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A PERSPECTIVE REVIEW ON HOMALIUM ZEYLANICUM BENTH

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ABSTRACT

Plant *Homalium zeylanicum Benth* belongs to Flacourtiaceae family and is distributed in evergreen and semi-evergreen forests, native to south India and srilanka.It is also found in Bangladesh, Laos. Myanmar, Nepal, Thailand and Vietnam. The various parts of plant including bark and leaf having many traditional medicinal uses, mainly in diabetes, wound healing. It has been traditionally used for treating several ailments including rheumatism, anti-inflammatory, and hepatoprotective and ant diabetic agent in Rayalaseema region of Andhra Pradesh. In Nigeria, it is used as traditional medicine for the treatment of malaria, ulcer, and inflammatory diseases and as an aphrodisiac. Various studies have been conducted to evaluate the medicinal properties of plant. A variety of phytoconstituents are identified and isolated from the *H.zeylanicum*.A perspective review of the ethanobotanical, phytochemical and pharmacological investigations of *H.Zeylanicum* are presented in this review.

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INTRODUCTION

Since ancient times a number of Indian medicinal plants have been used globally. There are many references to Indian medicinal plants and trade in spices in a number of historical documents. Herbal medicine has been used in India for thousands of years and is increasingly been used worldwide during the last few decades as evidenced by rapidly growing global and national markets of herbal drugs. Due to high prices and harmful side effects of synthetic drugs, people rely more on herbal drugs and this trend is growing, not only in developing countries but in developed countries too. India has 2.4% of world's area with 8% of global biodiversity. The forests of India are estimated to harbour 90% of India's medicinal plants diversity in the wide range of forest types that occur. The diverse approaches to herbal drugs have led to interesting hits and novel activities, which need further in depth drug development efforts, both as herbal as well as new single molecule drugs [1]. The world health organization (WHO) estimates that about 80% of the population is still depends up on these herbal medicines for their treatment of disease [2]. The number of studies on natural product are aimed to determine medicinal values of plants by investigation of existing scientific knowledge, traditional uses and discovery of potential therapeutic agents[3].

The genus *Homalium*, based on the single species *H. racemosum*, from Martinique, was established by Jacquin in 1760, and in 1763 a more extended description with a figure of the flower was given in his book entitled 'Selectarum Stirpium Americanarum Historia'.In 1775 Aublet described the new genus *Racoubea* from French Guiana, based on a single species, *R guianensis*, and with it the genus *Napimoga*, which has since been considered a more or less doubtful synonym of *Homalium*. Jussieu, in his Genera, referred Racoubea to *Homalium* as a synonym, a treatment which has been followed by all subsequent authors, and placed both *Homalium* and *Napimoga* in his group "Genera Rosaceis affinia." Robert Brown in 1818 made the genus *Homalium* the type of a new order, *Homalinae*, a classification retained by various authors down to 1857 [4]. There are more than 163 scientific plant names of species rank for the genus *Homalium* and among these 33 are accepted species, they are *H. densiflorum Spruce, H. guianense Warb, H. nicaraguense Blake, H. puberulum Klotzsch, H. mollicellum Blake, H. pleiandrum Blake, H. leiogynum Blake , H. hemisystylum Blake, H. racemosum Jacq, H.integrifolium Britton, H. pittieri Blake, H. trichocladum, H. pedicellatum Spruce,H. eleutherostylum Blake, H. columbianum Blabe, H. stenosepalum Blake, H. eurypetalum Blake, H. trichostemon Blake* [4].

Homalium zeylanicum Benth plant belongs to genus *Homalium* and family Flacourtiaceae distributed in evergreen and semi-evergreen forests, native to South India and Srilanka. It is also found in Bangladesh, Laos, Myanmar, Nepal, Thailand and Vietnam [5].it is cultivated for ornament and its wood is used commercially [6]. The various parts of plant including, bark and leaf having many traditional uses, mainly in diabetes, rheumatism and wound healing.

