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CHEMOSYSTEMATICS–CURRENT STATUS

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Key Word Index—Swain; plant chemosystematics; isoquinoline alkaloids; secondary metabolites.

Abstract—Tony Swain's pioneering contributions to chemosystematics are recalled. The distribution of isoquinoline alkaloids in plants is reviewed. The current use of secondary metabolites in plant systematics is analysed. © 1998 Published by Elsevier Science Ltd. All rights reserved

This contribution is not about Tony Swain but about a subject to which he made a major contribution during its formative years: the 1950s and particularly the 1960s. I am going to restrict my commentary to what is sometimes known as micromolecular systematics; that is to the distribution of low-molecular weight secondary metabolites and their systematic significance. While Swain did write a number of papers in this subject area, notably in the Filcopsida and Compositae [1–4], I think it is probable that his catalytic value in bringing together important compendia of papers in two books he edited, *Chemical Plant Taxonomy* [5] and *Comparative Phytochemistry* [6], had a greater overall impact on the development of the discipline.

In particular, there was his editorship of *Chemical Plant Taxonomy* in 1963 [5]. This was not the first book on chemical taxonomy, but its emphasis on the distribution of some major classes of metabolite in higher plants (a "big picture" approach) was exciting and offered an intellectual challenge that sustained the subject for two decades. And then, of course, Swain was also responsible for the establishment of two journals that are important repositories for papers with a chemotaxonomic message. First, there was *Phytochemistry*, and this was followed 12 years later by *Biochemical Systematics* which then almost immediately underwent a name change to *Biochemical Systematics and Ecology* as the founding editors recognised the beginning of the development of chemical ecology.

But let us return to *Chemical Plant Taxonomy*. What made this compilation so stimulating was that it bought together what were then many of the "big discoveries" in chemical taxonomy. For many chemists it opened their eyes to another outlet for natural products chemistry at a time when new techniques in chromatography and spectroscopy were beginning to speed up the comparative and identification processes of phytochemical analysis.

Several of the contributions focussed on observations of alkaloid distribution. One group of alkaloids that received particular attention were those derived from the condensation of two molecules of tyrosine to yield the 1-benzyltetrahydroisoquinoline alkaloid nucleus (Scheme 1). The concentration of these alkaloids in the major taxon then usually referred to as the Polycarpicae or Ranales was noted by several authors, notably by Hegnauer [5] and Kubitzki [7]. Modern classifications, such as those of Thorne [8] and Dahlgren [9], have accepted that these alkaloids are an important taxonomic markers of a group of genera that largely reflect the Polycarpicae and Ranales, which are known now as the Annoniflorae (Table 1) or Magnoliiflorae.

Perhaps the most telling inclusion in Table 1 is the Papaverineae (the families Papaveraceae and Fumariaceae). These families had traditionally been placed in the order Rhoeadales together with families such as the Capparaceae and Cruciferae, which do not produce 1-benzyltetrahydroisoquinoline alkaloids but are rich in glucosinolates. The chemical ambiguities of the Rhoeadales and the affinity of the Papaveraceae with the Polycarpicae was observed by Hegnauer [10, 11] and this evidence was accepted by Cronquist [12] who re-assigned the two families to a separate order, the Papaverales, which formed part of his Magnoliidae. To quote Cronquist [12]:

"The Papaverales characteristically contain iso-

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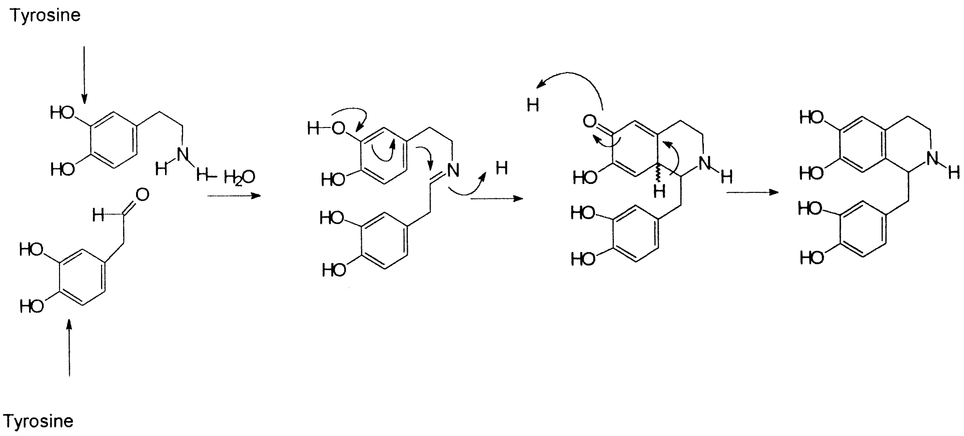


Scheme 1.

quinoline alkaloids (sometimes including berberine), a feature which links them to the rest of the Magnoliidae. Hegnauer (1956, 1961) has noted that 'The Polycarpicae (*sensu* Wettstein) together with the Papaveraceae form a very natural group characterized by the synthesis of alkaloids of the phenylalanine type.' The phenylalanine alkaloids of Hegnauer are apparently equivalent to the isoquinoline alkaloids of Manske and Holmes and some other authors."

