New Trends in the Utilization of Medicinal and Aromatic Plants

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Abstract

The use of medicinal and aromatic plants has never been out of focus throughout history. Our time, on the other hand, is witnessing a different approach to their utilization. For the first time in history, they have become industrial products for world-wide use. New concepts, such as nutraceuticals, cosmeceuticals, phytotherapy, aromatherapy, etc. are widening their use and new applications in functional foods, animal husbandry and agricultural pest management are taking place. New clinical evidence is also emerging on the effectiveness of medicinal plant products. The appearance of increasing number of monographs on plant drugs in national and international pharmacopoeias is a good indication that legislative and regulatory authorities have a more positive view towards the increased use of medicinal and aromatic plants in conventional medicine. This paper will focus on the above aspects from a global point of view.

INTRODUCTION

Especially in the last two decades, the upsurge of interest in the utilization of medicinal and aromatic plants for health care has increased in developed countries. This general trend gave rise to the flourishing of a herbal medicines industry. Since processed food and medicines are regulated products, regulatory authorities were soon in the scene and regulations best suited to the given country’s conditions were introduced and implemented.

Legislations may vary from country to country based on the strength of “regulatory bias” and general acceptance by the public and tradition within the tolerance limits of the country. In the USA, herbal medicines are generally regarded as dietary supplements under the Dietary Supplements Health and Education Act (DSHEA) of 1994 and approval of a herbal medicinal product by the Food and Drug Administration (FDA), at present, seems quite farfetched. However, in Europe, there are regulations for such products and regulatory differences among the countries are smoothened by the EU. In Europe, herbal medicines are a reality and herbal pharmaceutical industries are well established (Baser, 2003).

As to the standardization, the European Pharmacopoeia has made a positive move in the last decade. The 4th edition which was published in 2002 and its supplements contain more than 170 monographs related to herbal medicinal products. This is thanks to the extensive work of the phytochemistry experts at groups 13A and B. The European Scientific Cooperative on Phytotherapy (ESCOP) and World Health Organization (WHO) have also come up with their sets of monographs on herbal medicinal products. Although EP and ESCOP monographs are mostly on the herbal drugs used in Europe, the WHO monographs have a more global perspective (Baser, 2002).

TM/CAM

Recognizing the fact that 80% of the population in low and middle income countries rely on traditional medicine (TM) and up to 65% of the population in high-

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1 The paper is dedicated to the memory of late Ms. S. Wasuwat
income countries utilize complementary/alternative medicine (CAM), WHO developed in 2002 its WHO Traditional Medicine Strategy 2002-2005 to provide technical guidance to promote proper use of TM/CAM. (WHO, 2002). It has four main objectives: Policy; safety, quality, efficacy; access and proper use of TM/CAM.

TM/CAM therapies have beneficial effects but also carry some risks. The benefits include accessibility and affordability in many parts of the world. Although there is wide acceptance of TM in low and middle income countries, increased utilization of CAM in high income countries can be explained as follows: (i) Higher life expectancy with chronic and debilitating diseases for which conventional therapy offers little or no cure, (ii) increased concern about adverse effects of synthetic drugs, (iii) greater public access to health information.

The risks associated with TM/CAM therapies can be summarized as follows: (i) Direct risks involve unqualified practices, adverse effects or interactions and low quality products, (ii) indirect risks are missed or delayed diagnosis or refusal of effective treatments.

Apart from monographs and papers published on plant drugs describing adverse effects or interactions of TM/CAM medication therapies, Uppsala Monitoring Centre Sweden monitors adverse reactions of medicines including TM/CAM medications.

Adulteration has always been a major problem in phytotherapy. While in the past accidental or deliberate adulterations with physically similar other drugs or exhausted drugs were common place, recently more sophisticated adulterations are encountered. 24% of over 2500 chinese herbal medicines sold in Taiwan were shown to be adulterated with chemical drugs such as acetaminophen, hydrochlorothiazide, indomethacin, phenobarbital, theophyllin and corticosteroids (Huang et al, 1997).

WHO is drafting guidelines for growers and collectors of medicinal plants and consumers of TM/CAM medication therapies. Consumer awareness is a major concern. It is essential that there is decent and fair advertising of public and private information on safe use of TM/CAM medicaments especially for children, pregnant or lactating women and elderly, adverse reactions, short and long term toxicity and interactions with food and other drugs. Governments and Non-Governmental Organizations (NGOs) should implement the proper use of TM/CAM in their countries.

