Hypolipidemic activity of Mangiferin in cholesterol-fed mice

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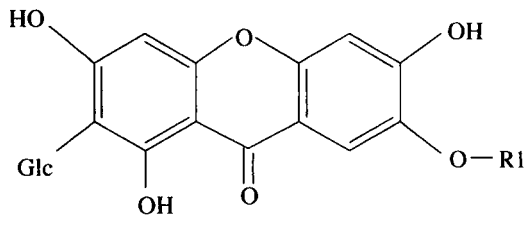
Abstract

The hypolipidemic activity of Mangiferin was investigated in normal and hyperlipidemic mice. Mangiferin (MF) (30 mg/kg) reduced the blood cholesterol level after oral administration to cholesterol-fed mice. However, MF did not change the blood cholesterol level in normal and TRITON-induced hyperlipidemia. The findings of the present study indicate that MF may be useful for the treatment of hypercholesterolemia in cholesterol-fed condition.

Key words Mangiferin, hypolipidemic effect, cholesterol.

Introduction

The rhizoma of *Anemarrhena asphodeloides* has been used in the Orient as traditional medicine for diabetes (polyuria and polydipsia) and contains xanthone compound, Mangiferin (MF) (Fig. 1).[1] In a previous study, we reported the hypoglycemic effect of MF.[2] In the course of screening for hypolipidemic drugs, we have examined the hypolipidemic effect of Mangiferin.



MF : R1=H
Glc: β-D-glucopyranosyl

Fig. 1 Structure of Mangiferin (MF)

Materials and Methods

Materials : Mangiferin was isolated by conventional method as previously reported.[3] The structure of MF was confirmed by spectroscopic method.[4] This was stored at room temperature until use.

Animals : Adult male ddY mice (SLC Co. Ltd. Shizuoka, Japan) (6 weeks old, body weight 22-25 g) were used for all studies. They were housed individually in an air-conditioned room at an ambient temperature of 24±1°C with a 12 h light-dark cycle. The animals were kept in this experimental animal room for 7 d with free access to food and water.

To determine blood lipid levels, blood samples were taken from the cavernous sinus using a capillary under non-anesthesia.

Hypercholesterolemic mice : Mice were fed a diet containing 1 % cholesterol and 0.5 % cholic acid. MF was administered orally once a day at the same time.

Effect of MF on blood triglyceride levels in TRITON-induced hyperlipidemic mice : After eigh-

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teen hours of fasting, mice were given MF orally and 3 hours later, TRITON WR-1339 (Sigma Co. Ltd, Tokyo, Japan) (400 mg/kg body weight) solution was administered intravenously. Blood samples were collected 18 hours after the administration of TRITON.

Determination of blood cholesterol and triglyceride level : Blood cholesterol levels in mice were determined using commercial reagents (Cholesterol E-Test Wako and Triglyceride G-Test Wako, Wako Pure Chemical Co. LTD).

All data were expressed as means±S.E.M and Student's t test was used for the statistical analysis. Values were considered to be significantly different when the p value was less than 0.05.

We complied with the guideline for experimental animals (Standards relating to the care and management, *etc.* of experimental animals, Notification No. 6, March 27, 1980 of the Prime Minister's Office).

Results

Effect of MF on blood lipid in normal mice

The mean blood cholesterol levels in normal mice after oral administration of MF are shown in Fig. 2. MF (30 mg/kg) had no effect on blood cholesterol. MF-treated mice showed a significant change in blood triglyceride level (data not shown).

Effect of MF on blood lipid in cholesterol-fed mice

The hypocholesterolemic effects of MF on the blood cholesterol levels of cholesterol-fed mice are shown in Fig. 3. MF (30 mg/kg)-treated mice showed a significant decrease in blood cholesterol at 3 weeks when compared with controls ($p<0.05$).

