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Research paper

Development of soy lecithin based novel self-assembled emulsion hydrogels

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ABSTRACT

The current study reports the development and characterization of soy lecithin based novel self-assembled emulsion hydrogels. Sesame oil was used as the representative oil phase. Emulsion gels were formed when the concentration of soy lecithin was >40% w/w. Metronidazole was used as the model drug for the drug release and the antimicrobial tests. Microscopic study showed the apolar dispersed phase in an aqueous continuum phase, suggesting the formation of emulsion hydrogels. FTIR study indicated the formation of intermolecular hydrogen bonding, whereas, the XRD study indicated predominantly amorphous nature of the emulsion gels. Composition dependent mechanical and drug release properties of the emulsion gels were observed. In-depth analyses of the mechanical studies were done using Ostwald-de Waele power-law, Kohlrausch and Weichert models, whereas, the drug release profiles were modeled using Korsmeyer–Peppas and Peppas–Sahlin models. The mechanical analyses indicated viscoelastic nature of the emulsion gels. The release of the drug from the emulsion gels was diffusion mediated. The drug loaded emulsion gels showed good antimicrobial activity. The biocompatibility test using HaCaT cells (human keratinocytes) suggested biocompatibility of the emulsion gels.

1. Introduction

Emulsion gels are defined as the biphasic systems formed by immobilization of a liquid in a 3D network formed by another immiscible liquid (Dickinson, 2012). The emulsion gels are generally classified into emulsion hydrogels and emulsion organogels on the basis of the continuum liquid phase, which is polar and apolar, respectively. Emulsion gels shows the beneficial features of both emulsions and gels therefore, possess many advantages over other types of formulations (Tokuyama and Kato, 2008). Emulsion gels can be used to deliver both hydrophilic and hydrophobic drugs by converting oil-in-water and water-in oil based emulsions into gelled system, respectively (Chen et al., 2006). Emulsion gels can also prolong the

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release of drugs having shorter half-life of even hydrophilic drugs by making w/o emulgel (Haneefa et al., 2013; Singla et al., 2012). Most of the newly discovered drugs are poorly soluble. Such drugs can be incorporated in oil phase of water-in oil emulsions and can be combined with gel to deliver in the form of emulsion gel. The loading capacity of the emulsion gels is far superior to the noisome and liposome containing formulations containing poorly soluble drugs (Khullar et al., 2011). The preparation of the emulsion gels do not need high end instruments thereby allowing development of low-cost formulations as compared to the conventional formulations. The main advantage of the emulsion gels is less greasy, easily washable and easy applicability, which improves the patient compliance of the emulsion gel based formulations (Alexander et al., 2013).

In recent years, the interest in the use of natural polymers for preparing biphasic pharmaceutical, nutraceutical and cosmetic formulations has markedly increased (Gilbert et al., 2013). Natural polymers are biocompatible, biodegradable, non-toxic, safe, cheap and easily available (Hamid Akash et al., 2015). These polymers help improving the stability of the formulations by decreasing the interfacial tension between the two immiscible liquid phases (Silva et al., 2015). The chemical or physical crosslinking renders emulsion gels as semi-solid (Guo et al., 2013). The physical stability of the gels depends on the extent of crosslinking (Alvarez-Lorenzo et al., 2013). The weak forces such as van der Waals interactions, π–π stackings and hydrogen bonds are responsible for the physical crosslinking. Guo et al. (2013) reported the use of whey protein based emulsion hydrogels (Guo et al., 2013). Tang et al. (2013) used soy protein isolate for stabilizing emulsion hydrogels (Tang et al., 2013).