Good Agricultural and Field Collection Practices Guideline refers to the utilization of proper agricultural techniques for the cultivation of high yielding and disease-resistant strains of medicinal plants, appropriate harvest and post harvest treatments to ensure the production of good quality drugs. The main concern of the field collection practice is collection of wildcrafting of medicinal plants in a sustainable way with utmost care shown not to damage the environment and to ensure the collection of correct plant materials at the right time utilizing appropriate techniques and tools. Again, the post harvest practices are important in order not to waste valuable materials by deterioration, contamination or infestation.

**Clinical Trials**

Herbal pharmaceuticals are subjected to clinical trials before registration with regulatory authorities. Similar set of rules that apply to synthetic medicines are demanded for herbal medicines. Due to complexity of the composition of herbal extracts, their clinical evaluation may require different parameters which complicate the trial design and evaluation even more. The extracts to be used in such trials should be well standardized and synergism, antagonism and additive effects between the components should be taken into consideration in order to better evaluate the results in terms of bioavailability, efficacy and long-term toxicity.

A preliminary survey has shown that globally 748 clinical trials have been conducted on 96 plant species or their combination formulas. Including reviews and mega-analysis reports, 823 papers have been published on clinical trials of herbal pharmaceutical materials. *Glycyrrhiza glabra* (Liquorice) tops the list with 67 clinical trials. Then follows, *Hypericum perforatum* (St John’s wort) (52), *Allium sativum* (Garlic)

**World Market of Herbal Medicines**

Due to antioxidant, free radical scavenger, tonic, phytoestrogenic, therapeutic, prophylactic and other useful physiological properties of various foodstuffs or medicinal and aromatic plants, major food companies are investing in the field of nutraceuticals or functional foods. In 2001, the global market for dietary supplements stood at $50.6 billion. The largest market was North America with sales to the tune of $16.3 billion, followed by Europe ($15.0 billion) and Asia ($7.8 billion). Japan was the 4th largest market in total sales with $7.2 billion. Herbs/Botanicals market had a share of $19.6 billion (39% of total sales) and was as big as the Vitamins and Mineral Supplements (VMS) market (Grünwald and Herzberg, 2002).

The herbal supplements market is experiencing some problems due to insufficient raw material supply. This is causing a drop in the quality of most products. Negative media coverage and loss of consumer confidence seem to be the main factors affecting the growth of herbal supplements market. Although the European market is also affected by the current situation in USA, the market growth rate was estimated at around 6% for 2002. This was attributed to the strong growth of the market in South America and Asia. The global growth rate was estimated at 8.7% (Grünwald and Herzberg, 2002).

**Synergy**

There are two main schools of thought concerning phyotherapy. The proponents of classical medicine consider phytomedicines as placebos. However, the supporters of phyotherapy value them as alternatives to synthetic medicines. The truth, to me, lies somewhere in between these two extreme opinions.

It is true that medicinal and aromatic plant products are consumed by a large segment of the population in each country due to their easy availability for public use. However, the quality of such drugs and their preparations vary over a wide range. This is the reason why conflicting reports are often circulated as to the efficacy or non-efficacy and even toxicity of such products.

For drugs like, senna, belladonna, opium, peppermint, digitalis, ephedra, etc., the safety and efficacy problem has long been solved and nobody questions their effectiveness in treating diseases. This is due to the fact that active ingredients in such drugs are known and quantified. However, for some drugs, although the efficacy can be proven but cannot be related to a single chemical. In such cases, standardization becomes a major problem in the absence of a single active principle. Fractionation of the active extract to isolate the possible active principle often leads to total loss of activity. Efforts, then, have in recent years been directed to the isolation of purified extracts containing a “certain balanced ratio” of components to render a stable activity in a dose-dependent manner. In such formulations, at least two single or groups of compounds are said to act synergistically to bring about the expected activity.

The most recent and notable example of this is the standardized ginkgo extract. It contains 24% flavonoids (mostly flavone glycosides and quercetin) and 6% terpenes (mainly ginkgolides composed of 2.9% bilobalide and 3.1% ginkgolides A, B, C, and J). Ginkgo extract is used in the treatment of cerebral dysfunction symptoms, dementia,
vertigo, tinnitus, peripheral arterial occlusive diseases and asthma. There are indications that it also an effective antioxidant with free radical scavenging activity.

