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Research article

Quantum chemical calculations on calcium oxalate and dolichin A and their binding efficacy to lactoferrin: An *in silico* study using DFT, molecular docking, and molecular dynamics simulations

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Table 1S. Mulliken atomic charges in (a) calcium oxalate and (b) dolichin A.

	Calcium oxalate		Dolichin A
Atoms	Mulliken Charge	Atoms	Mulliken Charge
O1	−0.487047	C1	0.053470
O2	−0.296518	C2	−0.207623
O3	−0.296685	C3	0.413936
O4	−0.487442	C4	1.106301
C5	0.159859	C5	−0.062279
C6	0.159815	C6	−0.502636
Ca7	1.248018	C7	−0.636732
		C8	−0.270781
		C9	−0.250321
		C10	−0.417233
		C11	−0.053538
		C12	−0.390965
		O13	−0.033183
		O14	−0.079191
		C15	−0.003285
		C16	0.245952
		C17	−0.223714
		C18	−0.753872
		C19	−0.358895
		C20	0.598209
		C21	−0.677274
		C22	−0.635403
		O23	−0.318311
		H24	0.273306
		O25	−0.277165
		H26	0.368357
		O27	−0.213114
		H28	0.261699
		H29	0.224813
		H30	0.232017
		H31	0.157836
		H32	0.209333
		H33	0.135759
		H34	0.180275
		H35	0.185616
		H36	0.210720
		H37	0.144818
		H38	0.245670
		H39	0.227868
		H40	0.200825
		H41	0.152421
		H42	0.125692
		H43	0.151573
		H44	0.109251
		H45	0.149797

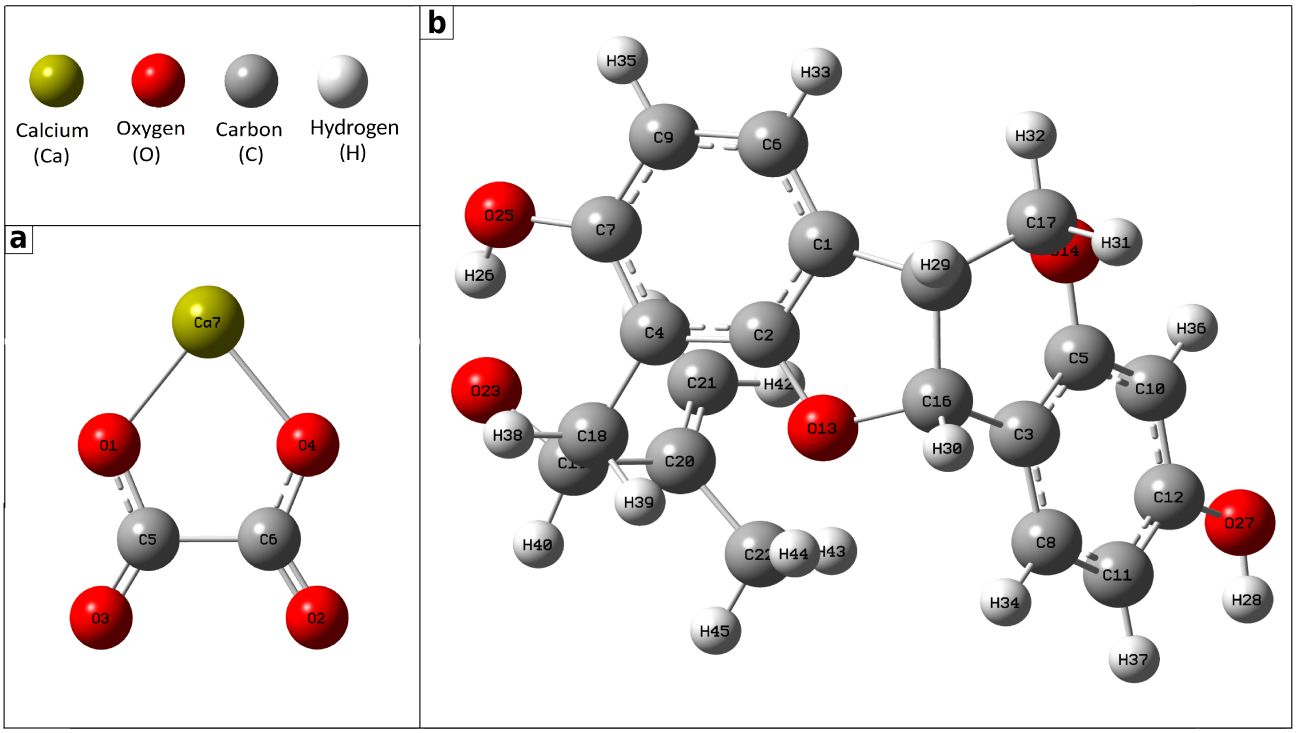

Figure 1S. Optimized structures of (a) calcium oxalate and (b) dolichin A.

