

Consolidation of network and experimental pharmacology to divulge the antidiabetic action of *Ficus benghalensis* L. bark

Pukar Khanal, BM Patil

Department of Pharmacology and Toxicology, KLE College of Pharmacy Belagavi, KLE Academy of Higher Education and Research, Belagavi 590010, India

*Corresponding Authors:

Pukar Khanal, Department of Pharmacology and Toxicology, KLE College of Pharmacy Belagavi, KLE Academy of Higher Education and Research, Belagavi 590010, India, E-mail: pukarkhanal58@gmail.com

Prof. Dr. B. M. Patil, Department of Pharmacology and Toxicology, KLE College of Pharmacy Belagavi, KLE Academy of Higher Education and Research, Belagavi 590010, India, E-mail: drbmpatil@klepharm.edu, bmpatil59@hotmail.com

Table S1: Chief phytoconstituents reported in *Ficus benghalensis*

Compound ID	Phytoconstituents	Type of Compound	Molecular Formula	Molecular Weight	Drug likeness score
C1	3-O-trans-p-coumaroyltormentric acid	Triterpenoid	C ₃₉ H ₅₄ O ₇	634.8419	1.10
C2	Lupeol acetate	Triterpenoid	C ₃₂ H ₅₂ O ₂	468.7541	0.32
C3	Ursolic acid	Triterpenoid	C ₃₀ H ₄₈ O ₃	456.7003	0.65
C4	Alpinumisoflavone	Isoflavanones	C ₂₀ H ₁₆ O ₅	336.338	0.40
C5	Mucuisoflavone A	Isoflavone	C ₄₀ H ₃₂ O ₁₀	672.6761	0.94
C6	Mucuisoflavone B	Isoflavone	C ₄₀ H ₃₂ O ₁₀	672.6761	0.91
C7	Mucuisoflavone C	Isoflavone	C ₄₀ H ₃₄ O ₁₀	674.692	1.07
C8	Isoderrone	Isoflavone	C ₂₀ H ₁₆ O ₅	336.338	0.27
C9	Isowighteone	Isoflavone	C ₂₀ H ₁₈ O ₅	338.3539	0.97
C10	Wighteone	Isoflavone	C ₂₀ H ₁₈ O ₅	338.3539	1.23
C11	Apigenin	Flavone	C ₁₅ H ₁₀ O ₅	270.2369	0.77
C12	3',4',5,7-tetrahydroxy-3-methoxyflavone	Flavonol	C ₁₆ H ₁₂ O ₇	316.2623	0.93
C13	Kaempferol	Flavonol	C ₁₅ H ₁₀ O ₆	286.2363	0.77
C14	Cyclomorusin A	Flavonoid	C ₂₅ H ₂₂ O ₆	418.44	0.07
C15	4-methoxybenzoic acid	Organic molecular entity	C ₈ H ₈ O ₃	152.14732	-1.28
C16	3,4-dihydroxybenzoic acid	Organic molecular entity	C ₇ H ₆ O ₄	154.12	0.74
C17	Daucosterol	Steroid saponin	C ₃₅ H ₆₀ O ₆	576.8473	0.51
C18	Sitosterol	Phytosterols	C ₂₉ H ₅₀ O	414.7067	0.88
C19	Benjaminamide	Ceramide	C ₄₂ H ₈₃ NO ₅	682.1121	-1.02
C20	Psoralen	Furocoumarins	C ₁₁ H ₆ O ₃	186.1635	-0.93
C21	α -amyrin	Triterpene	C ₃₀ H ₅₀ O	426.39	0.09

Table S2: Prospective targets of bioactives from *Ficus benghalensis* related to diabetes

