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Newly developed Japanese traditional food "Miso" which may possess blood pressure lowering effect.

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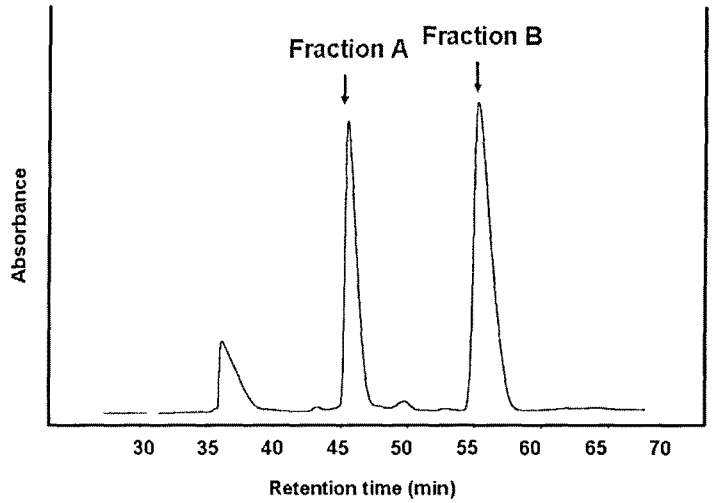
We have developed a new functional food by adding skimmed milk as a part of the raw material to make Japanese traditional food "Miso" - temporarily named "Milky Miso". The Milky Miso contained small peptides that possessed angiotensin converting enzyme (ACE) inhibitory activity. The peptides were thought to be degradation products of 'ソ-casein in skimmed milk by malted rice (*Aspergillus oryzae*) and we purified two of them so far; Tyr-Pro and Val-Tyr. Oral administration of Milky Miso (contain. 5% NaCl) decreasedblood pressure of spontaneously hypertensive rat (SHR/izm) while control Miso and 5% NaCl showed no significant effect on their blood pressure. Next, we checked its effect on humans, employing Double Blind Method. Twenty volunteers were divided into two groups, one group received 15 g of Milky Miso and the other group received 15 g of control Miso everyday for three months. During experimental period, arterial blood pressure of both groups showed no significant change, however angiotensin II concentration of Milky Miso group significantly decreased ($p=0.02$) at 6 weeks after start of the experiment. Because ACE is the key-enzyme for angiotensin II production, we concluded that the amount of ACE inhibitory peptides in Milky Miso taken in this experiment was not enough to decrease blood pressure that was regulated by many factors, however the amount was enough to prevent angiotensin II formation. Recently angiotensin II is believed to cause many pathophysiological events, such as cardio-vascular diseases, diabetes mellitus type II, renal malfunction, and atherosclerosis. It is suggested that daily intake of Milky Miso may have beneficial effect on those pathophysiological events.

Reversed phase HPLC pattern of ACE inhibitory peptides (isocratic elution)



Peptide A

α_{S1}-Casein

121 HSMKEGIHAQ QKEPMIGVNQ
141 QLAYFYPELF RQFYQLDAYP
161 SGAWYYVPLG TQYTDAPSFS

146 147
Tyr-Pro

MW =278.3

IC_{50} = 679.052 μg/ml (2440 μM)

Peptide B

α_{S2}-Casein

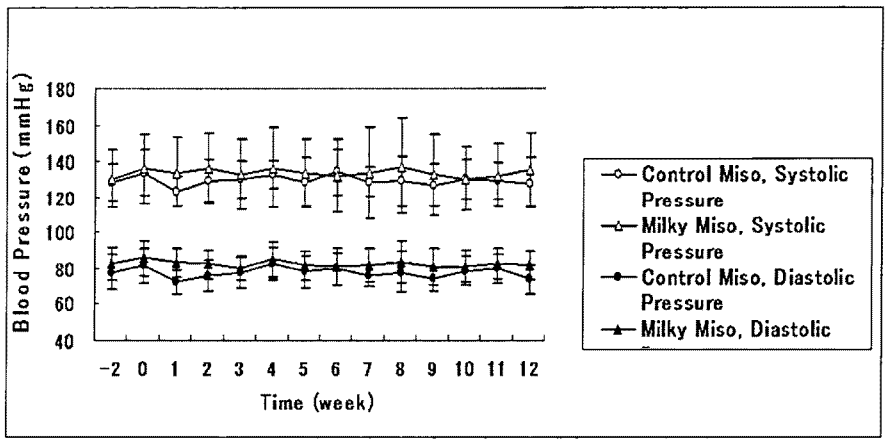
161 LNFNKKISQR YQKFALPQYL
181 KWVYQHQKAM KPWIQPKWKV
201 LPYVRYL · OH

183 184
Val-Tyr

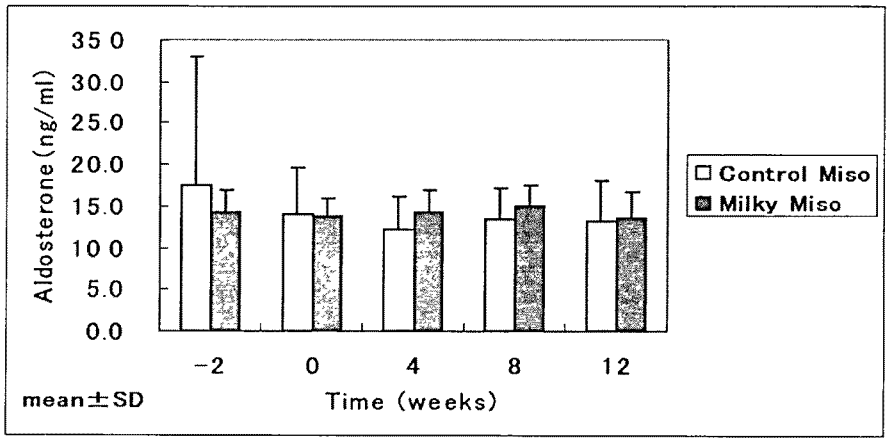
MW =280.3

IC_{50} = 6.167 μg/ml (22 μM)

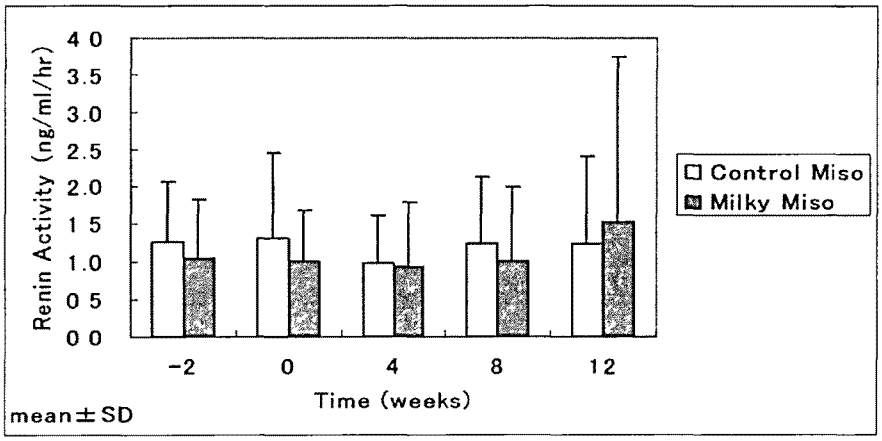
Effect of Milky Miso on blood pressure of human volunteers



Aldosterone



Renin Activity



Angiotensin II