The diterpene ginkgolides are known to be platelet activating factor (PAF) antagonists, therefore, reduce bronchoconstriction, bronchial hyperresponsiveness, platelet aggregation and allergic responses. They may also have an effect in cerebral insufficiency but their main function is antiinflammatory, hence antiasthma.

Flavonoids are also antiinflammatory. However, both groups of compounds act additively or synergistically to increase blood circulation to the brain. Antioxidant activity is particularly useful in the brain tissue improving cognitive function.

Cannabis extract (1 µM equivalent) is more effective than tetrahydrocannabinol (THC) in abolishing epileptiform bursting. THC (1 µM) inhibits excitatory postsynaptic potential (EPSP) generation indicating that it exerts an inhibitory presynaptic action and abolishes potnet muscarinic agonist oxotremorine methiodide (OXO-M) induced burst firing. Cannabidiol (CBD) (1 µM) has no effect upon EPSP generation or OXO-M induced epileptiform bursting. Cannabis extract (1 µM equivalent) reverses OXO-M induced synaptic inhibition and potentiates action potentials in control conditions. Cannabis extract also inhibits anandamine transport unlike THC alone. Other compounds within Cannabis affect the metabolism and action of ∆9 THC (Williamson, 2002a).

Other extracts for which synergy is suspected are ginseng, St. John’s wort, kava, valerian, rosemary and ginger. Synergy is an important feature of phytotherapy which should be investigated and then promoted (Williamson, 2002).

Biological Activities of Essential Oils and Aromachemicals

Aromatherapy is the use of natural essential oils and aromachemicals in therapy. One school of thought considers aromatherapy as “smell therapy” meaning effects are caused only by inhalation. However, in actuality, aromatherapy has been practiced in various forms ranging from inhalation therapy to massaging with oils and even oral consumption of aromatic waters. It may be more appropriate to call this form of therapy as “essential oil therapy” or “therapy with essential oil”. Aromachology is a term often used to describe the physiological effects of scents.

The most popular forms of practice of aromatherapy are as follows:

Vaporising essential oils in a small cup heated by a candle, inhaling essential oil vapours dropped in hot water, adding essential oils in a bathtub before entering, diluting essential oils in a vegetable or mineral oil before rubbing on skin.

Aromatherapy is used to treat a range of disorders including digestive problems, skin diseases (e.g., eczema, etc), headaches, insomnia, stress, cancer and for improving cognition. The effects of essential oils and aromachemicals on the nervous system, gastrointestinal system, immune system, respiratory system, antimicrobial and antifungal activities have been scientifically investigated in recent years.

Studies concerning the influence of essential oils and aromachemicals on the nervous system have been carried out. These studies have provided proof of aromatherapy and more significantly to the efficacy of essential oils or their components in conventional therapy (Buchbauer, 2002a).

Lavender oil and its components linalool and linalyl acetate have been shown to have sedative effects on both animals and human beings in a dose dependent manner. In studies using Electroencephalographs (EEG) on the use of inhaled compounds α-wave dominancy refers to a relaxed state and β-wave dominancy to stimulation. Lavender oil, sandalwood oil and apple aroma induced sedation as evidenced by α-wave dominancy, while jasmine odour increased β-wave activity hence induced stimulation. In an experiment with healthy volunteers R-(−)-, S-(+) and racemic linalool were tested. R-(−)-linalool found in lavender oil and the racemic mixture both showed sedative activity. S-(+)linalool which is obtained from coriander oil, however, showed the reverse (Sugawara et al., 1998).

Lavender oil positively affected mood by inducing a less depressed mood, and more relaxed feeling. Anxiety reduction was better and better performance was observed
in mathematical computations.

In studies to test the olfactory influence of learning, essential oils of lavender, jasmine, sage and rosewood were tested on 160 elementary school children at 3rd and 4th class. Significantly better learning results were obtained with lavender oil on anxious children due to sedating and stress reducing effect of its aroma. No significant results were obtained with the other tested oils. However, jasmine odour yielded rather worse learning results with lethargic children possibly due to stimulating effect of jasmine odour (Kerl, 1997).

