Original Article

Exploration of Elephant Foot Yam (*Amorphophallus paeoniifolius*) Starch: An Alternative Natural Disintegrant for Pharmaceutical Application

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ABSTRACT

Aim and Objectives: The aim of the current study is to isolate the starch from elephant foot yam (*Amorphophallus paeonifolius*) and investigate its potential as a disintegrant in tablet formulation as compare to standard corn starch. The objective of the study is to explore the applications of natural resources and develop an alternative to commercially available starches. **Materials and Methods:** Starch was isolated by a simple method, evaluated for phytochemical and physico-chemical properties. Tablets were prepared by wet granulation by varying concentrations of elephant foot yam or corn starch in the range of 2.5%, 5%, 7.5% and 10%. Further granules were evaluated for flow properties and tablets were evaluated for post-compression parameters. **Results:** It was found that the pH of the isolated starch sample was found to be neutral; it exhibited good swelling capacity and fair flow properties. P-XRD pattern showed a C-type diffraction pattern, SEM studies indicated that starch granules had a smooth surface. Granules possessed good flow properties and tablets complied with standard limits of weight variation. Hardness and friability were found in the range of 4.11-4.69 kg/cm^2 and 0.11-0.50% respectively. The wetting time was found in the range of 7 to 35 sec for elephant foot yam starch and 16-49 sec for corn starch. Disintegration time for elephant foot yam starch was found to be 28 to 84 sec and for corn starch, it was 40 to 90 sec. **Conclusion:** Formulations containing elephant foot yam starch showed a similar dissolution profile as that of corn starch. Stability studies were performed on F4 batch and it was found stable for three months.

Key words: Elephant foot yam, Corn starch, Disintegrant, Fast Disintegrating tablet, Disintegration time, Wetting time.

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INTRODUCTION

Excipients are a critical and integral part of pharmaceutical dosage forms and are used for various purposes along with active ingredients.[1] Excipients play a vital role to ease the manufacturing process of various dosage forms, modify physical properties of dosage form, improve patient compliance by imparting color and flavor, acts as a carrier for insoluble drug, modify the release pattern in case of fast disintegrating and prolong release dosage forms, improve stability and bioavailability of drug etc.[2] Stable and efficacious product can be obtained by addition of appropriately stable and compatible excipients in precise quantities in the formulation. Excipients range from simple to complex substances that can be challenging to characterize. Inappropriate use of excipient might lead to mild to severe toxic effects. It is a critical task of a formulator to select appropriate excipients to develop an efficacious and stable dosage form as per the requirements. Hence the development of the excipients is one of the key research areas in pharmaceuticals.

Starch is an immortal excipient!!! It is the major storage polysaccharide of higher plants found in the form of discrete granules.

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Starch granules consist of two major components namely amylose and amylopectin. Amylose is a linear polymer, consisting of α-1, 4 linkages, with chains arranged in helical form. Occasionally, a few branched chains may be present in amylose. Amylopectin is a branched polymer consisting of glucose units linked by both α-1, 4 and α-1, 6 bonds; as a result, it is highly polymerized.[3] Starch has varied applications in the food, plastic, paper, textile and pharmaceutical industries. In pharmaceuticals, they have been used for a variety of applications such as a diluent, glidant, thickening agent, binding agent and disintegrant.[4,5] Recently it was also used in certain novel applications such as solubility enhancer, preparation of microspheres, nanosponges, mucoadhesive agent and sustained release agent etc.[6-8] This is mainly attributed to low cost, renewable sources, high swelling capacity, biodegradable and abundant availability in the form of numerous edible food sources.[9] The most important sources available are various roots, cereals, rhizomes and tubers. It is present in these sources as granules with precise morphology in different plants, ranging from oval, polyhedral, round, elongated with varied size ranged from sub-microns to more than 100 μm in diameter.[10] It can be easily isolated from different sources by physical methods. Starch isolated from different botanical sources such as tubers, fruits, roots and seeds; had been studied by many researchers for various pharmaceutical applications.[11,12] With the increasing demand for starch in various industries it is necessary to explore the additional source of starch to meet the demands.

Elephant foot yam (*Amorphophallus paeoniifolius*) is a tropical tuber crop belonging to family *Araceae* grown primarily in tropical Pacific islands, Africa, South Asia and Southeast Asia. It has high productivity in the short growing season.[13] It is harvested for its edible corms, tubers and smooth petioles. The tubers have been used as traditional food sources in many countries like Indonesia, Malaysia, Philippines, Bangladesh and India. These are nutritionally rich because they contain proteins (≤5%), calcium, vitamins, fats (≤2%) and the majority of carbohydrates (≤18%).[14] It possesses certain health benefits like carminative, stimulant, expectorant, acute rheumatism etc.[15] Tubers might act as a substitute for potato, rice and corn as these are a rich source of starch; studies carried by Sukhija *et al.* (2016)[16] reported that elephant foot yam contains 18% of starch of the fresh weight of tubers. This starch comprises 10-30% of amylose and 70-90% of amylopectin. Besides, the properties of starch granules obtained from elephant foot yam are similar to starch granules extracted from previously mentioned sources.[17] Hence it can be utilized as an additional source of starch and ultimately could be explored as an efficient pharmaceutical excipient.

