Review Article

Traditional uses, Phytochemistry and Pharmacology of an Endangered plant - *Decalepis hamiltonii*. Wight and Arn.

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ABSTRACT

Decalepis hamiltonii. Wight and Arn. (Asclepiadaceae) has been extensively used in traditional systems of medicine for a wide range of ailments. Phytochemical studies have shown the presence of many valuable compounds such as saponins, tannins, flavonoids, phenolics, triterpenes, ketones, aldelydes, resinol, sterols, inositol, fatty acids, volatile flavour compounds, cardiac glycosides, volatile and essential oils. The wide spectrum of pharmacological activities in *D.hamiltonii* extracts includes antibacterial, antifungal, anti-inflammatory, antimalarial, antidiabetic, antiulcer, antipyretic, antiplasmodial antioxidant, cytoprotective, hepatoprotective and insecticidal properties. These properties have triggered acceleration in extraction and isolation of phytochemical compounds in recent years. The highly aromatic tuberous roots are endangered in its natural habitat due to habitat destruction and over-exploitation by destructive harvestation. Low availability is a serious bottleneck and there is an urgent need to focus on the conservation priorities of this globally endangered species.

Keywords: *Decalepis hamiltonii*, 2-hydroxy-4-methoxybenzaldehyde (2H4MB), aromatic root, volatile and essential oils.

INTRODUCTION

Plants are an exemplary source of traditional medicine and pharmaceutical drugs for human kind since time immemorial. About 80% of world population still dependent upon the herbal drugs for their health care. Roots account for 60% of the medicinal plants used in the traditional systems of medicine (Ayurveda, Siddha, Unani) as the principle material for drug preparation.[1]

Decalepis hamiltonii. Wight and Arn., is a globally endangered species exploited for its tuberous roots of therapeutic value.[2] Conservation Assessment and Management Plan included this species in red list of medicinal plants alarming the urgent need of its conservation. Moreover, lack of appropriate organized cultivation of this plant has hampered the research activities. The genus *Decalepis* has 4 scientific plant names of species rank, validated taxonomically and accepted as species names (www.theplantlist.org). viz. *Decalepis arayalpathra* (J.Joseph & V.Chandras.) Venter, *Decalepis hamiltonii* Wight & Arn., *Decalepis nervosa* (Wight & Arn.) Venter, *Decalepis salicifolia* (Bedd. ex Hook.f.) Venter. Except *D. hamiltonii* limited research has been reported on other three species. D.salicifolia *and D.arayalpathra* are critically endangered and endemic to southern forest of the Western Ghats, India.[3,4] Pure form of antifungal compound 2-hydroxy-4-methoxybenzaldehyde (2H4MB) was isolated from volatile oil of *D.salicifolia* roots.[5] Extracts of *D. arayalpathra* possess antiulcerative, gastric antisecretory[6], immunomodulatory, anti-cancerous properties.[7] *Decalepis nervosa* remains among the less-studied species of *Decalepis*.

The limited availability of these species decreased its scope of extensive investigation and there exists urgent measures of conservation and further exposure of the wide potentialities that has not been exploited. Therefore this review aims to provide a comprehensive overview of phytochemistry and biological activity of *Decalepis hamiltonii* and insights that have been emerged with possible uses to treat different diseases.

Geographical Distribution

D.hamiltonii (swallow root) of Asclepiadaceae family is a large glabrous climbing shrub liane, available during monsoon in Southern parts of India, dry hill tracts of Eastern and Western Ghats [8-10] (Table 1).

TRADITIONAL USES

D. hamiltonii used in Ayurveda, Siddha and Folk systems of medicines as general vitaliser, blood purifier, wound healer, bronchial asthma, fever, intrinsic haemorrhage, kushtha, erysipelas, poisoning, paediatric rejuvinative[11,12]. The root has a sweet taste containing 92% fleshy and 8% woody matter.[13] Chewing the roots and drinking Nannari (Herbal drink prepared from roots by Yanadi tribe) is regarded to give relief from digestive problems and increases appetite[14]. The roots are consumed as pickles, juices for its alleged health promoting properties[15] and also as decoction by the ancient tribes in the Western Ghats of India.[16-18] The presence of a volatile principle compound with bacteriostatic property allows it to be used as preservative in various food and pharmaceutical applications.[19-21] The roots are also used as a substitute for *Hemidesmus indicus* in ayurvedic preparation of ancient Indian medicine because of the similar aromatic properties[22]. It is used in the treatment of skin diseases,

nutritious disorders[17,23], epilepsy and central nervous system disorders[24].

The roots are used as a flavouring principle[25], culinary spice[8,26] preservative[27], demulcent, diaphoretic and diuretic. It is useful in curing diarrhoea and acts as a source of bioinsecticide for stored food grains[19].

