Plant Archives Vol. 20, Supplement 2, 2020 pp. 3313-3322 **e-ISSN:2581-6063 (online), ISSN:0972-5210**

SHOREA ROBUSTA GAERTN. F: A MULTI-THERAPEUTIC POTENTIAL INDIGENOUS DRUG

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Running Title: Multi-therapeutic potential of *Shorea robusta*
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Abstract

Shorea robusta Gaertn. f. is an Indigenous plant, commonly known as Sal, Shala, Indian Dammer, Holy tree. In ayurveda, bark and leaves of *S. robusta* were used to cure itching, leprosy, gonorrhea, wounds and stomach ulcers, disease of vagina, cough, pain in ear and head. It is used as anthelmintic, alexeteric, enrich the blood, prevent sweating, improve the complexion, etc. whereas, in Unani system of medicines *S. robusta* has been traditionally used to treat menorrhagia, eye irritation and in enlargement of spleen. It is a good blend of primary and secondary metabolites. Some pharmacological significant molecules isolated from *S. robusta* are bergenin, ursolic acid, caryophyllene oxide, calarene epoxide, Lupeol, β-humulene, α-amyrin, α-amyrin, β-Caryophyllene, etc. *S. robusta* has scientifically evaluated on experimental animals and reported to possess analgesic, anticancer, anticonvulsant, anti-diabetic, anti-hyperlipidemic, anti-inflammatory, antimicrobial, antioxidant, antipyretic, antiulcer, immunomodulatory, wound healing activity, etc. *S. robusta* is a plant drug having multi-therapeutic potential to cure a variety of health problems. It is worth to update the ethnopharmacological, phytochemical and pharmacological reports which might be a good source of information to the researchers working in these domains.
***Keywords*:** *Shorea robusta*; Sal; Holy tree; Ayurveda; Unani System of Medicine.

Introduction

In the human health care, herbal medicinal plants play a vital role. A large proportion of populations of growing countries have faith on herbal practitioners who are reliant on medicinal plants to fulfill the major healthcare needs (WHO, 1993). Generally, in villages (rural and tribal) of India about 7500 plants are utilized in local health. The traditional system of medicines for example Unani, Siddha, Ayurveda, Tibetan and Homeopathy use about 1200 plants. These traditional systems merged ancient beliefs and were passed on by oral tradition and/or guarded literature from one generation to another (Pushpangadan, 1995). The present effort is to review and compile updated information on various aspects of *Shorea robusta Gaertn. f.* (Figure 1), an herbal medicinal plant used in Indian traditional system of medicines for variety of purposes. *S. robusta* (Sal) belongs to family Dipterocarpacea, which is usually well-known as Shal, Sal in Hindi and Indian Dammer and Sal tree in English. It is a deciduous tree generally found in India, from Himachal to Orissa Eastern districts spreading to the Eastern Ghats of Andhra Pradesh (Kritikar and Basu, 1999).

(a) (b)

Fig. 1 : (a) *S. robusta* (close up view) and (b) Habit tree

Species of Sal indigenous to Western Ghats countries, South Asia, ranging South of Himalaya, from Myanmar in the east to India, Bangladesh, Bhutan and Nepal (Murugesa, 1988). In India, the species found from Himachal Pradesh to Assam, West Bengal, Tripura, Bihar, Orissa and Eastern districts of Madhya Pradesh and Andhra Pradesh (Murthy, 2011). The present critical review is centralized to traditional uses, scientific reports based on phytoconstituents as well as

pharmacological activities along with standardization studies and some miscellaneous scientific reports on *S. robusta* (Figure 2).