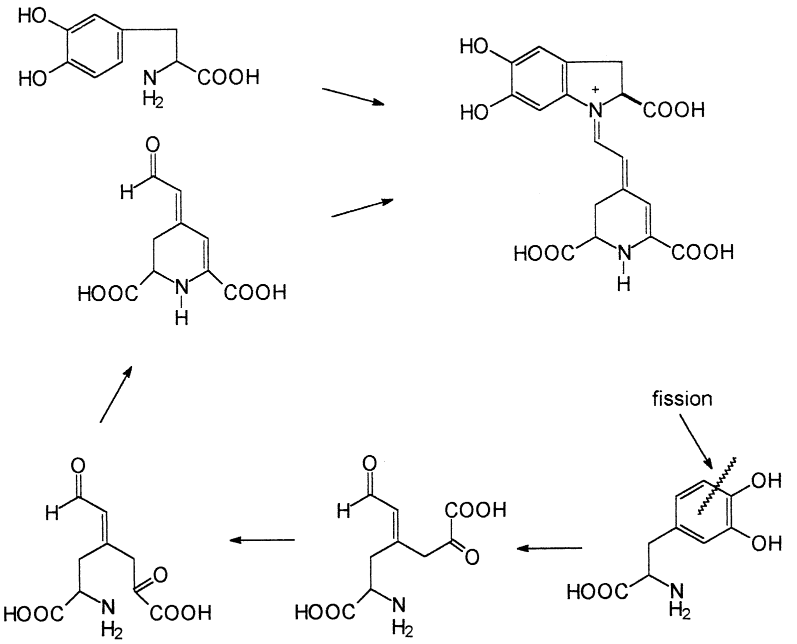
Another product of tyrosine that proved to be an early highlight for chemotaxonomy was the betalains. These coloured compounds are formed (Scheme 2) by the combination of dopa and betalamic acid (itself a modified dopa unit). Together with the related betaxanthins (proline + betalamic acid) these pigments only occur in a subset of the families which make up the order Caryophyllales (formerly the Centrospermae). To this day there is no better example of a type of compound being associated entirely with one taxonomic group—and their value as a systematic marker for that group is widely recognised [13].

The problem with such "big discoveries" is that they cannot be made with the same frequency and while *Chemical Plant Taxonomy* highlighted many such discoveries, new insights with a similar impact have proved difficult to achieve. Furthermore, as the available data rapidly increased through the 1970s and 1980s it became apparent that distribution patterns were often far less consistent than it had been assumed they would be. For example, the distribution of 1-benzyltetrahydroisoquinoline alkaloids has proved to be more widespread than originally anticipated

Table 1. Distribution of classes of 1-benzyltetrahydroisoquinoline alkaloids in major taxa; arranged according to the system of Thorne [8]

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Annoniflorae															
Annonales															
Winterineae															
Illicinae															
Magnoliineae	+		+												
Annonineae	+	+	+	+	+					+					
Aristolochineae	+		+	+	+										
Laurineae	+	+	+	+	+					+					+
Piperinae			+												
Berberidales															
Berberidineae	+	+	+	+	+	+		+		+	+	+			+
Papaverineae		+	+		+	+	+	+	+	+		+	+	+	+
Nymphaeiflorae															
Nymphaeales	+	+	+												
Rutiflorae															
Rutales	+		+		+			+	+						

1 = Benzylisoquinolines and bisbenzylisoquinolines; 2 = Proaporphines; 3 = Aporphines; 4 = Aristolochic acids and aristolactams; 5 = Protoberberines; 6 = Phthalideisoquinolines; 7 = Spiroisoquinolines; 8 = Protopines; 9 = Benzophenanthridines; 10 = Morphinans and Morphinanedienones; 11 = Hasubabans; 12 = Dibenzazonines; 13 = Rhoedines; 14 = Cularines; 15 = Pavines and isopavines.



Scheme 2.

and they occur in a number of orders outwith the Annoniflorae or Magnoliiflorae (i.e., in the orders Rutales, Fabales, Sapindales, Buxales, Cornales, Araliales, Capparales, Euphorbiales, Rhamnales, Liliales, Arecales [14]). The Rutaceae, in particular, illustrate this problem in that a few genera, notably *Zanthoxylum* [15], possess a wide range of alkaloids that appear to be analogous to those of the Papaveraceae (see Table 1). Unfortunately there is little evidence to support a link between Rutaceae or Rutales and Annoniflorae and the co-occurrence of these alkaloids currently seems to represent two disparate manifestations of identical biosynthetic pathways without any systematic significance. There are many comparable examples of such disjunct distributions for major classes of metabolites and these have often been presumed to represent parallel evolutionary developments.

