Chapter

Ocimum Phytochemicals and Their Potential Impact on Human Health

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Abstract

The genus *Ocimum* (Lamiaceae) is distributed all over the world and can be found in many environments. *Ocimum* species is a rich source of various phytochemicals including tannins, phenolic acids, anthocyanins, phytosterols, and policosanols. These phytochemicals have the potential to significantly impact human health. The economic importance of *Ocimum* is also evident; *Ocimum* oil and its constituents and derivatives are used as flavoring agents throughout the world in food, pharmaceutical, herbal, perfumery, and flavoring industry. The important advantages of *Ocimum* plants in various treatments are their safety besides being less expensive, efficacy and availability throughout the world. This paper will focus on the biological effects of *Ocimum* essential oils, with particular attention on the molecular mechanism underlying their action.

Keywords: *Ocimum* sp., essential oil, composition, biological activity

1. Introduction

Living plants produce a vast quantity of chemicals required for their performance and improvement. Some of these chemicals are primary metabolites, which consist of proteins (amino acids), carbohydrates, fats, nucleic acids, etc. but, besides these primary chemicals, the plants further provide just so-called secondary metabolites, which are specific to some taxonomic groups (families, genera). About 80% of the world's population still depends on the traditional system of medicine for curing several health hazards [1]. Despite the vast scientific development in contemporary medicine, Ayurvedic system of medicine is widely practiced and accepted by people not only in India but also in many developed countries. According to the World Health Organization (WHO), about 80% of patients in India still, rely on the practitioners of the traditional system of medicines. The therapeutic use of herbal crude medicines in different rural and urban communities is most of the time regulated by their traditional beliefs, and thus a majority of the herbal drugs are used as "folk" medicines and well practiced since long past. Furthermore, increasing dependency on medicinal plants in the industrialized communities have been found to the extraction and improvement of several remedies and chemotherapeutics from these plants and from traditionally established rural herbal remedies [2]. In these communities, herbal remedies become deeply engaged in the practice of minor conditions and again on the explanation of the increasing costs of specific health maintenance. Although synthetic drugs enhanced the demand against green remedies because of their rapid-acting implements, people have been turned up to understand the benefits correlated with essential remedies. Chemically prepared drugs may act at earlier, but they side effects which influence the human body separately in the long run, because medicinal plants work in an integrated or probiotic with limited or no negative effects on the body [3].

The genus *Ocimum* includes approximately 150 species, possessing a great variation in plant morphology and biology, essential oil content, and chemical composition [4]. The economic importance and global dissemination of *Ocimum*, with its many uses in cooking and folk medicine, make it important to investigate its pharmacological and toxicological effects in order to ensure its efficacy and safety. In India, among the medicinal herbs known for their healing properties, the genus *Ocimum* (commonly known as 'Basil' or 'Tulsi') is very important for its curative potential. Basils contain a wide range of essential oils rich in phenolic compounds and a wide array of other natural products including flavonoids and anthocyanins [5] having great pharmacological importance.

Nowadays, scientists are mainly focused on exploring the potential of plant antioxidants for curing several diseases. Antioxidants are compounds that can delay or inhibit the oxidation of lipids or other molecules by inhibiting the initiation or propagation of oxidative chain reactions [6]. Antioxidants counteract the harmful reactive oxygen species (ROS) and free radicals generated in the living organism during regular metabolism, especially under stress conditions. Several in vitro and in vivo studies have already proved the antioxidative property of beta-carotene, alfa-tocopherol, ascorbic acids, phenolics, flavonoids present in different plants [7].

Presently due to our regular stressful lifestyle, we are suffering from several types of diseases like aging, diabetes, degenerative disorders, etc., which mainly develop due to the development of ROS in our body. A dynamic balance is already operating in our body to reduce the harmful effects of generated ROS that is not adequate enough. Therefore, it is obvious to enrich our diet with antioxidants for developing protection. The purpose of this paper will focus on the recent research of the major nutrients and phytochemicals of *Ocimum* and their potential health benefits related to the dietary prevention of chronic diseases.

2. Health benefits of phytochemicals

"Phyto" in the word of phytochemicals is derived from the Greek word "phyto," which means plant. Phytochemicals are a naturally occurring group of chemicals in plants and plant-derived foods, which may function in reducing the risk of chronic diseases [8]. Although it is estimated at least more than 5000 dietary phytochemicals have been discovered, it is believed that a high percentage of phytochemicals in foods still remain unknown [8]. Critical reviews of studies available in the literature support the concept that phytochemicals (polyphenols, tocopherols, tocotrienols, carotenoids, and ascorbic acid) has been associated with the maintenance of good health as well as prevention/treatment of many health conditions including cancer, cardiovascular diseases, diabetes, hypertension, stroke, metabolic syndrome, and other degenerative diseases. It is largely accepted that the additive effects of the combinations of various phytochemicals in whole plant-based foods are shown to have stronger protective actions than single, isolated phytochemical compounds [9].

3. Role of secondary metabolites

New drug model seeks to meet on bringing compounds active toward target proteins. Even though newly pharmaceutical companies and support organizations take influence in molecular design, combinatorial chemistry and synthetic chemistry, natural productions, and especially those of plant source, remain as a prerequisite cause of new remedies, current medicine leads and other new synthetic entities (NCEs) [10, 11].

Plants produce a diverse array of compounds that can broadly be categorized into primary and secondary metabolites. Primary metabolites are the ones which are required for the normal growth and biological processes and are produced in the pathways that are crucial for plant survival. The other class of metabolites, though generally termed secondary, is also very crucial for plants from the ecological perspective.

These secondary metabolites are classified on the basis of their biosynthetic pathway and the following types are frequently observed-terpenes, phenylpropanoids, alkaloids, saponins, and glucosinolates. The availability of carbon, nitrogen, and sulfur along with energy from the primary metabolism governs the biosynthesis of these compounds [12].

