Comparison of Enset Starch with Other Widely Known Commercial Starches and Its Significant Applications in Pharmaceuticals

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Authors’ contributions

This work was carried out in collaboration with all authors. Author AG collected literatures and wrote the first draft of the manuscript. Author WD collected literatures and edited the manuscript and author AB collected literatures and edited the final manuscript. All authors read and approved the final manuscript.

ABSTRACT

Enset [Enset ventricosum (Welw.) Cheesman], a plant widely cultivated in south and southwest of Ethiopia has been shown to be a rich source of starch. A review regarding comparison of enset starch with other widely known commercial starches and its significant applications in pharmaceuticals was presented. After a brief historical introduction, details of the use of enset crop in Ethiopia were noticed. Many experimental studies suggested that, enset starch has potentials in pharmaceutical industries as tablet excipients as binder and disintegrant, sustained release agent, pharmaceutical gelling agent and other excipients. The review further compare the potentials of enset starch with commercially available other starch in terms of ease of availability, physical and chemical properties and efficiencies.

Keywords: Enset; Ethiopia; starch; pharmaceutical application; physical property.

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1. BACKGROUND

Starches are widely employed as versatile excipients in various firm dosages such as diluents, disintegrants, and binding agents in tablet formulations. These abundant are due to their suitable physico-chemical properties as well as their relative feasibility and inertness. The versatility of starches implies a need to continue to develop new starch excipients with suitable properties to meet the special needs of drug formulators and the demands of novel formulations [1].

Enset starch is obtained from Ethiopian drought resistant plant known as ensete ventricosum (Welw.). Enset known as false banana is a perennial, herbaceous, monocarpic and monocotyledonous crop belonging to the family Musaceae [2,3,4]. Enset has a physical resemblance with the banana plant as a result it is sometimes known as false banana [5,6]. Although enset produces banana like fruits; these fruits are not the edible part. The underground corm and the aerial pseudostem made up of overlapping leaf sheaths are edible after traditional fermentation processes [6]. The corm and pseudo stem of enset yield a high carbohydrate rich staple or co-staple food, for the quarter of the Ethiopian population that inhabits the south and south western part. Enset is a crop that tolerates prolonged drought periods, flooding and many diseases. Due to its drought tolerance, it is regarded as a priority crop in Ethiopia, where it makes a major contribution to the food security of the country [7].

In addition to the use of it as starchy foods it was reported that enset starch verified a number of similar physico-chemical properties, binding nature and disintegrating properties in granulated tablet formulations with potato starch [8]. Pharmaceutical properties of swelling and solubility of enset starch is lower than that of potato starch but it has higher than that of maize [9]. Other various studies reported the significant efficiencies of enset starch for pharmaceutical applications comparatively with commercially well known starch. This short review gives a background in the use of enset starch for pharmaceutical applications.

2. OVER VIEW OF ENSET CROP IN ETHIOPIA

In Ethiopia, over 80% of the Ensete production is concentrated in south and south western part of the country [10]. Enset foods used as staple food for about 20% of the whole Ethiopian population [6]. Ensete products such as Kocho (Fig. 1B) and Bulla are serving as the staple and co-staple food for many people in the southern part of the country [11]. The fermented Kocho is often stored in pits that are lined with enset leaves and left in a storage pit for a minimum of a month, even for several years. Fermentation played a significant role in Kocho preparation by enrichment of the product through development of flavours and aromas [12].
through biotechnological techniques and propagation of the clones to these regions could be of great value.

