Bora Rice: Natural polymer for drug delivery

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Abstract

Natural polymers play a vital part in the formulation of pharmaceutical dosage forms because of their use as excipients. Synthetic polymers have been introduced into drug delivery recently, the usage of natural polymers in drug delivery research continues to rise. It is not surprising that applications other than its caloric value have been found for starch. Various natural source of the polymer has been focused for delivery systems among them *Assam bora rice* starch seems to be a better candidate because of interesting properties such as non-toxic, biocompatible, biodegradable, mucoadhesive and non-immunogenic properties. *Assam Bora* rice, locally known as *Bora Chaul*, was first introduced in Assam, India, from Thailand or Myanmar by Thai-Ahom, now widely cultivated throughout the Assam. The starch obtained from *Assam Bora* rice is characterized by its high amylopectin content (i.e., > 95%) with a branched waxy polymer which shows physical stability and resistance towards enzymatic action. *Assam Bora* rice starch hydrates and swells in cold water, forming viscous colloidal dispersion or sols responsible for its bioadhesive nature. Moreover, it is degraded by colonic bacteria but remains undigested in the upper GIT. Due to the excellent adhesion and gelling capability, it is often selected as a mucoadhesive matrix in a controlled release drug delivery system. Carboxymethyl Assam Bora rice starch has also been applied for SPIONs stabilization, and further, it can effectively bind and load cationic anti-cancer drug molecule, Doxorubicin hydrochloride (DOX), via electrostatic interaction. This article provides a critical assessment of Assam bora rice literature and shows how the rice can be used in many ways, from food additives to drug delivery systems.

Keywords

Assam Bora rice, Starch, Natural polymer, Mucoadhesive agent, Drug delivery system

1. Introduction

Natural polymers have been widely explored as vehicles for the encapsulation and delivery of drugs and other bioactive compounds, drawing considerable interest. Their main advantages in terms of remarkable biological properties, controlled enzyme degradation, selective interactions with specific biomolecules, and versatility of modification enable them to be used for various drug delivery applications. Additionally, because of the reactive groups present in the indigenous biodegradable polymers, additional functional groups may be inserted, endowing the newly produced materials with great functionalities or changing their physical and chemical properties. Natural polymers include polysaccharides, proteins, peptides, polyesters, and several others. The Drug Delivery System has extensively investigated the natural polymers for their biocompatibility and processability. Polysaccharide and protein-based materials are more like the extracellular matrix, giving them minimally invasive features [1,2]. The backbones of polymers are also abundant in groups that can be modified, such as amino, carboxyl, and hydroxyl groups. Some natural polymers have shown stronger affinity to cell receptors and govern cellular processes such as adhesion, proliferation, and migration, which could be used to develop more selective and efficient usages. Enzyme-dependent degradation ensures their ability to build stimuli-responsive delivery systems in local locations[3]. Advances in drug delivery have driven the development of novel excipients that are safe, accomplish specialized functions, and directly or indirectly affect the rate and degree of release or absorption. Today, a wide variety of therapeutic excipients derived from plants are commercially available. Numerous investigations on the efficacy of plant-based materials as pharmaceutical excipients have been done. Synthetic polymers are toxic, expensive, have negative environmental consequences, require a long time to make, and are not as abundant as naturally occurring polymers. On the other hand, natural polymers are attractive for pharmaceutical applications because they are affordable, readily available, non-toxic, chemically changeable, potentially biodegradable, and biocompatible with few exceptions. The rationale for the rising importance of natural plant-based materials is that they are renewable and can provide a six continual supply of raw materials when cultivated or harvested sustainably [3,4]. Plant-based polymers have been studied for their potential application in various pharmaceutical dosage forms, including matrix-controlled systems, film coating agents, buccal films, microspheres, nanoparticles, and viscous liquid formulations such as ophthalmic solutions, suspensions, and implants.

