INTRODUCTION

Starch is one of the most abundant biopolymers on earth, next to cellulose and chitin (Tharanathan, 2005). It is one of the most important sources of food for humans, and, at the same time, it is also a renewable resource that could potentially be used in many industrial applications. It is found in plant roots, tubers, stalks and seeds, and is produced by staple crops such as corn, wheat and potato (Buléon, Colonna, Planchot, & Ball, 1998). Most of the starch produced worldwide is derived from corn. Other types of starch such as cassava, potato and wheat starch are also produced in large amounts. Only the starches extracted from these crops are commercially important (Zhu, 2020) and have applications in different areas, such as the food, textile and paper industries (BeMiller & Whistler, 2009; Sjöö & Nilsson, 2018).

Starch is synthetized in the chloroplast of plant cells as insoluble granules. These granules are formed by two different polymers: amylose and amylopectin. Amylose is a linear, or slightly branched, polysaccharide of glucose units joined by α-1-4 glycosidic bonds (Dimantov, Greenberg, Kesselman, & Shimoni, 2004). Amylopectin is a branched biopolymer featuring additional α-1-6 glycosidic bonds. The botanical source determines a variety of starch properties such as chemical composition, the amylose/amylopectin relation, molecular weight, molecular structure, the length of the α-glucan chains, the branching degree of amylopectin and the amount of non-carbohydrate impurities, as well as other thermal and rheological properties (Nwokocha, Aviara, Senan, & Williams, 2009).

Starch is a cheap and versatile biopolymer that has been used for many biomedical applications, including tissue engineering scaffolds, bone cements, drug delivery systems and stent (Beilvert...
et al., 2014; Torres & Arce, 2015; Zakaria, Muhammad, & Abdullah, 2017). The physiochemical and functional characteristics of starch vary from different plant sources. However, most of the studies carried out report the use of starch from commercial sources such as maize, corn, wheat and potato. This review reports a systematic revision of the state of knowledge of commercial and non-conventional starch nanoparticle applications (BeMiller & Whistler, 2009). There are two main sources considered yet.

Drug delivery systems and for novel applications that have not been supported researchers in their continued development and selection of conventional starch sources. This review can be used as a guide to developing tailor-made materials that might not be produced from unique properties of non-conventional starch nanoparticles allow non-conventional starches have been reported as suitable biopolymers to produce such delivery systems. It is worth noting that the unique properties of non-conventional starch nanoparticles allow developing tailor-made materials that might not be produced from conventional starch sources. This review can be used as a guide to support researchers in their continued development and selection of new natural sources for the development of starch nanoparticles for drug delivery systems and for novel applications that have not been considered yet.

2 | UNCONVENTIONAL STARCH SOURCES

The great diversity in the plant species that produce starch suggests that starches from non-conventional sources should be explored in order to develop novel products with unique properties and applications (BeMiller & Whistler, 2009). There are two main sources of unconventional starches. One source is formed by underutilized crops such as sago palm (Metroxylon sagu), quinoa (Chenopodium quinoa), young bamboo culm (Dendrocalamus asper), canna (Canna indica L.) and borne (Alocasia macrorhiza), among others (Abral et al., 2019; Araujo-Farro, Podadera, Sobral, & Menegalli, 2010; Ávila-Martín, Beltrán-Osuna, & Perilla, 2020; Felisberto et al., 2019; Valencia, Henao, & Zapata, 2012). A second source of unconventional starch is formed by the non-conventional varieties of traditional crops. For example, in Peru, smallholder farmers in the highlands are keepers of more than 4,000 varieties of potato (Meinzen-Dick, Devaux, & Antezana, 2009). Most of these native varieties are only used for human consumption and are not used to produce starch. Table 1 shows a list of starches extracted from non-conventional sources and their applications.

According to Zhu (2020), there are several reasons that justify the study of non-conventional starches such as sustainable and green production, waste and by-product utilization, local availability, cultural and social significance, and technological advantages over the common starches. The different characteristics of starches from different sources make them suitable for different applications. For example, rice starch has been used in the production of both cosmetic and medicated powders for topical application due to the size of their small granules. When applied to the skin, rice starch produces a soft effect which helps minimizing the appearance of fine lines, wrinkles and blemishes (Chew-Guevara, Pérez-Carrillo, Othon Serna-Saldívar, & de la Rosa-Millán, 2016). On the other hand, non-conventional starch extracted from sago has been used as a body powder and lubricant in certain surgical and diagnostic materials (Ahmad, Williams, Doublier, Durand, & Buleon, 1999; Builders & Arhewoh, 2016).

Torres, Troncoso, Díaz, and Amaya (2011) have reported the physicochemical properties of starches extracted from more than 30 varieties of Andean tubers, including several non-conventional varieties of potato. They reported the grain size, grain area, amylose/amylopectin ratio, as well as the gelatinization temperature and enthalpy. They used three varieties of the potatoes to prepare nanoparticles. They found that although these three varieties have similarities (amylose content and gelatinization temperature), they render nanoparticles with different properties, such as size and crystallinity (Torres, Troncoso, Vega, & Wong, 2015).

Gatto et al. (2016) studied the immunological response of animal cells to nanoparticles prepared from non-conventional starches of two different varieties of native Andean potatoes (var. NEG and PER). They found that these starch nanoparticles induce a dissimilar immune response. An altered inflammatory cytokine expression was induced by the administration of NEG nanoparticles which pushed the immune system to over-react and lead to abnormal migration of monocytes/macrophages. In contrast, the nanoparticles prepared with starch obtained from the PER variety displayed a minimal innate immune response. Thus, the nanoparticles from the PER variety could be used for the delivery of bio-active molecules, such as drug or gene delivery. On the other hand, the nanoparticles from the NEG variety could potentially be used for the preparation of biodegradable vaccine adjuvants.

3 | EXTRACTION AND ISOLATION OF STARCH

When using starch from non-conventional sources, the first experimental procedure that must be carried out at the laboratory is starch extraction from the plant tissue without inadvertent modification. It should be noted that the properties of starch such as granule size, gelatinization temperature, retrogradation and viscosity, among others, are also dependent on the starch preparation technique (Benmoussa & Hamaker, 2011; Grant, 1998). A variety of methods has been reported for the extraction of starch (Sit, Deka, & Misra, 2015; Torres, Troncoso, Díaz, et al., 2011; Villarreal, Ribotta, & Iturriaga, 2013). The starch sources (tubers, grains and roots) are usually soaked in water and wet ground. Sodium metabisulphite or another chemical agent is used to retard microbial growth and impede enzyme activity. Then, sequential filtration and washing steps are followed by a drying step. Usually, the processes performed to separate proteins from starch include toluene emulsification (Adkins & Greenwood, 1966), dimethyl sulphoxide dispersion (Banks & Greenwood, 1967) and ultrasonic sonication (Knorr, Zenker, Heinz, & Lee, 2004).

