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Section A – Basic Sciences; Section B – Applied and Technological Sciences; Section C – Allied Sciences

Available online at www.ijit.webs.com**Review Article****BIOCHEMISTRY AND PHARMACOLOGY OF AN INEVITABLY IMPORTANT PLANT *MURRAYA KOENIGII* SPRENG (RUTACEAE)****DEEPTI DUA² AND NUPUR S SRIVASTAV^{1*}**¹Amity Institute of Biotechnology, Sector-125 Amity University, Noida-201303 (UP), India²Amity Institute of Biotechnology, Sector-125 Amity University, Noida-201303 (UP), India
nsinha@amity.edu, ddua@amity.edu**ABSTRACT**

Murraya koenigii is a medicinal plant having high antioxidant potential. It is native to India. Aromatic leaves are highly valued as seasoning in southern and west-coast Indian cooking. A Pharmacological and Phytochemical study of the plant reveals the presence of bioactive compounds like carbazole alkaloids and polyphenols which are widely used for the prevention and treatment of various diseases. It is medicinally used as anti-bacterial, anti-trichomonal, anti-tumor, hepatoprotective, anti-inflammatory etc. Being a potential source of antioxidant enzymes it easily neutralizes free radical production and is highly evaluated in therapeutics. The present review emphasises on the potential of this plant in various aspects for human welfare and the therapeutics can be further analyzed. More studies are required to study the kinetics of the plant and its constituents.

KEY WORDS: *Murraya koenigii*, bioactive compounds, therapeutic properties, antioxidant enzymes**INTRODUCTION**

Murraya koenigii, a tree which produces aromatic leaves, is sub-tropical tree of the family Rutaceae, which is native to India. Its leaves are used in many dishes in India and neighbouring countries. Often used in curries, the leaves generally go by the name "curry leaves", though they are also translated as "sweet neem leaves" in most Indian languages (as opposed to ordinary neem leaves which are bitter).

It is a small tree, growing 4–6 m (13-20 feet) tall, with a trunk up to 40 cm diameter. The leaves are pinnate, with 11-21 leaflets, each leaflet 2–4 cm long and 1–2 cm broad. They are highly aromatic. The flowers are small, white, and fragrant. The small black shiny berries are edible, but their seeds are poisonous. In their fresh form, they have a short shelf life, and they don't keep well in the refrigerator. They are also available dried, though the aroma is largely inferior.

The leaves of *Murraya koenigii* are also used as a herb in Ayurvedic medicine. They are much valued as an anti-diabetic (1,2), antioxidant (3), antimicrobial, anti-inflammatory, hepatoprotective,

anti-hyper cholesterolemic, etc. They are rich in Vitamin C, and minerals calcium, phosphorus and iron, nicotinic acid and therefore serve as good nutritional supplements.

Curry leaves have the qualities of an herbal tonic. It has many herbal medicinal properties and is used widely in Ayurveda for its therapeutic properties (4). Curry leaves are your best bet against morning sickness during pregnancy. This prevents nausea and dry vomiting. These leaves have been used for proper functioning and strengthening of stomach when taken early in the morning. This is known to reduce stomach disorders, constipation and even dizziness. They are also known to be good for health of your hair and prevent premature greying of hair, nourish the hair root, and also are a growth stimulant for hair. A few curry leaves can be chewed daily to reduce weight and improper digestion.

A study published by P. Muthumani, et al., in the "Journal of Pharmaceutical Sciences and Research" in 2009 showed a significant decrease in the cancer cell number and tumor weight of rats with Dalton's ascitic lymphoma after treatment with curry leaf

extracts (5). The extract also showed significant anti-inflammatory activity in the rats. Chronic inflammation is a precursor to a number of diseases, including cancer, atherosclerosis and Alzheimer's disease.

Nutritional Value of Curry Leaves

The main nutrients found in curry leaves are carbohydrate, energy, fiber, calcium, phosphorous, iron, magnesium, copper and minerals. It also contains various vitamins like nicotinic acid and vitamin C, vitamin A, vitamin B, vitamin E, antioxidants, plant sterols, amino acids, glycosides and flavonoids. And nearly zero fat (0.1 g per 100 g) is found in curry leaves.

