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Evaluation of disintegrating properties of Abelmoschus esculentus mucilage

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ABSTRACT: Mucilage extracted from the pods of *Abelmoschus esculentus* (Ae) were subjected to toxicity studies for its safety and preformulation studies for its suitability as a disintegrating agent. The mucilage extracted is devoid of toxicity. Dispersible tablets of aceclofenac were prepared and compared with different concentrations viz; 2, 4, 6 and 8 %(w/w) of *Abelmoschus esculentus* mucilage powder and Ac-Di-Sol®. Eight formulations were prepared and evaluated for physical parameters such as thickness, hardness, friability, weight variation, drug content, disintegration time and drug dissolution. The formulated tablets had good appearance and better drug release properties. The study revealed that *Abelmoschus esculentus* mucilage powder was effective as disintegrant in low concentrations (4%). The mucilage was found to be a superior disintegrating agent than Ac-Di-Sol®. The study further revealed a poor relation between the swelling index and disintegrating efficiency. Studies indicate that the extracted mucilage may be a good source of pharmaceutical adjuvant, specifically a disintegrating agent.

Key words: Aceclofenac, *Abelmoschus esculentus* mucilage powder, superdisintegrants, tablets, pharmaceutical excipients.

INTRODUCTION

Mucilage and gums have been known since ancient times for their medicinal uses. In the modern era also they are widely used in the pharmaceutical industries as thickeners, water retention agents, emulsion stabilizers, suspending agents, binders and film formers[1-2]. Apart from its use in finished medicines, newer uses have been found in the preparation of cosmetics, textiles and paint paper. Hence the demand for these substances is increasing and new sources are getting tapped[3-4].Though, India, due to geographical and environmental positioning has traditionally been a good source for such products among the asian countries, a large quantity of this is still being imported from the European countries to meet up the ever-increasing demand[5]. Of all the orally administered dosage forms, tablet is most preferred because of ease of administration, compactness and flexibility in manufacturing. Because of changes in various physiological functions associated with aging including difficulty in swallowing, administration of intact tablet may lead to poor patient compliance and ineffective therapy. The paediatric and geriatrics patients are of particular concern. To overcome this, dispersible tablets[6] and fast-disintegrating tablets[7] have been developed. Most commonly used methods to prepare these tablets are; freeze-drying/Lyophilization[8], tablet molding[9] and direct-compression methods[10].

Abelmoschus esculentus is grown as a vegetable crop in the tropic, subtropic and warmer areas of the temperature zone. The mucilage from the fruit serves as a thickener in soup. Highly purified form of the gum has been evaluated as a plasma expander, as an intravenous circulating agent and as an emulsifying agent[11]. Whereas reasonable information is now available in literature on characterization and potential applications of this gum as a plasma expander and as an emulsifying agent in disperse systems, no published information is so far on the potential application of this gum as a disintegrating agent in tablet formulations. The present work is an attempt to extract and investigate the pharmaceutical properties of the gum and to assess its suitability as a disintegrant agent in the pharmaceutical formulations.

Aceclofenac,(2-[2-[2-(2,6-dichlorophenyl)aminophenyl]acetyl]oxyacetic acid), a nonsteroidal antiinflammatory drug (NSAID) has been indicated for various painful indications [12] and proved as effective as other NSAIDs with lower indications of gastro-intestinal adverse effects and thus, resulted in a greater compliance with treatment[13]. Aceclofenac is practically insoluble in water. For poorly soluble orally administered drugs, the rate of absorption is often controlled by the rate of dissolution.

MATERIALS AND METHODS

Aceclofenac (Aristo Pharmaceuticals Ltd, Mumbai, India), Ac-Di-Sol® and Microcrystalline cellulose (Maple Biotech Pvt. Ltd., Pune, India), Aspartame (Ranbaxy, New Delhi, India). Talc and magnesium

stearate were purchased from S.D. Fine Chem Ltd., Mumbai,India. *Abelmoschus esculentus* was procured from local market. All solvents used were of analytical grade and were purchased from S.D. Fine chemicals, Ltd, Mumbai, India.

Extraction of the mucilage

About 2kg of fresh immature fruit of *Abelmoschus esculentus* were purchased from local market. After removal of the seeds, the fresh immature fruits were sliced, homogenized and extracted with cold water containing 1% (w/v) sodium metabisulphate. The crude mucilage was centrifuged at 3000rpm for 5min and the gum was precipitated from the supernatant with acetone. The precipitated gum was washed several times with acetone, air dried for 1h and subsequently dried overnight in a desiccator. The dried gum was pulverized using end runner mill and screened through a 0.25 mm stainless steel sieve. This was stored in a well closed amber colored specimen bottle till ready for use.

