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Synthesis of pH-sensitive crosslinked guar gum-g-poly(acrylic acid-*co*-acrylonitrile) for the delivery of thymoquinone against inflammation

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ABSTRACT

The present work aims to synthesize the pH-sensitive crosslinked guar gum-g-poly(acrylic acid-*co*-acrylonitrile) [guar-g-(AA-co-ACN)] via microwave-assisted technique for the sustained release of thymoquinone. The synthesized material [guar-g-(AA-co-ACN)] was optimized by varying synthetic parameters viz. monomer concentration, reaction time, and microwave power to obtain the maximum yield of the crosslinked guar gum grafted product as well as maximum encapsulation of thymoquinone. The synthesized material [guar-g-poly(AA-*co*-ACN)] was characterized by FT-IR, SEM, XRD, NMR, zeta potential, and thermal techniques. This synthesized material was used to encapsulate thymoquinone (TQ) for effective nanotherapeutic delivery. In-vitro thymoquinone release behavior of guar-g-poly(AA-*co*-ACN) based nanoparticles (NpTGG) was investigated. The maximum thymoquinone release (78%) was achieved at pH 7.4 and time (6 h). The NpTGG also exhibited better antioxidant activity and hemocompatibility as compared to thymoquinone. Cytotoxicity of uar-g-(AA-co-ACN) and NpTGG was also evaluated against the human kidney VERO cell line and found to be nontoxic. Current research provides a cost-effective and green approach for the synthesis of guar-g-(AA-co-ACN) and NpTGG for sustained release of thymoquinone.

1. Introduction

The hydrogel is a lightly aggregated three-dimensional network of water-swollen hydrophilic polymeric chains [1,2]. They exhibit the capacity to hold huge amounts of water within their elastic network because of the hydrophilic moiety, cross-linking as well as porous structure [3]. Hydrogels attract the formulation scientist due to their water-retaining capacity, tunable stiffness, and structural simulation with living tissues. Natural polymer-based hydrogels are preferred over synthetic ones due to their safety, biocompatibility, and eco-friendly properties [4,5]. These properties make it an ideal candidate for biological applications [6]. These polymeric hydrogels very smartly respond to little alteration in their microenvironment which modulates their chain dynamics and system functioning [7]. Understanding biological microenvironments are crucial for drug targeting at the organ or intracellular level [8]. Natural material could be utilized for biomedical applications like drug delivery, cosmeceutical, and tissue engineering [9–11]. Moreover, the synthetic nature of these polymers has some limitations like systemic toxicities such as thrombosis, chronic inflammatory response. Therefore, there is an unmet need to develop/modify naturally occurring polymers to good biocompatibility, biodegradability, high water retention ability as well as little or no cytotoxicity.

Guar gum is a natural biocompatible, hyperbranched gum extracted from guar beans (*C tetragonoloba*) [12] made up of straight-chain mannose units linked by β-D-(1–4) randomly attached (1, 6) galactopyranose units as side chains [13]. Due to its diverse nature such as biocompatibility, hydrophilicity, biodegradability, eco-friendly nature, renewability, economic viability, suitability, and availability, guar gum and its modified forms are used in the pharmaceutical field [14]. The European Food Safety Authority recently declared that GG is non-genotoxic and can also be used in infant formulations. GG is non-ionic, stable at a wide range of pH, and compatible with various electrolytes, and has a higher content of galactomannan; which possesses several -OH groups that undergo intramolecular H-bonding, forming highly viscous pseudo-plastic and trimolecular tight coils in water [15]. Keeping the above facts in the mind, we have chosen Guar gum for drug delivery applications.

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