WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES

SJIF Impact Factor 6.041

Volume 5, Issue 11, 664-682 Review Article ISSN 2278 – 4357

THE ETHNOBOTANY, PHYTOCHEMISTRY AND BIOLOGICAL PROPERTIES OF *ALLOPHYLUS* SPECIES USED IN TRADITIONAL MEDICINE: A REVIEW

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Article Received on
14 Sept. 2016,

Revised on 04 October. 2016,
Accepted on 24 October 2016

DOI: 10.20959/wjpps201611-8039

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ABSTRACT

Allophylus (Family Sapindaceae) comprises about 255 species worldwide. Genus is having ethnopharmcological background and widely used in folk medicines. The aim of the present review is presentation and critical evaluation of the comprehensive information on ethnopharmacology of *Allophylus* especially its uses in traditional medicine, phytochemical constituents and biomedical research. *A. serratus* (Roxb.) Kurz., *A. cobbe* (L.) Raeusch., *A. laevigatus* (Turcz.) Radlk., *A. edulis* (A.St.-Hil., A.Juss. & Cambess.) Radlk. and *A. africanus* P. Beauv. are the phytochemically studied species of *Allophylus*. β-sitosterol and phenacetamide found in leaves of *A. serratus* are having antiulcer properties. Rutin, present in leaves of *A. serratus* has a wide range of biological activities. It has properties like antibacterial, antioxidant, anticancer, antiinflammatory and antiosteoporotic. Quercetin3-β-D glucoside is present in branches of *A. edulis* has antihypertensive action. L-quebrachitol found in twigs of *A. edulis* is antidiabetic. 11 acetoxy-4α-methoxy-eudesmane and Apigenin 8-c-β rhamnopyranoside Carissone have been found in fruits of *A. laevigatus*. In the present review, attempts have been made on critical discussion of identification and biological activities of important phytochemicals present in *Allophylus* which have been highlighted along with ethnobotanical knowledge and recent trends in research of this promising plant. Traditional knowledge alongwith present and future research on this plant will be helpful for the development of new drug targets for treatment of health problems like diabetes, bone fractures, osteoporosis, ulcers, wounds, cardiovascular disorders and bacterial infections. The present review compiles and critically

evaluates ethnobotanical uses, phytochemical research, pharmacological studies and clinical investigations of *Allophylus* possessing inhibitory action of the angiotensin converting enzyme, anti-hepatotoxic activity and negative ionotropic activity.

KEYWORDS: *Allophylus species*, Anti-osteoporotic, Antiulcer, antibacterial, wound healing, fracture healing.

1. INTRODUCTION

Allophylus of the family Sapindaceae is an important medicinal plant with a great ethnopharmacological value. The genus is found worldwide, in India particular, species of *Allophylus* are found to grow on upline edges of hills in Western Ghats Mountains in India as well as in mangroves associated with West Coast. *Allophylus* species have been described as medicinal i.e. *A. cobbe*, *A. serratus*, *A. abyssinicus* (Hochst.) Radlk., *A. africanus*, *A. cominia* (L.) Sw., *A. edulis*, *A. rubifolius* (Hochst. ex A.Rich.) Engl., *A. timorensis* (DC.) Blume, *A. occidentalis* (Sw.) Radlk., *A. racemosus* Sw. *A. zeylanicus* L. while *A. cobbe*, *A. serratus* and *A. rubifolius* (Hochst. ex A.Rich.) Engl. have importance in human nutrition.[1] *A. africanus* P. Beauv., *A. cobbe*, *A. macrobotrys* Gilg, *A. timorensis* (DC.) Blume are important in animal nutrition.[1]

Clinical investigations have proven that *A. serratus* and *A. abyssinicus* are biologically active.[2,3,4]

