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Heterogeneity of Rat Liver Sulfotransferases*

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Sulfation is generally an effective detoxification process by giving rise to the formation of ionized sulfates, which are more water soluble than the parent compounds and thereby facilitate their excretion into urine or bile. Sulfation of array of compounds such as phenols, alcohols, amines and hydroxylamines has provided the impetus to elucidate the multiple forms of sulfotransferases (ST).

Previous studies from this laboratory showed a wide variation in biliary metabolites of androsterone (AD) in Wistar rats. About half of the rats excreted large amounts of steroid glucuronides into bile, whereas the other rats excreted mainly steroid sulfates into bile. A remarkable feature of ST activity was a sex difference. ST activity toward AD was much higher in adult females than in adult males, whereas ST activity toward 4-nitrophenol (NP) was much higher in adult males. These results prompted us to investigate which ST isoenzymes are responsible for sulfation of AD.

Each Peak (I—V) obtained by DEAE-cellulose chromatography was precipitated in the 68% sat. ammonium sulfate and purified by affinity chromatography on PAP-agarose. Peak I, III and IV showed a prominent polypeptide band with a subunit molecular weight of 29,000. Peak II had subunit molecular weights of 28,000 and 36,000, whereas Peak V had subunit molecular weights of 29,000 and 36,000.

Several authors separated and purified ST isoenzymes and these STs were named in order of their elution from DEAE-cellulose column. Separation of AD-ST by DEAE-cellulose column provided the highest AD-ST activity in Peak I. The subunit molecular weight of Peak I was in good agreement with that of hydroxysteroid ST 1. Though characterizatrion of this enzyme is still incomplete, the close correspondence of chromatographic profiles and subunit molecular weight suggests that AD-ST isoenzyme (Peak I) should be hydroxysteroid ST 1. Application of Peak I to the affinity column resulted in 85-fold purification of AD-ST activity from cytosolic fractions. Peak I isoenzyme had comparatively low ST activity toward cortisol (CS) and was devoid of ST activity toward NP. Peak II appears to be a mixture of ST III and aryl ST I, whereas Peak V should mainly consist of aryl ST II. Peak III and IV could not be specified at present.

In this study, we demonstrated the existence of four partly resolved ST Peak I, II, III and IV active on AD. Previous study revealed a biphasic development of female ST activity toward AD : The enzyme activity increased after birth in parallel in both sexes, attained the highest activity at about 20 days of age, and began to decline after-

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ward. In contrast to males, female ST activity toward AD increased agein to high levels after 40 days of age. ST activity toward AD appears to be regulated by gonadal and progestational hormones. These studies indicate that further study is required to clarify which isoenzymes are responsible for developmental alteration, sex difference, induction or suppression of AD-ST activity.