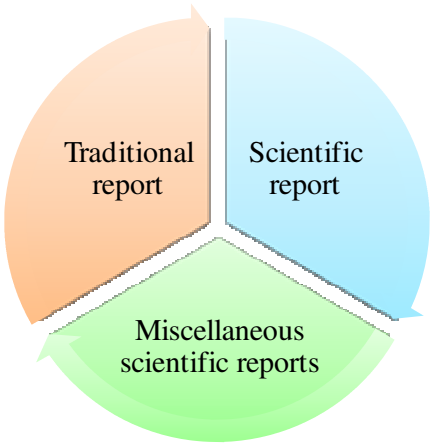


Fig. 2 : Centralized focus area on *Shorea robusta Gaertn*

Traditional reports

S. robusta has been traditionally used in a variety of health problems. According to in ayurveda, bark and leaves of *S. robusta* used in the cure of itching, leprosy, gonorrhea, wounds and ulcers, enrich the blood, prevent sweating, improve the complexion, in cough, disease of vagina, pain in ear and head. These are used as anthelmintic and alexeteric. Resin of this plant has been used as tonic to brain, blood purifier, lessens sweating and body temperature, effective for wounds, fractures, pains, burns, itching and ulcers, useful in dysentery and also good for vaginal discharges. Unani system of medicine reported use of resin in menorrhagia, ascites, obesity, ulcers, enlargement of spleen, wounds, in toothache, beneficial for eye burning and eyesores. All kinds of wounds, skin diseases and scabies treated with oil of *S. robusta* (Kritikar and Basu, 1999). The resin also used in dysentery, gonorrhea (Kritikar and Basu, 1999, Verma *et al*., 1993, Anonymous, 1972) astringent and in skin and ear troubles (Anonymous, 1972). It is also act as aphrodisiac and commonly given in weak digestion (Kritikar and Basu, 1999). Oleoresin gum used as ointment base with beeswax to heal foot crack, ulcers, wounds, burns, ear and eye troubles, skin disease (Pullaiah and Rani 1999, Patra *et al*., 1992, Misra and Ahmad 1997, Upadhyay *et al*., 1998). For the control of Hemorrhoids, swelling and pain, it also offers with cow ghee (Kaur *et al*., 2001). Seeds has been given in pus forming wounds (Singh, 1986), whereas oil of seeds used as good medication for scabies and skin disease. Flowers were also effective in Diarrhea, gonorrhea and leprosy (Chopra *et al*, 1956, The wealth of India, 1950).

Scientific Reports

Phytoconstituents reports

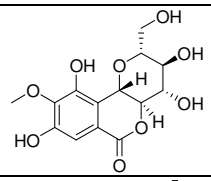
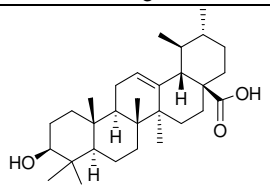
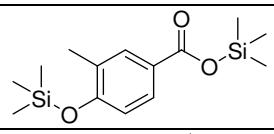
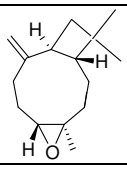
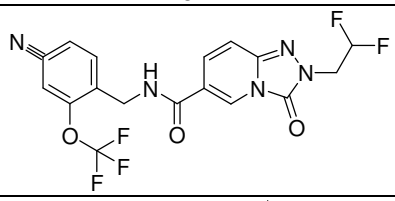
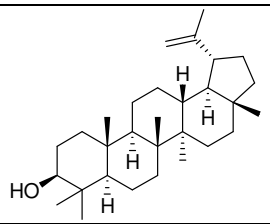
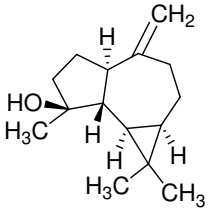
The chemical constituents present in plant are α-Amyrenone, Hopeaphenol, Asiatic acid, Benthamic acid and Uvaol (Soni *et al*., 2013; Merish *et al*., 2014), leucoanthocyanidin, and a terpene alcohol, furfural, monomethylether, dimethylether of homocatechol, alkybenzene derivatives, pentosans, lignan, amino acids, fatty acids, tannin triterpenoids, ellagic, chebulinic, gallic, phenolic and shorbic acids (Adlakha *et al*., 2014). Phytoconstituents reported from different parts of *S. robusta* listed in Table 1 and 2.

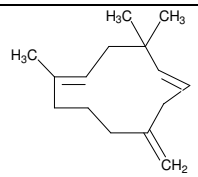
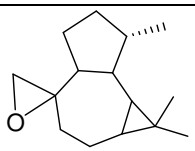
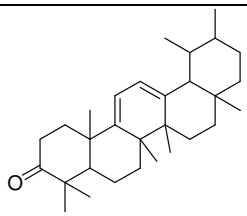
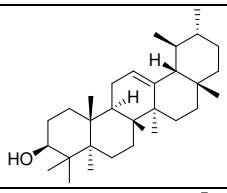
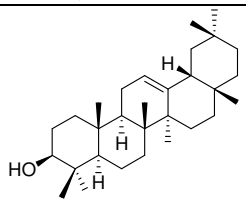
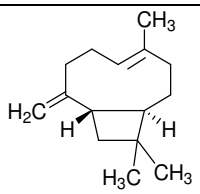
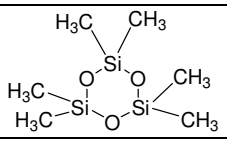
Table 1 : List of phytoconstituents reported from different parts of *S. robusta*

