

Use of Natural Halloysite as a Functional Cosmetics Carrier

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기능성 화장품의 캐리어로서 천연 할로이사이트의 활용

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천연 할로이사이트는 대부분 지름 15–125 nm범위의 내강으로 이루어진 튜브 구조의 형태를 가진다. 이러한 튜브형 할로이사이트는 액체 성분의 화장품을 내부에 담지하거나 고체상의 무기물 성분을 고정화하는데 사용될 수 있다. 이 논문에서는 기능성 화장품 성분의 담지기술과 고정화기술을 소개하고 할로이사이트가 화장품용 기재로 유용하게 활용된 두 가지 연구 사례를 기술하였다. 이 논문이 천연 할로이사이트를 응용한 화장품 연구에 많은 관심을 불러모을 수 있기를 기대한다.

주요어 : 기능성 화장품, 서방성, 보습제, 글리세롤, 자외선차단제, 이산화티타늄, 할로이사이트

Natural halloysite is mostly found in the form of a tubular structure with a 15–125 nm internal lumen. This kaolin clay can be used for encapsulating a liquid ingredient of cosmetics and for immobilizing an inorganic solid-phase ingredient. In this paper, the encapsulation and immobilization procedures are introduced and two example applications are reviewed to demonstrate the usefulness of halloysite as a cosmetics substrate. It may help attract more interest in cosmetic applications of halloysite and thus spur more research on the utilization of natural clays.

Keywords : cosmeceuticals, slow release, humectant, glycerol, sunscreen, titania, halloysite

1. Introduction

Halloysite is an aluminosilicate clay belonging to the kaolin group and with a composition of $\text{Al}_2\text{Si}_2\text{O}_5(\text{OH})_4 \cdot 2\text{H}_2\text{O}$ (Joussein *et al.*, 2005). Halloysite is mostly found in the form of a micro-tubular structure with a 15–125 nm internal lumen, a 30–250 nm outer diameter, and a length of less than a few microns (Fig. 1). Inside the halloysite lumen, organic or inorganic materials can be encapsulated

to allow new functionalities (Shchukin *et al.*, 2005). Its cytotoxicity testing revealed no toxic effect on fibroblast cells and human breast cancer cells for over 48 h (Suh *et al.*, 2011). Thus, the micron-sized tubular halloysite is considered a benign carrier appropriate for delivering active substances such as fragrances, cosmetics, and drugs (Levis and Deasy, 2002, 2003; Lvov *et al.*, 2008; Price *et al.*, 2001; Suh *et al.*, 2011).

Several research groups have shown interest in

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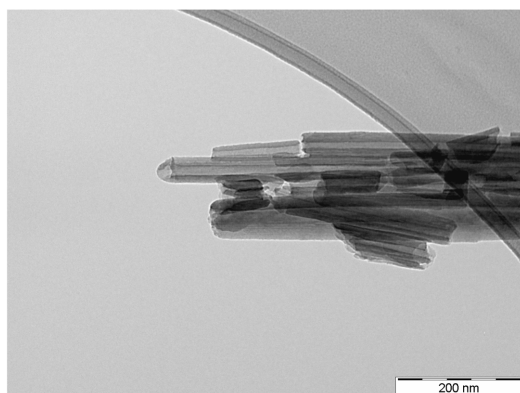


Fig. 1. Transmission electron microscopy (TEM) micrograph of natural halloysite.

controlling the delivery of active materials using tubular halloysite. Lvov group studied the *in-vitro* release of both hydrophilic and hydrophobic agents using halloysite (Price *et al.*, 2001). They showed that halloysite could be used for loading poorly water-soluble drugs up to a maximum load of 12 vol%, and for sustaining their release for over 5 h (Veerabadran *et al.*, 2007). And Deasy group carried out a physicochemical characterization of halloysite for use as a drug delivery carrier (Levis and Deasy, 2002). They revealed that the halloysite surface tends to be anionic and easily adsorbs cationic species from the aqueous solution. Based on this property, less water-soluble cationic drugs were adsorbed onto the halloysite surface to achieve sustained release (Levis and Deasy, 2003).