Protein ID	Short name of Protein	Full name of Protein
P1	ABCB1	ATP-binding cassette, sub-family B 1
P2	ADORA2A	Adenosine A2a receptor
P3	GAA	alpha-Glucosidase
P4	HTR2B	5-hydroxytryptamine receptor 2B
P5	HTR2C	5-hydroxytryptamine receptor 2C
P6	HTR4	5-hydroxytryptamine receptor 4
P7	HTR7	5-hydroxytryptamine receptor 7
P8	RXRA	Retinoid X receptor, alpha
P9	SI	Sucrase-isomaltase
P10	5HTR2A	5-hydroxytryptamine receptor 2A
P11	AKR1B1	Aldo-keto reductase family 1B1
P12	AKR1B10	Aldo-keto reductase family 1B10
P13	CDK6	Cyclin-dependent kinase 6
P14	CDKN2A	Cyclin-dependent kinase inhibitor 2A
P15	CYP19A1	Cytochrome P450, 19A1 (Aromatase)
P16	DHCR7	7-dehydrocholesterol reductase
P17	GSK3B	Glycogen synthase kinase 3 beta
P18	HMGCR	3-hydroxy-3-methylglutaryl-CoA reductase
P19	IGF1	Insulin-like growth factor 1
P20	IKBKB	Inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta
P21	KIT	V-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog
P22	LSS	Lanosterol synthase
P23	PGS1	Phosphatidylglycerophosphate synthase 1
P24	PPARA	Peroxisome proliferator-activated receptor alpha
P25	PPARG	Peroxisome proliferator-activated receptor gamma
P26	PRKCA	Protein kinase C alpha
P27	PRKCD	Protein kinase C, delta
P28	PTGS2	Prostaglandin-endoperoxide synthase 2
P29	PTPN1	Protein tyrosine phosphatase, non-receptor type 1
P30	SLCO1B3	Solute carrier organic anion transporter family, member 1B3
P31	SLCO1B1	Solute carrier organic anion transporter family, member 1B1
P32	ITGA4	Integrin, alpha 4
P33	ESRRB	Estrogen receptor Beta

Table S3: KEGG Pathway analysis of proteins regulated by bioactives of *Ficus benghalensis*

Pathway ID	Pathway Description	Count In Gene Set	Name of Genes	False Discovery Rate
04020	Calcium signaling pathway	7	PRKCA, 5HTR2A, HTR2B, HTR2C, HTR4, HTR7, ADORA2A	6.27E-05
00052	Galactose metabolism	4	AKR1B10, AKR1B1, SI, GAA	8.87E-05
04976	Bile secretion	5	SLCO, ABCB1, RXRA, SLCO1B1, HMGCR	8.87E-05
04151	PI3K-Aktsignaling pathway	8	KIT, CDK6, IKBKB, PRKCA, RXRA, GSK3B, IGF1, ITGA4	0.00028
05212	Pancreatic cancer	3	IKBKB, CDK6, CDKN2A	0.0103
04920	Adipocytokinesignaling pathway	3	RXRA, PPARA, IKBKB	0.0121
03320	PPARsignaling pathway	3	RXRA, PPARA, PPARG	0.0123
00100	Steroid biosynthesis	2	LSS, DHCR7	0.0156
00051	Fructose and mannose metabolism	2	AKR1B10, AKR1B1	0.0325
04152	AMPKsignaling pathway	3	IGF1, PPARG, HMGCR	0.0402
00620	Pyruvate metabolism	2	AKR1B10, AKR1B1	0.0423
04910	Insulin signaling pathway	3	IKBKB, PTPN1, GSK3B	0.0482
04930	Type II diabetes mellitus	2	IKBKB, PRKCD	0.0497

Table S4: Binding energy and hydrogen bond interaction of bioactives with protein-tyrosine phosphatase 1B(PDB: 1NNY)

S. No.	Compound	Binding energy (kcal/mol)	Hydrogen Bond Residues	Number of Hydrogen Bonds
1	Mucisoflavone A	-7.36	Arg 221, Lys 116, Gln 266, Asp48, Ala217, Asn 111, Glu 115	7
2	Mucisoflavone C	-6.47	Arg 221, Asp 48	2
3	Isowighteone	-8.51	His 208,Ser 205, Glu 75	3
4	Wighteone	-6.53	Arg 221, Cys 215	2
5	Psoralen	-6.08	Cys215, Gly218,Ile219, Arg221	4
6	Ursolic Acid	-8.93	Asp 48, Gln 266, Trp 179, Arg 221	5
7	3',4',5,7-Tetrahydroxy-3-Methoxyflavone	-6.61	Ser 203, Ser 80, Met 74	4
8	α -amyrin	-7.9	Cys 215	1
9	Sitosterol	-7.02	-	-