



Supplementary material

Phytochemical Composition and Cytoprotective Properties of the Endemic *Sideritis sipylea* Boiss Greek Species: A Valorization Study

Silvia Di Giacomo ¹, Antonella Di Sotto ^{1,*}, Apostolis Angelis ², Ester Percaccio ¹, Annabella Vitalone ¹, Marco Gulli ¹, Alberto Macone ³, Evangelos Axiotis ^{2,4,†} and Alexios Leandros Skaltsounis ^{2,4,†}

¹ Department of Physiology and Pharmacology “V. Erspamer”, Sapienza University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy

² Department of Pharmacognosy and Natural Products Chemistry, Faculty of Pharmacy, National and Kapodistrian University of Athens, 15771 Athens, Greece

³ Department of Biochemical Science “A. Rossi Fanelli”, Sapienza University of Rome, P.le Aldo Moro 5, 00185 Rome, Italy

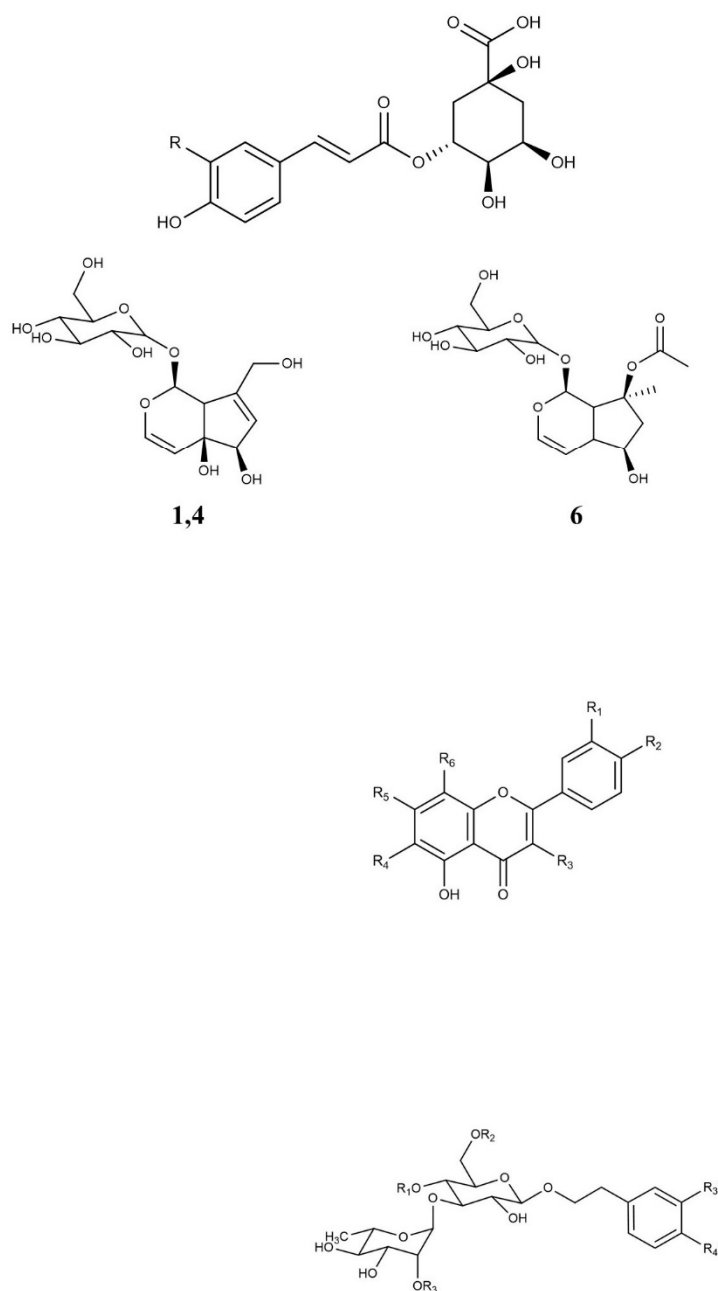
⁴ Natural Products Research Center “NatPro Aegean”, Gera, 81106 Lesvos, Greece

* Correspondence: antonella.disotto@uniroma1.it

† These authors equally contributed to the work.

Table S1. *S. sipylea* methanolic enriched extract fractions of increased polarity in mass (g) and their % (w/w) yields.

Fractions	Mass (g)	Yield (% w/w)
DCM 100%	0.0276	0.44
DCM / EtOAc (10%)	0.1636	2.64
DCM / EtOAc (50%)	0.2379	3.84
EtOAc 100%	0.3173	5.12
EtOAc / MeOH (10%) (S10)	0.9326	15.04
EtOAc / MeOH (20%) (S20)	1.5671	25.27
EtOAc / MeOH (50%) (S50)	1.4511	23.40
MeOH 100%	0.2462	3.97



Phenolic acids	R
Feruloylquinic acid (3)	OCH ₃
Chlorogenic acid (5)	OH

Iridoids
Melittoside derivatives (1),(4)
Ajugoside (6)