Lavender oil vapour and linalool significantly and dose-dependently induce anticonvulsive effects. This is possibly due to potentiation of GABA_A receptors. Lavender oil, lavender perfumes, leaf alcohol, hinokitol, pinene, eugenol, citronellol and citronellal bind at low concentrations (10-30 µM) to the potentiation site of GABA_A receptors and increase the affinity of GABA to the receptors (Aoshima and Hamamoto, 1999). Potentiation of GABA_A receptors by benzodiazepine, barbiturate, steroids and anesthetics induce anxiolytic, anticonvulsant and sedative activities.

In experiments to clarify the anticonvulsant mechanism of linalool, its effects on binding of an N-methyl-D-aspartate (NMDA) antagonist (MK801) and a GABA_A agonist (muscimol) to mouse cortical membranes showed a dose-dependent non-competitive inhibition on the antagonist binding but no effect on agonist binding suggesting a direct interaction with the NMDA receptor complex inducing anticonvulsant activity (Silva-Brum et al., 2001).

Pharmacokinetic basis of the anticonvulsant properties of linalool on glutamate binding sites were investigated (Elisabetsky et al., 1999). Linalool inhibits by means of competitive antagonism glutamate binding at CNS-membranes delaying NMDA and blocking quinolinic acid induced convulsions. It also inhibits the binding of glutamate to brain cortical membranes and significantly reduces K^-stimulated glutamate release and glutamate uptake but does not interfere with basal glutamate release (Silva-Brum et al., 2001a). These experiments provide proof that linalool can be considered as a promising antiepileptic drug.

A diagnostic method has been developed in brain research using linalool to determine the existence of unilateral supratentorial brain tumors (Daniels et al., 2001). Hypnotic or sleep promoting effects of lavender, lavender oil and linalool have been shown both in animals and human beings (Buchbauer, 2002). Local anesthetic effects of linalool were demonstrated (Re et al., 2000). Lavender flowers are used against states of restlessness, uneasiness, nervousness, difficulties in falling a sleep and anxiety. Lavender tea is taken as a sedative and to promote sleep (Schultz et al., 1997). Lavender bath relieves stress of the day and brings about calmness and relaxation. Lavender pillows are recommended for difficulties in falling asleep and for relaxation. Lavender oil is sedative, antistress, relaxant and sleep promoter (Buchbauer, 2002a). The use of lavender straw as bedding appeared to decrease incidence and severity of travel sickness, symptoms of travel sickness and stress such as retching, vomiting, foaming and chomping appeared to be less acute in pigs (Bradshaw et al., 1998). Lavender and lavender oil showed only very mild skin irritation and sensitisation effects in man, although allergic reactions were observed in some laboratory animals (Buchbauer, 2002). In a placebo controlled study, aromastream of lavender was tested against severe dementia in Alzheimer patients suffering from vascular dementia. 60% of the patients showed modest efficacy, sedation and calming (Holmes et al., 2002). Fragrance inhalation on sympathetic activity by normal adults was investigated. Inhalation of pepper, estragon, fennel or grapefruit oils resulted in 1.5 to 2.5-fold increase in relative sympathetic activity representing low frequency amplitude of systolic blood pressure (SBP-LF amplitude) compared with an odourless solvent. In contrast, fragrance inhalation of rose oil or patchouli oil caused 40% decrease in relative sympathetic activity. Pepper oil induced a 1.7-fold increase in plasma-concentration compared with the resting state, while rose oil caused a 30% decrease (adrenaline concentration) (Haze et al., 2002).
**Anticancer Effects**

Consumption of diets containing fruits and vegetables rich in monoterpenes such as \( \alpha \)-limonene reduces the risk of developing cancer of the colon, mammary gland, liver, prostate and lung (Reddy et al., 1997). Limonene, perillyl alcohol, geraniol, carveol, farnesol, nerolidol, citronellol, linalool, carvacrol and menthol have shown experimental evidence for the inhibition of induced tumors (Elson et al., 1999). Geraniol has been shown to sensitize human colon cancer cells to 5-fluorouracil treatment (Carnesecchi et al., 2002).

Mechanisms of action against cancer include inhibition of farnesyl transferase (perilla alcohol), increase of pro-apoptotic protein leading to apoptosis of tumor cells (perilla alcohol), and protein prenylation (nerolidol).

