MEDICINAL PLANTS:
Phytochemistry, Pharmacology and Therapeutics
– Volume 4 –

Dr. Vijay Kumar Gupta, Ph.D., FLS, London (born 1953-) Ex. Chief Scientist, CSIR- Indian Institute of Integrative Medicine, Jammu, India. He did his M.Sc. (1975) and Ph.D. (1979) in Zoology both from University of Jammu, Jammu-India. His research capabilities are substantiated by his excellent work on histopathology, ecology and reproductive biology of fishes, turtles, birds and mammals, which has already got recognition in India and abroad.

Dr. Gupta has to his credit more than 150 scientific publications and review articles which have appeared in internationally recognized Indian and foreign journals. Founder fellow, life member and office bearer of many national societies, academies and associations. He has successfully completed a number of research/consultancy projects funded by government, private and multinational agencies. His current areas of interest are histopathology, toxicology, pre-clinical safety pharmacology, reproductive efficacy studies of laboratory animals and biodiversity.

He is the Series Editor of the recently published multi-volume set of books, "**Comprehensive Bioactive Natural Products (Vols. 1-8)"**, published by M/S Studium Press, LLC, USA. He is also Editor-in-Chief of the books, "**Utilisation and Management of Medicinal Plants (Vols. 1-3)"**, "**Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics (Vols. 1-4)", "Traditional and Folk Herbal Medicine (Vols. 1-3)", "Natural Products: Research Reviews (Vols. 1-4)", "Bioactive Phytochemicals: Perspectives for Modern Medicine (Vols. 1-3)", "Perspectives in Animal Ecology and Reproduction (Vols. 1-10**)" and **"Animal Diversity, Natural History & Conservation (Vols. 1-5)"**. The Editor-in-chief of the American Biographical Institute, USA, has appointed him as *Consulting Editor* of *The Contemporary Who's Who*. Dr. Gupta also appointed as Nominee for the *Committee for the Purpose of Control and Supervision of Experiments on Animals* (CPCSEA, Govt. of India). The *Linnaean Society of London, U.K.* has awarded fellowship to him in November 2009 in recognition of his contribution towards the cultivation of knowledge in Science of Natural History. Recently, Modern Scientific Press, USA has nominated Dr. Gupta as the Editor of the *International Journal of Traditional and Natural Medicine*.

Dr. Gurdarshan Singh (born 1962), working as Senior Scientist in the PK-PD-Toxicology Division of Indian Institute of Integrative Medicine (CSIR), Jammu. He did his M.Sc. (1987), M.Phil. (1989) and Ph.D. (1993) in Zoology from University of Jammu, Jammu-India.

Dr. Singh has published 26 research papers, both in national and international journals of high repute and impact factor. He is also actively involved in both in-house and sponsored research projects for the generation of pre-clinical safety pharmacological data for IND (investigational New Drug) application. His main areas of research are toxicity and regulatory pharmacology of new chemical entities for drug development programme in addition to anti-allergy and anti-asthmatic screening of herbal as well as synthetic molecules.

Dr. Surjeet Singh (born 1958-) did his M.Sc. (1990) in Zoology and Ph.D. (2003) in the field of Inflammation from University of Jammu, Jammu-India and presently working as senior pharmacologist in the Department of Pharmacology, Indian Institute of Integrative Medicine(CSIR), Jammu.

He has an experience of 28 years in the field of inflammatory pharmacology, preclinical toxicology and safety and has published about 50 research papers and review articles in national and international journals. He is the life member of Indian Pharmacological Society and honour of the member *UNESCO Workshop* in 1992.

Dr. Anpurna kaul (born 1956-) working as Scientist in pharmacology Division of Indian Institute of Integrative Medicine(CSIR), Jammu- India. She has completed her Ph.D. in 1996 from University of Jammu, Jammu-India. Her field of research is immune-pharmacology.

Dr. Kaul has 35 research publications in national and international journals, 12 patents and also presented several research papers in various symposia/conferences. She has screened more than 4000 plant extracts/fractions and pure compounds on immune system by *in vivo* and *in vitro* methods. She has also actively participated in Indo-Malaysian research project as member and visited Malaysia in 2007 to attend *Women's Health and Asian Traditional Medicine* Conference.

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2016
Daya Publishing House®
A Division of
Astral International Pvt. Ltd.
New Delhi – 110 002

Cataloging in Publication Data--DK
Courtesy: D.K. Agencies (P) Ltd. <docinfo@dkagencies.com>

Medicinal plants : phytochemistry, pharmacology and therapeutics / editor-in-chief, V.K. Gupta ; editors, G.D. Singh, Surjeet Singh, A. Kaul.

volume 4 cm
Includes bibliographical references and index.
ISBN 978-93-5124-704-3 (Hardbound)
ISBN 978-93-5130-885-0 (International Edition)
ISBN 978-81-7035-767-4 (series)
ISBN 978-93-5130-096-0 (series) (international edition)

1. Medicinal plants--India--Analysis. 2. Materia medica, Vegetable--India. 3. Pharmacology--India. I. Gupta, V. K. (Vijay Kumar), 1953- editor. II. Singh, G. D. (Gur Darshan), 1962- editor. III. Surjeet Singh, 1958- editor. IV. Kaul, A. (Anpurna), 1956- editor.

