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International Journal of Pharmaceutics 187 (1999) 125–135

international journal of pharmaceutics

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Reduction of tablet coloration at tableting for oily medicine (tocopheryl nicotinate)☆

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Received 3 December 1998; received in revised form 27 March 1999; accepted 10 May 1999

Abstract

The powder (TN-PO) which adsorbed D,L-tocopheryl nicotinate (TN) as an oily medicine was prepared using porous calcium silicate (Florite®RE, FLR) as an adsorbing carrier. Tablets (TN-TAB) were produced by compression of TN-PO at different compression pressures. As TN-PO was compressed at the higher TN content in TN-PO and compression pressure, the more TN was exuded from TN-PO, and an increase in the degree of tablet coloration was observed. Therefore, FLR or colloidal silica (AEROSIL®200, AER) was newly added to TN-PO at compression to reduce the degree of tablet coloration. Further, the effects of addition of FLR or AER on the crushing strength, friability, porosity and disintegration property of the tablet and the dissolution property of TN from the tablet were studied. After addition of FLR or AER, a similar reduction of tablet coloration was observed. When the addition percentage of FLR to TN-PO exceeded 30%, the crushing strength of the tablet increased significantly. On the other hand, when TN-PO added with AER was compressed, no change was observed in the crushing strength of the tablet. The disintegration time of the tablet with added FLR was shorter than that of the tablet with added AER. At every addition percentage studied, the tablet with added FLR showed a higher releasing ability of TN compared with the tablet with added AER. These results indicate that it is possible to reduce tablet coloration by adding FLR or AER at compression of TN-PO. Further, it is considered that the differences in the crushing strength, disintegration property and dissolution property of TN between the tablets with added FLR or AER resulted in different liquid adsorbing and holding mechanisms of FLR particles and AER particles.

Keywords: Calcium silicate; Coloration; Compression; Oily medicine; Tablet; Tocopheryl nicotinate

☆ We designate this article as Part IV of 'Studies on Production of Higher Functional Pharmaceutical Preparations by Using Various Additives'. Parts I, II and III of the series are 'Application of calcium silicate for medicinal preparation. I' published in Chem. Pharm. Bull. 42 (1994) 2327–2331; 'Studies on the development of intragastric floating preparation. I' published in Chem. Pharm. Bull. 44 (1996) 1361–1366; and 'Studies on production of higher functional pharmaceutical preparations by using various additives. III' published in Chem. Pharm. Bull. 46 (1998) 1173–1176, respectively.

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0378-5173/99/$ - see front matter
PII: S0378-5173(99)00179-9

1. Introduction

Oily medicines have generally been produced and put on the market in soft capsule form (Takeuchi et al., 1992). To make a solid preparation of an oily medicine can be expected to improve its compliance and utility for patients and reduce the production cost (Kimura et al., 1989; Takeuchi et al., 1991). In our previous paper (Yuasa et al., 1994), we have reported that it was possible to granulate an oily medicine by adsorbing D,L-tocopheryl nicotinate (TN), an oily medicine, to porous calcium silicate (Florite®RE, FLR), which has a porous structure and an excellent liquid-holding ability. Our purpose in this paper is to study the tableting of TN using FLR as an adsorbing carrier. In addition, we studied the possibility of the reduction of tablet coloration by TN exudation at compression, because TN is expected to be exuded from TN-PO to the surface of the tablet by compression.

2. Materials and methods

2.1. Materials

D,L-Tocopheryl nicotinate (TN) was supplied by Sagami Kasei (Japan). The melting point and density are 38°C and 0.99 g/cm^3, respectively. Porous calcium silicate (Florite®RE, FLR, Eisai, Japan) was used as an adsorbing carrier for TN. FLR was used after drying at 80°C for 15 h. FLR or Colloidal silica (Aerosil®200, AER, Nippon Aerosil, Japan) was used as an additive at compression. Hydroxypropylstarch (HPS, Freund Industrial, Japan) was used as a disintegrator. Tween 80, a surfactant, was purchased from Kanto Kagaku (Japan).

2.2. Preparation of FLR powder with adsorbed TN

TN solutions of 10–60% concentrations were prepared by dissolving TN in ethanol. While stirring, 7 g of FLR was added to 100 g of TN solution, and was further stirred for 30 min in order to adsorb TN solution to the pores of FLR. FLR powder with adsorbed TN solution was recovered by suction filtering and dried at 80°C for 15 h. After being dried, FLR powder with adsorbed TN was passed through a 100-mesh (150 μm) sieve. Then six types of FLR powders with different contents of TN (TN-PO) were obtained.