**Antimicrobial Effects**

Recent studies have shown that the so-called superbugs – pathogenic microorganisms resistant to antibiotics such as MRSA (methicillin-resistant *Staphylococcus aureus*) cannot survive in the presence of essential oils, nor has there been any pathogen known to resist essential oils by mutating. This may well be due to the fact that bacteria are able to develop genetic mutation and resistance only against a specific drug such as methicillin. But their genetic system seems not to be able to develop defensive mutation versus many natural antibacterial terpenes, such as those found in essential oils. Due to the fact that several hundred terpenic compounds may exist in an essential oil and their concentrations may vary due to various reasons. All such variances make it impossible to trigger the genetic mechanisms which induce resistance when they are targeted by a single specific chemical (Khusal, 2002).

Essential oils are often more active against fungi than bacteria (Delespaul et al., 2000). Monoterpenes act on microorganisms through inhibition of the respiration of membranes, increase in membrane permeability that results in K+ leakage, loss of chemiosmotic control leading to the death of bacterium or yeast cell (Cox et al., 2000).

Essential oils are important for food preservation and also for their therapeutic effects on bacterial infections, fungal diseases, wounds, burns, acne, etc. Tea tree oil ex *Melaleuca alternifolia* (Myrtaceae) containing 32-45% terpinen-4-ol is effective against many gram positive and gram negative pathogens. Terpinen-4-ol alone has been shown to be more active (Buchbauer, 2002a).

Recent study of 96 essential oils (Allspice, bayleaf, carrot seed, cedarwood, celery seed, cinnamon, clove bud, gardenia, ginger root, jasmine, lemongrass, marigold, marjoram, mugwort, bitter orange, oregano, palmarosa, patchouli, spikenard, thyme) and 23 oil components (Benzaldehyde, carvacrol, (R)- and (S)-carvone, cinnamaldehyde, citral, estragol, eugenol, geraniol, geranyl acetate, isoeugenol, perillaldehyde, salicylaldehyde, terpineol, thymol) tested antibacterial activity on several strains of pathogenic bacteria: *Campylobacter jejuni*, *Escherichia coli*, *Listeria monocytogenes*, *Salmonella enterica*. The study stemmed from the need to find a comparable method to prove antibacterial activity of the tested material since the literature is full of information on materials tested in a plethora of different methods. The 27 oils and 12 compounds were active against all the species of bacteria.

Both the aldehydes (e.g., cinnamaldehyde, citral, citronellal, perillaldehyde, salicylaldehyde) and phenols (e.g., carvacrol, eugenol, isoeugenol, thymol) were found to be active in bactericidal assays. Monoterpenes with an exocyclic double bond (eugenol and estragol) were generally more active than the isomers with endocyclic double bonds (anethole and isoeugenol) (Friedman et al., 2002).

**Anticandidial Effects**

Candida infections, also called yeast infections, are difficult to treat due to the paucity of effective cure. Therefore, extensive research is conducted in this field. The difference between antibacterial antibiotics and antifungal agents can be explained by the difference between prokaryote bacteria and eukaryote fungi and yeasts.
Since humans and other mammals have eukaryotic origin like the fungi, it is not so easy to develop a mechanism to inhibit fungal and yeast infections without damaging human cells. This is the reason why there are more antibiotics than antifungal agents. The difference between mammals and fungi lies in their t-RNA-AA-acyltransferases, steroid synthesize systems (while cholesterol is the main steroid in mammals, it is replaced by ergosterol in fungi) and carbohydrate structure of the cell walls. An added difficulty in developing anticandidial remedies is due to the fact that Candida albicans is a yeast found naturally in the gut flora.

According to AMICBASE database 103,425 data exist on antimicrobial activity of nearly 6000 compounds and over 2000 microorganisms covering the period 1987-1999. In the database over 49,000 data exist on antifungal compounds and 6083 data relate to anticandidial compounds.

Ten phytochemicals with the strongest activity against Candida albicans are listed with their source and minimum inhibitory concentration (MIC) (ppm) values: lapachol (Chilopsis linearis, 0.03, Guiraud et al., 1994), polygodial (Polygonum hidropiper, 0.1-3.13, Himejima and Kubo, 1993), juglone (Juglans regia, 0.78, Clark et al., 1990), swartziadiolne (Swaartzia madagascariensis, 0.78, Hostettmann and Schaller, 1999), allicin (Allium sativum, 1.57-17.3, Yamada and Azuma, 1967), dehydrohispanolone (Ballota saxatilis, 1.5, Citoglu et al., 1998), 3,10β-Dihydroxy-α,10β-dimethyl-8-methylene-7-vinyl-tetradecahydro-5-oxa-acephenantrilen-4-one (2, Bills et al., 1996), hispanolone (Ballota saxatilis, 3.1, Citoglu et al., 1998), ballonigrin (Ballota nigra, 3.1, Citoglu et al., 1998), nagilactone E (Podocarpus sp., 3.13-50 [combined], Kubo et al., 1993).

