

## THE STEREOCHEMICAL INTEGRITY OF HYGRINE ENANTIOMERS IN VIVO AND IN VITRO

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Hygrine is an established precursor of the tropane ring system (O'Donovan and Keogh 1969) and we have shown (McGaw and Woolley 1977) that in Datura the dextrorotatory isomer, which has the  $2R$  configuration (Lukeš 1960), is preferentially used by the plant in the cyclisation process leading to the tropane ring. In the classification of the Solanaceae, Datura is placed in the Datureae whereas other well known tropane alkaloid bearing plants eg Atropa, Hyoscyamus and Physalis are collected together in the Solaneae tribe (Wettstein 1897). When we examined these latter plants for their ability to utilise (+) and (-)-hygrine- $[2'-^{14}C]$  there appeared to be little difference in the incorporation of the tracers into the tropane alkaloids (McGaw and Woolley 1979). This is a most unusual and contrasting result and we decided to investigate whether there was any possibility of racemisation of the optical isomers in aqueous solution or even the existence of an isomerase system in the plants.

The chemical stability was investigated by monitoring the optical rotation of D(+)-hygrine D(+)-tartrate in aqueous solution at neutral pH. There was no change in the specific rotation over a three week period.



To test the interrelationship within the plant, hygrine- $[2'-^{14}C]$  was synthesised (McGaw and Woolley 1977). By reducing N-methylpyrrolid-2-one with sodium borohydride- $^3H$  and coupling the resultant N-methylbutanal-1- $^3H$  with ethyl acetoacetate it was possible to prepare hygrine labelled with tritium in the asymmetric centre, C(2). The tracers were mixed giving a  $^3H/^{14}C$  ratio of 13.2. Since we knew that  $^{14}C$  labelled hygrine was a precursor of the tropane alkaloids it was possible to use it as an internal standard by which to monitor the uptake of tritium on a molecular basis. The double labelled precursor was resolved and the separate D(+)-tartrate salts were infiltrated into Physalis alkekengi plants. The  $^3H/^{14}C$  ratio in the isolated alkaloids remained substantially the same and we therefore feel that it is unlikely that there is any interconversion of hygrine isomers in vivo.

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