SUPPORTING INFORMATION

Synthesis and Antioxidant Evaluation of Lipophilic Oleuropein Aglycone Derivatives.

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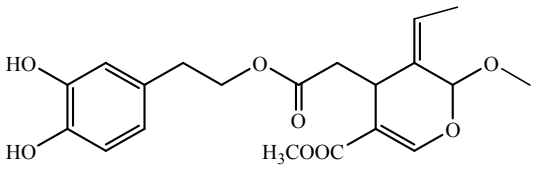
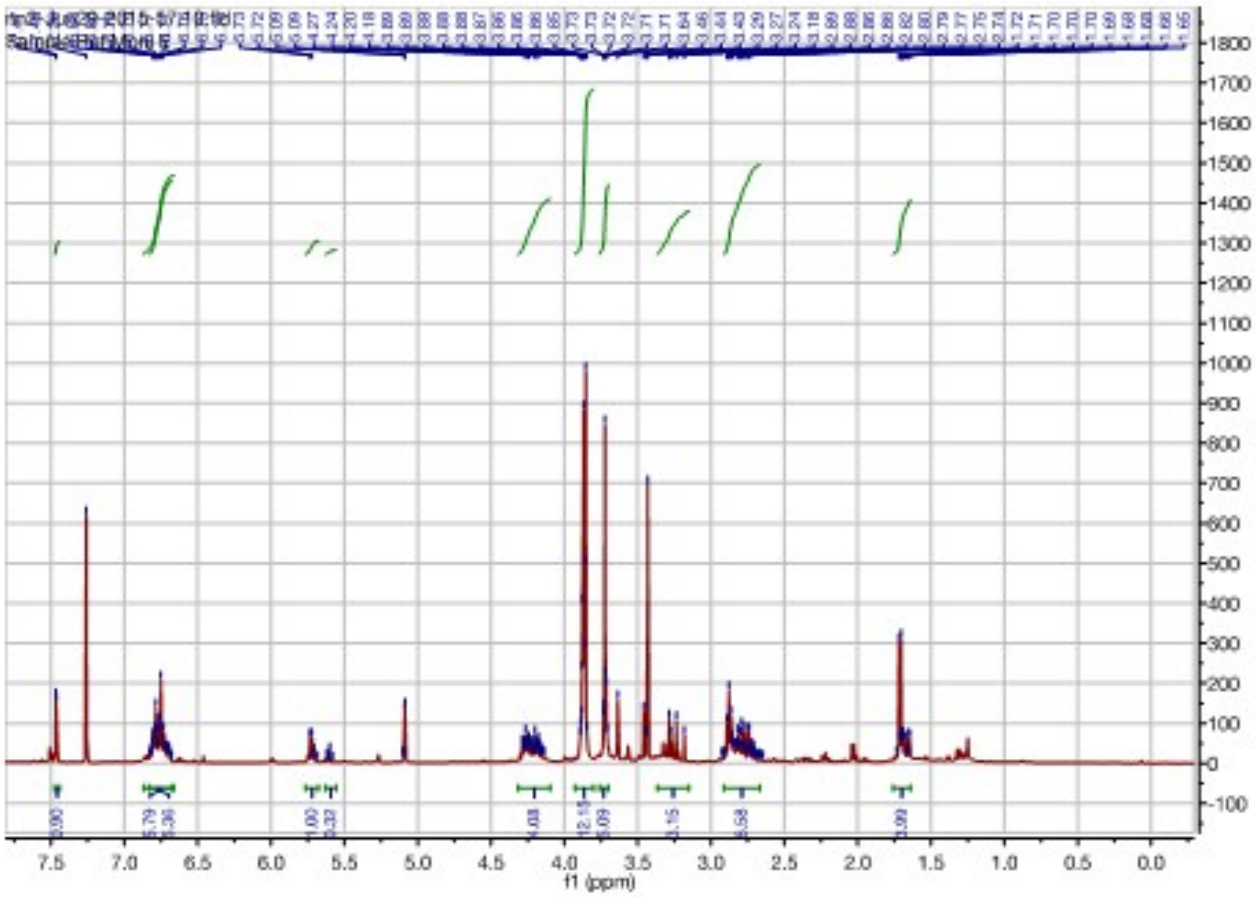
Table S1. Synthesis of Oleuropein Aglicone derivatives with 10% $Er(OTf)_3$ by Oleuropein

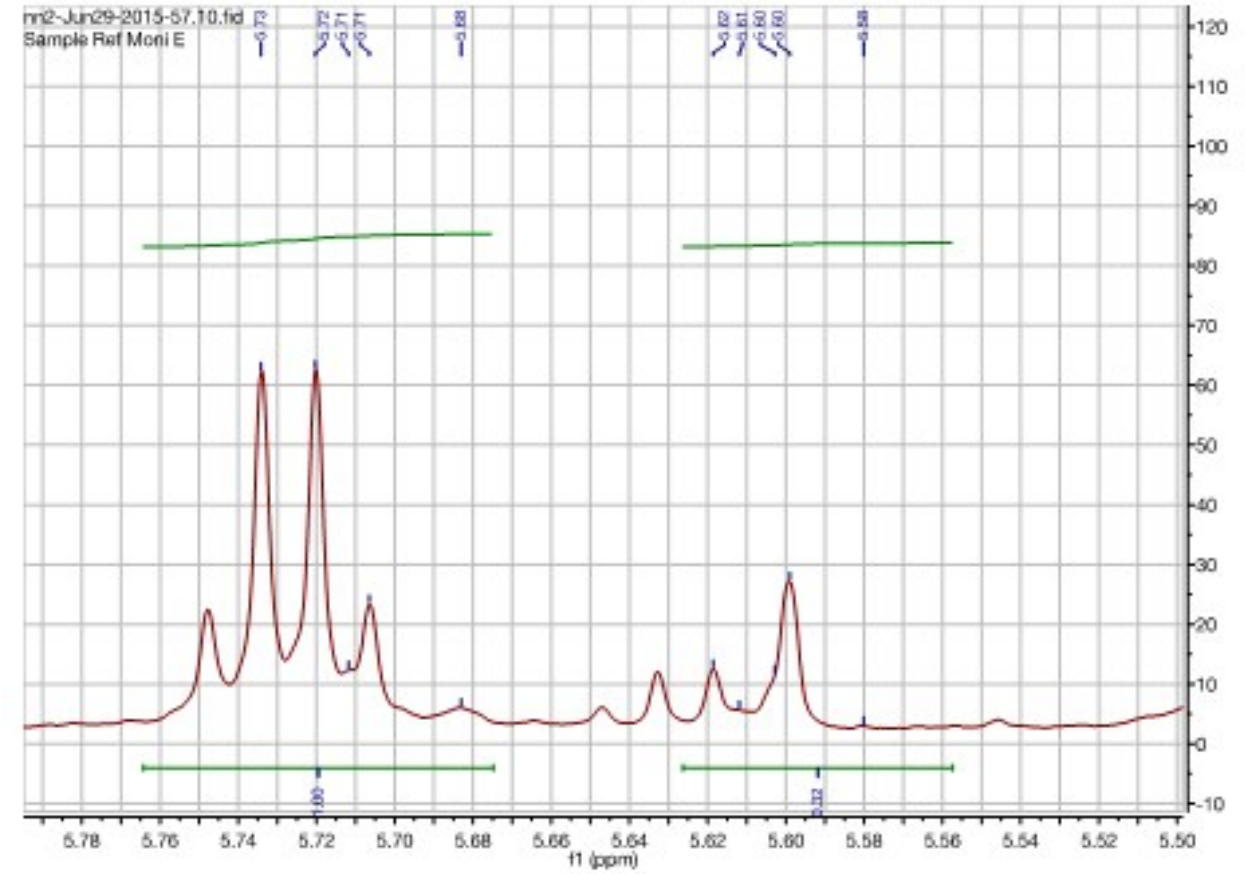
Entry	ROH	Time	Yield % [a]
1[b]	MeOH	1 h 30’	80
2[b]	EtOH	1 h 30’	80
3[c]	PhOH	4 h	78
4[c]	*trans*-Hexen-2-ol	4 h	75
5[c]	*cis*-Hexen-2-ol	4 h	80
6[c]	Octanyl alcohol	4 h	72
7[c]	Palmityl alcohol	4 h	60
8[c]	Oleyl alcohol	4 h	70

[a] Determinated by HPLC; [b] Oleuropein (0,92 mmol) was dissolved in MeOt/EtOH (4 mL) in the presence of $Er(OTf)_3$ (0.046 mmol) and refluxed at 80° C for 1h 30’.[c] Oleuropein (0,92 mmol) was dissolved in acetonitrile (4 mL) in the presence of $Er(OTf)_3$ (0.046 mmol) and the alcohol (1,104 mmol) refluxed at 80° C for 4h.



Methyl Oleuropein Aglicone (3)