2.3. Measurement of physical properties of TN-PO

The TN content in each type of TN-PO was determined by spectrophotometry after extracting TN with ethanol. The density of each type of TN-PO was measured by using an air comparison pycnometer (model 1000, Toshiba-Beckman, Japan). The specific surface area was measured by the air permeability method, employing a specific surface area meter (type SS-100, Shimadzu Seisakusho, Japan), and the apparent particle size of each type of TN-PO was determined by Eq. (1),

$$S_w = 6/\rho \cdot D \quad (1)$$

where S_w is specific surface area, ρ is density and D is apparent particle size. The angle of repose was measured by using a Konishi angle of repose meter (model FK, Konishi Seisakusho, Japan).

2.4. Observation of the surface of FLR powder and TN-PO

A scanning electron microscope (S-2250N, SEM, Hitachi, Japan) was used to observe the surface of FLR powder and TN-POs with 10, 30 and 60% TN contents.

2.5. Compression of TN-PO

A total of 250 mg of FLR or 300 mg of TN-PO with each TN content was compressed by using a universal testing machine (model TCM-5000C, Minebea, Japan) with a die and flat-faced punches of 1 cm^2 cross-section, and tablets with different TN contents were produced (TN-TAB). The compression pressures and compression speed were 500, 1000, 1500 and 2000 kg/cm^2 and 50 mm/min, respectively.

2.6. Compression of TN-PO with FLR or AER

To study the reduction of tablet coloration by exudation of TN at compression, the tablets with different addition percentages of FLR (TNF-TAB) or AER (TNA-TAB) were produced by compressing TN-PO (which was prepared from 60% TN solution) with different amounts of FLR or AER newly added. The compression pressure was 1000 kg/cm^2, which could produce a tablet having about 5 kgf of crushing strength when TN-PO was compressed without FLR or AER. The compression speed was 50 mm/min. The formulations of TNF-TAB and TNA-TAB are shown in Table 1.

2.7. Measurement of physical properties of tablets

The crushing strength and friability were measured by using a hardness tester (Kiya Seisakusho, Japan) and a friability tester, respectively. The porosity of TN-TAB and those of TNF-TAB and TNA-TAB were calculated following (Eq. (2)) and (Eq. (3)), respectively.

$$\varepsilon_1 = 1 - \{(\rho_{FLR}A_{FLR} + \rho_{TN}A_{TN})/(\rho_{FLR}\rho_{TN}V)\} \quad (2)$$

$$\varepsilon_2 = 1 - \{(\rho_{FLR}A_{FLR} + \rho_{TN}A_{TN} + \rho_E A_E) /(\rho_{FLR}\rho_{TN}\rho_E V)\} \quad (3)$$

where ε_1 and ε_2 are porosities of TN-TAB and TNF-TAB (or TNA-TAB), respectively, ρ_{FLR}, ρ_{TN} and ρ_E are densities of FLR, TN in TN-PO and FLR (or AER) added to TN-PO, respectively, A_{FLR}, A_{TN} and A_E are amounts of FLR, TN in TN-PO and FLR (or AER) added to TN-PO, respectively, and V is volume of each type of tablet.

2.8. Evaluation method of the degree of tablet coloration by TN exudation to tablet surface during compression

The surface color of the tablet was measured by using a color meter (Nippon Denshoku Kogyo, Japan) and then the color difference (ΔE) was calculated following a color difference equation (Eq. (4)) (JIS, 1980; Yuasa et al., 1995). The degree of TN exudation to tablet surface by compression was evaluated from the ΔE value.

$$\Delta E^*ab = \{(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2\}^{1/2} \quad (4)$$

where ΔE^*ab is color difference in the $L^*a^*b^*$ system, ΔL^* is difference between lightnesses of standard plate and tablet in the $L^*a^*b^*$ system and Δa^* and Δb^* are differences between chromaticity coordinates in the $L^*a^*b^*$ system. L^*, a^* and b^* were calculated following Eq. (5), Eq. (6) and Eq. (7), respectively.

$$L^* = 116(Y/Yn)^{1/3} - 16 \quad (5)$$

$$a^* = 500\{(X/Xn)^{1/3} - (Y/Yn)^{1/3}\} \quad (6)$$

$$b^* = 200\{(Y/Yn)^{1/3} - (Z/Zn)^{1/3}\} \quad (7)$$

where L^* is lightness in the $L^*a^*b^*$ system, a^* and b^* are chromaticity coordinates in the $L^*a^*b^*$ system, X, Y and Z are tristimulus values in the XYZ system and Xn, Yn and Zn are tristimulus values in the XYZ system at perfect reflection face.

