Further Investigations of Enhancing Effect of Medium-Chain Triglycerides on 
d- \( \alpha \)-Tocopherol Acetate Absorption from Lecithin-Dispersed Preparations in 
Rat Small Intestine

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The effect of medium-chain triglycerides (MCTG) in lecithin-dispersed \( d - \alpha \)-tocopherol acetate (VEA) preparation on intestinal absorption of VEA was investigated in rats using the \textit{in situ} loop experiment. When VEA preparations containing soybean phosphatidylcholine (PC) and various amounts of MCTG were administered, the amount of VEA absorbed in 2 h was not significantly different among them. However, the amounts of total VE, sum of VEA and \( d - \alpha \)-tocopherol (VE), remaining in the luminal fluid and the intestinal tissue were dependent on the MCTG content. Total VE remaining in the intestinal tissue after the administration of a VEA/PC/MCTG (5/16/1 by weight) preparation was nearly twice of VEA/PC (5/16) preparation, although the effect of MCTG varied with the increase or decrease in the MCTG content. Moreover, the increased tissue accumulation of total 
VE by the VEA/PC/MCTG (5/16/1) preparation resulted in an increase in the plasma VE concentration after the removal of the luminal fluid. No effect of pretreatment with PC/MCTG (1/1) dispersion on the tissue accumulation of total VE from VEA/PC (5/16) preparation was observed. Furthermore, the plasma concentration of VE from VEA and/or VE taken up in the tissue from the VEA/PC preparation was not increased by the treatment with the PC/MCTG dispersion. These results suggest that 
MCTG should coexist in the luminal VEA preparation to enhance the mucosal uptake.

A similar enhancing effect was also observed by the addition of the metabolite of MCTG, a 
medium-chain fatty acid. When caprylic acid was added to the VEA/PC preparation, the tissue 
cumulation of total VE was also increased in comparison with the VEA/PC preparation, and the 
increased amount was not significantly different from VEA/PC/MCTG (5/16/1) preparation.

\textbf{Keywords} — \( d - \alpha \)-tocopherol acetate; intestinal absorption; \( d - \alpha \)-tocopherol; lecithin-
dispersed preparation; medium-chain triglyceride; tissue uptake; rat

\section*{Introduction}

The intestinal lymphatic route of drug absorption is considered to be a minor route in general, 
except for water-insoluble compounds such as lipids\(^{1}\) and lipid-soluble vitamins.\(^{2,4}\) Moreover, 
such water-insoluble compounds are poorly absorbed from the gastrointestinal tract. For 
poorly absorbed drugs, development of dosage forms and the use of various absorption promoters 
have been extensively studied to improve their intestinal absorption. The lipid-dispersed preparations 
have also attracted special interest. Recently, we demonstrated that the intestinal absorption of a highly lipophilic compound, dolichol, can be improved by use of a liposome preparation.\(^{5}\) We also showed that a lecithin-dispersed preparation can enhance the bioavailabili-
ty of \( d - \alpha \)-tocopherol acetate (VEA).\(^{6,7}\) A lecithin-dispersed preparation containing 
medium-chain triglycerides (MCTG) gave a higher plasma concentration of \( d - \alpha \)-tocopherol 
(VE) and a higher rate of lymphatic transport in comparison with the liposome and the 
polyisorbate-80 solubilized preparations.

In the present study, the role of MCTG in the lecithin-dispersed aqueous preparation in 
increasing the absorption of VEA was examined using \textit{in situ} intestinal loop experiments in rats.

\section*{Materials and Methods}

\textbf{Materials} — VEA, VE, \( dl \)-tocol and MCTG (fatty acid composition; caprylic acid/caprylic acid, 1:3) were kindly supplied by Eisai Co., Tokyo. All other reagents were reagent

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grade commercial products.

Preparation of VEA Preparations — A chloroform solution containing PC (160 mg) and VEA (50 mg), without or with MCTG (5, 10, 50 or 100 mg) was evaporated under nitrogen gas using a rotary evaporator at room temperature in a round bottomed flask. The thin lipid film formed was hydrated in 10 ml of distilled water and was vortexed for 10 min at room temperature, followed by sonication (Ohtake Sonicator-5202, Tokyo; 20 kHz, 100 W) for 15 min on ice. The resultant VEA preparations were diluted with water to adjust the concentration of VEA at 2 mg in 5 ml of each preparation.

