

BIOSYNTHESIS OF WITHASOMNINE, A UNIQUE PYRAZOLE ALKALOID

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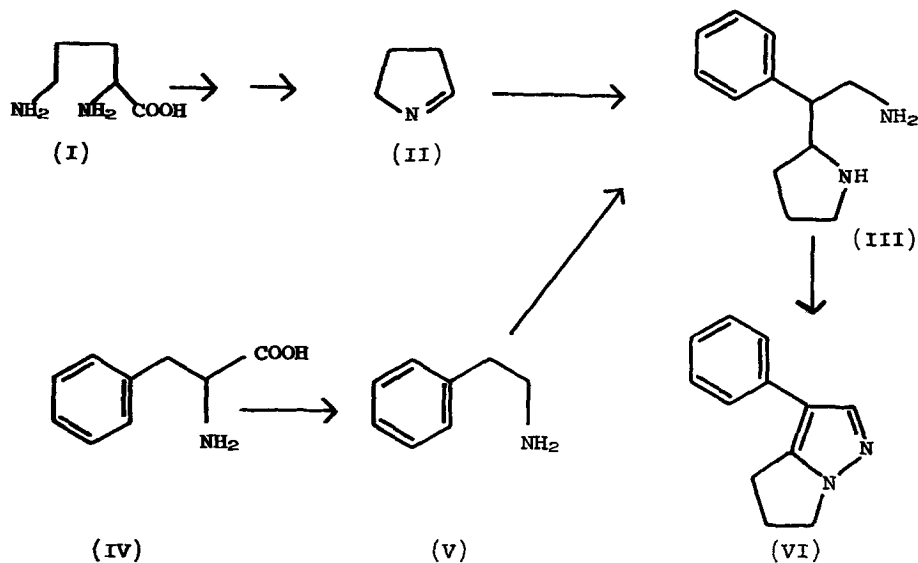
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Withania somnifera Dunal indigenous to Southern Europe, India and Africa is cultivated for drug purposes in India¹. Schwarting et al² have isolated in a pure state nine alkaloids from the roots of this plant - tropine, pseudotropine, 3-tropyl tigloate, choline, cuscohygrine, dl-isopelletierine, anahygrine, anaferine and an alkaloid whose constitution was not established.

More recently, Schröter et al³ have isolated an alkaloid from the roots of *W. somnifera* which they name Withasomnine and whose structure has been established by physical methods as 4-phenyl-1,5-trimethylenepyrazole (VI). Withasomnine has been shown to be identical with the unidentified alkaloid isolated by Schwarting⁴. On the basis of the simulated biosyntheses of other alkaloids of *W. somnifera* from Δ^1 -pyrroline (II) which have since been substantiated by tracer studies⁵, Onaka⁴ has suggested a biogenetic scheme for this alkaloid from ornithine (I) and phenylalanine (IV) and has achieved an in vitro synthesis of Withasomnine based on this scheme.

We now wish to report some preliminary studies on the biosynthesis of this alkaloid. D1-[3-¹⁴C]-phenylalanine (total activity 2.2×10^8 counts/min.) was fed by a wick arrangement to two, one year old, *W. somnifera* plants. The plants were grown on for fourteen days and then harvested. The crude alkaloidal mixture was isolated by conventional methods. 5 mg. of inactive Withasomnine was added, as carrier, to the mixture and the alkaloid was isolated on a preparative thin layer chromatogram (Silica G Merck); solvent system petroleum ether (B.P. 60-80°C)/Propanol 95:10, Rf 0.35. The alkaloid was purified to constant activity and had a percentage incorporation of 0.002%.

In a second experiment D1-[2-¹⁴C] ornithine (total activity 2.2×10^8 counts/min.) was fed to a further two plants by the same method and Withasomnine isolated as before. It was purified to constant activity and had percentage incorporation of 0.004%.



Our results to date substantiate Onaka's hypothesis on the biosynthesis of this alkaloid.

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