Some of the other chemical constituents present in curry leaf include carbazole alkaloids. Research studies he at the Department of Home Economics, Kenmei Women's Junior College, Hyogo in Japan showed that alkaloids found in curry leaves possess antioxidant properties. Carbazole alkaloids include mahanimbine, murrayanol, mahanineoenimbine, O-methylmurrayamine A, O-methylmahanine, isomahanine, bismahanine and bispyrayafoline. Further studies conducted at the Department of Horticulture at Michigan State University suggested that these chemicals had insecticidal and antimicrobial properties, specifically mosquitocidal properties.

Research studies conducted by Mylarappa B. Ningappa et al. at Jawaharlal Nehru Center for Advanced Scientific Research, Molecular Parasitology and Protein Engineering Laboratory, Bengaluru, India, have indicated that curry leaves or *Murraya Koenigii* as a good source of antioxidants. The presence of various vitamins like vitamin A, B, C and E help in reducing oxidative stress and free radical scavenging. Curry leaves can be added to your curries, vegetable stews and soup. They are also available in dried powder form.

Medicinal properties of curry leaves in Ayurveda

Curry leaves is an inexpensive condiment which has excellent medicinal properties (6). The leaves, fruits, bark and roots of curry leaf tree are used in indigenous medicine as tonic, stimulant and antifatulent. Curry leaves are extremely high in antioxidants, plant sterols, amino acids, glycosides, proteins and flavanoids. A few uses of curry leaves in Ayurveda are:

- **Gastrointestinal properties:** Curry leaves are an herbal tonic which strengthen and promote the function of stomach. They act

as mild laxatives and stimulate the digestive enzymes. In Southern India, curry leaves are eaten raw as a homeopathic remedy for dysentery and diarrhea. At the Sudhakarrao Naik Institute of Pharmacy, a study done on rats by S.V. Tembhrane and D.M. Sakarkar showed curry leaf extracts to increase gastrointestinal motility. The motility effects were felt by rats who both had and had not been given constipating agents. The results of the study showed great promise as a remedy for abdominal pain, constipation and gastroparesis (7). Usage of curry leaves is recommended as a cure for gastrointestinal issues in Ayurveda as they are considered to possess mild laxative properties.

- **Kidney disorders:** Research studies conducted by Ashish Pagariya and Maithili, V. concluded that the carbazole alkaloids present in curry leaves or *Murraya Koenigii* had anti-diarrheal properties. Experiments on lab rats showed that carbazole extracts from curry leaves had significantly controlled castor oil induced diarrhoea. It is a potent blood purifier and restorative of the degenerated blood cells. It helps in the building up and strengthening of liver, and also regulates metabolism of fatty acids associated with kidney disorders. The juice of the roots of curry leaf tree is beneficial in the treatment of pain helps in the breakdown of food. Tender curry leaves are useful in dysentery, diarrhea and piles treatment. Also used as a gall bladder stimulant.
- **Diabetes:** It is used in the treatment of diabetes due to heredity as well as diabetes caused due to obesity. It helps in reducing weight and hence is considered effective in reducing the level of sugar in blood. Perhaps one of the biggest health benefits of curry leaves is its use in diabetes control. Research conducted at the Department of Biochemistry and Molecular Biology in University of Madras, Chennai had showed that anti-hyperglycemic properties of curry leaves were beneficial in controlling blood glucose levels in diabetic rats.
- **Lowering cholesterol levels:** Curry leaves are also known to reduce bad LDL cholesterol level. Studies conducted at the Department of Biochemistry in University of Kerala, India have shown that curry leaves have the potential to reduce LDL cholesterol levels.