Preparation of PC Dispersions with or without MCTG — A chloroform solution of PC (10 mg) without or with MCTG (10 mg) was evaporated using a rotary evaporator. The thin lipid film formed was hydrated in 10 ml of distilled water, followed by sonication (20 kHz, 100 W) for 15 min on ice. The resultant dispersions were also diluted with water to adjust the concentration of MCTG at 0.08 mg/ml.

Preparation of VEA Preparation Containing Caprylic Acid — The stock chloroform solution of caprylic acid corresponding to 10 mg of MCTG was evaporated at room temperature. Ten ml of VEA/PC (containing 5 mg/16 mg in 1 ml) preparation was added to the thin film of caprylic acid, followed by sonication (20 kHz, 100 W) for 10 min on ice. This preparation was diluted with water similarly to the VEA preparations.

In Situ Absorption Study — Male Wistar rats weighing 180-250 g and fasted for 12 h were anesthetized with sodium pentobarbital (45 mg/kg, i.p.) and the rectal temperature was maintained at 37 °C in all the experiments. The small intestine was exposed through a midline incision and silicon tubes were inserted into the portion just below the pylorus and above the ileo-cecal junction. The bile duct remained intact. The mucosal side of the intestine was slowly rinsed with about 20 ml of saline warmed at 37 °C. It was again rinsed with about 10 ml of saline. Five ml of each VEA preparation warmed at 37 °C was slowly injected through the duodenal cannula and both ends of the cannulae were ligated. After 2 h, the residual fluid in the lumen was washed out with distilled water and the amount of total VE, sum of VEA and VE, remaining in the combined effluent was determined.

The intestinal tissue was also removed and homogenized by blender. The amount of total VE in the tissue was determined as described below.

The subtraction of the amount of total VE remaining in the lumen and the tissue from the dose of VEA gives the amount disappeared from the intestinal region, which was defined as the net absorption.

Pretreatment Study — Five ml of the preparation for pretreatment, PC alone or PC/MCTG (1/1 by weight), was administered in the same manner as the in situ absorption study. After 30 min, the luminal solution was withdrawn as completely as possible and the lumen was washed with additional water. Then, the VEA/PC (5/16) preparation was administered as usual.

Appearance of VE in Plasma from Intestinal Tissue — Five ml of each VEA preparation was administered in the small-intestinal loop in situ. After 2 h, the residual luminal fluid was washed out well with distilled water. Immediately, a blood sample (300 µl) was obtained from the tail artery and this was considered as 0-time blood sample. Blood samples were collected at 3, 6, 9, 12 and 15 h thereafter. After awakening, the rat was left undisturbed. The rectal temperature was maintained at 37 °C throughout the experiment.

Turbidity Measurement — The VEA preparations were diluted 10 times with sodium taurocholate solutions and the final concentrations of the bile salt were adjusted at 0, 1, 5 and 10 mM. They were subsequently incubated at 37 °C overnight for equilibrium. The turbidity was measured at 600 nm.

Assay Procedure for VEA and VE — VEA and VE remaining in the luminal fluid and the intestinal tissue were extracted with chloroform-methanol (2:1 v/v). The organic layer was dried under vacuum at 30 °C. The residue was redissolved in n-hexane and this solution was analyzed by high performance liquid chromatography (HPLC). The endogenous VE in the
intestinal tissue was extracted similarly and net tissue accumulation of VE was revised. HPLC conditions were as follows. HPLC (LC-5A, Shimadzu; Kyoto) equipped with a fluorescence HPLC monitor (RF-535, Shimadzu; the excitation and emission wavelengths were 290 and 325 nm, respectively) was operated by normal phase. The analytical column was Polygosil 60-5 (4 mm i.d. 100 mm, Chemco Scientific Co., Osaka). The mobile phase was n-hexane-isopropanol (100:0.4 v/v) and the flow rate was 0.9 ml/min.

