Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 4, 2015

Review Article

GERANIOL, A COMPONENT OF PLANT ESSENTIAL OILS–A REVIEW OF ITS PHARMACOLOGICAL ACTIVITIES

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Received: 11 Feb 2015 Revised and Accepted: 06 Mar 2015

ABSTRACT

Essential oils are a mixture of volatile and natural substances, identified and characterized by the strong odor, produced by aromatic plants as secondary metabolites. Their metabolites have a wide range of applications and have been commercially important to the pharmaceutical, food and cosmetic industries. One of the plants essential oil Geraniol, a monoterpene alcohol has the verity of pharmacological activities are reported in preclinical studies. Generally, monoterpenes are non nutritive dietary components found in the essential oils of citrus fruits and other plants. Geraniol has antibacterial, antiseptic, anti-inflammatory, *in vivo* and *in vitro* anticancer against in leukemia, hepatoma, melanoma and pancreatic cancer cell lines, and activity on lipid metabolisms and Mevelonate metabolisms. In this review, article highlights the important pharmacological activities of plant essential oil geraniol.

Keywords: Geraniol, **A**ntioxidants, Anticancer, Essential oil, Anti-inflammatory.

INTRODUCTION

Essential oils are also called volatile oils, are generally odorous aromatic. It is found in the various parts of the plant, and these are used in the cosmetic, medical and food industry [1]. These Essential oils are composed mainly of terpenes and phenilpropens, but the majority of essential oils contain predominantly (90%) terpenes [2]. These terpenes are in different forms as mono, di, try, tetra terpenes; in that mono terpenes have ten carbons, sesquiterpenes with fifteen carbons and diterpenes with twenty carbons [3]. These terpenes are isolated from many traditional and medicinal plants are using as the new class of pharmacological active molecules for various diseased conditions [4].

Recent trends of preclinical research focused on the herb oils that possess hypolipidemic, antiplatelet, antitumor or immune-stimulating properties that may be useful adjuncts in helping reduce the risk of cardiovascular disease and cancer [5]. It was found that, there were plenty of biologically active mixtures from the plant essential oils, mainly terpenoids like linalool, geraniol, boreneol, menthol, thujanol, citronnillol, α-terpineol and a variety of low molecular weight aliphatic hydrocarbons like phenols are thymol, carvacrol, eugenol, gaiacol and aromatic aldehydes are cinnamaldehyde, cuminal and phellandral [6]. Geraniol (fig. 1) (3, 7-dimethyl-2, 6-octadien-1-ol) an acyclic monoterpene mainly found in citurs fruits, lemongrass and aromatic herb oils [7]. Pure geraniol is colorless oily liquid and insoluble in water. It is primary part of rose oil, palmarosa oil, and citronella oil [8]. In this, review pointed out the various pharmacological effects of geraniol such as antimicrobial, antibacterial, anticancer, anti-inflammatory, anti-oxidant, HMG-CoA reductase activity, Neuroprotectivity and Hepatoprotectivity.

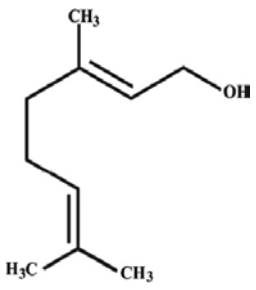

Fig. 1: Structure of geraniol

Antimicrobial activity

The success of treatments highly relates to the effectiveness of antimicrobial agents to eliminate the living microorganisms from an infected body [9]. Hence studying the antimicrobial activity of pharmacological agents is more important in therapeutics. Essential oils are mixtures of volatile secondary metabolites have antibacterial and antifungal activity [10]. Arldogan *et al.*, 2002 evaluated the antimicrobial activity of geraniol against bacteria and fungi by disc diffusion method individually and mixture of essential oils from *Rosa damascene*. In this case, geraniol inhibits *Staphylococcus aureus* strains and *Escherichia coli* strains by the inhibition zone was 8 mm reported [11].