Additionally, these compounds have been employed as stabilizers, disintegrants, solubilizers, emulsifiers, suspending agents, gelling agents, bioadhesives, and binders [5]. Natural polymers are biocompatible and free of unwanted effects because they are essentially polysaccharides. Native starch is a carbohydrate isolated from its botanical source with little processing to retain its intrinsic physicochemical properties following processing. Starch is one of the most popular biopolymers in sthe drug delivery system due to its versatility as an excipient in drug manufacturing, and its inexpensive cost. Starch possesses a wide variety of intrinsic physical and chemical features that dictate its functional properties and applications [6, 7]. Starch can be mainly obtained from crops including maize (Zea mays), rice (Oryza sativa), wheat (Triticum aestivum), and potato (Solanum tuberosum) (Solanum tuberosum). Due to the versatility of its applications and low cost, starch is one of the most often utilized biopolymers in drug delivery technology [8].

North-east India, notably Assam, is recognized as a confluence point for rice growing and is blessed with an abundance of rice varieties. Interestingly, starch has been proven to have applications other than caloric value. Numerous natural sources of the polymer have been targeted for use in delivery methods, including Assam bora rice starch appears to be a better candidate due to its unique qualities, which include non-toxicity, biocompatibility biodegradability, mucoadhesiveness, and non-immunogenicity [9]. Assam Bora rice (*Oryza sativa* L, Japonica variant) is a readily available Assamese glutinous rice with a high amylopectin content. Sticky rice starch is used in a range of pharmaceutical applications. Assam Bora rice, locally known as Bora Chaul, was introduced to Assam, India, by Thai-Ahom from Thailand or Myanmar. It is currently widely cultivated throughout Assam. The starch derived from Assam Bora rice is distinguished by a high amylopectin concentration (> 95%) and a branched waxy polymer that demonstrates physical stability and resistance to enzymatic action. Assam Bora rice starch hydrates and swells in cold water, generating viscous colloidal dispersion or sols that contribute to its bioadhesive properties. Additionally, it is destroyed by colonic bacteria but remains undigested in the upper gastrointestinal tract (GIT). It is frequently used as a mucoadhesive matrix in controlled release medication delivery systems due to its outstanding adherence and gelling properties. Assam Bora rice has a well-documented composition, physicochemical characteristics, shape, and medicinal applications [9,10].

This review focuses on the pharmaceutical applications and issues associated with using this native polymer in drug manufacturing technology, particularly in the formulation of conventional tablets and capsules and in specific controlled drug delivery systems. A breakthrough is likely to occur in using natural polymeric materials if the existing vigorous research on the use of natural polymeric materials is sustained and maintained. This advancement will likely address several disadvantages associated with this class of potential pharmaceutical excipients, thereby altering the landscape of the preferred pharmaceutical excipient for drug delivery in the future.

2. Physicochemical Properties of Assam Bora rice

Bora rice,, also known as sticky rice or glutinous rice, is a short-grain Asian variant used in many cuisines for its characteristic sticky texture and possesses an excellent gelling property. There is limited information on the structure and physicochemical properties of Assam Bora rice starch. Properties are normal to their biological origin. From the previous research, it has been demonstrated that the physicochemical properties of starch from Assam Bora rice are pretty similar to those of rice starches. Assam Bora rice is white or almost white, odorless, and tasteless. The amount of amylose in the product was nearly negligible. Bora rice starch contains a high concentration of amylopectin. Amylopectin is a complex molecule with three distinct types of branch chains. Bora rice, a rice variety high in amylopectin, has adhesive qualities and can thus be used alone or in conjunction with plant mucilage in appropriate proportions to develop matrix-type drug delivery systems. Due to its origin; the Assam Bora rice starch has a polygonal to spherical shape and a reasonably smooth surface. The infrared spectrum of starch is almost identical to the conventional infrared spectrum. In 1 M KOH, the inherent viscosity of Assam Bora rice starch is much higher than that of other rice starches. Moisture absorption capacity of Assam Bora rice starch increases as relative humidity increases. Assam Bora rice starch has high crystallinity. Starch granules s were revealed to be semicrystalline in nature, and crystallinity has been attributed to the well-ordered structure of amylopectin molecules within the granules, as amylopectin has been shown to alter the crystallinity level of starch granules. The degree of crystallinity of starch granules has an effect on a variety of starch properties, including gelatinization, resistance to hydrolysis (both acid and enzyme), and reactivity during chemical modification. The rigid structure of Assam Bora rice starch granules may account for the undigested nature of the Bora rice diet, which retains its bulk and medicinal benefits. Since Assam Bora rice starch is resilience to enzymatic hydrolysis, it is well suited for colon targeted drug delivery systems [2,4,11,12].

