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Review

Phytopharmacological importance of *Pelargonium* species

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World population relies on plant-based traditional system of medicine for their primary health care. With the emerging worldwide interest in adopting and studying traditional systems, it is essential to explore the potential of plant based health care systems. A number of herbs belonging to the genus *Pelargonium graveolens* are noted for their medicinal benefits in traditional system of medicine. A lot of medicinally important attributes have been assigned to the plants of *Pelargonium species*. They are rich source of monoterpenes, sesquiterpenes, coumarins, tannins, phenolic acids, cinnamic acids, flavones, flavonoids and flavonols derivatives. *Pelargonium*-derived essential oil is used in perfumery, cosmetics, soaps, creams, aromatherapy products exhibit good antioxidant activity and has potential immune modulating effects no natural killer cells. It further relieves congestion especially for the breast tissue, improves circulation and excellent for stimulating and cleansing the lymphatic system, promotes healthy immune system, helpful for detoxification, overcoming addiction, phlebitis, hemorrhoids, fluid retention and indigestion. The important plants of this species which have been so far explored mainly include *P. graveolens, P. sidoides, P. reniforme* and *P. radula* etc. The present review aims at exploring the current scientific findings on the various species of *Pelargonium*.

Key words: *Pelargonium*, phytochemistry, pharmacology, traditional system of medicine.

INTRODUCTION

Plants have great potential uses, especially as traditional medicine and pharmaceutical drugs. Since ancient times, plants have been an exemplary source of medicine. A large proportion of the world's population depends on the traditional medicine because of the scarcity and cost effectiveness of orthodox medicine (Ayo, 2010; Balunas and Kinghorn, 2005). Medicinal plants have been used for centuries as remedies for human diseases, because they contain chemical components of therapeutic values (Derwich et al., 2010) and have great important application in the field of agriculture, human and veterinary medicine, food and perfume industry (Butles 2004). Indigenous plants have been the traditional source of raw materials for the manufacture of medicines (Gupta, 1994). Due to its complex molecular active structures in the plant extracts they are able to interact with mammalian cell targets (Balunas and Kinghorn, 2005). Despite the advantages of the synthetic, combinatorial chemistry and molecular modeling, medicinal plants remain an important source of new drugs and drug leads. Of the 877 New Chemical Entities (NCEs) introduced between 1981 and 2002, nearly half (49%) of them were natural products, semi-synthetic natural products and their analogues or synthetic compounds based on natural products (Bhaskar and Rajalakshmi, 2010). The focus on plant research has increased all over the world and a large body of evidence has been collected to show the immense potential of medicinal plants used in various traditional systems. Such scientific studies have led to the isolation of chemical substances with therapeutic properties and many of the isolates have found their use as modern drugs while others have served as substrates for the synthesis of drugs (Nadro et al., 2006). In fact, modern pharmaceuticals still contain, at least, 25% drug derived from plants (Olaleye et al., 2006). During past several years, there has been growing interest among the usage of various medicinal plants for the treatment of different ailments. There is a need for documentation of research work carried out on traditional medicine. A number of herbs belonging to *Pelargonium* are noted for

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their medicinal benefits in traditional system of medicine (Prajapati et al., 2003) and is famous for its essential oil which is one of the top 20 essential oil in the world with wide application in perfumery, cosmetics and flavor industry (Douglas, 1969). A lot of medicinally important attributes have been assigned to *Pelargonium* species, the important plant species which have been so far explored include *P. graveolens, P. crispum, P. echinatum, P. grossalarioides, P. parriflorum, P. grandicalcaratum, Pelargonium magenteum, P. nerosum, Pelargonium fragrans, P. odorantissumum, P. peltatum, P. quercifolium, P. tricolor, P. xerophton, P. zonale, P. tomentosum, P. albrotanifolium, P. ionidiflorum, P. capitatum, P. citronellum, P. geranium, P. torento, P. radens, P. melissinum and P. nervosum* etc. *P.* accessions are popular as ornamental plants in North America and Europe, most of which originate from South Africa and now they are cultivated worldwide (Vander and Vorster, 1988). The common name *Geranium* has been erroneously used to refer to a plant that should correctly be called *Pelargonium* (Vander, 1977). China is now the main producer of *Geranium oil*. Other major producers are Egypt, Morocco, Reunion, India and the former Soviet Union but extensive industries of local importance exist in India. *Geranium* was introduced to India in the beginning of the twentieth century; *Rose–scented geranium (Pelargonium)* is found in various parts of India. The crop is grown in the Tamilnadu, Bangalore, Yercaud, Nilgiris, and Palani hills (Kodaikanal), Andhra Pradesh and agro climatic conditions of North Indian plains at Lucknow (Jain et al., 2001).

In India three cultivars of *Pelargonium* namely Algerian (Hemanti), Bourbon (Bipuli) and Egyptian (Kunti) are cultivated commercially (Rao and Bhattacharya, 1992). The present world production of *Geranium oil* is approximately 750 tonnes annually. Against its own requirement of approximately 200 tonnes, India produces less than 20 tonnes of *Geranium* oil and meets the requirement by imports (Navale and Mungse, 2002; Tembe and Deodhar, 2010). The aim of this paper is to review the traditional, phytochemical, pharmacological investigations of the *Pelargonium* spp. and highlight their potential as candidates for new drug discovery.

