In Silico Screening of Coffee Plant Natural Products as Lead Compounds for Stroke Remedy

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I.Supplementary Materials

I.1 Table

Number	Name	Molecular Mass (Da)	Hydrogen Bond Donor	Hydrogen Bond Acceptor	Lipophilicity (LOG*P*)	Molar Refractivity	PubChem CID
1	5-O-Caffeoylquinic acid	354	6	9	-0.645900	82.518768	5280633
2	Quercetin	302	5	7	2.010900	74.050476	5280343
3	3-O-Feruloylquinic acid	368	5	9	-0.342900	87.405968	9799386
4	4-O-Feruloylquinic acid	368	5	9	-0.342900	87.405968	10177048
5	5-O-Feruloylquinic acid	368	5	9	-0.342900	87.405968	73210496
6	4,5-Di-O-caffeoylquinic acid	312	5	6	-0.053101	77.145782	6474309
7	4-P-Coumaroylquinic acid	338	5	8	-0.351500	80.853966	5281766
8	5-P-Coumaroylquinic acid	338	5	8	-0.351500	80.853966	164893
9	16-O-Methylcafestol	330	1	3	4.060699	90.884766	68103163

10	16-O-Methyl Kahweol	328	1	3	4.141299	91.597771	68103165
11	Cafestol	316	2	3	3.406599	86.094566	108052
12	Kahweol	314	2	3	3.487199	86.807571	114778
13	Dehydrocafestol	298	1	2	4.211799	84.610771	101468593
14	Dehydro Kahweol	296	1	2	4.525099	86.256775	101468592

Table 1. List of molecule compounds that can be found in coffee beans. The informations here were retrieved from SCF Bio's online tool that predicts compounds in accordance with Lipinski's rule of five

#	Compound Name	Canonical SMILES	Pa value	Pi value
1	5-O Caffeoylquinic acid	C1C(C(C(CC1(C(=O)O)O)OC(=O)C=CC2=CC(=C(C=C2)O)O)O)O)O	0,785 (Antioxidant) 0,598 (Anti inflammatory) 0,346 (Antithrombotic) 0,233 (Antipyretic)	0,004 (Antioxidant) 0,032 (Anti inflammatory) 0,076 (Antithrombotic) 0,085 (Antipyretic)
2	Quercetin	C1=CC(=C(C=C1C2=C(C(=O)C3=C(C=C(C=C3O2)O)O)O)O)O	0,872 (Antioxidant) 0,689 (Anti inflammatory) 0,207 (Antithrombotic) 0,325 (Antipyretic)	0,003 (Antioxidant) 0,017 (Anti inflammatory) 0,198 (Antithrombotic) 0,038 (Antipyretic)
3	3-O-Feruloylquinic acid	COC1=C(C=CC(=C1)C=CC(=O)OC2CC(CC(C2O)O)(C(=O)O)O)O	0,727 (Antioxidant) 0,633 (Anti inflammatory) 0,315 (Antithrombotic)	0,004 (Antioxidant) 0,025 (Anti inflammatory) 0,092 (Antithrombotic)

			0,238 (Antipyretic)	0,081 (Antipyretic)
4	4-O-Feruloylquinic acid	COC1=C(C=CC(=C1)C=CC(=O)OC2C(CC(CC2O)(C(=O)O)O)O)O)O	0,713 (Antioxidant) 0,654 (Anti inflammatory) 0,283 (Antithrombotic) 0,250 (Antipyretic)	0,004 (Antioxidant) 0,022 (Anti inflammatory) 0,113 (Antithrombotic) 0,072 (Antipyretic)
5	5-O-Feruloylquinic acid	COC1=C(C=CC(=C1)C=CC(=O)OC2CC(CC(C2O)O)(C(=O)O)O)O	0,727 (Antioxidant) 0,633 (Anti inflammatory) 0,315 (Antithrombotic) 0,238 (Antipyretic)	0,004 (Antioxidant) 0,025 (Anti inflammatory) 0,092 (Antithrombotic) 0,081 (Antipyretic)
6	4,5-Di-O-caffeoylquinic acid	C1C(C(C(CC1(C(=O)O)O)OC(=O)C=CC2=CC(=C(C=C2)O)O)OC(=O)C=CC3=CC(=C(C=C3)O)O)O	0,806 (Antioxidant) 0,660 (Anti inflammatory) 0,267 (Antithrombotic) 0,211 (Antipyretic)	0,003 (Antioxidant) 0,021 (Anti inflammatory) 0,127 (Antithrombotic) 0,104 (Antipyretic)
7	4-P-Coumaroylquinic acid	C1C(C(C(CC1(C(=O)O)O)O)OC(=O)C=CC2=CC=C(C=C2)O)O	0,739 (Antioxidant) 0,674 (Anti inflammatory) 0,287 (Antithrombotic) 0,233 (Antipyretic)	0,004 (Antioxidant) 0,019 (Anti inflammatory) 0,110 (Antithrombotic) 0,085 (Antipyretic)

