

Flavonoids from leaves of *Syzygium samarangense* and its pharmacological potential: some recent insights

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Abstract

Syzygium samarangense is an indigenous herb growing ubiquitously in various parts of India. The present review aims to unravel the recent findings with respect to the flavonoids and their bioactivity isolated from the extracts and fractions of this plant. Extensive literature and compendial survey (2001-2019) was performed of existing bibliographic databases such as PubMed, AYUSH, Google scholar and databases of Traditional Knowledge and search strategies were designed a priori. Antibacterial, antifungal and anti-inflammatory activities were reported in *Syzygium* species. The flavonoids, isolated from *Syzygium samarangense*, studies were reported to exhibit activities like antidiarrheal, immuno-pharmacological, cytotoxic, antihyperglycaemic, antibacterial activity, analgesic and anti-inflammatory and antioxidant activity. In recent years many plants extracts containing flavonoids along with other secondary metabolites which have free radical scavenging properties accompanied with other activities like anti-inflammatory, hepatoprotective, nephroprotective, antiproliferative, neuroprotective and also cardio protective. The flavonoids fall under the category of typical phenolic compounds and are abundant in plants. The typical characteristic functional group in flavonoids is hydroxyl group substituted flavan moiety. These characteristic functional groups in flavonoids are free radical scavengers that impede the oxidation of biological molecules following conversion of ROS into inactive species. Hence oxidative stress induced disorder and diseases could be prevented with the help of antioxidants.

Keywords: Flavonoids, bioactive compounds, phytoconstituents, phenol

INTRODUCTION

Syzygium samarangense Merr et (Perry) belongs to the family Myrtaceae is a plant species commonly known as “Wax Apple” grows abundantly in the Malay peninsula,

Andaman & Nicobar Islands [1] and also in some parts of West Bengal. In West Bengal it's commonly named as “Jamrul”. Myrtaceae family plants are mostly popular due to their medicinal properties and are potent source of biologically active constituents like phenols

and flavonoids [2]. The flavonoids are used in treating diseases like asthma, bronchitis, inflammations, diabetes mellitus etc. In addition to their medicinal properties the leaf extracts have potent antioxidant activity, anti-mutation and anticancer activities. The chemical constituents present in the leaves of wax apple are flavonones, flavonol glycoside, ellagitannins, anthocyanidins, proanthocyanidins, triterpenoids, chalcones and volatile terpenoids [3]. The percentage of triterpenoid, tannins having γ terpinene and other related compounds are high in volatile oils present in the leaves *Syzygium* species [3]. Immunostimulant activity has been reported in hexane and ethanolic extracts of leaves thus helps reducing hyper motility in the gut [4][5]. Studies have shown that the seeds and leaves of the plant shows antimicrobial activities against *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Cryptococcus neoformans* [6]. Studies suggested that several *syzygium* species exhibited anti-inflammatory, anti-bacterial and antifungal activities [7].

The present review explores the role of the flavonoids found particularly in the leaves and their possible role in the putative effects of the plant which has not been collated extensively before the present study.

Presence of some rare flavonoids:

Characterization of flavonoids of rare variety has been identified and isolated from *Syzygium samarangense* leaves (syn. *Eugenia janvanica*) [8] two flavonoids those were reported are mearnsitrin and 2'-C-methyl-5'-O-galloylmyricetin-3-O- α -L-rhamnopyranoside.

There has been a greater interest in analyzing the flavonoid compounds because of the presence of bioactive compounds and pharmacological activities [9][10].

Reports were found that anti lipoperoxidative and anti-inflammatory were attributed to series of natural flavonoids and were assessed to possess promising results [11][12]. Hence the

rare flavonol mearnsitrin was recognized by spectral analysis [13]. The second compound isolated exhibited purple colour under UV and yellow under UV/NH₃ thus indicating presence of 4'-OH group [14].

Immunomodulatory effects of flavonoids [15]:

The acetone fraction of leaves extract has been studied and sixteen flavonoids were isolated. Immunopharmacological activities were demonstrated by the isolated flavonoids upon Human peripheral blood mononuclear cell (PBMC) which were the target cells while cell proliferation was resolved by 3H thymidine uptake. Therefore preliminary results exhibited isolated flavonoids outcomes upon the PBMC and the immunosuppressive activities thereafter. Since chalcones, proanthocyanidins and triterpenoids were already reported so the leaves extract were re-examined to infer its bioactivity obtaining sixteen flavonoids. They consist of five flavonones Pinocembrin, (-) Strobopinin, 3,8-methyl-pinocembrin, Demethoxymatteucinol, 7-hydroxy-5-methoxy-6,8-dimethyl-flavanone, two chalcones (stercurensin), 4,6'-dihydroxy-3',5'-dimethyl-2'-methoxy-chalcone, Four flavones glycosides, myricetin, epigallocatechin 3-O-gallate (one anthocyanidin), myricetin 3-O- α -rhamno-pyranoside, Mearnsitrin, two flavones (quercetin), Myricetin, Two dihydro-chalcones (uvangoletin), Myrigalone H. Isolated flavonoids were assessed on PBMC escalation.

