Utilization of Natural Polymer Wall Materials for Health-Effective Lycopene Encapsulation

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Abstract

Natural phytochemical carotenoids, pivotal for human health, enhance wellness, and exhibits anti-aging properties. Lycopene, distinguished by exceptional antioxidant properties, offers protection against oxidative stress. Studied extensively for its potential in medical interventions, it mitigates the risk of diseases like arteriosclerosis and breast cancer. However, lycopene's high antioxidant activity makes it prone to degradation from environmental stresses like oxygen and light, impacting processing and storage. Its water and ethanol insolubility contribute to poor bioavailability. Encapsulation technology addresses these challenges, gaining interest for health benefits in functional foods and cosmeceutical products. The process of lycopene encapsulation, with a specific focus on the selection of diverse wall materials, has demonstrated a substantial impact on both the physical and functional attributes of the encapsulated lycopene within natural biomaterials employed for biomedicine. Natural polymers assume a crucial role in the advancement of biomedicine, nutraceuticals and the functional food industry, particularly in the encapsulation of natural active compounds such as lycopene. Consequently, there is a discernible trend towards the extensive utilization of natural polymers. The choice of a suitable wall material is of paramount importance as it significantly determines the efficacy and success of the encapsulation process. The utilization of natural polymer wall materials presents potential strategies for health-effective lycopene encapsulation. This paper provides a comprehensive overview of lycopene encapsulation, specifically focusing on polysaccharides and proteins, including oligosaccharides and cyclodextrin. The incorporation of these natural polymers in lycopene encapsulation enhances the bioavailability and stability of lycopene, rendering it suitable for diverse biomedical and nutritional applications.

Keywords: Lycopene, Natural Polymer, Encapsulation, Inclusion, Complex

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Introduction

Lycopene, a natural phytochemical carotenoid, is abundantly present in red fruits and vegetables, including tomatoes, watermelons, carrots and gac (Fig. 1a). The aril, which is the seed membranous tissue of the gac fruit (Fig. 1b), is characterized by a high concentration of lycopene along with minor carotenoids such as beta-carotene and lutein. It is the abundance of lycopene that imparts the vibrant red color to the aril. Microscopic examination of the gac aril clearly demonstrates the presence of densely packed red lycopene microcrystals, typically ranging from approximately 10 to 20 µm in thickness (Fig. 1c). The absorption spectra of lycopene exhibit a distinctive triplet peak shape pattern, with the main absorption peak occurring at a wavelength of 475 nm (Fig. 1d). A naturally occurring red pigment lycopene possesses remarkable anti-aging properties and exhibits the highest antioxidant activity among carotenoids. It effectively combats free radicals, which can cause damage to biomolecules and DNA. In contrast, beta-carotene's anti-cancer efficacy has been questioned, as it has been found to potentially induce cancer in certain situations, particularly among smokers (Baker et al., 1999; Force, 2022). On the other hand, lycopene has been associated with a reduced risk of various cancers, including lung cancer, melanoma, breast cancer and prostate cancer, through multiple mechanisms. Notably, it has shown potential in preventing prostatic hyperplasia (Mirahmadi et al., 2020) and maintaining cardiovascular health. Furthermore, lycopene exhibits anti-inflammatory properties and enhances the immune system's functionality, among other beneficial effects (Caseiro et al., 2020; Falsafi et al., 2022; Li et al., 2021; Takehara et al., 2014).

Due to its diverse and remarkable health benefits, lycopene has garnered increasing attention among health enthusiasts. However, lycopene poses challenges due to its chemical structure, which is a long-chain hydrocarbon represented by the chemical formula $C_{40}H_{56}$ consisting of 11 conjugated and 2 unconjugated double bonds (Fig. 1d). Being a natural unsaturated oil, lycopene is insoluble in water, thereby limiting its extraction, absorption in the body and application in various products. Moreover, lycopene exhibits low stability and easily undergoes degradation when exposed to light, acidic conditions and oxygen. These factors, present during extraction, processing, storage and consumption, contribute to its rapid loss of effectiveness and consequently shorten its shelf life in finished products. Additionally, the inherently low bioavailability of lycopene, exacerbated by its water insolubility, hampers its efficient utilization in general processing (Acosta, 2009). In order to prevent lycopene degradation and enhance its hydrophilic properties, the utilization of encapsulation techniques becomes imperative.