General botanical description *Pelargonium*

Among the 250 *Pelargonium* (Geraniaceae) species of perennial small shrubs, approximately 80% occur in South Africa with the highest concentration of species growing in the winter rainfall region of the Southwestern Cape (Lis-Balchin, 1997; Vander and Vorster, 1988; Lis-Balchin, 1996). The genus *Pelargonium* includes annuals and herbaceous perennials, shrubs and deciduous plants, but most of the scented-leafed species are succulent perennial with a wide variety of growth habits and habitats. Leaves occur in a variety of shapes and sizes, may be covered with fine hairs and may be rough, sticky or have a velvety texture. Leaf edges may appear ‘curly’ or ‘crisped’ in some species. Flowers occur in a pseudo-umbel consisting of 1-50 individual flowers, but most have 5-10 florets. Flowers may be white, pink, mauve, lavender, pale yellow or burgundy. The *Pelargonium* species are divided into 16 recognized sections (Bakker et al., 2004) that are phylogenetically arranged (Van der Walt 1985). Taxonomically revised section *Pelargonium* contains a total of twenty-four species. Many of the species are aromatic and in particular *P. capitatum, P. graveolens and P. radens* are used in cultivation programmes for the ennoblement of geranium oil (Vander, 1985; Williams and Harborne, 2002; Lalli et al., 2008). Mild climate with low humidity is ideal for its growth. These species usually grow within short grassland and sometimes with shrubs and trees on stony soil varying from sand to clay-loam, shale or basalt. The plants are evergreen when cultivated, but die back in nature droughts and winter (Vander and Vorster, 1985).

Traditional uses

Indigenous plants have been the source of raw materials for the manufacture of medicines (Gupta, 1994). *Pelargonium* species are widely used by traditional healers in the areas of Southern Africa by Sotho, Xhosa, Khoi-San and Zulus for its curative and palliative effects in the treatment of diarrhea, dysentery, fever, respiratory tract infections, liver complaints, wounds, gastroenteritis, haemorrhage, kidney and bladder disorders (Watt and Breyer, 1962; Hutchings et al., 1996; Van Wyk et al., 1997).

Traditionally, roots have been used medicinally for a multitude of ailments; both the rhizome and herb have been used for different purposes since ancient times to treat malaria, inflammation, abdominal and uterine disorders. They were also used in decoction to wash patients suffering from fever (Watt and Breyer, 1962; Lis-Balchin 1996) and also directly chewed or powdered and mixed with food. Infusions and decoctions of the tubers are commonly taken, while a traditional method of using *Pelargonium* roots is to boil the tuber in milk (Latte and Kolodziej, 2004). The root extracts have been shown to have antibacterial, antifungal and antitubercular activity; this may justify its use by the people of South Africa in the treatment of coughs and tuberculosis (Mativandlela et al., 2006).

According to World Health Organization, ethanol extracts of the roots of two species of *Pelargonium* have been used in Germany since 1980s as herbal medicine (Helmstadter, 1996) with the brand name ‘Umckaloabo’ used for acute and chronic infections, especially those of the respiratory tract, ear, nose and throat infections (De Boer et al., 2002).

The leaves were used to treat wounds, abscesses and

externally used for treating neuralgia, throat infections and a wide range of skin diseases viz ringworm, ulcers and rashes (Vernin et al., 1983). In folk medicine *Pelargonium* was internally used as a stypic for metrorrhagia, menorrhagia, haematuria, haemorrhoids, syphilis, peptic and duodenal ulcers. Paracelsus described it as having cardiotonic and antidepressive activity and suggested for leucorrhoea as a mouth wash. It is commonly used for childhood ailments such as chicken pox, measles and mumps (Brendler and van Wyk, 2008). They are also useful in treating menstrual and menopausal problems, breast congestion, cellulite and fluid retention (Watt and Breyer, 1962; Hutchings et al., 1996).

It can also be used to treat shingles, herpes, eczema, dry skin, athlete's foot and is both moisturizing and regenerative for skin conditions (Miller 2002; Weiss 2007; Peterson et al., 2005; Verma et al., 2010). The boiled leaves of this herb are used to protect wounds against maggots (Smith 1895). In animals, the plant is used to prevent purging in horses and also to treat liver complaints in sheep and calves (Batten and Bokelman, 1966).

Pelargonium derived geranium monoterpene oil(s) responds well to the balancing effects of constipation, insomnia, restlessness, nervousness, anxiety, worry, high blood pressure, anger, frustration, emotional upsets, high cholesterol, low metabolic forces, slow to lose weight (Lis-Balchin, 1997; Buchbauer 1992). It is used in perfumery, cosmetics, soaps, creams, aromatherapy products (Lis-Balchin 1996; Herbet and Oliver, 2003) and has potential immune modulating effects on natural killer cells (Standen et al., 2006). *Pelargonium* essential oils show good antioxidant activity on bacterial and fungal organisms (Kolodziej 2003). Geranium oil relieves congestion especially for the breast tissue, improves circulation and excellent for stimulating and cleansing the lymphatic system, promotes healthy immune system, helpful for detoxification, overcoming addiction, phlebitis, hemorrhoids, fluid retention and indigestion (Lalli et al., 2008).

