CHEIRANTHUS ALLIONI – A UNIQUE CARDENOLIDE-BEARING PLANT

I. F. Makarevich

UDC 547.92/93+615.224:547.918

The results of chemical investigations of cardenolides and cardenolide glycosides of "plains erysimum" (Erysimum asperum, Cheiranthus allioni) have been generalized and analyzed. It has been shown that this plant is distinguished by the presence of an unusually large set of glycosides and aglycons and sugars of diverse chemical structures and by a wealth of isomeric compounds and genetically related substances. On the basis of chemotaxonomic characteristics, "plains erysimum" has been assigned unambiguously to the genus Cheiranthus (wallflower). The promising nature of the practical use of the plant is discussed. The review includes publications that appeared in 1969-1990.

The cardenolide-containing plants that have been subjected to chemical study relatively recently include Cheiranthus allioni hort. (Erysimum asperum, Erysimum marschalli (Stark) Boiss.) – "plains erysimum." This plant merits particular attention both from the number of cardenolides that it contains and, in particular, from the variety of their chemical structures.

Methods for isolating the native compounds of "plains erysimum" have been described previously [1, 5, 7].

The glycoside composition of the plant under study is complex. It includes not less than 50 cardenolides. The presence of such a large set of cardenolides and the wealth of isomers with similar polarities in them presents considerable difficulties for their isolation in the individual state. Nevertheless, the use of partition chromatography on cellulose in the toluene–butan-1-ol (2:1-3:2) system has basically permitted these difficulties to be overcome. In this connection it was important that the ratio between the support of the stationary phase and the total amount of substances to be separated was not less than 200:1 in the majority of cases.

We have isolated 33 native cardenolides (32 glycosides and one aglycon) in the individual state and have established their chemical structures. Half these substances proved to be new (indicated in Table 1 with asterisks). In the process of establishing their chemical structures, the hydrolysis of the cardiac glycosides isolated yielded a number of new aglycons and mono- and oligosaccharides.

Table 1 gives the chemical structures of 42 compounds, including 32 glycosides and 10 aglycons of "plains erysimum" grouped according to their aglycons.

As well as the six known monosaccharides obtained from the glycosides (D-glucose, L-rhamnose, L-glucomethylose, D-digitoxose, D-gulomethylose, and D-fucose) there was also a new one represented by L-glucomethylose [3, 6].

The cardiac glycosides isolated in the individual state were derivatives of ten aglycons – strophanthidin (I), cannogenol (VIII), digitoxigenin (XIII), bipindogenin (XX), strophanthidol (XXV), alliotoxigenin (XXIX), uzarigenin (XXXI), cannogenin (XXXV), sarmentogenin (XXXVIII), and 4,5-dehydrosarmentogenin (XL) and the monosaccharides listed above. The finding of such a number of cardiac aglycons and monosaccharides in one plant is a phenomenon that is, in itself, unusual. In any case, no other similar cardenolide-bearing plant has yet been found.

Among the substances studied there were cardenolides of two types – of the 5α- and 5β-series. Numerically, the compounds of the 5β-series predominated. The aglycons differed by their degree of hydroxylation, the positions of the hydroxy groups in the steroid nucleus,

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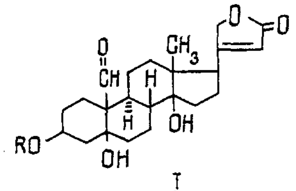
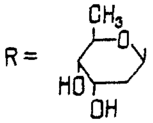
TABLE 1. Glycosides and Aglycons isolated from Cheiranthus allioni

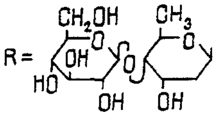


I

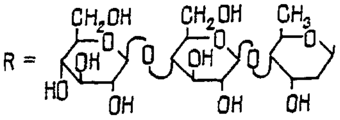
R = H, Strophanthidin, $C_{22}H_{32}O_6$, mp 144-146/230-233°, $[\alpha]_D$ + 44±2° [1]

II. 

