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CHEMICAL STUDY OF A NEW CARDIAC GLYCOSIDE FROM WORMSEED WALLFLOWER (*ERYSIMUM CHEIRANTHOIDES* L.)*

(Presented by Academician A. I. Oparin, 18 VIII 1960)

In the herb of wormseed wallflower, by the method of paper chromatography, 12 substances belonging to cardiac glycosides and aglycones were detected (see Fig. 1).

To obtain the glycosides, the comminuted herb was extracted with 96° alcohol. After evaporation of the solvent in vacuo, the extract was treated with water and purified with ether, then with $Pb(OH)_2$. From the aqueous solution the glycosides were extracted with a mixture of chloroform and alcohol (2 : 1). The solvent was distilled off, the residue was again dissolved in a small amount of water, and the treatment was repeated with a mixture of chloroform and alcohol (2 : 1). The sum of glycosides, obtained after concentration of the alcohol-chloroform extracts, was chromatographed on alumina. Development was carried out with chloroform, then with mixtures of chloroform and alcohol with a gradually increasing content of the latter. The operation of the column was monitored by paper chromatography. The eluates containing individual substances were collected separately. By this method we succeeded in isolating four substances in an individual crystalline state. Their principal physicochemical properties are given in Table 1.

Fig. 1. Chromatogram of cardiac glycosides and aglycones of wormseed wallflower on paper from the Leningrad Volodarsky Factory No. 2, grade M, in the solvent system chloroform—isoamyl alcohol—water (1 : 1 : 1), mobile phase—water saturated with organic solvents; 20°; 24 hours. 1 —purified extract of wallflower herb, 2 —erysimotoxin, 3 —strophanthidin, 4 —glycoside I, 5 —glycoside L. Values of R_f: a —0.02; —0.05; —0.11; —0.18; —0.27; —0.35; —0.45; —0.51; —0.55; —0.67; —0.74; —0.87.

The first two substances were identified with the previously known aglycone strophanthidin and the glycoside erysimotoxin (1). The remaining two proved to be cardiac glycosides new for wormseed wallflower, possessing high biological activity (according to data from the pharmacological laboratory). We named them, respectively, glycoside I and glycoside L.

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* From the dissertation of I. F. Makarevich.

Table 1

Properties of the glycosides and aglycones of wallflower mustard (*Erysimum cheiranthoides*)

Name	Mol. wt. and empirical formula	M.p., °C	$[\alpha]_D$	R_f	Biol. activity, mg/kg body weight of cat
Strophanthidin	405.0 $C_{23}H_{32}O_5$	232–233	+46.0°(ethanol)	0.11	0.33
Erysymotoxin	534.7 $C_{29}H_{42}O_9$	194–195	+28.6°(ethanol)	0.18	0.095
Glycoside-I	684.3 $C_{34}H_{50}O_{13}\cdot H_2O$	229–230	+17.1°(ethanol)	0.55	0.11
Glycoside-L		189–190	−25.3°(ethanol)	0.74	0.12

The chemical study of glycoside-I is the subject of the present communication. Glycoside-I crystallizes from acetone–ether in the form of colorless needles. The yield of crystalline product is 0.025–0.03% relative to the dry raw material. The glycoside is readily soluble in water and alcohol, and sparingly soluble in benzene and chloroform. It gives all the reactions characteristic of cardiac glycosides with a five-membered lactone ring: Legal, Raymond, and Kedde. With the Keller–Kiliani reagent it forms a dark-green coloration. In 84% sulfuric acid it dissolves with a green coloration, which after 15 min changes to orange, and after 2 hours to yellow.

The ultraviolet absorption spectrum of glycoside-I shows two maxima: the maximum at 220 mμ ($\log\varepsilon = 4.15$) indicates the presence in the glycoside of a five-membered lactone ring, and the maximum at 305 mμ ($\log\varepsilon = 1.49$) indicates an aldehyde group at C_{10}. The glycoside was analyzed after drying in high vacuum at 80° for 3 hr.

$$\begin{array}{ll} \text{Found \%:} & \text{C } 59.76;\ \text{H } 7.63 \\ C_{34}H_{50}O_{13}\cdot H_2O.\ \text{Calculated \%:} & \text{C } 59.63;\ \text{H } 7.65 \end{array}$$

Mol. wt.: found 684.3; calculated 684.79.

To determine its chemical structure, glycoside-I was subjected to stepwise hydrolysis. Under the action of the enzyme of snail pancreatic juice, it is cleaved into a pentose and a monoglycoside.

The sugar component that is split off strongly reduces Fehling’ s reagent, does not ferment with yeast, and on heating with hydrochloric acid readily forms furfural. The furfural obtained in this way forms with phloroglucinol a black-green precipitate of furfural phloroglucide, insoluble in alcohol, which is characteristic for distinguishing pentoses from methylpentoses.

