

Supplementary Materials

Essential Oils of *Laurus nobilis* L.: From Chemical Analysis to In Silico Investigation of Anti-Inflammatory Activity by Soluble Epoxide Hydrolase (sEH) Inhibition

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Table S1. List of terpenes in *L. nobilis* essential oils (area%) and yield%

	Class	LNMO1	LNMO2	LNMO3	LNMO4	LNMO5	LNCA	LNAB
Aliphatic monoterpenes	AM	0.52	1.05	0.94	1.34	0.74	1.16	0.85
Monocyclic monoterpenes	MM	3.03	1.47	1.81	1.42	1.41	1.93	1.73
Bi – and tricyclic monoterpenes	BM	16.78	19.52	23.66	15.79	13.14	19.1	15.27
Monoterpenes	M	20.33	22.04	26.41	18.55	15.29	22.19	17.85
Aliphatic monoterpenoids	AMO	1.45	4.35	1.37	3.19	12.74	3.93	11.1
Monocyclic monoterpenoids	MMO	16.29	15.24	13.32	14.19	12.98	17.73	13.72
Bi – and tricyclic monoterpenoids	BMO	42.43	45.38	40.75	41.43	32.38	43.06	34.42
Monoterpenoids	MO	60.17	64.79	55.44	58.81	58.1	64.72	59.25
Aliphatic sesquiterpenes	AS	-	-	-	-	-	-	-
Monocyclic sesquiterpenes	MS	0.51	0.53	0.9	0.61	0.48	1.18	1.32
Bi – and tricyclic sesquiterpenes	BS	1.17	0.9	2.15	1.5	1.62	1.89	3.3
Sesquiterpenes	S	1.68	1.43	3.05	2.11	2.1	3.07	4.62
Aliphatic sesquiterpenoids	ASO	-	-	-	-	-	-	-
Monocyclic sesquiterpenoids	MSO	0.10	-	-	-	0.06	-	-
Bi – and tricyclic sesquiterpenoids	BSO	1.91	2.2	3.39	0.83	2.38	1.29	2.11
Sesquiterpenoids	SO	2.01	2.2	3.39	0.83	2.44	1.29	2.11
Others	OT	16.11	8.65	10.58	18.8	21.57	7.74	15.35
EO's yield		0.46%	0.4%	0.24%	0.5%	0.46%	0.37%	1.1%

Abbreviations: AM- aliphatic monoterpenes; MM- monocyclic monoterpenes; BM-bi-and tricyclic monoterpenes; AMO- aliphatic monoterpenoids; MMO- monocyclic monoterpenoids; BMO- bi-and tricyclic monoterpenoids; AS- aliphatic sesquiterpenes; MS- monocyclic sesquiterpenes; BS- bi- and tricyclic sesquiterpenes; ASO- aliphatic sesquiterpenoids; MSO- monocyclic sesquiterpenoids; BSO- bi- and tricyclic sesquiterpenoids, OT- others.