Determination of swelling index

The swelling index is the volume in ml occupied by 1g of drug; including any adhering mucilage after it has been swollen in an aqueous liquid for 4h. The swelling index of *Abelmoschus esculentus* mucilage powder was determined according to the BP method[14]. One gram of *Abelmoschus esculentus* mucilage powder was taken in a 25 ml ground glass stoppered cylinder graduated over a height of 120 to 130 mm in 0.5 divisions. To this 25 ml of water was added and this was shaken vigorously every 10 m for 1h and then allowed to stand for 24h. The volume occupied by the disintegrating agent including adhering mucilage was measured. The swelling index was calculated from the mean of three determinations.

Physicochemical characterization of mucilage

The separated mucilage was evaluated for solubility, swelling index, loss on drying, ash value, microbial load, density, compressibility index and angle of repose. The evaluation was carried out as per the procedures described in IP and BP.

Evaluation of toxicity & Drug excipient compatibility study

Toxicity studies were carried out according to the method of Knudsen and Curtis[15]. Preformulation studies were carried out according to official monographs and drug-excipient compatibility studies were done by using FTIR.

Formulation of mouth dissolving tablets

Dispersible tablets of aceclofenac were prepared by the conventional direct compression technique using *Abelmoschus esculentus* mucilage powder and Ac-Di-Sol® at concentrations of 2, 4, 6, 8% w/w. The blend was then compressed on a Cadmach single-stroke punch machine. The composition of each formulation is given in Table1.

Table 1: Formulation of Dispersible Tablets of Aceclofenac

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8
Aceclofenac	100	100	100	100	100	100	100	100
AeM*	4	8	12	16	---	---	---	---
Ac-Di-Sol®	---	---	---	----	4	8	12	16
Magnesium Stearate	9	9	9	9	9	9	9	9
Aspartame	12	12	12	12	12	12	12	12
Talc	9	9	9	9	9	9	9	9
Flavour (orange)	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4
Microcrystalline cellulose	63.6	59.6	55.6	51.6	63.6	59.6	55.6	51.6
Total weight of tablet	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg

AeM* *Abelmoschus esculentus* Mucilage

Preparation and evaluation of mixed blend of drug and excipients

All ingredients were passed through sieve no. 60. Required quantity of each ingredient was taken for particular formulation and the blend was mixed by tumbling in a polythene bag. Prior to compression into tablets, the blend was evaluated for the following properties. Angle of repose, Apparent bulk density, Tapped density, Carr's index and Hausner ratio. The evaluation was carried out as per the reported procedures.

Evaluation of dispersible tablets

Tablets were evaluated for appearance, texture, taste, mouth feel, weight variation, hardness, friability, thickness, disintegration time, wetting time and stability. In weight variation test, twenty tablets were selected at random and average weight was determined using an electronic balance (Shimadzu, AX200, Japan). Tablets were weighed individually and compared with average weight. The Pfizer hardness tester and the Roche friabilator were used to test hardness and friability loss respectively. Thickness of tablet was determined by using dial caliper (Mitutoya, Model CD-6 CS, Japan). To measure wetting time of tablet, a piece of tissue paper was folded twice and placed in a small Petri dish containing sufficient water. A tablet was kept on the paper and the time for complete wetting of tablet was measured. Disintegration time was determined using USP tablet disintegration test apparatus (ED2L, Electrolab, India) using 900 ml of distilled water without disk at room temperature (30°).

Stability studies

The stability of selected formulations was tested according to International Conference on Harmonization guidelines for zone III and IV. The formulations were stored at accelerated (40± 2 ^{o} /75±5% RH) and long-term (30±2 ^{o} /65±5% RH) test conditions in stability chambers (Lab-Care, India) for six months following open dish method . At the end of three months, tablets were tested for disintegration time, hardness, friability, thickness, drug content and moisture uptake.

Dissolution Study

In vitro release of aceclofenac from tablets was monitored by using 900 ml of SIF (USP phosphate buffer solution, pH 7.4) at 37±0.5° and 75 rpm using programmable dissolution tester [Paddle type, model TDT-08L, Electrolab, (USP), India]. Aliquots were withdrawn at one minute time intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically (UV-1700, Shimadzu, Japan) at 274 nm.

