

EXTRACTION AND EVALUATION OF *MUSA PARADISIACA* STEM MUCILAGE AS A PHARMACEUTICAL EXCIPIENT

ABSTRACT

Aim: In present Pharmaceutical trend, natural excipients are gaining more importance because of their availability, safety, performance, and cost. The present work aimed at extraction of the mucilage from the stem of *Musa paradisiaca* (banana) and evaluation of extracted mucilage for its binding and disintegrating properties with Paracetamol as a model drug.

Methodology: The mucilage was extracted by aqueous extraction method followed by precipitation and evaluated for various physico-chemical properties. Drug-mucilage compatibility studies were conducted by FT-IR spectrometer. The extracted mucilage in three different concentrations was used to prepare 2 different sets of tablets for evaluation of its binding as well as disintegrating properties. Binding properties and disintegrating properties of the mucilage were compared with starch as standard binder and microcrystalline cellulose as standard disintegrant for the first and second set of tablets respectively. Wet granulation method was used to prepare total eight batches of 1 gm tablets of Paracetamol. Pre compression and post compression parameters of tablets were evaluated. Then the similarity factor for both (binding and disintegration test) were calculated by comparing test and standard tablets in each set.

Results and discussion: The results of the work shown that the mucilage extracted from the *Musa paradisiaca* stem (MPS) has similar binding properties as of starch and release retarding effect at increased concentration as disintegrating time was increased when compared to microcrystalline cellulose.

Conclusion: Thus, the mucilage can be used as a better binding agent in the tablet formulation and its high disintegrating time can be explored for its slow release or extended release effect.

Keywords: *Musa paradisiaca*, stem, mucilage, binding agent, disintegrating agent, natural excipient

1.INTRODUCTION

Excipients are pharmacologically inert ingredients which are added to the formulation to confer the therapeutic enhancement of an active ingredient in the final dosage form. Addition of an excipient to formulation ensures long term stabilization and bulking up solid formulation of drug when it is in small amounts.[1-4]. Excipients are known to have notable impact on the processability, efficiency and patient compliance related to dosage form [5,6] Tablets are one of the easily prepared and self administered dosage forms. Tablet formulation requires number of excipients, among which binding and disintegrating agents play a crucial role.

Binders or adhesives are essentially included to tablet formulation to render cohesiveness to powders; thereby they provide sufficient bonding properties to granules under compaction. With the addition of binder, inter particulate bonding strength within the tablet can be intensified and integrity of the tablet can be restored even after the compression with required hardness.[7,8&9]. Starch is a versatile excipient widely used as a binder due to its physico-chemical properties and its abundant availability from multiple sources. In general at concentration of 5–10% w/w freshly prepared starch paste is used as a binder for wet granulation. Binder ratio can be varied based on optimization studies. This ratio greatly influences the tablet parameters such as friability, hardness, disintegration time and drug dissolution rate. [10]

It is very essential to make a part of disintegrating agents during the formulation of oral solid dosage forms because they play active role in rapid break down of tablets into smaller fragments and expedites the dissolution. Microcrystalline cellulose (MCC) has wide range of applications in pharma industry and used as a disintegrating agent at concentration of 5–15 % w/w. [11]

Both binders and disintegrating agents can be derived from numerous sources like natural, semi synthetic and synthetic. Among which natural binders and disintegrating agents are preferred mostly due to their non toxicity, biodegradability, compatibility, safety and huge availability at low cost.

Musa paradisiaca (banana plant) is the largest herbivorous plant and found in the tropical and subtropical regions of the world. The fruits are good sources of potassium, calcium, phosphorus and nitrogen. The mucilage extracted from the leaves and peels has wide range of applications and known to possess binding, thickening, emulsifying, suspending and stabilizing properties. It is also used as a polymer to prepare matrix tablets for sustained release formulations. [12,13 &14]

Hence, the present study was aimed at extraction of mucilage from the stem of *Musa paradisiaca* first time for evaluation of its binding and disintegrating properties to formulate tablets using Paracetamol as model drug. Starch and micro crystalline cellulose were used as standard binder and disintegrant respectively.

2.MATERIALS AND METHODS

2.1.Materials: Fresh banana stem was collected from local forms in tirupati. Paracetamol was obtained as gift sample from Indian chemicals pvt ltd,tirupati,A.P. remaining chemicals were purchased from S.D.fine chemicals pvt.ltd

2.2.Methods:

2.2.1.Extraction of mucilage

Extraction process began with the collection and cleaning of the *Musa paradisiaca* stem (MPS). The cleaned stem was made into small pieces and soaked in water for 12 hours followed by boiling for 3 hours. Filtrate was collected by muslin cloth and the aqueous extracts were centrifuged at 3000 rpm for 10 minutes which gave a precipitate. The obtained precipitate was treated with 1-2 ml acetone to give solid form. The solid mucilage was collected by solvent evaporation and later it is dried. The precipitate was ground into fine powder, once the solvent was evaporated. [15]

2.2.2.Physicochemical characterisation of mucilage

The extracted mucilage powder was tested for the presence of carbohydrates by Molisch's and Ruthenium red tests [16].

Extracted mucilage was also tested for various physical properties like melting point(by capillary method), swelling index(by centrifugation [17] and measuring cylinder method [18]), pH, Loss on drying, Total ash[19], acid insoluble ash and water soluble ash[20] by standard procedures.

2.2.3.Standard curve of selected drug: (Paracetamol)

Standard curve of selected model drug Paracetamol from concentration of 10 to 100 µg/ml was obtained using UV-visible spectrophotometric method at 243nm in 0.1N HCl. [21]

2.2.4.Formulation of tablets:

The two sets of tablets were prepared by wet granulation method using Paracetamol as per composition shown in table -1 for binding (MB-1,MB-2,MB-3) and disintegrating(MD-1,MD-2,MD-3) properties. Test tablets represent the use of MPS extracted mucilage as binding and disintegrating agent and standard tablets(standard 1 and 2) represented use of starch(standard binder) and Microcrystalline cellulose (standard disintegrating agent) respectively.

