

Herbal Splendour, Medicinal Health & Modern Medicine

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SUMMARY

Plants have been the main source of healing agents from time immemorial and continued to be the source of drugs even today. Obviously earlier systems of medicines were based on the use of plants as therapy. Ayurvedha, Siddha, Unani and Tribal medicines are mainly based on the use of plants for curing diseases. This review article, projects highlights of the research work on medicinal herbs that were carried out in the Microbiology departments of three Institutes at Chennai - Madras Medical College, Dr. ALM PGIBMS & Presidency College. Many of the plants used as food in India especially, Tamil Nadu have medicinal properties. Besides nutritive value, the therapeutic usefulness various foods which are mainly of plant products are described in "Patharthaguna Vilakkam", an ancient compendium on Siddha medicine. Modern science provides evidence for their valid use because the vegetables, fruits, seeds, leaves, roots, have minerals, vitamins, proteins, good cholesterol and pharmaceutically important ingredients, including antimicrobial and immuno-modulatory principles. Modern science enables us to evaluate the efficacy of the claims on the useful products of traditional systems of medicines. It is well known that plants play a pivotal role in Human health.

Many of the drugs in various branches of medicines have their origin from plants. Initial use of plant in extract form was considered as non specific and isolation of specific active principle from the useful plant parts marked a new era in drug development from plants. Collaborative researches involving different disciplines - medical and paramedical have brought out newer information on the physiotherapeutic properties through evaluation on the usefulness of plants by *in vitro*, *in vivo* experimental studies followed by clinical trials. Getting patent for newer drugs of traditional sciences is strongly supported by DST. *In vitro* antimicrobial highlights of few potential plants from the studies conducted at Chennai revealed that *Phyllanthus amarus*, *Pongamia pinnata*, *Terminalia chebula*, *Terminalia catappa*, *Ocimum canum*, *Decalepis hamiltonii*, *Cassia auriculata*, *Lawsonia inermis* and *Plectranthus ambonicus* have appreciable antimicrobial properties and their minimum microbicidal value have been estimated.

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INTRODUCTION

Plants not only provide us food but also medicine. Forty eight percent of drugs in pharmacy are directly obtained from plants. 85% of the Chinese population and 65% of the Indian population rely on plants for medicine.

The earliest mention of the medicinal use of plants was in Rig Vedha which were written between 4000 & 1600 BC. In the Athurvana Vedha, prescription on various use of drugs are mentioned and in Ayurvedha, a upavedha, definitive properties of drugs and their uses in detail are described. Later, Charaka Samita of Ayurvedha (600 BC) list 341 plants and plant products for use in health management. Susruta samita described about more medicinal plants. Thus the Ayurvedic drug derived from single plant had increased to 600 species (2).

The WHO had listed over 21,000 plant species for medicinal purposes all over the world. In India 45,000 species of plants are distributed in 16 Agro climatic zones & 15,000 species of these are considered as medicinally important. The number of plants of medicinal value described in Ayurvedha are 7,500, in Sidha - 600(3), in Unani - 550, and in Homeopathy- 400. There are 4,600 ethnic communities in India using plant species for humans and veterinary health care.

Only 10-15% of the existing plants have been evaluated for their biological activity (1). Incidence of resistance gained by microbes for diseases like Malaria, Tuberculosis and Salmonellosis are an eye opener for the need on active research in finding newer drugs. Research on newer drugs of plants is a thrust area of research. Hence

research on the *in vitro* and *in vivo* anti-microbial efficacy and other pharmacological properties have been actively pursued through out the world.

Improvement in Evaluation Techniques

In the days of modern science, the evaluation techniques have undergone rapid improvement. Scientific use of chemicals as drugs to control microbial infections had its beginning in 1495 when mercury was used to treat syphilis (4). Use of plant extract as therapeutic substance preceded the use of chemical as drug. Ayurvedha, Siddha, which date back to more than two thousand years, seemed to have observed the usefulness of the plant extracts.

Medicinal plants, as natural industries for the synthesis of variety of chemicals either as primary or secondary metabolites, owe their healing power to one or more bioactive compounds. Unraveling these compounds for their therapeutic utilization is one of the thrust areas of research throughout the world. The annual global-trade on herbal preparations accounts for about 30,000 billion dollars per Year. There are 121 therapeutic agents of known structure from 90 species of plants. Yet there are few compounds like Chloroquinone from Cinchona bark which could not be synthesized but to be obtained only from plants (2).