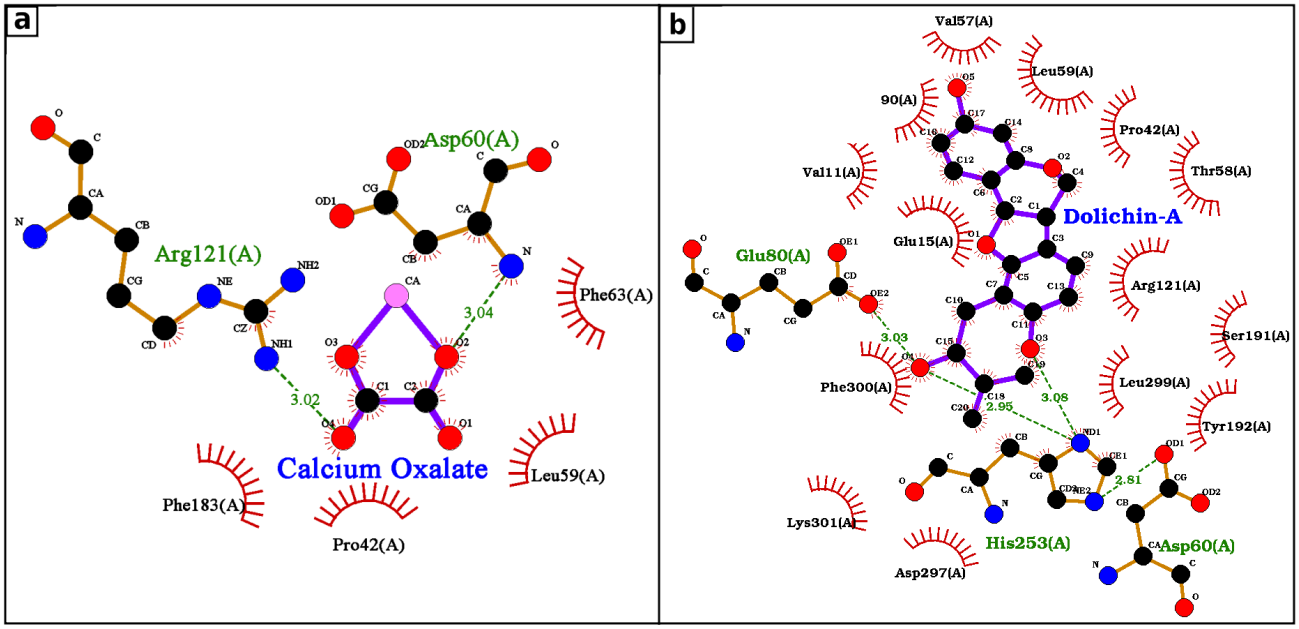

Figure 2S. Interactions of lactoferrin with (a) calcium oxalate and (b) dolichin A. Nonbonded residues are represented by spoked arcs, hydrogen-bonded residues are represented by green color, ligand name by blue color, and the hydrogen bond is represented by green-dotted lines.