ETHANOBOTANICAL REVIEW [5, 7]

Table 1: *Homalium zeylanicum.*

Synonym	**Blackwellia ceylanica**
Common name	Liyan, mukki
Family	Flacourtiaceae
Species	Zeylanicum
Genus	Homalium
Taxonamy	Kingdom : Plantae Phylum : Magnoliophyta Class : Magnoliatae Order : Violales Genus : Homalium
Vernacular names	English : Liyan,blackwellia zeylanica Gard, H.ceylanicum Gardner Kannada : Hulikaddi mara,Kala,Kalamattigu Malayalam : Kalavaram, Kalladamba Kaluvaluka,Manthalamukki Marathi : Homali Telugu : Manthralamukhi Tamil : Kaluvaluka,Manthalamukhi
Habit	Trees up to 25m tall
Habitate	Evergreen and Semi evergreen forests, native to south India and srilanka
Trunk & Bark	Bark smooth, grey, blaze white with orange speckles.
Branches and Branchlets	Branchlets slender, terete, glabrous.
Leaves	Leaves simple, alternate, distichous; stipules caducous, apex abruptly acuminate, base acute or rounded to sub attenuate, margin crenate, chartaceous.
Inflorescence / Flower	Inflorescence long, slender spikes with interrupted clusters of small flowers; flowers generally greenish white, sometimes few clusters crimson red in the same spike
Fruit and Seed :	Capsule; seeds small, many, oblong or angular.

Fig 1: Different parts of *Homalium zeylanicum*.

ETHANOPHARMACOLOGICAL REVIEW

TRADITIONAL USE [8]

Bark and leaf of the plant having many traditional uses in diabetes,rheumatism ,wound healing activity and hepatoprotective activities.

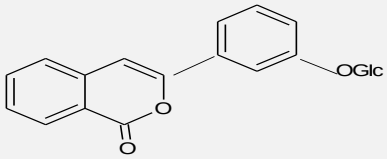
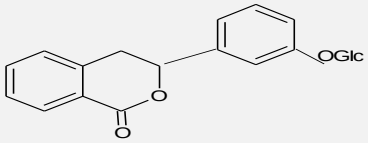
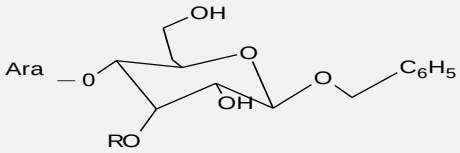
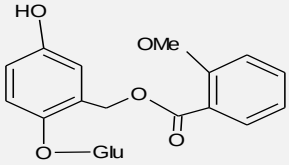
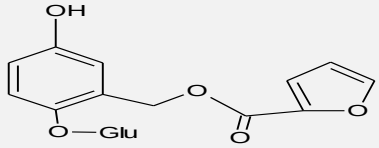
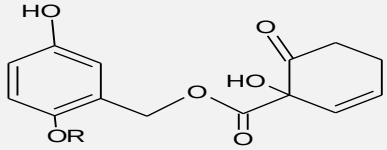
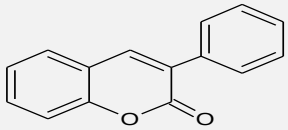
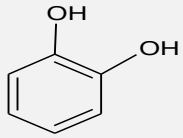
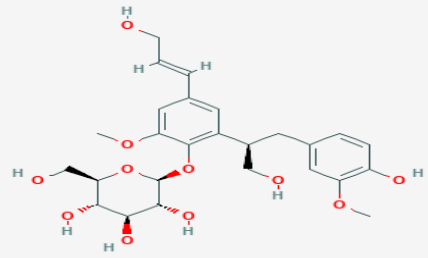
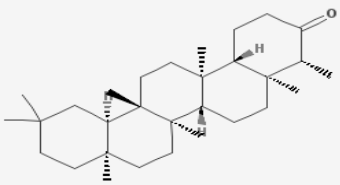
USES IN AYURVEDA AND SIDHHA[9]

