Antioxidant, Antimicrobial, Antidiabetic, Antiglycation, and Biocompatibility Potential of Aqueous *Zingiber officinale* Rhizome (AZOME) Extract

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Supplementary Info

Supp. Table 1: Chemical characterization (FT-IR) analysis of raw ZOME and AZOME extract.

S. No.	Wave number (cm^{-1}) in Raw ZOME	Wave number (cm^{-1}) in AZOME extract	FTIR functional group	Type of bond
1.	3270.57	3274.29	Alcohol, secondary amide	O-H stretch, N-H stretching
2.	2933.41	2928.19	Alkane	$-CH_2$ stretching
3.	1640.69	1644.92	Primary amines, Alkene, ketone water	N-H bending, C=C stretching, C=O, H-O-H
4.	1149.25	1150.78	Alcohol, amine	O-H stretching, C-N
5.	1077.07	1076.90	Amines, alcohol	C-N stretching, O-H
6.	995.01	996.68	Alkenes	=C-H
7.	932.89	931.65	Alkenes	=C-H
8.	858.54	859.99	Ether	C-O stretching

Supp. Table 2: Zone of inhibition for standard microbial strains by ZOME extract and Standard drug.

Zone of inhibition in millimeters (mm)												
Standard strains	**AZOME extract (µg/mL)**						**Standard drug (µg/mL)**					
	5	**25**	**50**	**100**	**250**	**500**	**5**	**25**	**50**	**100**	**250**	**500**
E. coli [MTTC 443]	-	13	15	16	17	21	-	20	23	28	28	28
P. aeruginosa [MTCC 1688]	-	14	15	17	19	21	-	20	23	24	26	27
S. aureus [MTCC 96]	-	13	14	16	18	20	-	17	19	21	22	22
S. pyogenes [MTCC 442]	-	12	14	16	18	20	-	16	19	21	21	21
C. albicans [MTCC 227]	-	13	14	16	19	21	-	18	21	22	22	24

Supp. Table 3: Minimum Inhibitory Concentration of AZOME extract and standard bactericidal drugs toward standard strains.

Minimum Inhibitory Concentration (MIC) in µg/mL					
Standard strains		***E. coli*** [MTTC 443]	***P. aeruginosa*** [MTCC 1688]	***S. aureus*** [MTCC 96]	***S. pyogenes*** [MTCC 442]
	AZOME extract	100	125	100	125
Antibacterial standard drugs	**Gentamycin**	0.05	1	0.25	0.5
	Ampicillin	100	100	250	100
	Chloramphenicol	50	50	50	50

	Ciprofloxacin	25	25	50	50
	Norfloxacin	10	10	10	10

Supp. Table 4: Minimum Inhibitory Concentration of AZOME extract and standard fungicidal drugs toward standard strains.

Minimum Inhibitory Concentration (MIC) in µg/mL				
Standard strains		***C. albicans*** [MTCC 227]	***A. niger*** [MTCC 282]	***A. clavatus*** [MTCC 1323]
	AZOME extract	100	125	100
Antifungal standard drugs	**Nystatin**	100	100	100
	Griseofulvin	500	100	100

Supp. Table 5: Qualitative phytochemical investigation of secondary metabolites in AZOME extract.

S. No.	Constituents (Secondary metabolites)	Presence of secondary metabolites in AZOME extract Present = + Absent = -
1.	Saponins	+
2.	Terpenoids	-
3.	Reducing Sugar	+
4.	Molish test (carbohydrate)	+
5.	Phenols	+
6.	Alkaloids	+
7.	Amino acids	+

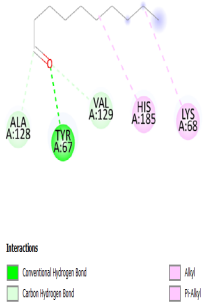
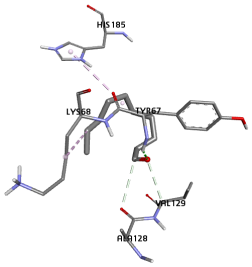
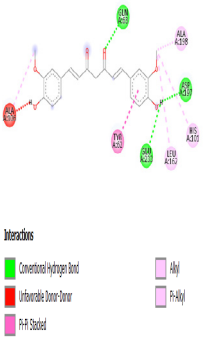
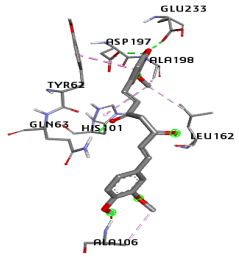
Supp. Table 6: Phytochemicals derived from AZOME extract with available standard drug and their binding affinity towards targeted antidiabetic proteins on different docking platforms (CB-Dock2, PyRx, and AutoDock Tools) with mentioned **Binding affinity** (kcal/mol) and **Inhibition constant** (mM/µM/nM).

