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Research Article

Physicochemical, ADMET and Druggable properties of Myricetin: A Key Flavonoid in *Syzygium cumini* that regulates metabolic inflammations

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Abstract

Syzygium cumini (Myrtaceae) is a potential medicinal plant traditionally used in indigenous systems of medicines practiced in India and elsewhere due to its functional properties against metabolic inflammations viz., anti-hyperglycemic, anti-inflammatory, cardio-protective, and antioxidant activities. Targeting metabolic inflammation has emerged as a standalone strategy to attenuate metabolic disease. Myricetin (3,5,7,3′,4′,5′-hexahydroxyflavone) is one of the flavonoids from stem bark, leaf, flowers, fruits, pulp and seeds of *S. cumini*. Therefore, attention has been paid to explore bioactive potentials of this compound in *S. cumini* owing to its exemplary therapeutic prospective and health-promoting effects. Antioxidant effect of Myricetin from *S. cumini* has been though experimentally demonstrated, therapeutic potential of Myricetin has not been fully explored. In the present study, physicochemical, ADMET and druggability properties of Myricetin - a key flavonoid compound in *S. cumini* have been evaluated. Data implicates that this molecule of GRAS standard can be a novel jumble-sale lead in drug discovery.

Keywords: Plant Based Natural Products (PBNPs); Drug Discovery; Pharmacological Activity; ADMET Properties; Flavonoid; Myricetin; *Syzygium cumini*

INTRODUCTION

Diabetes mellitus (DM) an epidemic, affects more than 170 million individuals worldwide. It is predominantly characterized by chronic, low-grade and systemic inflammation. Human body maintains blood glucose level within a narrow range, regulated by insulin - glucagon metabolism. Insulin induces liver cells to take up glucose from blood and store it in the form of glycogen whereas glucagon stimulates liver cells to secrete glucose into blood cells for production of ATP. Diabetics, a metabolic disorder results due to impairment of biochemical pathways responsible for production of insulin and the resultant metabolic inflammation. About 90 % of individuals have Type II diabetes which is characterized by high levels of glucose in blood.

As of now, there are five major classes of oral pharmacological agents available in the market to treat diabetes however, with side effects. Moreover, the limited long-term durability of immunotherapy and undesirable side effects of anti-diabetic drugs underlie the need for alternative therapeutics. Phytochemicals are rich source of plant based natural products (PBNPs) that are of pivotal importance with therapeutic potential in the management of diabetes.

Metabolic inflammation is well established as a critical feature of diabetes, and evident in the pancreas, liver, adipose tissue, muscle, and other organs actively involved in glucose metabolism. Furthermore, metabolic inflammation is profoundly modulated by various mediators of innate and adaptive immunity, making inflammation as the nexus within the crosstalk among key events in the pathogenesis of diabetes[1]. Given that metabolic inflammation is a key pathophysiological event that drives the progression of diabetes, protective effects of phytochemicals in metabolic inflammation needs in-depth investigation.

As said, plants provide a large repertoire of phytochemicals such as polyphenols, flavonoids, carotenoids and vitamins that are used as active ingredients of drugs in modern age[2]. Plant Based Natural Products (PBNPs) are associated with minimal side effects as compared to synthetic drugs and have gained much interest. More than 25000 phytochemicals

have been identified to date, including 8000 different types of polyphenols for their therapeutic potential[3].

Flavonoids consist of a large group of polyphenolic compounds having a benzo-γ-pyrone structure ubiquitously present in plants, synthesized through phenylpropanoid pathway. Secondary metabolites of phenolic nature including flavonoids are responsible for the variety of pharmacological activities[4]. Flavonoids, the most abundant polyphenol antioxidants in human diets, have been reported to be absorbed in humans, circulate in plasma and are excreted in urine. Flavonoids have antioxidant activity, free radical scavenging capacity, metal chelation activity, coronary heart disease prevention, hepatoprotective, anti-inflammatory, and anticancer activities[4]. As of now, more than 4000 varieties of flavonoids from various plant sources have been reported[5].

Myricetin, a common plant-derived flavonoid is well recognised for its nutraceuticals value. It is a key ingredient in various foods and beverages. Myricetin is a hexahydroxyflavone that is flavone substituted by hydroxyl groups at positions 3,3',4',5,5' and 7. Myricetin is a poly-hydroxyflavonol compound composed of light yellow crystals, soluble in methanol, acetonitrile, ethanol and other polar solvents. Its chemical formula is $C_{15}H_{10}O_8$ and the relative molecular mass is 318.24[6].