RESULTS AND DISCUSSION

The extracted and purified Ae gum is cream coloured and odourless. The gum is composed mainly of monosaccharide units of galactose, rhamnose and galacturonic acid. The average yield of dried mucilage obtained from *Abelmoschus esculentus* was 14%. To determine the safety level of extracted mucilage, acute toxicity studies were carried out. In this study it showed no manifestations of toxic syndromes. Acute toxicity studies were performed to assess the suitability of extracted mucilage for oral delivery. For that we have assessed hematological parameters for 15 days were observed. This study has inferred that there was no change in hematolological parameters, which was comparable with the control. Results of physicochemical characterization of mucilage are shown in Table 2.

Table 2: Results of Physicochemical Characterization of mucilage

SL.No.	Physicochemical Parameters	Results
1.	Solubility	slightly soluble in water, practically insoluble in ethanol, acetone, ether and chloroform
2.	Swelling ratio	28
3.	Loss on drying	0.9%
4.	Total ash	3.5%
5.	Acid insoluble ash	0.25%
6.	Microbial load: bacteria (CFUs/g) fungi (CFUs/g)	90 5
7.	Density of powder: Bulk density (g/cc) Tapped density (g/cc)	0.62 0.72
8.	Compressibility Index	15.05%
9.	Angle of repose	32^{0}

TABLE 3: Precompression Parameters of Various Formulations of Aceclofenac

Parameters	F1	F2	F3	F4	F5	F6	F7	F8
Bulk density (g/cc)	0.54	0.57	0.56	0.57	0.52	0.56	0.57	0.58
Tapped density (g/cc)	0.65	0.71	0.70	0.75	0.72	0.76	0.74	0.75
Bulkiness (cc/g)	1.76	1.74	1.89	1.85	1.77	1.73	1.92	1.77
Carr's Index (%)	16.2	21.4	22.4	22.8	22.9	22.6	27.7	24.1
Hausner ratio	0.95	1.21	1.25	1.38	1.29	1.28	1.35	1.33
Angle of repose (^{0})	27	30.2	31.2	31.38	28.3	27.7	32	30.5

Table 4: Post compression Parameters of Various Formulations of Aceclofenac

Parameters	F1	F2	F3	F4	F5	F6	F7	F8
Hardness (Kg/cm^2)	2.7	3.1	3.2	3.0	2.9	2.8	4.3	3.8
Friability (%)	0.81	0.91	1.23	1.35	0.96	0.88	1.03	1.1
Thickness (mm)	2.5	2.7	2.5	2.7	2.3	2.1	2.5	2.7
Weight variation	7.5	7.9	7.1	7.5	7.5	7.7	7.5	7.3
Content uniformity (%)	98.2	96.0	97.3	98.5	98.9	98.0	97.0	98.6

The IR spectra revealed that there was no compatibility related problems between the drug and excipients used in the formulation.

Since, the flow properties of the powder mixture are important for the uniformity of mass of the tablets, the flow of the powder mixture was analyzed before compression to tablets. Bulk density was found to be between 0.52 to 0.58 g/cc and tapped density between 0.65 to 0.76 g/cc, bulkiness between 1.73 to 1.92, Carr's index between 16 to 27%, Hausner ratio between 0.95 to 1.38 and angle of repose was found to be between 27 to 32^0, indicating fair to good flow properties. Results of Precompression parameters are shown in Table 3.

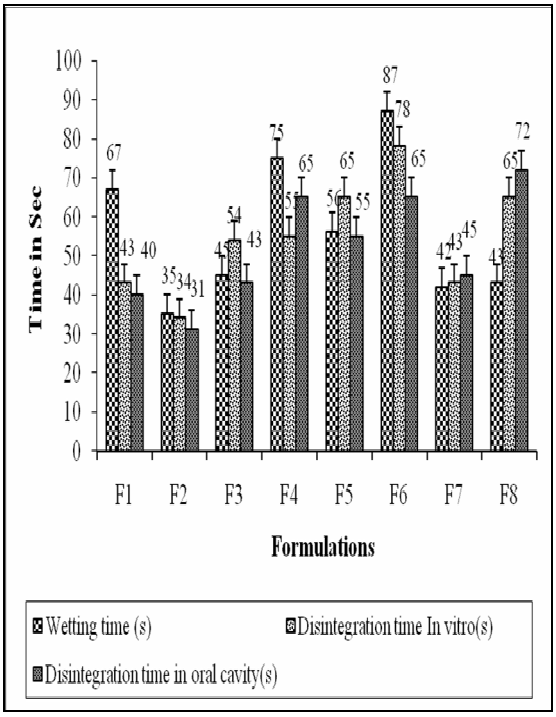
Tablets were prepared using direct compression. Tablets were obtained of uniform weight due to uniform die fill, with acceptable weight variation as per pharmacopoeial specification. Hardness of the all the formulations were measured in kg/cm^2. The hardness of all formulations was found to be 3-4 kg/cm^2. Drug content of all the formulations were found to be in the range of 96-99%, which is within acceptable limits. Friability values of all the formulations were within the limit i.e. is less than 1.0% indicated that tablets had a good mechanical resistance. Results of Post compression parameters are shown in Table 4.