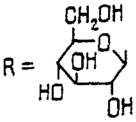
Erysimin (= strophanthidin-3-O-β-D-digitoxopyranoside), $C_{29}H_{42}O_9$, mp 176-178°, $[\alpha]_D$ +27±3° [1]

III. 

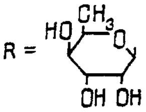
Erysimoside [= strophanthidin 3-(4'-O-β-D-glucopyranosyl-β-D-digitoxypyranoside)], $C_{35}H_{52}O_{14}$, mp 170-173°, $[\alpha]_D$ + 18.6±3° [1]

IV. 

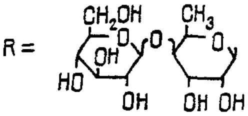
Glucoerysimoside [= strophanthidin 3-(O-β-D-glucopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1 → 4)-β-D-digitoxopyranoside)], $C_{41}H_{62}O_{19}$. mp 203-206°, $[\alpha]_D$ + 11.6±3°[5]

V. 

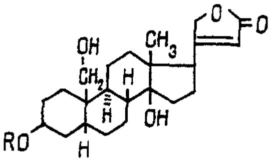
Glucostrophanthidin (= strophanthidin-3-β-D-glucopyranoside), $C_{29}H_{42}O_{11}$, mp 170-173, 234-236°, $[\alpha]_D$ + 18.8±2° [7]

VI. 

Desglucocheirotoxin (= strophanthidin-3-O-β-D-gulomethylopyranoside), $C_{29}O_{42}H_{10}$, mp 188-192°, $[\alpha]_D$ + 1.4± 2° [4]

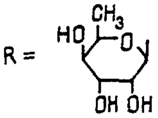
VII. 

Cheirotoxin [= strophanthidin 3-(4'-O-β-D-glucopyranosyl-β-D-gulomethylopyranoside)], $C_{32}H_{52}O_{15}$, mp 198-210°, $[\alpha]_D$ – 15.8±2° [7]

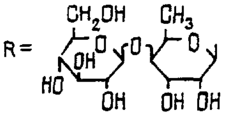


VIII

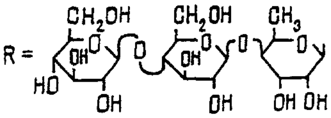
R = H, Cannogenol, $C_{23}H_{34}C_5$, mp 236-239°, $[\alpha]_D$ + 29.2±2° [1]

IX. 

Deglucoerycordin (= cannogenol-3-O-β-D-gulomethylopyranoside), mp 162-164°, $[\alpha]_D$ – 21.3 ± 2° [1]

X. 

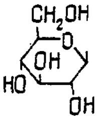
Erycordin [= cannogenol 3-(4' → 1)-O-β-D-glucopyranosyl-β-D-gulomethylpyranoside)], $C_{35}H_{54}O_{14}$, mp 200-203°, $[\alpha]_D$ – 25.3±2° [1]

XI. 

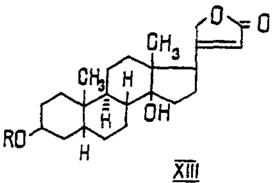
Glucoerycordin* [= cannogenol 3-(O-β-D-glucopyranosyl-(4' → 1)-O-β-D-glucopyranosyl-(4'' → 1)-O-β-D-gulomethylopyranoside)], $C_{41}H_{64}O_{19}$, mp 131-135°, $[\alpha]_D$ –22.2±3° [13]

TABLE 1 (continued)

XII. R =



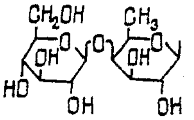
Glucocannogenol* (= cannogenol 3-O-β-D-glucopyranoside), $C_{29}H_{44}O_{10}$, mp 225-229°, $[\alpha]_D$ + 7.0 ± 2° [7]



XIII

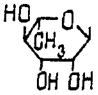
R = H. Digitoxigenin, $C_{23}H_{34}O_5$, mp, 236-256°, $[\alpha]_D$ + 18.5 ± 2° [1]