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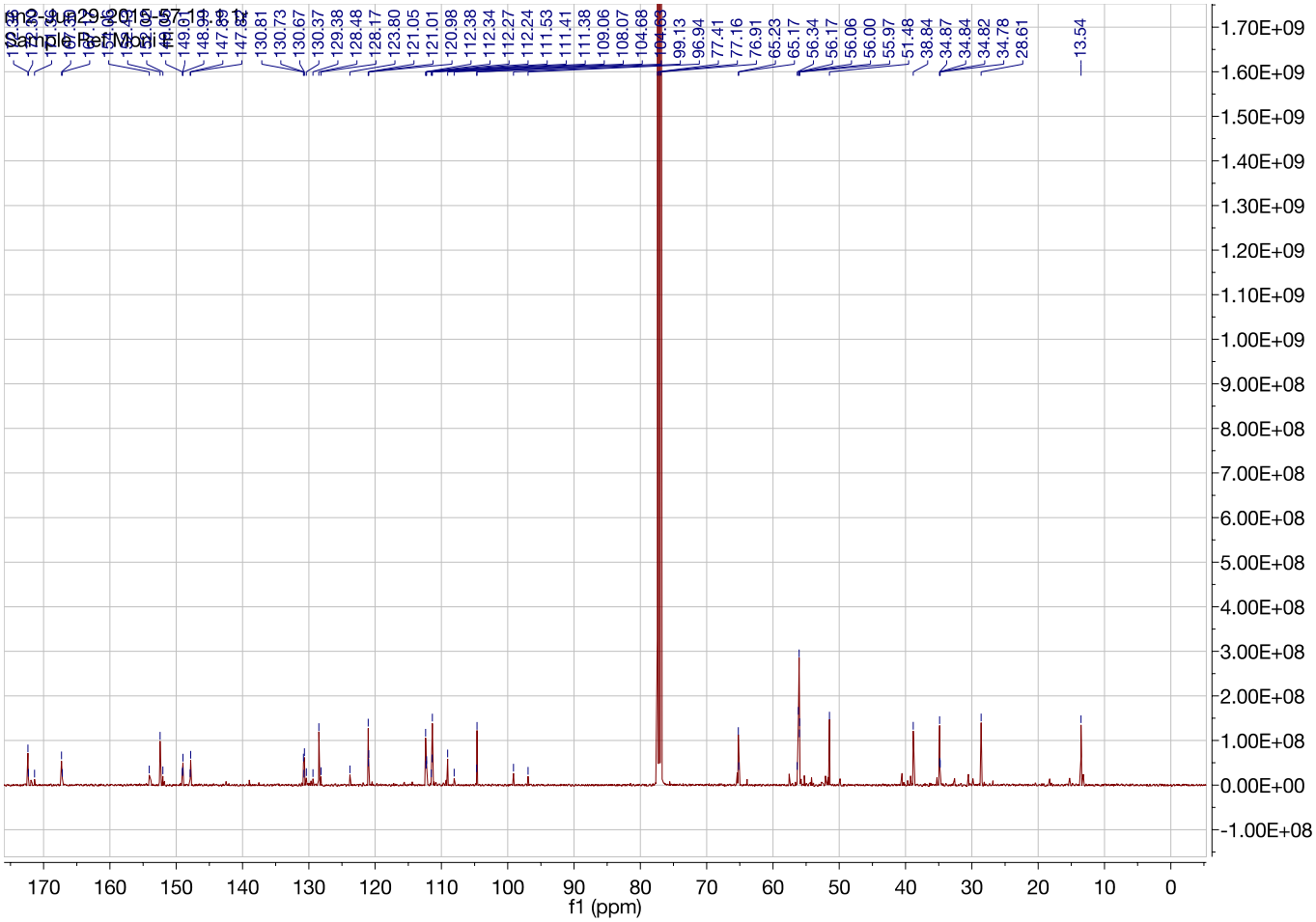
Sample Ref Moni E
f1 (ppm)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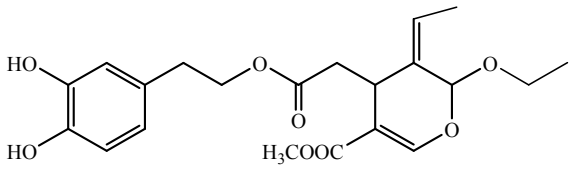
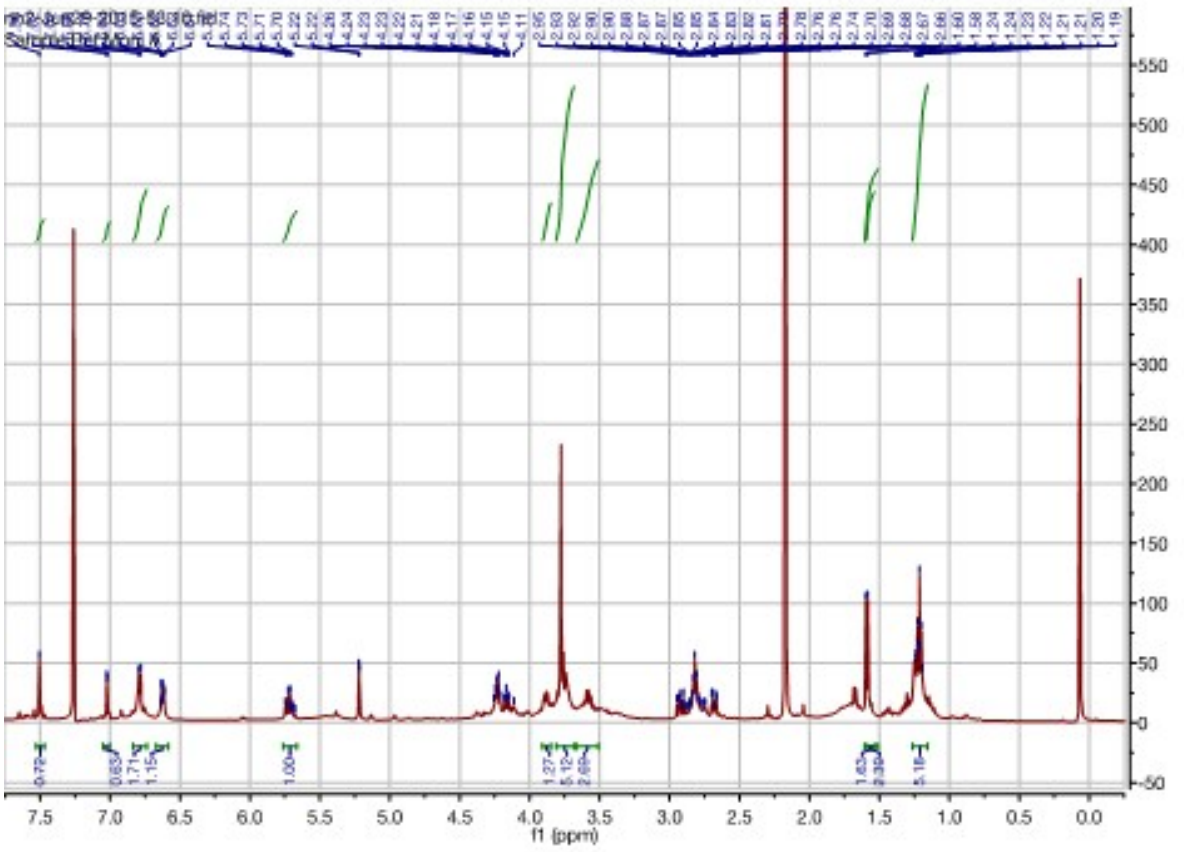
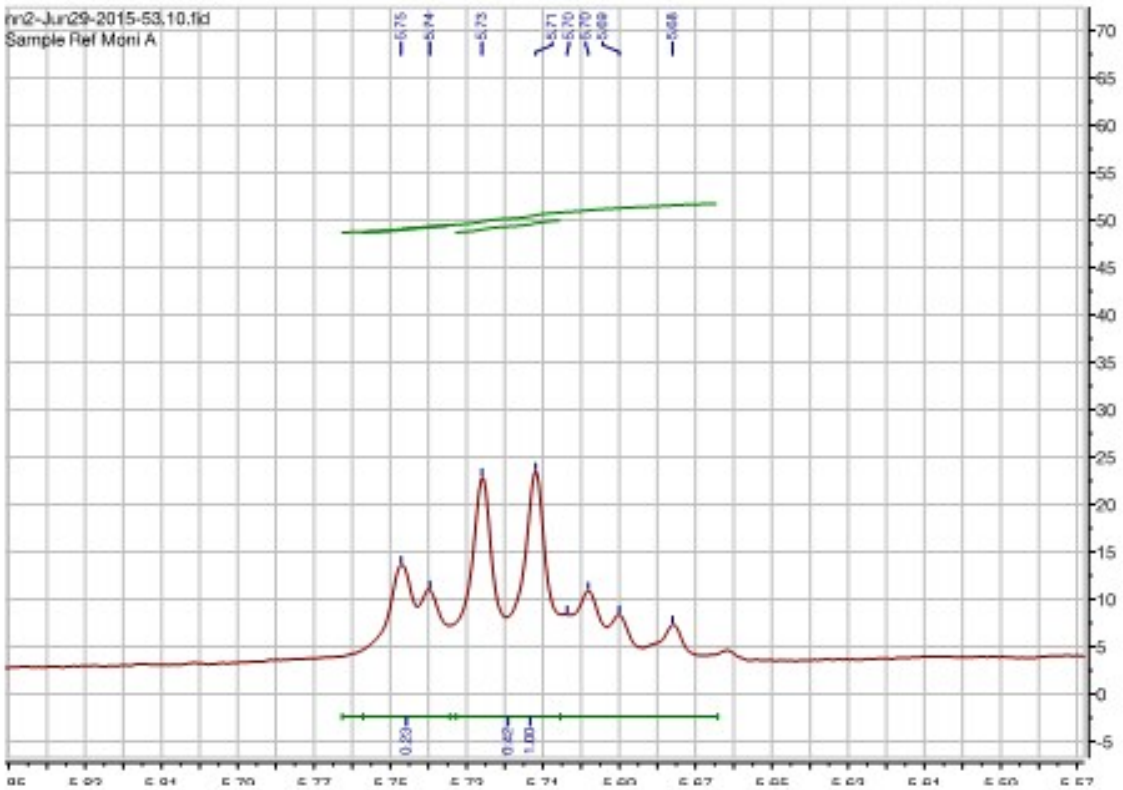


Ethyl Oleuropein Aglicone (4)