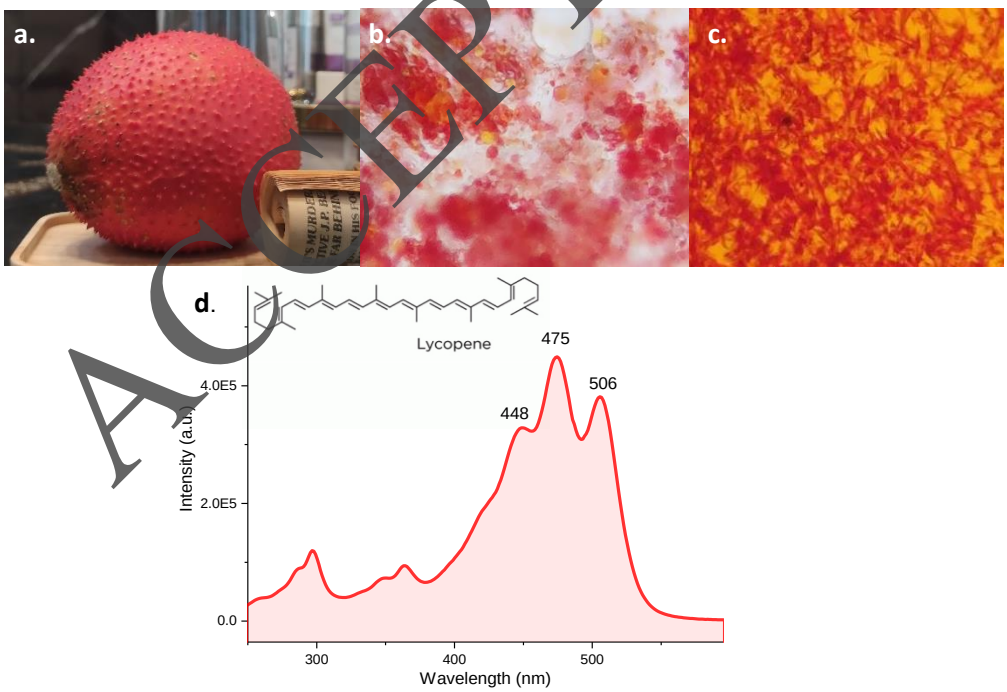


Fig. 1 Gac fruit and lycopene : (a) Gac fruit image, (b) Microscopy of lycopene and carotene pigments in gac seed membrane tissue (aril), (c) Microcrystals of lycopene extract and (d) Absorption spectra of Lycopene standard

Currently, researchers are actively working on developing processing technology to preserve and enhance the stability of lycopene while simultaneously improving its bioavailability. To tackle the mentioned challenges and bring new innovations to the market, a technology has emerged those entails encapsulating lycopene with other substances. This encapsulation process helps maintain the lycopene content and enhances its durability against environmental factors or specific systems. Additionally, encapsulation can improve the physical characteristics and water solubility of lycopene. In this process, lycopene molecules or small particles of various shapes and sizes, ranging from nanometers to millimeters, are enclosed within capsules, as depicted in Fig. 2. This technique, known as encapsulation, allows for the customization of properties based on the specific formation system, shape and size, making it suitable for different applications and the development of various finished products. Each encapsulation

method requires specific preparation techniques and therefore, a comprehensive understanding of the underlying principles is necessary for effective development and application.

Fig. 2 Resemblance of encapsulation particle characteristics to capsule structures

1. Lycopene encapsulation

Advancements in lycopene encapsulation technology have gained significant attention in both the food and cosmeceutical industries. The aim is to enhance the utilization of lycopene with greater efficiency, addressing its inherent limitations and weaknesses. Natural lycopene, being water-insoluble, faces challenges in absorption and bioaccessibility within the human body. Moreover, its susceptibility to light and oxygen degradation affects its antioxidant properties. Encapsulation technology seeks to improve these shortcomings and amplify the beneficial attributes of natural lycopene, such as its heightened antioxidant activity and targeted delivery to specific cells. By employing encapsulation techniques, the water solubility of lycopene can be improved, allowing for the formulation of a diverse range of health drink products, including both clear and turbid water-based beverages. Fig. 3 illustrates the conceptual diagram depicting the development of lycopene properties through lycopene retention technology. This innovative approach enables the surmounting of barriers associated with lycopene processing and utilization in the food and health food industry, leading to the creation of products with exceptional health-enhancing attributes (Fig. 4). The current technological trend is focused on developing diverse encapsulation models, aiming to make them available in the global market in the near future. By harnessing the potential of lycopene retention technology, these advancements hold promising prospects for elevating the nutritional and functional value of lycopene-enriched products, bolstering their significance in promoting overall health and well-being (Đorđević et al., 2015; Falsafi et al., 2022).

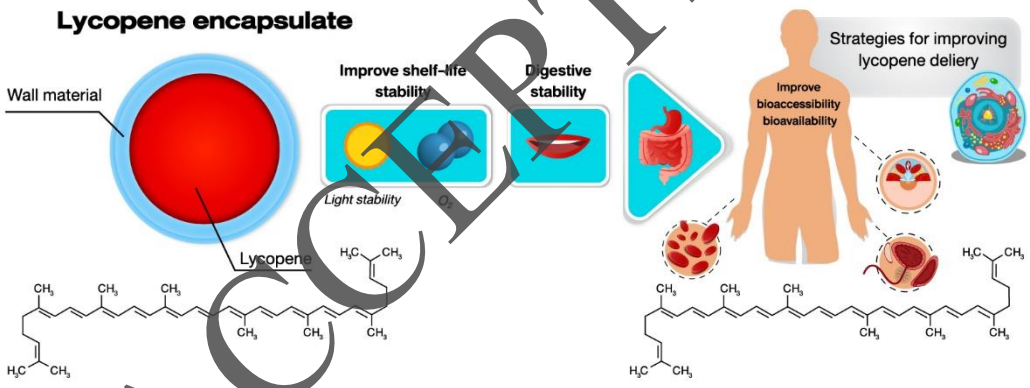


Fig. 3 The conceptual representation of enhancing lycopene properties using encapsulation technology

