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Euphosantianane E–G: Three New Premyrsinane Type Diterpenoids from *Euphorbia sanctae-catharinae* with Contribution to Chemotaxonomy

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Abstract: *Euphorbia* species were widely used in traditional medicines for the treatment of several diseases. From the aerial parts of Egyptian endemic plant, *Euphorbia sanctae-catharinae*, three new premyrsinane diterpenoids, namely, euphosantianane E–G (**1**–**3**), alongside four known triterpenes, 9,19-cyclolanostane-3β,24*S*-diol (**4**), 25-methoxycycloartane-3β,24*S*-diol (**5**), 25-methylenecycloartan-3β,24*R*-diol (**6**), and 25-methylenecycloartan-3β,24*S*-diol (**7**), were isolated and identified. The chemical structures were proven depending upon spectroscopic analysis, including FTIR, HRFABMS, and 1D/2D-NMR. The chemotaxonomic significance of the isolated compounds, especially diterpenes from *E. sanctae-catharinae* compared to those documented from different *Euphorbia* species was also studied via agglomerative hierarchical clustering (AHC). The Egyptian endemic *Euphorbia sanctae-catharina* was grouped with *E. bupleuroides*, *E. fidjiana*, *E. fischeriana*, *E. pithyusa* subsp. *cupanii*, *E. prolifera*, and *E. seguieriana*, where myrsinol diterpenoids were the characteristic compounds.

Keywords: endemic plant; *Euphorbia sanctae-catharinae*; euphorbiaceae; premyrsinane diterpenoids; euphosantianane E–G; chemotaxonomic significance

1. Introduction

From the times of ancient Egyptian civilization, medicinal plants have been used as resources of several medicinal treatments. Egypt has unique biodiversity, including different ecological zones such as the Nile-Delta areas, Mediterranean coasts, Red Sea coast, and deserts. Because of these variations in ecological and natural factors between these zones, it is characterized by a diversity of wild and/or endemic medicinal plants. It also includes 13 pharmacopeia ones, 60 endemic ones, and 529 species used for medical purposes [1,2]. The Sinai Peninsula and especially Saint Katherine is one of the most

interesting and promising resources of medicinal plants. The medicinal plants located in Sinai have shown unique phytochemicals with potent biological activities which have piqued the interest of many scientists, especially biologists and phytochemists, for further investigations [1,3–5].

It is well known that *Euphorbia* species all over the world have different chemical and biological diversity. Several *Euphorbia* plants have been used in folk medicines against several remedies, such as skin diseases, warts, gonorrhea, migraine, and intestinal parasites. Phytochemical characterization of these plants affords highly bioactive isoprenoids [6–8]. Diterpenes represent the main constituents from the plants of this genus, including jatrophanes, premyrsinanes, Abietanes, tiglianes, ingenanes, lathyranes, and myrsinols [6,7,9].

Several bioactivities were described for the different extracts and isolated metabolites of these plants, such as anti-inflammatory [10], antifungal [11], antiviral [12], antispasmodic [11], cytotoxic [9,13], antimutagenic [14], antibacterial [15,16], and hepatoprotective [6,7].

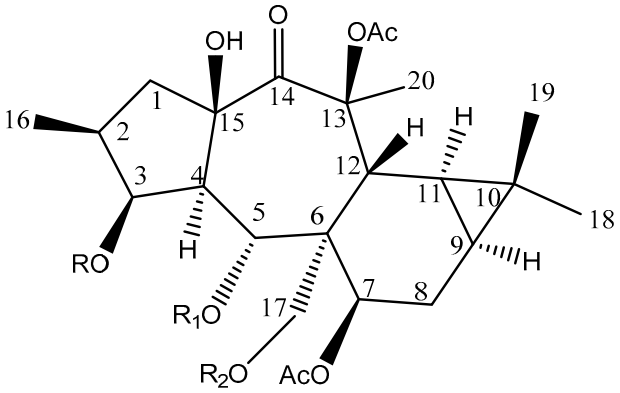
Among the 60 identified endemic species to Egypt, three *Euphorbia* species (*E. bivonae* Steud., *E. punctata* Delile, and *E. sanctae-catharinae* Fayed (synonym of *E. obovata* Decne.)) were recorded. Recently, our group successfully isolated and identified nine premyrsinanes diterpenoids as well as three flavonoids from *E. sanctae-catharinae* and evaluated their cytotoxic activities [9]. Continuing our work on the investigation of new metabolites from medicinal plants, we performed here the isolation and identification of seven terpenoids, including three new premyrsinanes (**1**–**3**, Euphosantianane E–G), alongside four known triterpenes (**4**–**7**) (Figure 1).

