route is usually used in case, if the child is severely ill or still very young. Due to the repulsion of oral liquids, rectal route is mainly used for

administered of the drugs to achieve systemic effects but this route is not accepted in some cultures.[3-4]

In particular, for the preterm and term infants liquid dosage forms (e.g. solution, drops, emulsions, suspensions) for per oral use are recommended. The poor stability of aqueous liquids is problematic. Substances like benzalkonium chloride, benzyl alcohol or parabens are commonly used as preservatives. Many such substances are known to be potentially allergenic which is a problem often underestimated. Moreover, preservatives can be toxic due to immature metabolic pathways in children.[5]

Fast-dissolving solid drug dosage forms for application onto the oral cavity for such population seem to be very appropriate. The delivery of drugs via the oral mucosa offers easy application, prevents drug degradation by gastrointestinal fluids, avoids first-pass metabolism and potentially improves bioavailability with rapid drug absorption and fast onset of drug action. Recently, the rapidly dissolving films have gained popularity as dosage forms and the pharmaceutical industry has recognized their potential for delivering medicinal products and has launched several products for the OTC market using this formulation technology. They are designed to dissolve/disintegrate in the mouth within a few seconds without additional water and the need to swallow. The fast-dissolving film is placed onto the patient's tongue where it is instantly wet by saliva, hydrated and adheres to the mucosa. The film then disintegrates and dissolves, releasing the drug for absorption by the mucosa.[6-9]

Material and methods:

The chemicals and solvents used in the present investigation are listed in Table below:

Table 1: List of Chemicals and Solvents

S.No.	NAME	SUPPLIER / MANUFACTURER
1	Montelukast Sodium	Gift sample from Replica Remedies PVT. LTD.,
2	Sodium starch Glycolate	Signet Chemicals Pvt. Ltd., Mumbai
3	Sodium Alginate	Central Drug House (P) Ltd., New Delhi
4	Pullulan	Nagase India PVT. LTD.
5	Eudragit	Evonik Pharmaceuticals, Bangalore
6	HPMC	Central Drug House (P) Ltd., New Delhi
7	PEG-400	Central Drug House (P) Ltd., New Delhi
8	Citric Acid	Central Drug House (P) Ltd., New Delhi
9	Aspartame	Sweetener India, Delhi

Method of preparation of (Drug Incorporated)

- Weighed accurate amount of polymer and socked in 10 ml ofwater.
- Required quantity of Montelukast sodium was dissolved in 10 mlof water.
- Added mentioned quantity of citric acid and aspartame to this solution and stirred for 45 minutes.
- Properly mixed the solution and added polymer solution to it with continuous stirring.
- At last, added plasticizer PEG 400 by continuous stirring.
- Stirred the final dispersion for next 45 minutes and then sonicated the solution for 15 minutes to remove air bubbles.
- Then after the dispersion was kept aside for one hour to settle down the foams.
- Meanwhile, lubricated the petri dish with the help of glycerol to terminate the chances of damage of the films while removing from the petri dish.
- Transferred the 2 ml of the final dispersion in the measuring cylinder and then cast the solution in the cleaned and dry petri dish (area of 28.26cm^2).
- The films were then kept under drying in vacuum tray dryer at 40°C for about 1-2 hours.
- The films were then removed and cut into the size of 2x2 cm^2
- containing 5mg of montelukast sodium.
- These films were then stored at room temp in suitable packaging

Table 2: Formulation of Oral Dissolving Films (Drug Incorporated)

Ingredients (Batch No. F5)	Quantity
Montelukast Sodium (mg)	176
Pullulan (gm)	0.9
PEG 400 (ml)	1
Citric Acid (mg)	200
Aspartame (mg)	10
Colouring Agent	q.s*
Flavouring Agent	q.s*
Water (ml)	10

Characterization and Evaluation

Characterization of films is accomplished via following tests:

Organoleptic evaluation

Special controlled human taste panels are used for such purpose. This in vivo taste evaluation is carried out on human volunteers. In-vitro taste evaluation of ODFs is performed by using taste sensors for screening.

In vitro taste assessing methods and technologies are appropriate and sufficient for high throughput taste sensing of such dosage forms. Both in vivo and in vitro techniques analyse the taste masking ability and sweetness level of taste masking agents.