Phytoconstituents	Part of Plant	Reference
9,10-dyhydroxystearic; Stearic acid; Palmitic acid; Arachidic acids	Sal fat	(Reddy and Prabhakar 1987)
1,2,4-Benzenetriol; Ethyl(trimethyl)silane; D-Mannitol 1,3,5,7-Tetraethyl-1-butoxycyclotetrasiloxane	Bark	(Marandi *et al*., 2016)
Shoreaphenol		(Patra *et al*., 1992)
Methyloct-5-yn-4-yl 2,2,2-trichloroacetate; Cyclooctene, 5, 6-dimethylene; Propyl octane-2-yl carbonate; n-Hexadecanoic acid (Palmitic acid); Phytol; Cyclohexane-1,3-dione; 2-allylaminomethylene-5,5-dimethyl; Trimethylsilyl 3-methyl-4- [(trimethylsilyl)oxy]benzoate; β -amyrin, friedelin; β-sitosterol; α-carotene; β-carotene; Lutein; Phenophytin; 7-methoxy-4'-5-dihydroxyisoflavone	Leaf	(Marandi *et al*., 2016, Chauhan *et al*., 2002)
Hexadecyltrichloroacetate; Cyclooctane, methyl-2-Decanol; Stearic acid; Hexamethylcyclotrisiloxane	Seed	(Marandi *et al*., 2016)
2α,3β,23-trihydroxy-11β-methoxy-urs-12-en-28-oic acid; Coumarin; β-amyrin; α-amyrin; Taraxasterol; Amino-glutethimide; Neoisolongifolene, 8-bromo-4-azapyrine; Cycloisolongifolene; Cyclotrisiloxane; Caryophyllene; (-)-Spathulenol; Cycloisolongifolene; Isolongifolene; Alloaromadendrene oxide-(1); (-)-Neoclovene-(I); dihydro-isoaromadendrene epoxide; Longifolenaldehyde; Spirooctane; Epiglobulol; β–Humulene; Tetrasiloxane, decamethyl-Silane; 3,25-epoxy-1,2,3,11tetrahydroxyurs-12-en-28-oic acid; Ursolic acid; 2α,3β-dihydroxy-urs-12-en-28-oic acid; 2α,3α-dihydroxy-urs-12-en-28-oic acid; 3β,23-dihydroxyolean-12-en-28-oic acid; 2α,3β,23-trihydroxy-urs-12-en28-oic acid; Nitro-L-arginine; Hexanoic acid; Caryophyllene; Caryophyllene oxide; Ledene oxide-(II); Calarene epoxide; Alloaromadendrene oxide-(1); Gamma-Gurjunenepoxide (2); Isocaryophillene; Anthracene; Culmorin; Butanoic acid; Corticosterone; 2-ethylacridine; Ursa-9(11), 12-	Resin	(Misra and Ahmad 1997, Rai and Bapuji, 1993, Vashisht *et al*., 2017)

dien-3-one β-Guaiene; Lanosterol; Ursa-9(11),12-dien-3-one; Ursa-9(11),12-dien-3-ol; β-amyrin; α-amyrin; Humulane-1, 6-dien-3-ol; Taraxasterol; Fluoranthene; Lupeol; 9-anthracene carbonitrile; Cytisine; 2,3-dimethylamphetamine; 3, 25-epoxy1,2,3-trihydroxyurs-12-en-28-oic acid		
Asiatic acid; 3,25-epoxy-1,2,3,11-etrahydroxyurs-12-en-28-oic acid; Phayomphenol; 7-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→6)-βD-glucopyranoside, 3,25-epoxy-1,2,3-trihydroxyurs-l2-en-28-oic Acid; 3,7-dihydroxy-8-methoxyflavone	Root bark	(Sharma *et al*., 2015)
Phenol; 3-(prop-2-en-1-yl) cyclohexene; Pentanoic acid, 4-oxo-, ethyl ester; 3-Octenoic acid, methyl(tetramethylene) silan; Butanedioic acid; diethyl ester; 3β-acetoxy-4,4,8,10,14-pentamethyl-17; 3β-acetoxy-4,4,8,10,14-pentamethyl-17; Naphthalene, hexahydro-1,6-dimethyl-4-(11H-Cycloprop [e]azulen-7-ol; 1R,4S,7S,11R-2,2,4,8-Tetramethyltricyclo Ledene alcohol; 2-(4a,8-Dimethyl-1,2,3,4,4a,5,6,7-octahy - Benzene, 1,3-bis(1,1-dimethylethyl)-2-me Ledene alcohol; 1-Fluoroforskolin; 5,9-Methano-benzocycloocten-1(2H)-one, 3, ClocortolonePivalate; Tris(2,6-dimethylphenyl)borane; 2,5-Bis(1-methyl-1-silacyclobutyl)-p-xyl Bis(2-ethylhexyl) phthalate; Methylprednisolone; Ursa-9(11),12-dien-3-ol; Tetracosanoic acid; tert-butyldimethyls, Ursa-9(11),12-dien-3-one	Oleo resin Oil	(Yusuf and Srinivasan, 2015)