PHYTOCHEMICAL PROPERTIES

Steam distillation, NMR and MS analysis of *D. hamiltonii* root volatiles revealed a volatile oil (0.68%) from fresh fleshy roots with 2-Hydroxy-4-methoxybenzaldehyde (2H4MB) crystallized out (96%) as the major component along with other minor flavour constituents responsible for the characteristic aroma and food preservative property[13] (Table 2).

Hydrodistillation of the roots yielded 0.33 % (v/w) of oil with a sweet aromatic odour. GC and GC-MS analyses revealed the presence of at least 18 components, with major components being 2H4MB, 4-O-methylresorcylaldehyde, benzyl alcohol, β-caryophyllene and α-atlantone. The oil chiefly consists of aromatic aldehydes (78.57%), monoterpene hydrocarbons (6.42%), alcohols (4.19%), and ketones (2.87%). The principal monoterpenes and phenolic components are β-phellandrene and trans-anethole respectively[18].

Table 1: Geographical Distribution and Vernacular names of *D. hamiltonii* in India

State	Area of distribution in India[11]	Language	Vernacular names
Andhra Pradesh	Kurnool, Chittoor, Nellore, Prakasam, Rangareddy, Mahabubnagar, Rayalaseema, Anantpur, Cuddapah.	Telugu	Neemam theega (chenchu tribes), maregugaddalu, Maredu kommulu, Barre sugnadhi
Karnataka	Hassan, Mysore, Bellary, Tumkur, Kolar.	Kanada	Magadi beru, Makali beru
Tamil Nadu	Chengalpattu, Coimbatore, Dharmapuri, Nilgiri, Kolli Hill.	Tamil	Mahali kizhangu, Mavilinga kilangu, Peru nannari
Kerala	Marayur, Chinnar, Idukki	Malyalam	Nannari
		Sanskrit	Sariba, Sveta sariva

Table 2: The percentage compositions of oil and root components of *D. hamiltonii*

Composition of the Essential Oil[13]		Composition of the volatiles [18]	
Compounds	*(%)*	*Compounds*	*(%)*
2-Hydroxy-4-methoxybenzaldehyde (2H4MB)	96.00	2-hydroxy-4-methoxybenzaldehyde (2H4MB)	37.45
Benzaldehyde	0.017	β-phellandrene	2.44
Isooctanol	0.213	1-ethyl-3,5-dimethyl benzene	1.50
Salicylaldehyde	0.018	β-pinene	2.01
Naphthalene	0.082	benzyl alcohol	3.16
Methyl salicylate	0.044	γ-hexalactone	0.81
Benzyl alcohol	0.016	2-hydroxybenzaldehyde	31.01
2-Phenylethyl alcohol	0.081	4-o-methylresorcylaldehyde	9.12
Ethyl salicylate	0.038	α-atlantone	2.06
Allyl nonanoate	0.010	γ-terpinene	1.97
p-Anisaldehyde	0.010	2-phenylethanol	1.03
Styrene	0.016	Unknown	1.02
4-Hydroxy-3-methoxy acetophenone	0.238	4-methoxybenzaldehyde	0.99
Methyl 3-hydroxy-4-methoxybenzoate$_3$	0.035	Geraniol	1.12
Vanillin	0.450	trans-anethole	1.14
Lauric acid	0.128	β-caryophyllene	1.19
Myristic acid	0.156	trans-α-bergamotene	1.04
Palmitic acid	0.550	trans-cadinol	0.88
Oleic acid	0.736	TOTAL	99.94
Stearic acid	0.407		
Docosanoic acid	0.149		
Tetracosanoic acid	0.022		
TOTAL	99.416		

Standard analytical assay procedure for the analysis of the volatile oils/estimation of 2H4MB in both fresh and dried roots was standardized based on steam hydrodistillation and gas chromatographic (GC) analysis[28]. The compounds 2H4MB, p-anisaldehyde, vanillin, borneol, salicylaldehyde, and bis-2, 3, 4, 6- galloyl-α/β-D-glucopyranoside (decalepin) were identified by MS, ^{1}H NMR, ^{13}C NMR and 2D NMR spectroscopic techniques from the methanolic root extract[29]. Moreover, 2H4MB is identified in dichloromethane extracts of different parts of root-tuber, peel, tuber without peel and medullary portion. Medullary (73.73 mg g^{-1} dry tissue) and peel (68.34 mg $g^{-1)}$ portions are rich in 2H4MB[2] (Table 3). Decalepin is claimed to be gastro protective in nature and perhaps inhibit $H^{+}K^{+}$ ATPase enzyme responsible for HCl secretion[50].

The other phytochemical constituents present in root extract are geraniol (Indian Medicinal Plants 2009), 4-0-methyl resorcylaldehyde (9-12%)[32], ketone, resinol, sterols, saponins, tannins, inositol, fatty acids[33,34], flavanoids, triterpenes such as α-amyrin, β- amyrin acetate, lupeol [35], steroids and cardiac glycosides. Cardiac glycosides were present in petroleum ether, ethyl acetate, acetone, methanol, and ethanol; and absent in aqueous, benzene and chloroform extracts. Steroid and glycoside constituents of petroleum ether extract could contribute to the antibacterial activity[36].