- **Radio-protective and chemo-protective properties:** Studies on the extracts of curry leaves have shown positive results in reducing the effects of chemotherapy, radiotherapy, protection against chromosomal damage, protection of bone marrow and prevention of free radicals in the body.
- **Hair:** leaves are known to promote hair growth and inhibit premature greying of hair. They bring about the growth of new hair which is healthier with normal melanin pigment. Curry leaves are believed to help in strengthening hair roots. Dry curry leaves powder mixed in oil can be applied to your hair with quick massage. The paste from curry leaves could also be applied in case of gray hair. Doing these on a regular basis can improve hair growth. These leaves have the property to nourish the hair roots. New hair roots that grow are healthier with normal pigment.
- **Skin Care:** Curry leaves are also helpful in skin care. Curry leaves help in healing the burns, bruises and skin eruptions. The juice or paste of the leaves can be applied on burns, cuts, bruises, skin irritations for quick recovery.
- **Eye:** Curry leaves contain high amounts of vitamin A and are good for eyesight. Vitamin A contains carotenoids which protect cornea, the eye surface. Deficiency of vitamin A may cause night blindness, cloud formations in front of the eye and loss of vision loss in some cases. Fresh curry leaf juice helps in maintaining the health of the eyes. Fresh juice of curry leaves suffused in the eyes, makes them look bright. It also prevents the early development of cataract.
- **Insect bites:** The fruits of the citrus curry leaf trees are berries and are edible. The juice of the berries mixed with lime juice is applied over the insect stings and bites of poisonous insects for treatment.
- **Protects against pathogen attack:** Research on curry leaves has revealed that they are also effective against fighting bacterial and fungal infections. The leaf extracts from the plant have been comparable to popular anti-biotic drugs.
- **Other uses:** Curry leaves benefit a wide range of health conditions, such as gastric reflux, constipation, traveller's diarrhoea, athlete's foot and candida. Eating curry may be especially beneficial for cold, damp

conditions such as fungal infections, sluggish metabolism, slow digestion, colds and the flu.

It is traditionally used as antiemetic, antidiarrhoeal, febrifuge and blood purifier (9). The whole plant is considered to be a tonic and stomachic. The leaves are used extensively as a flavouring agent in curries and chutneys. The oil derived from the leaves is also applied externally to bruises and eruptions. Studies indicate that it possesses antioxidant, antibacterial, anticarcinogenic, anti-lipid peroxidative, hypoglycaemic and hypolipidemic properties.

Helpful Compounds in Curry leaves

Curry leaves have been studied and found to have many phenols, flavonols, aminoacids and alkaloids which show them to have high antioxidant capacity as well. Amino acids such as alanine, tryptophan, tyrosine are some of the many acids found in the leaves. Carbazole alkaloids such as koenigine, mahanimbine, muconicine were extracted and have been found to demonstrate anticancer properties and antioxidant properties. Curry leaves have both hypoglycemic effect and also help in reducing triglycerides count. These tests have been done only on animals and are in very preliminary stages of testing for humans.

Curry leaves in cancer

The chemical constituents found in curry leaves such as phenols are helpful in fighting cancers such as leukemia, prostate cancer and colorectal cancers. Research on curry leaves at the Department of Medical Chemistry in Meijo University, Japan showed evidence of cancer fighting properties in carbazole alkaloids extract from curry leaves.

A chemical called mahanin, present in curry leaves has been found to be effective against the cure of cancer cells by causing controlled cell death.

Curry leaves due to the presence of this chemical can cause selective death of prostate cancer cells. They are coming up as a new chemotherapeutic treatment of prostate cancer. Also found to be effective in case of cancers of the female reproductive organ.

Curry leaves in liver protection

Curry leaves contain a range of beneficial chemicals which support and protect the health of the liver. In a study published in Experimental and Toxicological Pathology by the University of Mumbai in 2010 (8), researchers discovered that curry leaf extract protected liver cells from oxidation, chemical damage

and cirrhosis. Curry leaf compared favorably alongside pharmaceutical medications in the study and demonstrated significant hepato-protective potential. If taken regularly, curry leaves protect the liver, ensuring healthy detoxification, and preventing liver cancer. Liver plays a major role in the digestive system and it needs to be protected from attack of free radicals as well as viral and bacterial attacks. Research on curry leaves indicated that the tannins and carbazole alkaloids present in curry leaves exhibited good hepato-protective properties. They are also helpful in protecting liver from various diseases such as hepatitis and cirrhosis.