Table 1
Formulations of TNF-TAB and TNA-TAB

Materials	Addition percentage of FLR in TNF-TAB						Addition percentage of AER in TNA-TAB		
	0%	10%	20%	30%	50%	70%	10%	30%	70%
TN-PO (mg)	25.0	202.5	180.0	157.5	112.5	67.5	202.5	157.5	67.5
FLR (mg)	–	22.5	45.0	67.5	112.5	157.5	–	–	–
AER (mg)	–	–	–	–	–	–	22.5	67.5	157.5
HPS (mg)	75.0	75.0	75.0	75.0	75.0	75.0	75.0	75.0	75.0
Total (mg)	300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0	300.0

Table 2
Physical properties of TN-PO[a]

Concentration of TN solution (%)	TN content (%)[b]	Density (g/cm^3)	Apparent particle size (μm)	Angle of repose (°)
10	32.10 ± 0.5	2.15 ± 0.019	0.51 ± 0.002	33.0 ± 0.3
20	53.6 ± 1.5	1.60 ± 0.011	0.71 ± 0.002	36.0 ± 0.3
30	99.2 ± 1.3	1.58 ± 0.004	0.96 ± 0.006	39.0 ± 0.3
40	143.9 ± 1.5	1.36 ± 0.001	1.31 ± 0.007	40.5 ± 0.4
50	177.2 ± 2.3	1.32 ± 0.003	1.84 ± 0.019	43.0 ± 0.3
60	219.5 ± 3.2	1.28 ± 0.001	2.88 ± 0.024	41.0 ± 0.3

[a] Data represent means ± S.D. ($n = 3$).
[b] Weight percent of TN to FLR.

2.9. Disintegration test and dissolution test

Using a disintegration tester (HM-4D, Miyamoto Riken, Japan) the disintegration tests of TNF-TAB and TNA-TAB were carried out following the disintegration method in J.P.XII. Purified water was used as the medium.

The release profiles of TN from TNF-TAB and TNA-TAB were observed according to the paddle method (J.P.XII). A total of 900 ml of the first fluid added with 9 g of Tween 80 as a surfactant was used as the dissolution medium as well as in the previous paper; 5 ml of the sample solution was taken out, filtered through a membrane filter (pore size, 0.5 μm; Nihon Millipore, Japan) at appropriate intervals. The TN content was determined from the absorbance at 264 nm.

3. Results and discussion

3.1. Effects of TN content on physical properties of TN-PO

Table 2 shows the TN contents, densities, apparent particle size and angles of repose of TN-POs prepared with different concentrations of TN solutions. The density of TN-POs decreased with increasing TN content. This may be due to the fact that the density of TN (0.99 g/cm^3) is smaller than that of FLR (2.27 g/cm^3). The apparent particle size and angle of repose increased with the increasing TN content. Fig. 1 shows SEM photographs of a FLR particle or TN-POs with 10, 30 and 60% TN contents. It was observed that the pores in TN-POs were filled with TN with increasing TN content. These results suggest the following mechanism. When TN-POs were prepared, the amount of TN remaining in the upper parts of pores, on the surface and in the pores of the FLR particles increased with increasing TN content. The specific surface area of TN-PO decreased as the granulation occurred during the preparation of TN-PO, because TN remaining on the particle surface acted as a binder, and TN remaining in the pores reduced the surface area in the pores, causing the specific surface area of TN-PO to decrease. As a result, the apparent particle size increased with the increasing TN content. The angle of repose of TN-PO increased with the increasing TN content because a large friction occurred when the particles flowed since TN remaining on the surface of FLR particles adhered to other FLR particles.

3.2. Effects of TN content and compression pressure on mechanical strength of TN-TAB

The effects of TN contents and compression pressure on the crushing strength and friability of TN-TAB are shown in Fig. 2 and Fig. 3, respectively. In Fig. 2, the crushing strength became lower with higher TN content at every compression pressure studied, and TN-TABs with 99.2% or more of TN content showed about 10 kgf or less of crushing strength. We have already reported that FLR particles fracture brittlely and are deformed plastically, and have a high com-

