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QUINOVIC ACID GLYCOSIDES FROM *ZYGOPHYLLUM AEGYPTIUM*

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تم فصل سبعة مركبات صابونينية من الخلاصة الكحولية لنبات الزيجوفيلم ايجيبتيام وهى حمض الكينوفيك-٣-بيتا-أ-بيتا-دى- كينوفوبيرانوزيد (٢) وحمض الكينوفيك-٣-بيتا-أ-بيتا-دى-جلوكوبيرانوزيد (٣) و ٣-أ- [ألفا-ل-ارابينوزيل-(١ ← ٢)- بيتا-دى-كينوفوبيرانوزيل] حمض الكنوفيك (٤) و٣ بيتا-أ-بيتا-دى-كينوفوبيرانوزيل-حمض الكينوفيك-٢٨-أ- بيتا-دى-جلوكوبيرانوزيل استر (٥) و٣- بيتا-أ- [بيتا-دى-٢-أ- سلفونيل كينوفوبيرانوزيل] حمض الكينوفيك-٢٨-أ- بيتا-دى- جلوكوبيرانوزيل استر (زيجوفيلوزيدف) (٦) و ٣ بيتا-أ-بيتا- دى-جلوكو بيرانوزيل حمض الكينوفيك-٢٨-أ-بيتا-دى- جلوكوبيرانوزيل أستر (٧) ٣-أ-[بيتا-دى-٢-أ-سلفونيل جلوكوبيرانوزيل]-حمض الكينوفيك-٢٨-أ- [بيتا-دى جلوكوبيرانوزيل] استر (زيجوفيلوزيد ج) (٨) . هذا بالاضافة الي بيتا-سيتوستيرول جلوكوزيد (١) وقد تم التعرف على هذه المركبات بواسطة الخواص الطبيعية والطرق الطيفية المختلفة.

Seven known quinovic acid glycosides were isolated for the first time from the n-BuOH fraction of the 70% ethanol extract of Zygophyllum aegyptium A. Hosny sp. nov. These compounds were identified as: quinovic acid 3β-O-β-D-quinovopyranoside (2), quinovic acid 3β-O-β-D-glucopyranoside (3), 3-O-[α-L-arabinosyl-(1→2) β-D quinovopyranosyl] quinovic acid (4), 3-β-O-β-D-quinovopyranosnyl quinovic acid-28-O-β-D glucopyranosyl ester (5), 3-β-O-[β-D-2-O-sulphonyl quinovopyranosyl]-quinovic acid-28-O-β-D-glucopyranosyl ester (zygopylloside F) (6), 3-β-O-β-D-glucopyranosyl quinovic acid 28-O-β-D- glucopyranosyl ester (7), 3β-O-[β-D-2-O-sulphonyl glucopyranosyl]-quinovic acid-28-O-[β-D-glucopyranosyl] ester (zygophlloside G) (8), in addition to, β-sitosterol glucoside (1). The structure elucidation of these compounds was determined by physical, chemical and spectroscopic methods.

INTRODUCTION

The genus *Zygophyllum* (family Zygophyllaceae) is very common to desert plant and represented in Egypt by eleven species,[1-3] of which *Zygophyllum aegyptium* A. Hosny sp. nov. is restricted mainly to salty and sandy places of Egypt and Mediterranean region.[1-3] The genus is reputed for its folk medicine especially *Z. coccineum* L. which is known in Egypt as Kammun Quaramany and used in the treatment of gout, rheumatism, asthma and hypertension.[4-7] Recent work on the saponin content of this genus revealed the presence of several quinovic acid glycosides which are reputed for their potent anti-inflammatory and antiviral action.[8-16] However, *Zygophyllum aegyptium* A. Hosny sp. nov. has never been yet phytochemically investigated. The present study indicated the isolation and identification for the first time of seven quinovic acid glycosides from the plant, in addition to, ß-sitosterol glucoside.

EXPERIMENTAL

Melting points were uncorrected and measured on Stuart Scientific apparatus. Negative ion MS were recorded on a Varian-MAT 311A, glycerol matrix. NMR spectra were recorded on a Varian EM in pyridine-d_5 as solvent at 400 MHz for ^1H and 125 MHz for ^{13}C-NMR using TMS as internal standard.