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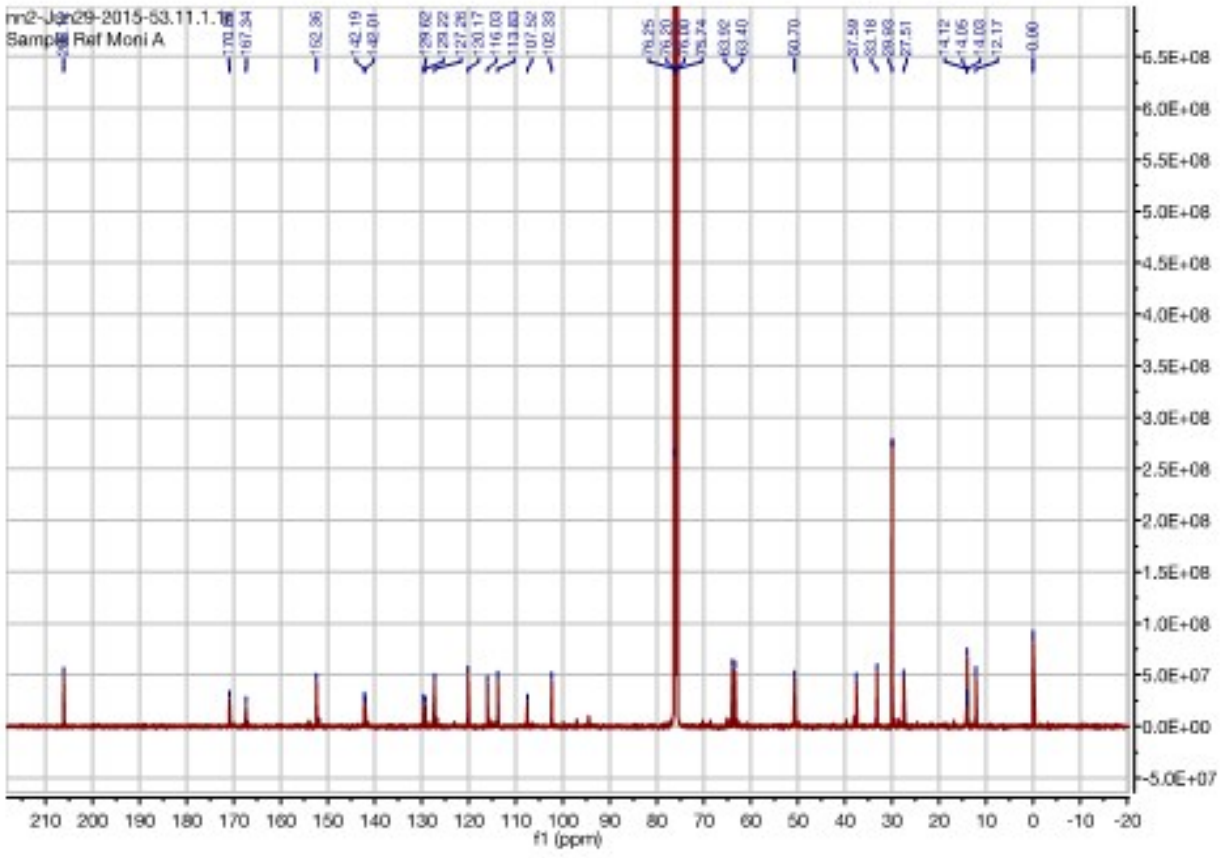
5.74
5.73
5.71
5.70
5.70
5.69
5.68
0.23
0.42
1.00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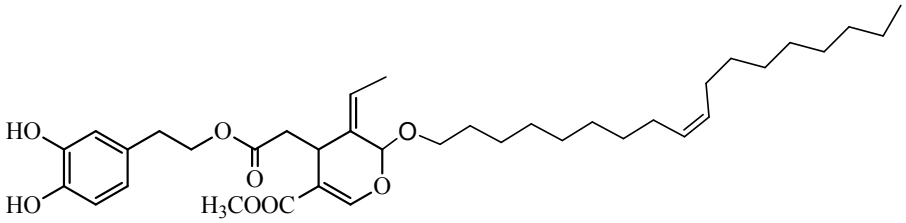
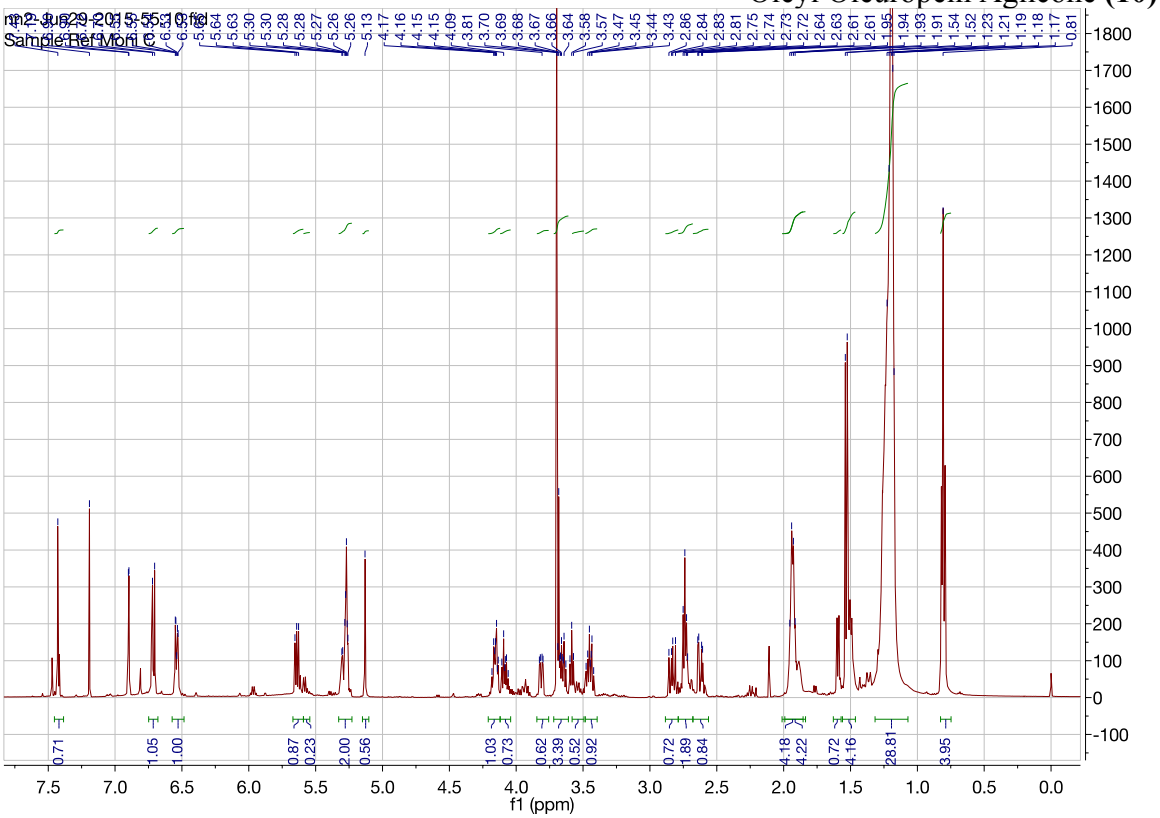
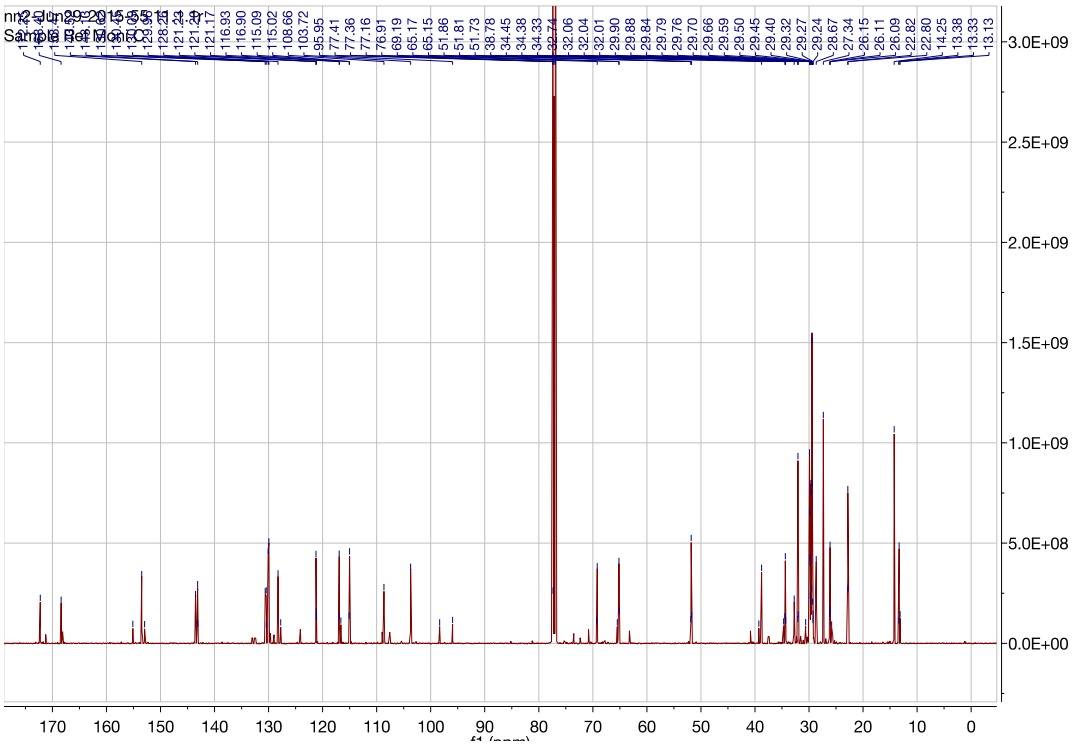
167.34
152.86
142.19
140.04
129.62
129.22
127.26
120.17
116.03
113.83
107.52
102.33
76.25
76.20
76.00
75.74
63.92
63.40
60.70
37.59
33.18
28.93
27.51
14.12
14.05
14.03
12.17
0.00
f1 (ppm)



