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ORIGINAL ARTICLE

Diisocyanate mediated polyether modified gelatin drug carrier for controlled release

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Abstract Gelatin is an extensively studied biopolymer hydrogel drug carrier due to its biocompatibility, biodegradability and non-toxicity of its biodegraded products formed *in vivo*. But with the pristine gelatin it is difficult to achieve a controlled and desirable drug release characteristics due to its structural and thermal lability and high solubility in aqueous biofluids. Hence it is necessary to modify its solubility and structural stability in biofluids to achieve controlled release features with improved drug efficacy and broader carrier applications. In the present explorations an effort is made in this direction by cross linking gelatin to different extents using hitherto not studied isocyanate terminated poly(ether) as a macrocrosslinker prepared from poly(ethylene glycol) and isophorone diisocyanate in dimethyl sulfoxide. The crosslinked samples were analyzed for structure by Fourier transform-infrared spectroscopy, thermal behavior through thermogravimetric analysis and differential scanning calorimetry. The cross linked gelatins were biodegradable, insoluble and swellable in biofluids. They were evaluated as a carrier for *in vitro* drug delivery taking theophylline as a model drug used in asthma therapy. The crosslinking of gelatin decreased the drug release rate by 10–20% depending upon the extent of crosslinking. The modeled drug release characteristics revealed an anomalous transport mechanism. The release rates for ampicillin sodium, 5-fluorouracil and theophylline drugs in a typical crosslinked gelatin carrier were found to depend on the solubility and hydrophobicity of the drugs, and the pH of the fluid. The observed results indicated that this material can prove its mettle as a viable carrier matrix in drug delivery applications.

1. Introduction

The use of natural polymers such as gelatin (Young et al., 2005), starch (Al-Karawi and Al-Daraji, 2010), chitosan (Sinha et al., 2004; Bertoldo et al., 2007; Subramanian and Vijayakumar, 2011), etc., as carriers in controlled drug delivery applications is gaining importance because of their inherent biocompatibility, biodegradability and biosafety (Young et al., 2005). But a common disadvantage of such natural polymers is their structural and thermal lability (Bigi et al., 2001), which require improvement for controlled and targeted

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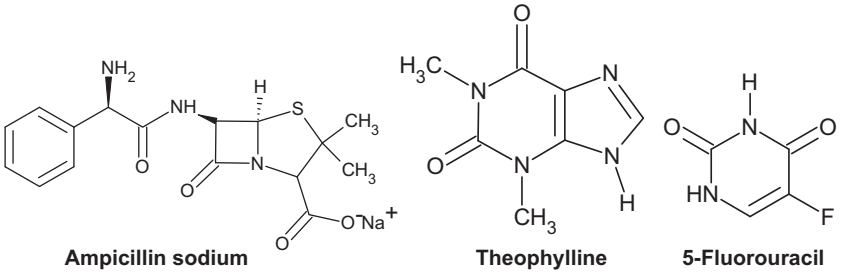
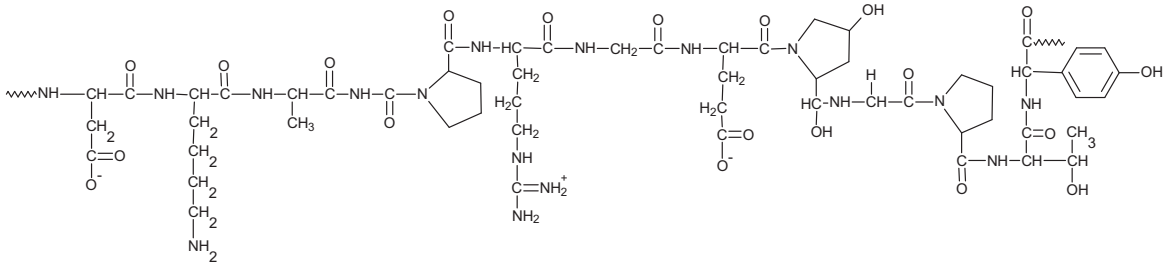