RS180.I4M43 2014 DDC 615.3210954 23

Published by : **Daya Publishing House®**
A Division of
Astral International Pvt. Ltd.
– ISO 9001:2008 Certified Company –
4760-61/23, Ansari Road, Darya Ganj
New Delhi-110 002
Ph. 011-43549197, 23278134
E-mail: info@astralint.com
Website: www.astralint.com

Laser Typesetting : **Classic Computer Services,** Delhi - 110 035

Printed at : **Thomson Press India Limited**

PRINTED IN INDIA

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Foreword

The previous volumes of the book series "*Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics*" have gained wide attention and praise from the scientific community as well as general readers. Medicinal plants have always been the source of new drugs and many important allopathic drugs have been discovered from medicinal plants. There are more than 400,000 plant species in the world and each plant has the potential to yield one or more potential drug considering the vast array of phytochemicals that a plant produces. Less than 2 per cent of the plants of the world have been scientifically studied and even then only partially. As such, medicinal plants can form the basis for discovery of new drugs against newly emerging diseases like AIDS, Ebola and bird flu, difficult to cure diseases like diabetes, cancer and rheumatoid arthritis, and diseases that have developed drug-resistant vectors like malaria, tuberculosis and filariasis, to name only a few. Most of the antibiotics used in the world today and in the recent past have developed antibiotic-resistant microorganisms, and as such, new antibiotics and other drugs are the necessity of the time. This discovery of novel drugs is more necessitated because many modern drugs have serious side-effects.

The present volume is a welcome addition to the existing scientific literature on the phytochemicals, pharmacological properties, and potential therapeutic uses of a number of plant species belonging to diverse genus and families. Each of the Chapters is a thorough review of the scientific literature, which will help researchers to develop new ideas and methods for investigating plant species in the continuous search of human beings to discover and develop more efficacious drugs. The various Chapters will contribute to the finding of more efficient sources of drugs against some of the common but most difficult to treat diseases prevalent today like cancer, diabetes, and cardiovascular disorders. Even plants used against gastrointestinal ailments are noteworthy for they can form the basis of affordable and readily available medicines.

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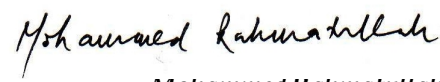
Rural persons in underdeveloped countries, because of lack of quality drinking water and proper sanitation facilities suffer most from gastrointestinal disease(s) and the Chapters on treatment of such ailments with plants can form an interesting and important addition to the scientific literature and possible discovery of novel drugs.

In short, this book is a timely addition to the existing scientific literature. Because the References cited in each Chapter are very much updated, the book can guide the readers to the latest trends in the field. This is important, because it will reduce repetition and redundancy. I hope that the scientists and readers will welcome the publication of this book with enthusiasm as this series of books richly deserve.



Mohammed Kahmatullah

Preface

Since the beginning of human civilization, medicinal plants have been used by mankind for its therapeutic value. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. Many of these isolations were based on the uses of the agents in traditional medicine. The plant-based, traditional medicine systems continue to play an essential role in health care, with about 80 per cent of the world's inhabitants relying mainly on traditional medicines for their primary health care.

All around the world there is talk about 'health for all' but it has been realized that modern pharmaceuticals are and will remain out of reach of a large proportion of the human population for the foreseeable future. This necessitates the use of other sources of human knowledge to provide common health benefits. Thus, Herbal medicine is now regarded as important but underutilized tool against disease. The World Health Organization (WHO) recognized this fact in the early 1970s and encouraged governments to effectively utilize local knowledge of herbal medicines for disease prevention and health promotion. Herbal medicines, however, suffer from a range of shortcomings. These include insufficient and unacceptable evidence of safety, efficacy, standardization and inconsistent production practices. The shortcomings are played well by the promoters of modern medicine and are less responsible for lower confidence level among the elite in the developing as well as developed countries. As the isolation and analytical techniques have become more powerful, and the capability to apply them in countries rich in medicinal herbs has increased, there is a growing interest in herbal medicine.