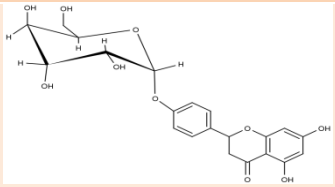
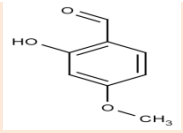
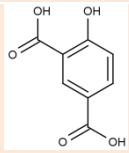
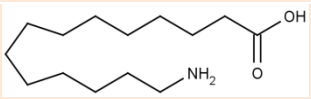
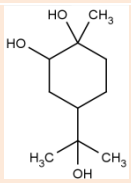
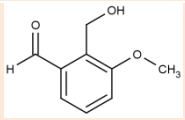
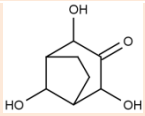
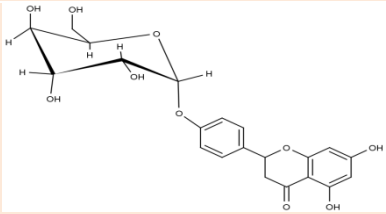
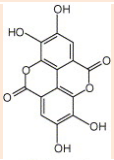
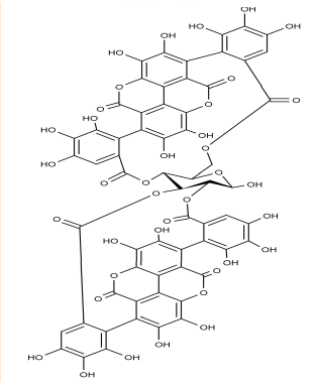
Five novel antioxidant compounds[26] and a polyphenolic antioxidant, dimeric derivative of gallic acid called Ellagic acid (2.27 mg/g extract or 0.39 g/kg of root powder) were identified and characterized from the root aqueous extracts[37] (Table 4). The dichloromethane/methanol root extracts constitutes Lupeol acetate and (2S)-5,7,4-trihydroxy flavanone 4-O-β-d-glucoside[38].

Twelve phenolic compounds *viz*., Gallic acid, Protocatechuic acid, Gentisic acid, Vanillic acid, Caffeic acid, Syringic acid, p-Coumaric acid, Ferulic acid, trans-Cinnamic acid, p-Hydroxybenzoic acid, 2H4MB and Vanillin were detected in swallow root phenolic acid extracts by HPLC analysis. These compounds include (5) hydroxybenzoate derivatives, (4) cinnamate derivatives and (2) hydroxybenzaldehyde derivatives. In total 12, 9, and 9 phenolic compounds were identified in free phenolic acids extracts (SRFP), Conjugated phenolic acids extracts (SRCP) and Insoluble-bound phenolic acids extracts (SRIBP) of swallow root respectively. The major phenolic compounds identified were: gentisic acid, 2H4MB, vanillin, vanillic acid and p-hydroxybenzoic acid in SRFP extracts; gallic acid and gentisic acid in SRCP extracts; 2H4MB, vanillic acid and p-hydroxybenzoic acid in SRIBP extracts[31]. There is need to evaluate the biological properties of several phytochemical compounds of *D.hamiltonii* such as the role of steroids and cardiac glycosides in broad spectrum antibacterial activities; gastro protective and possibly inhibition of $H^{+}K^{+}$ ATPase enzyme by Decalepin etc.[40] 2007).

Table 3: 2-Hydroxy-4-methoxybenzaldehyde (2H4MB) content in various parts of D.*hamiltonii*

Source	Percent composition in the volatile oils	Method of Identification and quantification	Ref
Roots	37.45%	Hydrodistillation, GC-MS analysis.	18
Fresh fleshy roots	96%	Steam distillation, GC–MS analysis.	13
Fresh and dried roots	> 90%	Steam hydrodistillation, GC analysis.	28
Roots of tissue culture derived plants	0.14% /1.0-1.5 cm root	FID and GC-MS analysis.	30
Roots of greenhouse grown plants	0.12 % /1.0-1.5 cm root		
Methanol root extract	Unknown	MS, ^{1}H NMR, ^{13}C NMR, 2D NMR Spectroscopic techniques.	29
Dicloromethane Extract	**Mean+/-SD**		
Whole tubers	62.6+/-1.21 (mg/100g)	TLC and GC-MS analysis.	2
Tubers without skin	54.7+/-0.89 (mg/100g)		
Central core or medullary portion	73.7+/-1.10 (mg/100g)		
Peel	68.3+/-0.79		
Methanol Extract	**Mean+/-SD**		
Free phenolic acids extracts (SRFP)	5.06 ± 0.239 (mg/g)	HPLC analysis.	31
Conjugated phenolic acids extracts (SRCP)	0.10 ± 0.003 (mg/g)		
Insoluble-bound phenolic acids extracts (SRIBP)	1.14 ± 0.06 (mg/g)		

Table 4: Chemical structures of some of the phytochemical compounds of *D.hamiltonii* root extracts.