PHYTOCHEMICAL PROPERTIES

Phytochemicals are natural bioactive compounds found in medicinal plants (Ayo 2010). The occurrence of Pelargonin (pelargonidin 3, 5-diglucoside) and malvidin 3, 5-diglucoside in flowers of *Pelargonium* cultivars was reported in *P. veitchianum*, *P. bertiana* and *P. cucullatum.* The indole alkaloids elaeocarpidine and its 20-H isomer epielaeocarpidine have been identified in leaves of *Pelargonium* species (Lis-Balchin, 1996). From 19 sections of *Pelargonium* species it is confirmed that flavonols are the major leaf vacuolar flavonoid constituents in the genus (Bakker et al., 2004; Williams et al., 2000).

Research on *Pelargoniums* is intensively focused on the chemical composition of the essential oils (Williams and Harborne, 2002) located in glandular hairs on both leaf surfaces (Vernin et al., 1983). The essential oil composition of the *P. graveolens* was significantly affected by crop duration and oil with best Citronellol: Geraniol ratio was obtained from January planted crops (Verma et al., 2010). Nearly 230 components have been detected in essential oils of *Pelargonium species.* It is a complex mixture of over 120 monoterpenes and sesquiterpenes such as pinene, phellandrene, myrcene, limonene, germacrene, caryophyllene (Li et al., 2009) and other organic compounds classified as terpenes, alcohols, esters, aldehydes, ketones and phenols etc., esters are citronellyl formate (5-8%) and geranyl formate (7%), monoterpenols are linalool (2-12%), citronellol (20-45%), geraniol (4-1%), ketones are menthone (1-4%), aldehydes citronellal (1%) and geranial (1-5%), coumarin, 5,6-dimethoxy,7-hydroxy-coumarin, and several related ethers, glycosides, and sulfates isolated from *Pelargonium* species (Kiran and Kaul 2005; Vernin et al., 1983). Other classes of chemicals including flavonoid methyl ethers and salicylic acid derivatives have been recorded in the leaf hairs or trichomes. Chemical analyses have led to characterization of about 65 metabolites including phenolic acids, cinnamic acids, tannins, flavornoids and coumarins in *P. graveolens* (Robert and Philip, 2003). The evidence of a high tannin content resulted in the isolation and identification of ubiquitous sterines, 12 amino acids, ethanolamine, tyramine, phenol carboxylic acid derivatives (e.g., caffeic acid, chlorogenic acid, paracoumaric acid), an anthocyanidine, gallocatechine and a remarkably high concentration of different coumarin derivatives (seven in total), of which Umckalin, the 5,6-dimethoxy-7-hydroxycoumarin, and its 7-O-glucoside were detected for the first time in the plant kingdom (Wagner et al. 1974; Bladt and Wagner 2007).

In *P. graveolens* whole plant extracts yield high quantity essential oils (Butles 2004; Kolodziej 2000). Thirty two compounds constituting 99.23% of geranium essential oil have been identified. The major components were citronellol (29.90%), trans-geraniol (18.03%), 10-epi-γ-eudesmol (8.27%), isomenthone (5.44%), linalool (5.13%), geranyl acetate (4.52%), γ- Cadinene (2.89%), geranyl butyrate (2.53%), geranyl tiglate (2.50%) and gemacrene D (2.05%). Geranium essential oil is rich in oxygenated components and commercial rhodinol (linalool + citronellol + geraniol) fraction (Rao et al., 2002; Fayed 2009). Galloyl C-glycosidic flavones, non galloyl flavones, phenolics (flavonoids and tannins), benzoic and cinnamic acid derivatives were reported in aerial parts (Goedecke et al., 2005; Ritika et al., 2000; Kolodziej and Kiderlen, 2007) and diterpene (reniformin), possessing a novel diterpene skeleton linked to a unique p-oxyphenethansulfonic moiety in the roots of *Pelargonium reniforme*. Novel ellagitannins with a 1- C4 glucopyranose core (pelargoniins) and 4-allyl-2, 5-

dimethoxyphenol-1-b-Dglucoside were also found. The four coumarins, scopoletin, the rare 7-hydroxy-5,6-dimethoxycoumarin and its 7-methyl ether and its 7-glucoside were identified in roots of *P. reniforme* and detected in roots of 11 other species: *P. betulinum*, *P. capitatum*, *P. cucullatum*, *Pelargonium hirtum*, *P. luridum*, *P. moreanum*, *P. myrrifolium*, *P. radula*, *Pelargonium reniforme*, *P. salmoneum*, *P. sidaefolium*, *P.triste* and *P. zonale* (Wagner and Bladt,1975). Tartaric acid is a characteristic constituent of the genus *Pelargonium* (Okudaetal, 1980). The occurrence of coumarin sulphates (5, 6-dimethoxycoumarin 7-sulphate and a mixture of 6- and 8- monosulfate of 6, 8-dihydroxy-5, 7-dimethoxycoumarin.), coumarin glycosides and proanthocyanidins was confined to *P. sidoides* (Herbert Kolodziej, 2007). *P. sidoides* and *P. reniforme* comprises a variety of phenolic and polyphenolic compounds and their roots express coumarins 6, 7, 8-trihydroxycoumarin and 8-hydroxy-5, 6, 7-trimethoxycoumarin. They are rich in flavonoids and hydrolysable tannins including a unique series of O-galloyl-C-glucosylflavones. The presence of umckalin, structurally related coumarins as active ingredient in Umckaloabo decreases upper airway infection and flu, palliates the severity of symptoms by improving the immune system (VanWyk et al., 2002; Matthys et al., 2007). The occurrence of tannins may explain the traditional use of the aerial parts as wound healing agent, which may be attributed, at least in part, to their astringent action. A similar rational explanation based on the presence of tannins and oligomeric proanthocyanidins may be provided for its use in traditional medicine for the treatment of gastrointestinal disorders such as diarrhea (Scholz, 1994). GC -MS analysis of *Geranium* (aerial parts) essential oils are presented in Table (1). (Jain et al., 2001; Robert and Philip, 2003)

