

**S U M M A R Y**

SUMMARY

The investigations reported in this thesis deal with the metabolism of arginine with special reference to <sup>the</sup> enzyme ornithine carbamoyltransferase in normal and tumour tissue of Rumex acetosa. L. cultivated in vitro.

Studies reported show that the enzyme ornithine carbamoyltransferase is low<sup>er</sup> in tumour than in normal tissue. This observation, along with the previous observations from this laboratory that arginase and ornithine  $\delta$ -ketoacid transaminase are high in tumour tissue would suggest that ornithine formed in tumour tissue is mainly channeled for glutamate formation rather than going for citrulline synthesis. Ornithine concentration itself seems to have a control over its formation by inhibiting arginase allosterically (Naik, 1970) and also having an inhibitory effect on ornithine carbamoyltransferase at high concentrations.

The enzyme ornithine carbamoyltransferase has been partially purified and characterized from tumour tissue. The kinetics of the purified enzyme showed some differences from that reported for this enzyme from other sources. The enzyme is specific for L-ornithine and carbamyl phosphate. It is inhibited by several metal ions such as  $Mn^{++}$ ,  $Cu^{++}$ ,  $Ni^{+++}$ ,  $Co^{++}$ ,  $Fe^{+++}$ ,  $Al^{+++}$ ,  $Zn^{++}$  and  $Hg^{++}$ . It is also inhibited

by phosphate, one of the products of reaction. The inhibition is competitive for carbamyl phosphate.

Most interesting observation made is the sigmoidal substrate saturation response for both substrates, with Hill coefficient values of more than one, indicative of cooperative binding. No definite proof, however, could be obtained as to the mechanism of reaction since the kinetic data did not clearly confirm to either sequential or ping pong patterns.

Also it has been possible to show that the enzyme is inhibited by several TCA cycle intermediates and purine nucleotides. The kinetics of AMP inhibition indicated an allosteric type of inhibition. It also seems that in this respect the tumour enzyme differs from normal one. This observation is of great significance to cancer biochemistry since it indicates that a higher concentration of adenine nucleotides will affect the formation of pyrimidine nucleotides required for an enhanced synthesis of nucleic acids, by controlling the activity of ornithine carbamoyltransferase and thus allowing the available carbamyl phosphate to go more for pyrimidine synthesis.