Pattnaik *et al.*, 1997 reported that geraniol along with few other aromatic constituents of essential oils were tested the antimicrobial activity against eighteen bacteria including Gram-positive cocci and rods, and Gram-negative rods and twelve fungi three yeast-like and nine filamentous [12]. In terms of antimicrobial activity, geraniol showed maximum efficacy [13, 14]. Mesa Arango *et al.*, 2009 reported the antifungal activity of geraniol and citronellal chemotypes from the essential oils of *Colombian Lippia alba* (mill.) N. E, at lower concentration of geraniol shows significant antifungal activity against *Candida krusei* and *Aspergillus fumigates* with GM-MIC values of 49.6 microg/ml and 176.8 microg/ml respectively [15]. The potential antibacterial activity of geraniol was demonstrated by Singh *et al.*, 2012 [16] against Gram-positive and Gram-negative bacteria pathogens and antifungal activity against dermatophytes, yeasts Aspergillus species and Candida albicans strains [17, 18]

Anti-inflammatory activity

Inflammation is a complex biological response of vascular tissues against aggressive agents such as pathogens, irritants, or damaged cells [19]. The immunosuppressive activity of geraniol was reported *in vitro* with lymphocyte proliferation assays and *in vivo* in a rat cardiac allograft transplant model [20]. It is an example of isoprenoid drugs that enters the mevalonate pathway and is capable of reverting the genetic or pharmacological inhibition [21]. Since available anti-inflammatory drugs exerted an extensive variety of side effects, whereas geraniol showed significant anti-inflammatory activity with fewer side effects [22]. Tricarico *et al.* 2013 reported geraniol modulates the enzymatic pathway and partially rescues the inflammatory phenotype associated with defective mevelonic

pathway [23]. Another study, geraniol along with other natural terpenes prevent the nimesulide induced cellular damage and inflammation on hepatocytes [24]. Tsai *et al.*, 2011 reported the essential oil of *Cymbopogon martinii* has the high content of geraniol which modulate/reduce the inflammatory markers TNF-α, IL-1β, and IL-8 secretion [25]. Citronellol and geraniol, the major components of rose oil, activated peroxisome proliferator-activated receptor (PPAR) α and γ, and suppressed Lipopolysaccharide (LPS)-induced cyclooxygenase-2 (COX-2) expression in cell culture assays, and also suppresses TNF-α induced neutrophil adherence at low concentration [26], indicating the anti-inflammatory activity of geraniol [27].

Anticancer activity

Numerous epidemiological studies consistently showed that high intake of fruits, and vegetables present productive action against different cancer types [28]. Hence diet derived terpenoids represent promising anticancer agents [29]. Geraniol has been reported to possess *in vivo* and *in vitro* anticancer activity against various cancers. Soon young Paik *et al.*, 2005 reported the essential oils from *Zanthoxylum schinifolium* had thirty three compounds and geranyl acetate was the most abundant among the constituents, this showed anticancer activity against HepG2 human hepatoma cell lines [30]. It also reported that geraniol inhibit growth of leukemia and melanoma cells [31], Hepatoma cells [32] and pancreatic cancer cells [33]. Furthermore, the compound has no cytotoxic activity, indicating that geraniol exerts mainly cytostatic effects on human colon cancer cells [34]. Carnesecchi *et al.*, 2004 reported that the treatment with geraniol at low concentration potentiates 5-Fluorouracil mediated growth inhibition of human colon cancer cell lines [35]. The anticarcinogenic action of geraniol was studied when administered continuously during the initiation and selection phase of hepatocarcinogensis [36]. Our previous study reported the anticancer effect of geraniol against chemically induced oral cancer in rats [7]. Geraniol inhibits cancer cell proliferation by modulating the expression of Proliferative cell nuclear antigen (PCNA), cyclin D1, and c-fos against DMBA-induced hamster buccal pouch carcinogenesis [37]. It invokes a $p21^{cip1}$ and $p27^{kip1}$ dependent antiproliferative mechanisms in human pancreatic adenocarcinoma cells [38]. Geraniol synergistically inhibits cholesterol biosynthesis and proliferation of Hep G2 cell line [39].

Apoptosis is programmed cell death; it has been recognized to play an important role in the maintenance of tissue homeostasis and cancer by the selective elimination of excessive cells [40]. Additionally, induction of apoptosis of cancer cells is recognized as a valuable tool for cancer treatment [41]. Geraniol inhibits cancer cell proliferation and DNA damage while induction of apoptosis specifically related to anticancer effect against initial phases of hepatocarcinogenesis [42]. At a molecular level, geraniol inhibited AKT signaling and activated AMPK signaling, resulting in mTOR inhibition leads to apoptosis in PC-3 Prostate cancer cells [43]. Geraniol regulates the expressions of apoptotic proteins Bcl-2, Bax and cytochrome-C thereby initiates apoptosis in coloncarcinogenesis [44, 34], Prostate cancer [45] lung adenocarcinoma [46] and Hepatocarcinogenesis [36].