The urge of current research work generated with the investigation of elephant foot yam starch as disintegrant. Starch was isolated from elephant foot yam, screened for physico-chemical and phytochemical properties. Further its potential as a disintegrating agent was compared with standard corn starch in tablet formulation. Verapamil Hydrochloride was used as a model drug, which is a calcium channel blocker and used in the treatment of high blood pressure, angina pectoris and supraventricular arrhythmias. More than 90% if the drug is absorbed within 1-2 h. After oral administration, half-life ranges from 2.8 to 7.4 hrs.[18] Major emphasis was given on exploring the new source of starch from elephant foot yam for pharmaceutical application.

MATERIALS AND METHODS

Materials

Verapamil hydrochloride was purchased from Swapnaroop drug agency. Elephant foot yam was purchased from the local market in Pune, Maharashtra, India and authenticated from Agharkar Research Institute Pune, India. All the other chemicals used were of analytical grade and purchased from Loba Chemicals.

Isolation and Purification of Starch from Elephant Foot Yam

Starch was isolated by the method reported by Carvalho *et al.* (2014).[19] with slight modification. Briefly, The Elephant foot yam tuber was peeled, cut into small pieces and immediately suspended in 0.1% (w/v) sodium metabisulphite solution. Then, the sample was homogenized and suspended in 4% NaCl. The slurry was filtered through a 100 μm sieve and the filtrate was centrifuged at 3000 rpm for 20 m. This procedure was repeated four times and the recovered starch was dried in an oven at 24 h at 40°C.

Evaluation of isolated starch

The isolated sample was subjected to Phytochemical and physico-chemical investigation.

Phytochemical screening of elephant foot yam starch

Phytochemical screening was performed for the presence of carbohydrates, polysaccharides, flavonoids, steroids, alkaloids, saponins, glycosides, proteins, ash value, as per the reported method.[20]

Physico-chemical test for isolated starch

Various physico-chemical properties like colour, taste, solubility, gelation temperature and pH of the isolated starch sample were measured. The pH of the 1% solution of isolated granules was measured using a digital pH meter (Systronics Instruments, India).

Swelling capacity

10 g Starch granules were added in a 100 ml measuring cylinder and tapped; the volume occupied by the granules was recorded (Vt). Then granules were dispersed in 70 ml of distilled water and final volume made with distilled water. After 24 hr. of standing the volume of the sediment (Vs) was determined. The swelling capacity was calculated using the equation:[21]

$$\text{Swelling index} = Vs/\ Vt$$

Where Vt was the initial volume of starch and Vs was the volume of sediment after swelling.

Powder flow properties

Bulk and tapped densities of the isolated starch granules were evaluated by bulk and tap density apparatus respectively. From these values, Carr's index and Hausner's ratio were calculated. The angle of repose was also determined for the starch granules. Calculations were done using the following equations:[22]

$$\text{Angle of repose, } \tan\theta = h/r$$

Where h = height of the granule heap and
r = radius of the heap

$$\text{Carr's index} = \frac{(\text{Tapped density} - \text{Bulk density}}{\text{Tapped density})} \times 100$$

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Powder X-ray diffraction (P-XRD) of starch granules

Powder X-ray diffraction (PXRD) pattern of starch was studied by X-ray diffractometer (D_8 advanced model of Bruker Axs.) with copper Kα value of 1.54060 radiations at a speed of 1°/m, diffraction angle of 2θ at 5°and 60° at 30 mA and 40 kV.[23]

Morphology of starch granules

Starch granules were observed using a Scanning Electron Microscope (SEM) (JEOL-Model 6390, Japan). The sample was sprinkled on a double-sided tape mounted on a SEM stub and coated with gold to make sample conductive and placed in the SEM chamber. Photomicrographs were taken using a scanning electron microscope apparatus at an accelerating voltage of 20 kV.[24]

Fourier transform infrared spectroscopy (FTIR) analysis and differential scanning calorimetry (DSC)

Spectra of powdered granules by mixing with KBR were recorded using Fourier transform Infrared Spectrophotometer (Shimadzu, Japan) within the operating range of 4000 to 400 cm^{-1}.

DSC analysis of starch granules was performed by using a differential scanning calorimeter equipped with a computer analyzer (JAPE DSC, Perkin Elmer, USA). The scan was carried out at a heating rate of 10°C/m under a nitrogen atmosphere over the temperature range of 30°C-300°C.[25]

Drug-excipient compatibility study

A binary mixture of drug with individual excipients was prepared and subjected for the accelerated temperature at 40°C / 75% RH for 1 month. After 1 month mixtures were characterized by FT-IR spectroscopy to check the compatibility.

Preparation of tablets

The application of the elephant foot yam starch as a tablet disintegrant was evaluated and compared with the standard corn starch. Tablets were prepared by wet granulation technique by using polyvinyl pyrrolidone 2% w/v solution in ethyl alcohol as a binder. Verapamil hydrochloride 80 mg was taken as standard drug dose per tablet, elephant foot yam starch and corn starch were used in the concentration of 2.5%, 5%, 7.5% and 10 % w/w respectively as a disintegrant, Microcrystalline cellulose was used as a diluent to achieve the final weight of 200 mg. All the solid ingredients were shifted through 80 mesh sieve. Weighted individually and mixed thoroughly. To this mixture 2%w/v solution of polyvinyl pyrrolidone was added and mixed to form the dough. This mass then extruded through 20 mesh sieve and dried in tray dryer for 30 min. Dried granules were further passed through 18 mesh sieve and mixed with 1% w/w of magnesium stearate and talc for lubrication. Prepared granules were evaluated for pre-compression parameters as discussed in powder flow properties. Granules were compressed by a 9 mm punch by a tablet compression machine (CIP, India). Formulation F1 to F4 contains elephant foot yam starch and F5 to F8 contains standard corn starch.[26]

Evaluation of tablet

The prepared starch tablets were evaluated through standard quality control parameters for tablets such

as thickness, weight variation, friability, disintegration, hardness and tensile strength as per standard methods.