Pure starch readily swells in the body, and it is rapidly degraded by enzymes. For some applications, modified starches are used to
| Botanical source                  | Scientific name                      | Applications                                                   | References                                                                 |
|----------------------------------|--------------------------------------|----------------------------------------------------------------|--------------------------------------------------------------------------|
| Native Andean potatoes           | Solanum tuberosum sbsp. Andigena     | Starch extraction                                             | Torres, Troncoso, Grande, and Díaz (2011)                                 |
| Native Andean potatoes           | Solanum tuberosum sbsp. Andigena     | Preparation of nanoparticles for biomedical applications     | Torres, Troncoso, Vega, et al. (2015), Torres et al. (2019), Gatto et al. (2016) |
| Native Andean potatoes           | Solanum tuberosum sbsp. Andigena     | Preparation of films for biomedical applications              | Torres, Troncoso, Diaz, et al. (2011), Torres, Troncoso, Gamucci, et al. (2015) |
| Sago palm                        | Metroxylon sagu                       | Preparation of films                                          | Abral et al. (2019)                                                      |
| Sago palm                        | Metroxylon sagu                       | Encapsulation of food ingredients                             | Zhu (2017)                                                               |
| Sago palm                        | Metroxylon sagu                       | Drug delivery                                                 | Muniyandy, Sathasivam, Veeramachini, and Janarthanan (2015)               |
| Quinoa                           | Chenopodium quinoa                    | Preparation of films                                          | Araujo-Farro et al. (2010)                                               |
| Quinoa                           | Chenopodium quinoa                    | Preparation of nanoparticles                                  | Velásquez-Castillo, Leite, Ditchfield, Sobral, and Moraes (2020)         |
| Quinoa                           | Chenopodium quinoa                    | Stabilization of emulsions                                    | Li, Xu, and Zhu (2019)                                                   |
| Banana                           | Musa paradisiaca                      | Edible films                                                  | Romero-Bastida et al. (2005)                                             |
| Okenia                           | Okenia hypogaea                       | Edible films                                                  | Romero-Bastida et al. (2005)                                             |
| Mango                            | Magnifera indica                      | Edible films                                                  | Romero-Bastida et al. (2005)                                             |
| Mango                            | Magnifera indica                      | Food industry                                                 | Bello-Pérez, Aparicio-Saguían, MÉNdez-Montealvo, Solorza-Feria, and Flores-Huicochea (2005) |
| Young bamboo culm                | Dendrocalamus asper                   | Starch extraction                                             | Felisberto et al. (2019)                                                |
| Bamboo                           | Bambusoideae                          | Food and biotechnology industry                                | Silva, Menis-Henrique, Felisberto, Goldbeck, and Clerici (2020)          |
| Achira                           | Canna indica L                        | Preparation of films                                          | Ávila-Martín et al. (2020)                                              |
| Achira                           | Canna indica L                        | Starch extraction                                             | Valencia et al. (2012)                                                  |
| Achira                           | Canna indica L                        | Starch extraction                                             | Piyachomkwan et al. (2002)                                              |
| Bore                             | Alocasia macrorrhiza                  | Starch extraction                                             | Valencia et al. (2012)                                                  |
| Pine nut                         | Araucaria angustifolia                | Pharmaceutical excipient                                      | Daudt, Külkamp-Guerreiro, Cladera-Olivera, Thys, and Marczak (2014)     |
| Chayote                          | Shechium edule                        | Preparation of films                                          | Aila-Suárez et al. (2013)                                               |
| Chayote                          | Shechium edule                        | Food coating                                                  | Martinez-Ortiz et al. (2019)                                             |
| Chayote                          | Shechium edule                        | Bioactivity evaluation                                         | Vieira, Pinho, Ferreira, and Delerue-Matos (2019)                       |
| Chayote                          | Shechium edule                        | Preparation of microcapsules                                  | Martinez-Ortiz et al. (2017)                                             |
| Chickpea                         | Cicer arietinum L                     | Starch extraction                                             | Hughes et al. (2009)                                                   |
| Lentil                           | Lens culinaris                        | Preparation of gels                                           | Joshi, Aldred, Panozzo, Kasapis, and Adhikari (2014)                    |
| Lentil                           | Lens culinaris                        | Starch extraction                                             | Chung, Liu, and Hoover (2009)                                           |
| Pea                              | Pisum sativum                         | Starch extraction                                             | Chung et al. (2009)                                                     |
| Pea                              | Pisum sativum                         | Preparation of films                                          | Corrales, Han, and Tauscher (2009)                                      |
| Pea                              | Pisum sativum                         | Preparation of noodles                                        | Yadav, Yadav, and Kumar (2011)                                          |
| Pea                              | Pisum sativum                         | Preparation of films                                          | Han, Seo, Park, Kim, and Lee (2006)                                     |
| Pea                              | Pisum sativum                         | Preparation of films                                          | Ma, Chang, Yang, and Yu (2009)                                          |
| Pea                              | Pisum sativum                         | Drug delivery                                                 | Yang et al. (2017)                                                      |
prepare nanoparticles. The processes used to modify starch include pregelatinization (Okunlola, Adebayo, & Adeyeye, 2015), oxidation (Zhang, Wang, Zhao, & Wang, 2012), cross-linking (Fang et al., 2008; Jain, Khar, Ahmed, & Diwan, 2008), acetylation (Tan et al., 2009; Tuovinen, Peltonen, & Järvinen, 2003) and hydroxypropylation (Santander-Ortega et al., 2010; Wu et al., 2016). For instance, hydroxyethyl starch, a starch derivative prepared by interacting starch with ethylene oxide in alkaline media, is often used as a plasma volume expander. Hydroxyethyl starch has been conjugated to anticancer molecules and therapeutic proteins to develop novel drug delivery systems (Paleos, Sideratou, & Tsiourvas, 2017).

Acetylated and hydroxypropylated starches are also among the most useful starches for drug delivery applications due to their hydrophobic nature. Acetylation is performed through the introduction of functional acetylated groups (CH₃CO) that react with the free hydroxyl groups present in the branched chains of the starch polymers to produce a specific ester (Sweedman, Tizzotti, Schäfer, & Gilbert, 2013). Reactive reagents such as anhydrous acetic acid, vinyl acetate and octenyl succinic anhydride (OSA) are used to carry out with esterification of starch in the presence of an alkaline catalyst (NaOH, KOH, Ca(OH)₂, Na₂CO₃) (Wang & Wang, 2002). For instance, OSA adds hydrophobic chains to the hydrophilic structure of starch (Chen, He, & Huang, 2014). Starch modified with OSA is an effective emulsifier used in the pharmaceutical and cosmetic industries (Fringant, Desbrières, & Rinaudo, 1996; Tuovinen et al., 2003, 2004).

Hydroxypropylated starch features a modified granular structure. The hydroxypropyl groups introduced into starch chains disrupt the inter- and intra-molecular hydrogen bonds, leading to an increase in motional freedom of starch chains in amorphous regions. As a result, hydroxypropylated starch, even with low degree of substitution, displays an improved solubility (Santander-Ortega et al., 2010). This improved solubility allows the preparation of nanoparticles using mild organic solvents such as ethyl acetate, avoiding the use of hazardous solvents (i.e. dichloromethane or dimethyl sulphoxide).

