

## **Mutagenic, Antimutagenic and Anticarcinogenic Properties of Medicinal Plants with Special Reference to *Melissa officinalis*: A Review**

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### **Abstract**

Mutations are the cause of innate metabolic defects in cellular systems, triggering morbidity and mortality in living organisms. Mutagens are not only involved in genotoxicity and carcinogenicity but also involved in the inception of several chronic diseases. One of the best ways to minimize the detrimental effects of mutagens is by use of natural antimutagens. Medicinal herbs have been on the forefront whenever we talk about antimutagenic and anticancer remedies. Medicinal plants have a vital role in the prevention and treatment of cancer. Present review attempts to furnish a brief overview on mutagenic, antimutagenic and anticarcinogenic properties of medicinal plants.

**Keywords:** Mutagenic, anticarcinogenic, medicinal herbs, *Melissa officinalis*.

### **Introduction**

For a long time plants have been providing essential nutritional values, medicinal properties and notable physiological effect to life and are a good source of food. Traditional medicine refers to the application, approach, knowledge and belief in incorporating plant or animal based properties in remedies, singularly or in combination, for the purpose of treating or preventing disease as well as to maintain the well-being of an individual. Population rise, inadequate supply of drugs, prohibitive cost of treatments, side effects of several allopathic drugs and development of resistance to currently used drugs for infectious diseases have led to increased emphasis on the use of plant materials as a source of medicines for a wide variety of human ailments. As such herbal remedies have been used to cure a variety of disorders or conditions such as diabetes, cardiovascular problems, weight control, dermal infirmities, sexual malfunctions and of course cancer. According to World Health Organization, more than 70% of the world's population uses traditional medicine in order to fulfill their health necessities. The principles underlying herbal medicines are relatively simple, although they are quite distinct from conventional medicine and herbal medicine. India in general and Jammu and Kashmir in particular is a rich source of medicinal plants and a number of plant extracts are used against diseases in various systems of medicine like ayurvedic, unani and siddha (Table 1). Only a few of them have been scientifically explored. Plant derived natural products such as flavinoids, terpenes and alkaloids (Osawa *et al.*, 1990) has soon received considerable attention in recent years due to their diverse pharmacological properties including cytotoxic and cancer chemo preventive effects.

### **Medicinal plants as mutagens**

Mutations are the cause of innate metabolic defects in cellular systems, triggering morbidity and mortality in living organisms. The mutagens are involved in the initiation and promotion of several human diseases, including cancer (Bhagavathy *et al.*, 2011).

Mechanism of mutagenesis is complex however many mutagens and carcinogens may act through the generation of Reactive Oxygen Species (ROS). ROS may play a major role as endogenous initiators of degenerative processes, such as DNA damage and mutation, which may be related to cancer, heart disease and ageing (Maryam *et al.*, 2010).

Somatic gene mutations are the basic events for the conversion of a normal cell to a mutant cell. This mutant cell is then converted to malignant cell through several genetic changes. Several chemicals have been implicated in cancer causation. Some of these are sodium azide, ethidium bromide, hydroxyl amine, ethylnitronitrosoguanidine (MNNG), N, N' bis-(1-naphthyl) N, N'-diphenyl -1, 1 biphenyl-4, 4'-diamine ( $\alpha$ -NPD), etc. (Prabhu *et al.*, 2010). Since plants are used in many areas for a number of purposes, there are many studies on plant extracts that examine their mutagenic properties for safe consumption. Because many plants synthesize toxic substances for defense against organisms including viruses, bacteria, and fungi, these compounds could have potentially deleterious effects in humans. Although there are a number of studies on the mutagenic effects of plant extracts, e.g., positive results have been reported from the Ames test using extracts of *Crinum macowanii*, *Catharanthus roseus*, *Combretum mkhzense*, *Diospyros whyteana*, *Plumbago auriculata*, *Ziziphus mucronata*, and *Chaetacme aristata*

A hydroalcoholic extract of *Ocotea duckei* leaves was found to be mutagenic for the *Salmonella typhimurium* TA97a, TA100, and TA102 strains, with or without S9 mix (Marques *et al.*, 2003). Deciga-Campos *et al.*, (2006) found that *Gnaphalium* sp. and *Valeriana procera* extracts induced mutations of *S. typhimurium* TA98 with or without S9 mix and of TA100 with S9 mix, respectively. The tubers of *Gloriosa superba* were found to contain potent mutagenic properties in an Ames mutagenicity test on *Salmonella* (Hemaiswarya *et al.*, 2009). It was also shown that compounds present in the methanolic extracts of the leaves of *Alchornea castaneaefolia* and *Alchornea glandulosa* were mutagenic in an Ames test (dos Santos *et al.*, 2010).

### Medicinal plants as anticancer drugs

The natural world has been providing life saving antibiotics, nutritive supplements and our most potent anti-cancer drugs. Natural products especially those from plants have been a valuable source of new cancer drugs for many decades. Medicinal plants are the most exclusive sources of life saving drugs for the majority of the world's population. The use of plant products in the treatment of cancer has been of recent interest.