The drug, lactose, and starch were mixed thoroughly (as shown in table -1), and added separately to sufficient volume of different %(2,10,15) of MPS mucilage of (MB-1,MB-2,MB-3). 10% starch solution was taken as standard binder (standard-1) and was slowly added to the powder blend and kneading was performed until wet mass with enough cohesiveness was obtained. Granules were made out of wet mass by using no:10 sieve and dried.

Similarly for testing disintegrating properties of mucilage, the drug, lactose and different quantities of MPS mucilage powder (25,50,100 mg) for test tablets (MD-1,MD-,MD-3) were taken and mixed. 100mg of MCC was used for standard-2 tablets as shown in table 1. Adequate volume of 10% starch was added to both test and standard tablets. Wet mass was kneaded until enough cohesiveness was obtained. It was passed through sieve no:10 and the resulted granules were dried.

The prepared granules of all formulations were then evaluated for pre compression parameters to evaluate flow properties and compressibility. These granules were compressed into tablets by single punch tablet punching machine

2.2.5.Evaluation of pre compression parameters [22]:

2.2.5.1.Angle of repose: The flow characteristics of granules were measured by angle of repose. Angle of repose is the maximum angle possible between the surface of a pile of powder and the horizontal plane. It was determined by fixed funnel method using the formula. $\tan \theta = h/r$, where, h = height of the pile, r = radius of the pile, θ = angle of repose

2.2.5.2. Bulk density: Definite quantity of granules were placed in a 100ml measuring cylinder and the volume occupied by granules without tapping was noted. The bulk density was calculated as the ratio of weight to volume. **Bulk density = weight of the granules ÷ volume of the granules**

2.2.5.3. Tapped density: For determining tapped density, the granules were taken into a graduated 100ml measuring cylinder. The volume occupied after tapping(x100) was noted. The tapped density was calculated by the formula **Tapped density = weight of the granules ÷ volume after tapping**

2.2.5.4.Compressibility index (or) Carr's index (C%): It is indirectly related to the relative flow rate, cohesiveness and particle size. It is simple, fast and popular method of predicting powder flow characteristics. Compressibility index value of granules was computed according to the equation. **Compressibility index = (tapped density- bulk density) ÷ tapped density ×100**

2.2.5.4.Hausner's ratio: Hausner's ratio of granules was determined by comparing the tapped density to the bulk density using equation. **Hausner's Ratio = Tapped density/Bulk density**

2.2.6.Evaluation of tablets[23,24]:

The prepared tablets were evaluated for drug content uniformity, weight variation, hardness, thickness, friability, disintegration time and *in vitro* dissolution profile.

2.2.6.1. Weight variation test:

In this test, 20 tablets were selected randomly from each formulation and individually weighed. Their average weight was calculated. The difference between the weight of each tablet and average weight was noted for all tablets. Then percentage variation of each tablet from average weight of tablet was calculated. The tablets meet the pharmacopeia specifications, when not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limits.

$$\% \text{ Weight variation} = \frac{\text{Weight average} - \text{weight individual}}{\text{Weight average}} \times 100$$

2.2.6.2. Friability test:

The friability of tablets was determined using Roche friabilator. It was expressed in percentage (%) loss. 10 tablets were randomly selected and their initial weight was noted. Then tablets were transferred into friabilator and was operated at 100 rpm. They were taken out, dedusted and the weight was noted again. Percentage loss was calculated. The percentage loss in friability should be less than 1%. It is the measure of surface strength of tablets calculated by

$$\% \text{ loss (F)} = \frac{\text{Initial weight} - \text{Final Weight}}{\text{Initial weight}} \times 100$$

2.2.6.3. Hardness:

Hardness indicates the ability of a tablet to withstand mechanical shock while handling during manufacturing process. Monsanto hardness tester was used to determine hardness and expressed in kg/cm². 5 tablets of each formulation were randomly selected and hardness of each tablet was determined. The average hardness was calculated. The tablet hardness should be in between 5 to 10 kg /cm²

2.2.6.4. Thickness:

Thickness of tablet was determined for 10 pre weighed tablets of each batch using a vernier calipers scale and average thickness was determined in mm.

2.2.6.5. Disintegration test:

Disintegration time is defined as the time required by a tablet to break into particles that can pass through sieve no.10. The method followed for disintegration test was according to USP. One tablet was introduced into each tube of basket of disintegration test apparatus and a disc was placed in each tube. The assembly was suspended in a beaker containing the 900ml of 0.1N HCl and the apparatus was operated for specified time. Disintegration time for 6 test and standard tablets was determined and average disintegration time was noted.

2.2.6.6. Drug content:

10 tablets were randomly selected and weighed. These were crushed and powdered in a motor. The powder equivalent to 500mg of drug was accurately weighed and transferred in to 100 ml of volumetric flask containing 0.1N HCl. Then it was shaken well and absorbance of the filtered sample was

measured to find out drug content by UV-spectrophotometer at 243nm after suitable dilution. The drug content was estimated using calibration curve and %drug content was noted for all batches of tablets..

$$\text{Drug content} = \frac{\text{Test absorbance}}{\text{Standard absorbance}} \times 100$$

2.2.6.7. Dissolution Test:

Dissolution test was conducted for all test and standard tablets using USP dissolution test apparatus-1 (basket model) in 900 ml of 0.1 N HCl as dissolution medium at $37 \pm 0.2^{\circ}\text{C}$. The tablet was placed in a dry basket. At the beginning of each test, the basket was lowered in to position before rotation. The apparatus was operated immediately at a specified speed of 75 rpm. A specimen from a zone midway between the surfaces of dissolution medium and the top of the rotating basket were taken which is not less than 10mm from the wall of the vessel at different time intervals. Volume of dissolution medium equal to the volume of the sample withdrawals in different time intervals was replaced. The test was performed and repeated for 3 times. For each tablet, the amount of dissolved active ingredient in the sample was calculated as a percentage of the stated amount by UV method with the help of standard curve. Dissolution study for 3 tablets of test and standard were conducted.

