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Letter to the editor:

PREVENTIVE ROLE OF *SAPINDUS* SPECIES IN DIFFERENT NEUROLOGICAL AND METABOLIC DISORDERS

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Sapindus, also known as soap nut is rich in saponins. The tree belongs to the family Sapindaceae which has six to twelve closely related species, primarily comprising of shrubs and small trees. Being one of the world's oldest cultivated medicinal plants, *Sapindus* boasts of various therapeutic uses. The use of this valuable tree has been traced back to the period of Ancient India, which is estimated to be around 5000 years ago. It is a deciduous tree with moderate length that grows naturally in the Southern states of India and also in some regions of Northern India. Sugars, fatty acids, trifoliosides, tannins, phenolic acids, steroids, carbohydrates, and triterpenoids are the primary phytoconstituents derived and reported from different parts of the plant (Arul et al., 2004). *Sapindus* is also used in Ayurvedic composition of shampoos and cleansers as an important component. Some tribes in India, use a decoction of the plant's aerial parts for the treatment of diabetes mellitus, as described in traditional reports. Contemporarily, *Sapindus trifoliatus* (ST) has been used for decades to treat colds caused by infection and inflammation, and is also used in combination with standard medicine to treat a variety of malignancies and conditions such as diabetes mellitus (Arulmozhi et al., 2004a). Soap nut powder contains potent antimicrobial activity and because of this it is widely used in cosmetic and contraceptive creams. Arthritis, common cold, constipation, nausea, and dental caries are also treated by using powdered seeds of the plant. It is also beneficial for skin disorders like eczema and psoriasis (Arulmozhi et al., 2004b). In addition, *Sapindus* species has also been used for thousands of years in traditional medicine to treat excessive salivation, epilepsy, chlorosis, and neuroleptic diseases (Arulmozhi et al., 2005a). Current biological and pharmacological updates on *Sapindus trifoliatus* have been reviewed below (Table 1).

Table 1: Current biological and pharmacological updates on *Sapindus* species

Key findings	Reference
Arul et al. assessed the anti-inflammatory activity of the ethanolic extract of *Sapindus trifoliatus* (ST) seeds in a migraine hyperalgesic model. The study reported significant inhibitory effects at a dose of 150 mg/kg, p.o. on leukocyte migration which indicated that the ethanolic extract of seeds can produce significant anti-inflammatory activity.	Arul et al., 2004
Arulmozhi et al. carried out an herbal-based study for the treatment of migraine. The findings revealed that, by using an isolated rat fundus, the aqueous extract of *Sapindus trifoliatus* (ST) showed affinity with 5-HT2B receptors. However, ST showed no specificity towards acute migraine targets (viz. 5-HT1B/1D receptors and -adrenoceptors).	Arulmozhi et al., 2004a
Saponins have been found in abundance in the ethanolic extract of ST. Saponins were shown to possess anti-diabetic and antioxidant properties. Furthermore, the plant is recognized for its protective action on lipid peroxidation and oxidative damage and thereby promoting cellular antioxidant response in alloxan induced diabetes.	Arulmozhi et al., 2004b
The results from this study have pointed out that in streptozotocin-induced diabetes, the extract of *Sapindus trifoliatus* (ST) has potential benefits on pancreas histological alterations. Moreover, the hydroalcoholic extract of ST fruits is reported to possess antihyperglycemic and antihyperlipidemic properties.	Arulmozhi et al., 2005a
In this study, the antihyperalgesic effect of the aqueous extract of *Sapindus trifoliatus* (ST) was observed, which is thought to be regulated by the antagonistic activity of dopamine D2. ST is also used in the treatment of hemicranias. It also has sedative properties which reduces locomotor activity in laboratory animals. The current findings support the use of ST in the treatment of hemicrania on an intellectual basis.	Arulmozhi et al. 2005b

