Pharmacogn J. 2018; 10(6)Suppl:s14-s26
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
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Review Article

Systematic Review *Andrographis serpyllifolia* (Rottler ex Vahl) Wight: An Ethno-Pharmaco-Botanical Perspective

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ABSTRACT
Andrographis serpyllifolia (Rottler ex Vahl) Wight, belonging to Acanthaceae, has been recorded in ethnobotanical archives as a plant possessing potent anti- snake and scorpion venom activity. Its leaf extract has been proven a highly effective drug to combat bovine mastitis. The present review compiles most of the available experimental data emphasising phytochemical profiles and the pharmacological actitvty of this medicinal geophyte. This kind of systematic review encompassing all experimentally proven aspects of the plant, gaps in research and potential areas for future investigation is not available in literature published with regard to this plant so far.
Key words: *Andrographis serpyllifolia,* Botany, Ethnobotany, Phytochemical screening, Pharmacological screening.

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History
- Submission Date: 13-10-2018;
- Review completed: 31-10-2018;
- Accepted Date: 08-11-2018

DOI : 10.5530/pj.2018.6s.3

Article Available online
http://www.phcogj.com/v10/i6s

INTRODUCTION

Andrographis serpyllifolia (Rottler ex Vahl) Wight, a member of the family Acanthaceae, is a valuable medicinal plant with significant therapeutic activity and is found incorporated in several ethnobotanical formulations. Though it is included in the Genus *Andrographis*, it has a form, architecture and structure not shared by any of its 42 or more sister species. Its habit certainly does not resemble *A. paniculata* a very well-known, much exploited drug with hepatoprotective activity. While *A. paniculata* assumes an upright, much branched herbaceous form with short life-cycle, *A. serpyllifolia* has evolved into a ground hugging prostrate, perennial, geophyte that successfully survives multiple geo-ecological challenges and grazing threats year after year. Except that it is endemic to the arid southern Indian peninsular states, very little is known about its life cycle, morphology, physiology geo-ecological adaptations, anatomy, cytology or ideal propagation methods. Most investigators have focused on the phytochemistry and pharmacological activity of this plant. The very fact that it exists effectively, interspersed among more vigorous grasses, in harsh geo-ecological conditions of high temperature, water scarcity, annual summer forest fires and herbivory, suggests several inbuilt mechanisms to combat the adverse edapho-climatic challenges.

MATERIALS AND METHODS

The preliminary search for mention of *A. serpyllifolia* was initiated among the various Floras, journals, Books, Publications of various Botanical Gardens and Internet search engines. The literature search spanned over a period of more than 200 years from 1800 to 2015. The Internet search engines accessed included Mobot, BoDD (The Botanical Dermatology Database which is a primary resource propelled by Cardiff University for Botany, Phytochemistry and medicine), Scopus. Google Scholar, Delta Key.

Publications reviewed included Elsevier, Springer, Jstor, Biomed, Pubmed other national and International journals.

Botanical garden reviews searched were Botanical Survey of India, Kew Botanical Gardens, Missouri Botanical Gardens, New York Botanical Gardens. Foundation for revitalization of local health traditions FRLHT, IISc Biodiversity Portal

The various Key words used were *Andrographis serpyllifolia*, Acanthaceae, geophytes, morphology, phytochemistry, alkaloids, phytochemical characterization, flavonoids, saponins, polysaccharides, anthraquinones, andrographolides, anti-microbial, anti-proliferative, antioxidant, anti-diabetic, hepatoprotective, anti-inflammatory, bio actives. Extensive literature survey reveals that only few researchers have been working actively in this arena and published some publications. Analysis of past research in *A. serpyllifolia* shows that the focus of study undertaken has been restricted to Ethnobotany, folklore usage, Pharmacological activity and Phytochemistry. Many aspects of basic and applied botanical study remain unexplored.

Cite this article: Krishnaswamy S, Kushalappa BA. Systematic Review of Andrographis serpyllifolia (Rottler ex Vahl) Wight: An Ethno-pharmaco-botanical Perspective. Pharmacog J. 2018;10(6) Suppl:s14-s26.

RESULTS

Distribution and Nomenclature

The occurrence of *A. serpyllifolia* has been described in different herbaria such as the Geneva Herbarium – De Candolle's Prodromus (G-DC) Bearing serial no 1144597462 and category Cat. G-DC-256977/1 as *Eriathera serpyllifolia* (Rottl. ex Vahl). *Andrographis serpyllifolia* was first described as *Justicia* by Robert Wight, who collected the herbarium specimen during Dec 1824 in the jungles of Mysore where he describes the occurrence as "rather common very procumbent". The nomenclature has been variously described as *Justicia nummularifolia* by Wallich, *Eriathera lobeloides* and *Eriathera serpyllifolia* by Nees. Herbarium records (Figure 1) , maintained at Kew Botanical Gardens indicate that *Andrographis serpyllifolia* (Vahl) Wight is an accepted name in the genu s Andrographis (family Acanthaceae) and is listed among the 42 species belonging to the Genus Andrographis in records (Tropicos) maintained by Missouri Botanical Gardens.

Synonyms

In botanical nomenclature a homotypic synonym (or nomenclatural synonym) is a synonym that comes into being through a nomenclatural act, when a taxon gets a new name, without being included in another taxon (of the same rank).

HOMOTYPIC_SYNONYM ***ANDROGRAPHIS HUMIFUSA* Wall.** Species

SYNONYM ***ANDROGRAPHIS HUMIFUSA* Wall. ex Nees** species

HOMOTYPIC_SYNONYM ***ANDROGRAPHIS ORBICULATA* Wall.** species

SYNONYM ***ANDROGRAPHIS ORBICULATA* Wall. ex Nees** species

HOMOTYPIC_SYNONYM ***ERANTHEMUM SERPYLLIFOLIUM* (Rottl. ex Vahl) Willd.** species

SYNONYM ***ERANTHEMUM SERPYLLIFOLIUM* (Rottl. ex Vahl) Willd. ex Roem. and Schult.** species

HOMOTYPIC_SYNONYM ***ERIATHERA NEESIANA* Wight and Arn.** species

SYNONYM ***ERIATHERA NEESIANA* Wight and Arn. ex Nees** species

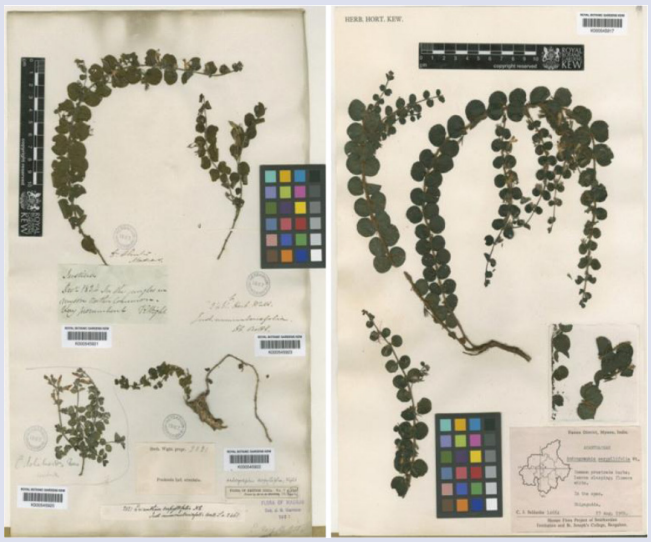


Figure 2: Herbarium records of *A.serpyllifolia* (KEW Botanical Gardens)

