Preparation of novel tragacanth gum-entrapped lecithin nanogels

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Abstract

Nanogel synthesis is gaining enormous interest in a large number of applications, such as drug delivery, wound care systems and tissue engineering. In the present work, we have investigated the preparation of Tragacanth gum (TG) nanoparticles in a water-in-oil nanoemulsion system. These nanoparticles exhibit stacked core-shell type of structure in which polygonal TG nanoparticles are covered by lipid structured lecithin (LC). The resultant nanoparticles comprise of amphillic nature, *i.e*. the hydrophilic TG core and hydrophobic LC shell which offers interesting features of immobilization of biomolecules. Copyright © 2019 VBRI Press.

Keywords: Tragacanth gum, lecithin, dioctylsulfosuccinate sodium salt, nanoemulsion, surfactant.

Introduction

Bioengineering of gels is a fascinating domain to develop nanoparticles with innovative features [**1**]. As a result, the nanogels become receptive to biomolecules and bioactive moieties. This needs a careful designing of the particles either by chemical functionalization or by the blending approach. Such a process opens up enormous possibilities of developing nanogels for human healthcare systems [**2, 3**]. Nanogels have been projected as drug carriers due to their novel properties, such as high surface area, biocompatibility, and prolonged drug delivery [**4-7**]. These nanohydrogels consist of functional groups or domains which are stimulated by triggering the external conditions, such as pH, temperature, ionic strength, and electric field [**4, 6-10**]. Within the hydrogels, natural gum polysaccharides have been used in drug delivery due to their high hydrophilicity, diverse functionality, biodegradability and biocompatibility. However, there are certain limitation of natural gums, viz, solubility, uncontrolled hydration, thickening and degradation which may limit their applications. A large number of studies have been carried out where these drawbacks can be minimized by modifications using various routes [**11, 12**].

Several reports are available for the synthesis of Tragacanth Gum (TG) nanogels for different applications and especially in drug delivery systems. A series of nanohydrogels based on TG were synthesized in the presence of different amounts of glycerol diglycidyl ether (GDE) and functionalized multi-walled carbon nanotubes for the loading and in-vitro release of indomethacine (IND) at different pH [**13**]. In further study, pH sensitive TG nanogels were prepared using 3-aminopropyltriethoxysilane, GDE, polyvinyl alcohol and glutaraldehyde as crosslinker for the release of IND [**14**]. Peppermint oil has been encapsulated within TG nanogel in the presence of aluminum and calcium ions as the crosslinkers and Triton X-100 as the surfactant [**15**]. The crosslinking helps in creating a network of hydrogel chains to develop an insoluble but swellable structure. Super paramagnetic TG nanogels were designed by sol-gel process for the controlled release of quercetin in which Fe_3O_4-SiO_2 nanoparticles as a magnetic core and *N*-vinyl imidazole as the functional monomer [**16**]. Recently, we reported the microwave assisted synthesis of polyitaconic acid grafted TG based nanohydrogels for controlled release of ampicillin [**17**].

In the present study, we have to choose TG due to its unique features, such as non-toxicity, pH stability, biocompatibility, eco-friendliness and safety for oral intake. The nanoparticles were prepared by using nanoemulsion process, in which dioctylsulfosuccinate sodium salt (AOT) along with lecithin (LC) was used as emulsifying agent [**18, 19**]. Both surfactants perform in a cohesive manner *i.e*., LC has complex structure comprising of fats, lipids and oils whereas, AOT consists of long alkyl chains with hydrophilic sulfosuccinate groups. LC was able to play multiple role as surfactant as well as stabilizing agent for the TG nanoparticles. These nanogels were characterized by TEM, DLS and EDX, with their projection in smart drug delivery applications.

Materials and methods

Materials

Tragacanth gum (TG) was purchased from Loba Chem, India and was purified by dissolution in water followed by re-precipitation in acetone. Dioctylsulfosuccinate sodium salt (AOT) and lecithin (LC) were supplied by Sigma Aldrich, India. Heptane and acetone were purchased from Merck, India. Ultra-pure water, resistivity 18 MΩ cm, produced by Millipore Milli-Q system was used throughout the experimental work. All the chemicals were used without any further purification.

