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Cloud point, fluorimetric and ^{1}H NMR studies of ibuprofen-polymer systems

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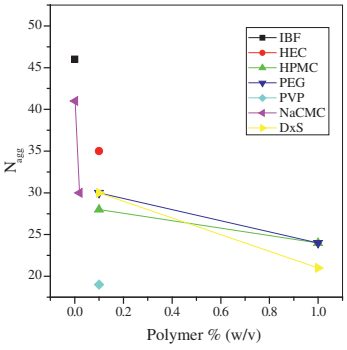
HIGHLIGHTS

- Much interest has been shown on interactions between amphiphilic drugs and polymers in a variety of fields, such as pharmaceuticals and bioscience.
- The ^{1}H NMR spectroscopy was used in the present investigation to probe the molecular investigation between ibuprofen and polymers.
- Aggregation number depends strongly on polymer percentage.

GRAPHICAL ABSTRACT

Average aggregation numbers of the total ensemble of ibuprofen micelles formed in solution, N_{agg}, as a function of the polymer percentage.



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ABSTRACT

Influence of six polymers viz. hydroxyethyl cellulose (HEC), hydroxypropyl methyl cellulose (HPMC), polyethylene glycol (PEG), polyvinyl pyrrolidone (PVP), sodium carboxy methyl cellulose (NaCMC) and dextran sulfate (DxS) on solution properties of amphiphilic drug ibuprofen (IBF) has been described in this work. As only HPMC showed the clouding behavior (among the polymers employed herein), its cloud point (CP) was studied in detail in presence of varying amounts of IBF containing different fixed concentrations of inorganic salts (NaCl, $NaNO_3$, Na_2SO_4, KBr and KNO_3). Presence of all these salts had CP reducing effect. By means of steady state fluorescence quenching studies, average aggregation number of IBF aggregates (N_{agg}) in the presence of varying amounts of the mentioned polymers were evaluated and discussed. ^{1}H NMR studies show that the magnitude of chemical shifts (δ) varies with the nature of the polymer.

1. Introduction

As drugs (especially, the amphiphilic ones) are almost invariably used in presence of a variety of additives (excipients), notwithstanding the knowledge of interaction and/or effect of drug molecules with the carrier, that of other foreign materials and their role toward drugs' therapeutic activity are required. Such a knowledge is essential in order to control/influence/employ (under specific conditions) the phenomenon of aggregation, swelling/deswelling, adsorption, solubilization, phase separation, etc.

Among drug carriers, cellulose derivatives and other water soluble polymers partake significant role. As such, the interaction of various drugs with carrying agents/vectors (like polymers) had

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been studied where almost the normally accepted polymer-surfactant interaction model was found to be operative [1–6] (Scheme 1). In the present work, we have studied the interaction of the sodium salt of ibuprofen (IBF) with several polymers viz. hydroxyethyl cellulose (HEC), hydroxypropyl methyl cellulose (HPMC), polyethylene glycol (PEG), polyvinyl pyrrolidone (PVP), sodium carboxymethyl cellulose (NaCMC), dextran sulfate (DxS) employing different experimental techniques. ^{1}H NMR studies have been used for detailed understanding of the interaction and fluorescence quenching was performed to evaluate the average aggregation number (N_{agg}).