2.2.7. Drug - excipients compatibility studies:

The FT –IR spectra were recorded for pure paracetamol, MPS mucilage and test tablets by using FT-IR spectrophotometer to find its compatibility with the formulation ingredients and drug.

2.2.8. Similarity Factor For Comparison Of Dissolution Profile Of Test And Standard Tablets[25]:

f1 and f2 are the two factors representing dissimilarity and similarity respectively to compare the dissolution profiles by mathematical approach. f2 is the simplest method for comparison of dissolution profiles. This was introduced by Moore and Flanner, adopted by the center for drug evaluation and research (US FDA) and by human medicines evaluation unit of the European agency for the evaluation of medical products (EMA). The similarity factor, f2 is defined as a logarithmic reciprocal square root transformation of one plus the mean squared (the average sum of squares) differences of drug percent dissolution between test and standard product.

$$f2 = 50 + \log\left\{ \frac{1}{n} \sum_{t=1}^n (R - T)^2 \right\}^{0.5} \times 100$$

(Where n = no of dissolution time for points, R_t = %drug dissolved from reference (standard) formulation, T_t = %drug dissolved from the test formulation, T =time)

The value of f2 ranges from 0-100 (a higher f2 value indicates closeness between the two dissolution profiles). Two dissolution profiles are considered similar if the f2 value is between 50-100.

2.2.9. Statistical analysis:

Statistical assessment of differences between two groups was performed by student's t-test and ANOVA Statistical significance was set accordingly at $p (\leq 0.05)$.

3. RESULTS AND DISCUSSION

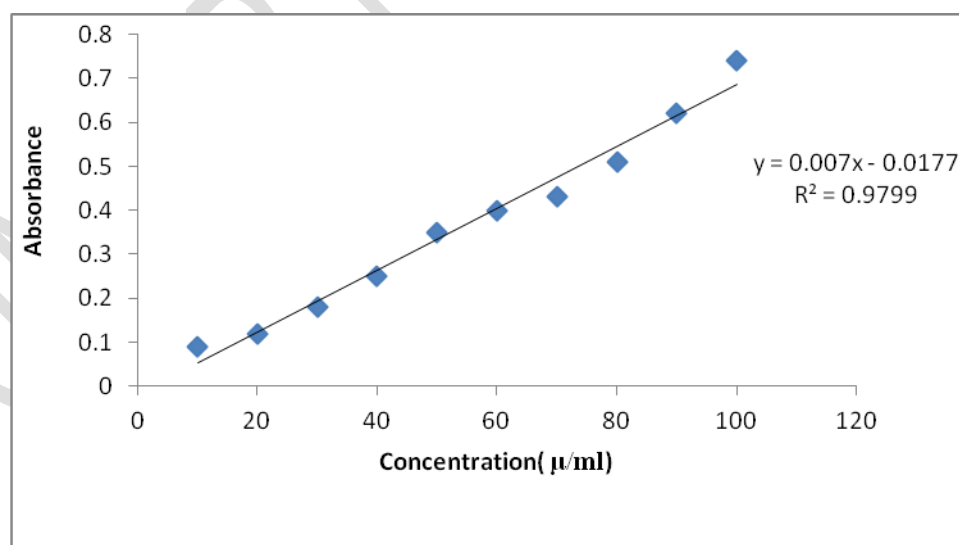
3.1.Physicochemical characterization of MPS mucilage: The phytochemical tests shown the presence of carbohydrates in MPS mucilage by observation of positive results in Molisch and ruthenium red test and results of all physical properties tested are listed in table-2.

Table- 2 Results of physical properties of Mucilage powder

S No	Parameters	Values
1	Swelling index by centrifugation method	1.05(water),1in(Hcl),1.15(in buffer)
2	Swelling index by measuring cylinder method	1.0(in water),1 in (Hcl).1.13(in buffer)
3	Melting point	180°C
4	Loss on drying (%)	2±0.05
5	P ^H	7.1±0.1
6	Total Ash (%)	0.2±0.1
7	Acid insoluble ash (%)	0.02±0.01
8	Water soluble ash (%)	0.1±0.1

The calibration curve of Paracetamol is shown in figure-1

Figure.1 Calibraion curve of Paracetamol



3.2.Evaluation of granules: The results of pre compression parameters are tabulated in table no.3.

Table-3 Micromeritic properties of granules

S.NO	Formulation code	Bulk density(g/cm)	Tapped density(g/cm)	Angle of repose(°)	Carr's Index	Hausner's ratio
1	MB-1	0.4±0.5	0.5±0.1	25.64±1	9.89±0.1	0.9±0.05
2	MB-2	0.3±0.1	0.4±0.1	26.68±0.57	21.35±0	0.8±0.1
3	MB-3	0.46±0.01	0.58±0.01	29.98±1	21.39±0.0	0.7±0.1
4	Standard-1	0.42±0.01	0.52±0.01	26.64±0.57	19.2±0.1	1.2±0.1
5	MD-1	0.23±0.01	0.26±0.01	25.63±0.57	11.5±0.1	1.1±0.1
6	MD-2	0.3±0.1	0.4±0.1	28.21±0.55	25±1	0.1±0.05
7	MD-3	0.45±0.01	0.51±0.1	29±1	20±1	1.1±0.05
8	Standard-2	0.2±0.1	0.3±0.1	35±1	33±1	0.7±0.1

*All values are represented as Mean±SD (n= 3).

3.3.Post Compression parameters: The prepared tablets were evaluated for different *in vitro* parameters (post compression parameters) and results are shown in the table no.4.