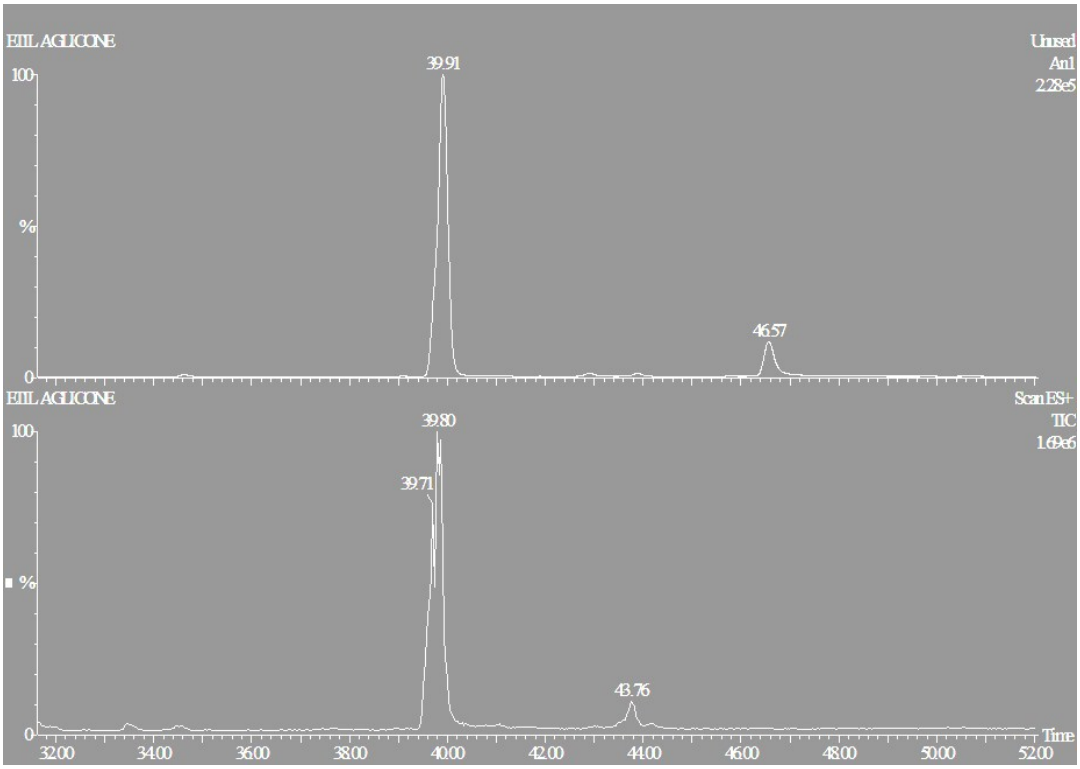
Oleyl Oleuropein Aglicone **(10)**



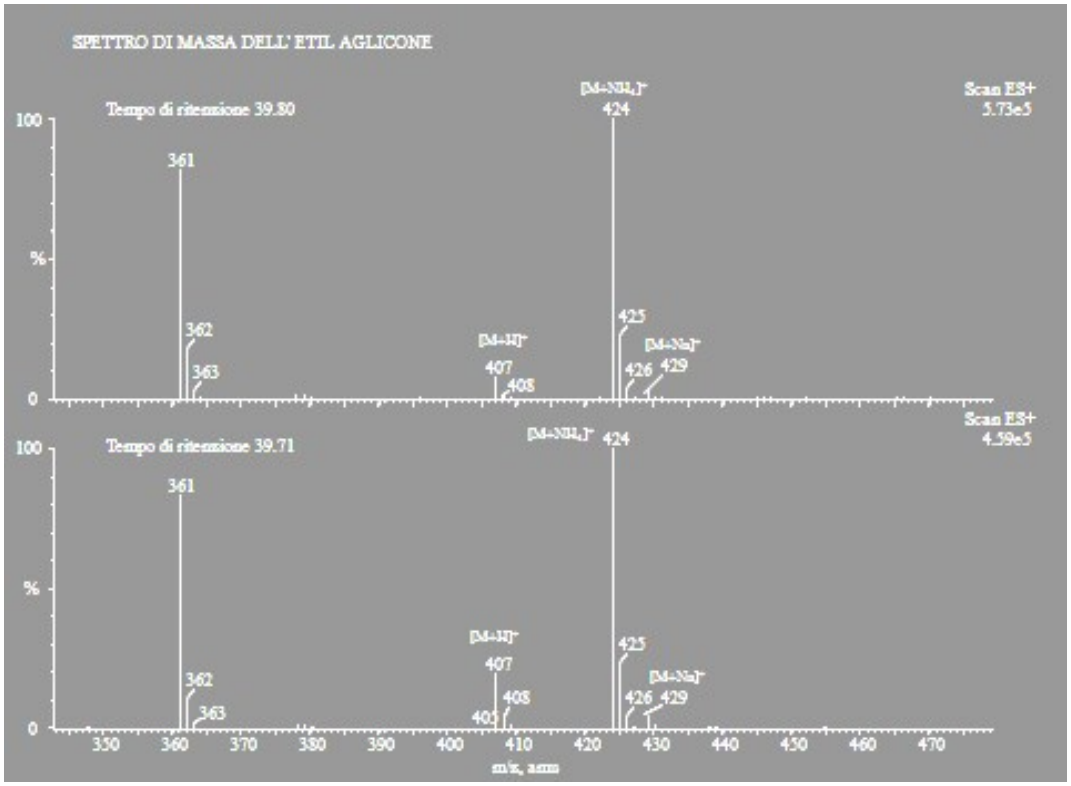


LC-MS spectrum of Ethyl Oleuropein Aglicone (4) : LC/UV/MS (A). ESI - MS spectra (B).

A



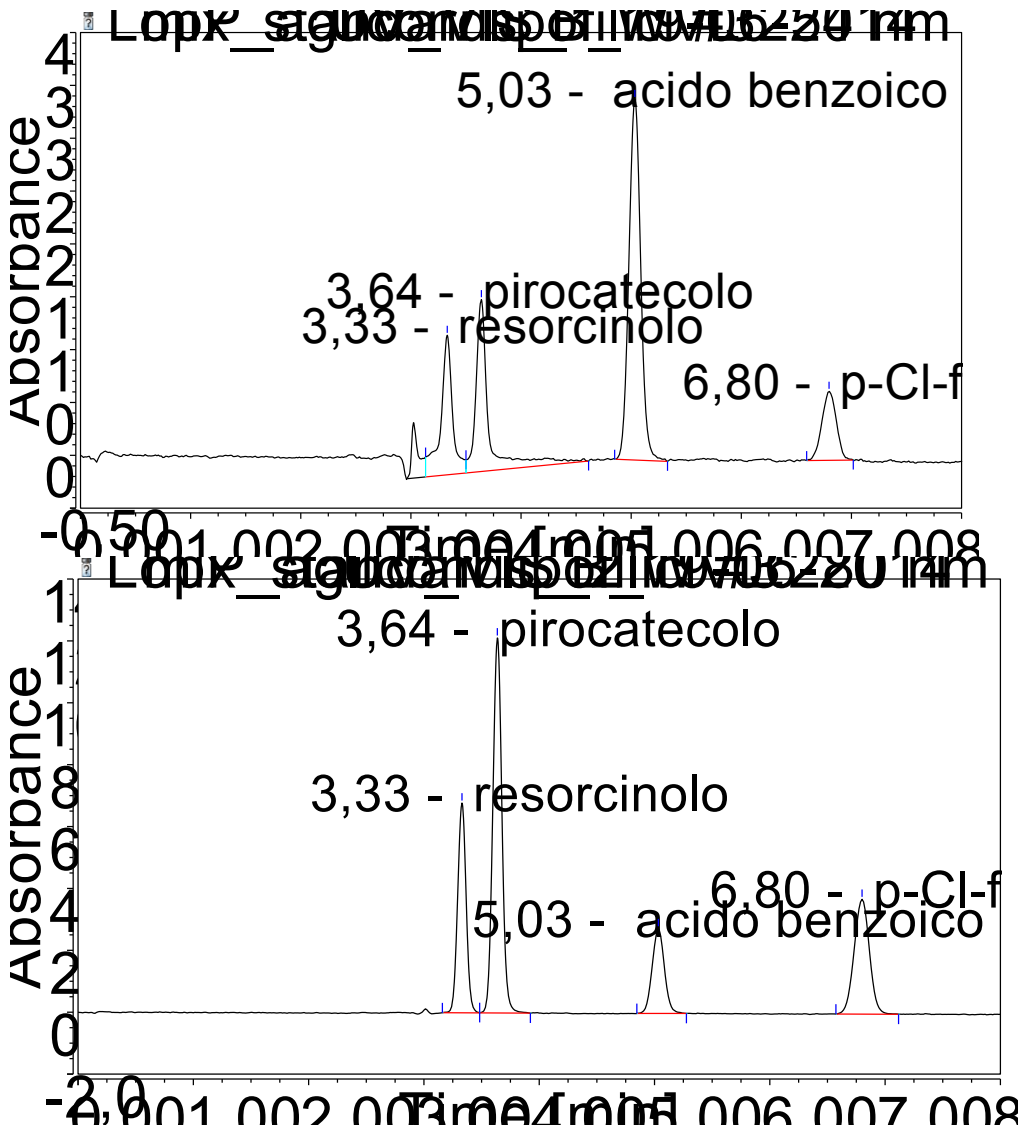
B



Determination of LogK$_{ow}$

To calibrate the RP-HPLC system, a suite of four well-defined organic compounds with known Log P has been used as standards. All of the standard substances are 99% grade and were obtained from Aldrich. Stock solutions containing 10 µg/ml of a single compound were prepared by dissolving them in mobile phase solution (40% water/CF_3COOH, PH= 2.4, 60% methanol). Multiple injections of single standards were performed to define the individual retention times and their reproducibility as well as stability of these selected compounds. Figure S1 shows the chromatograms registered to both wavelengths of 254 and 280 nm.

Figure S1. Chromatograms registered to both wavelengths of 254 and 280 nm



Capacity factor k′ was calculated for each compound according to equation showed in literature.[3] Table S1 gives the Log P values of standard compounds, their retention time and their capacity factors.

Table S2. Log P values of standard compounds

STANDARD	R.T.	T_0	k'	logk'	logKow
Resorcinol	3,330	3,013	0,105210753	-0,977939869	0,59
Pyrocathecol	3,637	3,013	0,207102556	-0,683814542	1,21
Benzoic acid	5,033	3,013	0,670428145	-0,173647762	1,94
p-Cl Phenol	6,797	3,013	1,255891138	0,098951996	2,39

Dead-time t_0 was determined from the chromatogram obtained on mobile phase at the beginning of each sequence of analysis and has been defined as the time of the negative peak maximum.

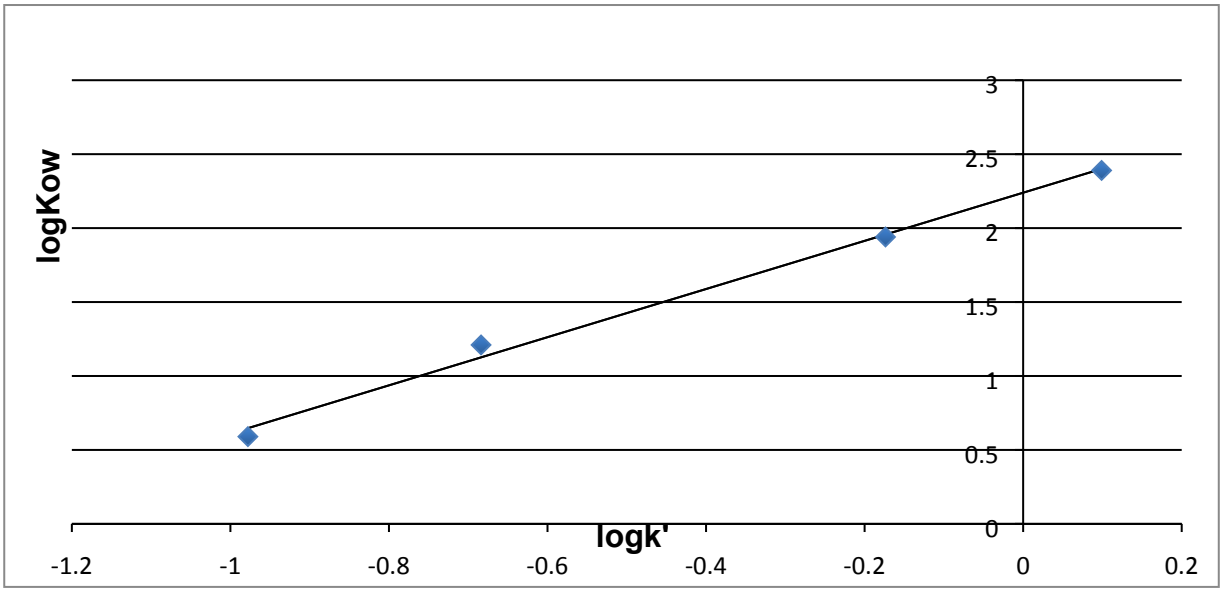
Log k′ were correlated with Log K_{ow} known values through a linear regression analysis[38] to obtain a "correlation curve" of the form

