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TRITERPENE GLYCOSIDES OF THE MEDICINAL PREPARATION HEDELIX®

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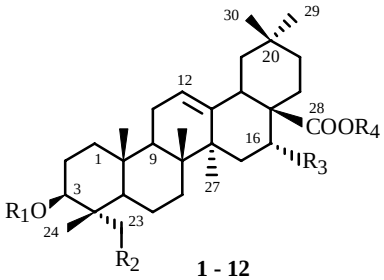
Leaves of common ivy (*Hedera helix* L.) have been used since antiquity in Europe to treat coughs [1]. The German medicinal preparation Hedelix® [2], which has recently appeared on pharmaceutical markets of CIS countries, is based on the extract of ivy leaves. It is indicated for catarrh of respiratory pathways and chronic inflammatory bronchitis.

The glycoside composition of Hedelix® is not well studied. The main component is known to be hederacoside C, hederagenin 3-O-α-L-rhamnopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(**1**→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranoside [1, 3].



1 - 12

	R_1	R_2	R_3	R_4
1:	Ara*p*α→	H	H	H
2:	Ara*p*α→	H	OH	H
3:	Ara*p*α→	OH	H	H
4:	Rha*p*α-(1→2)-Ara*p*α→	H	H	H
5:	Rha*p*α-(1→2)-Ara*p*α→	H	OH	H
6:	Rha*p*α-(1→2)-Ara*p*α→	OH	H	H
7:	^-O_3S→	H	H	H
8:	^-O_3S→	H	OH	H
9:	Ara*p*α→	OH	H	←βGlc*p*-(6←1)-βGlc*p*-(4←1)-αRha*p*
10:	Rha*p*α-(1→2)-Ara*p*α→	H	H	←βGlc*p*-(6←1)-βGlc*p*-(4←1)-αRha*p*
11:	Rha*p*α-(1→2)-Ara*p*α→	H	OH	←βGlc*p*-(6←1)-βGlc*p*-(4←1)-αRha*p*
12:	Rha*p*α-(1→2)-Ara*p*α→	OH	H	←βGlc*p*-(6←1)-βGlc*p*-(4←1)-αRha*p*

We investigated the prepared medicinal Hedelix® s.a. (Krewel Meuselbach, Germany) as drops for internal use (registration No. 3344/26.06.98-26.06.03 in Ukraine). The triterpene glycosides of the preparation were isolated as follows. The preparation was treated with *n*-hexane. The hexane layer was removed. The remainder was exhaustively extracted with water-saturated *n*-butanol. The *n*-butanol extract of glycosides was separated and analyzed by TLC. According to TLC, it contained several groups of triterpene glycosides. The butanol extract of glycosides was separated by column chromatography over silica gel as before [4]. General comments about the glycoside analysis have been reported [4, 5].

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We isolated glycosides and designated them **1**-**12** in order of increasing polarity. The yields were (mass % calculated per 100 g of preparation): 0.001 (**1**), 0.002 (**2**), 0.004 (**3**), 0.018 (**4**), 0.01 (**5**), 0.15 (**6**), 0.02 (**7**), 0.001 (**8**), 0.001 (**9**), 0.03 (**10**), 0.04 (**11**), and 0.18% (**12**).

Glycosides **1**-**12** were identified using authentic specimens of triterpene glycosides of known structure that we isolated from leaves and roots of Canary ivy *Hedera canariensis* [4, 6] and from common ivy *Hedera helix* [5, 7].

Total acid hydrolysis of **1**-**3** produced arabinose in addition to oleanic and echinocystic acids and hederagenin, respectively. Glycosides **1**-**3** are unchanged by alkaline hydrolysis but are methylated by diazomethane in ether. Their chromatographic mobilities are identical to the 3-O-α-L-arabinopyranosides of oleanic and echniocystic and hederagenin, respectively [4-6].

The carbohydrate compositions of **4**-**6**, according to total acid hydrolysis, include rhamnose and arabinose. The aglycons are oleanic and echinocystic acids and hederagenin. Glycosides **4**-**6**, like **1**-**3**, are unchanged in alkaline medium but methylated by diazomethane. This is consistent with the presence of unglycosylated carboxylic acids in their aglycons. Partial acid hydrolysis of **4**-**6** produced the progenins, which were identical according to TLC with glycosides **1**-**3**. Glycosides **4**-**6** have TLC traces similar to the 3-O-α-L-rhamnopyranosyl-(1→2)-O-α-L-arabinopyranosides of oleanic and echinocystic acids and hederagenin, respectively [4, 5].

Total acid hydrolysis of **7** and **8** produced oleanic and echinocystic acids, respectively. Monosaccharides were not found in the acid hydrolysate. However, sulfate was observed.

Therefore, the aglycons of **7** and **8** are not glycosylated and contain a sulfate. According to TLC analysis, we found that the chromatographic mobilities of **7** and **8** in various solvent systems were identical to those for oleanic and echinocystic 3-O-sulfates [7].

The total acid hydrolysates of **9**-**12** contained rhamnose, arabinose, and glucose for all glycosides. The aglycons were hederagenin (**9** and **12**) and oleanic (**10**) and echinocystic (**11**) acids. Glycosides **9**-**12** were hydrolyzed in alkaline medium to afford **3** and **4**-**6**, respectively. They were not methylated by diazomethane. This defined them as bisdesmosides. According to TLC analysis, **9**-**12** were identical to authentic specimens of hederagenin 3-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranoside [4-6] and oleanic, echinocystic, and hederagenin 3-O-α-L-rhamnopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides, respectively [4,5]. Furthermore, the ^{13}C NMR spectrum of **12** was identical to that of hederagenin 3-O-α-L-rhamnopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranoside [4].

Thus, the glycosides of Hedelix® are dominated by those of hederagenin. The highest contents were found for **6** and **12**, with the latter dominating.

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