[*Chem.-Biol. Interact.*, **130**, 879-889 (2001)] [Lab. of Biochemistry]

Molecular Cloning, Expression and Tissue Distribution of Hamster Diacetyl Reductase. Identity with L-Xylulose.

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Using rapid amplification of cDNA ends PCR, a cDNA species for diacetyl reductase was isolated from hamster liver. The encoded protein consisted of 244 amino acids, and showed high sequence identity to mouse lung carbonyl reductase and hamster sperm P26h protein, which belong to the short-chain dehydrogenase/reductase family. The enzyme efficiently reduced L-xylulose as well as diacetyl, and slowly oxidized xylitol. The K_m values for L-xylulose and xylitol were similar to those reported with L-xylulose reductase of guinea pig liver. The identity of diacetyl reductase with L-xylulose reductase was demonstrated by co-purification of the two enzyme activities from hamster liver and their proportional distribution in other tissues.

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Characterization of a Major Form of Human Isatin Reductase and the Reduced Metabolite.

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Isatin, an endogenous indole, has been shown to inhibit monoamine oxidase, and exhibit various pharmacological actions. However, the metabolism of isatin in man remains unknown. We have found high isatin reductase activity in the 105,000*g* supernatants of homogenates of human liver and kidney, and purified and characterized a major form of the enzyme in the two tissues. The K_m (10 μM) and k_{cat}/K_m (1.7 $s^{-1}\mu M^{-1}$) values for isatin at pH 7.0 were comparable to those for phenanthrenequinone, the hitherto best xenobiotic substrate of carbonyl reductase. The reduced product of isatin was chemically identified with 3-hydroxy-2-oxoindole, which was also excreted in human urine. The inhibitory potency of the reduced product for monoamine oxidase A and B was significantly lower than that of isatin. The results indicate that the novel metabolic pathway of isatin in man is mediated mainly by carbonyl reductase, which may play a critical role in controlling the biological activity of isatin.

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Prednisolone inhibits an IgE-mediated late-phase allergic cutaneous reaction by interfering with the activation of mast cells in mice.

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Epicutaneous antigen challenge in passively sensitized mice with IgE produces a biphasic cutaneous response which peaks 1 h (immediate-phase reaction) and 24 h (late-phase reaction; LPR) after the antigen challenge. In this model, anaphylactic degranulation and interleukin 6 (IL-6) expression between 4 and 8 h are observed in resident mast cells as the preceding stage of LPR. Prednisolone at a dose of 3 mg kg^{-1} clearly inhibited the LPR when administered 2 h before and 4 h after antigen challenge. Furthermore, 8 h after antigen challenge, prednisolone clearly inhibited the increase in the number of anaphylactic degranulated and IL-6-positive mast cells by administration 2 h before challenge, but did not affect it by administration 6 h after challenge. These data indicate that the inhibitory mechanism of prednisolone on LPR, at least, involves the inhibition of mast cell activation before LPR.

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A kampo formulation: Byakko-ka ninjin-to (Bai-Hu-Jia-Ren-Sheng-Tang) inhibits IgE-mediated triphasic skin reaction in mice: The role of its constituents in expression of the efficacy.

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We have demonstrated that oral administration of a Kampo formulation, Byakko-ka-ninjin-to, inhibited IgE-mediated triphasic skin reaction, including immediate phase response (IPR), late phase response (LPR) and very late phase response (vLPR), in passively sensitized mice with anti-DNP IgE antibody. Variant formulations of Byakko-ka-ninjin-to without Gypsum Fibrosum (Sekko), Glycyrrhizae Radix (Kanzo) or Oryzae Semen (Kobei) attenuated the inhibitory effect as compared with that of Byakko-ka-ninjin-to. These findings suggest that the effect of Byakko-ka-ninjin-to formulation on cutaneous inflammatory disease can differ from the sum of the effect of the individual constituents.