Table -4 Results of Post Compression parameters of tablet

S n o	Formulation code	Weight variation (%) (Mean±SD)	Friability (% loss) (Mean±SD)	Hardness (kg/cm ²) (Mean±SD)	Thickness (mm) (Mean±SD)	Disintegrati on time (min) (Mean±SD)	Drug content (%) (Mean±SD)	%Drug release in (Mean±SD)
1	MB-1	2.5±0.06	0.5±0.1	8.4±0.01	9.2±0.05	4.3±1.32	93±0.05	95±0.2
2	MB-2	2.8±0.09	0.6±0.1	8.6±0.05	8.9±0.1	5.1±0.05	90±1	90±0.3
3	MB-3	2.4±0.05	0.59±0.01	8.8±0.05	8.5±0.1	5.3±0.01	90±1	90±0.3
4	Standard-1	2.8±0.09	0.68±0.01	8±0.1	9.2±0.05	4.1±0.05	91±0.05	94±0.1

5	MD-1	2.8±0.09	0.36±0.02	8.4±0.1	8.5±0.1	6.0±0.05	92±0.5	94±0.1
6	MD-2	2.5±0.06	0.36±0.02	8.4±0.1	8.6±0.1	10.9±0.05	90±1	90±0.5
7	MD-3	2.9±0.02	0.67±0.05	8.6±0.1	8.3±0.1	9±0.01	92±0.5	90±0.2
8	Standard-2	2.5±0.06	0.43±0.02	6.8±0.05	9.2±0.05	5.5±0.01	92±0.5	93±0.1

3.3.1. In Vitro Dissolution Data:

Percentage drug release from three formulations MB-1,2,3 and standard -1 were compared. Dissolution profiles of MB-1,MB-2,MB-3 and Standard-1 are shown in figure-2. Percentage drug release from three formulations MD-1,2,3 and standard-2 were compared in table-5. Dissolution profiles of MD-1,MD-2,MD-3 and Standard-2 are shown in figure-3.

Figure- 2 Dissolution profile of tablets tested for binding properties.

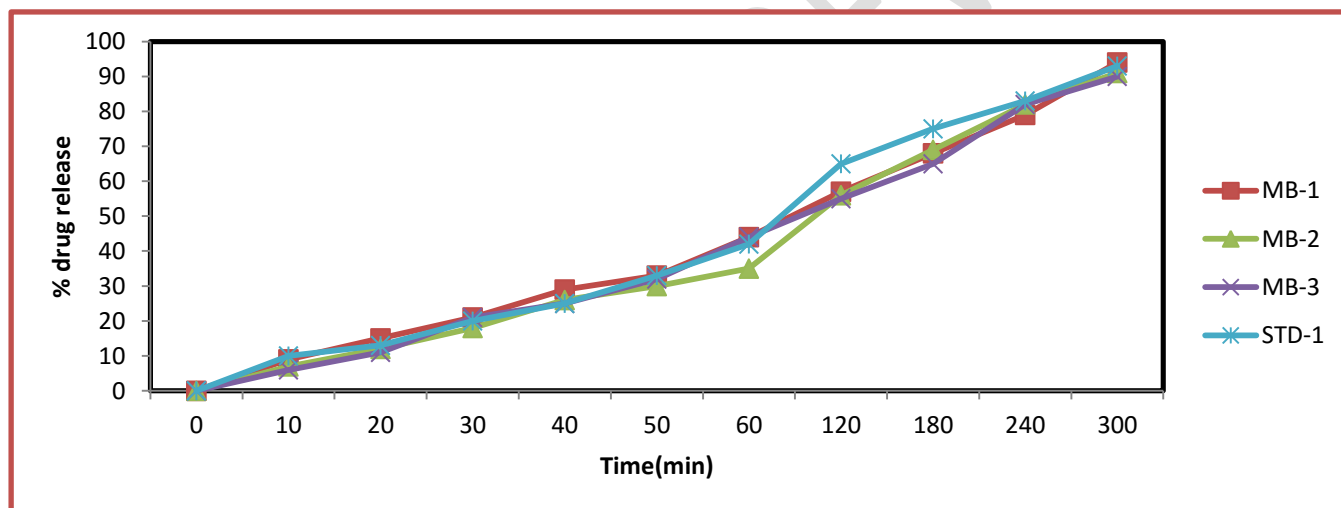
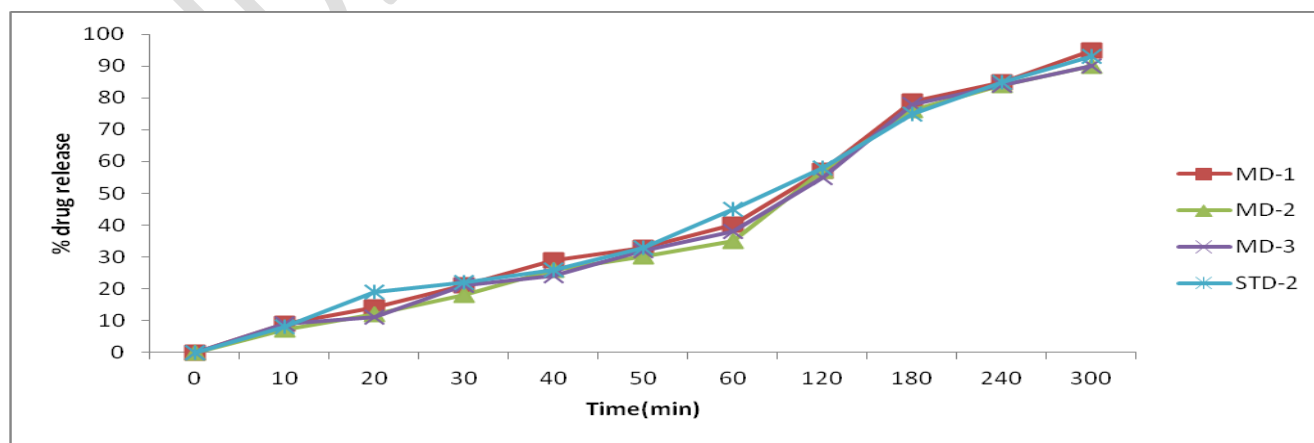


Figure-3 Dissolution profile of tablets tested for disintegration properties.