Key findings	**Reference**
In this study, the authors have shown that a hydroalcoholic extract of ST protected experimental rats from AlCl3-induced Alzheimer's disease (AD) based on behavioral, biochemical, and histopathological characteristics. This positive effect could be attributed to the hippocampus' inhibition of oxidative stress and plaque formation.	Bodhankar et al., 1974
The study reports the modulatory effect of ST on human platelet serotonin release. It was found that the aqueous extract of ST inhibited 5-HT2B receptors and platelet serotonin release significantly. It also inhibited adrenoceptors in the rabbit aorta, 5-HT1B/1D receptors in the rabbit saphenous vein and 5-HT2B receptors in the rat fundus.	Borad et al., 2001
Chen et al. reported that ST has analgesic effects in both the central and peripheral nervous systems. The current findings support the use of ST in the treatment of hemicrania in an ethno-medical setting. ST is likely to block both peripheral and central pain pathways, as well as have a modulatory role in NO-mediated nociceptive transmission.	Chen et al., 2019
The results obtained from the investigations suggested that ST-treated animals had considerably higher hyperglycemic levels during the oral glucose tolerance test (OGTT) than the vehicle-treated animals. Glibenclamide, a conventional hypoglycemic drug, was administered (10 mg/kg dose) and it showed a dramatic decrease in glucose levels during the GTT. ST has diabetogenic potential in normal animals, as reported by some authors.	Desai, et al., 1986
Findings from this study have shown that the aqueous extract at doses 50 mg/kg, 100 mg/kg, and 200 mg/kg, demonstrated skeletal muscle relaxant action. *Viola betonicifolia* and ST both had the same effect on the GABA(A) receptor, which renders them muscle relaxants.	Dixit and Gupta, 1982
The observations from this study discuss about the key inflammatory mediators, namely, 5-LO, COX, LTB4, and NOS. Topical use of ST dramatically reduced ear inflammation caused by acute and repeated TPA treatments, as well as acute capsaicin or arachidonic acid applications. The extract had no effect on oxazolone or DNFB-induced ear infection. ST possesses anti-inflammatory properties that may be mediated through the 5-LO and COX pathways.	Gandreddi et al., 2015
Grover et al. conducted a study on STZ-induced diabetic rats, by using extracts of ST for thermal and chemical hyperalgesia activity. The findings suggest that ST has an important role in modulating neuropathic pain through the adenosine receptor. ST stimulated the adenosine receptor (subtype A1) at the molecular level, which is related to a number of effectors such as adenylate cyclase, Ca2+ channel, K+ channel, ionositol phosphate, and neurotransmitter release.	Grover et al., 2005
Kamboj et al. isolated sapinmusaponins Q1 and R2, two new tirucallane-type triterpenoid saponins, as well as three prominent oleanane-type triterpenoid saponins from ST (3-5). Spectroscopic examination and chemical hydrolysis were used to identify their structures. Both sapinmusaponins Q and R were found to have a stronger anti-platelet aggregation activity than aspirin.	Kamboj and Dhawan, 1982
The findings from this study indicated that, extracts of *Sapindus mukorossi* and *Rheum emodi* protected primary hepatocyte and liver damage in a rat model of CCl 4-induced liver injury.	Lal et al., 1976
Pore et al. conducted a study on rats to evaluate the anti-ulcer activity of *Sapindus saponaria* L. leaves. Rats were administered with extracts of the fruits. Gastric secretion parameters including volume, pH, and acidity were estimated. The extracts were comparatively studied with cimetidine to evaluate its ability to relieve stress-induced lesions. In the acute experiments, the lesion index was significantly lowered. Extracts given orally for 30 days showed minimal change in body or organ weight of animals.	Pore et al., 2010