Mechanical properties

Thickness test

Thickness of a film is determined by using calibrated digital micrometre and then subsequently mean average is calculated. Generally, three readings from all the batches are determined and average is calculated. Weight variation of a film is calculated in triplicate by cutting the film and determining weight of each film. Uniformity in thickness is important to ascertain as it is directly proportional to dose accuracy of the film.[8]

Dryness test/tack test

This test is performed to find out the ability of a film to get adhered to a piece of paper pressed between strips. Obstinacy with which the film adheres with the piece of paper or any other accessory pressed in between the films is known as tack. Almost there are eight stages of film drying process which are identified viz dry-to touch, dry-to-recoat, and dry hard, set-to-touch, and dust-free, dry-through, tack-free and dry print-free. Primarily these tests are used to evaluate dryness of films in paint industry but are also adoptable for assessing orally fast disintegrating films. Dryness or tack test can also be performed by with the help of some newly invented instruments.[9]

Tensile strength

Tensile strength is defined as maximum stress applied at which the film breaks. Basically, this test is performed to measure the mechanical strength of films. It can be calculated from applied load at rupture divided by the strip cross-sectional area.

Percent elongation

Upon exerting stress on a film, the specimen stretches which is referred as strain. Strain is defined as change in length of film divided by its original/initial length of the film specimen. Percent elongation is related quantitatively to the amount of plasticizer used in film formulation. Increased plasticizer concentration in the film generally results in enhanced elongation of the strip.

Tear resistance

Tear resistance of film is the intricate function of its ultimate resistance to rupture. Maximum force required to tear the film is measured as tear resistance value. This test is typically attributed to plastic industry. The rate of loading employed is 2 in/min which is planned to determine the magnitude of force required to initiate tearing in the film specimen. The maximum amount of force necessary for tearing is generally found near the tearing onset which is ranked as tear resistance value.[10]

Folding endurance

Folding endurance is another procedure to estimate the mechanical properties of a film. It is measured by repeatedly folding a film at the same point until it breaks. Folding endurance value is number of times the film is folded without breaking.

Higher folding endurance value depicts the more mechanical strength of a film. A direct relation exists between mechanical strength and folding endurance of films. As mechanical strength is governed by plasticizer concentration so it is clearly evident that plasticizer concentration also indirectly affects folding endurance value.

Content uniformity

Contents of a film are determined by standard assay method specified for individual drug in different pharmacopoeia. This test is performed on 20 samples using analytical techniques. The acceptance value of the test is less than 15% in accordance with Japanese pharmacopoeia. According to USP27, the contents should range from 85% to 115% with the standard deviation of less than or equal to 6%. Content uniformity is worked out for estimating drug contents in individual film.[11]

Disintegration time

Disintegration apparatus mentioned in official pharmacopoeias is used for determining the disintegration time of a film. Normally, the disintegration time is the function of composition of film as it varies with the formulation and generally ranges from 5 to 30

s. Mostly, the USP disintegration apparatus is used for this test. There are no official guidelines available for determining disintegration time of orally fast disintegrating films. There are two methods for determining disintegration time of film:[12]

Slide frame method

A drop of distilled water is poured onto the film clamped into slide frames placed on petri dish. Time taken by the film to dissolve is noted.

Petri dish method

A film is placed onto 2 ml distilled water taken in petri dish. Time taken by the film to dissolve completely is considered as the disintegrating time.

In-vitro dissolution test

Standard official basket or paddle apparatus is used for conducting dissolution studies on films. Sink conditions should be maintained during dissolution.

Sometimes while performing this process, film floats over the medium making it difficult to perform the test properly. This problem is more likely to occur in case of paddle method thus the basket apparatus is mostly preferred. Media used are 6.8 pH phosphate buffer (300 ml) and 0.1 N HCl (900 ml). Temperature is maintained at 37 ± 0.5 °C and rotation speed of 50 rpm is usually adjusted. Samples of drug dissolved are collected at pre-determined intervals and are analysed by using UV-spectrophotometer. Despite its extensive use, dissolution test is still prone to noteworthy inaccuracy and tests let-down.

Visual inspection and surface morphology

Visual inspection of a prepared orodispersible film gives information about colour,

homogeneity and transparency. For surface morphology, scanning electron microscopy is performed. Absence of pores and surface uniformity depicts good quality of films.

Surface pH

The pH value of a film is usually determined by putting the prepared film in petri dish and subsequently film is made wet by using distilled water and noting pH by touching the film surface with a pH meter electrode. Determination of surface pH is vital as acidic or basic pH is liable to cause oral mucosal irritation.

Moisture uptake and moisture loss

Percent moisture loss is a parameter that determines the hygroscopicity of a film. Usually, this parameter is determined by first finding the initial weight of the film, afterward, putting this film in a desiccator for three days. Desiccator contains calcium carbonate. After three days, strips are taken out and weighed again. Moisture loss is determined by applying the following formula. Moisture uptake of a film is determined by first cutting the film with the dimension of 2 × 2 cm^2. Afterward these strips are exposed to environment with a relative humidity of 75% at room temperature for 7 days. Moisture uptake is determined as percent weight gain of the strips.

Stability studies of oral dissolving films

The purpose of stability testing is to provide evidence on how the quality of a drug substance or a drug product varies with the time under the influence of variety of environmental factors such as temperature, humidity, light etc.

