

Evaluation of *Abelmoschus* starch as tablet disintegrant

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Seed starch (16.0%w/w) obtained from *Abelmoschus moschatus* Linn. (Malvaceae) was employed as a disintegrant to paracetamol tablets at concentrations of 2.5-10.0% w/w. The granules prepared by wet granulation technique were evaluated for percentage of fines and flow properties. Tablet properties including thickness, content uniformity, average weight and weight variation, hardness, friability, disintegration time and drug dissolution were evaluated. With increasing *Abelmoschus* starch concentrations, the formulations disintegrate and dissolve rapidly due to its low viscosity and high swelling factor. The disintegrant efficiency of extracted starch was compared with that of the corn starch in tablets prepared using magnesium stearate, aerosol, corn starch and microcrystalline cellulose as diluent, drug and binder, respectively. The disintegration time for tablet formulations prepared using 10% w/w extracted starch was less (160 s) than that of the tablet formulations prepared using corn starch as a disintegrant (166 s). Dissolution studies showed that the drug release from the tablet containing 7.5 to 10% w/w was 70-90% in 1 hr. Tablets at 10% w/w concentration showed more optimum results as tablet disintegrant. Studies indicated that *A. moschatus* starch is a superior disintegrant in tablet formulation.

Keywords: Paracetamol, *Abelmoschus moschatus*, Muskdana, Ambrette plant, Seed, Starch, Disintegrant, Corn Starch.

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Introduction

A disintegrant is an excipient added to a tablet formulation to cause the tablet to break apart or disintegrate after administration¹. The drug must be released from the tablet matrix as quickly as possible to permit its rapid dissolution. A good disintegrant must be effective at low concentrations to avoid or reduce the influence on the tablet properties such as hardness, friability or compressibility. So the disintegrant is a crucial ingredient in the formulation of tablets and granules. Corn starch is the oldest and was the first most commonly used disintegrant in compressed tablets². So it is used as a standard for comparative studies.

Abelmoschus moschatus Linn. (Malvaceae), Ambrette plant commonly known as *Kasthuri benda* or Muskdana is found wild all over hilly region³. It is erect hispid herbs or undershrubs, 0.5-2.5 m in height, with a long slender tap root. Leaves extremely variable, lower suborbicular in outline, cordate, lower or palmately 3-7 lobed, upper narrower, hastate or sagittate at the base with linear-oblong or triangular lobes. Flowers regular, bisexual, yellow with purple

centre, involucre bracts 8-12, hairy. Fruits capsule, fulvous hairy, oblong lanceolate, acute. Seeds sub-reniform and blackish^{4,6}.

Ambrette oil obtained from seeds possesses an odour similar to that of musk and its aromatic constituents have long been used in perfumery industry. Different grades of essential, or aromatic absolute are marketed in Europe as high-grade perfumes⁷. The seeds are valued for the volatile oil present in the seed coat. Seed analysis reports the presence of 11.1% moisture, 31.5% crude fibre; 14.5% lipids, 13.4% starch, 2.3% protein, volatile oil (0.2-0.6%), calcium and resin⁸. The seeds are valued medicinally for their diuretic, demulcent and stomachic properties. They are also said to be antiseptic, carminative and aphrodisiac, cardiogenic, antispasmodic, deodorant and effective against *kapha* and *vata*, intestinal complaints and diseases of the heart, allays thirst and checks vomiting. According to Unani system of medicine seeds allay dyspepsia, urinary discharge, gonorrhoea, leucoderma and itch. The starch content reported in this plant is high therefore researches with its seeds starch in tablets of other active ingredients are necessary⁸. With increasing demand and search for natural starches with desirable properties for use in the pharmaceutical industries, the present work evaluates the possible use

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of *A. moschatus* seeds starch as disintegrant to paracetamol tablets.