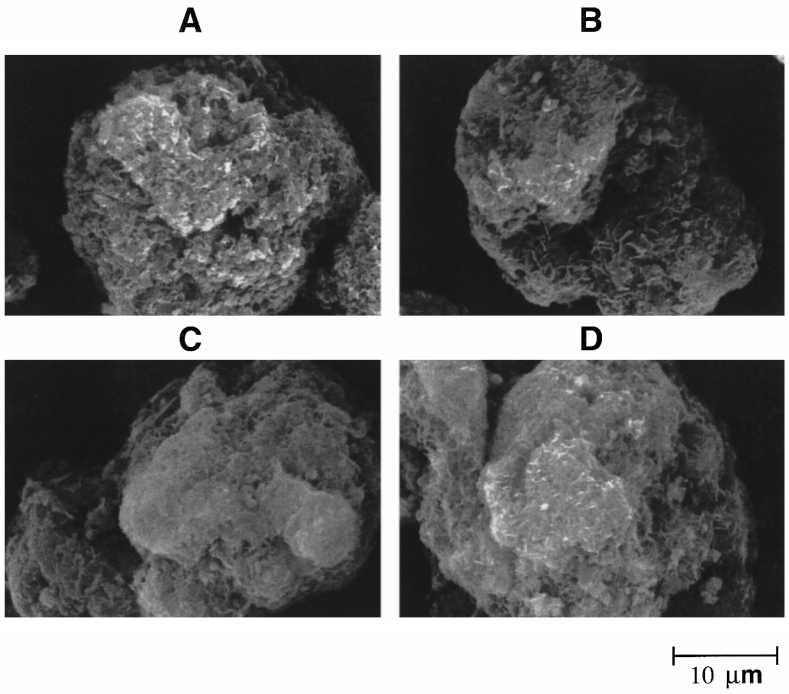

Fig. 1. SEM photographs of FLR particles and TN-POs with 10, 30 and 60% TN contents. (A) FLR particles, (B) TN-PO with 10% TN content, (C) TN-PO with 30% TN content, (D) TN-PO with 60% TN content.

pressibility (Yuasa et al., 1996). So, when FLR powder (without TN) or TN-PO with 32.1% TN content was compressed, the crushing strength became higher since the adhesion force among FLR particles depending on the compressibility, resulted in the high interparticle cohesion strength. On the other hand, when TN-POs with 99.2% or more of TN content were compressed, the amount of TN exuded by compression became larger. Therefore, TN layer appeared among the particles and the adhesion force among TN-PO particles became lower, with the result that the crushing strength became lower. In TN-TABs with 53.6 and 99.2% TN contents, the crushing strength became lower with higher compression pressure within the range from 500 to 1500 kg/cm^2. The reason was considered as follows. When TN-POs with 53.6 and 99.2% TN contents were compressed at 500 kg/cm^2 of compression pressure, a small amount of TN was exuded and formed liquid bridges among the particles, and the crushing strength became higher because of the adhesion force of the liquid bridges. When the compression pressure increased up to 1500 kg/cm^2, however, the amount of exuded TN became

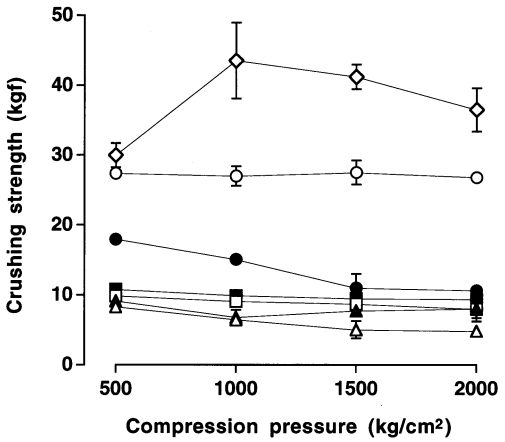

Fig. 2. Effects of TN content in TN-PO and compression pressure on crushing strength of TN-TAB. TN content (%): (◇) 0 (FLR tablet), (○) 32.1, (●) 53.6, (△) 99.2, (▲) 143.9, (□) 177.2 and (■) 219.5.

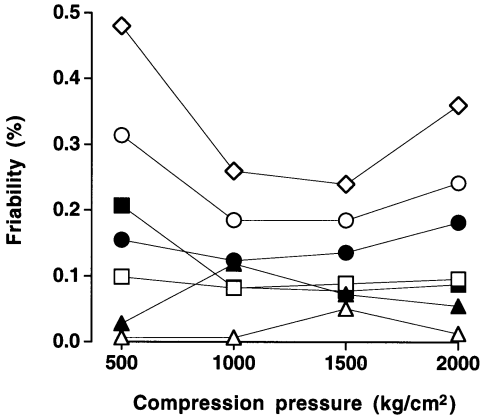

Fig. 3. Effects of TN content in TN-PO and compression pressure on friability of TN-TAB. TN content (%): (◇) 0 (FLR tablet), (○) 32.1, (●) 53.6, (△) 99.2, (▲) 143.9, (□) 177.2 and (■) 219.5.

larger and the adhesion force became lower. In TN-TABs with other TN contents, no effect of compression pressure on crushing strength was observed at 500 kg/cm^2 or more. However, at every TN content and compression pressure, TN-TABs had about 5 kgf or more of crushing strength.

In Fig. 3, the friability of TN-TABs was smaller than FLR tablets (without TN) and showed less than 0.4% at every TN content and compression pressure. The friability of TN-TABs decreased with increasing TN content up to 99.2%, whereas that of TN-TABs with 99.2% or more increased. This reason is not clear at the present.

