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ON THE ORIGIN OF THE C_3-UNIT IN (+)-PROTOLICHESTERINIC ACID

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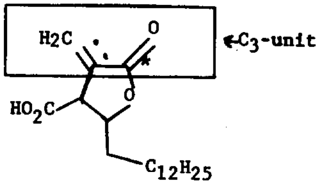
The series of aliphatic lichen acids is of unusual biosynthetic interest in that it appears to be a classic example of the derivation of a number of different natural products from a common sequence of biochemical reactions, which is furthermore related to the fundamentally important citric acid cycle and fatty acid cycle (at least formally). Both these contentions are supported by experiments described below which represent the first biosynthetical work on the aliphatic lichen acids. It has now been found that the C_3-unit of (+)-protolichesterinic acid (PLA) is derived from succinate, and seasonal studies now suggest that the aliphatic lichen acids may be more than shunt metabolites.

Initial experiments on the acetate biosynthesis of (+)-protolichesterinic acid[1] showed that it was indeed derived from a fatty acid derivative with normal head-to-tail linkage of acetate units plus a C_3-unit whose origin was not readily ascertained from the acetate data, although the equality of label in positions (.) suggested that it arose via a symmetrical intermediate.



On the basis of an earlier hypothesis,[2] we would have expected that acetate-[1-^{14}C]-label would be converted into succinate-[1,4,^{14}C]- label, followed by conversion to oxalacetate and condensation with a fatty acid derivative to give (1) with label in position (*). Positions (.) should not be significantly labeled, though what small amount of activity would be present should be distributed equally between each. It was disturbing that positions (.) were labeled to nearly the extent of (*). Furthermore, when a feeding experiment with succinic-[1,4^{14}C]-acid was run on a batch of fresh <u>Cetraria islandica</u> lichen, no incorporation was observed— the experiments being identical except for a time lapse of several weeks. In order to determine if a) the C_3-unit were derived from a source other than succinate and related metabolites or b) if seasonal variations were critical, we carried out simultaneous feeding experiments with acetate, succinic acid, glucose and pyruvate, labeled with ^{14}C in various positions, both in winter and summer. The winter experiment failed to give incorporation of any of the precursors. The summer experiment, however, was successful in incorporating succinic acid as well as acetate.

Succinic-[1,4^{14}C]-acid was incorporated into (1) to the extent of .001% or approximately a tenth the incorporation of acetate activity under the same conditions. Considering that a much smaller portion of (1) is derived from a non-acetate metabolic route, the experiments are in good agreement. The succinic acid experiment was surprisingly much more difficult to purify than the acetate runs. Analysis of suitable glpc derivatives showed that derivatives previously used could not be satisfactorily purified by multiple tlc. As either PLA or lichesterinic acid methyl esters were unstable to glpc, we chose to isolate the methyl ester of 2-methyl-4-ketoheptadecanoic acid, using glpc to constant radioactivity as the final purification stage. Reconversion of the ester to the free acid under standard conditions (1N NaOH 100°, 1 hr.) gave a satisfactory yield of material which was decarboxylated (copper chromite-quinoline) to give 34% of total radioactivity in a position corresponding to (*) in (1). The remainder of the molecule (isolated as n-propyl tridecyl ketone) contained 66% of the total activity.

Production of (1) in summer alone is in accord with seasonal variations observed in other chlorophyll-bearing organisms, and suggests that the key role in the biosynthesis of (1) belongs to the phycobiont, or algal component, of the lichen. A tempting hypothesis is that (1) may act as a source of sustenance for the dormant organism during the winter months.

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References

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