$$log\ K_{ow} = a\ logk^{'} + b$$

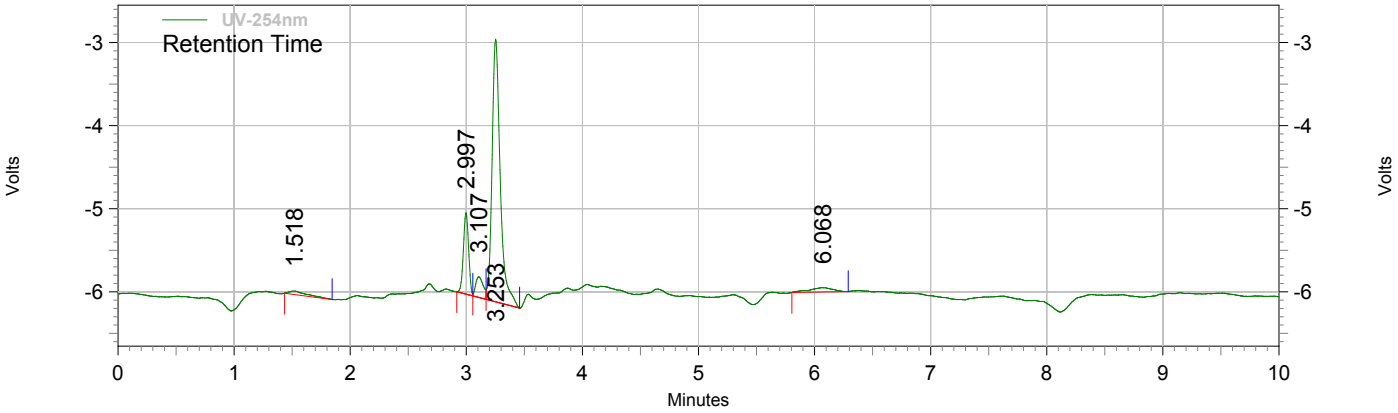
with a slope (a) of 1.628 and a regression coefficient of 0.994 (Figure S1)

Solutions containing 10 µg/ml of each unknown substances were prepared dissolving each 3,4-DHPEA-EA derivatives in the mobile phase. Three injections of each compound were performed to find the correct retention time. Capacity coefficient k′ of each derivative was calculated as for the known compounds. Log K_{ow} of each oleuropein derivative was finally found by correlation with Log k′ through the same linear regression determined before.

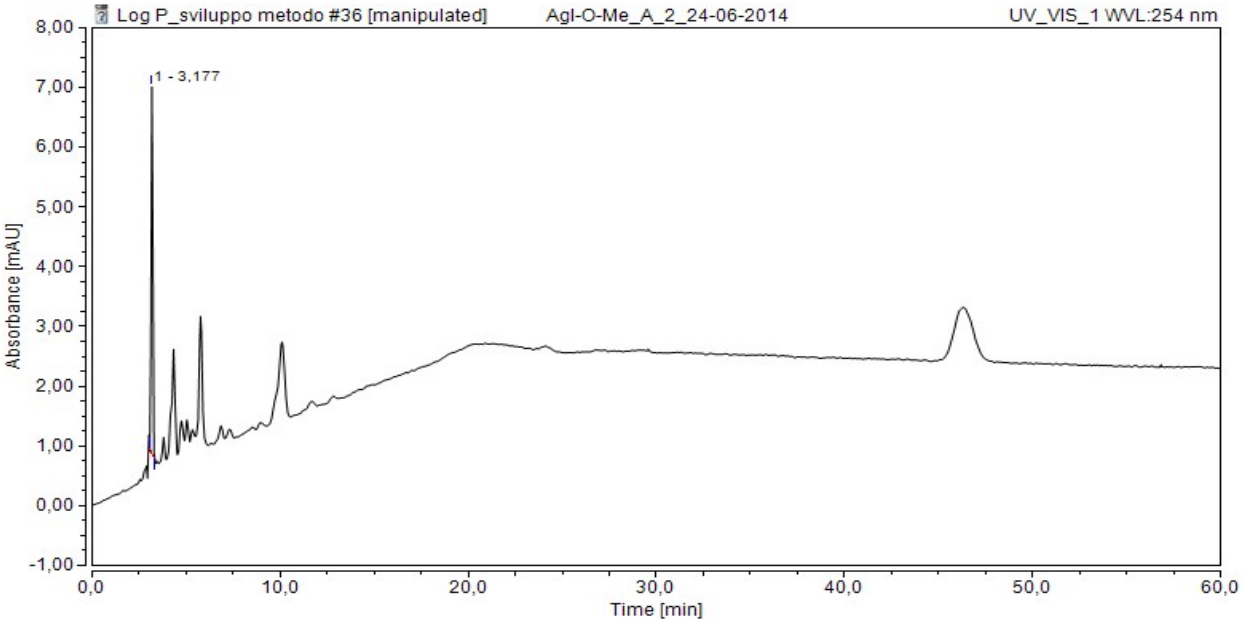
Figure S2. Linear Plot Log k′ correlated with Log K_{ow}



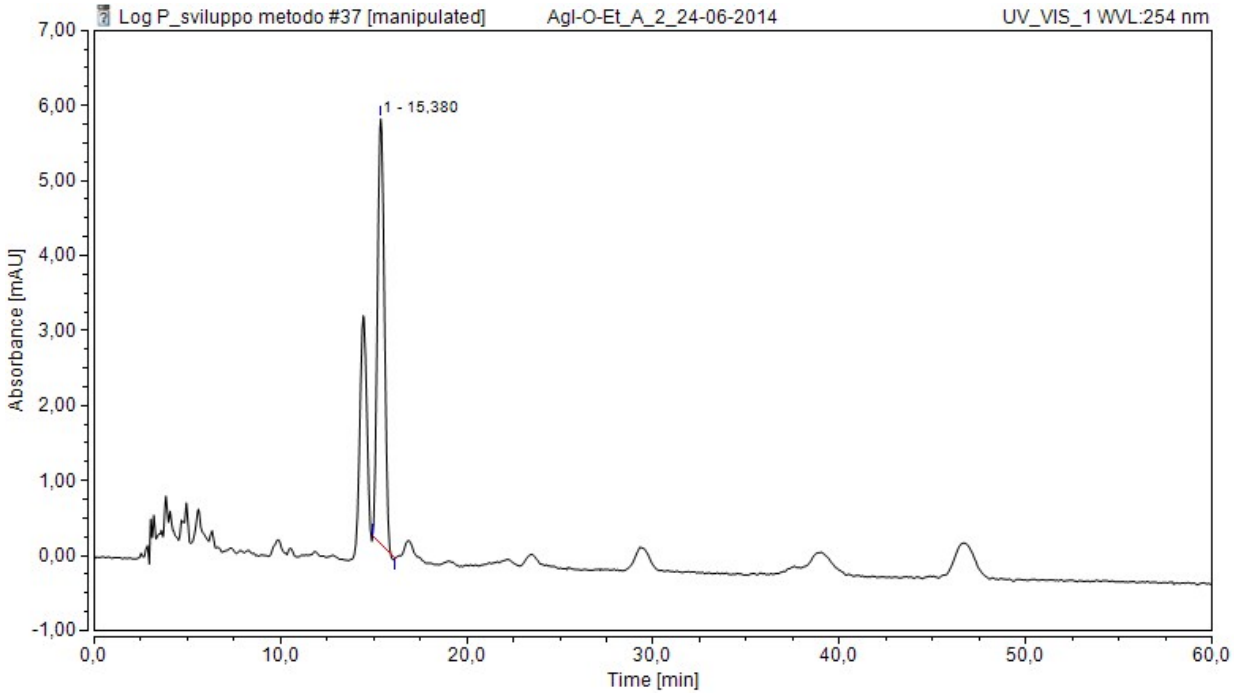
HPLC Chromatogram of Oleuropein Aglicone (2)



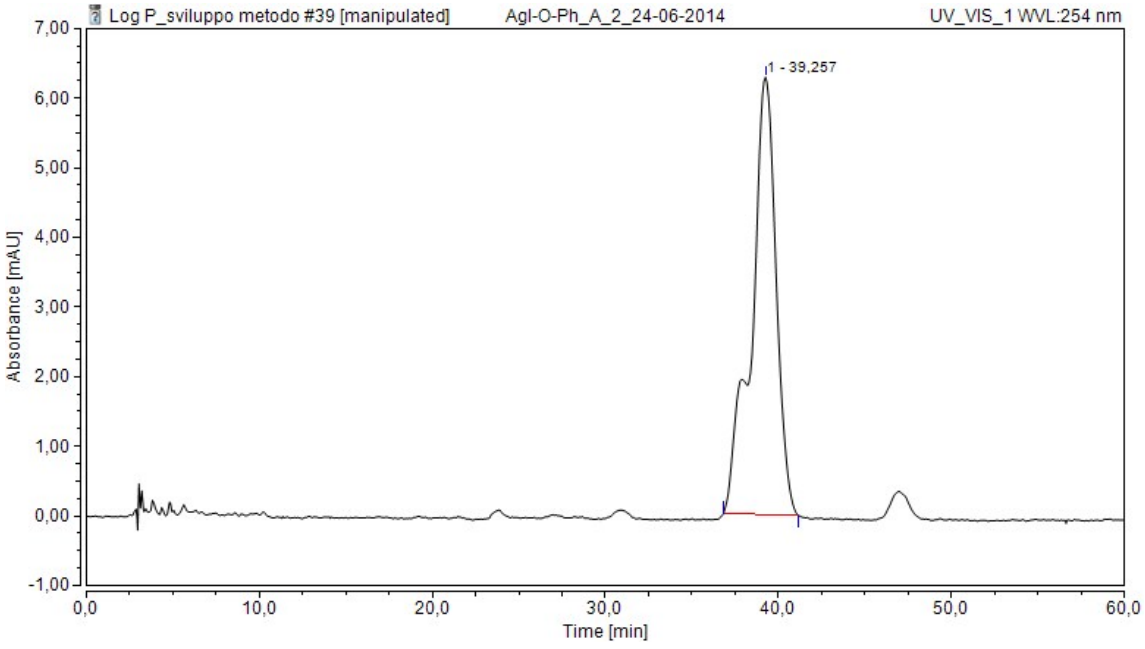
HPLC Chromatogram of Methyl Oleuropein Aglicone (3)