Materials and Methods

A. moschatus seeds were procured from local market, Ootacamund and authenticated in Medicinal Plant Collection unit, Government Arts College, Ootacamund. Paracetamol was used as model drug in the study, and it was purchased from Paxmy specialty chemicals, Chennai. Corn starch LR, microcrystalline cellulose, magnesium stearate and talc were all obtained from SD Fine chemicals, Mumbai. Aerosil was purchased from Degussa, Mumbai. All the other solvents and chemicals used were of analytical grade. Instruments used were Vernier calipers, Sartorius Moisture Analyzer, Brookfield Viscometer, Engineering labs, INC, Middlebord, USA, Rimek Rotary Tablet Compression machine (Karnavati Eng. Ltd., Ahmedabad). Monsanto hardness tester (Cadmach machineries, Ahmedabad), Friability tester (EF2 model, ElectroLab Mumbai.), Disintegration apparatus ED2 model, ElectroLab Mumbai and Dissolution apparatus-model TDT-06T (ElectroLab Mumbai). Digital pH meter was taken up from Merck, Mumbai and 160A-UV-vis spectrophotometer from Shimadzu, Tokyo, Japan.

Extraction of starch

The collected seeds were washed with running water to remove their impurities and other adhering organic matters. A proper steeping is essential for obtaining high yield and high quality starch. The washed seeds were cut into small pieces and were steeped in water containing 0.1-0.2% dilute sulphur dioxide for more than 20 h at 48-52°C to begin breaking the starch and protein bonds. The gluten bonds within the seeds begin to loosen and release the starch. The steeping is actually a controlled fermentation. Sulphur dioxide improves the fermentation by enhancing growth of favourable microorganisms, preferably lactobacillus, while suppressing detrimental bacteria, moulds, fungi and yeast. Solubles are extracted and the seeds soften. The softened seeds were then blended with 1% NaCl to free starch from the cells. Then the milky liquid is filtered through fine muslin with several washes, coarse and fine fibres and part of the protein were removed during filtration. It was added with 2 lt of water and kept for 12 h for effective settling. Residue is re-extracted again with 1% NaCl, refiltered and this is added to the first filtrate, on standing, starch

granules which have passed through muslin cloth settle out and the supernatant was then decanted and discarded. Starch protein matrix from the filtrate was further separated by sedimentation. Starch slurry was centrifuged, supernatant was decanted, the protein layer was scraped off and more water was added to the partly cleaned starch with centrifugation and decanting repeated 3 times. Heavy starch fraction was settled down to the bottom of the beaker and the lighter protein fraction remained suspended in the water, being removed during decanting. Wet starch was filtered and again purified to separate trace amount of proteins and soluble materials like gluten if any, by washing with 1% NaCl solution 3 times, once with 0.01M NaOH. Gluten, dissolves or swells and can be separated by filtration. Finally settled starch sediment was washed with water and dried at 30-40°C for half an hour in a tray drier. The dried product was stored in desiccators for further studies.

Physico-chemical and microbiological properties of starch

The physico-chemical properties such as solubility, ash values, swelling index¹⁰, viscosity¹¹, density¹², compressibility, loss on drying, flow properties¹³ and microbial load of the starch were determined according to Indian Pharmacopoeia procedure¹⁴. The pH of the starch was determined using a digital pH meter¹⁵.

Total microbial load of the isolated starch

The total microbial load is an important parameter, which decides the suitability of a substance for use as an excipient in pharmaceutical dosage form. According to many Pharmacopoeias, for synthetic and semisynthetic substances, the total aerobic count should not be more than 100 colonies forming unit (cfu) per gram and the total fungal count (including yeast and moulds) should not exceed 50 cfu/g. In case of excipients from natural origin, the total aerobic count should not be more than 1000 cfu/g and the total fungal count should not exceed 100 cfu/g.

Preparation of the medium

For bacteria

9 to 10 ml diameter petridishes were used and 15ml of liquefied Casein Soyabean Digest Agar medium at not more than 45°C was poured into the petridishes.

For fungi

The petridishes of 9 to 10 ml diam. were used and 15 ml of liquefied Sabourad dextrose Agar medium at not more than 45°C was poured.