Fig. 4 Versatile utilization of lycopene encapsulation technology: Lycopene encapsulation technology enables the production of dry powder or water-soluble forms, offering diverse applications for enhancing various finished products. This includes functional foods, dietary supplements and cosmeceuticals

The utilization of encapsulation technologies for lycopene encapsulation can be systematically categorized into diverse groups. This categorization hinges on factors such as the formulation of products or particles, the morphological attributes of the encapsulating material, the size or dimensions of the wall material and the synthesis techniques employed in the encapsulation process. These forms can be primarily classified into the categories of physical encapsulation or particle formation and molecular encapsulation. Furthermore, these forms can be manipulated and constructed to incorporate a variety of structural arrangements, as illustrated in Fig. 5. The simplest encapsulated particles where lycopene resides at the core (single core), encased by a protective wall material (Fig. 5a). Beyond this, more elaborate configurations emerge, such as active ingredients dispersed within a core matrix, enveloped by a wall material to sustain and stabilize its presence (Fig. 5b). Intriguingly, the concept extends to multi-layered coatings, serving sequential functions or controlled substance release. These layered structures can involve multiple core or shell layers, fostering targeted outcomes (Fig. 5c). The capsules feature dual-core particles, merging two or more active ingredients for targeted effects (Fig. 5d), or combining various encapsulate particles within a single capsule (Fig. 5e). A fundamental approach incorporates the dispersion of lycopene particles throughout the wall matrix (Fig. 5f). Further variations encompass lycopene dispersion within a hydrogel within the shell wall (Fig. 5g). Dispersal as emulsions, micelles, or liposomes introduces subtle disparities in particle structure (Fig. 5h). Emulsion systems or stacked micelles can accommodate multiple substances (Fig. 5i). Lycopene dispersion within polymers (Fig. 5j), the encapsulation of lycopene inclusion complex crystals (Fig. 5k) and lycopene adsorption on particle surface structure (Fig. 5l). Molecular encapsulation, specifically in the form of inclusion complexes, involves employing wall material molecules to encapsulate lycopene molecules via non-covalent interactions. Instead, these interactions rely on weak forces like Van der Waals interactions or hydrogen bonds. This encapsulation mechanism prevents lycopene from undergoing chemical alterations, allowing the delivery and release of lycopene molecules at target. Given lycopene's molecular mass of 536.85 Da and its elongated molecular structure, storage spaces as small as 174 Å per molecule can be employed. One example involves molecular encapsulation utilizing alpha cyclodextrin molecules, offering an effective means of accommodating lycopene molecules within their cyclodextrin cavities. Fig. 6 portrays an illustration of the inclusion complex's structural characteristics, highlighting the molecular encapsulation molecule structure and its self-assembly into an ordered crystalline arrangement. These multifarious encapsulation techniques unlock avenues for tailoring lycopene delivery systems. By optimizing stability, bioavailability and targeted actions, they augment the potential utility of lycopene in domains ranging from food to health industries.

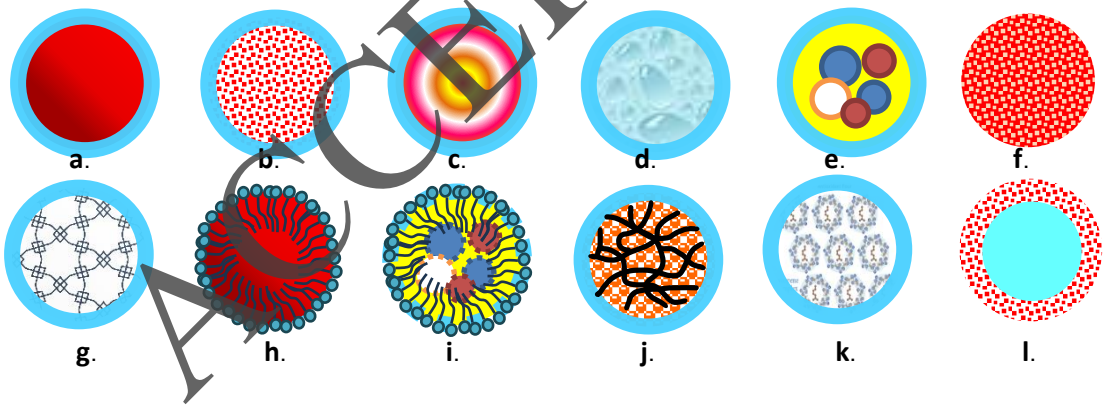


Fig. 5 Diagram depicting diverse lycopene encapsulation structures across various encapsulation technologies