Curry leaves in diabetes

Curry leaves are considered a good tonic for the spleen and pancreas and increase the number of cells of the islet of Langerhans which form insulin. They are rich in minerals and trace minerals such as iron, zinc and copper which are known to play a role in maintaining normal glucose levels in the blood. Hence, curry leaves may be effective in the treatment of diabetes.

Curry leaves are also significant in carbohydrate metabolism and restore the functions of liver and kidney enzymes which bring about the breakdown of carbohydrates. The antioxidant property of curry leaves is known to reduce the death of pancreatic cells and hence playing a crucial role in diabetes by reducing blood sugar levels.

Studies done on rats at the Department of Biochemistry and Molecular Biology at the University of Madras in India have shown an extract of curry leaves reduces oxidative stress on pancreatic cells and offers a therapeutic effect on damaged pancreatic cells in diabetic rats. The effects were comparable to those of the hypoglycemic drug glibenclamide and have great indications for use in humans (10).

Curry leaves in hair and skin care

All parts of the curry leaf tree can be utilized in preparing oil by steam distillation and applied on head to prevent premature graying of hair. Oil with curry leaves mixed in it provides nourishment to the hair root. Curry leaves are also known to induce hair growth and the new hair follicles are normal with normal concentration of pigments.

Studies have also reported that curry leaves can be used to maintain natural pigmentation of the skin, and is also known to possess some amount of sun protection factor. They are also known to improve the skin tone showing beautifying effects.

Curry leaves in neuro-protection

Studies indicated that chronic treatment with *Murraya koenigii* besides decreasing glycemic levels, offered neuroprotective benefits (11)

'Chutney' made with curry leaves, coriander, pepper and salt, taken with food regularly improves brain function. Taking bath once a week with essential oil made from curry leaves, using coriander leaves, gingelly oil, cow's milk and cumin is good for the brain, relieves vertigo.

Through recent research studies, for those seeking a holistic and alternative medicine approach to improving memory loss, the use of curry has been found to potentially improve cognitive function in the elderly. For senior adults searching for improved cognitive and memory function, growing curry plants has become a feasible option.

Curcumin is an ingredient of curry powder. One study showed that curcumin eliminated deposits of plaque in the brain that are thought to cause Alzheimer's. The curcumin in tumeric, as well as the other spices in curry powder, are reputed to sharpen the cognitive powers of the brain and lift the emotions. By regularly consuming curry, fine motor skills, such as handwriting improve and overall mental function is enhanced. Positive thinking and renewed interest in life also seem to increase as a result of consuming curry.

Free Radicals

All living organisms utilize oxygen to metabolize and use the dietary nutrients in order to produce energy for survival. Oxygen thus is a vital component for living. Oxygen mediates chemical reactions that metabolize fats, proteins, and carbohydrates to produce energy. While oxygen is one of the most essential components for living, it is also a double edged sword. Oxygen is a highly reactive atom that is capable of becoming part of potentially damaging molecules commonly called "free radicals."

These free radicals are capable of attacking the healthy cells of the body. This may lead to damage, disease and severe disorders. Cell damage caused by free radicals appears to be a major contributor to aging and diseases like:

- cancer
- heart disease
- decline in brain function
- decline in immune system etc.

Overall, free radicals have been implicated in the pathogenesis of at least 50 diseases. Since free radicals contain an unpaired electron they are

unstable and reach out and capture electrons from other substances in order to neutralize themselves. This initially stabilizes the free radical but generates another in the process. Soon a chain reaction begins and thousands of free radical reactions can occur within a few seconds on the primary reaction.

Control of free radicals

Normally free radical formation is controlled naturally by various beneficial compounds known as antioxidants. When there is deficiency of these antioxidants damage due to free radicals can become cumulative and debilitating.

Antioxidants are capable of stabilizing, or deactivating, free radicals before they attack cells.

Reactive oxygen species (ROS)

ROS is a term which encompasses all highly reactive, oxygen-containing molecules, including free radicals. Types of ROS include the hydroxyl radical, hydrogen peroxide, the superoxide anion radical, nitric oxide radical, singlet oxygen, hypochlorite radical, and various lipid peroxides. These can react with membrane lipids, nucleic acids, proteins and enzymes, and other small molecules.