Name of compound	Class of compound	Structure	Biological activity	Ref
(2S)-5,7,4-trihydroxy flavanone 4-O-β-d-glucoside	Flavone		Anti inflammatory activity	38
2-hydroxy- 4-methoxybenzaldehyde (2H4MB)	Polyphenolic compound		Antioxidant and antifungal activity	2
4-hydroxyisophthalic acid	Polyphenolic compound		Antioxidant activity and cytoprotective effect	39
14-aminotetradecanoic acid	Non Polyphenolic compound		Anti oxidant activity	
4-(1-hydroxy-1-methylethyl)-1-methyl-1,2-cyclohexanediol	Non Polyphenolic compound		Anti oxidant activity	
2-(hydroxymethyl)-3-methoxybenzaldehyde	Polyphenolic compound		Anti oxidant activity	
2,4,8trihydroxybicyclo[3.2.1]octan-3-one	Non Polyphenolic compound		Anti oxidant activity	
(2S)-5,7,4-trihydroxy flavanone 4-O-β-d-glucoside	Flavone		Anti inflammatory activity	38
Ellagic acid	Polyphenolic compound		Antioxidant activity and cytoprotective effect	37.
bis-2,3,4,6-galloyl-α/β-D-glucopyranoside(Decalepin	-		Antioxidant activity	29

PHARMACOLOGICAL PROPERTIES

Antibacterial activity

Several *in vitro* and *in vivo* studies were conducted to evaluate the antibacterial potential of phytochemicals from various extracts of *D.hamiltonii* against several gram positive and gram negative bacterial strains. The essential oil extracted from roots exhibit strong antimicrobial activity against foodborne pathogens and moderate activity against *Ps. aeruginosa* (11 mm) and *Pr. vulgaris* (12 mm)[18]. Out of 15 food borne pathogens evaluated for growth inhibition, 11 were inhibited by methanol extract and 9 nine by petroleum ether extract. The curative activity of these extracts was more than that of the respective standards against *B. cereus, B. megaterium and E. coli* indicating its usefulness in food preservation[41]. Petroleum ether extracts with 0.098µg/ml (MIC) and 0.049µg/ml (MID) exhibited higher activity against gram positive (*Staphylococcus aureus*, *Bacillus subtilis*) and gram negative bacteria (*E. coli, Klebsiella pneumonia*)[10].

All the extracts (except aqueous extract) of the roots exhibited antibacterial activity. Steroid and glycoside constituents could perhaps be the reason for antibacterial activity of the petroleum ether extract. Methanol and acetone extracts showed antibacterial activity against all the tested microorganisms except *Staphylococcus aureus* and *Shigella sonnie* respectively[36].

Crude petroleum ether extract obtained from the callus generated from *D.hamiltonii* leaves exhibited inhibitory activity-minimum against *Klebsiella pneumonia* (5mm), *Proteus vulgaris* (6mm) and maximum against *Salmonella typhi* (11mm). Antibacterial active constituents can be transmitted efficiently by *invitro* micropropagated clones implying large scale extraction of antibacterial principles and other curative chemicals through callus culture[20].

Antifungal activity

Aqueous root extract inhibited *A. alternata* mycelial growth by 100% and showed significant antifungal activity by poisoned food technique at different concentrations against phytopathogenic fungi - *Fusarium*, *Aspergillus*, *Penicillium*, *Drechslera* and *Alternaria alternata* species isolated from Sorghum, Maize and Paddy seeds. The petroleum ether extract showed the highest antifungal activity than benzene, chloroform, methanol and ethanol, suggesting that the active compound can be better extracted with petroleum ether. Aqueous extract totally inhibited both storage and field fungi. Then extracts showed better activity than the tested synthetic fungicides[42]. Minimal inhibitory concentration (MIC) of 2H4MB (petroleum extract) was determined by poisoned food technique using against various fungal pathogens (Table 5)[43,44].

Further Seeds (sorghum, maize and paddy) treated with 2H4MB (1g/ml) increased seed germination and seed vigour, with a corresponding decrease in seed mycoflora. The antifungal active compound was effective against all the 24 fungal species tested suggesting broad-spectrum antifungal activity[43]. Paddy seeds treated with 1 g/kg active compound significantly controlled seed borne fungi till 90 days of storage[44]. Methanol extract of *D. hamiltonii* at 3500 µg/ml concentration showed significant antifungal activity by poisoned food technique against *Alternaria alternata*, *Aspergillus flavus, Curvularia lunata, Drechslera oryzae*, *D. halodes*, *Pyricularia oryzae, Fusarium moniliforme* and *Trichoconis padwickii*[45].

The extracts (methanol, petroleum ether and aqueous) of leaf, stem, bark and root showed inhibitory activity against *Candida albicans* by micro-dilution assay with MIC ranging from 1.65-6.10µg/ml. Lowest MID and MFD were exhibited by aqueous extracts compared to methanol and Petroleum extracts. Moreover, the petroleum ether and methanol extracts of root and stem bark are rich in antifungal active compounds with fungistatic activities that showed higher inhibitory activities than leaf[10].