Lecithin is a naturally occurring zwitterionic phospholipid- based liquid surfactant (extracted from egg and soybean) (Vintiloiu and Leroux, 2008). It has been extensively studied as structuring agent for food, pharmaceutical and cosmetic applications (Rosa et al., 2015). It is a well known amphiphile which self-assembles at the oil-water interface into different supramolecular assemblies (Volkov and Deamer, 1996). These self-assembled supramolecular assemblies are composed of reverse micellar structures as the basic building blocks. These micellar structures are formed due to the weak van der Waals forces, hydrogen bonding and electrostatic interactions (Zhang, 2003). The well explored property of lecithin to form a supramolecular 3D network structure, in the presence of water and apolar phase, is exploited in the pharmaceutical and the food industries (Raut et al., 2012). Lecithin derived from soybean has been reported to be biocompatible and has been used for transdermal drug delivery applications (Willimann et al., 1992). Lecithin based organogels have been reported by many researchers (Bhatia et al., 2013; Kumar and Katare, 2005; Shchipunov, 2001), but emulsion hydrogels have not been explored much yet. The primary problem associated with the organogels is the greasy feeling upon application over the skin. The use of hydrogel based formulations, which offer a soothing effect and allow easy washing of the formulation, can help overcome this disadvantage. Nakagawa et al. (2012, 2014) reported the development and characterization of hydrogel formulations using hydrogenated soy lecithin (Nakagawa et al., 2012, 2014).

Sesame oil is extracted from the seeds of *Sesamum indicum L.* by successive expressions in hydraulic presses. The major fatty acid portions of sesame oil are oleic acid (40.0–50.0%) and linolic acid (35.0–45.0%). It is resistant towards oxidative deterioration due to the presence of sesamolin and sesamol (Mohamed and Awatif, 1998). Wright et al. (2006, 2011) reported phase behavior, microstructure, and rheological properties of ricinelaidic acid–sesame oil organogels (Wright and Marangoni, 2006; Wright et al., 2011). Abashzadeh et al. (2011) developed physical hydrogels of chitosan (and its water soluble derivatives such as carboxymethyl chitosan, sodium carboxymethyl chitosan), opened ring polyvinyl pyrrolidone and sesame oil for controlled delivery of triptorelin acetate (Abashzadeh et al., 2011). There are few patents in which researchers have used sesame oil as the oil phase for preparing emulsions (Boudy and Grollier, 1984; Wright, 1997) or gels (Ballard, 2010; Lin, 2011; Rojanapanthu et al., 2006). Hence, sesame oil was chosen as the apolar phase for the development of the emulsion gels.

Metronidazole, a nitroimidazole derivative, was incorporated within the developed emulsion gels. The drug is intracellularly absorbed by the bacteria, where the bacterial nitroreductase enzyme converts the drug into its active form. The active metabolite of the drug binds with the bacterial DNA and inhibits bacterial nucleic acid synthesis. This results in the bacterial cell death (Pal et al., 2009). It is one of the most frequently used antimicrobial drugs for the treatment of protozoal infections (*e.g.* trichomoniasis) and anaerobic infections (*e.g.* intra-abdominal, gynecological bone and joint, central nervous system, respiratory tract, skin, oral and dental) (Kaur et al., 2012). It is available commercially as several dosage forms, namely, solid (tablets, capsules), semisolid (gels, lotion, cream) and liquid (suspension, emulsions, injections). There are various semisolid products of this drug, such as Metro gel, Metro cream, Metro lotion, Vandazole gel, which are currently available in the market. The above-mentioned semisolid formulations are immediate release formulations (Wain, 1998). Since metronidazole is classified as BCS class I (high solubility and high permeability), it is invariably a drug of choice for developing sustained release formulations. Many research groups have reported controlled delivery of metronidazole from both hydrogel and organogel systems (Asnaashari et al., 2011; Krishnaiah et al., 2002; Latha et al., 2009; Lewis et al., 2000; Obitte et al., 2010).

Though there are few reported literatures on the development of hydrogels using hydrogenated soy lecithin, the application of these hydrogels in drug delivery have not yet been explored (Nakagawa et al., 2012). In the present study, the self-assembled emulsion hydrogels of soy lecithin were developed as delivery matrices. Sesame oil was used as the representative vegetable oil for the development of emulsion gels. The ability of the developed emulsion gels to deliver metronidazole was studied in-depth. The method described for the preparation of the emulsion gel in this study is very simple and varies only a little from the reported method of lecithin based organogel preparation (Raut et al., 2012). A group of formulations was made and five formulations were selected as the representative formulations for further analysis. The developed gels were found to be emulsion hydrogels. The gels were characterized thoroughly by microscopy, FTIR spectroscopy, X-ray diffraction studies, viscosity analysis and mechanical analysis. Metronidazole was