Procedure

Plate count method

The total aerobic microbial count in the substance was examined by Plate count method. One gram of starch was dissolved in 10 ml of pre-sterilized buffer sodium chloride peptone solution and the pH was adjusted to 7.0 (step 1). Five test tubes were taken and 9 ml of buffer sodium chloride peptone solution was transferred into all test tubes and sterilized by autoclave at 121°C for 15 minutes (step 2). The pretreated samples (from step 1) were made serial dilution from 10^{-1} to 10^{-8} using test tubes (from step 2). Casein Soyabean Digest Agar and Sabourad Dextrose Agar plates were spreaded with the 100 μ l of the serial dilutions, i.e., 10^{-1} , 10^{-2} , 10^{-3} , 10^{-4} up to 10^{-5} , respectively. Casein soyabean digest agar plates were incubated at 30-35°C for 5 days and Sabourad Dextrose Agar plates were incubated at 25°C for 5 days and on the 5th day the plates were examined for microbial contamination and number of colony forming units (cfu) were counted.

Observation and interpretation of results

If no evidence of growth is found, the preparation being examined passes the test. If evidence of microbial growth found and if it is within the specified limit, then also the sample passes the test. If evidence of microbial growth is found, more than the specified range the preparation being examined fails the test. In order to count the colonies on a petriplate, an instrument called Colony Counter has been used.

Evaluation of safety profiles

Acute toxicity studies¹⁶

Wistar Albino rats (150-200 g) of either sex were obtained from the colonies maintained at Animal House, Sri Adichunchanagiri College of Pharmacy and housed six animals per cage with paddy husk as bedding. Animals were housed at temperature of $25 \pm 2^\circ\text{C}$ and relative humidity 30-60%. A 12:12 light and dark cycle was followed. Each animal in a group was recognized by the mark of picric acid. Eighteen hours before the experiment, food was withheld. The acute toxicity studies were performed according to Organization for Economic Co-operation and Development (OECD) guidelines. At the end of 28th day, mortality of the animals was observed.

Granulation and evaluation

Paracetamol was used as a model drug for the study. Tablet formulation was prepared by wet

granulation technique¹⁷. All the powders were passed through BSS-80 mesh. Required quantities of paracetamol and other recipients except the glidant and the lubricant were mixed thoroughly and a sufficient volume of granulating agent (starch in water) was added slowly. After enough cohesiveness was obtained, the mass was sieved through 8 mesh. The granules were dried at 40°C for 3-4 h and then passed through 22 mesh. Aerosil and magnesium stearate were finally added as glidant and lubricant. The prepared granules were then evaluated for percentage of fines, loss on drying and flow properties (by measurement of angle of repose). The bulk and tapped densities of the granules were assessed in accordance with the USP 25 using a tapped volumeter apparatus (Erweka, SVM101, Heusenstamm, Germany). Compressibility of the granules was calculated from the difference between the tapped and bulk densities divided by the tapped density and the ratio expressed as a percentage.

Compression and evaluation of tablets

The tablets were compressed (10 mm diam. standard concave punches) using a Rotary tablet compression machine (10 station, Rimek, Ahmedabad, India). The batch size prepared was of 80 tablets. The tablets were evaluated for average weight and weight variation, content uniformity, thickness, hardness, friability, disintegration time and *in vitro* dissolution profile¹⁸⁻¹⁹. Totally 4 batches (2.5-10.0% w/w) were prepared to evaluate the disintegrant properties.

Dissolution studies²⁰

The dissolution rate of paracetamol from the tablets was studied in a paddle type dissolution test apparatus (Electro lab, Mumbai, India) operated at 50 rpm. The dissolution medium was 900 ml phosphate buffer with pH 7.8 at $37 \pm 0.5^\circ\text{C}$. At different time intervals, 5 ml samples were withdrawn and immediately replaced with 5 ml samples of fresh buffer solution maintained at the same temperature. The amount of paracetamol in each sample was analyzed spectrophotometrically at 249 nm with Shimadzu UV-vis spectrophotometer.

Results and Discussion

A. moschatus seeds have been reported to contain 16.0% (w/w) starch. It was partially soluble in water and insoluble in organic solvents. The microbial and fungal counts were determined and found to be absent; however, it has to be confirmed on long term

storage conditions. The acute toxicity studies carried out established the safety of the starch. The pH of the starch was found to be 7.4 which being near to neutral, it may be less irritating in gastrointestinal tract and hence was suitable for uncoated tablets. The prescribed phytochemical tests confirmed only carbohydrates and starch and low viscosity and high swelling factors were found. The hygroscopic after

purification was found to be minimum. The Loss of Drying (LOD) was 2 % (w/w) whereas the gelling concentration was in the range of 2-4 %. The results are shown in Table 1.