XIV. R =



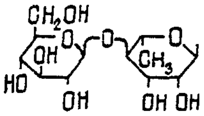
Glucodigifucoside [= digitoxigenin 3-(4'-O-β-D-glucopyranosyl-β-D-fucopyranoside)], $C_{35}H_{54}O_{13}$, mp, 188-192°, $[\alpha]_D$ 5.6 ± 3° [1]

XV. R =



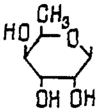
Evomonoside (= digitoxigenin 3-O-α-L-rhamnopyranoside), $C_{29}H_{44}O_8$, mp. 239-242°, $[\alpha]_D$ −28.9±2° [1]

XVI. R=



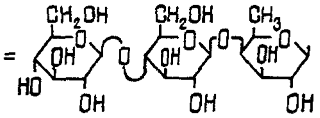
Evobioside [= digitoxigenin 3-O-(4-O-β-D-glucopyranosyl-α-L-rhamnopyranoside)], $C_{35}H_{54}O_{13}$, mp, 267-271°, $[\alpha]_D$ −24.3± 2° [1]

XVII. R =



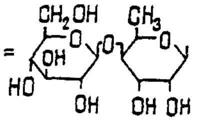
Digitoxigenin gulomethyloside (= digitoxigenin 3-O-β-D-gulomethylopyranoside), $C_{29}H_{44}O_8$, mp, 150-152°, $[\alpha]_D$ −22.0 ± 2° [1]

XVIII. R =

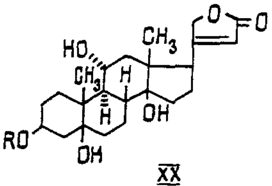


Digifucocellobioside [= digitoxigenin 3-O-(O-β-D-glucopyranosyl-(1 → 4')-O-β-D-glucopyranosyl-(1 → 4'')-fucopyranoside)], $C_{41}H_{64}O_{18}$, mp 270-275°, $[\alpha]_D$ − 6.4± 2° [11]

XIX. R =



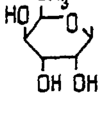
Glucodigigulomethyloside* [= digitoxigenin 3-O-(4'-O-β-D-glucopyranosyl-β-D-glucomethylpyranoside)], $C_{35}H_{54}O_{13}$, mp 197-198°, $[\alpha]_D$ − 34.3 ± 2° [11]



XX

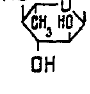
R = H. Bipindogenin, $C_{23}H_{34}O_6$, mp 260-262°, $[\alpha]_D$ + 30.0 ± 2° [3]

XXI. R =



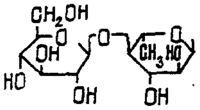
Bipindogulomethyloside* (= bipindogenin 3-O-β-D-gulomethylopyranoside), $C_{29}H_{44}O_{11}$, mp. 150-154/168-170°, $[\alpha]_D$ − 16.0 ± 2° [11]

XXII. R =



Alliside* (= bipindogenin 3-O-α-L-glucomethylopyranoside), mp $C_{29}H_{44}O_{10}$, mp 180-183°, $[\alpha]_D$ − 47.7 ± 3° [3]

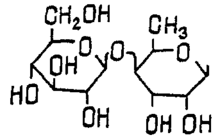
XXIII. R=



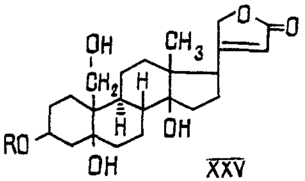
Glucoalliside* [= bipindogenin 3-O-(4'-O-β-D-glucopyranosyl-α-L-glucomethylopyranoside)], $C_{35}H_{54}O_{15}$, mp 203-206°. $[\alpha]_D$ −47.1 ± 2° [6]

TABLE 1 (continued)

XXIV. R =



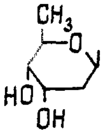
Glucobipindogulomethyloside* [= bipindogenin 3-O-(4'-O-β-D-glucopyranosyl-β-D-gulomethylopyranoside)], $C_{35}H_{54}O_{15}$, mp, 192-195, $[\alpha]_D$ −31.0 ± 2° [10]