VE concentration in the plasma was determined by HPLC under the conditions as described above, except that the mobile phase was n-hexane-isopropanol (100:0.8 v/v) and the flow rate was maintained at 1.6 ml/min. To 100 µl of each plasma sample, 100 µl of distilled water and 300 µl of ethanol were added and the mixture was extracted with 2 ml of n-hexane containing a known concentration of dl-tocot, an internal standard. The organic layer was evaporated to dryness and the residue was redissolved in n-hexane. An aliquot of the n-hexane solution was injected into the HPLC after filtration through a 0.5 µm pore size teflon membrane (Nihon Millipore Kogyo, Yonezawa).

Statistical Analysis — Statistical analysis was carried out by a Student’s t-test.

### Table I. Intestinal Absorption of VEA from Lecithin-Dispersed VEA Preparations

<table>
<thead>
<tr>
<th>Dosage form</th>
<th>% remaining in lumen VEA</th>
<th>% remaining in tissue VEA</th>
<th>% absorbed in 2 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>VEA/PC</td>
<td>48.8±3.3</td>
<td>14.5±0.3</td>
<td>19.5±2.3</td>
</tr>
<tr>
<td>(5/16)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>45.4±2.3</td>
<td>11.7±0.5</td>
<td>22.9±1.8</td>
</tr>
<tr>
<td>(5/16/0.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>57.1±2.8</td>
<td></td>
<td>34.4±2.9</td>
</tr>
<tr>
<td>(5/16/1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>26.7±1.7</td>
<td>9.3±2.1</td>
<td>40.0±3.7</td>
</tr>
<tr>
<td>(5/16/1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>36.0±2.9</td>
<td></td>
<td>53.4±3.8</td>
</tr>
<tr>
<td>(5/16/5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>35.8±2.3</td>
<td>8.5±1.9</td>
<td>31.6±2.0</td>
</tr>
<tr>
<td>(5/16/10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCTG</td>
<td>44.3±1.7</td>
<td></td>
<td>45.2±1.9</td>
</tr>
<tr>
<td>(5/16/0.88)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VEA/PC/MCFA</td>
<td>50.5±2.9</td>
<td>6.1±2.7</td>
<td>28.2±3.6</td>
</tr>
</tbody>
</table>

Dosage forms are expressed as weight ratio of the components and the dose of VEA was 2 mg/5 ml/rat. Each value is expressed as the mean ± S.E. of 3–4 rats.

Upper line: % of dose for VEA or VE calculated in terms of VEA. Lower line: % of dose for total VE (sum of VEA and VE).

a) p < 0.05; b) p < 0.01; c) p < 0.001, compared with VEA/PC (5/16) preparation.

**Results**

**Effect of MCTG on the Intestinal Absorption of VEA**

The effect of MCTG on the absorption of VEA from the small intestine was examined by an in situ loop experiment for 2 h. As shown in Table I, the absorption of VEA, expressed as percent of dose, from VEA preparations containing MCTG was not significantly different from the preparation without MCTG. However, the rate of tissue accumulation of total VE from VEA/PC/MCTG (5/16/1 and 5/16/5 by weight) preparations was greater than from VEA/PC (5/16 by weight) preparation.

**Effect of Medium-Chain Fatty Acid (MCFA) on VEA Absorption**

In the intestinal lumen, MCTG is hydrolyzed and one of the products is MCFA. The effect of MCFA on the absorption of VEA from the small intestine was examined in comparison with VEA/PC (5/16) and VEA/PC/MCTG (5/16/1) preparations and the result was shown in Table I. The addition of MCFA, caprylic acid, instead of MCTG to VEA/PC preparation resulted in higher tissue accumulation of total VE similarly to the VEA/PC/MCTG preparation. When the VEA/PC/MCFA preparation was administered, the absorption in 2 h was not signifi-
Intestinal Absorption of Vitamin E

TABLE II. Effect of Pretreatment with MCTG on Intestinal Absorption of VEA from VEA/PC (5/16) Preparation

