

A REVIEW ATORVASTATIN TABLET BY USING FINGER MILLET (ELEUSINE CORACANA) STARCH AS NATURAL DISINTEGRANT

HANUMANT JI SHARMA 1*, JIYA SHARMA 2* RAVINDRA MISHRA 3*

DEPARTMENT OF PHARMACY, VIVEK COLLEGE OF TECHNICAL EDUCATION BIJNOR (U.P.)

Abstract

The demand for millets and their products is becoming popular globally due to their various health-promoting properties. The major constituent of the millet is its starch which contributes about 70% of total millet grain and decides the quality of millet-based food products. The application of starch for various purposes is dependent upon its physicochemical, structural, and functional properties. A native starch does not possess all the required properties for a specific use. However, product-specific properties can be achieved by modifying the structure of starches. Information deficit on millet starch has undermined its potential use in new food product design. The objective of this review is to examine the chemical composition, characterization, structural chemistry, digestibility, hydrolysis, and modification techniques of the millet starches. The review paper also discusses the various applications of native and modified starches in the food industry.

Key word-: rapidly digestible starch (RDS), slowly digestible starch (SDS), Atorvastatin

Introduction

The nutritional quality of a food product is a key parameter considered by the consumers for their healthy lifestyle and overall physical wellbeing. New food product design considers ingredients that are not only cheap and easily available but, at the same time, have functionality and nutrition. Millets are one such food material. Millets were cultivated and consumed in Asia, mostly India, and China, and also in some regions of the African continent, even before the rise of today's common cereals (wheat, and rice) [1]. Millets are small-seeded grains that belong to two tribes, Chlorideae and Paniceae, the Poaceae family. These are broadly categorized into two types: Major and Minor millets. The major millets are Pearl (Pennisetum glaucum), Proso (Panicum miliaceum), finger (Eleusine coracana), and foxtail (Setaria italica) millets. However, the minor millets comprise barnyard (Echinochloa colona), little (Panicum miliare), Kodo (Paspalum scrobiculatum), black fonio (Digitaria iburua), white fonio (Digitaria exilis), and teff (Eragrostis tef) millets (Fig. 1) [2]. Besides their nutritional benefits, millets have a short cultivation period, less water requirement, high adaptability towards adverse climatic conditions, and better productivity on the marginal lands than the major cereal crops. These agro-climatic requirements of millets

make them favorable in semi-arid areas of Africa and Asia, where now the other major crops seem to fail [3]. However, the cultivation, production, and consumption of millets vary with the geographical regions. For instance, China mainly cultivates the foxtail millet, while pearl millet is mainly cultivated in India, Africa, Nepal, and North America focuses on proso millet cultivation [4]. Millets are not commercially produced and consumed as compared to other common cereals. The possible reasons behind this might be the lesser area under their cultivation, awareness among people, and smaller size of these grains which makes their processing troublesome. These factors lead to the higher prices of decorticated grains and flour of millets as compared to other cereal crops. In India, many of these millets are consumed against wheat/rice/maize during the fasting time of Hindu rituals.

Saleh et al., [5] extensively reviewed the millets for their nutritional quality and potential health benefits. Nutritionally, millets contain 60–70% carbohydrates, 1.5–5% fat, 6–19% protein, 12–20% dietary fiber and 2–4% minerals [6]. Besides this, these are a rich source of vitamin B, lipids, dietary fiber, polyphenols, and minerals, depending upon their specific type [7]. The credit for millet's worldwide acceptance and consumption goes to its nutritional properties as it is gluten-free and possesses a high content of fiber, protein, and antioxidants. Being gluten-free, these are suitable for consumption by people suffering from celiac disease. Millets are also known to lower the release of blood glucose, which makes them effective against diabetes [[8], [9], [10]]. Epidemiological studies showed that millet consuming persons are less prone to diabetes [5,11], as millets reduce the release of blood glucose. The Glycemic index (GI) of finger millet was found lower than the wheat and rice [12]. Millets have 3–5 times the nutritional value of wheat or rice [11]. Finger millet has calcium content three times that of milk and ten times that of wheat, brown rice, and maize [12]. Initiatives to create awareness among farmers, processors, health workers, and consumers by highlighting various benefits of the millets have been reported [10]. However, to make different possible uses of millets in food products, research is to be carried out on various properties of millet and its derived components.