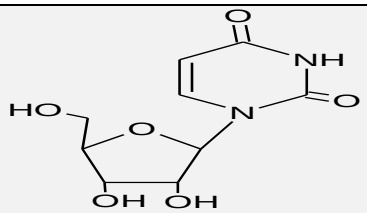
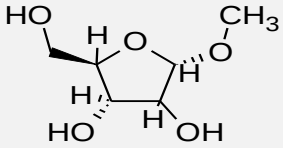
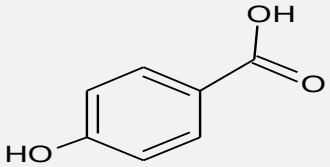
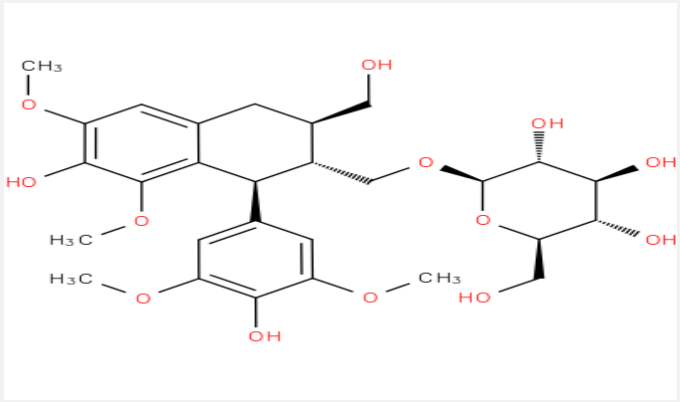
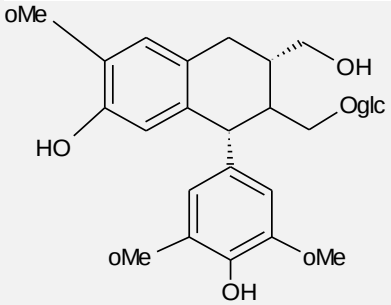
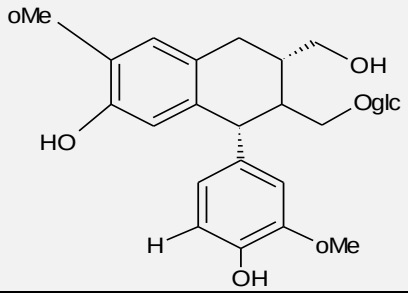
An Ayurveda, siddha and unani medicine employs a large number of medicinal plants for treatment of skin diseases which includes cuts, wounds and burns. Medicinal plants have been used since olden time for treatment of various ailments of skin and dermatological disorders especially cuts, wounds and burns. Research into traditional wound healing remedies fall into three categories: (1) herbal remedies; (2) the use of animal, insect products as wound healing agents; (3) the use of organisms to effect wound healing. A review on the exploration of herbal drug used in wound healing activity includes use of leaf of homalium zeylanicum.

PHYTOCHEMICAL REVIEW [10, 11]

A variety of phytoconstituents are identified and isolated from *homalium zeylanicum* which include mainly

Table 2: Phytoconstituents of *Homalium zeylanicum.*

NAME OF COMPOUND	STRUCTURE
Homalicine	
Dihydrohomalicine	
Homaloside-A R- Benzoyl	
Homaloside B	
Homaloside C	
Homaloside D R=GIu(6-o-benzoyl)	
3-phenyl coumarin	
4'-O-methyl-epigallo catechin And 4'-O-methyl-epigallocatechin penta acetate (Catechol)	
Icariside E54	
Friedeline	

Uridine	
methyl-α-arabinofuranoside	
4-hydroxybenzoic acid	
(+) lyoniresinol3α-O-β-D -glucopyranoside	
5'-methoxyisolariciresinol-3α-O-β-D-glucopyranoside	
(–) isolarisiresinol-3α-O-β-D –glucopyranoside	

Rachala vinod kumar *et al* were conducted a chemical examination of bark and leaf of Homaliun zeylanicum yielded phenolic compounds 3 Phenyl coumarin (1) and 4'-O-Methyl-Epigallo catechin (2). The structures of the compounds were established on the basis of various NMR spectral data. The extracts of bark, leaf and their isolated compounds showed both antioxidant and anticancer activities in in vitro mode. The acetate derivative of compound 2 showed significant anticancer activity against human cancer cell line IMR-32 (IC50 6.26 µg/ml) in the MTT assay[11].

Two new benzenoid glucosides-homaliside A and homaloside D- and 1-hydroxy-6-oxocyclohex-2-enoic acid methyl ester isolated and their structure established,isolation and characterisation of homaloside B,homaloside C, 6-O-(3,4dimethoxycinnamoyl catalpol) and 3- hydroxyl-β-ionyl-β-D-glucopyranoside together with salireposide and salirepin also isolated from homalium zeylanicum benth [12].

A study conducted on the synthesis and biological screenings of Homalicine and dihydrohomalicine showed the presence of 3- [3'- (beta – D – glucopyranosyl - oxyphenyl)] isocoumarin and (-) -3- [3' - (beta - D - glucopyranosyloxyphenyl)] -3, 4-dihydroisocoumarin from the acetone extract of the roots of homalium zeylanicum. The total synthesis of homalicine and dihydrohomalicine,which not only confirm the structural assignments but also makes them available for biological evaluation and antimicrobial activity [13].

