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Research Article

PREDICTION OF ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION ACTIVITY OF THE COMPONENTS OF *MADHUCA LONGIFOLIA* AND ITS INHIBITING TARGET MOLECULE

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ABSTARCT

Objectives: *Madhuca longifolia* is a versatile tropical tree mostly cultivated or harvested in the wild in South Asia for its edible flowers and oil seeds. Mahua trees are vegetatively propagated; they act as soil improvers, and also help in soil reclamation and erosion control. *M. longifolia* is a plant of great importance due to its scientifically proven uses such as antioxidant activity, immune suppression, and neuroprotective activity, which is because of the various chemical constituents present in different parts of the plant. The aim of our study is to analyze the absorption, distribution, metabolism, and excretion (ADME) properties and pathways analysis of active components of *M. longifolia.*

Methods: The detailed study of these chemical constituents is done using PubChem and software's such as Rasmol and Pymol. Swiss ADME was used to find out the ADME properties of the chemical constituents present in the plant. The pathway analysis was done using a literature survey and Swiss TargetPrediction.

Results: The research has identify the potentially active compound from the plant with its inhibitory target protein.

Conclusion: The ADME result demonstrates the potential pharmacological activity of the plant compound, which can be studied through *in vivo* model against its potential inhibitory target molecules.

Keywords: *Madhuca longifolia*, Rasmol, Pymol, PubChem, Absorption; distribution; metabolism; and excretion properties.

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INTRODUCTION

Madhuca longifolia belongs to the *Sapotaceae* family commonly known as butternut tree, which is a fast-growing tree found widely in Nepal, India, and Sri Lanka. The common Indian name for *M. longifolia* is Mahua, Mahwa, or Iluppai. It is cultivated in warm and humid regions. It is a deciduous tree that can grow up to 20 m of height. The ethnomedicinal uses of *M. longifolia* contain various phytochemical compounds such as flavonoids, Vitamins A and C, histidine, glutamic acid, tannins, volatile oil, beta-carotene, and xanthophylls. The aqueous and alcoholic extract of *M. longifolia* has been reported to show analgesic activity [1]. *M. longifolia* is a multipurpose tree. Large numbers of Mahua trees are found in India and the estimated production of its flowers is more than 1 million tonne in the country. Tribes of West Bengal, such as Lodhas, Santals, and Mundas, have been using different parts of Mahua as medicine [2]. The presence of some bioactive substances in leaves supports the traditional medicinal uses of *M. longifolia*. The presence of quercetin was reported in *M. longifolia* leaf through high-performance thin-layer chromatography technique. Madhucic acid, Madhushazone, and Madhusalmone were isolated from *M. longifolia* fruits. A isoflavone (3,4-dihydroxy-5,2-dimethoxy-6,7-methylenedioxy) was isolated from the fruits of *M. longifolia* [3].

Recent researches on *M. longifolia* were against diclofenac-induced toxicity in female Wistar albino rabbits, bio fabrication, and characterization of flavonoid loaded Ag, Au, pyrolysis characteristics, fuel properties, and compositional study of *M. longifolia* butter [4,5]. Absorption, distribution, metabolism, and excretion (ADME) and toxicological profiling are critical parts of any drug development program, and essential for compliance with regulatory guidelines [6-9]. In this experiment, the ADME properties of each compound were analyzed using SWISS ADME, and the inhibiting target molecule of each compound was found using Swiss TargetPrediction. This work would help in analyzing the pharmacological activities of the active compounds of *M. longifolia* against its inhibitory target molecules.

METHODS

Active compounds of *M. longifolia*

M. longifolia has various active compounds present in different parts of the plant. Few important ones are Vitamins A and C present in flower, alpha-spinasterol, alpha-terpineol (bark), and important amino acids such as alanine, glycine, cysteine (seeds), alpha- and beta-amyrin acetates (fruit) and xanthophylls, and erythrodiol (leaves).

