

[J. Biochem. 98, 1349 (1985)]

Kinetic and Structural Properties of Diacetyl Reductase from Hamster Liver. HIDEO SAWADA*, AKIRA HARA, TOSHIHIRO NAKAYAMA, KAZUNORI SEIRIKI

Kinetic and physicochemical properties of hamster liver diacetyl reductase have been examined. The kinetic studies on the reduction of diacetyl and NADPH to acetoin and NADP⁺ suggest that the reaction follows an Ordered Bi Bi mechanism in which NADPH binds first before diacetyl. The enzyme is a tetrameric glycoprotein of single subunits of a Mr of 23,500 with a sedimentation coefficient of 6.0 S. The enzyme does not contain Zn, Cu or Fe. The amino acid composition revealed an unusually low proportion of proline residues. The modification of thiol and arginine residues of the enzyme caused the loss of the activity, but the presence of NADPH prevented it. The enzyme transferred the *pro* 4S hydrogen atom of NADPH to the substrate and the binding of the enzyme to NADPH resulted in a red shift of the absorption spectrum of the cofactor.

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Basic Study for the Clinical Application of Fluoropyrimidines to Cancer Chemotherapy (Part I)-Metabolism of Fluoropyrimidines in Cancer Patients. TADASHI HORIUCHI, SHOJI SUGA, HIDEO SAWADA*, HAKUTAKA HASHIZUME, HIDEAKI AOYAMA, KENJI INA, KIYOJI KIMURA

Thymidine phosphorylase activity in resected stomach and breast cancer specimens was dominant compared to that of uridine phosphorylase, which suggesting that 5-fluorouracil is mainly metabolized, via 5-fluoro-2'-deoxyuridine, to an active form, 5-fluoro-2'-deoxyuridine 5'-monophosphate. Both 1-(2-tetra hydrofuranyl)-5-fluorouracil and 5'-deoxy-5-fluorouridine were activated by thymidine phosphorylase to form 5-fluorouracil. The thymidine phosphorylase activity in tumor tissues was over 5-fold higher than that in normal tissues. This observation would indicate that the compounds would exert a tumor-selective toxicity in cancer patients.

[Yakugaku Zasshi, 105, 271 (1985)]

Interaction of Membrane Lipids with Carbonyl Reductase in Guinea Pig Liver Microsomes. SHIGEYUKI USUI, AKIRA HARA, TOSHIHIRO NAKAYAMA, HIDEO SAWADA*

Membrane lipids affecting guinea pig liver microsomal carbonyl reductase were investigated. The reductase in microsomes treated with 67% acetone was activated about three times that of intact microsomes, and inhibited by the addition of acetone-extracted lipids in which fatty acids gave strong inhibition on the reductase in acetone-treated microsomes and the purified reductase. On the other hand, the activity of the reductase was inactivated by phospholipase treatment and delipidation of microsomes with sodium deoxycholate, and recovered by the addition of phospholipids. The purified reductase was also activated by phospholipids. These results indicate that the membrane lipids take part in carbonyl reductase activity.