2. Results and Discussion

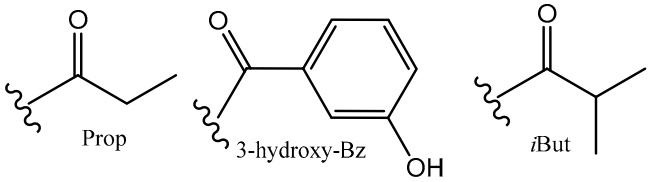
2.1. Structure Elucidation of the Isolated Compounds

The chemical characterization of the CH_2Cl_2–MeOH extract of the air-dried powder of the Egyptian endemic plant, *E. sanctae-catharinae*, using different chromatographic tools, afforded three new premyrsinane types diterpenes (**1**–**3**) alongside four known triterpenes (**4**–**7**), presented in Figure 1. The chemical structures of these seven isolated compounds were established depending upon the modern spectroscopic analysis.

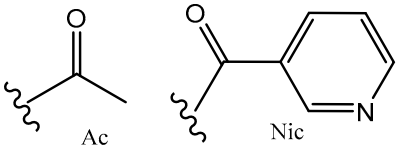
Euphosantianane E (**1**) was isolated as a colorless oil and exhibited positive optical rotation ($[\alpha]_D^{25}$ + 18.0 in MeOH). The chemical formula was assigned as $C_{36}H_{46}O_{13}$ (cal. 686.2938) depending upon the HRFABMS that exhibit molecular ion peak at *m/z* 709.2930 $(M + Na)^+$ and displayed 14 degrees of unsaturation. FTIR absorption bands characteristic for OH and carbonyl esters were observed, respectively, at 3380 and 1732 cm^{-1}, alongside with the aromatic ring absorption bands at 1442 and 723 cm^{-1}. ^{1}H-NMR spectrum (Table 1) of **1** exhibited proton signals for three oxygenated methines at δ_H 5.35 br t (J = 3.48 Hz), 6.42 d (J = 11.46 Hz) and 4.77 d (J = 6.72 Hz); one methylene at δ_H 4.35 d (J = 11.70 Hz) and 4.67 d (J = 11.70 Hz); three characteristic methyles singlets of acetates at 2.11 s (6H) and 2.12 s. Additionally, four singlet methyl signals at δ_H 0.94 s, 1.04 s (6H), and 1.57 s, as well as one triplet methyl signal at δ_H 0.98 t (J = 7.5 Hz). Additionally, two methine protons characteristic to cyclopropane moiety were identified at δ_H 0.73 m (2H). ^{13}C-NMR (Table 1) spectrum displayed 36 carbon signals that were characterized by DEPT-135 and HMQC experiments to 12 quaternary carbons (including five carbonyl esters at δ_C 173.5, 170.8 (2 × C), and 170.0, 168.9; one ketone at δ_C 204.1 and two oxygenated carbons at δ_C 84.2 and 85.7); 12 methines (including three oxygenated at δ_C 78.2, 70.6 and 70.5); four methylene carbons (including one oxygenated at δ_C 62.8); and eight methyl groups (including three methyles of acetates at δ_C 20.8, and 21.4 (2 × C) and one methyl of propanoyl group at δ_C 8.8). 1D and 2D-NMR spectra of **1** were closely related to previously reported premyrsinanes with clear differences in type of substitution in C-5. A complete assignment of **1** was compatible with previously reported euphosantianane A [9].

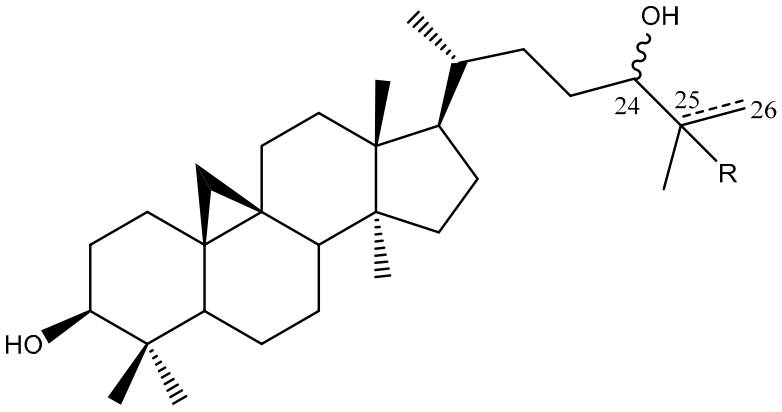


1 R= Pro, R_1= 3-hydroxy-Bz, R_2= Ac
2 R= Pro, R_1=Pro, R_2= Nic
3 R= iBut, R_1=Ac, R_2= Nic



Pro: Propanoyl
3-hydroxy-Bz: 3-hydroxy benzoyl
iBu: isobutanoyl
Nic: nicotinoyl
Ac: acetyl





4 R= H, 24*S* OH
5 R=OMe, 24*S* OH
6 = 24*R* OH, Δ^{25}
7 = 24*S* OH Δ^{25}

Figure 1. Isolated compounds from *Euphorbia sanctae-catharinae*.