The active compound of the flower of *M. longifolia* is Vitamin A ($C_{20}H_{30}O$) and Vitamin C ($C_6H_8O_6$). The active compound of *M. longifolia* bark is alpha-amyrin acetate ($C_{32}H_{52}O_2$), alpha-spinasterol ($C_{29}H_{48}O$), alpha-terpineol ($C_{10}H_{18}O$), and oleic acid ($C_{30}H_{48}O_3$). The active compound of *M. longifolia* fruits is alpha-amyrin acetate ($C_{32}H_{52}O_2$), beta-amyrin acetate ($C_{32}H_{52}O_2$), beta-sitosterol ($C_{29}H_{50}O$), dihydroquercetin ($C_{25}H_{34}N_2O_7$), and quercetin ($C_{15}H_{10}O_7$). The active compound of *M. longifolia* seeds is alanine ($C_3H_7NO_2$), arachidic acid ($C_{20}H_{40}O2$), cysteine ($C_3H_7NO_2S$), glycine ($C_2H_5NO_2$), isoleucine ($C_6H_{13}NO_2$), leucine ($C_6H_{13}NO_2$), linoleic acid ($C_{18}H_{32}O_2$), myristic acid ($C_{14}H_{28}O_2$), oleic acid ($C_{18}H_{34}O_2$), palmitic acid ($C_{16}H_{32}O_2$), quercetin ($C_{15}H_{10}O_7$), and stearic acid ($C_{18}H_{36}O_2$). The active compound of *M. longifolia* leaves is beta-sitosterol ($C_{29}H_{50}O$), carotene ($C_{40}H_{56}$), erythrodiol ($C_{30}H_{50}O_2$), myricitin ($C_{15}H_{10}O_8$), n-hexacosanol ($C_{26}H_{54}O$), n-Octacosanol ($C_{28}H_{58}O$), quercetin ($C_{15}H_{10}O_7$), stigmasterol ($C_{29}H_{48}O$), and xanthophylls ($C_{40}H_{56}O_2$).

Analysis of ADME property

The ADME properties of each compound were analyzed using SWISS ADME (http://www.swissadme.ch/). The canonical smiles of each compound were taken from PubChem (https://pubchem.ncbi.nlm.nih.gov/) and pasted into SWISS ADME to predict ADME parameters,

pharmacokinetic properties, drug-like nature, and medicinal chemistry of each compound.

Analysis of inhibitory target molecule

Analysis of the inhibitory target molecule was done using Swiss TargetPrediction (http://www.swisstargetprediction.ch/) a part of Expasy (https://www.expasy.org/medicinal_chemistry). This website is used to estimate the most probable macromolecular targets of a small molecule.

RESULTS

ADME properties of *M. longifolia*

Table 1 represents the ADME analysis of the active compounds of *M. longifolia*. Many compounds have obeyed the Lipinski rule and few compounds were observed to show high gastrointestinal (GI) absorption. Fig. 1 represents the ADME chart of the compounds. GI absorption in the following compounds was high – Vitamin A, Vitamin C, alpha-terpineol, dihydroquercetin, quercetin, glycine, isoleucine, leucine, linoleic acid, myristic acid, oleic acid, palmitic acid, and stearic acid. GI absorption in the following compounds was low – alpha-amyrin acetate, alpha-spinasterol, oleic acid, beta-amyrin acetate, beta-spinasterol, arachidic acid, cysteine, carotene, erythrodiol, myricitin, n-Hexacosanol, n-Octacosanol, Stigmasterol, and xanthophylls.

Inhibitory analysis of *M. longifolia*

Table 2 represents the inhibitory target molecule of the active compound of *M. longifolia* with its probability and known actives.