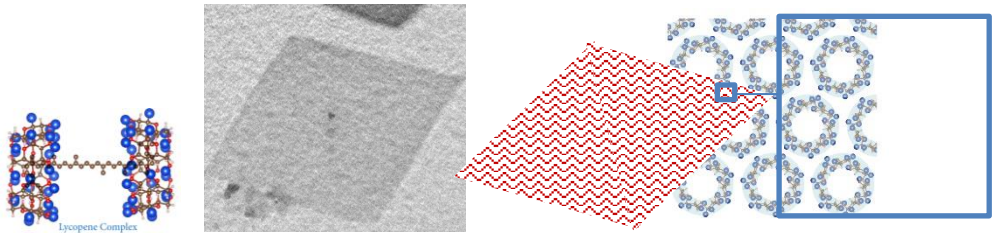


Fig. 6 Diagram depicting molecular encapsulation structure and self-assembly into an ordered crystalline form

2. Wall Materials in Lycopene Encapsulation

Encapsulation involves the entrapment of lycopene within a protective matrix or wall material, thereby shielding it from adverse conditions and enhancing its stability, bioaccessibility and functionality. Wall materials play a crucial role in lycopene encapsulation, significantly influencing the physicochemical properties of the encapsulated product. A diverse range of wall materials has been investigated for lycopene encapsulation, encompassing natural

polymers, proteins, lipids and synthetic polymers. Natural polymers like starch, cellulose and chitosan exhibit biocompatibility and biodegradability, making them attractive options for food and pharmaceutical applications. Proteins such as whey protein, casein and gelatin have also shown excellent encapsulation capabilities due to their ability to form stable complexes with lycopene. Lipid-based wall materials, including liposomes and micelles, effectively improve lycopene solubility and enhance its bioavailability. Various types of wall materials are employed in lycopene encapsulation technology, each offering distinct advantages and disadvantages. Synthetic polymers, specifically biopolymers, are derived from natural sources and undergo structural modifications to achieve specific properties. Widely employed in various encapsulation formulations, these polymers, such as polyvinyl alcohol (PVA), polylactic acid (PLA), Polyethylene Glycol (PEG), Carboxymethyl Cellulose (CMC) and poly(ε-caprolactone) (PCL) play a crucial role in lycopene encapsulation technologies (Cao-Hoang et al., 2011; dos Santos et al., 2015; Komijani et al., 2022; Kusdemir et al., 2023; Li, Y. et al., 2023; Sharma et al., 2021).

The choice of wall material plays a crucial role in determining the stability and solubility of encapsulated lycopene. Certain materials, like chitosan and whey protein, have demonstrated the ability to enhance lycopene stability by protecting it against oxidation and degradation induced by light and heat. Additionally, utilizing hydrophilic carriers such as cyclodextrin derivatives holds promise for improving the water solubility of lycopene, facilitating its incorporation into water-based products. The selection of the appropriate wall material depends on specific encapsulation objectives, including providing stability and insulation for lycopene, ensuring safety for consumption, promoting efficient absorption and achieving desired physical characteristics. These considerations are integral to the intended application and play a pivotal role in effectively controlling the delivery and release of lycopene in target cells. Apart from the technical aspects, the cost of raw materials and the efficiency of manufacturing processes and technologies also hold significant importance in the selection of the appropriate wall material. These economic considerations play a crucial role in ensuring the viability and feasibility of encapsulation technology, making it commercially viable for various industries. Overall, a comprehensive evaluation of these factors is imperative to make informed decisions and to successfully develop lycopene encapsulation technology that meets specific requirements and maximizes the benefits of this valuable phytochemical in various applications including functional foods, dietary supplements and cosmetic formulations to enhance their antioxidant and health-promoting properties.

2.1 Natural polymers

Natural polymers, intricate and complex organic compounds widely distributed in the natural environment, are prevalent in organisms like mammals, plants and microbes. Derived from renewable sources, these biopolymers, natural synthesized by living organisms, form a diverse group of high-molecular-weight molecules with repeating building blocks—nucleotides, amino acids, or sugars. Polynucleotides (e.g., DNA or RNA), polypeptides (proteins) and polysaccharides (polymeric carbohydrates) play crucial roles in cellular processes. Polysaccharides forms a substantial thick hydrophilic polymeric coating around a lycopene core material. The principal mechanism for particle formation and stabilization involves 'steric repulsion', which contributes to the high stability of the system. Their minimal environmental impact positions them as pivotal in developing sustainable and eco-friendly products. Renowned for renewability, biodegradability and biocompatibility, natural polymers find value in various biomedical applications, from tissue engineering to trauma repair and drug delivery. Recent advancements emphasize the exploration of natural polymers in biomedicine, especially in developing biomaterials with antibacterial and antioxidant properties. The growing interest in these materials reflects their potential to address contemporary challenges in health and environmental sustainability (Zhang et al., 2024).

