Food Reviews International

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/lfri20

Antimicrobial, Antioxidant and Other Pharmacological Activities of *Ocimum* Species: Potential to Be Used as Food Preservatives and Functional Ingredients

Javad Sharifi-Rad, Charles Oluwaeun Adetunji, Olugbemi T. Olaniyan, Stephen Kayode Ojo, Micheal Olugbenga Samuel, Banjo Temitope Temitayo, Osahon Itohan Roli, Olaogun Oluwatoyin Nimota, Banjo Temitope Oluwabunmi, Juliana Bunmi Adetunji, Farukh Sharopov, Natália Cruz-Martins & María del Mar Contreras

To cite this article: Javad Sharifi-Rad, Charles Oluwaeun Adetunji, Olugbemi T. Olaniyan, Stephen Kayode Ojo, Micheal Olugbenga Samuel, Banjo Temitope Temitayo, Osahon Itohan Roli, Olaogun Oluwatoyin Nimota, Banjo Temitope Oluwabunmi, Juliana Bunmi Adetunji, Farukh Sharopov, Natália Cruz-Martins & María del Mar Contreras (2021): Antimicrobial, Antioxidant and Other Pharmacological Activities of *Ocimum* Species: Potential to Be Used as Food Preservatives and Functional Ingredients, Food Reviews International, DOI: 10.1080/87559129.2021.1934693

To link to this article: https://doi.org/10.1080/87559129.2021.1934693

Published online: 13 Jul 2021.

FOOD REVIEWS INTERNATIONAL
https://doi.org/10.1080/87559129.2021.1934693

Taylor & Francis
Taylor & Francis Group

Antimicrobial, Antioxidant and Other Pharmacological Activities of *Ocimum* Species: Potential to Be Used as Food Preservatives and Functional Ingredients

Javad Sharifi-Rad[a,b], Charles Oluwaeun Adetunji[c], Olugbemi T. Olaniyan[d], Stephen Kayode Ojo[e], Micheal Olugbenga Samuel[f], Banjo Temitope Temitayo[g], Osahon Itohan Roli[h], Olaogun Oluwatoyin Nimota[h], Banjo Temitope Oluwabunmi[i], Juliana Bunmi Adetunji[j], Farukh Sharopov[k], Natália Cruz-Martins[l,m,n], and María del Mar Contreras[o]

[a]Phytochemistry Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran; [b]Facultad De Medicina, Universidad Del Azuay, Cuenca, Ecuador; [c]Department of Microbiology, Biotechnology and Nanotechnology Laboratory, Edo University Iyamho, Edo State, Nigeria; [d]Laboratory for Reproductive Biology and Developmental Programming, Department of Physiology, Edo University, Iyahmo, Edo State, Nigeria; [e]Department of Microbiology, Federal University, Oye-Ekiti, Ekiti State, Nigeria; [f]Cardiometabolic Research Unit, Department of Physiology, College of Health Sciences, Bowen University, Iwo, Osun State, Nigeria; [g]Institute for Human Resources Development, Federal University of Agriculture, Abeokuta, Ogun State, Nigeria; [h]Department of Anatomy, College of Basic Medical Science Edo University Iyamho, Nigeria; [i]Department of Biological Sciences, Crawford University, Igbesa, Ogun State, Nigeria; [j]Nutritional and Toxicological Research Laboratory, Department of Biochemistry, Osun State University, Osogbo, Osun State, Nigeria; [k]Department of Pharmaceutical Technology, Avicenna Tajik State Medical University, Rudaki, Dushanbe, Tajikistan; [l]Faculty of Medicine, University of Porto, Porto, Portugal; [m]Institute for Research and Innovation in Health (I3s), University of Porto, Porto, Portugal; [n]Laboratory of Neuropsychophysiology, Faculty of Psychology and Education Sciences, University of Porto, Porto, Portugal; [o]Department of Chemical, Environmental, and Materials Engineering, University of Jaén, Campus Las Lagunillas, Jaén, Spain

ABSTRACT

Ocimum plants are commonly used culinary herbs and fragrant ornamental plants. Beyond this feature, the present review firstly describes scientific studies on the antimicrobial and antioxidant activities of several *Ocimum* species. Secondly, the use of *Ocimum* plants as ingredients for food preservation, such as meat, fish and dairy products was covered. Thirdly, the phytochemical composition has been reviewed to reinforce further standardization to be *Ocimum* plants used as preservatives. Finally, other pharmacological properties (cardioprotective activity, anti-diabetic activity, hepato-renal protective activity, anticancer activity) are also reviewed. Overall, these plants can serve to promote food preservatives and functional ingredients, but there are still some challenges to be overcome as this review points out.