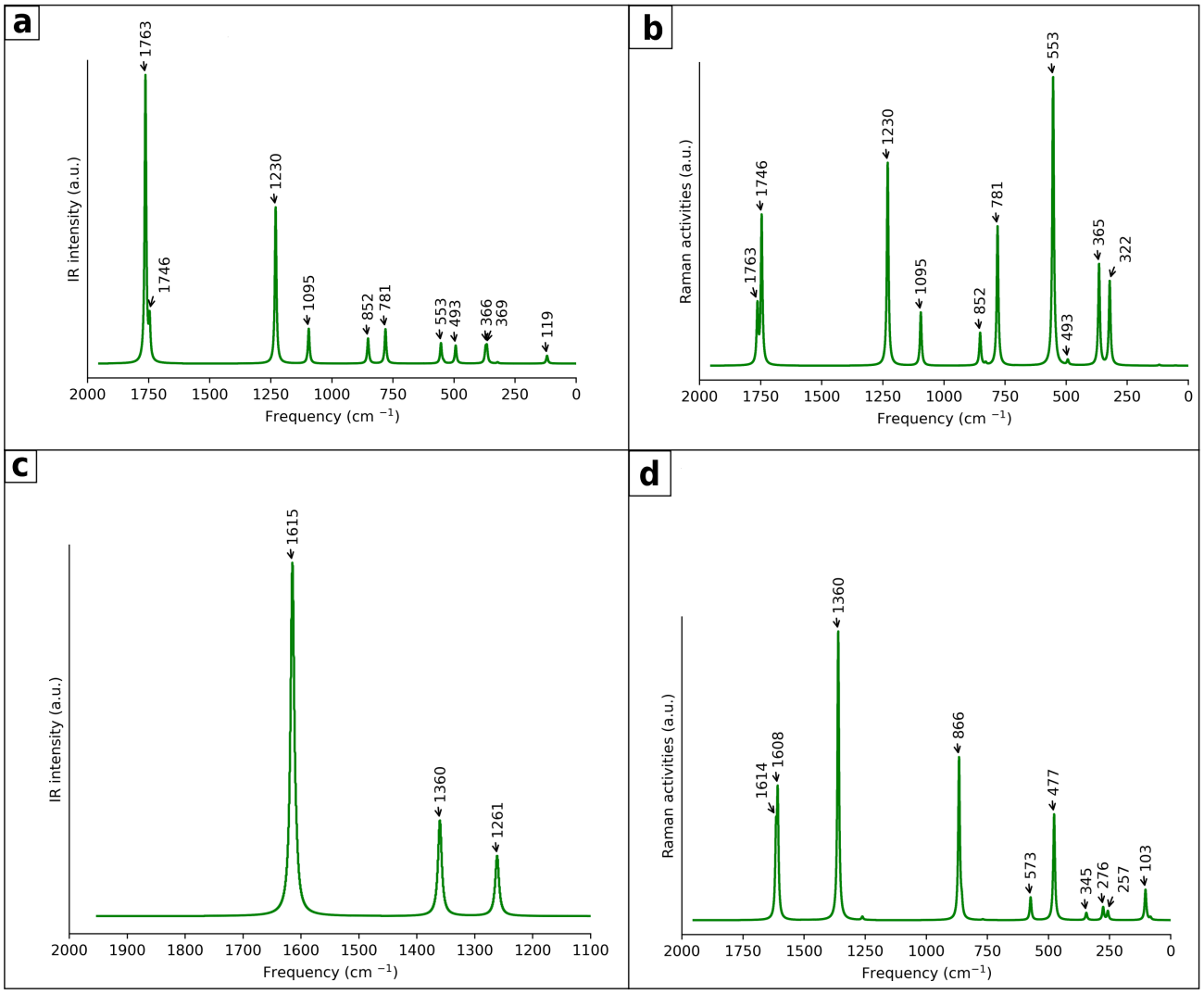

Figure 3S. Calculated (a) IR spectra (b) Raman spectra of calcium oxalate in the gas phase. Calculated (c) IR spectra (d) Raman spectra of calcium oxalate in the water solvent.