4. Classification of secondary metabolites

Metabolites are the mediators and amounts of metabolism. The term metabolite is commonly confined to narrow fragments. Metabolites have specific functions,

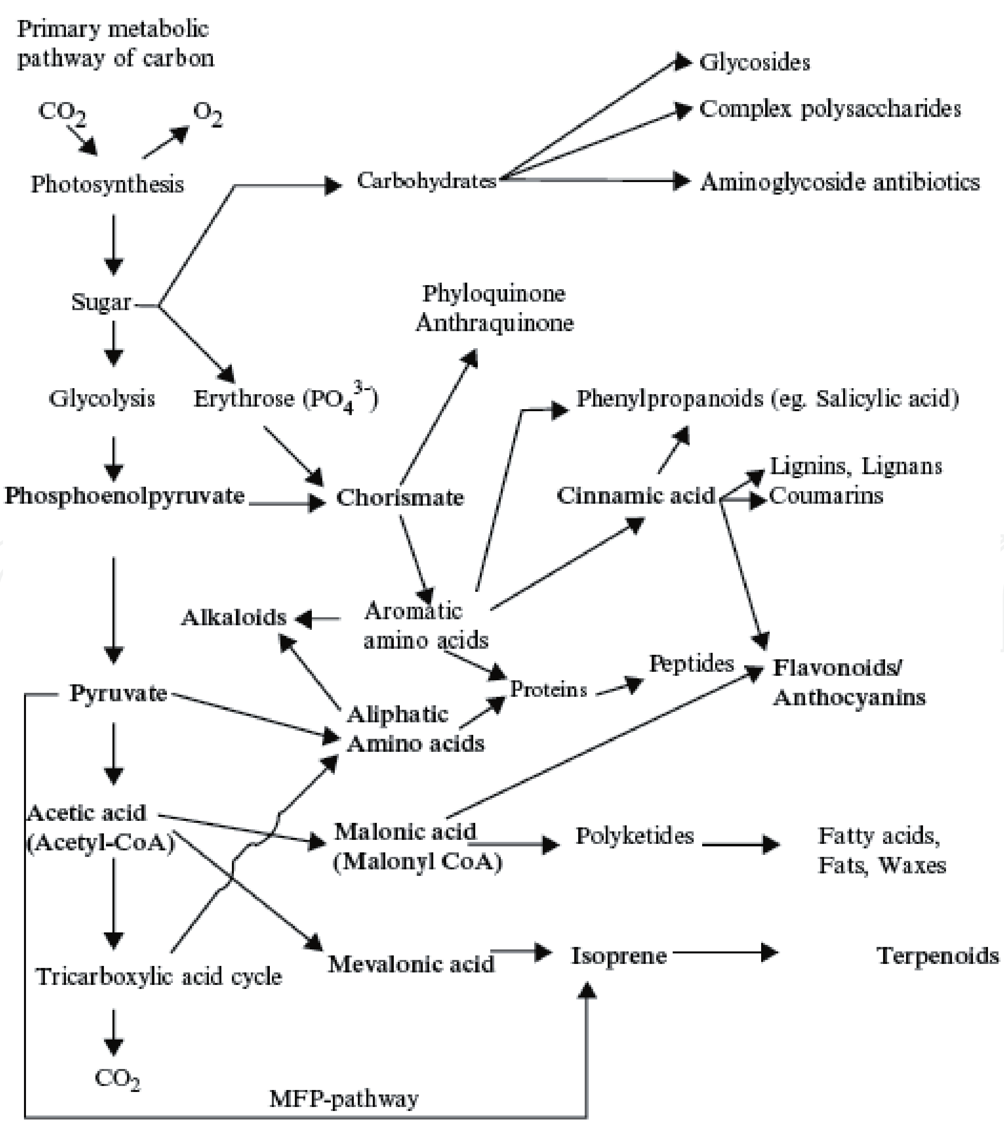

Figure 1.
Major pathways of biosynthesis of secondary metabolites [15].

consisting of fuel, structure, signaling, stimulatory and inhibitory effects on enzymes, and the catalytic activity of their holding (mostly as a cofactor to a stimulant), defense and interaction with distinct pathogens. Plant metabolites are categorized based on their biosynthetic pathways. The pathways of biosynthesis are responsible for the occurrence of both primary and secondary metabolites (**Figure 1**) [13, 14]. Plant secondary metabolites can be classified on the basis of chemical structure (for example, having rings, containing a sugar), composition (consisting of nitrogen or not), their solubility in numerous solvents, or the pathway by which they are synthesized (e.g., phenylpropanoid, which provides tannins).

5. Essential oil of *Ocimum* species

Since ancient times, essential oils are known for their medicinal use, and they are very much interesting and impressive natural plant commodities. They continue to be of paramount importance until the present day. Essential oils have been tested as perfumes, flavors for foods and beverages, or to provide both bodies and care for thousands of years [16].

Species	Class of compounds	Reference
O. basilicum L.	**Monoterpene hydrocarbons** α-Phellandrene, α-pinene, α-terpinene, α-terpinolene, α-myrcene, β-phellandrene, β-pinene, camphene, *cis*-β-ocimene, *cis*-ocimene, δ-3-carene, β-ocimene, (E)-β-ocimene, limonene, myrcene, *ρ*-cymene, sabinene, terpinolene, thujene, γ-terpinene	[18–20, 23]
	Oxygenated monoterpene α-Citral, α-fenchyl acetate, α-terpineol, borneol, bornyl acetate, camphor, carvacrol, carvone, 1,8-cineole, *cis*-linalool oxide, *cis*-rose oxide, citronellol, endo-fenchol, estragol, eugenol, exo-2-hydroxycineole-acetate, fenchone, geranial, geraniol, geranyl acetate, hotrienol, *iso*-neomenthol, *iso*-pinocamphone, *trans*-pinocamphone, L-camphor, L-carvone, lavandulol, linalool, linalool *cis*-furanoid, linalool *trans*-furenoid, linalyl acetate, menthol, menthone, methyl chavicol, myrtenal, myrtenol, neral, nerol, ocimene oxide, pinocarvone, P-menth-1,8-dien-4-ol, piperitone, pulegone, terpinen-4-ol, terpinyl formate, *trans*-linalool oxide, *trans*-myroxide, *trans*-sabinene hydrate, *trans*-*p*-menth-2-en-1-ol, thymol, verbenone, (Z)-sabinene hydrate	[18, 19, 21, 25]
	Sesquiterpene hydrocarbons β-acoradiene, β-bourbonene, β-caryophyllene, β-cedrene, β-copaene, β-cubebene, β-elemene, β-guaiene, β-ocimene, β-selinene, cyclohexane, 2,4 diisopropenyl-1-methyl-1-vinyl, 1,4,7-cycloundecatriene,1,5,9,9-tetramethyl, α-acoradiene, α-amorphene, α-bulnesene, α-cadinene, α-cedrene, α-copaene, α-cubebene, α-guaiene, α-gurjunene, γ-gurjunene, α-7-epi-selinene, α-humulene, aromadendrene, α-(Z)-bergamotene, α-zingiberene, epsilon-muurolene, dehydroaromadendrene, germacrene-A, bicycloelemene, bicyclogermacrene, cadinene, cadina-3,5-diene, *cis*-calamene, *cis*-muurola-4(14),5-diene, (E)-β-farnesene, (E)-caryophyllene, 1-epibicyclosesqui-phellandrene, germacrene-B, germacrene-D, guaia-1(10),11-diene, iso-caryophyllene, isoledene, longifolene, δ-selinene, St α-ylangene, *trans*-α-bisabolene, *trans*-α-bergamotene, *trans*-β-farnesene, *trans*-β-ocimene, *trans*-caryophyllene, valencene, γ-cadinene, γ-terpin, δ-cadinene, γ-muurolene, (Z)-calamenene	[19, 26, 21–24]