4 | PREPARATION OF STARCH-BASED NANOPARTICLES

The isolated starch granules are formed by two different biopolymers, amylose and amylpectin, that form lamellas composed of intermittent amorphous and semicrystalline phases. These lamellas aggregated in an onion-like fashion to form the starch granule (Blanshard, Bates, Muhr, Worcester, & Higgins, 1984). The semicrystalline lamellas are densely packed through the ellipsoid nanoscale ‘blocklets’ with dimensions of 20–500 nm (Gallant, Bouchet, & Baldwin, 1997). This structure can be modified by a variety of physical and chemical methods in order to obtain nanoparticles.

Table 2 shows some of the methods reported to produce starch nanoparticles. Roughly, these methods follow either a ‘top-down’ or a ‘bottom-up’ approach. The ‘top-down’ approach consists on breaking down the native structure of the starch granules. This structure can be attacked by acid, alkaline or enzymatic hydrolysis (LeCorre, Vahanian, Dufresne, & Bras, 2012; Torres, Arroyo, Tineo, & Troncoso, 2019). The hydrolysis is carried out to degrade the amorphous regions of starch granules, leaving crystalline lamellae of amylpectin which are more resistant to the hydrolysis. The nanoparticles obtained by hydrolysis are sometimes called starch
nanocrystals (LeCorre et al., 2012), since the amorphous phases are removed from the starch granules. In fact, the degree of crystallinity of the nanoparticles produced by hydrolysis is higher than the degree of crystallinity of the starch sources. Torres et al. (2019) showed that the degree of crystallinity of starch nanoparticles produced by the acid hydrolysis of potato starch ranged 40%–60% while the crystallinity of the Andean potato starches ranged 38%–44%. In addition to the chemical attacks, there are physical methods to destroy the native structure of the starch granules, including nanomilling (Patel, Chakraborty, & Murthy, 2016), ultrasonication (Bel Haaj, Magnin, Pétrier, & Boufi, 2013), reactive extrusion (Song, Thio, & Deng, 2011), and gamma radiation (Lamanna, Morales, García, & Goyanes, 2013).

On the other hand, using the ‘bottom-up’ approach, the nanoparticles are obtained from a build-up of amylose and amylpectin molecules in a controlled manner that is regulated by thermodynamic means such as self-assembly (Tan et al., 2009). Two of the most used bottom-up techniques are emulsion and nanoprecipitation. An emulsion is formed by two immiscible liquids (e.g. oil and water) with one of the liquids being dispersed as small droplets in the other. The nanoprecipitation techniques take advantage of the principle of the interfacial deposition of a polymer after the

| Techniques                  | Nanoparticles’ size               | Reference                                         |
|-----------------------------|-----------------------------------|---------------------------------------------------|
| 'Top-down' techniques       |                                   |                                                   |
| Acid hydrolysis             | 65–278 nm                         | Torres, Troncoso, Vega, et al. (2015)             |
|                             | 40–100 nm                         | Gatto et al. (2016)                               |
|                             | 50–100 nm                         | LeCorre et al. (2012)                             |
|                             | 5–30 nm                           | Putaux, Molina-Boisseau, Momaur, and Dufresne (2003) |
| Enzymatic hydrolysis        | ~145 nm                           | LeCorre et al. (2012)                             |
|                             | 60–120 nm                         | Sun, Li, Dai, Ji, and Xiong (2014)                |
|                             | 50–100 nm                         | Hao, Chen, Li, and Gao (2018)                     |
|                             | ~137 nm                           | Foresti, Williams, Martínez-Garcia, and Vázquez (2014) |
| Reactive extrusion          | 160 nm                            | Song et al. (2011)                                |
| Ultrasonication             | 30–100 nm                         | Bel Haaj et al. (2013)                            |
|                             | 35–50 nm                          | Haaj, Magnin, and Boufi (2014)                    |
|                             | 20–60 nm                          | Sun, Fan, & Xiong (2014)                          |
| γ-radiation                 | 20–30 nm                          | Lamanna et al. (2013)                             |
| Nanomilling                 | 335–946 nm                        | Bai et al. (2008)                                 |
|                             | 245 nm                            | Patel et al. (2016)                               |
| 'Bottom-up-techniques'      |                                   |                                                   |
| Emulsification              | <200 nm                           | Paulos, Mrestani, Heyroth, Gebre-Mariam, and Neubert (2016) |
|                             | 93.2 nm                           | Ji, Luo, Xiao, and Peng (2016)                    |
|                             | 83 nm                             | Chin, Mohd, Siti, and Pang (2014), Chin, Azman, and Pang (2014) |
|                             | 200 nm                            | Ding, Zheng, Zhang, and Kan (2016)                |
|                             | 96.9 nm                           | Zhou, Luo, and Fu (2014a)                         |
|                             | 91.4 nm                           | Zhou, Luo, and Fu (2014b)                         |
| Nanoprecipitation           | 300–400 nm                        | Chin, Pang, and Tay (2011)                        |
|                             | 30–75 nm                          | Qin, Liu, Jiang, Xiong, and Sun (2016)            |
|                             | 207.9–475.6 nm                    | Wu et al. (2016)                                  |
|                             | 92–263 nm                         | Farrag et al. (2018)                              |
|                             | 223–324 nm                        | Mahmoudi-Najafi et al. (2016)                     |
| Nano-spray drying           | ~500–1,000 nm                     | Pérez-Masiá et al. (2015)                         |
|                             | 208–235 nm                        | Hategékimana, Masamba, Ma, and Zhong (2015)       |
|                             | 300–500 nm                        | Shi, Li, Wang, and Adhikari (2012a)               |
|                             | 1,000–2,000 nm                    | Shi, Li, Wang, and Adhikari (2012b)               |
displacement of a semipolar solvent, miscible with water, from a lipophilic solution.

Some investigations report the use of combined techniques to prepare nanoparticles with tailored properties. Ding and Kan (2016) fabricated starch nanoparticles of 600–700 nm using a combination of sonication and W/O nanoemulsion cross-linking technique. Wang, Chen, Luo, and Fu (2016) fabricated starch nanoparticles with an average particle size of 80.5 nm by using an ionic W/O micro-emulsion followed by a cross-linking reaction. Torres et al. (2019) studied the characteristics of nanoparticles obtained using three different types of non-conventional potato starches and four different preparation methods, including acid hydrolysis, a combination of acid hydrolysis and ultrasonication, nanoprecipitation, and nanoprecipitation with the addition of a cross-linking agent (Figure 1). They found that both acid hydrolysis-based methods and nanoprecipitation-based methods yield nanoparticles with an elliptical shape, with diameters ranging from 79.6 to 362.9 nm and 34.03 to 194.7 nm, respectively. However, the acid-based methods were found to preserve the original starch crystalline structure, whereas the nanoprecipitation fully disrupted the granule organization.