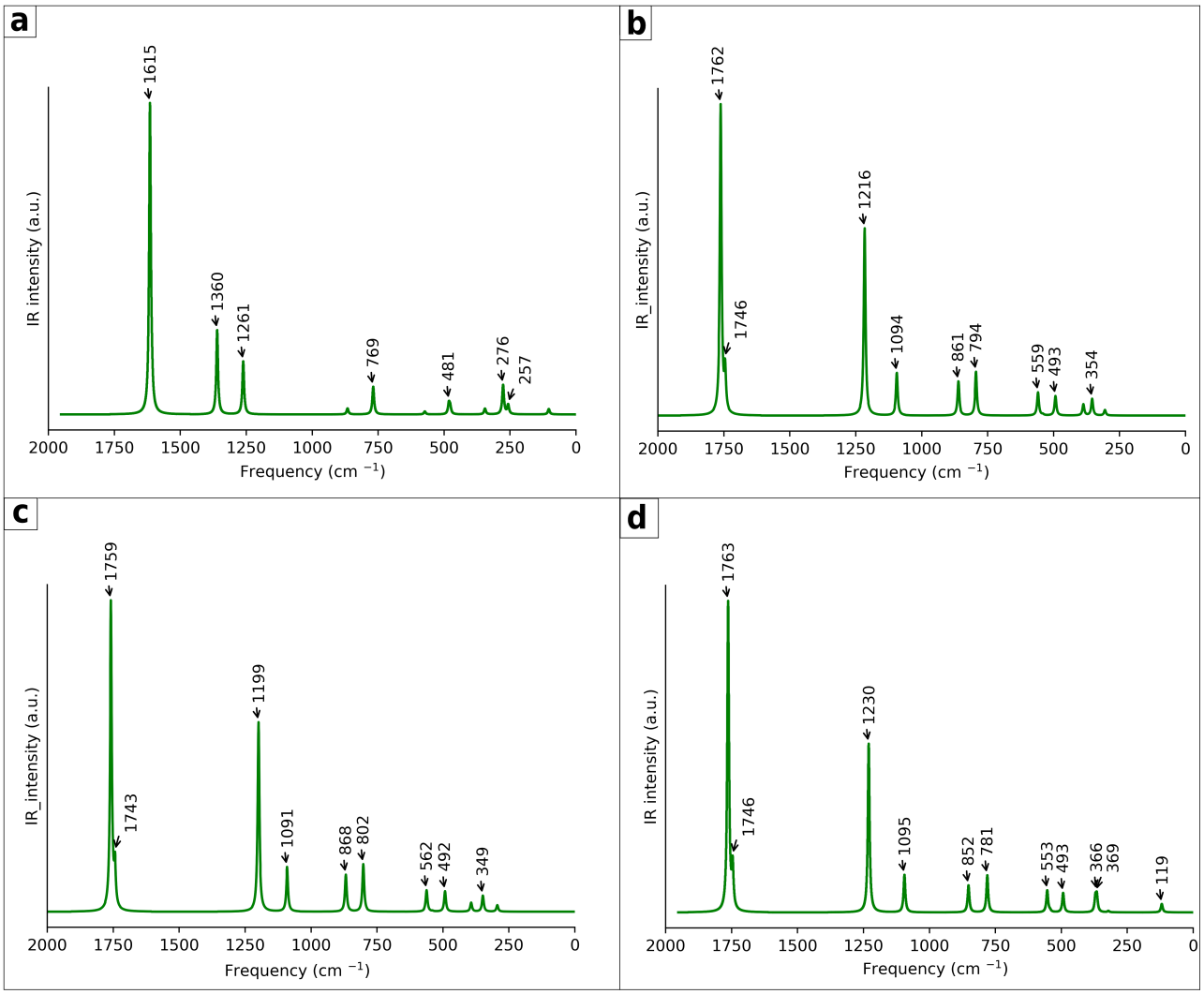

Figure 4S. Calculated IR spectra of calcium oxalate by DFT method at B3LYP/6-311++G(d,p) level of calculation (a) water solvent (b) CCL4 solvent (c) THF solvent and (d) gas phase.

Table 2S. Thermodynamic parameters at different temperatures.

Temperature (K)	Thermal Energy (kcal/mol)	Heat Capacity (cal/mol-K)	Entropy (cal/mol-K)
50	16.390	8.462	56.042
100	16.865	10.609	63.917
150	17.462	13.324	69.528
200	18.197	16.031	74.308
250	19.061	18.456	78.595
300	20.037	20.557	82.513
350	21.111	22.362	86.127
400	22.269	23.913	89.483
450	23.499	25.249	92.612
500	24.791	26.403	95.543