It was first described in 18th century from the bark of *Myrica nagi* Thunb. Myricaceae[7], later from the leaves of *Myrica rubra* and other plants. This compound is very common in berries, vegetables, teas and wines produced from various plants[8]. Although Myricetin occurs throughout the Plant Kingdom, it is produced mainly by members of the families: *Mangifera indica* (Anacardiaceae)[9,10], *Marantodes pumilum* (Primulaceae)[11], Polygonaceae[12], and Primulaceae[13]. Myricetin plays a vital role as cyclooxygenase 1 inhibitor, it down-regulates phorbol ester-induced cyclooxygenase-2 expression in mouse epidermal cells by blocking activation of nuclear factor *kappa* B[14]. Myricetin serves as an antineoplastic agent, an antioxidant, a food component and a hypoglycemic agent. It is a hexahydroxyflavone and a 7-hydroxyflavonol.

Pharmacological studies have proved that Myricetin possesses a variety of biological activities such as anti-inflammatory, antitumor, antibacterial, antiviral, anti-obesity, cardio-protective, neuro-protective, and hepatoprotective effects. Studies have demonstrated its activity against DNA polymerases, RNA polymerases, reverse transcriptases, telomerases, kinases and helicases[15].

Myricetin is used in the management of non-insulin-dependent diabetes, by stimulating the uptake of glucose without functional insulin receptors[16]. The effect of Myricetin was evaluated in diabetes mellitus-associated kidney injuries and dysfunction in an experimental mouse model induced by 5 consecutive injections of low-dose streptozotocin (STZ). Data revealed that Myricetin (Oral, 100 mg/kg/day, for 6M) inhibited IκBα/NF-κB pathway independent of nuclear factor erythroid 2-related factor (Nrf2) regulation. Furthermore, it activated glucagon-like peptide 1 receptor (GLP-1R) and its long-term oral administration (200 mg/kg, for 40D) validates its gluco-regulatory effects[17]. Based on the results it was concluded that Myricetin acts as a natural class B GPCR antagonist for the treatment of T2D. Accumulating evidence suggests that Myricetin possesses antidiabetic properties that are mediated via regulation of the transport of glucose through the function of glucose transporter-2 in *Xenopus laevis* oocytes[18]. Karunakaran et al.[19] reported the in vitro effect of Myricetin on high glucose-induced β-cell apoptosis, possibly via cyclin-dependent kinase 5 (CDK5) inhibition. Myricetin (20 μM) significantly protect β-cells reducing apoptosis in INS-1 cells and rat islets that were incubated with glucose at the concentration of 30 mM for 24 and 48 h, respectively.

Many countries have developed and marketed health products containing Myricetin. Its antioxidant potentials and cholesterol-lowering effect have been acknowledged. Nowadays, people pay more attention in finding ways to strengthen the body using plant based natural products instead of using chemical drugs that have more toxic and side effects, this aspect encourage scientists to take-up research on Myricetin. As a result, studies focusing on its pharmacological effects are available, but a complete report on pharmacological activity of Myricetin is still lacking. Therefore, ADMET reports pertaining to Myricetin has been envisaged to provide a theoretical baseline support for the development of Myricetin based drugs for clinical use in the days to come.

Ramya et al.[20] pointed out that, all parts of *S. cumini* are rich in polyphenols (Table 1). The extracts of various parts of *S. cumini* contains phytochemicals including tannins, anthocyanins, terpenes, flavanols and aliphatic-acids. Both fruit and flowers of *S. cumini* are rich in anthocyanins as Cyanidin, Delphinidin, Peonidin, Pelargonidin, Petunidin and Malvidin[21]. Seeds of *S. cumini* contain Rutin and Quercetin while leaves have been reported to contain kaempferol, Myricetin, Quercetin and their glycosides. *S. cumini* has been reported to contain Ellagic acid, Triterpenoids, acetyl Oleanolic acid, Quercetin, Isoquercitin, Myricetin and Kaempferol[20]. *S. cumini* possesses enormous phytochemicals, of all, Myricetin has been widely reported for hypoglycemic, antimicrobial, hypolipidemic, anti-allergic, anti-inflammatory, cardio-protective, hepatoprotective and antineoplastic properties[3,6,20,22].