Chemical constituents in the leaves:

Dose-dependent spasmolytic activity was showed by *S. samarangense* from the four potent flavonoids segregated from the hexane extract [16]. Studies showed evidence that 2',4'-dihydroxy-6'-methoxy-3',5'-dimethylchalcone from *S. samarangense* exhibited significant differential cell toxicity against MCF-7 cell line and consequential selective cell toxicity against yeast mutant strain RAD 52 [17]

2',4'-dihydroxy-6'-methoxy-3'-methylchalcone, 2',4'-dihydroxy-6'-methoxy-3'-methyl

dihydrochalcone, 2'-hydroxy-4',6'-dimethoxy-3'-methylchalcone, betulin, lupeol, epibetulinic acid, α - and β -carotene are separated from the hexane extract of the leaves and β -D-sitosterylglucoside exhibited activity against prolylendopeptidase [18]. High antidiabetic activity were exhibited by methanolic extracts of leaves [19], 5-O-methyl-4'-desmethoxy matteucinol and 2', 4'-dihydroxy-6'-methoxy-3',5'-dimethyl chalcone in hyperglycaemic mice blood glucose were significantly lowered after 15 minutes of glucose load, while 2',4'-dihydroxy-6'-methoxy-3',5'-dimethylchalcone significantly reduced blood glucose in alloxan induced diabetic mice.[20].

Flavonoids with spasmolytic activity

Flavonoids from hexane extract were found to possess spasmolytic activity. Though flavonoids have been traditionally established for their spasmolytic activity researchers found that series of triterpenoids and flavonoids have propyl endopeptidase activity [21], so they have studied the effect of these fractions of *S. samarangense* upon the isolated jejunum of rabbit which were reported to be rare C methylated chalcones and flavones. Mostly flavonol, flavones and isoflavone has spasmolytic activity [22][23][24].

Antihyperglycaemic Flavonoids

Proanthocyanidins, Ellagitannins and flavonol glycoside were reported to be found in leaves of *S. samarangense*, 4',6'-dihydroxy-2'-methoxy-3',5'-dimethylchalcone this compound was yielded from the aerial parts. Flavonoids present in this leaves are rare because of C methylated group. The chemical conformation of the structures attributes to antihyperglycaemic activity due to additive effect of the C-5'-CH₃ and the olefinic moiety next to the -C = O group. 2',4'-Dihydroxy-3',5'-dimethyl-6'-methoxychalcone 1, and one of the flavanone 5-O-methyl-4'-desmethoxy-matteucinol 2 were separated from the leaves.

Antibacterial effects

It has been reported that the leaves and seeds of the plant shows antimicrobial activities against *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and *Cryptococcus neoformans* [25]. Several species were reported to possess anti-inflammatory, anti-bacterial and antifungal activities.

Evaluation of Myricitrin and 3,5-di-O-Methyl Gossypetin (an new compound) from *Syzygium samarangense* [25]

Study showed that the compound Myricitrin and 3,5-di-O-Methyl Gossypetin both exhibited ability to reduce oxidative stress. The oxidative stress was induced by sodium arsenate for the former and ultraviolet rays for latter on human keratinocytes.

Since ROS generation is considered responsible for pathologies. Hence pre-treatment with the mentioned flavonoids was able to nullify the negative effects induced by oxidative stress, hence alteration in GSH (glutathione) level, reactive oxygen species production, peroxidation was observed. Mitogen activated protein kinase modulation was observed. Finally both the compounds exhibited their scavenging activity of free radicals through nuclear transcription factor by stimulating antioxidant properties. Both the compound holds substantial future prospect in anti-inflammatory and antioxidant activity.

DISCUSSION

These aforesaid functional groups characteristic to the plant species are necessary for the flavonoids possibly scavenger of free radical which helps in impeding oxidation of biological molecules followed by conversion of ROS donating H₂ atom into inactive species. Hence antioxidants proves to be more advantageous because of their ability to lower the oxidative stress induced diseases.. Since the deleterious effects of ROS are impending crisis, so to combat the process free radical scavenging is necessary, even though our defense mechanism has innate capability to

admonish but in long term process external source of antioxidants are required.

Some of the innate antioxidant in our system includes alpha lipoic acid, glutathione, vitamins A, C, E, some endogenous enzymes, minerals such as Zn, Cu, Se, Mn proves beneficial to maintain redox homeostasis. When there is disruption in the intracellular redox equilibrium, pathway of oxidative stress gets stimulated and therefore need of exogenous antioxidants replenishment becomes necessary. Recently reported that there are 92 compounds separated from leaves of *Syzygium samarangense* whose main components comprises of flavonoids and tannins [26] Five new triterpenoid has been reported they are sysamarin A to E (oleanane triterpenoid).

The present review aptly summarises the role of these flavonoids found particularly in the aerial parts of the plant and explore their possible role and mechanism in the amelioration of certain disorders not studied before in such depths.

CONCLUSION

The review on the flavonoid behind the role of *Syzygium samarangense* as a potential antioxidant and having free radical scavenging activity are evident. The justification regarding the therapeutic activity in the mitigation and prevention predominantly depends upon the outcome of the bioactive components attributed to those pathological conditions which are yet to be explored. Proper emphasis to be given upon the identification, characterization and isolation of the constituent. Exploring the bioactive component having the potential to exhibit the therapeutic efficacy is a major concern. Therefore, further studies in this genre of medicinal plants requires utmost importance since antioxidants are gaining more popularity nowadays, if that could be obtained from natural source future prospects in the field of herbal medicines will promise for new avenues.

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Conflict of interest

None

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