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Soy protein may have a hypercholesterolemic effect in rats and may potentiate lipoprotein susceptibility to peroxidation when its dietary level leads to methionine deficiency

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nine sites. A model study was performed by sequential hydrolysis of purified α_{s1} -casein with immobilized pepsin (EC 3.4.23.1) and/or α -chymotrypsin (EC 3.4.21.1) (cleavage of Phe-X peptidic bonds) and immobilized thermolysin (EC 3.4.24.4) (cleavage of X-Phe peptidic bonds). Biochemical characterization of the hydrolysates was performed by analyzing: i) the molecular weight using size-exclusion chromatography; ii) the individual aromatic amino acid composition of the peptides using reversed-phase high-performance liquid chromatography and spectrophotometric analysis [Perrin et al (1995) *J Chromatogr* 664, 267-276]; iii) the global amino acid content.

Peptidic fractions showed a decreased phenylalanine content (reduction of phenylalanine concentration about three times). This could not, however, be directly used for phenylketonuria treatment due to the presence of free phenylalanine that had been released by proteolysis.

Further elimination of free phenylalanine was achieved by size-exclusion chromatography, hydrophobic affinity chromatography or electro dialysis.

We demonstrated that the residual phenylalanine level in the peptidic fraction was the consequence of the resistance of the hydrophobic fragment $CN\alpha_{s1}$ -f(21-32) containing four phenylalanyl residues to the enzymes.

The hydrolysates have a more neutral taste and technofunctional properties than the mixture currently in use.

Soy protein may have a hypercholesterolemic effect in rats and may potentiate lipoprotein susceptibility to peroxidation when its dietary level leads to methionine deficiency. C Moundras, C Rémésy, MA Levrat, C Demigné (*Laboratoire des maladies métaboliques, Inra-*

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It is widely accepted that casein, compared to soy protein, is hypercholesterolemic. However, this effect depends on various factors, such as animal species, age, sex, dietary protein level and the presence of cholesterol in the diet. Casein and soy protein differ in their amino acid composition and the supply of methionine may be deficient with soy protein diets. Besides their effects on protein synthesis and growth, the sulfur amino acids are the precursors of important intracellular compounds such as taurine and glutathione (GSH). GSH is the major intracellular-SH molecule, and may be involved in a number of processes, including cellular protection against oxidative stresses.

The aim of the present study was to further investigate the effect of dietary protein on lipid metabolism (particularly cholesterol). In parallel, lipoprotein susceptibility to in vitro Cu-induced peroxidation was examined in rats adapted to moderate (13%) protein levels, with or without methionine supplementation (0.4%). This methionine level was selected to produce plasma and liver methionine concentrations similar to those present in casein fed rats: as a result, liver GSH concentrations were greatly elevated by methionine supplementation in soy protein fed rats (from 1.20 to 3.87 $\mu\text{mol/g}$ liver).

In this experiment, it turned out that soy protein failed to lower plasma cholesterol and there was even a slight cholesterol-raising effect (+18%), despite a higher rate of bile acid excretion than in the rats adapted to the casein diet. In contrast, soy protein feeding resulted in a marked triglycerides-lowering effect. Methionine supplementation of the soy protein diet counteracted its hypercholesterolemic effect. It also elevated the plasma triglyceride levels. The elevation of plasma cholesterol in rats fed soy protein was characterized by higher cholesterol lev-

els in the LDL and HDL1 fractions, paralleled by a striking induction of HMG-CoA reductase and cholesterol 7 α -hydroxylase activities. This induction was lower when the soy protein diet was supplemented with methionine. The [VLDL + LDL] susceptibility to Cu-induced peroxidation was markedly enhanced in rats adapted to soy protein, compared to those receiving casein. It is noteworthy that methionine supplementation only partially recovered the lipoprotein resistance to peroxidation, despite the high GSH status in such conditions.

In conclusion, it appears that the potential cholesterol-lowering effect of some plant proteins requires that the sulfur amino requirements of the organism are fulfilled. When this supply is inadequate, various disturbances of lipid metabolism may be observed, and especially the susceptibility of lipoproteins to oxidative stress.

Importance of cation concentrations on the stability of parenteral nutrition solutions. R Collomp, E Peroux, JM Pons (*Laboratoire de fabrication, Pharmacie centrale CHU, 06730 Saint-André-de-Nice, France*)

This study was designed to determine the influence of cation concentration on the stability of nutrient solutions for parenteral use.

Four nutrient solutions were modified by reducing their calcium and magnesium concentrations and by increasing their potassium phosphate content.

The influence of cations on stability can be estimated by calculation of the critical aggregation number (CAN): $CAN = a + 64b + 729c$, where a is the molar concentration of monovalent cations, b is the molar concentration of divalent cations and c is the molar concentration of trivalent cations [Bumham et al (1983) *Int J Pharmacol* 13, 9-22]. For industrial preparations, the limit of destabilization is set empirically at $CAN = 200$.

The overall stability of emulsions, expressed in exploitable days, is estimated by determining the evolution of five parameters over a period of time: the height of creaming, the average diameter of oil droplets, the percentage of oil, pH and osmolality. Tests are performed on tubes and on bags over a period of 14 days.

The modified nutrient solutions having fewer divalent cations exhibited improved stability, even when their monovalent cation concentration was increased. This phenomenon was correlated with a decrease in CAN, although this parameter was not always linearly related to the global stability of the emulsions (eg, samples P2 and P4).

Cation composition of the mixtures.

| | P1 | P'1 | P2 | P'2 | P3 | P'3 | P4 | P'4 |
|---------------------------|------|------|------|------|------|------|------|------|
| Na ⁺ (mmol/L) | 28.6 | 39.9 | 36.3 | 34.6 | 26.6 | 32.4 | 42.8 | 38.6 |
| K ⁺ (mmol/L) | 24.6 | 34.3 | 31.2 | 34.9 | 24.6 | 28.9 | 33.6 | 41.7 |
| Ca ²⁺ (mmol/L) | 3.6 | 2.4 | 4.6 | 2.1 | 3.6 | 1.7 | 4.0 | 2.4 |
| Mg ²⁺ (mmol/L) | 2.2 | 1.2 | 2.8 | 1.0 | 2.2 | 0.9 | 2.3 | 1.2 |
| CAN | 424 | 304 | 541 | 268 | 422 | 228 | 480 | 310 |

P1, P2, P3, P4: original formulas; P'1, P'2, P'3, P'4: new formulas; CAN: critical aggregation number.