3.3. Effects of TN content and compression pressure on TN exudation from TN-TAB at compression

Fig. 4 shows the color difference (ΔE) of the surface color of each type of TN-TAB studied. At every compression pressure, it was observed that the ΔE value was larger than that of FLR tablets (without TN) and increased with increasing TN contents, that is, increasing degree of tablet coloration. In TN-TABs with 32.1 and 53.6% TN contents, no change in ΔE value was observed up to 500 kg/cm^2 of compression pressure, whereas when the compression pressure exceeded 500 kg/cm^2, the ΔE value increased with increasing compression pressure. In the TN-TABs with other TN contents, a significant increase in ΔE value was observed up to 500 kg/cm^2 of compression pressure, whereas the increase in the ΔE value with increased compression pressure was slight when compression pressure exceeded 500 kg/cm^2. This can be considered as follows. When TN content in TN-PO was 99.2% or more, TN was exuded from TN-PO by compression at up to 500 kg/cm^2 of compression pressure. This TN filled the interparticle space among TN-PO particles, increasing the ΔE value. In TN-TABs with 32.1 and 53.6% TN contents, at up to 500 kg/cm^2 of compression pressure, TN was not exuded to the space among TN-PO particles since TN was entrapped in TN-PO, with no change in ΔE value. When the compression pressure exceeded 500 kg/cm^2, the ΔE value of TN-TABs with 32.1 and 53.6% TN contents increased, causing TN to start to be exuded from TN-PO to the space among TN-PO particles.

Fig. 5 shows the porosity of each type of TN-TAB. The porosity of TN-TABs was lower than that of FLR tablets and decreased with higher TN contents. In TN-TABs with 32.1 and 53.6% TN contents, the porosity significantly decreased up

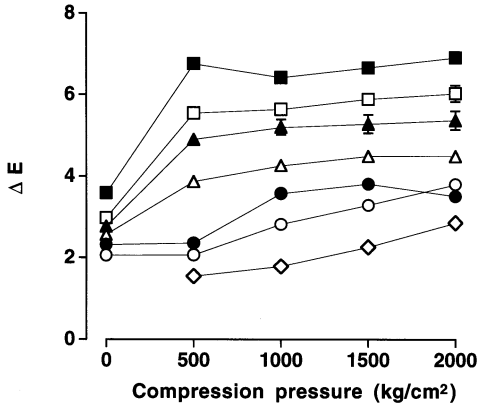

Fig. 4. Effects of TN content in TN-PO and compression pressure on color difference (ΔE) of TN-TAB. TN content (%): (◇) 0 (FLR tablet), (○) 32.1, (●) 53.6, (△) 99.2, (▲) 143.9, (□) 177.2 and (■) 219.5. *The data for FLR powder (compression pressure is 0 kg/cm^2) could not be obtained, since FLR powder has no flat and smooth reflection face due to its petal structures.

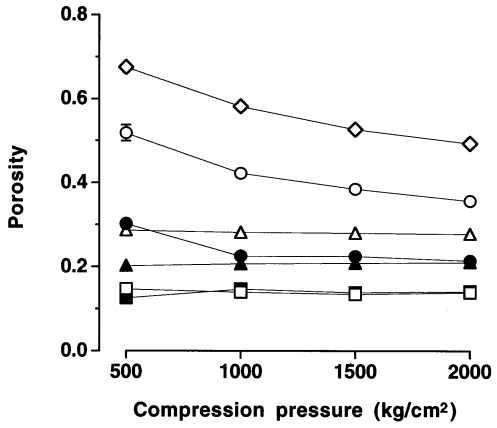

Fig. 5. Effects of TN content in TN-PO and compression pressure on porosity of TN-TAB. TN content (%): (◇) 0 (FLR tablet), (○) 32.1, (●) 53.6, (△) 99.2, (▲) 143.9, (□) 177.2 and (■) 219.5.

to 1000 kg/cm^2 of compression pressure, whereas when compression pressure exceeded 1000 kg/cm^2 the decrease in the porosity with higher compression pressure was slight. This can be considered as follows. TN-POs in TN-TABs with 32.1 and 53.6% TN contents had a lot of pores without TN, since TN contents were lower than the other TN-TABs. These pores significantly decreased by compression when compression pressure was up to 1000 kg/cm^2, with the result that a significant change occurred in the porosity up to 1000 kg/cm^2 of compression pressure. On the other hand, TN-TABs with 99.2% or more of TN content showed approximate porosities at every compression pressure.

These results suggest that it is possible to produce TN-TAB which has a satisfactory mechanical strength at every TN content and compression pressure, whereas the degree of tablet coloration became larger by exudation of TN in the tablet with higher TN content and compression pressure.