8	5-P-Coumaroylquinic acid	C1C(C(C(CC1(C(=O)O)O)OC(=O)C=CC2=CC=C(C=C2)O)O)O	0,753 (Antioxidant) 0,650 (Anti inflammatory) 0,321 (Antithrombotic) 0,221 (Antipyretic)	0,004 (Antioxidant) 0,023 (Anti inflammatory) 0,089 (Antithrombotic) 0,096 (Antipyretic)
9	16-O-Methylcafestol	CC12CCC3=C(C1CCC45C2CCC(C4)C(C5)(CO)OC)C=CO3	0,468 (Antioxidant) 0,314 (Anti inflammatory) 0,321 (Antithrombotic) 0,221 (Antipyretic)	0,008 (Antioxidant) 0,148 (Anti inflammatory) 0,089 (Antithrombotic) 0,096 (Antipyretic)
10	16-O-Methyl Kahweol	CC12C=CC3=C(C1CCC45C2CCC(C4)C(C5)(CO)OC)C=CO3	0,488 (Antioxidant) 0,391 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)	0,007 (Antioxidant) 0,100 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)
11	Cafestol	CC12CCC3=C(C1CCC45C2CCC(C4)C(C5)(CO)O)C=CO3	0,470 (Antioxidant) 0,274 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)	0,008 (Antioxidant) 0,188 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)
12	Kahweol	CC12C=CC3=C(C1CC	0,492	0,007

		C45C2CCC(C4)C(C5)(CO)O)C=CO3	(Antioxidant) 0,345 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)	(Antioxidant) 0,126 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)
13	Dehydrocafestol	CC12CCC3=C(C1CCC45C2CCC(C4)C(=C5)CO)C=CO3	0,315 (Antioxidant) 0,456 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)	0,021 (Antioxidant) 0,071 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)
14	Dehydro Kahweol	CC12C=CC3=C(C1CCC45C2CCC(C4)C(=C5)CO)C=CO3	0,339 (Antioxidant) 0,534 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)	0,018 (Antioxidant) 0,047 (Anti inflammatory) - (Antithrombotic) - (Antipyretic)

Table 2. Compound prediction results retrieved from the PASS Server

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Table 3. ADMET results

Number	Name	GI absorption	BBB permeation	P-gp substrate	CYP-inhibitor	Skin permeation	Lipinski score	Bioavailability Score	Synthetic accessibility
1	4,5-Di-O-caffeoylquinic acid	Low	No	Yes	No	-8.37 cm/s	No (3 violation)	0.11	4.86
2	Dehydro Kahweol	High	Yes	Yes	Yes (CYP2C9)	-5.15 cm/s	Yes	0.55	5.92
3	5-O Caffeoylquinic acid	Low	No	No	No	-8.76 cm/s	Yes (1 violation)	0.11	4.16
4	5-O Feruloylquinic acid	Low	No	No	No	-8.62 cm/s	Yes	0.11	4.25
5	5-P Coumaroylquinic acid	Low	No	No	No	-8.41 cm/s	Yes	0.56	4.07
6	Kahweol	High	Yes	Yes	Yes (CYP2D6)	-5.80 cm/s	Yes	0.55	6.01
7	4-P-Coumaroyl quinic acid	Low	No	No	No	-8.41 cm/s	Yes	0.56	4.04
8	Quercetin	High	No	No	Yes (CYP1A2)	-7.05 cm/s	Yes	0.55	3.23
9	4-O Feruloylquinic acid	Low	No	No	No	-8.62 cm/s	Yes	0.11	4.22
10	3-O Feruloylquinic acid	Low	No	No	No	-8.62 cm/s	Yes	0.11	4.25
11	16-O Methyl Kahweol	High	Yes	Yes	Yes (CYP2D6)	-5.51 cm/s	Yes	0.55	6.08