The thickness of 10 tablets was checked by vernier caliper and the mean thickness value was calculated.

Weight of 20 tablets was recorded (Shimadzu, Japan) and percent relative standard deviation was calculated. The Friability test was carried out by the friability test apparatus (Electrolab, India.) taking 20 tablets for each batch. The drum was rotated at 25 rpm for 4 min; tablets were dropped from a height of 6 inches. At the end of the test, tablets were de-dusted and the percent weight loss was calculated from the difference in original weight and weight after rotation tablets. Tablet hardness was determined by using Pfizer hardness tester.

Wetting time

Circular tissue papers were placed in the petri dish, 10 ml of amaranth solution was added in petri dish. One tablet was then placed carefully on the surface of the tissue paper and the time required for the amaranth solution to reach the upper surface of the tablet was noted.[27]

In-vitro disintegration time

The average disintegration time of six tablets for each batch was determined in distilled water at 37 ± 2°C. Time in second was noted for the entire tablet to break completely into the particle which passed through the screen of tubes. Disintegration efficiency ratio (DER) was calculated by the following equation as reported earlier by Itiola *et al.* (2016).[28]

$$DER = (Ca / Fr)/D_T$$

Where Ca was hardness, Fr was friability of the tablet and D_T was disintegration time.

The disintegration parameter, DER*c* was determined using the formula $DERc = DER_{test} / DER_{reference}$

Where, DER_{test} = Disintegration efficiency ratio of tablets containing elephant foot yam starch and $DER_{reference}$ was the Disintegration efficiency ratio of tablets containing corn starch at the same concentration.

When DER*c* > 1, the DER of elephant foot yam starch was considered to possess better disintegration property than the corn starch and vice versa.

In-vitro dissolution test

It was carried out by the IP I dissolution test apparatus, briefly, 900 of 0.1 N HCl was added in a dissolution vessel and the temperature of the dissolution medium was maintained at set at 37.5 ± 0.5°C. The rotational speed of the paddle was set at 50 rpm. The 5 ml of sample was withdrawn at the time interval of 2 m., sink conditions were maintained by adding the fresh medium. The samples were analyzed for drug content at λ_{max} of 278 nm. Cumulative percentage of drug release was calculated.[29]

Stability studies

The stability study of the tablets was carried out by keeping the sample in the stability chamber at 40 ± 2°C/75± 5% RH the ICH (International conference on harmonization of the technical requirement for registration of pharmaceutical for human use) guidelines. The optimized batch was selected for stability study and was evaluated for hardness, friability, wetting time and disintegration time after 1-month interval.

Statistical analysis

Statistical analysis was performed using Microsoft Excel software (MS Office 2010). Data were expressed as means ± SD and the results were taken from individual experiments performed in triplicate. Student t-test was performed to analyze the statistical significance between two readings and the *p* values of 0.05 or less were considered to be statistically significant.

RESULTS AND DISCUSSION

Phytochemical screening

Starch is isolated from elephant foot yam successfully without the use of any harsh chemicals and complicated method. Phytochemical screening of isolated sample showed the presence of carbohydrate further it was also confirmed the presence of polysaccharide, starch by an iodine test. These results were in agreement with the results reported by Rahman *et al.* (2011).[30] All the other phytoconstituents were found absent except protein, this indicates an isolated sample is free from other phytoconstituents. The purity of the sample was confirmed by ash value. Total ash is indicative of the amount of residue remaining after the ignition of the sample under standard conditions. Such residue might be either physiological ash derived from plant components like plant tissue or non-physiological ash as a result of contamination from soil or other extraneous matter.[31] For isolated starch ash value was found 0.10% ± 0.08, this value was slightly lower than the ash value reported by Sukhija *et al.* (2015).[32] (Table 1).

Physico-chemical evaluation

Isolated starch was white in colour, bland in taste with near about neutral pH (determined in the concentration of 1% w/v solution). It was practically insoluble in cold water and other organic solvents but formed a

Table 1: Phytochemical properties of the elephant foot yam starch.