There are different strategies to use these nanoparticles as drug carriers. For instance, the active substances can be dissolved in a liquid inner phase (Ding, Lin, & Kan, 2018; Nallasamy et al., 2020; Yang et al., 2017), using hollow-core nanoparticles (nanocapsules). When using solid-core structures, the drugs can be dissolved in the starch matrix that forms the nanoparticles. Another strategy used is to absorb the active substance at the nanoparticle surface. These strategies have been also used for the preparation of other drug delivery systems from different biopolymers, such as polylactic acid (PLA), chitosan and bacterial nanocellulose (Table 3). Table 3 also lists some important properties of the starch-based drug delivery systems and the other biopolymers systems, including size, shape and biocompatibility.

5 | STARCH-BASED NANOPARTICLES FOR DRUG DELIVERY APPLICATIONS

The use of nanoparticles in drug delivery systems is aimed at enhancing the therapeutic efficacy of the drugs by allowing a

![Figure 1](image-url)
According to Srikaeo (2016), polysaccharides are still understudied as drug delivery carriers in spite of the fact that they feature advantages such as preventing non-specific protein adsorption, providing neutral coating with low surface energy and allowing modification with various ligands due to high proportion of reactive groups in their backbone.

Starch-based nanoparticles have been used to develop novel drug delivery systems. Table 4 shows a list of the different starch-based systems for oral, parental and topical drug delivery using starches extracted from conventional and non-conventional sources. Starch-based nanoparticles have been used to deliver ciprofloxacin (Mahmoudi Najafi, Baghaie, & Ashori, 2016), curcumin (Pang, Chin, Nadirah, Hiang, & Yazid, 2015), sodium diclofenac (El-Naggar, El-Rafie, El-Sheikh, El-Feky, & Hebeish, 2015), doxorubicin hydrochloride (Xiao et al., 2016), hydroxychloroquine (Sleightholm, Yang, Yu, Xie, & Oupicky, 2017), hydroxyurea drug (Alwaan, Jafar, & Allebban, 2019) and 5-fluorouracil (Ding et al., 2018), among other drugs and active agents. Figures 2 and 3 show the schematic diagram of the preparation of ciprofloxacin and doxorubicin hydrochloride-loaded starch nanoparticles, respectively.

Oral delivery is a common route for the administration of drugs. In order to be effective, drugs administrated orally must be stable and maintained in the active form under the acidic and enzymatic conditions of the gastrointestinal tract. The active substance must pass through the different tissues that form the gastrointestinal tract, mucus layer and intestinal epithelium, in order to finally enter the portal vein and reach the systemic circulation (Chen, Sonaje, Chen, & Sung, 2011). The environmental conditions make difficult for some drugs to remain active. The pH of the stomach environment is 1.2–3.0, whereas the pH in the intestine is 6.5–8.0 (Wang & Zhang, 2012). Thus, pH-responsive drug delivery systems have been developed for oral delivery applications. One of the strategies followed to design pH-responsive polymers is to add carboxylic groups in their structure (Wang et al., 2015; Zhang et al., 2016). The solubility of these carboxylic acid groups varies according to the pH of the media. In pH < 6, their solubility decreased, while in pH > 6, their solubility increases.

Recently, Jong, Ju, and Zhang (2017) used hydroxyethyl starch to synthesize a pH-responsive polymer. This polymer was prepared via hydrophobic modification of hydroxyethyl starch (HES) with propynylglycidyl ether (PGE), and then, pH-responsive carboxylic acid group was connected to propynyl group via thiol-yne click reaction with NAC (N-acetyl-cysteine). They prepared nanoparticles with this modified starch and loaded them with doxorubicin. These nanoparticles perform drug release by the conversion of hydrophilic and hydrophobic with the change of the pH value in aqueous solution. They were able to protect drugs under acidic conditions and showed good in vitro drug release under neutral conditions.

Parenteral administration is another universal route for the administration of drugs due to the easy access of injected drugs to systemic circulation. The rapid action of the injected drug is often followed by a fast decline in the systemic drug levels. The development of new polymeric nanoparticles has the objective of providing sustained and slow drug release for long durations, reducing the frequency of injections and improving the quality of treatment (Nikam, Pawar, Jadhav, & Bairagi, 2013). Narayanan, Nair, and Menon (2015) used hydroxyethyl starch to prepare starch nanoparticles through a simple, two-step cross-linking-precipitation route. The results showed that these nanoparticles were effective in encapsulating two chemically distinct drugs (indomethacin and ibuprofen sodium) with varying hydrophobicities. They also found that the controlled

| Type of nano-object | Processing technique | Size | Shape | Loaded drug | Biocompatibility | Reference |
|---------------------|---------------------|------|-------|-------------|-----------------|-----------|
| Starch from non-conventional sources | Acetylated starch nanocrystals | Acid hydrolysis | 108–727 nm | Nanocrystals | Doxorubicin hydrochloride | Rat hepatocytes | Xiao et al. (2016) |
| Starch nanoparticles | Nanoprecipitation | 135.1 nm | Nanoparticles | Curcumin | – | Acevedo-Guevara, Nieto-Suaza, Sanchez, Pinzon, and Villa (2018) |
| Starch nanoparticles | Nanoprecipitation | 119.1–723 nm | Nanoparticles | Quercetin | – | Farrag et al. (2018) |
| Other polymer sources | PEG-PLA nanoparticles | Precipitation polymerization | ~200 nm | Nanospheres | Cisplatin | L929 cells | Deng and Lei (2013) |
| | Thiolated trimethyl chitosan nanoparticles | Polyelectrolyte complexation | 100–200 nm | Spherical | Insulin | Caco-2 cells | Yin et al. (2009) |
| | Bacterial nanocellulose | Static cultivation | ~100 nm | Nanofibres | Octenidine | HaCaT cells | Moritz et al. (2014) |
| Starch (source) | Active component/model drug | Application | Reference |
|----------------|-----------------------------|-------------|-----------|
| **Starch from conventional sources** | | | |
| Cholesterol/imidazole-modified oxidized starch | Curcumin | Cancer therapy | Xu et al. (2020) |
| Pure starch | 7-Phenyl-2, 4, 6-hepta-trienoyl hydroxamic acid | Cancer therapy | Alp, Damkaci, Guven, and Tenniswood (2019) |
| Hydroxyethyl starch (HES) | Hydroxychloroquine (HCQ) | Cancer therapy | Sleightholm et al. (2017) |
| Pure starch cross-linked with gum arabic | Hydroxyurea drug | Cancer therapy | Alwaan et al. (2019) |
| Modified (semisynthetic) starch | Doxorubicin (DOX) | Cancer therapy | Wu et al. (2018) |
| Hydrazine-modified starch | Doxorubicin (DOX) | Cancer therapy | Zohreh, Hosseini, and Pourjavadi (2016) |
| Retrograded starch | 5-Fluorouracil | Cancer therapy | Ding et al. (2018) |
| Corn starch | FTY720 | Cancer therapy | Masoudipour, Kashanian, Azandaryani, Omidfar, and Bazyar (2017) |
| Esterified modified potato starch | Doxorubicin (DOX) | Cancer therapy | Chen et al. (2019) |
| Potato starch | Paclitaxel | Cancer therapy | Putro, Ismadji, Gunarto, Soetaredjo, and Ju (2020) |
| Wheat starch | Minocycline hydrochloride | Topical drug delivery | Marto, Gouveia, et al. (2018), Marto, Ruivo, et al. (2018) |
| Pregelatinized starch | Topical lipophilic molecules | Topical drug delivery | Marto et al. (2016) |
| Maize starch | Flufenamic acid, testosterone | Topical drug delivery | Santander-Ortega et al. (2010) |
| Carboxymethyl corn starch | Clonidine | Topical drug delivery | Saboktakin et al. (2014) |
| Pure maize starch | Indomethacin, acyclovir | Topical drug delivery | El-Feky et al. (2015) |
| Pure maize starch | Diclofenac sodium | Topical drug delivery | El-Naggar et al. (2015) |
| Pregelatinized starch | Human neutrophil elastase inhibitor (ER143) | Topical drug delivery | Marto, Ruivo, et al. (2018) |
| Pregelatinized starch | Minocycline hydrochloride | Topical drug delivery | Marto, Gouveia, et al. (2018) |
| Corn starch | Ginkgo biloba extracts | Oral drug delivery | Wang et al. (2020) |
| Anionic carboxymethyl starch | Bovine serum albumin | Oral drug delivery | Zhang et al. (2017) |
| Cationic quaternary ammonium starch | Doxorubicin (DOX) | Oral drug delivery | Jong et al. (2017) |
| Hydroxyethyl starch | Insulin | Oral drug delivery | Minimol, Paul, and Sharma (2013) |
| Esterified starch | Insulin | Oral drug delivery | Zhang et al. (2013) |
| Corn starch | Insulin | Oral drug delivery | Jain et al. (2008) |
| Soluble potato starch | Insulin | Transnasal drug delivery | Narayanan et al. (2015) |
| Hydroxyethyl starch | Indomethacin, ibuprofen sodium | Parental drug delivery | Maghsoudi et al. (2017) |
| Soluble starch | Curcumin | Anticariogenic | Li, Yang, Lu, Ma, and Zhang (2018) |
| Hydroxyethyl starch | Flavonoid morin | Hyperuricemia therapy | Bashir Pathan, Subhashrao Misal, Bairagi, and Mallikarjuna Setty (2016) |
| Esterified modified corn starch | Irbesartan | Hypertension treatment | Mahmoudi Najafi et al. (2016) |
| Acetylated corn starch | Ciprofloxacin | Antibiotic delivery | Shi et al. (2016) |
| Soluble starch | Ciprofloxacin | Antibiotic delivery | Paulos et al. (2016) |