The present volume includes twenty nine original research and review articles written by eminent scientists and researchers from within India and abroad, the notable amongst which include: Phytochemistry, Pharmacology and Therapeutics of *Coptis*; Pharmacological Activities and Therapeutic Potential of *Sarca asoca* and its Phytoconstituents; Anticancer Activity of Indian Medicinal Plant Bael, *Aegle marmelos* (L.) Correa in Mice Transplanted with Ehrlich Ascites Carcinoma; Efficacy and Pre-

clinical Safety Pharmacological Evaluation of Lavangadi Vati; Pharmacological and Phytochemical Screening of Methanolic Extract of *Callicarpa arborea* Roxb.; Ionic Liquids: Green Solvents for the Extraction of Phytoconstituents; Elderberry, its Constituents and Use in Treating Gastrointestinal Ailments; A Review on Pharmacognosy, Phytochemistry, Pharmacology and HPTLC Fingerprint Profile of *Averrhoa bilimbi* L.; *Ficus* Genera: A Promising Genera for Development of New Anti-Diabetic Drugs?; The Cytotoxic Effect of *Phellinus durrisimus* with respect to other Anticancer Drugs Evaluated by Extended Lethality Assay of Brine Shrimps (eLABS); Activity of *Centella asiatica* (Linn).U. Extracts on Bacterial Flora of Human Skin; Antibacterial Effect of *Lantana camara* L. Leaf Extracts; Protective Activity of Ethanolic Extract of *Citrus medica* Linn Peel on Rat Models of Inflammatory Alveolitis; Antigenotoxic Potential of *Punica granatum* in Breast Cancer Patients; Curry Leaf (*Muraya koenji* L. Spreng): Its Phytochemisty and Pharmacological Properties; Anti-allergic and Anti-anaphylactic Activity Profile of Ethanolic Extract of *Pothos scandens* in Rodents; Anticancer Activity of Methanol Extract of Green Tea against Cervical Cancer; Therapeutic Activity of Comparative Extraction of *Quercus borealis* (Oak) Leaves with Solvents of Different Polarities against *Trypanosoma evansi*; Therapeutic Evaluation of Methanolic Extract of *Moringa oleifera* Seeds against *Trypanosma evansi*; Evaluation of Gastric Ulcer Protective Activity of *Acorus calamus* Linn in Laboratory Animals; UV-VIS and HPLC Studies on *Amphiroa anceps* (Lamarck) Decaisne; Novel Synthesis of Silver Nanopeptides Using Protein Extracts of *Selaginella intermedia* (Bl.) Spring; Pharmacological and Phytochemical Screenings of *Bidens sulphurea* Cav.; Cytotoxic Activity of Stem Bark of *Ficus racemosa* against Non-small Cell Lung Carcinoma A549 Cells; Natural Product Chemistry of Anti-Helminthic Plants; Medicinal Plants Modulating Cannabinoid Receptors and Endocannabinoid Metabolizing Enzymes.

The chapters included in the present volume "***Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics - Vol. 4***" are likely to lead further researches in this direction and it is hoped that this publication would attract world wide audience of researchers and the academicians of allied disciplines engaged in research of new drug from plant resources.

V.K. Gupta

Contents

Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics Vol. 4 (2016)
Editors: **V.K. Gupta *et al.***
Published by: **DAYA PUBLISHING HOUSE, NEW DELHI**
Pages **375–389**

18

Curry Leaf (*Muraya koenigii* L. Spreng): Its Phytochemisty and Pharmacological Properties–A Review

Kaliyaperumal Ashokkumar[1]* and Arun S.K. Shunmugam[1]

ABSTRACT

Murraya koenigii, L. Spreng, a medicinally important herb of Indian origin, and very popularly used in Indian cuisine are the daily basis. The study of literature reveals some remarkable phytochemistry and pharmacological activities of the plant. The whole plant of M. koenigii are rich in carotenoids, alkaloids and flavonoids and it keeps several biological activities such as immunomodulatory, anticancer, antidiabetic, antibacterial, antimicrobial, antiulcer, anti-diarrhea, antiamnesic, anthelmintic, and antioxidant properties. M. koenigii also is rich in simple phenolic acid such as gallic, caffeic, tannic, ferulic and vanillic acids. Based on the above consideration, it is not surprising that M. koenigii have been attracting greater interest. Therefore, this article reviews the most updated information of the phytochemical properties and pharmacological effects of M. koenigii extract as well as its miscellaneous uses.

Keywords: Carbazole alkaloids, *Murraya koeingii*, Phytochemical and pharmacological activities.

Introduction

Medicinal plants hold several bioactive compounds, which are helpful in improving the life and treatment of disease. The leaves of curry leaves contain

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carbohydrates, proteins, enzymes, fats, oils, carotenoids, terpenoids, flavonoids, sterols and simple phenolic compounds etc. Natural products are the source of synthetic and traditional herbal medicine and are still the primary health care system. The presence of various life-sustaining constituents in plants made scientists to investigate these plants for their uses in treating certain infectious diseases and management of chronic wounds (Nayak, 2006). Recent research has focused on the natural plant products are alternatively for disease control and cure. Medicinal plants are cheaper, more available in most of the population throughout the world. Thus, there is a need to encourage the use of healing plants as potential sources of new drugs. There has been as highly increased interest in herbal remedies in several parts around the world (Daniyan and Muhammad, 2008).