KEYWORDS

Aromatic herb; basil; food preservative; functional ingredient; *Ocimum*

Introduction

Medicinal plants are rich sources of biologically active molecules employed in the treatment of various diseases in traditional and modern medicine.[1–3] This has promoted the quest for researching a wide pool of plant extracts as a potential source of new therapeutic drugs and food preservatives.[3,4] Among them, *Ocimum* (family Lamiaceae) is a plant genus growing worldwide, prominently wild, in tropical and sub-tropical areas, although indigenous from Asia and African continents. *Ocimum* genus is generally known as basil. "The Plant List" website lists 76 accepted names while 18 are unresolved

CONTACT María del Mar Contreras mcgamez@ujaen.es Department of Chemical, Environmental, and Materials Engineering, University of Jaén, Campus Las Lagunillas, 23071 Jaén, Spain

names.[5] The major diversity appears to be in Africa, with various *Ocimum* species and forms vary in growth habit, colour, and aromatic composition making complex the real identity of basil.[6]

Ocimum plants have been recognised as a good repository source of essential oils and aroma compounds, as culinary herbs and even as attractive and fragrant ornamental plants. This makes them excellent culinary herbs to flavour foods that are used in several regions worldwide, e.g. *Ocimum bassilicum* L. (sweet basil), *Ocimum gratissimum* L. (clove basil), *Ocimum tenuiflorum L.* (syn. *Ocimum sanctum* L.) are renowned culinary herbs.[7–9] The latter and *Ocimum gratissimum* are known as Tulsi in Hindi or Tulasi in Sanskrit (holy basil) and have been used in the Ayurveda for more than 3000 years for its healing properties. Moreover, the extracts and essential oils of *Ocimum* plants worldwide have been traditionally used for the treatment of gastroenteritis and chronic diarrhea, skin infections, headaches, respiratory tract infections, etc.[4,10–13] Some *Ocimum* species have also been traditionally used to treat diabetes mellitus in Africa and Asia.[14,15] Essential oil of *O. basilicum* has been applied to treat upper respiratory tract infections, while extracts from *O. gratissimum* L. have revealed to be useful in the treatment of *Leishmania* and as medicine to treat central nervous system diseases.[16,17]

In this context, this review firstly extensively describes the antimicrobial and antioxidant properties of *Ocimum* plants, including *O. basilicum, O. gratissimum*, and *O. sanctum*, as well as their promising use as antimicrobial and antioxidant agents, serving as key ingredients for food preservation and to extend the shelf life of foodstuffs. Moreover, the phytochemical composition is also reviewed and it could serve to reinforce further standardization to be used in foods applications. Additionally, in view of the aforementioned ethnopharmacological potential of *Ocimum* plants, some other pharmacological properties are described for adequate health care delivery to human being to promote the formulation of functional ingredients.

Antimicrobial and antioxidant effects of *Ocimum* spp.: *in vitro* and *in vivo*

Antimicrobial activity of Ocimum *spp*

The discovery of antibiotics was a great achievement in the history of health and diseases, as there was an effective treatment of the myriads of diseases caused by microorganisms. This succor was soon cut-short owing to the emergence of resistant bacteria against prevailing antibiotics.[13,18] In this context, finding natural sources of antimicrobial components is attractive and *Ocimum* plants have been extensively studied, possessing a wide range of antimicrobial spectrum.[19] Fig. 1 summarizes the antimicrobial properties reported for some *Ocimum* species, which are described in this section, including the activity of solvent and aqueous extracts and essential oils. Firstly, studies on *O. basilicum* are described and then about other *Ocimum* species.