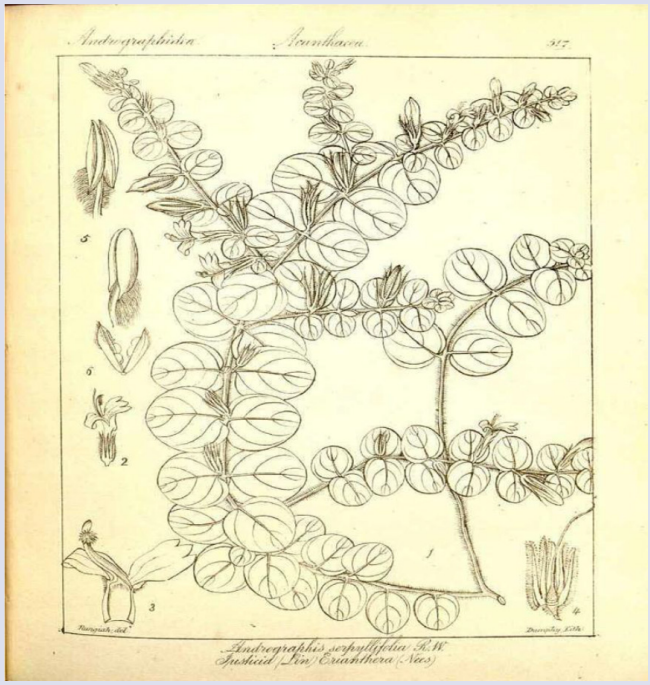


Figure 1: Herbarium records of *A.serpyllifolia* (KEW Botanical Gardens)

HOMOTYPIC SYNONYM ***ERIATHERA SERPYLLIFOLIA* (Rottl. ex Vahl) Nees** species

SYNONYM ***JUSTICIA NUMMULARIFOLIA* Wall.** species

HOMOTYPIC_SYNONYM ***JUSTICIA SERPYLLIFOLIA* Rottl.** species

SYNONYM ***JUSTICIA SERPYLLIFOLIA* Rottl. ex Vahl** species

Botanical Description and Identification

The widely accepted taxonomical description is as follows:

Kingdom: Plantae

Division: Tracheophyta

Sub division: Angiospermae

Class: Magnoliopsidae

Sub class: Gamopetalae

Order: Lamiales

Family: *Acanthaceae*

Genus: *Andrographis*

Species: serpyllifolia (Rottler ex Vahl) Wight

The key identification features of this plant listed by Gamble are orbicular or sub-reniform, sessile villous leaves presence of much bearded anthers, glabrous capsule pointed at both ends, deeply curved spoon shaped retinacula and deeply rugose small seeds. The micro-morphology of *A. serpyllifolia* shows presence of numerous diacytic stomata on both adaxial and abaxial leaf surfaces, restricted presence of abundant sessile glandular trichomes on the abaxial leaf surfaces, reticulate pollen ornamentation with echinate sulcus outlined with smooth morus and deeply reticulate, highly pitted and convoluted spermoderm or seed testa reminiscent of human brain.[1] These three features may serve as pharmacognostic markers aiding in accurate identification and quality control of this herb. Further correlation of the impact of morphological adaptation

of each organelle, its functional role in plant body and potential bioactive accumulation was discussed.

Floras

A. serpyllifolia has been described in many Floras of South India. Robert Wight has included this species as *A. serpyllifolia* in his book *Icones Plantarum Indiae Orientalis* published in 1850 and the same has been included in the Flora of British India Vol II, Page 506 and subsequently in Flora of Madras by Gamble in 1923, Flora of Coorg District, S N Yoganarasimhan, Flora of Tamil Nadu, VOL. II, 1987, Flora of British India Gamble, J.S. 1982. Flora of the Presidency of Madras, Vol. II. Botanical Survey of India, Calcutta. pp: 1045-1051.

Embryology and seed development

Investigations in this plant have been sporadic and spaced out over long periods of time. After its first identification and description in 1824, it was only mentioned in 1960 when the sequential stages of embryogenesis in *A. serpyllifolia* were described.[2] The embryo sac has a bifurcated chalazal part. During fertilization both synergids and antipodal cells disintegrate to form ruminate endosperm. *A. serpyllifolia* is the only Acanthoideae member to possess large multinucleate suspensor cells. The seeds have been described as albuminous, with a large embryo and the seed coat almost dissolved but with a thick walled persistent endosperm. The systematic study of the development of endosperm reveals three components: (1) a binucleate densely cytoplasmic chalazal haustorium; (2) a large binucleate micropylar haustorium; and (3) a central chamber which develops into the actual endosperm. Several authors reported ruminate morphology in some members of Acanthaceae, which develops due to uneven activity of endosperm or the seed coat and is seen as an adaptation for efficient aeration and germination of the seed.[3] In *A. serpyllifolia*, the convoluted ruminate condition of endosperm is due to the unequal destruction of the integument. The mature seed is nearly naked because the seed coat is almost completely digested. The embryo has a long suspensor. The micropylar cells of the suspensor are hypertrophied and multinucleate.

Ethnobotany

Scientists have gathered information on traditional and folklore usage following extensive interaction with tribal communities in Palani Hills, Tamil Nadu, Andhra Pradesh, Telangana and Karnataka. Variously called Kattuppooraankod, Siyan kodi (Tamil), Kaasina Sara or belesoppu in Kannada, leaf paste of *A. serpyllifolia* has been used in treatment of snake and scorpion bites.[4] Elsewhere, the whole plant of *A. serpyllifolia* was reported to be effective against snakebite[5] Decoction of the leaves is used to cure fever and cough. A native formulation comprising about 500 grams each of leaves and roots of *A. serpyllifolia* , 15 flakes of *Allium sativum* bulb and *Piper nigrum* (9 nos.) ground to a paste, rolled into boluses of egg size and orally administered thrice a day for a period of 9–21 days to combat mastitis in cattle.[6] Efficacy against bacterial infections is corroborated by the study by many researchers (Table 2) where broad spectral anti- microbial activity is attributed to different parts of *A. serpyllifolia.*

Antimicrobial and antioxidant activities were analyzed in the selected ethno-medicinal plants (EMP): *Andrographis serpyllifolia* Vahl., *Dioscorea hispida* Dennst., *Glycosmis mauritiana* Tanaka., *Nothapodytes nimmoniana* Blume and *Rauvolfia densiflora* (Wall.) Benth and Hook and included in the Tribal Medicine formulation (TMF).[7] While evaluating the antifungal activity, it was found that ethanol extracts of EMP drugs showed efficient antifungal activity against *Aspergillus flavus* viz., *A. serpyllifolia* (19.6±0.6), *D. hispida* (16.9±0.5), *G. mauritiana* (17±0.4) *N. nimmoniana* (16±0.3) and *R. densiflora* (15.5±0.4). These plant drugs and their formulations used by the tribal practitioners could justify further investigation on these ethno-medicinal plant drugs for the biological activity and isolation of active constituents using bio-assay guided fractionation.

Toxicity studies and Safety

While establishing the effect of ethanolic leaf extract of *A. serpyllifolia* on experimentally induced typhoid using *Salmonella typhi*, it was proved that the extract was quite safe for long term administration.[8] The acute oral toxicity study of ethanolic extract of *A. serpyllifolia* leaves was performed on 24 h fasted rats by single dose administration each of 2000 and 4000 mg/kg through oral route (Per.os). There was no mortality and rats showed no toxic signs such as anorexia, depression, lethargy, jaundice and dermatitis throughout the examination during the 14 days observation period. Ethanolic extract of *A. serpyllifolia* leaves was found to be safe up to 4000 mg/kg (P.O.). Since ethanol is considered "GRAS"(Generally Recognized As Safe by FDA), it was concluded that ethanolic leaf extract of *A. serpyllifolia* was safe for long term administration and did not induce toxic effects in experimental rats.

The ethanolic extracts of *A. serpyllifolia* were proved to be safe for prolonged use while establishing the anti-diabetic effect of *Andrographis lineata* and *A. serpyllifolia* leaf extracts *in vitro* and *in vivo* studies.[9] The 3-[4, 5-dimethylthiazol-2-yl]-2, 5-diphenyltetrazolium bromide (MTT) assay of the EtALL (Ethanolic extract of *A.lineata*) and EtASL (ethanolic extracts of *A. serpyllifolia*) extracts in 3T3-L1 cell line confirmed that there was no toxicity effect for both the extracts from 6.5 to 50 µg/ml concentrations. Further, normoglycemic male Wistar rats orally fed with EtASL extracts at increasing dosage level (100, 500, 1000, 2000 and 4000 mg/kg body weight) were observed continuously for 2 h under behavioral, neurological and autonomic profiles. After a period of 24 to 72 h of incubation they were observed for lethality or death. The test animals showed no change in behavior, erratic movements or any abnormality during the entire duration of the experiment lasting for 28 days. Hence it was deduced that *A. serpyllifolia* extracts are safe even for chronic administration.

