

IRIDOIDS FROM ENDEMIC CHILEAN BIGNONIACEAE

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Abstract - Several iridoids were isolated from 4 species of endemic Chilean *Bignoniaceae*.

Introduction

The family of *Bignoniaceae* includes about 120 genera and 700-800 species mainly distributed in Tropical and Subtropical areas of the world, though several genera are typical of temperate regions.¹ In the Chilean Flora, which is characterized by a high number of endemisms as a consequence of the unique geographic position, only few *Bignoniaceae* species are present, pertaining to four genera: *Tecoma*, *Campsidium*, *Argylia* and *Eccremocarpus*. *Bignoniaceae*, as part of the iridoid-containing *Sympetaleae*, present these methylcyclopentane monoterpenes as chemosystematic markers, though their occurrence is restricted to *Tecomae* and *Eccremocarpeae* among the five tribes forming the family. The aim of this paper is a short communication of the results obtained during the last years in the study of iridoid components of endemic Chilean *Bignoniaceae*.

Iridoids from Chilean Bignoniaceae

The most common *Bignoniaceae* species in Chile is probably *Jacaranda mimosaeifolia* D. Don, which however is not endemic, having being introduced, as in other South American countries, to arborize urban areas. The study of the polar components of the leaves of this species, collected in Valparaiso, led to the isolation of a cyclohexanone, jacaranone, a phenylpropanoid glucoside verbascoside (=acteoside) and a new glucose ester, named jacaranosio,² whereas iridoids were totally absent. The last compounds were found in all the endemic species studied, each of these species pertaining to one of the aforementioned genera.

Tecoma fulva (Cav.) G. Don is a small tree growing in the North of Chile. The leaves of this species contain plantarenaloside (I) and stansioside (II)³, two aldehydic iridoid glucosides usually co-occurring and already found in other *Bignoniaceae* of *Tecoma* and *Campsis* genera.

Stems and leaves of *Campsidium valdivianum* (Phil.) Skotts., a voluble species of the Southern Regions of the country, also contain I and II, together with two related glycosides, III and IV, where the glucose moiety is substituted by gentiobiose.⁴

The Northern part of Chilean II Region is characterized by a semiarid climate with absence of significant rains for several years. The herbal species *Argylia radiata* (L.) D. Don well adapted itself to these extreme conditions by the metamorphosis of the underground parts in large tuberous roots and the reduction of the vegetative period of the aerial parts to the month of September. Roots are used in popular medicine as a stomach tonic. This plant resulted particularly rich in iridoids, which can be divided into three groups, according to the types of

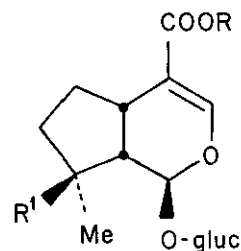
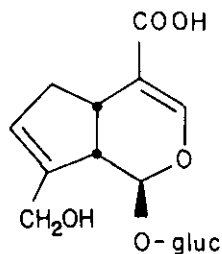
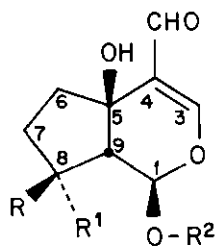
structure: a) iridoid glucosides, including: plantarenalloside (I)⁵, a series of compounds with carboxylic function at C(4), i.e. geniposidic acid (V), mussaenosidic acid (VI)⁶, the new 7-deoxy-8-epiloganic acid (VII) and 7-deoxygardoside (VIII)⁷, and finally catalpol (IX)³, probably the most common iridoid; b) the iridoids of the second group, characterized by esterification of the secondary alcoholic function at C(6) of catalpol by the C(11) carboxyl of another unit of iridoid glucoside, including argylioside (X)⁵ and radiatoside A-D (XI-XIV)^{6,8}; compounds made by the junction of two iridoid units were already known, but in all the previous examples one of the units was a secoiridoid and, in this regard, the substances isolated from *A. radiata* represent a new class of dimeric iridoids, for which we propose the name of bisiridoids; c) a new non-glucosidic iridoid of isoiridomyrmecin-type, named argyol (XV).⁹

Iridoids from Eccremocarpus scaber

The research on *Eccremocarpus scaber* Ruiz. et Pav. completes the study of the four genera present in the Chilean Flora. The genus *Eccremocarpus* belongs to *Eccremocarpeae*, a small tribe constituted only by three species distributed in the Andes.¹ By preliminary separation of the ethanolic extract of the whole plant and subsequent column chromatography, three iridoids were isolated: mussaenoside (XVI) and two new non-glucosidic iridoids XVII and XVIII, named eccremocarpol A and B, respectively, whose structures were assigned mainly on the basis of analysis of nmr spectral data.