Species	Class of compounds	Reference
	Oxygenated sesquiterpenes α-Cadinol, α-humulene oxide, alloaromadendrene, β-basibolol, β-basibolol isomer, β-eudesmol, cubenol, caryophyllene oxide, 1,10-di-epi-cubenol, dihydroactinidiolide, isospathulenol, muurolol, spathulenol, T-cadinol, viridiflorol, (Z)-nerolidol	[19, 21]
	Triterpene Alphitolic acid, betulin, betulinic acid, 3-epimaslinic acid, euscaphic acids, oleonolic acid, pomolic acid, ursolic acid, basilol, ocimol	[27]
	Aromatic compounds 4-Allylphenol, anethole, anisaldehyde, benzyl alcohol, cuminaldehyde, estragole, ethyl cinnamate, methyl benzoate, methyl cinnamate, methyl eugenol, methyl salicylate, *p*-methoxycinnamaldehyde, phenethyl alcohol, phenyl acetaldehyde, safrole, benzaldehyde, *cis*-hex-3-enyl acetate	[21]
O. kilimandscharicum Guerke	**Monoterpene hydrocarbons** α-Phellandrene, α-pinene, α-terpinene, γ-terpinene, β-pinene, camphene, limonene, D-limonene, β-ocimene, (E)-β-ocimene, myrcene, ρ-cymene, terpinolene, thujene, α-terpinolene, isosylvestrene, γ-himachalene	[28, 29, 34]
	Oxygenated monoterpene α-Citral, α-terpineol, borneol, bornyl acetate, camphor, linalool, citronellol, geraniol, myrtenol, 1,8-cineole, eugenol, terpinen-4-ol, *trans*-sabinene hydrate, (Z)-sabinene hydrate, α-campholenal, isoborneol, endo-borneol, globulol	[29–31, 34]
	Sesquiterpene hydrocarbons α-Copaene, α-gurjunene, α-humulene, β-caryophyllene, β-copaene, β-cubebene, β-elemene, δ-cadinene, γ-muurolene, *trans*-caryophyllene, germacrene-D, germacrene-B, β-selinene	[31, 32, 34]
	Oxygenated sesquiterpenes Cubenol, caryophyllene oxide, spathulenol, α-cadinol, viridiflorol	[28, 32]
	Phenolic compounds Vanillin	[33]
O. gratissimum L.	**Monoterpene hydrocarbons** α-Pinene, *cis*-ocimene, *trans*-ocimene, β-pinene, α-terpinene, p-cymene, myrcene, α-phellandrene, A^3-carene, sabinene, limonene, γ-terpinene, terpinolene, cis-sabinene hydrate	[35–39]
	Oxygenated monoterpene Camphor, eugenol, methyl eugenol, 1,8-cineole, trans-sabinene hydrate, linalool, δ-terpineol, terpinen-4-ol, α-terpineol, thymol, carvacrol, eugenol, methyleugenol	[36, 39–41]
	Sesquiterpene hydrocarbons *trans*-Caryophyllene, germacrene-D, α-farnese, β-bisabolene, *cis*-β-ocimene, *trans*-β-ocimene, α-copaene, β-elemene, β-caryophyllene, α-humulene, germacrene-D, β-selinene, trans-β-Farnesene, β-bisabolene, γ-cadinene, δ-cadinene, γ-muurolene, β-cubebene, α-cubebene	[33, 36, 40, 41]
	Sesquiterpenes oxygenated β-Caryophyllene epoxide	[36]
	Aromatic compounds Methyl cinnamate	[36]
O. canum Sims.	**Terpenoids** Cyclosativen	[42]

Species	Class of compounds	Reference
	Monoterpenes hydrocarbon α-Thujene, α-pinene, camphene, β-pinene, limonene, γ-terpinene, terpinolene, sabinene, myrcene, α-terpinene, *p*-cymene, (Z)-β-ocimene, (E)-β-ocimene, perillene, (E)-β-epoxyocimene, α-phellandrene, α-terpinene, *cis*-β-ocimene, *cis*-sabinene hydrate, carene, tricyclene	[43, 45, 48]
	Oxygeneated monoterpenes Eugenol, linalool, 1,8-cineole, 5-isopropyl-2-methylbicyclo[3.1.0]hexan-2-ol, fenchone, *trans*-linalool oxide (furanoid), camphor, δ-terpineol, terpinen-4-ol, α-terpineol, fenchyl acetate (endo), isobornyl acetate, borneol, thymol, menthone, geranial, α-fenchyl acetate, bornyl acetate, exo-2-hydroxycineole acetate, verbenone, camphenol, myrtenyl acetate	[43, 46, 48]
	Sesquiterpenes hydrocarbon α-Copaene, β-elemene, β-caryophyllene, germacrene D, β-bisabolene, E, E-α-farnesene, δ-cadinene, α-cadinene, *trans*-α-bergamotene, aromadendrene, α-humulene, *epi*-bicyclosesquiphellandrene, bicyclogermacrene, δ-guaiene, calamenene, (E)-α-bisabolene, valencene, *trans*-α-bergamotene, γ-muurolene, α-muurolene, epi-α-muurolol, elemol, β-selinene, α-selinene, (Z,E)-α-farnesene, *trans* β-ocimene, (E)-β-farnesene	[45, 46, 49]
	Oxygenated sesquiterpenes α-Cadinol, spathulenol, (Z)-nerolidol, caryophyllene oxide, β-eudesmol, viridiflorol	[42, 46]
	Aromatic compounds Methyl eugenol, estragole, benzyl benzoate	[45, 47]
	Esters 1-Octen-3-yl acetate	[44]
	Others Naphthalene	[46]
O. tenuiflorum L. *syn. O. sanctum* L (purple type)	**Monoterpenes hydrocarbon** α-Pinene, β-pinene, β-terpinene, D-limonene, camphene, sabinene, myrcene, *p*-cymene, limonene, α-terpinene, *α*-thujene, *α*-myrcene, α-terpinolene, terpinolene, γ-terpinene, (E)-β-ocimene, β-myrcene, *α*-camphene, β-terpinolene, β-*cis*-ocimene	[50–52]
	Oxygeneated monoterpenes Linalool, menthol, methyl chavicol, α-citral, carvone, lavandulol, hotrienol, eugenol, 1,8-cineole, globulol, borneol, bornyl acetate, camphor, thymol, geranial, citronellol, E-linalool, β-citral, carvacrol, methyl chavicol, α-fenchyl acetate, myrtenol, terpinen-4-ol, *trans*-sabinene hydrate, *cis*-geraniol, *cis*-*α*-terpineol, *cis*-linalool oxide, eucalyptol, *cis*-linalool oxide (furanoid), *trans*-linaool oxide (furanoid), δ-terpineol	[52–54]
	Sesquiterpenes hydrocarbon Caryophyllene, β-farnesene, germacrene-D, isoledene, β-selinen, β-cubebene, β-elemene, β-caryophyllene, β-bourbonene, α-humulene, γ-muurolene, bicyclogermacrene, δ-cadinene, α-copaene, *trans*-caryophyllene, selinene, β-elemene, *β*-guaiene, β-bisabolene, α-guaiene, germacrene-B, valencene, (E)-β-farnesene, *trans*-α-bergamotene, α-cubebene, β-germacrene, α-farnesene, α-caryophyllene, α-selinene, (Z)-β-farnesene	[50, 52–54]