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Column chromatography: silica gel and RP-$_{18}$; spray reagents: 10% H_2SO_4 for saponins and aniline-diphenylamine-phosphoric acid for carbohydrates.[14] TLC: with precoated plates of silica gel 60 F_{254} (E. Merck) using the following systems:
1-$CHCl_3$-MeOH (80:20).
2-$CHCl_3$-MeOH-H_2O (75:20:2).
3-$CHCl_3$-MeOH-H_2O (70:25:3).

Plant material

Aerial parts of *Zygophyllum aegyptium* A. Hosny sp. nov. were collected from desert road between Qantara and Ismailia in may 1995. The plant was kindly identified by Dr. Amal I. Hosny (Dep. of Taxonomy, Faculty of Science, Cairo University).

Extraction and Isolation

The air dried powdered aerial parts of *Z. aegyptium* A. Hosny sp. nov. (2 kg.) were extracted with 70% ethanol. The concentrated alcoholic extract (25 g) was diluted with distilled water and fractionated successively with $CHCl_3$ and n-BuOH. The dried n-BuOH residue (10 g) was chromatographed on a column of silica gel using $CHCl_3$-MeOH gradient. Elution with $CHCl_3$-MeOH (92:8) afforded compound (1). Compound (2) was eluted by $CHCl_3$-MeOH (90:10) followed by compound (3) which was eluted by $CHCl_3$-MeOH (88:12). Elution with $CHCl_3$-MeOH (85:15) gave compound (4), while elution with $CHCl_3$-MeOH (80:20) afforded a mixture of compounds (5) and (6) which were isolated on RP-$_{18}$ column chromatography using MeOH-H_2O (30:70). Elution with $CHCl_3$-MeOH (75:25) from the main column afforded a mixture of compounds (7) and (8) which were finally isolated on RP-$_{18}$ column using MeOH-H_2O (70:30) as eluent.

Compound 1: 300 mg, spherical crystals (MeOH), m.p. 275-8°, HR_f 55 (system 1), identified by direct comparison with authentic sample as ß-sitosterol glucoside.

Compound 2: 43 mg, needles (MeOH), m.p. 210-2° HR_f 52 (system 1), negative FAB-MS m/z 631 $[(M-H)^+]^-$ (100), m/z 587 $[(M-H)^+-CO_2)]^-$ (30), m/z 485 $(M-H^+$-quinivose$)^-$ (17), m/z 441 $(M-H^+$-quinivose-$CO_2)^-$ (22), ^{1}H-NMR: δ 0.82 (3H, d, J= 6 Hz), 0.89 (3H, s), 0.97 (3H, s), 1.12 (3H, s), 1.17 (3H, s), 1.25 (3H, d, J= 6 Hz), (Me x 6), 1.50 (3H, d, J= 6 Hz, quinivose Me), 3.24 (1H, m, H-3), 4.71 (1H, d, J= 7.6 Hz, H-1´ quinivose), 6.03 (1H, t, J= 2.5 Hz, H-12). ^{13}C-NMR see Table 1.

Compound 3: 22 mg, amorphous, HR_f 47 (system 1), negative FAB-MS m/z 647 $[(M-H)^+]$ (100), m/z 603 $(M-H^+-CO_2)^-$ (8), m/z 441 $(M-H^+$-gluc.-$CO_2)^-$ (21), ^{1}H-NMR δ 0.82 (3H, d, J= 6 Hz), 0.89 (3H, s), 0.97 (3H, s), 1.12 (3H, s), 1.17 (3H, s), 1.25 (3H, d, J= 6 Hz) (Me x 6), 3.24 (1H, m, H-3), 4.65 (1H, d, J= 8Hz H-1´ glucose), 6.03 (1H, t, J= 2.5 H-2, H-12) ^{13}C-NMR see Table 1.

Compound 4: 52 mg, needles, m.p. 192-4°, HR_f 45 (system 2), negative FAB-MS m/z 763 $(M-H)^+$ (100), m/z 719 $(M-H^+-CO_2)$ (12), m/z 631 $(M-H^+$-arabinose$)^-$ (13), m/z 485 $(M-H^+$-arabinose-quinivose) (10), ^{1}H-NMR δ 0.82 (3H, d, J= 6 Hz), 0.92 (3H, s), 1.00 (3H, s), 1.13 (3H, s), 1.18 (3H, s), 1.25 (3H, d, J= 6 Hz), (Me x 6), 1.50 (3H, d, J= 6 Hz, quinivose Me.), 3.14 (1H, m, H-3), 4.69 (1H, d, J= 7.5 Hz H-1´ quinivose), 5.16 (1H, d, J= 6.6 Hz H-1´´ arabinose), 6.03 (1H, m, H-12). ^{13}C-NMR see Table 1.