**Starch extracted from non-conventional sources**

| Starch | Active component/model drug | Application | Reference |
|--------|-----------------------------|-------------|-----------|
| Broken rice starch | Doxorubicin hydrochloride (DOX) | Cancer therapy | Xiao et al. (2016) |
| Acetylated dioscorea starch | - | Release of water-insoluble drugs | Paulos et al. (2016) |

(Continues)
| Starch (source)          | Active component/model drug | Application                                     | Reference                      |
|-------------------------|-----------------------------|-------------------------------------------------|--------------------------------|
| Assam Bora rice starch  | Metronidazole (MTZ)         | Colon-targeted drug delivery systems            | Ahmad et al. (2012)            |
| Pea starch              | Quercetin                   | Evaluation of release kinetics                   | Farrag et al. (2018)           |
| Sago palm starch        | Curcumin                    | Bioavailability of curcumin                      | Chin, Mohd, et al. (2014)      |
| Sago palm starch        | -                           | pH-responsive drug carriers                      | Tay, Pang, and Chin (2012)     |
| Sago palm starch        | Paracetamol                 | pH-responsive drug carriers                      | Chin, Romainor, Pang, Lee, and Hwang (2019) |
| Sago palm starch        | Curcumin                    | Bioavailability of curcumin                      | Pang et al. (2015)             |
| Banana starch           | Curcumin                    | Oral drug delivery                               | Acevedo-Guevara et al. (2018)  |
| Jackfruit seed starch   | Ibuprofen                   | Colon-targeted drug delivery                     | Das and Das (2019)             |
| Jack bean starch        | -                           | Nanoparticle disintegrants in drug delivery systems | Oladebeye (2020)              |
| Cassava (Manihot esculentus) starch | Rifampicin              | Tuberculosis treatment                           | Christianah and Rodrigues (2016) |
| Cassava (variety H-165) starch | Curcumin                  | Cancer therapy                                  | Athira and Jyothi (2015)       |

**FIGURE 2** Comparison between two drug-loading methods used for ciprofloxacin loading on starch nanoparticles (StNPs). (a) Flow chart of the coating method. Ciprofloxacin is added into the initial solution before the starch nanoparticles are produced by an emulsion technique followed by high-pressure homogenization (HPH), (b) flow chart of the adsorption method. The starch nanoparticles are produced first; then, ciprofloxacin is adsorbed onto starch nanoparticles. Reproduced with permission from Shi, Li, Liu, Adhikari, and Wang (2016)

**FIGURE 3** Scheme for the preparation of hollow starch nanoparticle (HSNPs) loaded with doxorubicin hydrochloride (DOX·HCl) via a sacrificial hard-template process. CaCO₃ nanoparticles are used as template. EDTA (ethylenediaminetetraacetic acid) is used to remove the template. Reproduced with permission from Yang et al. (2017)
release of drugs was achieved by the combination of two different release mechanisms, diffusion and erosion.

Topical drug delivery has also been reported for starch-based nanoparticles. Some of the requirements for the materials used in topical drug delivery include skin compatibility, skin protection, sensory properties and environmental compatibility (Röper, 2002). In addition to the nanoparticles, vehicles, such as ointments, creams, lotions and gels, are used for topical drug delivery (Raposo, Simões, Almeida, & Ribeiro, 2013). Starch nanoparticles can be tailor-made in a variety of sizes and shapes, and their surface polarity can be modified to improve skin penetration and prolong the residence time of drugs (Escobar-Chavez et al., 2012; Liu, Jiao, Wang, Zhou, & Zhang, 2008). Starch-based nanoparticles have been used for topical delivery of a variety of drugs such as flufenamic acid (Santander-Ortega et al., 2010), human neutrophil elastase inhibitor (ER143) (Marto, Ruivo, et al., 2018), minocycline hydrochloride (Marto, Gouveia, Gonçalves, Ribeiro, & Almeida, 2018), clonidine (Saboktakin, Akhyari, & Nasirov, 2014), acyclovir (El-Feky, El-Rafie, El-Sheikh, Mehez, & Hebeish, 2015) and diclofenac sodium (El-Naggar et al., 2015).

Several works report the use of starch-based drug delivery systems for cancer treatments. Chemotherapy is among the most common methods for cancer treatment (Wicki, Witzigmann, Balasubramanian, & Huwyler, 2015). Chemotherapeutic drugs show poor stability and solubility in blood circulation and lack selective delivery. These drugs are generally toxic to both cancerous and healthy cells (Gewirtz, 1999; Quintela-Fandino et al., 2017). Starch nanoparticles have been shown to help to overcome some of the problems associated with chemotherapy. Targeted starch drug delivery systems have been shown to avoid high concentration intake of chemotherapeutic drugs and thus decrease the possibilities of side effects (Alexiou et al., 2000).