Species	Class of compounds	Reference
	Sesquiterpenes oxygenated α-Cadinol, alloaromadendrene, caryophyllene oxide, cubenol, t-cadinol, spathulenol, viridiflorol	[53, 54]
	Aromatic compounds *p*-Methoxycinnamaldehyde, estragole, benzaldehyde	[51, 54]
O. tenuiflorum (white type)	**Monoterpene hydrocarbons** α-pinene, camphene, β-pinene, limonene, (E)-β-ocimene, *p*-cymene, γ-terpinene, camphene hydrate, carene, terpinolene, sabinene hydrate, terpinene, ocimene, limonene, terpinene, phellandrene, myrcene, sabinene, camphene, thujene, tricyclene	[55–57]
	Oxygeneated monoterpenes Linalool, borneol, eugenol, methyl eugenol, 1,8-cineole, α-terpineol, geraniol, *trans*-linalool oxide (furanoid), δ-terpineol, terpineol, terpinen-4-ol, δ-terpineol, camphor, fenchone, *trans*-sabinene hydrate, eucalyptol	[56–59]
	Sesquiterpenes hydrocarbon β-Elemene, β-caryophyllene, α-humulene, germacrene D, β-selinene, α-selinene, α-cubebene, δ-cadinene, elemol, bicyclogermacrene, α-cadinene, copaene, β-elemen, α-guaiene, γ-muurolene, δ-cadinene, amorphene, cubebene, α-bisabolene, cadinene, β-bisabolene, muurolene, germacrene, humulene, farnesene, sesquiphellandrene, bergamotene, guaiene, elemene, bourbonene, zingiberene	[55–59]
	Sesquiterpenes oxygenated Spathulenol, caryophyllene oxide, viridiflorol, β-eudesmol, γ-eudesmol	[60, 61]
	Aromatic compounds Estragole	[55, 60]

Table 1.
Compositions of species-wise distribution of bioactive compounds in Ocimum species.

Chemical diversification is of special significance if at the genus or species level both terpenes and phenylpropenes can be formed in the essential oil. Most Lamiaceae preferentially accumulate mono-(and sesqui-)terpenes in their erratic oils but some genera show oils too rich in phenylpropenes [17].

The action of essential oils begins by entering the human body via three possible different ways including direct absorption through inhalation, ingestion or diffusion through the skin tissue.

Table 1 presents published compositions of species-wise distribution of bioactive compounds in *Ocimum* species.

6. Biological activities of *Ocimum* species

The genus *Ocimum* (family Lamiaceae), collectively known as basil, is composed of a diverse and rich source of essential oil containing plants. The main issues of concern with the use of herbal drugs remain safety, validation of claims and standardization of product. Different species and forms of *Ocimum* spp. vary in growth habit, color, and aromatic composition, making the true botanical identity of basil difficult (**Figure 2**). There exist the problems of significant variation in the content of *Ocimum* plants across and within species, with the implication of varied

