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High barrier function to moisture, oxygen and odor of novel poly(vinylalcohol -acrylic acid-methylmethacrylate) (POVACOAT®) as a coating film

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Abstract
Purpose: POVACOAT is a newly developed aqueous polymer which is poly (vinyl alcohol) derivative grafted with acrylic acid and methyl methacrylate. POVACOAT is applied to coating film, granulation binder and solid dispersion carrier etc. This study focused on the improvement of moisture permeability of POVACOAT under higher relative humidity conditions by adding a pharmaceutical pigment. **Methods:** In order to evaluate the moisture permeability, the aluminum casing with the isolated film which was attached on the opening part (40 mm × 40 mm) was used. The aluminum casing was heat-sealed, after 3.0 g of calcium chlorides was put into the inside as a moisture absorption agent. The increase in weight per 24 hours of the calcium chloride under various relative humidity was measured, and the moisture permeability coefficient was calculated. **Results:** The moisture permeability coefficients of POVACOAT film showed a typical sigmoid change as relative humidity increased. It was found that the permeability coefficients under higher relative humidity were excellently modified to be in a level of 1/6 against simple POVACOAT film by adding talc.
Keywords: PVA copolymer, POVACOAT, pharmaceutical excipient, film coating, moisture permeability

1. Introduction

POVACOAT [1)] is a newly developed aqueous polymer which is poly (vinyl alcohol) derivative grafted with acrylic acid and methyl methacrylate. The chemical structure is shown in Fig. 1. POVACOAT is applied to coating film[5)], granulation binder[3,5)], solid dispersion carrier[2,4)] and so on. POVACOAT was registered to Drug Master Files of US as DMF18033, and Master Files of Japan as 219MF20003.

Many investigators reported that drug degradation under higher humidity conditions occurred due to hydrolysis reaction. In this study, the moisture permeability of simple POVACOAT film was evaluated first. Furthermore, the improvement of moisture barrier tendency under relative humidity condition, i.e., 75% R.H. at 40°C, was studied by adding commonly used pharmaceutical pigment.

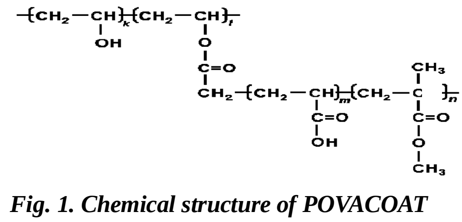

Fig. 1. Chemical structure of POVACOAT

2. Materials and methods

2.1. Materials

POVACOAT (Type F; Daido Chemical Corp., Japan), talc (Nippon Talc, Japan) and titanium dioxide (Toho Titanium, Japan) were used and hydroxypropylmethylcellulose (HPMC, TC5-R, Shin-Etsu Chemical, Japan) was used as a reference polymer. Calcium chloride (Wako Chemical, Japan) was used as a moisture absorption agent.

2.2. Measurement of moisture permeability

In order to evaluate the moisture permeability, the aluminum casing with the isolated film which was attached on the opening part (40 mm × 40 mm) was used (Fig. 2). The aluminum casing was heat-sealed, after 3.0 g of calcium chloride was put into the inside. The increase in weight per 24 hours of the calcium chloride under various relative humidity was measured. The moisture permeability was denoted by the coefficient of permeability in unit of mg・cm/cm²・day・cmHg.

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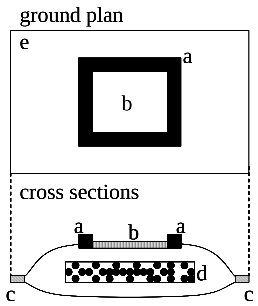


a; silicon type adhesive, b; a casting film
c; heat-seal, d; calcium chloride, e; aluminum casing

Fig. 2. Schematic diagram of moisture permeability experiment

3. Results and discussion

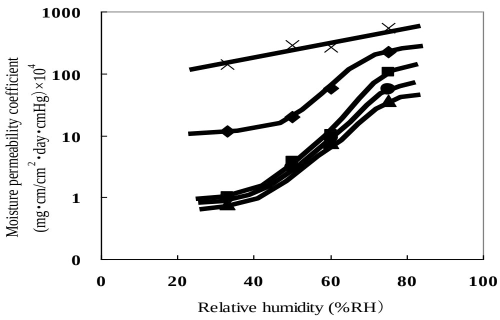
3.1.Moisture permeability of simple POVACOAT film

The moisture permeability coefficients under various relative humidity by using the casting films of POVACOAT and HPMC were measured. The results are shown in Fig. 3.