We have already reported that FLR and colloidal silica (Aerosil®200, AER) have about 4 to 14 times as greater liquid holding ability than other additives (Yuasa et al., 1994). Therefore, FLR or AER was newly added to TN-PO at compression and we subsequently attempted a reduction in the degree of tablet coloration by readsorbing TN, exuded from TN-PO, to FLR or AER particles.

3.4. Effects of addition of FLR or AER on TN exudation at compression

Fig. 6 shows the ΔE values of TN-TAB (no addition), TNF-TAB (added with FLR) and TNA-TAB (added with AER). In comparison with TN-TAB, the ΔE value of TNF-TAB or TNA-TAB decreased with addition of increasing percentage of FLR or AER, respectively, showing that the tablet coloration was reduced by compressing TN-PO with FLR or AER. It was considered that this was due to a decrease in the amount of TN exuded to the surface of the tablets, because TN exuded from TN-PO at compression was readsorbed to the pores in the added FLR particles or to the interparticle space among the added AER particles. The degree of the change in the ΔE values was almost the same regardless of addition percentage of FLR or AER.

This result showed that it was possible to reduce the tablet coloration, caused by TN exudation to tablet surface, by compressing TN-PO with added FLR or AER. Then we studied the effects of addition of FLR or AER on the mechanical strength, disintegration property and release property of TN from TNF-TAB and TNA-TAB.

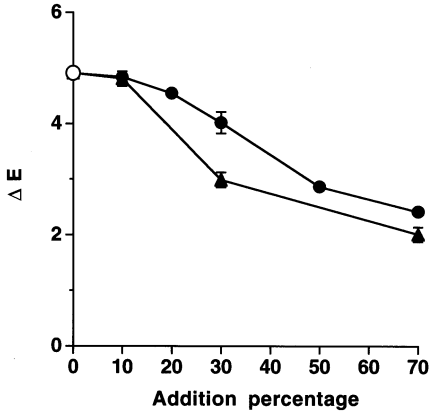

Fig. 6. Effects of addition percentage of FLR and AER to TN-PO on color difference (ΔE) of TNF-TAB and TNA-TAB. (○) TN-TAB, (●) TNF-TAB and (▲) TNA-TAB.

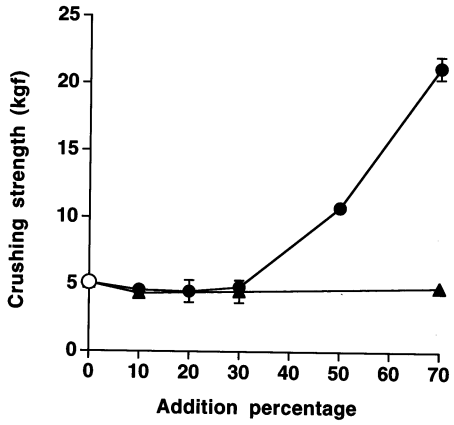

Fig. 7. Effects of addition percentage of FLR and AER to TN-PO on crushing strength of TNF-TAB and TNA-TAB. (○) TN-TAB, (●) TNF-TAB and (▲) TNA-TAB.

3.5. Effects of addition of FLR or AER on mechanical strength and porosity of TNF-TAB and TNA-TAB

The crushing strengths of TN-TAB, TNF-TAB and TNA-TAB are shown in Fig. 7. In TNF-TAB, the crushing strength showed approximately the same value up to 30% of FLR addition percentage, whereas when the addition percentage exceeded 30% the crushing strength significantly increased. The reason was considered as follows. When FLR addition percentage exceeded 30%, almost all of TN exuded from TN-PO at compression was entrapped to the pores in FLR newly added. Consequently, the cohesive strength among particles in TNF-TAB came to depend on that among FLR-FLR particles, which is derived from the physical property of FLR itself. In TNA-TAB, on the other hand, no change in the crushing strength was observed by varying the addition percentage of AER. This was thought to be caused because TN exuded from TN-PO at compression was readsorbed to TN-PO particles by forming liquid bridges. When the addition percentage of AER increased, the interparticle cohesion strength came to depend on that among AER particles, and no significant change was shown in the crushing strength.

Fig. 8 shows the porosities of TN-TAB, TNF-TAB and TNA-TAB. The porosity increased with increasing addition percentage both TNF-TAB and TNA-TAB. The degree of the increase in the porosity of TNA-TAB was markedly larger than that of TNF-TAB. This is explained as follows. The mean particle diameter of an AER particle is about 200 Å, and AER particles cannot be easily deformed plastically. Therefore AER particles are more difficult to densify than FLR particles at compression. As a result, the porosity significantly increased because the total volume increased with the increasing AER addition percentage.

