약제학회지(1991), 제21권 제1호
J. Kor. Pharm. Sci., Vol. 21, No. 1, 51-55(1991)

The Entrapment of Vitamin E Acetate in Porous Spheres

Yoon-Jeong Yang†, Bong-Jin Bae, Kyu-Sik Lee and In-Koo Chun*

*Lamy Cosmetics Co., Ltd. and *College of Pharmacy, Dongduck Women's University*
*Kyungki-do 467-800, Korea and *Seoul 136-714, Korea*

(Received March 11, 1991)

다공성 미소구체 중 초산토코페롤의 봉입에 관한 연구

양윤정†· 배봉진 · 이규식 · 전인구*
라미화장품연구소, *동덕여자대학교 약학대학

(1991년 3월 11일 접수)

Porous spheres composed of natural waxes and inorganic materials containing vitamin E acetate as a drug were prepared by impregnation method. Furthermore, the amount of vitamin E acetate entrapped in the spheres and the release rate of vitamin E acetate from the spheres were studied. The impregnation of vitamin E acetate was carried out by dipping the spheres in vitamin E acetate solutions. Entrapment mechanism of vitamin E acetate could be expressed in terms of Langmuir's adsorption isotherm. The amount of vitamin E acetate entrapped in porous spheres was influenced by the structure and concentration of the polymer used in vitamin E acetate solutions, and the concentration of vitamin E acetate. Release characteristics of vitamin E acetate from the spheres were investigated by withdrawing samples periodically and analyzing them by spectrophotomer.

Keywords—porous sphere, vitamin E acetate, entrapment, release characteristics, kinetic analysis

Efforts have been ongoing for a long time to blend cosmetics with scrubbing materials.[1] The primary purpose of such efforts is to cleanse and beautify the skin. Initially, sand was used as a scrubbing agent; some other agents that have been used include endocarps (seeds of natural plants), waxes and splited synthetic resins. However, these agents could cause a minor skin trauma or may compromise the barrier properties of the skin due to the mechanical abrasive action. The development of porous spheres allowed for a scrubbing action which could overcome these disadvantages.[2-4] The porous spheres are composed of natural waxes and inorganic substances. This research investigated the kinetics of entrapment of vitamin E acetate[5] in porous spheres (Lamy Cosmetics Co., Ltd.) and also the release characteristics and the influence of polymers on the entrapment and release of the drug.

Experimentals

Materials

All reagents used were of analytical grade quality. Some special materials used and their suppliers are as follows; porous spheres (Lamy Cosmetics Co., Ltd., Korea), isopropyl myristate and isopropyl palmitate (Inolex Chem. Co., USA), viny-

†To whom correspondence should be addressed. This paper was presented in the 28th scientific meeting of the Society of Cosmetic Chemists of Japan held on June 21-22 in Kobe, Japan in 1990.

lpyrrolidone/vinyl acetate copolymers [molar ratio 7 : 3 (PVP/VA E 735), 6 : 4 (PVP/VA E 535), 3 : 7 (PVP/VA E 335)], alkylated vinylpyrrolidone polymer (Antaron V-216), vinylpyrrolidone/dimethylaminoethylmethylmethacrylate copolymer (Copolymer 958, Gaf Co., West Germany).

Impregnation of Vitamin E Acetate into Porous Spheres

Vitamin E acetate was entrapped into porous spheres by impregnation.[6] Porous spheres used had a porosity of 20.74 v/v% and a particle size of 149-297 μm. Twenty gram of the spheres were soaked in 50 m*l* of a 5-50 w/w% vitamin E acetate solution at room temperature and then the mixture was operated under pressure and vacuum alternately three times at intervals of 5 min. After filtration, drying was done at 30℃ for 24 hrs. Free drug on the surface of the dried spheres was washed off by using 250 m*l* of washing solution, which was a mixture of ethanol and cyclohexane (7 : 3 v/v%) and agitating at 380 rpm for 5 min. The washed spheres were dried at room temperature for 24 hrs to completely remove all organic solvents.

Assay for Drug Content

0.5 g of vitamin E acetate-containing spheres were accurately weighed and extracted with 5 m*l* of cyclohexane at 80℃. After cooling, the solidified mass was separated by centrifugation.[7] The supernatant was suitably diluted with cyclohexane. The drug amount extracted from the spheres was measured by determining the absorbance of the solution at 285.5 nm[8] and calculations were done for the amount entrapped in the spheres.