^{1}H–^{1}H COSY correlations of H-4 (δ_H 2.37, dd, J = 3.78, 11.5 Hz)/H-3 (δ_H 5.35 brt, J = 3.48 Hz), H-4/H-5 (δ_H 6.42 d, J = 11.46 Hz), H-9 (δ_H 0.73 m)/H-8 (δ_H 3.50 brd, J = 6.54 Hz), and H-8/H-7 (δ_H 4.77, d, 6.72 Hz) confirmed the oxygenation of C-3 (δ_C 78.2), C-5 (δ_C 70.5), and C-7 (δ_C 70.6). Additionally,

H_3-16 (δ_H 1.04, s), H-12 (δ_H 3.48, s), and H-5 showed correlation with C-3, C-5, and C-7 in HMBC analyses, respectively (Figure 2). The HMBC spectra showed the following correlation: H-17 at δ_H 4.67 (d, J = 11.70 Hz)/C-5 (J^3); H-3/C-15 (84.2; J^3); H-4/C-15 (J^2); H-4/C-14 (204.1; J^3); H_3-20 at δ_H 1.57(s)/C-14 (J^3); H-12/C-13 (δ_C 85.7; J^2) confirmed the hydroxylation of C-15, oxygenation of C-13 and C-17, and localization of ketone group in C-14 (Figure 2). As described in several reports, the premyrsinanes isolated from *Euphorbia* plants are usually characterized by variation of functionality at C-3, C-5, C-7, and/or C-17 [9,17,18]. The 1D and 2D-NMR as well as mass spectrum exhibited the replacement of 3-methylbutyryl moiety (euphosantianane A, Hegazy et al., 2018) with 3-hydroxy benzoyl moiety. This substitution was deduced depending upon the HMBC correlations of H-5/(O=C)-1" (δ_C 168.9; J^3), H-3" at δ_H 7.39 d (J = 1.56 MHz)/C-1", and H-7" at δ_H 7.58 dd (J = 1.68, 7.98 MHz). Further, the hydroxylation of C-4" was confirmed with the aromatic quaternary carbon at δ_C 161.9 (C-4") alongside the HMBC correlations of H-6" at δ_H 6.80 t (J = 9.18 MHz)/C-4".

The relative configuration of **1** was determined depending upon NOESY correlations (Figure 3). The *trans* and α orientation H-4 and H_2-17, respectively, was established depending upon the biosynthetic pathways of these types of myrsinols [9,17,18]. Starting from this reference point, NOESY correlations of H-4α/H-3 and H-3/H-2 deduced the α configuration of H-3 and H-2. NOESY correlations of H-12β/H-5, H-9α/H-11α, and H-11α/H-20 elucidated the β orientation of H-5 and Me-20. From all these described data, **1** was assigned as premyrsinol-3β-propanoyl-5α-(3-hydroxy)-benzoyl-7β,13β,17α-triacetate (Euphosantianane E).

Euphosantianane F (**2**, Figure 1) was isolated as a colorless oil and exhibited positive optical rotation ($[\alpha]_D^{25}$ + 24.4 in MeOH). Based on the HRFABMS ion peak at *m/z* 685.3089 (M), the molecular formula of **2** was determined as $C_{36}H_{47}NO_{12}$ (cal. 685.3098), exhibiting 14 degrees of unsaturation. FTIR bands for OH and carbonyl esters were characterized at 3441 and 1736 cm^{-1}, respectively, in addition to the aromatic ring absorption bands at 1434 and 741 cm^{-1}. 1D-NMR data (Table 1) and 2D (^1H–^1H COSY, HMQC, and HMBC, Figure 2) exhibited that **2** is very close to euphosantianane A (Hegazy et al., 2018), except the substitution at C-5 and C-17 was replaced by propanoyl and nicotinoyl, respectively. This substitution was deduced by the downfield shift of C-5 by 1.9 ppm to be at δ_C 70.7 and the upfield shift of C-17 by 1.0 ppm to be at δ_C 62.6, in addition to the HMBC and ^1H–^1H COSY related to propanoyl and nicotinoyl substituents, respectively. Depending on NOESY, compound **2** showed the same stereochemistry of **1**. Thus, **2** was identified as premyrsinol-3β,5α-dipropanoyl-7β,13β-diacetyl-17α-nicotinoate (euphosantianane F).

Euphosantianane G (**3**, Figure 1) was obtained as a colourless oil and exhibited positive optical rotation ($[\alpha]_D^{25}$ 53.2 in MeOH). The HRFABMS ion peak assigned at *m/z* 708.3090 $(M + Na)^+$ indicated the molecular formula as $C_{36}H_{47}NO_{12}$ (cal. 685.3098) with 14 degrees of unsaturation. Hydroxyls and carbonyl ester FTIR bands at 3430 and 1728 cm^{-1}, respectively, as well as the aromatic ring absorption bands at 1458 and 716 cm^{-1} were identified. 1D-NMR data (Table 1), ^1H–^1H COSY and HMBC (Figure 2) of **3** are very close to euphosantianane D [9] (Hegazy et al., 2018), with the usual exception of different substitutions at C-3 and C-5, in which isobutanoyl and acetyl groups were inserted, respectively. The downfield shift of C-3 by 1.3 ppm found at δ_C 78.6 deduced the substitution of this carbon with the acetyl group instead of 3-dimethylbutanoyl in euphosantianane D [9]. One methylene group was detected in ^1H and ^{13}C-NMR at δ_H 2.15 m and δ_C 27.6, respectively, along with at two methyle groups at δ_H 1.05 d (J = 7.02 Hz; 6H) and at δ_C 8.9 that were characterized by DEPT-135 and HMQC. Strong ^1H–^1H COSY and HMBC correlations of H_3-3'/H-2', H_3-3'/C-2' (J^2), H_3-3'/(C=O)-1' (δ_C 175.1, J^3), and H-3 at δ_H 5.20 s/(C=O)-1' were observed that deduced the localization of isobutanoyl group at C-3 (δ_C 78.6). The NOESY experiment confirmed that **3** has the same absolute configuration of **1** and **2**. Thus, **3** was identified as premyrsinol-3β-isobutyroyl-5α,7β,13β-triacetoyl-17α-nicotinoate (euphosantianane G, **3**).

