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Carboxymethyl guar gum nanoparticles for drug delivery applications: Preparation and preliminary *in-vitro* investigations

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ABSTRACT

Carboxymethyl guar gum (CMGG) synthesized from commercially available polysaccharide was formulated into nanoparticles *via* ionic gelation using trisodium trimetaphosphate (STMP) as cross-linking agent. Characterisation using a range of analytical techniques (FTIR, NMR, GPC, TGA and DLS) confirmed the CMGG structure and revealed the effect of the CMGG and STMP concentration on the main characteristics of the obtained nanoformulations. The average nanoparticle diameter was found to be around 208 nm, as determined by dynamic light scattering (DLS) and confirmed by scanning electron microscopy (SEM) and nanoparticle tracking analysis (NTA). Experiments using simulated gastric and intestinal fluids evidenced significant pH-dependent drug release behaviour of the nanoformulations loaded with Rhodamine B (RhB) as a model drug (loading capacity in excess of 83%), as monitored by UV–Vis. While dose-dependent cytotoxicity was observed, the nanoformulations appeared completely non-toxic at concentrations below 0.3 mg/mL. Results obtained so far suggest that carboxymethylated guar gum nanoparticles formulated with STMP warrant further investigations as polysaccharide based biocompatible drug nanocarriers.

1. Introduction

Guar gum (GG) is a non-ionic natural polysaccharide sourced from the seeds of *Cyamopsis tetragonolobus* (*Leguminosae* family) and consists of linear chains of (1, 4)-β-*D*-mannopyranosyl units with α-*D*-galactopyranosyl units attached *via* (1, 6) linkages (Fig. 1). Because of its ability to produce highly viscous aqueous solutions at lower concentrations, guar gum is used in many applications in industries such as, textile, petroleum, paper, food, explosives and pharmaceuticals [22] - it is biocompatible, biodegradable, non-toxic, low-cost and amenable to chemical modifications, properties that make it an ideal material for developing drug delivery formulations [25]. However, native guar gum has also shortcomings such as, uncontrolled rates of hydration, high swelling, thickening effect, instability upon storage, high susceptibility to microbial attack and the difficulty to control viscosity due to relative fast biodegradation [37]. Various strategies were developed in order to overcome these issues, offering the opportunity to tailor the physical and chemical properties of guar gum, thus yielding materials that may find a wide range of applications. Many approaches dependent on chemical modification of guar gum were aimed at meeting the requirements of special applications [26] and included derivatization reactions such as, methylation [28], sulfation [36], hydroxyalkylation [12,13], carboxymethylation [7,10], or phosphorylation [20]. Carboxymethylation in particular has been found to improve water solubility while increasing the solution viscosity, to lower biodegradability and hence increase the shelf life compared to that of the native polysaccharide [19].

Carboxymethyl guar gum was formulated as microparticles tailored for drug delivery applications [21] and the studies indicated that these drug microcarriers were able to avoid rapid clearance by phagocytes and thus had an extended circulation into the blood stream [2,14]. Microencapsulation of sensitive macromolecules such as, proteins into derivatized carboxymethyl guar gum was also achieved by using multivalent metal ions solutions (Ca^{2+} and Ba^{2+}) as cross-linkers [33]. The maximum retention of bovine serum albumin (BSA) in the beads was only about 50% under the studied conditions, which could be due to the lower rates of cross-linking. Microspheres of carboxymethyl guar gum loaded with abacavir sulfate were formulated using water-in-oil (w/o) emulsions and glutaraldehyde (GA) as cross-linker; it was found that the beads extended the *in vitro* release time in both acidic and alkaline pH conditions when compared with unmodified GG [32]. Carboxymethyl guar gum was also combined with gelatine to obtain semi-interpenetrating polymer networks (semi-IPN) in the form of

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