XXV

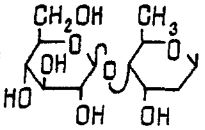
R = H. Strophanthidol, $C_{23}H_{34}O_6$, mp, 140-142°, $[\alpha]_D$ + 36.0 ± 4 [4]

XXVI. R =



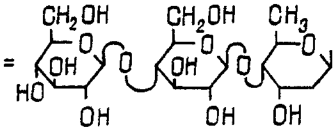
Helveticoside (= strophanthidol 3-O-β-D-digitoxopyranoside), $C_{29}H_{44}O_9$, mp 166-171°, $[\alpha]_D$ +27.1 ± 3° [4]

XXVII. R =

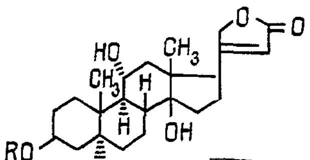


Erysimosol [= strophanthidol 3-O-(4'-O-β-D-glucopyranosyl)-β-D-digitoxopyranoside)], $C_{35}H_{54}O_{14}$, mp 172-176°, $[\alpha]_D$ + 21.6 ± 3° [4]

XXVIII. R =



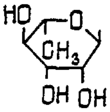
Glucoerysimosol* [= strophanthidol 3-O-(O-β-D-glycopyranosyl- (4 → 1)-O-β-D-glucopyranosyl-(4 → 1)-β-D-digitoxopyranoside)], $C_{41}H_{61}O_{19}$, mp 260-262°, $[\alpha]_D$ + 15.8 ± 3° [5]



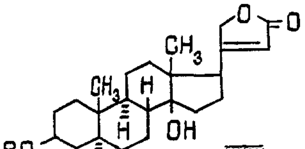
XXIX

R = H. Alliotoxigenin*, $C_{23}H_{34}O_5$, mp 295-301°, $[\alpha]_D$ + 25.8 ± 3° [2]

XXX. R =



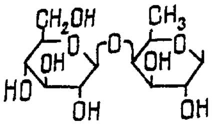
Alliotoxin* (= alliotoxigenin 3-O-α-L-rhammopyranoside), mp 262-272°, $[\alpha]_D$ −40.0 ± 3° [2]



XXXI

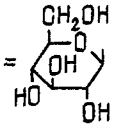
R = H Uzarigenin, $C_{23}H_{34}O_4$, mp. 240-256° $[\alpha]_D$ −14.0 ±2° [6]

XXXII. R =



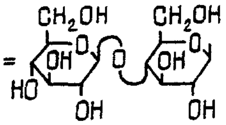
Cheiroside A = cheiroside H [= uzarigenin 3-O-(4'-O-β-D-glucopyranosyl-β-D-fucopyranoside], $C_{35}H_{54}O_{13}$, mp 295-297°, $[\alpha]_D$ −23.7 ± 2° [6]

XXXIII. R =



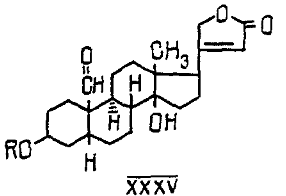
Deglucouzarin (= uzarigenin 3-O-β-D-glucopyranoside), $C_{29}H_{44}O_9$, mp 269-273/277-279°, $[\alpha]_D$ −17.1 ± 2° [8]

XXXIV. R =



Neouzarin* [= uzarigenin 3-O-(4'-O-β-D-glucopyranosyl-β-D-glucopyranoside)], $C_{35}H_{54}O_{14}$, mp 268-277/292-300°, $[\alpha]_D$ − 18.7 ± 2°

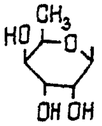
TABLE 1 (continued)



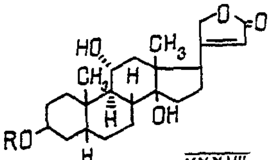
XXXV

R = H. Cannogenin, $C_{23}H_{32}O_5$, mp 145/185; 200-210°, $[\alpha]_D$ -15.0 ± 2° [4]