Meanwhile, only a couple of research on functional cosmetics using halloysite has been reported. Suh *et al.* (2011) demonstrated a cosmetic skincare application of halloysite for glycerol loading. Glycerol is widely used in cosmetics as a humectant. They extended the release rate of glycerol using halloysite over 20 h. Suh and Cho (2015) studied on the synthesis of a hybrid powder, in which the light-scattering nanoparticles are loaded into halloysite for sunscreen purposes. Immobilizing the light-scattering nanoparticles into halloysite and using them as sunscreens agents may reduce unwanted side effects on the skin while keeping their merits intact. In this paper, I reviewed the main concepts introduced in the previous studies to encourage practical research on the cosmetic applications of halloysite.

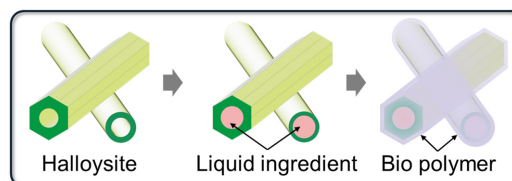


Fig. 2. Conceptual process for applying halloysite to a slow-release system of liquid ingredients.

2. Concepts of Halloysite Utilization as a Cosmetics Carrier

2.1. Sustained Release of a Liquid Ingredient

The encapsulation process of a liquid ingredient inside the halloysite lumen is shown in Fig. 2. The loading is accomplished via the suspension of the halloysite in the solution of a liquid agent in deionized (DI) water. If necessary, the concentration of the active agent needs to be reduced so that its viscosity can be adjusted as appropriate. After the addition of halloysite, the suspension is sonicated and is placed in a vacuum jar for some period, after which ambient air is allowed to enter the jar. The vacuum process is repeated three to four times to increase the loading efficiency. After the vacuum process, the sample is kept for a few days under atmospheric pressure, which may further increase the loading efficiency. After loading, the halloysite is separated from the solution via centrifugation and is washed with DI water.

Furthermore, the layer-by-layer (LbL) shell assembly of the polymers on a tubular halloysite further retards the release of the liquid ingredient, depending on the thickness and molecular weight of the polymer layers (Kelly *et al.*, 2004; Veerabadran *et al.*, 2009). For example, polyethylenimine (PEI) and polyacrylic acid (PAA) can be used to encapsulate the halloysite microtubes. Initially, negatively charged halloysite particles are suspended in a solution containing PEI for a period, after which the halloysite particles are removed from the solution via centrifugation and are resuspended in a PAA solution. The halloysite samples are washed with water before resuspension in consecutive polyelectrolyte solutions. Several bilayers of PEI/PAA can be deposited over the surfaces of the halloysite particles filled with a liquid ingredient.

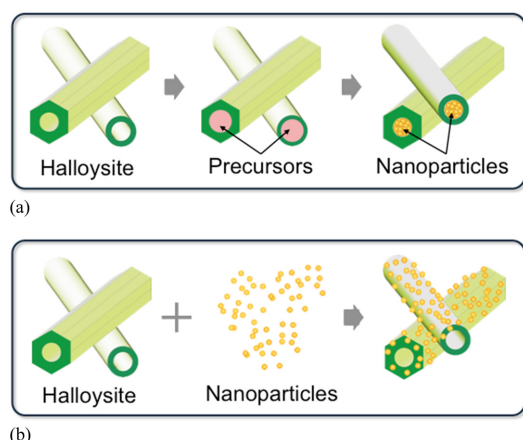


Fig. 3. Conceptual procedures for using halloysite as a substrate for immobilization of solid-phase materials: (a) *in situ* precursor solution method and (b) *ex situ* nanoparticle colloidal method.

2.2. Immobilization of a Solid-phase Ingredient

The immobilization procedures of a solid-phase ingredient inside the halloysite lumen and outside its surface are depicted in Fig. 3. The hybrid powder of halloysite and solid nanoparticles can be prepared by either of two methods. The first method is an *in situ* precursor solution method that generates solid nanoparticles inside halloysite by vacuum-pulling the nanoparticle precursor into the halloysite lumen. The second entails an *ex situ* nanoparticle colloidal method based on the direct loading of nanoparticles into halloysite.