Unlike banana, enset is monocarpic and only once in its life cycle [14]; fruits contain several seeds which are hard and about 1 to 2 cm long. Sprouting occurs only when the main shoot with the meristem is artificially decapitated at the junction between the pseudostem and corm at the soil surface; while in banana sprouting occurs spontaneously. Enset is a diploid plant with the haploid chromosome number \( n = 9 \), whereas Musa species, including edible banana, have different ploidy levels and chromosome numbers (diploid, triploid or tetraploid), with \( n = 7 \), \( n = 9 \), \( n = 10 \), and \( n = 11 \) [13]. Enset is the main crop of a sustainable indigenous African system that ensures food security in a country that is food deficient. It is one of the major agricultural products in Ethiopia and feed about 13 million people and more than 20% of the population in southern Ethiopian highlands [12]. The recurrent droughts have led to the expansion of enset cultivation to other (west and north) parts of the country [15]. Moreover, the crop has indisputable value in accordance with cultural beliefs, medicinal value and backyard animal production interventions (Table 1). The crop is highly resistant to adverse environmental conditions such as excessive rain and extended drought. It has been witnessed during the great famine of Ethiopia from 1888 to 1892 and it's named as “tree against hunger” [15]. From true history, heartfelt appreciation given by Emperor Menelik II of the plant said it was appropriately called worqe, literally meaning "my own gold" [16].

3. PHARMACEUTICAL APPLICATION OF ENSET STARCH

3.1 Properties of Enset Starch

Enset starch accounts for more than 90% of bulla on its dry weight basis and composed of moisture (14.0%), ash (0.16%), fat (0.25%), protein (0.35%), and amylose (29.0%) [17]. The fat and protein content of enset starch are significantly higher than potato starch and lower than that of maize starch [17]. Scanning electron micrographic study showed that enset starch has a characteristic shape that is somewhat angular and elliptical with the average volumetric particle diameters of about 46 μm. Study conducted by Gebre-mariam and Schmidt, [18] showed the properties of swelling and solubility of enset starch is lower than potato starch and it has higher property than that of maize. Based on this study, the differential scanning calorimetric (DSC) analysis of a starch revealed that the onset, peak and end temperature of gelatinizations to be 61.8, 65.2 and 71.7°C, respectively. Another study showed that, native enset starch has similar binding and disintegrating properties with potato starch in granulated tablet formulations [19]. In addition, sodium starch glycolate prepared from enset starch verified similar disintegrant competence to that of Primojel® (Sodium starch glycolate produced by carboxymethylation and cross-linking of potato starch) [17]. This investigation proved the potentials of application of enset starch for modification to swap the commercialized modified starches from abroad with inexpensive and cheap local products. Furthermore, various studies revealed the similarity of enset starch with in amylose content, granule size, X-ray diffraction pattern and gelatinization temperature with that of potato starch. But in some properties such as swelling power and solubility enset starch has lower than that of potato starch. The expression patterns of granules of the enset starch are angular and elliptical in shape that is discovered in different pattern from potato starch [8].

Starch is the most abundant storage reserve carbohydrate in plants. It is found in many different plant organs, including seeds, fruits, tubers and roots, where it is used as a source of energy during periods of dormancy and regrowth [20]. Native starches from different sources with highly different functionalities are investigated and commercially available on the market. Each starch may be named as according to its plant source, e.g. potato starch, maize starch, etc and these groups are markedly different from each other with the existence of chemical composition and physical properties [21]. A great deal of attention has been devoted to starch and its derivatives mainly in the context of the food, plastics and pharmaceutical industries. This because of starch physicochemical properties can be easily altered through chemical or enzymatic modification and physical treatment [19]. Starch both for food and pharmaceutical industry has commercially obtained majorly from cereals sources such as corn and wheat; from tubers and roots particularly potato and cassava. Recently more attention has been focused on the development of some of the starch from different botanical sources as excipients in pharmaceutical formulations [21]. There are different studies on enset starch have brought
the possibility of using enset starch as pharmaceutical excipients as alternatives of common starches like corn and potato.

3.2 Tablet Excipients (Binder and Disintegrant)

A pharmaceutical excipient is defined as an inactive ingredient added deliberately to the medicinal formulation [22]. Excipients are used to convert pharmacologically active compounds into pharmaceutical dosage forms suitable for administration to patients [23]. They are also necessary in ensuring the manufacturing process is thriving and the quality of the formulation can be guaranteed. The appropriate selection of excipients in the formulation is critical in development of a successful product [24].