From thousands of years, plants have been utilized as medicines (Ruffa *et al.*, 2002). Major constituents of more than 50% of all the drugs in clinical use are natural products and their derivatives. One of the potential uses of plant-derived compounds is as antimutagenic agents (Calomme *et al.*, 1996; Ammar *et al.*, 2007). As a result of human civilization and global environmental pollution, the rate of mutations has increased and one of the ways to neutralize the effect of such mutagenic agents is to identify those substances that can antagonize their effect. Plants are the promising source of antimutagens which occur in them as secondary metabolites. These antimutagens may help in strengthening the cell defences against environmental mutagens/stress. Nowadays, there is an increasing interest in natural compounds that can act as protectors against diseases (Aydin *et al.*, 2004). Several therapeutic properties of medicinal plants are known in obstetrics and gynecology (Abo *et al.*, 2000), respiratory disorders (Neto *et al.*, 2002), skin disorders (Graf, 2000), cardiac diseases (Ankli *et al.*, 2002), and mental health (Ahmad *et al.*, 1998). It has been suggested that halving the rate of mutations would delay the onset of most cancers and might be adequate in the lifetime of many individuals (Loeb *et al.*, 2003). There are different classes of secondary metabolites present in the plants exhibiting antimutagenic activities.

From the earliest times, herbs have been prized for their pain-relieving and healing abilities and today we still rely largely on the curative properties of plants. According to World Health Organization, 80% of the people living in rural areas depend on medicinal herbs as primary healthcare system. The synthetic anticancer remedies are beyond the reach of common man because of cost factor. Herbal medicines have a vital role in the prevention and treatment of cancer and medicinal herbs are commonly available and comparatively economical. A great deal of

pharmaceutical research done in technologically advanced countries like USA, Germany, France, Japan and China has considerably improved quality of the herbal medicines used in the treatment of cancer. Some herbs protect the body from cancer by enhancing detoxification functions of the body. Certain biological response modifiers derived from herbs are known to inhibit growth of cancer by modulating the activity of specific hormones and enzymes. Some herbs reduce toxic side effects of chemotherapy and radiotherapy.

Scientists all over the world are concentrating on the herbal medicines to boost immune cells of the body against cancer. By understanding the complex synergistic interaction of various constituents of anticancer herbs, the herbal formulations can be designed to attack the cancerous cells without harming normal cells of the body (Larkin, 1983; Saxe, 1987).

Most plants synthesize toxic substances which act as a defensive mechanism against insects and herbivores. In addition to that, the poisonous substances may also affect organisms that feed on them including humans. Therefore, it is reasonable that while some medicinal plants may suppress the effects of mutagens, others may have toxic or mutagenic effects (Vicentini *et al.*, 2001). Thus, studies of their mutagenic as well as antimutagenic potential are necessary to establish the safe use of these medicinal plants.

Apart that, the plant has the potential to treat Herpes Simplex Virus infection, minimize inflammations and to reduce *in vitro* carcinogenic effects. *A. vasica*, also known as Malabar Nut Tree is part of Acanthaceae plant family which is used widely among Indians for the treatment of inflammation (Chakraborty and Brantner, 2001), cold, cough, chronic bronchitis (Amin & Mehta, 1959), cataract (Patel *et al.*, 2012), asthma, piles, glandular tumor & to cure fresh wounds (Ayyanar and Ignacimuthu, 2008; Dhuley, 1999; Palasuwan *et al.*, 2005). The pharmacological activities may be due to the presence of vasicine, vasicinone and vasicinol, which are the major alkaloids found in *A. vasica* (Padmaja *et al.*, 2011). *Carica papaya* (papaya) belongs to the family Caricaceae, native to all tropical countries. The plant is well known for its fruits & its parts are used for microbial infections (Sharmeen *et al.*, 2012), treating burns and wounds, fever, intestinal nematode infection, asthma, and gastric (Runnie *et al.*, 2004; Starley *et al.*, 1999; Stepek *et al.*, 2004). Moreover, according to Mazzio and Soliman (2009), the extract of papaya leave showed antitumor activity when tested in Neuro-2A cell lines.

### ***Melissa officinalis* used as antimutagenic and anticarcinogenic drug**

Lemon balm (*Melissa officinalis* L.) belonging to the Lamiaceae family is a perennial herb. It grows wildly in Europe and the Middle Asia and is used as aromatic, culinary and medical herb (Kato- Noguchi, 2003). This plant is successfully cultivated and popularized by the agricultural research organizations of Taiwan. It is also applied for tea and steeped wine manufactures in Taiwan due to its health profit. Reports indicated that lemon balm had many beneficial effects such as anti-bacterial, sedative, spasmolytic, mnemonic improvement, and could reduce excitability, anxiety, stress, gastrointestinal disorders and sleep disturbance (Mentle *et al.*, 2000; Perry *et al.*, 1999).