Oxidative stress

Oxidative stress means an unbalance between pro-oxidants and antioxidant mechanisms. This results in excessive oxidative metabolism. This stress can be due to several environmental factors such as exposure to pollutants, alcohol, medications, infections, poor diet, toxins, radiation etc. Oxidative damage to DNA, proteins, and other macromolecules may lead to a wide range of human diseases most notably heart disease and cancer.

Antioxidants

Antioxidants are substances that may protect your cells against the effects of free radicals. Antioxidants have the ability to scavenge free radicals and therefore reduce oxidative stress. Antioxidative compounds oppose reactive oxygen species (12), hinder oxidative degradation of lipids and consequently enhance the nutritional value of food (13).

The curry leaf is nutritionally rich as it contains abundant quantities of vitamin E, which is an efficient antioxidant. Curry leaf is a good source of vitamin A, calcium and folic acid. Curry leaves offer antioxidant support and helps prevent cancer of the skin and stomach. In a study published in Nutrition Research by Jawaharlal Nehru University in 2003, curry leaves significantly reduced the incidence of cancer cells in the stomach and skin tissues. The

protective and chemopreventative mechanism in curry leaves is attributed to the high level of antioxidants found in the plant, and to increasing the body's own antioxidants, such as superoxide dismutase (14).

Interest in greater use of curry leaf has been stimulated since its high antioxidant and anticarcinogenic potential were reported (15, 16). In a study published in Plant Foods for Human Nutrition in 2009, several Indian leafy vegetables were compared for their antioxidant activity. Interestingly, total antioxidant activity and free radical scavenging activity were highest in curry leaves. This shows that curry leaves and their extract hold great promise to mediate the immune system and metabolic processes.

Antioxidants from food

There are several nutrients in food that contain antioxidants. Vitamin C, vitamin E, and beta carotene are among the most commonly studied dietary antioxidants (17).

Vitamin C is the most important water-soluble antioxidant in extracellular fluids. Vitamin C helps to neutralize ROS in the water or aqueous phase before it can attack the lipids.

Vitamin E is the most important lipid soluble antioxidant. It is important as the chain-breaking antioxidant within the cell membrane. It can protect the membrane fatty acids from lipid peroxidation. Vitamin C in addition is capable of regenerating vitamin E. Beta carotene and other carotenoids also have antioxidant properties. Carotenoids work in synergy with vitamin E (18, 19).

Antioxidant deficiencies

A diet low in fats may impair absorption of beta carotene and vitamin E and other fat-soluble nutrients. Fruits and vegetables are important sources of vitamin C and carotenoids. Whole grains and high quality vegetable oils are major sources of vitamin E. Many plant-derived substances are known as "phytonutrients," or "phytochemicals". These also possess antioxidant properties. Phenolic compounds such as flavonoids are such chemicals. These are found in several fruits, vegetables, green tea extracts etc.

Antioxidants within the human body

Apart from diet, the body also has several antioxidant mechanisms that can protect itself from ROS mediated damage. The antioxidant enzymes – glutathione peroxidase, catalase, and superoxide dismutase (SOD) are such enzymes. They require micronutrient cofactors such as selenium, iron, copper, zinc, and manganese for their activity. It has

been suggested that an inadequate dietary intake of these trace minerals may also lead to low antioxidant activity.