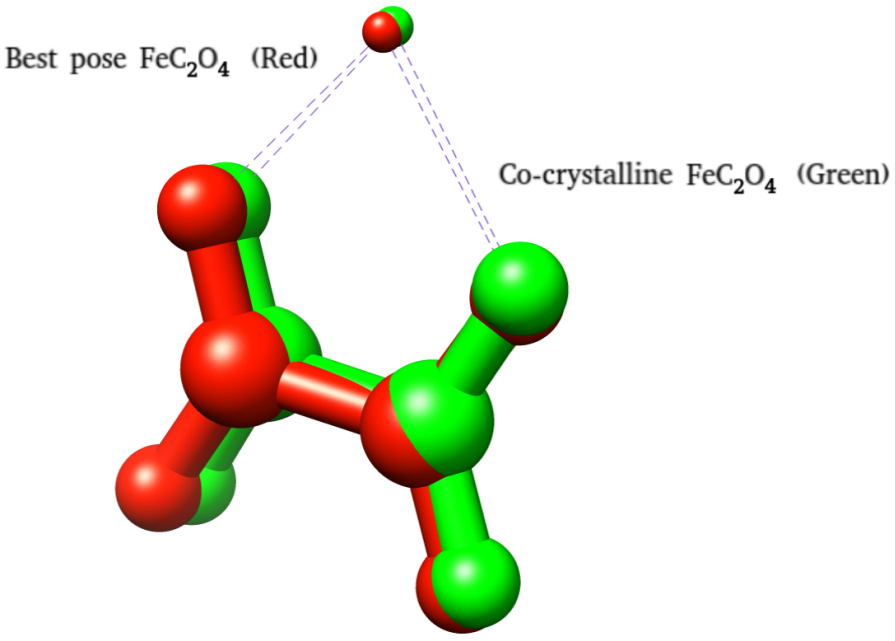

Figure 5S. Co-crystalline ligand of lactoferrin in 1BKA.PDB (green) and best pose of co-crystalline ligand after molecular docking in the vicinity of original position (red) in the lactoferrin.

Table 3S. Binding energy of lactoferrin with different chemicals found in *M. uniflorum* using PyRx.

Chemical compounds	Binding energy (kcal/mol)
Dolichin A	**−9.3**
Dolichin B	−9.1
Stigmasterol	−8.4
Stigmast5en3ol	−8.3
Vit-E	−8.1
Isolongifolol acetate	−8
Ethyl hexopyranoside	−6.8
Hexatriacontane	−6.4
Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl) ethyl ester	−6.4
Ethyl L-phenylalanate	−6.2
9-Methyl-10,12-hexadecadien-1-ol acetate	−6.2
3-Cyclopentylpropionic acid, 2-diethylaminoethyl ester	−6.2
9-12,Octadecadienoic acid	−6.1
hexadeconoic acid	−6
Heneicosane	−5.9
Heptadecanoic acid	−5.8
Hexadecanoic acid	−5.7
(R)-(-)-14-Methyl-8-hexadecyn-1-ol	−5.6
Eicosane	−5.5
3-Methylheptadecane	−5.4
N-(2-Hydroxyethyl)octanamide	−5.4
Benzeneacetaldehyde	−5.1
Benzeneethanamine	−5
dioxapentacyclo[20.8.1.17,16.01,22.07,16] dotriacontane	−0.3