Now, some 35 years on from *Chemical Plant Taxonomy* the impression is of a subject that has stalled; the promise has not been fulfilled and chemical taxonomy still plays a peripheral role in systematics. Today the growth area of biochemical systematics is in DNA-sequencing which is now burdened with the unfair expectation that it will solve our problems. So what went wrong for micromolecular systematics? We can point to a number of factors which have had a negative impact on its development:

(1) Secondary metabolite biosynthesis within a species has proved to be a more plastic phenomenon than was originally supposed. Extrinsic factors such as soil nutrients, UV levels, drought, salinity and ambient temperature can all impact on the level and type of metabolite produced [16]. This makes interpretation of what is and what is not a valid chemical marker for a taxon very difficult.

(2) The genetic coding for the enzymes that perform secondary metabolic processes may often be retained within a species without being expressed. The old idea that evolution was often accompanied by the loss of ability to perform a biosynthetic process [17] has had to be revised as we realise that when production ceases to be expressed, the capacity is retained in the genetic code and may be re-expressed at a later date. Such re-expression may be phylogenetically distant from the original source [18], which would lead to the disjunct distribution of compounds such as the 1-benzyltetrahydroisoquinoline alkaloids. This could be the case in the alkaloids of the Annoniflorae and Rutales that would not then represent parallel evolutionary events. Thus, we must consider a vastly more complex evolutionary scenario than was originally supposed.

(3) The absence of comprehensive data on the distribution of metabolites in a series of taxa means that many attempts at taxonomic interpretation based on these markers are tentative and make suppositions that are not made with more traditional morphological or anatomical markers. For this reason the use of powerful computer-driven cladistic analysis programmes to analyse micromolecular data has rarely been attempted as it needs comprehensive data sets.

(4) Ironically, the successes in advancing analytical techniques to the level where traces of a metabolite can be detected have made it difficult to unambiguously establish its absence from a taxon.

(5) Sadly many chemical studies which have supposedly been performed for "chemotaxonomic purposes" have lacked credibility from the perspective of traditional taxonomists. There are many examples of failure to attend to the essential basic requirement of adequate vouchering of material, over-interpretation of data without due consideration to other systematic parameters, and inadequate thought as to what makes a valid taxonomic marker.

The above has made rather gloomy reading. Am I leading up to a declaration that chemical taxonomy does not work? No, this is not the case. What I am saying is that the problems confronting it are far more complex than originally imagined and that these make it very difficult to use secondary metabolites as the sole or primary markers in a taxonomic scheme. However, as hypothesis testers and problem solvers, used in a reactive rather than a proactive manner, they have shown themselves to be very valuable. Let us end on an upbeat note by looking at a few examples.

A number of taxonomically difficult families have been placed on the basis of their secondary metabolite profiles. The Bonnetiaceae, which consists of the two genera *Bonnetia* and *Archytaea*, is better associated with the Guttiferae than with the Theaceae because of the presence of xanthones [19]. Placement of the Bretschneideraceae in the Capparales rather than the Sapindales is supported by the occurrence of glucosinolates [20]. The South American family Rhabdodendraceae has a complex taxonomic history in which it has been variously associated with the Rutales, Caryophyllales and Rosales. Negative evidence (i.e. the absence of metabolites typical of the order) suggests that affinities are definitely not with the Rutales [21] but fail to give a strong indication as to the true affinity of this family.

At lower taxonomic levels, many classes of metabolites have proved useful in establishing taxonomic relationships. From our own work, the distribution of indole and carbazole alkaloids, 8-prenylated coumarins and monoterpene or sesquiterpene dominated volatile oils have been combined to confirm the division of the genus *Murraya* (Rutaceae) into two taxa [22]. One of these has close chemical affinity with the genera *Glycosmis* and *Clausena* and the other with *Micromelum* and *Merrilia*.

That there is considerable continuing endeavour in chemical taxonomy is amply demonstrated by browsing through any number of *Biochemical Systematics and Ecology*, the journal initiated by Tony Swain in 1973. Today much of the work reported therein is focussed on more limited studies within genera or within wide-ranging species and is contributing much to our knowledge of how metabolic profiles vary between populations and factors that may impact on this. While this is a far cry from the "big picture" chemical taxonomy of the 1960s, it is certainly producing information which will have a lasting value to the taxonomy of higher plants.

I suspect that Tony Swain, if available for comment, would be satisfied that his efforts in encouraging and supporting the early development of this discipline have not been wasted.

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