Role of inhibitory target molecules

The role of inhibitory target molecules was analyzed which is discussed here. Gamma-amino-N-butyrate transaminase is responsible for the catabolism of gamma-aminobutyric acid and inhibition of neurotransmitters in the central nervous system (CNS) [10]. Peroxisome proliferator-activated receptor (PPAR) alpha binds to peroxisome proliferator response elements which initiate the transcriptional regulation of target genes. It may inhibit the ligand-induced transcriptional activity of PPARs alpha and gamma [11]. Fatty acid-binding protein intestinal actively accelerates the transport of lipids to specific parts in the cell. Metabotropic glutamate receptor 2 is the major excitatory neurotransmitter in the CNS and activates both ionotropic and metabotropic glutamate receptors [12]. The active compound Metabotropic glutamate receptor 6 is reported to cause neuronal excitability and synaptic transmission. This is by modulation of a variety of ion channels and other regulatory and signalling proteins. Tyrosine-protein kinase FYN encodes a membrane-associated tyrosine kinase that is involved in controlling cell growth. Tyrosine-protein kinase LCK controls a wide variety of cellular processes. High-affinity choline transporter is involved in pain regulation and pain inhibition [13].

Voltage-gated calcium channel alpha-2/delta subunit 1 plays roles in the trafficking of these channels, both to the plasma membrane and to specific subcellular domains. PPAR-gamma is a key regulator of metabolism, proliferation, inflammation and differentiation, and upregulates tumor suppressor genes. PPAR-alpha is involved in cell proliferation, cell differentiation and in immune and inflammation responses PPAR-alpha, which is a nuclear transcription factor. Free fatty acid receptor 1 is involved in the metabolic regulation of insulin secretion. Fatty acid-binding protein adipocyte is an important mediator of inflammation [14]. Vasopressin V2 receptor has the primary property to respond to the pituitary hormone arginine vasopressin. Aldose reductase is implicated in the development of diabetic complications by catalyzing the reduction of glucose to sorbitol. PPAR-alpha is involved in cell proliferation, cell differentiation and immune, and inflammation responses. Carboxylesterase 2 is responsible for the hydrolysis of various xenobiotics [15]. 11-beta-hydroxysteroid dehydrogenase 1 catalyzes the conversion of the stress hormone cortisol to the inactive metabolite cortisone. Protein-tyrosine phosphatase 1B is essential for catalytic activity. It acts as a negative regulator of insulin signaling by dephosphorylating the phosphotyrosine residues of insulin receptor kinase. Cytochrome P450 51 is involved in drug metabolism and synthesis of cholesterol, steroids, and other lipids. Adenosine A2a receptor plays an important role in cardiac rhythm and circulation, cerebral and renal blood flow, immune function, pain regulation, and sleep. Adenosine A3 receptor is involved in the inhibition of neutrophil degranulation in neutrophil-mediated tissue injury. Butyrylcholinesterase is involved in the detoxification of poisons including organophosphate nerve agents and pesticides, and the metabolism of drugs, including cocaine, heroin, and aspirin [16].

Microtubule-associated protein is associated with several neurodegenerative disorders such as Alzheimer's disease, pick's