In the food industry, natural polymers have gained popularity due to their inherent functionality, biocompatibility and safety for consumption. Many of these polymers are established components of food, addressing consumer concerns. Their wide availability and cost-effectiveness further enhance their attractiveness in diverse applications. These polymers can be broadly categorized into two major groups: polysaccharides and proteins, both of which find extensive utility as lycopene retention agents. Among the polysaccharide group, starch, amylose (Jain et al., 2020), pectin (Aguirre & Santagapita, 2017; Sampaio et al., 2019; Zhang et al., 2023), sugars and biopolymers, cellulose (Sharma et al., 2021), gum, chitin and chitosan (Li et al., 2017) are commonly employed, while the protein group encompasses whey protein (Jain et al., 2018; Zhang et al., 2023), collagen (Aredo et al., 2019) and gelatin (Charpashlo et al., 2021). A notable trend is the exploration of novel encapsulation strategies involving the synergy of natural polymers with synthetic counterparts such as PVA and PLA (Li et al., 2017). This combination enhances the properties of the encapsulation, rendering it suitable for more demanding applications.

Li et al. (2017) developed a self-assembly method utilizing a green tea catechin derivative, oligomerized (-)-epigallocatechin-3-O-gallate (OEGCG), as a carrier for oral lycopene delivery. Lycopene-loaded OEGCG nanoparticles (NPs) were prepared through nano-precipitation, followed by chitosan coating to form a protective shell. This not only improved lycopene bioavailability but also effectively shielded it from degradation owing to EGCG's antioxidant properties. The self-assembled natural polymer nanostructure of OEGCG combined with lycopene holds promise for oral drug delivery across various applications. Gessica L.A. Sampaio et al. (Sampaio et al., 2019) explored the encapsulation of a lycopene-rich watermelon concentrate in alginate and pectin beads. These particles exhibited robust lycopene protection against varying conditions of temperature and pH. Polysaccharide with Ionic gelation shows a promiseng method for obtaining stable lycopene-rich dried ingredients.

2.1.1 starch

Certain natural polymers, such as amylose from polysaccharides, possess a molecular structure conducive to molecular encapsulation, enabling their use as carriers for various forms of active ingredients. They can serve as both molecular encapsulation and physical encapsulants, utilization as particle-based constituents through coating. Consideration of D-glucopyranose sugar rings linked by α1→4 bonds have characteristic of the chemical structure of amylose. In the case of amylopectin, branches of amylose chains are formed at α1→6 positions (Mottiar & Altosaar, 2011). Different levels of starch structure and architectural configurations in nature are illustrated in Figures 7 and 8 (Li & Gilbert, 2018; Tran et al., 2011). A secondary structure of amylose exhibits a double helix configuration of its chain backbone, as depicted in Fig. 7. This double helix can undergo detachment and transformation into a single helix form, resulting in a cavity with a molecular helix gap diameter of approximately 5.4 Å, as illustrated in Fig. 8.a (top) for the amylose single helix structure. This unique single helix structure offers potential for molecular confinement of small bioactive substances or compatible forms. When organic substances are confined within the single helix cavity, it triggers a reorganization leading to the formation of novel crystal structures, transitioning from the inherent double helix nature of amylose A (Fig. 8.b) and amylose B (Fig. 8.c) structures into amylose V (Fig. 8.d) structures. These structural changes can be readily identified through crystal structure analysis. An illustrative example of the selected area of the X-ray diffraction pattern obtained from TEM of amylose V-structured rice starch, synthesized under carbon dioxide and ethanol conditions and presented in Fig. 8.e.

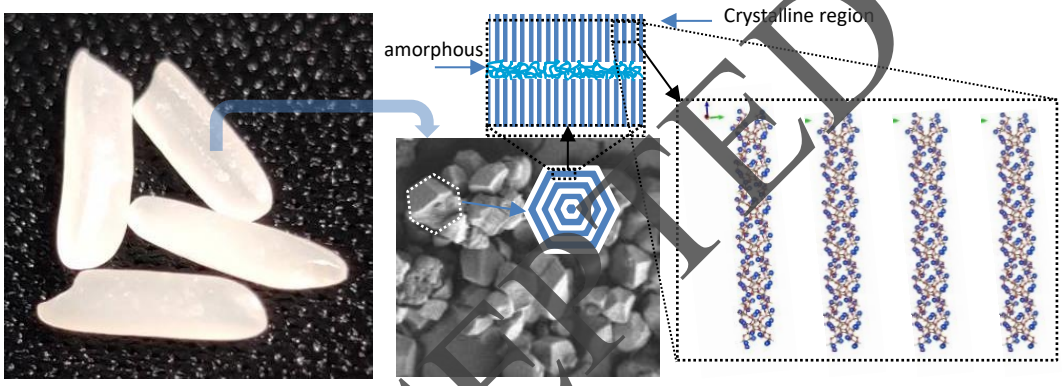
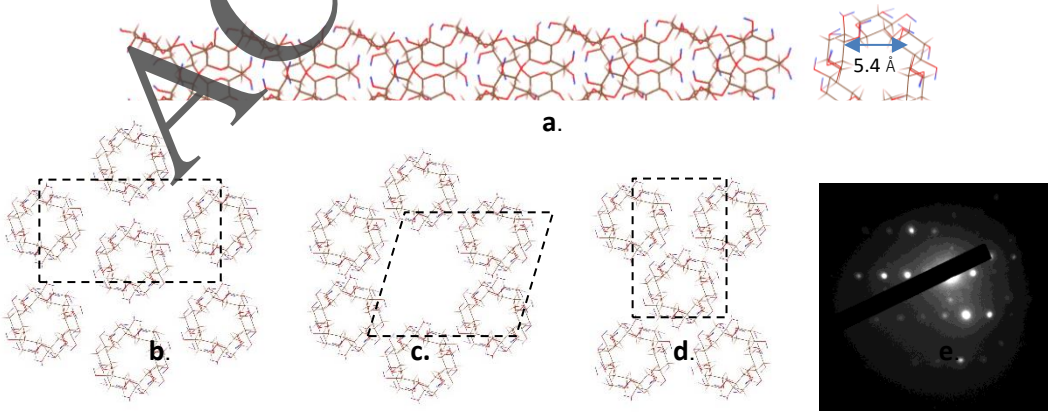