The ethanolic extract of the whole plant was subjected to a preliminary separation according to the charcoal method.⁹ Paper chromatography analysis of the 50% aqueous ethanolic fraction showed the presence of a complex mixture of compounds probably of iridoid type, as confirmed also by the positive reaction with the vanillin reagent. Subsequent column chromatography of the fraction on silica gel in CHCl₃: MeOH 9:1 afforded pure XVI, identified by analysis and comparison of physical and spectral data,¹¹ eccremocarpol A (XVII) and eccremocarpol B (XVIII). *Eccremocarpol A*, XVII, $[\alpha]_D^{25} -29^\circ$ (MeOH), is an oily substance with no significant absorption in the uv spectrum; ¹H Nmr (methanol-d₄, 400 MHz), δ : 1.87 (1H, dd, J= 7.5 and 14.0 Hz, H-4a); 1.92 (1H, ddd, J= 3.0, 5.0 and 14.0 Hz, H-4b); 1.98 (1H, ddd, J= 1.0, 5.0 and 8.0 Hz, H-5); 2.77 (1H, dd, J= 4.0 and 8.0 Hz, H-9); 3.40 (3H, s, OMe); 3.46 (3H, s, OMe); 3.56 (1H, d, J= 13.0 Hz, H-10a); 3.97 (1H, d, J= 13.0 Hz, H-10b); 4.07 (1H, dd, J= 1.0 and 8.0 Hz, H-6); 4.72 (1H, dd, J= 3.0 and 7.5 Hz, H-3); 4.94 (1H, d, J= 4.0 Hz, H-1). ¹³C Nmr (methanol-d₄), ppm: 29.1, C(4); 35.6, C(5); 40.6, C(9); 54.4, OMe; 55.4, OMe; 60.7, C(10); 60.9, C(7); 63.2, C(8); 77.4, C(6); 95.3, C(3); 98.7, C(1). Elem. anal (calcd for C₁₁H₁₆O₆): C, 53.56; H, 7.42 (C, 53.65; H, 7.37%).

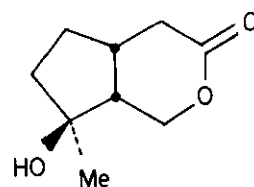
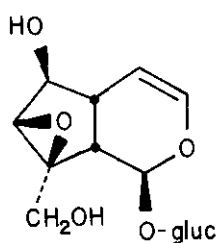
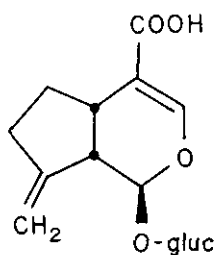
Eccremocarpol B, XVIII - Oily, $[\alpha]_D^{25} -18.5^\circ$ (MeOH). ¹H Nmr (methanol-d₄), δ : 1.66 (1H, dd, J= 3.5 and 14.0 Hz, H-4a); 2.38 (1H, ddd, J= 1.0, 10.0 and 14.0 Hz, H-4b); 2.57 (1H, ddd, J= 1.0, 4.5 and 14.0 Hz, H-5); 2.65 (1H, dd, J= 3.0 and 4.5 Hz, H-9); 3.46 (3H, s, OMe); 3.50 (3H, s, OMe); 3.84 (2H, AB system, H-10); 3.99 (1H, d, J= 6.5 Hz, H-7); 4.10 (1H, d, J= 6.5 Hz, H-6); 5.07 (1H, dd, J= 1.0 and 3.5 Hz, H-3), 5.14 (1H, d, J= 3.0 Hz, H-1). ¹³C Nmr (methanol-d₄), ppm: 35.0, C(4); 36.7, C(5); 37.3, C(9); 54.4, OMe; 55.4, OMe; 63.8, C(10); 75.9, C(7); 76.9,