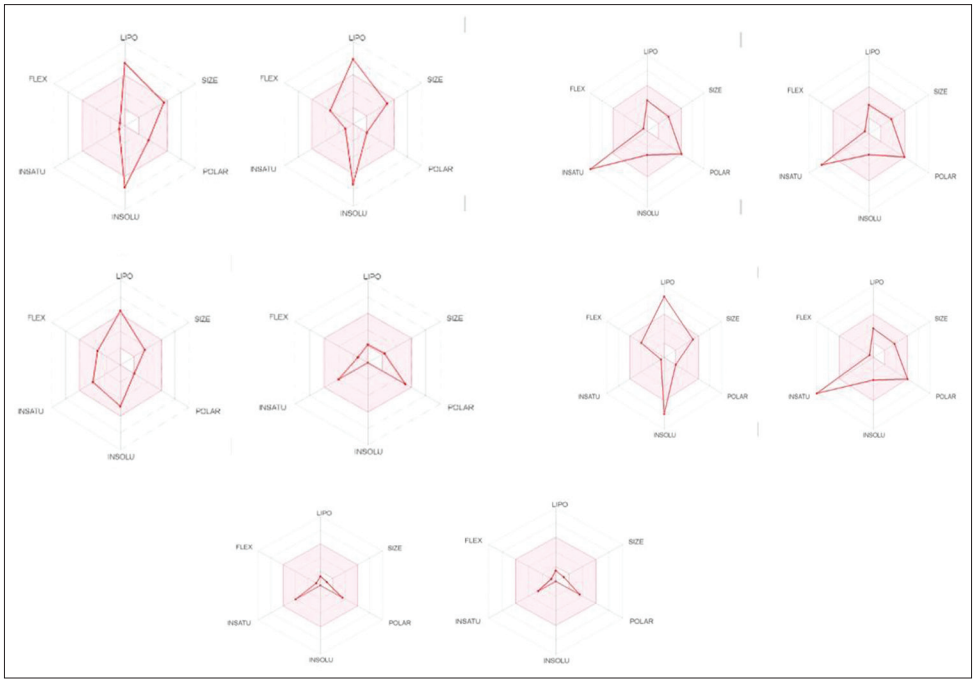

Fig. 1: Absorption, distribution, metabolism, and excretion analysis

Table 1: Absorption, distribution, metabolism, and excretion analysis of active compounds of *Madhuca longifolia*

Plant parts	Compound	TPSA (Å)	GIA	NRB	NHBD	NHBA	LIPINSKI	BA	LOG KP (cm/s)
Flower	Vitamin A	20.23	High	5	1	1	YES,1 V MLOGP>4.15	0.55	−4.01
	Vitamin C	10.22	High	2	4	6	YES,0 V	0.56	−8.54
Bark	Alpha-amyrin acetate	26.30	Low	2	0	2	YES,1 V MLOGP>4.15	0.55	−2.36
	Alpha-spinasterol	20.23	Low	5	1	1	YES,1 V MLOGP>4.15	0.55	−2.92
	Alpha-terpineol	20.23	High	1	1	1	YES, 0 V	0.55	−4.83
	Oleic acid	57.53	Low	1	2	3	YES,1 V MLOGP>4.15	0.56	−3.77
Fruit	Alpha-amyrin acetate	26.30	Low	2	0	2	YES,1 V MLOGP>4.15	0.55	−2.36
	Beta-amyrin acetate	26.30	Low	2	0	2	YES,1 V MLOGP>4.15	0.55	−2.25
	Beta-sitosterol	20.23	Low	6	1	1	YES,1 V MLOGP>4.15	0.55	−2.20
	Dihydroquercetin	127.45	High	1	5	7	YES, 0 V	0.55	−7.8
	Quercetin	131.36	High	1	5	7	YES, 0 V	0.55	−7.05
Seeds	Alanine	63.32	High	1	2	3	YES, 0 V	0.55	−8.95
	Arachidic acid	37.30	Low	18	1	2	YES, 1 V MLOGP>4.15	0.56	−1.61
	Cysteine	177.24	Low	7	4	6	YES, 0 V	0.55	−11.37
	Glycine	63.32	High	1	2	3	YES, 0 V	0.55	−9.04
	Isoleucine	63.32	High	3	2	3	YES, 0 V	0.55	−8.32
	Leucine	63.32	High	3	2	3	YES, 0 V	0.55	−8.18
	Linoleic acid	37.30	High	14	1	2	YES, 1 V MLOGP>4.15	0.56	−3.05
	Myristic acid	37.30	High	12	1	2	YES, 0 V	0.56	−3.35
	Oleic acid	37.30	High	15	1	2	YES,1 V MLOGP>4.15	0.56	−2.60
	Palmitic acid	37.30	High	14	1	2	YES,1 V MLOGP>4.15	0.56	−2.77
	Quercetin	131.36	High	1	5	7	YES, 0 V	0.55	−7.05
	Stearic acid	37.30	High	16	1	2	YES,1 V MLOGP>4.15	0.56	−2.19
Leaves	Beta-sitosterol	20.23	Low	6	1	1	YES, 1 V MLOGP>4.15	0.55	−2.20
	Carotene	0.00	Low	10	0	0	NO, 2 V MW>500. MLOGP>4.15	0.17	0.12
	Erythrodiol	40.4 6	Low	1	2	2	YES, 1 V MLOGP>4.15	0.55	−3.63
	Myricitin	151.59	Low	1	6	8	YES, 1 V NH or OH>5	0.55	−7.40
	n-Hexacosanol	20.23	Low	24	1	1	YES,1 V MLOGP>4.15	0.55	0.26
	n-Octacosanol	20.23	Low	26	1	1	YES,1 V MLOGP>4.15	0.55	0.86
	Quercetin	131.36	High	1	5	7	YES, 0 V	0.55	−7.05
	Stigmasterol	20.23	Low	5	1	1	YES,1 V MLOGP>4.15	0.55	−2.74
	Xanthophylls	40.46	Low	10	2	2	NO, 2 V MW>500 MLOGP>4.15	0.17	−1.95

