피부개선첨가물로의 기능을 지닌 arbutin-montmorillonite 복합소재 합성 및 특성

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The synthesis and characterisation of arbutin-intercalated montmorillonite as skin improvement supplement

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One class of delivery vehicle that has received attention in the recent years is represented by layered materials, which can intercalate therapeutic compounds between their layers. Because the release of drugs from drug intercalated layered materials is potentially controllable, these new materials can be used as delivery hosts in the pharmaceutical field [1]. Natural clay minerals are suitable to be used in modified DDS, which are designed to provide therapeutic levels of the drug to the site of action and maintain them throughout the treatment. These goals may be achieved by modifying the rate and/or time and/or site of drug release in comparison with conventional formulations by delaying (extended release systems), targeting (site-specific release systems) and improving drug solubility. New strategies are focused on increasing drug stability and simultaneously modifying drug delivery patterns (particulate delivery systems) [2-3].

Montmorillonite clay (MMT) belongs to the smectite group, composed of silica tetrahedral sheets layered between alumina octahedral sheets. The imperfection of the crystal lattice and the isomorphous substitution induces a net negative charge that leads to the adsorption of alkaline earth metal ions in the interlayer space. Such imperfection is responsible for the activity and exchange reactions with organic compounds [4]. MMT also contains dangling hydroxyl end-groups on the surfaces. It has a large specific surface area, exhibits good adsorbance ability, high cation exchange capacity, standout adhesiveness, and drug-carrying capability. Thus, MMT is a common ingredient in pharmaceutical products, both as excipient and as active support. The intercalation of organic species into layered inorganic materials provides a useful and convenient route to prepare organic–inorganic hybrids that combine the properties of both the inorganic host and the organic guest [5].

Arbutin is an active ingredient found at high concentration in certain plants, especially in bearberry (Arctostaphylosuva-ursi). It was also reported that the depigmentation effect of arbutin works through an inhibition of the melanosomal tyrosinase activity, rather than suppression of the expression and synthesis of tyrosinase in human melanocytes [6-7]. It is a competitive inhibitor of tyrosinase and its inhibitory concentration is nontoxic to melanocytes. For arbutin, liposomal formulations have emerged as attractive alternatives for topical delivery due to their biocompatibility, non-toxicity, suitability for both hydrophilic and lipophilic compounds. However,

a novel type of liposome named as “deformable liposome” has been reported as a proper carrier for topical delivery of skin whitening agents and other therapeutic agents for the treatment of skin disorders [8]. Also, Arbutin is glucosylated hydroquinone, and may carry similar cancer risks, although there are also claims that arbutin reduces cancer risk. The German Institute of Food Research in Potsdam found that intestinal bacteria can transform arbutin into hydroquinone, which creates an environment favorable for intestinal cancer [9].

Herein, we introduced a new method with practical value of intercalating and stabilizing arbutin within an inorganic layered material MMT. Meanwhile, toxicity assessment also pointed out the margin of safety and toxicity rankings for feasibility of arbutin-MMT composites in practical applications.

Experimental

The experiments were carried out to determine the optimum pH value for intercalation of arbutin into the interlayer of MMT from 5wt% to 50wt%. These studies were performed by treating arbutin and MMT mixture at different pH and constant temperature, time and concentration. The reaction mixtures were filtered and concentration of arbutin in the filtrate was determined by UV spectroscopy at max = 294nm. MMT–arbutin hybrid was characterized by X-ray diffraction(XRD) and Fourier transformed infrared(FT-IR).