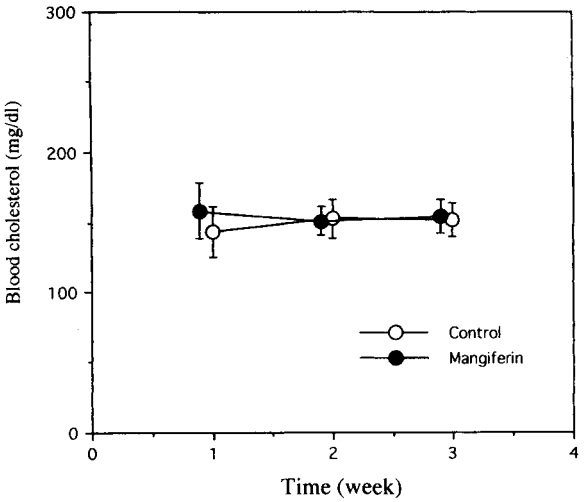

Fig. 2 Effect of MF on blood cholesterol in normal mice. Each value represents the mean±S.E. from 3-5 mice.

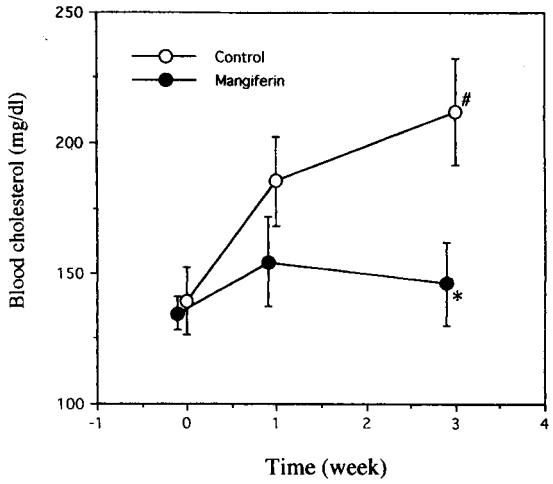

Fig. 3 Effect of MF on blood cholesterol in cholesterol-fed mice. Each value represents the mean±S.E. from 3-6 mice.
Significantly different from controls, $*p<0.05$.
Significantly different from baseline, $\#p<0.05$.

Effect of MF on blood lipid in TRITON-induced hyperlipidemic mice

The effect of oral administered MF on TRITON-induced hypercholestemia is shown in Table I. MF-treated animals did not change blood cholesterol and triglyceride levels when compared with controls.

Table I Effect of Mangiferin in Triton-induced hyperlipidemic mice.

	Normal	Control	Mangiferin
Blood cholesterol (mg/dl)	139±13	451±62#	469±34
Blood triglyceride (mg/dl)	189±24	2857±249##	2635±308

Each value represents the mean±S.E. from 3~5 mice.
Significantly different from normal mice, $\#p<0.05$, $\#\#p<0.01$.

Discussion

One of the most common lipid abnormalities is hypercholesterolemia which causes arteriosclerosis. The present results show that Mangiferin reduces

blood cholesterol levels in cholesterol-fed mice. However, no difference in blood cholesterol levels was observed between control and MF-treated groups in TRITON-induced hypercholesterolemia. TRITON induces the cholesterol synthesis by increase of HMG-CoA reductase and induces the triglyceride synthesis by increase of VLDL synthesis in liver.[4,5] These findings indicate that MF does not affect the VLDL synthesis and HMG-CoA reductase in liver. These findings suggest that the hypocholesterolemic action of MF may be due to the inhibiting absorption of cholesterol in the small intestine. But the hypocholesterolemic mechanism by MF is unknown. In the preliminary study, we examined the dose-dependence (10, 30, 90 mg/kg) after treatment of MF, and we found that it showed antidiabetic activity at 30 and 90 mg/kg after oral administration. Therefore, we studied the effect of lipid metabolism of MF at the dosage of 30 mg/kg.

In a previous study, we also showed hypoglycemic activity of Mangiferin on diabetic mice.[2] Diabetics also often have elevated blood cholesterol levels. It may be useful that MF has a beneficial effect on hyperglycemia and hyperlipemia in diabetics. This is the first report of the hypocholesterolemic activity of Mangiferin in mice. It is therefore interesting that xanthone compound (Mangiferin) has a significant hypocholesterolemic effect.

The findings of the present study indicate that MF may be useful for the treatment of hyperlipidemia. Further investigations will be needed to elucidate the mechanism of these effects.

和文抄録

マンギフェリン (MF) の脂質低下作用について正常および高コレステロールマウスで検討した。MF はコレステロール食マウスのコレステロール値を低下させた。しかし、正常および Triton 誘発高脂質血症のコレステロール値には影響を与えなかった。これらのことから MF の高コレステロール血症に対する有効性が示唆された。

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