Antibacterial activity of Ocimum *spp*

Taechowisan et al.[20] observed that the ethyl acetate extract of *O. basilicum* leaves tested against nine *S. aureus* isolates with *fem*B gene, of which six were methicillin-resistant (MRSA) with *mec*A gene, gave a growth inhibition zone size ranging from 10.3 ± 0.6 to 17.5 ± 1.2 mm, while the control, *S. aureus* ATCC25923 had an inhibition zone of 25.6 ± 0.8 mm. It was also noted that most MRSA strains had minimum inhibitory concentrations (MIC) less than 0.09 mg/ml and minimum bactericidal concentration (MBC) ≤0.09 mg/ml, including the control strain.[13] Adam and Omer[10] reported an inhibition zone of 7.8 mm against *Escherichia coli* and *Pseudomonas aeruginosa* at the lowest concentration (6.25 µg/ml), while the antibacterial activity detected against *S. aureus* was of 4.4 mm. According to Khalil,[21] *O. basilicum* ethanol leaf extract at different concentrations (50–200 mg/ml) revealed a high inhibitory activity at the highest dose against *E. coli* (21 mm), followed *S. aureus* (16 mm). The study of Kaya et al.[22] using three different solvents for extraction, resulted in that methanol leaves extract (of 5 ml) displayed the highest antibacterial activity compared with acetone and chloroform extracts: the inhibition zones ranged from 13 mm (*E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853) to 15 mm (*Listeria monocytogenes* ATCC 7644). *S. aureus* ATCC 29213 had an

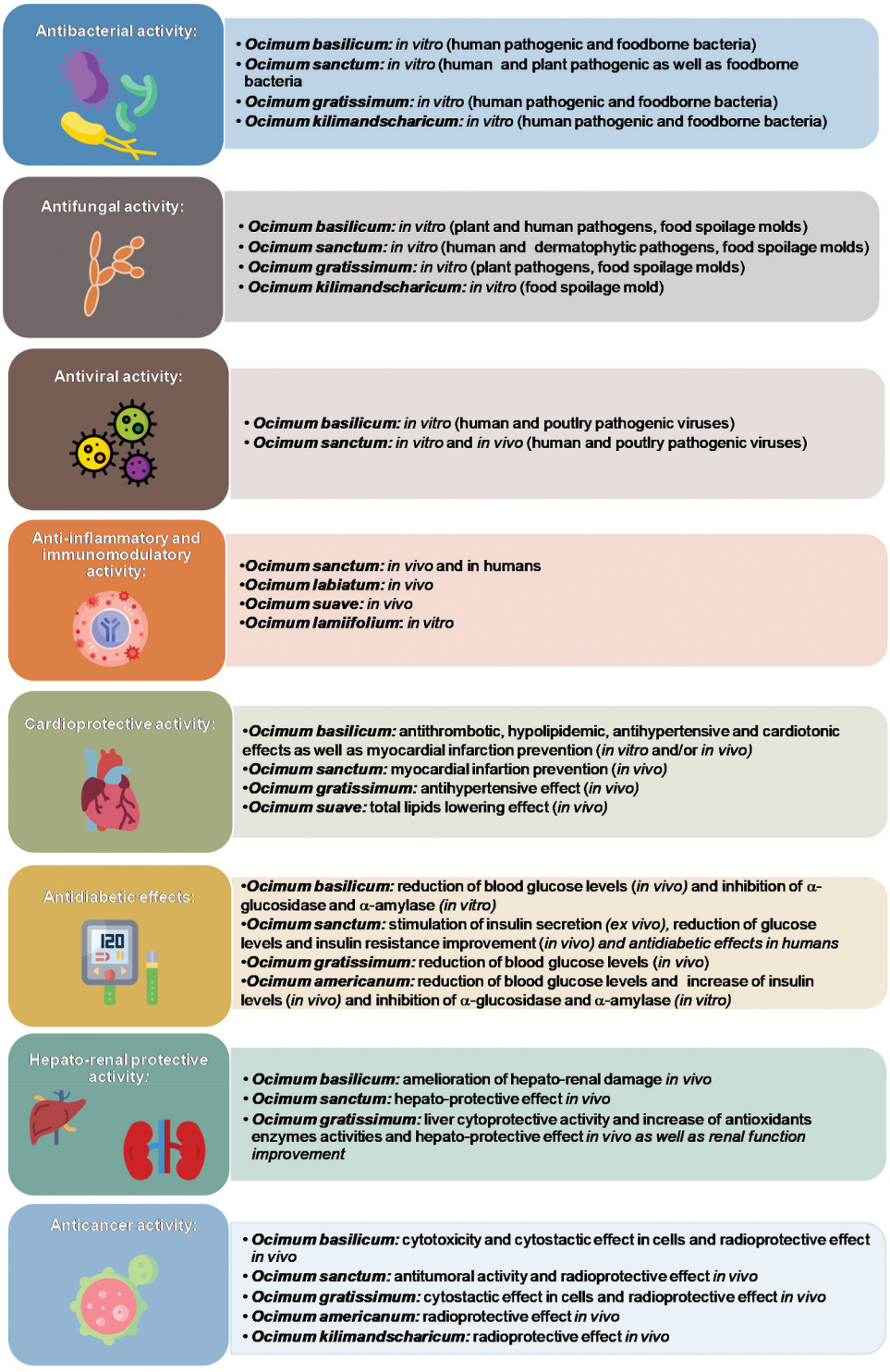

Figure 1. Scheme summarizing the antimicrobial activity, the antioxidant activity and other biological properties (*in vitro, in vivo* and/or in humans) of extracts from *Ocimum* spp. described here and in the review on clinical trials by Jamshidi and Cohen.[9] The icons have been designed using resources from Flaticon.com.