1.1 Distribution and general morphology of the genus *Allophylus*

Allophylus is the largest genus in the Sapindaceae family. According to recent literature, there are about 255 species of *Allophylus*, distributed worldwide. The genus is widely distributed in tropical and subtropical regions of the America, Africa, Mascarine Island, Madagascar, Indian Archipelago and the Pacific.[5] Nine species of *Allophylus* are found in India i.e. *A. serratus*, *A. cobbe*, *A. chartaceus* (Kurz.) Radlk., *A. villosus* (Roxb.) Blume, *A. concanicus* Radlk., *A. dimorphus* Radlk., *A. subfalcatus* Radlk., *A. triphyllus* (Burm.f.) and *A. rheedii* (Wight.) Radlk.[5] *Allophylus* species are normally found to be growing as erect trees or erect shrubs, lianas or scandent shrubs or rarely woody climbers.[6] Leaves are pinnately compound, alternate, exstipulate and tri-foliolate.[7] Some West Indian species of *Allophylus* are uni-foliolate but all Central American species are tri-foliolate.[8] Flowers are minute, irregular, polygamo-dioecious, pedicellate, and white or yellowish in colour with 4 sepals and

4 petals. Generally, eight stamens are inserted in the bisexual flowers and surround the ovary. The filaments are connate at the base and the fruit is indehiscent.[9,5]

2. USES

2.1. Uses in ethnomedicine

Species of *Allophylus* have long been used worldwide against various disorders. Leaves of *A. cobbe* are used against diarrhea, dysentery, bone fractures and dislocations.[10,11] Leaves *A. cobbe* are used for mouth wash.[12] Stem bark of *A. cobbe* is peeled down towards the roots and used to prepare bandages to tie over an injured area and fractured bones in Sri Lanka.[13]

In Maharashtra (India), two species are found namely *A. cobbe* and *A. serratus*. In field surveys, we observed that both the species are called by the same name- *Tipan* (in Marathi language) by local people in Maharashtra. The fresh leaves of these species are tied over the bone fractures for quick recovery. The fresh leaves as well as dry powder of leaves are also taken with small amount of jaggery at early morning with empty stomach, for relief from joint pains.[14]

Where *A. serratus* is concerned, a whole plant is medicinally useful.[15] It is astringent, bitter, anti-inflammatory, vulnerary, digestive and carminative while also useful for the treatment of constipation, bone fractures, dislocations, ulcers, wounds, dyspepsia, anorexia and diarrhea.[15] Fruits of this species are sweet, cooling and a nourishing tonic.[15,16]

A. rubifolius is used as a remedy on boils on skin.[17] In Oman, the leaves of *A. rubifolius* are used against wound healing.[18] It has been noted by authors that reintroduction of leaves of *A. rubifolius* in regular diet in people of Oman is accepted as relevant cultural practice in the control of diseases. In Dhofar, the Southern region of Oman, the leaf paste of *A. rubifolius* combined with *Anogeissus dhofarica* A.J. Scott. is applied around infected wounds.[19]

In Caroline Islands, *A. ternatus* Lour. is used to treat the leg swelling and action of the medicine is said to be anodyne.[1] *A. timorensis* is used in Phillipines against malaise while *A. species* is used to treat burns and sores in the same region.[1] Another species- *A. occidentalis* in Haiti is said to be useful as a remedy on common cold, tetanus, toothache, tuberculosis and as a depurative and this species acts mainly on the veneral system.[1] *A. cominia* is used for medicinal purposes in Dominian Republic Haiti against various diseases like common cold, dysentery, dyspepsia, hemoptysis, stomach ache, tetanus, tooth ache, tuberculosis and as