PHARMACOLOGICAL ACTIVITIES

Antibacterial activity

The antimicrobial activity of extracts of *Pelargoniums* and their constituents is reported against bacterial (*S*taphylococcus *aureus, Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa and Haemophilus influenzae),* fungal (*Microsporum canis, Microsporum gypseum, Aspergillus* fumigatus*, Mucor racemosus, Rhizopus nigricans*) and pathogens as well as opportunistic yeasts such as *Candida albicans, Candida glabrata, Candida krusei* and *Cryptococcus neoformans* (Kolodziej, 2000; Kolodziej et al., 2003; Latte and Kolodziej, 2000). *Pelargonium glutinosum, Pelargonium pseudoglutinosum, Pelargoniums scabrum* and *Pelargonium sublignosum* exhibited considerable antimicrobial activity against the Gram-positive bacteria (*S. aureus and Bacillus cereus*) and Gram-negative bacterium (*K. pneumonia*). *P. tomentosum and Pelargonium vitifolium* were found to be non-toxic and showed promising antimicrobial activities. Essential oils *P. graveolens, P. tomentosum, P. odaratissimum, Pelargoniumm denticulatum* and *Pelargonium ficifolium* have been found to possess good antibacterial activity against *S. aureus, Proteus vulgaris, B. cereus* and *Staphylococcus epidermidis* (Lis-Balchin et al., 1998, 2003). The extracts of both *P. sidoides* and *P. reniforme* have modest direct antibacterial activity with isolated coumarins and phenolics having minimum inhibitory concentration values from 200 to 1000 mcg/mL in agar dilution assays (Kayser and kolodziej, 1997). Unsaturated fatty acids from the roots, especially linoleic acid, had antimycobacterial activity at 2 mcg/ml. (Seidel and Taylor, 2004; Mativandlela et al., 2006).

Immune modulator of *P. sidoides* extracts, coumarins, and phenolics has been documented in a variety of functional assays, (Kolodziej et al., 2003; Kayser et al., 2001) including enhancement of interferon-beta synthesis and activation of natural killer cell activity (Koch et al., 2002). Tannins from the plant induced nitric oxide synthase and cytokine gene expression in a macrophage-like cell line (Kolodziej and kiderlen, 2007). Methanol, acetone and water extracts from the roots and leaves of *P. reniforme* (Curtis) showed significant antimicrobial activity against the gram-positive (*B. cereus, S. epidermidis, S. aureus, Micrococcus kristinae and Streptococcus faecalis*) and gram-negative bacteria (*Salmonella pooni, P. aeruginosa* and *K. pneumonia)*. Both the roots and leaves had similar antibacterial activity on gram-positive bacteria however, the roots showed more activity against gram-negative bacteria than the leaves (Adewusi and Afolayan, 2009).

Antibacterial effect of *P. sidoides* in the form of drug was detected on eight *Neisseriae spp*, four *H. influenzae*, four *S. pneumoniae*, four *S. epidermidis* and four Moraxella *catharralis* (Hakan et al., 2009). Root extracts of *P. reniforme* (CURT) and *P. sidoides* (DC) inhibited the growth of *H. influenzae, M. catarrhalis* and *S. pneumonia* (Mativandlela et al., 2006; Lalli et al., 2008). In *P. radula* the main flavonoids, isoquercitrin and rutin, contribute significantly to the overall antimicrobial activity of the plant. Both (flavonoid isoquercitrin F1 and flavonoid rutin F2) fractions demonstrated strong inhibitory activity against *S. aureus, P. rettgeri, Candida tropicalis and Microsporum gypseum. Staphylococcus sp*. (Coagulase-negative) and *Candida lusitaniae* were strongly inhibited only by fraction F1 and *Fusarium graminearum* only by fraction F2. The methanolic and petroleum spirit extracts were more potent antibacterial agents than steam distilled volatile samples against *S. aureus, P. vulgaris, B. cereus* and *S. epidermidis*. Citral, citronellal, citronellic acid, geraniol, linalool and alpha- pinene showed most potent antimicrobial activity in the *Pelargonium* oil (Lis-Balchin et al., 1998).

P. graveolens (geranium oil) is being used as potent oil

Table 1. GC -MS analysis of *Geranium* (aerial parts) essential oils.

