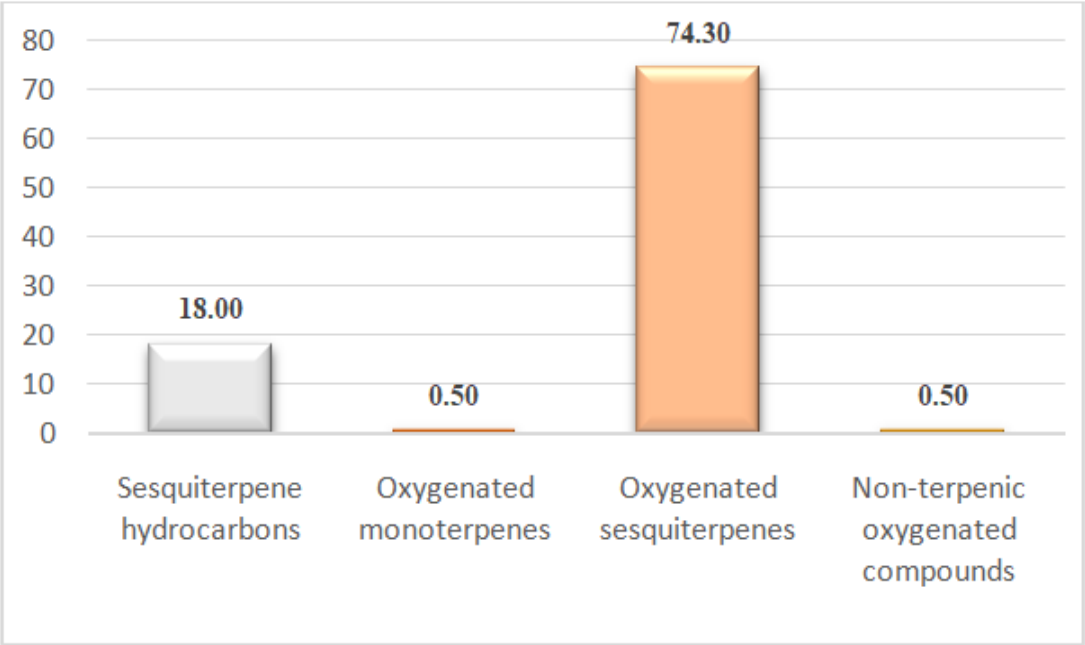


Fig 1: Variation of the contents of the different chemical classes of the essential oil of the aerial part of *I. montana*

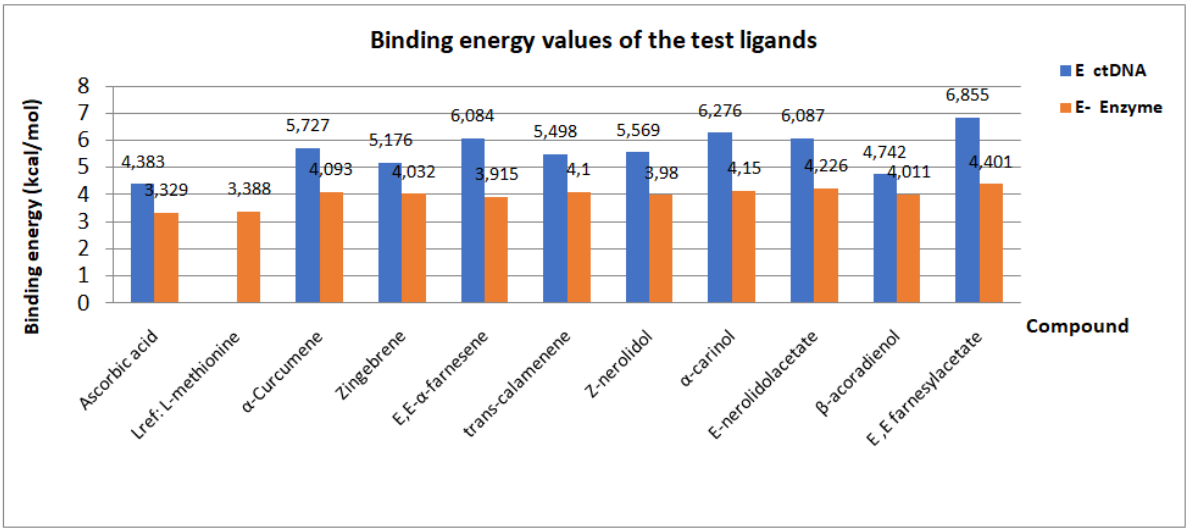


Fig 2: Binding energy values of the test ligands; Lref: reference ligand, ascorbic acid: control ligand

