

BIOSYNTHESIS OF THE C₉₋₁₀ UNIT OF CEPHAELINE

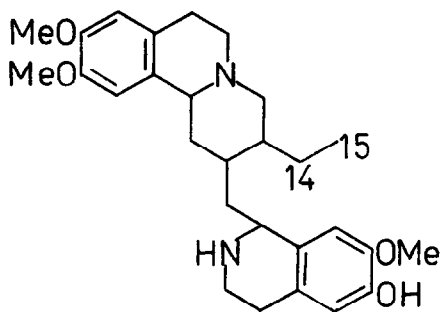
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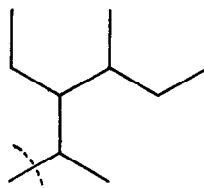
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Alkaloids related to corynantheine, strychnine, aspidospermine, and ibogaine all contain a C₉₋₁₀ unit which is believed to arise from the same precursor, and which appears in the alkaloid cephaeline (I) as the unit (II). This unit has recently been shown to arise from geraniol in catharanthine and vindoline (1,2,3,4) and in quinine (5). The geraniol appears to arise from mevalonic acid which is also a specific precursor of the above alkaloids (6). We now present evidence that neither leucine nor intermediates in carbohydrate biosynthesis are good precursors of the C₉₋₁₀ unit, that radioactivity from glycolic acid is widely randomized in cephaeline, but that glycine is a specific precursor of this C₉₋₁₀ unit in cephaeline.



I



II

All radioactive compounds were fed in quantities of 100 μ c, by the wick method, to four three-year old cephaelis ipecacuanha plants for periods of ten days, after which time cephaeline was isolated. The plants were shown to be actively synthesizing alkaloids by concurrently feeding tyrosine-3-C¹⁴ which gave rise to radioactive cephaeline with a specific activity of 1.3×10^5 d p m/mM. Succinic acid-1,4-C¹⁴, succinic acid-2,3-C¹⁴, and glycerol-1,3-C¹⁴ gave rise to cephaeline of very low activity, whereas leucine-U-C¹⁴-6, 7-H³ gave inactive cephaeline.

Glycine-2-C¹⁴ (100 μ c) gave rise to cephaeline (80 mg) with a specific activity of 5.5×10^4 d p m/mM (0.01% incorporation). A portion of it was subjected to a Kuhn-Roth oxidation to yield sodium acetate (C₁₄ and C₁₅) containing 15.1% of the activity of the cephaeline. A Schmidt reaction on the acetic acid yielded methylamine (isolated as the N-methylbenzamide) which contained all the activity of the acetic acid. The carbon dioxide was inactive. Conversely the cephaeline obtained from the feeding of glycine-1-C¹⁴ was essentially inactive.

Glycollic acid-1-C¹⁴ also gave rise to cephaeline of very low activity. Glycollic acid-2-C¹⁴ resulted in cephaeline (159 mg) which had a specific activity of 2.8×10^4 d p m/mM (0.02% incorporation). However the acetic acid obtained from C₁₄ and C₁₅ by Kuhn-Roth oxidation contained only 4.8% of the original activity and this was divided between the two carbon atoms. These values are compatible with randomization of activity such as has been demonstrated when radioactive acetic acid has been fed to cephaelis ipecacuanha (7).

The data obtained from the feeding of glycine-2-C¹⁴, wherein C₁₅ contains approximately one sixth of the total activity of the cephaeline and C₁₄ is inactive, would be in agreement with glycine acting as a specific two carbon unit precursor of mevalonic acid and the C₉₋₁₀ unit. If this is so the keto analog glyoxylic acid should also be a specific precursor of this unit. Recently glyoxylic acid-2-C¹⁴ has been shown to be an effective precursor of β -carotene in chloroplasts (8). Glyoxylic acid-1-C¹⁴ did not incorporate radioactivity into the β -carotene, and we have found that, in an analogous fashion, glycine-1-C¹⁴ is a very poor precursor of cephaeline.

Our results suggest that the oxidation state of a two carbon compound may exert a major effect on whether or not it is capable of acting as a specific precursor for the C₉₋₁₀ unit of these alkaloids. It appears that acetic acid is not normally a specific precursor of this unit, but that radioactive acetic acid is partially or completely randomized throughout not only the C₉₋₁₀ unit but also the rest of the molecule (7,9,10). Our results suggest a similar fate for glycollic acid whereas glycine seems to act as a specific precursor for the C₉₋₁₀ unit. Confirmation of such a neat distinction must await further feedings and further degradations and this approach is being actively pursued.

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