Curry leaf *M. koenigii* (Rutaceae), is a perennial plant commonly known as Curry Veppilai (Tamil) and "Curry Patta" (Hindi) is widely used as a spice and throughout the India and other tropical countries (Joseph and Peter, 1985). *M. koenigii*, a medicinally important herb of Indian origin, has been used for centuries in the Ayurvedic system of medicine, and very popularly used in Indian cuisine are the daily basis. *M. koenigii* is an aromatic and deciduous shrub occurred throughout the India up to an altitude of 1500 m and cultivated for mainly aromatic leaves, Anonymous (1998). It is native to India and commonly occurs in the foothills of Himalaya, Assam, Sikkim, Tamil Nadu, Kerala, Andhra Pradesh and Maharashtra. Moreover, it found in evergreen and deciduous forests of peninsular India (Lal *et al.,* 2003).

The *M. koenigii* plant is widely used as an herb, spice, condiments and also used to treat various types of ailments in the Indian traditional system. In the traditional system of medicine, it is used as antiemetic, antidiarrheal, dysentery, febrifuge, blood purifier, tonic, stomachic, flavoring agent in curries and chutneys. The oil is used externally for bruises, eruption, in soap and perfume industry (Prajapati *et al.,* 2003). Several parts of *M. koenigii* have been used for traditional medicine for the treatment of rheumatism, traumatic injury and snake bite, and it has been reported to have antioxidant (Ninjappa *et al.,* 2008), antimicrobial (Goutam and Purohit, 1974), anti-diabetic and anti-dysenteric activities (Kong *et al*., 1986; Kesari *et al.,* 2007; Mishra *et al.,* 2009; Yankuzo *et al.,* 2011). It has also used as anti-inflammatory (Muthumani *et al.,* 2009), anticancer (YihKok *et al.,* 2012; Muthumani *et al.,* 2009), antinociceptive (Patil *et al.,* 2012), anthelmintic (Sharma *et al.,* 2010), anticholinesterase and antiamnesic activity (Tembhurne and Sakarkar, 2011). Based on the above interest and attention, the present study contributes up to date review on phytochemical and pharmacological properties of *M. koenigii*.

Phytochemical Properties

The leaves of *M. koenigii* are well to do in minerals, proteins, carbohydrate, fiber, minerals, carotene, nicotinic acid, Vitamin C, Vitamin A, calcium, oxalic acid, crystalline glycosides, alkaloids, flavonoids, terpenoids, koenigine, resin (Kong *et al*., 1986; Tee and Lim, 1991; Tiwari *et al*., 2011; Rakesh and Arora, 2012; Prajapati *et al.,* 2003). *M. koenigii* have been identified as containing a rich profile of simple phenolic acids including tannic, gallic, caffeic, cinnamic, chlorogenic, ferulic, and vanillic

acids (Singh *et al.,* 2004). It also contains girinimbine, iso-mahanimbine, koenine, koenigine, koenidine, koenimbine, mahanimbicine, bicyclomahanimbicine, phebalosin, coumarine as Murrayoneimperatoxin are isolated from leaves (Narasimhan, 1975; Rastogi and Mehrotra, 1980; Knölker and Reddy, 2002; Schmidt *et al.,* 2012).

Triterpenoid alkaloids like cyclomahanimbine and tetrahydromahanimbine are also present in the leaves (Kureel *et al*., 1969; Hesse *et al.,* 2013). Murrayastine, murrayaline, pyrayafolinecarbazolealkaloids and many other chemical compounds have been reported in the leaves of *M. koenigii* (Furukawa *et al*., 1986). The bark mainly contains the carbazole alkaloids as murrayacine, murrayazolidine, murrayazoline, mahanimbine, girinimbine, koenoline and xynthyletin (Rastogi and Mehrotra, 1980; Gruner, 2011; Hesse *et al.,* 2013). The pulp of fruits generally contain 64.9 per cent moisture, 9.76 per cent total sugar, 9.58 per cent reducing sugar, 0.17 per cent non-reducing sugar and negligible amount of tannin and acids. It also contains 13.35 per cent of vitamin C. The pulp of fruits contain trace amount of minerals 1.97 per cent phosphorus, 0.082 per cent potassium, 0.811 per cent calcium, 0.166 per cent magnesium and 0.007 per cent iron. It also contains a noticeable amount of protein (Parmar and Kaushal, 1982).Furthermore, the isolated phytochemical components and its biological activities were summarized (Table 18.1).