Table 2 : Bioactive phytoconstituents isolated from *S. robusta*

Part of Plant	Chemical constituents	Chemical structure	Reference
Leaves	Bergenin		(Mukherjee *et al*., 2013)
	Urosolic acid		(Mukherjee *et al*., 2013)
	Trimethylsilyl 3-methyl-4 [(trimethylsilyl)oxy]benzoate		(Marandi *et al*., 2016)
Resin	Caryophyllene oxide		(Vashisht *et al*., 2017)
	Calarene epoxide		(Vashisht *et al*., 2017)
	Lupeol		(Vashisht *et al*., 2017)
	(-)-Spathulenol		(Vashisht *et al*., 2017)

	Beta humulene		(Vashisht *et al*., 2017)
	Alloaromadendrene oxide-(1)		(Vashisht *et al*., 2017)
	Ursa-9(11),12-dien-3-one		(Vashisht *et al*., 2017)
	Alpha amyrin		(Vashisht *et al*., 2017)
	Beta amyrin		(Vashisht *et al*., 2017)
Flower	β-Caryophyllene		(Marandi *et al*., 2016)
Seed	Hexamethylcyclotrisiloxane		(Marandi *et al*., 2016)

Pharmacological reports

Various investigations have been carried out and published on the pharmacological activities of *S. robusta* plant. These biological activities are because of crude extract and its isolated phytocompounds which can be of great interest in future for the advancement or development of plant based integral medicines. Pharmacological properties of *S. robusta* have been depicted in Figure 3.

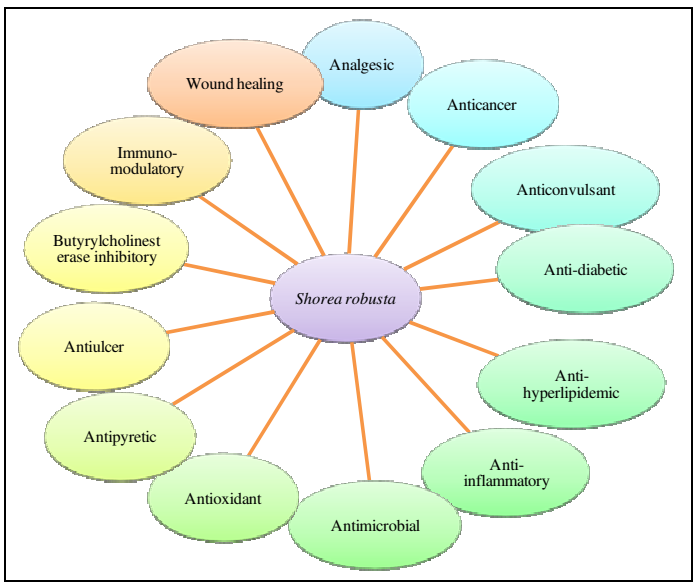


Fig. 3 : Pharmacological properties of *S. robusta*.

Analgesic activity

S. robusta has been used since long time as analgesic agent. Pharmacologically the activity was reported in the 70% ethanolic extract of resin of *S. robusta*. The extract at doses 30, 100, 300 mg/kg intraperitoneally determined by different pain models like hot plate and tail flick. Significant central and peripheral analgesic effect produced by the extract in Wistar albino rats and Swiss mice. The analgesic properties were proved from hike in reaction time in both hot plate and tail flick method (Wani *et al*., 2012). The Aqueous and methanolic extract of *S. robusta* leaves were examined by tail flick method and writhing method induced by acetic acid. Intraperitoneal doses of extract 200 and 400 mg/kg were injected to animals showed decreasing writhing movements and peripheral analgesic activity. This study concluded the analgesic activity of leaves of *S. robusta* (Chattopadhyay *et al*., 2012). The alcoholic and aqueous extract of bark at dose 300 mg/kg was evaluated in Swiss albino rats making use of Immersion test, writhing induced by 4% NaCl solution and tail clip method showed significant analgesic activity (Mohod, 2014). A significant analgesic activity showed by ethyl acetate extract of stem bark of *S. robusta* at doses (100 and 300 mg/kg) evaluated by hot plate, formalin induced paw licking methods and tail flick. The phytochemical analysis revealed the presence of flavonoids abundantly which has credited to inhibit the pain perception (Singh *et al*., 2016).

Antipyretic activity

S. robusta has been found to offer antipyretic activityproved experimentally. The 70% ethanolic extract of resin of *S. robusta* possessed antipyretic activity at dose 30, 100, 300mg/kg. This activity was studied making use of Brewer's method in which pyrexia is induced by yeast in wistar rats which results significantly dose-independentdecrease in the body temperature. The standard drug etoricoxib (10mg/kg) were used (Wani *et al*., 2012)