GIA: Gastrointestinal absorption, NRB: Number of rotatable bond, NHBD: Number of hydrogen bond donor, NHBA: Number of hydrogen bond acceptor, BA: Bioavailability, V: Violation

disease, frontotemporal dementia, corticobasal degeneration, and progressive supranuclear palsy. Carbonic anhydrase II is associated with osteopetrosis and renal tubular acidosis. Carbonic anhydrase I encode a cytosolic protein that is found at the highest level in erythrocytes. Transient receptor potential cation channel subfamily M member eight plays a role in prostate cancer cell migration. Niemann-Pick C1-like protein 1 plays a critical role in regulating lipid metabolism. Vitamin D receptor is involved in immune response and cancer. Muscarinic acetylcholine receptor M2 triggers calcium ion release into the cytosol. DNA polymerase beta it translocates to the nucleus on DNA damage. Plasma retinol-binding protein results in defective delivery and supply to the epidermal cells [17].

DISCUSSION

The ethanolic extract of *M. longifolia* has a significant role in nephroprotective and hepatoprotective activity against acetaminophen-induced necrotic damage of hepatic and renal tissue. Ether benzene-95% crude ethanolic extract of leaves and bark of *M. longifolia* shows a remarkable reduction in the time taken to heal a wound [18]. The methanolic extraction proved to have potential benefits of anti-