A successful attempt was made to formulate fast dissolving oral films of Montelukast sodium using different concentration of different film forming polymers. In present work ten formulations were prepared. The formulated films were characterized for physicochemical parameters.

PREFORMULATION STUDIES OF PURE DRUG IDENTIFICATION OF DRUG

The IR spectrum obtained of pure drug shows characteristics peaks as given below and depicted in figure.

Table 3: IR Spectrum of Montelukast Sodium

Functional Group Presents	Standard Wave Range Cm^{-1}	Peaks
C – Cl (Aliphatic)	800 – 600	794.70
C – S (Aliphatic)	700 – 600	669.32
C = N (Aromatic)	1600 -1430	1496.81
C = O (Aliphatic)	1870 -1660	1685
C = C (Aromatic)	1645 – 1600	1606
C – H (Aliphatic)	2960 – 2850	2937

Drug excipients compatibility study:

Physical compatibility:

The sample were kept in open (O), closed (Cl) and controlled conditions (CO). Both open and closed vials are kept at accelerated conditions (40°C/75%RH) and observed after the end of the every week for four weeks to determine physical incompatibility.

Table 4: Drug Excipient Physical Compatibility Study

Combination (1:1) ratio	Conditions in which vials are kept											
	After I week			After II week			After III week			After IV Week		
	Co.	Cl.	O	Co.	Cl.	O	Co.	Cl.	O	Co.	Cl.	O
Pullulan	W	W	W	NC	NC	NC	NC	NC	NC	NC	NC	NC
PEG 400	Clr	Clr	Clr	NC	NC	NC	NC	NC	NC	NC	NC	NC
Citric Acid	W	W	W	NC	NC	NC	NC	NC	NC	NC	NC	NC
Aspartame	OW	OW	OW	NC	NC	NC	NC	NC	NC	NC	NC	NC
Pullulan+ Montelukast Sod.	W	W	W	NC	NC	NC	NC	NC	NC	NC	NC	NC
PEG400+Montelukast Sod.	W	W	W	NC	NC	NC	NC	NC	NC	NC	NC	NC
Citric Acid+Montelukast Sod.	W	W	W	NC	NC	NC	NC	NC	NC	NC	NC	NC
Aspartame+Montelukast Sod.	OW	OW	OW	NC	NC	NC	NC	NC	NC	NC	NC	NC

***Clr = Clear, W = White, Ow = Off White, NC = No Change**

Chemical Compatibility:

Compatibility study of pure drug Montelukast Sodium with other excipients were carried out prior to the formulation of films. IR spectra of pure drug and DSC of physical mixture of drug-excipients were obtained, which are depicted below. All the characteristics peaks of Montelukast sodium were present in spectra at respective wavelengths. Thus, it shows compatibility between drug and excipients. There was no significant change in the chemical integrity of the drug.