In addition to these three new premyrsinane diterpenes, euphosantianane E–G (**1**–**3**), four known triterpenes, 9,19-cyclolanostane-3β,24*S*-diol (**4**) [19], 25-methoxycycloartane-3β,24*S*-diol

(**5**) [20], 25-methylenecycloartan-3β,24*R*-diol (**6**), and 25-methylenecycloartan-3β,24*S*-diol (**7**) [21,22], were characterized (Figure 1).

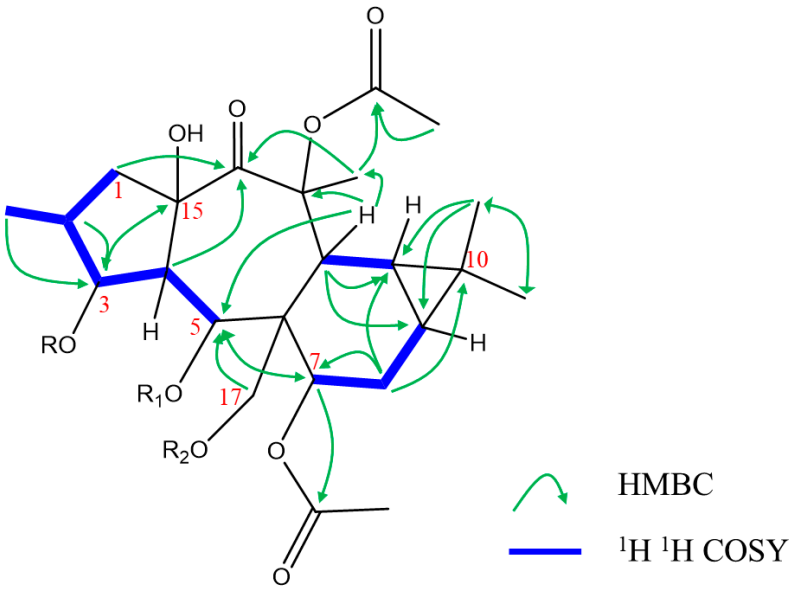


Figure 2. Selected significant ^{1}H ^{1}H COSY, and Key HMBC correlations of **1**–**3**.

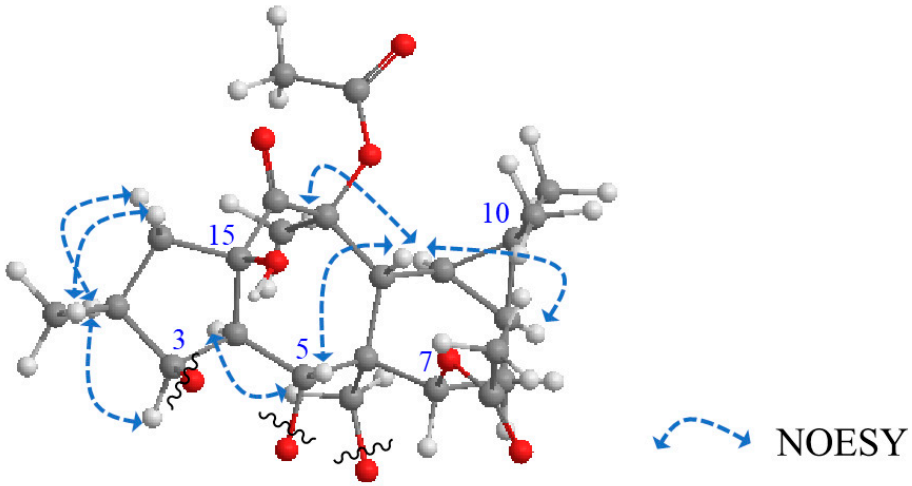


Figure 3. Significant NOESY correlations of **1**–**3**.

Table 1. ^{1}H (600 Hz) and ^{13}C (150 Hz) NMR ($CDCl_3$) of **1**–**3** [a,b].