depurative and drug action is veneral.[1] An infusion of leaves of *A. edulis* is ethnically used for intestinal disorders and as a throat antiinflammatory agent in Uruguay.[20] Leaves and young stem of *A. edulis* are used in popular phytotherapy in Missiones Province (Argentina) in the form of infusions and concoctions, either alone or combined with *Ilex paraguariensis* St. Hil. (*yeraba mate*) as refresher, digestant and in the treatment of hepatitis.[21] In West Africa root and twigs of *A. africanus* are supposed to be diuretic and used for the treatment of gastritis, hookworm, veneral diseases, burns, sores and fever.[22] In Nigeria, leaves, roots and bark of *A. africanus* (African false currant) is used against diarrhea, pile, toothache, helminthes, veneral diseases and cough.[23] An herbal practitioner of Tripura State in India has described that roots of *A. racemosus* (*Chaonti*) mixed with other plant parts and used against the jaundice.[24] Another practitioner from Khumlong (India) has described that leaves or roots of *A. racemosus* mixed with other plants are used against pneumonia.[25] People in the Shengena Forest Reserve in Tanzania use the roots of *A. ferrugineus* Var. *Ferrugineus* (Sapindaceae) against stomach gas, coughing, round worms and fever.[26] In Sri Lanka, all plant parts of *A. zeylanicus* are used for preparation of medicinal oil which is used for fracture healing whereas leaves and bark used to prepare poultice[27] where only leaves are used for healing of fractures and dislocations of bone.[11] Extract of leaves and stem of *A. zeylanicus* is combined with seeds of *Peuraria thunbergiana* Benth. and used for treatment of paralysis by *Chakma* community, the largest indigenous ethnic group in Arunachal Pradesh State in India.[28]

2.2. Role in human nutrition

Fruits and leaves of some species of *Allophylus* are edible and are eaten in various regions of the world. Fruits of *A. cobbe* are edible.[29] In India, the berries of *A. cobbe* are eaten raw which are tasted very sweet.[30,31] and eaten after ripening.[7] Fruits of *A. serratus* are sweet, cooling and nourishing tonic.[15] Fruits of *A. rubifolius* are edible and are eaten in days of food scarcity by tribals in Tanzania.[32] In Oman, the leaves of *A. rubifolius* are eaten for wound healing.[18]

Sixth Annual report (1995-96) of M.S. Swaminathan Research Foundation, Madras, stated that in South India, *Malyali* tribals named '*Malasar*' eat the fruits of *A. cobbe*. In their local language, they call this plant as '*korangu peetha*' and after fermentation of the fruits beverage similar to wine is produced which is used for drinking in *Malasar* tribals.[33] In Peru, the fruit of *A. cobbe* is added in the traditional beverage–*chicha*.[34]

2.3. Role in Animal Nutrition

Some *Allophylus* species have potential role in animal nutrition. Komwihangilo *et al.* conducted studies on farming systems perspective with view in agro-pastoral areas of semi-arid central Tanzania to investigate feeding values of indigenous browsing species as described by goat keepers based on their accumulated knowledge.[35] The fast stomach fill, palatability and promoting growth of kids were some of the most prominent qualities or 'advantages' *A. africanus* of (specific name misspelled in original text as *africana*).[35] They also observed that *A. africanus* is responsible for 63% stomach fill for feeding of goat in semiarid Central Tanzania.[35] Fruits of *A. timorensis* are eaten by Pacific pigeons (*Ducula pacifica*) in Tonga Forest.[36] Leaves of *A. abyssinicus* as well as leaves and fruits of *A. macrobotrys* are eaten by Gorilla in Bwindi Impenetrable National Park, Uganda.[37] Further analysis of fruits and leaves in the diet of Mountain Gorilla and investigated that the leaves of *A. abyssinicus* are rich in protein while fruits of *A. macrobotrys* show higher neutral detergent fibre content.[37] Some of the plants eaten by Bwindi Gorillas containing condensed tannins compared to plants consumed by Gorillas in the Virunga region.[38] but phenolics (including condensed tannins) are common in the diet of Western Lowland Gorilla especially during times of food scarcity.[39,40] In Eastern Madagascar noted that fruits of *A. cobbe* (L.) Raeusch. are eaten by fruit eating bats (*Eidolon dupreanum*).[41]