Phytochemical screening and quantification in leaf extracts of Homalium zeylanicum was carried out with an intention of finding the type and diversity of phytochemicals present. The phytoconstituents in the plant were extracted using ethyl acetate methanol and water as solvents. The methanolic and aqueous extract showed the positive results for the presence of steroids,triterpenoids,alkaloids,carbohydrates,flavonoids and phenolic compounds [14].

PHARMACOLOGICAL REVIEW

Herbal Medicine is the oldest form of medicine known to mankind. Medicinal plants can contain a variety of phytochemicals as well as minerals, vitamins and trace elements. Some of the phytochemicals are pharmacologically active and can exert a therapeutic action on the body. In recent years; the use of herbal products has been increasing in developing countries. An overview of pharmacological activities of Homalium zeylanicum has been listed here.

ANALGESIC AND ANTI-INFLAMMATORY EFFECT

K.Siva Sankara Prasad et al evaluated Ethanolic extract of *Homalium zeylanicum* for its analgesic and anti-inflammatory potential using acetic acid induced writhing test in mice, sub plantar carrageenan induced nociception, the tail-clip test and carrageenan induced oedema in rats. Three doses of the extract (100, 200, 400 mg/kg) were used for the assessment. *Homalium zeylanicum* ethanolic extract demonstrated strong dose-dependent analgesic and anti-inflammatory activities in all the models employed and it found to possess comparable efficacy with that of standard analgesic and anti- inflammatory drugs. The results indicated that *Homalium zeylanicum* showed better analgesic and anti-inflammatory properties suggesting that its traditional use in the treatment of pains and inflammatory diseases may be effective [15]

ANTHELIMINTIC ACTIVITY

A Study on the evaluation of anthelimintic activity in the ethyl acetate and methanolic bark extract of homalium zeyanicum were carried out, all phytochemical screening methods were done by using standard methods, were as anthelmintic method was done at three different concentration on adult earthworm phertima posthuma, the parameters like the time of paralysis and the time of death were determined. Both the extracts showed significant activity in the dose dependent manner. The methanolic extract showed significant activity than that of standard drug albendazole.this might due to the presence of secondary metabolite tannins which are responsible for the activity [16].

ANTIMICROBIAL ACTIVITY

Antimicrobial activities of leaf extracts of homalium zeylanicum were evaluated. The leaves of the plant were extracted with ethyl acetate, methanolic and aqueous solvents. Antimicrobial activity of the plant extracts were evaluated by determining the minimum inhibitory concentration values. Different pathogenic organisms including four Bactria (B.subtilis, S. aureus, P.aeruginosa, E.coli) and one fungus (A.niger) were evaluated for antimicrobial activity. Fluconazole antibiotic was used as Standard for antifungal activity and amoxicillin drug was used as a standard for antibacterial activity. The antibacterial activity of the ethyl acetate, methanolic and aqueous solvents leaf extracts of plants was depends on their phyto chemical composition. The diameters of the inhibition zones were measured in millimetre. Homalium zeylanicum had shown the high antibacterial activity on gram negative than gram positive. This will be of immense advantage in fighting the menace of antibiotic refractive pathogens that are so prevalent in recent times [17].

ANTIDIABETIC ACTIVITY

Homalium zeylanicum has been widely used in traditional system of medicine for diabetes. Many natural sources have been investigated with respect to suppression of glucose production from the carbohydrates in the gut or glucose absorption from the intestine. Alpha-amylase catalyses the hydrolysis of alpha-1, 4-glycosidic linkages of starch, glycogen and various oligosaccharides. Alpha-glucosidase further breaks down the disaccharides to simple sugars, readily available for intestinal absorption. The inhibition of their activity in the digestive tract of humans is considered to be effective tool to control diabetes. In addition, these effects may leads to diminished absorption of monosaccharides. Therefore, effective and nontoxic inhibitors of alpha-amylase and alpha-glucosidase have long been sought. This study was performed to evaluate the antidiabetic activity by inhibition of α-amylase enzyme using spectrophotometer. The results of antidiabetic activity using α-amylase inhibitory assay of the ethyl acetate, methanol and aqueous leaves extracts of H. zeylanicum shows all the tested extracts exhibited the dose dependent inhibition of enzyme. The extracts was exhibited IC50 less than 100µg/mL will be considered active in comparison with other tested extracts. H. zeylanicum leaf methanoilc extract exhibited the high antidiabetic activity by reducing 78.88% enzyme inhibition at 0.40 mg/ml concentration and IC50 value was found to be 0.15 mg/ml. This reflected that methanolic extract of H. zeylanicum leaves contains certain compound(s) with alpha glucosidase inhibitory activity. It was concluded that methanolic leaf extract of HZB possess high antidiabetic activity due to the presence of flavonoids and extract concentration of 200µg/ml was found to be sufficient for 50% inhibition of α-amylase [17].