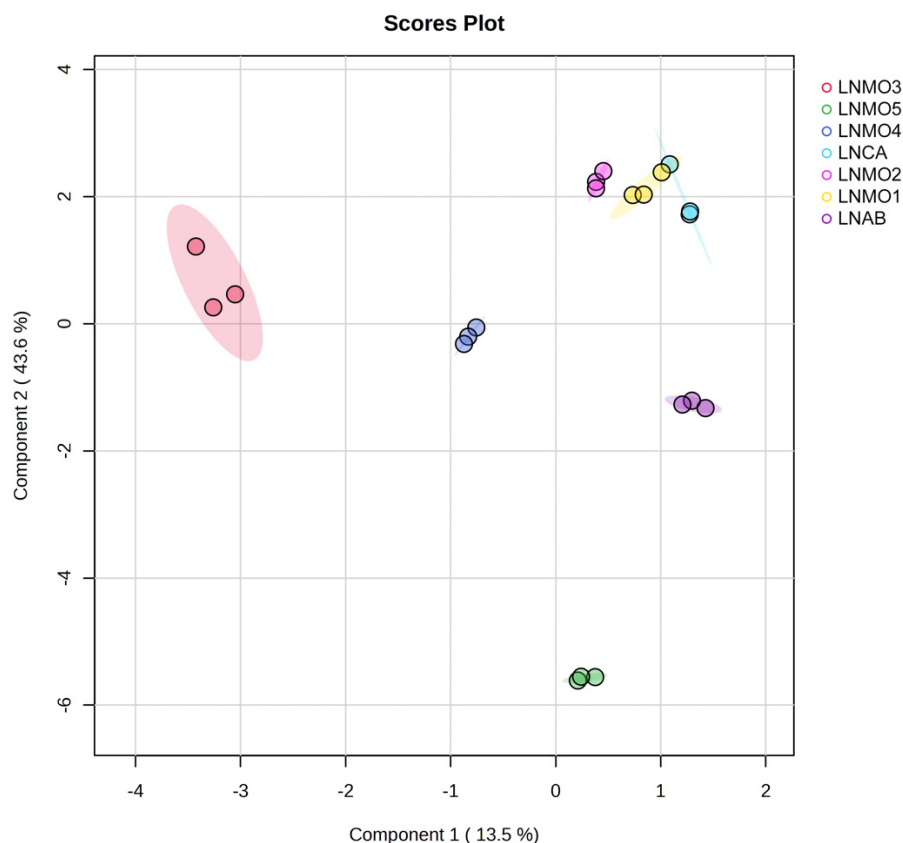


Figure S1. A 2D score plot of the PLS-DA of the essential oils of *L. nobilis* varieties.

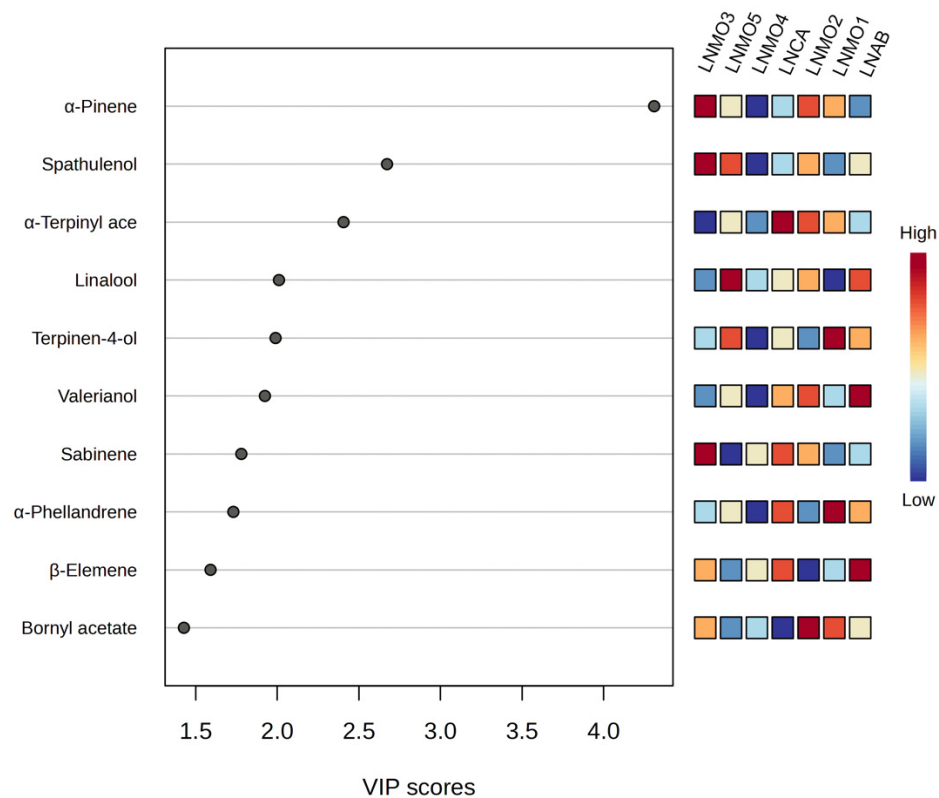


Figure S2. VIP plot in component 1.

