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Research Article

Polydimethylsiloxane–Indomethacin Blends and Nanoparticles

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Abstract. A series of blends of polydimethylsiloxane (PDMS) and indomethacin (IMC), containing 20–80 wt.% IMC were obtained and characterized by differential scanning calorimetry, Fourier transform–infrared spectroscopy, and powder X-ray diffraction in order to observe the mutual influence of the two components. The main thermal transitions of PDMS remained un-changed. Both the solvent (tetrahydrofuran, THF) and the PDMS influenced the crystalline form of IMC. The blends were subsequently re-dissolved in THF, with or without cross-linking reagents added and precipitated into diluted aqueous solutions of siloxane-based surfactants. The resulted nanoparticles were analyzed by dynamic light scattering and scanning electron microscopy. Most of the particles had diameters between 200 and 300 nm. The surfactants, the IMC content and the cross-linking influenced the particles size and polydispersity, as well as the nanoparticle yield. The maximum drug release from selected aqueous formulations was 30%.

KEY WORDS: indomethacin; nanoparticles; polydimethylsiloxane.

INTRODUCTION

Polysiloxanes have many biomedical uses, especially in implantology, transdermic applications and drug delivery (1–3). They are well-known for their biocompatibility (especially referring to high molecular weight homologs) and at the same time, they are among the most tested materials concerning safety (2,4,5). Apart the biological inertness, polysiloxanes are characterized by hydrophobicity, permeability to diffusion of different substances, including gases, water vapors and drugs, as well as by specific visco-elastic properties (2). The controlled release of active drugs with polydimethylsiloxane (PDMS) goes back to the 1960s (6). At the present, there are numerous commercially available products in which silicones are used as actives or excipients. For example, silicones act as antifoams in gastroenterology, being very effective in anti-acid formulations (6). The drug release from silicone-containing formulations is controlled by its diffusion through the silicone network (6,7).

In our previous work, we tested the possibility of using PDMS as a core polymer in nanoparticles obtained by precipitation in the presence of different stabilizers, having a siloxane-organic structure (8–10). We have shown that cross-linking of PDMS may occur in the nanoparticles (9,10), and that improved stability of the particles is obtained after this step. Taking into account the properties of polysiloxanes, in particular of PDMS, they can be considered an interesting alternative as polymer matrix for nanoparticles encapsulating drugs or other active principles, for oral or topical formulations.

The anti-inflammatory non-steroidal drugs (AINS) are used in rheumatoid and osteoarthritis and in local inflammation (11). The oral therapy with AINS is very efficient, but the clinical use is often limited due to potential side effects, like irritations and ulcerations of the gastro-intestinal mucous membrane (12). These well-known side effects of AINS oral administration accelerated the development of alternative pharmaceutical formulations, such as creams, gels, and topic foams, which allow the local adsorption to the inflammation site, without adverse systemic reactions (13). Nevertheless, effective drug encapsulation for oral or parenteral use is very important for limiting side effects and maintaining efficiency. Indomethacin (IMC) is a hydrophobic, model AINS drug in many investigations.

Different applications have been proposed for drug-loaded nanoparticles, like targeted drug delivery, controlled release, increasing bioavailability of poor water-soluble drugs (14,15). The nanoparticles used for this purpose, roughly having dimensions between 10 and 1,000 nm, may be nanocapsules or nanospheres. Several characteristics of the particles were recognized as key parameters for magnified efficacy of nanoparticles for therapeutic applications: particle size, particle shape, surface characteristics and release of therapeutics (16).

By combining IMC and PDMS, improved results might be obtained in topical applications (due to the substantivity of PDMS) or oral administration (due to the low density and antifoam properties of PDMS). These potential benefits prompted a basic investigation on the mutual influence of the drug and the matrix, in order to better understand processes like blending, encapsulation or release. In this study, the approach was to mix PDMS and IMC in different proportions in a common organic solvent. The obtained blends were investigated by DSC, FT-IR, and powder X-ray diffraction and their properties are considered the model for nanoparticles obtained thereof. The nanoparticles were prepared by re-dissolving the blends in THF and precipitation in water in the presence of siloxane-based

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