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Formulation And Evaluation Of Medicated Soft Lozenges Of Montelukast Sodium

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ABSTRACT:

Lozenges are solid dosage forms that include one or more medications that are supposed to dissolve or disintegrate slowly in the mouth, or medicated candies that dissolve slowly in the mouth to lubricate and soothe sensitive throat tissue. The objective of the present study was formulation and evaluation of Medicated Soft Lozenges of Montelukast sodium by using PEG 1500 as a lozenges base while Dextrose as a sweetener. The drug excipients interaction study was done by FTIR, the compatibility of Montelukast sodium with PEG 1500 and Dextrose the studies of FTIR showed that all above characteristic peaks of Montelukast sodium were observed near about their respective values so it has been concluded that there is no incompatibility between excipients and pure drug. Formulations were prepared by melting and moulding technique. The Medicated Soft lozenges of Montelukast sodium were evaluated for physical appearance, thickness, weight variation, hardness, friability test, drug content, disintegration time, in- vitro drug release and stability study. All prepared batches showed good in- vitro dissolution studies. The best result from lozenges batches was from F2 which gives Thickness of 5.12 mm, Weight variation of 0.24 mg, Hardness of 6.5 kg/cm^{-1}, Friability of 0.695%, Drug content of 98.32%, Disintegration time of 30 min and In- vitro drug release of 80%. The main selection criteria for the best formulation was in-vitro drug release of the formulations equal to the in-vitro drug release of the pure drug which is not less than 70%, which complies with the IP standards and hardness of the formulation batches. Hence it can be concluded that Medicated Soft Lozenges of Montelukast sodium can be successfully formulated by melting and mould technique.

KEYWORDS: Medicated soft lozenges, antileukotriene, Montelukast sodium.

INTRODUCTION:

Lozenges and pastilles have been produced in pharmacy during the twentieth century and are still manufactured commercially. Lozenges are solid medications that dissolve in the mouth or pharynx. They are meant to treat local irritation or infection of the mouth or pharynx and may also be used for systemic medication absorption. They may include one or more medicaments in a flavoured and sweetened base. They have the ability to distribute drugs in several directions into the mouth cavity or on the mucosal surface[1,2].Though the lozenge dissolves in around 30 minutes, the rate of breakdown and absorption is determined by the patient by sucking on the lozenge until it dissolves[1,3,4]. As a result, there may be significant variations in the amount of medication supplied each time the lozenge is taken[1,5]. Moulding or compression are used to make lozenges, depending upon their type[1,2,5]. Moulded lozenges are also called as pastilles, while troches are compressed lozenges[1].Lozenges should dissolve slowly in the mouth and have a smooth texture, with no sharp edges. Lozenges come in a variety of shapes, including flat, circular, octagonal, biconvex, and bacilli, which are short rods or cylinders[1,5].The majority of lozenge formulations are accessible as over-the-counter (OTC) medicines that do not require a prescription from a physician, although others are prescribed by physicians[1,5].

Soft lozenges –
Soft lozenges have grown popular due to their ease of preparation and ability to be used with a wide range of medications[2,3,6]. The bases are commonly made up of a combination of polyethylene glycols, acacia, or other related substances[2,3,4,6]. Pastilles is one of the type of soft lozenges that contains a drug in a glycerogelatin, gelatin, or acacia: sucrose base, which is soft variety of lozenges[2,3,6]. Soft lozenges are related to a historical type of medicine known as "confection," which is making a comeback. Confections are soft, saccharinated masses that contain therapeutic ingredients[2,6]. The use of polymers (polyethylene glycols) as the dosage form matrix has greatly improved their present use[2,6]. They're simple to use, easy to carry, have a pleasant flavour, and easy to store at (at room temperature)[2,3,6]. Many

drugs exhibit unpleasant bitter taste when administered by oral route and bitter taste lead to non- compliance of the patient due to discomfort. Hence elimination of bitter taste and increase in bioavailability has been a main concern for medicated soft lozenges with simultaneous increase in oral feel.

Leukotriene receptor antagonist drugs

Leukotriene receptor antagonist or leukotriene modifier is also known as antileukotriene, are the drugs that acts as a leukotriene-related enzyme inhibitor (arachidonate 5-lipoxygenase) or a leukotriene receptor antagonist (cysteinyl leukotriene receptors) and thus inhibits the function of these inflammatory mediators. Immune system produces leukotrienes which serves to promote mucus secretion in asthma and COPD, inflammation, bronchoconstriction and microvascular permeability. Leukasts are a term used to describe antagonists of leukotriene receptors[7].