3.3.2. Drug excipient compatibility studies: FT-IR spectra of model drug paracetamol, MPS mucilage and best formulations MB-1 and MD-1 are shown in Figure 4,5,6 and 7 respectively and observed wave number and functional groups were mentioned in table-5. MB-1 and MB-1 tablets were selected as best tablet sets based on comparison of results of in-vitro evaluation tests of test and standard tablets.

Figure-4 FT-IR spectrum of Paracetamol

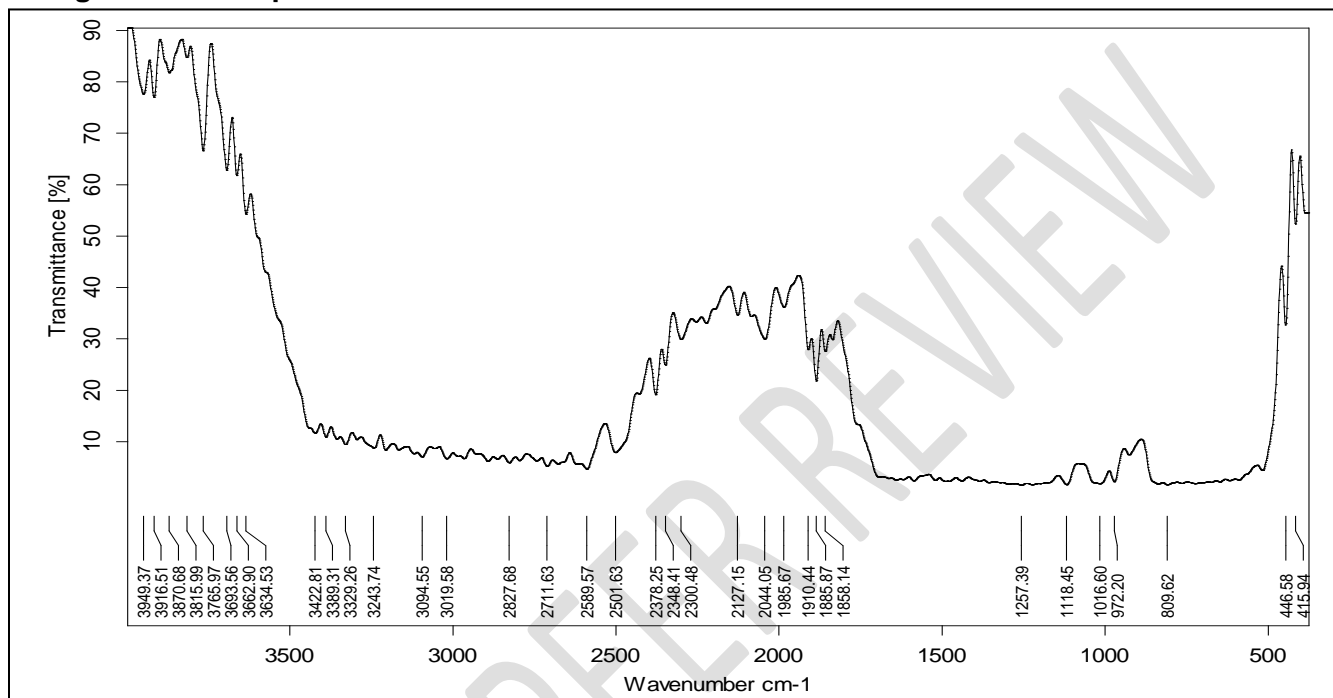


Table-5 Data of FT-IR analysis

S NO	WAVE NO	GROUPS
Paracetamol		
1	3329-3019	OH and CH ₃
2	1257	Amide and CH
Mucilage of MPS		
1	3429-3019	OH
2	2923-2983	CH
3	1128	C-C and C-O-C
MB-1		