Preparation of lecithin-TG nanogel

Tragacanth gum-Lecithin nanogels (nTG-LC) were prepared by water-in-oil nanoemulsion process using AOT as the surfactant. Oil phase consisted of 100 mg of LC and 800 mg of AOT in 10 mL of heptane. Water phase comprised aqueous solution of 1% TG. 100 µL of water phase (comprising of TG) was added to 10 mL oil phase (comprising of lecithin, AOT and heptane) and the whole mixture was then placed on constant stirring for 30 min. After reaction completion, the nanoemulsion was destabilized by the addition of acetone as non-solvent, so that nanoparticles of nTG-LC settled down. The nTG-LC nanoparticles were obtained as precipitate and were repeatedly washed with acetone and were dried under vacuum oven at 60°C for 24 h. The acetone washing removes AOT and a large fraction of superficial lecithin shell leaving behind a small amount of lecithin around TG nanoparticles.

Characterization of lecithin-TG nanogels

The morphology and size of nTG-LC nanogels were observed under a JEOL JEM-1400. HRTEM operated at 200 kV equipped with Olympus Soft Imaging Solutions GmbH (software: iTEM; TEM Camera: Morada 4008 × 2672 pixel max) recording system. For HRTEM analysis, the samples were prepared by placing one drop of the aqueous nTG-LC nanoparticles on a carbon-coated copper TEM grid and dried at vacuum oven. Size of the nanoparticles in wet condition was observed by particle size analyzer (LITESIZER™500) by Anton Paar. The particle size analysis was employed based on the concept of laser light scattering by particles in constant Brownian motion. The elemental analysis of nTG-LC nanoparticles was monitored by energy dispersive X-ray analysis (EDX) RONTEC's EDX Model QuanTax 200 (SDD technology, USA). The samples were put on carbon tap and placed on aluminum sample stub and coated with carbon using Auto-Fine Coater JFC-1600 (Joel, USA Inc., USA). Triplicate measurements of EDX analysis at different locations were analyzed.

Results and discussion

The objective of this work is to synthesize nTG-LC nanoparticles using water-in-oil nanoemulsion method. The schematic representation for the development of nTG-LC nanoparticles by nanoemulsion process is depicted in **Fig. 1**. The system containing TG in water phase while lecithin and AOT in heptane as oil phase provided nanoemulsion with micelles being in the size range of 30-75 nm. This approach involves the simple, green and facile route for the development of TG nanoparticles with excellent and long term stability. Nanoemulsion functionalization was strongly affected by the addition of AOT as surfactants. Due to its amphiphilic nature, it protects the water phase by creating polar-organic phase boundary and forms the micelles structure.

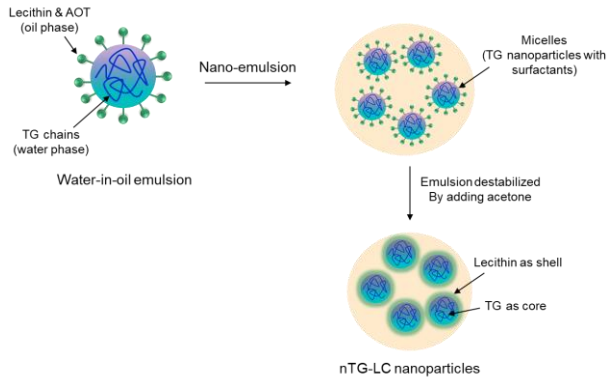

Fig. 1. Schematic representation for the development of lecithin-nTG nanoparticles.

The TEM images of nTG-LC nanoparticles demonstrated the polygonal shapes of the nanoparticles which is strongly stabilized by lecithin. **Fig. 2**, depicts the shape and size of the nTG-LC nanogels in both low and high magnifications. The average particle size of the nTG-LC was observed to be 58 ± 4 nm with stacked structure of the nanoparticles. It seems that the nanoparticle of TG was stacked within the lecithin lipid chains and gains the polygonal shape.