Table 1: Myricetin in different parts of *Syzygium cumini*

Part	Plant Based Natural Products (Bioactive Lead Molecules)	Ref
Bark	**Myricetin**, Quercetin, Kaempferol	20, 47
Flower	Kaempferol, **Myricetin**, Dihydromyricetin, Myricetin-3-L-Arabinoside, Isoquercetin, Quercetin, Quercetin-3-D-galactoside	20, 48
Fruit	**Myricetin**, Quercetin, Myricetin Deoxyhexoside	20, 49
Leaf	Catechin, Kaempferol, **Myricetin**, Myricetin 3-O-B-D-glucuronopyranoside, Myricetin-4□-methyl ether 3-O-A-rhamnopyranoside, Myricetrin 4□□-O-acetate, Myricetrin 4□□-O-acetyl-2-o-gallate, Quercetin -3-o-α-rhamno_ pyranoside	20, 50
Seed	Quercetin, **Myricetin**, Rutin, 3,5,7,4-tetrahydroxy flavanone	20, 51

MATERIALS AND METHODS

ADMET prediction

Physicochemical properties were computed using FAF-Drugs4 (28961788)/ RDKit - open-source CIP. Selected phytocompounds were subjected to ADMET prediction using QikProp (version 4.3, Suite 2015-1; Schrödinger, LLC: New York, NY) and toxicity prediction using TOPKAT (Accelrys, Inc., USA). Qik-Prop develops and employs QSAR/QSPR models using partial least squares, principal component analysis and multiple linear regression to predict physico-chemically significant descriptors[23]. Druggabiity scores were computed using FAF-Drugs4 (28961788)/ FAF-QED (28961788) - open-source CIP.

RESULTS AND DISCUSSION

In the present study, the selected biomolecule Myricetin -

Chemical kingdom: Organic compounds

Super class: Phenylpropanoids and polyketides

Class: Flavonoids

Subclass: Flavans

PubChem Identifier: 161557

ChEBI Identifier: 28429

Synonyms: DIHYDROMYRICETIN

Canonical SMILES: Oc1cc2O[C@H](c3cc(O)c(c(c3)O)O)[C@H](C(=O)c2c(c1)O)O

InChI Key: KJXSIXMJHKAJOD-LSDHHAIUSA-N

Myricetin was evaluated for its Physico-chemical, ADMET and Drugable properties. The 2D and the 3D structures of the molecules have been provided in Fig. 1 and Fig. 2. The calculated molecular weight of the selected molecule was 320.25 g/mol; the LogP value of Myricetin was 0.89; LogD value of the compound was 1.36; calculated LogSw value of the compound was -2.38; total number of stereocenters were = 2; Stereochemical complexity was estimated as 0.133; calculated Fsp3 value of Myricetin was = 0.133; Topological polar surface area of Myricetin was = 147.68 Å2; the number of hydrogen bond donors in the compound was = 6; number of hydrogen bond acceptors in Myricetin was = 8; number of smallest set of smallest rings (SSSR) in Myricetin = 2; size of the biggest system ring was 10; number of rotatable bond was = 1; number of rigid bonds in Myricetin = 18; number of charged groups in the compound = 0; total charge of the compound was = 0; the calculated Number of carbon atoms were 15; calculated Number of heteroatoms was = 8; the calculated Number of heavy atoms in Myricetin was = 23; the calculated ratio between the number of non-carbon atoms and the number of carbon atoms in Myricetin was = 0.53. Summary of data for physicochemical properties is provided in Table 2.