Fig. 7 Diverse starch structural hierarchies, polysaccharide amylose organizes into a double helix secondary structure, exhibiting various degrees of order and disorder, alongside combined crystal and amorphous multilevel structures in natural starch grains.



(b.) and B type (c.) amylose crystal structures. When organic molecules are Encapsulated Within the Helix Through Hydrophobic Inclusion Complexes (Only the Amylose Helix Structure is Depicted), the Helix Uncoils and Self-Organizes into an Ordered Rearrangement, Forming the Crystal Structure of V Amylose Pattern (d.) (Pozo et al., 2018) (Sarko & Wu, 1978; Sarko & Zugenmaier, 1980). Corresponding example of selected area electron diffraction pattern for V type amylose structure (e.) in Transmission Electron Microscopy (TEM)

Rocha et al. (2012) employed modified starch (Capsul®) in the microencapsulation of lycopene via spray drying, offering a potential solution to mitigate lycopene instability when applied in cakes (Rocha et al., 2012). Stability tests demonstrated that microencapsulation provided enhanced protection compared to free lycopene, with

microcapsules uniformly coloring the studied food system. Souza et al.(2018) conducted microencapsulation of a lycopene-rich tomato concentrate via spray drying, examining the influence of encapsulating agents (maltodextrin, whey protein isolate and modified starch Capsul) (Souza et al., 2018). Formulations with maltodextrin and modified starch exhibited superior lycopene concentrations, antioxidant capacity and storage stability, highlighting starch's potential as a viable encapsulating substance for lycopene. Jain et al. (2020) explored lycopene encapsulation in emulsions and hydrogel beads using dual modified rice starch. The modified rice starch exhibited better adsorption at the oil-water interface, enhancing resistance against the gastrointestinal environment. The study suggests the potential use of modified rice starch in designing food-grade delivery systems for improved lycopene stability and controlled release in the gastrointestinal tract (Jain et al., 2020).

2.1.2 Cellulose

Cellulose, an abundant and naturally occurring polysaccharide, serves as a versatile material for lycopene encapsulation. Recognized for its non-toxic nature and inherent durability, cellulose provides substantial protection against oxidation. Sharma et al. (2021) employed carboxymethyl oil palm empty fruit bunch cellulose (CM-OPEFBC), carnauba wax and palm oil to formulate lycopene-loaded nanostructured lipid carriers (NLC) for topical administration (Sharma et al., 2021). In this study, cellulose acted as an encapsulation shell, contributing to the formation of small, uniformly spherical particles within the lipid matrix. Cellulose played a crucial role in stabilizing lycopene, enhancing its skin penetration upon topical application. The NLC demonstrated superior drug loading capacity and colloidal stability, presenting advanced systems for lycopene stability and delivery in the pharmaceutical industry. Gao et al. (2023)utilized nanocellulose derived from pomelo peel, specifically cellulose nanofibrils (CNFs) and cellulose nanocrystals (CNCs), as Pickering stabilizers for lycopene-loaded Pickering emulsions (Gao et al., 2023). CNF-based emulsions exhibited higher stability than those stabilized with CNCs, attributed to the gel structure induced by CNFs' longer fibrils. Nanocellulose, derived from cellulose nanofibers or nanocrystals, offers a new potential platform for lycopene encapsulation due to its exceptional mechanical properties, biocompatibility, high surface area-to-volume ratio, numerous hydroxy surface groups and unique structure.