No.	Euphosantianane E (1)		Euphosantianane F (2)		Euphosantianane G (3)	
	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1*α*	3.15 dd (8.05, 13.86)	42.8, t	2.64 dd (10.85, 14.64)	41.1, t	3.16 dd (8.10, 13.62)	42.8, t
1*β*	1.64 t (13.26)		1.60 m		1.61 m	
2	2.26 qd (1.56, 7.56)	35.1, d	2.31 m	33.8, d	2.25 m	34.0, d
3	5.35 br t (3.48)	78.2, d	5.46 br dd (3.06, 6.12)	78.7, d	5.20 s	78.6, d
4	2.37 dd (3.78, 11.5)	50.1, d	3.01 dd (3.30, 10.50)	50.4, d	2.37 brd (11.6)	50.4, d
5	6.42 d (11.46)	70.5, d	5.79 d (8.80)	68.5, d	6.23 d (11.52)	69.0, d
6	—	47.8, s	—	48.2, s	—	47.7, s
7	4.77 d (6.72)	70.6, d	4.90 d (6.54)	68.8, d	4.68 d (6.54)	70.7, d
8*α*	3.50 br d (6.54)	22.1, t	2.34 d (7.44)	23.2, t	2.32 d (7.14)	22.4, d
8*β*	1.84 t (16.92)		1.72 t (13.92)		1.88 br d (17.40)	
9	0.73 m	18.9, d	0.75 m	19.4, d	0.79 m	19.0, d

Table 1. *Cont.*

10	—	18.4, s	—	19.1, s	—	18.4, s		
11	0.73 m	23.8, d	0.75 m	23.3, d	0.79 m	23.9, d		
12	3.48 s	37.4, d	3.47 br d (6.11)	36.0, d	3.45 br d (3.42)	35.0, d		
13	—	85.7, s	—	79.8, s	—	85.5, s		
14	—	204.1, s	—	210.2, s	—	204.2, s		
15	—	84.2, s	—	83.6, s	—	84.1, s		
16	1.04 s	13.9, q	0.92 d (5.01)	15.2, q	0.77 d (5.04)	14.2, q		
17*α*	4.35 d (11.70)	62.8, t	4.55 d (12.18)	62.6, t	4.49 d (11.82)	64.4, t		
17*β*	4.67 d (11.70)		5.28 d (12.30)		5.86 d (11.94)			
18	0.94 s	29.5, q	1.07 s	28.8, q	1.05 s	29.6, q		
19	1.04 s	14.9, q	0.94 s	15.3, q	0.92 s	14.9, q		
20	1.57 s	25.0, q	1.57 s	23.0, q	1.72 s	24.6, q		
	3-*O*-Prop		**3-*O*-Prop**		**3-*O*-*i*But**			
CO	—	173.5, s	CO	—	172.9	CO	—	175.1, s
2′	2.26 qd (7.62)	27.5, t	2′	2.32 q (7.14)	27.6, t	2′	2.15 m	27.6, d
3′	0.98 t (7.5)	8.8, q	3′	1.15 t (6.66)	8.8, q	3′	1.05 d (7.02)	8.9, q
	5-*O*-3-hydroxy-Bz			**5-*O*-Prop**		4′	1.05 d (7.02)	8.9, q
CO	—	168.9, s	CO	—	170.1, s		**5-*O*-Ac**	
2″	—	129.6, s	2″	2.36 q (7.14)	27.6, t	CO	—	170.1, s
3″	7.39 d (1.56)	111.9, d	3″	0.95 t (7.56)	8.8, q	2″	2.00 s	21.3
4″	—	161.9, s		**7-*O*-Ac**			**7-*O*-Ac**	
5″	6.92 (8.40)	117.9, d	CO	—	175.1, s	CO	—	170.8, s
6″	6.80 t (9.18)	136.1, d	2‴	1.94 s	21.5, q	2‴	2.10 s	21.4
7″	7.58 dd (1.68, 7.98)	119.2, d		**17-*O*-Nic**			**17-*O*-Nic**	
	7-*O*-Ac		CO	—	164.9, s	CO	—	165.7, s
CO	—	170.8, s	2⁗	—	129.7, s	2⁗	—	129.7, s
2‴	2.11 s	21.4, q	3⁗	9.22 s	128.4, d	3⁗	9.15 s	128.3, d
	13-*O*-Ac			8.30 d (7.44)	137.4, d	4⁗	8.21 d (7.50)	137.1, d
CO	—	170.8, s		7.37 m	123.9, d	5⁗	7.48 m	123.9, d
2⁗	2.11 s	21.4, q		7.67 d (7.74)	153.7, d	6⁗	7.68 d (7.44)	150.4, d
	17-*O*-Ac		4⁗					
CO	—	170.0, s	5⁗					
2⁗′	2.12 s	20.8, q	6⁗					

[a] Coupling constant [*J*] in Hz are given in parentheses, [b] s, quaternary, d, methine, t, methylene, q, methyl.

2.2. Study of Chemosystematic Significance

Euphorbia is one of the most diverse and very large genera among flowering plants. It has a worldwide distribution, and it is found as herbs, shrubs or trees. It is characterized by the presence of milky latex. More than 2000 species are distributed at cosmopolitan, but especially tropical, subtropical, and warm-temperate regions [23]. *Euphorbia* is represented by 36 species in the flora of Egypt. Three of these *Euphorbia* are endemic to Egypt, namely, *E. bivonae* Steud., *E. punctata* Delile, and *E. sanctae-catharinae* Fayed (synonym of *Euphorbia obovata* Decne).