It has been reported that nanoparticles readily accumulate in cancer tissue at much higher concentrations than in normal tissue. This retention effect of cancerous tissues is due to the leaky vasculature and limited lymphatic drainage of cancer tumours (Maeda, 2001; Maeda, Wu, Sawa, Matsumura, & Hori, 2000; Zhang et al., 2019). In addition, the tumour extracellular pH is from 5.7 to 6.9 in cancer cells, which is lower than that in normal tissues (Wike-Hooley, Haveman, & Reinhold, 1984). Thus, pH-responsive drug delivery systems are suited to improve the effectiveness of cancer treatments. This can be achieved by the utilization of pH-labile chemical bonds (pH-sensitive polymer–drug conjugates), such as hydrazone, cissacitinyl and acetal bonds (Fleige, Quadir, & Haag, 2012; Shalviri et al., 2013). The imidazole functional group is commonly used to provide pH sensitiveness to a drug delivery system. It allows absorbing protons under acidic conditions (pH ~6.0–6.5) and exhibits a pH-induced hydrophilic–hydrophobic transition (Radovic-Moreno et al., 2012; Wang et al., 2014).

Starch-based drug delivery systems can improve tumour accumulation of chemotherapeutics avoiding immunogenic responses (Hu et al., 2016; Li et al., 2015; Liu, Jiang, & Hunziker, 2016). Xu et al. (2020) prepared pH-responsive nanoparticles for tumour-targeted anticancer drug delivery using oxidized starch modified by cholesterol and imidazole to obtain amphiphilic cholesterol/imidazole-modified oxidized starch (Cho-Imi-OS) nanoparticles loaded with curcumin (Figure 4). They found that the cumulative release

![Diagram](image_url)  
**Figure 4** Scheme for the preparation of curcumin-loaded nanoparticles based on cholesterol/imidazole-modified oxidized starch (Cho-Imi-OS) via a dialysis method. The pH of the tumour cells environment triggers the breakdown of curcumin-loaded nanoparticles. (DMSO, dimethyl sulphoxide; PBS, phosphate-buffered saline) Reproduced with permission from Xu et al. (2020)
of curcumin is much more and faster at pH 5.5 (65%) than that at pH 7.4 (38%). The results suggest that the starch nanoparticles gradually swell and disassemble due to the protonation of imidazole groups at acidic pH, leading to trigger the release of encapsulated curcumin.

6 | CONCLUSIONS

We have reviewed the most recent reports of nanoparticles prepared from pure and modified starches for drug delivery applications. More than 25 non-conventional sources of starch have been reported. Both conventional and non-conventional starches have been used to prepare nanoparticles for drug delivery systems, using a variety of techniques such as acid hydrolysis, emulsification and nanoprecipitation, among others. The investigations of delivery systems prepared with conventional starch often report their use in a specific therapy together with in vitro and in vivo tests. The non-conventional starches reported for the preparation of nanoparticles for drug delivery applications include dioscorea, pea, sago palm, banana, jackfruit, jack bean and cassava starch. Most of the investigations dealing with the use of these non-conventional starches report the characteristics of the nanoparticles prepared together with the loading and unloading properties, showing the potential applications of these systems. Further investigations should report in vitro and in vivo tests of non-conventional starch drug delivery systems for specific diseases and treatments.

ACKNOWLEDGEMENTS

The authors thank the Vice-Rectorate for Research (VRI) of the Pontificia Universidad Catolica del Peru for financial support.

REFERENCES

Abrah, H., Basri, A., Muhammad, F., Fernando, Y., Hafizulhaq, F., Mahardika, M., ..., Stephane, I. (2019). A simple method for improving the properties of the sago starch films prepared by using ultrasonication treatment. Food Hydrocolloids, 93, 276–283. https://doi.org/10.1016/j.foodhydro.2019.02.012

Acevedo-Guevara, L., Nieto-Suaza, L., Sanchez, L. T., Pinzon, M. I., & Villa, C. C. (2018). Development of native and modified banana starch nanoparticles as vehicles for curcumin. International Journal of Biological Macromolecules, 111, 498–504. https://doi.org/10.1016/j.ijbiomac.2018.01.063

Adkins, G. K., & Greenwood, C. T. (1966). The isolation of cereal starches in the laboratory. Starch – Stärke, 18, 213–218. https://doi.org/10.1002/star.19660180703

Ahmad, F. B., Williams, P. A., Doublier, J., Durand, S., & Buleon, A. (1999). Physico-chemical characterisation of sago starch. Carbohydrate Polymers, 38, 361–370. https://doi.org/10.1016/S0144-8617(98)00123-4

Ahmad, M. Z., Akhter, S., Ahmad, I., Singh, A., Anwar, M., Shamim, M., & Ahmad, F. J. (2012). In vitro and in vivo evaluation of Assam Bora rice starch-based bioadhesive microsphere as a drug carrier for colon targeting. Expert Opinion on Drug Delivery, 9, 141–149. https://doi.org/10.1517/17425247.2012.633507

Alía-Suárez, S., Palma-Rodríguez, H. M., Rodríguez-Hernández, A. I., Hernández-Uribe, J. P., Bello-Pérez, L. A., & Vargas-Torres, A. (2013). Characterization of films made with chayote tuber and potato starches blending with cellulose nanoparticles. Carbohydrate Polymers, 98, 102–107. https://doi.org/10.1016/j.carbpol.2013.05.022

Alexiou, C., Arnold, W., Klein, R. J., Parak, F. G., Hulin, P., Bergemann, C., ..., Lübke, A. S. (2000). Locoregional cancer treatment with magnetic drug targeting. Cancer Research, 23, 6641–6648.

Alp, E., Damkaci, F., Guven, E., & Tenniswood, M. (2019). Starch nanoparticles for delivery of the histone deacetylase inhibitor CG-1521 in breast cancer treatment. International Journal of Nanomedicine, 14, 1335–1346. https://doi.org/10.2147/IJN.S191837

Alwan, I. M., Jafar, M., & Allebban, Z. (2019). Development of biodegradable starch nanocrystals/gum Arabig hydrogels for controlled drug delivery and cancer therapy. Biomedical Physics & Engineering Express, 5, 25021. https://doi.org/10.1088/2057-1966/aaf4c4

Araujo-Farro, P. C., Podadera, G., Sobral, P. J. A., & Menegalli, F. C. (2010). Development of films based on quinoa (Chenopodium quinoa, Willdenow) starch. Carbohydrate Polymers, 81, 839–848. https://doi.org/10.1016/j.carbpol.2010.03.051

Athira, G. K., & Jyothi, A. N. (2015). Cassava starch-poly(vinyl alcohol) nanocomposites for the controlled delivery of curcumin in cancer prevention and treatment. Starch – Stärke, 67, 549–558. https://doi.org/10.1002/star.201400199

Ávila-Martín, L., Beltrán-Osuna, A. A., & Perilla, J. E. (2020). Effect of the addition of citric acid and whey protein isolate in Canna indica L. starch films obtained by solvent casting. Journal of Polymers and the Environment, 28, 871–883. https://doi.org/10.1007/s10924-019-01648-z

Bai, S. H., Bukhari, N. I., Hay, Y. K., Kang, Y. B., Majeed, A. B. A., & Nadeem, M. (2008). Effect of surfactants on the size-distribution of starch nanoparticles during wet grinding. Technical Proceedings of the 2008 NSTI Nanotechnology Conference, 1, 356–359.