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>% remaining in lumen VEA</th>
<th>% remaining in tissue VEA</th>
<th>% remaining in tissue VE</th>
<th>% absorbed in 2 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>48.8 ± 3.3</td>
<td>14.5 ± 0.3</td>
<td>19.5 ± 2.3</td>
<td>8.8 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>63.2 ± 3.0</td>
<td></td>
<td>28.3 ± 3.4</td>
<td></td>
</tr>
<tr>
<td>Distilled water</td>
<td>43.1 ± 1.3</td>
<td>18.2 ± 2.5</td>
<td>16.7 ± 4.0</td>
<td>9.5 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>61.3 ± 3.7</td>
<td></td>
<td>26.2 ± 5.1</td>
<td></td>
</tr>
<tr>
<td>PC dispersion</td>
<td>46.7 ± 0.8</td>
<td>14.8 ± 2.8</td>
<td>19.4 ± 3.3</td>
<td>12.2 ± 0.5</td>
</tr>
<tr>
<td></td>
<td>61.4 ± 2.4</td>
<td></td>
<td>31.5 ± 3.7</td>
<td></td>
</tr>
<tr>
<td>PC/MCTG (1/1) dispersion</td>
<td>45.5 ± 1.6</td>
<td>14.5 ± 1.3</td>
<td>15.5 ± 2.1</td>
<td>15.2 ± 1.8</td>
</tr>
<tr>
<td></td>
<td>60.1 ± 2.1</td>
<td></td>
<td>30.7 ± 3.8</td>
<td></td>
</tr>
</tbody>
</table>

The pretreatment was carried out for 30 min and the dose of VEA was 2 mg/5 ml/rat. Each value is expressed as the mean ± s.e. of 3–4 rats. Upper and lower lines are the same as in Table I.

significantly greater than both the VEA/PC and the VEA/PC/MCTG (5/16/1) preparations. The VEA/PC/MCFA preparation reduced the amount of total VE remaining in the luminal fluid and the effect was not significantly different from the VEA/PC/MCTG preparation. The VEA/PC/MCFA preparation enhanced the tissue accumulation of total VE in comparison with the VEA/PC preparation, but was not different from the corresponding VEA/PC/MCTG preparation.

Effect of Pretreatment with MCTG on Intestinal Absorption of VEA from VEA/PC Preparation

To clarify the action of MCTG, the effect of pretreatment with PC/MCTG (1/1) dispersion for 30 min on the intestinal absorption of VEA from VEA/PC (5/16) preparation was investigated. Results are summarized in Table II. The pretreatment with the PC/MCTG dispersion as well as the aqueous dispersion of PC alone did not affect the absorption of VEA.

Appearance of VE in Plasma after Accumulation in Intestinal Tissue

In order to investigate whether the tissue accumulation of total VE reflects on the plasma concentration, the change in VE plasma concentration was examined after washing out the residual luminal fluid of the 2-h loop experiment in situ. Our previous study showed that the plasma concentration of endogenous VE in the rat was almost constant all day and the plasma concentration did not significantly change for initial 3 h after the administration of VEA preparations. Moreover, as shown in Table I, the absorption in 2 h after the administration was not different between VEA/PC (5/16) and VEA/PC/MCTG (5/16/1) preparations. From these background data, the increase in VE plasma concentration after the tissue accumulation of the vitamin was estimated by subtracting the VE concentration just before washing out the luminal fluid. Results are shown in Fig. 1. Cmax for VEA/PC/MCTG (5/16/1) preparation (2.2 ± 0.1 µg/ml; p < 0.001) was higher than

![Fig. 1. Appearance of VE in Plasma from Intestinal Tissue Treated with VEA Preparations](image-url)

VEA preparations containing 2 mg of VEA were administered in the loop of the small intestine for 2 h in situ. Changes in the plasma concentration of VE were monitored after washing out the VEA preparation remaining in the lumen. Results are expressed as the mean ± S.E. of 3–4 rats.

VEA preparations: ○, VEA/PC (5/16); ●, VEA/PC/MCTG (5/16/1).
VEA/PC (5/16) preparation (1.3 ± 0.1 µg/ml) and area under the plasma concentration-time curve (AUC) up to 15 h for the preparation containing MCTG (23.7 ± 3.8 µg·h/ml; p<0.05) was approximately twice of the preparation without MCTG (11.2 ± 3.8 µg·h/ml).