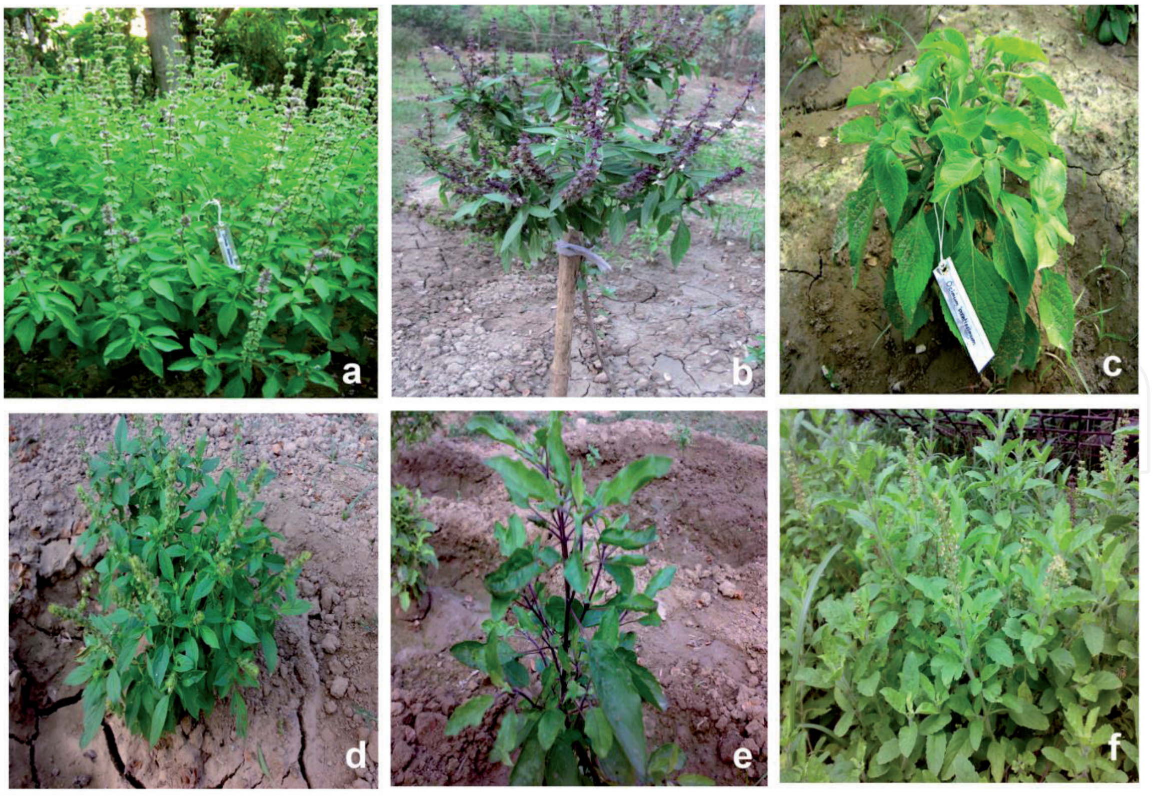

Figure 2.
Different species of Ocimum (a) Ocimum basilicum L.; (b) Ocimum kilimandscharicum Guerke; (c) Ocimum gratissimum L.; (d) Ocimum canum Sims.; (e) Ocimum tenuiflorum L. syn. O. sanctum L. (purple type); (f) Ocimum tenuiflorum (white type).

biological activities. During the last two decades, it has been shown that *Ocimum* oil and its constituents possess different biological activities including antioxidant, antimicrobial, anticancer, and anti-inflammatory properties.

6.1 Oxidant activity

Anti-oxidants play an important function in protecting the body against free radicals. They achieve this by stopping the formation of new free radicals species, converting older ones to free radicals, less toxic molecules that can be easily mopped up and preventing radical chain reaction [62]. The principal function of anti-oxidants is in suspending the oxidation of other molecules, by inhibiting the initiation or propagation of oxidizing chain reactions by free radicals and thereby reducing oxidative damage to the human body [63]. Two great mechanisms of procedure have been proposed for antioxidants [64]. The initial is a chain breaking method by which the initial antioxidant provides an electron to the free radical stage in the systems. The second technique involves the destruction of ROS/reactive nitrogen species initiators (secondary antioxidants) by cutting off chain starting catalysts (**Figure 2**). The potential role in the food industry and human health, antioxidants are getting acceptance all across the globe. Antioxidants are defined as a substance that easily in small amounts, can inhibit or prohibit the oxidation of readily oxidizable elements. The antioxidant is also defined as a substance qualified of inhibiting special oxidizing stimulants or a substance that serves with oxidizing agents prior to creating damage to other fragments or a substance that sequesters metal ions or even a substance efficient of the recovering system such as iron transporting protein [65].

Natural antioxidants have been studied intensively during the past years which are mainly phenolic compounds. Moreover, oxidation is a degenerative process in biological systems due to the endogenous reactive oxygen species (ROS). Reactive oxygen species (ROS) are chemical properties originate in the body during metabolism that is overmuch reactive and may have one or expanded unpaired electrons. Oxidative stress, i.e., an inequality between ROS and antioxidant defenses have deleterious aftereffect, such as the peroxidation of membrane lipids and the aggression on biomolecules (proteins, membrane enzymes, carbohydrates and DNA) [66].

Various *Ocimum* species and their extracts or essential oils have been determined to achieve antioxidant activity [67, 68]. Phenolic acids, hydroxycinnamates, and flavonoids are perhaps the major antioxidants [67]. Vitamin antioxidants (e.g., ascorbic acid and carotenoids) are secondary contributors to the overall antioxidant capacity [69]. In essential oils, unsaturated terpenes having a cyclohexadiene structure (e.g., terpinene) and secondary cyclic oxygenated terpenes (e.g., thymol) may lead to antioxidant capacity, while acyclic unsaturated oxygenated monoterpenes (e.g., linalool), aromatic oxygenated monoterpenes (e.g., eugenol), methylchavicol (estragole), sesquiterpene hydrocarbons (e.g., α-bergamotene, germacrene D, γ-cadinene, δ-cadinene, β-selinene, sesquiterpenes oxygenated (e.g., spathulenol) may act as pro-oxidants [68].

Different test methods have been applied, and it becomes to be understood between the complete essential oil and individual components [70–73]. A strong chelating effect on metals as iron or copper has been reported to diminish the presence of ROS obtained from reactions bar with these metals [74]. In addition, the antioxidant actions of *Ocimum* essential oils have also been found employing metal-independent oxidative processes [75] or controlling stable free radicals, such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical [71, 76]. The DPPH test, a test widely used to measure the ability to donate hydrogen atoms [77], was applied to measure the antioxidant capacities of *Ocimum* species extracted by different solvent systems; these include the methanol extracts of *O. basilicum* L., *O. canum* Sims., *O. gratissimum* L., *O. kilimandscharicum* Guerke, *O. sanctum*, *O. tenuiflorum* [67, 71, 76, 78–80]; the ethanol extracts from *O. basilicum* L., *O. gratissimum* L., *O. kilimandscharicum* Guerke, *O. sanctum* [76, 79, 81–83].

Particular attention has been focused on the scavenger ability to inhibit the process of low-density lipoprotein (LDL) cholesterol oxidation since it represents a major prevention mechanism against atherosclerosis. Various experimental evidence, using in vitro and in vivo preclinical models, showed a strong action of *Ocimum* essential oils [84]. Moreover, Aqueous extracts *Ocimum sanctum* and 70% ethanol extracts *Ocimum basilicum* L. were able to reduce 5-lipoxygenase-driven cellular recruitment of leukocytes and the damaging consequences of their ability to release ROS while leaving unimpaired the generation of prostaglandins, which promote microvascular blood flow and act as immunomodulators [85–87].

In many cases, the antioxidative activity (**Figure 3**) of essential oils cannot be attributed to the main compounds; minor compounds and synergistic effect may significantly contribute to the activity.