Table 5: *In vitro* antifungal activity of *2H4MB* from petroleum ether extract of *D.hamiltonii* roots

Fungal species	MIC of 2H4MB (µg/ml)	Ref
Fusarium graminearum	200	43
F. Semitectum	250	
F. solani	250	
D. halodes	300	
A. columnaris	650	
A. niger	700	
Seed-borne fungal pathogens from paddy seeds		
D. tetramera	350	44
F. proliferatum	350	
F. oxysporum	400	
A. alternate	450	
T. padwickii	600	
P. oryzae	650	

Hepatoprotective activity

Treating liver diseases with herbal drugs is age old tradition in India, China and Japan (Girish et al. 2009). Adult male albino rats were used for the hepatoprotective studies of this plant (Table 6). The probable reason for hepatoprotective activity of the extracts could be free radical scavenging activity/ increasing the antioxidant capacity by the bioactive antioxidant principles.

Anti-inflammatory activity

The methanol root extract has potential anti-inflammatory activity at doses of 250 and 500 mg/kg fed orally in the carrageenan-induced rat paw edema and cotton pellet–induced chronic inflammatory models[48]. Lupeol acetate and (2S)-5,7,4-trihydroxy flavanone 4-O-β-d-glucoside isolated from roots inhibited the proliferation of mitogen induced peripheral blood mononuclear cells employing [^{3}H] thymidine uptake assay with an IC_{50} value of 8 and 0.5 µg/ml respectively. These compounds exhibit anti inflammatory activities by down regulating TNF-α and

IL-2 specific mRNA, besides up regulating the synthesis of mRNA of IL-10[38].

Ethanolic root extract showed maximum inhibition in carrageenan (34.48 %) followed by histamine (25.35%) and serotonin (21.71%) induced acute inflammation[49]. Powdered root (250 mg/kg) showed 35.55% inhibition in Carrageenan, 42.62% in 5HT, 36.62% in bradykinin induced acute inflammation in Albino rat models. Ethanolic root extract and powdered root exhibited a progressive inhibition of 25.26 % (3rd day), 31.25 % (5th day), 33.90 % (7th day), 44.82% (9th day), 50.40% (11th day), 46.01% (13th day)[49] and 36.84% (3rd day), 36.45% (5th day), 51.45% (7th day), 66.39% (13th day) respectively in the chronic inflammatory model induced with formaldehyde[50].

Basic pharmacological data of *D.hamiltoni*

Type of extract	Dose range tested	Solvent	Minimal active concentration	Model used (incl. information whether it is an *in vitro* or in vivo study	Controls (positive and negative)	Basic pharmacological data	Ref
Essential oil	Diluted with equal volumes of 4% DMSO in H2O at concentration ranges of 1:0, 1:1, and 1:2.	4% DMSO in H2O	concentration range of 1:0	*In vitro* antibacterial activity	Paper disks treated with antimicrobial standards alone served as control	Strong antimicrobial activity against Bacillus cereus, Bacillus megaterium, Escherichia coli, Micrococcus luteus, Micrococcus roseus, and Staphylococcus aureus	18
Petroleum ether, benzene, chloroform, ethyl acetate and Methanol	1 to 100 mg/ml	Petroleum ether, benzene, chloroform, ethyl acetate and Methanol	-	*In vitro* Susceptibility Testing	Chloramphenicol, clidamycin, clotrimazole, gentamycin, nystatin and tetracycline	Methanolic extract inhibited growth of 11 of 15 selected organisms, whereas the petroleum ether and ethyl acetate extracts inhibited nine and seven organisms respectively.	41
Petroleum ether callus extract	1g/20ml	Petroleum ether	5mg/ml.	*In vitro* antibacterial activity	Petroleum ether (- control) and Gentamycin antibiotic 50mg/ml (+ control)	Protects against food pathogens like- Bacillus subtilis and Staphylococcus aureus.	20
Leaves, stem bark, root	100mg to 0.049µg/ml	Petroleum ether, ethyl acetate and Aqueous	0.098 and 0.049µg/ml of petroleum ether extracts were recorded as MIC and MID respectively	*In vitro* antibacterial activity	Ampicillin (+control) and DMSO (- control).	The aqueous extracts of root and stem bark exhibited lower MID values against Staphylococcus aureus, Bacillus subtilis and E. coli, Klebsiella pneumoniae, except the same extract of leaf.	10
Petroleum ether, benzene, chloroform, ethyl acetate, acetone, ethanol and methanol	10µl (contains 5mg/ disc)	DMSO	-	*In vitro* antibacterial activity	DMSO(– control)	Different degrees of antibacterial activity against 7 gram positive bacteria (Escherichia coli, Klebsiella pneumonia, Salmonella typhi, Proteus mirabilis, Vibrio cholera, Shigella sonnie, Serritia sp) and 2 gram negative bacteria (Staphylococcus aureus and Bacillus subtilis).	36