Anti-inflammatory activity

S. robusta leaves have been inhibit the inflammation in rats. Methanolic extract of leaves were assessed for Anti-inflammatory activity against carrageenan inducing inflammation in paw at doses 200 and 400 mg/kg. At both doses level significance anti-inflammatory activity produced in Wistar rats (Jyothi *et al*., 2008). Experimentally acute inflammation test was conducted on male Wistar albino rats, in one group carrageenan was used to induce edema in paw and cotton pellet induced sub-acute inflammation in other group of animals. In rat's pretreatment with 70% ethanolic extract at doses 100, 300mg/kg showed significantly decline in granulation tissue formation and edema volume (Wani *et al*., 2012). Chattopadhyay *et al*, has stated the anti-inflammatory activity of leaves of *S. robusta*. Inflammation was induced by carrageenan and dextran induced paw edema and cotton pellet induced granuloma in Swiss albino male mice and adult male Wistar rats. Aqueous and methanolic extract at 400 mg/kg p.o has shown dose dependent inhibition of paw edema compared to standard group (Diclofenac sodium). In cotton pellet induced inflammation both extract inhibited granuloma weight in dose dependent manner. The aqueous extract (400 mg/kg) has shown significantly (P <0.001) higher inhibition of granuloma weight compared to diclofenac sodium (Chattopadhyay *et al*., 2012). Ethyl acetate extract of *S. robusta* stem bark has found to provide relief to rats against carrageenan and formalin induced inflammation. These experiment rats were administered with stem bark leaves at two dose level 100 and 300 mg/kg. Both the doses shown significantly anti-inflammatory activity credited to flavonoids, tannins and phenols (Singh *et al*., 2016).

Antimicrobial activity

S. robusta is reported with antibacterial activity. The aqueous extract of floral part of *S. robusta* shown antibacterial activity against gram +ve bacteria (*Staphylococcus aureus*, *Bacillus subtilis*) and gram –ve (*Klebsiella pneumonia* and *Serratia marcescens*). This study found that extract of gynoecia has good inhibitory property compared to petal extract. The antibacterial effects of extract at concentration of 4 mg/well were compared with standard antibiotic Penicillin. Phytochemical analysis indicates the presence of tannins, flavonoid, cardiac glycosides and steroids may involve killing Bacteria (Duddukarni *et al*., 2011). The crude benzene, petroleum, methanol and aqueous extract of oleoresin of *S. robusta* were tested for antibacterial and antifungal activity by disc diffusion method against various gram -ve and gram +ve bacteria and some fungi such as *Proteus vulgaris, Escherichia coli, Pseudomonas fluorescence, Bacillus licheniformis, Bacillus subtilis, Bacillus coagulans, Baccilus cereus, Staphyococcus griseus, Staphylococcus epidermidis, Staphylococcus aureus, Penicillium chrysogenum, Aspergillus flavus, Candida albicans, Aspergillus niger.* The aqueous extract shown activities against bacteria whereas methanol, petroleum and benzene extract possesses antibacterial and antifungal properties were compared with standard antibiotics (Murthy 2011). Antimicrobial activity of ethanolic and methanolic extract of *S. robusta* resin evaluated against some bacterial strain. A parallel study was conducted again to compared antimicrobial activity with five standard antibiotics such as Ciprofloxacin, Gentamycin, Kanamycin, Ofloxacin, Penicillin. The ethanolic extract found more effective against *S. aureus* and *Pseudomonas sp* whereas methanolic extract potent against E. *coli* and *S. typhi* strains. Preliminary phytochemical study ensures the presence of secondary metabolites likes terpenoids, saponins and alkaloids in the resin of plant may be responsible for antimicrobial activity against resistant microbial strains. Current research found *S. robusta* as a potent antimicrobial agent can be used in Pharmaceutical formulations and medicines to cure infectious diseases (Banerjee *et al*., 2014).The ethanolic extract of bark, leaf, flower and seed were tested by standard disc diffusion method against 4 grams +ve bacterial strain viz. *Bacillus cereus, Streptococcus pneumonia, Bacillus subtilis, Staphylococcus aureus* and 8 grams –ve strains include *Enterobacter aerogenes, Pseudomonas aeruginosa, Salmonella paratyphi, Proteus mirabilis, Escherichia coli, Vibrio cholera and Klebsiella pneumonia, Proteus vulgaris*. Minimum zones of inhibition were found against *P. aeruginosa* and *B. Subtilis*. The seeds and bark shown higher antibacterial activities followed by leaf and flower. However, leaves possess considerable size of zones against *S. faecalis* and *S. aureus*. Seeds exhibited higher antibacterial activities validates its ethnic utilization against gastritis, dysentery and diarrhea (Marandi *et al*., 2016). Resin of *S. robusta* evaluated against gram +ve and gram –ve bacterial strain by paper disc diffusion method. The resin methanolic extract inhibits the growth of gram +ve and gram –ve pathogens similar to