1	3247-3143	OH & CH ₃
2	1015	C-C
3	854	NH ₄
MD-1		
1	3011-3457	OH & CH ₃
2	1495	C-C

Figure-5 FT-IR spectrum of Mucilage of MPS

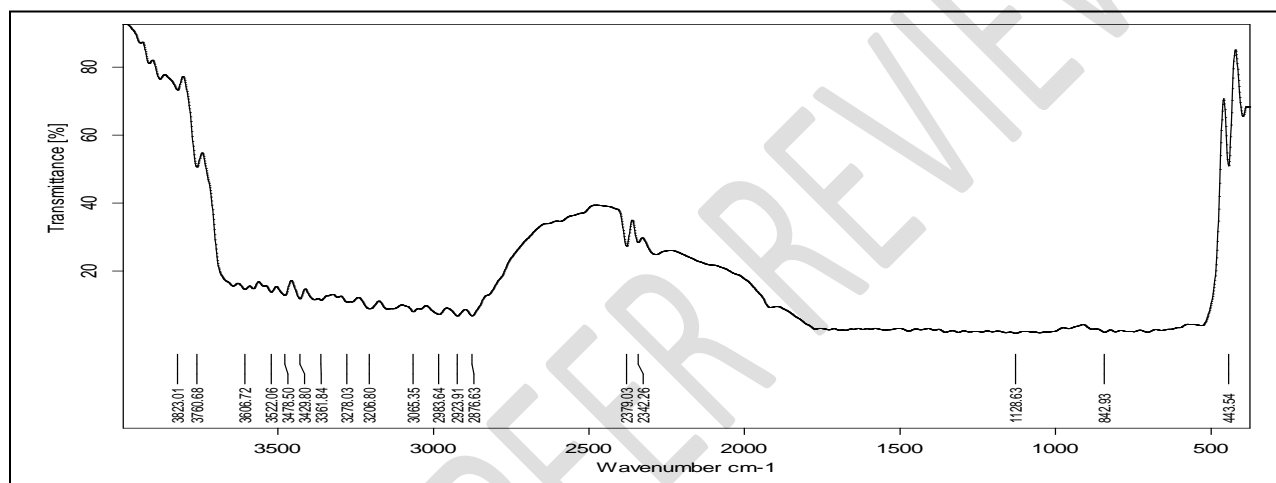


Figure-6 FT IR spectrum of MB-1

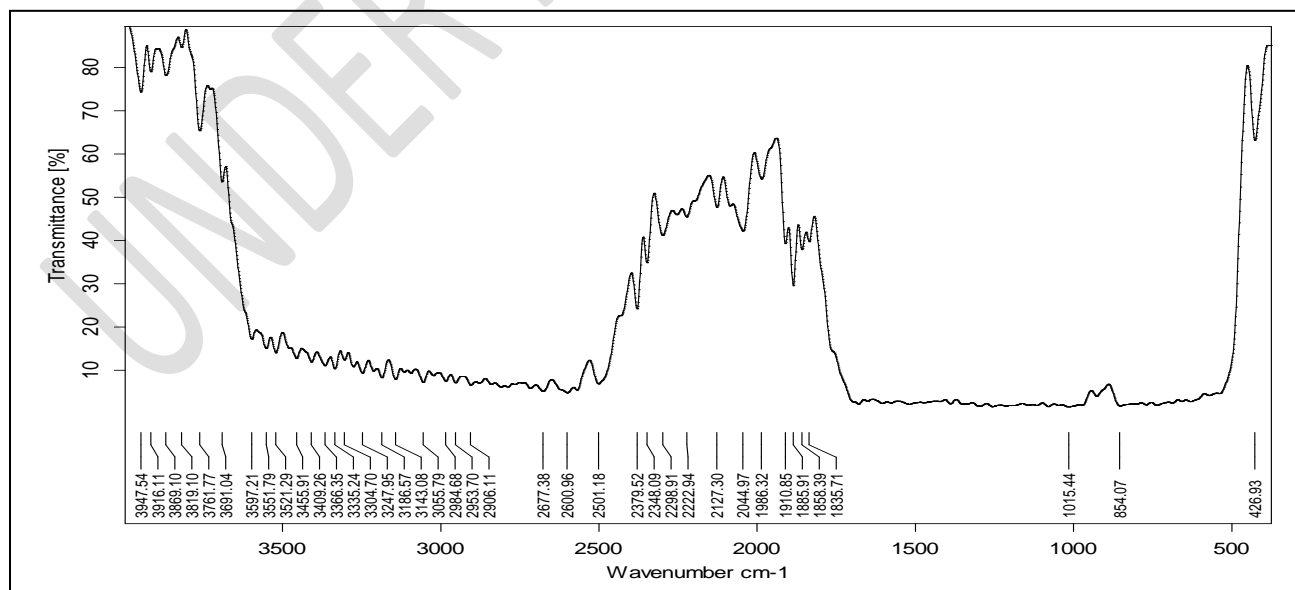
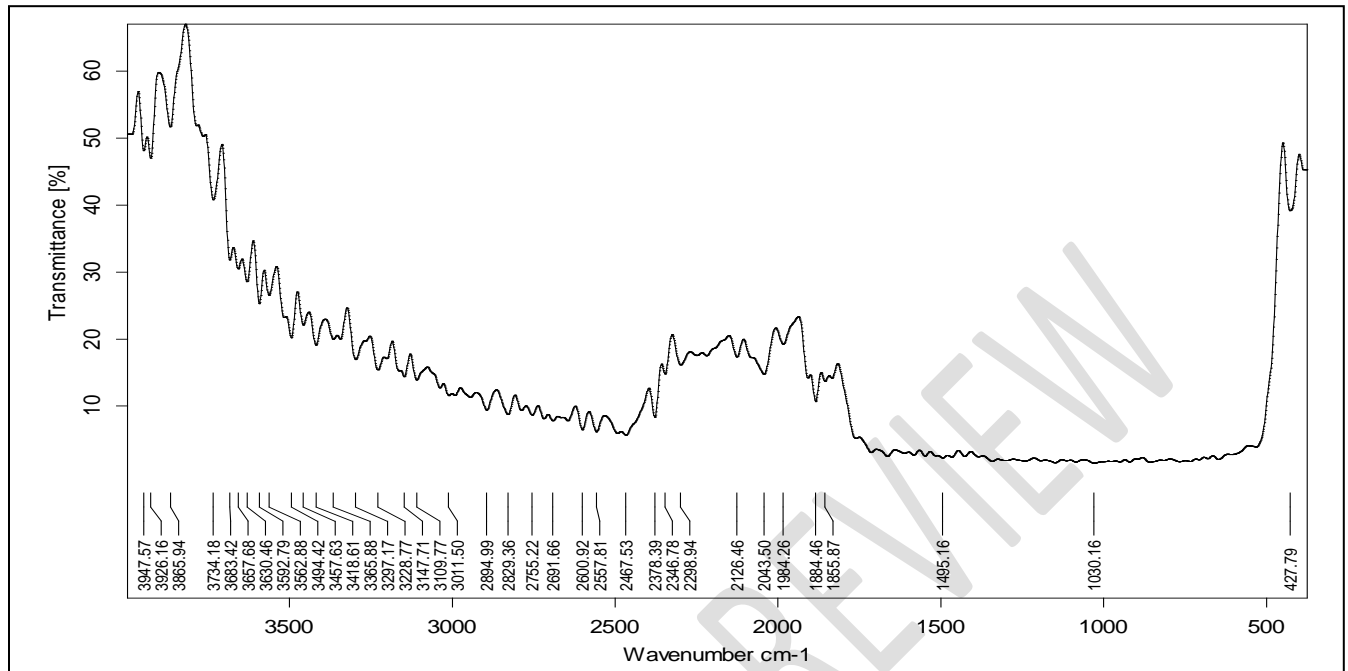


Figure-7 FT –IR spectrum of MD-1



3.4. Comparison of dissolution profiles of selected best formulations with their respective standard tablets: Comparison studies for dissolution profiles were conducted for both best test formulations (MB-1 & MD-1) with their respective standard tablets in order to know the value of similarity factor (f_2) in their dissolution profiles. Comparative dissolution profile of standard-1 and MB-1 is shown in figure-8 and standard-2 and MD-1 is shown in figure-9.

