Encapsulation of the Glabridin using the gamma-Cyclodexrin based MOFs(COFs)

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Abstract

A glabridin is an active ingredient in the root extract of licorice (Glycyrrhiza glabra) and brownish powder. It is an isoflavane, part of plant-derived molecules, the natural phenols. Glabridin is insoluble in water and oil, but soluble in organic solvents such as propylene glycol. Glabridin is known for properties such as skin whitening, anti-inflammatory, cell-protective abilities and antioxidant. The stability of glabridin is greatly affected by various environmental factors such as pH, temperature, light, heat, and oxygen. It is also known to reduce absorption in vivo because it conferred low polarity and water solubility. This makes it difficult to apply glabridin in cosmetic formulations. Gamma-cyclodextrins are widely applied in various fields such as food, pharmaceutics, and cosmetics. They are bio-friendly and could encapsulate the hydrophobic component which is unstable in external environment. Gamma-cyclodextrin based metal-organic frameworks (COFs) are formed by gamma-cyclodextrin as an organic ligand and potassium ion as a inorganic metal center. COFs have the various properties such as biodegradable, highly porosity, large surface areas, and nontoxicity. In this study, COFs encapsulated glabridin was synthesized to stabilize the glabridin in the external environment and increase the solubility in water. The characters of COFs encapsulated the glabridin were investigated with scanning electron microscope (SEM), X-ray diffraction (XRD), nuclear magnetic resonance (NMR) and fourier-transform infrared spectroscopy (FT-IR). Then, the water solubility was evaluated and the stability of COFs encapsulated glabridin was confirmed by high-performance liquid chromatography (HPLC) measurement for 6 months. The COFs encapsulated the glabridin were successfully synthesized. The shapes of COFs were similar cubic crystals and the COFs crystalline was maintained after encapsulating the glabridin. The encapsulated glabridin peak was confirmed with NMR data. In this study, porosity COFs were used as encapsulated glabridin carrier. It could conclude that the COFs encapsulated the glabridin was successfully synthesized and had high stability from the external environment and solubility in water. The synthesized COFs could apply for various fields such as drug delivery, food, and cosmetics.

Keywords: Glabridin, gamma-Cyclodextrin, COFs, Stability

Introduction.

Metal–organic frameworks (MOFs) are porous substances composed of inorganic metal ions and organic ligands. Their organic ligand functionalization allows for pore and shape control, so they have potential for adsorption, encapsulation, storage, and catalysis. Although MOF traditionally contains potentially toxic components, the COFs synthesized in this study was made using gamma-cyclodextrin and is biocompatible and can be applied to drug delivery through encapsulation. [1-3] Gamma-cyclodextrins (γ -CD) are widely applied in various fields such as food, pharmaceutics, and cosmetics. They are bio-friendly and could encapsulate the hydrophobic component which is unstable in external environment. γ -CD based metal-organic frameworks (COFs) are formed by γ -CD as a organic ligand and potassium ion as a inorganic metal center. COFs have the various properties such as highly porosity, large surface areas, and non-toxicity [4-6]. Glabridin is the main component of the hydrophobic flavonoid fraction of licorice extract that has anti-inflammatory, antioxidative and skin whitening effects. However, effective of Glabridin is limited in cosmetic products, because of poor solubility, poor stability and unsatisfactory skin penetration. [7-8] In this study, COFs encapsulated glabridin was synthesized to stabilize the glabridin in the external environment and increase the solubility in water. The characters of COFs encapsulated the glabridin were investigated with scanning electron microscope (SEM), X-ray diffraction (XRD), nuclear magnetic resonance (NMR), fourier-transform infrared spectroscopy (FT-IR), and High-performance liquid chromatography (HPLC).

Materials and Methods.

The COFs were prepared by dissolving gamma-cyclodextrin and KOH in water, followed by vapor diffusion of ethanol in to the solution including PEG20000 and succinated chitosan at room temperature. After 1 day, the synthesized Chito-COFs were washing with centrifuge and neutralized with acetic acid and then, drying process conducted. To encapsulate the glabridin, The Chito-COFs and glabridin was put into ethanol and stirred for 24 hours. The morphology of synthesized Chito-COFs encapsulated the glabridin was analyzed by SEM [S-4800, Hitachi, Japan] and the crystallinity was characterized using XRD [SmartLab, Rigaku, Japan]. The FT-IR spectra were recorded on an FT-IR-Raman spectrometer Thermo-Nicolet and collected in the 4000-650 cm^{-1} range. To investigate the encapsulated glabridin, the H^1 NMR spectra was recorded under the condition (500 MHz, 298 K). The stability of Chito-COF-glabridin was analyzed using HPLC for 6 months at various temperature.

Results.

Surface morphology of γ -CD, CD-MOF, Chito-COF and Chito-COF-glabridin was analyzed by SEM. SEM micrographs shown in Figure 1(a) reveal that pure γ -CD has irregular and rough surface.