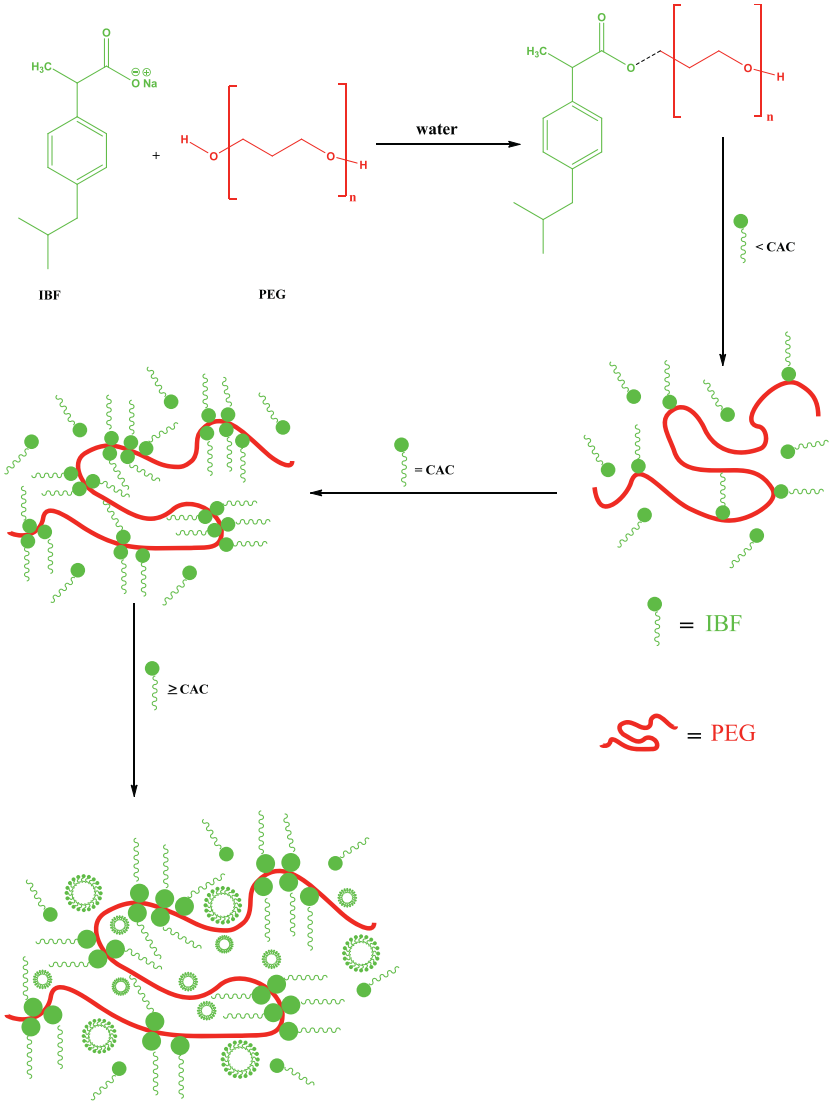
Out of the polymers employed in the study, only HPMC was found to show clouding phenomenon and hence the cloud point of HPMC in presence of different [IBF] was checked. The cloud point studies of IBF-polymer-water systems were further investigated in presence of certain inorganic salts like NaCl, $NaNO_3$, Na_2SO_4, KBr and KNO_3. Though there have been a number of studies on the CP of cellulose ethers with various types of surfactants (cationic, anionic, nonionic, Gemini, etc.,) [7–17], the case in the presence of an amphiphilic drug is not so and, therefore, studies concerning their effects on cellulose ethers in presence and absence of different types of additives is expected to be useful for the advancement of the field in addition to their practical applications. The concentrations of drugs as well as the salts were varied in the study and the various thermodynamic parameters at CP were computed and discussed.

The chosen model drug, IBF, contains a carboxylic acid group (Scheme 1). It is a non-steroidal anti-inflammatory drug that is commonly used for relief of symptoms of arthritis, fever, primary dysmenorrheal (menstrual pains), and as an analgesic. Ibuprofen also has an antiplatelet effect (protects from blood clots) [18]. The sodium salt of IBF is surface active having high critical micelle concentration (90 mM at 25 °C) [2]. In a recent report on its interaction with some biocompatible polymers it was shown that the anionic IBF interacted more strongly with cationic polymers as compared to the nonionic ones whereas the anionic polymers showed the least interaction [2].

2. Experimental

2.1. Chemicals

The drug sodium salt of ibuprofen ($C_{13}H_{17}NaO_2$, (RS)-2-(4-(-methylpropyl)phenyl)propanoate (IBF, ⩾99%, Sigma, USA)), polymers hydroxyethyl cellulose (HEC, Otto, Mumbai),



Scheme 1. Conceptual drawing showing the molecular interaction mechanism between IBF and polymers (exemplified with PEG).