6.2 Antimicrobial

For thousands of years, folk medicine has used *Ocimum* leaf for the treatment of infections. Such protective properties have been confirmed by several studies performed in the last decades using *Ocimum* essential oil [29] or isolated compounds. Gram-positive and Gram-negative bacteria, as well as antiprotozoal and also *anti-Trichomonas vaginalis*, resulted sensitive to the antiproliferative action of *Ocimum oil* and its derivatives [29, 88–90]. At present, the exact mechanism responsible for the antimicrobial activity of *Ocimum* oil and its derivatives is still not completely

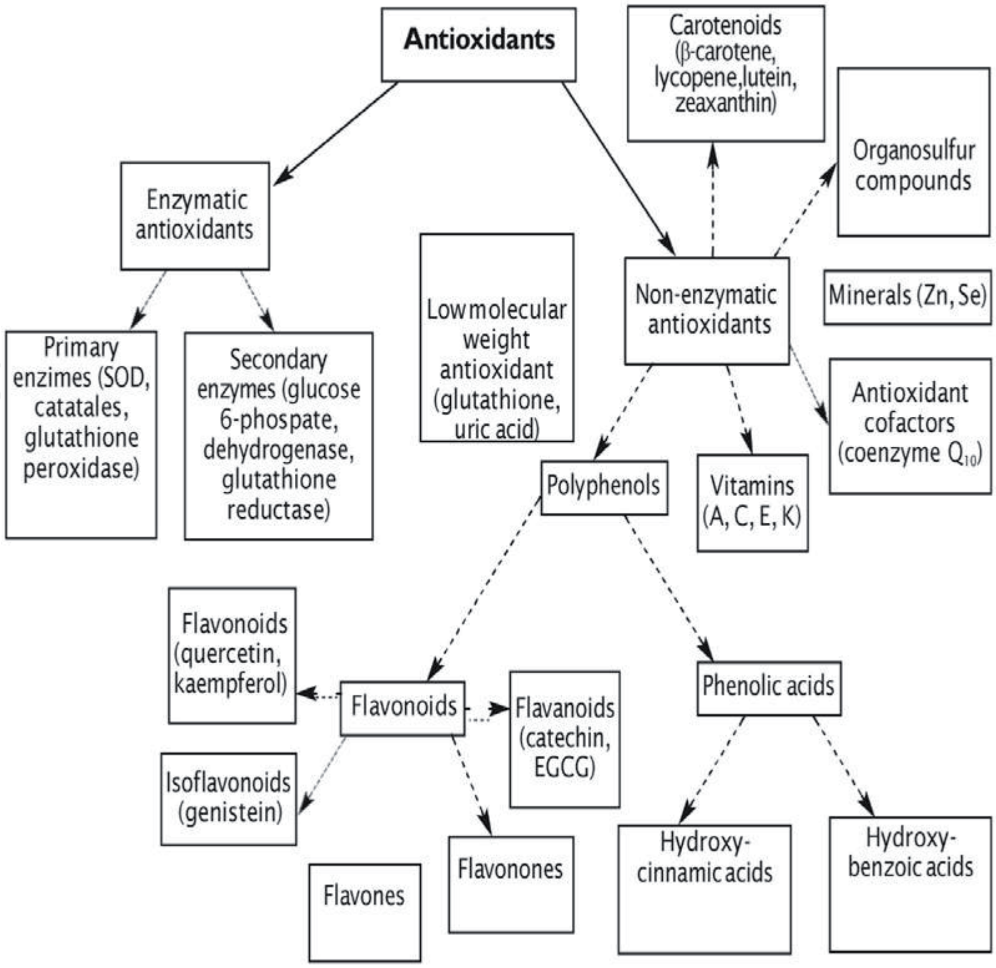

Figure 3.
Types of antioxidants.

clarified, although various modes of action in the bacterial cell have been discussed including degradation of the cell wall, damage to cytoplasmic membrane and membrane proteins, leakage of cell contents, coagulation of cytoplasm, and depletion of proton motive force [91–93].

The antibacterial and antifungal activities of *Ocimum* species have been studied on various bacteria and fungi [29, 94–96]. These studies indicate that essential oils are more efficient antifungals and antibacterials compared to the polar extracts [97–99]. *Ocimum sanctum* essential oils showed remarkable antimicrobial activity against bacteria and other microorganisms, such as periodontopathogens [100], mainly due to the presence of oxygenated monoterpenes in their chemical compositions [101].

The essential oil and methanol extracts of five *Ocimum* species have an appreciable activity against seven human pathogenic bacteria [29], essential oils of *Ocimum* species showed strong antimicrobial activity against all seven microorganisms tested. Oils of seven *Ocimum* taxa (*O. americanum* L., *O. basilicum* L., *O. campechianum* Mill., *O.* x *citriodorum* Vis., *O. kilimandscharicum* Baker ex Gürke and three botanical varieties and cultivars of *Ocimum basilicum* L.: 'Genovese', var. difforme and var. purpurascens)) showed strong antimicrobial activity against all 8 microorganisms tested by Carovic-Stanko et al. [102].

Among the antifungal activities, the *in vitro* antifungal activity of *O. basilicum* L. essential oil against Aspergillus flavus fungal growth and aflatoxin B1 production [103], essential oils of *O. basilicum* L. showed strong antifungal activity against *A. flavus*, and the main components were linalool, 1,8-cineol, eugenol, methyl cinnamate, α-cubebene, caryophyllene, β-ocimene and α-farnesene.

6.3 Anticancer activity

For a long time, the polyphenols of the *Ocimum* oil of the diet have been considered to play a role for the prevention of certain types of cancer in the Asian origin [104]. Even more than in *Ocimum* oil, constituents present in *Ocimum* leaf extract has shown strong antioxidant potency and inhibition of cancer cell proliferation, thus suggesting the protection against the genotoxic action of the ROS as one of the mechanisms explaining the anticancer effects of these compounds. Indeed, either methanol aqueous *Ocimum basilicum* L. leaf extract or the isolated constituents eugenol epoxide free radical scavenging activity and growth inhibition at low micromolar concentration on human breast cancer cell lines (MCF-7 and MDA-MB-231) [105, 106] and Human cancerous cell lines (HL60-promyelocytic blood leukemia cells) [107]. Such findings were further confirmed by other in vitro reports, testing the effects of *Ocimum basilicum* L. against four different humans cancer cell lines viz. human cervix adenocarcinoma HeLa cells, human melanoma FemX cells, human chronic myelogenous leukemia K562 cells, and human ovarian SKOV3 cells [108]. Furthermore, Karthikeyan et al. [109] demonstrated regression of tumors caused by orally administrated aqueous and ethanolic extracts of *Ocimum sanctum* in mice that developed spontaneous soft tissue sarcomas.

