

The Isolation of Isoflavonoids from Bacteria

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Summary The isoflavonoids genistein and prunetin have been isolated for the first time from a bacterium, *Mycobacterium phlei*.

THE flavonoid-isoflavonoid family constitutes the largest single group of naturally occurring oxygen heterocyclic compounds.¹ However, the isolation of these metabolites has so far been restricted to the higher plants and they have never been found in micro-organisms or algae.² We report the isolation of the isoflavones genistein (5,7,4'-trihydroxyisoflavone) and prunetin (5,4'-dihydroxy-7-methoxyisoflavone) from the bacterium *Mycobacterium phlei* (ATCC 10142).

Genistein (3 mg./l.)[†] and prunetin (2 mg./l.), along with 6-methylsalicylic acid (3 mg./l.),[‡] were isolated from the culture medium of *M. phlei* when the organism was grown at 37° for 5 days (shake) in an iron-deficient medium of the

following composition: L-asparagine, 21 g.; sodium citrate, 1.05 g.; glycerol, 150 ml.; K₂HPO₄, 2.1 g.; MgSO₄·7H₂O, 2.25 g.; deionised water to make a final volume of 1.5 l. When cultured in medium of normal iron content, no trace of the isoflavones or 6-methylsalicylic acid was observed. Instead, substantial quantities (100 mg./l.) of anthranilic acid were isolated from the medium.

The isolation of genistein and prunetin from *M. phlei* provides the first example of isoflavonoid production by a micro-organism and is yet another illustration of the profound effect that iron exerts on the metabolism of micro-organisms. Micro-organisms grown under conditions of iron-deficiency are well known to show enhanced production of aromatic metabolites capable of iron chelation. White and Snow³ have established that most species of mycobacteria grown in media deficient in iron produce members of a class of compound known as the mycobactins.

[†] Identical with material synthesized by the method of Ollis.⁹

[‡] Identical with material kindly supplied by Dr. J. D. Bu'Lock.

The isolation of 2,3-dihydroxybenzoic acid⁴ and its various amino-acid conjugates^{5,6} from several species of microorganisms have also been shown to be dependent upon the growth media being iron-deficient. In addition, Ratledge and Winder⁷ have observed greatly enhanced production of salicylic acid by *M. smegmatis* and *M. tuberculosis* when the media were depleted in iron. These workers have also isolated 6-methylsalicylic acid from a strain of *M. phlei* (NCTC 525) different from the one employed by us, although again this organism was cultured in iron-deficient medium.⁸

The production of metabolites, generally considered to be characteristic of both the higher plants (genistein and prunetin) and of some fungi (6-methylsalicylic acid), by *M. phlei* serves to emphasize the unique position held by the mycobacteria and affords a unique opportunity to study the biosynthesis of these compounds in a single system.

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