Sr. No.	Test		Result
	Carbohydrates	Molisch test	Positive
		Barfoed's test	Positive
	Protein	Biuret test	Positive
	Non reducing sugar	Benedict's test	Positive
	Starch	Iodine Test	Positive
	Steroids	Salkowski test	Negative
		Liebermann–Burchard test	Negative
	Glycosides	Keller–Killani test	Negative
	Flavonoids	Ferric chloride test	Negative
		Lead acetate test	Negative
	Alkaloids	Mayer's test	Negative
	Saponins	Foam test	Negative
	Ash value (%)	---	0.10 + 0.08

colloidal solution in hot water. It attained gelation in the temperature range of 65-70°C ± 0.05. When the starch is heated in presence of excess water it undergoes phase transition of order-disorder at a particular range of temperature is known as gelation. The phase transition is the result of water uptake by amorphous region, water diffusion into starch granules, hydration and swelling of granules. This leads to uncoiling and dissociation of double helices ultimately loss in crystallinity. Swelling destabilizes amylopectin crystallites and high-temperature crystallites undergo melting.[33]

Swelling capacity

Swelling capacity is the ability of starch granules to trap the water via hydrogen bonding. Swelling may be attributed to the disruption of double-helical order in the crystalline lamellae of amylopectin as a result of water uptake by the granules, excess absorption of water exert more pressure on the crystallites, hence granule gradually starts swelling. The presence of a high amount of amylopectin enhances swelling conversely, amylose restricts the swelling.[34] For elephant foot yam starch swelling capacity was found to be 1.68 ± 0.04 (Table 2). These results indicated that at room temperature starch exhibits good swelling and water retention ability. Results of the above mentioned parameters were in agreement with research reported by Pawar and Varkhade.[35] Higher swelling in elephant foot yam starch might be attributed to the presence of a high amount of amylopectin (70-90%). The swelling capacity of starches is a tool to predict the swelling of tablets during disintegration that results in quicker dissolution.[36]

Powder flow properties

Powder flow properties are of crucial importance during manufacturing. Densities of the powder influence certain unit operations such as mixing and segregation. Particle size and shape have a potential impact on density and packing behavior eventually these affects die filling and compression of tablet.[37] Bulk and tapped density for elephant foot yam starch was determined and found to be 0.65 ± 0.005 and 0.9 ± 0.001 g/ml respectively. From these values, Carr's compressibility index and Hausner's ratio were determined and found to be 27.77± 0.002 % and 1.385± 0.004 respectively (Table 2). These values were representative of cohesiveness of starch which affects flowability. The angle of repose was also determined and it was 30°C. These values indicate the fair flow properties of isolated starch. Obtained results were in agreement with the study carried out by Kumar *et al.* (2015).[24] Hence it was decided to prepare tablets by wet granulation technique.

Powder X-ray diffraction

Powder X-ray diffraction (PXRD) patterns were traced by using a X-ray diffractometer and the X-ray diffraction pattern of the sample was shown in (Figure 1). It showed intermediate intensity peaks at diffraction angles of 2θ = 17.52 and 18.22, these values represent B-type diffraction pattern which is observed in most of the tubers starches. B-type diffraction pattern represents

Table 2: Physico-chemical properties of the elephant foot yam starch.

Sr. No.	Parameter	Results*
1.	Colour	White
2.	Taste	Tasteless
3.	Gelation temperature(°C)	65-70 ± 0.25
4.	pH	6.8 ± 0.19
5.	Solubility	Forms colloidal solution in hot water, insoluble in cold water and other organic solvents
6.	Swelling capacity	1.68 ± 0.04
7.	Bulk density (g/ml)	0.65 ± 0.005
8.	Tapped density (g/ml)	0.9 ± 0.001
9.	Carr's compressibility index (%)	27.77 ± 0.002
10.	Hausner's ratio	1.385 ± 0.004
11.	Angle of repose (⁰)	30 ± 0.024

*All the values stand for the means of three determinations ± standard error of the mean

crystalline forms of the starch.[38] A strong peak at 2θ = 23.12 and a weak peak at 15.01 resembles A-type diffraction pattern, this is most abundant in cereal starches. Elephant foot yam starch illustrated diffraction patterns of C-type, which was a superposition of A and B type diffraction patterns. Results were inconsistent with reported by Sundaramoorthy *et al.* (2014).[39] The double helices in both A and B type diffraction pattern are identical as it has parallel double helices in a hexagonal arrangement with twelve glucose residues but these differ in mode of packing of helices and water content. A-type crystalline structure associated with four water molecules forms dense packing and B-type structure has a more open hexagonal pattern with 36 water molecules. This type of diffraction patterns are influenced by the chain length of amylopectin, amylose content and biological origin of starch.[40]

Scanning electron microscopy

The morphology of starch granules was determined by scanning electron microscopy (Figure 2). SEM studies indicated that the elephant foot yam starch granules possess a smooth surface with a varying shape such as elliptical, polygonal and round. The sample was free from cracks or signs of damage. Morphology of the elephant foot yam starch was found in agreement with studies carried out by Sundaramoorthy *et al.* (2014).[39] Particle shape and size could be a key parameter for compaction as these influences the packing behavior of the starches.[41]

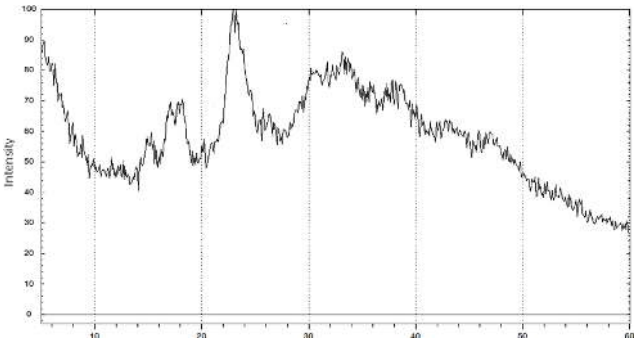


Figure 1: PXRD of Elephant foot yam starch.

