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EFFICACY AND PATEINT-CENTERED OUTCOMES OF ANTIASTHMATIC ORODISPERSIBLE TABLETS IN ACUTE ASTHMA EXACERBATION

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ABSTRACT

Objective: The main objective of this study is to formulate salbutamol sulphate as mouth-dissolving tablets by using lepidium sativum mucilage as a natural superdisintegrant for rapid action to relieve. **Methods:** The formulation of the salbutamol sulphate using different concentrations of lepidium sativum mucilage (2%-8%, w/w) as a natural superdisintegrant and compared with the semisynthetic and synthetic superdisintegrants that are already present, like crospovidone and croscarmellose sodium. An attempt was made to extract Lepidium sativum and evaluate its various physiochemical characterizations. **Results:** The formulated tablets are evaluated for different physical tests like weight variation, hardness, friability, and disintegration time, and the results are shown with the limits. The in vitro release of all the formulations is studied and assessed that all are released by first-order kinetics. From all the formulations, F4, which contains lepidium sativum with an 8% concentration, performed at the least disintegration time of 18 seconds, resulting in a higher in vitro release rate of 95% at the end of 30 minutes. Hence, the f4 batch is considered an optimized batch. This study proposed that the natural superdisintegrants performance has better disintegrating properties than the widely used synthetic superdisintegrants in the formulation of the mouth-dissolving tablets. **Conclusion:** As per the results, the Lepidium sativum mucilage acts as a natural super disintegrating agent and has better disintegrating properties than the synthetic super disintegrants.

KEYWORDS: Mouth dissolving tablet, Salbutamol Sulphate, Lepidium sativum, Crospovidone, croscarmellose sodium.

INTRODUCTION

The oral route of drug administration is the common route of drug administration for drug delivery due to its convenience, easy to use and coast effective.[1] In oral drug deleviery system the most popular is the solid dosage form which are tablets and capsules.[2] But the most common drawback of these dosage form, is the dysphagia in the all age group of people, mainly paediatrics and geriatric patients because in these patient the physiological changes are obsereved most.[3] Mouth dissolving drug delivery system is a novel formulation which have the ability to disintegrate within few seconds when placed in the mouth without the use of the water which aims to enhance the bioavailability of drug and rapid action. Formulating the better dosage form for the administration of drug to achieve better patient compliances and rapid action of time.[4] Salbutamol sulphate is a beta-2 adrenergic agonist mainly bronchiodailater which is used to treat the diseases like asthma and COPD.[5] The half-life of salbutamol sulphate is 2-5 hrs and it is weakly protein bound. According to BCS (biopharmaceutics classification system) classification salbutamol sulphate is classified as class III drug with high solubility and low permeability. Salbutamol sulphate can activate the beta-2 adrenergic receptor in the smooth muscles of the airways which results in the relaxation of the smooth muscles. Salbutamol sulphate is metabolised in the liver due to these the bioavailability of drug is reduced, and the bioavailability is enhance by mouth dissolving.[6] The excipients are added to the formulation to improve the stability of the delivery system, systemic bioavailability, patient acceptability and safety and efficacy during use or storage. The excipients like superdisintegrants, binder, lubricant, etc., has been used to formulate the mouth dissolving tablets.[7] The present study is to formulate the mouth dissolving tablets of salbutamol sulphate for the management of the asthma by direct compression method. The aim of the present study was to extract the mucilage of lepidium sativum and evaluate its flow properties, swelling index, melting point and disintegration properties of mucilage and compared with the commonly used superdisintegrants i.e., crospovidone and croscarmellose sodium in mouth dissolving tablets. All the formulation batches are evaluated with its different physical tests like weight variation, hardness,

friability, disintegration time, in-vitro drug release.

MATERIAL AND METHODS

Material

Salbutamol sulphate, lepidium sativum seeds, crospovidone, croscarmellose sodium, microcrystalline cellulose, sodium saccharine, magnetic stearate, talc.

Methods

Extraction of mucilage of lepidium sativum seeds

The extraction of mucilage from the seeds of Lepidium sativum. Weigh accurately about 50 g of Lepidium sativum seeds. Add the 400 ml of distilled water to the seeds and soak them for 12 hrs. Then the seeds (soaked seeds) were blended at 2000 rpm for 15-20 min. Then the obtained mix was filtered through the 8 folds of muslin cloth. Then again, blend the seeds by adding 100 ml of distilled water. They refilter it. The precipitation of the filtrate was done using 400 ml of acetone. Then filter out the precipitate, which gives the coagulant mass, using muslin cloth. Then the coagulant mass was dried in the dryer at 60°C for 16-18 hrs. Then spraying with the acetone to dry the mucilage to obtain the mucilage flakes from the petri dish. Then the obtained flakes were dried in a dryer at 60°C for 5 min. Then the obtained mass was ground in the pestle mortar and passed through the sieve number 80 and then packed in an airtight container.[8]

Evaluation of physicochemical parameters of mucilage

The dried and purified extracted mucilage powder was evaluated for its micrometric properties, solubility, swelling index, viscosity and loss on drying.