Phytochemical screening of the 80% Ethanolic extract of stem, root, leaves and whole plant showed that the heavy metal sequestration in the different plant parts was well within permissible limits.[10] Heavy metal analysis by Atomic Spectrophotometer (AAS) revealed highest accumulation of 2.08 ppm Cadmium in the root (Table 1). But since this value is low compared to permissible limits of 2000 ppm, the ethanolic extracts of *A. serpyllifolia* were deduced to be safe from causing heavy metal toxicity and hence safe for human consumption as a drug.

Screening for Phytochemicals

Various workers have screened *A. serpyllifolia* for its phytochemical activity and the quantitative estimation results are summarized (Table 2). The earliest investigations into the plant's phytochemical profile were conducted in 1968 when scientists isolated the molecule Serpyllin from *A. serpyllifolia.11* Its structure has been established as 5-hydroxy-7, 8, 2′, 3′, 4′-pentamethoxyflavone by spectral and synthetic evidence. The synthesis of 5, 6, 7, 2′, 3′, 4′-hexamethoxyflavone is also reported by the same researchers. Phytochemical screening of whole plant extracts, using various polar and non-polar solvents, revealed presence of alkaloid, tannins, steroids, terpenoids, phlobatannin, anthraquinones, flavonoids, saponins and phenolic compounds. Quantitative analysis revealed the presence of saponins (4.2%) in high concentration followed by tannins (4.12%), phenolics (1.4%), alkaloids (1.2%) and flavonoids (0.98%)[12] (Table 4). Investigators working on hepatoprotective activity of *A. serpyllifolia* ethanolic leaf extract reported isolation of Quercetin (0.08196%w/w) and rutin (0.20461% w/w) by HPTLC.[13]

Table 1: Accumulation of heavy metals in different plant parts of *A. serpyllifolia* as analysed using Atomic Spectrophotometer (AAS_AA700).

PLANT SAMPLE	MERCURY (ppm)	LEAD (ppm)	CADMIUM (ppm)	ARSENIC (ppm)
LEAF	-VE	-VE	1.63	> 0.2
STEM	-VE	1.036	1.91	> 0.2
ROOT	-VE	1.036	2.08	> 0.2
WHOLE PLANT	-VE	1.036	1.41	> 0.2

Table 2: Quantitative Estimation of Bioactives in *A. serpyllifolia*.

Phytocompound	Concentration in Extract
Saponins	4.2%
Tannins	4.12%
Phenolics	1.4%
Alkaloids	1.2%
Flavonoids	0.98%
Quercetin	0.08196%
Rutin	0.20461%

An efficient mobile phase was developed for thin layer chromatography in a combination ($CHCl_3$: MeOH 95: 5) that separated compounds over a wide range of R_f values in the roots and five components in the aerial parts.[14] A new flavone 5-hydroxy-7, 8, 2'3'4-pentamethoxyflavone, named Serpyllin was isolated from the leaves of *A. serpyllifolia* in 1999.[15] Subsequently, the same authors isolated two new acylated flavone glucosides, skullcapflavones (2-O-B-D-30-E-cinnamoyl glucopyranoside and 12'-O-B-D-glucopyransode in addition to Andrographidine C from whole plant extracts.

A very detailed phytochemical investigation of root extract carried out using NMR spectroscopy yielded six pure crystalline compounds[16] (Table 3). Described as Compound AS-01 to AS- 06, these six compounds were determined to be either flavonoid or Andrographolide derivatives.

Pharmacological activity Screening

Various solvent and aqueous extracts of *A. serpyllifolia* have been screened for multiple applications and have proven to possess a wide range of curative and therapeutic activities. Some of the efficacies proven in animal models are

- Anti-Microbial Activity
- Anti-Oxidant Activity
- Anti-Diabetic Activity
- Anti-Lipidemic Activity
- Anti-Proliferative Activity
- Anti-Inflammatory Activity
- Hepatoprotective Activity
- Anthelmintic Activity

In an experiment conducted on Sprague-Dawley rats infected with *S. typhi* (MTCC 734) treatment with ethanolic extract of *A. serpyllifolia* leaves was administered in test dosages of 200 mg / kg and 400 mg/Kg of body weight.[7] Eight cases of animals in each group treated with ethanolic extract of *A. serpyllifolia* extract at dose level of 200 mg/kg showed 75.0% to 87.5% protection and 100% protection at higher dose of 400 mg/kg on widal blood culture and typhidot tests respectively. The ethanolic leaf extract was shown to possess antimicrobial activity against *S. typhi* and could be recommended for clinical applications in treatment of typhoid.

Investigation into the antibacterial activity of *A. serpyllifolia* leaf and stem extracts (acetone and aqueous) was carried out by, against four human pathogenic bacterial species viz., *Bacillus cereus, Staphylococcus aureus, Escherichia coli* and *Klebsiella pneumoniae* by agar well diffusion method.[17,18] The aqueous stem extract and acetone extract of leaf and stem showed significant activity against Gram positive bacteria such as *Bacillus cereus, Staphylococcus aureus* and moderate activity against Gram negative bacteria *like Escherichia coli, Klebsiella*. The bio-efficacy was found comparable to the activity exhibited by standard drug Ciprofloxacin (10 mg/g). The stem extract showed a higher inhibitory effect than the leaf extracts. The results of this study suggest that *A. serpyllifolia* leaf and stem extract possess significant antibacterial activity against some of the tested pathogens. The aqueous extract showed highest antibacterial activity against *Staphylococcus aureus* (17.50 ± 0.07 mm); followed by acetone extract (15.49 ± 0.21 mm). The highest inhibition zone observed for aqueous extract of *A. serpyllifolia* leaves against *Bacillus cereus* was 13.15 ± 0.23 mm followed by 11.46 ± 0.11 mm for Acetone extract. (Table 4).

These results confirmed the observation of previous studies by other scientist groups[9] The antibacterial activity reported in *A. serpyllifolia* in the present study may be due to the presence of glycosides, alkaloids, saponin, steroids, tannins and terpenes. Other investigators reported significant antimicrobial activity of *Andrographis serpyllifolia* extract from root, stem and leaf.

A comparative evaluation of the antimicrobial activity of the crude methanolic extracts of *Memecylon malabaricum* Clarke. (leaves), *Cochlospermum religiosum* Linn. (leaves and flowers) and *Andrographis serpyllifolia* Vahl. (leaves) using the standard disc diffusion assay against eight strains of both clinical and plant-associated bacterial species, viz., *Staphylococcus aureus, Salmonella typhi, Enterobacter aerogenes, Pseudomonas aeruginosa, Xanthomonas oryzae pv. oryzae, Xanthomonas axonopodis pv. malvacearum, Bacillus cereus* and *Micrococcus sp* was conducted.[19] The phytochemical screening of methanolic extract of leaves of *A. serpyllifolia* revealed the presence of sterols, cardiac glycosides, saponins, flavonoids, tannins and phenols. Amount of total phenolics varied slightly in plant materials and ranged from 19 to 49.5 mg/g of leaf extract. The highest amount of total phenolics was found in *A. serpyllifolia* (49.5 mg/g) and the lowest in *M. malabaricum* (19 mg/g). The extracts of the plant at a concentration of 1.25 mg/disc showed moderate activity against *Staphylococcus aureus, Salmonella typhi* and *Xanthomonas oryzae pv. oryzae* indicating a broad spectrum activity.

Anti-oxidant activity

Aqueous (ASAE) and methanol (ASME) extracts of *A. serpyllifolia* were reported to contain phenolic acids up to 3-5%, in addition to Andrographolide which is present at ~2% level.[20] Aqueous extract exhibited ~2 and 10 fold higher free radical scavenging and reducing power activities than those of methanol extract and the isolated Andrographolide, suggesting that *Andrographis* species may contain antioxidant components other than Andrographolide as well. Further, about 70-80% of DNA and red blood cells were protected against oxidant-induced damages at 4 mg/mL and there was about 80% inhibition of proliferation of highly metastatic MDA-MB-231 cells at 10 mg/mL, which suggests the anticancer potential of *A. serpyllifolia*. Identification of phenolic acids contributing to antioxidant potency revealed that Gentisic (48%) followed by Gallic (25%), Protocatechuic (14%) and Cinnamic (11%) acids in ASAE, while Protocatechuic (59%), followed by Ferulic (30%) and p-Coumaric (8%) acids in ASME contributed to the activity. Thus, phenolics and androgra-

Table 3: Structure elucidation of Compounds isolated from *A. serpyllifolia* root.