ciprofloxacin (Vashisht *et al*., 2016). *S. robusta* ethanolic extract along with its ethyl acetate soluble fractions and residual ethanolic fractions reported with antimicrobial activity by using disc diffusion method at concentrations 20, 30, 50 mg/ml of extracts while 10, 20, 30 mg/ml of fractions. Extracts and fractions have shown promising antimicrobial activity against bacterial and fungal pathogens (Biswas *et al*., 2020). Antimicrobial activity of various extracts such as methanol, petroleum ether, acetone, chloroform, and water of oleoresin of *S. robusta* evaluated by using disc diffusion method against bacteria (*Micrococcus luteus* and *Proteus vulgaris*) and fungal strain (*Aspergillus niger* and *Candida albicans*). 150µl of extracts impregnated into discs. Gentamycin and Nystatin used as positive control for antibacterial and antifungal activity respectively. The aqueous and methanolic extract showed great antibacterial activity, while antifungal activity shown by the chloroform extracts (Thampi and Kumar 2015). Antimicrobial activity of methanolic extract of leaves of *S. robusta* was reported by agar well diffusion method against *Staphylococcus aureus* and *Klebsiella pneumonia* at various concentrations (1000, 750, 500 and 250 µg/mL). Antibiotic Tetracycline used as positive control (Archana and Jeyamanikandan 2015). Some contraindications to antibacterial activity of resin of *S. robusta* were reported by a study carried out against *Escherichia coli, Proteus vulgaris, Baccilus cereus,* and *Staphylococcus aureus* using spread plate method. Ethanol, acetone, DMSO, and chloroform extract were compared with standard antibiotic amoxicillin (Gaurea and Bapat, 2016).

Anticancer activity

The two isolated compounds alpha amyrin and beta amyrin from methanolic extract of bark of *S. robusta* investigated for inhibitory activity on hepatocellular carcinoma by molecular docking studies. The docking was done on human oncogene protein 121p. The binding of alpha and beta amyrin with human Ras protein was found to be -9.36 kcal/mol and -8.90 kcal/mol respectively (Kamaraj *et al*., 2019).

Anticonvulsant activity

The methanolic and aqueous extract of *S. robusta* leaves were evaluated at dose 10, 300, and 500 mg/kg against seizures induced by PTZ, picrotoxin, strychnine induced seizures and maximum electroshock method. Out of both the extracts methanolic extract possessed significant anticonvulsant activity with ideal dose 300 and 500 mg/kg (Jogpal *et al*., 2019).

Anti-diabetic activity and Anti-hyperlipidemic activity

The 70% ethanolic extract of bark of *S. robusta* evaluated for hypoglycemic and anti-hyperlipidemic activity in alloxan monohydadrate (120 mg/kg) induced diabetic rats. Significant hypoglycemic effects possessed by 500mg/kg extract in diabetic rats compared to Glibenclamide (600mg/kg). Various biochemical parameters viz. glucose, protein, hemoglobin, lipid profile, plasma insulin, MDA, GSH, urea, AST altered normal on treated with ethanolic extract. Hence it is claimed that ethanolic extract of *S. robusta* has shown valuable effects on blood glucose levels and improves lipid profile. This data scientifically proved the folklore use of *S. robusta* and as ingredient in various ayurvedic formulations (Sudha and Prasanna, 2013). The ethanolic extract of bark of *S. robusta* has been studied in alloxan monohydrate (150 mg/kg) induced diabetic rats. Extract at two different doses 200mg/kg and 400mg/kg administered orally shown significant hypoglycemic activity. Preliminary phytochemical studies reveal the presence of flavonoids, alkaloids, terpenoids, steroids and tannins. This study partially concludes antidiabetic property of *S. robusta* (Biswas *et al*., 2015). In other study single intraperitoneal (i.p.) injection of Streptozotocin (50mg/kg) was used to induce diabetes in rats. The ethanolic extract (100, 200mg/kg) and 100 mg/kg chloroform and n-butanol fraction of leaves administered orally restored the serum biochemical parameters like blood glucose level and lipid profile. Ethanolic extract/ fraction shown more significant beneficial effects i.e. decrease blood glucose, maintain body weight and sugar and improve lipid metabolism in diabetic rats (Velayutham *et al*., 2015). Kumawat reported the protective effects of 70% ethanolic extract of *S. robusta* resin. Diabetic peripheral neuropathy in rats was induced by single intaperitoneal injection of Streptozotocin. Various biochemical parameters, anti-nociceptive activity and histopathology (H&E) assessed after treatment with ethanolic extract. *S. robusta* extract increases pain threshold in diabetic rats earlier shown significant hyperalgesia. Activity of super oxide dismutase (SOD) and catalase restored to normal whereas malondialdehyde (MDA) and nitric oxide (NO) level significantly ($P<0.05$) reduced. Moreover, diabetic rats shown loss of myelin sheath, loose and disorganized sciatic nerve fibers, these amendments were also play vital role in treatment. Current research observed that resin of *S. robusta* possess hypoglycemic and protective effects (Kumavat *et al*., 2019).