They show stronger activity than the synthetic antifungal agent ketokonazol (MIC 62.5 µg/mL). Lapachol, a naphtaquinone from Chilopsis linearis tops the list with MIC 0.03 µg/mL. Polygodial, a sesquiterpene dialdehyde from Polygonum hidropiper is second in rank. 32 fold increase in anticandidial activity was obtained when polygodial was used together with trans-anethole, a anticandidial phenylpropanoid from Pimpinella anism (Anise). Similar enhancement of activity was observed with warburganal, another anticandidial sesquiterpene dialdehyde from Warburgia ugdandensis with trans-anethole (Kubo, 1993).

Oregano oil was as effective as amphotericin B in protecting mice from systemic candidiasis. Giving whole essential oil was more effective than its isolated component carvacrol, supporting the view that synergy between certain components is more effective than single compounds (Anon., 2002). A patent has recently been issued for the treatment of candidial nail disease by a mixture of camphor, menthol, thymol and the oil of Eucalyptus citriodora at 750 ppm dose (Nair et al., 2002).

**Other Effects of Essential Oils**

Certain essential oils and aromachemicals have shown the following effects:

1. **Plant Growth Promoting Activity.** A Japanese patent claims that linalool vapour is effective on enhancing the growth of vegetables such as horseradish, kidneybeans and lettuce (Sato et al., 1995).

2. **Plant Growth Inhibitory Activity.** Inhibitory activity of essential oils is expressed against (1) both seedling and sprout growth, (2) seed germination but not sprout emergence. The inhibitory effect of essential oils is exerted not only against other plant species but also against the progeny of producing plant particulary for seed germination and seedling growth. S-(+)–Carvone, a monoterpenic ketone, found in Caraway (Carum carvi) or dill (Anethum graveolens) oils inhibits the sprouting of potatoes (Bang, 1997). Pulegone also has antisprouting activity for potatoes. Minhostachys plants (Muna) containing pulegone in their oil have been used by the Inka Indians in the potato stores to prevent sprouting. Oil v apours of Allium sativum (garlic), Carum carvi (caraway), Salvia officinalis (sage), Minhostachys verticillata (Muna), Mentha piperita (peppermint), Mentha arvensis (cornmint), Mentha spicata (spearmint), Rosmarinus officinalis (rosemary) inhibited the sprouting of potatoes (Bang, 1997). Coridothymus capitatus herb and its oil inhibits the germination of its own seedlings (Vokou, 2002).
monoterpenic cyclic ether isolated from Eucalyptus oil, which is the model compound for the herbicide Cinmethylin was found to be active on grass weeds and some dicotyledonous weeds (Vokou, 2002). Methyl jasmonate emitted by sagebrush plants (Artemisia tridentata susp. tridentata) has recently been shown to inhibit the germination of nearby growing tobacco (Nicotiana attenuata) plants (Preston et al., 2002). Inhibitory monoterpenes camphor and the cineole epimers are the major constituents in sagebrush emissions. Seed germination of a weedy monocot, Echinochloa crusgalli, and dicot, Cassia obtusifolia, was inhibited by 1,8-cineole, while root growth of Cucumis sativa (Muller, 1966) and shoot growth of E. crusgalli (Romagni et al., 2000) were reduced by applications of camphor and 1,4-cineole, respectively.

