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REVIEW PAPER

Nanoencapsulation and delivery of curcumin using some carbohydrate based systems: A review

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ABSTRACT

Nanoencapsulation is commonly used to improve nutritional properties, rheological behavior and flavor profile of phytochemicals. The particles commonly utilized to encapsulate the functional ingredients are natural polymers such as polysaccharides and proteins. There is an ever-growing interest for use of polysaccharides to encapsulate hydrophobic phytochemicals like curcumin. Curcumin is a polyphenol compound with numerous health benefits including anti- inflammatory, antioxidant capacity and anti-cancer activity. However, poor solubility of this compound in gut has been led to restricting of its bio accessibility. Encapsulation of curcumin with biopolymers is one of the most effective methods to increase its bioavailability. In the present article, we will briefly review the recent studies focused on application of carbohydrate polymers including starch, β-cyclodextrin, pectin, Arabic gum, carrageenan gum, soluble soy bean polysaccharide (SSPS) and Enteromorpha prolifera polysaccharide as a carrier of curcumin.

Keywords: *Curcumin; Nanoencapsulation; Polysaccharides*

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INTRODUCTION

Turmeric has been broadly utilized for treatments of inflammatory conditions and other diseases [1]. Its therapeutic benefits are mainly attributed to its main constituent, curcumin. The chemical structure of curcumin is presented in Fig 1. Curcumin has been well known for its health benefits including anti- inflammatory, antioxidant capacity and anti-cancer activity [2]. Due to poor water solubility of curcumin and its instability toward light, heat, oxidation and alkalinity, it cannot directly apply in various formulations. Thus, it is essential to protect this phytochemical before its industrial utilization [3, 4].

In recent decades, nanoencapsulation is extensively used in food and pharmaceutical industries. It is well documented that encapsulation have the ability for improvement of the stability of phytochemicals [4]. Phytochemicals can be encapsulated by various materials, including biopolymers, minerals, lipid and surfactants. In the present work, we will focus on application some carbohydrate polymers to fabricate the nano and microcapsules. Natural polymers like gum exudates and seed gums have unique advantages in nanoencapsulation of phytochemicals due to their non-toxicity and biocompatibility [5, 6]. Natural polymers can be applied individually or in combination with other biopolymers or salts depending on of demanded functionality. In the present work, we will briefly review the recent studies focused on application of carbohydrate polymers including starch, β-cyclodextrin, pectin, Arabic gum, carrageenan gum, soluble soy bean polysaccharide (SSPS) and *Enteromorpha prolifera* polysaccharide as a carrier of curcumin.

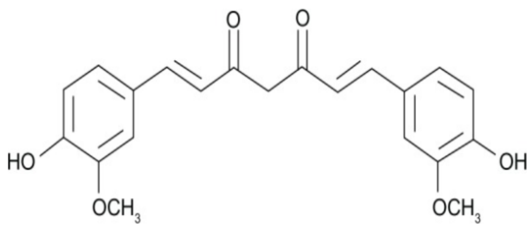

Fig 1. Chemical structure of curcumin

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Table 1. Example of polysaccharides that have recently applied for encapsulation of curcumin

Polysaccharides	References
Starch	Joye and McClements [9]
β-cyclodextrin	Tønnesen, Másson and Loftsson [10]
Pectin	Yan, Qiu, Wang and Wu [11]
	Zhou, Wang, Hu and Luo [12]
	Hu, Huang, Gao, Huang, Xiao and McClements [13]
	Cho, Jung, Lee, Kwak and Hwang [14]
	Huang, Huang, Gong, Xiao, McClements and Hu [15]
	Alkhader, Billa and Roberts [16]
Soluble soy bean polysaccharide (SSPS)	Chen, Ou and Tang [17]
	Chen, Ou, Chen and Tang [18]
Arabic gum	Shahgholian and Rajabzadeh [4]
	Sheikhzadeh, Alizadeh, Rezazad and Hamishehkar [19]
	Tan, Xie, Zhang, Cai and Xia [20]
Carrageenan	Xu, Jin, Zhang, Li, Lin, Huang, Ye and Li [21]
Enteromorpha prolifera polysaccharide	Li, Jiang, Chi, Han, Yu and Liu [22]

Encapsulation of curcumin

Polysaccharides

Polysaccharide are commonly non-toxic, easy-access, eco-friendly, and biocompatible [7]. Furthermore, the functional characteristics of carbohydrate polymers can be improved by physicochemical and enzymatic modifications [8]. The recent polysaccharides employed to encapsulate curcumin were tabulated in Table 1.

Starch

Starch, as a natural biopolymer contains two neutral constituents including amylose and amylopectin. The functional properties of starch can be improves by physic-chemical and enzymatic modifications [9]. In a recent study, sodium octenyl succinate modified starch (SOSMS) used for encapsulation of curcumin [23]. Encapsulated curcumin had more solubility in simulated gastric fluid (SGF). Moreover, the authors showed that the SOSMS can improve the stability of curcumin against alkaline condition. The fabricated capsules exhibited more oxidization and thermal stabilities.