Banks, W., & Greenwood, C. T. (1967). The fractionation of laboratory-isolated cereal gereal starches using dimethyl sulphoxide. Starch – Stärke, 19, 394–398. https://doi.org/10.1002/star.19670191202

Bashir Pathan, I., Subhashrao Misal, N., Bairagi, S., & Mallikarjunya Setty, C. (2016). Palmitic acid grafted maize starch (PaGMS) nanoparticles as potential drug carrier for Ibesarten. In vitro and in vivo evaluation. Current Nanommedicine, 6, 156–164. https://doi.org/10.2174/2146818730666160622082419

Beilvert, A., Faure, F., Meddahi-Pellé, A., Chaunier, L., Guillois, S., Chaubet, F., ..., Bizeau, A. (2014). A resorbable shape-memory starch-based stent for the treatment of salivary ducts under sialendoscopic surgery. The Laryngoscope, 124, 875–881. https://doi.org/10.1002/lary.24380

Bel Haaj, S., Magrin, A., Pétrier, C., & Boufi, S. (2013). Starch nanoparticles formation via high power ultrasonication. Carbohydrate Polymers, 92, 1625–1632. https://doi.org/10.1016/j.carbpol.2012.11.022

Bello-Pérez, L. A., Aparicio-Saguilán, A., MÉNdez-Montealvo, G., Solorza-Feria, J., & Flores-Huicochea, E. (2005). Isolation and partial characterization of mango (Magnifera indica L.) starch: Morphological, physicochemical and functional studies. Plant Foods for Human Nutrition, 60, 7–12. https://doi.org/10.1007/s11130-005-2534-z

BeMiller, J., & Whistler, R. (2009). Starch (3rd ed.). London, UK: Academic Press.

Benmoussa, M., & Hamaker, B. R. (2011). Rapid small-scale starch isolation using a combination of ultrasonic sonication and succrose density separation. Starch – Stärke, 63, 333–339. https://doi.org/10.1002/star.201000083

Blanshard, J. M. V., Bates, D. R., Muhr, A. H., Worcester, D. L., & Higgins, J. S. (1984). Small-angle neutron scattering studies of starch granule structure. Carbohydrate Polymers, 4, 427–442. https://doi.org/10.1016/0144-8617(84)90025-0