Antioxidant activity

Antioxidant activity of leaves of *S. robusta* evaluated through CCl_4 induced oxidative stress in hepatocytes. After CCl4 treatment, entire variables *viz.* SOD, CAT, GPx, glutathione, vitamin C and Vitamin E recorded decline. Methanolic extract at doses 400µg/ml restored variables near to normal, suggesting Pharmacological effect of *S. robusta* to reduce the oxidative stress. This study concluded that *S. robusta* possess a liver protective effect against CCl4 induced oxidative stress and shown antioxidant and anti-lipid per oxidative activities (Suganya *et al*., 2014). The methanolic extract of *S. robusta* resin was screened for antioxidant activity by using DPPH assay and reducing power assay method. In DPPH assay, the half inhibition concentration of ascorbic acid and extract of *S. robusta* resin is 31.91 and 35.60 µg/ml respectively. The DPPH assay activity of resin extract is close to reference as ascorbic acid. The reducing power of *S. robusta* extract found dose dependent. All the doses showed significantly higher activities than the control, indicating presence of hydrophilic polyphenolic compound responsible for greater reduction power (Vashisht *et al*., 2016). The antioxidant activity of *S. robsuta* bark evaluated through DPPH, iron reducing power activity, superoxide anion scavenging and hydroxide peroxide scavenging activity. The ethanolic extract of bark experimentally shown capacity to scavenge reactive oxygen species and protect cells from oxidative damage and could be a beneficial against oxidative stress. GC-MS analysis of extract identified seventeen compounds and noticeable amount of α and β amyrins which play a vital role as antioxidants. Current research ensures *S. robusta* as an available source of natural antioxidants with subsequent health benefits (Muniyappan

and Rethinam, 2018). Different extracts such as methanol, petroleum ether, acetone, chloroform, and water of oleoresin of *S. robusta* assessed for free radical scavenging activity by Hydrogen peroxide method. All methanolic extract has shown significant 64.7% scavenging (Thampi and Kumar, 2015). The methanolic extract of *S. robusta* leaves showed antioxidant activity against DPPH and α-Amylase Inhibition assay. The extract has 30.24% radical scavenging effect (Archana and Jeyamanikandan 2015). Antioxidant activity of *S. robusta* methanolic extract of oleoresin was reported by using DPPH and iron chelating method. This extract revealed a significant dose dependent inhibition of DPPH (Yusuf and Srinivasan, 2015).

Antiulcer activity

Gastro protective effects of resin of *S. robusta* at two different doses 150 and 300 mg/kg were evaluated againstethanol and pyloric ligation (PL) induced gastric ulcers in rats. The antiulcer effect of aqueous extract was claimed with stabilization of various antioxidant markers like Superoxide dismutase (SOD), Glutathione peroxidase (GP_X), Glutathione –S-transferase, (GST), catalase (CAT) and lipid peroxidation (LPO) in ethanol induced group of animals. In another PL group of animal's plant extract shown destruction in gastric juice volume (65.44%), pepsin (44.39%), total acidity (26.98%) and protein (23.82%) while carbohydrate (22.67%) and mucin (41.46%) increase in gastric juice. Moreover, pH of gastric juice also increases from 1.23 to 4.54. This current study clearly proved that Sal extract decrease gastric acid and pepsin secretion indicating plant have both gastric cytoprotective and gastric anti-secretory effects (Muthu *et al*., 2013).

Butyrylcholinesterase Inhibitory activity

The ethanolic extract of de oil cake of *S. robusta* evaluated for Butyrylcholinesterase Inhibitory activity by using Ellman's method at concentration ranging from 12.5 to 200 µg/mL. The inhibition was found to be concentration dependent and maximum at 200 µg/ml. This study concluded that *S. robusta* used for symptomatic treatment of Alzheimer's disease (Shekhar and Kumar, 2014).

Immunomodulatory activity

The bark of *S. robusta* consumed with traditional claim that it boosts immunity. The hydroalcoholic extract of bark of *S. robusta* evaluated by various immunological models. Mice treated orally with 100 and 300 mg/kg doses of hydroalcoholic extract for 14 days when challenged with Sheep red blood cells (5 x 109 cells/ml). Among two doses 300 mg/kg altered the total and differential WBCs count, potentiated the effect on cellular and humoral response and phagocytosis. This study revealed significant stimulating immunomodulatory response of plant due to presence of flavonoids, polyphenols and terpenoids. Hence, this data supports the use of *S. robusta* bark as a potent natural health product for enhancing immunity (Kalaiselvan and Gokulakrishnan, 2012).