The antidiabetic activity of homalium zeylanicum stem bark ethanol extract against alloxan induced diabetes was evaluated using standard drug metformin.diabetes was induced in male wistar rats by intraperitoneal injection of alloxan(90mg/kg). Ethanol extract of HZB stem bark were administered to the experimental rats (250mg and 500mg/kg,p.o.for 28days).study concluded that in ethanol extract treated animals, the hyperglycemia by alloxan was controlled significantly by restoration of the levels of of serum glucose as compared to the normal and standard drug metformin treated groups [18].

In-vitro and in-vivo studies on the antidiabetic activity of homalium zeylanicum were designed to explore the ant diabetic potential of stem bark extracts using Streptozotocin induced diabetic model. The crude aqueous suspension, hexane, ethyl acetate, methanol and aqueous stem bark extracts of Homalium zeylanicum were examined each at a concentration of 50g/L using an in vitro method and compared to control and standard (Insulin). The methanolic extract showed a significant inhibitory effect on in vitro glucose diffusion. The in-vitro inhibitory activity cannot be always related to in vivo activity so a preclinical study was conducte using glibenclamide (0.02g/kg b.w) as a reference standard the results shows that that administration of HZACS to STZ induced diabetic rats at a dose of 0.5g/kg b.wt. Produced a significant reduction (61%), ($p<0.0001$) in blood glucose level. Among the different solvent extracts MEHZ at a dose of 0.5g/kg b.wt. Produced a significant reduction (69%), ($p<0.0001$) in blood glucose level in the diabetic rats while the other extracts could produce less antihyperglycemic activity. The administration of MEHZ at a dose of 0.5g/k.g b.w along with 2g/k.g b.w glucose load has significantly improved the glucose tolerance in the diabetic rats with consistent decrease in the blood glucose with a maximum fall of 41.96%. The antidiabetic activity of MEHZ stem bark may be due to its stimulating effect on the remnant beta cells or improvement in insulin action at cellular level or it could also be due to its insulin like effect. However the methanolic extract was found to be more effective than the hexane, ethylacetate and aqueous extract. This study concluded that the methanolic extract showed a significant antidiabetic activity and was more effective in reducing the blood glucose levels compared to that of standard drug glibenclamide **[19].**

HEPATOPROTECTIVE ACTIVITY

The hepatoprotective effect of the extract of the stem of the plant (200-600 mg/kg) was evaluated by the assay of liver function parameters, namely total and direct bilirubin, serum protein and albumin, total cholesterol, alanine aminotransaminase (ALT), aspartate aminotransaminase (AST), and alkaline phosphatase activities (ALP), antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), reduced glutathione (GSH) and histopathological study of the liver.Administration of the extract of the stem of the plant caused a significant ($p<0.05 – 0.001$) dose-dependent reduction of high levels of liver enzymes (ALT, AST and ALP), total cholesterol, direct and total bilirubin as well as elevation of serum levels of total protein, albumin and antioxidant enzymes (SOD, CAT, GPx and GSH). Histology of the liver sections from extract and silymarin-treated animals showed reductions in the pathological features compared to the paracetamol-treated animals.The chemical pathological changes were consistent with histopathological observations suggesting marked hepatoprotective effect of the extract of H. letestui stem. Study concluded that the hepatoprotective potential which may be due to the antioxidant activity of its phytoconstituents **[20].**

ANTIOXIDANT ACTIVITY

The antioxidant potential of leaf and bark of the plants was evaluated through successive extraction methods by using hexane, chloroform, ethyl acetate and methanol. The extracts were subjected to invitro assays as DPPH, hydroxyl, nitricoxide and superoxide along with its biochemical estimation. Amongst all, the ethyl acetate extracts of bark is found to be most potent compared with that of the leaves. H. nepalense has the highest amount of total phenolic and flavonoid contents followed by H. mentosum and H. zeylanicum, respectively, and significant antioxidant behaviour. This study reported antioxidant activity, total phenolic and flavonoid contents of the leaves and bark part of three Indian Homalium species. In order to realise medicinal values from potential plant sources, it is important to measure the antioxidant activity using various radicals and oxidation systems. From this study it is established that leaves and bark of H.nepalense possess better antioxidant quality than other Homalium species that need further study and clinical tests. Bark of the plant was proved to be more potent than the leaves. These three Indian Homalium species have shown better scavenging activities than the reported West African species of H. letestui **[21].**