***β*-cyclodextrin**

The photochemical stability of encapsulated curcumin with β-cyclodextrin has been evaluated by Paramera *et al* [23]. They found that not only β-cyclodextrin did not improve the stability of curcumin, but led to a decrease in its stability. The similar observation has been reported by Tønnesen *et al* [10]. who that encapsulation of curcumin with cyclodextrin resulted in an increase in its sensitivity against photodegradation. This effect may be attributed to the ability of curcumin to form inter/intra interactions which leads to its instability against photodegradation [23]. The release rate of curcumin is mainly dependent on the type of encapsulator used. Paramera *et al* [23]. exhibited that the encapsulation of curcumin in β-cyclodextrin led to improvement of the stability of curcumin during storage period. Furthermore, the authors also found that the encapsulated curcumin had more thermal stability.

Pectin

In a recent study, Yan *et al* [11] developed a nanoparticle by electrostatic interaction between heat-denatured lactoferrin (LF) with positive charge and negatively charged pectin. The fabricated complex at optimized conditions showed a spherical shape with an average diameter and zeta potential of 208 nm and−32 mV, respectively. Encapsulation efficiency (EE) and loading capacity (LC) were obtained 85.3% and 13.4%, respectively. The authors stated that the synthesized nanocapsules can be introduced as suitable delivery systems to improve water solubility, controlled release, and antioxidant capacity of curcumin.

In a similar research, a nano-gel was manufactured from low density lipoprotein (LDL)/pectin as potential oral delivery vehicles for curcumin [12]. Surprisingly, the mean average diameter and the charge of LDL/pectin nanogels at optimized conditions were 58 nm and −41 mV, respectively. The shape of nanoparticles was spherical with a smooth surface, and homogeneous size distribution. The developed nanogels had an appropriate stability in SGF and enabled controlled release of curcumin. Collectively, the fabricated nanogels can be introduced as a promising vehicle for oral delivery of curcumin.

Hu *et al*[13]. investigated the physic chemical properties of zein/pectin complextion. Zein is a positively charged protein with a hydrophobic nature and pectin is an anionic biopolymer. At pH below acid association constant, anionic biopolymer have negative charge and can interact with cationic polymers and form nanoparticles [24]. Curcumin was load into the core–shell nanoparticles at a high EE (>86%). The shape of developed nanoparticles was spherical with the size of 250 nm, and polydispersity index of 0.24. The authors reported that the nanoparticles could be useful for loading of curcumin into pharmaceutical products.

It has been proven that proteins have stabilizing effect on curcumin, and it has been also reported that this stabilizing effect may be due to interaction of proteins with polysaccharides and the formation of electrostatic complexes. In a recent study, the nanoparticles based on sodium caseinate (NaCas) and high-methoxyl pectin (HMP) were fabricated by Cho *et al.* [14]. These electrostatic interactions were very stable against pH, so that they remained unchanged at various pH. In general, it was found that the fabricated capsules may be a better carrier than NaCas at an acidic medium.

Huang *et al* [15]. developed a shell by combining of alginate and pectin to cover the zein nanoparticles. They reported that when 30% of pectin was replaced with alginate, the stability of nanoparticles considerably enhanced against high ionic strengths (2000 mM NaCl). It also was found that antioxidant and radical scavenging activities of the curcumun encapsulated by these core–shell nanoparticles were notably more when compared to that solubilized in ethanol solutions.

Alkhader *et al* [16]. formulated a nanoparticle based on chitosan-pectinate that able to retain its integrity in SGF. They reported that developed delivery system could deliver curcumin to the colon for treatment of colorectal cancer. The mean average of dimater and the charge of the nanoparticle were 206.0 nm and +32.8 mV, respectively. Furthermore, the EE of the curcumin inside of capsules was, on average, 64%.

Soluble soy bean polysaccharide (SSPS)

Chen *et al* [17]. developed a nanoparticles by complexation of soy protein isolate (SPI) and curcumin, and use of SSPS as coating. They stated that when the pH reached to 7, the core–shell complex was formed without any influence on the particle size and morphological characteristics of the complexes; while, as the pH decreased up to 4, the particle size of nanoparticles considerably increased. Contrary to what was expected, the authors showed that the encapsulation of curcumin into fabricated nanoparticles had no effect on the bioavailability of curcumin. However, the encapsulated curcumin had more thermal stability and better controlled release characteristics than free one. It also was found that the freeze-dried nanoparticles had good redispersion property.

More recently, nanoparticles based SSPS and curcumin were fabricated by Chen *et al* [18]. The results exhibited that the value of EE for curcumin at optimized pH (4.0) was 67.3%. The interaction between curcumin and SSPS led to aggregation of SSPS and as a result formed nanoparticles with compact structure. The encapsulation of curcumin into mentioned nanoparticles notably enhanced the stability of curcumin against temperature. Furthermore, in vitro bio-availability of curcumin has also improved. Overally, the authors suggested that SSPS/curcumin nanoparticles can be used as a food grade nanovehicle to improve the water solubility, heat stability, and bioavailability of curcumin.

