Supplementary Materials

Ketoprofen-LDH Nanohybrid for Transdermal Drug Delivery System

Myung-Chul Park, Hark Kim, Dae-Hwan Park, Jae-Hun Yang, and Jin-Ho Choy*

*Center for Intelligent NanoBio Materials (CINBM), Department of Chemistry and Nano Science, and Department of BioinspiredScience, EwhaWomans University, Seoul 120-750, Korea. *E-mail: jhchoy@ewha.ac.kr*

Received February 24, 2012, Accepted March 15, 2012

Experimental

The KP-LDH nanohybrid was prepared by the coprecipitation method. A mixture of $Zn(NO_3)_2 \cdot 6H_2O$, $Al(NO_3)_3 \cdot 9H_2O$, and KP ($C_{16}H_{14}O_3$) molecules dissolved in solution of ethanol and deionized water was titrated with NaOH solution to pH 8.0 at ambient temperature with vigorous stirring. The precipitate was aged for 24 hours and then washed with decarbonated water, and freeze-dried.

Powder X-ray diffraction (XRD) analyses were carried out on a Rigaku X-ray diffractometer with CuKα radiation (λ = 1.5418 Å). Fourier transform infrared (FT-IR) spectra were collected on a Jasco FT/IR-6100 spectrometer with the KBr disk method. To determine content of KP loaded in KP-LDH, the KP-LDH was dissolved in solution of 1 N HCl and KH_2PO_4 buffer (pH 7.4) (1:9 = v:v ratio). The suspension was then filtered through a 200 nm PTFE membrane, and then quantitatively measured by high performance liquid chromatography (HPLC, Agilent Technologies) with UV detector (λ_{max} (KP) = 250 nm).

In-vitro release of KP from the KP-LDH was carried out using a USP dissolution apparatus 2 (a paddle stirring with 50 rpm method). The each KP-LDH and equivalent KP only was suspended in mixed solution of 720 mL of phosphate buffer solution (PBS, pH 7.4) and 180 mL of ethanol. The pH value of buffer solution was continuously maintained at 7.4 and the temperature at 35 ± 0.5 °C in a water bath incubator, which is similar to the topical skin condition. The amount of released KP was periodically monitored by HPLC installed with UV detector at 250 nm.

In-vitro transderrmal permeation experiments were carried out using the common two-chamber Franz diffusion cell (Lab Fine, Inc.) method. It consists of donor and receptor chambers between which a membrane is positioned. The exposed surface area of the membrane available for KP drug permeation was 0.77 cm^2. The skin of each hairless female nude mouse (Orient Bio Inc.) was excised after sacrificed. The skin was carefully cleaned with normal saline solution and removed the most of a layer of fat and blood vessel by ethanol. The donor cell was filled with the KP-LDH suspended in solution of PBS (pH 7.4) and ethanol (1:1 = v:v ratio). In preparation of colloidal solution of the KP-LDH, ethyl alcohol was added in order to enhance the transdermal delivery efficiency due to the fact that the ethyl alcohol may achieve the enhanced penetration of drugs through fluidization or de-lipidization of the stratum corneum lipid, softening of the stratum corneum keratin, degradation of skin enzyme or solvent drag. The receptor compartment was filled with PBS (pH 7.4) only. As-prepared suspension of KP-LDH in donor cell was treated on the mouse skin, and then the aliquot of released media in receptor compartment were isolated at specified time intervals. Each experiment was carried out for 24 hours to achieve a steady-state flux. The temperature of diffusion medium was maintained at 35 ± 0.5 °C by thermostatic water pump and the medium was mechanically stirred. The cumulative amount of penetrated KP was then analyzed by HPLC.