Swelling index

To conduct the investigation, a 100 mL stoppered graduated cylinder was used. 1 gram of lepidium sativum mucilage initial bulk volume was determined. Enough water was supplied. sufficiently to guarantee 25 mL of homogeneous dispersion by shaking briskly every 10 minutes for one hour, and then letting it stand for twenty-four hours. The sediment volume of the swelled mass was measured 24 hours after the dispersion was kept at room temperature.[9]

Viscosity

For four hours, one gram of powdered fenugreek gum was suspended in 75 milliliters of distilled water. To reach the 1% concentration, 100 milliliters of distilled water were added. After two hours of homogenization with a mechanical stirrer, the mixture's viscosity was measured at 5 r/min using a Brookfield viscometer, spindle SC4-18 (Brookfield viscometer, DV-2+LV).[10]

Characterization of drug and excipients

Drug-excipient compatibility studies

The compatibility studies between the salbutamol sulphate and lepidium sativum mucilage was studied using the FT-IR spectrophotometer. The samples were scanned and the graph was plotted using KBr pellet method. The spectra of salbutamol sulphate, lepidium sativum mucilage and the mixture of salbutamol sulphate and lepidium sativum mucilage. The spectral range was obsereved between 3500 cm^{-1} to 600 cm^{-1} wavelength.

Formulation of mouth dissolving tablets

Mouth dissolving tablets containing 6 mg salbutamol sulphate and different proportion of natural and synthetic super disintegrants i.e., lepidium sativum mucilage, crospovidone and croscarmellose sodium. Microcrystalline cellulose as binder and diluent. Sodium saccharine as sweetener, magnesium stearate as lubricant and talc as glidant were prepared using direct compression method. The formulae used to formulate the tablets were illustrated in table 1. All the ingredients were passed through sieve no. 60 individually. The blended mixture was compressible into tablets with 6.5 mm punch using 8-station Karnavati tablet punching machine. As the all formulations of all the batches(MD1-MD12) is provided in Table 1.

Table 1: formula of different formulations of salbutamol sulphate of mouth dissolving tablets.

Composition	MD 1	MD 2	MD 3	MD 4	MD 5	MD 6	MD 7	MD 8	MD 9	MD 10	MD 11	MD 12
Salbutamol sulphate	6	6	6	6	6	6	6	6	6	6	6	6
Lepidium mucilage	2	4	6	8	-	-	-	-	-	-	-	-
Crospovidone	-	-	-	-	2	4	6	8	-	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	-	-	2	4	6	8
Microcrystalline cellulose	86.4	84.4	82.4	80.4	86.4	84.4	82.4	80.4	86.4	84.4	82.4	80.4
Sodium saccharine	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Magnesium stearate	3	3	3	3	3	3	3	3	3	3	3	3
Talc	2	2	2	2	2	2	2	2	2	2	2	2

Evaluation of tablets

Weight variation

The weight variation is an important parameter in the weight of a tablet. According to the IP, the weight variation is studied by taking 20 random tablets from the formulation batch and then weighing the individual and collective 20 tablets using a digital weighing balance. The average weight of one tablet was determined from the collective weight of the tablet. Then both the individual and average weight were compared.

Hardness

The hardness of the tablets was determined using a Monsanto hardness tester. For the hardness of the tablets,

three tablets from each formulation batch were randomly selected, and the individual tablet was placed in the Monsanto hardness tester, and after it, the pressure was applied to break the tablets, and the average reading was noted. The hardness of the tablet was measured in kg/cm². For the orodispersible tablets, the hardness was kept to be lower than the other tablets. The hardness for the orodispersible tablets should be in the range of 3-5 kg/cm².

Friability

The friability test of tablets was determined to assess the ability of the tablets to withstand the packaging, handling, and transportation of the tablets. Friability was the removal of the fine particles that were on the surface of the tablets in the container, due to which the weight of the tablets decreased. For testing the friability of the tablets, we use the Roche friabilator. The Roche friabilator consists of a plastic chamber that revolves at 25 rpm in which we place the tablets of 6.5 mg or nearer to it because the weight of the tablet is less than the 650 mg. The loss of the weight of tablets was measured and is expressed in percentage. The formulae for calculating the friability were.

Wetting time

Wetting time is the important parameter in the formulation of orodispersible tablets. Wetting time is the time taken for the tablets to disintegrate. Wetting time can indicate the inner structure of the tablets and the nature of excipient, i.e., hydrophilicity nature. The lower the value of the wetting time, the faster is the disintegration of tablets. The process to determine the wetting time was first to place a double-folded tissue paper in a small Petri dish and then pour 6 ml of phosphate buffer pH 6.8 into the Petri dish. Place the tablet on the tissue paper and note the time taken for the tablet for complete wetting. Three tablets were randomly selected for each formulation, and the average time was calculated.