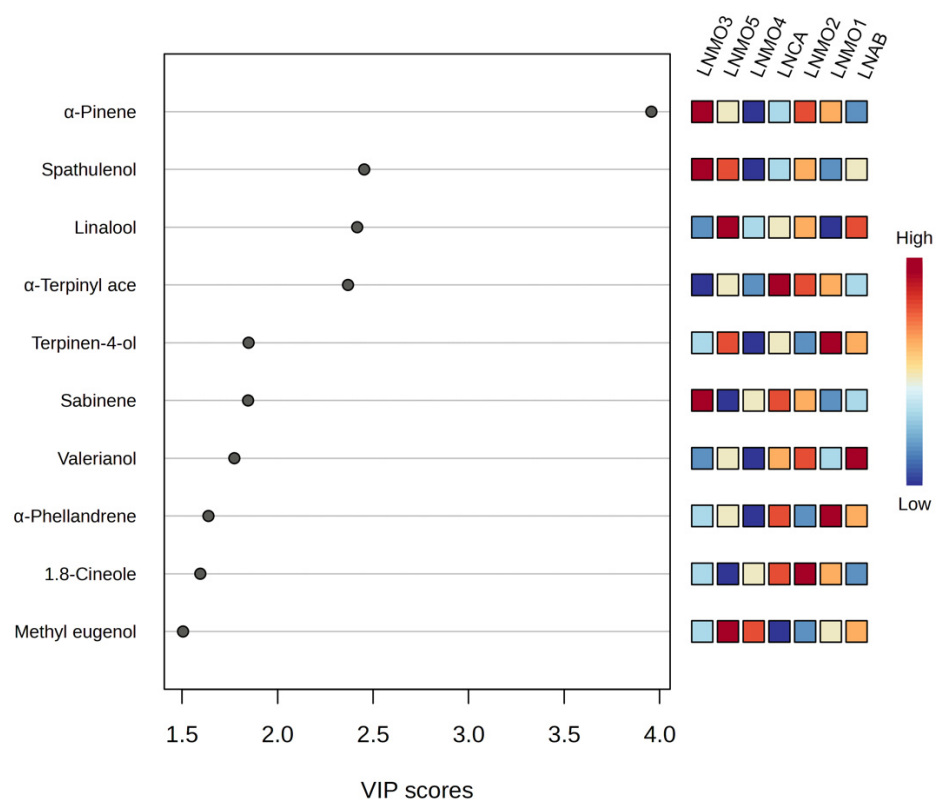


Figure S3. VIP plot in component 2.

Re-docking of the known inhibitor 4A0 co-crystallized in the protein structure of sEH

The compound 4A0 co-crystallized in the protein structure of sEH (PDB code: 4Y2X[1]) as reference to define molecular docking parameters. Specifically, Glide software (Schrödinger Suite) [2–6] was used in the Extra Precision (XP) mode to reproduce the binding mode of the compound ADUA as reported in the crystal structure. The generated molecular docking pose replicated a similar binding mode observed for the co-crystallized form of this ligand, as shown in Figure S4.

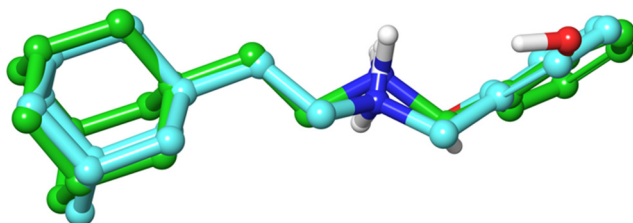


Figure S4. The binding mode of 4A0 (in cyan) superimposed to its pose (in green) in the crystal structure of sEH (PDB code: 4Y2X).