In our previous work on the chemical composition of the endemic *E. sanctae-catharinae* of Egypt, nine premyrsinanes diterpenes and three flavonoids were isolated and identified from *E. sanctae-catharina*. Moreover, in the present study, four cycloartane triterpenes and three new myrsinol compounds were identified for the first time from the endemic *E. sanctae-catharinae*.

In order to correlate the chemical composition of this endemic species to Egypt with other *Euphorbia* species, agglomerative hierarchical clustering (AHC) analysis was performed. Based on diterpenoid chemical composition from 32 *Euphorbia* species in addition to *E. sanctae-catharinae*, the AHC analysis revealed these plants categorized into nine groups (Figure 4). The largest group comprised ten *Euphorbia* species (*E. amygdaloides*, *E. bungei*, *E. characias*, *E. dendroides*, *E. esula*, *E. formosana*, *E. helioscopia*, *E. peplus*, *E. sororia*, and *E. tuckeyana*). These species showed a close correlation to each other due to the presence of jatrophane diterpenoid compounds. These species mainly contained jatrophane

terpenoids, where amygdaloidins A–L were reported in *E. amygdaloides* [24]. Helioscopinolides A, B, and C were reported in *E. formosana* [25], while euphocharacins A–L were isolated from *E. characias* [26]. The jatrophane diterpenoids euphodendrophanes A–P, abeodendroidin, and epiabeodendroidin F were isolated from *E. dendroides* [27–29], while esulatin A–M, esulone A, and esulone B were isolated from *E. esula* [30].

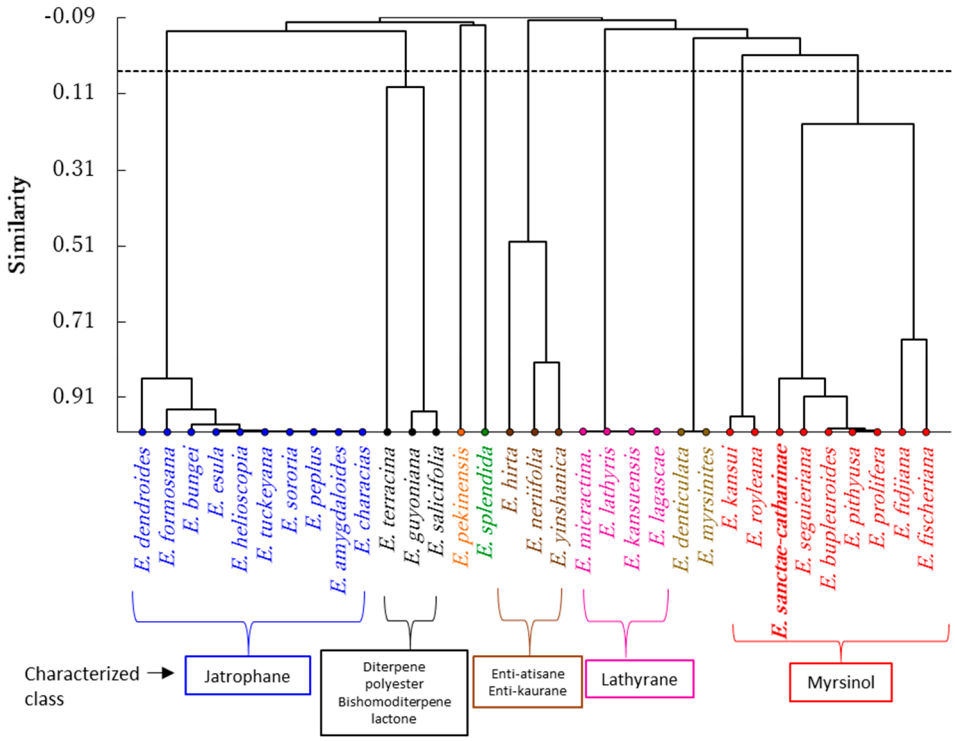


Figure 4. Agglomerative hierarchical clustering (AHC) of 32 *Euphorbia* species and the present studied endemic *Euphorbia* (*E. sanctae-catharinae*) based on the terpenoid compounds.

Corea et al. [31] identified several types of jatrophane compounds in *E. peplus*, such as pepluanin A, B, and C, euphopeplin A, 2α,5α,7β,8α,9α, 14β-hexaacetoxy-3β-benzoyloxy-15-hydroxyjatropha-6(17), 11*E*-diene, and 5α,8α,9β,10β, 14α-pentaacetoxy-3β-benzoy-loxy-15-hydroxypepluane. However, *E. helioscopia* was reported as a rich plant with jatrophane diterpenes, where it contained euphohelin A–E, euphoheliosnoids A–C, and helioscopianoids A–Q [32–34]. Sororianolide A–C were identified from *E. sororia* [35], while tuckeyanol A and B and euphotuckeyanol were isolated from *E. tuckeyana* [36].