Millets are used for the production of various food and beverage products such as fermented/non-fermented flatbreads, beer, porridge, and non-alcoholic drinks [13]. Production and quality of such products depend greatly on the composition, of structures, properties, and interactions their major component, starch. Depending upon their hydrolysis by α -amylase, starch is categorized as rapidly digestible starch (RDS), slowly digestible starch (SDS), and resistant starch (RS) [14]. RS has many health benefits. While providing the feeling of fulfillment, it escapes the digestion process and reaches the colon where it ferments and acts as a prebiotic for the bacteria beneficial for the digestion process [15]. Millets are known to contain a good amount of resistant starch (RS), which is why they are highly preferred [6]. Kodo millet starch has high RS and low SDS in comparison to widely used rice and wheat [16]. Starch is present in the form of granules which can be isolated by various chemical, physical and enzymatic methods like centrifugation, filtration, and gravity sedimentation [17], for its numerous food and non-food uses. Every starch differentiates from others in their physio-chemical and structural properties, depending upon the source of origin, variety, and type [18]. In their native state, starches do not always have those physical and chemical properties, which otherwise required for their specific applications.

But their modification brings numerous changes in their properties making them suitable for applications in food, and non-food industries [19]. The modification also enhances their functional properties resulting in resistant starch for their use in functional foods [20]. In short, it unlocks new paths for their application. It can be done by using physical, chemical, enzymatic methods, or even hybrids of these treatment methods. The most commonly used modification treatment methods are acid hydrolysis (AHT), hydrothermal (HTT), dry heat (DHT), ultra-high-pressure (UHP) treatments, enzymatic modification (EMT), the addition of crosslinkers, and esterification [21]. These methods increase the water-binding capacity (WBC) and reduce the syneresis of starch for their better application [22,23]. Besides this, the starch modification also claims health benefits such as resistance towards digestion, promoting colon health and prebiotic activity, and lowering of blood glucose and cholesterol levels [20]. Unfortunately, compared to other cereals, millets are still lacking in their exploration and application, despite their increased utilization interest. To the best of our knowledge, the information regarding the starch characterization of some millets such as barnyard, black fonio, white fonio, little and teff millets is scanty. Understanding the various properties of millet starches would greatly contribute towards their further development and utilization as alternative functional crops. This review focuses on various native and modified millet starches, their properties, and possible applications. The data and information generated and combined in this paper will provide the required user information for the efficient utilization of millet starches during new product design.

Properties:-

1. Should be elegant product having its own identity while being free of defects such as chips, cracks, discoloration and contamination.
2. Should have strength to withstand the rigors of shocks encountered in its production, packaging, shipping and dispensing.
3. Should have the physical stability to maintain its physical attributes overtime.
4. Must be able to release the medicament agent(s) in the body in a predictable and reproducible manner.
5. Must have a suitable chemical instability over time so as not to allow alteration of the medicinal agent(s).

Methods for starch isolation from millets

Starch granules are tightly associated with the protein matrix of the grains. To solubilize the protein fraction and obtain starch from the grains, various methods and chemical reagents are used [24]. Millet starches are usually extracted by the three wet milling methods (Fig. 2), in which the flour or the millet kernels are soaked in the aqueous solution for several hours to facilitate the starch isolation from the other components of millets [25]. Generally, there are three successive phases

Preparation of standard of Atorvastatin calcium

Accurately weighed 10 mg of Atorvastatin calcium was dissolved in 10 ml of methanol to obtain a solution of 1000 μ g/ml. 1ml of this solution was diluted to 10 ml using methanol to a solution of 100 μ g/ml, this solution served as the stock solution. Into a series of 10ml volumetric flasks, aliquots of standard solution (i.e., 0.1, 0.2, .0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1ml) were added and volume was made up to 10ml using methanol. The absorbance of these solutions was measured against reagent blank at 243.90 nm(\approx 244nm). A standard curve between concentration and absorbance was plotted