Wound healing activity

Dutta *et al* reported that *S. robusta* resin in combination with flax seed oil, Yashada bhasma useful in wound contraction, increased the hydroxyproline and collagen content also improved tensile strength. These effects together make this combination a vital usable for anti-aging activities especially for better skin health (Datta *et al*., 2011). The wound healing activity of ethanolic extract of *S. robusta* resin evaluated in incision and excision wound modals of rats. The ethanolic extract at doses 10 and 30 % applied locally on wounds and shown dose-dependent effects in healing process i.e. rise in hydroxyproline content and tensile strength, acceleration in wound contraction of rats. This results revealed wound healing activity of resins of Sal (Wani *et al.*, 2012). *S. robusta* has been used from ages for the treatment of wounds. The wound healing effects of leaves of *S. robusta* and its two fractions was studied on incision, excision, and dead space wound models. In rats some parameters evaluating such as the wound closure rate, tensile strength, hydroxyproline content, period of epithelization, granulation tissue weight and histopathology. Three types of topical formulations were prepared a) aqueous and methanol extract (2.5 and 5.0 g) mixed with 100g ointment base b) fraction 1 and 2 (5.0g) and 100 g ointment base, c) 0.025 g of isolated compound (bergenin and urosolic acid) with 10 g ointment base. Animals treated with 5 g fractions and extract showed significant reduction in wound area 96.55% and 96.41% with faster epithelization (17.50 and 17.86), whereas the isolated compound heal the wound faster. This data confirmed the traditional use of *S. robusta* leaves in wound healing (Mukherjee *et al*., 2013). Methanolic extract, Petroleum ether, benzene insoluble fraction of methanolic extract (F1) and Essential oil of *S. robusta* resin possessed significant wound healing activity. Fraction, extract and essential oil were assimilated with yellow paraffin wax (10% w/w) and these prepared ointments applied to incisions and excision wounds of Wistar rats. Wounds heal faster with the application of F1 and Essential oil compared to plain base and framycetin (standard). Tensile strength, wound contraction of F1 found to be 53%, 99% respectively which is higher than that of control group of animals. Protein and hydroxyproline content greater in F1 (20.8 and 3.5% w/w) and Essential oils (17.4 and 2.8% w/w) group than control group (9.95 and 1.48%) of rats. Histopathology examination showed complete epithelization and formation of new blood vessels in F1 group. This study indicates that essential oil and triterpene-rich fraction of *S. robusta* have maximum wound healing activity and confirm the traditional statements on this plant of healing of wounds (Khan *et al*., 2015). The formulation of ethanolic extract of *S. robusta* resin was prepared in two different concentrations 10% w/w and 30% w/w and studied for wound healing activity. Dose dependent effect of resin extract was found in wound contraction and epithelization period. Phytochemical studies revealed the presence of anthraquinone glycosides, tannins, triterpenoids, carbohydates, saponins and flavonoids (Shakya and Bashyal, 2018).

Miscellaneous Scientific Reports

Singh *et al* reported biochemical Analysis and isolation of leaf protein concentrates from the Leaves of *S. robusta*. It has good potential to use in production of leaves protein contents (LPC). Newly fresh and matured leaves yield high amount of LPC (5.96 g) per 100 g leaves. It was additionally found to contain exceptionally high measure of ash (9.24%), which comprised of calcium, Phosphorus, Potassium, Iron, Sulfur micronutrients. Looking at all the biochemical examination, LPC's recovered from Sal shows genuinely great amount of protein-37.25%, fat-7.41%, nitrogen free concentrate 37.85%, total carbohydrates 45.5%, total soluble sugar-1.94% along with low amount of anti-nutritional

factors such as total phenolics and total saponins (Singh *et al*., 2014). Another study reported comparison of different extract of *S. robusta* on the basis of Pharmacognostic evaluation. Microscopic characters, Ash value, extractive value, Thin layer chromatography and identification test has performed. Methanol, ethanol and Chloroform soluble extractive value reported to 44.85%, 48.57% and 4.48% respectively. The presence of phytoconstituents like amino acids, triterpenoids, alkaloids and flavonoids were confirmed by identification test followed by TLC (Vashisht *et al*., 2017). Standardization of oleo resin of includes organoleptic study, Physico-chemical constants, fluorescence analysis of extracts and powder, TLC profiling and heavy metal determination. All these evaluated parameters widely accepted and helpful in quality assessment of herbal drugs (Rasheed *et al*., 2012).

Conclusion and Prospects

S. robusta is a medicinal plant of vital importance owing to its diverse traditional uses Phyto-chemical constituents and therapeutic profile. The anticancer, anticonvulsant anti-diabetic and antimicrobial activity of *S. robusta* is a ray of light in treating the death causing diseases throughout the world. This review exposes that this plant is a strongest source of new potential phyto-constituents with various pharmacological properties. Identification of more compounds and their activities claimed traditionally suggests a promising future of this plant.

Conflict of Interest

No conflict of interest.

Acknowledgement

Acknowledged to Chandigarh University, Mohali, Punjab, India and Career Point University, Hamirpur, Himachal Pradesh, India for providing necessary facilities.

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