Tablets were formulated using natural excipients by wet granulation technique (Table 2). The physico-chemical parameters supported the applicability of the selected excipient as tablet disintegrant. Percentage of fines was determined by passing the granules through sieves 22 and 44. The particles which pass through 44 are considered as fines (Table 3). The compressibility index and angle of repose indicated that the powder is having good flow with moderate compressibility. Percentage porosity values of the powders ranged from 30.29% to 38.32%, indicating that the granules are loosely packed and confirming that the particles are not of greatly different sizes. All these results indicate that the granules possessed satisfactory flow properties, compressibility and porosity (Table 4).

Totally 80 tablets were prepared by using starch of *A. moschatus* at four different concentrations, viz. 2.5, 5.0, 7.5 and 10.0% (w/w). Starch (10% w/w) was used as standard disintegrant for comparison. Its performance was compared with starch at optimum concentration (10% w/w) and it was found better than starch in tablet formulations with less disintegration time (160 s) compared to that of starch (166 s) (Table 5). All the tablets showed uniform thickness

Table 1—Characterization of extracted starch

| | | |
|-----|--|---|
| 1. | Percentage yield (%w/w) | 16.0 |
| 2. | Macroscopy | Smooth and yellowish powder |
| 3. | Phytochemical screening | Only carbohydrates present |
| 4. | pH | 7.4 |
| 5. | Solubility | Partially soluble in water and insoluble in ethanol |
| 6. | Viscosity (CP) | 2.132 |
| 7. | Swelling index | 7.6 |
| 8. | % Loss on drying | 2.26 |
| 9. | Gelling concentration (%w/v) | 2.0-4.0 |
| 10. | Total ash (% w/w) | 4.12 |
| 11. | Acid insoluble ash (% w/w) | 1.24 |
| 12. | Water soluble ash (%w/w) | 1.62 |
| 13. | Angle of repose | 34° 20' |
| 14. | Loose bulk density (g/cm ³) | 0.4420 |
| 15. | Tapped bulk density (g/cm ³) | 0.5460 |
| 16. | Bulkiness | 1.5424 |
| 17. | Compressibility (%) | 18.02 |
| 18. | Porosity (%) | 32.72 |
| 19. | Microbial load | Absent |

Table 2—Batch details for the evaluation of disintegrant property of starch

| Sl. No | Name of the ingredient | Category | mg/tab |
|---------------------|-------------------------------|--------------|--------------------------|
| 1. | Paracetamol | Active | 250 |
| 2. | Gelatin (7.5%w/w) | Binder | 28.125 |
| 3. | Extracted starch (2.5-10%w/w) | Disintegrant | Variable (9.375 to 37.5) |
| 4. | Microcrystalline cellulose | Diluent | Variable (44.25 to 72.5) |
| 5. | Magnesium stearate (1% w/w) | Lubricant | 3.75 |
| 6. | Aerosil (0.5% w/w) | Glidant | 1.805 |
| Total tablet weight | | | 375.00 |

Table 3—Percentage of fines of batches with different disintegrant concentration

| Disintegrant | Concentration of disintegrant (%) | Retained on sieve 44(g) | Passed through sieve 44(g) | % of fines |
|-------------------------------------|-----------------------------------|-------------------------|----------------------------|------------|
| | | | | |
| <i>Abelmoschus moschatus</i> starch | 2.5 | 24.0 | 5.8 | 24.56 |
| | 5.0 | 24.3 | 5.4 | 24.42 |
| | 7.5 | 25.2 | 4.8 | 25.26 |
| | 10.0 | 25.9 | 4.3 | 26.78 |

Table 4—Granular properties of batches using *Abelmoschus moschatus* starch

| Parameters | Disintegration concentration (%) | | | |
|--|----------------------------------|--------|--------|--------|
| | 2.5 | 5.0 | 7.5 | 10.0 |
| Angle of repose | 28°19' | 28°45' | 28°86' | 28°58' |
| Loose bulk density (g/cm ³) | 0.312 | 0.367 | 0.365 | 0.389 |
| Tapped bulk density (g/cm ³) | 0.410 | 0.418 | 0.416 | 0.401 |
| Loss on drying (%) | 1.02 | 1.45 | 1.26 | 1.48 |