Carotenoids and Flavonoids

The fresh curry leaf leaves contain 9744 ng, 212 ng; 183ng/g was found in lutein, α-tocopherol and carotene respectively.3121. mg/100 g of total carotene, 7.1 mg/100 g of β-carotene was found in fresh curry leaf, and it was reported by Bhaskarachary *et al.* (1995). Siong (1991), reported that 14570 µg/100g of total carotenoids and out of total carotenoids, lutein was 5252µg/g and β-carotene was 9328 µg/g. Air dried curry leaf leaves contain 924.3 mg/kg, 85.9 mg/kg, 5.9 mg/kg and 0.2 mg/kg were found in rutin, quercetin, myricetin, and kaempferol respectively. Also, total flavonoid concentration was 1415.5 mg/kg were analyzed by RP-HPLC (Ashokkumar *et al.,* 2013). In addition, its contain 21 per cent quercetin yield compared to standard was analyzed by HPLC (Vijayanand and Wesely, 2011).

Pharmacological Activities

Immunomodulatory Activity

Aqueous extract of *M. koenigii* 1 g/kg and 2 g/kg doses were evaluated for its immunomodulatory potential in Wistar rats (Sathyae *et al.,* 2011). The results showed that 1 g/kg and 2 g/kg doses are produced the decrease in cell-mediated immune response (30.05 per cent and 55.36 per cent suppression of inflammation, respectively). Methanol extracts of *M. koenigii* showed that significant increase in a phagocytic index by rapid removal of carbon particles from the blood stream (Shah *et al.,* 2008). Furthermore, the extracts increased the antibody titre against ovalbumin and stimulate the T-cells in mice.

Table 18.1: Phytochemical Components Isolated from Various Parts of Curry Leaf and their Biological Effects

Sl.No.	Phytochemical Components Isolated	Parts Used	Biological Activity	References
1.	Mahanine	Leaves	Hepatoprotective	Roy *et al.*(2004)
2.	Girinimbiol and Girinimbine	Leaves	Hypoglycaemic and hepatoprotective effect	Adebajo *et al.* (2006)
3.	Xanthotoxin, isobyakangelicol and minor furocoumarins	Seeds	–	Adebajo and Reish, 2000
4.	Bismurrayafoline	Leaves	Antioxidative activity	Tachibana *et al.* (2001)
5.	Koenimbine, O-methyl murrayamine A, O-methylmahanine, isomahanine, bismahanine and bispyrayafoline	Leaves	Antioxidant activity	Tachibana *et al.* (2003)
6.	Mahanimbine	Leaves	Mosquitocidal	Mathur *et al.* (2011)
			Antimicrobial and Antioxidant activity	Reisch *et al.* (1994), Prakash and Natarajan (1974)
			Toxicity on *Culex quinquefsciatus* larvae	Kureel *et al.* (1969b)
	mahanimbine	Leaves	Antidiabetic and hypolipidemic	Dineshkumar *et al.* (2010)
7.	8,8'-bis koenigine	Leaves	–	Wang *et al.* (2003)
8.	Benzisofuranone derivative, six known carbazole alkaloid and three known steroids	Stem and bark	Anti-microbial activity	Rahman and Gray, (2005)
9.	Monoterpene and sesquiterpenes such as α-terpinene, terpinen-4-ol, linolol and β-ocimene	Seeds	–	Mallavarapu et al. (1999)
10.	Mahanimbinine	Leaf	–	Kureel *et al.* (1970)
11.	Mahaninbicine and Bicyclomahanimbicine.	Leaf	–	Kureel *et al.* (1969a)
12.	Cyclomahanimbicine, bicyclomahanimbicine, and mahanimbimbidine	Leaf	–	Kureel *et al.* (1969b)
13.	9-carbethoxy-3-methylcarbazole, 9-formyl-3-methylcarbazole, and 3-methyl carbazole	Root	Hepatoprotective	Chakrabarty *et al.* (1997)
14.	Murrastifoline-F	Root	–	Bringmann *et al.* (2001)
15.	Mahanimbine, Girinimbine, Isomahanimbine, Murrayazoline, Murrayazolidine, and Mahanine	Leaves	Hepatoprotective	Gupta and Singh (2007)
16.	Murrayanol	Leaves	Mosquitocidal	Mathur *et al.* (2011)
			Antimicrobial	Reisch *et al.* (1994)

