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Long-term Supplementation of *Syzygium cumini* (L.) Skeels Concentrate Alleviates Age-related Cognitive Deficit and Oxidative Damage: A Comparative Study of Young vs Old Mice

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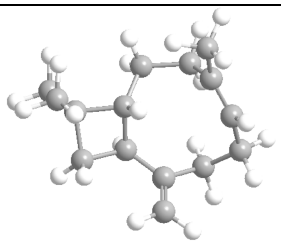
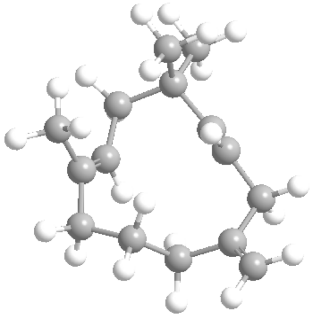
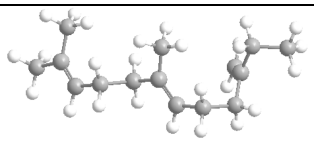
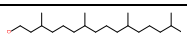
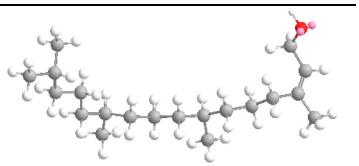
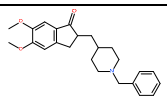
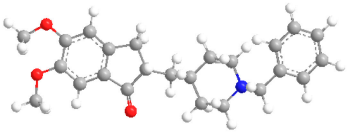
Supplementary Materials

Supplementary Table S1. Physiochemical properties, 2D(Chemdraw) and 3D (Chemdraw 3D), and chemical descriptors of investigated compounds A–E.

Compound Name	2D Structure	Chemical Properties	Chemical Analysis	3D Structure
Caryophyllene (A)		Boiling Point: 576.5 [K] Melting Point: 323.21 [K] Critical Temp: 737.59 [K] Critical Pres: 20.27 [Bar] Critical Vol: 716.5 [cm3/mol] Gibbs Energy: 196.63 [kJ/mol] Log P: 4.48 MR: 67.73 [cm3/mol] Henry's Law: -1.45 Heat of Form: -112.68 [kJ/mol] tPSA: 0 CLogP: 6.453 CMR: 6.6238 LogS: -4.156 pKa: N/A	Chemical Formula: $C_{15}H_{24}$ Exact Mass: 204.19 Molecular Weight: 204.36 m/z: 204.19 (100.0%), 205.19 (16.5%), 206.19 (1.2%) Elemental Analysis: C, 88.16; H, 11.84	
Humulene (B)		Boiling Point: 586.4 [K] Melting Point: 299.71 [K] Critical Temp: 755.3 [K] Critical Pres: 20.53 [Bar] Critical Vol: 722.5 [cm3/mol] Gibbs Energy: 137.25 [kJ/mol] Log P: 4.83 MR: 71.02 [cm3/mol] Henry's Law: -1.75 Heat of Form: -125.84 [kJ/mol] tPSA: 0 CLogP: 6.773 CMR: 6.7758 LogS: -4.195 pKa: N/A	Chemical Formula: $C_{15}H_{24}$ Exact Mass: 204.19 Molecular Weight: 204.36 m/z: 204.19 (100.0%), 205.19 (16.5%), 206.19 (1.2%) Elemental Analysis: C, 88.16; H, 11.84	
(E)-.beta.-Farnesene (C)		Boiling Point: 547.44 [K] Melting Point: 204.51 [K] Critical Temp: 705.83 [K] Critical Pres: 16.04 [Bar] Critical Vol: 819.5 [cm3/mol] Gibbs Energy: 298.05 [kJ/mol] Log P: 5.13 MR: 72.95 [cm3/mol] Henry's Law: -1.12 Heat of Form: -22.43 [kJ/mol] tPSA: 0 CLogP: 6.787 CMR: 7.0582 LogS: -3.608 pKa: N/A	Chemical Formula: $C_{15}H_{26}$ Exact Mass: 206.20 Molecular Weight: 206.37 m/z: 206.20 (100.0%), 207.21 (16.5%), 208.21 (1.3%) Elemental Analysis: C, 87.30; H, 12.70	

