[*The Prostate*, **47**, 59-65 (2001)] [Lab. of Pharmaceutics]

Myristoleic Acid, a Cytotoxic Component in the Extract from *Serenoa repens*, Induces Apoptosis and Necrosis in Human Prostatic LNCaP Cells.

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The extract from *S. repens* has been used for the treatment of benign prostatic hyperplasia and nonbacterial prostatitis. We identified myristoleic acid as one of the cytotoxic components in the extract. It was demonstrated that the extract from S. repens and myristoleic acid induced mixed cell death of apoptosis and necrosis in LNCaP cells. Cell death was demonstrated to associate partially with caspase activation. These results suggest that the extract and myristoleic acid may develop attractive new tools for the treatment of prostate cancer.

[*Biol. Pharm. Bull..*, **24**, 1400-1403 (2001)] [Lab. of Pharmaceutics]

Antidiabetic Effect of an Acidic Polysaccharide (TAP) from *Tremella aurantia* and Its Degradation Product (TAP-H).

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Continuous oral administration of the polysaccharide (TAP) solution (0.5 g/l) and the TAP-H (degradation product of TAP) solution (1.5 g/l) ionstead of water for 10 weeks were found to depress plasma glucose increases in diabetes using NIDDM model mice. TAP and TAP-H significantly lowered levels of insulin, total-cholesterol and triglyceride in the blood of the mice. In excretion to feces, TAP and TAP-H significantly increased the total bile acid, while the cholesterol content of both groups was less than that of the control. Furthermore, TAP and TAP-H significantly decreased the plasma lipoperoxide level.

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Glycated High-Density Lipoprotein Induces Apoptosis of Endothelial Cells via a Mitochondrial Dysfunction.

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This study set out to clarify whether glucose-modified HDL affects the function of endothelial cells by examining the apoptosis of cultured human aortic endothelial cells (HAECs) exposed to a glycated-oxidized HDL (gly-ox-HDL) prepared in vitro. Incubation of HAECs with 100 μg/mL of gly-ox-HDL fro 48 h showed apoptotic features and the degree of apoptosis was dose-dependent on the glucose used in the preparation of gly-ox-HDL. Stimulation of HAECs with gly-ox-HDL elicited a marked increase in caspase 3 activity and the expression of active caspase 3 and caspase 9, whereas concomitant treatment with a caspase 3 inhibitor significantly blocked gly-ox-HDL-induced apoptosis of HAECs. The release of cytochrome c into cytosols markedly increased in HAECs during the treatment with gly-ox-HDL. The increased expressions of Bax and Bad were detected in HAECs incubated for 24 h with gly-ox-HDL, but gly-ox-HDL failed to interfere with the expression of Bcl-2 and Bcl-x. Taken altogether, additional oxidation of HDL under hyperglycemic conditions may induce endothelial apoptosis through a mitochondrial dysfunction, following the deterioration of vascular function.

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Modulation of Reactive Oxygen Species in Endothelial Cells by Peroxynitrite Treated Lipoproteins.

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We prepared *in vitro* lipoproteins oxidatively modified by peroxynitrite (NO_2-lipoprotein) and investigated the effect of NO_2-lipoprotein on viability of cultured endothlial cells. After exposure of a high-density lipoprotein (HDL) to peroxynitrite, some intermolecular complexes of apolipoproteins in HDL were detected on immunoblotting with monoclonal antibodies against apolipoprotein AI and AII, suggesting that nitration of HDL by peroxynitrite causes intermolecular cross-linking of the apolipoproteins in the particles. Increased radical production in NO_2-lipoprotein-treated HAECs implied that reactive oxygen species such as superoxide anions and hydroxyl radicals may contribute to the mechanism of the toxic effect induced in endothelial cells by NO_2-lipoprotein.