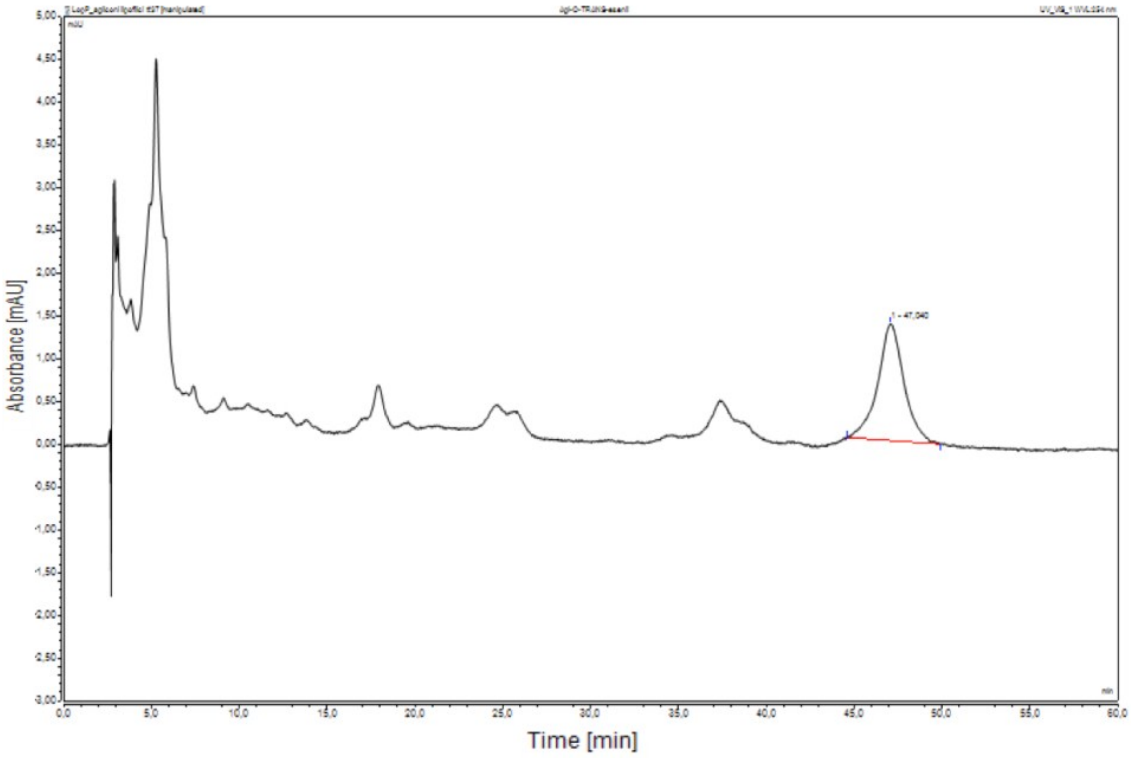
HPLC Chromatogram of Ethyl Oleuropein Aglicone (4)



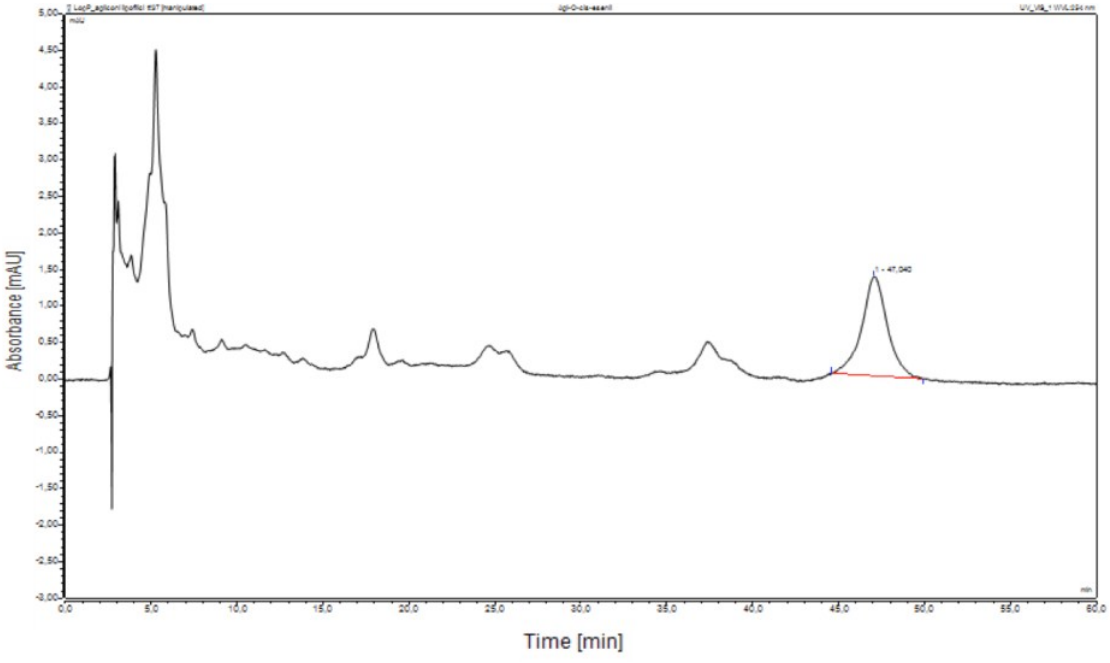
HPLC Chromatogram of Phenyl Oleuropein Aglicone (5)



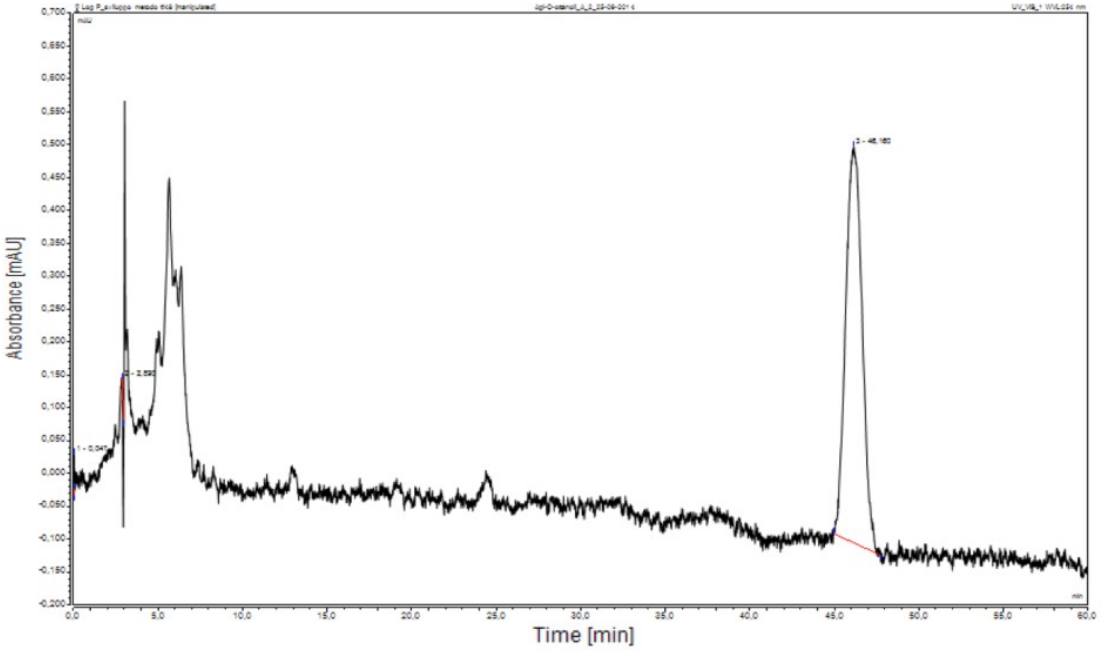
HPLC Chromatogram of trans-Hexenyl Oleuropein Aglicone (6)



HPLC Chromatogram of cis-Esenyl Oleuropein Aglicone (7)



HPLC Chromatogram of Octyl Oleuropein Aglicone (9)



Measurement of oxygen radical absorbance capacity ($ORAC_{FL}$)

Fig.S3 FL fluorescence decay curve induced by AAPH

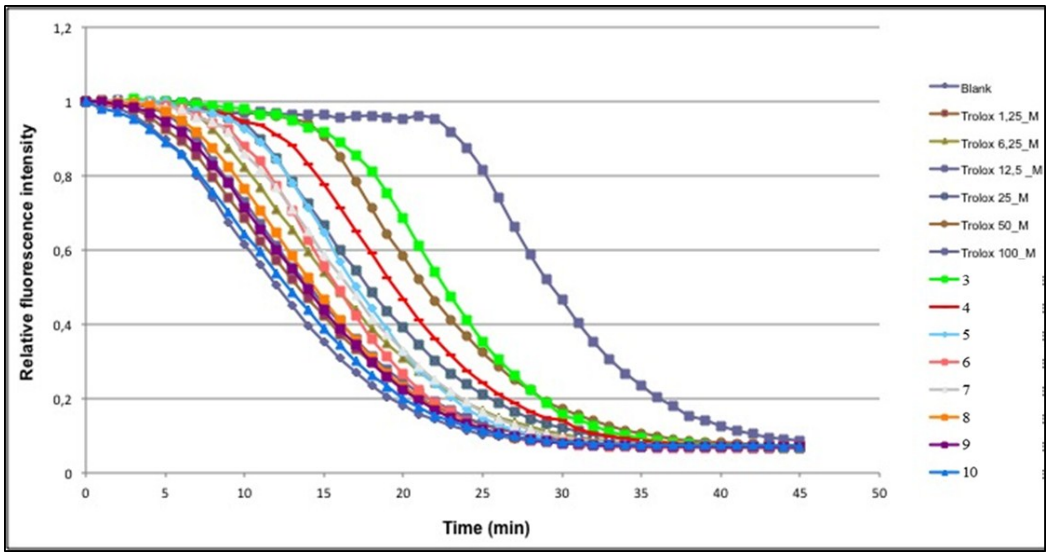
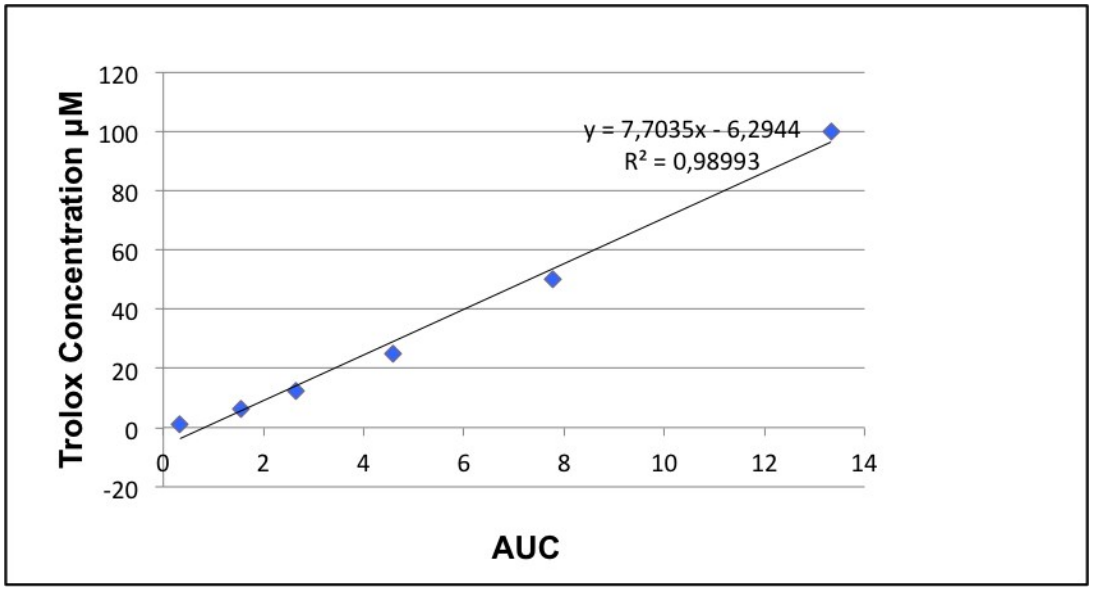


