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

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**INTRODUCTION**

Diabetes mellitus (DM) an epidemic, affects more than 170 million individuals worldwide. It is predominately 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. Diabetes, 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 diabetes². 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 age². 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
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. 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. As of now, more than 4000 varieties of flavonoids from various plant sources have been reported.

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 polyhydroxyflavonol compound composed of light yellow crystals, soluble in methanol, acetonitrile, ethanol and other polar solvents. Its chemical formula is C_{15}H_{10}O_{7} and the relative molecular mass is 318.24.

It was first described in 18th century from the bark of Myrica nagi Thunb. Myricaceae7, 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. Although Myricetin occurs throughout the Plant Kingdom, it is produced mainly by members of the families: Mangifera indica (Anacardiaceae)8,9, Marantodes pumilum (Primulaceae)10, and Primulaceae11. 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. 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, telomerasens, kinases and helicases.

Myricetin is used in the management of non-insulin-dependent diabetes, by stimulating the uptake of glucose without functional insulin receptors. 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 hCa/NF-κB pathway independent of nuclear factor erythroid 2-related factor (Nrf2) regulation. Furthermore, it activated gluagon-like peptide 1 receptor (GLP-1R) and its long-term oral administration (200 mg/kg, for 40D) validates its gluco-regulatory effects. 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 antioxidant properties that are mediated via regulation of the transport of glucose through the function of glucose transporter-2 in Xenopus laevis oocytes. Karunakaran et al. 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. pointed out that, all parts of Syzygium cumini are rich in polyphenols (Table 1). The extract of various parts of Syzygium cumini contains phytochemicals including tannins, anthocyanins, terpenes, flavanols and aliphatic-acids. Both fruit and flowers of Syzygium cumini are rich in anthocyanins as Cyanidin, Delphinidin, Peonidin, Pelargonidin, Petunidin and Malvidin. Seeds of Syzygium cumini contain Rutin and Quercetin while leaves have been reported to contain kaempferol, Myricetin, Quercetin and their glycosides. Syzygium cumini has been reported to contain Ellagic acid, Triterpenoids, acetyl Oleanolic acid, Quercetin, Isoquercitin, Myricetin and Kaempferol. Syzygium 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.

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

| Part     | Plant Based Natural Products (Bioactive Lead Molecules) | Ref |
|----------|--------------------------------------------------------|-----|
| Bark     | Myricetin, Quercetin, Kaempferol                        | 28, 47 |
| Flower   | Kaempferol, Myricetin, Dihydromyricetin, Myricetin-3-L-Arabinoside, Isoquercetin, Quercetin, Quercetin-3-D-galactoside | 28, 48 |
| Fruit    | Myricetin, Quercetin, Myricetin Deoxyhexose            | 28, 49 |
| Leaf     | Catechin, Kaempferol, Myricetin 3-O-8-B-D-glucuronopyranoside, Myricetin-4'-methyl ether 3-O-A-rhamnopyranoside, Myricetin 4'-O-acetate, Myricetin 4'-O-acetyl-2-o-gallate, Quercetin-3-O-α-rhamno, pyranoside | 28, 50 |
| Seed     | Quercetin, Myricetin, Rutin, 3,5,7,4-tetrahydroxy flavanone | 28, 51 |
MATERIALS AND METHODS

ADMET prediction

Physicochemical properties were computed using FAF-Drugs4 (28961788)/ RDKit - open-source CIP. Selected phytochemicals 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. Druggability 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(c3O)O)O][C@H](C(=O)c2c(c1)O)O
InChI Key: KJXSIXMJHKAJOD-LSDHHA1USA-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 = 147.68 Å2; the number of hydrogen bond donors in the compound was = 6; number of hydrogen bond acceptors in Myricetin = 8; number of smallest set of smallest rings (SSSR) in Myricetin = 2; size of the biggest system ring = 10; number of rigid 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 = 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.

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 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 a 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 (3.0 20 LD50, 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  |

Myricetin was 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 800; PIN ENSP00000313681 (SPHK1) Spingosine kinase 1 phosphorylates spingosine to spingosine-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 cytoscope network of predicted human target of Myricetin is provided in Fig. 4. The Predicated Pa-Pi-Pmax and the probable bioactivity of the compound are given in Table 8.

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            |                 |

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 monoxygenase 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 | Lipoygenase 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 overwhelming biological role in human health-care6-24. Myricetin plays an important role as antioxidant15, anticancer25,26, anti-inflammatory27,28, anti-amyloidogenic29, antibacterial30, antiviral31, and anti-diabetic32 agent. Myricetin has a proven record of an inverse association with risk of T2D33. In Myricetin, arylxoy 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 catedol moiety34. Therefore, Myricetin has been proposed to be a potent antioxidant35.

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 diabetes36. Therefore, production and elimination of ROS is an important step in the pathogenesis of diabetes37. 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 disease38. It has been demonstrated that Myricetin significantly lowers the plasma glucose levels in streptozotocin-induced diabetes in rats39 and insulin resistance40. 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 adipocytes41.

ATPases use ATP for catalytic function; several ATPases such as Hsp70 ATPase42 are inhibited by Myricetin. Toxicological screenings including behavioral, histomorphological, hematological and biochemical parameters using seed extracts35, fruit44, and leaf45 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. 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 adjunct treatment against COVID-19 and other viral infections due to its physicochemical 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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