- I R = H ; R¹ = Me , R² = glucose
 II R = Me ; R¹ = H ; R² = glucose
 III R = H , R¹ = Me ; R² = gentiobiose
 IV R = Me ; R¹ = H ; R² = gentiobiose

V

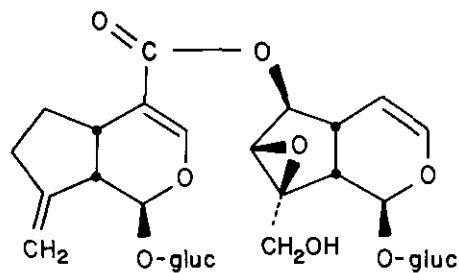
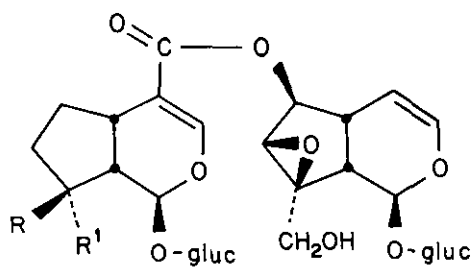
- VI R = H ; R¹ = OH
 VII R = H ; R¹ = H
 XVI R = Me ; R¹ = OH



VIII

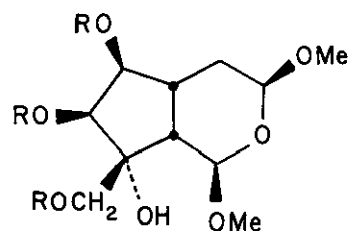
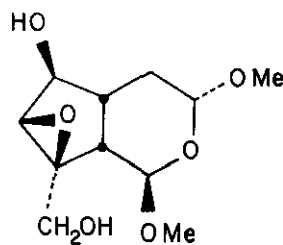
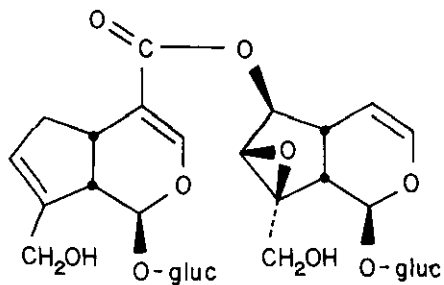
IX

XV



- X R = Me ; R¹ = H
 XI R = OH ; R¹ = Me
 XIV R = H ; R¹ = Me

XII



XIII

XVII

XVIII R = H

XIX R = Ac

C(6); 81.2, C(8); 91.1, C(3); 97.0, C(1). Elem anal. (calcd for $C_{11}H_{20}O_7$): C, 50.08; H, 7.67 (C, 49.99; H, 7.63%).

The ^{13}C nmr spectrum of XVII shows 11 peaks: 9 of them pertain to the monoterpene iridoid skeleton and the remaining 2 to methoxy groups (54.4 and 55.4 ppm). The two signals at lowest field (95.3 and 98.7 ppm) can be assigned to hemiacetal or acetal functions in position 1 and 3, on the basis of the basic structure and the chemical features of iridoid compounds, biogenetically derived from the ring closing of the precursor iridodial. In the 1H nmr spectrum the same groups are also evident in the doublet at δ 4.94 ($J=4.0$ Hz) and the doublet of doublets at δ 4.72 ($J=3.0$ and 7.5 Hz). The comparison of these data with the corresponding ones in xylomollin¹² and the series of compounds synthesized by Whitesell et al.¹³ allows to assign the methoxy groups at positions 1 and 3, as well as to determine the stereochemistry of the corresponding chiral centres. The signal at δ 4.94, assigned to H-1, resulted coupled with the doublet of doublets at δ 2.77, assigned to H-9, which was on his on its side also coupled with a complex signal at δ 1.98, attributed to H-5. The assignment of the last proton was also confirmed by its couplings with one of the protons of the methylene in position 4 (δ 1.87, dd) and with H-6 (δ 4.07, dd). As regard the remaining part of the structure, the accord with the iridoid skeleton lets us assume the presence of a cyclopentane ring, whose substituents were determined by comparison with reported data for catalpol and related compounds.¹⁴