3.6. Disintegration property and release property of TN from TNF-TAB and TNA-TAB

Fig. 9 shows the disintegration time of TN-TAB, TNF-TAB and TNA-TAB. The disintegration time of TNF-TAB added with 10% FLR was about 2 min and it was shorter than that of about 6 min with TN-TAB (0% addition percentage). Furthermore, it was observed that the disintegration time was shorter with the greater addition percentage of FLR. In addition, TNA-TAB with 30% or more of AER showed almost the same disintegration time as TNF-TAB. By visual inspection during the disintegration test, it was observed that TNF-TAB disintegrated into smaller flakes than TNA-TAB. The reason may be explained as follows. When FLR was added to TN-PO at compression, the amount of TN form-

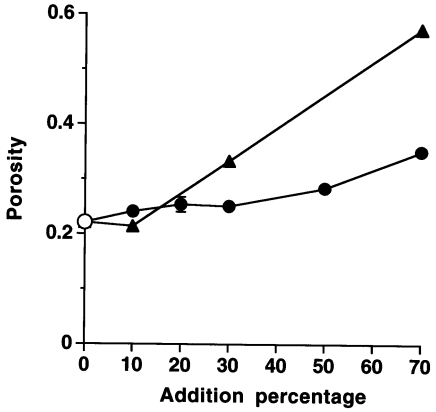

Fig. 8. Effects of addition percentage of FLR and AER to TN-PO on porosity of TNF-TAB and TNA-TAB. (○) TN-TAB, (●) TNF-TAB and (▲) TNA-TAB.

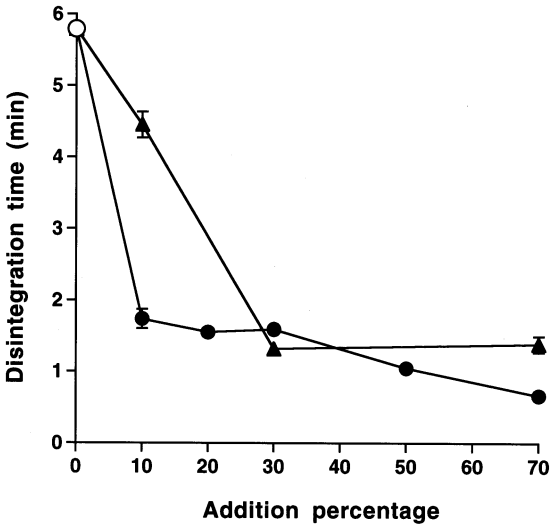

Fig. 9. Effects of addition percentage of FLR and AER to TN-PO on disintegration time of TNF-TAB and TNA-TAB. (○) TN-TAB, (●) TNF-TAB and (▲) TNA-TAB.

ing liquid bridges among the particles decreased, because TN exuded from TN-PO by compression was readsorbed to FLR newly added particles. When AER was added to TN-PO at compression, TN exuded from TN-PO was readsorbed by forming liquid bridges among AER particles.

The release profiles of TN from TNF-TAB and TNA-TAB are shown in Fig. 10. The percentage of TN released from TNF-TAB or TNA-TAB increased with increasing addition percentage of FLR or AER. Furthermore, it was observed that the percentage of TN released from TNF-TAB, as shown in Fig. 10A, was larger than that from TNA-TAB, as shown in Fig. 10B. This may be due to the fact that the effective surface area of TN in TNF-TAB participating in the dissolution became larger because TNF-TAB disintegrated into smaller flakes compared with TNA-TAB.

As mentioned above, the tablet coloration caused by TN exudation from TN-PO was reduced by addition of FLR or AER to TN-PO at compression, but the crushing strength, disintegration property and release property of TN were different between TNF-TAB and TNA-TAB. It was considered that this difference resulted from different liquid adsorbing and holding mechanisms of FLR and AER. So we considered the models of the existent state of TN in the tablet at compression, which are shown in Fig. 11.

When TN-PO with HPS as a disintegrator is compressed, as shown in Fig. 11A, TN is extruded by compression and readsorbed by forming liquid bridges to the particles of TN-PO and HPS. It was considered that the interparticle space was decreased as these liquid bridges were formed, with the result that the penetration rate of water into TN-TAB decreased, and therefore the disintegration time was longer and the release rate of TN was slower.