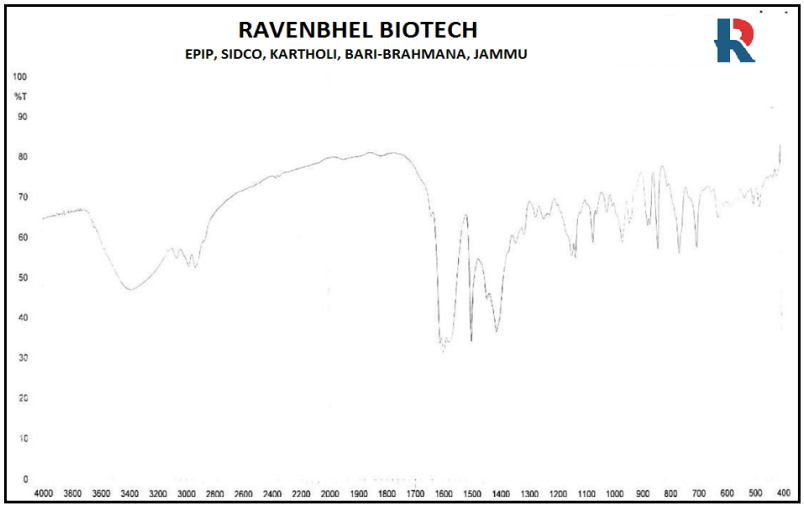

Figure 1: FTIR Spectrum of Montelukast Sodium

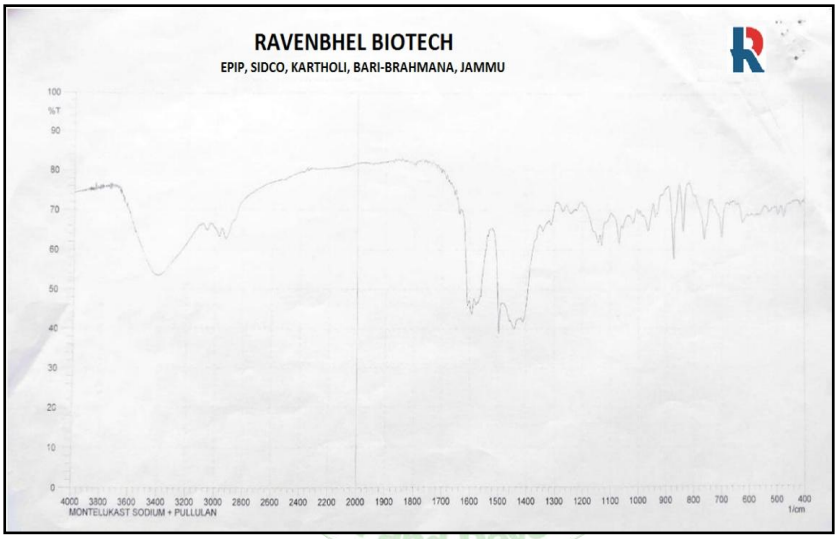

Figure 2: FTIR Spectrum of Montelukast Sodium+Pullulan

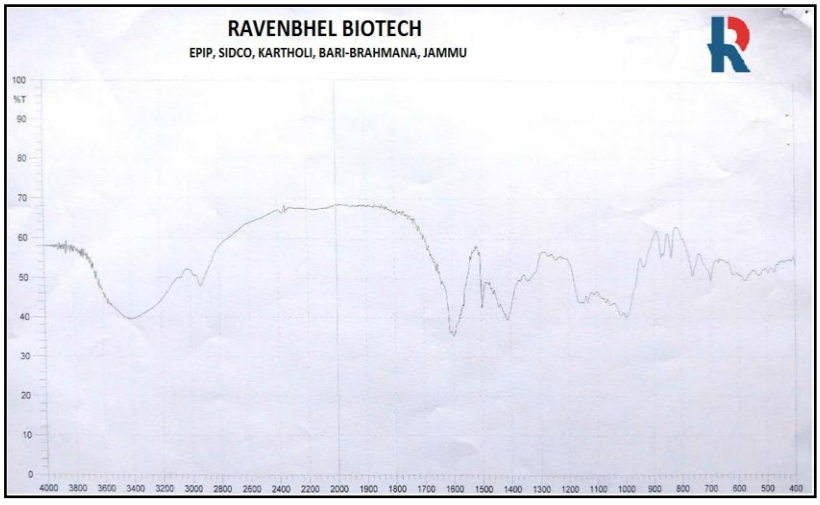

Figure 3: FTIR Spectrum of Montelukast Sodium+SSG

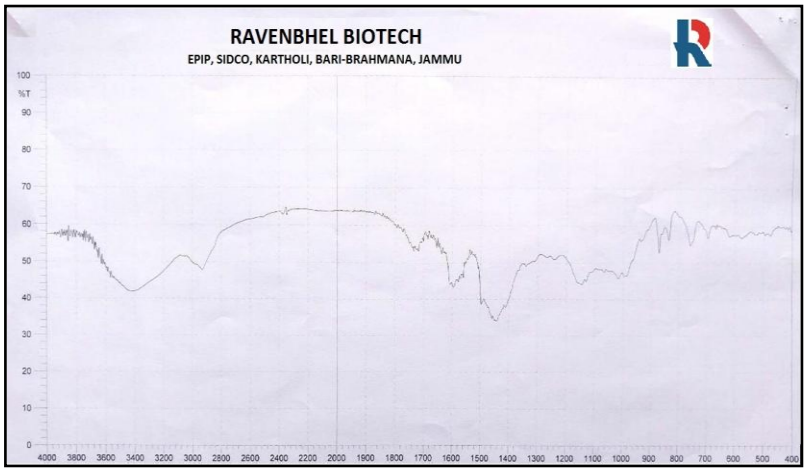

Figure 4: FTIR Spectrum of Montelukast Sodium+Eudragit

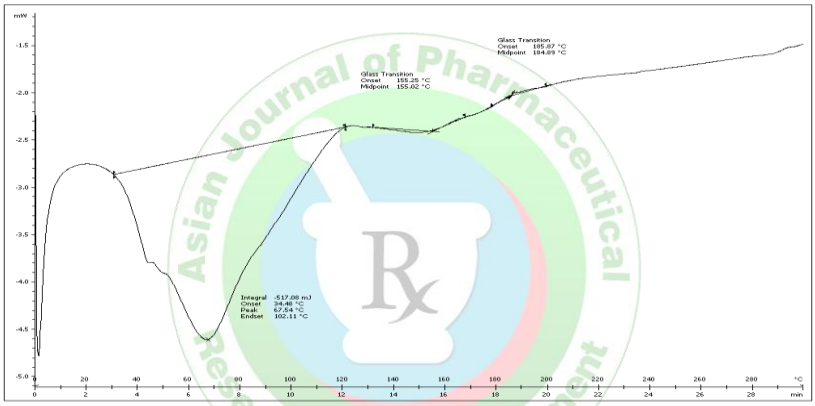

Figure 5: DSC of Montelukast Sodium

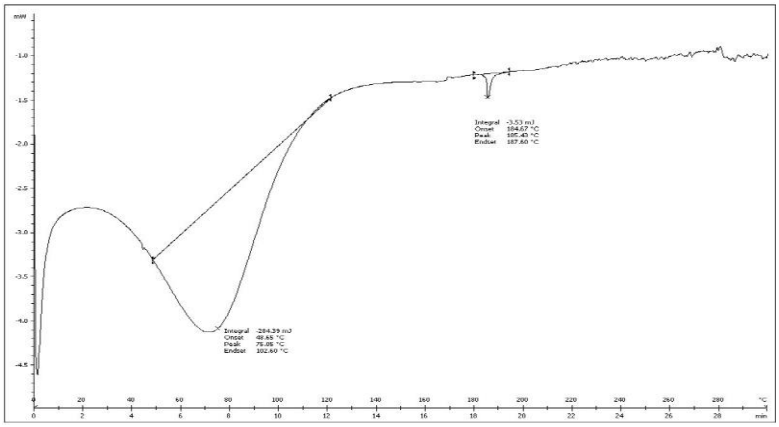

Figure 6: DSC Of Physical Mixture: Optimized Formulation

Table 5: IR Compatibility Study of Drug with Different Polymers

Combination (Drug+polymer)	IR Peaks	Liquefaction	Compatibility
Montelukast Sodium	794,669,1496,1685, 1606,2937	No	Compatible
Montelukast Sodium + SSG	796,664,1493,1681, 1604,2936	No	Compatible
Montelukast Sodium + Pullulan	798,665,1491,1680, 1602,2941	No	Compatible
Montelukast Sodium + Eudragit	801,675,1502,1690, 1600, 2920	No	Compatible
Montelukast Sodium + Sodium Alginate	790,668.1490,1685, 1606,2925	No	Compatible
Montelukast Sofium + SSG+Eudragit+Pullul and+Sodium Alginate	793,678,1502,1681, 1606,2936	No	Compatible

Evaluation of Montelukast Sodium Oral Dissolving Films

Appearance

Formulations containing lower concentration of pullulan were transparent, higher concentration of pullulan were translucent and films containing eudragit and sodium alginate were opaque in appearance. HPMC films were also transparent but the films containing pullulan had good texture and feel.

WEIGHT OF FILM

Films of area 4 cm^2 were weighed using electronic balance and the average weight was calculated. The weight of films range from 18-23 mg.

THICKNESS OF FILM

The thickness of three randomly selected films was determined using a standard Vernier caliper. The thickness of films were range from 0.037- 0.053.

SURFACE pH OF FILM