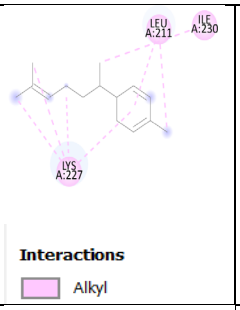
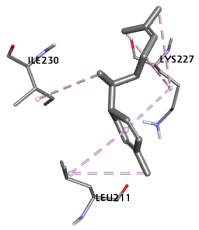
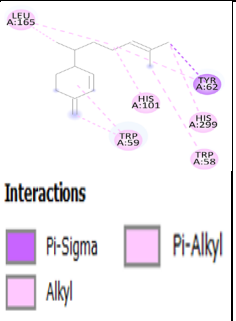
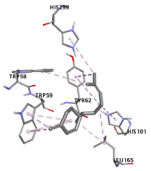
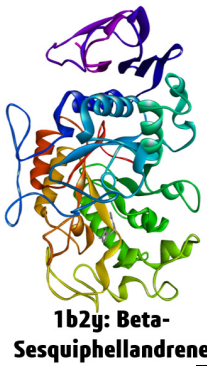
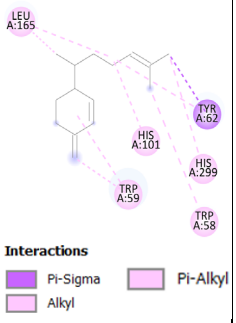
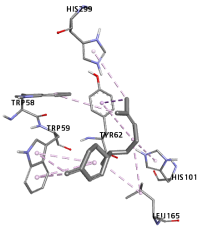
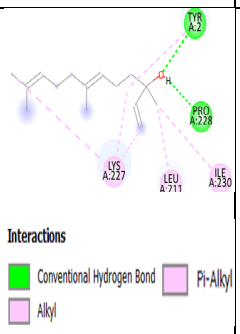
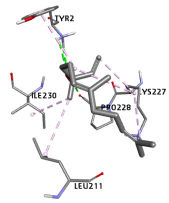
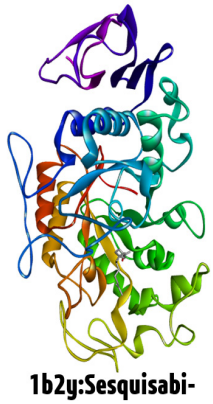
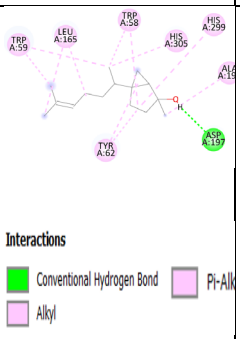
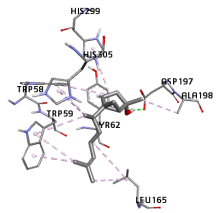
S. No.	Phytochemical compound in AZOME extract	PubChem CID	CB-DOCK2			PyRx			Auto Dock Tools		
	Ligands		Targeted Antidiabetic Protein docked on different docking tools: 1B2Y= α-amylase; 3TOP= α-glucosidase; 7WSM= GLUT4								
			1B2Y	3TOP	GLUT 4	1B2Y	3TOP	7wsm		1B2Y	3TOP	GLUT4
		Binding Affinity (kcal/mol) and Inhibition constant (Ki) (mM/µM/nM)										
1.	Decanal	8175	-4.5	-5.5	-4.7	-4.3	-5.0	-4.8		-2.89 & 7.60 mM	-3.41 & 3.19 mM	-3.86 & 1.48 mM
2.	Curcumin	969516	-8.6	-8.7	-9.0	-7.8	-7.6	-8.5		-6.24 & 26.88 uM	-6.24 & 26.50 uM	-5.67 & 69.79 uM
3.	Zingiberene	92776	-6.1	-7.8	-6.7	-6.0	-7.8	-6.2		-5.02 & 207.80 uM	-5.15 & 169.24 uM	-5.12 & 176.38 uM
4.	Beta-Bisabolene	10104370	-6.5	-7.3	-6.8	-7.3	-7.0	-7.1		-5.53 & 88.25 uM	-6.02 & 38.74 uM	-6.06 & 36.22 uM
5.	Beta-Sesquiphellandrene (SQP)	519764	-6.1	-7.6	-6.5	-6.2	-6.2	-6.1		-4.86 & 275.92 uM	-5.30 & 129.45 uM	-5.68 & 68.50 uM
6.	Trans-Nerolidol	5284507	-6.2	-7.1	-6.5	-6.4	-5.3	-6.1		-3.39 & 3.28 mM	-3.76 & 1.76 mM	-4.11 & 966.02 uM
7.	Sesquisabinene Hydrate	20055539	-7.0	-7.3	-7.0	-6.8	-6.0	-6.7		-5.04 & 200.63 uM	-5.54 & 87.03 uM	-4.84 & 281.36 uM
8.	1,2-Benzenedicarboxylic acid, diethylester	6781	-5.8	-6.5	-6.1	-5.8	-4.9	-6.1		-3.65& 2.12 mM	-4.54 & 469.54 uM	-3.58 & 2.38 mM
9.	Alpha-Bisabolol	10586	-7.3	-7.4	-7.4	-7.3	-6.9	-7.5		-4.70 & 356.42 uM	-5.09 & 187.10 uM	-5.25 & 142.85 uM
10.	Zingiberenol	13213649	-7.2	-7.6	-7.1	-7.0	-6.9	-7.1		-5.03 & 204.84 uM	-5.05 & 198.79 uM	-5.17 & 162.47 uM
11.	Zingerone	31211	-6.4	-7.1	-6.3	-6.4	-7.1	-6.4		-3.62 & 2.20 mM	-4.50 & 504.92 uM	-4.05 & 1.08 mM
12.	Beta-Selinenol or β-eudesmol	91457	-8.0	-7.1	-7.7	-8.0	-6.9	-7.8		-6.17 & 30.16 uM	-6.83 & 9.79 uM	-6.62 & 14.01 uM
13.	Carotol	442347	-7.0	-7.2	-7.3	-7.5	-6.6	-7.7		-5.41 & 107.94 uM	-6.05 & 36.64 uM	-6.16& 30.44 uM
14.	Caryophyllene oxide	1742210	-7.9	-7.3	-7.5	-7.9	-6.1	-7.2		-5.76 & 60.02 uM	-6.20 & 28.43 uM	-6.72 & 11.82 uM