Many reports indicated that low polar extract of *Melissa officinalis* (lemon balm) leaves, especially its essential oil, had good antioxidant and antitumoral activities (DeSousa *et al.*, 2004; Marongiu *et al.*, 2004; Mimica-Dukic *et al.*, 2004). Dastmalchi *et al.*, (2008) demonstrated that ethanolic extract of lemon balm cultivated in Iran could present good antioxidant activity. Capecka *et al.*, (2005) also found that methanolic extracts of lemon balms cultivated in Poland had good radical scavenging ability. There is no thorough report concerning anti-proliferative activity of the polar extract from lemon balm leaves for cancer cells. Marnett and DuBois (2002) indicated that cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) are rate-limiting enzymes in the biosynthesis of prostaglandins. COX-1 is constitutively expressed in most mammalian tissues and plays a role in tissue homeostasis. COX-2, an inducible isoform, could be stimulated by carcinogens, growth factors, inflammatory cytokines and tumor promoters (Shen *et al.*, 2008). Abnormal or excessive COX-2 expression has been suggested in many pathological conditions such as angiogenesis, inflammation and tumor promotion (Rao *et al.*, 2001). An inhibition of the activity or expression of COX-2 was an important target for antiinflammation or cancer chemoprevention (Shen *et al.*, 2008). However, the suppressing activity of the extract of lemon balm leaves is still unavailable.

**Table 1. A list of some of the important medicinal plants of Jammu and Kashmir used in treatment of Cancer and various other diseases.**

S. No.	Botanical Name	Common Name	Family	Chemical Constituents	Uses
1.	<i>Artemisia annua</i> L.	Sweet Wormwood	Asteraceae	Artemisinin, Camphor	Cancer treatment, Parasite, Malaria.
2.	<i>Aconitum heterophyllum</i>	Atis root, Atis	Ranunculaceae	Alkaloids, Atisin	Analgesic, anti-inflammatory, anti-pyretic, aphrodisiac, induce appetite.
3.	<i>Bergenia ciliata</i>	Zakhm-e-hayat	Saxifragaceae	Bergenin, Catechin, Gallic acid	To dissolve kidney stones and as a diuretic.
4.	<i>Chrysanthemum cinerariifolium</i> L.	Pyrethrum, Insect Plant	Asteraceae	Yejuhua lactone, Asteglasine, Sesquiterp, Amyrins, Lupeol, Arteglasin, Acacetin, Flavinoids, Linalool, Thymol	Wide variety of medicinal properties, including anti-HIV-1, antibacterial and antimycotic, acts as natural source of insecticide.
5.	<i>Bupleurum falcatum</i>	Sickle leaf hare's ear	Apiaceae	Tripenoid Saponins, Saikosaponin a, Saikosaponin b4, Saikosaponin c, Olyscaccharides, Bupleurans	Anti-inflammatory, Antitussive, Diaphoretic, Hepatoprotective.
6.	<i>Ferula jaeschkeana</i> L.	Heeng	Apiaceae	Resin, Endogenous gum, Volatile oil, Asaresinotannols, Ferulic acid, Umbelliferone	To treat tumors, chronic wounds.
7.	<i>Juglans regia</i>	Walnut	Juglandaceae	Nucin, mucilage, albumin, mineral matter, cellulose and water.	Treatment of skin troubles, anti-scorbutic pickle, sore and slightly ulcerated throats.
8.	<i>Melissa officinalis</i>	Lemon balm	Lamiaceae	Trans-ocimene, cis-ocimene, cis-3-hexenol, citronellal, linalool, geraniol.	Antibacterial activity, Antioxidant
9.	<i>Origanum vulgare</i>	Oregano	Limaceae	Carvacrol, thymol, limonene, pinene, ocimene, caryophyllene	Antioxidant, Antimicrobial activity.
10.	<i>Podophyllum hexandrum</i> Royle	Indian Mayapple	Berberidaceae	Podophyllin	Anticancerous
11.	<i>Rumax nepalensis</i> L.	Jangli Palak	Polygnaceae	Anthraquinone, Nephthaline, Chrysophanol, Glucopyranoside, Nepodin.	Applied to skin sores, Syphilitic ulcers
12.	<i>Scutellaria species</i>	Blue Skullcap, Hoodwort, Mad dog Skullcap	Limiaceae	Flavinoids, diterpenes, tannin, beta elemene, calamenene	Antitumor, hepatoprotective, antioxidant, anticonvulsant, antibacterial, antiviral.
13.	<i>Taxus wallichiana</i> Zucc.	Himalayan Yew	Taxaceae	Abeo-baccatin, bujanone, bujanol.	Anticancer drug, paclitaxel.

## Conclusion

Untoward mutations are associated with a number of serious diseases for which useful medications are few and treatment is often limited to deal with symptomatology, many of the environmental pollutants, residues of pesticides and toxins present in food and drugs are common agents of mutagenic damage in human population. Science has long acknowledged the value of healing substances found in nature, such as digitalis, aspirin, penicillin, insulin, steroids, etc. There has been a resurgence of interest, both scientifically and popularly, in the utilization of natural approaches. Experiments on cell lines and in animals demonstrated that herbal drugs having anticancer role by inducing apoptosis and differentiation, enhancing the immune system, inhibiting angiogenesis and reversing multidrug resistance. However, the mechanism of the anticancer role has not yet been fully elucidated. Further research is needed to explore the molecular mechanism of herbal drugs.

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