Table 2: Analysis of inhibitory target molecule

Plants parts	Compound	Target	Target class	Probability	Known active (3d/2d)
Flower	Vitamin A	Plasma binding retinol	Secreted protein	0.418947321	3/2
		Retinoid X receptor alpha	Nuclear receptor	0.418947321	2/13
		Retinoid X receptor beta	Nuclear receptor	0.106099949	0/2
	Vitamin C	Glycogen synthase kinase-3 beta	Kinase	0.141787381	0/2
		Protein kinase C alpha	Kinase	0	0/168
		Protein-tyrosine phosphatase 1B	Phosphatase	0	0/9
Bark	Alpha-amyrin Acetate	Carboxylesterase 2	Enzyme	0.128531578	0/12
		11-beta-hydroxysteroid dehydrogenase 1	Enzyme	0.128531578	153/29
		Protein-tyrosine phosphatase	Phosphatase	0.120225751	7/70
	Alpha-spinasterol	Androgen receptor	Nuclear receptor	0.705989664	23/106
		Muscarinic acetylcholine receptor M2	Family A G protein-coupled receptor	0.306043655	0/2
		Acetylcholinesterase	Hydrolase	0.306043655	0/1
	Alpha-terpineol	Androgen receptor	Nuclear receptor	0.120677312	80/78
		Cytochrome P450 19A1	Cytochrome P450	0.091839166	88/138
		Carbonic anhydrase II	Lyase	0.091839166	17/0
	Oleic acid	Protein-tyrosine phosphatase 1B	Phosphatase	0.971605984	63/72
		DNA polymerase beta	Enzyme	0.771064571	5/12
		Aldo-keto reductase family 1 member B10	Enzyme	0.754299393	7/7
Fruit	Alpha-amyrin acetate	Carboxylesterase 2	Enzyme	0.128531578	0/12
		11-beta-hydroxysteroid dehydrogenase 1	Enzyme	0.128531578	153/29
		Protein-tyrosine phosphatase 1B	Phosphatase	0.120225751	7/70
	Beta-amyrin acetate	Prostaglandin E synthase	Enzyme	0.128531578	6/13
		Androgen receptor	Nuclear receptor	0.120225751	12/106
		11-beta-hydroxysteroid dehydrogenase 2	Enzyme	0.120225751	6/11
	Beta-sitosterol	Androgen receptor	Nuclear receptor	0.120225751	12/106
		HMG-CoA reductase	Oxidoreductase	0.614311102	36/7
		Cytochrome P450 51	Cytochrome P450	0.614311102	2/2
	Dihydroquercetin and quercetin	NADPH oxidase 4	Enzyme	1	7/8
		Vasopressin V2 receptor	Family A G protein-coupled receptor	1	1/1
		Aldose reductase	Enzyme	1	17/72
Seeds	Alanine	Gamma-amino-N-butyrate transaminase	Transferase	0.03397069	2/0
		Histone deacetylase 3 transporter	ERASER	0	0/1
		Betaine transporter	Electrochemical transporter	0	2/0
	Arachidic acid	Peroxisome proliferator-activated receptor alpha	Nuclear receptor	0.364127943	77/9
		Peroxisome proliferator-activated receptor delta	Nuclear receptor	0.364127943	30/7
		Fatty acid-binding protein intestinal	Fatty acid-binding protein family	0.34052608	0/1
	Cysteine	Metabotropic glutamate receptor 2	Family C G protein-coupled receptor	0	3/0
		Metabotropic glutamate receptor 3	Family C G protein-coupled receptor	0	2/0
		Metabotropic glutamate receptor 6	Family C G protein-coupled receptor	0	1/0
	Glycine	Tyrosine-protein kinase FYN	Kinase	0	0/1
		Tyrosine-protein kinase LCK	Kinase	0	0/1
		High-affinity choline transporter	Electrochemical transporter	0	0/1
	Isoleucine	Voltage-gated calcium channel alpha-2/delta subunit 1	Calcium channel auxiliary subunit alpha2delta family	0.125817531	30/5
		Adenosine A3 receptor	Family A G protein-coupled receptor	0.095255918	3/2
		Excitatory amino acid transporter 3	Electrochemical transporter	0.074316474	0/3
	Leucine	Voltage-gated calcium channel alpha-2/delta subunit 1	Calcium channel auxiliary subunit alpha-2/delta family	0.135105168	31/5
		Adenosine A3 receptor	Family A G protein-coupled receptor	0.095255918	3/2
		Excitatory amino acid transporter 3	Electrochemical transporter	0.074316474	0/3
	Linoleic acid	Peroxisome proliferator-activated receptor gamma	Nuclear receptor	0.747488284	429/22
		Peroxisome proliferator-activated receptor alpha	Nuclear receptor	0.747488284	270/18
		Peroxisome proliferator-activated receptor delta	Nuclear receptor	0.747488284	192/10
	Myristic acid	Peroxisome proliferator-activated receptor alpha	Nuclear receptor	0.95528599	229/9
		Peroxisome proliferator-activated receptor delta	Nuclear receptor	0.580792647	138/7

(Contd...)

Table 2: (*Continued*)