Table S2. Interactions of the known inhibitor 4A0 and major chemical components with the enzyme sEH.

Compounds	Type of interactions	Amino acids
4A0	Hydrogen bonds	Tyr383, His524, Gln 384
	Salt bridges	Asp 335
	Hydrophobic contacts	Leu408, Met419, Phe267
1,8-Cineole	Hydrophobic contacts	Leu408, Met419, Phe267
α -Terpinyl acetate	Hydrogen bonds	His524
	Hydrophobic contacts	Leu408, Met419, Phe267
Sabinene	Hydrophobic contacts	Leu408, Met419, Phe267
Eugenol	Hydrogen bonds	Asp335, His524
	Hydrophobic contacts	Leu408, Met419, Phe267
α -Pinene	Hydrophobic contacts	Leu408, Met419, Phe267
Linalool	Hydrogen bonds	Asp 335
	Hydrophobic contacts	Leu408, Met419, Phe267
Methyl eugenol	π - π interactions	Tyr 383
	Hydrophobic contacts	Leu408, Met419, Phe267
Terpinen-4-ol	Hydrogen bonds	Asp 335
	Hydrophobic contacts	Leu408, Met419, Phe267

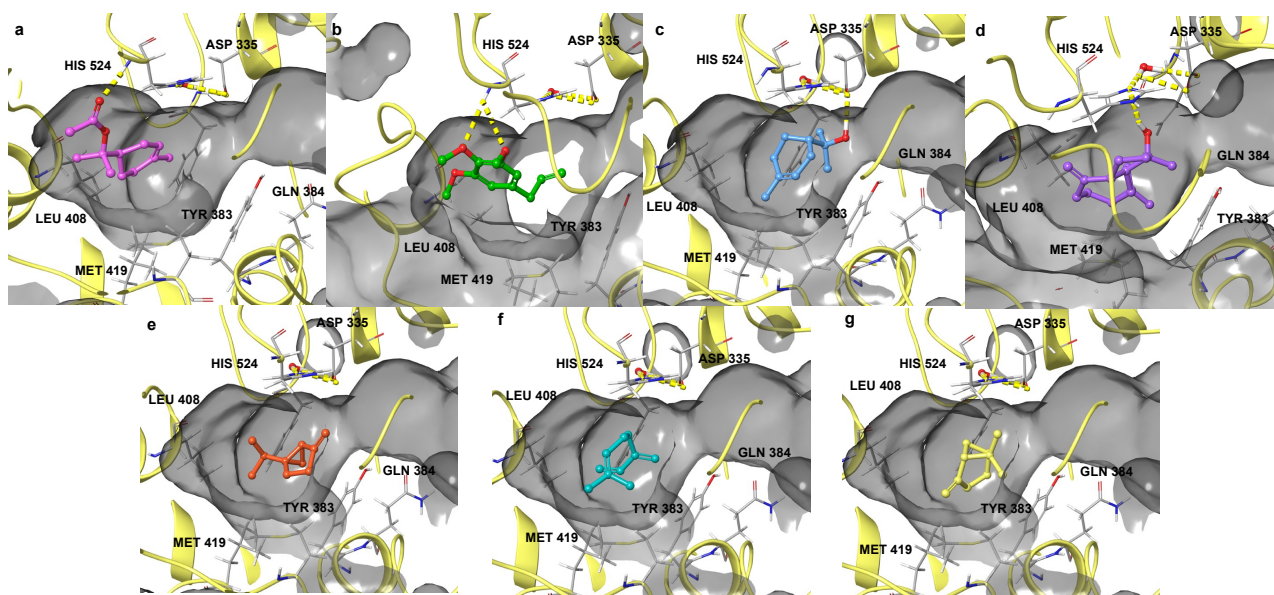


Figure S5. Binding mode of (a) α -terpinyl acetate (9.16–13%), (b) elemicin (2.05 – 0.57%), (c) α -terpineol (2.91 – 0.91%), (d) spathulenol (1.76 – 0.57%), (e) sabinene (10.57 – 4.85%), (f) myrcene (1.02 – 0.38%), and (g) β -pinene (3.77 – 2.44%). Hydrogen bonds are shown as dotted yellow lines.