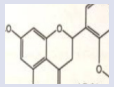
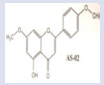
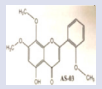
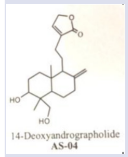
Compound	Description	Molecular Formula	Melting Point		Molecular weight	Test parameters	Result	Inference	Conclusion	Remarks
Compound AS-01 	Pale yellow needles	$C_{17}H_{16}O_5$	163°C		300.3059	Fecl3 Test	Positive	Phenols	5-hydroxy,7, 2'dimethoxy flavanone	
				UV Spectrum	262 - 320 nm	Flavone moiety				
				IR Spectrum	3342 cm-1 and 1672 cm-1	Phenolic hydroxyl and flavanone carbonyl				
Compound AS-02 	Yellowish Crystals	$C_{17}H_{14}O_5$	178°C		298.2901	UV Spectrum	265 - 320 nm	Flavone moiety	5-hydroxy,7, 4-dimethoxy flavone	
				IR Spectrum	3300 cm-1 and 1650 cm-1	Phenolic hydroxyl and flavanone carbonyl				
				NMR	3.946 and 3.963	Two Phenolic methoxyls				
Compound AS-03 	Yellow needles	$C_{18}H_{16}O_6$	178°C		328.316	UV Spectrum	265 - 320 nm	Flavone moiety	5-hydroxy,7,8, 2-trimethoxy flavone	First proof of occurrence in Andrographis genus
				IR Spectrum	3300 cm-1 and 1650 cm-1	Phenolic hydroxyl and flavanone carbonyl				
				NMR	3.914 , 3.964 and 3.951	Three Phenolic methoxyls				
Compound AS-04 	Very bitter Amorphous Powder	$C_{20}H_{29}O_4$	176 - 178°C		333.44	UV Spectrum	203 - 221 nm	Unsaturated Lactone Ring system	14-deoxyandrographolide	An analogue of Andrographolide (Aerial parts of A. paniculata)
				IR Spectrum	3333 cm-1 , 1643 and 1744 cm-1	Hydroxyl unsaturated Lactone Carbonyl				
				NMR	3.914, 3.964 and 3.951	Ent-labdane skeleton				

Table 3: **Structure elucidation of Compounds isolated from *A. serpyllifolia* root..**

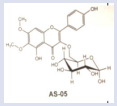
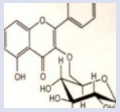
Compound	Description	Molecular Formula	Melting Point	Molecular weight	Test parameters	Result	Inference	Conclusion	Remarks
Compound AS-05 (Ethanolic Extract) 	Yellow amorphous powder	$C_{22}H_{24}O_{12}$	182°C	480.4188	IR Spectrum	3400 cm-1 1600 cm- 11060 cm- 11120 cm-1	Hydroxyl CarbonylSugar moiety	5, 4'-dihydroxy-6.7-dimethoxy-flavone-3-0-glucoside	Trivial name: Eupalitin-3-0-B-D-glucoside, First proof of occurrence in Andrographis genus
		$C_{23}H_{24}O_{12}$	178-180°C		Shinoda Test	Positive			
					$Fecl_3$				
Compound AS-06 (Methanolic Extract) 	Yellow needles			492.429 Positive Positive			Flavonoid glycoside	Kaempferol1-3-OB-glucopyranoside	First proof of occurrence in Andrographis genus
			Molisch's Test						

Table 4: Evaluation of anti-bacterial activity of *A. serpyllifolia* leaf extracts.

Pathogen	Aqueous Leaf Extract	Acetone leaf extract
B. cereus	13.15 ± 0.23	11.46 ± 0.11
S. aureus	17.50 ± 0.05	10.50 ±0.19
E. coli	8.78± 0.16	9.29 ± 0.28
K. pneumoniae	8.14 ± 0.14	6.08 ± 0.10

Table 5: Composition of Polysaccharides isolated from *A.serpyllifolia* leaves (mg/g).

Rhamnose	08
Arabinose	23
Xylose	03
Mannose	10
Galactose	26
Glucose	30
Uronic acid	110

pholide in *A. serpyllifolia* may be implicated in anticancer properties as observed in traditional therapies.[21]

Anti-oxidant activity of ethanolic leaf extract of *A. serpyllifolia* was proved by analyzing biochemical markers such as Lipid peroxidation (LPO), Superoxide dismutase (SOD), Catalase (CAT) and Reduced Glutathione (GSH) in Carbon tetrachloride induced hepatotoxicity in Wistar Rats.[22] Treatment with standardized extract at 150 mg, 250 mg and 500 mg/kg significantly reduced lipid peroxidation from 0.62±0.07 to 0.40±0.09, SOD from 204.2±13.0 to 101.2 ±0.08, increased catalases from 30.2±1.2 to 35.4±1.3 and GSH from 40.5± 2.8 to 59.6±3.7.

Anti-diabetic Activity

Investigators concluded that ethanolic whole plant extract of *A. serpyllifolia* showed lower serum glucose level in normal rats.[23] Hydro-ethanolic extract of whole plant was concentrated under reduced pressure in a rotary evaporator and completely dried to constant weight. The dried extract was suspended in 2% gum acacia to prepare the test solution. A fortnight –long acute toxicity study, carried out on mice as per the OECD guideline-423 (Organization for Economic Co-operation and Development) established that this drug did not cause mortality, autonomic or behavioral responses such as tremors, convulsions, diarrhea, lethargy, drowsiness or coma and hence is safe for use.

Assessing the Oral Glucose Tolerance Test (OGTT) conducted on fasting rats, maximum reduction in serum glucose level was observed after 4 hours at dosage levels of 100, 200 mg/kg body weight of the extract. In normal rats the serum glucose level reduction at 4 hours was 20.85% by 100 mg/kg body weight and 35.56% by 200 mg/kg body weight. In alloxan induced diabetic rats, continuous administration of the extract significantly reduced the serum glucose levels from fifth day to till the end of experiment. The extract was also found to reduce the elevated serum biomarker enzymes as well as improve parameters like lipid profile and body weight and thus may be valuable in diabetes treatment. These results indicate that *A. serpyllifolia* extracts are able to ameliorate biochemical damages induced by alloxan in diabetic rats.

Scientists demonstrated similar results using streptozotocin induced Diabetes in rats while comparing anti-diabetic activity of *Andrographis lineata* and *A. serpyllifolia*.[24] The treatment with EtALL and EtASL extract (400 mg/kg b.w.) on fasting blood sugar and oral glucose tolerance test in treated normoglycemic rats showed hypoglycemic effect. When the streptozotocin induced diabetic rats were administered with EtALL and EtASL 400 mg/kg b.w. in chronic model (28 days) there was a significant reduction in plasma glucose, plasma insulin level, total cholesterol, low density lipoprotein (LDL)-C triglyceride, glucose-6- phosphatase and fructose -1, 6- bisphosphatase levels. Glycogen content (liver and muscle), high density lipoprotein (HDL) cholesterol, hexokinase, was significantly increased compared with the diabetic control rats in both the extracts treated rats. The above findings reiterated the significant anti-diabetic potential of the extracts in ameliorating induced-diabetic condition in treated rats.