Montelukast sodium

Montelukast Sodium is bronchodilator and anti-inflammatory. It is selective cysteinyl leukotriene receptor antagonist and monosodium salt of montelukast, usually administered orally. Montelukast sodium effectively and competitively inhibits the inflammatory mediator leukotriene D4 from binding to the cysteinyl leukotriene 1 (CysLT1) receptor (LTD4). LTD4 inhibition blocks leukotriene-mediated inflammatory results in events such as eosinophil and neutrophil migration, leukocyte adherence to vascular endothelium, monocyte and neutrophil aggregation, increased airway swelling, increased capillary permeability, and bronchoconstriction[8].

MATERIALS AND METHODS:

Materials:

Montelukast Sodium was obtained as a gift sample from Lupin Limited in Chilkalthana, Aurangabad. PEG1500 and Dextrose were obtained from Research-Lab Fine Chem Industries, Mumbai. All of the chemicals utilized in the formulation and analysis in this project were of pharmaceutical grade and analytical grade and of high purity.

Preparation of medicated soft lozenges:

The soft lozenges of Montelukast sodium were prepared by melting and moulding technique. The PEG 1500 base was placed in a beaker and melted on a magnetic stirrer with hot plate to approximately 45°C. As the base was melted dextrose was added and stirred continuously and heated up to 146°C to form a transparent mixture of base and sweetener. The temperature was brought down to 60°C and Montelukast sodium was into the transparent mixture and mixed uniformly. Flavouring agent and colouring agent were added to the mixture. Mixture was poured into the pre calibrated moulds and allowed to cool at room temperature to form medicated soft lozenges. Each lozenges containing 10mg of Montelukast sodium, PEG 1500 in 1st formulation (F1) -500mg, 2nd formulation (F2) -1000mg, 3rd formulation (F3) -1500mg and 2000mg of dextrose as per formula given in the table 1.

Table 1. Formulation of medicated soft lozenges of Montelukast sodium.

Ingredients/ Formulations	F1	F2	F3
Drug	10 mg	10 mg	10 mg
PEG1500	500mg	1000mg	1500mg
Dextrose	2000mg	2000mg	2000mg
Flavouring agent	q.s	q.s	q.s
Colour	q.s	q.s	q.s

Evaluation of Lozenges:

A. Physical Appearance: The lozenges were evaluated for various parameters for visually for colour, shape [9,10].

B. Diameter and Thickness: The diameter and thickness of the lozenges are vital for uniformity in the size of the lozenges. Vernier calliper was used to determine it [9,10].

C. Weight Variation: Weight variation is used to verify that the weight of lozenges in a batch is uniform. Weighing 20 lozenges from each formulation separately, calculating the average weight, and comparing the individual weight of the lozenges to the average is how the USP weight variation test was carried out [9,10].

D. Hardness: Lozenges' hardness determines their resistance to breakage or shipping during storage, transportation, and handling prior to use[5,9,10]. Monsanto hardness testers were used to determine the hardness of the lozenges, and the force required to break them was recorded[2,4]. In terms of kg/cm^2 the hardness was measured[9,10].

E. Friability Test [2,4,11]

The friability of the lozenges was determined by using the Roche friabilator. The 20 lozenges from each batch were weighed first and placed in a friabilator and rotated at 25rpm for 4 minutes. After 4 minutes, the lozenges were removed, made free from dust, and reweighed.

F. Drug Content Uniformity-
Each batch's lozenges were taken and triturated separately. Powder equivalent to dose of drug was transferred to a beaker and Phosphate buffer pH 6.4 was added to the beaker and it was agitated for 5 minutes. Finally, to bring the volume up to 100ml, phosphate buffer pH 6.4 was added, and the solution was filtered through Whatman filter paper. Finally, the solution was diluted suitably, and the absorbance of the resulting solution was measured spectrophotometrically at 280 nm using a UV/ Visible spectrophotometer Jasco V630 against a blank of Phosphate buffer pH 6.4 to estimate the drug content[2,9,10].

G. Disintegration Test: The disintegration time of lozenges from each batch is determined by using the USP Disintegration equipment. At 37°C, disintegration time was measured in phosphate buffer pH 6.4[5].