3. Bora rice as a natural polymer

3.1 Drug Delivery Applications[2,10-15]:

With advancement in vesscience and technology. Innovations in the field of public health care and medication conveyance have turned out to be one of the most promising fields for researchers across the globe. Newer designs are developed sto establish controlled drug delivery systems that provide beneficial and advantageous therapeutic potency and efficacious release of drug at the target site compared to the traditional regimens that demand frequent dosing. The use of distinct and appropriate polymers as excipient also have a vital role to play in the development of specific drug delivery systems. The utilization of natural polymers in drug delivery has attracted a lot of attention from the researchers worldwide. Natural polymers exhibit various advantages like cost-effectiveness, enhanced bioavailability, easy accessibility, conservative, and most importantly, lesser unwanted effects. Bora rice has evolved as one of the promising natural polymers that are very stable and being designated as 'GRAS' (Generally regarded as safe), which is the primary criteria for any excipient to be used for administrative and pharmaceutical purposes [35]. Bora rice also finds its application in medication conveyance as it has been characterized by some special properties. As it is obtained from natural origin, the margin of safety is much higher when compared to synthetic polymers. However, some of the utilities of bora rice as excipients in different drug delivery systems have been investigated.

a. Bora rice starch as directly compressible agents:

Assam Bora Rice Starch(ABRS) exhibits the property of a binder and directly compressible agents in the formulation of tablets. In order to study these properties of bora rice starch, a model medication comprising atorvastatin was used for developing tablets that were prepared under different conditions. The tablets were prepared with acid-altered ABRF, untreated ABRF, thermally treated ABRF, and spray-dried ABRF, which were further, analyzed, and compared with tablets utilizing microcrystalline cellulose. The study results indicated that thermally and untreated ABRF did not attain the required hardness when prepared without a binding agent. However, spray dried, and acid-modified tablets were used as directly compressible agents. Studies were also performed to evaluate the compression properties, Young's modulus, uniformity in weight, dissolution, tensile strength, friability, toughness, the drug-content profile of ABRFs. Also, the mechanical properties of ABRFs were analyzed using Kawakita's and Heckel method, and the results f the study signified the possible use of ABRFs as directly compressible agents for tablet dosage forms when compared to starch.

b. Plasma volume expander properties:

The chemical composition of bora rice starch indicates the presence of amylopectin that is also present in the structure of glycogen, and hence it was studied for its polymer expanding properties. The characterization of the bora rice starch was the subject to various analytical and other related studies like 1H NMR, Mark-Houwink relationship, FTIR studies, the relationship between viscosity and molecular weight, and osmotic pressure utilizing inward estimation technique. The result of the studies indicated that bora rice starch could be efficiently used as a plasma volume expander.

c. Importance of bora rice in the development of targeted drug delivery system:

Towards the development of targeted drug delivery systems, a series of experimental studies were performed using bora rice starch. ABRS was used to establish a novel colon-targeted tablet(compression covered) that was meant to target the 5-FU receptor site. Spray-dried lactose and microcrystalline cellulose were used to prepare the center tablet that was further coated with ABRS which played the role of a targeted drug carrier. The study results inferred that ABRS could potentially be used as a drug carrier in targeted delivery systems. Further research into the field also indicated that ABRS exhibits biocompatible mucoadhesive properties utilized in the development of mucoadhesive microspheres (MAMs).To achieve targeted delivery, the MAMs were prepared by means of a double emulsion solvent evaporation system.

d. Bora rice starch as biopolymeric polymer:

A series of in vitro dissolution studies were performed for the microbeads prepared by ionotropic gelation method following SUPAC-MR rules that incorporated the mixture of sodium alginate and pregelatinized bora rice. The microbeads were analysed using different parameters like mucoadhesion, surface morphology, pharmacotechnical boundaries, and drug-polymer compatibilities. Further, the result of the studies indicated that bora rice starch could be efficiently used as a biopolymeric excipient in drug delivery systems, and in medication transporter frameworks, it can also be used as drug release modulators.