On paper chromatography in various solvent systems the sugar showed R_f values identical with those of d-xylose. From an alcohol–ether solution the sugar readily crystallizes in the form of prisms with m.p. 145–147°; $[\alpha]_D^{22} = +18.4^\circ$ (aqueous solution, after 2 hours, $c = 0.71$). In a mixed sample with authentic d-xylose, the sugar of glycoside-I gives no depression of the melting point. The osazone was obtained in the form of yellow needle-like crystals with m.p. 162–163°. A mixed sample with the osazone of authentic d-xylose has the same melting point.

By its properties, the sugar obtained upon enzymatic hydrolysis of glycoside-I proved identical with d-xylose. It is a rather rare occurrence for pentoses to be found as constituents of cardiac glycosides. After cleavage of d-xylose from glycoside-I, a monoglycoside is obtained, crystallizing from methanol in the form of long spear-shaped plates with m.p. 194–195°; $[\alpha]_D^{22} = +28.2^\circ$ (ethanol, $c = 1.05$).

The monoglycoside also undergoes all the reactions characteristic of cardiac glycosides with a five-membered lactone ring. A positive Keller-Kiliani reaction (blue coloration) indicates that this glycoside contains a 2-deoxysugar.

In 84% sulfuric acid the glycoside dissolves with a brown coloration, which changes to green and then to blue.

$C_{29}H_{42}O_9$.	Found	% :	C 65.02;	H 8.06
	Calculated	% :	C 65.15;	H 7.92

Mol. wt.: found 534.3; calculated 534.65.

Acid hydrolysis of the monoglycoside proceeds very readily, with cleavage of one molecule of 2-deoxysugar. At room temperature, with a 0.2 N solution of H_2SO_4, crystallization of the aglycone in the form of rhombic prisms begins after only 1.5 hours. After recrystallization from alcohol the aglycone has m.p. 176-177°, and from a mixture of chloroform and benzene 232-233°; $[\alpha]_D^{20} = +46.1^\circ$ (ethanol, $c = 0.94$).

The aglycone is soluble in alcohol and chloroform, less readily in benzene, and very sparingly soluble in water. It gives positive Legal and Liebermann reactions and a negative Keller-Kiliani reaction. In 84% H_2SO_4 it dissolves with a yellow-green coloration, which changes to orange and then to green.

$C_{23}H_{32}O_6$.	Found	% :	C 68.07;	H 7.91
	Calculated	% :	C 68.29;	H 7.97

Mol. wt.: found 405.0; calculated 404.51.

Authentic strophanthidin and a mixed sample with the aglycone of glycoside-I have the same melting point. On paper chromatograms in various solvent systems these aglycones behave identically. The aglycone of glycoside-I, as does strophanthidin, gives a monoacetyl derivative crystallizing from methanol as colorless prisms with m.p. 242–243°; $[\alpha]_D^{20} = +53.2^\circ$ (ethanol, $c = 1.00$).

$$C_{25}H_{34}O_7. \quad \begin{array}{lll} \text{Found} & \%: & \text{C } 67.29;\ \text{H } 7.71 \\ \text{Calculated} & \%: & \text{C } 67.24;\ \text{H } 7.67 \end{array}$$

Mol. wt.: found 447.01; calculated 446.54.

It follows from the foregoing that the aglycone of glycoside-I is completely identical with strophanthidin.

From the acid hydrolysate, after separation of the aglycone, a crystalline 2-deoxysugar was obtained, melting at 109–110°. By paper chromatography and by physicochemical properties this sugar was identified as *d*-digitoxose.

Comparison of the molecular rotations of glycoside-I ($[M]_D = +177$), the monoglycoside ($[M]_D = +150.6$), and the aglycone ($[M]_D = +186.7$) according to Klyne's rule (2) shows that both digitoxose and xylose are linked by β-glycosidic bonds (see Table 2).

Table 2

Comparison of the molecular rotations of methylglycopyranosides of *d*-digitoxose and *d*-xylose with the molecular rotations of these same sugars in glycoside-I

Name of sugar	$[M]_D$ of methylglycopyranosides, α	$[M]_D$ of methylglycopyranosides, β	Molecular rotation of the sugar components in glycoside-I ΔC	Configuration of sugars in glycoside-I
d-Digitoxose	+311	+60(3)	−36.1	β
d-Xylose	+252.7	−108.5(4)	−33.6	β

Thus, glycoside-I is strophanthidin (3)—β-D-digitoxoso-β-D-xyloside. Its structure may be expressed by the following most probable formula:

[[structural formula of glycoside-I shown]]

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Note: Figure translations are in progress. See original paper for figures.

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