On the other hand, COFs and Chito-COF made of γ -CD have a uniform and stacked shape. (Figure 1 (b), (c)) Similarly, Chito-COF-glabridin has a uniform shape and dense surface morphology as shown in Figure 1(d). The crystallinity of Chito-COF was maintained after encapsulating the glabridin. It could be co-relation with SEM images.

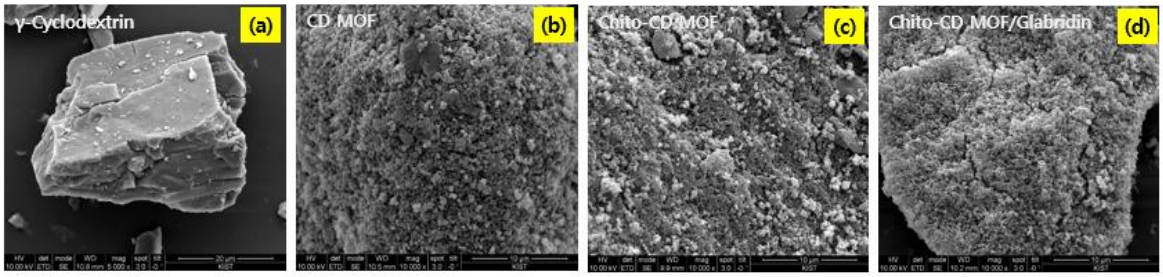

Figure 1. SEM images of COFs ; (a) γ -CD, (b)COF, (C)Chito-COF, (d)Chito-COF-glabridin

The XRD pattern of pure γ -CD, Glabridin, Chito-COF, and Chito-COF-glabfidin are shown in Figure 2. The XRD analysis can help to identify the crystalline or amorphous nature of the polymer. Also, The XRD pattern of COF revealed its crystalline nature. In the peak of Chito-COF-glabridin, pure γ -CD and glabridin peaks could not be observed, but the COFs peak was observed. It can be concluded that Chito-COF-glabridin retains its crystal structure even after integration into a succinated chitosan and encapsulation a glabridin.

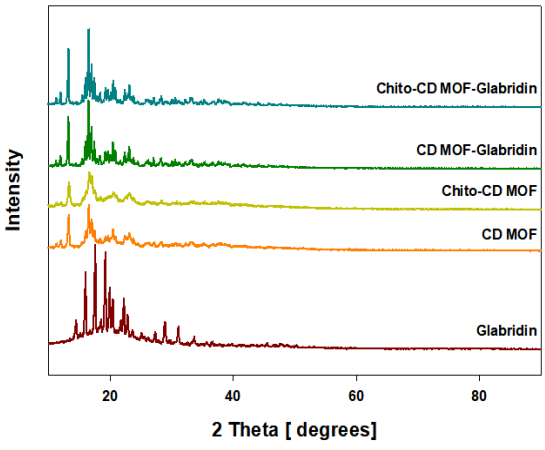

Figure2. XRD data of COFs and glabridin

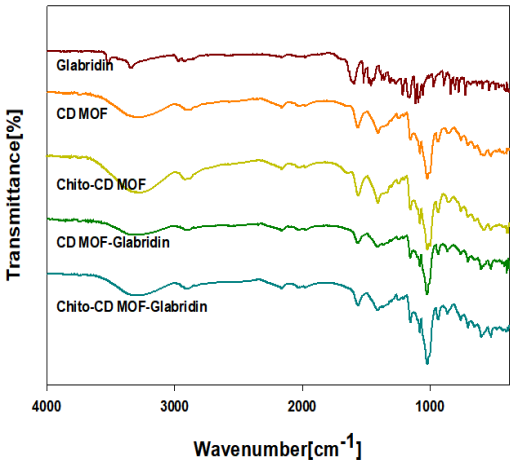

Figure 3. FT-IR of COFs and glabridin

FTIR spectra of γ -CD, Glabridin, COFs, and Chito-COF-glabridin is shown in Fig. 3. Incorporated Chito-COF-glabridin developed a weak interaction with the available functional group present on succinated chitosan and glabridin.

The ^{1}H NMR spectra glabridin, COFs, and Chito-COF-glabradin were recorded and used to confirm the glabridin encapsulation. The peaks the originated glabridin were shown at COF-glabridin and Chito-COF-glabridin in ^{1}H NMR spectra (Figure 4). It could be concluded that the Chito-COFs were successfully encapsuled the glabridin.