Compound 5: 156 mg, needles (MeOH), m.p. 240-2°, HR_f 62 (system 3), negative FAB-MS m/z: 793 $(M-H^+)^-$ (100), m/z 749 $(M-H^+-CO_2)$ (25), m/z 587 $(M-H^+$-glucose-$CO_2)$-(11), m/z 441 $(M-H^+$-gluc. -CO_2-quin.) (13), ^{1}H-NMR δ 0.77 (3H, d, J= 6 Hz), 0.91 (3H, s), 0.96 (3H, s), 1.16 (3H, s), 1.19 (3H, s), 1.24 (3H, d, J= 6 Hz) (Me x 6), 1.50 (3H, d, J= 6.6 Hz, quinivose Me), 3.14 (1H, m, H-3´), 4.65 (1H, d, J= 7.6 Hz, H-1´ quinivose), 6.03 (1H,m, H-12), 6.32 (1H, d, J= 7.6 Hz, H-1´´ gluc), ^{13}C-NMR see Table 1.

Compound 6: 30 mg, amorphous, HR_f 59 (system 3), negative FAB-MS m/z; 873 $(M-H)^+$

(100), m/z 829 (M-H^+-CO_2) (6), m/z 711 (M-H^+-gluc.)$^+$ (17), m/z 665 (M-H^+-gluc.-CO_2) (15), m/z 587 (M-H^+-gluc.-CO_2-SO_3) (3), m/z 441 (M-H^+-gluc.-CO_2-SO_3-quinivose), m/z 97 $(SO_4H)^+$ (30), m/z 80 (SO_3) (35), ^{1}H-NMR δ 0.76 (3H, d, J= 6Hz), 0.87 (3H, s), 1.12 (3H, s), 1.16 (3H, d, J= 6 Hz), 1.19 (3H, s), 1.28 (3H, s) (Mex6), 1.56 (3H, d, J= 6 Hz, quinivose Me), 3.15 (1H, m, H-3), 4.72 (1H, d, J= 7.5 Hz, quinivose H-1´), 6.02 (1H, t, J=2.5 Hz, H-12), 6.35 (1H, d, J= 8.1 Hz, H-1´´´ gluc.), ^{13}C-NMR Table 1.

Compound 7: 92 mg, amorphous, HR_f 48 (system 3), negative FAB-MS m/z; 809 $(M-H^+)^-$ (100), 765 $(M-H^+-CO_2)^-$ (20), 603 $(M-H^- -CO_2$-gluc.) (10), 441 (M-H^+-CO_2 -2 gluc.) (7), ^{1}H-NMR δ 0.75 (3H, d, J= 6 Hz), 0.80 (3H, s), 1.11 (3H, s), 1.14 (3H, d, J= 6 Hz), 1.17 (3H, s), 1.28 (3H, s) (Me x 6), 3.70 (1H, dd, J= 11.5, 4.5 Hz; H-3), 4.70 (1H, d, J= 8 Hz, H-1´ glucose), 5.97 (1H, t, J= 2 Hz, H-12), 6.34 (1H, d, J= 8 Hz, H-1´´´ gluc.), ^{13}C-NMR see Table 1.

Compound 8: 41 mg, amorphous, HR_f 45 (system 1), Negative FAB-MS m/z 911 ((M$^+$-2H$^+$ +Na$^+$) (12), 889 $(M-H^+)^-$ (100), 845 (M-H^+-CO_2) (6), m/z 727 (M-H^+-gluc.) (10), m/z 683 (M-H^+- gluc.-CO_2) (12), m/z 603 (M-H^+-gluc.-CO_2-SO_3)$^-$ (3), m/z 97 $(SO_4H)^-$ (37), m/z 80 $(SO_3)^-$ (32); ^{1}H-NMR δ 0.73 (3H, d, J= 6Hz), 0.81 (3H, s), 1.11 (3H, s), 1.14 (3H, d, J= 6 Hz), 1.16 (3H, s), 1.28 (3H, s) (Me x 6), 3.70 (1H, m, H-3), 4.82 (1H, d, J= 8 Hz, H-1´ glucose), 5.95 (1H, t, J= 2.5 Hz, H-12), 6.34 (1H, d, J= 8 Hz, H´´´ 1 glucose), ^{13}C-NMR Table 1.