Table 6: Hepatoprotective activity of *D.hamiltonii* roots

Type of Extract	Hepatotoxic inducer	Dosage	Increased levels	Decreased levels	Restored levels	Ref
Aqueous	CCl4	50, 100 and 200 mg/kg b.wt.	-	lipid peroxidation, protein carbonylation,	antioxidant enzymes and glutathione	26,47
Methanol	CCl4	50, 100 and 200 mg/kg b.wt	total protein	GPT, GOT, ALP, LDH, lipid peroxidation	GSH, Catalase, GPx and GR	31
Methanol	acetaminophen	50, 100 and 200 mg/kg b.wt	CAT, SOD, GSH, ascorbic acid	LPO	ALT, AST, ALP, bilirubin, total protein	36

Anti-arthritic activity

Arthritis induced by formalin was used as a model for evaluation of ethanolic extract of *D.hamiltonii* roots with probable activity against the proliferative phase of inflammation i.e. chronic inflammation. Progressive inhibition of 25.26%, 31.25%, 33.90%, 44.82%, 50.40%, 46.01% was observed on 3rd day, 5th day, 7th day, 9th day, 11th day and 13th day respectively. There was significant inhibition of formaldehyde induced paw edema by ethanolic root extracts suggesting its competency in treatment of arthritis and related disorders. The roots possess potent anti-inflammatory activity possibly due to inhibition or release of inflammatory mediators like serotonin and histamine[49]. Perhaps it can emerge as an alternative to Non Steroidal Anti Inflammatory Drugs and corticosteroids in inflammatory disorders.

Anti typhoid activity

Antityphoid activity of *D.hamiltonii* was reported against typhoid causing organisms by agar diffusion technique. Among the different extracts used (petroleum ether extract, chloroform extract, ethyl acetate extract, ethanolic extract and water extract), petroleum ether and chloroform extracts showed significant activity with the zone of inhibition of 15,14,15mm and 10,10,6mm respectively against *S. typhi, S. paratyphi A* and S. *paratyphi B*.[51] This study revealed the anti typhoid activity but the active principles with potent activity need to be isolated.

Insecticidal property

The root powder of *D. hamiltonii* has been found to have bioinsecticidal activity on storage pests (*Sitophilus oryzae* L., *Rhizopertha dominica* F. and *Tribolium castaneum* Hbst.) at lethal and sublethal levels[32,19,52]. Organic extracts of the roots showed insecticidal activity against stored grain insect pests such as *Rhyzopertha domonica, Sitophilus oryzae, Stigobium pancieum, Tribolium castaneum* and *Callosobruchus chinensis*. The methanol extract (LC_{50}=0.14 mg/cm^2) was most toxic against *S. oryzae,* followed by ethyl acetate, hexane and acetone. It has been extensively used as preservative and bioinsecticide in food grains storage due to the presence of strong aroma and 4-0-methyl resorcylaldehyde (9-12%)[53]. The toxic effect of methanolic extract on adults and also on various life stages of stored grain insect pests can be exploited as the source of a new ecofriendly bioinsecticide and grain protectant of natural origin.

Antidiabetic activity

In vivo studies has shown that the oral administration of aqueous, methanol and petroleum ether extracts at a dose of 200 mg/kg body weight decreased the blood glucose levels by 69.43 %, 62.04%, and 49.61% respectively. The extract has showed significant glucose uptake 76.39%, 72.19% (aqueous), 58.98%, 57.58%, 59.25% (methanol) and 59.49% (petroleum ether) at 6th hour without and with insulin when compared to control group respectively[54].

In vitro study of antidiabetic activity by rat hemi diaphragm method revealed direct insulin like effect of *D.hamiltonii* root extracts that can enhance the peripheral use of glucose in alloxan induced diabetes in male wistar albino rats. Root ethanol extracts (0.05 and 0.1%) in STZ induced diabetic rats significantly reduced the blood glucose level, risk of oxidative stress, DNA damage and ameliorated liver damage and diabetic condition, which signifies its anti-diabetic activity[21].

Oral administration of ethanolic extracts (100, 200 and 400mg/kg) once daily up to 28 days to alloxan induced diabetic wistar albino rats lowered blood glucose, glycosylated hemoglobin, restored body weight and increased insulin levels significantly. Triglycerides, total cholesterol, VLDL and LDL levels were significantly decreased, whereas, HDL levels, reduced glutathione (GSH), catalase (CAT) and reduced reactive thiobarbituric acid levels (TBARS), superoxide dismutase (SOD) were increased[12]. The higher dose of alcoholic extract (200 mg/kg) and aqueous extract (400 mg/kg) produced maximal serum glucose lowering effect in both normal and STZ induced diabetic albino rats. The alcoholic extract exhibited higher hypoglycemic and antidiabetic activity than aqueous extract and standard gliclazide (2 mg/kg). The oral acute toxicity (LD_{50}) of alcoholic and aqueous extracts was found to be 1000 and 2000 mg/kg respectively. Thus the alcoholic extracts possess beneficial effects on serum glucose levels in normal and STZ induced diabetic albino rats[55]. The antihyperglycemic activity of these extracts may be due to, free radicle scavenging, regeneration of pancreatic beta cells and enhanced peripheral glucose uptake by skeletal muscle. The mechanism of the hypoglycemic and antidiabetic effect of extracts needs to be elucidated for prevention or early treatment of diabetic disorder.

