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The Distribution of Iridoids in *Labiatae Sensu Lato*

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SUMMARY. Iridoids, present in many plants used in the popular medicine, are important taxonomic markers in *Sympetalae*. The distribution of this compound in the families *Verbenaceae* and *Labiatae* have been of great value to delimit the boundary between the two families. In this work we show the distribution of these compound in *Labiatae sensu lato*.

RESUMEN. "La distribución de Iridoids en *Labiatae sensu lato*". Los iridoides, presentes en muchas plantas usadas en la medicina popular, son importantes marcadores taxonómicos en las *Sympetalae* y su distribuición en las familias Verbenaceae y Labiatae ha sido de gran valor para la delimitación entre estas familias. En este trabajo mostramos la distribuición de estes compuestos en *Labiatae sensu lato*.

INTRODUCTION

Iridoids are present in many herbal preparations used as bitter tonics, sedatives, febrifuges, cough medicines, remedies for wounds and as hypotensives. Nevertheless, for a long time, they were not considered particularly important as a pharmacologically active class of compounds. More recently, however, several investigations have revealed that iridoids exhibit a wide range of bioactivity including cardiovascular, hypoglycemic, antiinflammatory, antitumor, antiviral and immunomodulator activities, among others[1].

Iridoids have also been extensively used as taxonomic markers in *Sympetalae*. The presence or absence of certain types of iridoids has been a valuable chemotaxonomic indicator [2-6]. Iridoids can be divided into two main groups, carbocyclic and seco-iridoids, which are abundant in *Lamiales* and *Gentianales* (sensu Dahlgren [7]), respectively.

Among the families where carbocyclic iridoids have been found *Verbenaceae* and *Labiatae* deserve comments. Many species from these taxa have been used in the traditional medicine and some of the proclaimed activity could be related to these compounds. As iridoids have been demonstrating interesting biological activities and the chemotaxonomy is one of the criteria for selecting plants for phytotherapeutic investigation, the aim of this work is to show the distribution of this compound in the new system for the classification of the *Labiatae*.

The classification of the *Labiatae* and its relation to the family *Verbenaceae* is still being discussed. Most recently Cantino *et al.* [8] proposed to limit the *Verbenaceae* to the subfamily *Verbenoideae* and to transfer the other subfamilies to *Labiatae*, which would then be subdivided in eight subfamilies.

As previously reported by Rimpler *et al.* [4], in the former family *Verbenaceae*, the species of the subfamily *Verbenoideae*, with a ventral plantation, accumulate C-4 carboxylated iridoids, such as for instance theviridoside (Fig. 1a). On the other hand, the species with ovules dorsally attached, occurring in the subfamilies *Viticoideae, Chloanthoideae* and *Caryopteridoideae*, as well as in the *Labiatae*, did accumulate mainly C-4 decarboxylated iridoids, such as ajugol [4, 6] (Fig. 1b). It thus appears that the distribution of

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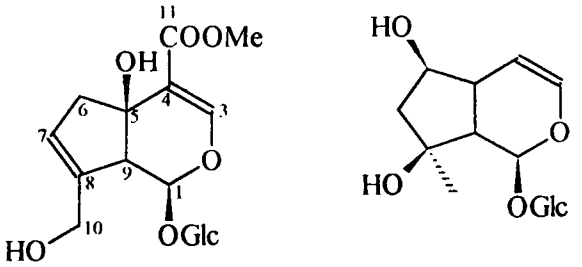

1a. theviridoside **1b.** ajugol

Figure 1. Examples of C-4 carboxylated (1a) and C-4 decarboxylated iridoids.

iridoid types in these families supports the revised classification by Cantino *et al.* [8], which was based on morphological characters.

METHODOLOGY

The occurrence of the iridoids in the genera of *Labiatae* were obtained in the Chemical Abstracts and in some additional reviews [6, 9-13].

