Materials Chemistry and Physics 208 (2018) 183–188

Contents lists available at ScienceDirect

Materials Chemistry and Physics

journal homepage: www.elsevier.com/locate/matchemphys

Spherical silica hybrid liposome particles with controlled release of *citrus unshiu* peel extracts

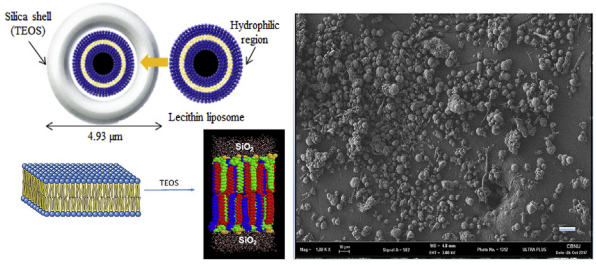
Hyesun Lee, Jeong Ho Chang*

Center for Convergence Bioceramic Materials, Korea Institute of Ceramic Engineering and Technology (KICET), Chungbuk, 28160, South Korea

HIGHLIGHTS

- Spherical silica hybrid liposomes particles were prepared by sol-gel reaction.
- *Citrus unshiu* extract was used for controlled release and cosmetic applications.
- Efficient amounts of *citrus unshiu* extract load and release were calculated.
- Release kinetic model was fitted to pseudo-second-order kinetic model.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 7 October 2017
Received in revised form
21 December 2017
Accepted 7 January 2018
Available online 9 January 2018

Keywords:
Silicified liposome particles
Citrus unshiu peel extract
Sustained release
Kinetic

ABSTRACT

This paper reports the controlled release of *citrus unshiu* extract from spherical silica hybrid liposome (silicified liposomes) particles. Silicified liposome particles were synthesized by silicification through the sol-gel reaction with TEOS as a silica source of the hydrophilic region of lecithin. In addition, we achieved the various characterization analyses such as SEM-EDS, DLS, FT-IR, and TGA, respectively. The silicified liposomes particles effectively entrapped as much as 314.2 mg/L solution of the *citrus unshiu* peel extract. After the *citrus unshiu* peel extract was entrapped in the silicified liposomes, the controlled release profile was investigated and the results showed that the maximum release was 41.4%. The release kinetics were fitted to various kinetic models, such as pseudo-first, pseudo-second-order kinetic and intra-particle diffusion models. The pseudo-second-order kinetic model showed good matching with the experimental release results. Furthermore, the antioxidant activity of *citrus unshiu* peel extract was measured by the DPPH free radical scavenging method.

1. Introduction

Recently, several studies on various phospholipid liposomes have been conducted to investigate their potential for application, in smart drug delivery systems due to their advantages of safety, biocompatibility, and higher loading efficiency in comparison to other materials [1]. Among the phospholipids, lecithin has been widely used due to its excellent biocompatibility and emulsifying properties [2]. Furthermore, in the field of cosmetics, phospholipid liposomes are utilized as a functional carriers or scaffolds to entrap active ingredients effectively and release them on the skin [3,4]. Phospholipid liposomes are also called phospholipid vesicles, and they are composed of amphipathic molecules such as hydrophobic acyl (or fatty acid) chains and hydrophilic head groups [5]. In aqueous solution, phospholipids spontaneously form bilayers that have strong affinity with the cell membranes. The encapsulation of active ingredients in the liposome vesicles is usually performed in the hydrophobic regions using an impregnation process [6].

* Corresponding author.
E-mail address: jhchang@kicet.re.kr (J.H. Chang).

https://doi.org/10.1016/j.matchemphys.2018.01.027
0254-0584/

Although, phospholipid vesicles have been used for the delivery of active ingredient compounds in cosmetic or drug delivery formulations, they are not efficacious due to the high flexibility and lower loading capacity of the active ingredients [7,8]. To overcome these disadvantages of using liposomes, we synthesized silicified liposomes by sol-gel silicification with tetraethyl orthosilicate on the hydrophilic regions of phospholipid liposomes. Moreover, the stability of these silicified phospholipids was enhanced by coupling with inorganic or supported lipid bilayer (SLB) materials such as sericite or mica [9].

The dried peel extract of the *Citrus unshiu* Markovich fruit has been used in traditional medicine, and it has been widely investigated recently regarding its biological activity, such as anti-oxidant, anti-allergic and anti-bacterial functions because it includes biologically active compounds [10–12]. *Citrus unshiu* peel extract contains high levels of phenolic compounds, which have strong anti-oxidant activity [13].

In this study, we prepared silicified liposome particles with a uniform diameter of 5 μm for controlled release of the anti-oxidant *Citrus unshiu* peel extract as a drug delivery system for practical application in the cosmetic fields. The kinetics of loading and release of *Citrus unshiu* peel extract properties have been studied using various kinetic models. Furthermore, the anti-oxidant activity of *Citrus unshiu* peel extract was investigated by the 1,1-diphenyl-2-picryl-hydrazyl (DPPH) free radical scavenging method as a function of time.