Weigh a glass-stoppered, shallow weighing bottle that has been dried under the same conditions to be employed in the determination. Transfer to the bottle the quantity of the sample, accurately weighed around 1 gm, cover it and accurately weigh the bottle and the contents. Distribute the sample as evenly as practicable by gentle sidewise shaking to a depth not exceeding 10 mm. Dry the substance by placing the loaded bottle in the drying chamber at 105°C for 3 hours, remove the stopper and leave it also in the chamber. Dry the sample to constant weight. After drying is completed, open the drying chamber, close the bottle promptly and allow it to cool to room temperature (where applicable) in a desiccator before weighing. Weigh the bottle and the contents. The bottle was removed from oven and reweighed; loss on drying was calculated by following equation.

Millet starch content and composition

Millet contains 51–79% starch, similar to other cereals. Starch content varied from 71–81% and 51–69% respectively in finger millets [30] and pearl millet [31]. Millet starches usually contain around 20–30% of amylose and 70–80% of amylopectin. The presence of other constituents as impurities in the starch granules (Table 1) significantly affects its functionality [32]. For instance, millet starches mostly contain polar phospholipids (comprising 89% of total lipid content), with the remaining

Millet starch functionality

The possible applications of millet starch in food product development are more or less influenced by its functionalities such as swelling, solubility, thermal, gelatinization, viscosity, rheological, digestibility, and textural properties as discussed in the following sections.

Millet starch hydrolysis

Many factors control the rate and extent of starch hydrolysis. Some of these factors are amylose: amylopectin ratio, starch modification, amylose lipid complex, structure and size of granules, processing methods, and presence of constituents such as fiber and polyphenol in millet [6,120]. Among all the factors listed above, interactions among the three major constituents i.e. starch-lipid-proteins play a key role in glycemic property. Anti-nutrients, α -amylase inhibitors, and starch

...

Starch modification

The ability of the starch to get easily modified makes it one of the most important and demanded ingredients in food and non-food use. Starch modification is mainly achieved via derivatization (such as etherification, esterification, cross-linking), by decomposition (via acid hydrolysis and starch oxidation), by enzymatic, and physical treatments (such as heat moisture (HMT), ultra-high pressure (UHP)). The effect of some of the treatments/modification methods on some of the millet starch

Applications of millet starches

Starch is a versatile biomaterial used all over the world for its different applications in foods, textiles, pharmaceuticals, and engineering sectors. The desired functionality or role of starch in a specific field is determined by its physicochemical and functional properties.

Millet starch is used either in its native or modified forms in the food and non-food industry. But, in its native form, it has limited functionality and therefore limited industrial applications. Generally, native and

Conclusion

Millet is grown in the semi-arid region of the world where conventional cereals find difficulty in their cultivation. It offers health-promoting benefits, but still, these are underutilized. Starch is a major component of millets but is neglected for its utilization as raw material for the production of starch, unlike the other conventional sources. Similar to other starches, millet starches mainly act as a structuring agent, texture modifier, binder, and viscosity regulator. To the best of...

...

Reference

1. Kunle OO, Ibrahim YE, Emeje M., Shaba S, Kunle Y. Extraction, Physicochemical and Compaction Properties of Tacca Starch – A potential Pharmaceutical Excipient. *Starch/Stärke* 2003; 55: 319 -325
2. Mital, H.C. and Ocran J. 1968; Suitability of Cassava and Yam starches as tablet disintegrant. *Pharm. Acta. Helv.* 43:493
3. Khan K. A. and Rhodes C. T. (1972); Effectiveness of some tablet disintegrants in on insoluble direct compression base. *Pharm. Acta. Helv.* 43: 493
4. Nasipuri R. N. (1979); Evaluation of yam starch as a tablet binder and disintegrant part 1, Before storage, *Nigerian journal of Pharmacy* 10 (4), 182
5. Wiki. The free Encyclopedia: www.wikipedia.org.
6. Lachman, L., Lieberman, H.A and Kanig J.L (Edi) 3rd Edition (1986) *Lea and Febiger*, Philadelphia PP. 301 – 303