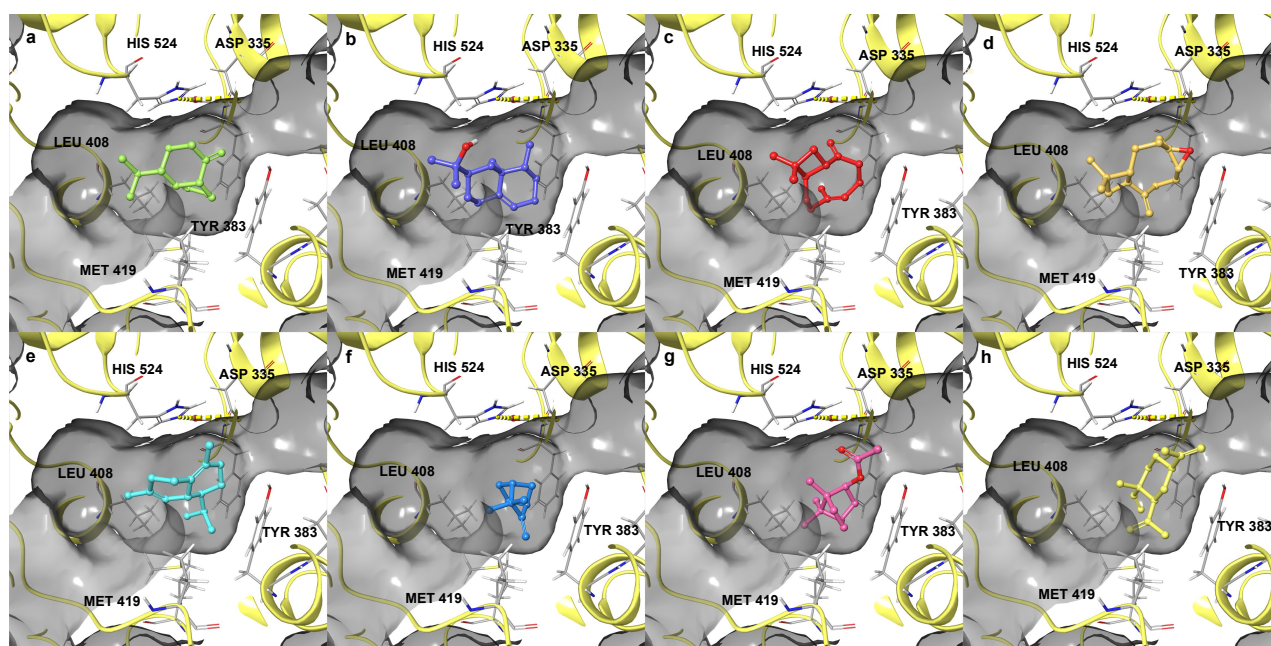


Figure S6. Binding mode of (a) γ -amorphene (0.73 – 0.08%), (b) valerianol (0.55 – 0.15%), (c) E-caryophyllene (0.79 – 0.32%), (d) caryophyllene oxide (0.83 – 0.16%), (e) δ -cadinene (0.55 – 0.11%), (f) camphene (0.90 – 0.10%), (g) bornyl acetate (0.82 – 0.13%), and (h) β -elemene (0.79 – 0.20%).