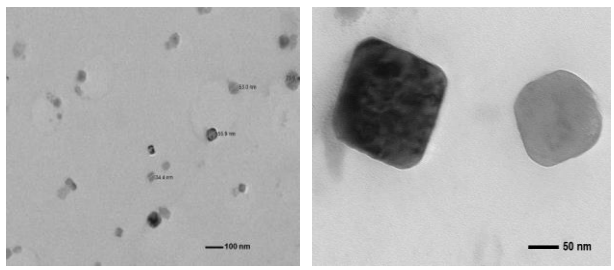

Fig. 2. TEM images of nTG-LC nanoparticles at different magnification.

The hydrogel character of the nanogel was demonstrated by particle size analyzer, in which the particle size was observed in the wet condition and the results are shown in **Fig. 3**. The average particle size of the nTG-LC nanoparticles was observed to be 326 nm. The zeta potential of the nanoparticles was observed in the range of −11.21 mV and depicts the long term stability of the nanoparticles.

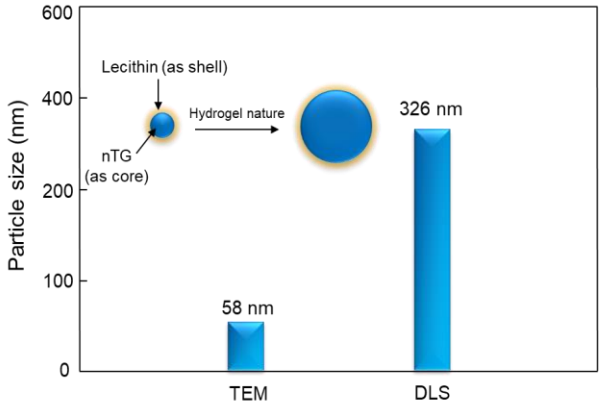

Fig. 3. Variation of the particle size of nTG-LC nanoparticles.

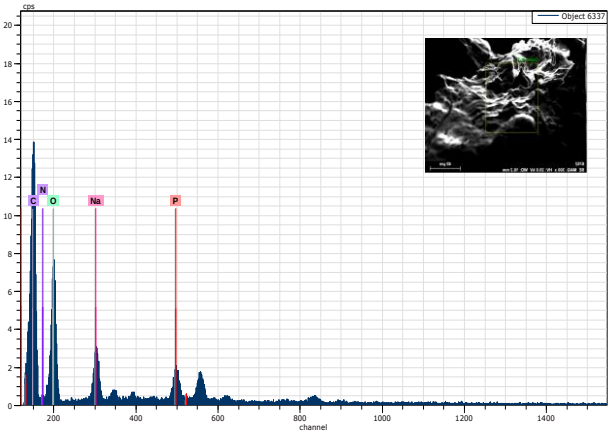

Fig. 4. EDX spectrum of nTG-LC nanoparticles.

The elemental analysis of nTG-LC nanoparticles was monitored by EDX and results are shown in **Fig. 4**. The EDX spectrum of nTG-LC nanoparticles shows a distinctive energy peaks at around 0.2 and 0.3 keV, characteristic of carbon oxygen and nitrogen along with a peak at 2 keV, which confirmed the presence of phosphorous in the nanoparticles. Furthermore, the EDX pattern of the nanoparticles was found to be C, O, N and P in the ratio of 50.26 ± 1.68%, 32.53 ± 2.6%, 14.3 ± 1.4% and 2.94 ± 0.8%, respectively. EDX spectrum of the nanoparticles confirm the presence of lecithin in the nanoparticles.

Conclusions

In this investigation, a beautiful approach was utilized to develop TG embedded within the lecithin shell to have a multi component nanoparticles. The water-in-oil nanoemulsion process was employed for the synthesis of nTG-LC nanogels with stacked type of core shell particles in which the nTG was bound in lipid structured lecithin. The polygonal shaped lecithin-TG nanoparticles with average particle size of 50 nm was observed. These different structures of nTG-LC nanoparticles are unique and could be used as promising material in drug delivery applications, especially anti-cancer therapy. These nanoparticles comprises both hydrophilic core and hydrophobic shell in which different drugs may be entrapped. We have been working on the entrapment of cisplatin anticancer drug within these nanoparticles which will be communicated soon.

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