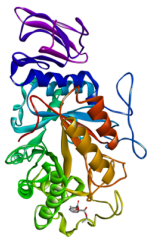
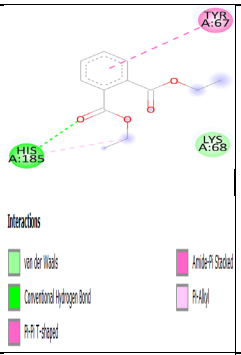
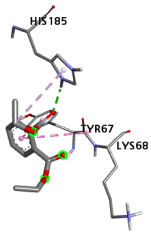
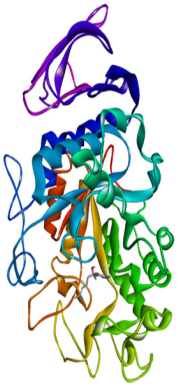
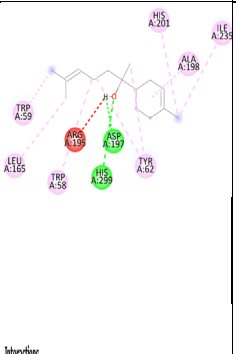
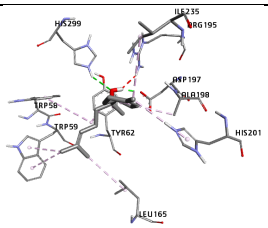
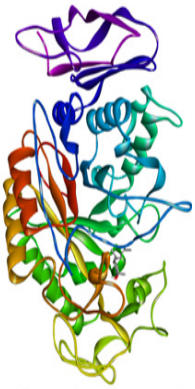
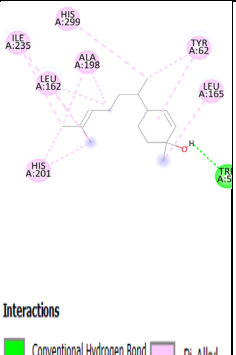
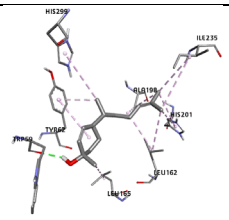
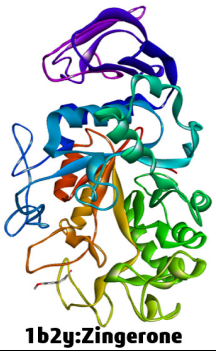
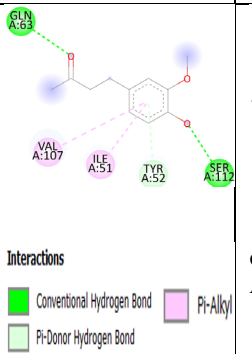
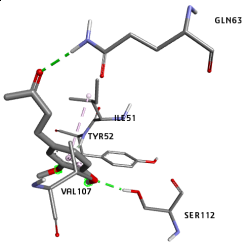
15.	Farnesol	445070	-6.3	-7.1	-6.7	-6.4	-5.8	-6.6		-3.98 & 1.22 mM	-4.04 & 1.09 mM	-4.01 & 1.14 mM
16.	4-(l-Adamantyl) phenyl acetate	523825	-5.8	-6.5	-6.4	-5.8	-6.6	-6.5		-3.80 & 1.64 mM	-4.32 & 678.17 uM	-4.41 & 588.23 uM
17.	Alpha-curcumene	92139	-6.5	-7.5	-6.8	-6.4	-7.5	-6.8		-4.57 & 444.60 uM	-4.80 & 302.42 uM	-5.19 & 158.07 uM
18.	Palmitic acid	985	-5.1	-5.8	-5.4	-5.1	-7.1	-6.4		-2.44 & 16.18 mM	-1.70 & 56.78 mM	-2.51 & 14.43 mM
19.	Alpha-Bergamotene	86608	-6.6	-7.1	-6.6	-6.8	-6.8	-6.3		-5.13 & 172.40 uM	-5.81 & 55.27 uM	-5.33 & 123.83 uM
20.	Franesyl Acetate	638500	-6.3	-7.1	-7.2	-6.2	-6.5	-6.4		-3.86 & 1.49 mM	-4.93 & 244.46 uM	-4.62 & 409.95 uM
21.	Linoleic acid	5280450	-5.9	-6.2	-5.7	-5.7	-6.1	-5.8		-2.74 & 9.85 mM	-2.88 & 7.69 mM	-3.32 & 3.66 mM