Key findings	Reference
This study reports the usage of *Sapindus* saponaria L. extracts which showed anti-ophidian efficacy and could be administered as an adjuvant or supplement to serum therapy. It contains a large number of possible enzyme inhibitors that are important in a variety of pathophysiological human and animal diseases.	Sirisha et al., 2018
The findings from this study indicated that high-dose alcohol extracts of *Sapindus mukorossi* can boost HDL and APL levels as well as lower LDL, AST, TC, TG, c-GT, ALT and ALP levels in NAFLD-rat model. The morphology of hepatic tissue and liver cells recovery of LSEC were also observed by using optical and electron microscopes. The study reported that alcoholic extracts of *Sapindus mukorossi* can regulate blood fat levels and improve pathological alterations in hepatic tissues, demonstrating the effects of fat down-regulation and liver safety.	Lu et al., 2016
Findings from this study have shown that *Sapindus* saponins have the potential to be developed into a human microbicidal contraceptive. In this research *Sapindus* saponins were compared with *Trichomonas vaginalis.* The findings showed that *Trichomonas vaginalis* has ten times lower affinity than its actual spermicidal concentration when used with *Sapindus* saponins. Final findings suggest that *Sapindus* saponins altered Trichomonas' inhibitory mechanisms, bypassing host immunity and has a microbicidal contraceptive use in human.	Tiwari et al., 2008
The study reports the usage of *Sapindus mukorossi* stem bark for inflammation-related illness due to the presence of polyphenols, flavonoids, and other compounds in polar extract/fractions which may reduce inflammation and pain-inducing mediators.	Tungmunnithum et al., 2018
Porsche et al. reported that *Sapindus mukorossi* aqueous extract and chloroform methanol extract of fruit pericarp showed antifungal activity. It was studied for the first time against 2 major fungal infections, *Venturia inaequalis* and *Botrytis cinerea*. The findings show aqueous extract (1 % v/v) reduced *B. cinerea* disease severity on grapes by 63 % on average.	Porsche et al., 2018
Chaudhary et al. confirmed in their study that dietary shell powder supplementation (SSP) of soapnut (*Sapindus mukorossi*) had no benefit on the egg laying quality, but increased serum and seminal plasma testosterone levels by 0.02 percent. It lowered embryonic mortality in broiler breeders, confirming that it has 0.026 % nutritional supplementation efficacy. As a result, SSP improved broiler breeder reproductive performance.	Chaudhary et al., 2019
Polli et al. conducted a biological activity on the extract of secondary metabolites of *Sapindus saponaria* named (E-G6-3-2) to evaluate the antioxidant and anticholinesterasic properties. They suggested that *Curvularia sp.* (E-G6-3-2) appears to be a promising source of bioactive secondary metabolites, such as asperpentyn, a substance with therapeutic value. Spectroscopic and mass spectrometric analysis of extract confirmed that asperpentyn came from the epoxyquinone family, which has an appealing structural complexity and a wide range of biochemical processes, including enzyme inhibitory activity.	Polli et al., 2021
Samiksha et al. conducted research on insect-repellent potential of *Sapindus mukorossi* (SM) extract. The study showed that SM has resistance against *Bactrocera cucurbitae*. Tritrypsin inhibitor extracted from SM seed can inhibit the growth and development of B. cucurbitae larvae by altering their physiological and biochemical processes and can be used as a biocontrol against pests and various bacterial strains.	Samiksha et al., 2019

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Key findings	Reference
As per Wei et al. aqueous extract of *Sapindus mukorossi* yielded two phytochemicals, Mukurozioside IIa and Mukurozioside IIb. They demonstrated cytotoxic activity in greater extents than the positive control group. The IC_{50} values of MCF-7, MDA-MB-231, and MDA-MB-435s remained comparatively higher than their parent fraction II, which show that their individual action is weaker than their parent fraction. As a result, they show synergistic effect in fraction II with themselves or other compounds and contributed to the anticancer action.	Wei et al., 2021
According to Hu et al. the pulp extract of *Sapindus mukorossi* produced significant anti-fungal action, showing new unknown oleanane-type and lupane-type triterpenoid saponins with 12 known relative components. Spectroscopic investigation and chemical approaches were used to identify their structures. *Trichophyton rubrum* was inhibited by -a-L-arabinopyranoside with a MIC80 of 8 mg/mL. In this study they found that *Trichophyton rubrum* and *Candida albicans* were resistant to a-L-rhamnopyranosyl (1/2) oleanolic acid, but not to 3-O-a-L-arabinopyranosyl (1/3) oleanolic acid.	Hu et al., 2018
Bera et al. had observed the effect of dietary saponin rich soapnut (*Sapindus mukorossi*) shell powder on growth performance, immunity, serum biochemistry and gut health of broiler chickens. It was observed that it strengthened the immunity of broiler chicken and health with low belly fat, serum cholesterol, triglyceride, glucose, and pathogenic gut bacteria load. The optimal dose of saponins in the form of soapnut shell powder was administered at 150 mg/kg diet for 3 weeks (21–42 days). Findings show that the selective antimicrobial activity against gut pathogens boosted specific immunity by using the optimal dose of saponins.	Bera et al., 2019
Sirisha et al. performed molecular docking and *in vitro* studies of soap nut trypsin inhibitor (SNTI) against phospholipase a 2 isoforms in therapeutic intervention of inflammatory diseases. They suggested that membrane, cytosolic, and pancreatic PLA2 proteins have mostly been docked with ST ligand molecules. Kampferol, an ST seed endosperm secondary metabolite, inhibited cytosolic PLA2 by a significant amount. SNTI, a protease inhibitor isolated from ST seed endosperm, showed a good interaction with membrane PLA2 in both *in silico* and *in vitro* experiments. *In vitro* studies and docking interaction profiles indicate that some ST compounds are immunomodulators with anti-inflammatory properties.	Sirisha et al., 2018

Conflict of interest

The authors declare no conflict of interest.

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