In order to clarify the action of MCTG on the transfer process from the tissue to the circulation, the effect of the administration of PC/MCTG (1/1) dispersion in the intestinal loop on the rate of VE appearance in the plasma was examined after the pretreatment for 2 h with VEA/PC (5/16) preparation. As shown in Fig. 2, the plasma concentration of VE up to 9 h was not affected by the treatment with MCTG.

**Effect of Sodium Taurocholate on Turbidity of VEA Preparations**

In order to investigate the effect of bile on the particle size on VEA preparations, the turbidity change of each preparation was measured in the presence of sodium taurocholate. The results are shown in Fig. 3. As is evident from the figure, the initial turbidity was markedly varied in the preparations, suggesting that the particle size of the preparation is dependent on the

**Discussion**

Lipoidal preparations have been extensively studied to improve drug absorption from the gastrointestinal tract. Recently, it was reported that liposomes, emulsions, and lipid-surfactant mixed micelles prepared from various lipids enhanced drug absorption from various regions of the gastrointestinal tract. Lecithin, which has been used as a major component of liposomes, is of interest as a component of dosage forms of drugs. Our previous paper showed that lecithin-dispersed aqueous preparation of VEA containing MCTG is an effective dosage form to enhance the absorption and that both lecithin and MCTG are important components for the enhancement. Moreover, on the intestinal absorption of VE, Gallo-Torres et al. reported that MCTG has an effective function in the intestinal absorption of the vitamin. Thus, in the present study, the site of action of MCTG in the lecithin-dispersed preparation on
the intestinal absorption of VEA was investigated.

When lecithin-dispersed preparations containing various amounts of MCTG were administered by the in situ loop experiment, the rates of absorption of VEA in 2 h were not significantly different among them. However, the ratio of VE, in the form of VEA or VE, remaining in the luminal fluid and the intestinal tissue changed markedly, which was dependent on the MCTG content. VEA/PC/MCTG (5/16/1) and (5/16/5) preparations increased the accumulation of total VE in the intestinal tissue (Table I). It was reported that these two preparations increased the plasma concentration and AUC of VE up to 24 h, suggesting that the increased tissue accumulation is related to the increase in the bioavailability. Gallo-Torres et al. reported that VE administered as MCTG emulsion was accumulated in the small-intestinal wall more than the emulsion of long-chain triglycerides. It has been shown that the time course of intestinal absorption of a lipid soluble drug from oil-in-water emulsions reflects that of the oils. Since medium-chain glycerides are absorbed rapidly from the small intestine, the tissue accumulation would be affected by the MCTG-containing formulation only in the early stage. Thus, in order to clarify the relationship between the amount of VE accumulated in the tissue in the initial 2 h and the bioavailability, the change in VE plasma concentration was examined after washing out the luminal fluid in in situ 2 h-loop experiments for VEA preparations containing various amounts of MCTG. In this experiment, the amount of VE accumulated in the tissue at 2 h could not be measured practically, but the amount of total VE remaining in the luminal fluid was not significantly different from ones shown in Table I. VEA/PC/MCTG (5/16/1) preparation increased VE concentration in the plasma and AUC of VE up to 15 h, which were about 2 times greater than VEA/PC (5/16) preparation (Fig. 1). Furthermore, as shown in Fig. 4, the tissue accumulations of total VE from VEA preparations with various MCTG contents (Table I) are correlated well with AUCs of VE up to 24 h after the intraduodenal administration, supporting strongly the relationship between the initial accumulation of total VE in the intestinal tissue and the extent of bioavailability of the vitamin.

It has been reported that orally-administered VEA was hydrolyzed by the presence of bile and pancreatic juice in the intestinal lumen before the passage of the intestinal mucosa, and we also reported that unchanged VEA was not detected in the plasma nor in the thoracic lymph following intraduodenal administration of VEA preparations. In this study, not only VE but also VEA was detected in both intestinal loop and tissue (Table I) and the ratio of VE to VEA was not dependent on the preparations of VEA. This might be due to dilute bile and pancreatic juice in the loop. However, the mucosal uptake would not be so different between VEA and VE, because the rate of absorption of VE from VEA micellar solution was similar to that from VE micellar solution.

