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

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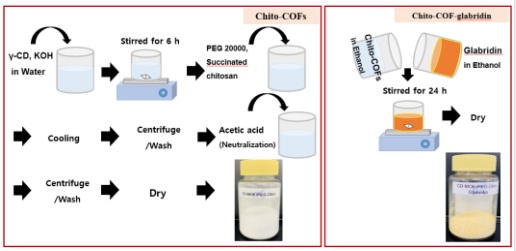
Introduction:

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 & 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 H1 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 & Discussion:

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.

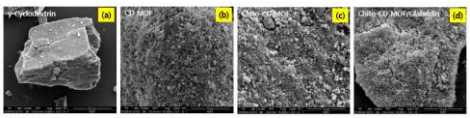


Figure 1. SEM images of COFs ; (a) γ -CD, (b)COF, (C)Chito-COF, (d)Chito-COF-glabridin

Results & Discussion:

The XRD pattern of pure γ -CD, Glabridin, Chito-COF, and Chito-COF-glabridin 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.

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.

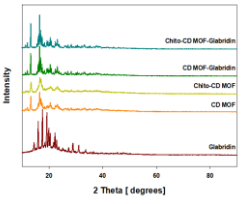


Figure2. XRD data of COFs and Glabridin

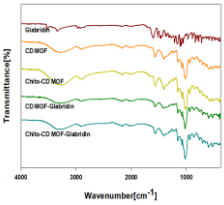


Figure3. FT-IR of COFs and Glabridin

The 1H 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 1H NMR spectra. (Fig. 4) It could be concluded that the Chito-COFs were successfully encapsuled the Glabridin.

The stability of Chito-COF-glabridin was analyzed using HPLC. The initial content of Chito-COF-glabridin was 5.00 ±0.50%. After 6 months storage at 4℃, room temperature, and 45℃, 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. (Fig. 5)

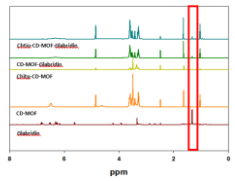


Figure 4. 1H NMR data of COFs and Glabridin

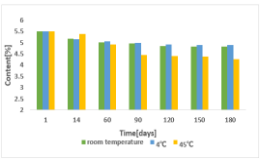


Figure 5. Stabilization of Chito-COF-glabridin at various temperature

Conclusions:

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.

Acknowledgements:

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