The surface pH of the film was determined in order to investigate the possibility of any side effect in vivo. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to the neutral as possible. The pH of films range from 6.43-6.98.

FOLDING ENDURANCE:

Folding endurance was determined by repeatedly folding the film at same possible position until it breaks. The folding endurance of films range from 209-269.

DISINTEGRATION TIME

2 ml of distilled water was placed in petridish and one film was added on the surface of the water and the time measured until the film was dissolved completely. The disintegration time range from 8-33 seconds.

DRUG CONTENT STANDARD PREPARATION:

Weighed accurately 5 mg of Montelukast sodium dissolved in 100 ml pH

6.8 phosphate buffer. Dilute 1 ml of this solution to 10 ml with pH 6.8 Phosphate buffer.

TEST PREPARATION:

A sample of size 2x2 cm^2 which were placed in the beaker containing 100 ml of distilled water. Dilute 10 ml of this solution to 10 ml with distilled water.

PROCEDURE:

Absorbance of standard preparation and test preparation was taken using UV double beam spectrophotometer.

The drug content of films was found to be between 96.29-99.87%.

Table 7: Physical Characterization of Fast Dissolving Oral Films

PARAMETERS	FORMULATION CODE									
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**
Weight variation	19.37 ±0.452	22.07 ±0.323	20.64 ±0.337	21.50 ±0.547	23.69 ±0.601	17.71 ±0.432	22.75 ±0.231	18.75 ±0.652	20.68 ±0.125	22.83 ±0.385
Thickness	0.040 ±0.010	0.048 ±0.012	0.037 ±0.081	0.053 ±0.090	0.048 ±0.001	0.050 ±0.042	0.047 ±0.065	0.051 ±0.032	0.053 ±0.089	0.036 ±0.042
Surface pH	6.67	6.95	6.43	6.87	6.98	6.89	6.58	6.98	6.87	6.74
Folding endurance	209	219	230	238	260	218	232	246	257	269
Disintegration time	29 ±0.58	23 ±0.15	17 ±0.56	25 ±0.65	8 ±0.12	37 ±0.18	40 ±0.85	30 ±0.45	27 ±0.89	33 ±0.56
Drug content	96.47 ±0.45	98.53 ±0.89	97.32 ±0.41	96.58 ±0.67	99.87 ±0.85	98.87 ±0.78	98.47 ±0.23	96.23 ±0.68	97.30 ±0.44	97.83 ±0.49