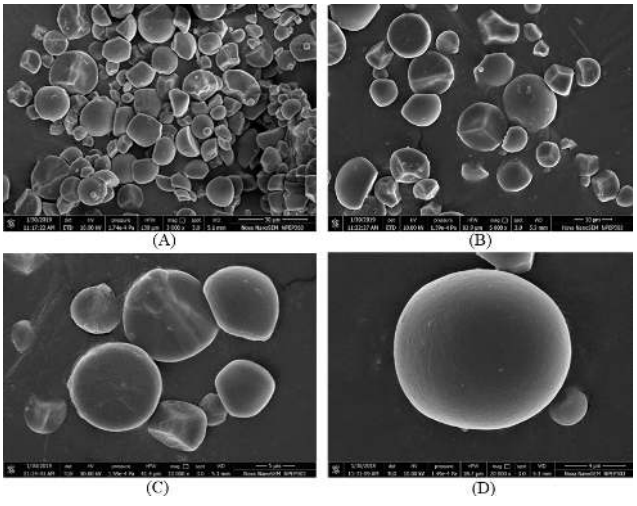


Figure 2: SEM images of elephant foot yam starch at different resolution (A) 3000 X (B) 5000 X (C) 10000 X (D) 20000 X.

FTIR and DSC studies

The FTIR spectrum showed curve resembling starch. The spectrum showed several distinct absorbances at 1153.22, 1078.98 cm^{-1} which could be attributed to the C=O bond stretching. An extremely broad at 3300.57 cm^{-1} observed due to hydrogen-bonded hydroxyl groups. Characteristic absorption bands of anhydroglucose ring stretching vibrations were observed at 1003.77, 929.52, 859.32, 758.49, 738.60 and 703.89 cm^{-1}.[42,43] FTIR spectrum was depicted in Figure 3.

DSC thermogram of elephant foot yam starch is shown in Figure 4. DSC depicts information about enthalpy and melting temperature. DSC thermogram shows an onset peak at 49.99°C, reaching the endotherm at 97.30°C and ends at 154.31°C. ΔH was found to be 299.09 J/gm. These results are

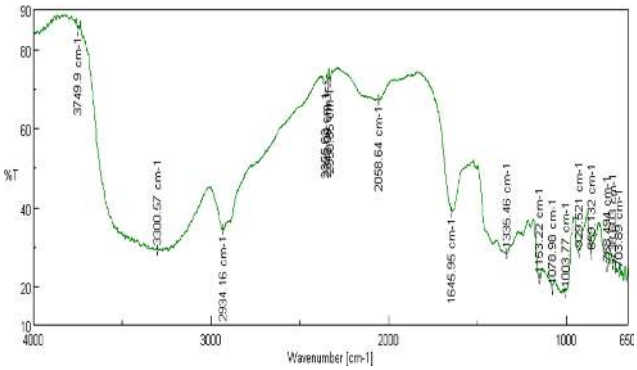


Figure 3: FTIR spectrum of elephant foot yam starch.

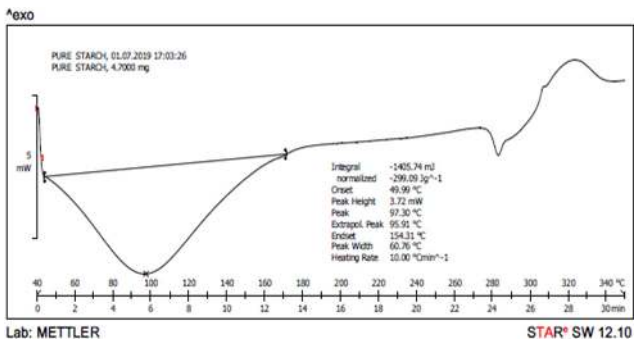


Figure 4: DSC thermogram of elephant foot yam starch.

characteristics of the starches. Results were in agreement with results reported by Pachuau *et al.* (2018).[44]

Drug excipient compatibility studies

Drug excipient compatibility studies were carried out to by FITR spectroscopy. FTIR spectrum of pure verapamil hydrochloride was compared with FTIR spectra drug excipient mixture. FTIR spectra of the pure drug showed a characteristic peak at 2914.88 cm^{-1} correspondings to C-H stretching of a methyl group, peak at 2543.65 cm^{-1} represents N-H stretching of protonated amine, peak at 2236.06 cm^{-1} depicts C=N group of alkyl nitrile, peaks at 1691.96 and 1510.67 cm^{-1} showed stretching of a benzene ring, peak at 1261.22 cm^{-1} represents C=O stretching. These values were in agreement with the values reported by Johnson and Akers (2007).[45] Similar peaks were obtained for a mixture of drug and excipients with very slight variation. The peak at 2957.3 cm^{-1} showed C-H stretching, 2542.68 cm^{-1} indicated N-H stretching, 2236.06 cm^{-1} corresponded to C=N group, 1609.38 and 1501.46 cm^{-1} showed benzene ring stretching, 1261.22 cm^{-1} showed C=O stretching. All the peaks of the drug are visible. These results were indicative of compatibility between drug and excipient (Figure 5).

Evaluation of granules

Granules were prepared by wet granulation technique and evaluated for pre-compression parameters as listed in the powder flow properties of elephant foot yam. The results of these parameters were shown in Table 3. Prepared granules exhibited good flow properties.