Anti-proliferative activity

In a comparative study conducted to prove inhibition of galectin-3 mediated cellular interactions by pectic polysaccharides, four plants used as dietary sources *Decalepis hamiltonii* (swallow root -SRPP), *Hemidesmus indicus* (HPP), *Nigella sativa* (black cumin-BCPP) *Andrographis serpyllifolia* (APP), *Zingiber officinale*-(ginger-GRPP) and citrus pectin (CPP) were examined.[25] Inhibition of (a) galectin-3 of MDA-MB-231 cells induced hemagglutination of red blood cells (b) galectin-3 mediated interaction between normal /metastatic human buccal cells (NBC)/ (MBC) and; (c) invasion of MDA-MB-231 and MBC in the invasive chamber were assessed. Results indicated that SRPP inhibited hemagglutination at Minimum Inhibitory Concentration (MIC) of 1.86 μg ml−1 equivalent of carbohydrate as opposed to those of BCPP (130 μg ml−1), APP (40 μg ml−1), HPP (40 μg ml−1) and CPP (25 μg ml−1). About 4 % Pectic polysaccharides were isolated from *A. serpyllifolia* leaves (Table 5) Agglutination inhibitory activity against MDA-MB-231-galectin-3 induced hemagglutination of rabbit Erythrocytes was observed at 40μg / ml concentration of the APP. These galectin inhibitors are believed to be safer since they exert their effects by binding to galectin-3 found only in cancer cells and not in normal cells. In the advanced stages of the disease, metastasis, which is essentially the ability to spread to other tissues and organs, makes cancer potentially fatal. It was concluded that a safe compound that could particularly block galectin-3 that induces metastasis i.e., galectin inhibitors may be found in *A. serpyllifolia*.

Anti- inflammatory Activity

Anti- inflammatory and analgesic properties of *A. serpyllifolia* were proved in clinical studies involving Wistar rats and Albino mice.[26] *A. serpyllifolia* methanolic root extract shows moderate potency in the inhibition of 5-LOX (5-Lipoxygenase) which is a key enzyme in leukotriene biosynthesis.[27] Leukotrienes (LTs) constitute a group of bioactive lipids that are generated by the 5-LO pathway. 5-LO expression is typically restricted to certain types of leukocytes, such as granulocytes (neutrophils, eosinophils and basophils) and monocytes/macrophages, which constitute the major source of LTs due to high 5-LO expression and enzymatic activity. 5-LO expression can also be detected in dendritic cells, mast cells and B-lymphocytes. LTs primarily mediate inflammatory and allergic reactions by enhancing chemotaxis of migrating neutrophils and triggering vascular permeability and edema formation in inflamed tissues. Methanolic root extract of *A. serpyllifolia* exhibited higher anti-inflammatory activity than chloroform extract in *in vitro* studies involving carrageenan induced Rat paw edema and TPA (12-0-tetradecanoylphorbol-13-acetate) induced Ear Edema. Higher analgesic activity was attributed to methanolic root extract than chloroform extract in *in vivo* studies. Potent analgesic activity was recorded at 100 and 200 mg / kg in acetic acid induced writhing test. However similar results were not

Appendix (Compiled by Authors)

S/N	Pharmacological activity		Plant part used (A. serpyllifolia Extract)	Test	Observation	Reference
1	Anti-Microbial Activity	a.	Ethanolic extract of leaves	Salmonella typhimurium	Effective in treatment of typhoid.	Gupta *et al.*
		b.	Leaf acetone Extract	Escherichia coli and Klebsiella pneumoniae	Moderate activity against Gram negative bacteria	C. Alagesaboopathi (2012)
			Stem Acetone extracts	Escherichia coli and Klebsiella pneumoniae	Moderate activity against Gram negative bacteria	
			Leaf aqueous Extract	Bacillus cereus, Staphylococcus aureus	Significant activity againt Gram positive bacteria	
			Stem Aqueous extracts	Bacillus cereus, Staphylococcus aureus	Significant activity againt Gram positive bacteria	
		c	Extract from root, stem and leaf.	Unspecified bacteria	Significant antimicrobial activity	Revathi et al. Coopoosamy and Naidu
		d	Ethanolic extract of leaves	Escherichia coli, Staphylococcus aureus and Bacillus subtilis	Significant antimicrobial activity	G Panduranga Murthy et.al (2015)
		e	Ethanolic extract of leaves	Aspergillus flavus, Aspergillus niger, fusarium oxysporum, Rhizopus stolonifer	Significant antifungal activity	
		a	Aqueous (ASAE) and extracts	Phenolic acids + Andrographolides	Better free radical scavenging and reducing power activities compared to Methanolic extract and isolated Andrographolide	Satisha U V et al.
			Phenolic Acid Profile of Aqueous Extract of A.S	Gentisic Acid	48%	
				Gallic Acid	25%	
				Protocatechuic Acid	14%	
				Cinnamic Acid	11%	
			Methanol (ASME)	Phenolic acids + Andrographolides	Moderate free radical scavenging and reducing power activities compared to Aqueous extract	
2	Anti-Oxidant Activity		Phenolic Acid Profile of Methanolic Extract of A.S	Protocatechuic Acid	59%	
				Ferulic Acid	30%	
				p-Coumaric Acid	8%	
		b	70% Ethanolic Root Extract	DPPH (1,1-diphenyl-2picryl-hydrazyl) Free radical scavenging test	14.59% inhibition at dose of 100 µg/ml which was less than Gallic Acid standard of 0.5 µg/ml which showed 16.18 % inhibition	K Ravishankar, KVRNS Ramesh and Ganga Rao (2008)
					Significant anti-oxidant activity comparable to silymarin	
		c	70 % Ethanolic Leaf Extract	Carbon Tetra Chloride induced Hepatotoxicity in Wistar rats	Reduced lipid peroxidation from 0.62+0.07 to 0.40+0.09, SOD from 204.2+13.0 to 101.2 +0.08, increased catalases from 30.2+1.2 to 35.4+1.3 and GSH from 40.5+ 2.8 to 59.6+3.7.	Ch.V.Rao, Shyam Sundar Gupta and Joni Sharma,(2014)

Appendix (Compiled by Authors)

S/N	Pharmacological activity		Plant part used (A. serpyllifolia Extract)	Test	Observation	Reference
3	Anti-Diabetic activity	a	Hydro-ethanolic extract	Oral Glucose Tolerance Test (OGTT) conducted on normal fasting rats and Alloxan induced diabetic rats	Reduced elevated serum biomarker enzymes as well as improved lipid profile and body weight	N. Sanjeevaiah and A. Jithan (2013)
		b	Ethanolic leaf extract	Streptozotocin induced Diabetes in rats.	Strong inhibitory activity for α-glucosidase which was comparable with Acarbose.	Sudarshana Deepa et. al., (2013)
4	Anti-proliferative activity		Leaf Extract	Inhibition of (a) galectin-3 of MDA-MB-231 cells induced hemagglutination of red blood cells (b) galectin-3 mediated interaction between normal / metastatic human buccal cells (NBC)/(MBC) and; (c) invasion of MDA-MB-231 and MBC in Rabbit erythrocytes	Inhibition of galectin-3 mediated cellular interactions by pectic polysaccharides	Sathisha U V et. al. (2007)
5	Hypolipidemic activity		Aqueous root extract	Atherogenic diet induced hyperlipidemic model in Male albino rats (Wistar strain)	Inhibition of cholesterol biosynthesis and presence of andrographolides, terpenoids, flavonoids and lignans, slightly increased the HDL- cholesterol level	Bharath Chelluboina and K Manga (2009)
6	Anti-Inflammatory Activity	a.	Ethanolic Root Extract	Carageenan induced Rat Paw oedema	38.95% inhibition @ 200mg /Kg comparable to Diclofenac sodium Standard dose @ 25 mg/Kg	K Ravi Shankar and Ganga Rao B (2008)
				Histamine induced Rat Paw oedema	38.76% inhibition @ 200 mg/Kg comparable to Diclofenac sodium Standard dose @ 25 mg/Kg	
		b.	Methanolic Root Extract	Inhibition of 5 LOX	Higher anti-inflammatory activity in vitro	Kandati V, Govardhan P, Reddy ChS, Nath AR, Reddy RR (2012)
					Higher analgesic activity in vivo	
7	Hepatoprotective Activity		70 % Ethanolic Leaf Extract	Carbon Tetra Chloride induced Hepatotoxicity in Wistar rats	Significant hepatoprotective activity due to presence of flavonoids like Quercetin and Rutin	Ch.V.Rao, Shyam Sundar Gupta and Joni Sharma.
				a. Reversal of altered enzyme profiles	Significant restoration of altered enzyme activity at dose levels of 150 mg/kg (19.84-47.4%), 250 mg/kg (27.84-55.86%) and 500 mg/kg (52.20-74.65%)	
				b. Reduced lipid peroxidation	Anti- hepatotoxic activity comparable to Silymarin	
8	Anthelmintic Activity	a	Aqueous root extract	Earthworms (Pheretima posthuma) comparable to round worms parasitizing human intestines	At Test dose of 20 mg / ml, casued paralysis within 28 mins followed by mortality in 74 mins	K Ravishankar et.al. (2007)
		b	Ethanolic root extract		At Test dose of 20 mg / ml, casued paralysis within 12.5 mins followed by mortality in 28 min comparable to Albendazole and Piperazine citrate	