2.4. Other Uses

Allophylus yield good quality of timber which is durable, hard, used for various purposes like construction of buildings, bows, fishing equipments and fuel-wood. Saplings of *A. timorensis* (vern. *Kitahk*) are used for making handles of flying fish-nets in Pingelap (Canada) and useful for making fish traps, fishing poles.[42] The wood of *A. cobbe* (wt. 40 lb per cft.) is moderately hard and used as fuelwood and roofing.[29] Wood of *A. rubifolius* is used for building.[43] Final Report of Darwin Initiative for the survival of Species -2001 states that *A. abyssinicus* is useful for shade, medicine, fuelwood, charcoal and bee-forage.[44] stem of *Allophylus spp*. (locally called as enchanie-mbae in Kenya) is narrow, straight and durable which is used for making arrow shafts are used for hunting and self defense by Loita Maasai community (a community in Southwestern Kenya).[45] Wood of *A. puberulus* (Cambess.) Radlk. is used by local people in Brazil as firewood.[46]

3. PHYTOCHEMISTRY

Most of the species of *Allophylus* contain medicinally important phytochemicals viz. rutin (antiosteoporotic), β-sitosterol (cardioprotective), phenacetamide (antiulcer) in *A. serratus*, L-quebrachitol (antidiabetic) in *A. edulis*, carissone, apigenin 8-c-β rhamnopyranoside (antiradical) in *A. laevigatus* which have contributed its medicinal properties and increased importance in medicinal biology. Phytochemical investigation alongwith biological action of remaining species of *Allophylus* is necessary, as among 255 species very few are phytochemically analysed and there is a lack of knowledge of biological action of too many species.

Screening of several samples of leaves and barks of *A. cobbe* which gave negative tests for alkaloids when tested in the field, but laboratory assays showed the presence of traces of alkaloids.[47] After large scale extraction of the leaves, the crude 'alkaloid' fraction was found to be an extremely complex mixture of non-alkaloidal material. Benzylamide has been isolated from leaves of *A. cobbe*.[48] In a preliminary phytochemical survey of plants in Crocker range, at Sabah, Malaysia, it was found that leaves of *A. cobbe* contained saponin while it lacked alkaloids, steroids and triterpenes.[49] Leaves of *A. serratus* contain β-sitostrerol and an antiulcer compound phenacetamide.[3] From the fruits of *A. laevigatus*, a new sesquiterpene, 11 acetoxy-4α-methoxy-eudesmane, has been isolated alongwith the known comounds carissone and apigenin 8-c-β rhamnopyranoside.[50]

A. edulis is commonly used as a source of sesquiterpenes[51] flavonoids, phenolic compounds[52] and tannins, essential oils.[53] *A. edulis* has also been reported to contain two flavonoid glycosides which are effective against ulcer.[48,54] Fatty acids have been found to be present in the seed oils of *A. edulis*.[55] This species shows presence of phenolic compounds, cyanogenic glycosides, flavonoids, naphthoquinones, anthraquinones, alkaloids, steroids and terpenoids.[21] Two closely migrating, not well separated spots of polyprenols were observed upon absorption chromatography of *A. edulis*.[56]

Cynolipids of types II, III, and IV occur in the species *A. occidentalis* (Sw.) Radlk and *A. concina*.[57] TAG fraction and CL isolated from *A. dregeanus* exhibited a composition different from that of *A. natalensis*, are characterized by very high amounts of C20 FA, which in total contribute to 80% (Cynolipid I) and 44.1% (Cynolipid III).[58]