The first record on the efficacy of phytochemical as an antimicrobial agent was of quinine from the bark of Cinchona species for *Plasmodium vivax*, a protozoan, by Joseph Pelletier & Joseph Caventou in 1820. The Chinese emperor, in his pharmacopoeia 2700 BC had mentioned on the use of Ephedra in a variety of diseases other than syphilis (5).

Since then, greater attention has been given to the study on efficacy of plant extracts against microbial pathogens of human namely bacteria, fungi, protozoan and viruses. Whenever an extract was found to be efficacious, the follow-up action was to isolate its antimicrobial principles and later to understand its pharmacokinetics.

The first chemist to investigate on plant products in India was W.O Shangnessy in 1840 of Kolkata Medical college. Later his associate Warder & Hooper, isolated Abrin, a toxin protein from the seeds of *Abrus precatorius*. Later several phytochemicals have been studied extensively for their pure active constituents and these have been included in Modern pharmacopoeia Morphine from *Papaver* sp., Ephedrine from

Ephedra sp., Emetine from *Ipecac*, Senna glycosides from *Cassia* sp., and Reserpine from *Rauwolfia serpentina*.

During the later part of this century collaborative investigations among Ethnobotanists, Biochemists, Microbiologists and Pharmacologists have resulted in unraveling the efficacy of substantial number of compounds. This gave greater impetus to the development of Phytochemistry and phytochemical pharmacology.

Scientific investigations of a medicinal plant is extremely essential because contrary to the belief, a newer and unrelated activities was found in plants. For instance leaves of well known medicinal plant *Catharanthus roseus* (*Vinca rosea*) had been

Table: 1 - *In Vitro* Minimum bactericidal value in mg/ml of the Seitz filtered aqueous extracts

S. No	Bacteria	Extracts						
		Terminalia chebula		Ocimum canum L	Cassia auriculata L	Plectranthus ambonicus		Lawsonia inermis
		UR	R			Non vareigated	Variegated	
1	Strep pyogenes	13.5	24	-	-	-	-	18.5
2	Staph aureus ATCC 25923	13.5	24	-	-	-	-	18.5
3	Staph aureus	13.5	24	-	-	-	-	18.5
4	Staph epidermidisl	-	-	-	-	-	-	-
5	E coli ATTC 25922	13.5	24	-	5	-	-	-
6	Escherichia coli	13.5	24	-	-	-	-	-
7	Shigella sonnei	13.5	24	-	-	-	-	-
8	Salmonella typhi	13.5	24	10	20	-	-	-
9	S paratyphi A	13.5	24	-	10	-	-	-
10	S. paratyphi B	13.5		10	20	-	-	-
11	Vibrio cholerae	13.5	24	10	2.5	27.5	17.5	-

L - Leaf, UR - Unripe Fruit, R - Ripe Fruit

used for the treatment of diabetes in Mexico but a detailed investigation of the plants led to the isolation of alkaloid leurosine and P 1534 leukoblastine which have antitumor activity on lymphocytes leukaemia, inhibiting the growth of human choriocarcinoma transplanted into hamster cheek pouch (6) but found to lack any chemicals that is related to Diabetes mellitus.

It is estimated that now more than two thirds of the world populations rely on plant based drugs. About 7,000 medicinal compounds used in the western pharmacopoeias are derived from plants (7). In the USA, approximately 25% of all prescribed drugs contain one or more bioactive compounds derived from vascular plants (8). The bioactive compounds are

not only derived from higher plants, but are also derived from lower plants like fungi.

Need for Newer Drugs from Plants

A worldwide resurgence of interest on the exploration of newer drugs from the plants and their utilization for human health care has come for various reasons namely:

1. Reports of acquiring resistance by disease causing organisms to the existing antibiotics as in the case of chloroquinone.
2. Plants are seen as goldmines by industrialists in their attempt to exploit a variety of phytochemicals as drugs.