H. In –Vitro Release Profile:
This study was carried out by using USP II dissolution apparatus (paddle type). Lozenges containing 10mg of Montelukast sodium from each batch, that is F1 equivalent to 2.51gm, F2 corresponding to 3.01gm, and F3 equivalent to 3.51gm, were placed in the vessel. The USP II paddle method was used to conduct the dissolution study in 900ml of Phosphate buffer pH 6.4 at 50rpm, maintaining a temperature of 37±2°C. Samples (5ml) of the solution were withdrawn at 5 minutes time interval and replaced immediately with an equal volume of fresh Phosphate buffer pH 6.4, the solution withdrawn were diluted up to 10ml with Phosphate buffer pH 6.4 and absorbance of this solutions was measured at 280nm using double beam UV visible spectrophotometer[5].

I. Stability Study:
The capacity of a particular formulation in a certain container to remain within its physical, chemical, therapeutic, and toxicological standards is known as drug stability. The purpose of this study was to demonstrate how the quality of a drug substance or drug product changes over time as a result of various environmental conditions such as temperature, humidity, and light. Medicated soft lozenge of Montelukast sodium were packed in a container and exposed to 37°C at 80% RH for three months according to the guidelines from International Council for Harmonization (ICH). Soft lozenges of Montelukast sodium were evaluated for the physical and chemical parameters[1,3,9,10]

RESULT AND DISCUSSION:

Evaluation of Medicated soft lozenges:
The results of various evaluation parameters are depicted in Table 2.

Table 2. Evaluation for Medicated soft lozenges.

Parameters	F1	F2	F3
Physical Appearance	Colour: Green Shape: Round	Colour: Green Shape: Round	Colour: Green Shape: Round
Thickness (mm)	5.10	5.12	5.14
Weight Variation (mg)	0.33	0.24	0.34
Hardness (kg/cm$^{2)}$	5.9	6.5	6.7
Friability Test (%)	0.527	0.695	0.725
Drug Content (%)	96.12	98.32	97.53
Disintegration time (min)	22	30	33

In –Vitro Release Profile: The results of invitro drug release are depicted in table no 3.

Table 3. Invitro Drug Release Profile.

Time (min)	Drug (%)	F1 (%)	F2 (%)	F3 (%)
5	16	25	28	16
10	30	34	33	37
15	43	45	44	48
20	59	60	58	59
25	70	69	67	66
30	80	77	80	79

The In-Vitro Drug Release of Pure drug was found to be 80%, and that of 1st Batch (F1) was 77%, 2nd Batch (F2) was 80% and 3rd Batch (F3) was 79%, which was found to be not less than 70 % therefore, Drug release Profile of Pure drug and all the batches complies with the IP Specifications. In- Vitro Drug release of Pure Drug and F2 batch was identical in terms percent drug which was 80% within 30 mins as per IP Specification. Hence, the Formulation F2 was selected as optimized batch.

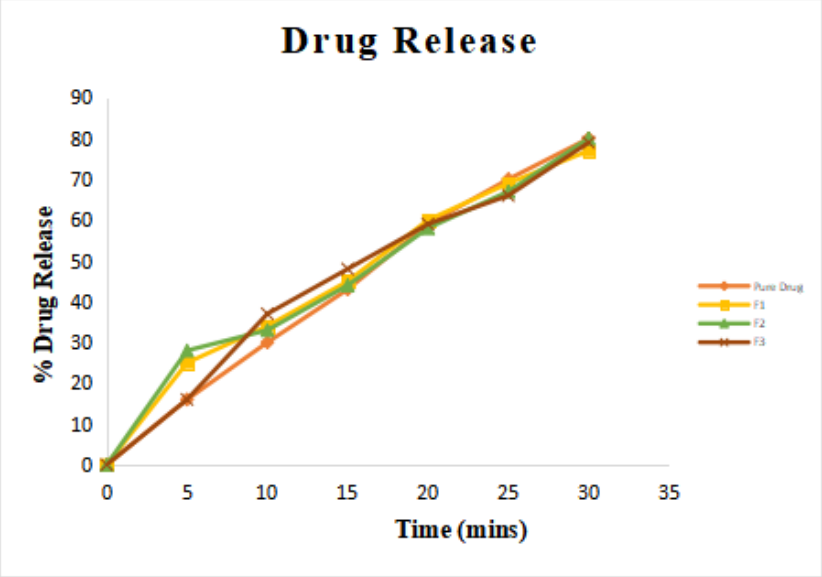

Fig 1. Comparison of in vitro dissolution profile of Pure Drug and All Batches.

Optimization of the Lozenges batches:
Considering the In-Vitro Drug Release profile , F2 batch the Formulation F2 was selected as optimized batch.