Ethanolic extract of leaves of *A. rubifolious* best inhibited DPPH radicals at 89.93% after 15 min. of incubation at a test concentration of 50 µg/ml for the lowest Ic50 values 7.11 µg/ml.[18] Due to antioxidant potential, these leaves have been reintroduced in diet of people in Oman. 10 Kg leaves of *A. serratus* were extracted in a glass percolator with 25l ethanol a; then the extract was vaccum dried and suspended in hexane to separate oily impurities and again extracted with water saturated n-butanol which was then subjected to column chromatography over silica gel and showed the presence of compounds like- quercetin, pinitol, luteolin-7-O-β-D-glucopyranoside, rutin and apigenin-4'-O- β -D-glucoside out of which rutin was found effective antiosteoporotic.[2]

4. BIOLOGICAL ACTIVITIES

4.1. Antiosteoporotic activity

Kumar *et al.* investigated antiosteoporotic activity of *A. serratus* leaves. Compounds isolated from *A. serratus* leaves i.e. quercetin, pinitol, luteolin-7-O-β-D-glucopyranoside, rutin and apigenin-4'-O- β -D-glucoside were tested for osteogenic activity.[2] Osteogenic activity was tested *in vitro* using calvarial osteoblasts obtained from Sprague Dawley rats by applying method of Ishizuya *et al.* .[2,59] Cultured osteoblasts at ~80% confluence were trypsinised and treated with isolated compounds after which alkaline phosphatase activity was measured spectrophotometrically in which Alkaline phosphatase activity, a measure of osteoblast differentaiation was increased due to rutin.[2]

4.2. Wound healing and antiinflammatory activity

Most of the species of *Allophylus* have powerful tissue healing ability e.g. *A. abyssinicus, A. cobbe, A. serratus* and *A. zeylanicus*. In the Ethiopian folk medicine, leaves of *A. abyssinicus* are used for treatment of wounds, burns, skin diseases and to arrest bleeding. Yesuf and Asres assessed wound healing and antiinflammatory activity of leaves of *A. abyssinicus*.[4] They extracted the leaves of *A. abyssinicus* with 80% (v/v) methanol by maceration. The dried extracts were again extracted in chloroform, acetone and methanol by soxhlet method.[4] They formulated different solvent fractions by using simple ointment base and hydroxypropyl methylcellulose gel at 5% and 10% concentrations and applied topically on wound and studied wound healing activity using excision, incision and dead space wound models in Swiss albino mice using 1% CMC as control for incision and dead space models while 0.2% nitrofurazone for excision model.[4] In excision model, the period of epithelization for the 10% methanol and aqueous fractions was found to be 17.54±0.33 and 19.34±0.76 days,

respectively.[4] Ointments prepared from the 10% chloroform, 10% acetone and 5% methanol fractions showed faster period of epithelization compared with respective negative control groups. In incision model, treatment with 200mg/Kg of the methanolic fraction showed highest tensile strength of wound.[4]

In vivo antiinflammatory activity of fractions of leaf extracts of *A. abyssinicus* was also evaluated on the basis of carrageenan-induced mice hind paw oedema, in which the plant extracts and indomethacin (control) were administered orally to the Swiss albino mice.[4] 0.1ml of 1% carrageenan in normal saline was used as an oedema inducing agent.[4] 80% methanolic fraction and indomethacin found to be blocking both phases, i.e. blocking histamine and serotonin release in the first phase and preventing the release of some of the inflammatory mediators by blocking prostaglandin's action in the second phase.[4]

4.3. Antiulcerogenic and ulcer healing activity

Dharmani and Palit investigated antiulcerogenic and ulcer healing property of ethanolic leaf extracts of *A. serratus*.[3] They used PUD (peptic ulcer disease) models as-CRU (cold restraint), AL (alcohol), ASP (aspirin), PL (pyloric ligation) in albino rats.[3] The plant extract was found responsible for significant protection against peptic ulcer in all the models.[3] They speculated that the reduction in acid output and peptic activity and increase in mucin secretion were the major mechanisms behind the protection in PL model while reduced acid output was the major reason in CRU model whereas the tremendous increase of mucus content and a possible increase in prostaglandin level could be the protective mechanism in the AL and ASP models.[3] They concluded that leaves of *A. serratus* contain β-sitostrerol and an antiulcer compound phenacetamide. They have further suggested that the extract of *A. serratus* can be effectively used as an antiulcer drug by knowing the precise mechanism of its action.[3]