inhibition zone of 15 mm, whereas *Streptococcus pyogenes* ATCC 19615 had 13 mm when methanol extract was used. Chloroform and acetone extracts revealed no activity against both Gram-positive and Gram-negative bacteria tested, except for *P. aeruginosa* ATCC 27853. Different phytochemicals could be solubilized in the different extracts, although the characterization study was not provided.

Other *Ocimum* species have also revealed antibacterial effects. Shiju[23] studied the activity of Tulsi extract (*O. sanctum*) against *E. coli* and *S. aureus* and found to be higher at a concentration of 100 µg (100%), with the maximum inhibition zones being 16 mm and 17 mm, respectively. In another study, *O. sanctum* leaves aqueous and ethanolic extracts (50–150 mg/ml) revealed antibacterial activity against *E. coli, S. aureus* and *P. aeruginosa* inhibition zones up to 18.52 mm, 16.62 mm, and 19.72 mm for *E. coli, S. aureus*, and *P. aeruginosa*, respectively. Root extract showed no inhibitory activity against the studied strains.[24] *O. sanctum* leaves aqueous, chloroform, and ethanolic extract (at 100 µg disc concentration) also revealed to be effective against a wide range of microorganisms: *S. aureus* (inhibition zone of 54%-87%), *Staphylococcus epidermidis* (74%-92%), *Streptococcus pyogenes* (82%-97%), *Streptococcus mutans* (71%-95%), *Streptococcus pneumoniae* (87%-92%), *Micrococcus luteus* (77%-97%), *Bacillus cereus* (74–77%), *Bacillus subtilis* (79%-77%),[25] thus revealing the high efficacy of *O. sanctum* extracts and supposing it as upcoming antibacterial agents in place of synthetic ciprofloxacin. Methanolic leaves extracts of *O. sanctum* (Black and green Tulsi) also revealed to be effective against *Klebsiella pneumoniae* with inhibition zone of 16 mm, *Salmonella typhi* (13–14 mm), *S. aureus* (12–17 mm) and *Streptococcus* spp. (14–16 mm), at the highest dose tested (5000 µg/ml), while only Black Tulsi extract was found to be effective against *E. coli* (16 mm).[26]

O. sanctum antibacterial activity was also assessed against *Xanthomonas citri* using 25 Xcmi strains. The average activity was 19.05 mm and fourteen of the 25 strains showed higher activity than the average, while the other 11 Xcmi strains showed less activity.[27] This study corroborates the potential use of *Ocimum* spp. not only for the treatment of human pathogens or against foodborne bacteria, but also against bacterial pathogens of economic plants.

Prasad et al.[4] evaluated the antibacterial activity of different extracting solvents on five *Ocimum* plant leaves (namely, *O. sanctum* purple, *O. sanctum* green, *O. gratissimum, O. basilicum* and *O. kilimandscharicum* Gürke – Camphor basil) against Gram-positive and Gram-negative bacteria. *Ocimum* spp. isoamyl extract was the most active and those that led to highest inhibition zone, being 24 mm (*O. sanctum* purple) to 32 mm (*O. sanctum* green) against *B. subtilis*; 22 mm (camphor basil) to 28 mm (*O. basilicum)* against *S. typhi*. When looking at the antibacterial effect against *S. aureus*, the inhibition zones obtained to isoamyl extracts were 12 mm (Camphor basil) to 21 mm (*O. gratissimum*), while no activity was detected to *O. sanctum* green. Similar findings were reported by other studies on *E. coli* and *S. aureus*, although with different species of *Ocimum* plants.[21] In another comparative study, *O. kilimandscharicum, O. sanctum* and *O. gratissimum* antibacterial activity was also examined against Gram-positive (*B. subtilis, B. cereus*) and Gram-negative (*E. coli, P. aeruginosa*) bacteria. Among the *Ocimum* species studied, *O. kilimandscharicum* was those with higher antibacterial activity (maximum inhibition zone on *B. subtilis* and 25 mm on *E. coli*). Gram-negative bacteria were highly susceptible to all *Ocimum* species extracts, whereas Gram-positive were resistant to leaf extracts, except *O. kilimandscharicum*.[28]