S/No.	Identity compounds	Quality (%)
1	Cis -3-Hexenol*	91
2	a-Pinene*	96
3	6-Methyl-5-heptene-2-one*	93
4	Myrcene*	91
5	a-phelleandrene*	91
6	p-Cymene*	94
7	Limonene*	98
8	Cis-b-Ocimene*	97
9	Trans-b-Ocimene*	95
10	Cis –Linalool oxide*	91
11	Terpinolene*	98
12	Trans-Linalool oxid*	91
13	Linool*	96
14	Cis-Rose oxide*	94
15	Trans –Rose oxide*	94
16	Menthone*	97
17	Citronellal	91
18	Iso-isopulegol	98
19	Isomenthone*	96
20	Terpinen-4-ol*	96
21	Neoisomenthol	97
22	a-terpineol*	91
23	Nerol*#	90
24	Citronellol*#	96
25	Neral	97
26	Piperitone	93
27	Geranio*	91
28	Geranial*	94
29	Citronellyi formate*	96
30	Geranyl formate *	90
31	a-Cubebene*	94
32	Phenylethyl propanoate	78
33	Citronellyl acetate	91
34	a-Copene*	98
35	a-Ylangene*	99
36	b-Bourbonene*	98
37	Geranyl acetate	91
38	b-Caryophyllene*	99
39	Trans-a- bergamotene	90
40	Aromadendrene	95
41	a-Guaiene	95
42	a-Humulene*	98
43	Alloarmadendrene*	99
44	Citronellyl propanoate*	91
45	Germacrene D*	97
46	g- Muurolene*	99
47	Geranyl propanoate*	95
48	d-Cadinene*	99
49	Cis-Calamenene*	98
50	Citronellyl-n-butyrate*	91
51	a-Agarofuran	93

Table 1. Contd.

52	Germacrene B	99
53	Geranyl –n-butyrate*	96
54	Phenylethyl tiglate*	83
55	10-Epi-g-eudesmol*	90
56	Hinesol	90
57	g-Eudesmol	99
58	Gerany valerate	Tent
59	Geranyl tiglate	91
60	Citronellyl hexanoate	Tent
61	Geranyl hexanote*	Tent
62	Citronellyl heptanoate	Tent
63	Geranyl heptanoate*	Tent
64	Geranyl octanoate*	Tent
65	Geranyl octanoate*	Tent

Components marked as (*) are common to Neetu Jain et al., 2001; Robert et al., 2003 and those marked as (#) and indicated as tent are unresolved Components and tentatively assigned respectively (Jain et al., 2001; Robert et al., 2003).

on the pathogenic vignal bacteria such as *Atopobium vaginae*, *Gardnerella vaginalis*, *Bacteroides vulgatus*, *Streptococcus agalactiae*. H_2O_2-producing lactobacilli, non H_2O_2 producing lactobacilli, *C. albicans*, *C. glabrata*, *Candida parapsilosis* and *Candida tropicalis* (Schwiertz et al., 2006; Lis-Balchin et al., 1998; Bayoub et al., 2010; Seidel and Taylor, 2004; Mativandlela et al., 2006) and have been used to extend the shelf life of foods, beverages, pharmaceutical and cosmetic products. The essential oil from the fresh aerial parts exhibited antimicrobial activity against *B. subtilis*, *S. aureus*, *Enterococcus fecalis, C. glabrata*, *C. krusei*, *C. neoformans*, *Mycobacterium tuberculosis* and *Mycobacterium intracellulare*. Geranium oil shows inhibition properties on *S. aureus* and *C. albicans* (Serkedjieva, 1997). High concentration of α-pinene (37.4%), β-pinene (16%) and limonene (13.3%), are believed to actively inhibit the growth of microorganisms (Derwich et al., 2010; Gabriella et al., 2010).

The profound antimicrobial activity of *Pelargoniums* may partly explain their wound-healing properties (Stjepan et al., 2005; Lis-Balchin 1996). These extracts broad spectrum antimicrobial activity may be caused by the coumarins and phenolic acids (Verma et al., 2010) and may be potential sources of effective agents for nosocomial and wound infections (Cosentino et al., 1999; Karaman et al., 2003; Lalli et al., 2008).

Antitubercular activity

Immune modular of the host is a potential course for antimycobacterial activity. Root extracts of *P. reniforme and P. sidoides* evaluated for antitubercular assays by BACTEC method revealed that acetone, chloroform and ethanol extract of *P. reniforme* showed activity against M. tuberculosis exhibiting a minimum inhibitory concentration of $5x10^3$ mg/L. The reputed benefit of the two *Pelargonium* species in respiratory tract infections may be due in part to a stimulation of the immune system (Mativanlela et al., 2006; 2007).

Bronchitis

Pelargonium containing phytopharmaceuticals are currently used in Europe to treat respiratory tract infections (Matthys et al., 2007). The herb *P. sidoides* has long been used to treat cough, sore throat, congestion, and other respiratory ailments. Its extract has been shown to safely and effectively treat acute upper respiratory tract infections such as bronchitis, tonsillopharyngitis, sinusitis, and the common cold (Watt and Breyer, 1962). Currently available data from 6 high quality randomized clinical trials suggests there is encouraging evidence that *P. sidoides* is effective compared to placebo for patients with acute bronchitis. The clinical research on EPs 7630 has been shown to reduce the duration and severity of acute upper respiratory tract infections (Timmer et al., 2008).