2.1.3 Proteins

Proteins, as natural polymer materials, are highly esteemed for lycopene encapsulation due to their exceptional bioaccessibility upon ingestion. Globular proteins form a thin polymeric coating around a lycopene core material. The primary mechanisms governing particle formation and stabilization rely on “electrostatic repulsion”, representing a strategic approach to enhance the stability of lycopene. When selecting encapsulation matrices, proteins from edible sources stand out, offering the advantage of being consumable food materials. Proteins possess a unique chemical structure with diverse chemical interactions, including amino groups, carboxyl groups and peptide bonds. Charged amino acid side chains can form ionic bonds and polar amino acids are proficient in establishing hydrogen bonds. Additionally, hydrophobic side chains interact through weak van der Waals forces. The majority of bonds formed by these side chains are noncovalent, allowing for versatile modifications in various formulations by altering conditions such as pH, solvent type, ionic strength, and cross-linking with other polymers. Moreover, proteins exhibit diverse structural levels, encompassing secondary structures and larger formations, which contribute to the varied morphological structures of encapsulated substances. This versatility, coupled with various functional attributes, holds significant potential for designing additional functionalities or exploiting synergistic effects for lycopene. Ho et al.'s investigation delved into the physicochemical stability of lycopene-loaded emulsions, particularly those stabilized by plant or dairy proteins like soy, pea, whey and sodium caseinate, that enhance the physicochemical stability and bioavailability of lycopene (Ho et al., 2017). Notably, emulsions stabilized by specific proteins, such as soy and pea proteins, exhibited improved stability. Jain et al. (2018) introduced an innovative approach involving the development of lycopene-loaded whey protein isolate nanoparticles, without intricate equipment-intensive methods, which served as a robust drug delivery system, demonstrating heightened bioavailability of lycopene and anti-cancer activity (Jain et al., 2018). In vitro assessments on MCF-7 breast cancer cells showed significant cytotoxic effects, enhanced oral bioavailability by modulating lycopene release and facilitating absorption through lymphatic pathways. Additionally, prophylactic anticancer efficacy was demonstrated in an experimentally induced breast cancer animal model. Gheonea et al. (2021) employed complex coacervation and freeze-drying for the microencapsulation of lycopene from tomato peels. The resulting powder, with whey protein isolate and acacia gum as components, exhibited heightened antioxidant activity, suggesting its viability as a stable, functional ingredient with supplementary health benefits. Lin et al. (2022) investigated alginate-based and soy protein isolate-stabilized emulsion gel beads for lycopene encapsulation, highlighting the pH-dependent influence on gelation and interactions between alginate and protein-coated droplets. These findings indicate the potential of proteins in controlling release and enhancing storage stability of lycopene-encapsulated compounds in emulsion gel beads through pH modulation.

Whey protein, a natural polymer, also exhibits versatility in formulation as nano fiber structures. Charpashlo et al. (2021) utilized a gelatin-based strategy to formulate whey protein into sub-micron fiber structures via multilayered electrospinning, enhancing lycopene bioaccessibility (Charpashlo et al., 2021). Chen et al. (2023) encapsulated lycopene complex-stabilized emulsions using whey protein isolate and Tricholoma lobayense polysaccharide, resulting in emulsion-based nanofibers with heightened photostability and thermostability (Chen et al., 2023). This approach demonstrated improved targeted release in the small intestine, facilitating effective lycopene absorption and intracellular antioxidant activity, therefor a natural protein proposes a promising design for safe electrospun fiber-based delivery systems, highlighting enhanced bioaccessibility for lipophilic compounds, particularly beneficial for

functional food industries. Moreover, employing composite proteins in conjunction with other natural polymers allows for the formulation of diverse morphology structures and functional varieties. For example, microencapsulation formulations via spray drying (Jia et al., 2020; Kha et al., 2015), emulsification formulations through complex coacervation and freeze-drying and covalent modifications (Aguirre & Santagapita, 2017; Chen et al., 2023; Gheonea et al., 2021; Lv et al., 2021; Zhang et al., 2023).

2.2 Oligosaccharide-Based

Oligosaccharide-type wall materials, such as cyclodextrin, have been extensively explored in various studies for encapsulating lycopene with diverse functionalities. Oligosaccharides possessing appropriate structures readily undergo molecular encapsulation through non-covalent interactions with compatible structures. Complex interactions can be easily formed through simple mixing or kneading processes (Bockuviene et al., 2021). These applications encompass using cyclodextrin as a matrix for thickening, as a surfactant and as a molecular encapsulation agent in the form of a cyclodextrin inclusion complex. The molecular structure of beta-cyclodextrin, found within the macro ring, exhibits dimensions that closely resemble those of the inner region of a single-helical amylose ring (Fig. 9a). Upon molecular confinement, where molecules are encapsulated within the cavity gap of the cyclodextrin macro ring, various encapsulation forms can manifest. This confinement resembles threading cyclodextrin molecules with molecular chains, creating a novel and organized arrangement forming a complex crystal lattice. When both sides of a lycopene molecule are enfolded, the lycopene molecule undergoes a reorganization, leading to an orderly structure, exemplified by the lateral complex molecule structure along the a-axis in Fig. 9b. A top-down view along the c-axis mimics the crystal structure of amylose, as depicted in Fig. 9c. This arrangement typically undergoes reorganization to form rectangular crystallized particles due to the molecular lattice, as illustrated in Fig. 9d. The crystal form and morphology of cyclodextrin-lycopene inclusion complexes are typically showcased through microscopic images (Fig. 10a) compared with the raw solely cyclodextrin (Fig. 10 b.), including SEM and TEM, as presented in Fig. 10 (c. and d.). Hence, cyclodextrin finds extensive application in the food and pharmaceutical industries (Augustin & Hemar, 2009; Đorđević et al., 2015; Saffarionpour, 2019; Szente & Szejtli, 2004), as well as in the encapsulation of various health-active phytochemicals extracted from plants (Ghosh et al., 2022; Muñoz-Shugulí et al., 2021; Smaoui et al., 2021), including lycopene (Falsafi et al., 2022; Santos et al., 2021). Nerome et al. (2013) employed supercritical antisolvent precipitation to prepare lycopene beta-cyclodextrin inclusion complex nanoparticles (Nerome et al., 2013). Mele et al. (Mele et al., 1998; Mele et al., 2002) utilized α-, β- and γ-cyclodextrin for lycopene and carotenoids encapsulation through a simple kneading procedure. Blanch et al. (2007) (Blanch et al., 2007) focused on the stabilization of all-trans-lycopene from tomatoes by encapsulating it with α-, β- and γ-cyclodextrins also by using a supercritical fluid extraction (SFE) process. Fernández-García and Pérez-Gálvez (2017), alongside. de Oliveira et al., (2011) employed a simple mixing and solvent evaporate method in their cyclodextrin in lycopene encapsulation (de Oliveira et al., 2011; Fernández-García & Pérez-Gálvez, 2017). The modification of cyclodextrin and its application to other natural polymers, coupled with advancements in synthesis techniques, represents a promising approach. This strategy holds the potential to enhance the properties of lycopene and introduce new functionalities to the encapsulated product.