Therefore, the predominance of jatrophane compounds in theses *Euphorbia* species reflected the similarity of the chemistry of these species and led to a clustering of them together in one group of the AHC (Figure 4). Nevertheless, different diterpenoid classes such as lathyrane, *enti*-atisane, ingole, and bishomoditerpene lactone were also isolated from some of these species [24,34].

On the other hand, *E. kansuensis*, *E. lagascae*, *E. lathyris*, and *E. micractina* were closely related to each other and grouped together (Figure 4). This group was characterized by lathyrane-type diterpenoids, where *E. lagascae* has been reported to possess latilagascene A–F and jolkinol B [37]. While euphorbia factor L_8, euphorbia factor L_{7a} and $_{7b}$, euphorbia factor L_3, jolkinol B, isolathyrol, 7-hydroxylathyrol, and lathyrol were isolated from *E. lathyris* [38,39].

Another group comprised *E. hirta*, *E. neriifolia*, and *E. yinshanica* and was characterized by the presence of *enti*-atisane and *enti*-kaurane diterpenoids [40–42]. *Euphorbia guyoniana*, *E. salicifolia*, and *E. terracina* represented another group, and these plants are characterized by the presence of diterpene polyester and bishomoditerpene lactone. Terracinolide A and B were identefied in *E. terracina* [43], guyonianin C–F were isolated from *E. guyoniana* [44,45], and euphosalicin 1–3 as well as salicinolide were idenfied in *E. salicifolia* [46].

Our studied endemic species, *E. sanctae-catharinae*, was grouped with *E. bupleuroides*, *E. fidjiana*, *E. fischeriana*, *E. pithyusa* subsp. *cupanii*, *E. prolifera*, and *E. seguieriana*. However, the Pearson correlation coefficient analysis revealed that *E. sanctae-catharinae* showed a close correlation to *E. bupleuroides* (0.888), followed by *E. prolifera* (0.880), then *E. pithyusa* subsp. *cupanii* (0.870) based on the composition of the terpenoid composition (Figure 4). Myrsinol diterpenoids were the main constituents of these *Euphorbia* species [9,47–49], while other diterpenoid compounds such as abietane, *ent*-kaurane, *ent*-atisane, and lathyrane types as well as cycloartane triterpene were also identified in these plants [6,50]. Hegazy et al. [9] identified several myrsinol compounds form *E. sanctae-catharinae*, such as euphosantianane A–D. In addition, the present study revealed the presence of an additional three new myrsinol compounds (euphosantianane E–G). However, *E. prolifera* was richer in the myrsinol diterpenoids where it comprises numerous compounds including for examples, proliferin A–D, euphorprolitherin B and D, euphorbiaproliferin A–I, and euphorbialoid [17,47–49,51,52].

Euphorbia pithyusa subsp. *cupanii* was reported to have myrsinol compounds [18], while Jeske et al. [50] stated that *E. seguieriana* contained 12 myrsinol compounds. Therefore, the results exhibited that our studied endemic species (*E. sanctae-catharinae*) was grouped with theses *Euphorbia* species due to the predominance of myrsinol diterpenes. Nevertheless, the present phytochemical study showed the presence of four cycloartane triterpenes (25-methylenecycloartan-3β,24*R*-diol, 9,19-cyclolanostane-3β,24*S*-diol, and 25-methylenecycloartan-3β,24*S*-diol,) which was already reported from some *Euphorbia* species like, *E myrsinites* [53], *E. denticulate* [54], and *E. spinidens* [55].

On the other hand, cycloartane triterpenes were identified in both *E. denticulate* and *E. myrsinites*, and thus grouped together. However, *E. kansui* and *E. royleana* were similar to each other, chacterized by ingole compounds [56–58], while either *E. pekinensis* or *E. splendida* showed dissimilarity with all tested *Euphorbia* species.

From previously reported flavonoids from *Euphorbia* species, flavonoid and their glycosides were isolated and identified from some of these plants, such as *E. condylocarpa*, *E. virgata*, *E. chamaesyce*, *E. hirta*, and *E. magalanta* [59–62], in addition to *E. sanctae-catharinae* [9]. For example, quercetin-3-*O*-*α*-rhamnopyranoside and kaempferol-3-*O*-rhamnoside were isolated from *E. condylocarpa* collected from Iraq [60], and this is in total agreement with the isolated compound from *E. sanctae-catharinae*.

3. Conclusions

From the Egyptian endemic plant, *E. sanctae-catharinae*, three new premyrsinanes, euphosantianane E–G (**1**–**3**), alongside the known triterpenes (**4**–**7**), were characterized using modern spectroscopic tools. For first time, the chemotaxonomic significance of isolated compounds from *E. sanctae-catharinae* especially diterpenes compared to those documented from different *Euphorbia* ecospecies was also studied, and it was found to be closely correlated to *E. bupleuroides*, *E. prolifera*, and *E. pithyusa* subsp. *cupanii* based on the composition of the terpenoid compound classes.