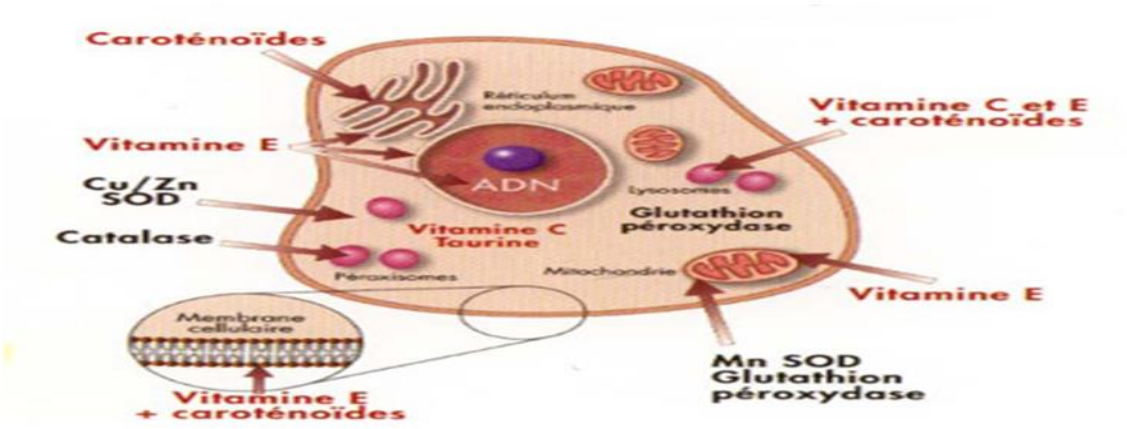


Fig 3: Sites of action of antioxidant nutrients (in red) and antioxidant enzymes (in black) (OPARA, 2002).

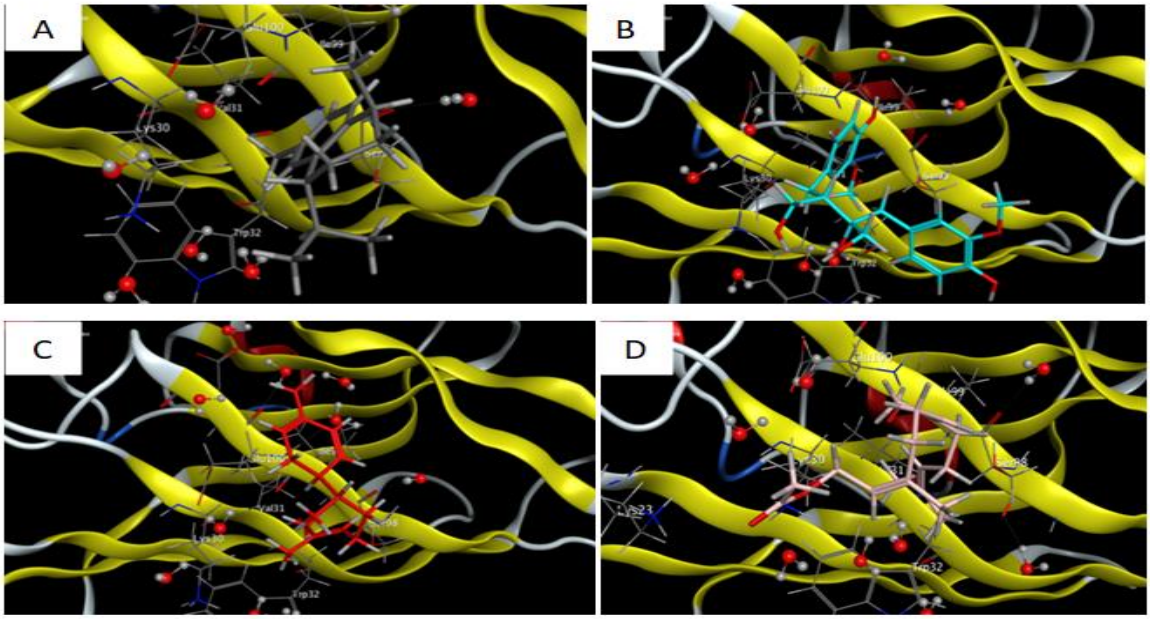


Fig.4. 3D representations of the best pose interactions between the ligands and their receptor. The proteins are represented in solid ribbon model and the ligands are represented in stick model. A. interaction between trans-Calamenene and SODs, B. interaction between α-Carinol and SODs, C. interaction between Zingebrene and SODs. D. interaction between Z.E-Farnesyl acetate and SODs.