The characteristic and therapeutically most important natural substances of EPs7630,a herbal drug preparation from *P.sidoides* roots, are polymeric polyphenolic compounds (Kolodziej et al., 2003). The mechanism of action is ascribed to the ability of EPs7630 to antagonize bacterial adhesion and/or invasion to intact epithelia, thus protecting the upper respiratory tract from bacteria colonisation and infection (Conrad et al., 2007). It is an

effective and well tolerated treatment of acute bronchitis in adults, children and infants outside the strict indication for antibiotic treatment (Matthys et al., 2007).

Antifungal activity

According to Food and Agriculture Organization (FAO), one quarter of the world's food crops are affected by mycotoxins each year. About five billion people in developing countries worldwide are at risk of chronic exposure to aflatoxins through contaminated foods (Shephard, 2003) and aflatoxicosis has recently been recognized as sixth amongst the ten most important health risks identified by the World Health Organization for developing countries (Williams et al., 2004). The leaf essential oil of *P. graveolens* exhibit a broad fungitoxic spectrum against *Aspergillus fumigatus, Aspergillus terreus, Aspergillus alternata, F. oxysporum, H. oryzae* and *T. viride* (Singh et al., 2008) first reported the anti-aflatoxigenic nature of *P. graveolens* oil with complete inhibition of aflatoxin B1 production even at 0.50 gL^{-1} suggesting the relevance in enhancing shelf-life of commodities by controlling microorganisms and minimizing health hazards by inhibiting aflatoxin B1 elaboration in food by use of the essential oil of *P. graveolens*. The oil was found to be highly efficacious, showed better fungitoxicity against *A. flavus* at concentrations lower than the earlier reported oils and synthetic fungicides (Helal et al., 2007).

The antimycotic investigation revealed that *Pelargonium* extracts showed significant growth inhibition against *Aspergillus flavus, A. niger and Penicillum notatum*. The inhibitory effect of *P. reniforme* on the growth of the fungi may also justify its use in the treatment of liver diseases (Adewusi and Afolayan, 2010). Both acetone and ethanol root extracts of *P. reniforme* and only the ethanol root extract of *P. sidoides* inhibited the growth of *Aspergillus niger* and *Fusarium oxysporum* significantly at a concentration of $5x10^3$ mg/L (Mativandlela et al ., 2006). In addition, both the roots and leaves were observed to be effective against the fungal strains tested, though the leaves had better activity suggesting that compounds identified in the roots of the plant may be similarly present in the leaves but with different concentrations of active compounds (Adewusi and Afolayan, 2009).

Moulds and mycotoxins contaminate stored food commodities which results in qualitative as well as quantitative losses. Most of the synthetic antimicrobials used for preservation of stored food items produce side effects in the form of residual and mammalian toxicity (Bajaj and Ghosh, 1975). Plant products have been recommended as safe alternatives of such synthetic antimicrobials as they would be biodegradable, renewable in nature and safe to human health (Varma and Dubey, 1999). Plant products, especially essential oils, are recognized as one of the most promising groups of natural products for the formulation of safer antifungal agents (DonPedro, 1985; Varma and Dubey, 2001).

Antioxidant activity

Polyphenols are the major plant compounds with free radical quenching and antioxidant activity. This activity is believed to be mainly due to their redox properties (Zheng and Wang, 2001) which play an important role in adsorbing and neutralizing free radicals, quenching singlet and triplet oxygen or decomposing peroxides (Afolayan et al., 2007). Methanol and water extracts assessed by three established *in vitro* methods namely, 2,2´-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH) and ferric ion reducing power showed that the *P. reniforme* extract possessed strong scavenging activity-antioxidant activity, moderate reducing power thus validates its traditional use in the treatment of liver diseases. Flavonoids and hydrolysable tannins of *P. reniforme* showed marked antioxidant effects using a DPPH radical generating system and a luminol-dependent chemiluminescence assay (Latte and Kolodziej, 2004).

Regarding structure–activity relationships, the antioxidant potentials generally increased in the order of C-glucosylsoO-glycosidesoaglyconesogalloylatedC glucosyls in the series of the tested flavonoids, while for tannins the presence of galloyl and DPPH entities were important determinants (Kolodzieja, 2007). The presence of significant amount of phenolic compounds in the leaves and roots may account for its high antioxidant activity (Sofidiya et al., 2008) and exhibit concentration dependent antioxidant activity suggesting that similar antioxidant compounds are found in both plant parts implying that leaves may substitute for its roots in medicinal formulations especially in the treatment of liver diseases (Adewusi and Taylor., 2009). The Geranium essential oils reduced the concentration of DPPH free radical with an efficacy (EC_{50}=66.45 µg/ml) near to that of standard ascorbic acid (Fayed 2009).

Antioxidant activity was displayed by a number of methanolic extracts of representative species and cultivars of *Pelargonium* (Lis-Balchin and Deans 1996; Latte and Kolodziej, 2004) established that the flavonoids and hydrolyzable tannins isolated from *P. reniforme* produced higher anti-oxidant activity than ascorbic acid. Potent anti-oxidant activity was observed for the crude extracts of *P. betulinum* (IC_{50}: 4.13±0.14 µg/ml) and *P. crispum* (IC_{50} : 4.49±0.18 µg/ml). *P.cordifolium* and *P. scabrum* also showed potent radical scavenging activity.