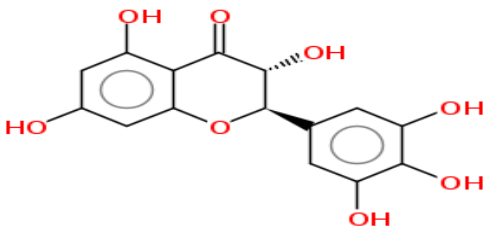

Figure 1: 2D structure of Myricetin

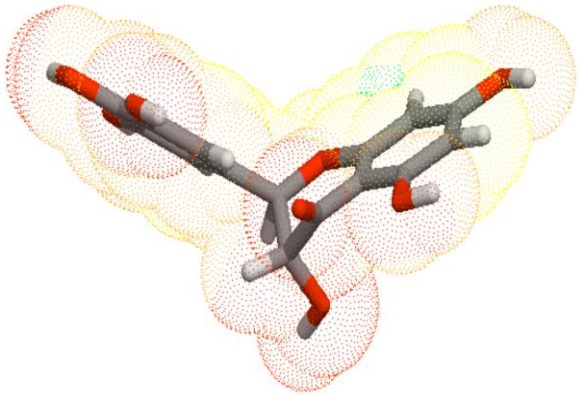

Figure 2: 3D structure of Myricetin

Table 2: Physicochemical Properties of Myricetin

PHYSICOCHEMICAL PROPERTY	VALUE
Molecular weight	320.25 g/mol
LogP	0.89
LogD	1.36
LogSw	-2.38
Number of stereocenters	2
Stereochemical complexity	0.133
Fsp3	0.133
Topological polar surface area	147.68 Å2
Number of hydrogen bond donors	6
Number of hydrogen bond acceptors	8
Number of smallest set of smallest rings (SSSR)	2
Size of the biggest system ring	10
Number of rotatable bonds	1
Number of rigid bonds	18
Number of charged groups	0
Total charge of the compound	0
Number of carbon atoms	15
Number of heteroatoms	8
Number of heavy atoms	23
Ratio between the number of non-carbon atoms and the number of carbon atoms	0.53

The compound when tested for Human Intestinal Absorption (HIA+) recorded a calculated value with a probability of 0.965; Blood Brain Barrier (BBB-) had a probability value of 0.571, The compound when tested for overall ADMET properties Boiled egg model indicated that the compound lies will within the permissible limits (Fig. 3); Caco-2 permeable (Caco2-) had a probability value of 0.896; for P-glycoprotein substrate (Substrate) the calculated value had a probability = 0.563; P-glycoprotein inhibitor I (Non-

inhibitor) recorded a calculated value with a probability of 0.930; while for P-glycoprotein inhibitor II (Non-inhibitor) the calculated value (probability) was = 0.838. for CYP450 2C9 substrate (Non-substrate) the calculated value had probability of 0.790; CYP450 2D6 substrate (Non-substrate) the calculated value had probability of 0.912; CYP450 3A4 substrate (Non-substrate) the calculated value had probability of 0.653; CYP450 1A2 inhibitor (Inhibitor) the calculated value had a probability of 0.911; CYP450 2C9 inhibitor (Non-inhibitor) the calculated value had a probability of 0.582; CYP450 2D6 inhibitor (Non-inhibitor) the calculated value had a probability of 0.929; CYP450 2C19 inhibitor (Non-inhibitor) the calculated value had a probability of 0.903; CYP450 3A4 inhibitor (Inhibitor) the calculated value had a probability of 0.695; CYP450 inhibitory promiscuity (High CYP Inhibitory Promiscuity) the calculated value had a probability of 0.582.

Ames test (Non AMES toxic) the calculated value had a probability of 0.722; Carcinogenicity (Non-carcinogens) the calculated value had a probability of 0.945; Biodegradation (Not ready biodegradable) the calculated value had a probability of 0.867; Rat acute toxicity (3.020 LD_{50}, mol/kg) the calculated value had a probability was Not applicable; hERG inhibition (predictor I) (Weak inhibitor) the calculated value had a probability of 0.978; hERG inhibition (predictor II) (Non-inhibitor) the calculated value had a probability of 0.816. Summary of ADMET properties tested has been provided in Table 3.