In-vitro drug release:

The in-vitro dissolution study was carried out in simulated saliva solution pH 6.8 phosphate buffer using USP basket apparatus at 37±0.5°C. Samples were withdrawn at regular time intervals and analysed by UV-Visible spectrophotometer. By this method cumulative drug release and cumulative percentage of drug retained were calculated.

The study was carried out at 37°C with stirring speed of 75 rpm in 900 ml of pH 6.8 phosphate buffer dissolution medium. 5 ml of samples were withdrawn at predetermined time intervals of 2,4,6,8 and 10 minutes and replaced with the same volume of buffer. The samples were collected and the absorbance was determined at 287 nm UV-Visible spectrophotometer.

The results of in-vitro release data obtained for all formulations were fitted in two popular models of data treatments as follows:

i. Zero-order kinetic model (cumulative percent drug released vs time) ii First-order kinetic model (log cumulative percent drug remaining vs time).

Table 8: Dissolution Parameters for Formulations

S.No	Formulation code	$t_{25\%}$ (min)	$t_{50\%}$ (min)	$t_{70\%}$ (min)	$t_{90\%}$ (min)	Cumulative % drug release in 10 minutes
1.	F1	2.47	5.47	8.13	>10	82.94
2.	F2	2.74	6.10	8.46	>10	87.36
3.	F3	2.00	4.00	6.00	>9	97.21
4.	F4	1.35	3.00	4.22	>8	97.52
5.	F5	1.00	2.00	2.10	>6	98.57
6.	F6	2.98	6.00	8.23	>10	79.87
7.	F7	3.00	5.47	8.12	>10	82.48
8.	F8	2.13	4.47	7.10	>10	89.36
9.	F9	2.00	4.00	6.01	>10	95.58
10.	F10	1.48	2.49	4.47	>10	98.01

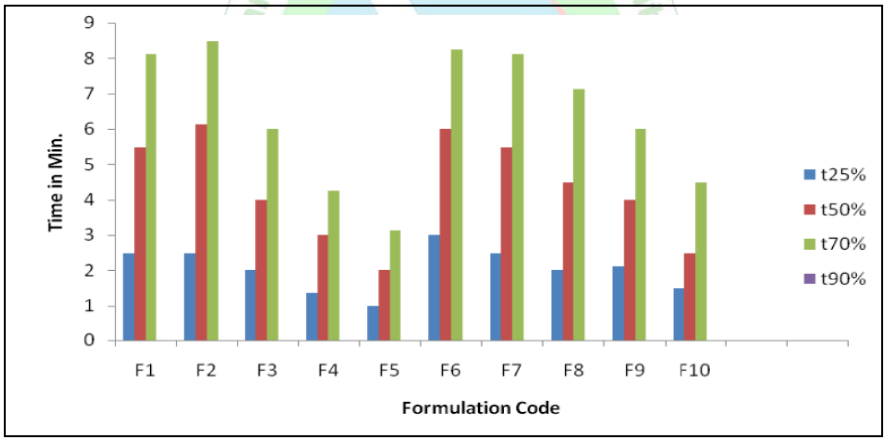

Figure 7: Comparison of Dissolution Parameters (T25%, T50%, T70%, T90%) of Fast Dissolving Films of Montelukast Sodium

Assay of Content Uniformity

The result of assay and content uniformity of all batches is shown in table. Content uniformity and assay complies in all batches as all batches are within the specified limit of 95% to 105% as per USP. The formulation F5 shows maximum drug content which is 99.87%.

Table 9: Result of Assay of Content Uniformity

Batch No.	Assay (%)	Content Uniformity
F1	96.47 ± 0.45	Complies
F2	98.53 ± 0.89	Complies
F3	97.32 ± 0.41	Complies
F4	96.58 ± 0.67	Complies
F5	99.87 ± 0.85	Complies
F6	98.87 ± 0.78	Complies
F7	98.47 ± 0.23	Complies
F8	96.23 ± 0.68	Complies
F9	97.30 ± 0.44	Complies
F10	97.30 ± 0.44	Complies

Data treatment

The in vitro release data were plotted for various kinetic models. To find out mechanism of drug release from all the formulations of Montelukast sodium mouth dissolving films, the data were fitted according to zero order and first order pattern as illustrated in table.