Figure-8 Dissolution profile of Standard-1 and MB-1 for binding properties

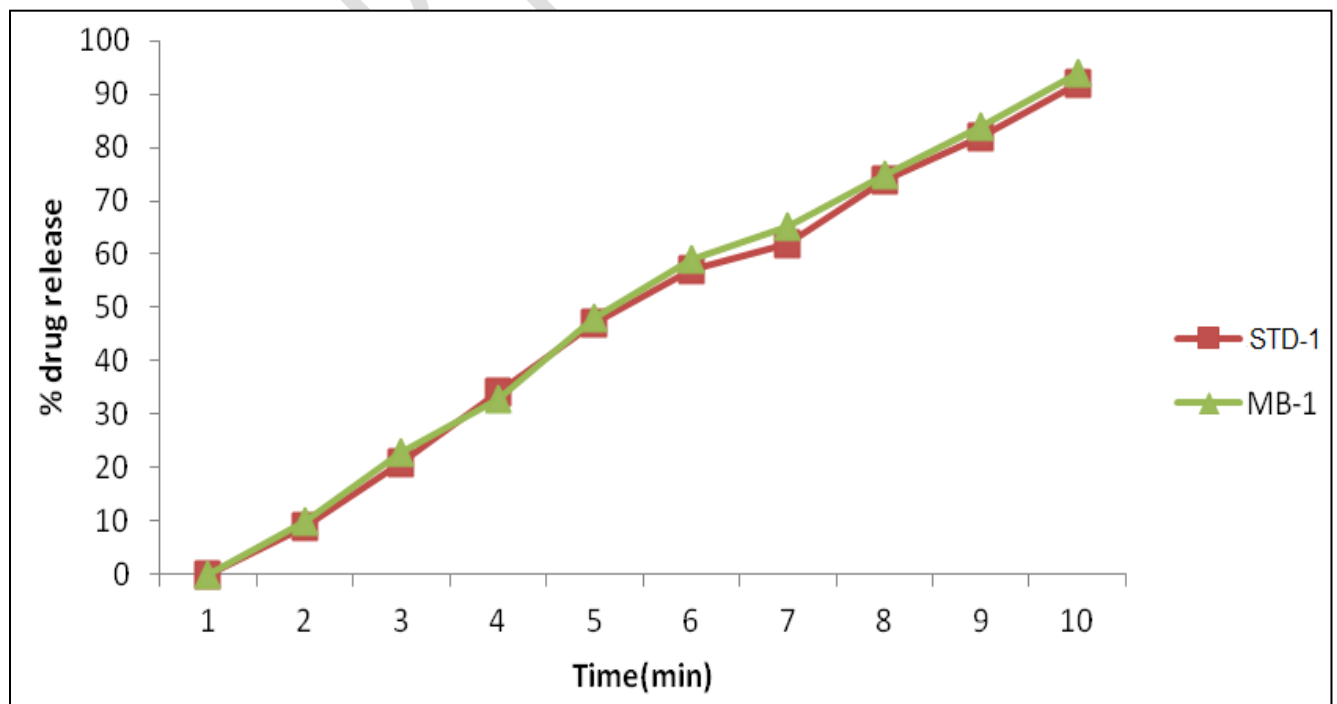
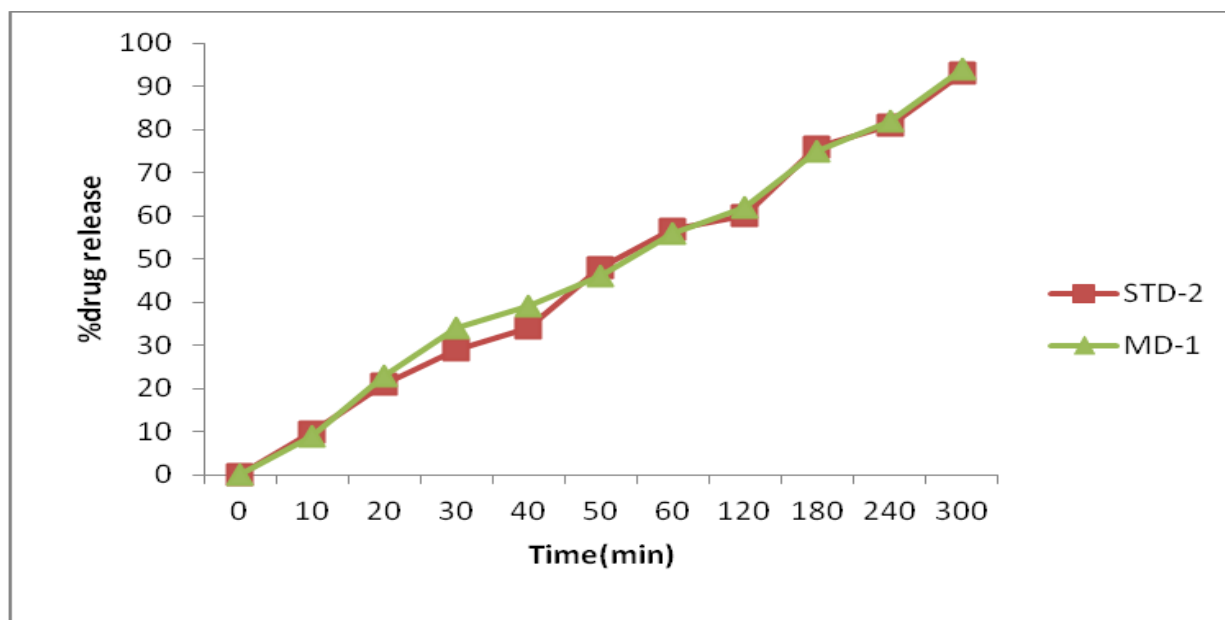