3.2 Upcoming challenges of bora rice in drug delivery

Even though bora rice has multiple functional versatilities, there are many properties that lower the efficiency of bora rice, making it a less dependable pharmaceutical excipient in innovative and conventional formulations. Before selecting an excipient for any particular formulation, it is vital to analyze the basic informations associated with that excipient and is considered the basis of the final selection. Absorption properties and intrinsic moisture content are vital properties that can provide preliminary information about the excipient. Moisture content can affect properties like flow, tensile strength, and compaction properties of the tablets and granules. The moisture content of the bora rice starch is directly associated with the degree of relative humidity (RH) present in the atmosphere and the environment into which the starch material is stored. Thus, the moisture content of bora rice elevates with an increase in the sorption of moisture when the RH of the environment increases [2].In the case of bora rice, the process of moisture sorption occurs in different phases that begin with the tight binding of water molecules to the anhydrous glucose units. The initial step continues until a stoichiometric ratio of 1:1(water: anhydrous glucose) is attained throughout the bora rice starch grains. With an increase in water absorption, the stoichiometric ratio results as 1:2 (water: anhydrous glucose), imparting the qualities of bulk water influencing the compaction and flow properties of starch. From the research studies, it has been observed that there is a sharp fall in the Granules' flowability at 60% RH, and the flowability completely stops at 70% RH.

High moisture content has been found to produce adverse effects on the flow properties of the granules resulting in a serious variation in their weight. Hence, these weight variation issues produce serious issues during the production of capsules, tablets, and granules packaging into sachets, especially when automated systems are employed for large batch production. Furthermore, it has been observed that bora rice starch forms cake when exposed to high RH. Studies have indicated that the highest strength of tablets can be attained when the ratio of water: anhydrous glucose stoichiometry corresponds to 1:1 and 1:2 and is considered to be the equilibrium moisture content state. This stoichiometry can be obtained by storing the bora rice starch at RHs 60% and 70%, respectively. Thus, the concentration of moisture is an essential parameter for powder and granules, primarily when bora rice starch is employed in high concentrations or when it is used as diluents in the formulation[11-13]. On the other hand, moisture content also has an influential role in the compaction properties of bora rice starch.

Further, the poor flow property exhibited by the rice starch is also responsible for producing minimal lubricant sensitivity adding on more hindrances in the use of bora rice in drug delivery. To get rid of these obstacles, science-based pieces of information on the formulation, drug-delivery system, potency, dosage efficacy, and the degree of side effects should be considered during the design set of the drug delivery system incorporating bora rice as an excipient. Hence, it is the prime duty of the researchers to bring a revolution by designing and developing a drug delivery system that can exploit the potential benefits of bora rice polymer in terms of commercial utilities to overcome the hindrances and challenges on the use of bora rice in drug delivery systems[15].

4. Conclusion

Native starches are a safe biopolymer with several pharmaceutical applications. They are obtained from botanical sources and processed to pharmaceutical standards. Various natural source of the polymer has been focused for delivery systems among them Assam bora rice starch seems to be a better candidate because of interesting properties such as non-toxic, biocompatible, biodegradable, mucoadhesive and non-immunogenic properties. Starch isolated from Assam Bora rice revealed that it exhibits the same kind of physicochemical properties as rice starches. The therapeutic potential of Assam Bora rice, as evidenced by its extraordinarily high amylopectin concentration, is presented and studied as a matrix operator for controlled release drug delivery systems. As a result, the remarkable properties of Bora rice can be used to accelerate the development of drug delivery systems. Bora rice starch may be zutilized as an excipient in the future to deliver drugs with poor physical and chemical qualities in a controlled/sustained/prolonged manner. Additionally, there is no patent on bora rice starch, which opens up new possibilities for researching the potential commercial benefits of bora rice starch polymer. Bora rice starch is also being used in nano-sized colloidal, vesicular, and specialized carrier systems. According to the aforementioned literature, the use of bora rice for nanotechnology may have an additive or synergistic effect on water-insoluble pharmaceuticals' delivery, increasing their physicochemical qualities and changing their pharmacokinetics and pharmacodynamics.

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