The correlation coefficient (R^2) values of all formulations showed that the formulations follow first order release pattern, as indicated by their high regression coefficient. The R^2 value of zero order was found to be very low i.e 0.63 while that for first order was found to be 0.98 which indicates that the release from formulation F5 was found to be nearly first order release, governed by dissolution through polymer. The release of drug from polymer also depends upon polymer viscosity. High molecular weight polymer retards release of drug from formulation.

Table 10: Kinetic Value Obtained From In Vitro Release

Formulation Code	Zero order		First order	
	Ko (mg/h)	R^2	K_1 (hr^{-1})	R^2
F1	7.497	0.567	0.487	0.957
F2	7.537	0.482	0.489	0.977
F3	7.597	0.457	0.487	0.969
F4	7.447	0.460	0.402	0.970
F5	8.517	0.628	0.478	0.965
F6	8.123	0.541	0.458	0.832
F7	7.737	0.529	0.263	0.991
F8	6.487	0.466	0.289	0.9439
F9	7.861	0.601	0.378	0.9074
F10	8.154	0.643	0.432	0.8987

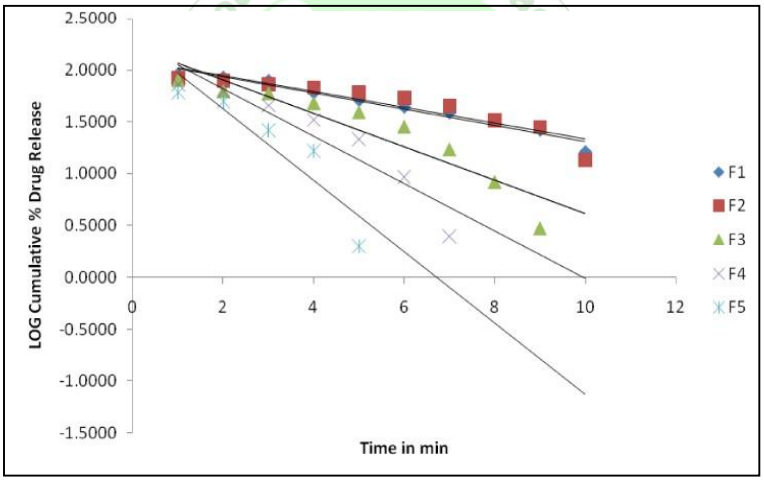

Figure 10: Cumulative Percent Drug Released Vs Time Plots (Zero Order) Of Formulations F1, F2, F3, F4 and F5 in pH 6.8 Phosphate Buffer

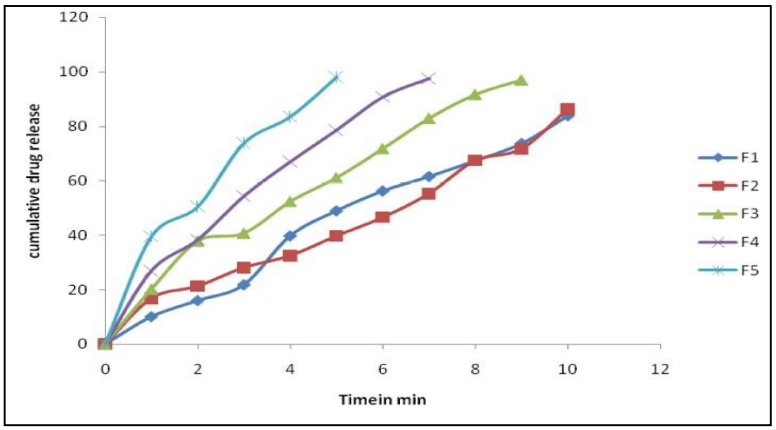

Figure 11: Log Cumulative Drug Remaining Vs Time Plots (First Order) Of Formulations F1, F2, F3, F4 and F5 in pH 6.8 Phosphate Buffer

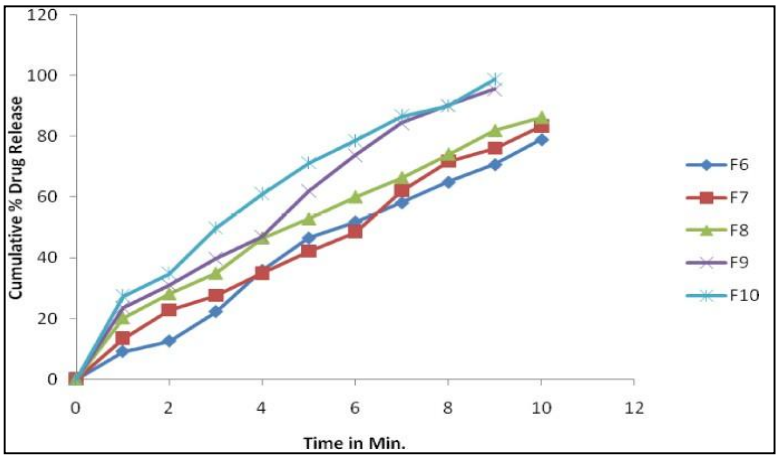

Figure 12: Cumulative Percent Drug Released Vs Time Plots (Zero Order) Of Formulations F6, F7, F8, F9 and F10 in pH 6.8 Phosphate Buffer