observed in albino mice subjected to pain stimulus at 55°±0.5°C by hot plate method. This observation implies that the activity of plant extract is expressed through peripheral mechanisms rather than central mechanisms. Peripherally-induced neuropathic pain is initiated by damage to the peripheral nervous system (PNS) while persistence of pain appears to rely on maladaptive processes within the central nervous system (CNS).[28] Correlating both *in vitro* and *in-vivo* data, it was concluded that *A. serpyllifolia* methanolic root extract possibly consists of more anti-inflammatory and analgesic active principles than chloroform extract.

While reviewing herbal plants that are traditionally used for their anti-inflammatory activity, it was observed that chloroform and methanolic root extracts of *A. serpyllifolia* showed moderate inhibitory activity on 5-LOX but showed significant anti-inflammatory efficacy.[29] This implied that the efficacy of plant extract may possibly be mediated through processes other than just inhibition of 5-LOX.

Hypo-lipidemic Activity

Hypolipidemic activity screening was carried out in Male albino rats (Wistar strain).[30] Aqueous root extract exhibited moderate efficacy in lowering the elevated serum cholesterol. It was concluded that the lipid lowering effect of *A. serpyllifolia* aqueous root extract in rats may be due to inhibition of cholesterol biosynthesis and presence of andrographolides, terpenoids, flavonoids and lignans. The drug showed protective action as it slightly increased the HDL- cholesterol level in atherogenic diet induced hyperlipidemic model.

Hepatoprotective Activity

Investigating the effect of standardized leaf extract of *A. serpyllifolia* on carbon tetrachloride-induced hepato-toxicity in Wistar rats, scientists analyzed different biochemical parameters used to quantify hepatotoxicity.[31] The standard biochemical parameters assessed for hepatotoxicity include tests for Serum enzymes, Aspartate transaminase (AST), Alanine transaminase (ALT), Serum alkaline phosphatase (ALP) and total serum bilirubin (TBIL). Antioxidant parameters like Lipid peroxidation (LPO), Superoxidase dismutase (SOD), Catalase (CAT) and Reduced glutathione (GSH) were determined. High hepatic serum enzymes are indicative of cellular leakage resulting from severe damage of liver cells. When liver cell plasma membrane is damaged, various enzymes contained within the cytosol are released into the blood stream. Estimation of activity of serum marker enzymes like ALT, AST, ALP aids in assessment of efficiency of Liver Function. Leaf extract was prepared using 70% ethanol, concentrated under reduced pressure at 40oC in a rotavapor and lyophilized to get 20 % of solid residue or extract. Quantitative phytochemical screening of this crude ethanolic extract indicated presence of flavonoids Quercetin (0.08196% w/w) and Rutin (0.20461% w/w). Test dosages of this crude extract were fixed at 150 mg, 250 mg and 500 mg/kg body weight of the test animal. Based on the results of the tests listed above, it was concluded that altered biochemical profiles caused by exposure to Carbon tetra chloride could be reversed to normalcy using *A. serpyllifolia* leaf extract at optimal dose of 250mg/kg. This dual protective property of damage reversal followed by protection from further damage was attributed to the presence of flavonoids Quercetin and Rutin in *A. serpyllifolia* leaves.

Anthelminthic Activity

Scientists evaluated the ethanolic and aqueous root extract of *A. serpyllifolia* and demonstrated in earthworms (*Pheretima posthuma*) that at concentration of 20 mg/ml, aqueous extracts caused paralysis followed by mortality within 28 mins and 74 mins respectively.[32] Ethanolic extract at the same concentration of 20 mg/ml was comparatively more potent inducing paralysis within 12.5 mins and mortality within 28 mins. Earthworms were chosen as test organisms owing to their close anatomical and physiological resemblance to round worms that parasitize human intestines. The anthelmintic activity displayed by root extracts was comparable to the pharmacological activity of standardized drugs Albendazole and Piperazine Citrate. It was concluded that *A. serpyllifolia* root extract possesses good anthelmintic activity.

DISCUSSION

Investigators working on *A. serpyllifolia* have largely focused on the phytochemistry and pharmacology. Studies on the Pharmacognostic, Botanical, Geoecological aspects which may directly influence the phytochemical profile of the plant have been inadequate.

A few scientists working on the ethno pharmacology of *A. serpyllifolia* report that leaf and whole plant extracts have been used as an antidote for snake bite and scorpion bite in ethnomedicine. This may imply presence of bio actives with definite activity on the Central Nervous System or Peripheral Nervous system or Neurotransmission channels. It may be worthwhile to investigate the class of botanical compounds that could prove to be a potential candidate to arrest neurodegeneration or synaptic lapses. The phytochemical screening of leaf and root extracts of *A. serpyllifolia* show significant proportions of Saponins and Tannins in leaves and root extracts. While the primary role of saponin and tannins may be to protect the plant from herbivory and pests, their pharmacological potential is immense. The anti-oxidant activity, oxidative stress induced diabetes demonstrated by various researchers may be attributed to saponins. A group of reviewers, while reviewing the therapeutic attributes of ginseng saponins called ginsenosides discussed the pharmacological effects of the saponins, including the effects on the cardiovascular system, immune system and central nervous system as well as the anti-diabetes and anti-cancer effects.[33] It was reported in a review article that more than 100 ginsenosides have been isolated from roots, leaves, stems, flower buds and berries of Asian ginseng and American ginseng and these ginsenosides exhibit considerable structural variation.[34] A similar effort to separate fractions of *A. serpyllifolia* saponins may prove valuable in terms of drug discovery.

The anti-microbial activity of this plant's extracts may be due to the presence of relatively high content of Tannins or water-soluble polyphenols which have been proven to inhibit growth of many fungi, yeasts, bacteria and viruses. Ethnopharmacology reports mention that *A. serpyllifolia* leaf extract is highly effective in curing Bovine mastitis. Scientists treated three strains of pathogenic bacteria with condensed tannins (CT) purified from eight different woody plant species to investigate their inhibition effect on the growth of these bacteria *in vitro*. *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* were tested against low (0, 2, 4 and 8 mg CT/ml) and high dose levels (0, 50 and 100 mg CT /ml) of CT extracted from different plant species. *S. aureus* and *E. coli* exhibited dose dependent and susceptibility ($P < 0.01$) when exposed to 4 mg/ml of the following tannin monomers which exhibited differential inhibitory activity: Catechin > Ellagetannin > Tannic Acid > Epi-Catechin > Gallotannin.[35] In the presence of high dose levels at 0, 50 and 100 mg tannin extract/ml, inhibition zones of growth were varied among plant species. The findings indicated that source and concentration are important factors that influence antimicrobial activity of tannins. Estimates of the polyphenol profile of *A. serpyllifolia,* demonstrated presence of almost 48 % of Gentisic acid which is a crystalline dihydroxybenzoic acid with a broad spectrum of biological activity, such as anti-inflammatory, anti-rheumatic and antioxidant properties but the activities of individual tannin monomers need to be evaluated.[20] It was shown that ethanolic extract of *A. serpyllifolia* exhibited highest anti-fungal activity among the tested ethno-medicinal plants against *Aspergillus flavus* which is an opportunistic human and animal pathogen, causing aspergillosis