Evaluation of tablets

Verapamil hydrochloride tablets containing different concentration of elephant foot yam starch or corn starch were prepared by wet granulation technique. Starch as a disintegrant was added intra-granularly. Prepared tablets were evaluated for various parameters.

Weights of all the tablets were within the limit of uncoated tablets according to United States Pharmacopoeia (2011, USP34). Tablets exhibit satisfactory thickness. Friability expresses the resistance of the tablet against abrasion and chipping. Friability of the tablet was determined and it was found to be in the range of 0.20-0.50% and 0.18-0.43% for elephant foot yam and corn starch respectively, which was less than 1%. Mechanical strength is the integral property of the tablet. It is an indication of a tablet's resistance to breakage during transportation and handling. The hardness of the tablet was observed between 4.11-4.69 kg/cm^2 for elephant foot yam starch and 4.16-4.53 for corn starch. Obtained values confirm the good mechanical strength of the formulations. Tablet hardness was reduced with a higher concentration of both the starches as it tends to weaken the tablet structure at higher concentration (Table 4).[46]

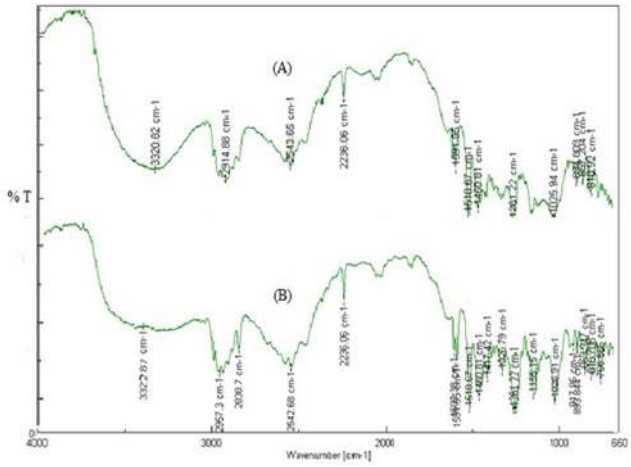


Figure 5: FTIR spectra of (A) Pure Verapamil Hydrochloride (B) Mixture of Verapamil Hydrochloride and other excipients used in the formulation.

Table 3: Results of pre-compression parameters of granules containing elephant foot yam starch (F1 F4) and corn starch (F5-F8).

Formulation Code	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility index (%)	Hausner's ratio	Angle of repose (°)
F1	0.49 ±0.002	0.56 ± 0.04	12.50 ± 0.006	1.143 ± 0.005	28° ± 0.07
F2	0.48 ± 0.05	0.54 ± 0.001	11.11 ± 0.003	1.125 ± 0.003	27° ± 0.03
F3	0.52 ± 0.007	0.59 ± 0.008	11.86 ± 0.005	1.135 ± 0.009	29° ± 0.09
F4	0.50 ± 0.08	0.57 ± 0.004	12.28 ± 0.009	1.140 ± 0.004	30° ± 0.06
F5	0.55 ± 0.009	0.63 ± 0.009	12.70 ± 0.005	1.145 ± 0.002	29° ± 0.01
F6	0.51 ± 0.002	0.58 ± 0.009	12.07 ± 0.004	1.137 ± 0.004	28° ± 0.03
F7	0.47 ± 0.005	0.54 ± 0.001	12.96 ± 0.008	1.149 ± 0.001	29° ± 0.08
F8	0.48 ± 0.004	0.55 ± 0.006	12.73 ± 0.002	1.146 ± 0.005	27° ± 0.04

*All the values expressed as means of five determinations ± standard error of the mean

Table 4: Evaluation of post compression parameters.						
Formulation code	Thickness (mm) **	Weight variation ***	Friability (%) ***	Hardness (kg/cm²) **	Wetting time (Seconds) *	Disintegration time (Seconds)
F1	2.12 ± 0.06	199.9 ± 0.06	0.20 ± 0.08	4.69 ± 0.25	35 ± 0.25	64 ± 1.06
F2	2.20 ± 0.16	200.1 ± 0.09	0.34 ± 0.05	4.35 ± 0.17	26 ± 0.36	50 ± 2.02
F3	2.13 ± 0.25	200.2 ± 0.04	0.47 ± 0.06	4.20 ± 0.31	12 ± 0.44	35 ± 1.36
F4	2.16 ± 0.03	199.8 ± 0.07	0.50 ± 0.03	4.11 ± 0.26	7 ± 0.19	28 ± 1.54
F5	2.21 ± 0.68	200.2 ± 0.01	0.18 ± 0.07	4.53 ± 0.30	49 ± 0.22	90 ± 1.66
F6	2.16 ± 0.07	199.9 ± 0.05	0.26 ± 0.02	4.42 ± 0.19	33 ± 0.40	76 ± 1.14
F7	2.22 ± 0.18	200.1 ± 0.12	0.35 ± 0.06	4.25 ± 0.42	24 ± 0.29	53 ± 1.68
F8	2.15 ± 0.24	200.1 ± 0.02	0.43 ± 0.04	4.16 ± 0.38	16 ± 0.17	40 ± 1.71