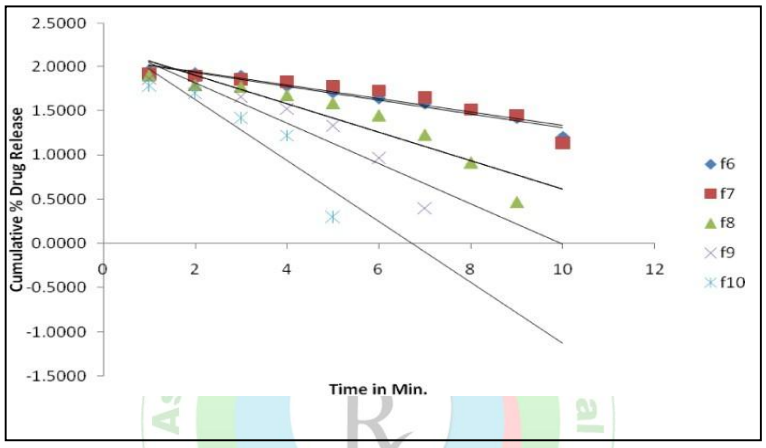

Figure 13: Log Cumulative Drug Remaining Vs Time Plots (First Order) Of Formulations F6, F7, F8, F9 and F10 in pH 6.8 Phosphate Buffer

The aim of the present research work was to develop mouth dissolving films of Montelukast sodium. For the research to be successful, the work to be done should be logically and properly based upon the literature surveyed. The objective of the research work was to develop a safe and stable dosage form for the effective treatment of asthma and seasonal allergies.

During preformulation study, Montelukast sodium used in the research work was analysed for the determination of absorption maxima, organoleptic characteristics, assay, moisture content, solubility determination and identification by FTIR and DSC spectrum. FTIR study showed no interaction between drug and polymer. The results were similar to certificate of analysis provided by the manufacturer and as reported in official compendia. Hence drug sample was considered as a pure and used for further studies. Solubilitystudy do Montelukast Sodium showed that it was soluble in hot as well as cold water and insoluble in ethanol (95%). Drug-excipients compatibility were carried out for proper selection of the excipients. The physical compatibility studies (visual observation only) was carried out by mixing drug with various excipients in the ratio of (1:1) for a period of one month (4 weeks), at different temperature and humidity conditions, under open, closed and controlled conditions. No change in colour was observed when physical mixture of Montelukas Sodium API with all excipients used in the table formulation was kept in above mentioned ratio at different temperature and humidity conditions. So, the excipients to be used were found to be physically compatible with Montelukast sodium and hence suitable for use in formulation.

The preliminary batches were planned for the formulation and development of placebos of fast dissolving film by using solvent casting method. Total 10 formulations were prepared by using concentration of polymer i.e pullulan in different proportion. In formulations F5 to F6 various concentration of pullulan were incorporated as well as in other formulation trails taken with different concentration of different natural i.e Sodium alginate, SSG and synthetic i.e HPMC, eudragit to find out best suitable polymer for the film formation. Among all formulations, formulation F5 was found to be satisfactory. The placebos were evaluated for various parameters such as physical appearance, weight variation, thickness, surface pH and disintegration time.

F5 formulation came out with best result after various evaluations and so it was further prepared by incorporating Montelukast Sodium API. This formulation was then evaluated for various parameters along with assay, content uniformity and dissolution. The results obtained from the F5 formulation complied with the specifications given for ODF. A batch to batch was also observed after obtaining the results. Further, various batches were prepared with various concentration of PEG-400 and evaluated. It was observed

that the batch with the higher concentrations of PEG-400 retarded release of drug from formulation.

In vitro release studies showed that the formulation F5 match with the required dissolution profile, the drug release retarded in F1, F2 and F3 formulations due to different concentration of polymer and plasticizer, which did not match with the required dissolution profile. The in vitro release of formulation F5 was found to be most promising as it was in accordance required dissolution profile.

The dissolution data was fitted to various pharmacokinetic models and it was found that the formulation showed first order release.

Further stability study was conducted on films of F5 formulation and stored for one month in air tight plastic pack. Films were then evaluated for assay, content uniformity, pH, weight and in vitro release profile. No significant changes were observed in any of studied parameters during the study period. The prepared fast dissolving films exhibited good film characteristics features as indicated by the thickness measured, folding endurance, disintegration time, and drug content. The films were found to be uniform, flexible and 99.87% of drug was released by the formulation F5 within ten minutes which was desirable for the fast absorption, thus it could be concluded that the developed formulation was stable.

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