カルボニル還元酵素の単離およびその特性

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Purification and Properties of Carbonyl Reductase from Rabbit Ridney

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ABSTRACT An enzyme catalyzing the metabolic reduction of acetohexamide, an oral antidiabetic drug, has been purified from the cytosolic fraction of rabbit kidney to apparent homogeneity by various chromatographic techniqes. The purified enzyme consists of a signal polypeptide chain with a molecular weight of 28,000 on sodium dodecyl sulfate-polyacrylamide gel electrophoresis.

The enzyme requires NADPH as a cofactor and has an optimal pH of 6.0. A variety of xenobiotic carbonyl compounds including acetohexamide are effectively reduced by the enzyme. Flavonoids (quercetin and quercitrin) are potent inhibitors for the enzyme, but pyrazole or barbiturates have little effect on the enzyme activity.

These findings clearly indicate that the enzyme can be classified as one of the carbonyl reductases. The enzyme also shows both prostaglandin 9-ketoreductase and 3α-hydroxysteroid dehydrogenase activities. Judging from the Kcat/Km values of the enzyme for 4-pyridylketones with a straight-chain alkyl group, a hydrophobic pocket that binds most strongly to a straight-chain alkyl group of five carbon atoms in length appears to be located in the substrate binding region of the enzyme.

抄録　経口糖尿病薬アセトヘキサミドを基質として、ウサギ腎臓の可溶性画分からケトン薬物還元酵素の単離、精製に成功した。本酵素は、分子量数 28,000 の単量体で、補酵素として NADPH を要求した。芳香族ケトン類を良い基質とするとともに、PG−9−ケト、3−ケトステロイドなどのレダクターゼ活性を有することが判明した。ま

た、本酵素の組成はウサギ肝臓やニワトリ腎臓より単離されたカルボニルレダクターゼのそれと高い類似性を示した。アセトヘキサミドおよび4－ピリジルケトン誘導体に対する本酵素の反応性は、基質の疎水性に依存して増大するが、直鎖のアルキル炭素数が6以上になると減少する傾向にあった。従って、本酵素の基質結合領域には、炭素数5程度の疎水性ポケットの存在が考えられた。

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