Release Studies

Release studies were carried out using a basket type dissolution apparatus and 125 m*l* of a mixture (8 : 2 v/v%) of 50% aqueous ethanol and cyclohexane as the dissolution medium. The release studies was conducted at 25℃. One gram of the impregnated spheres was placed into the net of 100 mesh nylon,[9] fastened 2.5 cm high from the bottom of the vessel, and rotated at 100 rpm. The dissolution apparatus was tightly sealed throughout the release studies for the prevention of evaporation. Samples were withdrawn at given time intervals and diluted suitably with the dissolution medium. Absorbance was measured at 285.5 nm and the drug amount released was calculated from the previously prepared calibration curve.

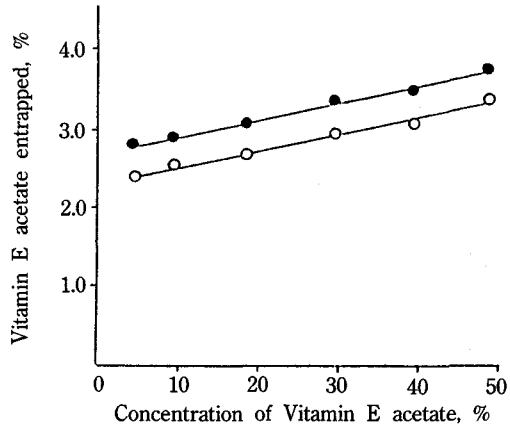

Figure 1—Effect of concentration of Vitamin E acetate, on the amount of Vitamin E acetate entrapped. Key: Solvent; ○, IPM; ●, IPP.

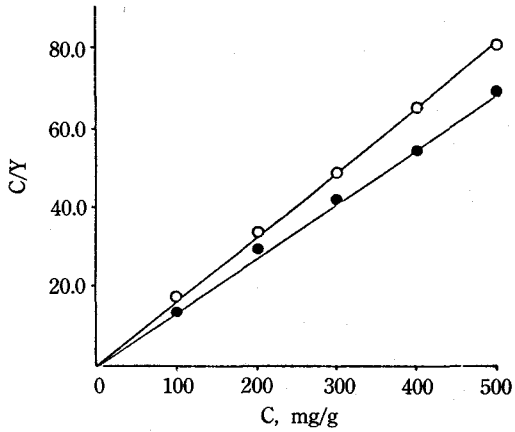

Figure 2—Plots of C/Y vs. concentration of Vitamin E acetate (C). The symbols are the same as those in Fig. 1

Results and Discussion

Kinetics of Entrapment

Fig. 1 shows the relationship between the concentration of the vitamin E acetate solution and the amount of drug entrapped at each concentration, while making the vitamin E acetate-containing spheres. As can be seen from Fig. 1, the amount of drug entrapped increased slowly with

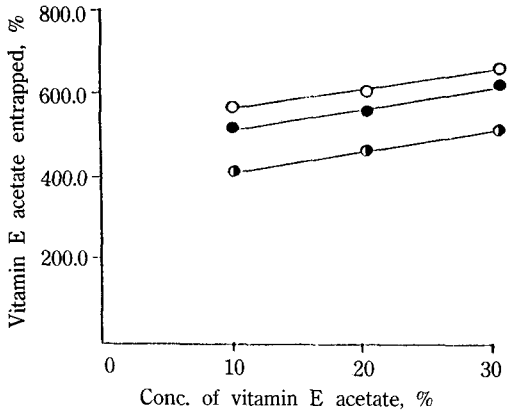

Figure 3—Effect of structure of polymers on the amount of vitamin E acetate entrapped. Key: ○, Copolymer 958; ●, PVP/VA E735; ◑, Antaron V-216.

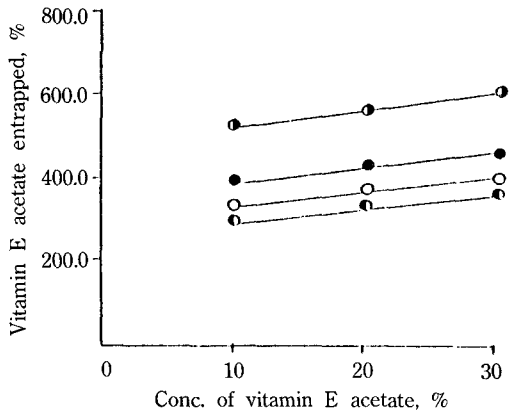

Figure 4—Effect of molar ratio of PVP/VA E grades on the amount of vitamin E acetate entrapped. Key: ◑, 7 : 3; ●, 6 : 4; ○, 5 : 5; ◐, 3 : 7.