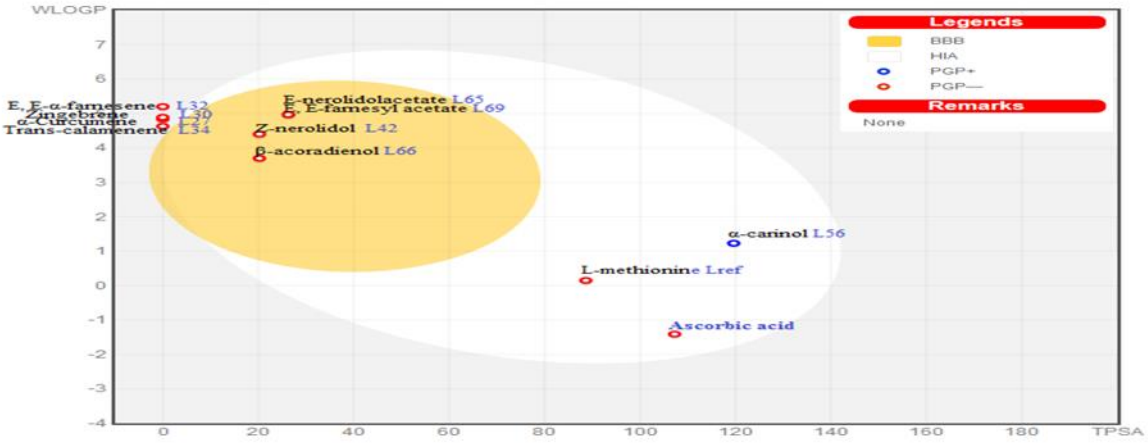


Fig 5: BOILED-Egg plot. Points located in the BOILED-Egg's yolk (yellow) represent the molecules predicted to passively permeate through the blood-brain barrier (BBB). whereas the ones in the egg white are relative to the molecules predicted to be passively absorbed by the gastrointestinal tract; the blue dots indicate the molecules for which it was expected to be effluated from the central nervous system (CNS)

Table 1: Some properties of all compounds For Antioxydants Drug.

Molecules	Energies(Kcal/mol)	LogP	LogS	Toxcicity
Hexanal	-2.10017e+000	1.77	-1.38	No
Z-hex-3-en-1-ol	6.05208e+000	1.94	-0.93	No
β-Citronellene	1.09326e+001	3.55	-3.92	No
6-methyl-hept-5-en-2-one	6.02568e+000	2.32	-1.48	No
1,8-Dihydro cineole	-2.50281e+000	2.55	-2.41	No
Octanal	-2.50281e+000	2.55	-2.41	No
Nonal	4.80498e+000	1.91	-2.53	No
α-terpineol	3.87834e+001	4.27	-5.91	No
theaspirane 1	4.34100e+001	4.27	-5.91	No
cis-3-hexenyl tiglate	1.21711e+001	2.85	-2.38	No
α-Cubebene	3.87834e+001	4.27	-5.91	No
α-ylangene	4.34100e+001	4.27	-5.91	No
α-Copaene	4.34100e+001	4.27	-5.91	No
β-Bourbonene	4.34100e+001	4.27	-6.41	No
Cyprene	4.88527e+001	4.27	-6.41	No
cis-α-Bergamotene	3.91656e+001	4.73	-5.29	Yes
α-gurjunene	5.36129e+001	4.27	-6.41	No
Aristolene	2.95612e+001	4.58	-5.17	No
(E)-β-Caryophyllene	3.91656e+001	4.73	-5.29	No
β-Copaene	4.34100e+001	4.27	-5.91	No
β-ghurjunene	2.59488e+001	4.89	-4.87	No
Aromadendrene	4.88527e+001	4.27	-6.41	No
α-Humulene	4.28781e+001	5.04	-3.92	No
allo-Aromadendrene	5.36129e+001	4.27	-6.41	No
γ-Muurolene	2.95612e+001	4.58	-5.17	No
Germacrene-D	3.17611e+001	4.89	-4.74	No
α-Murolene	2.95612e+001	4.58	-5.17	No
Delta-cadinene	2.61312e+001	4.73	-4.80	No