4. Materials and Methods

4.1. General Experimental Procedures

As described in our previously reported protocol by Hegazy et al. [9].

4.2. Plant Material

The aerial parts of *E. sanctae-catharinae* were collected from Wadi Jibaal, Protectorate of Saint Katherine, South Sinai, Egypt during the flowering stage in April 2016 under the permission of the Protectorate for scientific purposes. A voucher specimen (#16-212) has been deposited in the herbarium of the National Research Centre. The authentication of the plant was kindly performed by Prof. Mona Marzouk, Professor of Taxonomy, NRC, Cairo, Egypt.

4.3. Extraction and Isolation

Air dried aerial parts (one kg) were ground, and extracted with CH_2Cl_2:MeOH (1:1) at room temperature, filtered and then concentrated under vacuum afforded black gum (63 g). The extract was then subjected to silica gel flash column chromatography (5 × 60 cm) and eluted with n-hexane/EtOAc step gradient. Eight main fractions (ES-1:ES-8) were obtained after thin layer chromatography (TLC, Kieselgel 60 F254, 0.25 mm, Merck, Darmstadt, Germany) examinations of similar ones. Fraction ES-4 (724 mg), subjected to further fractionation via reversed phas ODS column (3×60 cm) with MeOH: H_2O 4:1, afforded 3 main subfractions (ES-4A–C) after TLC examinations. Subfraction ES-4B, eluted by MeOH:H_2O (4:1) by a reversed phase HPLC (20 × 250 cm), afforded compounds **1** (2.8 mg), **3** (3.2 mg), **6** (14.6 mg), and **7** (12.9 mg). Moreover, subfraction ES-5 (564 mg) was further fractionated over ODS column (3 × 60 cm) with MeOH: H_2O 7:3 that afforded 2 main subfractions (ES-5A,B). Subfraction ES-5B was eluted by MeOH:H_2O (85:15) over a reversed phase HPLC (20 × 250 cm) and afforded compounds **2** (3.4 mg), **4** (15.1 mg), and **5** (7.8 mg).

*4.4. Spectroscopic Data of Euphosantianane E–G (**1**–**3**)*

Euphosantianane E (premyrsinol-3β-propanoyl-5α-(3-hydroxy)-benzoyl-7β,13β,17α-triacetate, **1**): colorless oil; $[\alpha]_D^{25}$ +18.0 (c 0.01, MeOH); FT-IR (KBr): 3380, 1732, 1462 and 728 cm^{-1}; ^1H and ^{13}C-NMR spectral data, see Table 1 and Supplementary Materials (S1–S9); HRFABMS: *m/z* 709.2930 $(M + Na)^+$; $C_{36}H_{46}O_{13}$ (cal. 686.2938).

Euphosantianane F (premyrsinol-3β,5α-dipropanoyl-7β,13β-diacetyl-17α-nicotinoate, **2**): colorless oil; $[\alpha]_D^{25}$ + 24.4 (c 0.01, MeOH); FT-IR (KBr): 3441, 1736, 1434 and 741 cm^{-1}; ^1H and ^{13}C-NMR spectral data, see Table 1 and Supplementary Materials (S10–S17); HRFABMS: *m/z* 685.3089 (M), $C_{36}H_{47}NO_{12}$ (cal. 685.3098).

Euphosantianane G (premyrsinol-3β-isobutyroyl-5α,7β,13β-triacetoyl-17α-nicotinoate, **3**): colorless oil; $[\alpha]_D^{25}$ + 53.2 (c 0.01, MeOH); FT-IR (KBr): 3430, 1728, 1458 and 716 cm^{-1} ^1H and ^{13}C-NMR spectral data, see Table 1 and Supplementary Materials (S18–S25); HRFABMS: *m/z* 708.3090 $(M + Na)^+$, $C_{36}H_{47}NO_{12}$ (cal. 685.3098).

4.5. Statistical Analysis

A data matrix of 15 terpene classes from 33 *Euphorbia* species was subjected to agglomerative hierarchical clustering (AHC). This matrix was designed based on the numbers of the identified terpenoid compounds from 32 *Euphorbia* species (collected from the literature review) as well as that identified in the present study from the endemic species to Egypt (*E. sanctae-catharinae*). This analysis was performed by XLSTAT statistical computer software package, version 2018 (Addinsoft, New York, NY, USA).

Supplementary Materials: The Supplementary Materials are available online.

Author Contributions: A.I.E., T.A.M., and M.-E.F.H. contributed to the extraction, isolation, purification, identification, and manuscript preparation. A.M.A.-E. contributed to the evaluation of chemotaxonomic significance. A.M.A., A.A.S., S.L.A.-R., and B.A.D. contributed to guiding experiments, and manuscript preparations. M.-E.F.H. was the group leader, organizing and guiding the experiments, structure elucidation, and manuscript writing. All authors discussed the results, commented on the paper, and approved the final manuscript.

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Sample Availability: Samples of the compounds **1–7** are available or not from the authors.