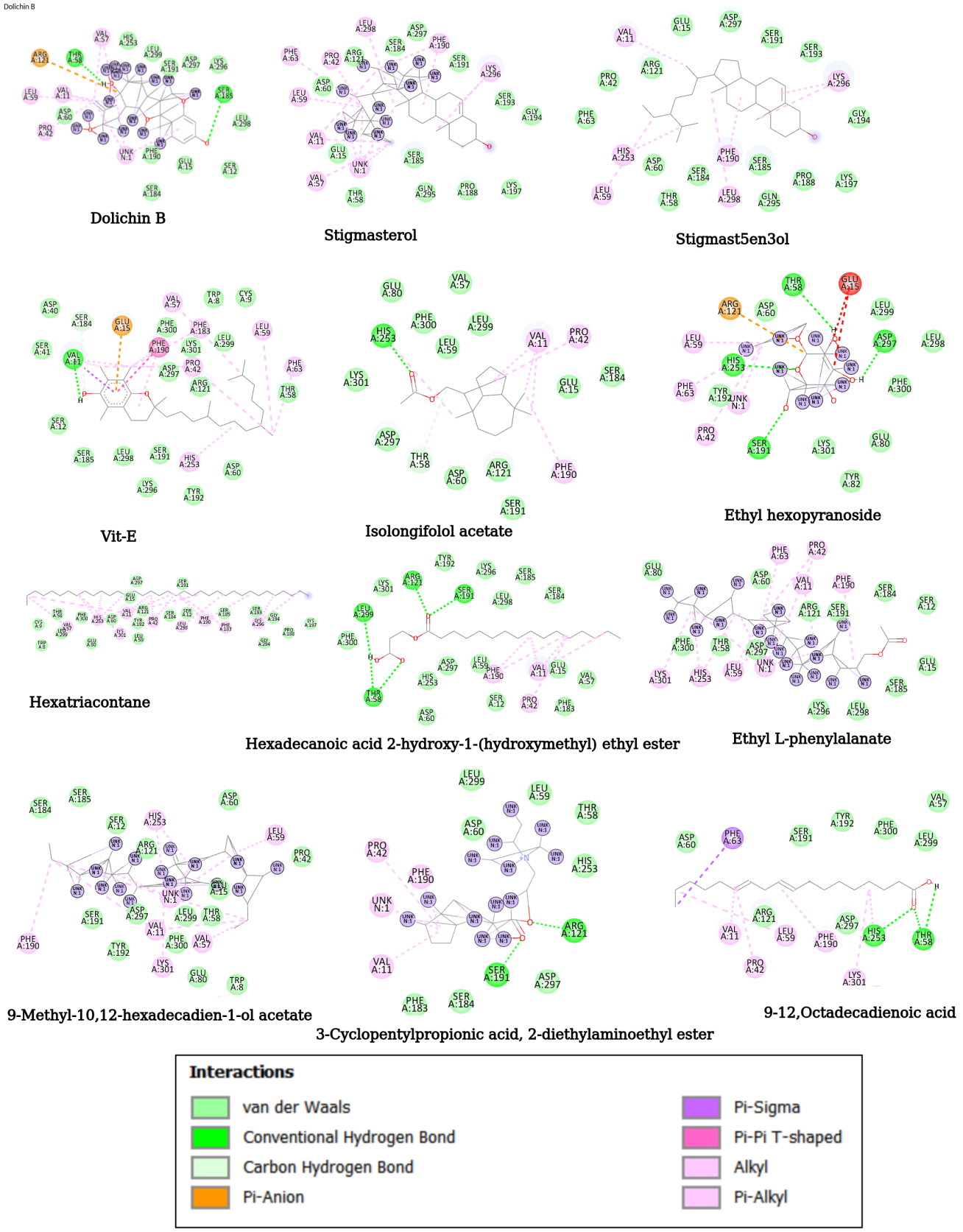

Figure 6S. Two-dimensional visualization of the docking images of lactoferrin with different chemicals found in *M. uniflorum.*