Arabic gum

Shahgholian and Rajabzadeh [4] used from Arabic gum and bovine serum albumin (BSA) to encapsulate curcumin using coacervation technique. Various conditions including pH, BSA/Arabic gum, ratio and content of curcumin were tested to optimize the polyelectrolyte complex formation. They reported that the optimum complex formation was pH of 3.7 and BSA/Arabic gum with respective ratio of 2:1. At these conditions, EE was 92%. The result of SEM analysis showed a sponge-like coacervate phase. Furthermore, the mean average diameters of particles were between 40 to 80 µm. Due to high EE and facility of coacervation assay, it seems that the BSA/Arabic gum emulsification-coacervation can be used is an efficient method to encapsulate curcumin.

In another study, Sheikhzadeh et al. [19] assembled nanoparticles by interaction between sodium caseinate and Arabic gum. FTIR analysis confirmed the interactions of curcumin with sodium caseinate and Arabic gum. Optimum nanoencapsulation conditions were determined using response surface methodology (RSM). The optimum encapsulation circumstances were found to be: 0.21 wt% sodium caseinate, 0.5 wt% Arabic gum, and pH =5. At this condition, mean average diameter, turbidity and EE were found to be 72 nm, 0.29 and 81%, respectively. Small size of fabricated nanoparticles as well as high EE obtained indicated that these nanoparticles could be employed in different pharmaceutical products as functional ingredient.

In this line, Tan *et al.* [20] fabricated polysaccharide-based nanoparticles by formation of chitosan (CS) and Arabic gum complex as a new carrier for curcumin. They optimized the nanoencapsulation formulation. Their results revealed that optimum encapsulation conditions were as follow: pH 4.0 and CS to Arabic gum ratio of 1:1. In this point, a highly positively charged hydrophilic nanoparticle with high degree of homogeneity was obtained. Electrostatic interaction between Arabic gum and CS was confirmed by FT-IR and X-ray analyses. The nanoparticles had a particles size in the range of 250–290 nm. The EE and LC of curcumin were more than 90% and 3.8%, respectively. Furthermore, use of developed nanoparticles led to improvement of the antioxidant capacity of curcumin. Also, encapsulation of curcumin resulted in a considerable enhancement in the stability of curcumin and delaying in curcumin release in SGF. Totally, based on literature review, CS-Arabic gum nanoparticles could be employed as an efficient delivery system to deliver curcumin pharmaceutical products.

Carrageenan

Carrageenan forms a rigid gel in the presence of K^+ or Ca^{2+}. Xu *et al* [21]**.** Investigated the protective effect of a complex of carrageenan and lysozyme on curcumin stability. It was found that the EE and LC of encapsulated curcumin were 71 ± 0.02% and 50.71 ± 0.71%, respectively. Their results also exhibited that the curcumin loaded in carrageenan/lysozyme complex increased the thermal stability of curcumin. The protection effect of fabricated encapsulator was also confirmed by 2, 2-diphenyl-1-picrylhydrazyl free radical (DPPH) measurement.

Enteromorpha prolifera **polysaccharide**

Li *et al* [22]. used from *Enteromorpha prolifera* polysaccharide (EP) and chitosan (CS) for formation of nanoparticles, and then applied the nanoparticles as carrier of curcumin. The developed nanoparticles had a spherical shape with zeta potential of−16.27 mV and particle size of 230-330 nm. The existence of hydrogen and electrostatic interactions between fabricated nanoparticles and curcumin was confirmed by Fourier transform infrared spectroscopy (FT-IR), X-Ray Diffraction (XRD) and differential scanning calorimetry (DSC) analyses. The results obtained in their study showed that the encapsulation of curcumin into the nanoparticles improved the stability of curcumin against thermal degradations. Moreover, sustained release of curcumin *in vitro* was observed. The authors compared the cellular uptake curcumin nanoparticles to free ones, and observed that the cellular uptake of encapsulated curcumin was greatly more than free curcumin during incubation for 3 h. Additionally, results of MTT assay proven that the encapsulated curcumin had good cytotoxic activity against B16F10 cells. In overall, the results showed that the developed nanoparticles can be introduced as promising vehicle for delivery the hydrophobic anti-tumor drugs such as curcumin.

Future trend

It is clear that encapsulation had a considerable stabilizing effect on the stability of curcumin. The literature review demonstrated that nanoencapsulation can be utilized as an effective approach for improvement of water dispersion, heat stability, and even controlled release of curcumin. There is a large body of knowledge in employment of polysaccharides to encapsulate curcumin. However, there are only few works on application of novel source of polysaccharides like plant seed gums as carrier for encapsulation of curcumin. The physico-chemical features of gums are mainly dependent on their structural and chemical properties, and hence it is essential to fabricate new nanoparticles based novel polysaccharides/curcumin to enhance the release properties and stability against in vivo conditions.

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