As can be seen till now the species and the solvent used for extraction, and the plant part affect the antibacterial activity, being leaves the most interesting part. According to Ba-Hamdan et al.,[29] the antibacterial activity of methanolic extracts of *O. basilicum* revealed a better effect against the Gram-positive bacteria (*Bacillus* spp., *Micrococcus* spp., MRSA, *S. aureus, S. epidermidis* and *S. pneumoniae*), ranging from 10.7 ± 0.58 to 15.3 ± 0.58 mm, as compared with ethanolic extracts (varying from 8.7 ± 1.2 to 14 ± 2 mm). A similar scenario was found when using methanol extract (10.7 ± 2.5 to 12 ± 2.6 mm) to the Gram-negative bacteria (*Acinetobacter* spp., *E. coli, K. pnuemoniae*, and *P. aeruginosa*) when compared with ethanol extract (9 ± 1.7 to 10.3 ± 1.5 mm). It was also evident from the report of Kaya et al. that different extraction solvents affect the final bioactive effect of extracts, alcoholic extracts were more effective than hexane.[22] Alternatively, the antibacterial activity of chloroform *O. sanctum* extract was more effective than methanol extract against all tested strains

(*E. coli, P. aeruginosa, Salmonella typhimurium* and *S. aureus*).[30] Similar findings were stated by Rathnayaka,[31] testing various *O. sanctum* leaves extracts using different solvents (water, chloroform and alcohol) against foodborne pathogens (*Salmonella enterica, Vibrio parahaemolyticus, E. coli* and *L. monocytogenes*), where a positive antibacterial activity was stated against all the tested foodborne microbial pathogens, except to *L. monocytogenes* that was resistant to three of five solvent extracts.

Concerning essential oils, Al Abbasy et al.[12] assessing the antibacterial activity of that obtained from basil against three Gram-positive and four Gram-negative pathogenic bacteria found that only two Gram-positive bacteria (*S. aureus* and *B. cereus*) and two Gram-negative bacteria (*E. coli* and *S. typhimurium*) were sensitive. *B. cereus* showed the highest susceptibility (25 mm), followed by *E. coli* (11 mm), *S. typhimurium* (10 mm) and *S. aureus* (9 mm). *S. epidermidis, K. pneumoniae* and *P. aeruginosa* were found to be highly resistant to *O. basilicum* essential oil. Other authors have also shown the susceptibility of *E. coli* and *S. aureus* against basil essential oil.[11] *O. sanctum* essential oil was also found highly effective (at 4.5 and 2.25% concentration) against *S. aureus* growth, including MRSA, and *E. coli*, completely inhibiting their growth, while to *P. aeruginosa* a partial inhibition was found at the same concentrations; for the latter the extract only exerted bacteriostatic effects.[32] Moreover, it has been shown that essential oils from the first and second cutting collection stages possess higher antibacterial properties than the others.[33] For instance, comparing the inhibition zones of essential oils with the control disc (tetracycline), essential oil of both cutting stages had better results against *E. coli, P. aeruginosa* and *S. aureus.*

Interestingly, Silva and co-workers reported a combination study between *O. basilicum* leaves essential oil, done by steam distillation, and standard antibiotics. The authors found a MIC value for *O. basilicum* essential oil and imipenem used alone against the *S. aureus* strains of 1024 mg/ml and 4 mg/ml, respectively. However, when the two antibacterial agents were combined, *O. basilicum* oil in association with imipenem revealed MIC values of 32 and 0.125 mg/ml, respectively, suggesting the existence of synergy between compounds against *S. aureus* strains.[34] A contrary scenario was found to ciprofloxacin: the MIC value of ciprofloxacin alone is 2 mg/ml, but when combined with *O. basilicum* oil, an increase in MIC value to 4096 mg/ml was stated, and a reduction in the single MIC value to 0.5 mg/ml, respectively. Similar observations were reported for *P. aeruginosa* strains. Moreover, nanoemulsion of *O. basilicum* essential oil for encapsulation showed enhanced antibacterial activity (MIC) against enteric bacterial pathogens, *E. faecalis, S. aureus, Salmonella paratyphi*, and *K. pneumoniae*.[35]