4.4. Antidiabetic Activity

A. cominia and *A. cobbe* are the species of *Allophylus* used against diabetes. Faz *et al.* characterized the leaves of *A. cominia* extracting them in chloroform by means of maceration and reflux.[60] The composition of thus obtained extract was characterized which indicated the predominant alcohol as an aliphatic chain with eight carbon atoms, an unsaturation and an OH^- group in addition to fatty acids, proteins, and in trace quantities, tri-terpenes and steroids.[60] The pharmacological evaluation of the composition obtained and showed a marked hypoglycemic effect on rats.[60]

A. cominia is popularly used in Cuba for the treatment of diabetes by consuming in the form of decoction.[61] Effect of incubation with aqueous extract obtained from leaves of vegetable species *A. cominia* on the reception of glucose at peripheral level, specifically in muscular tissue was studied and verified in an *ex-vivo* assay. Their results indicated that the active metabolites present in extract caused the reception of glucose when being applied in an equivalent dose to 1.5g/Kg. They concluded that those metabolites could be acting by an insulin-mimetic type mechanism of action at peripheral level which facilitates glucose peripheral absorption.[61]

Diaz *et al.* analyzed twig powder of *A. edulis* (*chal chal*) occurring in Uruguay and Brazil.[62] *A. edulis* is used locally in the form of infusion to treat diabetes.[63] During the analysis, they found presence of quebrachitol in material.[62] A phytochemical L-quebrachitol is a sugar substitute for diabetes.[64] The observations by Musalmah *et al.* showed that this compound neither prevented hypoglycemia nor raised blood sugar content.[65] Diaz *et al.* found that hypoglycemic effects in hyperglycemic rats due to L-quebrachitol and they pointed out that the local use of *A. edulis* is related to its L-quebrachitol quantity.[62] L-quebrachitol have been previously isolated from the leaves of *A. cobbe* in Vietnam.[66]

4.5. Antihypertensive Activity

Jose *et al.* compiled an extensive review on 321 plants showing antihypertensive activity.[67] They speculated that inhibition of Angiotensin converting enzyme (ACE) is a modern therapeutic target against hypertension.[67] Within the enzyme cascade of the rennin angiotensin system, ACE removes histidyl-leucine from angiotensin I, physiologically active octapeptide angiotensin II, one of the most potent known vasoconstrictors.[67] Therfore, a rationale for treating hypertension would be to administer drugs or natural compounds which selectively inhibit ACE.[67] The literature on plants and chemically defined molecules from natural sources with *in-vitro* anti-hypertensive potential is pertinent to the inhibition of ACE.[67] Arisawa *et al.* extracted branches of *A. edulis* with hexane, $CHCl_3$ and H_2O which showed inactive while extracts in 70% ethanol and butanol showed active natural sources as anti-hypertensive potential and identified it as a flavonoid Quercetin3-β-D-glucoside.[52] Later chemically defined natural compounds catechin and epi-catechin belonging to class flavonoid, were isolated from *A. edulis* found responsible for inhibition of angiotensin converting enzyme.[68]

4.6. Antibacterial Activity

Chavan and Gaikwad investigated antibacterial activity of young and mature leaf extracts (aqueous and ethanolic) of *A. cobbe* and *A. serratus* extracts.[69] 25 µl of 1mg/ml each of extract was tested by agar well diffusion method against bacteria namely *Staphyllococcus aureus* and *Bacillus subtilis*.[69] Aqueous and ethanolic extracts of young and mature leaves of *A. cobbe* and *A. serratus* exhibited good antibacterial potential against *B. subtilis* as compared to that of Cefotaxime.[69] These species are locally used for wound healing.[69] They speculated that leaf extract may be inhibiting the wound attacking microflora.[69]