Figure 1 Chemical structures of drugs.

drug release applications. In this context, gelatin a well-known and widely used biopolymer drug carrier has been chosen for improving its drug release characteristics, because the high solubility, and poor mechanical and thermal stability of gelatin under physiological conditions may not facilitate a desirable sustained drug release. Hence it is necessary to modify its solubility in biofluids to have a controlled release characteristic with improved drug efficacy and broader application as a carrier for a wide range of drugs. Several chemical modifications such as crosslinking with formaldehyde (Digenis et al., 1994), glutaraldehyde (Narayani and Panduranga Rao, 1996), 1,4-diisocyanato butane, hexamethylene diisocyanate,



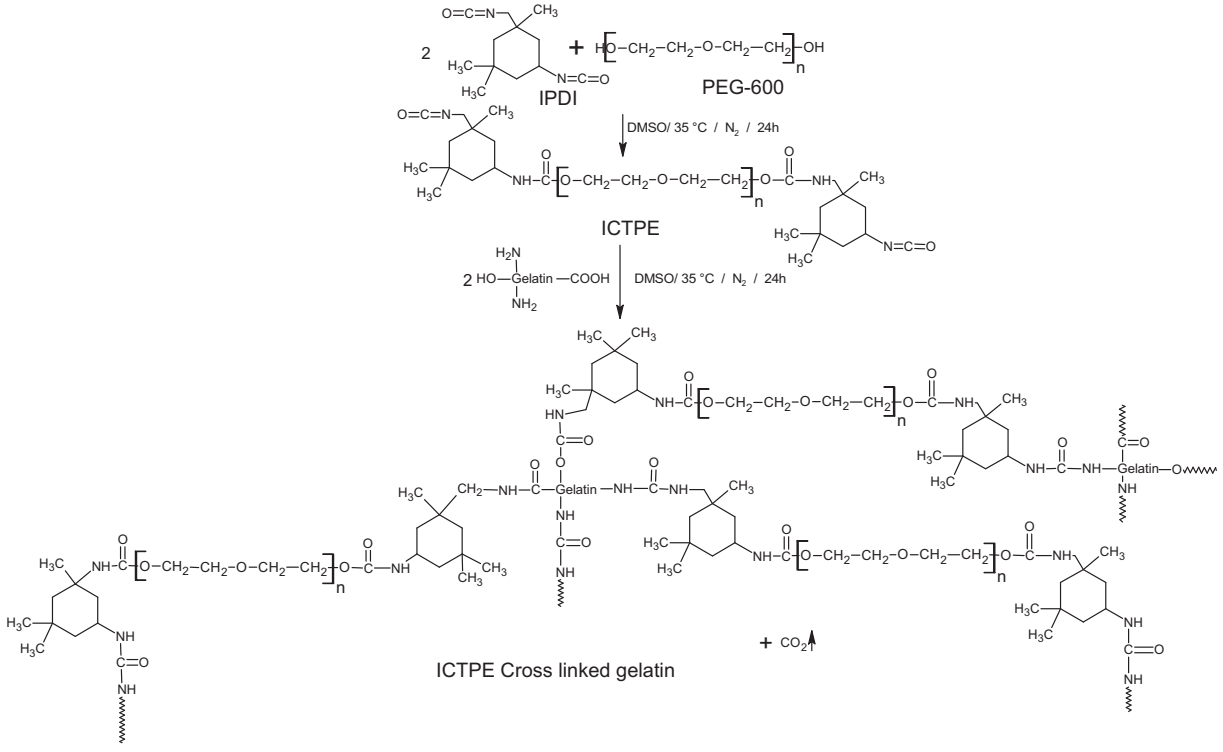


Figure 2 Crosslinking reactions of gelatin with ICPTE.