The *in situ* precursor solution method is used to load solid nanoparticles into halloysite by adding halloysite in the early formation stages of the nanoparticles (Fig. 3a). A precursor solution is prepared and the halloysite powder is added to the solution. Next, the solution is vacuum pulled. Subsequently, the powder is collected by centrifugation and is washed with anhydrous ethanol or DI water to remove the residual precursor. Then, the collected powder is dispersed in a medium, and the resulting mixture undergoes a chemical reaction at a certain temperature for a predetermined period. After cooling the resulting solution to room temperature, the hybrid powder is collected by centrifugation and is washed with DI water.

The nanoparticle colloidal method is used to immobilize solid nanoparticles, which are prepared separately, directly into halloysite (Fig. 3b). First,

the solid nanoparticles are prepared in a separate process and are collected by centrifugation. The collected nanoparticles are added to DI water and are dispersed with ultrasonic waves to prepare a colloidal solution. Then, halloysite powder is added to the colloidal solution and the resulting mixture is vacuum pulled. Subsequently, the hybrid powder is collected by centrifugation and is washed with DI water.

3. Examples of Halloysite-cosmetics Hybrid Materials

3.1. Humectant-loaded Halloysite

On the basis of the previous research done by Suh *et al.* (2011), a cosmetic skincare application of halloysite for a liquid-ingredient loading is summarized. Glycerol, which is widely used in cosmetics, is a good candidate for such purpose. It is a skin-friendly humectant that promotes skin moisture retention. It also helps maintain the water balance in the intercellular matrix, and in so doing, maintains the skin's homeostasis. Halloysite microtubes with an about-15-nm internal lumen were used as cosmetic micro-containers for slowing down the release of glycerol. The halloysite was filled with glycerol in water to estimate its cosmetic-ingredient retention capability.

Glycerol loading occurs via two mechanisms: the entrapment of the glycerol inside the hollow tubules and its adsorption onto the surface of the tubules. The active agent glycerol initially releases via desorption mainly from the exterior surface of the halloysite, and then via diffusion from the ends of the microtubules (Price *et al.*, 2001). As such, the adsorbed portion of glycerol was washed off a few times to examine only the release from the inside lumen. Besides, glycerol-loaded halloysite was coated layer by layer with polyelectrolytes to additionally reduce the release rate.

The release profile of glycerol at a loading efficiency of 19 ± 3 mass% from a halloysite sample is shown in Fig. 4. The release took place in a steady manner for 28 h, indicating that halloysite is considered as a good container for glycerol's sustained release. Furthermore, no initial burst implies that most of the glycerol was loaded within the micro tubular lumen. The total release time of glycerol from the halloysite microtubes well exceeded

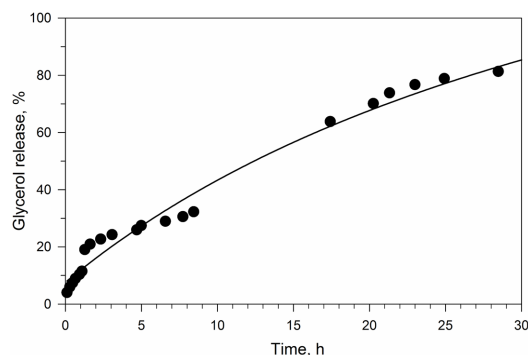


Fig. 4. Controlled release of the glycerol loaded inside the lumen of halloysite.

20 h, which is considered enough time for cosmetic applications. It is also found that despite the same basic crystalline structures among different samples, their performance strongly depended on their physical shapes such as the extent to which they contain open ends, well-developed hollow tubules, and edge pockets, as well as on their uniformity.