Antioxidant Activity

Antioxidant activity of leaves and bark extract of *M. koenigii* was evaluated on streptozotocin induced diabetic in Wistar albino rats. Aqueous leaf extract demonstrated highest DPPH free radical scavenging activity at 89.32 ±1.65 than the methanolic, chloroform and n-hexane extracts 76.34 ± 1.56, 67.89 ± 1.54 and 59.56 ± 1.32 respectively at a concentration of 100 µg/ml. Besides this, aqueous leaves extract also revealed highest Ferric-reducing antioxidant power assay value *i.e.* 76.32 ± 1.87 than the other extracts at a concentration of 100 µg/ml (Sahu *et al.,* 2013). Ningappa *et al.* (2008) were evaluated, the *in vitro* antioxidant properties of different extracts (water, alcohol, alcohol: water, hexane or chloroform extracts of curry leaves (*M. koenigii* L.) using various assays. In results, alcohol: water (1:1) extract of curry leaves possessed the highest antioxidant and free radical scavenging activity. It was inhibited membrane lipid peroxidation by 76 per cent, at 50 µg/ml, scavenged 93 per cent of superoxides at 200 µg/3 ml and scavenged approximately 90 per cent of hydroxyl and 1,1-diphenyl-2-picrylhydrazayl radicals at 4–5-fold lower concentrations compared to the other tested extracts. The selected green leafy vegetable, the total antioxidant activity was highest in *M. koenigii*as compared to that of methanol extracts of *Amaranthus* sp., *Centella asiatica* and *Trigonellafenum graecum* (Gupta and Prakash, 2009). Crude methanolic extract was observed the most excellent DPPH scavenging activity (EC 50-0.187mg) compared with BHT standard (EC 50-0.59mg). β-carotene bleaching assay of an ethyl acetate fraction of methanol extract has potential antioxidant activity (77.8 per cent; BHT- 74.1 per cent) at 1 mg/ml concentration (Juhi *et al.,* 2009).

Das *et al.* (2011) studied the antioxidant effect of curry leaf powder for assessing the formation of lipid peroxides, free fatty acids (FFA) and thiobarbituric acid substances (TBARS) in raw ground and cooked goat meat patties during refrigerated storage. Fresh goat meat with curry leaf powder had an acceptable odour up to 5 days whereas in the control sample, it was up to 3 days. Raw goat meat with curry leaf powder had substantially lower free fatty acids content than control sample for 9 days refrigerated storage. Curry leaf powder (CLP) significantly inhibited the rate of lipid peroxides and TBARS formation in uncooked meat than control. Curry leaf powder in cooked goat meat patties showed significant antioxidant effect as indicated by TBARS values measured by distillation as well as extraction method. These results show that CLP at concentrations as low as 0.2 per cent are a very effective inhibitor of primary and secondary oxidation products in raw ground and cooked goat meat patties and has been potential as a natural antioxidant in raw and cooked meat systems. Mitra *et al.* (2012), observed that aqueous extracts of *M. koenigii* leaf have significant protection to rat cardiac tissue against cadmium-induced oxidative stress probably due to its antioxidant activity. Antioxidant activity of *M. koenigii* could be beneficial to people who are exposed to cadmium either environmentally or occupationally.

Antidiabetic Activity

Dusane and Joshi (2012), observed the extracts of *M. koenigii* in pancreatic beta cell protection and functional pancreatic islets that produce insulin. Yadav *et al.*

(2002) studied, feeding of diet containing various doses of curry leaves (5, 10 and 15 per cent) to normal rats for 7 days as well as mild diabetic (blood-glucose glucose levels >175 mg/dl induced by alloxan 35 mg/kg IP) and moderate diabetic rats (blood-glucose glucose levels >250 mg/dl induced by STZ 60 mg/kg IP) for 5 weeks showed varying hypoglycemic and anti-hyperglycemic effect. In normal rats, reduction in blood glucose was almost negligible (approximately 4 per cent with 10 and 15 per cent diet). In mild and moderate diabetic rats, feeding of 5, 10 and 15 per cent diet caused a maximal reduction in blood sugar by 13.1, 16.3 and 21.4 per cent (NS, P<0.05 and 0.005) and 3.2, 5.58, 8.21 per cent (NS) respectively, Yadav *et al.* (2002). Khan *et al.* (1995), conducted an experiment to find out the effect of *M. koenigii* on carbohydrate metabolism using rats as experimental animals, and it showed significant hypoglycemic action.

Anti-hyperglycemic activity of leaves and bark extract of *M. koenigii* was evaluated in the streptozotocin induced diabetic in Wistar albino rats. The leaf and bark extract was demonstrated LD_{50}> 3 g/kg and LD_{50}> 3.6 g/kg respectively with low toxicity. Remarkable loss body weight retrieval (+14.37 g) was demonstrated by using *M. koenigii* leaf aqueous extract. Among all the different polarity of leaf and bark extracts, the aqueous and methanolic leaf extract at the dose levels of 300 mg/kg body weight produced a significant decrease in fasting blood-glucose level by 64.16 and 60.84 per cent respectively with respect to be initial fasting blood-glucose level after 15 days of the treatment was reported by Sahu *et al.* (2013).

Xie *et al.* (2006), observed curry leaf (*M. koenigii*) extract possesses the property to decrease blood cholesterol and blood-glucose levels in diabetic ob/ob mice. Mice received daily intraperitoneal injections of 80 mg/kg curry leaf extract for 10 consecutive days. The extract significantly decreased blood cholesterol level from 277.6 ± 16.6 mg/d (day 0) to 182.0 ± 15.3 mg/d (day 10, $p < 0.01$ compared with the change in the vehicle group). The extract also considerably decreased blood-glucose level from 387.0 ± 15.6 mg/dl (day 0) to 214.0 ± 26.6 mg/dl (day 10, $p < 0.01$). In addition, the body weight was reduced after extract treatment. These data suggested that curry leaf may be proven to be of clinical importance in improving the management of high-cholesterol level and type 2 diabetes.