RESULTS AND DISCUSSION

The data obtained in the survey suggest a sound distinction between *Verbenoideae* and the rest of *Verbenaceae sensu lato,* which according to the iridoid content are more closely related to *Labiatae*. This correspondence is based in the fact that the vast majority of the isolated iridoids outside *Verbenoideae* is C-4 decarboxylated, such as ajugol, harpagide, reptoside, melittoside and monomelittoside, or iridoids are absent at all.

Table 1 shows the distribution of the genera of *Labiatae* in the eight subfamilies, according to Cantino *et al.* [8]. The table also shows the genera formerly included in *Verbenaceae* and transferred to *Labiatae*. The subfamily *Viticoideae* is formed exclusively by genera once classified as *Verbenaceae;* no verbenaceous genera were incorporated into *Nepetoideae, Lamioideae* and *Pogostemonoideae*.

The distribution of iridoids in the different subfamilies of *Labiatae* is also presented in Table 1. These compounds were reported for species from all subfamilies. Although the majority of the products are C-4 decarboxylated, in *Lamium* and *Phlomis* they are C-4 carboxylated or present a methyl group attached to C-4. The occurrence of carboxylated iridoids in other species is rare: in *Physostegia* and *Scutellaria* (together with C-4 decarboxylated products) and in the formerly verbenaceous *Caryopteris odorata, Clerodendrum inerme, Premna corymbosa* and *P. latifolia* and some species of *Vitex* [6]. In the other species transferred to *Labiatae* the iridoids are C-4 decarboxylated.

Aucubin, the most widespread iridoid, was never reported in *Labiatae sensu* Cronquist [14], although aucubin derivatives (melittoside and

Subfamily	Genera	Genera formerly *Verbenaceae*	Genera with iridoids	Genera from *Verbenaceae* with iridoids	Types
Nepetoideae	134	0	2	0	C4-methyl C4-carboxylated (special stereochemistry)
Lamioideae	56	0	13	0	C4-carboxylated, C4-decarboxylated and C4-methyl
Teucrioideae	23	18	6	4	C4-decarboxylated (mainly) C4-carboxylated and C4-formyl
Chloanthoideae	17	10	3	2	C4-decarboxylated (catalpol-type)
Viticoideae	15	15	6	6	C4-decarboxylated (mainly) C4- carboxylated
Pogostemonoideae	7	0	2	0	C4-decarboxylated
Ajugoideae	6	1	1	0	C4-decarboxylated
Scutellarioideae	4	1	2	1	C4-decarboxylated

Table 1. Iridoid distribution in Labiatae *sensu lato* (number of genera is indicated).

catalpol, among others) have been isolated. It means that in this family aucubin is quickly transformed into another iridoids [15]. The absence of an enzymatic system could be considered as a plesiomorphic character and indicate that aucubin-bearing *Viticoideae* and *Chloanthoideae* are, in a chemical view, more primitive.

In the subfamily *Nepetoideae* where are placed the aromatic *Labiatae* such as *Mentha* spp., *Origanum* spp, *Rosmarinus* spp., *Cunila* spp, etc., iridoids are largely absent. Although this kind of product occur in *Nepeta* and *Satureja* they are structurally different. The iridoids found in *Nepeta cataria* (nepetalactone, epi-nepetalactone, nepetaside and 1,5,9- epi-deoxyloganin) are uncommon, particularly the last one, which is the only iridoid presenting three stereochemical centers [16]. In *Satureja* the iridoids present an unusual substitution pattern, C-4 methyl group, which also occurs in *Lamium amplexicaule*.

The biosynthesis of iridoids, especially carboxylated –dominant in *Verbenaceae sensu stricto*– is a plesiomorphic character and the presence of decarboxylated iridoids or their absence is an apomorphy [17]. In subfamily *Nepetoideae*, the largest of the *Labiatae*, iridoids are rarely found, being common in the other subfamilies where C-4 decarboxylated iridoids predominate. It means that, chemically, *Verbenaceae sensu stricto* is primitive in relation to *Labiatae (sensu* Cantino *et al.* [8]) and that subfamily *Nepetoideae* is more advanced than the other ones. This assertion is in accordance with the pollen morphology: hexacolpate pollen present in species of *Nepetoideae* is considered an apomorphic character.

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