I.2 Figure

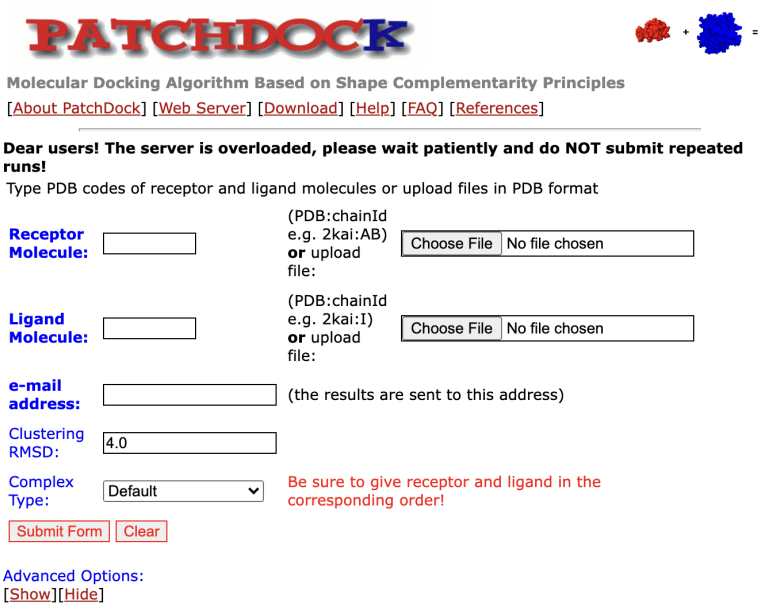

Figure 1. The PatchDock docking web service's user interface.

Receptor	Ligand	Complex Type	Clustering RMSD	User e-mail	Receptor Site	Ligand Site	Distance Constraints
4q7p.pdb	3mep.pdb	Default	4.0	muhammad.arief@student.i3l.ac.id	-	-	-

Solution No	Score	Area	ACE	Transformation	PDB file of the complex
1	2152	237.60	-43.03	2.34 -0.43 -2.47 28.36 -5.39 23.04	result.1.pdb
2	1938	207.90	-105.89	2.38 0.92 2.01 2.86 -9.64 36.10	result.2.pdb
3	1858	215.00	-16.38	-1.93 -0.11 0.99 19.08 -14.12 24.62	result.3.pdb
4	1854	193.70	-86.75	2.08 0.63 -0.60 8.98 2.60 33.02	result.4.pdb
5	1844	203.80	-85.97	-1.72 0.28 -0.16 8.86 -19.14 17.01	result.5.pdb
6	1830	210.50	-73.01	0.36 0.10 -1.49 26.75 -7.24 6.78	result.6.pdb
7	1808	196.50	-43.16	-2.36 -0.34 0.92 17.06 -10.57 32.11	result.7.pdb
8	1802	198.20	-52.18	-1.01 0.70 1.20 26.23 -3.27 5.31	result.8.pdb
9	1798	206.20	-70.14	-0.55 -0.33 -2.57 19.78 2.70 11.26	result.9.pdb
10	1778	217.30	19.87	-0.13 0.50 -1.45 13.37 -12.81 -4.92	result.10.pdb
11	1772	203.70	-111.96	-1.96 0.82 0.26 27.98 -11.66 14.77	result.11.pdb
12	1760	186.60	-46.21	-0.59 0.20 -0.84 23.13 -8.43 -6.72	result.12.pdb
13	1756	209.50	-64.65	-2.80 -0.21 1.30 8.50 9.14 29.24	result.13.pdb
14	1714	197.20	-83.05	2.23 -1.03 1.64 -4.70 12.07 14.77	result.14.pdb
15	1708	189.60	-54.95	-2.25 0.22 2.58 2.09 7.38 33.71	result.15.pdb
16	1692	183.30	-33.84	-2.18 -1.03 -1.66 -3.43 -13.03 14.43	result.16.pdb
17	1682	201.30	-86.87	2.24 -1.33 -2.36 28.69 -11.27 16.37	result.17.pdb
18	1672	173.40	-24.16	2.00 0.46 0.38 -2.10 10.95 28.15	result.18.pdb
19	1652	195.60	-77.59	-2.34 -0.59 -2.04 -4.52 -2.80 28.26	result.19.pdb
20	1628	197.90	5.12	-0.82 0.09 0.13 16.40 -14.86 -3.50	result.20.pdb

show next 20 »»

Figure 2. The docking results shown from the PatchDock results page.