Figure-9 Dissolution profile of Standard-2 and MD-1 formulation



3.5. DISCUSSION: MPS mucilage was extracted and evaluated first time for its binding and disintegrating effects in tablet formulations. MPS mucilage was tested initially for physicochemical properties. The MPS mucilage was slightly soluble in water and insoluble in all other solvents like ethanol, acetone, ether etc. The swelling index of MPS mucilage (Table 1) was above one in water, acid and buffer indicated good water absorbing capacity. The results of remaining all physical properties given in table no-1 indicated its identification characteristics. The results of chemical tests revealed that the MPS mucilage was chemically carbohydrates in nature. Then, the MPS mucilage was used to prepare tablets using paracetamol as model drug to find its binding and disintegrating properties, for that, 2 sets of tablets were prepared as shown in table-1 as MB and MD sets. Three batches of tablets were prepared by wet granulation method (MB-1,MB-2,MB-3) with three different percentage MPS stem mucilage binding properties along with the standard (standard-1) tablets using starch as reference binder. Similarly, three batches of tablets were prepared (MD-1, MD-2,MD-3) with three different amounts of MPS stem mucilage for testing disintegrating properties along with standard (std-2) tablets using microcrystalline cellulose as reference disintegrating agent.

The granules were evaluated for different precompression parameters before punching in to tablets. Then tablets were evaluated for different in vitro parameters.

The granules of all batches of formulations have shown good to excellent flow properties as per the results of precompression parameters shown in table -2. The % weight variation, hardness, and friability of all tablets were within IP limits. The drug content of all tablets was between 90-93% which was within limits

In post compression parameters, though the hardness of tablets prepared for testing binding properties (MB-1, MB-2 & MB-3) was increased with increase in concentration of MPS mucilage, there was no significant difference ($p < 0.05$) in hardness of tablets prepared with different concentrations. (table-4)

Drug and mucilage compatibility was confirmed by FT-IR spectra which demonstrated that there were no changes in characteristic peaks of drug in both formulations prepared with MPS mucilage (MB & MD)

3.6. Evaluation of binding effect: The disintegration time of tablets (MB-1-MB-3) was increased with significant by ($p < 0.05$) increase in concentration of MPS mucilage might be due to its increased binding or adhesive property at high concentration which was also proved by increased hardness at high concentration of MPS mucilage.

The % drug dissolved in 5 hours was also decreased with increase in MPS mucilage concentration might be due to increased hardness and disintegration time. It was found that MB-1 tablets have shown near values to that of standard -1 tablets indicated that the MB-1 tablets are performing similar to standard tablets prepared with starch paste in place of MPS mucilage. Hence, the similarity factor (f_2) was calculated by comparing the dissolution profiles of MB-1 and Standard-1 tablets, which was found to be 86.4. It confirmed the similarity between MB-1 and standard-1 tablets as the value of similarity factor (f_2) was above 50.

The increased hardness, disintegration time and decreased % drug release in dissolution studies with increased concentration of MPS mucilage as binder revealed that the MPS mucilage at 2% concentration has satisfactory binding properties with that of starch.

These studies also demonstrated, decreased rate of release of drug at high concentrations can be further explored for its retarding drug release effect for the development of prolonged release tablets.

3.7. Evaluation of disintegration effect:

The MPS mucilage was also tested for its disintegrating properties using microcrystalline cellulose as standard disintegrating agent. The hardness and disintegrating time of tablets prepared for testing disintegration properties (MD-1-MD-3) were increased with increased quantity of MPS mucilage. There was a no significant difference ($p < 0.05$) in hardness of MD tablets but there was a significant difference in disintegration time of MD tablets.

The % drug dissolved in 5 hours was decreased with increase in MPS mucilage in MD tablets due to increased hardness and disintegration time. Among MD-1, MD-2 and MD-3 tablets MD-1 tablets possessed hardness, disintegration time and % drug dissolution values near to the standard-2 tablets indicated 25mg of MPS mucilage shown similar results with that of 100mg microcrystalline cellulose as

disintegrant. Hence, the similarity factor for MD-1 and standard-2 tablets was calculated by comparing their dissolution profiles which was found to be 66.2, it revealed that the 25 mg of MPS stem mucilage has similar disintegrating properties as that of 100 mg of microcrystalline cellulose.

The f₂ (similarity factor) of MB & MD revealed that MPS mucilage has more similarity (86.4) with starch as binding agent than similarity with (66.2) microcrystalline cellulose as disintegrating agent. Hence it was concluded that *Musa paradisiaca* stem mucilage can be used as better binding agent in the formulation of tablet dosage forms. Both tests (binding and disintegrating) confirmed the release retarding effect of *Musa paradisiaca stem* mucilage at increased concentrations.

4.CONCLUSION

The present study was performed on mucilage of *Musa paradisiaca* stem which has carbohydrate content. The mucilage has shown similar binding property when compared to starch as standard binder and the disintegrating property was also similar when compared with the reference disintegrating agent microcrystalline cellulose. But, both disintegrating and binding tests confirmed the release retarding effect of mucilage at increased concentrations, thus the mucilage can be explored for further use in sustained or controlled release formulations.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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