in immune-compromised individuals and highest activity against *Eschericia coli.*[34] The polysaccharide profile of *A. serpyllifolia leaves* includes significantly high amount of Uronic acid at 110mg/g. Carbohydrate metabolism involves major pathways like Glycolysis and Kreb's cycle and minor pathways like Hexose monophosphate pathway (HMP) for production of pentoses and NADPH and Uronic acid pathway for oxidation of glucose. While the two major pathways are important for energy generation and occur in cytosol of all cells, HMP and Uronic acid pathways occur in the cytosol of Liver. Uronic acids are a class of sugar acids in which the terminal hydroxyl group of an aldose or ketose is oxidized. The main function of Uronic acid pathway is formation of UDP-glucuronate via Glycosaminoglycans (GAGs) synthesis and provides a pool of toxins for several conjugation reactions with bilirubin and steroids making them more easily soluble and hence easily excreted. The human body uses the process of glucuronidation (linkage process where uronic acids form glycosidic bonds with thiol, amine and hydroxy groups or esterification with the carboxyl and hydroxyl groups) to make alcohols, phenols, carboxylic acids, mercaptans, primary and secondary aliphatic amines and carbamates more water-soluble and in this way, allows for their subsequent elimination from the body through urine or faeces (via bile from the liver) at a significantly increased rate. Thus Uronic acid may aid in easy detoxification. Further, Glucuronic acid or uronic acid derived from glucose, is a common building block of proteoglycans and glycoglycerolipids such as Heparin, an anti-coagulant. Accumulation of Uronic acid in the leaves of *A. serpyllifolia* indicates its potential as a hepatoprotective drug.

Higher therapeutic value of *A. serpyllifolia* is attributed to aqueous extracts of various plant parts by most researchers. Methanol and 70% Ethanol have also been used by a few workers to demonstrate anti-inflammatory, hepatoprotective and anti lipidemic activities. Most of the pharmacological screening is conducted using the wholesome crude extract and specific fractions and their related activity is not clear. Pure fractions may be valuable source of therapeutic or curative moieties that may contribute significantly to drug discovery.

Although there are ample Ethnopharmacological references in public domain, there seems to be no classical Ayurvedic plant reference for *Andrographis serpyllifolia.* This lacuna may be due to its limited geographic spread or if indeed there is mention, it may be described by some other name. It may be part of Siddha preparations which are ill-documented and are often verbally transmitted through generations, rather than in well documented Ayurvedic formulations.

CONCLUSION

A. serpyllifolia is a slow growing plant with unique morphology and is endemic to South India. It is evident that the various signature compounds produced in the roots and aerial parts of the plant have wide therapeutic applications. While its present occurrence may not be as common as observed by workers more than a century ago, it is quite sparse in distribution currently and is not yet listed under the Rare, Endangered and Threatened species. It is important that this slow growing plant, trying to survive under constant risk of acute water scarcity, grazing, forest fires, habitat disruption and destruction is at least brought under "vulnerable" tag. The compounds characterized by various workers may serve well either as pure drugs or as part of synergistic polyherbal formulations. Developing pharmacognostic markers will go a long way in accurate identification and prevent adulteration of this drug. A keen understanding of the growth parameters is necessary to develop practical cultivation practices that lead to production of abundant herbage. Plant Biotechnology has much to offer via its tissue culture techniques. Efficient Micropropagation systems can provide adequate and perennial source of planting material facilitating large scale cultivation. Establishing specific organ cultures that could serve as bio-factories synthesizing valuable identified and de novo synthesised therapeutic bioactives would be beneficial and plausible alternative to inevitable destructive harvesting of this geophyte with a good chunk of its therapeutic properties stored in the roots.

ACKNOWLEDGEMENT

We are grateful to Cambium Biotechnologies, Bangalore, India, for providing facility and financial support for the conduct of this research.

CONFLICT OF INTEREST

The authors declare that there is no conflict ot interest

ABBREVIATIONS

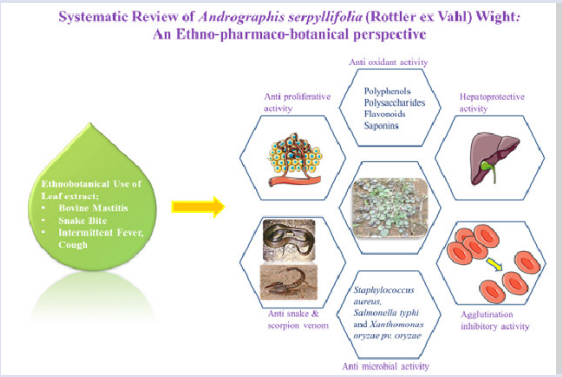
G-DC: Geneva Herbarium – De Candolle's Prodromus; **FRLHT:** Foundation for Revitalisation of Local Health Traditions; **IISc:** Indian Institute of Science; **EMP:** Ethno-Medicinal Plants; **TMF:** Tribal Medicine formulation; **GRAS:** Generally Recognized As Safe by FDA; **Per os:** "by opening" or "by way of the opening; **P.O:** Per opening (oral drug delivery route); **MTT:** 3-[4, 5-dimethylthiazol-2-yl]-2, 5-diphenyltetrazolium bromide; **EtALL:** Ethanolic extract of A.lineata; **EtASL:** Ethanolic extracts of A.serpyllifolia; **AAS:** Atomic Spectrophotometer; **Ppm:** Parts per million; **HPTLC:** High performance thin layer chromatography; **NMR spectroscopy:** Nuclear Magnetic resonance spectroscopy; **MTCC:** Microbial Type Culture Collection and Gene Bank; **ASAE:** Aqueous extracts of A.serpyllifolia; **ASME:** Methanol extracts of A.serpyllifolia; **SRPP:** Decalepis hamiltonii swallow root Pectic Polysaccharides; **HPP:** Hemidesmus indicus Pectic Polysaccharides; **BCPP:** Nigella sativa (black cumin) Pectic Polysaccharides; **APP:** Andrographis serpyllifolia Pectic Polysaccharides; **GRPP Zingiber officinale:** (ginger) Pectic Polysaccharides; CPP: citrus pectin Pectic Polysaccharides; **LPO:** Lipid peroxidation; **SOD:** Superoxide dismutase; **CAT:** Catalase; **GSH:** Reduced Glutathione; **OECD:** Organization for Economic Co-operation and Development; **OGTT:** Oral Glucose Tolerance Test; **LDL:** Low density lipoprotein; **HDL:** High density lipoprotein; **MIC:** Minimum Inhibitory Concentration; **5-LOX, 5-LO:** 5-Lipoxygenase; **LTs:** Leukotrienes; **TPA:** 12-0-tetradecanoylphorbol-13-acetate; **PNS:** Peripheral nervous system ; **CNS:** Central Nervous System; **AST:** Aspartate transaminase; **ALT:** Alanine transaminase; **ALP:** Serum alkaline phosphatase; **CT:** Condensed tannins; **HMP:** Hexose monophosphate pathway; **NADPH:** Nicotinamide Adenoside Dinucleotide Phosphate; **GAGs:** Glycosaminoglycans.