The second compound (XVIII) presents several structural analogies with XVII. Again the analysis of nmr data shows the presence of two acetalic functions at positions 1 and 3, comprehensive of two methoxyls, the lack of substituents at positions 4, 5 and 9 and the presence of a primary hydroxy group at C(8), which is further substituted by an oxygenated function. Principal differences are instead the absence of the epoxide function at C(7)/C(8) and the presence of two coupled secondary hydroxy functions, attributable to positions 6 and 7. By treatment of XVIII in anhydrous pyridine and acetic anhydride, the triacetyl derivative XIX is obtained, where, as expected, H-1 and H-3 remain practically unchanged and H-6 and H-7 are shifted to lower field. XIX - 1H nmr ($CDCl_3$), δ : 1.71 (1H, dd, $J=3.5$ and 14.0 Hz, H-4a); 1.92 (3H, s, Ac); 1.93 (3H, s, Ac); 1.99 (3H, d, Ac); 2.31 (1H, dd, $J=1.0, 10.0$ and 14.0 Hz, H-4b); 2.39 (1H, dd, $J=3.0$ and 4.5 Hz, H-9); 2.42 (1H, dd, $J=4.5$ and 10.0 Hz, H-5); 3.36 (3H, s, OMe); 3.40 (3H, s, OMe); 4.12 (2H, AB system, H-10); 4.88 (1H, dd, $J=1.0$ and 3.5 Hz, H-3); 4.98 (1H, d, $J=6.5$ Hz, H-7); 5.00 (1H, d, $J=3.0$ Hz, H-1); 5.20 (1H, d, $J=6.5$ Hz, H-6).

When the general structure of the molecule has been determined in such a way, it remains to solve the rather complex problem of the stereochemistry assignment. Since a β configuration is assigned to H-5, as in all known natural iridoids, the practical null value of $J_{5,6}$ (H-6 is sharp doublet at δ 4.10 with $J_{6,7}=6.5$ Hz) must result from a dihedral angle between H-5 and H-6 near to 90° and therefore from a *trans* relationship for the two protons, assigning a β configuration to the hydroxyl at position 6. The coupling constant value between H-6 and H-7 is compatible with both *trans* and *cis* relationships, however it appears much closer to that reported in posoquenin¹⁵ ($J=6.0$ Hz; 6- β -OH and 7- β -OH) than to that in

avicennoside¹⁶ ($J=10.0$ Hz; 6- β -OH and 7- α -OH). A confirmation of the 7- β -OH assignment comes from the comparison of chemical shift values of C(6), C(7) and C(8) in XIX with those of the couple 10-decinnamoylglobularinine/10-decinnamoylglobularimine,¹⁷ epimers at C(7), and the same data, together with the values of C(9), can be also used for the assignment of stereochemistry at C(8) and interpreted on the basis of the so called "rule of the epimer pairs at C(8)"¹⁸ In particular the chemical shift value of C(9) appears indicative: its resonance frequency results shielded by the steric influence of the hydroxy group in position 8, to which α configuration is therefore assigned. The formation of 7- β , 8- α diol in iridoids by opening of 7/8 epoxide ring was discussed by Davini *et al.*¹⁹ Regards the other part of the molecule, the configuration at C(3) was inverted in consideration of the coupling constant values of H₂-4 with H-3.

Although the presence of XVII and XVIII in the extract of the plant partially purified by the charcoal method was checked by tlc, the possibility of their formation from the corresponding unstables emiacetales during the purification process, the unique step involving the use of MeOH, cannot be totally excluded.

The iridoids found in Chilean *Bignoniaceae* confirm the presence of two main chemosystematic markers for the family in this class of natural products, as already proposed by us⁹: a) catalpol and its derivatives, b) compounds with oxygenated functions at C(4), i.e. plantarenaloxide and stansioside. In accordance with the biogenetic sequence proposed by Gottlieb²⁰, the presence of these iridoids appears in agreement with the phylogenetic position proposed for *Bignoniaceae* at the beginning of *Scrophulariales*, coming from *Gentianales*, and in particular *Rubiaceae*, where secoiridoids and iridoids with oxygenated group at C(4) are predominant, and going towards *Scrophulariaceae* and *Lamiaceae*, where catalpol- and aucubin-type structure are prevalent.

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