An example of clinical study is through the control of the bacterial biofilm on teeth to maintain the oral health. In a randomized controlled clinical trial, a mouthrinse based on *O. sanctum* extract (obtained by maceration with ethanol) was as effective as chlorhexidine in reducing plaque and gingivitis.[36] Similarly, results were found by Penmetsa et al.[37]

Concerning the mechanism of action, it seems that *Ocimum* components could degrade the cell wall, as observed using scanning electron microscopy. They may cause some damage to the cytoplasmic membrane proteins, the binding of proteins, leakage of cell contents, coagulation of cytoplasm and depletion of the proton motive force.[22]

Antifungal activity of Ocimum *spp*

The antifungal activity of essential oils and extracts of several *Ocimum* spp., including *O. basilicum*, have been also described. As before, it depends on the sample type, species, and fungi type. The variety is also another factor that affects the antifungal potency concentration.[38] The most studied one is *O. basilicum*. It has showed to a 100% mycelia growth inhibition against the plant pathogen *Rhizoctonia solani* at 500 μg/ml, while to the others species was at 750–1000 μg/ml.[39] In a similar study, the antifungal activity of *O. basilicum* methanolic-chloroform extract and hydrodistilled essential oil was determined by Hadush et al. against *Aspergillus niger* and *Rhizoctonia bataticola*.[11] No inhibitory activity was found by the solvent extract while the essential oil revealed a fungal growth inhibition zone up to 8.00 ± 0.71 mm and 12.75 ± 0.35 mm, respectively (10 and 20 μL).[11] Similar findings were reported by Sethi et al.[39] Abou El-Soud et al. also stated antifungal effects to *O. basilicum* essential oil

against the human pathogenic *Aspergillus flavus* mycelial growth and aflatoxin B1 production.[40] *O. basilicum* essential oil revealed dose-dependent (500–1000 ppm) antifungal effects up to 100%, while noticeable aflatoxin B1 production inhibition was stated. Alternatively, *O. basilicum* crude extracts of varying solvents yielded no antifungal activity (*Candida albicans* 845981, *C. crusei* ATCC 6258, *C. albicans* 90028 and *Saccharomyces cerevisiae* (Pakmaya)) at the concentrations tested by Kaya et al.[22] In this regard, probably higher dose are required in line with results on *O. forskolei* essential oil, which showed a MIC value of 8.6 mg/ml.[41]

Concerning food spoilage fungi species, the growth inhibition potential of a food grade basil extract against *Fusarium* species (*F. verticillioides, F. oxysporum, F. proliferatum*, and *F. subglutinans*) was shown at varying concentrations during a 14 days incubation period by Kocić-Tanackov and coworkers. Concentrations at 0.35% and 0.70% (v/v) inhibited some species, while at 1.50% all species were susceptible. Also, a reduced growth of aerial mycelium was observed, along with hyphae deformations.[42] Jakowienko et al. (2011) assessed the antifungal activity of essential oils from two varieties of sweet basil (5–10 µl/disc) on *Botrytis cinerea, Cladosporium herbarum, A. flavus, Eurotium* spp., and *Alternaria* sp. Among them, *E. chevalieri* was the most sensitive to the two varieties studied (Wala and Fine Verde), with mean inhibition zones at 90 and 62.5 mm, respectively, while the most resistant fungi was *A. flavus* (mean growth inhibition diameters were 6.8 and 7.3 mm, respectively). It was clearly observed that both oils under same experimental conditions had higher antifungal activity than cycloheximide and methyl thiophanate.[38]

In addition to *O. basilicum* the antifungal activity of other *Ocimum* spp. essential oils against *R. solani* revealed to be dose-dependent. All essential oils tested, except *O. sanctum* and *Ocimum americanum* L., had inhibitory effect on fungal mycelia growth at 750–1000 µg/ml.[39] Nonetheless, other studies on *O. sanctum* extracts have revealed opposite results against other fungi. This can be influenced for the chemical composition and the dosage tested. In another work, *O. sanctum* extracts (aqueous and alcoholic extracts, and hexane, benzene, chloroform, ethyl acetate, methanol, and water fractions) were determined against different clinically isolated fungi, like *Trichophyton mentagrophytes, Trichophyton rubrum, Microsporum canis, Microsporum gypseum and Epidermophyton floccosum*; the results varied in function of the fungi species tested and the sample type, with the lowest MIC values against *T. mentagrophytes* (125 ± 25 µg/ml) for the methanol fraction.[43] Moreover, *O. sanctum* has been discovered to possess fungicidal activity against all forms of dermatophytic fungus and up till now there is no data on side effects.[43]

