[*Planta Medica*, **64**, 195-290 (1998)] [Lab. of Hygienics]

Inhibitory Effect of Delphinidin from *Solanum Melongena* on Human Fibrosarcoma HT-1080 Invasiveness *in vitro*.

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We investigated the inhibitory effect of eggplant (*Solanum melongena L. var.marunasu* HARA) extract on human fibrosarcoma HT-1080 cell invasion of reconstituted basement membrane (Matrigel (MG)). We found that the effective component of the plant extract was delphinidin, a flavonoid pigment contained in the peel. The extract and delphinidin did not affect tumor cell adhesion to MG or haptotactic migration to MG. HT-1080 secretes matrix metalloproteinase(MMP)-2 and MMP-9, which degrade extracellular matrix as part of the invasive process. Delphinidin slightly inhibited the activity of MMPs, which may have been responsible, in part, for the inhibition of tumor cell invasiveness.

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Carbonyl Reductase Purified from Rabbit Liver Is Not the Product of a Carbonyl Reductase Gene (RCBR5 or RCBR6) Cloned from the Rabbit Liver cDNA Library.

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Six peptides were obtained by the digestion of carbonyl reductase purified from rabbit liver. The amino acid sequences were virtually identical to the corresponding regions in amino acid sequences deduced from two cloned carbonyl reductase genes (RCBR5 and RCBR6). However, there was a difference of one amino acid residue between the sequences of peptides from the purified enzyme and deduced from the two cDNAs. The purified carbonyl reductase was confirmed to exhibit no activity towards menadione, even though the transient expression of the two cDNA for rabbit liver carbonyl reductase has been reported to cause a marked increase of menadione reductase activity in COS7 cells. Based on these results, it is concluded that the carbonyl reductase purified from rabbit liver is not the product of cloned carbonyl reductase gene (RCBR5 or RCBR6).

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Activation of Human Liver 3α-Hydroxysteroid Dehydrogenase by Clofibrate Derivatives.

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The $NADP^+$-dependent dehydrogenase activity of a predominant isozyme of human liver 3α-hydroxysteroid dehydrogenase was activated by antihyperlipidemic drugs, such as bezafibrate and clinofibrate, and by clofibric acid and fenofibric acid (active metabolites of clofibrate and fenofibrate, respectively). The activation increased both *K*m and *k*cat values for the coenzyme and substrates. Kinetic analysis showed that bezafibrate, clinofibrate clofibric acid were non-essential activators. The combined activators experiments with one of the above drugs and sulfobromophthalein (BSP), a known activator specific for this enzyme indicated that BSP and the drugs bind to an identical site on the enzyme. These results suggest that the long-term therapy with the antihyperlipidemic drugs influence the metabolism of steroid hormones, bile acids and several ketone-containing drugs mediated by the enzyme.

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Dual Effect of Anti-inflammatory 2-Arylpropionic Acid Derivatives on a Major Isoform of Human Liver 3α-Hydroxysteroid Dehydrogenase.

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Nonsteroidal anti-inflammatory drugs have been shown to be potent inhibitors of mammalian 3α-hydroxysteroid dehydrogenase. Here, we report that the drugs of 2-arylpropionic acid class act as both activators and inhibitors for a predominant isoform of the human liver enzyme which is involved in the metabolism of steroid hormones, bile acids, drug ketones and xenobiotic aromatic hydrocarbons. Flurbiprofen, fenoprofen, ibuprofen, naproxen, ketoprofen and suprofen stimulated the activity of the human enzyme at low concentrations, whereas at higher concentrations they inhibited the activity. Comparison of the effects of the structurally related compounds with the drugs revealed that the essential structure required as the activator molecule is 2-phenylpropionic acid with a hydrophobic substituent on the aromatic ring.