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In-situ synthesis of polyacrylate grafted carboxymethyl guargum–carbon nanotube membranes for potential application in controlled drug delivery

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ABSTRACT

Sustainable hydrophobic membranes were prepared in-situ from the composites of poly (diethylene glycol dimethacrylate) grafted carboxymethyl guargum (CMG-g-PDEGDMA)/ carboxy functionalized multiwalled carbon nanotube (f-MWCNT). The composite membranes were applied for transdermal delivery of hydrophobic diclofenac sodium. The uniform dispersion of f-MWCNT resulted into stronger–matrix filler interaction, particularly at 1 wt.% f-MWCNT concentration. The membrane was most hydrophobic and least drug eluting. At higher f-MWCNT loading i.e. at 2 and 3 wt.% the membranes were less hydrophobic and faster drug eluting as a consequence of relatively poor matrix–filler interaction and copolymer wrapping. The most hydrophobic formulation (1 wt.%) had released 16.4% of the encapsulated drug, while the least (3 wt.%) had released 42% after 20 h study in a Franz diffusion cell under physiological condition.

1. Introduction

Transdermal delivery or patch therapy has received maximum compliance of a patient because of its elementary, non-invasive approach [1,2]. Apart from being the mildest drug delivery approach, it further resists secondary infections through obstructing fast pass metabolism and thus eliminates toxicity [3–7]. The sustained release of the drug molecules eventually reduces therapeutic complications between intra and inter patient variability. A transdermal patch is composed of (i) a liner, which protects the patch during storage and is removed before use, (ii) the drug, which is encapsulated within the patch in the sol state, (iii) an adhesive layer, which adheres the components of the patch together and also adheres the patch to the skin, (iv) the membrane, which encapsulates the drug and controls the release and (v) the backing, which protects the patch from the external environment [8]. Membrane is the key component of a patch since it acts as drug encapsulator cum sustained releaser. Majority of the membranes is prepared from different synthetic polymers such as various acrylates [9–12], poly (vinyl alcohol) [13–15], poly (ethylene glycol) [16,17], and poly (propylene oxide) [18,19] mainly due to advantages of high mechanical strength and stability. However, due to increased environmental awareness, many biopolymers are experimented of late as an alternate membrane polymer. Some latest example, include guar gum [20,21], locust bean gum [22], agar agar [23,24], xanthan gum [25], etc. Although polysaccharides are excellent viscosifiers yet the membranes are not

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mechanically stable. In addition, the hygroscopic nature of the polysaccharides wanes the level of control over the drug release rate since the absorption of water molecules facilitates faster elution of the drug molecules [26]. So, it is important that the polysaccharide membranes should maintain optimum hydrophobicity for both better drug encapsulation and controlled release. In this project, we have used CMG instead of guargum, due to its higher water solubility than the later, and grafted it with PDEGDMA (CMG-g-PDEGDMA) to impart hydrophobic character. It was apprehended that increase in synthetic content in CMG could improve environmental as well as mechanical stabilities of the membranes [27,28]. The material world has dramatically changed with the advent of polymer nanotechnology. Addition of various nanofillers in polymers has drastically improved various physico-mechanical properties [29,30]. f-MWCNT is an important nanofiller which has been used primarily to improve thermal and electrical conductivities in various thermoplastic polymer composites [31–33]. However, it has not been investigated in the area of medicinal biotechnology so far mainly due to its cytotoxic effects [34]. The reason that we have selected f-MWCNT because the proposed membranes will be used in vitro, in particular, outside the body, where the chances of contamination with cellular masses is minimized. f-MWCNT was added in the grafting stage to facilitate uniform dispersion in the absence of a compatibilizer. f-MWCNT could be an excellent adsorbent for the drug molecules, hence could increase the encapsulation efficacy of the membranes. On top of that, it could further promote the hydrophobicity of the membranes. The newly developed membranes were used to encapsulate and regulate the release of a model hydrophobic drug, diclofenac sodium or only diclofenac. Diclofenac has been the most popular pain killer drug for a long period of time. Withal, it is connected with certain vital issues like limited plasma solubility, extremely low half-life (2.5 h) and chronic side effects from long term administration. Controlled delivery through the skin could resolve most of these problems, in particular, extension of the half-life period of the drug molecules which in turn cuts the effects of drug overload. The noble composite membranes were thoroughly characterized and the release kinetics were investigated in a Franz diffusion cell under physiological condition. The role of both PDEGDMA and f-MWCNT have been discussed in the manuscript for understanding the release data of the drug molecules.

2. Experimental

2.1. Materials

CMG with a degree of substitution 0.6 was generously supplied by the Hindustan Gums and Chemicals Ltd., Haryana, India. DEGDMA was a gifted sample from Berger Paints India Ltd., Howrah, India. f-MWCNT with 2 wt.% carboxy functionalization (outer diameter 10–20 nm, length 10–30 μm, purity >95 wt.% and ash <1.5 wt.%) was generously supplied by the Cheap Tubes Inc. Barttelboro, USA. Benzoyl peroxide, the grafting initiator and hydroquinone the quencher, of, standard laboratory grades, were purchased from the Loba Chem, Mumbai, India. Diclofenac sodium was a gift sample received from the Ranbaxy Int. Gurgaon, Haryana, India.

2.2. Graft copolymerization of PDEGDMA on CMG and synthesis of in-situ nanocomposites

2.2.1. Methodology

One anhydroglucose unit (AGU) of CMG was dissolved in 50 ml distilled water at a pH of 7.0 under constant stirring. Desired DEGDMA and benzoyl peroxide (concentrations are mentioned in Table 1) were added and the temperature was gradually raised to 75 °C under continuous stirring. The reagents were allowed to react for 3 h at 75 °C under nitrogen. After 3 h, the reaction was quenched with adequate amount of saturated hydroquinone. The kettle temperature was lowered to 30 °C and the whole mass was allowed to stand overnight. Next day, the reacted mass was poured into excess acetone to settle down the graft copolymer. The settled mass was filtered carefully, washed three times with acetone, dried in an air oven and finally vacuum dried to drive away all the absorbed acetone. The hard mass was pulverized, sieved and finally dissolved in water to form CMG-g-PDEGDMA sol. The sol was cast onto plane Teflon sheet and dried to constant weight. The extent of grafting of PDEGDMA was determined gravimetrically, the working formula of which is described in the following section. In-situ nanocomposites were synthesized using the conditions that produced a maximum level of grafting. Different concentrations of f-MWCNT used for the synthesis of nanocomposites are given in Table 1. f-MWCNT was first dispersed in CMG-DEGDMA-benzoyl peroxide for 2 h and then the copolymerization was carried out. The whole process was repeated in

Table 1
Sample designation and composition of in-situ DEGDMA grafted CMG hydrogel nanocomposites.

Sample designation	CMG (mole)	PDEGDMA (mole)	Initiator conc. (wt.%) w.r.t. PDEGDMA	MWCNT w.r.t. total mass	Deborah number
CMG-g-PDEGDMA$_{1.0/0.1}$	1.0	1.0	0.1	0.0	5.29
CMG-g-PDEGDMA$_{1.0/0.1/0.5}$	1.0	1.0	0.1	0.5	6.69
CMG-g-PDEGDMA$_{1.0/0.1/1.0}$	1.0	1.0	0.1	1.0	10.47
CMG-g-PDEGDMA$_{1.0/0.1/2.0}$	1.0	1.0	0.1	2.0	5.67
CMG-g-PDEGDMA$_{1.0/0.1/3.0}$	1.0	1.0	0.1	3.0	6.33