3. Pest Control. Traditionally, aromatic plants such as sage, sweet basil, cinnamon have been used as insect deterring agents. Essential oils have antifeedant, repellent and other lethal effects against insects, mollusks and other animals. Eleven essential oils were tested for insecticidal activity against Drosophila auraria eggs, larvae and adults (All the oils exhibited insecticidal activity. They prevented egg hatching and caused death of larvae or adult flies). Both surviving and dead larvae had several kinds of malformations. Mentha pulegium and Mentha spicata oils proved most effective on eggs; Satureja thymbra, Coridothymus capitatus, Origanum vulgare subsp. hirtum on larvae and Mentha pulegium on adults. Mortality reached 100% within 30 min of exposure and carvacrol-rich essential oils were second in effectiveness. Geraniol is a repellent of houseflies but attractant of honeybees setting an ideal case in pest control strategies since a good agricultural compound should simultaneously repel pest insects and attract beneficial insects. β-caryophyllene, a common sesquiterpene of many essential oils has been shown to be effective against cabbage butterfly larvae. Terpinen-4-ol, main component of teatree oil is most effective as mosquito repellent. (Vokou, 2002). Wintergreen oil (Gaultheria procumbens) is the essential oil most used for controlling mites in honey bees (Amrine et al., 2002). Menthol and peppermint oil are also used for the same purpose (http://www.wvu.edu/~agexten/varoa/treatmix.htm). House dust mites which occur in “household dust” are causative agents of many allergic diseases, such as bronchial asthma, allergic rhinitis, and atopic dermatitis. The essential oil and its sesquiterpenes obtained from Taiwania cryptomerioides have recently been shown to have antimite activity against two major allergenic household mites: Dermatophagoides pteronyssinus and D. farinae (Chang et al., 2001).

4. Animal Repellent Activity. Snails were repelled by Origanum vulgare subsp. hirtum leaves or essential oil. Presence of the antifeedant oil caused reduction of daily consumption rates regardless of the species. Ethylacetate extract of the molluscicidal plant Origanum compactum immobilized all the furcocercariae of Schistosoma haematobium after 15 min of exposure. The apparent cercaricidal activity was attributed to the presence of terpenoids and flavonoids in the extract. Encouragingly, several non-target aquatic organisms were largely unaffected by exposure to concentrations of the extract that kill S. haematobium (Lahlou, 2002). A patent exists on a repellent mixture for dogs and cats containing pennyroyal oil, musk ambrette, d-limonene, benzaldehyde, anethole, vanillin, cinnamic alcohol, some esters and γ-lactones (Rod, 1986).

5. Enhancement of Soil Respiration. A number of soil bacteria can metabolize essential oils. This facilitates the decomposition process and may contribute to soil fertility. Repeated additions of Satureja thymbra oil to the soil kept CO₂ release high. Many essential oils tested activated soil respiration to a comparable degree. Soils exposed or not exposed previously to essential oils responded similarly. There is evidence that some bacteria can also biodegrade organic pollutants with similar isoprenoid structure. Some monoterpenoids (e.g., carvone, limonene) induce biodegradation of polychlorinated biphenyls (PCB). Possible application areas for these features can be organic farming and pollution control (Vokou, 2002).

6. Skin Penetration Enhancing Activity. Several oils and terpenes have been shown to induce increased and faster transdermal absorption of drugs. Equal effects at smaller doses and even enhanced effects at reduced doses were observed in such combinations.
Menthone and carvone enhanced the penetration of 5-fluorouracil, tamoxifene. The penetration of prednisolon and caffeine was enhanced by a-terpineol and terpinen-4-ol. Further enhancements were as follows: Domperidon, propranolol, haloperidol, chlorpromazine, dihydrotestosterone by limonene; methylsalicylate, leuprorelin acetate by camphor; metoprolol, propranolol, ketoprofen, azidothymidine by linalool and nifedipine by lavender oil (Buchbauer, 2002, 2002a). Acyclic terpene alcohols such as geraniol, farnesol, nerolidol, α-bisabolol were proved to be best enhancers, better than terpene hydrocarbons, for diclofenac sodium and 5-fluorouracil, e.g., geraniol showed 20 times increase.

Use of Medicinal and Aromatic Plants in Veterinary Medicine

The utilization of medicinal and aromatic plants in treating diseases in domesticated animals has been as old as their use for humans. In recent years there is an increasing interest in research into the utilization of plants, plant extracts and essential oils in veterinary medicine. Many successful applications especially in the field of natural antimicrobials look promising. Several products have entered the market particularly for pigs and poultry as well as horses and domestic pets.