Binder are used to impart cohesive qualities to the powder material are or granulating agent. They improve the free flowing qualities of granules by imparting desired hardness and size as well as impart cohesiveness to the tablet formulation [22,25]. As such, Solution binders are generally considered the most effective, and this is therefore the most common way of incorporating a binder into granules [26]. The binders effects on the granule properties have been received greater attention by different researchers. Result reported by Bhutanis and Bhatia 1975 [27] showed the amount of moisture retained by granules after drying increase with the increasing concentration of binding agents. The following table (Table 1) summarizes comparative elucidation of some physico-chemical properties of potato, maize and enset starch.

Tablets must have sufficient strength to withstand the stresses of subsequent manufacturing operations such as coating, packaging, and distribution processes. However, once the tablet is taken by the patient, it must break up rapidly to ensure rapid dissolution of the active ingredient in immediate - release preparations. To overcome the cohesive strength produced by the compression process and to break down the tablet into the primary particles as rapidly as possible, the disintegrants are combined with other excipients during the tableting process [22]. Several mechanism of action of disintegrants have been suggested, such as facilitating water uptake, swelling of particles, exothermic wetting reaction, particle repulsion and particle deformation recovery. There are also groups of disintegrants that function by producing gases [27].

Table 1. Comparative elucidation of some physicochemical properties of potato, maize and enset starch

| Test            | Investigations         | Result | References |
|-----------------|------------------------|--------|------------|
| Potato starch   | Bulk density (g/cm³)   | 0.833  |            |
|                 | Tapped density (g/cm³)| 1.071  |            |
|                 | True density (g/cm³)   | 1.798  | [1]        |
|                 | Carr’s index (%)       | 22.22  |            |
|                 | Hausner ratio          | 1.28   |            |
|                 | Swelling temperature (°C) | 65    |            |
|                 | Bulk density (g/cm³)   | 0.462  | [28]       |
|                 | Tapped density (g/cm³)| 0.658  |            |
| Maize starch    | True density (g/cm³)   | 1.478  | [28]       |
|                 | Carr’s index (%)       | 29.79  |            |
|                 | Hausner ratio          | 1.42   |            |
|                 | Swelling temperature (°C) | 64    |            |
|                 | Bulk density (g/cm³)   | 0.70   |            |
|                 | Tapped density (g/cm³)| 0.83   |            |
| Enset starch    | True density (g/cm³)   | 1.52   | [28]       |
|                 | Carr’s index (%)       | 15.93  |            |
|                 | Hausner ratio          | 1.19   |            |
|                 | Swelling temperature (°C) | 80    |            |
There are different commonly used disintegrants, of all the starch is by far the most widely used material. Swelling action of starch when exposed to water and capillary action, it has been generally accepted as a disintegrating agent [29,30]. The native starch has been widely used as a tablet disintegrant due to its softening effects that it has on tablet at effective concentration. The increasing stipulates for more rapid disintegration, dissolution and improved bioavailability of drugs administered by conventional oral tablets has resulted to some extent in its replacement by more active disintegrants like super-disintegrants. Super-disintegrants include sodium starch glycolates, cross-linked polyvinylpyrrolidone and cross-linked carboxymethyl cellulose [21]. But due to the higher cost of super-disintegrants, pharmaceutical formulators are looking for alternative cheaper disintegrants. The disintegrant characteristics of pregelatinized starches from various botanical sources were also examined in tablet formulation [31,32].