Results and Discussion

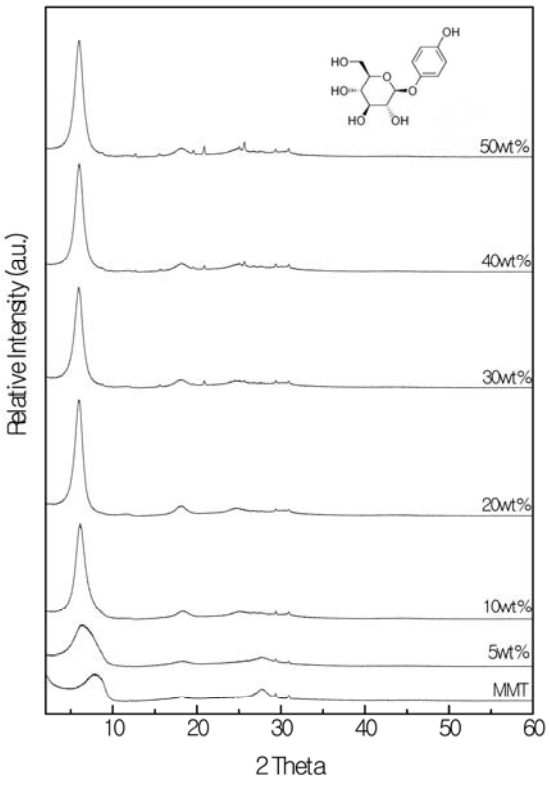
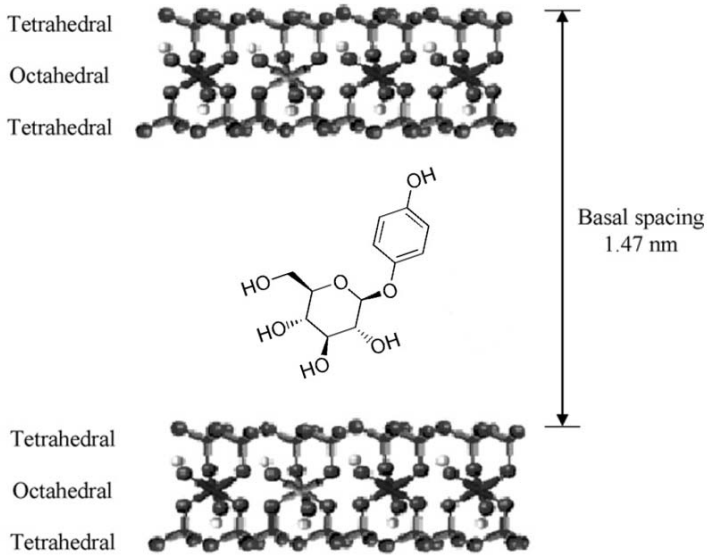


Fig. 1. XRD patterns of MMT and MMT–arbutin hybrid materials.

Fig. 1 shows the XRD pattern of MMT and MMT–arbutin hybrid prepared under optimized conditions. The characteristic peak of (001) plane for MMT and MMT–arbuyin hybrid is observed at 7.4◦ and 5.948◦, with basal spacing of 1.18 and 1.47nm, respectively. According to the Bragg's law, the peak shifting fromhigher diffraction angle to lower diffraction angle is due to increase in the d-spacing which indicates that arbutin has been effectively intercalated into the interlayer of MMT (Scheme 1) and is lying flat on the surface of MMT as a monolayer.



Scheme 1. Possible structural arrangement of MMT–arbutin.

Fig. 2 depicts the FT-IR spectra of MMT, and MMT–arbutin hybrid. MMT shows the characteristic absorption bands at 3400cm^{-1} due to -OH stretching band for adsorbed water. The bands at 3620 and 3698cm^{-1} are due to -OH band stretch for Al-OH and Si-OH. The shoulders and broadness of the structural -OH band are mainly due to contributions of several structural -OH groups occurring in the MMT. The overlaid absorption peak at 1640cm^{-1} is attributed to -OH bending mode of adsorbed water. The characteristic peak at 1115 and 1035cm^{-1} is due to Si-O stretching (out-of-plane) and Si-O stretching (in-plane) vibration for layered silicates, respectively. Peaks at 915, 875, and 836cm^{-1} are attributed to AlAlOH, AlFeOH, and AlMgOH bending vibrations, respectively. Arbutin showed a broad band appearing at 3328cmcm^{-1} due to O-H/N-H stretching vibrations. The bands at 2970, 2898, and 2853cm^{-1} are due to aliphatic C-H stretching vibrations. Acid carbonyl group of arbutin gave band at 1710 and 1500cm^{-1}. The C=O stretching vibrations appears at 1620cm^{-1}. Bands at 1262 and 1119cm^{-1} are due to the C=O-C and morpholino C–O–C stretching vibrations, respectively, while the bands at 1230 and 953cm^{-1} due to O-H bending and hydroxyl C-O stretching vibrations, respectively. In the IR spectra of MMT–arbutin hybrid, not only characteristic bands belonging to MMT and arbutin appear in the spectrum but also several new absorption bands appears at 1300, 1383, and 1454cm^{-1} which indicates that arbuyin interacts strongly with the MMT layers.