Flavonoid	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆
Apigenin (17)	H	OH	H	H	OH	H
Apigenin-7- <i>p</i> -coumaroyl-glucoside (16)	H	OH	H	H	<i>p</i> -coumaroyl-glu	H
Apigenin-7- <i>O</i> -glucoside (11)	H	OH	H	H	<i>O</i> -glu	H
Isoscutellarein 7- <i>O</i> -allosyl-(1→2)-glucoside (12)	H	OH	H	H	<i>O</i> -all-glu	OH
Luteolin 7- <i>O</i> -allosyl-(1→2)-[6''- <i>O</i> -acetyl]-glucoside (13)	OH	OH	H	H	<i>O</i> -(6''- <i>O</i> -acetyl)-β-glu	H
4'- <i>O</i> -methylisoscuteallarein 7- <i>O</i> -allosyl-(1→2)-glucoside (14)	H	OCH ₃	H	H	<i>O</i> -all-glu	OH
4'- <i>O</i> -methylisoscuteallarein 7- <i>O</i> -allosyl-(1→2)-[6''- <i>O</i> -acetyl]-glucoside (15)	H	OCH ₃	H	H	<i>O</i> -(6''- <i>O</i> -acetyl)-β-glu	OH
4'- <i>O</i> -methylisoscuteallarein 7- <i>O</i> -[6'''- <i>O</i> -acetyl]-allosyl-(1→2)-[6''- <i>O</i> -acetyl]-glucoside (18)	H	OCH ₃	H	H	<i>O</i> -(6'''- <i>O</i> -acetyl)-β-D-all-(1→2)] 6''- <i>O</i> -acetyl-β-D-glu	OH
Xanthomicrol or Hypolaetin trimethyl ether (19)	H	OH	H	OCH ₃	OCH ₃	OCH ₃

Phenylethanoid glycosides	R ₁	R ₂	R ₃	R ₄
Echinacoside (7)	feru	glc	H	OH
Lavandulifolioside (8)	caff.	api	api	OH
Isoverbacoside (9)	H	caff.	H	OH
Leucoseptoside A (10)	feru	H	H	OH

*feru = feruloyl; caff = caffeoyl; glc = glucose; api = apiose

Figure S1. Chemical structures of the identified compounds from S10, S20 and S50 fractions respectively from wild *S. sipylea* Boiss. The numbers in parentheses refer to Table 2 in the main manuscript.

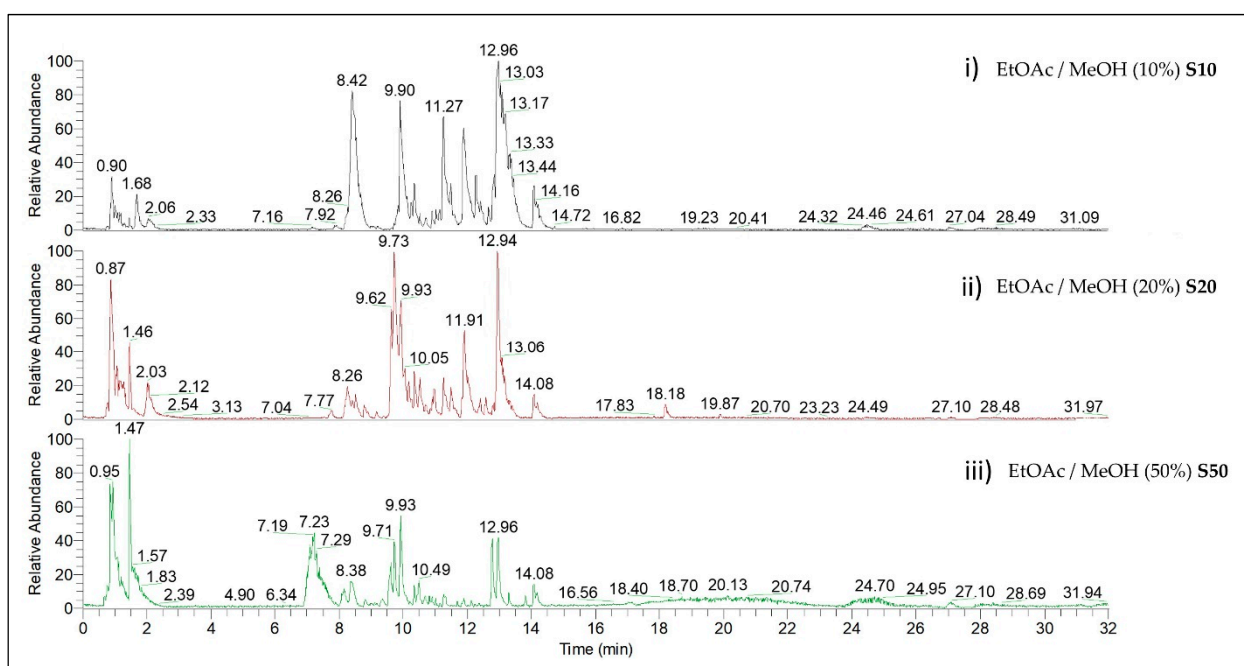


Figure S2. UPLC-ESI (-)-HRMS chromatograms of (i) EtOAc / MeOH (10%) (S10), (ii) EtOAc / MeOH (20%) (S20), and (iii) EtOAc / MeOH (50%) (S50) fractions of the methanol extract from wild *S. sipylea*

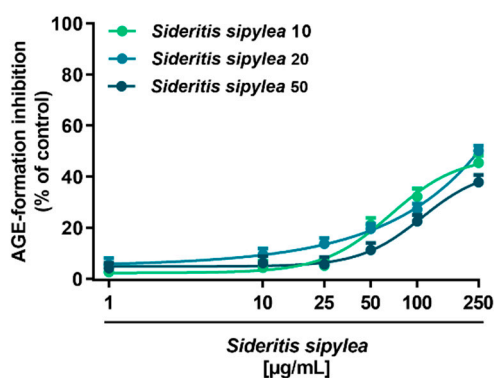


Figure S3. AGE formation inhibition by S10, S20 and S50 fractions from *S. sipylea* Boiss. Data represents the average and standard error of at least six replicates from at least two experiments.