α-cadinene	3.90002e+001	3.78	-3.23	No
α-calacorene	3.54879e+001	3.78	-3.54	No
β-calacorene	4.47669e+001	3.92	-4.36	No
E-nerolidol	3.54879e+001	3.78	-3.54	No
epi-globulol	8.54552e+001	1.23	-2.09	No
caryophyllene oxyde	8.54552e+001	4.40	-4.25	No
Globulol	5.49887e+001	3.47	-4.79	No
Humulene epoxyde II	4.77798e+001	4.25	-3.09	Yes
β-oplopenone	5.30337e+001	3.80	-3.98	No
viridiflorol	4.03789e+001	3.70	-4.64	No
Zingiberenol	2.38235e+001	4.25	-3.09	Yes
1,10-diepi-cubenol	8.27697e+000	5.38	-5.86	No
Aromadendreneepoxyde II	4.99269e+001	3.48	-4.96	Yes
eudesma-4(15)-en-6-one	3.57237e+001	3.69	-2.29	No
Cadin-4-en-7-ol	4.09548e+001	3.78	-3.23	No
T-Muurolol	3.54879e+001	3.78	-3.54	No
β-eudesmol	4.47669e+001	3.92	-4.36	No
α-Cadinol	3.54879e+001	3.78	-3.54	No
Z-Z-farnesol	1.60145e+001	4.40	-4.25	No
α-eudesmol	2.18401e+001	5.20	-6.01	No
β-bisabolol	2.76289e+001	4.58	-4.67	No
Curcumen-15-al	2.19599e+001	4.35	-4.75	No
Eudesm-7(11)-en-4-α -ol	4.93225e+001	4.06	-3.67	No
Shyobunol	5.30337e+001	3.80	-3.98	No
Ledol	5.91711e+001	3.47	-4.79	No
8,11,14-Heptadecatrien-2-one	8.27697e+000	5.38	-5.86	No

Table 2: Results of Energy balance of all complexes formed with Anti-Angiogenic Drug molecules.

Mol	Binding Energy (Kcal/mole)	Rmsd -refine	Energy -Conf	Energy Place	Energy Refine	RMSD
Hexanal	-2.995	3.099	-5.978	-30.237	-6.069	0.060
Z-hex-3-en-1-ol	-3.212	1.877	16.055	-25.903	-7.039	0.035
β-citronelle	-3.119	1.951	22.989	-28.863	-7.362	0.054
6-methyl-hept-5-en-2-one	-3.233	1.389	-13.936	-31.409	-7.485	0.091
1,8-Dihydro cineole	-3.236	3.617	56.560	-19.787	-3.236	0.964
octanal	-3.300	2.294	-2.944	-18.824	-7.818	0.036
Nonal	-3.328	4.524	8.706	-26.487	-7.175	0.097
α-Terpineol	-3.662	3.119	18.409	-7.545	-8.734	0.460
theaspirane 1	-3.855	2.107	36.675	-17.982	-8.6748	0.043
cis-3-hexenyl tiglate	-3.823	1.502	24.584	-35.636	-7.214	0.314
α-cubebene	-3.2146	1.769	43.839	-28.440	-7.631	0.050
α-ylangene	-3.127	3.108	49.812	-15.673	-7.395	1.021
α-Copaene	-2.992	2.247	52.798	-22.361	-7.083	0.032
β-borbonene	-3.337	3.347	47.716	36.622	-7.866	0.047
Cyprene	-3.135	3.115	66.442	18.991	-6.310	0.990
cis-α-bergamotene	-3.134	2.411	48.391	-31.669	-7.557	0.106
α-gurjunene	-3.554	3.400	38.933	26.525	-6.757	1.067
Aristolene	-3.367	3.118	58.719	8.070	-7.860	1.001
E-β-caryophyllene	-3.154	2.911	47.761	-7.266	-8.735	0.151
β-copaene	-3.234	3.119	45.917	34.860	-7.894	0.363
β-gurjunene	-3.449	2.925	66.064	20.565	-5.556	0.055
nomadendrene	-3.081	2.897	24.397	74.377	-5.253	0.126
α-humulene	-2.927	4.158	62.965	199.949	-5.524	0.132
Allo-aromadendrene	-3.084	3.389	71.830	22.228	-7.042	0.141
γ-muurolene	-3.549	3.947	45.821	56.752	-9.566	0.057
germacrene D	-2.955	2.368	40.212	66.737	-6.414	0.183
α-muurolene	-3.634	3.691	45.824	14.940	-10.259	0.174
E,E-α-farnesene	-3.915	1.511	-1.997	-5.738	-3.758	1.154
γ-cadinene	-3.947	4.325	41.094	8.636	-10.755	0.051
α-cadinene	-3.463	2.752	43.859	-12.451	-7.455	1.014
α-calacorene	-3.359	2.115	44.733	-9.132	-7.069	1.021
β-calacorene	-3.360	2.116	44.733	-9.132	-7.071	1.039
E-nerolidol	-3.752	2.877	32.588	-3.852	-8.647	1.142
epi-globulol	-3.438	1.944	62.730	-24.761	-8.619	1.102
caryophyllene oxyde	-3.370	2.137	54.1124	12.223	-8.315	1.128