XXXVI. R =



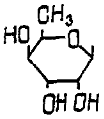
Cheiranthoside* (= cannogenin 3-O-β-D-gulomethylopyranoside), $C_{29}H_{42}O_9$, mp 154-156°, $[\alpha]_D$ -41.3 ± 3° [4]



XXXVII

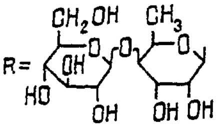
R = H. Sarmentogenin, $C_{23}H_{34}O_5$, mp 265-267°, $[\alpha]_D$ + 21.5 ± 2° [9]

XXXVIII. R =

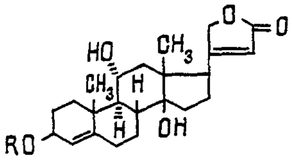


Sarmentogulomethyloside* (= sarmentogenin 3-O-β-D-gulomethylopyranoside), $C_{29}H_{42}O_9$, mp, 307-309°, $[\alpha]_D$ -33.5 ± 3° [9]

XXXIX. R =



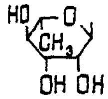
Gulosarmentoglucoside* (= sarmentogenin 3-O-(4'-O-β-D-glucopyranosyl-β-D-gulomethylopyranoside)], $C_{35}H_{54}O_{14}$ mp, 204-207°, $[\alpha]_D$ - 23.9 ± 3° [9]



XL

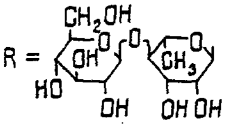
R = H. 4,5-Dehydrosarmentogenin. $C_{23}H_{32}O_5$, mp. 296-302°, $[\alpha]_D$ + 26.2 ± 3° [12]

XLI. R =



Ch-30* (= 4-dehydrosarmentogenin 3-O-α-L-rhamnopyranoside), $C_{29}H_{31}O_9$, mp 268-275° $[\alpha]_D$ -38.2 ± 2° [12]

XLII. R =



Ch-31* [= 4,D-dehydrosarmentogenin 3-O-(4'-O-β-deglucopyranosyl-α-L-rhamnopyranoside)], $C_{35}H_{52}O_{14}$, $[\alpha]_D$ -44.1 ± 2° [12]

the degree of oxidation of the substituent at C-10 (CH_3, CH_2OH, CHO), and the presence of an isolated double C=C bond in the steroid moiety.

A characteristic feature of "plains erysimum" is, as already mentioned, the presence of a multiplicity of isomeric groups of cardenolides. At the present time, they number 11. Each group contains from two to five isomers.

It is impossible to single out a number of biogenetically related glycosides differing by the lengths of their carbohydrate chains and the natures of the attachment of the D-glucose units to the monoglycosides.

1. Erysimin (II), erysimoside (II), glucoerysimoside (IV);
2. Desglucoerycordin (IX), erycordin (X), glucoerycordin (XI);
3. Helveticosol (XXVI), erysimosol (XXVII), glucoerysimosol (XXVIII);
4. Alliside (XXII), glucoalliside (XXIII);
5. Desglucocheirotoxin (VI), cheirotoxin (VII);
6. Evomonoside (XV), evobioside (XVI);
7. Desglucouzarin (XXXIII), neouzarin (XXXIV);
8. Digitoxigenin gulomethyloside (XVII), glucodigigulomethyloside (XIX);
9. Glucodigifucoside (XIV), digifucocellobioside (XVIII);
10. Bipindogulomethyloside (XXI), glucobipindogulomethyloside (XXIV);
11. Sarmentogulomethyloside (XXXVIII), gulosarmentoglucoside (XXXIX);
12. Ch-30 (XLI) and Ch-31 (XLII).

In the living plant, in each of these groups both the hydrolysis of the D-glucose units and the addition of such units may take place under the influence of enzymes [22]. As a result, mono-, di-, and triglycosides are present in the living plant in a definite equilibrium, with the diglycosides predominating. This equilibrium can change profoundly in the direction of an accumulation of oligosides during the process of slow drying of the plant, as has been shown previously by N. K. Abubakirov et al. in the case of other glycoside-bearing plants [22].