Plants parts	Compound	Target	Target class	Probability	Known active (3d/2d)
		Free fatty acid receptor 1	Family A G protein-coupled receptor	0.580792647	164/3
	Oleic acid	Fatty acid-binding protein adipocyte	Fatty acid-binding protein family	1	5/4
		Anandamide amidohydrolase	Enzyme	1	7/17
		Peroxisome proliferator-activated receptor gamma	Nuclear receptor	1	223/24
	Palmitic acid	Fatty acid-binding protein adipocyte	Fatty acid-binding protein family	0.935895337	20/3
		Peroxisome proliferator-activated receptor alpha	Nuclear receptor	0.935895337	152/9
		Fatty acid-binding protein muscle	Fatty acid-binding protein family	0.935895337	10/5
	Quercetin	NADPH oxidase 4	Enzyme	1	7/8
		Vasopressin V2 receptor	Family A G protein-coupled receptor	1	1/1
		Aldose reductase	Enzyme	1	17/72
	Stearic acid	Peroxisome proliferator-activated receptor alpha	Nuclear receptor	0.929299884	121/9
		Peroxisome proliferator-activated receptor delta	Nuclear receptor	0.929299884	135/7
		Fatty acid-binding protein adipocyte	Fatty acid-binding protein family	0.723067577	13/3
Leaves	Beta-sitosterol	Androgen Receptor	Nuclear receptor	0.120225751	12/106
		HMG-CoA reductase	Oxidoreductase	0.614311102	36/7
		Cytochrome P450 51	Cytochrome P450	0.614311102	2/2
	Carotene	Adenosine A1 receptor	Family A G protein-coupled receptor	0.086885855	0/1
		Adenosine A2a receptor	Family A G protein-coupled receptor	0.086885855	0/1
		Adenosine A3 receptor	Family A G protein-coupled receptor	0.086885855	0/3
	Erythrodiol	Protein-tyrosine phosphatase 1B	Phosphatase	0.120225751	7/70
		Butyrylcholinesterase	Hydrolase	0.31401521	8/2
		Cytochrome P450 19A1	Cytochrome P45	0.222719907	12/157
	Myricitin	Microtubule-associated protein tau	Unclassified protein	1	1/1
		Lysine-specific demethylase 4D-like	Eraser	1	½
		G-protein coupled receptor 35	Family A G protein-coupled receptor	1	2/4
	n-Hexacosanol	Transient receptor potential cation channel subfamily M member 8	Voltage-gated ion channel	0.177292204	0/1
		Carbonic anhydrase II	Lyase	0.177292204	0/3
		Carbonic anhydrase I	Lyase	0.177292204	0/3
	n-Octacosanol	Transient receptor potential cation channel subfamily M member 8	Voltage-gated ion channel	0.177292204	0/1
		Carbonic anhydrase II	Lyase	0.177292204	0/3
		Carbonic anhydrase I	Lyase	0.177292204	0/3
	Quercetin	NADPH oxidase 4	Enzyme	1	7/8
		Vasopressin V2 receptor	Family A G protein-coupled receptor	1	1/1
		Aldose reductase	Enzyme	1	17/72
	Stigmasterol	Androgen Receptor	Nuclear receptor	0.689284537	35/102
		Niemann-pick C1-like protein 1	Other membrane protein	0.639333184	9/13
		HMG-CoA reductase	Oxidoreductase	0.639333184	50/7
	Xanthophylls	Vitamin D receptor	Nuclear receptor	0.082221517	0/57
		Androgen receptor	Nuclear receptor	0.082221517	0/52
		Protein-tyrosine phosphatase 1B	Phosphatase	0.082221517	0/16

inflammatory, anti-pyretic, and analgesic properties because of the presence of flavonoids in the plants. The methanolic extract of the bark is known to have antidiabetic and anti-hyperglycemic activity. The aqueous extract of leaves has been prevent to have an effective antiulcer property [2]. Anticancer activity of *M. longifolia* was reported in Ayurvedic literature and some *in vitro* cell line studies also confirmed its antiproliferative property. The bark is used for rheumatism, chronic bronchitis, diabetes mellitus, ulcers, tonsillitis, and bleedings. The flowers have been traditionally used as an analgesic, diuretic, cooling agent, tonic, aphrodisiac, astringent, demulcent and for the treatment of helminths, acute and chronic tonsillitis, pharyngitis, and bronchitis. Leaves are expectorant and also used for chronic bronchitis and Cushing's disease [18].

