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Study on Glycylproline Dipeptidyl Aminopeptidase Activity in Chinese Serum

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Glycylproline Dipeptidyl Aminopeptidase (GPDAP; EC 3.4. 14.1), discovered in rat liver and kidney by Hops-Havu and Glenner (1) in 1966, is an enzyme which cleaves the N-terminal X-proline from peptides. The enzyme has been purified by Nagatsu group (2) from human submaxillary gland to apparent homogeneity. An approximate molecular weight of 225,000 was estimated by gel filtration. Chromogenic substrates of the type X-proline-*p*-nitroanilide (X=Gly, Ala, Lys, Arg, Glu, or Asp) have been studied, and the glycyl-proline-*p*-nitroanilide had the highest activity among the substrates at the optimum pH 8.7 (3). The enzyme activity has also been demonstrated in normal and pathological human sera (4-6).

In the present study, we used glycylproline-*p*-nitroanilide (a gift from Dr. Y. Kasahara, Fujizoki Pharm. Co., Tokyo) as substrate to determine the serum GPDAP activity kinetically at 37°C and pH 7.9. The within-run and run-to-run precision of the test were 0.4-0.7% (C.V.) and 0.6-2.6% (C.V.) respectively (7). The determination of enzyme activity was linear at least up to 400 U/L (correlation coefficient=0.9998). The reference range for normal Chinese was determined to

be 68.2±16.0 U/L (mean ± SD; range 38.8-100.5) from 140 apparently healthy adults (age 24-79 years). There was no significant difference between male (70.2+15.1 U/L) and female (66.3±16.6 U/L), ($p>0.1$, $n=70$ each). These data generally agreed with values reported for other populations.

The serum GPDAP activity of patients with liver diseases was significantly ($P<0.001$) higher than the normal control; 125.1±40.5 U/L (range 69.1-200.2) in 10 acute hepatitis, 119±38.8 U/L (41.9-221.8) in 42 chronic active hepatitis, 93.5±38.5 U/L (34.0-228.5) in 45 cirrhosis, and 186.7±116.9 U/L (61.5-681) in 40 primary hepatoma. Its activity increased in the order of cirrhosis, hepatitis and hepatoma. Those results indicated that the determination of serum GPDAP may be used as a diagnostic aid for liver diseases.

On the order hand, the serum GPDAP activity was determined to be 46.6±30.9 (8.4-126.6) in 44 leukemia patients. It was significantly ($p<0.001$) lower than the normal. And 50% of the patients had serum level less than the lower limit of the reference range. Other preliminary results indicated that the serum GPDAP activity increased in pancreatic cancer, and decreased in gastric cancer, but not altered in lung cancer patients. The cause of the alternation of serum GPDAP activity in patients with neoplastic diseases and with liver diseases remains to be elucidated. But the fact of the alternation in pathological sera and its possible application as diagnostic aids are intriguing and require further study.

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