- **Superoxide dismutase:** One of the most effective intracellular enzymatic antioxidants is superoxide dismutase (SOD) (EC1.15.1.1). Superoxide dismutase is the antioxidant enzyme that catalyses the dismutation of $O_2^{\bullet-}$ to O_2 and less-reactive species H_2O_2 . While this enzyme was isolated as early as 1939, it was only in 1969 that McCord and Fridovich proved the antioxidant activity of SOD (43).
- **Catalase:** Catalase (EC 1.11.1.6) is an enzyme present in the cells of plants, animals and aerobic (oxygen requiring) bacteria (21). Catalase is located in a cell organelle called the peroxisome. The enzyme very efficiently promotes the conversion of hydrogen peroxide to water and molecular oxygen. It has one of the highest turnover rates for all enzymes. One molecule of Catalase can convert 6 million molecules of hydrogen peroxide to water and oxygen each minute.
- **Glutathione peroxidase (GPx):** There are two forms of the enzyme glutathione peroxidase, one of which is selenium-independent (glutathione-S-transferase, GST, EC 2.5.1.18) while the other is selenium-dependent (GPx, EC 1.11.1.19). These two enzymes differ in the number of subunits, the bonding nature of the selenium at the active centre and their catalytic mechanisms. Glutathione metabolism is one of the most essential of anti-oxidative defence mechanisms (21). The substrate for the catalytic reaction of GPx is H_2O_2 , or organic peroxide ROOH. GPx decomposes peroxides to water (or alcohol) while simultaneously oxidising GSH. Significantly, GPx competes with catalase for H_2O_2 as a substrate and is the major source of protection against low levels of oxidative stress.
- **Vitamin C:** Vitamin C (ascorbic acid) is a very important, and powerful, antioxidant that works in aqueous environments of the body, such as is present in the lungs and in the lens of the eye. Its primary antioxidant partners are Vitamin E and the carotenoids, as well as working along with the antioxidant enzymes. Vitamin C protects membranes against oxidation (22). The positive effect of Vitamin C in reducing the incidence of stomach cancer is most probably due to the inhibitory action in the generation of *N*-nitroso compounds by interrupting the reaction between nitrites and amine groups. A consistent protective effect of Vitamin C has also been found in lung and colorectal cancer. Recent studies indicate the ability of ascorbic acid to regulate factors that may influence gene expression, apoptosis and other cellular functions (23). In many studies Vitamin C protects against cell death triggered by various stimuli and a major proportion of this protection has been linked with its antioxidant ability. Studies of the anti-apoptotic activity of Vitamin C have revealed a role of Vitamin C in modulation of the immune system.
- **Vitamin E:** Vitamin E is a fat-soluble vitamin that exists in eight different forms. α -tocopherol is the most active form of vitamin E in humans and is a powerful biological antioxidant which is considered to be the major membrane bound antioxidant employed by the cell (24). Its main antioxidant function is protection against lipid peroxidation (25). It has been demonstrated that the intake of Vitamin E [200 IU (international units)/day] reduced the incidence of colorectal cancer by triggered apoptosis of cancer cells by inducing p21waf1/cip1, a powerful cell cycle inhibitor (26). Generally, the protective effect of Vitamin E is a result of the inhibition of free radical formation and activation of endonucleases. Other study reported negative results for Vitamin E in combination with Vitamin C and beta-carotene to prevent colorectal cancer adenoma over a period of 4 years (27). Since Vitamin C regenerates Vitamin E, it has been proposed that addition of Vitamin E hinders the protective effect of Vitamin C against oxidative damage (28).
- **Glutathione:** The major thiol antioxidant is the tripeptide, glutathione. Glutathione (GSH) is a multifunctional intracellular non-enzymatic antioxidant. It is considered to be the major thiol-disulphide redox buffer of the cell. Glutathione is highly abundant in the cytosol (1–11 mM), nuclei (3–15 mM), and mitochondria (5–11 mM) and is the major soluble antioxidant in these cell compartments (29). The reduced form of glutathione is GSH, glutathione, and the oxidised form is GSSG, glutathione disulphide. Oxidised glutathione GSSG is

accumulated inside the cells and the ratio of GSH/GSSG is a good measure of oxidative stress of organisms (30).

The main protective roles of glutathione against oxidative stress are that (i) glutathione is a cofactor of several detoxifying enzymes against oxidative stress, e.g. glutathione peroxidase (GPx), glutathione transferase and others; (ii) GSH participates in amino acid transport through the plasma membrane; (iii) GSH scavenges hydroxyl radical and singlet oxygen directly, detoxifying hydrogen peroxide and lipid peroxides by the catalytic action of glutathione peroxidase; (iv) glutathione is able to regenerate the most important antioxidants, vitamins C and E back to their active forms; glutathione can reduce the tocopherol radical of vitamin E directly, or indirectly, via reduction of semi-dehydroascorbate to ascorbate.

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