4.7. Antimalarial Activity

Oladosu *et al*. determined the antimalarial potential of different parts of *A. africanus in vivo* for suppressive, curative and cytotoxic activities in mice receiving 0.2 mL of a standard inoculum size of 1×10^7 infected erythrocytes of *Plasmodium berghei* (NK-65) intraperitoneally.[70] *A. africanus* extracts suppressed parasitaemia following administration to infected mice by 92.82%–97.81% on day 7 post-infection against 96.81% for Chloroquine.[70] The infected extract-treated animals had significantly moderate ($P < 0.05$) packed cell volume as compared with the infected, untreated animals.[70]

4.8. Insecticidal Activity

A. cobbe known to be exhibiting significant nematicidal activity against the root knot nematode *Meloidogynae incognita*.[71] CH_2Cl_2 and hexane extracts of stem found to be 54% effective and methanolic 25% effective against the larvae of Mexican bean beetle (*Epilachna varievestis* Muls.)[71] Castillo *et al*. evaluated the antiinsectan activity of extracts from different vegetative parts of ten plant species native to Uruguay.[72] They observed that twig extracts of *A. edulis* exhibited strong settling inhibition (SI) activity (%SI=77±4) against the feeding generalist insect *Myzus persicae* (Hemiptera).[72]

4.9. Genotoxicity

Yajia *et al.* evaluated the genotoxic potential of aqueous extract of *A. edulis* obtained by decoction (concentrations: 12, 6-ethnotherapeutic dose-3, 1.5 and 0.75g/L) and analysed by means of the *Allium cepa* L. test for general toxicity and genotoxicity.[21] They obtained dose dependent effects on root length growth (RL) of upto 68.3% of the controls (r= -0.88) and macroscopic abnormalities (MA) (range-30.58-94.82%; r=0.90) such as c-tumours and necrosis.[21] They observed decrease in mitotic index (MI) with respect to controls, which was also in a dose dependant way(r=-0.94).[21] They observed a significant correlation occurred

between MI and RL (r=0.93) and MI and MA (r= -0.90). They reported that mitotic abnormalities included micronuclei, pycnotic nuclei, binucleated cells, c-metaphases, sticky metaphases, arrested anaphases and telophase bridges.[21]

CONCLUSION

The various species of *Allophylus* exhibit the presence of medicinally important phytochemicals such as 11 acetoxy-4α-methoxy-eudesmane, Apigenin 8-c-β rhamnopyranoside Carissone, Phenacetamide, β-Sitosterol, Rutin, Quercetin, Pinitol, Luteolin-7-O-β-D-glucopyranoside, Apigenin-4'-O- β -D-glucoside, sesquiterpenes, phenacetamide, L-quebrachitol and fatty acids as well as bioactivity of these compounds is proven by clinical experiments. As the leaves, fruit and stem are found to be used against wound healing, fracture healing, cuts, ulcer healing. Hence, the systematic analysis and evaluation of bioactive molecules will definitely open up new avenues for development of drugs against the various diseases like cancer, cardiovascular diseases, diabetes, bacterial infections and painful diseases like osteoporosis, arthritis, burns, cuts, wounds and fractures.

Presence of valuable phytochemicals such as L-quebrachitol, Rutin, 11 acetoxy-4α-methoxy-eudesmane, Apigenin 8-c-β rhamnopyranoside, Carissone, Phenacetamide, β-Sitosterol, Quercetin, Pinitol, Luteolin-7-O-β-D-glucopyranoside, Apigenin-4'-O- β -D-glucoside, sesquiterpenes, phenacetamide, and fatty acids underlines the importance of *Allophylus* species in medicinal biology. Bioactivity of these compounds is proven by clinical experiments. Leaves, stem and roots of *Allophylus* species are used in traditional medicine. However, only leaves and fruits of the most of the species have remained focus of interest of scientists while stem and roots are neglected parts. It is necessary to evaluate phytochemicals from these parts as they have contributed in ethnomedicine. Present knowledge with future research in phytochemistry and clinical investigation of this medicinal plant can surely open up new avenues for new drug targets for dreaded diseases like cardiovascular diseases, diabetes, bacterial infections, painful diseases like osteoporosis, arthritis, burns, cuts, wounds and fractures.