Table: 2 - In Vitro Minimum fungicidal value in mg /ml of the Seitz filtered Aqueous extracts

S. No	Fungi	Extracts					
		Lawsonia inermis	Terminalia catappa		Decalepis hamiltonii RB	Terminalia chebula	
			Ripe FR	Unripe FR		Unripe FR	Ripe FR
1	Epidermophyton floccosum	2.31	1.5	0.4	-	0.67	0.6
2	Microsporum gypseum	2.31	0.375	0.4	0.537	0.67	0.6
3	Trichophyton mentagrophytes	4.62	1.5	0.4	-	0.67	0.6
4	Candida albicans	18.5	-	-	-	0.67	0.6
5	Mucor	-	-	-	2.15	0.67	0.6
6	Rhizopus	-	-	-	2.15	0.67	0.6
7	Penicillium	-	-	-	-	0.67	0.6
8	Aspergillus flavus	-	—	-	-	-	-
9	Aspergillus niger	-	—	-	-	-	-

- lack of fungicidal properties

3. Need for an honest attempt to evaluate the usefulness of plant drugs due to the existing threat to the precious flora as realized by the international organization like IUCN (International Union for Conservation of Nature) had given necessary impetus for aggressive research on medicinal plants. IUCN had estimated that 10-20% of the plant species would have become extinct.

A review of the reference on the past investigations on the isolation, characterization of active principles from the medicinal plants clearly reveal us that:

1. more than 90% of the plants remain to be analyzed for bioactive components.
2. even in respect to the chemically well studied plants, not all the isolated and identified biochemicals were tested for their biological, pharmacological and toxicological effects.

In vitro standard protocols have been evolved to obtain uniformity and reproducibility and consistency. *In vitro* antimicrobial Assay of National committee for Clinical Laboratory Standards (NCCLS) prescribe protocols for the *in vitro* antibacterial(9) and antifungal (10) evaluation. Standardization of inoculum for *in vitro* antibacterial assay is also available (11). Standard *in vitro* antiviral (12) and *in vitro* safety (13) protocols. Also standard protocols have been evolved for isolation and characterization of compounds (14) and estimation of anti-inflammatory property and other specific physiological activities.

Another visible lacuna in the traditional systems and a stumbling block in utilization of the time honoured medicinal plants is the lack of knowledge about the

possible toxic effects of these plants on the human organ and tissues. It is interesting to note that some of the plants like *Tribulus terrestris* (Puncture vine), mentioned in the traditional systems of medicine and described in Indian Materia Medica (15) for its diuretic property, has been found to possess profound toxic effect on liver due to possible nitrate poisoning (16). Hence screening of every potential medicinal/health plants to observe the presence or absence of toxicity in their useful parts by suitable safety study experiments in suitable animal model, is a prerequisite for making it as a potential drug for human use. Hence it is imperative to evaluate the medicinal properties of Indian medicinal plants to facilitate discovery of newer cost effective medicines for human and veterinary beings by utilizing Drug Development Programme of DST, Government of India.

Evaluation on the safety of the plant extracts and on isolated active principle by *in vitro* (13) assay are also available. More than these - the conduct of clinical trials in volunteers have been standardized in order to identify the safety of the drug during long period of usage. Statistical analysis of the experimental data is uniformly suggested to justify the significance of the results by adopting suitable statistical softwares like ANOVA.

RESULTS

Intensive studies on *Phyllanthus amarus* had shown the efficacy of the whole plant in the control of Hepatitis - B and its safety had been ensured through safety studies in animal models and human volunteers. Clearance of HBsAg had been carried out and the clearance rate was highest from a species collected from Chennai. *Phyllanthus amarus* collected from other than Tamil

Nadu state did not show appreciable HBs Ag clearance (18,19). All these results obtained from 28 National and International centres had resulted in development of the drug named as "VIROHEP" by Prof. S.P. Thyagarajan and a patent had been obtained in the name of University of Madras. Similarly detailed study on another plant *Pongamia pinnata* (20) resulted in the observation of *in vitro* antiviral activity for HSV and clinical trials (21) suggested its usefulness in clearance of Herpes infections. Seitz filtered extract was adopted as suitable method for *in vitro* estimation of antimicrobial properties of aqueous extract by a modified serial tube two fold dilution method and had reported that Seitz filtration did not affect antimicrobial activity of Henna leaf extract (22). Since then Seitz filtered aqueous extract of useful plant parts have been tested for the bactericidal and fungicidal properties. The impressive antibacterial activity for 14 gastroenteritis bacteria have been reported. The flower buds and seed extract of *Cassia auriculata* (Tanners Cassia) and the ripe fruit of *Terminalia chebula* (Chebulic myrobalan) (23), were found to possess antibacterial activity on gastroenteritis bacteria. (Tables 1 & 2). Varietal variation had been reported in the fruits of Bael tree (24). However, there was no difference in the antibacterial activity between the leaf extracts of *Plectranthes ambonicus*, namely, of the variegated and non variegated varieties. Extracts of both varieties did have marked inhibitory activity on *Vibrio cholerae* and lack of activity on other nine gastroenteritis bacteria (25). However, a plant of high esteem, *Ocimum teniflorum* (Holy basil) was found to lack bactericidal activity while Hoary basil (*Ocimum canum*) was found to possess appreciable antibacterial activity (26). It is interesting to note that fruit rind extracts of *Terminalia catappa*