Acid hydrolysis

Ten mg of each glycoside was refluxed with 1M trifluoroacetic acid for 2 hours. The solution in each case, was evaporated under vacuum, the residue, was extracted with 1ml distilled water and identified by TLC (precoated silica gel) alongside authentic sugars using acetonitrile-water (85:15, triple run). The aglycone was dissolved in hot chloroform-methanol (1:1) and identified by comparison with authentic sample (TLC.).

Alkaline hydrolysis

Ten mg of compound (6) was refluxed with 5% KOH for about 6 hours. The reaction mixture was neutralized with dilute HCl and extracted with n-BuOH saturated with water. The butanol residue was chromatographed on a column of silica gel and eluted with $CHCl_3$-MeOH (85:15) to give a compound identical to compound (2) (TLC).

RESULTS AND DISCUSSION

The crude saponin fraction of the air dried aerial parts of *Zygophyllum aegyptium* A. Hosny sp. nov. afforded seven known saponins from the plant after repeated column chromatography over silica gel and RP_{18} materials.

Acid hydrolysis of compounds 2-8 gave one and the same aglycone, which was identified by direct authentication, as quinovic acid (mmp and co-chromatography).

Compound (1) was identified as ß-sitosterol glucoside by direct comparison with authentic sample (mmp and co-chromatography).

Compound (2) showed a molecular formula $C_{36}H_{56}O_7$ (DEPT ^{13}C-NMR and FAB-MS). The negative FAB-MS spectrum of (2) showed a molecular anion peak at m/z 631 $[M-H^+]^-$ and further peaks at m/z 587 $[M-H^+-CO_2]^-$, m/z 485 for [M-H^+-146 (deoxyhexose)] and m/z 441 for M-H^+-146-CO_2]. The sugar moiety was identified as ß-D quinivose from comparison of the ^{1}H and ^{13}C-NMR spectra of (2) with reported data.[9,17] The ^{1}H and ^{13}C-NMR anomeric signals at δ 4.71 and 106.8 respectively are in full agreement with an ether linked ß-D quinivose moiety at C-3 of quinovic acid.[8-16] As such, compound (2) was assigned the structure quinovic acid 3ß-O-ß-D-quinovopyranoside.

Similarly compound (3) was identified as quinovic acid 3ß-O-ß-D- glucopyranoside from its acid hydrolysis (D-glucose by TLC) and by comparison of its ^{1}H and ^{13}C-NMR (Table 1) with literature.[9,10,18]

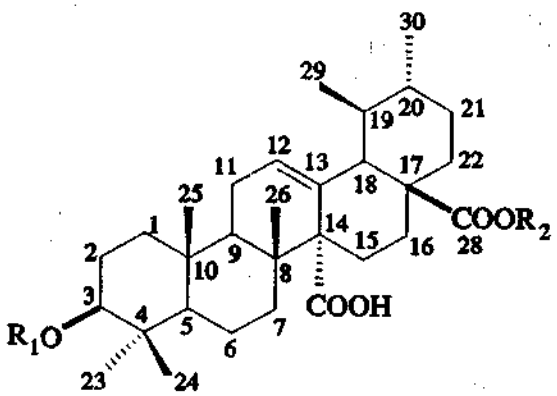
Acid hydrolysis of compound (4) afforded L-arabinose and D-quinivose (TLC). The presence of two anomeric protons at δ 4.65 and 5.14 indicated the presence of two sugar units. This was confirmed by FAB-MS which showed a quasi-molecular ion peak at m/z 763 $[M-H^+]^-$

and further peaks at m/z 631 and m/z 485 indicating successive losses of arabinose and arabinose + quinivose moieties respectively from the molecular ion peak. The ^{13}C-NMR of compound **(4)** (Table 1) further supported this conclusion where two anomeric carbons at δ 104.8 and 106.8 were observed. Moreover, it indicated that the extra arabinose moiety was linked to C-2 of quinivose due to upfield shifts of both C-1 (2 ppm) and C-3 (1 ppm) of quinivose and downfield shifts of C-2 of quinivose (8.5 ppm) in comparison with compound 2.