Monga et al. [110] studied the antimelanoma and radioprotective activity of essential oils obtained by 50% alcoholic aqueous leaf extract from five species of *Ocimum* viz. *Ocimum sanctum* (SE), *Ocimum gratissimum*, *Ocimum basilicum*, *Ocimum canum*, and *Ocimum kilimandscharicum*, were evaluated using C57BL and Swiss albino mice tumorigenesis; growth inhibition has in fact been associated with (a) reduction of tumor volume (b) blockage of messengers of pathways involved in cell proliferation was evident in all the oils but the greater was shown by that obtained from *Ocimum tenuiflorum* (syn. *O. sanctum*) compared to other *Ocimum* species. In various experiments and test systems, some mono-and sesquiterpenes showed activity, where camphor, 1,8-cineole and limonene were of greatest interest. Camphor, 1,8-cineole and limonene, the anti-inflammatory compound of *Ocimum kilimandscharicum* oil, showed a strong time-and dose-dependent cytotoxic effect on human ovarian cancer cell [111]. The potential antitumor effects of camphor have been shown previously [112, 113], and the mechanistic action of camphor against cancer included the improvement of immune function [114] and the radiosensitizing effect on transplantable mammary adenocarcinoma in mice [112]. Ursolic acid showed some potentiating effect on the anticancer activity of rosmarinic acid, cinnamic acid, caffeic acid, sinapic acid, and ferulic acid on various cell lines [106].

6.4 Cardiovascular protection

For decades, investigation on the health-promoting effects of Asian diet has been revealed that *Ocimum* oil consumption is a key factor in the cardiovascular protection found in Asian origin [115]. It is well established that the healthful properties of *Ocimum basilicum* L. oil depend largely on its Cardiac glycosides and catecholamines content [116]. But, many arguments prove that in *Ocimum* oil there are little bioactive components, much than Cardiac glycosides and catecholamines, effective for its cardiovascular protective properties: among them, the ethanolic fraction of *Ocimum* oil, and in specific omega-3 fatty acids have proved antioxidant, anti-platelet aggregation, vasodilatory, and anti-inflammatory effects, all engaged in this health beneficial action [117–119].

Oxidation of LDL cholesterol is one of the key steps in the induction of atherosclerotic lesions by increasing damage to the arterial side through several processes, including growth factor and chemotactic protein expression, inflammation, and build up local macrophages [120, 121] have indicated that ethanolic leaf extract of *Ocimum basilicum* L. oil strongly inhibits copper sulfate-induced oxidation of LDL, as a result of the step of different indicators of lipid oxidation [phospholipids (PL), cholesterol ester (CE), triacylglycerol (TG)].

Although the contraction of plasmatic cholesterol and LDL is the primary technique regulating the antiatherogenic activity of *Ocimum basilicum* L. extract, other implements are further identified [121]. It is well settled that local leukocyte and monocyte recruitment into the vessel wall is initial walk-in atherogenesis. This fact takes combined with the statement in the endothelial cells of adhesion fragments such as intercellular adhesion fragment-1 (ICAM-1) and vascular adhesion fragment-1 (VCAM-1). Aqueous extract of *Ocimum gratissimum* L. showed the capacity to reduce LPS-stimulated expression of BEAS-2B cell in human lung epithelial cells inhibiting its mRNA levels. Moreover, Li et al. [122], investigating the action of distillate and residue fractions of basil essential oil (viz. estragole, methyl eugenol, linoleic acid, α-cadinol, and α-bergamotene) in-a Raw 264.7 cells line, have demonstrated that residue fractions prevents the expression of gene and suppressed the production of cytokines (TNF-a, IL-b, IL-6) in LPS-induced Raw264.7 cells, which contribute to treating various disorders caused by extreme oxidative stress.

6.5 Anti-inflammatory

The inflammatory response involves long been compartmentalized into multiple attributes commonly termed redness, heat, pain, and edema. Inflammatory injuries lead to the discharge of a variety of fundamental mediators, cytokines, and chemokines that balance cellular infiltration that consequentially brings about resolving inflammatory response and restoration of tissue scrupulosity. However, immutable inflammatory stimuli or dysregulation of mechanisms of the resolution phase can lead to chronic inflammation [123, 124].

Ocimum extracts contain numerous constituents which could have anti-inflammatory effects. The anti-inflammatory effects of *Ocimum* oil phenolics, in RAW 264.7 macrophage cells have been described by Aye et al. [125]. When added to murine macrophages stimulated with bacterial lipopolysaccharide (LPS), *Ocimum* oil phenolics did not cause cytotoxicity in RAW 264.7 macrophage cells in vitro, as evaluated by a significant increase in the production of nitric oxide [125]. Additionally, NO is a significant inflammatory mediator generated by NOS (neuronal, inducible, and endothelial) under physiological and pathophysiological conditions [126]. It further serves as a crucial mediator during the inflammatory process. Enhanced NO production and iNOS expression contributes to the great cytotoxic function of LPS stimulated macrophages [127]. Thus, the reduction in NO production indicates the anti-inflammatory activities of the treatment in the cells. However, *Ocimum basilicum* L. ethyl acetate extract and butanol extract inhibited the growth of normal RAW 264.7 macrophage cells [128]. Also, *Ocimum basilicum* L. crude methanolic extract suppressed the induction of iNOS and the subsequent production of NO in LPS-stimulated RAW 264.7 macrophage cells [129, 130]. To test the anti-inflammatory activity of the *Ocimum basilicum* L. methanolic extracts has been determined by PBMC (peripheral blood mononuclear cells) in mitogenic lymphocyte proliferative assay, methanolic extracts enhanced the functional activity of these immune-competent cells, as evaluated by a significant inhibitory effects of methanolic leaf extracts, PHA activated PBMC proliferation could be suggestive of suppression of T cell proliferation [130]. This effect arose from its pivotal role in immune regulation [131, 132], T cell activation provides a target for pharmacological modulation aimed at achieving clinically useful immune-suppression [133].