To further retard the glycerol release, the halloysite filled with glycerol was coated with a few layers of polyionic polymers. Halloysite has a tubular structure with a silica layer exposed on its surface, and tends to have an anionic surface with hydroxyl ions adsorbed on it, except at a very low pH. Hence, the initially negatively charged halloysite surface was adsorbed with the cationic polymer PEI and then with the anionic polymer PAA. Glycerol must diffuse through the polymer shells after traveling through the narrow lumen to reach the open ends of the halloysite. The polymer shells provide an additional barrier through which glycerol must diffuse and in turn slow down its release. However, there was no noticeable release-rate difference between before and after the multilayer coatings of the polymers. This result indicates that the LbL nanoassembly does not have a significant influence on the glycerol release rate. This is partially related to a small molecular weight of glycerol in that small and mobile glycerol molecules can easily pass through the openings of the LbL nanoshells (Byrne and Deasy, 2005). It can also be attributed to the higher solubility of glycerol in water, which helps the glycerol molecules diffuse through water due to their high concentration gradient (Levis and Deasy, 2003). The layers of

higher-molecular-weight polymers like chitosan or gelatin may cause higher retardation in the release rate of glycerol (Veerabadran *et al.*, 2009). Further, a more perspective approach to slowing down the glycerol release will be to admix small nanoparticles, which will make the ends of the tube lumen narrower (Lvov and Price, 2007).

3.2. Sunscreening Agent-immobilized Halloysite

The use of inorganic ultraviolet (UV) filters, such as TiO_2 and ZnO nanoparticles, has been increasing significantly, especially in sunscreen products for children and people with sensitive skin (Serpone *et al.*, 2007). The sunscreen is required to block the UV solar radiation over the whole UVB (290–320 nm) and UVA (320–400 nm) ranges, while being transparent to visible light for cosmetic aesthetics. To satisfy the cosmetic efficacy, TiO_2 nanoparticles in the range of 20–50 nm have been considered as an optimal material (Barnard, 2010; Barnard, 2011; Murphy, 1999).

On the other hand, TiO_2 nanoparticles of this size range have also been used as catalysts because of their high photoactive efficiency (Barnard, 2010; Barnard, 2011; Jiang *et al.*, 2008). The photoactive surfaces of the TiO_2 nanoparticles produce reactive oxygen species (ROS), such as $\cdot\text{OH}$, O_2^- , and H_2O_2 (Hirakawa and Nosaka, 2002; Hirakawa *et al.*, 2007; Nel *et al.*, 2006), which are known to be cytotoxic, e.g., to DNA plasmids and to the whole human skin cells (Dunford *et al.*, 1997; Serpone *et al.*, 2007). Moreover, as the dermal exposure to TiO_2 nanoparticles occurs regularly during the use of sunscreen products, nanoparticles penetration through the skin has become a growing concern (Barry, 2001; Bennat and Muller-Goymann, 2000; Lademann *et al.*, 2011; Lademann *et al.*, 1999; Menzel *et al.*, 2004; Nel *et al.*, 2006; Newman *et al.*, 2009; Oberdörster *et al.*, 2005; Tinkle *et al.*, 2003). In particular, the TiO_2 nanoparticles may enter the human body through the skin when a sunscreen lotion containing TiO_2 nanoparticles is rubbed on a skin area burned by the sun or damaged by acne.

Recently, Suh and Cho (2015) provided two synthetic methods to fabricate hybrid sunscreen powders, in which TiO_2 nanoparticles are immobilized onto halloysite. As described in the previous section of this paper (Fig. 3), they suggested two

fabrication routes: the *in situ* generation of the nanoparticles inside halloysite and the *ex situ* immobilization of the nanoparticles. The toxicity of the sunscreen nanoparticles can be prevented by immobilizing them in halloysite, reducing the chance of direct exposure of the skin to the nanoparticles themselves. As a result, the ROS generated by the UV light remain in the proximity of the nanoparticles inside the halloysite microtubes without entering in contact with the skin. In addition, the nanoparticles are located inside the lumen so that they cannot infiltrate through the halloysite.