7. Banker, G.S. and Anderson, N.R.; Tablets In: The theory and practice of Industrial Pharmacy.
8. Singh, P., Desai, S.J., Simonelli, A.P. and Higuchi W.I. (1968); Role of wetting on the rate of drug release from inert matrices. *J. Pharm.Sci.*, 57: 217-226
9. Ganderton, D. (1969); The Effect of distribution of magnesium stearate on the penetration of a tablet by water. *J. Pharm. Pharmacol.*, 21 (Suppl.): 95-185
10. Ganderton, D. and Shotton E. (1961); the strength of compressed tablet III. The relationship of particle size, bonding and capping of sodium chloride, aspirin and hexamine. *J. Pharm. Pharmacol.*, 12:144T-152T
11. Nogami H., Hagai, T., Fukuola E. and Sonobe, T. (1969); Disintegration of aspirin tablets containing potato starch and microcrystalline cellulose in various concentrations. *Chem: Pharm. Bull.*, 17 (7): 1450-1455
12. Kurup, T.R.R and Pipel, N. (1977) The tensile strength and Disintegration of griseofulvin tablets. *Powder Technol.*, 16: 843 – 847.
13. Kanig J.L and Rudnic, C. (1984). The mechanisms of Disintegration action. *Pharm. Technol.*, 8; 50-62
14. Shangraw, R., Mitrevej, A., and Shah, M. (1980) New era of Tablet disintegrants. *Powder Technol.*, 4: 49-57
15. Marzaro, G.; Guiotto, A.; Chilin, A. *Exp. Opin. Ther. Pat.* 2012, 22, 223.
16. Alafeefy, A. M.; Kadi, A. A.; Al-Deeb, O. A.; El-Tahir, K. E.; Al-Jaber, N. A. *Eur. J. Med. Chem.* 2010, 45, 4947.
17. Gineinah, M. M.; El-Sherbeny, M. A.; Nasr, M. N.; Maarouf, A. R. *Arch. Pharm.* 2002, 335, 556.
18. Rather, B. A.; Raj, T.; Reddy, A.; Ishar, M. P.; Sivakumar, S.; Paneerselvam, P. *Arch. Pharm.* 2010, 343, 108.
19. Lew, J.; Qi, Z.; Huang, Q.Q.; Paudel, H.; Matsuura, I.; Matsushita, M.; Zhu, X.; Wang, J.H. Structure, function, and regulation of neuronal Cdc2-like protein kinase. *Neurobiol Aging*. **1995**, 16(3), 263-8.
20. Moeslein FM, Myers MP, Landreth GE, The CLK family kinase, CLK1 and CLK2, phosphorylate and activate the tyrosine phosphate PTP-1B *J Biol Chem* 1999, 274(38), 26697-704.
21. www.uniprot.org
22. Martin L.; Latypova X.; Wilson C.M.; Magnaudeix A.; Perrin M.; Yardin C.; Terro F. Tau protein kinases: Involvement in Alzheimer's disease. *Ageing Research Reviews*. **2012**, 6
23. Rosenthal, A.S.; Tanega, C.; Shen, M.; Mott, B.T.; Bougie, J.M.; Nguyen, D.T.; Misteli, T.; Auld, D.S.; Maloney, D.J.; Thomas, C.J. Potent and selective small molecule inhibitors of specific isoforms of Cdc2-like kinases (Clk) and dual specificity tyrosine-phosphorylation-regulated kinases (Dyrk). *Bioorg Med Chem Lett*. **2011**, 21, 3152-8.