increasing concentration of vitamin E acetate. Fig. 2 shows the relationship between C (the concentration of vitamin E acetate) and C/Y according to equation 1, which reveals the straight line. This indicates the Langmuir type adsorption isotherm[10] for the entrapment

$$C/Y = C/Ym + 1/b\ Ym \quad (1)$$

Where C is the concentration (mg/g) of vitamin E acetate in the solution, Y is the amount (mg/g spheres) of vitamin E acetate entrapped, Ym is the saturable amount (mg/g spheres) of vitamin E acetate in the spheres, and b is the equilibrium constant.

The equilibrium constant (b) was found to be different slightly from each other depending on the kind of solvent used.

Effect of Polymers on the Amount Entrapped

The effect of increasing vitamin E acetate concentration on the amount entrapped has been discussed earlier. This section will discuss the use of pyrrolidone polymers in order to investigate the correlation between the structure of polymer and the influence of polymer on the amount entrapped. The polymers used were PVP/VA E 735, Antaron V-216 and Copolymer 958 at a concentration of 5% each, and the amount of drug entrapped in the spheres was plotted as a function of increasing concentration of vitamin E acetate in the polymer solution. As indicated in Fig. 3, it was found that drug amount entrapped increased with increasing concentration of vitamin E acetate and the rank order for the effectiveness of the polymers in increasing the amount entrapped was copolymer 958>PVP/VA E 735>Antaron V-216. Fig. 4 shows, as a result of Fig. 3, the linear relationship between C and C/Y. In an attempt to look into the effect of copolymer according to its molar ratio, the amount entrapped was plotted as a function of increasing drug concentration of polymer solution at a concentration of 5% each for PVP/VA E 735 (molar ratio 7 : 3), PVP/VA E 635 (6 : 4), PVP/VA E 535 (5 : 5) and PVP/VA E 335 (3 : 7). As can be seen from Fig. 4, it was found that the drug amount entrapped increased in the rank of PVP/VA E 735>PVP/VA E 635>PVP/VA E 535 >PVP/VA E 335 with increasing proportion of PVP in the PVP/VA copolymer. The effect of polymer concentration in vitamin E acetate solution on the amount entrapped was also studied. Copolymer 958 was used in the concentrations of 1, 3 and 5% each in 0-30% vitamin E acetate solutions. As shown in Fig. 5, it was found that the amount entrapped increased depending on increasing concentrations of the polymer and vitamin E acetate.

Drug Release Characteristics

Fig. 6 shows the release pattern of vitamin E acetate from the spheres prepared using different polymer solutions. According to Higuchi's diffu-

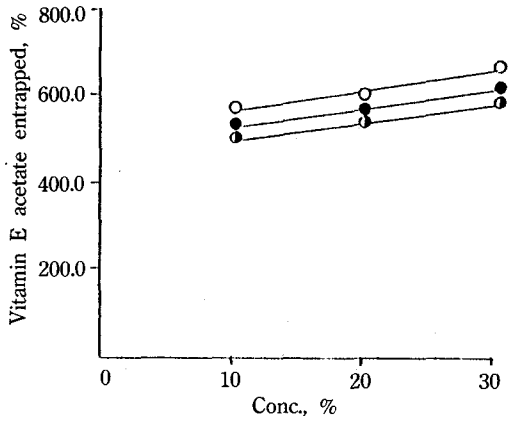

Figure 5—Effect of polymer (Copolymer 958) concentration on the amount of Vitamin E acetate. entrapped. Key: ○, 5%; ●, 3%; ◑, 1%.

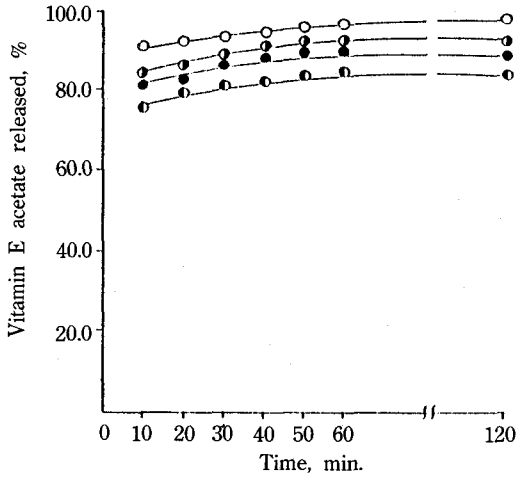

Figure 6—Release of Vitamin E acetate from spheres. Key: ◑, Antaron V-216; ●, PVP/VA E735; ◐, Copolymer 958.