Anticancer Activity

M. koenigii, a medicinally important herb of Indian origin and its leaves have a rich source of polyphenols used to inhibit the proteolytic activity of the cancer cell proteasome, and cause cell death (Noolu *et al.*, 2013). Girinimbine has been isolated from stem bark of *M. koenigii*, was used to show the in-vitro anti-tumor promoting activity by measuring the percentage inhibition of induced early antigen EA of Epstein Barr virus EBV on the surface of Raji cells. This study results shown that the girinimbine strongly inhibited the induction of EA of EBV more than 90 per cent when tested at 16.0 and 32.0 µg/ml Yih *et al.* (2012).

Syam *et al.*(2011), isolated girinimbine carbazole from the bark of *M. Koenigii* and its significantly induced programmed cell death in HepG2 cells suggesting the necessity for further evaluations in preclinical human hepatocellular carcinoma models. Bhattacharya *et al.*(2010)study results provide evidence for the involvement

of death receptor mediated extrinsic pathway of apoptosis in mahanine induced anticancer activity in MOLT-3 cells, but not in K562 cells, which are deficient in FasFsL. Additionally, three carbazole alkaloids pyrayafoline, mahanine, and murrafoline, showed significant activity against HL-60 cells by inducing apoptosis through of capsase-9/capsase-3 pathway, through mitochondrial dysfunction (Ito *et al.,* 2006). Roy *et al.* (2004), observed the down regulation of cell survival factors by activation of capsase-3 through mitochondrial dependent pathways and disruption of cell cycle progression could be an additional mechanism. In addition, the mean number of neoplasms in the colon and intestines were significantly low as demonstrated by morphological and histological studies in the *M. Koenigii* treated animals (Khan *et al*., 1996).

The effect of extract of *M. koenigii* on parameters studied to evaluate the antitumor activity enabled to conclude that it has significant antitumor activity. Nevertheless, further investigations are essential for the isolation of the principle of extract of *M. koenigii* and its mechanism of action (Muthumani *et al.,* 2009). Khanum *et al.* (2000) studied the antioxidant potential of curry leaves in rats treated with a known chemical carcinogen, dimethyl hydrazine hydrochloride (DMH). Observed a 50 per cent reduction was seen in the micronuclei induced by DMH and a 30 per cent reduction in the activity of γ-glutamyltranspeptidase when the rats were fed a curry leaf-supplemented diet (Khanum *et al.,* 2000). These results indicated that curry leaves have been high potential as reducer of the toxicity of DMH.

Antimicrobial Activity

Benzoisofuranone derivatives along with six known carbazole alkaloids and three known steroids were isolated from stem bark of *M. Koenigii*. These compounds are found to be effective in range 3.13 - 100 µg/ml concentration (Rahmanand Gray, 2005). Literature survey revealed that methanolic extract of 21 plant species were screened for in vitro anti-bacterial activity against multi resistant bacterial isolates including Gram positive and Gram-negative strains. Study showed that *M. koenigii* shown maximum antibacterial activity and *Staphylococcus epidermidis* was significantly inhibited by *M. koenigii* (Panghal *et al.,* 2011).

Mahanimbine, mahanine and murrayanolare three carbazole alkaloids isolated from the acetone extract of the fresh leaves of *M. Koenigii.* Among them, murrayanol showed an IC50 of 109 µg/ml against hPGHS-1 and an IC50 of 218 µg/ml against hPGHS-2 in anti-inflammatory assays, while mahanimbine displayed antioxidant activity at 33.1 µg/ml. All these three carbazole alkaloids were mosquitocidal and antimicrobial and exhibited topoisomerase, I and II inhibition activities (Furukawa *et al*., 1986). Some of the carbazole alkaloids isolated from *M. koenigii* have also been studied for their anti-TB activity (Choi *et al.,* 2006).

Antibacterial Activity

The 3 carbazole alkaloids *viz.* mahanine, mahanimbine, andmahanimbicine and essential oils from the leaves of *M. koenigii* were evaluated for the effects on growth of five antibiotic-resistant pathogenic bacteria and three tumor cell lines (MCF-7, P388 and Hela). Mahanimbine and essential oil demonstrated potent dose-

dependent antibacterial and cytotoxic effect (<=5.0 µg/ml). Additionally, significant antitumor activities against MCF- 7, Hela and P388 cell lines were also noted (Nagappan *et al.*, 2011; Kusuma *et al.*, 2011). Erkan (2012), observed the complete inhibition of growth of *L. innocua* with both Solvent-free microwave extraction(SFME) and conventional hydro-distilled oil essential oils, at 400 and 600 µg/ml (minimum inhibitory concentration), respectively. The SFME-essential oil at 300 µg/ml provided 92 per cent inhibition and indicating it has potential as a natural antimicrobial agent. Das and Biswas (2012), reported the leaves of *M. Koenigii* ethyl acetate extract to have antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus* (Gram positive), and dichloromethane extract showed antibacterial activity against *Pasteurella multocida* and *Proteus vulgaris* (Gram negative).