Fig. S4 Linear plot of AUC *vs* Trolox concentrations



DPPH radical scavenging activity

Fig. S5 Absorbance induced by DPPH

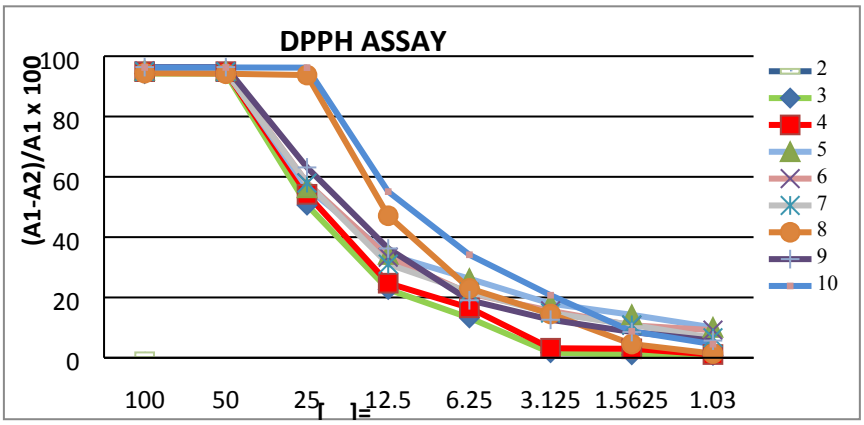


Fig. S6 Linear plot DPPH Assay of Methyl Oleuropein Aglicone (3)

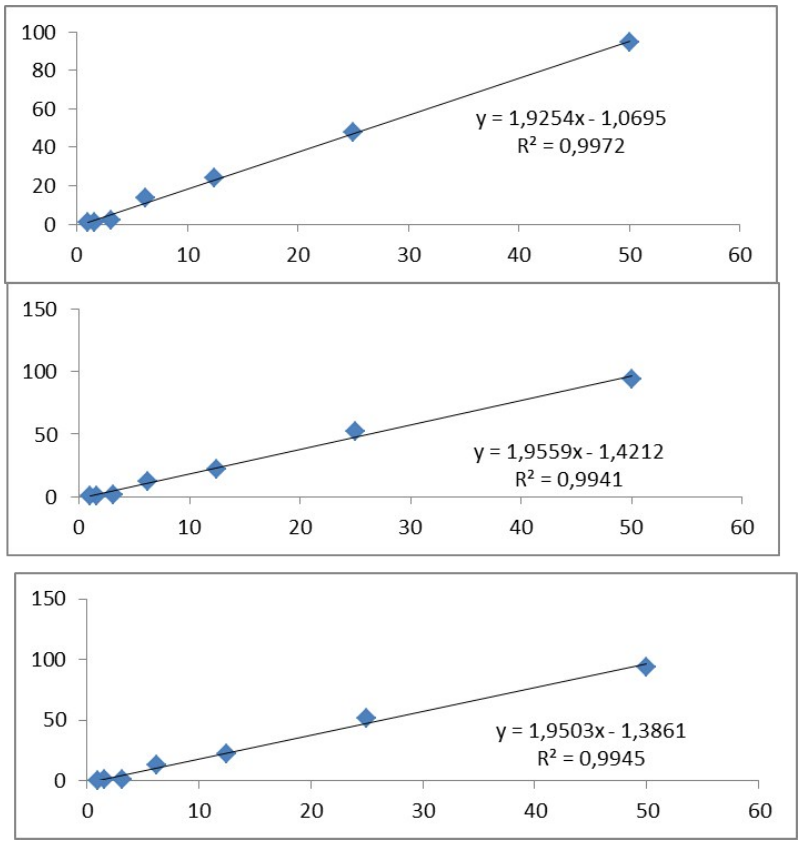


Fig. S7 Linear plot DPPH Assay of Ethyl Oleuropein Aglicone (4)

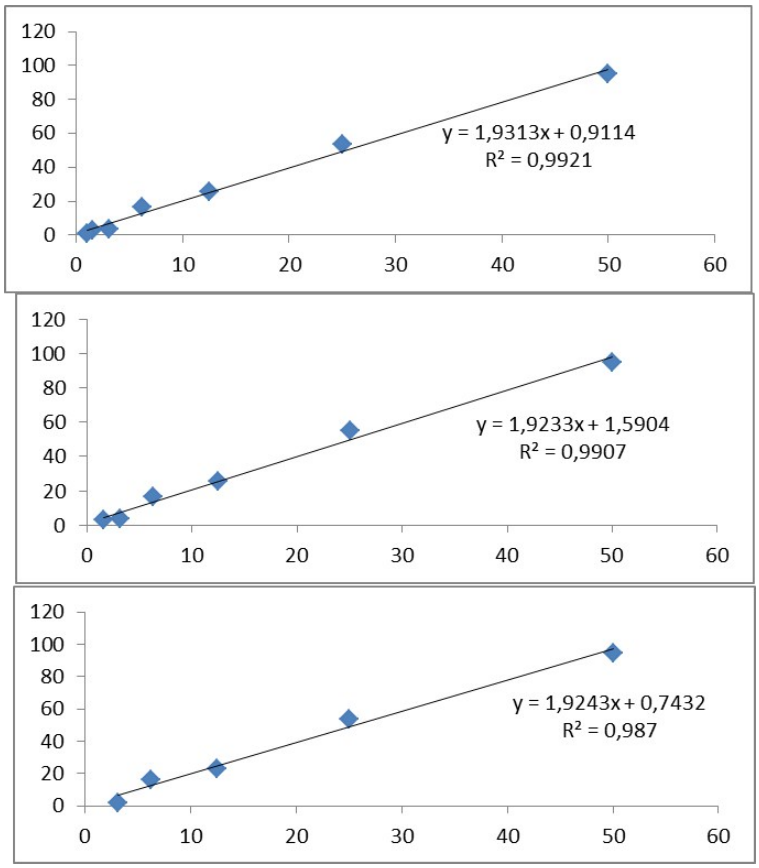


Fig. S8 Linear plot DPPH Assay of Phenyl Oleuropein Aglicone (5)

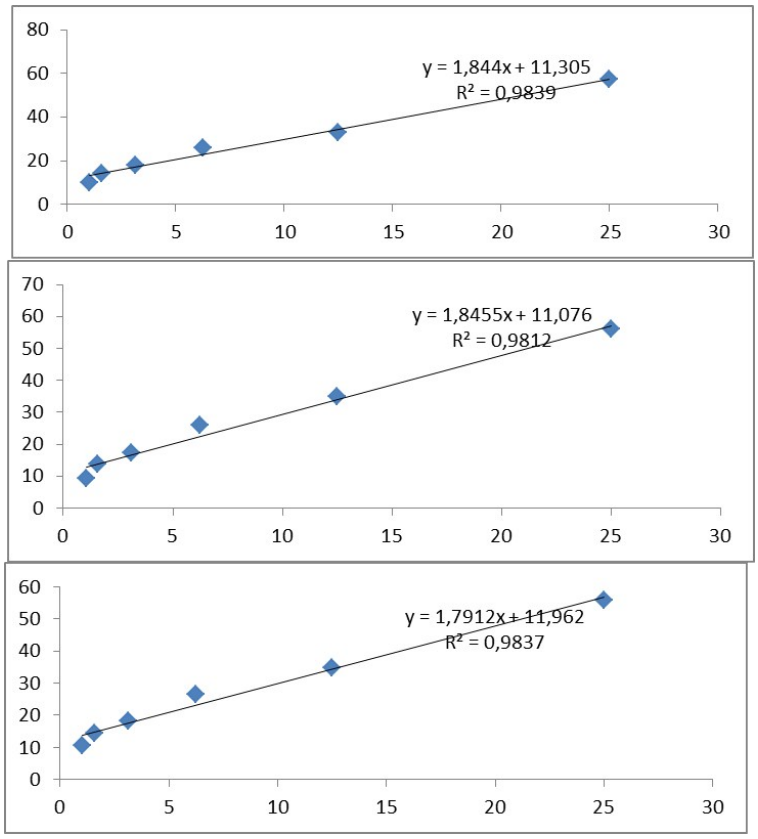


Fig. S9 Linear plot DPPH Assay of trans-Hexenyl Oleuropein Aglicone (6)