Caprylic acid is one of the metabolic products of MCTG in the lumen. There are many reports concerning the enhancing effect of MCFA on drug absorption. Kajii et al. reported that enhancing effect of sodium caprylate on drug penetration across the intestinal membrane was

Fig. 4. Relationship between the Amount of Total VE Accumulated in Intestinal Tissue after 2-h Absorption Experiment in Situ and AUC of VE up to 24 h after the Intraduodenal Administration of VEA Preparations with Different MCTG Content

AUCs of VE quoted from the reference 7) were plotted against the amounts of total VE accumulated in the intestinal tissue (Table I) for 5 VEA preparations. The correlation coefficient was 0.910 and the correlation was significant by t-test (p < 0.05).
probably due to the perturbation of the mucosal membrane.\textsuperscript{16} Yata \textit{et al.} demonstrated that the calcium-chelating ability would be important for the promoting effect of MCFA.\textsuperscript{17} Gallo-Torres \textit{et al.} pointed out that MCFA are approximately 100 times more soluble in water than long-chain fatty acids, which would create suitable conditions for faster uptake of VE by the intestinal mucosa.\textsuperscript{11} Hollander \textit{et al.} reported that caprylic acid influenced the rate of lymphatic appearance of vitamin A.\textsuperscript{18} In this study, the effect of MCFA on VE accumulation in the mucosal tissue was examined. As is evident from Table I, the VE accumulation from VEA/PC/MCFA preparation was increased similarly to the corresponding VEA/PC/MCTG preparation. These results suggest that MCTG can enhance the uptake of VEA by the intestinal mucosa by many ways even after being hydrolyzed to MCFA in the lumen.

Moreover, bile plays an important role in VE absorption from VEA preparations. It is well known that bile is necessary for the intestinal absorption of fats\textsuperscript{19} and lipophilic drugs\textsuperscript{20} because it forms mixed micelles with smaller particle sizes. Our previous study showed that a bile salt, sodium taurocholate, reduces the particle size of the VEA/PC/MCTG (5/16/1) preparation more markedly (from 1–2 μm to about 80 nm) than the VEA/PC (5/16) preparation.\textsuperscript{21} The result of turbidity measurements showed that the degree of the particle size reduction by the addition of sodium taurocholate was the greatest in the VEA/PC/MCTG (5/16/1) preparation in those containing MCTG (Fig. 3). Interestingly, the turbidity in the presence of 5 mM sodium taurocholate followed in the reverse order of the amount of total VE accumulated in the tissue shown in Table I except for the preparation without MCTG. These results suggest that the action of bile in the intestinal lumen would also be important in mucosal uptake of VEA and/or VE from VEA preparations, although precise mechanisms of the uptake of the vitamin would be different between VEA/PC/MCTG (emulsions)\textsuperscript{21} and VEA/PC (liposomes)\textsuperscript{21} preparations.

On the effect of MCTG on the property of the mucosal membrane, the effect of pretreatment of the intestinal mucosa with MCTG was investigated by using the VEA/PC (5/16) preparation. The pretreatment with MCTG did not significantly affect anyone of the amounts of VE remaining in the luminal fluid, the tissue accumulation, or the absorption (Table II). Furthermore, the plasma concentration of VE from VEA and/or VE taken up in the mucosal tissue from the VEA/PC (5/16) preparation was not increased by the following treatment with PC/MCTG (1/1) dispersion (Fig. 2). These results suggest that the site of action of MCTG on the absorption of the vitamin is neither the change in the properties of the mucosal membrane nor the transfer process from intestinal mucosa to the circulation. It is probably in the lumen, where bile is present, to make up to the suitable condition for the mucosal uptake by coexisting in VEA preparations. This coexistence effect has been reported for a poorly absorbed drug, bromthymol blue.\textsuperscript{9}

In conclusion, there is a most suitable ratio of the components of the VEA/PC/MCTG preparation for VEA uptake and following accumulation in the mucosal tissue. For the enhancement of VEA uptake and/or accumulation in the tissue, both MCTG and MCFA are concerned and it is necessary for MCTG to coexist in the lecithin-dispersed VEA preparation. The enhanced tissue accumulation would be followed by the slow elevation of VE concentration in the plasma thereafter.

References

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