Złote et al. [134] studied the capacity of phenolic-rich fraction obtained from the elicited basil leaves to inhibit the activity of two enzymes of inflammatory process (LOX and COX). This research found that a higher LOX and COX inhibition efficiency was positively correlated with the increased contents of rosmarinic, benzoic and *o*-coumaric acids determined after elicitation of basil. This result partially corresponds with the study of [135]. More recently, to gain insight into the mechanism of action and pharmacological value of the anti-inflammatory activity of aqueous and methanolic extracts of *Ocimum basilicum* L. in macrophage (RAW264.7) and human chondrosarcoma (SW1353) cell lines, and human primary chondrocytes to correlate their efficacy in terms of management of osteoarthritis (OA). Raina et al. [136] evaluated aqueous extract of *O. basilicum* L. significantly accustom the production of inflammatory mediators such as NO, PGE2, LTB4, and MMPs increased than the methanolic extract. The regulation of these inflammatory intermediaries is pivotal in OA, as it would have a direct effect on (1) chondrocyte survival, (2) production of proinflammatory cytokines, prostaglandins and leukotrienes, and (3) production of extracellular matrix-degrading enzymes such as MMPs. Due to the significant side-effects related to the use of NSAIDs, the check for natural products that would regulate the inflammatory cascade related to OA, without engaging chondrocyte survival, is extremely important. To investigate the anti-inflammatory effect of *Ocimum basilicum* L. oil, Rodrigues et al. [137] investigated an acute and chronic in vivo test as paw edema, peritonitis, and vascular permeability and granulomatous inflammation model. The anti-inflammatory mechanism of action was also analyzed by the participation of histamine and arachidonic acid pathways. These researchers found that the *Ocimum basilicum* L. essential oil and estragole significantly reduced paw edema induced by carrageenan and dextran. The smallest quantities of *Ocimum basilicum* L. essential oil (50 mg/kg) and estragole (30 mg/kg) revealed effectiveness in the decrease of paw edema created by histamine and arachidonic acid, vascular permeability inhibition and leukocyte emigration in the peritoneal fluid. These dosages were carried out of decrease the assured inflammatory process. The results followed between the *Ocimum basilicum* L. essential oil and estragole determine efficacy in anti-inflammatory activity, however, the essential oil is higher efficacious in the acute and chronic anti-inflammatory action. Dextran is a high molecular weight polysaccharide, which differently to carrageenan, induces anaphylactic reactions characterized by extravasation and formation of edema due to mastocyte degranulation with release of histamine and serotonin. Carrageenan induces an inflammatory response through opinion with sulfated polysaccharides, initially encouraging the free of chemical substances which encourage multifactorial facts, mostly concerning the free of substance P, bradykinin, histamine, serotonin, cytokines, and nitric oxide and, subsequently on commodity arise from the arachidonic acid pathway [138].

6.6 Antidiabetic

Diabetes mellitus is a chronic metabolic disorder caused by an absolute or relative lack of insulin and or reduced insulin activity which results in hyperglycemia and abnormalities in carbohydrate, fat and protein metabolism [139, 140]. The hypoglycemic effect of *O. tenuiflorum* L., *O. canum* Sims. and *O. gratissimum* L. in animals with alloxan-induced diabetes was applied to potentiation of glucose-induced insulin free and parallel increased peripheral uptake of glucose [141, 142]. Successive studies have reported a greater link of antidiabetic deal with the antioxidant effects of *Ocimum* oil. The character played by OS for diabetes complications such as retinopathy, nephropathy, and cardiovascular disease are well set up so that dietary antioxidant compounds was fixed to protect from the damages of oxidative stress and free radicals in diabetic cases [143].

In animal experimental designs of alloxan-induced diabetes, both antioxidant and hypoglycemic effects of *O. basilicum* L., *O. tenuiflorum* L., *O. canum* Sims. and *O. gratissimum* L. have been reported. By treating alloxan-diabetic rabbits [141, 142, 144], made a significant decrease in blood glucose levels as corresponded with diabetic control rabbits. Such a hypoglycemic work was related to its powerful antioxidant potentiality: in evidence, in interact, the rabbits studied with *Ocimum* oil showed further a renewal of the levels of malondialdehyde and most of the enzymatic and nonenzymatic endogenous antioxidants [141, 142, 144]. Similar results were achieved in alloxan-diabetic rats: the control, of *Ocimum tenuiflorum*-rich extracts showed significant hypoglycemic, hypolipidemic, and antioxidant effects in all the investigated diabetic rats [145, 146]. In an identical empirical design, *O. gratissimum* L. led to a decrease in the sugar level in plasma and a rise in superoxide dismutase, catalase, and glutathione peroxidase activities in liver and kidney. Furthermore, an opposed reaction against hepatic and renal toxicity in diabetic rats was also observed [147, 148]. Furthermore, the effects of *Ocimum sanctum* leaf polyphenols have been investigated also in insulin-secreting pancreatic β-cells, whose OS-induced alterations contribute to the pathogenesis of diabetes [149].

7. Future direction and conclusion

Despite the many appreciations of science and industry, present practice is filled with stress. Mobile devices and the web have vastly enhanced the pace of life so that many people feel that they are now going down in an endless-increasing ocean of data, while technical culture has overwhelmed us with growing vulnerability to unhealthy prepared and packed food and a profusion of pesticides, food container components, and many toxic modern chemicals. Urban citizens are nevertheless dealt with growing prosperity disparity, social segregation, excessive turbulence, air, water and soil pollution and disconnection from nature. Therefore, while industrialization experiences served to stronger lifespans and impressive expansions in human populations, it is now agreed that the extremest causes of death and disease on the globe are preventable lifestyle-related chronic diseases [150].

The biodiversity of essential oils containing the small molecular terpenoids remains an enchanted field of investigation, and the continuous usage of this reward in a broad field of studies suggested these demands in the consequent [151]. Screening, identifying, and dealing with this vast biodiversity will require a progressing progress of precise, rich-throughput experimental methods including new driving procedures.

The beneficial health effects of *Ocimum* oil compounds have also been proven by many randomized, crossover, controlled, human studies on biomarkers of health performed in the last decades. Several preclinical studies suggest that such beneficial effects may be mainly ascribed to the phenolic compounds. Further development of biotechnology with the genomic and metabolomic analyses and genetic engineering will advance a variety of fields involving bioactive compounds ranging from food and animal nutrition to plant protection. Although many biological activities as antimicrobial or antioxidative and other effects have been intensively studied and well documented. However, well studies are needed to further characterize the *in vivo* effects of individual *Ocimum* derivatives applied as specific agents or in a mixture, consisting of their safety analysis on mortals. Moreover, a better evidence of their molecular procedure of activity may appropriate the system to a better application in human pharmacology.

In inference, the tendency of the last moments in the treatment of herbal productions have indicated that nature prospects and trust in pure and healthful products including medicines, cosmetics, household products, since easily as foodstuffs of plant and animal origin have belonged to a vital issue. So, indeed a well-balanced risk-benefit assessment of bioactive essential oils is one of the major challenges and policymakers must be convinced that review on natural products as the volatile terpenoids in essential oils is a huge task to ensure the ultimate human and animal welfare [151].

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