Some aglycons are also, apparently, biogenetically linked with one another: for example, sarmentogenin (XXXVII), alliotoxigenin (XXIX), 4,5-dehydrosarmentogenin (XL), and bipindogenin (XX). They are all hydroxylated in the 11α position and differ by the presence or absence of an OH group at C-5 or of a double bond in the 4:5 position. If it is accepted that biosynthesis takes place from less complex to more complex, it may be assumed that the precursor of bipindogenin (XX), sarmentogenin (XXXVII), and alliotoxigenin (XXIX) is 4,5-dehydrosarmentogenin (XL). The hydrogenation of the latter at the isolated C=C bond may give sarmentogenin (XXXVII) or alliotoxigenin (XXIX), or a mixture of them, while the hydration of (XL) leads to bipindogenin (XX).

The main glycosides of "plains erysimum" are: glucoerysimoside, erysimoside, glucoalliside, cheirotoxin, glucobipindogulomethyloside, erycordin, cheiroside A, glucodigifucoside, digifucocellobioside, and neouzarin.

Attention is attracted also by one other important feature of the glycosides of "plains erysimum." Among the main components there are two glycosides that are bipindogenin derivatives — (XXIII) and (XXIV). Before investigations of this "erysimum," bipindogenin and its glycosides were regarded as rare and difficultly accessible; their presence in such plants as lily of the valley and erysimum, where they are present in insignificant amounts, was known. "Plains erysimum" is an exception in this respect. The level of bipindogenin glycosides in it is about 0.4% (on the weight of the plant). An investigation of the native bipindogenin glycosides as substances with a cardiotonic action appears of interest. Hitherto, there had been not one drug based on glycosides of 11-α-hydroxyaglycons, because of their unavailability. At the same time, if one bears in mind the experience of the use of hormonal steroids where the presence or absence of an oxygen-containing substituent at C-11 greatly affects their specific biological action, it may be assumed that for cardiac glycosides containing 11α-hydroxyaglycons, as well, a peculiarity of their cardiotropic action will be observed. These investigations are waiting to be performed. Nevertheless, "plains erysimum" must be regarded as a promising source of 11-α-hydroxycardenolides.

The large variety of cardiac glycosides with different structures in "plains erysimum" gives grounds for recommending them for detailed pharmacological study both in the form of the purified total material and as individual glycosides, particularly the bipindogenin derivatives that have been mentioned, with the aim of their use in medical practice. In view of the chemical structures of the glycosides present in the extremely complicated native complex, it may be hoped that they will possess not only the pharmacotherapeutic properties of many other cardenolide glycosides that are used but also new ones.

The chemical investigations of the cardenolide composition of "plains erysimum" that have been performed give grounds for unambiguously assigning it to the genus Cheiranthus. This conclusion is relevant, since among botanists there has been no established opinion either in this respect or in the matter of the name of the plant: Russian botanists recognize three of them: Cheiranthus allioni hort., Erysimum marschalli (Stark) Boiss., and Erysimum allioni hort. [16]. In the opinion of systematists, this hybrid of obscure origin [14] is an annual herbaceous plant which was introduced into cultivation on an experimental field of the All-Union Scientific-Research Institute of Drug Chemistry and Technology (Khar'kov) by Professor I. G. Zoz. Objective indications in favor of the conclusion we have drawn that the plant under discussion belongs to the genus Cheiranthus are the following. In the first place, not one cardenolide of the 5α-series has been found in representatives of the genus Erysimum. And this, moreover, when many species of erysimum have been studied in detail chemically. At the same time, as shown above, cardenolides of the 5α-series form a considerable component of Cheiranthus allioni, while cheiroside A (a glycoside of the 5α- series) is one of the main components not only of Ch. allioni but also of another Cheiranthus species — Ch. cheiri, from which it was first isolated [17-19]. Furthermore, common main glycosides for both species of wallflower are glucoalliside, cheirotoxin, and glucoerysimoside [20, 21].

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