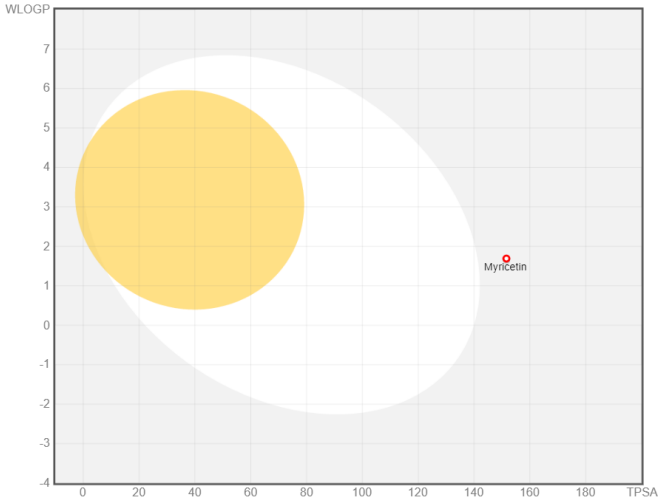

Figure 3: ADMET Boiled Egg Model of Myricetin

Table 3: ADMET Properties of Myricetin

ADMET PROPERTY	VALUE	PROBABILITY
Human Intestinal Absorption	HIA+	0.965
Blood Brain Barrier	BBB-	0.571
Caco-2 permeable	Caco2-	0.896
P-glycoprotein substrate	Substrate	0.563
P-glycoprotein inhibitor I	Non-inhibitor	0.930
P-glycoprotein inhibitor II	Non-inhibitor	0.838
CYP450 2C9 substrate	Non-substrate	0.790
CYP450 2D6 substrate	Non-substrate	0.912
CYP450 3A4 substrate	Non-substrate	0.653
CYP450 1A2 inhibitor	Inhibitor	0.911
CYP450 2C9 inhibitor	Non-inhibitor	0.582
CYP450 2D6 inhibitor	Non-inhibitor	0.929
CYP450 2C19 inhibitor	Non-inhibitor	0.903
CYP450 3A4 inhibitor	Inhibitor	0.695
CYP450 inhibitory promiscuity	High CYP Inhibitory Promiscuity	0.582
Ames test	Non AMES toxic	0.722
Carcinogenicity	Non-carcinogens	0.945
Biodegradation	Not ready biodegradable	0.867
Rat acute toxicity	3.020 LD50, mol/kg	Not applicable
hERG inhibition (predictor I)	Weak inhibitor	0.978
hERG inhibition (predictor II)	Non-inhibitor	0.816

Lipinski's rule of 5 violations for the compound was recorded as 1; the compound is within the range of Veber rule and was ascertained as Good; likewise it is in the limits of Egan rule and therefore considered as Good; Oral PhysChem score (Traffic Lights) was recorded as 2; GSK's 4/400 score was Good; Pfizer's 3/75 score was Good; Weighted quantitative estimate of drug-likeness (QEDw) score was 0.418; Solubility value for the compound was = 29492.46; Solubility Forecast Index was Good for Myricetin (Table 4). The calculated molecular and bioactivity score for the compound Myricetin is given in Table 6, 7.

Table 4: Druggability Properties of Myricetin

DRUGGABILITY PROPERTY	VALUE
Lipinski's rule of 5 violations	1
Veber rule	Good
Egan rule	Good
Oral PhysChem score (Traffic Lights)	2
GSK's 4/400 score	Good
Pfizer's 3/75 score	Good
Weighted quantitative estimate of drug-likeness (QEDw) score	0.418
Solubility	29492.46
Solubility Forecast Index	Good Solubility

Table 5: Molecular Properties - Calculated values of Myricetin

MOLECULAR PROPERTY	VALUE
miLogP	0.42
TPSA	147.67
Natoms	23
MW	320.25
nON	8
nOHNH	**6**
Nviolations	**1**
Nrotb	1
Volume	254.34

Table 6: Bioactivity scores - Calculated values of Myricetin

BIOACTIVITY PROPERTY	VALUE
GPCR ligand	0.09
Ion channel modulator	0.03
Kinase inhibitor	0.01
Nuclear receptor ligand	**0.27**
Protease inhibitor	**0.08**
Enzyme inhibitor	**0.32**

Table 7: Predicted Human Target Proteins

Protein identifier	HGNC symbol	Combined score STITCH database
ENSP00000354558	mTOR	700
ENSP00000216117	HMOX1	800
ENSP00000261769	CDH1	800
ENSP00000386884	CXCR4	800
ENSP00000313681	SPHK1	700

Myricetin when evaluated for its Human Target Proteins listed in the Human Genome Organisation (HUGO) Project for its effect on Predicted Human Target Protein with Protein Identifier Number (PIN) ENSP00000354558 (mTOR) protein kinase nucleates a major eukaryotic signalling network that coordinates cell growth with environmental conditions and plays a fundamental role in cell and organismal physiology, recorded a combined score of 700; PIN ENSP00000216117 (HMOX1), a Heme oxygenase cleaves the heme ring at the alpha methane bridge to form biliverdin. Biliverdin is subsequently converted to bilirubin by biliverdin reductase recorded a combined score of 800; PIN ENSP00000261769 (CDH1), Cdh1 is one of the substrate adaptor protein of the anaphase-promoting complex (APC); plays a pivotal role in controlling cell division at the end of mitosis (telophase) and in the subsequent G1 phase of cell cycle recorded a combined score of 800;