Londhe et al.[28] described the antifungal activity of hydrodistillates essential oils of *O. gratissimum, O. sanctum* and *O. kilimandscharicum* against the food spoilage mold *A. niger*, stating maximum antifungal potential. *O. gratissimum* had the largest inhibition zone (29 mm) followed by *O. sanctum* (20 mm) and *O. kilimandscharicum* (16 mm). Among these species, the findings by Mohr and coworkers showed that the essential oil of *O. gratissimum*, obtained by hydrodistillation, is also an effective inhibitor of phytopathogenic fungi, with MICs varying from 31.25 to 125 µg/ml. *F. oxysporum* f. sp lycopersici and *R. solani* were the most sensitive, with growth inhibition potential compared to the positive control ketoconazole at 500 µg/ml.[44] This is in line with results obtained by other authors.[11,39] Other study have revealed that the essential oil of *Ocimum campechianum* Mill., rich in methyleugenol, exhibited antifungal activity against *F. oxysporum* and *Colletotrichum gossypii* phytopatogens (IC_{50}, 0.7–0.8 µl/ml,) as well as the mycelial growth and spore germination of the fungi.[45]

Finally, as for other microorganisms, *Ocimum* components are able to disrupt cell wall and cell membrane, as well as to provoke denaturation based on the previous literature.

Antiviral activity of Ocimum *spp*

In the assessment of a potential antiviral agent, cytotoxicity evaluation is considered very important owing to the extract selective nature for virus-specific activity, with little or no effects on the host cells metabolisms. Yucharoen et al. tested the effect of dichloromethane and methanol extracts of *O. basilicum, O. sanctum*, and *O. americanum* on African Green Monkey (GMK) cells, the 50% cytotoxicity dose (CD_{50}) value were with doses of 110 µg/ml for both dichloromethane and methanol

extracts of *O. sanctum* and *O. americanum* and 56 μg/ml for both dichloromethane and methanol extracts of *O. basilicum*. Then, all samples were tested against anti-herpes simplex virus (HSV) and the extract showed HSV activities at various steps of the viral multiplication cycle. For example, the extract-pretreated cells when infected with HSV-2 G had effective doses at 50% (ED_{50}) for *O. sanctum* methanol extract and *O. americanum* dichloromethane extract at 66.96 and 59.1 μg/ml, respectively, and with therapeutic indexes (TI = CD_{50}/ED_{50}) of 1.644 and 1.865, respectively. The antiviral activity after the addition of extracts both during and after HSV adsorption was also evaluated. Both *O. americanum* and *O. basilicum* extracts affected HSV-2 G during adsorption. The authors reported the ED_{50} of *O. americanum, O. sanctum* and *O. basilicum* methanol extracts on HSV-2 G as 46.95, 44.49 and 35.83 μg/ml, respectively, with TI at 2.345, 2.473 and 1.563, respectively. The ED_{50} of *O. americanum* and *O. basilicum* dichloromethane extracts on HSV-2 G were 41.95 and 30.58 μg/ml, respectively, and the TI were 2.623 and 1.835, respectively. In contrast, HSV-1 F was inhibited less than 50% during adsorption by all extracts.[46] In another work, the antiviral activity of *O. basilicum* against new Castle Disease (NCD) virus, an important poultry pathogen with considerable financial losses to poultry business, was assessed by Al-Amri and coworkers. The maximum non-toxic concentrations, ranged from 50 to 500 μg/ml, were used for antiviral activity. The reduction in viral titer after the *O. basilicum* extract administration from Tissue Culture Infected Dose of 50% ($TCID_{50}$) was found to be 10^{-1} with 500 μg/ml concentration when compared with control virus at 10^{7} titer. The extract was also found to prevent the cytopathic effect of NCD virus, and thus indicating inhibition of viral replication.[47] Moreover, the antiviral activities of *O. basilicum* extracts (aqueous and ethanolic) and selected purified components were assessed against DNA viruses, herpes viruses (HSV), adenoviruses (ADV) and hepatitis B virus, and RNA viruses, coxsackievirus B1 (CVB1) and enterovirus 71 (EV71). The EC_{50} varied between 0.4 mg/L and 16.9 mg/L for the compounds and from 51.4 to > 100 mg/L for the extracts, depending on the virus. In general, aqueous extract had stronger antiherpetic activity than the ethanolic extract, both showed mild activity against adenoviruses and low activity against CVB1. Moreover, of the 11 purified components assayed, linalool revealed inhibitory activity with a broad spectrum.[48]