(Indian almond) were found to exhibit remarkable antifungal activity on dermatophytic fungi (27). Likewise, highly appreciable antifungal property was found in the fruit rind extracts of ripe and unripe fruits of Chebulic myrobalan (*Terminalia chebula*) and were also found to be fungicidal to all opportunistic and dermatophytic fungi (28).

MBC (Minimum Bactericidal concentration) of the seitz filtered extracts of the useful plant part for the susceptible bacteria and its Minimum Fungicidal Concentration (MFC) for susceptible fungi had been estimated. (Tables 1 & 2)

CONCLUSION

Modern science has helped us to get a clear and better understanding of the "Herbal Splendour". Improvements in the evaluation techniques both *in vitro* and *in vivo* enable us to understand the antimicrobial efficiency of the traditional medicinal plants. Completion of *in vivo* antibacterial studies are confined to handful plants like *Phyllanthus amarus* and *Pongamia pinnata*. Safety studies had been carried out only for few plants/plant parts, namely *Phyllanthus amarus*, *Pongamia pinnata*, *Terminalia chebula* and *Aegle marmelos*. In the Indian context, only few plants like *Phyllanthus amarus* has crossed through all scientific investigations and developed into a drug with a patent. Studies on other plants have helped to understand their specific profile on their efficacy to clinically important bacteria, fungi and few viruses. Plant parts of Chebulic myrobalan have very high antibacterial and antifungal activities while certain plants have narrow activity as in *Aegle marmelos*.

Similar estimations on *in vitro* profile for plant ingredients of traditional medicines in relation to infectious diseases

would create a useful database that would facilitate *in vivo* safety study followed by clinical trial and ultimately help in the development of many newer drugs of plant origin. India, being basically an agricultural country and major section of the people are

in the rural areas, the evaluated herbal traditional medicine by modern science is the solution for the cost – effective management and treatment of diseases and maintenance of good health.

REFERENCES:

1. Washington DC (1983). Plants the potentials for extending production of medicines & other usefulness, workshop proceedings, OTA– BP-F-23 congress, Office of the Technology Assessment, 313.
2. Bhattacharya Supriya Kumar (2004). Handbook of Medicinal Plants, Pointer publication Jaipur, 2.
3. Kannusami Pillai, Padardha Guna vilakkam B, Rathina Naicker & Sons (1949). Chennai –79, 1-380.
4. Micheal J. Pelczar, Jr. Chan ECS and Krieg NR (1993). Microbiology Concepts and Applications, Mc Graw Hill Inc. 15.
5. Taylor N (1965) Plant drug that changed the world. London, George Allan & Unwin Ltd., 87, 105.
6. Rastogi RP and Mehrota BN eds. (1999). Compendium of Indian Medicinal plants, Central Drug Research Institute, Lucknow and National Institute of Science Communication, New Delhi, 1, 92.
7. Caufield C (1991). In the rain forest: The University of Chicago Press Chicago, 9.
8. Farnsworth NR, Morris RW. Higher plants, the sleeping giant of drug development. *Am J Pharmacol* 148: 46-52.
9. National Committee for Clinical Laboratory Standards NCCLS (1984). Methods of antimicrobial susceptibility testing of anaerobic bacteria. Tentative Standard M11-NCCLS, Villanova, PA, USA.
10. National Council for Clinical laboratory standards (NCCLS) reference (1997). Method for broth dilution antifungal susceptibility testing of yeasts approved std. M27A, NCCLS, Wayne PA. USA.
11. Working Party Report (1991). Working party of the British society for antimicrobial chemotherapy. A guide to antibiotic sensitivity testing. *J Antimicrobial. Chemotherapy* 27(D): 1-50.
12. Serkedjieva J and Ivancheva S (1999). Antiherpes virus activity of extracts from the medicinal plant, *Geranium sanguineum* L. *J Ethnopharmacology* 64: 59-68.
13. Mosmann T (1983). Rapid calorimetric assay for cellular growth and survival application for proliferation and cytotoxicity assays. *J Immunol Meth* 65: 55-63.
14. Aneja R, Mukerjee SK and Seshadri TR (1958). Synthesis of Benzo-furan derivatives- I. Karanjketone, Karakjin and Pongapin. *Tetrahedron* 2: 203-210.
15. Nadkarini AK (1982). Indian material medica, Popular prakashan pvt. Ltd., Mumbai, 1: 47.
16. Kingsbury JM (1961). Poisonous plants of US & Canada, Prentice Hall Inc., New Jersey, 18,205.
17. Thyagarajan SP, Thiruneelakandan K, Subramanian S and Sundaravadeivelu S (1982). *In vitro* inactivation of HBsAg by *Eclipta alba* Hassk and *Phyllanthus niruri* Linn. *Ind J Med Res* 76: 124-130.
18. Thyagarajan SP, Subramanian S, Thirunalasundari T, Venkataraman PS and Blumberg BS (1988). Effect of *Phyllanthus amarus* on chronic carriers of Hepatitis –B virus. *Lancet* 2: 764-766.