Phytol (D)		Boiling Point: 752.1 [K] Melting Point: 311.44 [K] Critical Temp: 777.23 [K] Critical Pres: 11.37 [Bar] Critical Vol: 1137.5 [cm3/mol] Gibbs Energy: 45.05 [kJ/mol] Log P: 6.96 MR: 97.17 [cm3/mol] Henry's Law: 1.6 Heat of Form: -516.77 [kJ/mol] tPSA: 20.23 CLogP: 8.483 CMR: 9.5811 LogS: -5.139 pKa: 14.594	Chemical Formula: $C_{20}H_{42}O$ Exact Mass: 298.32 Molecular Weight: 298.56 m/z: 298.32 (100.0%), 299.33 (22.2%), 300.33 (2.5% Elemental Analysis: C, 80.46; H, 14.18; O, 5.36	
Donepezil (E)		Boiling Point: 964.14 [K] Melting Point: 624.13 [K] Critical Temp: 952.21 [K] Critical Pres: 14.84 [Bar] Critical Vol: 1122.5 [cm3/mol] Gibbs Energy: 222.62 [kJ/mol] Log P: 4.01 MR: 113.97 [cm3/mol] Henry's Law: 10.3 Heat of Form: -301.37 [kJ/mol] tPSA: 38.77 CLogP: 4.59759 CMR: 11.1212 LogS: -4.609 pKa: 9.287	Chemical Formula: $C_{24}H_{29}NO_3$ Exact Mass: 379.21 Molecular Weight: 379.50 m/z: 379.21 (100.0%), 380.22 (26.4%), 381.2 Elemental Analysis: C, 75.96; H, 7.70; N, 3.69	

K: kelvin, cm3/mol: centimeter cube in one mole, kJ/mol: kilojoules in one mole.

Supplementary Table S2. Adsorption, Distribution, Metabolism, Excretion and Toxicological properties of the investigated compounds (A–D) in comparison to donepezil (E) drug.

ADMET	A	B	C	D	Donepezil (E)
Physiochemical Properties					
Formula	$C_{15}H_{24}$	$C_{15}H_{24}$	$C_{15}H_{26}$	$C_{20}H_{40}O$	$C_{24}H_{29}NO_3$
Molecular Weight	204.35	204.35	206.37	296.53	379.49
No.of Heavy Atoms	15	15	15	21	28
No.arom.Heavy Atoms	0	0	0	0	12
Fraction Csp3	0.73	0.6	0.6	0.9	0.46
No. of rotatable bonds	0	0	7	13	6
No.of H.bond Acceptor	0	0	0	0	4
No. of H.bod donors	0	0	0	0	0
Molar Refractivity	68.78	70.42	72.8	98.94	115.31
Topological polar surface Area (TPSA) A^2	0	0	0	20.23	38.77
Lipophilicity (Log $P_{o/w}$)					
iLOGP	3.29	3.3	4.02	4.71	3.92
XLOGP3	4.38	4.79	6.21	8.19	4.28
WLOGP	4.73	5.04	5.43	6.36	3.83
MLOGP	4.63	4.53	4.93	5.25	3.06
Silicos-IT Log P	4.19	4.19	4.94	6.57	4.91
Consensus Log P (average of all above predictions)	4.24	4.37	5.1	6.22	4
Water Solubility					
Log S (ESOL)	−3.87	−4.12	−4.57	−5.98	−4.81
Solubility (mg/ml)	2.78E-02	1.53E-02	5.56E-03	3.10E-04	5.87E-03
Class	Soluble	Moderately soluble	Moderately soluble	Moderately soluble	Moderately soluble
Log S (Ali)	−4.1	−4.52	−6	−8.47	−4.81
Solubility (mg/ml)	1.64E-02	6.15E-03	2.09E-04	9.94E-07	5.92E-03
Class	Moderatel y soluble	Moderately soluble	Moderately soluble	Poorly soluble	Moderately soluble
Log S (SILICOS-IT)	−3.77	−3.77	−4.08	−5.51	−6.9
Solubility (mg/ml)	3.49E-02	3.49E-02	1.70E-02	9.06E-04	4.78E-05
Class	Soluble	Soluble	Moderately soluble	Moderately soluble	Poorly soluble
Pharmacokinetics					
GI absorption	medium	medium	Low	Low	High
BBB permeant	No	No	No	No	Yes
P-gp substrate	No	No	No	Yes	Yes
CYP1A2 inhibitor	No	No	Yes	No	No
CYP2C19 inhibitor	Yes	No	No	No	No
CYP2C9 inhibitor	Yes	Yes	Yes	Yes	No
CYP2D6 inhibitor	No	No	No	No	Yes
CYP3A4 inhibitor	No	No	No	No	Yes
Log Kp (skin permeation) cm/s	−4.44	−4.15	−3.15	−2.29	−5.58
Drug Likeness					
Lipinski Violation	1	1	1	1	0
Ghose Violation	0	0	0	1	0
Veber Violation	0	0	0	1	0
Egan Violation	0	0	0	1	0
Muegge Violation	1	1	2	2	0
Bioavailability	0.55	0.55	0.55	0.55	0.55
Medicinal Chemistry					

Pan Assay Interference Structure (PAINS)	0	0	0	0	0
Brenk	1	1	1	1	0
Leadlikeness	2	2	2	2	2
Synthetic Accessibility	4.51	3.78	3.18	4.3	3.36

XLOGP3: pure atom-additive model, LOGP: octanol-water partition coefficient, Log S: water solubility of a drug, CYP: Cytochrome P450, Log Kp: Skin permeability.