ADME is an abbreviation used in pharmacokinetics and pharmacology for ADME and describes the disposal of a compound within an organism. The path of any new molecule to reach its target involves the passage through many barriers, as well as the survival of the complicated biological systems. A prerequisite in drug discovery and development in conducting drug metabolism and pharmacokinetics studies, often referred to as ADME toxicity studies [19]. Absorption – how much of the drug and how quickly is it absorbed? (bioavailability). Absorption takes place in the GI tract. The surface area and pH of the organ influence the rate of absorption of the compound. Absorption is the movement of drug from its site of administration into the body. Small molecules diffuse easily than large molecules. Lipid soluble drugs are absorbed faster. Acidic drugs get well absorbed in the stomach (ph-2) and basic drugs get well absorbed in the small intestine (ph-8.0). Most of the drugs get absorbed in the intestine than in the stomach because the surface area of the stomach is smaller than that of the intestine. LogP tells us about the hydrophilic and hydrophobic balance. More the value of logP is hydrophobic and its less soluble. Lower the value of logP, the compound is hydrophilic and it

is more soluble [20]. Distribution – where is the drug administered and what is the rate and extent of distribution. After absorption, the drugs are distributed in blood. After GI tract absorption, it is taken up by the hepatic portal system. Lipids are absorbed into the lymphatic system and through thoracic duct, it is delivered into the blood. Lipophilicity plays an important role in distribution [21]. The capillaries in CNS are sealed by connective tissue; hence, only small molecules can cross the blood–brain barrier [22]. Metabolism – how fast is the drug metabolized, what is the mechanism of action and what metabolite is formed and it is active or toxic. It depends on race, age, the health of the patient, depends on whether the patient is taking another drug. The liver is the primary site but it can happen anywhere in the bloodstream. Biotransformation is the process of making a compound more hydrophilic so that it can be excreted out from the body. This happens in two phases, i.e., Phase I metabolism – the compound is modified chemically by the process such as oxidation, reduction, and hydrolysis. These changes create sites for Phase II metabolism. In Phase II conjugation of the Phase I, metabolite takes place with polar groups, for example, glucuronic acid and sulfates. This alters the activity and it becomes more hydrophilic and less lipid soluble so it gets excreted easily. Excretion – how is the drug excreted and how quickly? Some drugs are unchanged but some drugs get changed into urine or bile and are excreted out [23].

Scientists are more interested in estimating the drug-likeness properties that are bioavailability, pharmacokinetics (how body responds to the drug), pharmacodynamics (how drug acts on the body), solubility, toxicity, lipophilicity, permeability, logP, logD, kinetic and thermodynamic solubility, the volume of distribution, and biotransformation [24]. The underlying goal and end-game for all ADME studies are to better understand a compound's metabolite-mediated toxicity and safety profile to make a concrete decision on whether the compound can progress to late-stage preclinical and clinical studies to enable filing for an investigational new drug, new drug agreement, or a biologics licensing agreement. ADME studies can be used in molecular docking, pharmacophore modeling, *de novo* designing, fragment-based screening, to find structure-activity relationships [25,26]. Transporters play an important role in the ADME of drugs. Recently, various *in vitro* and *in vivo* methods have been established for studying transporter function and drug transporter function [9,27].

There are some rules or models for classifying a compound, whether it is a good drug or a bad drug. The most widely accepted one is Lipinski's rule of 5. Lipinski's rule – devised by Lipinski and coworkers. If two parameters are out of range, "poor absorption or permeability is possible." The compound may get absorbed in GI tract if any one of the parameter doesn't work properly. Hence, the rules are: (1) Molecular weight <500, (2) number of H-bond acceptors<10 (any O and N atoms), (3) number of H-bond donors <5 (N-H or O-H groups), (4) LogP >5 then it is hydrophobic, and (5) LogP id 0–5 then it is very hydrophilic [28,29].

CONCLUSION

The article has elaborated on the ADME and inhibitory potential of *M. longifolia*. The role of all target molecules is much essential. The active compound of *M. longifolia* can be further studied through *in vitro* and *in silico* methods for its potential pharmaceutical values.

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Paper correction and project design: Jerine Peter S, Nagesh Kishan Panchal, Work analysis: Ankitha V, Sai Lakshmi, Poojita Karchalkar, Correspondence: E P Sabina.

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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