Germacrene D-4-ol	-3.2506	3.089	33.487	28.563	-7.371	1.028
Globulol	-3.3849	2.333	23.513	8.360	-8.326	0.443
humuleneepoxyde	-3.497	4.006	66.206	15.868	-7.562	1.085
β-oplopenone	-3.354	3.472	36.251	-10.682	-7.188	1.009
viridiflorol	-3.677	2.241	62.639	-3.894	-8.881	1.051
zingeberenol	-3.564	1.479	27.119	-6.487	-8.541	0.268
1,10-diepi-cubenol	-3.444	1.224	5.152	-6.843	-6.786	0.394
Aromadendrene epoxyde	-3.686	2.888	63.107	35.337	-8.540	0.228
eudesma-4(15)-en-6-one	-3.470	2.992	54.987	23.426	-6.505	1.002
cadin-4-en-7-ol	-3.915	3.048	48.475	0.407	-9.423	0.165
Trans-murolol	-3.655	1.986	40.394	-25.627	-8.789	0.047
β-eudesmol	-3.578	0.959	8.875	-42.053	-7.934	0.987
α-cadinol	-3.075	2.841	35.815	14.554	-6.960	0.079
Z,Z-farnesol	-3.999	2.529	30.995	-3.686	-10.632	0.091
α-eudesmol	-3.571	0.959	8.867	-42.053	-7.918	1.139
β-bisabolol	-3.557	3.699	35.043	2.230	-8.104	0.975
ar-curcumen-15-al	-3.996	1.585	43.186	-9.686	-11.653	0.100
eudesma-7,11-en-4-α-ol	-3.880	2.907	49.672	-14.152	-10.567	0.236
Shyobunol	-3.433	2.084	70.682	-18.550	-7.232	0.070
Ledol	-3.415	4.383	62.169	13.782	-8.088	0.189
heptadec-8,11,14-trien-2-one	-3.839	2.294	17.951	4.9099	-6.093	1.133

Table 3: The docking energies of best compounds of Superoxide Dismutase inhibitors

N°	Compound	DE(kcal/mol	ETOR (kT)	EVDW(kcal/mol	EIE (kcal/mol)
Lref	**methionine**	**-3.388**	**597.446**	**3321.887**	**-8885.99**
L32	E,E-α-Ffarnesene	-3.915	587.582	3334.543	-8901.72
L27	α-Curcumene	-4.093	592.789	3321.371	-8883.31
L30	Zingebrene	-4.032	587.551	3310.948	-8864.58
L34	trans-Calamenene	-4.100	600.347	3337.831	-8889.85
L42	Z-Nerolidol	-3.980	594.720	3419.679	-9023.10
L56	α-Carinol	-4.150	620.680	3443.616	-9049.99
L65	E-Nerolidol acetate	-4.226	586.014	3331.509	-8884.12
L66	β-Acoradienol	-4.011	614.614	3403.857	-9020.57
L67	Z,E-Farnesyl acetate	-4.175	610.880	3331.462	-8913.68
L69	E,E-Farnesyl acetate	-4.401	594.807	3372.486	-8940.57
DE: docking energy; ETOR: Torsion energy; VDW: Van der Waals; EIE: Electrostatic Interaction Energy					