Conclusion

This work examines the advantageous effect of clay mineral as active ingredient carrier for

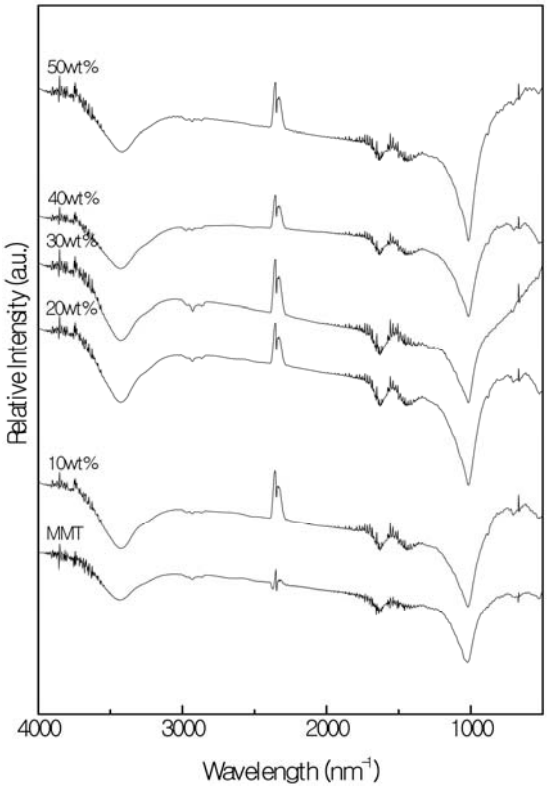


Fig. 2. FT-IR spectrum of MMT and MMT–arbutin hybrid materials.

arbutin, skin lightening agent. The intercalation of arbutin into the interlayer of montmorillonite (MMT) at different pH and initial concentration is demonstrated.

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References

1. Chen, B.Y., Lee, Y.H., Lin, W.C., Lin, F.H., Lin, K.F., Biomed. Eng. *Appl. Basis Comm.*, **18**, 30 (2006).
2. Forni, F., Iannuccelli, V., Coppi, G., Bernabei, M.T., *Arch. Pharm.*, **322**, 789 (1989).
3. Lee, W.F., Chen, Y.C., *Appl. Polym. Sci.*, **91**, 29342941 (2004).
4. Wang, S.F., Shen, L., Tong, Y.J., Chen, L., Phang, I.Y., Lim, P.Q., Liu, T.X., *Polymer Degradation and Stability*, **90**, 123 (2005).
5. Viseras, C., Cerezo, P., Sanchez, R., Salcedo, I., Aguzzi, C., *Appl. Clay Sci.*, **48**, 291 (2010).
6. E.V. Curto, C. Kwong, H. Hermersdorfer, H. Glatt, C. Santis, V. Virador, J.V. Hearing and T.P. Dooley, *Biochem. Pharmacol.*, **57**, 663 (1999).
7. M.H. Schmid and H.C. Korting, *Adv. Drug Deliv. Rev.*, **18**, 335 (1996).
8. M. Trotta, E. Peira, M.E. Carlotti and M. Gallarate, *Int. J. Pharm.*, **270**, 119 (2004).
9. O'Donoghue, J L, *Journal of Cosmetic Dermatology*, **5 (3)**, 196 (2006).