Builders, P. F., & Arhewoh, M. I. (2016). Pharmaceutical applications of native starch in conventional drug delivery. Starch – Stärke, 68(9-10), 864–873. http://dx.doi.org/10.1002/star.201500337
Li, G., Xu, X., & Zhu, F. (2019). Physicochemical properties of docetyl succinyl anhydride (DOSA) modified quinoa starch. Food Chemistry, 300, 125201. https://doi.org/10.1016/j.foodchem.2019.125201
Li, J., Yang, Y., Lu, L., Ma, Q., & Zhang, J. (2018). Preparation, characterization and systemic application of self-assembled hydroxyethyl starch nanoparticles-loaded flavonoid Morin for hyperuricemia therapy. International Journal of Nanomedicine, 13, 2129–2141. https://doi.org/10.2147/IJN.S158585
Li, M., Tang, Z., Zhang, D., Sun, H., Liu, H., Zhang, Y., ... Chen, X. (2015). Doxorubicin-loaded polysaccharide nanoparticles suppress the growth of murine colorectal carcinoma and inhibit the metastasis of murine mammary carcinoma in rodent models. Biomaterials, 51, 161–172. https://doi.org/10.1016/j.biomaterials.2015.02.002
Liu, K., Jiang, X., & Hunziker, P. (2016). Carbomethoxy-based amphiphilic nano delivery systems for cancer therapy. Nanoscale, 8, 16091–16156. https://doi.org/10.1039/C6NR04489A
Liu, Z., Jiao, Y., Wang, Y., Zhou, C., & Zhang, Z. (2008). Polysaccharides-based nanoparticles as drug delivery systems. Advanced Drug Delivery Reviews, 60, 1650–1662. https://doi.org/10.1016/j.addr.2008.09.001
Ma, X., Chang, P. R., Yang, J., & Yu, J. (2009). Preparation and properties of glycerol plasticized-pea starch/zinc oxide-starch bionanocomposites. Carbohydrate Polymers, 75, 472–478. https://doi.org/10.1016/j.carbpol.2008.08.007
Maaran, S., Hoover, R., Donner, E., & Liu, Q. (2014). Composition, structure, morphology and physicochemical properties of lablab bean, navy bean, rice bean, tepary bean and velvet bean starches. Food Chemistry, 152, 491–499. https://doi.org/10.1016/j.foodchem.2013.12.014
Maeda, H. (2001). The enhanced permeability and retention (EPR) effect in tumor vasculature: the key role of tumor-selective macromolecular drug targeting. Advances in Enzyme Regulation, 41, 189–207. https://doi.org/10.1016/S0001-8322(00)00013-3
Maeda, H., Wu, J., Sawa, T., Matsumura, Y., & Hori, K. (2000). Tumor vascular permeability and the EPR effect in macromolecular therapeutics: A review. Journal of Controlled Release, 65, 271–284. https://doi.org/10.1016/S0168-3659(99)00248-5
Maghsoodi, A., Yazdian, F., Shahmoradi, S., Ghaderi, L., Hemati, M., & Amoabediny, G. (2017). Curcumin-loaded polysaccharide nanoparticles: Optimization and anticariogenic activity against Streptococcus mutans. Materials Science and Engineering: C, 75, 1259–1267. https://doi.org/10.1016/j.msec.2017.03.032
Mahmoudi Najafi, S. H., Baghaie, M., & Ashori, A. (2016). Preparation and characterization of acetylated starch nanoparticles as drug carrier: Ciprofloxacin as a model. International Journal of Biological Macromolecules, 87, 48–54. https://doi.org/10.1016/j.jbiomac.2016.02.030
Martínez-Ortíz, M. A., Palma-Rodríguez, H. M., Montalvo-González, E., Sáyago-Ayerdí, S. G., Utrilla-Coello, R., & Vargas-Torres, A. (2019). Effect of using microencapsulated ascorbic acid in coatings based on resistant starch chayote texture on the quality of guava fruit. Scientia Horticulturae, 256, 108604. https://doi.org/10.1016/j.scienta.2019.108604
Martínez-Ortíz, M. A., Vargas-Torres, A., Román-Gutiérrez, A. D., Chavarría-Hernández, N., Zamudio-Flores, P. B., Meza-Nieto, M., & Palma-Rodríguez, H. M. (2017). Partial characterization of chayote starch-based films added with ascorbic acid encapsulated in resistant starch. International Journal of Biological Macromolecules, 98, 341–347. https://doi.org/10.1016/j.jbiomac.2017.02.016
Marto, J., Gouveia, L. F., Gonçalves, L. M., Gaspar, D. P., Pinto, P., Carvalho, F. A., ... Almeida, A. J. (2016). A Quality by Design (QbD) approach on starch-based nanocapsules: A promising platform for topical drug delivery. Colloids and Surfaces B: Biointerfaces, 143, 177–185. https://doi.org/10.1016/j.colsurfb.2016.03.039
Villarreal, M. E., Ribotta, P. D., & Iturriaga, L. B. (2013). Comparing meth-
Vieira, E. F., Pinho, O., Ferreira, I. M. P. L. V. O., & Delerue-Matos, C. (2019). Chayote (Sechium edule): A review of nutritional composition, bioactivities and potential applications. Food Chemistry, 275, 557–568. https://doi.org/10.1016/j.foodchem.2018.09.146
Villarreal, M. E., Ribotta, P. D., & Iturriaga, L. B. (2013). Comparing meth-
Wang, M., Sen, J., Zhai, Y., Lian, H. E., Luo, C., Li, L., ... He, Z. (2015). Enteric polymer based on pH-responsive aliphatic polycarbonate functionalized with vitamin E to facilitate oral delivery of tacrolimus. Biomacromolecules, 16, 1179–1190. https://doi.org/10.1021/bm501847u
Wang, T., Wu, C., Fan, G., Li, T., Gong, H., & Cao, F. (2020). Ginkgo biloba extracts-loaded starch nano-spheres: Preparation, characterization, and in vitro release kinetics. International Journal of Biological Macromolecules, 106, 148–157. https://doi.org/10.1016/j.ijbiomac.2016.03.039
Wang, X., Chen, H., Luo, Z., & Fu, X. (2016). Preparation of starch nanoparticles in water in oil microemulsion system and their drug delivery properties. Carbohydrate Polymers, 138, 192–200. https://doi.org/10.1016/j.carbpol.2015.11.006
Wang, X., & Zhang, Q. (2012). pH-sensitive polymeric nanoparticles to improve oral bioavailability of peptide/protein drugs and poorly water-soluble drugs. European Journal of Pharmaceutics and Biopharmaceutics, 82, 219–229. https://doi.org/10.1016/j.ejpb.2012.07.014
Xiao, H., Yang, T., Lin, Q., Liu, G., Zhang, L., Yu, F., & Chen, Y. (2016). Acetylated starch nanocrystals: Preparation and antitumor drug delivery study. International Journal of Biological Macromolecules, 89, 456–464. https://doi.org/10.1016/j.jbiomac.2016.04.037
Xu, Y., Yi, Y., Lei, J., Mo, X., Shao, Z., Wu, Y., ... Mu, C. (2020). pH-Responsive nanoparticles based on cholesterol/imidazole modified oxidized-starch for targeted anticancer drug delivery. Carbohydrate Polymers, 233, 115858. https://doi.org/10.1016/j.carbpol.2020.115858
Yadav, B. S., Yadav, R. B., & Kumar, M. (2011). Suitability of pigeon pea and rice starches and their blends for noodle making. LWT - Food Science and Technology, 44, 1415–1421. https://doi.org/10.1016/j.lwt.2011.01.004
Yang, J., Li, F., Li, M., Zhang, S., Liu, J., Liang, C., ... Xiong, L. (2017). Fabrication and characterization of hollow starch nanoparticles by gelation process for drug delivery application. Carbohydrate Polymers, 173, 223–232. https://doi.org/10.1016/j.carbpol.2017.04.002
Yin, L., Ding, J., He, C., Cui, L., Tang, C., & Yin, C. (2009). Drug permea-
bility and mucoadhesion properties of thiolated trimethyl chitosan nanoparticles in oral insulin delivery. Biomaterials, 30(29), 5691–5700. https://doi.org/10.1016/j.biomaterials.2009.06.055
Zakaria, N. H., Muhammad, N., & Abdullah, M. M. A. B. (2017). Potential of starch nanocomposites for biomedical applications. IOP Conference Series: Materials Science and Engineering, 209, 01207. https://doi.org/10.1088/1757-899X/209/1/012087
Zhang, L., Zeng, Z., Hu, C., Bellis, S. L., Yang, W., Su, Y., ... Wu, Y. (2016). Controlled and targeted release of antigens by intelligent shell for improving applicability of oral vaccines. Biomaterials, 77, 307–319. https://doi.org/10.1016/j.biomaterials.2015.11.009
Zhang, Y., Chi, C., Huang, X., Zou, Q., Li, X., & Chen, L. (2017). Starch-
based nanocapsules fabricated through layer-by-layer assembly for oral delivery of protein to lower gastrointestinal tract. Carbohydrate Polymers, 171, 242–251. https://doi.org/10.1016/j.carbpol.2017.04.090
Zhang, Y., Lin, R., Li, H., He, W., Du, J., & Wang, J. (2019). Strategies to improve tumor penetration of nanomedicines through nanoparticle design. Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, 11, e1519. https://doi.org/10.1002/wnn.1519
Zhang, Y., Wang, X., Zhao, G., & Wang, Y. (2012). Preparation and properties of oxidized starch with high degree of oxidation. Carbohydrate Polymers, 87, 2554–2562. https://doi.org/10.1016/j.carbpol.2011.11.036
Zhang, Z., Shan, H., Chen, L., He, C., Zhuang, X., & Chen, X. (2013). Synthesis of pH-responsive starch nanoparticles grafted poly (l-glutamic acid) for insulin controlled release. European Polymer Journal, 49, 2082–2091. https://doi.org/10.1016/j.eurpolymj.2013.04.032
Zhou, G., Luo, Z., & Fu, X. (2014a). Preparation and characterization of starch nanoparticles in ionic liquid-in-oil microemulsions system. Industrial Crops and Products, 52, 105–110. https://doi.org/10.1016/j.indcrop.2013.10.019
Zhou, G., Luo, Z., & Fu, X. (2014b). Preparation of starch nanoparticles in a water-in-ionic liquid microemulsion system and their drug loading and releasing properties. Journal of Agricultural and Food Chemistry, 62, 8214–8220. https://doi.org/10.1021/jf5018725
Zhu, F. (2017). Encapsulation and delivery of food ingredients using starch based systems. Food Chemistry, 229, 542–552. https://doi.org/10.1016/j.foodchem.2017.02.101
Zhu, F. (2020). Underutilized and unconventional starches: Why should we care? Trends in Food Science & Technology, 100, 363–373. https://doi.org/10.1016/j.tifs.2020.04.018
Zohreh, N., Hosseini, S. H., & Pourjavadi, A. (2016). Hydrazine-modified starch coated magnetic nanoparticles as an effective pH-responsive nanocarrier for doxorubicin delivery. Journal of Industrial and Engineering Chemistry, 39, 203–209. https://doi.org/10.1016/j.jiec.2016.05.029

How to cite this article: Troncoso OP, Torres FG. Non-conventional starch nanoparticles for drug delivery applications. Med Devices Sens. 2020;3:e10111. https://doi.org/10.1002/mds.3.10111