The fact that the antibiotics used in animal nutrition are causing bacteria cross-resistance to the generation of antibiotics intended for use in human medicine has led to the ban by the European Union on the use of antibiotics as growth promoters in animals. The introduction of a total ban on antibiotics as feed additives from 2006 onwards will greatly affect the pig and poultry industry (Fink-Gremmels, 2002). Following the ban on certain antibiotics used as growth promoters in animal nutrition particularly in pigs and poultry, increasing efforts are undertaken to replace them with pre- and probiotics, and plant products such as herbs, extracts and essential oils. Many herbs and essential oils, generally those containing phenolic monoterpenes such as thyme and oregano have both antimicrobial and appetizing properties. Therefore, when added in feed, they improve feed consumption leading to better body weight and protect the feed from microbial contamination. Their antioxidant effects help improve the quality of meat produced from such animals.

Our group has conducted two different field trials on broilers and laying hens using a mixture of six essential oils: oregano, laurel leaf, trilobed sage leaf, myrtle leaf, fennel seed and citrus peel as feed additives. Superior performance results were obtained. Essential oil mixture supplemented diets increased carcass yield while decreasing small intestinal and abdominal fat weight numerically, and reduced the death rate. Laying hens produced approximately eight more eggs than control, each weighing 1 gram more, and performed the best feed conversion rate (Bozkurt and Baser, 2002, 2002a).

CONCLUSIONS

Rich biodiversity of the world will continue to be exploited for the benefit of mankind. Last two decades have witnessed the development of a more systematic and methodological approach in research into investigating medicinal and aromatic plants for new therapeutic or other useful leads and to their commercialization. Many new plant drugs and novel properties of known drugs have been discovered. Plant drugs have found their way to national and international pharmacopoeias. The new edition of the European Pharmacopoeia contains around 170 plant drugs. This trend is likely to continue.

The popularity of dietary supplements and nutraceuticals will grow stronger as worldwide research intensifies into antioxidant and free radical scavenging activities of medicinal and aromatic plants. These hybrid products of foods and pharmaceuticals are becoming commodities of our daily lives. This is because not only the pharmaceutical but also food industries have commercial interest in this emerging field.

New scientific evidence on synergy obtained in the last decade regained credibility to plant extracts and essential oils as pharmaceutical aids and started challenging the common belief in industry that single compounds make better drugs.

Aromatherapy and aromachology as well as other forms of TM/CAM will
continue to be popular. New clinical and research evidence will keep these areas as the treasurehouse of discovering useful natural products. Rapid developments should be expected in the extensive utilization of essential oils in food, feed and pharmaceutical industries. The fact that 26 natural aromachemicals proposed as “sensitizers” in the European Cosmetics Directive (Amendment 38, Article 1, Point 6A of Directive 76/768/EEC) is seen as a serious threat to the essential oil and aroma trade and industry since these chemical are ingredients of almost all essential oils. The directive brands these chemicals as hazardous and drastically limits their use in cosmetic products.

The utilization of medicinal and aromatic plants and their secondary metabolites in agriculture and veterinary medicine have never been so popular. Especially the uses of essential oils and aromachemicals as antimicrobial, pesticidal, herbicidal and other therapeutical agents are seen as promising for developing new agricultural or veterinary products.

Combinatorial chemistry and high throughput screening (HTS) techniques were hoped to increase the chances and reduce the cost of developing new medicines. However, their value as a source of useful lead molecules has been questioned and natural products are still considered to be a more economical source of chemical diversity (Harvey, 2000). As less than 10% of the world’s biodiversity has been tested for biological activity, many more useful lead molecules are likely to be discovered in coming years.

Advances in chemical and biological research techniques directly affect the natural products research and those new techniques find their application almost simultaneously. Many new techniques and applications are being discovered by natural product scientists.

Biotransformations, the nature’s way to produce new molecules will continue to be a popular field among the techniques of biotechnology. The discovery of new useful molecules through this technique for use in flavour & fragrance, food and pharmaceutical industries should be expected. The beauty of this technique is the production of natural molecules from natural starting materials.

The last decade has also witnessed the emergence of a better awareness of the conservation of biodiversity. Biopiracy has been widely condemned as a “dirty word” and intellectual property rights of ethnic communities and nations on the traditional use of natural products are now considered seriously when useful information is to be commercialized.

Sustainable harvesting or wildcrafting of medicinal and aromatic plants has been a major concern for UN agencies (e.g., WHO), NGOs and the industry. Following a few proposals, WHO is now considering the introduction of a guideline for Good Field Collection Practice.

The future of basic and applied research and development in the field of medicinal and aromatic plants looks quite bright. I personally look forward to hearing many interesting and exciting reports during the congress in coming days.

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