When TN-PO added with FLR and HPS is compressed, as shown in Fig. 11B, TN is extruded by compression and readsorbed to the pores in

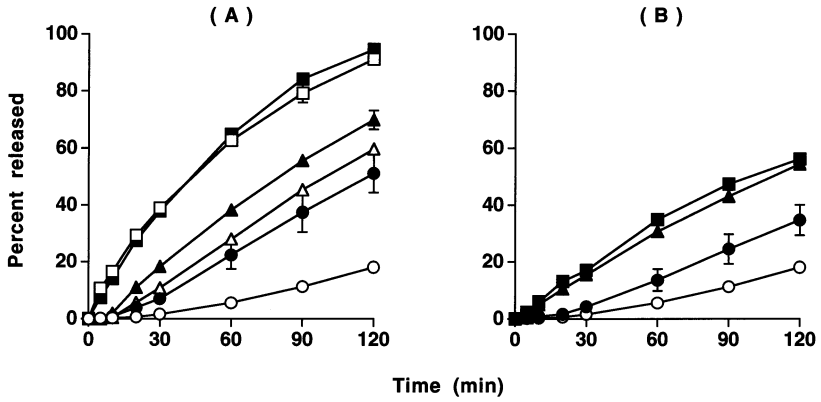

Fig. 10. Profiles of TN from (A) TNF-TAB and (B) TNA-TAB. Addition percentage (%): (○) 0, (●) 10, (△) 20, (▲) 30, (□) 50 and (■) 70.

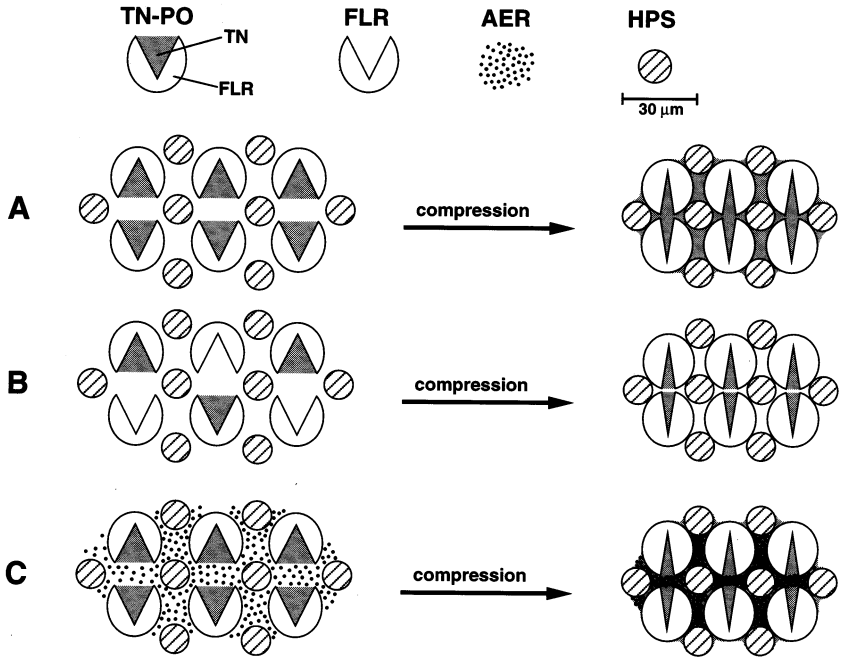

Fig. 11. Models of existent state of TN at compression of (A) TN-PO, (B) TNF-TAB and (C) TNA-TAB.

newly added FLR, with the result that a lot of interparticle space without TN is formed. In addition, we confirmed, by determining the pore size distributions in the tablets produced from FLR or AER alone, that the mean interparticle pore diameters among FLR or AER particles in the tablets were about 250 and 150 Å, respectively. It was considered that, since the interparticle space in TNF-TAB, that is the mean pore diameter, was larger than that in TNA-TAB, water easily penetrated into the TNF-TAB. As a result, the disintegration time was shorter and the release property of TN was improved in comparison with TN-TAB and TNA-TAB.

When TN-PO with added AER and HPS is compressed, as shown in Fig. 11C, TN is extruded by compression and readsorbed by forming liquid bridges to the particles of TN-PO, AER and HPS. When the percentage of added AER increased, the disintegration time became shorter because the interparticle space without TN bridges increased. Furthermore, because the mean pore diameter of TNA-TAB is smaller and the amount of TN forming bridges to the particles in TNA-TAB is larger, it may be difficult for water to penetrate into TNA-TAB. As a result, the release rate of TN from TNA-TAB was slower than that from TNF-TAB, as shown in Fig. 10.

4. Conclusion

This study suggests that when the powder (TN-PO) in which TN (as an oily medicine) is adsorbed to FLR is compressed, the degree of tablet coloration caused by TN exudation from TN-PO becomes larger with higher TN content and compression pressure. It has been clarified that the reduction of tablet coloration at tableting of TN is possible by compressing TN-PO added with FLR or AER, both of which have a high liquid holding ability. Especially, when FLR is added at compression, a shorter disintegration time and a higher release property of TN are attained than when AER is added. This may be due to the fact that the liquid adsorbing and holding mechanism of FLR differs from that of AER.

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