Invitro dissolution profile of F2 batch:

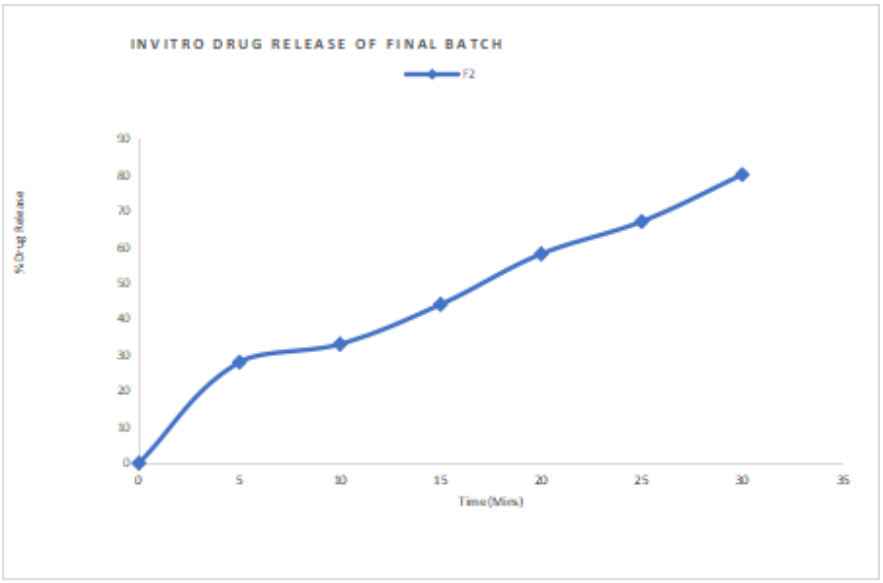

Fig.2. *Invitro* dissolution profile of F2 batch

Release Kinetics and Correlation Coefficients of F2 Batch:
The release kinetics of F2 Batch was First order release with R^2 =0.9922

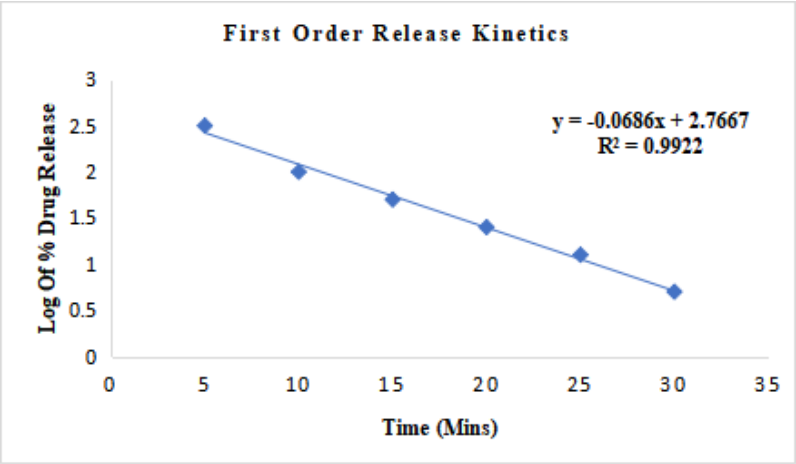

Fig.3. First Order Release Kinetics of F2 Batch.

Stability Study:

The stability study was conducted as per ICH guidelines for optimized batch i.e. F2 for three months and results of stability study were depicted in table no 4. The results showed that there was no significant change in physical and chemical parameters of the lozenges, therefore the formulation was found to be stable.

Table. 4 Stability Study of F2 Batch.

Parameters	**F2**
Physical Appearance	Colour- Green Shape- Round
Thickness (mm)	5.10
Weight Variation (mg)	0.27
Hardness (kg/cm^2)	6.4
Friability Test (%)	0.693
Drug Content (%)	98.32
Disintegration Time (min)	30

CONCLUSION:

The conclusions from the current study were drawn such as- Medicated Soft Lozenges of Montelukast sodium with PEG 1500 as the base of the lozenges can be successfully formulated by melting and mould technique using dextrose as sweetening agent. Medicated Soft Lozenges of Montelukast sodium were prepared by melting and mould technique and was found to be good without chipping, capping, and sticking. The in-vitro dissolution profiles of medicated soft lozenges formulation of Montelukast sodium were found that the drug release up to 80% in 30 mins. The release kinetics of the formulation was found to be first order release kinetics with R^2 = 0.9922. Hence the objective of the formulation and evaluation of Medicated Soft Lozenges of Montelukast sodium was achieved successfully.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation**.**

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