CYTOTOXIC ACTIVITIY

In addition to radical scavenging activity,cytotoxic activity was also tested for the extracts and isolated compounds. Chromatographic partition of the ethyl acetate extract (40 g) of dry leaf (1.0 kg) H. zeylanicum on silica gel using n hexane/ethyl acetate mixtures of increasing polarity, led to the isolation of the 3-phenyl coumarin (1). Similarly Chromatographic partition of the ethyl acetate extract (50 g) of dry bark (1.0 kg) H. zeylanicum on silica gel using n-hexane/ethylacetate mixtures of increasing polarity, led to the isolation of the stigmasterol and the 4'-O-methyl epigallocatechin (2). Compound 2 was acetylated using pyridine/acetic anhydride to get a penta acetate derivative (3). Cytotoxic activity was tested using 3-(4, 5- dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) assay12. Three human cancer cell lines IMR-32 (neuroblastoma cell line), MCF-7 (breast adinocarcinoma cell line) and Hep-G2 (hepatoma cell lines) were used. The assay was dependent on the reduction of the tetrazolium salt MTT (3-(4, 5-dimethylthazol2-yl)-2, 5-diphenyl tetrazolium bromide) by the mitochondrial dehydrogenase of viable cells to form a blue formazan product dissolved in DMSO and measured at 570 nm. The extracts and their isolated compounds of bark and leaf of H. zeylanicum showed in vitro anticancer activity but, Ethyl acetate extract of leaf and Hexane extract of bark showed potential cytotoxicity against IMR-32 cell lines (IC50 1.76 & 4.21 µg/ml). Similarly, compound 3 showed potential cytotoxicity against IMR-32 cell lines (IC50 6.26 µg/ml) when compared with its parent compound 2 (IC50 32.2Mg/ml) which may have further therapeutic value **[11].**

REVIEW ON WOUND HEALING ACTIVITY

Wounds generally termed as physical injuries that result in an opening or breaking of the skin. There are different types of wounds which range from mild to potentially fatal. Wound healing is impaired in diabetic patients with infection or hyperglycaemia. Diabetes mellitus is one of the major contributors to chronic wound healing problems. The diabetic patients with ulcer become at high risk for major complications which include infection and amputation. In traditional medicine plants are generally used for treatment of various acute and chronic diseases and abnormalities in the body. Due to the present fast life of the humans a drastic increase in chronic disease conditions mainly diabetes has been determined. Most of these patients tend to face a tremendous problem when they get an infected wound.

Sandhya *et al* in 2011 made a review on plants as potent ant diabetic and wound healing agents this review contain a list of the plants used in traditional medicine for the treatment of wounds and diabetes were screened [22].
List plants having traditional claim on wound and diabetes [23-27]

Table 3: Name of plants.

Homalium Zeylanicum	Bambusa arundinaceae
Linum usitatissmum	Cynadon dactylon
Biophytum sensitivum	Paspalum serobiculatum
Cipadessa baccifere	Phragmites karka
Chloroxylon swietenia	Triticum aestivum
Filicum decipens	Sida cordata
Acacia nilotica	Cieba pentandra
Nerium oleander	Grewia tiliafolia
Calotropis procera	Pterocarpus marsupium
Barleria Montana	Acacia polycantha
Aerva lanata	Mimosa pudica
Ficus bengalensis	Argyreia nervosa

CONCLUSION

In India large number of wild species is available and it is important to protect and preserve endangered species. Herbal medicine may offer testimony of their safety and efficacy, and its demand is increasing more due to their lack in side effects. Homaliun zeylanicum Benth is widely available tree. Based on this complete literature study, that the plant HZB is being used traditionally, due to their therapeutic potential to treat various diseases. It contain variety of bioactive phytoconstituents like homalicine,dihydrohomalicine,vacciniin,homaloside A B C D ,coumarin,catechin.On the basis of pharmacological investigations various activities including analgesic, anti-inflammatory, ant diabetic, anthelmintic ,hepatoprotective and antioxidant were reported from the extracts of different parts and phytoconstituents of this plant. These activities and isolated compounds provide scientific observations for some of the therapeutic claims.

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