The binding property of enset starch was compared and better results have been obtained. In one study, the binding and disintegrant properties of enset starch has been compared and evaluated with starch of potato. The comparisons were made with Dipyrone, chloroquine phosphate, and paracetamol tablets have been formulated with tablet prepared with potato starch. The results of comparison of such properties showed that, enset starch had a better binding ability giving tablets of lower porosity and friability, but higher crushing strength than potato starch [33]. Further this study showed enset starch has a reduced characteristics of disintegrant than potato starch. As such, the results of this study evident although enset starch is a less effective disintegrant than potato starch, it can be used as an alternative source of starch in tablet formulations. Study conducted by Wondimu and Gebre-Mariam 2012 [1] revealed that, pregelatinized enset starch demonstrated comparable binding and disintegrant property with that of commercially available partially pregelatinized corn starch. Sodium starch glycolate is the sodium salt of a relatively low substituted carboxymethyl ether of a native starch prepared by both crosslinking and substitutions. In one study, the disintegration efficiency of a sodium starch glycolate prepared from enset starch was evaluated in α-lactose monohydrate and dicalcium phospahe dehydrate tablets by comparing similar tablets containing sodium starch glycolate from potato starch (Primojel®) or croscarmellose sodium, NF (Ac-Di-Sol®) [21]. The study showed the disintegration efficiency of sodium starch glycolate prepared from enset starch was as efficient as Primojel®. Study conducted by [9] investigated the effect of the type and quantity of disintegrant on the stability and various other attributes of the tablets. The study conducted using twelve Acetylsalicylic Acid (ASA) 81 mg tablets and formulation by direct compression method. Based on the study the author concluded that, type of disintegrant significantly affects the stability of enteric coated ASA 81 mg tablet. As such, tablets of desired quality and optimum stability were obtained using pregelatinized enset starch as disintegrant.

### 3.3 Sustained Release Agent

Biodegradable polymers have been used for the development of sustained release dosage forms of pharmaceutical drugs. Studies on various species of modified starch have shown a promising result in the formulation of sustained release dosage and drug action. Enset starch was used by cross-linked with sodium hexametaphosphate (SHMP) in solid phase systems under different microwave powers and reaction times were studied. From the experiment it was found that, the cross linked enset starch sustained the release of the drug for nearly a day [14]. Comparative study of the physicochemical, drug loading and releasing properties of cross-linked cassava, enset and potato starches, using sodium hexametaphosphate (SHMP) as cross-linking agent also showed that cross-linked enset starch loaded higher amount of drug in 0.1 N HCl, 0.9% NaCl and pH 7.4 phosphate buffered saline media as compared to cross-linked cassava and potato starches. After 12 h, cross-linked enset starch matrix released about 90% of the drug, indicating its ability to sustain drug release and their potential to be used as drug-release-sustaining pharmaceutical excipients [34]. Another study conducted by Nugusu et al. [35] evident, the starch acetate with degrees of substitution of 2.142 and 0.672 evaluated for direct compressibility and drug release sustaining properties. From the result, enset starch showed high degree of acetylation renders it to sustain the drug release for more than 12 hrs and highly compressible was reported.
3.4 Pharmaceutical Gelling Agent

There was discouraging situation in use of native starches for pharmaceutical gelling agent has been reported. This was due to the need for a high concentration and heating to obtain a viscous gel and its poor stability compared to other gelling agents [36]. Several reports indicated that carboxymethylation improves aqueous dispersibility and cold storage stability of starch pastes. These improved properties suggest the potential application of CMS as a pharmaceutical gelling agent. The use of carboxymethylated enset starch as pharmaceutical gelling agents have been investigated [36]. The study showed nine different topical gel formulations of ibuprofen were prepared and subsequently evaluated with respect to cosmetic qualities, pH, drug content, viscosity, spreadability, extrudability, in vitro drug release, anti inflammatory activity and stability. The ibuprofen gels exhibited significantly higher anti-inflammatory activity in mice compared to the standard 1% indomethacin gel and they were found to be non-irritant and physicochemically stable. This evident the potential use of carboxymethylated enset starch as effective gelling agents in topical preparations.

4. CONCLUSION

The present review illustrated details about pharmaceutical applications of Enset [Enset ventricosum (Welw.) Cheesman] starch. Numerous studies revealed that Enset starch has amylose content, granule size, X-ray diffraction pattern and gelatinization temperature which is comparable to potato starch. Enset starch demonstrated various pharmaceutical applications, including binder, disintegrant, super disintegrant, and gelling agent. The cross-linked and acetylated form of enset starch showed their potential use as a novel drug delivery system. Hence it can be concluded that enset starch can be used as alternative starches in pharmaceutical industries, especially in Ethiopia, where almost all of the starch used are imported from abroad.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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