Likewise, PIN ENSP00000386884 (CXCR4) C-X-C chemokine receptor type 4 also known as fusin or CD184 is a protein that in humans is encoded by the CXCR4 gene recorded a combined score of 800; PIN ENSP00000313681 (SPHK1) Sphingosine kinase 1 phosphorylates sphingosine to sphingosine-1-phosphate (S1P) SK1 is normally a cytosolic protein but is recruited to membranes rich in phosphatidate (PA), a product of Phospholipase D (PLD) recorded a combined score of 700 in the STITCH database respectively. Overall results indicated that this lead molecule is of GRAS standard and can be used on the Human Target Protein candidates tested (Table 7). The cytoscape network of predicted human target of Myricetin is provided in Fig. 4. The Predicated *Pa*-*Pi*-*P*max and the probable bioactivity of the compound are given in Table 8.

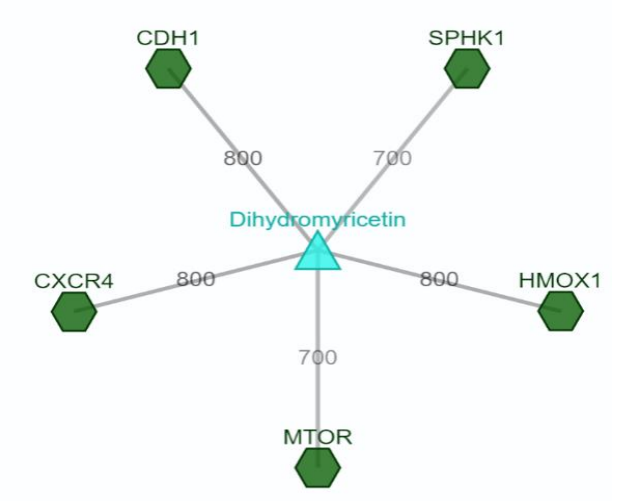

Figure 4: Cytoscape network of predicted human targets of Myricetin

Table 8 Predicated Pa-Pi-Pmax and bioactivity of Myricetin

Pa	Pi	Pmax	Bio-Activity
0.964	0.001	0.964	Peroxidase inhibitor
0.948	0.001	0.948	Cystathionine beta-synthase inhibitor
0.903	0.004	0.903	Apoptosis agonist
0.869	0.003	0.897	Antioxidant
0.867	0.002	0.981	Monophenol monooxygenase inhibitor
0.86	0.004	0.860	Aldehyde oxidase inhibitor
0.839	0.001	0.839	Carbonic anhydrase III inhibitor
0.818	0.001	0.818	Fatty acid synthase inhibitor
0.811	0.001	0.811	Creatine kinase inhibitor
0.807	0.003	0.807	Interleukin 4 antagonist
0.789	0.002	0.789	Carbonic anhydrase VI inhibitor
0.784	0.004	0.784	Lipoxygenase inhibitor
0.782	0.002	0.945	Carbonic anhydrase XIII inhibitor
0.764	0.002	0.764	Xanthine dehydrogenase inhibitor
0.754	0.007	0.754	Transcription factor NF kappa B inhibitor
0.712	0.003	0.712	NOS3 expression enhancer
0.692	0.004	0.692	Pyruvate kinase inhibitor
0.687	0.002	0.708	Xanthine oxidase inhibitor
0.672	0.002	0.672	Histone deacetylase SIRT1 stimulant
0.672	0.002	0.672	Histone deacetylase stimulant
0.655	0.014	0.759	Antiinflammatory
0.632	0.002	0.632	DOPA decarboxylase inhibitor
0.631	0.004	0.631	Estrogen antagonist
0.618	0.003	0.618	Estrogen receptor beta antagonist
0.609	0.003	0.609	HIV-1 integrase (3'-Processing) inhibitor
0.604	0.006	0.938	Hepatoprotectant
0.602	0.006	0.692	Hypoxia inducible factor 1 alpha inhibitor
0.600	0.002	0.613	Carbonic anhydrase VII inhibitor
0.584	0.004	0.584	P-glycoprotein inhibitor
0.578	0.009	0.905	Hypoglycemic
0.562	0.017	0.873	Spasmolytic
0.561	0.004	0.851	Lipid peroxidase inhibitor
0.533	0.013	0.533	Transcription factor STAT inhibitor
0.514	0.002	0.514	NAD(P)H dehydrogenase (quinone) inhibitor
0.512	0.004	0.512	Topoisomerase II inhibitor
0.511	0.003	0.511	HIV-1 integrase (Strand Transfer) inhibitor
0.506	0.008	0.771	Angiogenesis stimulant
0.503	0.011	0.503	Heat shock protein 90 antagonist
0.500	0.003	0.500	HIV-1 integrase inhibitor
0.493	0.003	0.493	Telomerase inhibitor