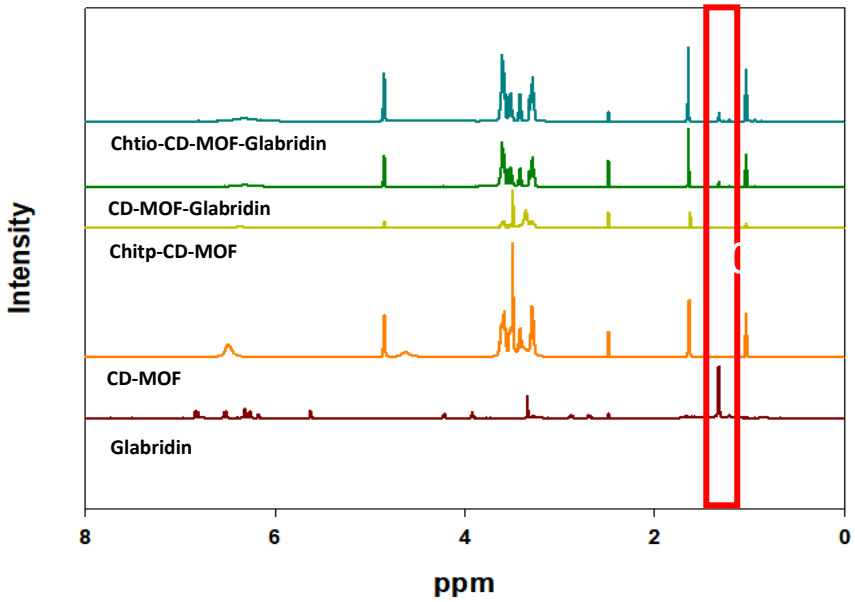

Figure 4. ^{1}H NMR data of COFs and glabridin

The stability of Chito-COF-glabridin was analyzed using high-performance liquid chromatography(HPLC). The initial content of Chito-COF-glabridin was 5.00 ±0.50%. After 6 monthss storage at 4°C, room temperature, and 45°C, the residual glabridin in Chito-COF-glabridin were 5.03±0.03%, 4.35±0.06%, and 4.26±0.04%, respectively. It concludes that the initial content of Chito-COF-glabridin was maintained more than 85% for 6 months at various temperature.

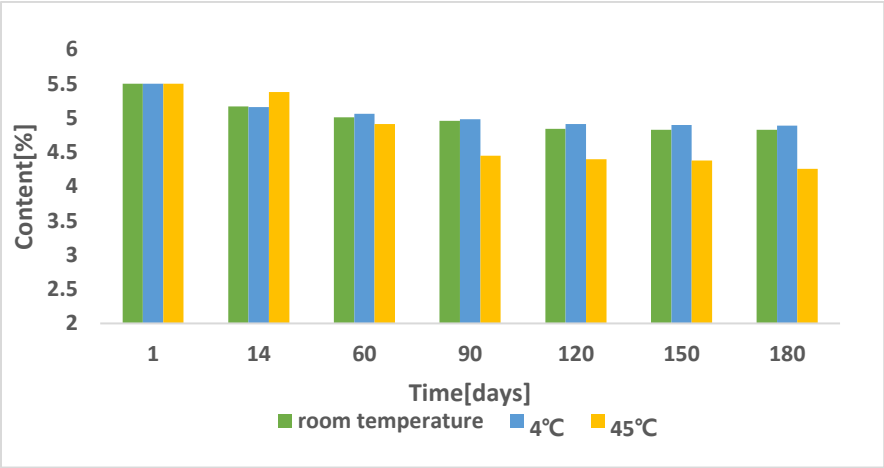

Figure 5. Stabilization of Chito-COF-glaridin at various temperature

Discussion.

In this study, MOF was synthesized using biocompatible γ -CD and succinated chitosan was attached to the COFs to improve skin delivery effect of active substances. The crystalline structure of the synthesized Chito-COFs was confirmed through SEM images and XRD patterns. It was confirmed that glabridin was encapsulated in the porous space of Chito-COFs through FTIR spectra and NMR spectra. The content of glabridin captured in Chito-COF-glabridin was confirmed through HPLC measurement for 6 months, as a result, it was confirmed that the stability was significantly increased than that of the raw material glabridin. In addition, while raw material glabridin is insoluble in water, Chito-COF-glabridin has solubility in water, which is expected to be easy for cosmetic formulations.

Conclusion.

The COFs were successfully synthesized by modified vapor diffusion method. The synthesized COFs used as encapsulated glabridin carrier. The COFs have the uniform shape framework and the crystallinity was maintained after encapsulating the glabridin. The glabridin was encapsulated through the hydrogen bonding with COFs. The Chito-COF-glabridin was maintained the content of glabridin up to more than 85% at various temperature for 6 months, which the glabridin could be protected from external environment. In conclusion, the synthesized COFs could be a promising system and apply for various fields such as drug delivery, food, and cosmetics.

Acknowledgments.

This work was supported by the Technology Innovation Program (or Industrial Strategic Technology Development Program (10077704, Hybrid composite based on LDH and MOF for improved skin permeability and On/Off controllable function of physiologically active substance) funded By the Ministry of Trade, Industry &Energy (MOTIE, Korea).

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