24. Mott, B.T.; Tanega, C.; Shen, M.; Maloney, D.J.; Shinn, P.; Leister, W.; Marugan, J.J.; Inglese, J.; Austin, C.P.; Misteli, T.; Auld, D.S.; Thomas, C.J. Evaluation of substituted 6-arylquinazolin-4-amines as potent and selective inhibitors of cdc2-like kinases (Clk). *Bioorg Med Chem Lett.* **2009**, *19*, 6700-5.
25. Ogawa, Y.; Hagiwara, M. Challenges to congenital genetic disorders with “RNA-targeting” chemical compounds. *Pharmacol Ther.* **2012**.
26. Nguyen, T.B.; Lozach, O.; Surpateanu, G.; Wang, Q.; Retailleau, P.; Iorga, B.I.; Meijer, L.; Guéritte, F. Synthesis, Biological Evaluation and Molecular Modeling of Natural and Unnatural Flavonoidal Alkaloids, Inhibitors of Kinases. *J Med Chem.* **2012**, *55(6)*, 2811-9.
27. Cuny, G.D.; Ulyanova, N.P.; Patnaik, D.; Liu, J.F.; Lin, X.; Auerbach, K.; Ray, S.S.; Xian, J.; Glicksman, M.A.; Stein, R.L.; Higgins, J.M. Structure-activity relationship study of beta-carboline derivatives as haspin kinase inhibitors. *Bioorg Med Chem Lett.* **2012**, *22*, 2015-9.
28. Coffman, K.; Brodney, M.; Cook, J.; Lanyon, L.; Pandit, J.; Sakya, S.; Schachter, J.; Tseng-Lovering, E.; Wessel, M. 6-Amino-4-(pyrimidin-4-yl)pyridones: Novel glycogen synthase kinase-3b inhibitors. *Bioorg Med Chem Lett.* **2011**, *21*, 1429-33
29. Huber, K.; Brault, L.; Fedorov, O.; Gasser, C.; Filippakopoulos, P.; Bullock, A.N.; Fabbro, D.; Trappe, J.; Schwaller, J.; Knapp, S.; Bracher, F. 7,8-Dichloro-1-oxo- β -carbolines as a Versatile Scaffold for the Development of Potent and Selective Kinase Inhibitors with Unusual Binding Modes . *J Med Chem.* **2012**, *55*, 403-13.
30. Nguyen, T.B.; Lozach, O.; Surpateanu, G.; Wang, Q.; Retailleau, P.; Iorga, B.I.; Meijer, L.; Guéritte, F. Synthesis, Protein Kinase Inhibitory Potencies and in Vitro Antiproliferative Activities of Meridianin Derivatives. *J Med Chem.* **2011** *54(13)*:4474-89.
31. Debdab, M.; Carreaux, F.; Renault, S.; Soundararajan, M.; Fedorov, O.; Filippakopoulos, P.; Lozach, O.; Babault, L.; Tahtouh, T.; Baratte, B.; Ogawa, Y.; Hagiwara, M.; Eisenreich, A.; Rauch, U.; Knapp, S.; Meijer, L.; Bazureau, J.P. Leucettines, a class of potent inhibitors of cdc2-like kinases and dual specificity, tyrosine phosphorylation regulated kinases derived from the marine sponge leucettamine B: modulation of alternative pre-RNA splicing. *J. Med. Chem.* **2011**, *54*, 4172–4186.
32. Krishnamurty, R.; Brock, A.M.; Maly, D.J. Protein kinase affinity reagents based on a 5-aminoindazole scaffold. *Bioorg Med Chem Lett.* **2011**, *21*, 550-4.
33. Fedorov, O.; Huber, K.; Eisenreich, A.; Filippakopoulos, P.; King, O.; Bullock, AN.; Szklarczyk, D.; Jensen, L.J.; Fabbro, D.; Trappe, J.; Rauch, U.; Bracher, F.; Knapp, S. Specific CLK Inhibitors from a Novel Chemotype for Regulation of Alternative Splicing. *Chem Biol.* **2011**, *18*, 67-76.