Studies on Myricetin has been surmounting in recent times due to its overwhelmed biological role in human health-care[6,24]. Myricetin plays an important role as antioxidant[16], anticancer[25,26], anti-inflammatory[27,28], anti-amyloidogenic[29], antibacterial[30], antiviral[31], and antidiabetic[32] agent. Myricetin has a proven record of an inverse association with risk of T2D[33]. In Myricetin, aryloxy radical in B-ring promotes antioxidant activity due to the presence of a pyrogallol moiety with a 3′,4′,5′-trihydroxy-substituted phenyl group (FRS) than a catechol moiety[34]. Therefore, Myricetin has been proposed to be a potent antioxidant[35].

Diabetes has a close association with metabolic inflammation and oxidative stress. Chronic inflammatory responses, including production of cytokines, results impaired insulin secretion and β-cell dysfunction that ultimately leads to diabetes[36]. Therefore, production and elimination of ROS is an important step in the pathogenesis of diabetes[37]. Myricetin has antioxidant as well as anti-inflammatory effects therefore, plays a pivotal role in preventing the onset of diabetics and the long term complications associated with the disease[38]. It has been demonstrated that Myricetin significantly lowers the plasma glucose levels in streptozotocin-induced diabetes in rats[39] and insulin resistance[40]. Myricetin inhibits glucose uptake in rat adipocytes by disrupting glucose-transporter subtype 4 (GLUT4). Furthermore, Myricetin blocks metabolic uptake of methylglucose by inhibiting GLUT4. However, phosphorylation of insulin receptor substrate-1 via insulin receptor tyrosine kinase remains unaffected by Myricetin in insulin-stimulated rat adipocytes[41].

ATPases use ATP for catalytic function; several ATPases such as Hsp70 ATPase[42] are inhibited by Myricetin. Toxicological screenings including behavioral, histomorphological, hematological and biochemical parameters using seed extracts[43], fruit[44], and leaf[45] of *S. cumini,* had no toxic effect. Silva et al.[45] demonstrated that acute administration of hydro-alcoholic extract of *S. cumini* leaf at doses as high as 2 g/kg produced no toxic effects in experimental models. Dang et al.[46] demonstrated that owing to poor absorption, Myricetin showed low oral bioavailability. Studies have established that Myricetin has a therapeutic effect on different types of tumors, inflammatory diseases, atherosclerosis, thrombosis, cerebral ischemia, diabetes, Alzheimer's disease and pathogenic microbial infections[6]. Furthermore, Myricetin significantly enhances the immunomodulatory functions, suppresses cytokine storms, and improves cardiac-dysfunction. Myricetin possesses an antiviral potential, therefore, can be used as an adjuvant treatment against COVID-19 and other viral infections due to its physiochemical and biomolecular properties.

CONCLUSION

Prevention and cure of diseases using phytochemicals especially flavonoids has been well established. Fruits and vegetables are rich sources of flavonoids. Myricetin has a potential use as a nutraceutical. Its antimicrobial and antioxidant role have shown promising results. Also, preclinical studies have revealed antidiabetic, anticancer, immunomodulatory, anti-cardiovascular, analgesic and antihypertensive activities. The data presented in this paper towards physicochemical, ADMET and druggable properties of Myricetin can used as a baseline information to take-up in-depth research investigation on this molecule as a lead GRAS candidate for the development of novel drug in the days to come.

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