Antiulcer activity

In Indian traditional medicine, several plants have been used to treat gastric ulcers[56]. Antiulcer properties have been attributed generally to phenolics[57,58] and occasionally to polysaccharidesof plant extracts.[59-61] Maximum protection upto 72% at 200 mg/kg b.wt was recorded by aqueous extract of swallow root in swim stress-induced ulcers with an ulcer index (UI) of 6.0 ± 0.01. Additionally, the extract normalized 2.4 folds of increase in gastric mucin, possessed reducing power, antioxidant, free radical scavenging ability (IC_{50} 0.17 µg/ml), DNA protection (80%) at 0.2 µg and proton pump inhibition. Toxicity studies indicated no lethal effects in rats fed up to 5g/kg b.w[50].

Srikanta et al. 2007 reported a pectic polysaccharide from swallow root (*D.hamiltonii*; SRPP) containing a sulfonamide group and phenolics with known sugar composition [rhamnose: arabinose: xylose: galactose in the ratio of 16:50:2:32 (w/w), with 141 mg/g of uronic acid)[62]. This compound was proved to be an effective

antiulcer compound (80%-85%) and possess a multi-potent role in the upregulation of mucin, antioxidant levels, modulation of oxidative status, inhibition of H^+, K^+-ATPase activity (IC_{50} of 77 µg/ml) evident from the *in vivo* study against swim and ethanol stress induced ulcers in Wistar albino rats. Moreover, it also inhibits *H.* pylori (MIC-150µg/ml). This phenolic polysaccharide has potential role in preventing gastric ulceration. Toxicity studies in albino wistar rats did not show any significant differences in the serum total protein suggesting no adverse effects on the major organs. Swollen root pectic polysaccharide identified as antiulcer component is inexpensive, effective and nontoxic suggesting its potential as an alternative for ulcer management.

Antipyretic activity

The methanol extract of *D.hamiltonii* possess antipyretic activity. The elevated rectal temperature of the albino rats (Wistar strain) after 18 h of subcutaneous injection of yeast suspension decreased with methanol extract at doses of 250 and 500 mg/kg in dose-dependent manner 4 h after pyrexia when compared with control (Paracetamol). LD_{50} study of the test extract ingested up to 2000 mg/kg did not produce any lethality[48].

Antioxidant activity

D.hamiltonii root extracts are a cocktail of antioxidants. Srivastava et al. 2006 has first reported the antioxidant activity of the roots and founds that methanolic and aqueous extracts showed high antioxidant activity measured as scavenging of DPPH, superoxide and hydroxyl radicals and inhibited microsomal lipid peroxidation. These extracts exhibited strong reducing power and metal chelating activity.

Six compounds with antioxidant activity were isolated from methanolic extract of the root viz., 2H4MB, p-anisaldehyde, vanillin, borneol, salicylaldehyde, and bis-2,3,4,6-galloyl-α/β-D- glucopyranoside /Decalepin. The purified compounds showed inhibition of lipid peroxidation, hydroxyl radical, superoxide anion and 1,1-diphenyl-2picrylhydrazyl radical scavenging[29]. Ellagic acid isolated from the aqueous extract of the roots exhibited free radical-scavenging activity, inhibited LDL oxidation and showed cytoprotective effect against xenobiotic-induced oxidative stress in Ehrlich Ascites tumor cells[37].

Different concentrations of dichloromethane extracts subjected to antioxidant assay by DPPH (1,1 dihydroxy 2-picryl hydrazyl) has shown radical scavenging activity in medullary (44%), peel extracts (46.7%) and 67.3% activity in β-carotene linoleate model system (b-CLAMS). At 100ppm medullary, peel extracts and standard 2H4MB showed 43.46%, 45.7% and 69.64% antioxidant activity respectively. Similarly hydroxyl radiacle scavenging activity was found to be 48.36, 46.86, 48.26 and 73.26 in whole tuber, medullary, peel and standard 2H4MB respectively[2].

Ethanol extract also showed significant antioxidant activity[12]. DPPH radical scavenging activity indicated an IC_{50} of 0.046, 0.06 and 0.128 µg /ml for SRCP, SRIBP and SRFP, respectively. SRCP exhibited higher reducing power and DNA protectivity (80%). Phenolics compounds that contributed to antioxidant activity are gallic, gentisic, protocatechuic and p-coumaric acids[31].