The synthesized TiO_2 nanoparticles showed a strong extinction tendency across most of the UVB and UVA spectra, whereas halloysite is nearly transparent (Fig. 5). The UV-vis extinction of the nanoparticle suspensions can be determined by measuring the transmittance of the radiation between 250 and 500 nm (Tadros, 2008). The absorbance, $A = -\log(I/I_0)$, is calculated from the Beer–Lambert law, where I/I_0 , I , and I_0 represent the transmittance, intensity of the light transmitted through the sample, and intensity of the incident light, respectively (van de Hulst, 1981). The higher extinction capability of TiO_2 nanoparticles over halloysite is attributed to the dependence of the light scattering efficiency on the material optical properties, such as the refractive index (Murphy, 1999; van de Hulst, 1981). The broad-spectrum protection shown by the TiO_2 nanoparticles can impart high values of sun protection factor (SPF) at relatively low concentrations (Schueller and Romanowski, 2003). The hybrid powders show an intermediate absorbance between halloysite and bare TiO_2 nanoparticles at the same concentration, indicating the extent of the TiO_2 nanoparticle immobilization on halloysite. Here, the hybrid powder was prepared by following the nanoparticle colloidal method. The hybrid powder at 0.01 mass%, four times higher concentration than that of bare TiO_2 nanoparticles, showed higher absorbance in the UVB wavelength range than the bare TiO_2 nanoparticles at 0.0025 mass%. Notably, the increase of the hybrid powder concentration may not cause any problems in the cosmetic formulation, as the allowance on the concentration of sunscreens agents are based on the effective ingredients, i.e., TiO_2 . The sunscreen active concentration allowed by the US Food and Drug Administration (FDA)

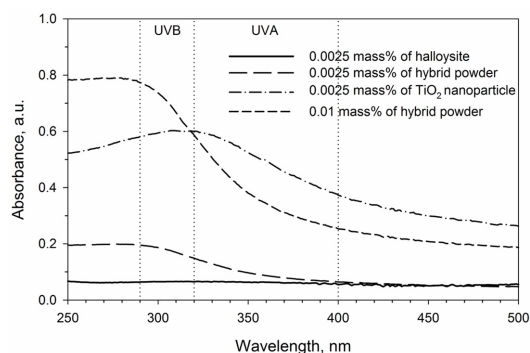


Fig. 5. Ultraviolet (UV) extinction efficiencies of halloysite-titania hybrid powders.

is 25 mass% for TiO_2 nanoparticles (Schueller and Romanowski, 2003). Although the increase in the total solid concentration can limit the usability, the adoption of a natural clay mineral in cosmetics is preferable for some applications.

The order of the representative extinction performance, which is defined by integrating the UV light absorbance with respect to wavelength over the UVB (290–320 nm) and UVA (320–400 nm) ranges, was TiO_2 nanoparticles > hybrid powder produced by the nanoparticle colloidal method > hybrid powder produced by the precursor solution method. The outer surface of halloysite in the hybrid powder prepared by the *in situ* precursor solution method is covered by a much smaller number of nanoparticles than that prepared by the *ex situ* nanoparticle colloidal method. Considering a rather narrow halloysite inner lumen and the TiO_2 particle size ($15 \times 70 \text{ nm}^2$), a higher amount of TiO_2 nanoparticles can be immobilized in the case of the nanoparticle colloidal method. Despite the lower sunscreens efficiency, however, the precursor solution method would be considered more advantageous if the contact between the photocatalytic particles and the skin has to be avoided.

4. Conclusions

Halloysite, a naturally occurring benign clay mineral, possesses potential advantages in the applications of cosmeceuticals. Halloysite is proven to be useful for the sustained release of a liquid ingredient as demonstrated by the extended release of glycerol

in aqueous environments. It also appears effective to immobilize a solid nanomaterial like a sun-screening agent, titania, both in the lumen and onto the outside surface. Furthermore, layer-by-layer coatings of biocompatible polymers such as chitosan may enhance its applicability. The unique surface characteristics of halloysite will provide more chance to multiply its merits; the outer surface comprises a silicate SiO_2^- layer, whereas the inner surface comprises an alumina Al_2O_3^+ layer. All these schemes may be integrated to attain the full functionality of active ingredients. It should be noted that halloysite can be employed to suppress negative side effects of active ingredients such as toxicity while minimally sacrificing their intended functions. Therefore, it is expected that tubular halloysite will find a wide range of applications in cosmetics, such as humectants, sunscreens, anti-ageing agents, nutrients, fragrances, deodorants, and other functional agents. More studies on the cosmetic applications of halloysite should be undertaken to offer its high potential for everyday use.

Acknowledgments

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