The sugar linkage was assigned to C-3 of quinovic acid where C-3 of the glycoside **(4)** was shifted downfield (10 ppm) in comparison with C-3 of free aglycone.[10] As such, the structure of **(4)** was deduced as 3ß-O-[α-L-arabinosyl-(1→2) ß-D quinovopyranosyl] quinovic acid which was confirmed by comparison with literature data.[11,13]

The acid hydrolysis of compound **(5)** afforded D-quinivose and D-glucose [TLC]. The ^{1}H-NMR of **(5)** showed two anomeric protons at δ 4.65 (ether linked) and δ 6.32 (ester linked). Comparison of its FAB-MS and ^{13}C-NMR with literature data[11,19] confirmed its identity as 3-ß-O-ß-D-quinovopyranosnyl quinovic acid-28-O-ß-D glucopyranosyl ester.

Acid hydrolysis of compound **(6)** afforded D-quinivose and D-glucose (TLC) as that of **(5)**. The ^{1}H-NMR of **(6)** revealed two anomeric protons for an ether linked sugar at δ 4.73 (1H, d, J= 7.6 Hz) and an ester linked sugar at δ 6.33 (1H, d, J= 8.0 Hz), an olefinic proton at δ 5.99, four tertiary and two secondary methyl groups characteristic of quinovic acid urs-12-ene skeleton at δ 0.76-1.28 and an extra methyl doublet at δ 1.57 (3H, d, J= 6.0 Hz) associated with the quinivose moiety.



Compound	R_1	R_2
2	ß-D-quinivose	H
3	ß-D-glucose	H
4	α-L-arabinose(1→2)ß-D-quinivose	H
5	ß-D-quinivose	ß-D-glucose
6	2-O-sulphonyl ß-D-quinivose	ß-D-glucose
7	ß-D-glucose	ß-D-glucose
8	2-O-sulphonyl ß-D-glucose	ß-D-glucose

Table 1: ^{13}C-NMR data for compounds (2-8) in Pyridine d-$_5$.

	2	3	4	5	6	7	8
1	39.4	39.0	39.1	38.9	38.9	39.0	39.6
2	26.8	26.7	26.7	26.7	26.8	26.8	26.7
3	88.7	88.7	88.5	88.5	89.3	88.8	89.2
4	40.1	39.4	39.5	39.4	39.4	39.5	40.2
5	55.9	55.6	55.8	55.7	55.7	55.7	55.8
6	18.7	18.6	18.5	18.5	18.5	18.6	18.5
7	37.2	37.8	37.6	37.5	37.6	37.6	37.5
8	40.1	40.0	40.1	40.1	40.2	40.1	40.2
9	47.3	47.2	47.2	47.3	47.3	47.2	47.2
10	37.3	37.1	37.1	37.0	37.0	37.0	37.0
11	23.4	23.3	23.4	23.5	23.5	23.5	23.4
12	129.3	128.9	129.0	129.6	129.6	129.0	129.6
13	134.2	134.1	134.0	133.3	133.3	133.8	133.3
14	56.9	56.8	56.8	56.8	56.8	57.1	56.8
15	25.6	25.5	25.4	25.5	25.5	25.7	25.5
16	26.4	26.4	25.9	26.2	26.2	26.4	26.2
17	48.9	48.7	48.7	49.1	49.0	49.1	49.0
18	55.0	54.9	55.0	54.8	54.7	54.9	54.7
19	37.8	37.5	37.8	37.5	37.5	37.5	37.5
20	39.4	39.4	39.4	39.1	39.1	39.2	39.1
21	30.7	30.6	30.1	30.2	30.3	30.3	30.3
22	37.6	37.0	37.0	36.4	36.5	36.6	36.5
23	28.1	28.8	27.9	28.1	28.1	28.1	28.1
24	17.1	17.1	16.8	17.1	17.1	17.0	17.1
25	16.6	16.5	16.5	16.6	16.6	16.7	16.6
26	19.0	18.9	18.9	19.2	19.1	19.2	19.2
27	178.1	178.1	178.1	178.1	178.1	178.6	178.0
28	180.2	180.1	180.2	176.7	176.7	176.7	176.6
29	18.3	18.3	18.2	18.2	18.2	18.3	18.2
30	21.4	21.4	21.4	21.2	21.2	21.3	21.2
1`	106.7	106.9	104.1	106.7	104.1	107.0	104.3
2`	76.0	75.8	84.2	76.0	81.2	75.7	81.0
3`	78.4	78.8	77.8	78.4	77.7	78.7	78.3
4`	76.9	71.8	67.6	76.9	76.7	71.8	71.8
5`	72.7	78.3	72.4	72.7	72.2	78.3	77.5
6`	18.8	62.9	18.5	18.8	18.5	63.0	62.9
1``			106.8	95.7	95.8	95.7	95.7
2``			73.8	74.2	74.2	74.2	74.1
3``			74.3	78.8	78.9	78.9	78.9
4``			69.1	71.3	71.3	71.2	71.2
5``			67.0	79.2	79.3	79.3	79.3
6``				62.3	62.4	62.3	62.4