HMG-CoA reductase activity

3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate limiting enzyme in the biosynthesis of cholesterol and other sterols, catalyzes the formation of mevalonate, is required for DNA synthesis and proliferation [47]. Increased level of mevalonate promotes call growth and proliferation, so it is important to inhibit the mevalonate synthesis during the development of new chemotherapeutic agents [48]. Robin *et al.*, 2004 reported geraniol exerts HMG-CoA reductase activity in MCF-7 human breast cancer cell [49].

Antioxidant activity

Antioxidants have been reported to prevent oxidative damage caused by free radical and can be used in Cardiovascular, Neurological diseases, Cancer and Inflammatory diseases [50]. Our previous study reported the antioxidant activity of geraniol against 4-Nitroquinoline-1-oxide induced oral carcinogenesis in rats [7, 51]. Geraniol enhance the production of antioxidants by activating Nuclear factor E2-related factor 2 (Nrf2) is a key component to cellular redox homeostasis; thereby Product cellular oxidative damage caused by free radicals in the diseased model. [52]. Khan AQ *et al.*, 2013 reported geraniol protects 12-O-tetradecanoyl phorbol-13-acetate induced oxidative damage by expressions of antioxidant response markers, glutathione (GSH) content and the activity other antioxidant enzymes [53]. In addition, geraniol inhibits abnormal cell proliferation occurring in skin carcinogenesis by modulating the activities of Phase II detoxification agents and through free radical scavenging potential was reported by Manoharan *et al.*, 2012 [54], and it modulates Phase I and Phase II detoxification enzymes in experimental oral carcinogensis is reported by madankumar *et al.*, 2013 [7], which shows the strong antioxidant efficacy of geraniol.

Anti-ulcer activity

Silva *et al.*, 2012 reported the monoterpene constituent of essential oils has the anti-ulcer activities in experimental models of edema induced by different phlogistic agents and gastric lesions were induced by acetic acid [55]. De Carvalho KI *et al.*, 2013 studied Oral treatment with geraniol in ethanol induced gastric ulcer in experimental rats, significantly decreased the number of ulcerative gastric lesions by 70 % to 99 %, and it was participates in the gastroprotective effects against different ulcerogenic agents by increasing GSH levels (an endogenous antioxidant factor) and decreasing MPO activity (an inflammatory marker) in gastric and duodenal tissue [56]. Plant essential oils have antiulcer activity against aspirin plus, pylorus, ligation, aspirin and ethanol induced rats and terpenes possessed with significant antiulcer activity against different ulcer causing agents in experimental animal models [57].

Neuroprotectivity

Neuroprotective effect of geraniol was reported by Prasad and Muralidhara, 2014 by assessing the ameliorative effect of geraniol against an acrylamide induced oxidative stress, mitochondrial dysfunction and neurotoxicity in a Drosophila melanogaster model [58]. Brain derived Neurotrophic factors and glial cell derived neurotrophic factors, could prevent or halt the progress of neurodegeneration in Parkinson's disease [59]. Neuroprotective efficacy of geraniol was affirmed by improved motor coordination, expressions of neurotrophic factors, and inhibiting oxidative stress, increasing the counts of dopaminergic immunoreactive neurons and it prevents oxidative stress-related neurodegenerative disorders such as Parkinson's disease [60].

Hepatoprotectivity

Ong *et al.*, 2012 reported the Dietary isoprenic derivatives such as geraniol on hepatocarcinogenesis may involve a block in carcinogen activation, induction of phase 2 enzymes and an antioxidant activity, as well as interference with cellular processes including cell communication, proliferation, apoptosis, differentiation and remodeling of preneoplastic lesions [61]. Singh *et al.*, 2012 studied the preventive effective of natural terpenes on Nimesulide induced cellular damage from elevated SGPT, SGOT, bilirubin and histo-pathological changes, Antioxidants and key redox enzymes (iNOS, mtNOS, Cu/Zn-SOD, Mn-SOD, GPx and GR) were studied significantly to ensuing hepatoprotectivity [62].

CONCLUSION

Plant essential oils are the most important source for exploring potentially useful structural compounds for developing new therapeutic drugs. Geraniol, an important constituent of essential oil of ginger, lemon, lime, lavender, nutmeg, orange, rose, etc. It is an acyclic mono terpenoid and is the main component of oil-of-rose and palmarosa oil has been used to treat various diseases for several years. The present review reports the diverse pharmacological potentials which are explored by different researchers. However, more biological potentials are still untapped. The geraniol and related metabolites are used in the traditional system of medicine for various diseases related to the human race.

CONFLICT OF INTERESTS

Declared None

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