The moisture permeability coefficient of the HPMC film was gradually increased with the increase of relative humidity while that of POVACOAT film showed a typical sigmoid change. In case of lower humidity condition, POVACOAT film is assumed to exist in lower mobility state of polymer segments due to strong hydrogen bonding [6)]. Therefore, the diffusion coefficient of water might be small. On the other hand, under the higher humidity condition, for example 75% R.H., the increase of moisture uptake might decrease the glass transition temperature of polymer. Accordingly the diffusion coefficient of water is assumed to be larger.

3.2.Effect of addition of talc on moisture permeability

In order to improve the moisture permeability of POVACOAT under higher humidity conditions, the effect of pigment addition was investigated. Talc and TiO_2 were used as powdery additives. It was found that talc was very effective to decrease the moisture permeability in a level of 1/6 against simple POVACOAT/talc (30 w/w%) film as shown in Fig. 3. TiO_2 addition was not effective. The permeability (P) is defined from concentration of diffusant in film (S) multiply diffusion coefficient (D) of it. (P=S・D). It is assumed that addition of talc might increase tortuosity against diffusion pathway due to



◆; POVACOAT only ■; Talc 10%, ●; Talc 30%,
▲; Talc 50%, ×; HPMC only

Fig. 3. Plots of moisture permeability coefficient against relative humidity

its sheet-like small crystalline property –a well-known modification method in film industry–, leading to the depression of moisture permeability.

The mechanical properties such as the strength and elongation of the film were confirmed to be comparable with simple POVACOT film (data not shown).

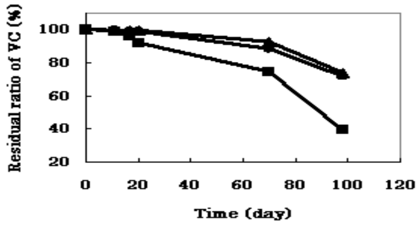
3.3. Oxygen barrier function of talc formulation

Oxygen barrier effect of POVACOAT casting film containing 30 w/w% of talc was evaluated and the result is shown in Fig. 4. The experiment was carried out in the similar manner of moisture permeability testing as follows: the mixture of ascorbic acid powder and 1 w/w% $CuSO_4$ as an oxidization catalyst for ascorbic acid was put into the inside of aluminum casing and heat-sealed. Residual contents of ascorbic acid under storage at 40°C and 75% R.H. were measured according to the JP assay of ascorbic acid (titration method).

Oxygen barrier effect of 30% talc–added POVACOAT film was found to be the same level to the aluminum sealing as a control.

3.4. Film Coating performance of talc formulation

In order to evaluate the applicability of talc formulations, coating experiment of tablets was carried out by using a perforated coating machine



●;POVACOAT(30w/w% talc) ■; HPMC ▲; Control(Alminum)

Fig. 4. Oxygen barrier effect of the films

(Dria-coater500; Powrex Japan). Table 1 shows the operational parameters of coating. The film coating process for talc formulation could be achieved in the same manner of simple POVACOAT formulation.

Table 1. Operational parameters of coating

Feeding, Tablet size	3.9 kg, 8φ12R 200mg
Inlet / Outlet temperature	70°C / 47°C,
Inlet-air velocity	3.6 m^3/min
Atomize / Pattern air	120 / 110L/min
Revolution speed of drum	12 rpm
Spray rate	30 g/min
Concentration of solution (25% aqueous ethyl alcohol)	14% (POVA 7%,Talc 7%)

Obtained film coating tablets with varying film amounts were stored under 40°C and 75% R.H. for the estimation of moisture uptake of tablets. Over 5 wt% of coating amounts was found to be very effective to moisture barrier as expected from the casting film experiments. Talc/POVACOAT formulations are already used in the marketed products as also an odor resistance coating film.

4. Conclusion

The moisture permeability of POVACOAT film showed a sigmoid change as relative humidity increased. It was found that the permeability coefficients under higher relative humidity were excellently modified to be applicable to the actual products by adding talc.

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