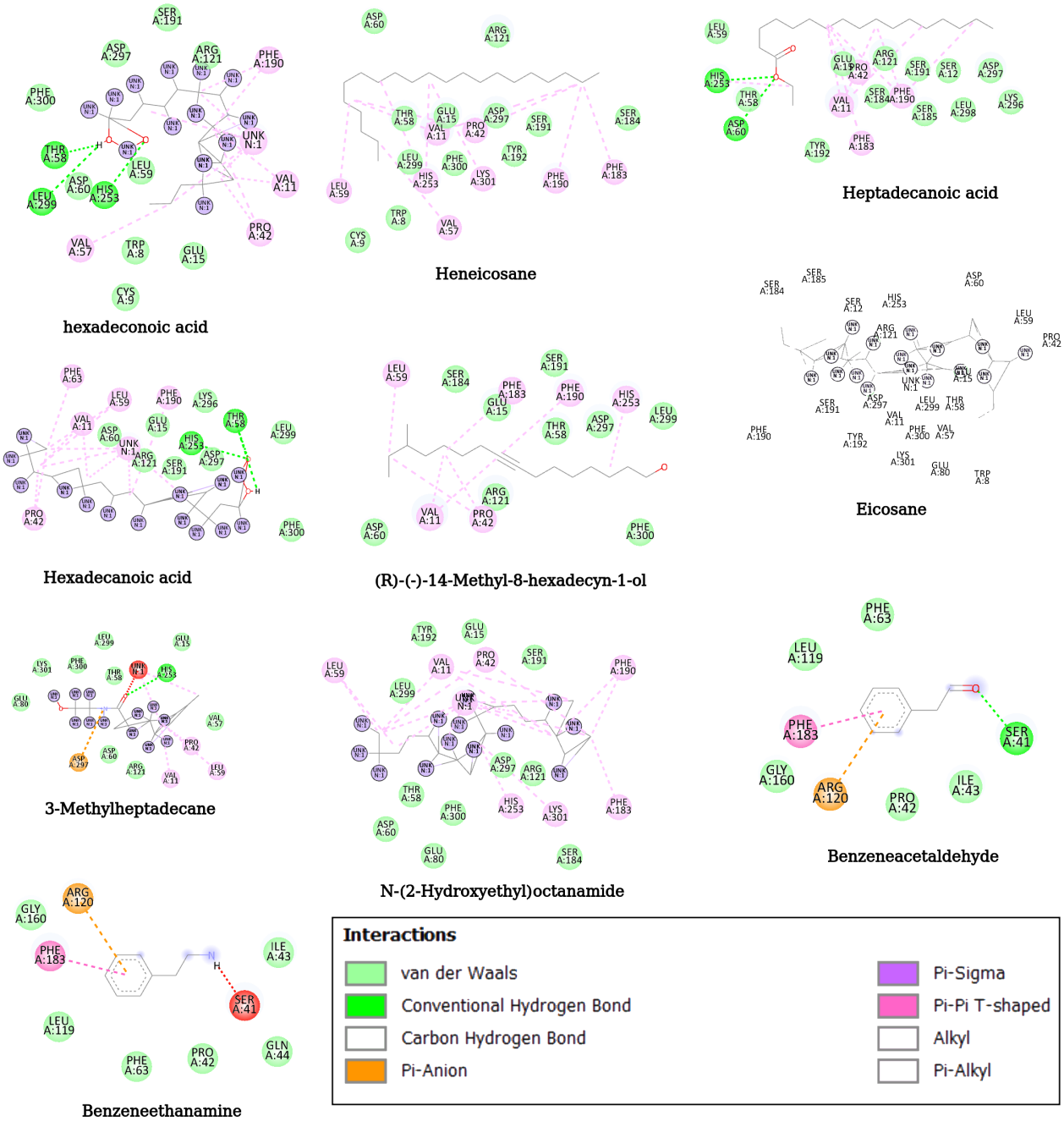

Figure 7S. Two-dimensional visualization of the docking images of lactoferrin with different chemicals found in *M. uniflorum.*

Table 4S. RMSFs values for residues in Complex and Apo.

Residues number	RMSF (Complex form) (Å)	RMSF (Apo form) (Å)
11	1.01	1.01
15	0.97	1.04
42	1.03	0.99
57	0.89	0.71
59	0.67	0.56
60	0.61	0.56
63	0.73	0.70
80	0.79	0.67
92	0.92	0.88
117	0.88	0.81
121	0.56	0.73
122	0.56	0.66
123	0.63	0.70
124	0.63	0.82
183	1.64	1.53
190	1.02	1.19
191	0.83	1.02
192	0.87	1.01
253	0.70	0.59
297	0.83	1.16
299	0.84	0.84
300	0.75	0.77
301	0.72	0.75

Table 5S. The physicochemical properties of dolichin A. Here, molecular weight (MW) in g/mol, molar refractivity (MR) and total polar surface area (TPSA) in $Å^2$.

MW	molecular fomula	Heavy atoms	Aromatic heavy atoms	Fraction Csp3	Rotatable bonds	H-bond acceptors	H-bond donors	MR	TPSA
340.37	C20H20O5	25	12	0.3	3	5	3	93.58	79.15

Table 6S. Water solubility properties of Dolichin A.

ESOL Log S	ESOL Solubility (mg/ml)	ESOL Class	Ali (Log S)	Ali Solubility (mg/ml)	Ali Class	Silicos-IT (LogSw)	Silicos-IT Solubility (mg/ml)	Silicos-IT class
-4.10	0.027	Moderately soluble	-4.49	0.011	Moderately soluble	-4.29	0.02	Moderately soluble

Table 7S. Lipophilicity properties of Dolichin A.

iLog P	XLog P3	WLog P	MLog P	Silicos-IT Log P	Consensus Log P
2.64	3.16	2.86	1.9	3.29	2.77

Table 8S. Pharmacokinetics properties of Dolichin A.

GI absorption	BBB permeant	Pgp substrate	log Kp (cm/s)
High	No	Yes	-6.13

Table 9S. Druglikeness properties of Dolichin A.

Lipinski violations	Ghose violations	Veber violations	Egan violations	Muegge violations	Bioavailability Score
0	0	0	0	0	0.55

Table 10S. Toxicity properties of Dolichin A.