In-vitro Disintegration time

The disintegration test indicates how fast and efficiently a tablet breaks down into smaller particles in the liquid medium. The disintegration test is used to establish that the absorption of the drug by the body is not as had envisioned. The procedure to determine the disintegration time of tablets. First, the disintegration apparatus was maintained at 37°C ± 2°C, and the apparatus was filled with distilled water. Then randomly select the six tablets from each formulation and place them individually in the six cylinders of a disintegration test apparatus. Then the apparatus was operated, causing the up-and-down movement of the basket in the apparatus. Then the time is noted for the complete disintegration of each tablet. The average time was taken for the disintegration of the tablets.

In-vitro Dissolution test

The in vitro dissolution test is an important test in the post-compressional parameter. The in vitro dissolution test is used to determine the drug release profile. Here is the procedure to perform an in vitro dissolution test for the orodispersible tablets. For the orodispersible tablets, the in vitro dissolution test was performed by USP type II apparatus that is paddle type. The temperature of the water bath is maintained at 37°C ± 0.5°C, and the speed of the paddle was set at 50 rpm. The 500 ml of phosphate buffer pH 6.8 is poured in the vessel, which acts as a dissolution medium. A randomly selected tablet is placed in the vessel of the dissolution test apparatus. The 5 ml sample was withdrawn from the vessel at every 5-minute interval up to 30 minutes, and the sink condition should be maintained. The samples were filtered, and then the sample was analyzed in the UV-Visible spectrophotometer at 272 nm, and the absorbance is noted, and the percent drug release and the percent cumulative drug release are calculated.[11-16]

RESULTS

The lepidium sativum mucilage was extracted and evaluated for the physiochemical characterization are illustrated in table 2. The swelling index, viscosity and loss on drying of lepidium sativum mucilage was observed and found to be in the optimum range.

Table 2: physiochemical characterization of lepidium sativum mucilage.

Parameters	Results
Percentage yield	24.9
pH	6.8
Loss on drying	8.21%
Swelling index	238%
Bulk density	0.382 g/cm^2
Tapped density	0.431 g/cm^2
Carr's index	11.36%
Hausner's ratio	1.12
Angle of repose	25.13°C

All the formulation batches of salbutamol sulphate mouth dissolving tablets were formulated using the different concentration of natural and synthetic superdisintegrants by direct compression method and compared the natural and synthetic superdisintegrants and the optimised range were used. The tablets were formulated and evaluated. The evaluation results of all the formulated batches were illustrated in table 3.

Table 3: The physical characterization of mouth dissolving tablets of salbutamol sulphate.

Formulation batch	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Wetting Time (Sec)	Disintegration time (sec)	Friability (%)	% Drug release
MD 1	100	6.3	4.6	6	19	0.16	95.482
MD 2	101	6.2	4.7	4	20	0.17	97.721
MD 3	104	6.4	4.7	7	21	0.12	96.359
MD 4	101	6.4	4.5	5	18	0.25	98.641
MD 5	98	6.5	4.8	6	24	0.28	97.539
MD 6	97	5.9	4.9	4	20	0.15	95.941
MD 7	100	6.1	4.7	5	23	0.19	92.163
MD 8	100	6.0	4.9	3	22	0.16	97.956
MD 9	95	6.4	4.9	7	30	0.23	92.762
MD 10	100	5.8	5.2	6	33	0.24	91.928
MD 11	105	6.3	4.8	6	27	0.27	94.531
MD 12	100	5.9	5.1	7	29	0.24	96.358

DISCUSSION

The method used to extract the lepidium sativum mucilage from the lepidium sativum seed was found too reproducible. The physiochemical characterization of the mucilage powder observed and the powder shows the higher swelling index in the distilled water. The flow properties of the mucilage powder attributed to the uniform mass of the tablets which is important parameter for compression of tablets. The flow properties of mucilage powder like carr's index, hausner's ratio and angle of repose were found to be 14.63%, 1.17, 23.4°C respectively which indicates the optimum flow properties. The FT-IR suggests the graph and after compared the characteristic peaks of salbutamol sulphate, lepidium sativum mucilage and the physical mixture of salbutamol sulphate and lepidium sativum and after analyzing the graph indicates the mucilage did not interfere the drug and it found to be compatible. The mouth dissolving tablets are formulated and evaluated for the required parameters. The weight variation test of all the formulated tablets was passed. The hardness found between 4.5 to 5.2 Kg/cm^2 and the thickness was found between 5.8 to 6.5 mm. this both parameters were studied for the mechanical strength of the tablets. The percent friability was found within the prescribed limits indicating the physical integrity of tablets. The wetting time of all the formulated batches were found to be 5 to 25 seconds. The disintegration time of all the formulated batches were found to be 18 to 33 seconds. The percent drug release was found to be 98.641% to 91.928%. from all the formulation batches, the F4 batch formulated with the lepidium sativum mucilage showed the least wetting time 5 seconds, which directly indicates the high-water absorption ratio. This study analyze that the higher the concentration of lepidium sativum mucilage decreases the disintegration time and optimized the percent drug release. Lepidium sativum mucilage in the higher concentration 8% act as a superdisintegrants and disintegrate the tablet within 18 seconds which fulfil the criteria of mouth dissolving tablets. The percent drug release 98.641% at 30 minutes indicates the better choice of the natural superdisintegrants than the synthetic superdisintegrants.

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