Appendix A. Species of *Allophylus* and their plant parts used in folk medicines worldwide

Name of the species	Part used	In the form of	Medicinal Uses	Reference
A.edulis	Twig	Infusion	Diabetes	[63]
	Leaves	Tisane	Throat anti-inflammatory agent & for intestinal disorders	[20]
	Leaves &young stem	Infusion (alone/mixed with *Ilex paraguariensis)*	Refresher, digestant and, to a lesser extent, in the treatment of hepatitis	[21]
	Fruits	-	Sweet, Cooling and nourishing tonic	[15]
A.cobbe	Leaves	-	Bone fractures	[73,31]
	Leaves	Juice	Rashes	[31]
	Leaves	Ground with quick lime	Stomach ache	[31]
	Leaves	-	Mouth wash	[12]
	Bark	Bandages	Bone fractures	[13]
	Roots	Decoction	Diarrhoea	[31]
	Roots	-	Diarrhoea and dysentry	[74]
	-	-	Diarrhoea and dysentry	[10]
A.cominia	Leaves	Decoction	Diabetes	[61]
	-	-	Common cold, dysentery, dyspepsia, hemoptysis, stomach ache, tetanus, tooth ache, tuberculosis and as depurative	[1]
	-	-	Iron loss and menstrual cramping	[75]
A.ferrugineus	Roots	Infusion	Stomach gas, cough, round worms, fever	[26]
A.occidentalis	-	-	Common cold, tetanus, toothache, tuberculosis, and as a depurative	[1]
A. racemosus	Roots	Mixed with other plants	Jaundice	[24]
A.rubifolius	Leaves	Leaf paste mixed with *Anogeissus dhofarica* applied around wound	Wound infections	[19]
	Leaves	-	Wound healing	[18]
	-	-	Boils (skin)	[17]
A.serratus	Leaves	-	Bone fractures	[15]
	Fruits	-	Sweet, Cooling and nourishing tonic	[15]
A.timoriensis	-	-	Malaise	[1]

	Roots	Mixed with other plants	Pneumonia	[25]
A.zeylanicus	-	-	Fractures and dislocations	[26]

-Literature not found.

Appendix B. Phytochemicals isolated from various species of *Allophylus*

Species	Name of compound isolated	Source	Biological activity of compound	Reference
A.edulis	Quercetin3-β-D glucoside	Branches	Anti-hypertensive	[52]
	L-quebrachitol	Twig	Antidiabetic	[62]
A.cobbe	Rutin	Stem	Osteogenic	[2]
	L-quebrachitol	Leaves	Antidiabetic	[66]
	Benzylamide	Leaves	Nil	[48]
A.laevigatus	11 acetoxy-4α-methoxy-eudesmane	Fruit	Nil	[50]
	Apigenin 8-c-β rhamnopyranoside	Fruit	Nil	[50]
	Carissone	Fruit	Nil	[50]
A.serratus	Phenacetamide	Leaves	Antiulcer	[77,3]
	β-Sitosterol	Leaves	Antiulcer	[77]
	Rutin	Leaves	Antiosteoporotic	[2]
	Quercetin	Leaves	Nil	[2]
	Pinitol	Leaves	Nil	[2]
	Luteolin-7-O-β-D-glucopyranoside	Leaves	Nil	[2]
	Apigenin-4'-O- β -D-glucoside	Leaves	Nil	[2]

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