Investigation of Organogel Based Nanodispersion as a Novel Drug Delivery System

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論　文　内　容　の　要　旨

Introduction: Poor water solubility of drug molecules is one of the major obstacles in the development of an effective drug delivery system (DDS) for various routes. Poorly soluble drugs result in suboptimal dosing and subject to poor bioavailability and decreased therapeutic responses which make their formulation difficult or even impossible. Hence, it is a challenge for the researchers to develop a DDS for effective delivery of poorly water-soluble drugs without compromising safety and therapeutic efficacy. With the advances in technology, currently available drug delivery strategies for hydrophobic drugs are based on nanoparticle systems and offer several advantages including low drug toxicity, enhanced bioavailability, ease of administration through various routes. Despite several advantages, nanoparticle-based DDSs have certain limitations especially instability, immediate drug release owing to their large surface area, limited drug encapsulation efficiency, inadequate biocompatibility and so on.

Considering these developments and limitations, the current research aims to develop an organogel nanodispersion for the safe and effective delivery of hydrophobic drugs. Characterization of developed nanoemulsion along with its in vitro biocompatibility study reveals the feasibility of organogel nanoemulsion as a promising drug carrier. Besides, in vitro and in vivo studies confirms the possible application of G/W nanoemulsion for anticancer drug delivery via various routes of administration.

Chapter 1: The first chapter of the thesis discusses the background and objective of this research. This chapter also highlights the novelty of this study and how this study was useful over currently available drug delivery systems.

Chapter 2: This chapter provides a comprehensive review of drug delivery systems. It also focuses on the use of organogel in drug delivery systems, application of organogel for transdermal, oral, parenteral, and ocular preparations, challenges with the use of organogel.

Chapter 3: In this chapter, we successfully developed a gel-in-water (G/W) nanoemulsion using 12-hydroxystearic acid and lipiodol that form organogel, encapsulate hydrophobic drugs and remain

dispersed in water by ultrasonication. Nanoparticles were ~ 200 nm in diameter with narrow size distribution and higher encapsulation efficiency (~97%). G/W nanoemulsion has shown excellent stability over six months independent of storage temperature compared to oil-in-water (O/W) nanoemulsion and suggests the feasibility of G/W nanoemulsion as a novel DDS.

Chapter 4: Chapter 4 focuses on the in vitro and in vivo evaluation of G/W nanoemulsion that determines its application as an effective drug carrier. Biocompatibility of nanogel emulsion was confirmed in vitro as no significant change in the mitochondrial activity and metabolic function of primary rat hepatocytes was observed. In vitro and in vivo antitumor efficacy of paclitaxel-loaded G/W nanoemulsion towards murine melanoma cells (B16F10) denotes successful drug delivery from organogel droplets.

Chapter 5: This chapter concentrates on the potential application of G/W nanoemulsion for intravenous delivery of anticancer drugs. A significant decrease in tumor volume and tumor weight was noticed after intravenous administration of paclitaxel-loaded G/W (G/W-PTX) nanoemulsion via the tail vein. This result suggests site-specific antitumor efficacy along with successful drug delivery from G/W nanoemulsion by intravenous route. Additionally, in vitro drug release study suggests sustained drug release from nanogel droplets with 66% drug release after 48h.

Chapter 6: In chapter six we successfully develop a nanogel dispersion using beeswax as an organogelator for topical drug delivery to the posterior segment of eye. Physicochemical characteristics of developed emulsion reveal the possible application of G/W nanoemulsion as an eye drop. The fabricated nanoemulsion was found biocompatible to primary rat hepatocytes and HUVEC cells in vitro even at higher concentrations (0.1 – 10%). The prospect of gel-in-water nanoemulsion as an eye drop was confirmed by enhanced corneal permeability and excellent ocular tolerance study in vivo.

Chapter 7: Finally, chapter 7 concludes with a summary of key findings in this thesis and future studies that can be embraced for further expansion of the current study.

〔作成要領〕

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