DHA enhanced strong the antioxidant profile in brain by alleviating the activities of SOD, CAT, and GPx compared to liver[63]. The protective activity of aqueous extracts in male Wistar rat brain at high dose (in all the brain regions except cerebellum) and low dose (in striatum, cortex, and pons) can be attributed to its potent antioxidant constituents that prevents cholinesterase inhibition by inducing the Dichlorvos (2,20-dichlorovinyl dimethyl phosphate – DDVP) detoxifying enzymes.[64]

The aqueous root extracts rich in polyphenols exhibited strong antioxidant activities compared to that of the standard compounds such as α-Tocoperol, Rutin and Butylated hydroxytoluene (BHT) determined by antioxidant assays[65].

4-hydroxyisophthalic acid (4-HIPA) a potent free radical quencher isolated from the *D.hamiltonii* roots is a potent scavenger of superoxide ($O_2^{\cdot-}$), hydroxyl ($^{\cdot}OH$), nitric oxide ($^{\cdot}NO$), and lipid peroxide ($LOO^{\cdot}$) physiologically relevant free radicals with IC_{50} values in the nanomolar (2–187) range. 4-HIPA in a dose dependent fashion prevented CCl_4 induced protein carbonyl formation in rat liver tissue and showed significant ferrous ion-chelating activity, as a measure of its antioxidant capacity. It also exhibits a concentration dependent secondary antioxidant activity like reducing power, metal chelating activity and inhibition of protein carbonylation.[66] Hence, this plant with rich source of antioxidants could be used in the prevention of free radical mediated diseases and general health tonic.

Cytoprotective activity

The role of natural products is gaining more popularity in both developed and developing countries and much appreciated towards their applications as ‘‘alternatives” against chronic diseases such as diabetes, ulcer and cancer. A dose dependent cytoprotection was shown by SRFP, SRCP and SRIBP of root extracts evaluated on cultured NIH 3T3 fibroblast cells exposed to tertbutyl hydroperoxide showed a dose dependent protection between 0.03 and 0.15 µg/ml concentrations. At 0.12 µg/ml SRCP showed 87% cytoprotection (on NIH 3T3 cells) followed by SRIBP (65%) and SRFP (47%)[31].

4-HIPA demonstrated cytoprotective activity in primary hepatocytes and Ehrlich Ascites tumour (EAT) cells against oxidative stress inducing xenobiotics at LC_{50} concentration (hepatocytes – CCl4 and ethanol) (EAT cells – HCH, CHP, and CCl4). 4-HIPA dose dependently ameliorated toxicant-induced cytotoxicity by maintaining the intracellular GSH, ROS scavenging and LPO inhibition. This study opens up new avenues to exploit plant sources such as *D.hamiltonii* for application of novel bioactive molecules in both prevention and amelioration of degenerative diseases.[66]

CONCLUSION

Decalepsis hamiltonii as a potential resource has seldom been commercially tapped. The roots have emerged as a good source of the traditional medicines for the treatment of wide range of ailments of the central nervous system, gastrointestinal tract, respiratory system, endocrine system, infectious disorders, nutrition disorders, inflammation, bronchial asthma, intrinsic haemorrhage, diarrhoea, skin disease and to combat malarial parasites. The roots are edible and in view of the long history of human use, it can possible be exploited as source of a new ecofriendly bioinsecticide, grain protectant, serve as a new source of natural antioxidants or nutraceuticals along with potential applications in human health. The extracts and the compounds isolated from *D. hamiltonii* showed a wide spectrum of pharmacological activities including antibacterial, antifungal, anti-inflammatory, antimalarial, anticancer, antidiabetic, antiulcer, antipyretic, antioxidant, cytoprotechtive, hepatoprotective and insecticidal properties. SRPP can serve as a potential alternative for ulcer management. Further exploration is needed to identify the active principles responsible for the alleged health promoting activity to elucidate their mode of action, avoiding adulteration and to authenticate the genuine drugs or developing commercial formulation based on field, animal trails and toxicological experiment. The over-exploitation and destructive harvesting has endangered this plant in its natural habitat and there is an urgent need to conserve this globally endangered species.

Future needs of research

The pharmacological activity of *Decalepsis hamiltonii* extracts and research with its bioactive constituents provide scientific evidence which underpins the traditional therapeutical claims made such as gastrointestinal tract, infectious disorders, nutrition disorders, inflammation, and skin disease. However, to-date there is no scientific and methodological investigation so far been reported in literature regarding its mechanism of action, potential anticancer source of antioxidants and antimetastatic compounds, anti-inflammatory and anti-arthritic agent that blocks histamine and serotonin pathways which could serve as an effective alternative to non steroidal anti inflammatory drugs and corticosteroids in inflammatory disorders. The other challenging questions which should be addressed answered in the coming years are: Does the extracts nullify STZ in the blood itself or prevent its transport across into pancreatic and hepatic cells?/wipes off ROS or is it a chain-breaking antioxidant?/activate liver enzymes?/prevent alkylation of DNA.

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