The flavonoid derivatives detected in the tested *Pelargonium* extracts (Lalli et al., 2006) may contribute to their observed *in vitro* anti-oxidant activities. The *Pelargonium* species, in particular *P. betulinum, P. crispum, P. tomentosum and P. cordifolium* are possible

Table 2. *In vitro* antioxidant, antibacterial and antifungal activity of toxicity properties of selected *Pelargoniums .sp.*

Species	Antioxidant activity IC_{50} (ug ml)	Antibacterial activity MIC (µg ml^{-1})	Antifungal activity MIC(µg ml^{-1})
P. betulinum	4.31±0.14	1000	2000
P. capitatum	Nd	1000	1500
P. citronellum	23.7.±3.68	3000	1000
P. citronellum	84.01±16.08	3000	500
P. cordifolium	5.01±0.55	1500	750
P. crispum	4.49±.18	2000	1330
P. cucullatum	40.18±5.65	1500	1000
P. cucullatum	10.91±0.54	3330	2000
P. glutinosum	16.41±0.33	2000	1000
P. glutinosum	29.17±0.78	2000	2000
P. graveolens	14.49±0.46	2000	3330
P. greytonense	Nd	3200	1500
P. hermanniifolium	13.50±0.73	1500	1500
P. hispidum	12.78±0.45	2000	3000
P. panduriforme	Nd	2000	2000
P. panduriforme	91.58±4.45	2000	1000
P. papilionaceum	81.24±13.44	4000	1190
P. pseudoglutinosum	52.38±0.67	2000	540
P. quercifolium	17.15±0.58	8000	2000
P. quercifolium	61.87±3.19	2000	1000
P .radens	Nd	2500	2000
P. scrabroide	Nd	2000	1000
P. scabrum	7.15±0.11	2000	380
P. sublignosum	17.61±3.18	2000	500
P. tomentosum	28.16±2.65	2000	2330
P. vitifolium	Nd	4000	2000
Controls	4.72±0.14	2.5(a)	2.5(b)

Abbreviations: Nd: not determined due to insufficient extract for testing (a) Ciprofloxacin (b) Amphotericin and minimum inhibitory concentration (MIC) determinations for the Antimicrobial and Antifungal activity.

sources of anti-oxidant compounds since these extracts were relatively non-toxic (Table 2. Lalli et al., 2008).

Anticancer activity

Geranium essential oil is becoming popular for the treatment of dysentery, hemorrhoids, inflammation, heavy menstrual flows, and even cancer. Monoterpenic essential oils are natural antioxidants (Yanishlieva et al., 1999) that are active against certain cancers (Kris-Etherton et al., 2002). Indeed, a number of dietary monoterpenes have antitumoral activity that can prevent the formation or progress of cancer and cause tumor regression. Most of the principle components present in *geranium* essential oils are monoterpenes. Monoterpenes have shown prevention of mammary, lung, skin, liver and fore stomach cancers in rat models (Haag et al., 1992). The major constituents in *geranium* essential oil, citronellol and trans-geraniol may be attributed to the anticancer activity. Zhuang et al. (2009) reported that citronellol, an oil soluble compound derived from the *geranium,* has anticancer and anti-inflammatory properties. Burke et al. (1997) investigated the anticancer activity of geraniol and found the significant (60-90%) inhibition of the anchorage-independent growth of human MIA PaCa-2 pancreatic tumor cells. Some of the major chemical compounds (citronellol, citronellyl formate, geraniol and citronellyl acetate) of *P. graveolens* oil, possess marginal antitumour activities (Fang et al., 1989).

The anticancer activity of the *geranium* essential oils on two human promyelocytic leukemia cell lines (HL-60 and NB4) using trypan blue assay showed the anticancer activity with the LC_{50}:62.50 and 86.5 µg/ml in NB4 and HL-60 cell line respectively, demonstrating the potential of the essential oils for cancer treatments (Fayed, 2009). Many authors reviewed that *P. graveolens* has potential antitumor activity against uterine cervical neoplasia (De Moura et al., 2002; Duke and Ayensu, 1985). Analysis of

geranium essential oil showed citronellol and trans-geraniol as the major constituents which are known to possess antioxidant and anticancer properties (Haag et al., 1992).

Geraniol sensitizes colonic cancer cells to 5-FU treatment, by increasing the cytotoxicity of the drug, resulting from the facilitated transport of 5-FU and the blockade of the morphological and functional differentiation of the cancer cells (Carnesecchi et al., 2002). Geraniol inhibited the growth of leukemia and melanoma cells (Shoff et al., 1991), hepatoma cells (Yu et al., 1995), and pancreatic cancer cells (Burke et al., 1997). The antiproliferative effects of geraniol on hepatoma and melanoma cell growth have been ascribed to inhibition of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, a key enzyme of mevalonate biosynthesis (Elson, 1995). Geraniol caused a 50% decrease of ornithine decarboxylase activity, a key enzyme of polyamine biosynthesis, which is enhanced in cancer growth. Geraniol also activated the intracellular catabolism of polyamines, indicating that polyamine metabolism is presumably a target in the antiproliferative properties of geraniol. Carnesecchi (2001) reported a potent antiproliferative effect of geraniol on the growth of human colon cancer cells. Geraniol has no cytotoxic effect, is mainly cytostatic, and inhibits DNA synthesis, leading to the accumulation of Caco-2 cells in the S phase (Carnesecchi et al., 2004).