Carcinogenicity	Hepatotoxicity	Nephrotoxicity	Mutagenicity	Immunotoxicity	Predicted LD50	Predicted Toxicity class
inactive	inactive	inactive	inactive	active	500mg/kg	4

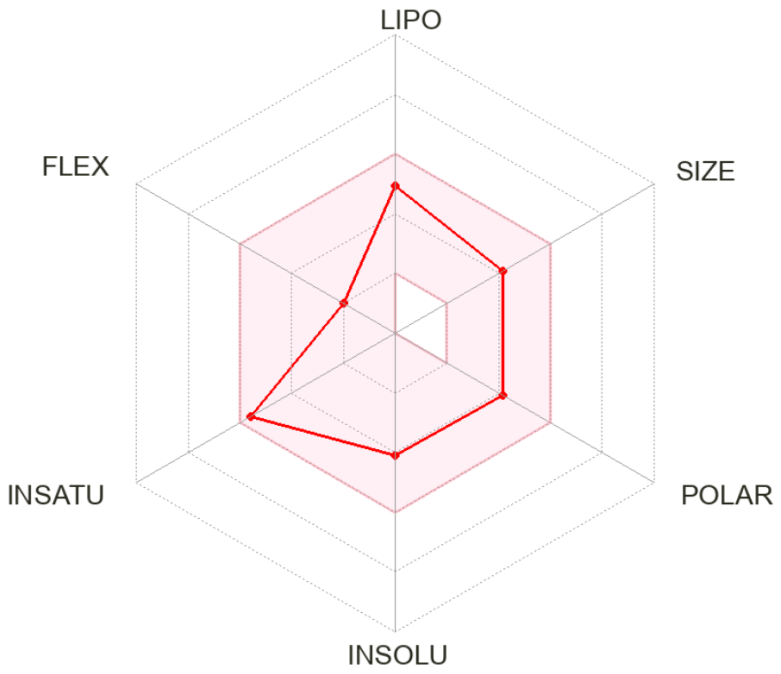

Figure 8S. Bioavailabiity radar for dolichin A using SwissADME. Pink region represents the optimal range for each physicochemical properties for druglikeness.

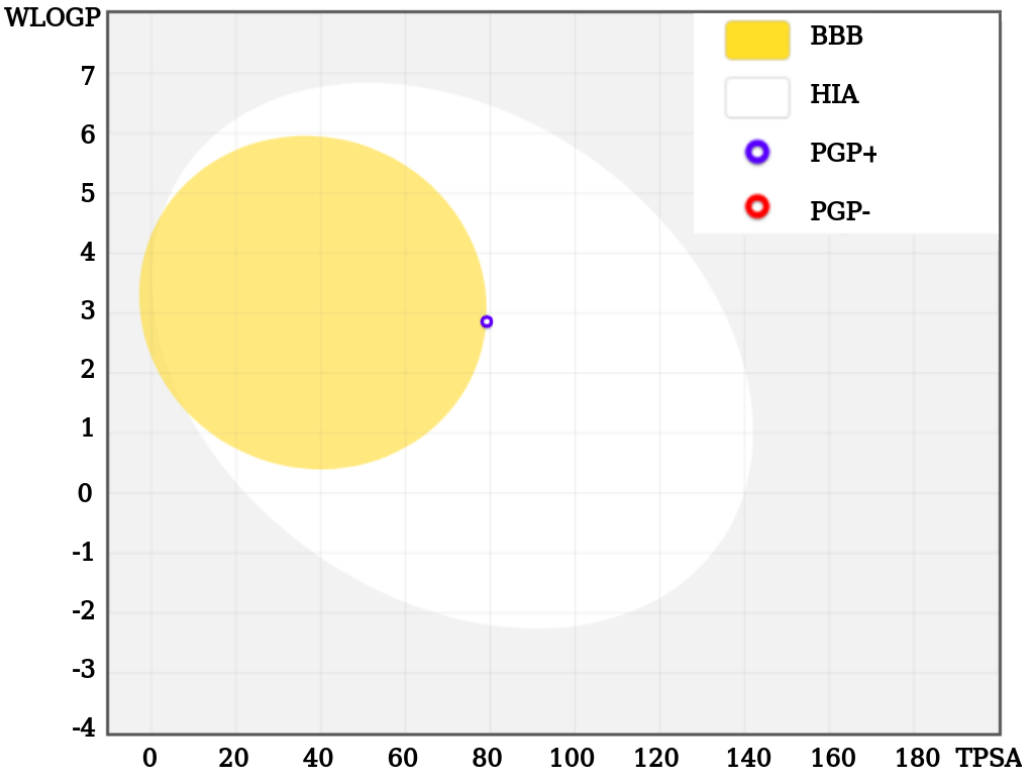

Figure 9S. BOILED-Egg model of dolichin A using SwissADME.