22.	Cis-Vaccenic acid	5282761	-5.5	-6.1	-5.7	-5.5	-5.1	-5.6		-1.84 & 45.02 mM	-2.28 & 21.32 mM	-2.56 & 13.36 mM
23.	Geranylgeraniol	5281365	-7.1	-7.1	-7.0	-5.8	-6.6	-6.8		-4.06 & 1.06 mM	-3.64 & 2.16 mM	-4.36 & 641.94 uM
24.	Oleic acid amide	445639	-5.5	-6.2	-5.8	-5.4	-5.2	-5.6		-3.18 & 4.68 mM	-1.99 & 35.00 mM	-3.97 & 1.22 mM
25.	Cetyl amide	69421	-5.4	-6.2	-5.6	-4.7	-5.1	-5.6		-2.99 & 6.46 mM	-2.44 & 16.26 mM	-2.95 & 6.91 mM
26.	2-Butanone,4-(4-hydroxy-3-methoxy phenol)	129849736	-6.2	-6.7	-6.3	-6.1	-6.6	-6.3		-3.67 & 2.04 mM	-3.69 & 1.97 mM	-4.00 & 1.16 mM
27.	Notrachelogenin	479756	-7.7	-8.9	-8.8	-7.6	-8.0	-9.3		-3.83 & 1.57 mM	-3.65 & 2.12 mM	-4.14 & 922.68 uM
28.	Shogaol	5281794	-7.0	-7.4	-7.0	-6.3	-7.0	-7.1		-3.80 & 1.64 mM	-4.28 & 725.28 uM	-4.36 & 638.49 uM
29.	Gingerol	442793	-6.6	-7.0	-7.1	-6.2	-7.2	-7.1		-2.69 & 10.60 mM	-3.75 & 1.80 mM	-3.46 & 2.90 mM
30.	Beta-Phellandrene	11142	-6.0	-6.5	-5.6	-5.8	-6.5	-5.9		-4.50 & 500.65 uM	-5.20 & 154.72 uM	-5.05 & 197.58 uM
31.	Geraniol	637566	-5.8	-6.2	-5.6	-5.7	-5.9	-5.4		-3.78 & 1.71 mM	-3.65 & 2.12 mM	-4.12 & 953.29 uM
32.	Ar-curcumene or alpha-curcumene	92139	-6.5	-7.5	-6.8	-6.4	-7.3	-6.9		-4.57 & 444.60 uM	-4.80 & 302.42 uM	-5.19 & 158.07 uM
33.	Vanillylacetone	31211	-6.4	-7.1	-6.3	-6.5	-6.5	-6.3		-3.61 & 2.27 mM	-4.50 & 504.92 uM	-4.05 & 1.08 mM