All values are expressed as mean ± standard error of the mean, n = 6*/10**/20***

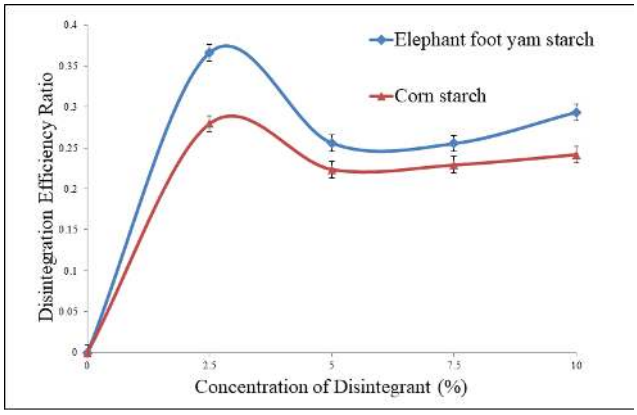
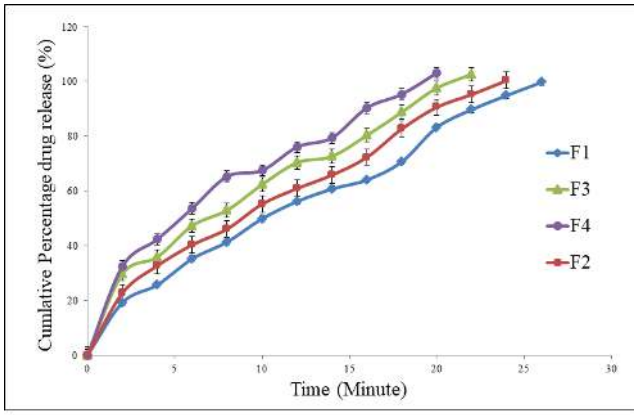


Figure 6: Disintegration efficiency plot for elephant foot yam starch and corn starch, Standard deviations of triplicate determinations were used for error bars.



(A)

Figure 7: *In-vitro* drug release profile of formulations containing (A) Elephant foot yam

Wetting time

Wetting time is a significant measure for understanding the ability of disintegrant to swell in presence of a specific volume of water.[47] The wetting time was found to be in the range of 7 to 35 sec for elephant foot yam starch and 16-49 sec for corn starch (Table 4). Tablets containing elephant foot yam possessed less wetting time as compared to standard corn starch and was increased with increasing concentration of starch. This might be attributed to the rapid penetration of water inside the pores of tablets. As a result of fast wetting; the tablet also disintegrates fast as compare to tablets containing corn starch (Table 4).

Disintegration time

The disintegration time for elephant foot yam starch tablets was observed in the range of 28 to 84 sec and disintegration time for corn starch tablets was found to be in the range of 90 to 40 sec (Table 4). The swelling was the accepted mechanism for starch as a disintegrant. The increased concentration of starch resulted in a reduction in disintegration time. All the tablets passed the official limit of the disintegration test for uncoated tablets. The disintegration efficiency ratio is a measure of the balance between the mechanical and disintegration property of the tablet. Tablet with a better balance of disintegration and mechanical strength possess a higher disintegration efficiency ratio.[48,49] For current formulations comparison of disintegration efficiency ratio was shown in Figure 6. These results were inconsistent with research carried out by Pachuau *et al.* (2018).[44] The DER*c* value is the range between 1.11 to 1.31 which is more than 1. This confirmed that elephant foot yam starch exhibited better disintegration efficiency ratio as compared to corn starch. The results of the post-compression parameters were summarized in Table 4.

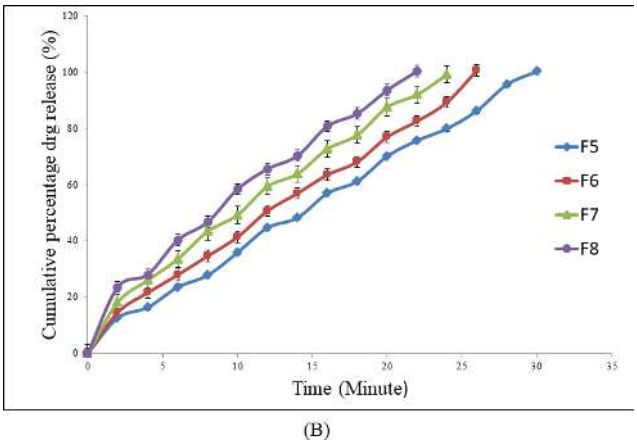
In-vitro dissolution studies

The dissolution profiles of verapamil hydrochloride tablets containing different concentrations of the elephant foot yam starches in 0.1 N HCl were shown in Figure 7. These results indicated that formulation containing elephant foot yam starch exhibited similar drug release characteristics as that of corn starch.

Table 5: Stability data of F4 batch.

Parameter	1 Month	2 Month	3 Month
Hardness (Kg/cm^2)	4.12 ± 0.16	4.36 ± 0.31	4.49 ± 0. 27
Friability (%)	0.56 ± 0.06	0.53 ± 0.08	0.44 ±0.02
Wetting time (Seconds)	8 ± 0.27	7 ± 0.19	9 ± 0.22
Disintegration time (Seconds)	25 ± 1.48	30 ± 1.39	22 ± 1.21

*All the values expressed as means of five determinations ± standard error of the mean



(B) Corn starch, Standard deviations of triplicate determinations were used for error bars.