sion[11] (Eq. 2) and first-order release[12] (Eq. 3) models, the release rate constants of vitamin E acetate from the spheres were calculated. The results are summarized in Table I. As indicated in Table I, the correlation coefficients (r) by Eq. 2 are larger than those by Eq. 3, indicating that the release of vitamin E acetate from the spheres followed Higuchi's diffusion model.

$$Q' = K't^{1/2} \quad (2)$$

Where Q' is the total amount of vitamin E acetate released from the spheres within a certain period of time (t), and K' is the release rate constant.

$$\log A' = -\frac{Kt}{2.303} + \log A_o \quad (3)$$

where A' is the amount of vitamin E acetate remaining in the spheres ($A_o - Q'$), A_o is the initial amount of vitamin E acetate in the spheres, and K is the first-order release rate constant.

Table I—*Comparison Linearization of Release Rates by First-Order (K) and Diffusion Model (K') for Vitamin E Acetate Spheres Using Polymers.*

Polymer, 5%	Diffusion model		First-order kinetic	
	K', mg/min$^{1/2}$	r	K, min	r
No polymer	13.03	0.9927	−0.014	0.9801
PVP/VA E 735	15.06	0.9916	−0.020	0.9752
Antaron V-216	15.72	0.9916	−0.018	0.9714
Copolymer 958	18.52	0.9908	−0.006	0.9702

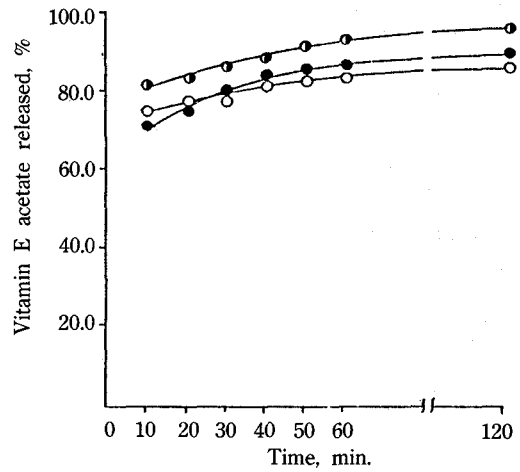

Figure 7—Effect of polymer (PVP/VA E735) concentration on release of Vitamin E acetate. Key: ◑, 5%; ○, 10%; ●, 15%.

Effect of Polymer Concentration on Drug Release

The experiment outlined above revealed that there was a slight change in the rate of drug release in accordance with the kind of polymers which were added to the vitamin E acetate solution. On the other hand, it was observed that the release rates of vitamin E acetate from the spheres were slightly increased with increasing conce-

Table II—*Time Required to Release 50% of Vitamin E Acetate (T_{50}) from Spheres against Concentration of PVP/VA E735.*

PVP/VA E735 concentration (%)	T_{50} (min)
0	14.72
5	11.02
10	10.94
15	10.50

ntration of PVP/VA E 735 in vitamin E acetate solution (Fig. 7). However, marked change in release rate was not observed. The times (T_{50}) required to release 50% of vitamin E acetate from the spheres are summarized in Table II. With increasing concentration of the polymer, T_{50} was reduced somewhat but there was no significant change.

Conclusions

Vitamin E acetate, as a model drug, was entrapped in the porous spheres by impregnation. The kinetics of entrapment of vitamin E acetate and its release characteristics were found to be as follows; First, the drug entrapment followed the Langmuir adsorption isotherm. Second, the drug amount entrapped increased with increasing concentration of vitamin E acetate and the effectiveness of the polymers in increasing the amount entrapped had the rank order of vinylpyrrolidone/dimethylaminoethylmethyl methacrylate copolymer>vinylpyrrolidone/vinyl acetate copolymer (molar ratio 7 : 3)>alkylated vinylpyrrolidone polymer. The molar ratio of vinylpyrrolidone/vinyl acetate copolymer influenced the drug entrapment in the rank order of 7 : 3 > 6 : 4 > 5 : 5 >3 : 7. Third, the release of vitamin E acetate from the spheres appeared to follow the Higuchi's matrix diffusion model, and the release patterns varied depending on the kind and concentration of polymers added in vitamin E acetate solution.

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