Wetting time was used as a parameter to correlate with disintegration time in oral cavity. This is an important criterion for understanding the capacity of disintegrants to swell in presence of little amount of water. Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of dispersible tablets. The wetting time of formulated tablets was found in the range of 35- 87s. *In vitro* and *In vivo* dispersion time was 31-72 s for all the formulations. The disintegration times of all the formulations were within official requirements that are less than 180 s. Comparison between disintegration time

in oral cavity, wetting time and disintegration time (*In vitro*) for *Abelmoschus esculentus* mucilage powder formulations are shown in Figure1. Disintegration time in oral cavity was found between 34-78 s for *Abelmoschus esculentus* mucilage powder. This showed good correlation between disintegration time in oral cavity and wetting time for all formulations.

All designed formulations using *Abelmoschus esculentus* mucilage powder and Ac-Di-Sol® showed rapid dissolution and percent cumulative drug release (%CDR) at the end of 12 min was between 79-99%. The results are shown in Figure 2.

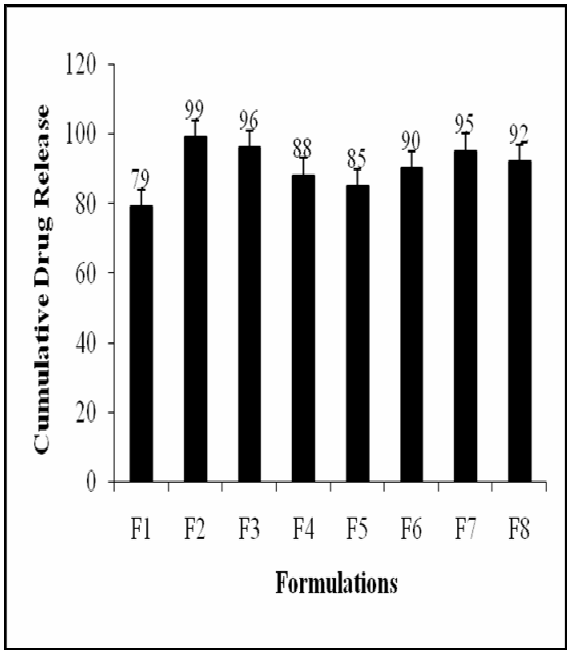
Figure1: Comparison between disintegration time in oral cavity, wetting time and disintegration time (*in vitro*) for Aceclofenac Formulations



Batch F2 was selected as optimized batch containing *Abelmoschus esculentus* mucilage powder as super disintegrant in 4% w/w concentration. It has less disintegration time. The dissolution study was carried out and 99% of drug release was occurring within 12 min.

When tablets were kept at real time (30±2 ^{o} /65±5% RH) and accelerated (40±2 ^{o} /75±5% RH) storage conditions, both disintegration time and hardness values decreased significantly indicating that tablets have lost the mechanical integrity leading to more friability loss. These results indicate that, at higher relative humidity, tablets containing high concentration of *Abelmoschus esculentus* mucilage get softened and hence, must be protected from atmospheric moisture.

Figure 2: Comparison of *In Vitro* Release of Various Aceclofenac Formulations



CONCLUSION

From the present study, it can be concluded that natural super disintegrants like *Abelmoschus esculentus* mucilage powder showed better disintegrating property than the most widely used synthetic super disintegrants like Ac-di-sol® in the formulations of FDTs and may be used as disintegrant at the level of 4%w/w in tablet formulations. As primary ingredients are cheap, biocompatible, biodegradable and easy to manufacture. They can be used as superdisintegrants in place of currently marketed synthetic superdisintegrating agents.

FUTURE PERSPECTIVES

The present investigation is a primary platform to indicate the suitability of *Abelmoschus esculentus* mucilage as a tablet disintegrant. The work can further be extended for evaluation of its suitability as suspending agent, gelling agent, emulsifying agent and other similar pharmaceutical applications considering the easy and ample availability of the plant. The work can go a long way to evaluate herbal pharmaceutical excipients.

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