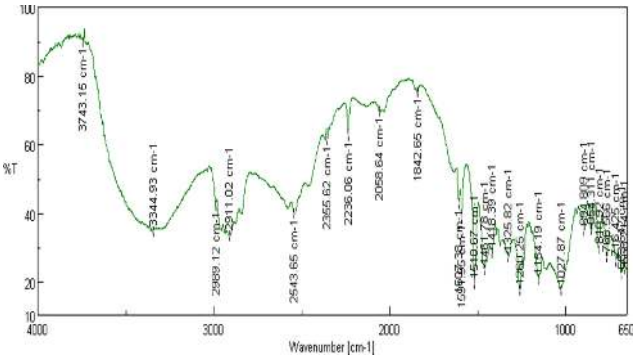


Figure 8: FT-IR spectra of optimized tablet indicating the stability of the drug within the formulation.

Prompt enhancement in the dissolution of drug with enhanced starch concentration might be due to swelling of starch granules that leads to penetration of dissolution medium in the pores of tablets and generation of hydrodynamic pressure for faster, complete disintegration and ultimately quicker dissolution of tablets. The faster disintegration was responsible for accelerating the dissolution of the tablets by exposing a large surface to the dissolution medium. Drug release from all the formulations was within the Unites States Pharmacopoeia limits (80% drug release within 30 m). Drug release from F4 formulation was similar to standard corn starch at the same concentration. It also showed quicker wetting and disintegration time; apart from this other parameters tested were also found to be within the standard limits. Hence this batch was considered as an optimized batch and further stability studies were carried out on the same batch.

Stability Studies

Stability studies were performed on the F4 batch. The results of the stability indicated that more significant difference was not observed for tested parameters before and after the storage. It was found to be stable 40°C / 75% RH for 3 months (Table 5).

FTIR spectrum of optimized formulation was carried out and compared with FTIR spectra pure verapamil hydrochloride to check the stability of drug within a formulation. Various peaks at 2969.12 cm^{-1} represent to C-H stretching of a methyl group, peak at 2543.65 cm^{-1} corresponds to N-H stretching of protonated amine, peak at 2236.06 cm^{-1} showed C=N group of alkyl nitrile, peaks at 1607.38 and 1510.67 cm^{-1} indicative of stretching of a benzene ring, peak at 1260.25 cm^{-1} represents C=O stretching. Similar peaks were reported earlier for a pure drug. These results were suggestive that the drug was stable in the formulation (Figure 8).

CONCLUSION

Disintegration is an important prerequisite for the dissolution of drugs. Starch was isolated from elephant foot yam by a simple and inexpensive process. The obtained product exhibited the characteristics of starch. This study had shown that tablets prepared from elephant foot yam starch showed similar or better disintegrant properties as that of standard corn starch. Elephant foot yam starch could be developed commercially as potential disintegrants more profoundly it could be explored as an alternative to commercially available starches for pharmaceutical use. In the future it could be modified by various techniques to avail other novel benefits such as a directly compressible excipient, increase in solubility, controlled release polymer, carrier for poorly water-soluble drug etc.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this research article.

ABBREVIATIONS

P-XRD: Powder X-ray diffraction; **SEM:** Scanning electron microscope; **FTIR:** Fourier transform infrared spectroscopy; **DSC:** Differential scanning calorimetry; **NaCl:** Sodium Chloride; **HCl:** Hydrochloric acid; **rpm:** revolutions per minute; **kV:** Kilovolts; **°C:** Degree Celsius; **µm:** Micrometer; **mg:** Milligram; **ml:** Millilitre; **m:** Minutes; **hrs.:** Hours; **RH:** Relative humidity; **w/v:** Weight by volume; **DER:** Disintegration efficiency ratio; **nm:** Nanometers; **J/gm:** Joule per gram; **kg/cm²:** kilogram per square centimeter.

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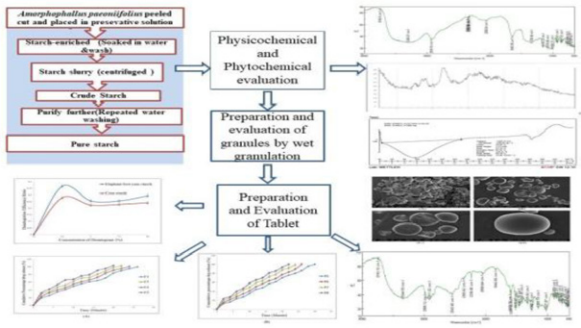
PICTORIAL ABSTRACT



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SUMMARY

- Present research work was dealing with the isolation of starch from elephant foot yam and explore its potential as a disintegrating agent as compare to standard corn starch.
- Starch isolated from elephant foot yam by a simple process and screened for phytochemical and physico-chemical properties. Studies showed that isolated sample exhibit the typical characteristics of starches and free from other foreign organic matter.
- Tablets were prepared containing elephant foot yam starch or corn starch by wet granulation and evaluated as per standard methods.
- All the formulations passed the limit as per the standards for both pre and post-compression parameters. Disintegrating potential for elephant foot yam starch was compared with corn starch by application disintegration test. Further, it was confirmed by disintegration efficiency plot, ratio and wetting time.
- It was disintegration was almost similar or even better for elephant foot yam as compared to corn starch and it can be explored commercially as an alternative disintegrant for corn starch.

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