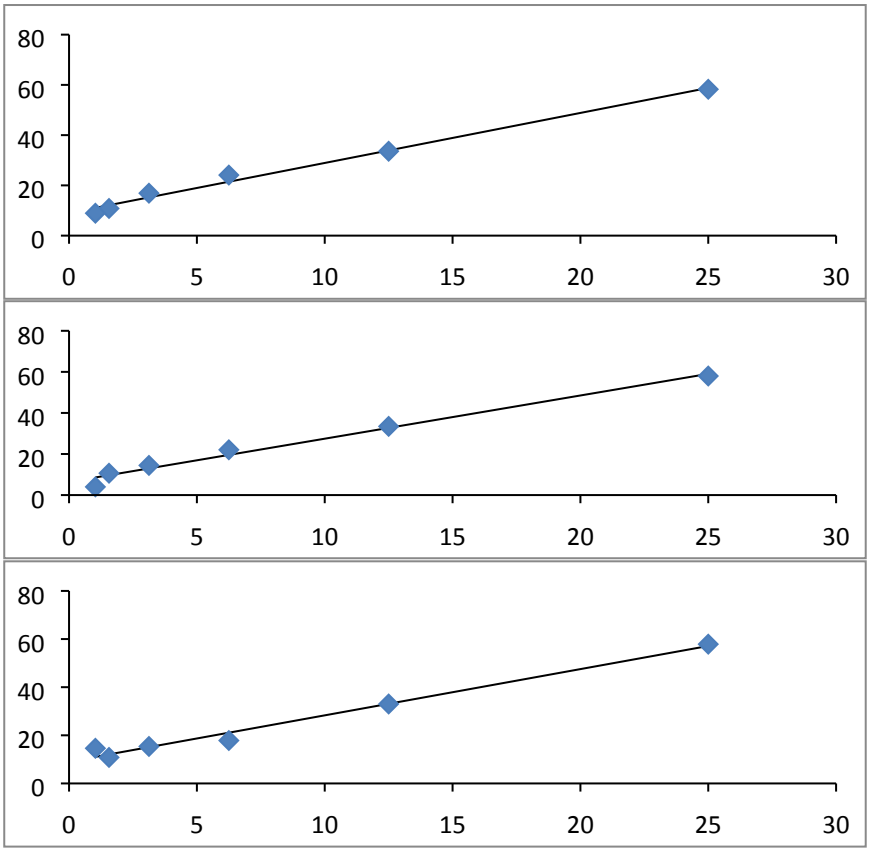


Fig. S10 Linear plot DPPH Assay of cis-Hexenyl Oleuropein Aglicone (7)

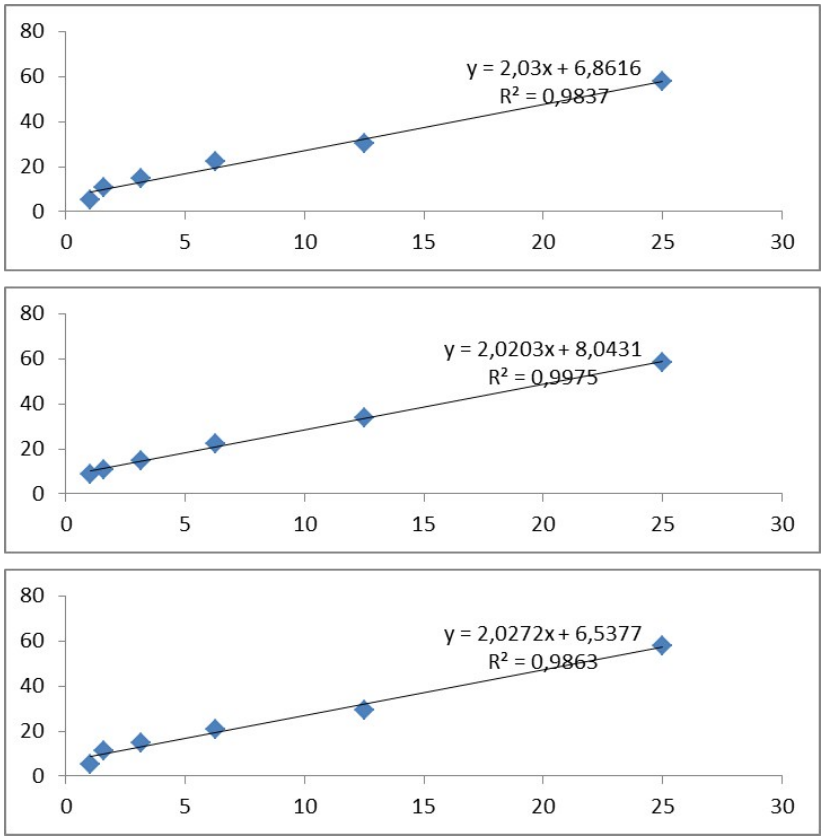


Fig. S11 Linear plot DPPH Assay of Palmityl Oleuropein Aglicone (8)

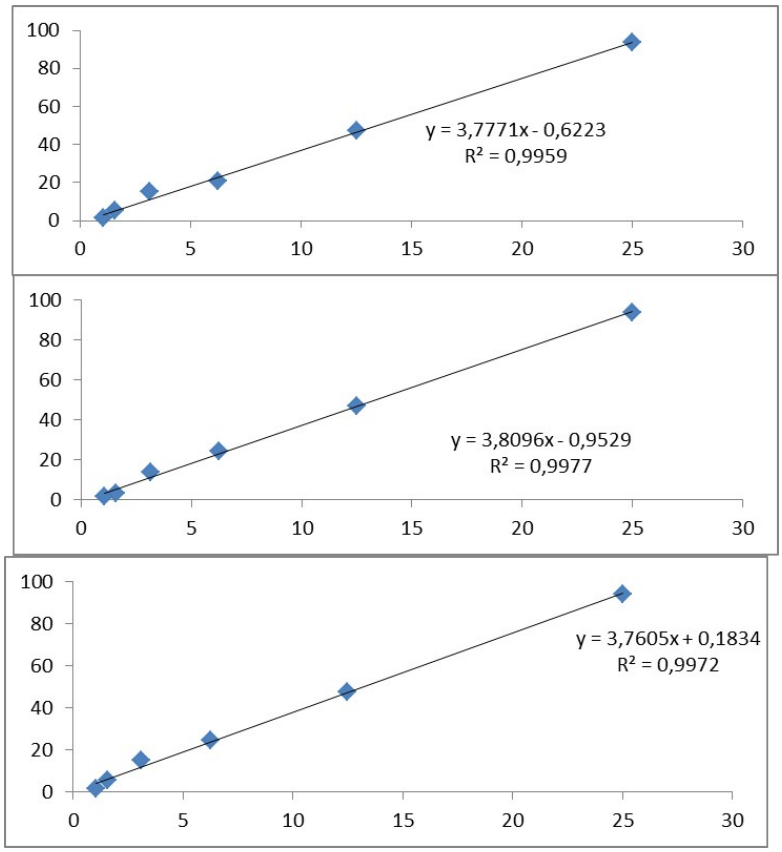


Fig. S12 Linear plot DPPH Assay of Octyl Oleuropein Aglicone (9)

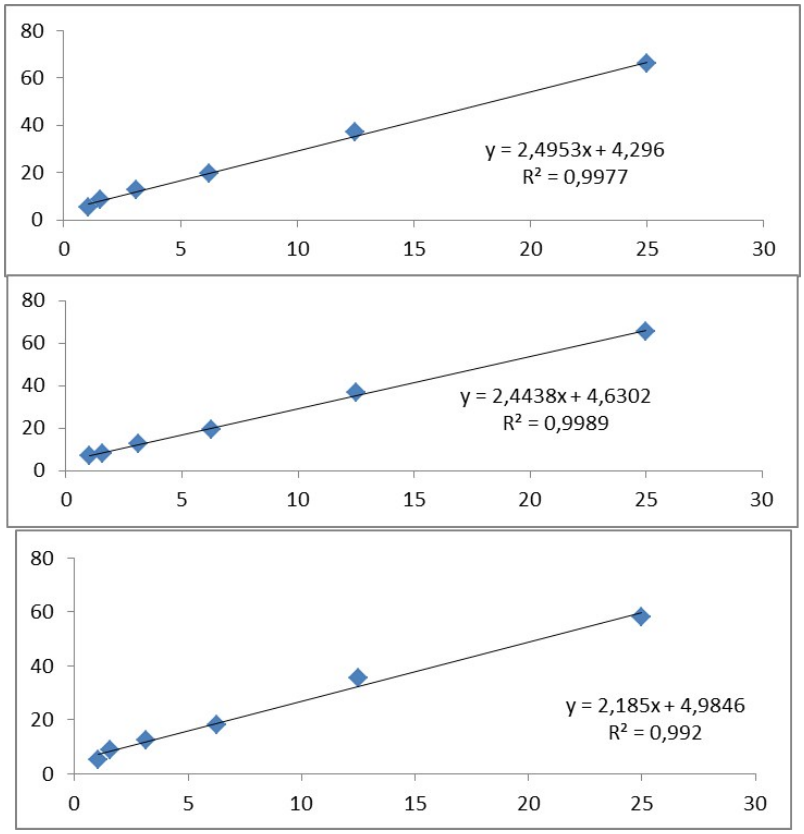


Fig. S13 Linear plot DPPH Assay of Oleyl Oleuropein Aglicone (10)

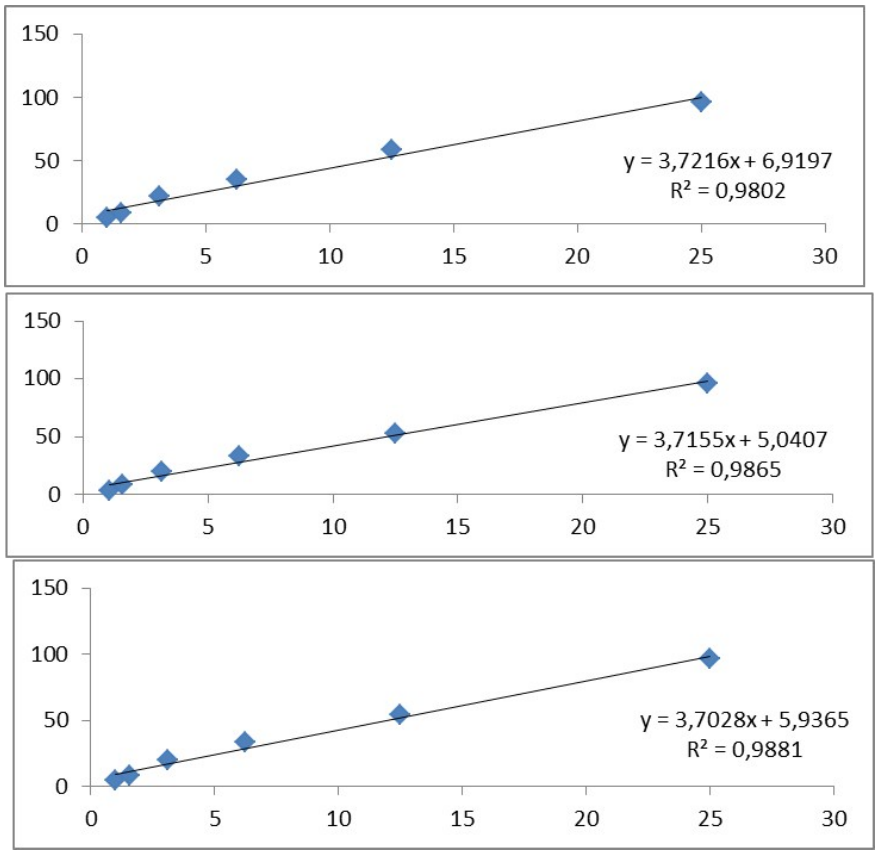


Fig. S14 IC50 of Oleuropein Aglicone derivates in DPPH Assay