2. Experimental

2.1. Chemical and materials

Lecithin (1,2-diacyl-*sn*-glycero-3-phosphatidylcholine) was purchased from TCI (Portland, OR, USA). Hydrochloric acid, tetraethyl orthosilicate (TEOS), 1,1-diphenyl-2-picryl-hydrazyl (DPPH) were purchased from Sigma-Aldrich (St. Louis, MO, USA). *Citrus unshiu* peel extracts (Model. CEXD-011126) were supplied by the JSK BIO Company (Deajeon, South Korea). All chemicals were used without further purification.

2.2. Preparation of silicified liposomes

As reported previously, silicified liposome particles were prepared based on the modified methods of Kang et al. [9]. In brief, 1 g lecithin was dissolved in 40 mL ethanol and added to 60 mL distilled water. The mixture was homogenized at 80 °C for 1 h in oil bath. Then, 2 g of the TEOS was added dropwise to the mixture, and the mixture was agitated for 8 h. The mixture was centrifuged at 3000 rpm to remove extra liposomes in the supernatant. The obtained Si-Liposomes were washed several times with ethanol and dried overnight at room temperature. The prepared silicified liposomes were stored at 4 °C.

2.3. Characterization of silicified liposomes

The morphology of silicified liposome particles was characterized by the scanning electron microscopy (SEM; SM-300, Topcon Co., Tokyo, Japan) at an acceleration voltage of 20 kV and energy dispersive X-ray spectroscopy (EDS, Thermo Electron Corporation). The specimens were sputter coated with gold in order to prevent charging on a carbon tape. Size distribution was determined using a dynamic light scattering instrument (DLS, Photal DLS-8000, Otsuka Electronics Co., Tokyo, Japan) with a wavelength of 632.8 nm. The particle size of silicified liposomes was measured at each 8 h, 16 h, 24 h and 48 h of stirring time, respectively. Infrared spectra of prepared silicified liposomes were recorded using fourier transform infrared spectroscopy (FT-IR; Jasco 460 plus, Jasco Co., Tokyo, Japan). FT-IR spectra were obtained at 4000-650 cm^{-1} region at a resolution of 4 cm^{-1} using KBr pressed-pellet method. To evaluate decomposition behavior of the silicified liposomes and *Citrus unshiu* peel extract loaded silicified liposomes, thermogravimetric analysis (TGA; SDT Q900, TA instruments Inc., USA) was performed in nitrogen (N_2) atmosphere from 30 to 700 °C at a heating rate of 10 °C/min.

2.4. Drug loading and release behavior of citrus unshiu peel extract from silicified liposomes

Citrus unshiu peel extract was selected as the model drug for the present study. *Citrus unshiu* peel extract was loaded on the silicified liposome particles were prepared by dispersion in phosphate buffer solution (PBS, pH 7.4) of 314.2 mg/L. The loading capacity (q_e, mg/g) of *Citrus unshiu* peel extract at each sampling time t (min) on the silicified liposomes was calculated according as (Eq. (1)):

$$q_e = \frac{V(C_0 - C_t)}{W} \quad (1)$$

where q_e is the amount of *Citrus unshiu* peel extract loaded at equilibrium (mg/g), V is the volume of the PBS (L), C_0 and C_t are initial and finial *Citrus unshiu* peel extract concentration (mg/L) and W is the mass of dried silicified liposomes (g).

The prepared *Citrus unshiu* peel extract loaded silicified liposomes were centrifuged at 3000 rpm and washed once with PBS. Then 0.01 g of dried *Citrus unshiu* peel extract loaded silicified liposomes were placed in 20 mL of PBS. The release study of *Citrus unshiu* peel extract from silicified liposomes was carried out in pH 7.4 PBS with constant agitation at 100 rpm/min at room temperature. The release profile was obtained by measuring absorbance of the samples at 340 nm with a UV-Vis spectroscopy (Jasco 550 plus, Jasco Co., Tokyo, Japan). To investigate the *Citrus unshiu* peel extract release mechanisms, the drug release data were fitted in 4 kinetic models: zero-order, first-order, Higuchi and Korsmeyer-Peppas [14,15].

2.5. DPPH radical scavenging activity

The potential antioxidant activity of *Citrus unshiu* peel extract was estimated spectrophotometrically at 517 nm using 1,1-diphenyl-2-picryl-hydrazyl (DPPH) free radical scavenging method [16,17]. Briefly, the 2 mL of various concentration of *Citrus unshiu* peel extract (0.1–20 wt. %) were added to 2 mL of 0.1 mM DPPH solution. After incubation at room temperature for 30 min, the absorbance of mixture was measured using UV-Vis spectrophotometer. The antioxidant activity (K_D) of *Citrus unshiu* peel extract as calculated using the following Eq. (2):

$$KD\ (\%) = \frac{Abs_c - (Abs_i - Abs_j)}{Abs_c} \times 100 \quad (2)$$

where Abs_c was the absorbance value of the blank sample, Abs_i was the absorbance of the samples and Abs_j was the absorbance of the samples alone.

3. Results and discussion

3.1. Characterization of silicified liposomes

Nanoporous silicified liposome particles were successfully synthesized by the silicification of tetraethyl orthosilicate (TEOS) on the hydrophilic region of lecithin liposomes. Schematic images of a