Table 3.a: The docking energies of Superoxidase inhibitors

Compound	**DE (kcal/mol)**	**ETOR (kT)**	**EVDW (kcal/mol**	**EIE (kcal/mol)**
Hexanal	-2.995	597.332	3342.402	-8948.86
Z-hex-3-en-1-ol	-3.212	596.126	3345.720	-8943.17
β-Citronellene	-3.119	592.205	3348.598	-8936.64
6-methyl-hept-5-en-2-one	-3.233	598.320	3341.958	-8936.61
1,8-Dihydro cineole	-3.236	627.105	27816.57	-8907.44
Octanal	-3.300	593.151	3346.690	-8951.89
Nonal	-3.328	589.330	3343.336	-8941.91
α-Terpineol	-3.214	601.468	3349.357	-8932.99
theaspirane 1	-3.855	3749.304	613.157	-8946.55
cis-3-hexenyl tiglate	-3.823	647.190	6321.043	-4319.38
α-Cubebene	-3.214	610.306	3384.991	-9032.64
α-ylangene	-3.127	612.301	8762.842	-8967.10
α-Copaene	-2.992	601.373	3363.417	-8934.37
β-Bourbonene	-3.337	611.035	3347.124	-8930.44
Cyprene	-3.135	619.038	3277.628	-8829.95
cis-α-Bergamotene	-3.134	596.942	3361.550	-8933.92

α-gurjunene	-3.554	597.944	3267.282	-8859.29
Aristolene	-3.367	616.120	3336.980	-8846.42
(E)-β-Caryophyllene	-3.154	603.505	3357.169	-8943.25
β-Copaene	-3.234	603.198	3360.764	-8940.74
β-ghurjunene	-3.449	619.054	3317.916	-8855.46
Aromadendrene	-3.081	602.405	3341.775	-8903.09
α-Humulene	-2.927	592.172	3341.092	-8893.32
allo-Aromadendrene	-3.084	605.290	3332.595	-8888.61
γ-Muurolene	-3.549	584.796	3324.077	-8877.05
Germacrene-D	-2.955	591.711	3319.690	-8875.09
α-Murolene	-3.634	586.472	3324.826	-8877.57
Delta-cadinene	-4.033	587.266	3348.037	-8915.92
α-cadinene	-3.463	592.018	3329.039	-8895.14
α-calacorene	-3.359	612.513	3303.220	-8867.23
β-calacorene	-3.360	609.525	3344.146	-8866.00
E-nerolidol	-3.752	597.883	3307.371	-8861.73
epi-globulol	-3.438	615.302	3325.806	-8872.41
caryophyllene oxyde	-3.370	619.009	3288.317	-8837.21
Germacrene D-4-ol	-3.370	590.998	3318.289	-8810.04
Globulol	-3.384	617.196	3335.690	-8905.43
Humuleneepoxyde II	-3.497	597.785	3297.471	-8816.91
β-oplopenone	-3.354	602.155	3254.729	-8748.37
Viridiflorol	-3.677	638.614	3306.393	-8864.61
Zingiberenol	-3.564	593.478	3397.712	-8993.73
1,10-diepi-cubenol	-3.444	6.790	0.272	-6.263
Aromadendreneepoxyde II	-3.686	612.929	3385.184	-8991.95
eudesma-4(15)-en-6-one	-3.470	601.660	193548.1	-8878.01
Cadin-4-en-7-ol	-3.915	593.034	3398.624	-8982.18

T-Muurolol	-3.479	593.141	3360.039	-8960.44
β-eudesmol	-3.578	599.518	3314.986	-8820.03
α-Cadinol	-3.075	600.368	3415.881	-9012.55
Z-Z-farnesol	-3.999	594.783	3420.311	-9039.54
α-eudesmol	-3.571	591.404	3298.312	-8874.92
β-bisabolol L60	-3.557	605.394	3307.140	-8804.15
Curcumen-15-al	-3.996	599.566	3421.137	-9028.64
Eudesm-7(11)-en-4-α -ol	-3.880	606.410	3424.604	-9031.10
Shyobunol	-3.433	614.361	3404.770	-8993.88
Ledol	-3.415	614.888	3389.227	-8993.63

Table4: Predicted toxicity risks

Ligands	Mutagenic	Tumorigenic	Irritant	Reproductive effective
Lref				
Ascorbic acid				
L27				
L30				
L32				
L34				
L42				
L56				
L65				
1-Analog structure L65				
2-Analog structure L65				
L66				
L69				
1-Analog structureL69				
green = good, yellow = tolerable, red = bad.				