Anthelmintic Activity

Methanolic extract of *M. koenigii* showed anthelmintic activity against *Pheretima posthuma* worms in a dose dependent manner giving the shortest time of paralysis and death with 100 mg/ml concentration (Anil *et al.*, 2011). The results showed that methanolic extract cause paralysis at 18 min and the time of death at 45 min against the earth worm. Uma *et al.* (2010), studied ethanolic and aqueous extracts from the *M. koenigii* leaves were investigated for their anthelmintic activity against *Pheretima posthuma*. Three concentrations (25, 50, and 100 mg/ml)of each extract were studied in activity, which involved the determination of time of paralysis and time of death of the worm. Results showed that both the extracts exhibited significant anthelmintic activity at highest concentration of 100 mg/ml.

Antiamnesic Activity

Vasudevan and Parle (2009), investigated the effects of *M. koenigii* leaves (MKL) on cognitive functions, brain cholinesterase activity and total serum cholesterol level in young and aged mice fed orally with a diet containing 2 per cent, 4 per cent and 8 per cent w/w of MKL for 30 days consecutively. The memory scores were measured using various exteroceptive and interoceptive behavioral models. The *M. koenigii* leaves diets produced a significant dose-dependent improvement in the memory scores of young and aged mice and significantly reduced the amnesia induced by scopolamine (0.4 mg/kg, i.p.) and diazepam (1 mg/kg, i.p.). Similarly, brain cholinesterase activity and total cholesterol levels were reduced by the *M. koenigii* leaves diets (Vasudevan and Parle, 2009). Iyer and Mani(1990) studied dose dependent memory improvement in young and aged mice by the administration of ethanolic extracts of *M. koenigii* leaves for 15 days. The results showed that *M. koenigii* leaves produced significant dose-dependent improvement in the memory scores of young and aged mice and significantly reduced the amnesia induced by scopolamine (0.4 mg/kg, intraperitoneally) and diazepam (one mg/kg, intraperitoneally). In addition the results also indicated to reduce the brain cholinesterase activity and total cholesterol level.

Cytotoxic Activity

In leaf extract of *M. koenigii,* the ethyl acetate and dichloromethane soluble partitionates showed less cytotoxicity than n-hexane fraction was observed Das and

Biswas, (2012). Ito *et al.* (2006) isolated 10 carbazole alkaloids from *M. koenigii* and examined their effects on the growth of the human leukemia cell line HL-60. Three carbazole alkaloids, mahanine, pyrayafoline-D and murrafoline-I, showed significant cytotoxicity against HL-60 cells.The isolated carbazole alkaloid koenolinefrom root bark of *M. koenigii* exhibited the cytotoxic activity against the KB cell culture system (Manfred *et al*., 1985;Knölker and Bauermeister,1990; Knölker and Bauermeister, 1993). Koeniginequinone A and koeniginequinone B, isolated from the stem bark of *M. koenigii*, showed cytotoxic activity (Saha and Chouwdhury, 1998; Knölker and Reddy, 2003).

Conclusion

Nowadays, ethno-botanical and traditional uses of natural compounds, particularly of plant origin achieve much attention as they are well tested for their efficacy and generally believed to be safe for human use. An ethno-botanical approach signifies an effective method which may increase the outcomes of phytochemical research. The health properties of native Indian plants are limited. The enormous number of edible plants used as foods and medicines by the Indian population creates opportunities for the discovery of the novel physiologically active compounds. Comprehensive screening of literature offered on *M. koenigii* exposed the very fact that is a common remedy among the varied ethnic teams, Ayurveda practitioners for treatment of diversity of ailments. However, little or no efforts are placed by the scientific community to find the useful potential of this plant. *M. koenigii* has been screened for a few pharmacological activities and found to possess anti-diabetic, anti-cancer, cytotoxic, antiulcer, anti-diarrheaactivity, antioxidant property, antibacterial and antimicrobial drug potential and many other helpful therapeutic properties. Furthermore, alternative components of plant like seeds, leaves and seed oil, that too possesses vital medicinal advantages, has to be evaluated scientifically for their medicinal potential. Hereafter, the isolated principles from the plant have to be required to be evaluated victimization scientific experimental animal models and clinical trials to understand the molecular mechanism of action, in detection of lead molecule from natural resources.

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