19. Geetha J, Manjula R, Malathi S, Usha K, Chari T, Raghuraman K, Thyagarajan SP and Madhanagopalan (1992). Efficacy of essential phospholipids substances of soya bean oil and *Phyllanthus niruri* in acute viral Hepatitis. *J General Medicine* 4(3): 53-58.
20. Elanchezian M, Rajarajan S, Rajendran P, Thyagarajan SP and Subramanian S (1993). Antiviral properties of the seed extract of an Indian medicinal plant, *Pongamia pinnata* Linn. against Herpes simplex viruses: In vitro studies on Vero cells. *J. Med. Microbiology* 38: 262-264.
21. Rajarajan S, Thyagarajan SP, Subramanian SS, Sundaram M and Venkataraman TK (1990). A study on the clinical efficacy of two medicinal plants *Pongamia pinnata* (Linn) Merr. (*Pongamia glabra* Vent). *Thespesia populnea* (L) Sol. against certain skin disorders of viral, bacterial and fungal origin. *Medicinal & Aromatic plant Abstracts* 12(3): 195.
22. Rajarajan S, Kavitha K, Anand D, Mayuran S, Thyagarajan SP and Subramanian S (2002). In vitro antibacterial and antifungal properties in the aqueous leaf extracts of Henna (*Lawsonia inermis* L.). *Indian Journal of Applied Microbiology* 2(1): 59-61.
23. Rajarajan S and Selvi Rao M (2004). A study on the in vitro antibacterial activity in the seitz-filtered aqueous from the Ripe fruit, Unripe Fruit and Leaf Gall of *Terminalia chebula* (*Chebulic myrobalan*). *Biomedicine* 24 (2&3): 7-11.
24. Palaniswami KS (2003). Studies on the in vitro antibacterial properties in three varieties of an Indian medicinal plant, *Aegle marmelos* (L.) Correa and on the in vivo safety of their useful plant parts in wistar rats. Ph.D. Thessis. University of Madras.
25. Rajarajan S, Balasubramanian R, Priyadharshini M, Anand D, Thyagarajan SP and Subramanian S (2002). In vitro antibacterial properties in the Leaf extract of two varieties of country boarge (*Plectranthus ambonicus*. (Lour).spreng). *Biomedicine* 22(1&2): 83-86.
26. Rajarajan S, Yasoth Kumar N, Anand D, Rathina Kumar SS, Thyagarajan SP and Subramanian SS (2004). A study on the in vitro antibacterial activities in the Leaf of *Ocimum tenuiflorum* Linn. and *Ocimum americanum* Linn. For gastroenteritic bacteria. *Indian Journal of Applied Microbiology* 4(1): 5-7.
27. Rajarajan S, Shanbhag Gayathri N Anand D, Thyagarajan SP and Subramanian SS (2003). A study on the in vitro antifungal properties in the aqueous extracts of unripe fruit and ripe fruits of *Terminalia catappa* Linn. *Indian Journal of Applied Microbiology* 1: 67-69.
28. Selvi Rao M, Rajarajan S, Thyagarajan SP and Subramanian S (2004). A study on the in vitro antifungal activity in the Unripe and ripe fruits of *Terminalia chebula* Retz. *Indian Journal of Applied Microbiology* 4(1): 23-25.