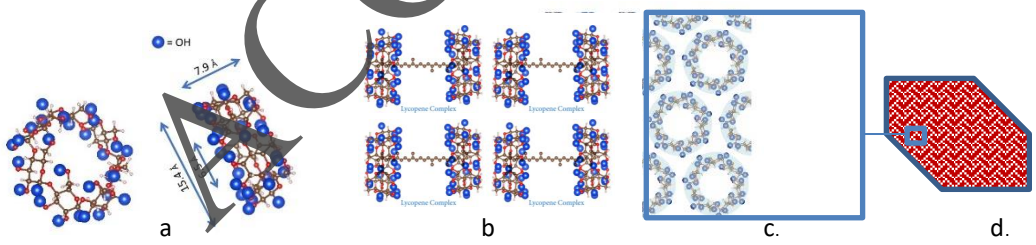


Fig. 9 Schematic representation of beta-cyclodextrin molecular structure (a.). Potential configuration of lycopene crystal structure in beta-cyclodextrin, forming columnar structures along the a-axis (b.) and c-axis (c.) within the lycopene encapsulation crystal (d.)

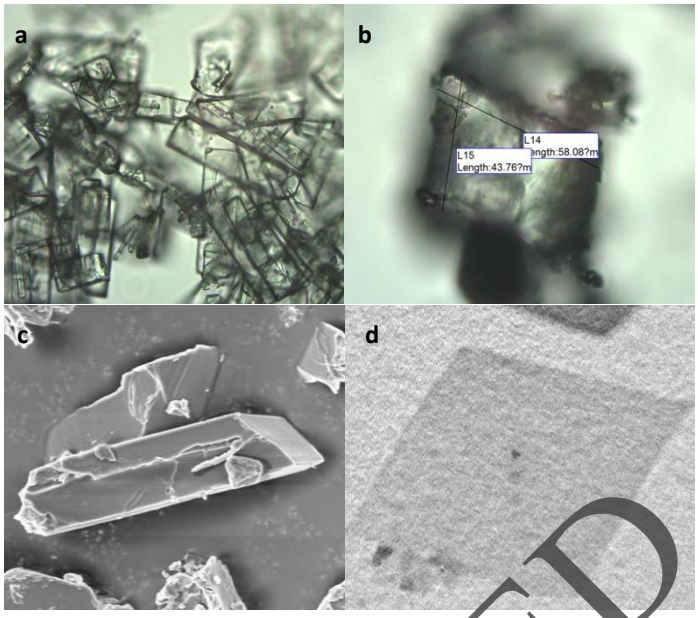


Fig. 10 Microscopic photograph at 400x magnification illustrating the angular crystalline structure of lycopene encapsulation within beta-cyclodextrin (a.) in comparison to the raw beta-cyclodextrin (b.). Additionally, a FESEM image at 10,000x magnification depicting the crystal with dimensions of approximately 2 μm in length and width (c.), along with a TEM image of a single crystal at approximately 400 nm (d.)

Conclusion

The encapsulation of lycopene employing diverse natural polymer wall materials presents a promising avenue for enhancing its stability, solubility and bioavailability. The selection of a suitable wall material is contingent upon the specific application and desired product characteristics for advancing the incorporation of lycopene into various health-related products. Natural polymers assume a crucial role in the realm of wall materials for lycopene encapsulation, offering attributes such as low toxicity, biocompatibility, chemical and environmental stability, improved bioaccessibility and heightened bioavailability, potentially augmenting functionality. Polysaccharides, proteins and cyclo-oligosaccharides, with their diverse chemical and molecular structures, provide a benefit for designing innovative lycopene encapsulation properties through a flexible method for modifications in the preparation process. The exploration of multi-composite modifications and the utilization of active polymers as wall materials showcase substantial possibilities in the development of lycopene encapsulation.

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