Geranium oil is one of the top 20 essential oils in the world which has wide application in perfumery, cosmetics and flavour industry. It forms a part of many high grade perfumes (Douglas 1969). It has antifungal (Wollman et al., 1973) insect repellant (Osmani et al., 1974; Osmani and Sighamony, 1980) and antibacterial (Aggarwal et al., 2000) activity because of which it finds extensive use in medicinal and agrochemical field. The oil has a wide application in aromatherapy (Ranade, 1988) and food product industry (Leung 1980). Essential oils are the volatile fraction of aromatic and medicinal plants after extraction by steam or water distillation. They have been used for their pharmaceutical potential since early times, and even now are still subject to a great deal of attention. They are valuable natural products used as raw materials in many fields, such as perfumes, cosmetics, aromatherapy, spices and nutrition (Buchbauer, 2000; 2004). There is an increasing world-wide interest in screening plants to study the biological activities of their oils with particular focus on their chemical, pharmacological and therapeutic properties (Luqman et al., 2007).

Antihelmintic activity

Nematicidal activity of essential oil of *P. graveolens* (cv. Algerian) and its major constituents namely citronellol, geraniol and linalool were determined against the root-knot nematode *Meloidogyne incognita*. Geraniol was found to be the most effective constituent followed by citronellol and linalool. The water distillate of the fresh flowers *Pelargonium endlicherianum* exhibit anthelmintic activity (Leela et al., 1992).

Antiplasmodial activity

The non-volatile extracts of *Pelargonium panduriforme* (provenance SBG) exerted the greatest antimalarial activity against the choloroquine-resistant Gambian FCR-3 strain of *Plasmodium falciparum* by hypoxanthine incorporation assay. *P. citronellum* (provenance NBG), *P. citronellum* (provenance SBG), *P. quercifolium* (provenance SBG) and *P. radens* possessed similarly potent antimalarial activity.

The *Pelargonium citrosa* leaf extracts having significant biting deterrency completely inhibited the larval, pupal and adult developments of malarial vector, *Anopheles stephensi*. The highly bioactive compounds of *P. citrosa* leaf extracts could be used to develop naturally occurring insecticides; an alternative to the expensive and environmentally harmful organic insecticides (Jeyabalan et al., 2003).

Insecticidal activity

Insecticidal properties of geranium oils have been reported for many years (Deans and Ritchie, 1987). *Pelargonium* species have an antifeedant action on insects (Lis-Balchin, 1996).

A rare agonist of excitatory amino acid receptors, L-quisqualic acid ($C_5H_7N_3O_5$) from petals of zonal geranium *(Pelargonium hortorum*) with paralytic effects on the Japanese beetle (*Pelargonium japonica)* was identified by high-resolution–MS and NMR (1H, 13C, COSY, heteronuclear sequential quantum correlation, heteronuclear multiple bond correlation) analysis. By establishing zonal geranium as a natural source of L-quisqualic acid, it presents unique opportunities for the pursuit of botanically based formulations for insect pest management (Range et al., 2010; Ballou, 1929; Held and Potter, 2003)

CONCLUSION

Human beings have been using natural products of plant sources for thousands of years either in the pure forms or as crude extracts for the treatment of various diseases. The *Pelargonium* extracts can potentially be used as novel antioxidant, antimicrobial, anticancer agents in the food, cosmetic and pharmaceutical industries. Plant extracts of remaining species have not been tested against the fungal pathogens, bacteria, which are

associated with either primary or secondary infections of bronchitis, tuberculosis etc., and appears to be the most promising species requiring further investigation. There is necessity for further studies of the *Pelargonium* species, focusing on the *in vivo* studies, isolation and structure elucidation of true antimicrobial, antioxidant and anticancer compound/s, since they have potential use as therapeutic agents in managing diseases associated with free radicals and to determine the metabolic pathways involved in their degradation. The oil may be recommended as an easily available and renewal source of antifungal and anti aflatoxigenic agent over the synthetic antimicrobials for enhancing the shelf-life of food commodities by controlling fungal infestation. Consumption of foods prepared with geranium or their essential oils may have significant health benefits.

There are large numbers of scented species, hybrids and cultivars of *Pelargonium* which are at present unexploited, but exhibit some potential as odourants for the perfumery and food industry, antimicrobial agents and insecticides (Lis-Balchin and Dean 1996; Lis- Balchin, 1988). These *Pelargoniums* have thus represented an attractive source of fascinating secondary metabolites. The actual composition of the active components is as yet unknown. Although the root of this plant is used in the treatment of liver disorders by several ethnic groups, there is paucity of scientific evidence in the literature regarding its usage in liver disorders. The role of L-quisqualic acid in defending zonal geranium against other insect pests and pathogens also warrants further investigation. *Pelargonium* spp. possess various pharmacological activities as discussed in literature, however, there has been very little commercial exploitation and it is imperative that more clinical and pharmacological studies are necessary to provide a rational basis for validation of their potential therapeutic applications.

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