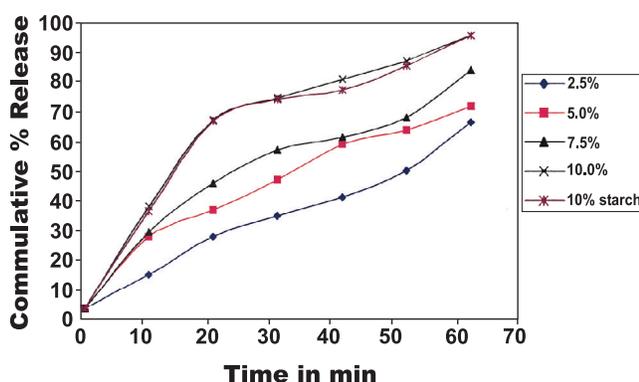
Table 5—Tablet properties of batches using *Abelmoschus moschatus* starch

| Parameters | Disintegrant concentration (%) | | | | Corn starch 10.0 |
|--------------------------------|--------------------------------|---------------|---------------|---------------|------------------|
| | 2.5 | 5.0 | 7.5 | 10.0 | |
| Average wt and wt variation | 373.23 (1.67) | 381.28 (1.35) | 381.15 (1.02) | 381.78 (1.07) | 381.80 (1.10) |
| Content uniformity | 98.35 | 97.36 | 97.18 | 99.42 | 99.49 |
| Thickness (mm) | 3.98 | 3.97 | 3.98 | 3.97 | 3.99 |
| Hardness (kg/cm ²) | 4.5 | 5.6 | 6.0 | 6.2 | 6.4 |
| Friability (%) | 0.434 | 0.625 | 0.712 | 0.817 | 0.821 |
| Disintegration time (sec) | 194 | 187 | 176 | 160 | 166 |

Table 6—Physical evaluation of 10% w/w concentration tablets after 15 and 30 days

| S. No | Evaluation | Observation (in days) | | |
|-------|-------------------------------|-----------------------|-----------------------|-----------------------|
| | | 0 | 15 | 30 |
| 1 | Physical appearance | * | No significant change | No significant change |
| 2 | Weight variation (%) | 1.07 | 1.12 | 1.15 |
| 3 | Hardness (Kg/m ²) | 6.2 | 5.9 | 5.5 |
| 4 | Friability (%) | 0.817 | 0.814 | 0.809 |
| 5 | Disintegration time (sec) | 160 | 162 | 164 |

*White coloured tablets

Fig. 1—Comparative dissolution profile of paracetamol tablets prepared with *A. moschatus* and corn starch

and average percentage deviation of 20 tablets of each formula was less than $\pm 5\%$ and hence the formulations cleared the test for uniformity of weight. The tablets were evaluated for hardness as per Indian Pharmacopoeia procedure using Monsanto hardness tester. All the formulated batches have acceptable hardness and the incorporation of *A. moschatus* seed starch to the formulations produced tablets with short disintegration time and fast dissolution rates compared with those of official starch. Dissolution studies showed that the drug release from the tablet containing 7.5 to 10% (w/w) disintegrant was 70-90% in 1 hr. Tablets at 10% (w/w) concentration showed more optimum results as tablet disintegrant. These tablets were stored for 30 days and no physical change was observed (Table 6). The comparative dissolution profile of the paracetamol tablets prepared with *A. moschatus* starch and corn starch as disintegrant is shown in Figure 1.

Conclusion

There was no significant difference between the extracted starch and the corn starch in terms of disintegration time. It could be said that the extracted starch and corn starch showed comparative

effectiveness as disintegrant in paracetamol tablets. Dissolution studies showed that the drug release from the tablet containing 7.5 to 10% (w/w) disintegrant was 70-90% in 1 hr. Hence, it can be concluded that *A. moschatus* seed starch could compete favourably with corn starch as disintegrant in tablet formulations.

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