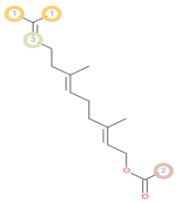
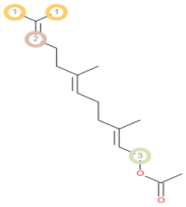
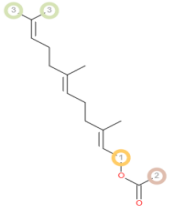
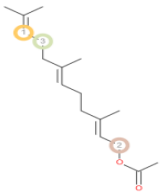
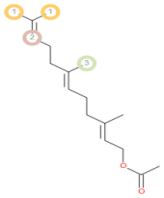
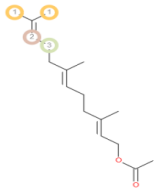
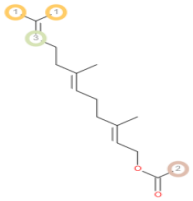
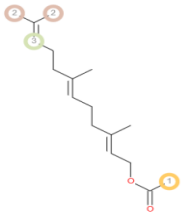
Table 5: ADMET profile of the test ligands, the control ligand (ascorbic acid) and Lref By using admetSAR

ADMET PROFILE	**HIA**	**BBB**	**CYP inhibition/substrate**	**Ames toxicity**	**Carcinogenicity**	**LD50**
Ascorbic acid	0.8150	0.9785	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	1.318
Lref	0.4786	0.9384	Substrate/non inhibitor	Nontoxic	Non carcinogenic	1.235
L27	0.9887	0.9962	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	2.06
L30	0.9790	0.9960	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	1.938
L32	0.9698	0.9962	Non substrate/non inhibitor	Nontoxic	carcinogenic	1.599
L34	0.9906	1.0000	Substrate/non inhibitor	Nontoxic	Non carcinogenic	2.596
L42	0.9645	0.9890	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	2.768
L56	0.9683	0.4757	Non substrate/ inhibitor	Nontoxic	Non carcinogenic	2.401
L65	0.9703	0.9859	Substrate/non inhibitor	Nontoxic	Non carcinogenic	2.276
L66	0.9826	0.9800	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	3.225
L69	0.9703	0.9932	Non substrate/non inhibitor	Nontoxic	Non carcinogenic	1.981

Table 6: Pharmacokinetics and Medicinal Chemistry properties for best molecule

		Pharmacokinetics		Medicinal Chemistry	
Molecule		**GI absorption**	**Log K_p (skin permeation)**	**Leadlikeness**	**Synthetic accessibility**
Ascorbic acid		High	-8.54 cm/s	**No; 1 violation: MW<250**	3.47
Lref		High	-8.54 cm/s	**No; 1 violation: MW<250**	2.43
α-Curcumene	L27	Low	-3.71 cm/s	No; 2 violations: MW<250, XLOGP3>3.5	2.31
Zingebrene	L30	Low	-3.88 cm/s	No; 2 violations: MW<250, XLOGP3>3.5	4.81
E, E-α-farnesene	L32	Low	-3.20 cm/s	No; 2 violations: MW<250, XLOGP3>3.5	3.72
trans-calamenene	L34	Low	-3.90 cm/s	No; 2 violations: Rotors>7. XLOGP3>3.5	2.61
Z-nerolidol	L42	High	-4.23 cm/s	No; 2 violations: MW<250, XLOGP3>3.5	3.53
α-carinol	L56	High	-7.57 cm/s	No; 2 violations: MW>350, Rotors>7	3.45
E-nerolidolacetate	L65	High	-3.80 cm/s	No; 2 violations: Rotors>7, XLOGP3>3.5	3.43
β-acoradienol	L66	High	-4.90 cm/s	No; 2 violations: MW<250, XLOGP3>3.5	4.53
E,E Farnesylacetate	L69	High	-3.72 cm/s	No; 2 violations: Rotors>7, XLOGP3>3.5	3.27

Table7: Results of the P450 sites of metabolism prediction study of the E,E Farnesylacetate best ligand molecules.

Names of P450 isoenzymes	E,E-Farnesyl acetate L69	Names of P450 isoenzymes	E,E-Farnesyl acetate L69	Names of P450 isoenzymes	E,E-Farnesyl acetate L69
1A2		2C8		2D6	
2A6		2C9		2E1	
2B6		2C19		3A4