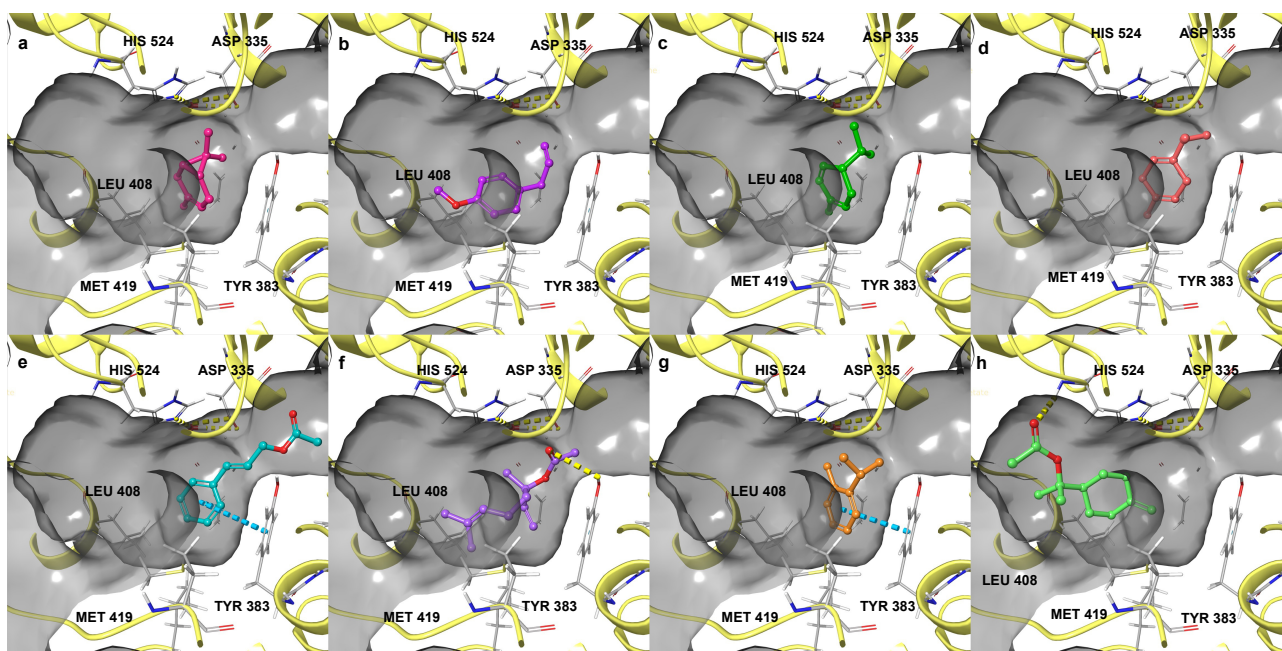


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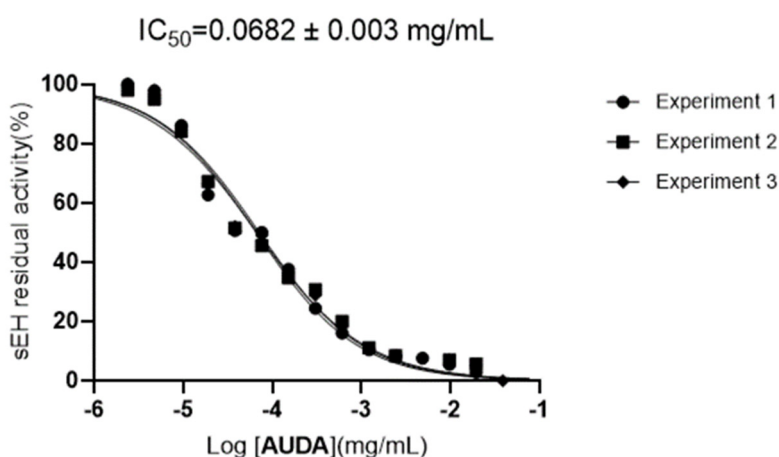


Figure S8. IC_{50} of AUDA (reference compound) on sEH. Data are expressed as means of three experiments \pm SD.

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