34.	Farnesene	5281516	-5.8	-6.9	-6.3	-5.5	-6.8	-5.7		-2.31 & 20.27 mM	-4.71 & 349.89 uM	-4.11 & 969.09 uM
35.	Aromadendrene Oxide	91753455	-7.9	-7.9	-7.6	-7.2	-6.4	-7.4		-6.33 & 22.92 uM	-5.71 & 65.20 uM	-6.21 & 27.99 uM
36.	Gamma-Sitosterol	457801	-9.3	-10.0	-9.8	-9.2	-9.1	-9.7		-6.79 & 10.61 uM	-5.89 & 48.35 uM	-7.48& 3.29 uM
	Standard Drugs											
37.	Metformin	4091	-5.3	-5.1	-5.2	-5.0	-5.3	-5.0		-5.60 & 77.96 uM	-6.66 & 13.20 uM	-3.92 & 1.33 mM
38.	Acarbose	41774	-8.1	-7.8	-8.6	-8.2	-8.0	-8.4		-1.57 & 70.70 mM	-0.65 & 334.99 mM	+0.96
39.	2-DGP (2-deoxyglucose-6-phosphate)	108108	-5.9	-6.1	-5.7	-5.6	-5.5	-5.7		+0.56	+0.11	+0.44

Supp. Table 7: Targeted protein (1b2y; 3top & 7wsm) complexed with AZOME extract's phytocompounds (ligands) showing its interacting amino acids with atom residue including Grid box spacing (Å) are mentioned.

S. No.	**Ligands**	**Protein-Ligand Interaction**			
		3D confirmation	**2D confirmation**	**Ligand interaction with amino acids**	**Sapacing (Å) Center Grid Box**
1.	Decanal			 ALA A:128, TYR A:67, VAL A:129, HIS A:185, LYS A:68	x center= 17.989; y center= 21.315; z center= 49.322
2.	Curcumin			 ALA A:106; TYR A:62; GLU A:233; LEU A:162; HIS A:101; ASP A:197; ALA A:198; GLN A:63	x center= 17.982; y center= 21.783; z center= 49.349

3.	Zingiberene			 LEU A:211;ILE A:230;LYS A:227	x center= 17.989; y center= 21.315; z center= 49.322
4.	Beta-Bisabolene			 LEU A:165;TYR A:62;HIS A:101;HIS A:299;TRP A:59; TRP A:58	x center= 17.989; y center= 21.315; z center= 49.322
5.	Beta-Sesquiphellandrene (SQP)			 LEU A:165;TYR A:62;HIS A:101;HIS A:299;TRP A:59; TRP A:58	x center= 17.989; y center= 21.315; z center= 49.322
6.	Trans-Nerolidol			 TYR A:2;PRO A:228;LYS A:227;LEU A:211;ILE A:230	x center= 17.989; y center= 21.315; z center= 49.322
7.	Sesquisabinene Hydrate			 TRP A:59;LEU A:165;TRP A:58;HIS A:305;HIS A:299;ALA A:198;TYR A:62;ASP A:197	x center=17.989; y center= 21.315; z center= 49.322

8.	1,2-Benzenedicarboxylic acid, diethyl ester	 1b2y:1,2-Benzenedicarboxylic acid, diethylester		 TYR A:67; HIS A:185; LYS A:68	x center= 17.989; y center=21.315; z center=49.322
9.	Alpha-Bisabolol	 1b2y:Alpha-Bisabolol		 HIS A: 201; ALA A:198; ILE A:235; TRP A:59; LEU A:165; TRP A:58; ARG A:195; ASP A:197; HIS A:299; TYR A:62	x center= 17.989; y center= 21.315; z center= 49.322
10.	Zingiberenol	 1b2y:Zingiberenol		 ILE A:235;HIS A:299;LEU A:162;ALA A:198;HIS A:201;TYR A:62;LEU A:165;TRP A:59	x center= 17.989; y center= 21.315; z center= 49.322
11.	Zingerone	 1b2y:Zingerone		 GLN A:63;VAL A:107;ILE A:51:TYR A:52;SER A:112	x center= 17.989; y center= 21.315; z center= 49.322