REFERENCES

1. Krishnaswamy S, Kushalappa AB. Correlative Evaluation of the Impact of Adaptive Plant Morphology on Bioactive Accumulation Based on Micro-Morphological Studies in *Andrographis serpyllifolia* (Rottler ex Vahl) Wight. Not Sci Biol. 2017;9(2):263-73
2. Mohan RHY. The Development of the Seed in *Andrographis serpyllifolia.* American Journal of Botany. 1960;47(3):215-9. www.jstor.org/stable/2439252.
3. Nitin ML, Dongarwar NM. A Ruminate Embryo In Blepharis Repens (Vahl.) Roth (Acanthaceae). J Plant Develop. 2014;21:55-61.
4. Alageshaboopathi C. International Journal of Biosciences. 2013;3(2):42-53. IJB | ISSN: 2220-6655 (Print) 2222-5234 (Online)http://www.innspub.net.
5. Sekhar J, Penchala PG, Sudarsanam G, Prasad GP. Ethnic information on treatments for snake bites in Kadapa district of Andhra Pradesh. Life Sci Leaflets. 2006;67:25-6.
6. Balakrishnan NMN, Unnikrishnan PM. Revitalizing Ethnoveterinary Medical Traditions a Perspective from India Chapter 5 Page 107 62650683-Ethnoveterinary-Botanical-Medicine-Herbal-Medicines-for-Animal-Health.pdf
7. Panduranga MG, Chandrasekhar KB, Leelaja BC, Lokesh S. Antimicrobial and

Antioxidant Activities of Tribal Medicine formulation (TMF) accomplished for Wound related remedies in Biligirirangana Hill area of Chamarajanagara district, Karnataka (India). IJPC. 2015;5(8):260-76.
8. Gupta SS, Sharma J, Kumar GR, Pandey G, Mohapatra PK, Rawat AS, *et al.* Effect of *A. serpyllifolia* leaves extract on experimentally induced Typhoid Using *Salmonella typhi.* British J of Pharm Res. 2014;3(2):230-9.
9. Shyam SG. Effect of *Andrographis serpyllifolia* Leaves Extract on Experimentally Induced Typhoid Using *Salmonella Typhi.* British Journal of Pharmaceutical Research. 2014;4(2):16-31. ISSN: 2231-2919.
10. Revathi SL, Kumar S, Sudarshana DV, Kumar S. Antimicrobial Activity of *A. serpyllifolia* (Rohl.Ex.Vahl) Wright. Interna J of Pharma Sci and Health Care. 2014;1(2):2249-5738.
11. Govindachari TR, Parthasarathy PC, Pai BR, Kalyanaraman PS. Chemical investigation of *Andrographis serpyllifolia*, isolation and structure of serpyllin, a new flavone. Tetrahedron. 1968;24(24):7027-31.
12. Narasimhamurthy K. Phytochemical screening and *In vitro* assessment of antimicrobial and antioxidant potential of *Andrographis serpyllifolia* - An endemic medicinal plant from South India. International Journal of Advanced Research. 2014;2(2):917-28.
13. Rao CV, Lubna A, Shyam SG. Phytochemical And Pharmacological Review on *Andrographis serpyllifolia*: Potential Herbal Cure-All Mintage. Journal of Pharmaceutical and Medical Sciences. 2014;3(Suppl 3).
14. Kumar H, Hullatti KK, Sharanappa P, Sharma P. Comparative antimicrobial activity and TLC-bioautographic analysis of root and aerial parts of *Andrographis serpyllifolia.* Intern J Pharmacy and Pharm Sci. 2010;2(1):52-4.
15. Damu AG, Jayaprakasam B, Gunasekar D, Blond A, Bodo B. Two acylated flavone glucosides from *Andrographis serpyllifolia.* Phytochem. 1999;52(1):147-51.
16. Ravishankar K, Ganga RB. Pharmacological Activities of *Andrographis serpyllifolia.* LAP Lambert Academic Publishing. 2012.
17. Alageshaboopathi C. Ethnobotanical Studies on useful Plants of Kanjamalai Hills of Salem district of Tamil Nadu, Southern India. Archives of Applied Science Research. 2011;3(5):532-9.
18. Alagesaboopathi C. Screening of antibacterial potential of leaves and stem extracts of *Andrographis serpyllifolia* (Vahl) Wight – An endemic medicinal plant of India. Journal of Pharmacy Research. 2012;5(12):5404-7.
19. Ravishankar RJBA, Pradeepa VS. Evaluation of the antimicrobial activity of three medicinal plants of South India. Malaysian Journal of Microbiology. 2011;7(1):14-8. http://dx.doi.org/10.21161/mjm.2290914
20. Satisha UV, *et al.* Inhibition of galectin-3 mediated cellular interactions by pectic polysaccharides from dietary sources. Glycoconj J. 2007;24(8):497-507.
21. Venkateshaiah SU, Jayaram S, Dharmesh SM. Antiproliferative, Antioxidant and Cyto/DNA Protective Properties in *Andrographis serpyllifolia*: Role of Andrographolide and Phenolic Acids. J Complement Integr Med. 2009;6(1):1553-3840.
22. Sanjeevaiah N. Pharmacological Screening of *A.serpyllifolia* for Antidiabetic Activity. 2013. www.ijapbc.com/files/25-2328.pdf
23. Sanjeevaiah N, Jithan A. Pharmacological screening of *A. serpyllifolia* For Antidiabetic Activity. Intern J of Advances in Pharma. 2013;2(3):2277-4688.
24. Deepa VS, Kumar PS, Vadivukkarasi B, Tilton F. Molecular Docking Studies On Selected Phytocompounds From Different *Andrographis Sp* Against Ppar-Γ And C/Ebp-A Receptors For Type-2-Diabetes. Asian J of Pharma and Clinical Research. 2013;6(2):196-9.
25. Sathisha UV, Smitha J, Shylaja MD. Antiproliferative, Antioxidant and Cyto/DNA Protective Properties in *Andrographis serpyllifolia*: Role of Andrographolide and Phenolic Acids. Journal of Complementary and Integrative Medicine. 2007;6(1). ISSN (Online) 1553-3840, DOI: https.//doi.org/10.2202/1553-3840.1252
26. Kandati V, Govardhan P, Reddy CS, Nath AR, Reddy RR. *In-vitro* and *in-vivo* anti-inflammatory activity of *A. serpyllifolia* (Rottl. E. Vahl.) Wt. Inter Current Pharma J. 2012;1(8):199-204.
27. Dieter S, *et.al.* 5-Lipoxygenase: Underappreciated Role of a Pro-Inflammatory Enzyme in Tumorigenesis Front. Pharmacol. 2010;1:143
28. Meacham K, Shepherd A, Mohapatra DP, Haroutounian S. Neuropathic Pain: Central vs. Peripheral Mechanisms. Curr Pain Headache Rep. 2017;21(6):28.
29. Rajesh KS, Akanksha C, Prayag Y, Raghuveer I, Vihangesh D. Traditionally used herbal plants in anti-inflammatory activity: An Overview. Journal of Pharma Research. 2013. ISSN: 2319-5622
30. Chelluboina B, Manga K. Hypolipidemic activity of Andrographis serpyllifolia Wt.Ic. Pharm Res. 2010; 3(4):769-770.
31. Shyam SG, Joni S, Rao CV. Effects of Flavonoids From *Andrographis serpyllifolia* Leaves Extract on Carbon Tetrachloride-Induced Hepatotoxicity in Wistar Rats. Indian Journal of Applied Research. 2014;4(5).
32. Ravishankar KB, Ganga R, Appala R, Chandralekha G,Vinod K. Antimicrobial and Anthelmintic activity of *Andrographis serpyllifolia* root extract. International Journal Chem Sci. 2007;5(3):1145-9.
33. Chun-Su Y, Chong-Zhi W, Sheila MW, Lian-Wen Q. Chemical and pharmacological studies of saponins with a focus on American ginseng. J Ginseng Res. 2010;34(3):160-7.
34. Jia L, Zhao Y. Current evaluation of the millennium phytomedicine--ginseng (I): etymology, pharmacognosy, phytochemistry, market and regulations. Curr Med Chem. 2009;16(19):2475-84
35. Pinchak WE, Min BR, Merkel R, Walker S, Tomita G, Anderson RC. Comparative antimicrobial activity of tannin extracts from perennial plants on mastitis pathogens. Scientific Research and Essay. 2008;3(2):066-73. Available online at http://www.academicjournals.org/SRE ISSN 1992-2248

GRAPHICAL ABSTRACT



SUMMARY

This systematic review examines the investigations conducted in Ethnobotanical, Botanical and pharmacological aspects of Andrographis serpyllifolia documented over more than 200 years (Years 1800 to 2017). The review summarizes evidence from herbaria, floras, thirty three high-quality studies, including Scanning Electron microscopic exploration, phytochemical screening, pharmacological efficacies and in vitro experiments with Sprague-Rawley, Wistar and Albino rats.

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Cite this article: Krishnaswamy S, Kushalappa BA. Systematic Review of Andrographis serpyllifolia (Rottler ex Vahl) Wight: An Ethno-pharmaco-botanical Perspective. Pharmacog J. 2018;10(6)Suppl:s14-s26.