The negative FAB-MS of compound (6) showed a molecular anion peak at m/z 873 and further peaks at m/z 711, 667, 587, 441 which could be assigned for successive losses of glucose unit, glucose unit + CO_2, glucose unit + CO_2 + SO_3.

The presence of OSO_3H moiety was further indicated by fragment ions at m/z 97 $(SO_4H)^-$ and m/z 80 $(SO_3)^-$. The ^{13}C-NMR of compound (6) showed downfield shift of C-2 and upfield shift of the anomeric carbon of quinivose unit linked at C-3 of the aglycone, while the other sugar signals were corresponding to an ester glucose unit linked at either C-27 or C-28. This was confirmed from alkaline hydrolysis of compound 6 which afforded D-glucose and a compound identical to compound (2). The data of this compound were identical with those reported for zygopylloside F which has been first assigned as C-27 glucosyl ester[10] by HMBC and revised to C-28 glucosyl ester by further 2D-NMR analysis from other *Zygopyllum* species.[11]

Acid hydrolysis of compound (7) gave only D-glucose by TLC. The negative FAB-MS of (7) showed [M-H$^+$] at m/z 809 with successive peaks at m/z 765, 603 and 441 assigned for successive losses of CO2, glucose + CO_2 and two glucose units + CO_2. The ^{1}H and ^{13}C-NMR spectra of (7) exhibited signals for an ether linked glucose unit at δ 4.70, 107 respectively and an ester linked glucose unit at δ 6.34, 95.7 respectively. Comparison of ^{13}C-NMR of compound (7) with those reported for 3-ß-O-ß-D-glucopyranosyl quinovic acid 28-O-ß-D-glucopyranosyl ester[11,20] proved their identity.

The acid hydrolysis of compound (8) yielded D-glucose (TLC). The ^{1}H-NMR and ^{13}C-NMR of compound (8) (see exp. and Table) indicated the presence of also two glucose units, one of them is linked at C-3 as ether group and the other as ester at C-28 as seen in compound (7). However compound (8) showed an extra sulphate group at C-2 of the glucose unit linked at C-3 as previously discussed in compound (6). From these data, compound 8 was identified as 3ß-O-[ß-D-2-O-sulphonyl glucopyranosyl]-quinovic acid-28-O-[ß-D-glucopyranosyl] ester (zygophlloside G), which was confirmed by comparison with literature data.[11]

Compounds 2-8 have been previously isolated and completely characterized from other *Zygophyllum* species,[8-14] however this is the first report for their isolation from *Zygophyllum aegyptium* A. Hosny sp. nov.

It was observed that all quinovic acid glycosides containing quinivose moiety or sulphated quinivose moiety (compounds 2, 4, 5 and 6) gave an orange-red colour with 10% H_2SO_4 as spraying agent after heating a relatively a short time (10 min at 140°) in comparison with those containing glucose units only (compounds 3, 7 and 8) which gave a violet colour. Compounds (5) and (6) are intensely bitter in taste compared with the other isolated glycosides and are principally responsible for the bitterness observed with the bearing *Zygophyllum* species. They form a gel in chloroformic eluents blocking the silica gel upon a trial for their isolation column and consequently they were isolated on RP_{-18}.

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