O. sanctum extracts have been tested against several virus types, generally, showing dose-dependent effect and inhibited virus replication at higher concentrations (e.g. 10 to 15 mg/ml), including human pathogens, such as influenza A virus,[49] and animal ones, such as NCD virus,[50,51] infectious bursal disease (IBD) virus,[51] orthomyxovirus and paramyxovirus.[52] In particular, Ghoke and co-authors on influenza A virus subtype H9N2 using embryonated chicken egg model, the maximum non-toxic concentration (MNTC) from *O. sanctum* extracts was determined at 135 mg/0.1 ml, which showed no evidence of mortality till hatching in the specific pathogen free (SPF) embryonated chicken eggs (ECEs) (SPF ECEs). The concentrations of antiviral drugs tested were also non-toxic to the embryos at doses of 16 μg/0.1 ml and 2.66 μg/0.1 ml for amantadine hydrochloride and oseltamivir, respectively. In another work, *O. sanctum* crude extract, terpenoid and polyphenol fractions showed significant virucidal activity, being higher for the two first samples. Also, the therapeutic effect was maintained for longer period of time (up to 72 h post-incubation).[49] Moreover, Patil, assessing the *in vitro* cytotoxicity of *O. sanctum* (Tulsi) crude extracts on MDBK cells (bovine kidney cells) and African Green Monkey cells (Vero cell) against orthomyxovirus and paramyxovirus, observed that the IC_{50} values in mammalian cells indicated no cytotoxicity effect in the evaluated cells, which was found useful and safe.[52] The antiviral effect against paramyxovirus and orthomyxovirus was dependent on the solvent used for extraction.

Furthermore, an *in vivo* study was conducted by Varshney et al.[51] The 50% infectious dose (ID_{50}) of NCD virus was calculated to be $10^{9.5}$/ml, while that of IBD virus was $10^{3.5}$/ml. Chickens fed with *O. sanctum* aqueous extract and subsequently challenged with NCD virus, were observed with clinical signs found to be mild as compared to control group of chicken. Exhibition of paralysis in leg and wings was absent in treated chickens, while two of six unfed chickens exhibited paralysis in one leg and wings at the determined ID_{50}. Comparing the body weight of chicken fed with *O. sanctum* and the unfed, fed chicken were found healthier with a fewer loss in body weight as compared to unfed groups.

Treated chickens showed mild hemorrhagic lesions in intestines whereas unfed chickens challenged with NCD virus showed more hemorrhage.

Finally, some of the aforementioned studies have reported that in the mechanisms of action can be implied a specific inhibition of a stage in viral intracellular multiplication and non-specific interference with virus-cell interactions like masking/blocking the some important glycoproteins.[52]

Antioxidant activity of Ocimum *spp*

Free radicals are molecular fragments containing an unpaired electron in atomic or molecular orbitals, such as superoxide, hydroxyl, peroxyl ($RO_2^{\bullet}$), alkoxyl ($RO^{\bullet}$), and hydroperoxyl ($HO_2^{\bullet}$) radicals.[2] To avert free radicals' buildup, the body has different levels of antioxidants defense mechanisms produced endogenously. Moreover, antioxidants can be consumed exogenously. These compounds prevent the oxidation of other molecules by inhibiting the initiation or propagation of oxidizing chain reactions. They can protect the human body from free radicals, reduce lipid oxidation and oxidative stress damage, in addition to retard the progress of many chronic diseases. Also, lipids oxidation causes deterioration in many food systems, leading to reduced-flavors and formation of toxic compounds lowering the quality and nutritional value of foods.[53–55]

Artificial antioxidants are often used in industry, but due to their carcinogenic potential, a growing interest on natural antioxidants has emerged since antioxidants-rich compounds have a vital role in ailments management.[56] Therefore, natural antioxidants have attracted interest because of their safety and potential nutritional, therapeutic benefits and low side effects.[56] In this sense, medicinal plants, particularly those with less toxic compounds, continue to play an important role in the modern healthcare system or to be used as antioxidant additives.[57,58]

Concerning *O. basilicum*, several *in vitro* assays or test tube, such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical inhibition, have been applied to reveal the antioxidant properties of different cultivars.[59–61] Extracts and essential oils have shown antiradical properties.[59–68] Teofilovic and coworkers showed that the antioxidant activity of *O. basilicum* extracts was highly variable (DPPH assay, IC_{50}, 0.22 to 20.49 μg/ml), depending on the solvent used for extraction, conditions and plant fragmentation. Best solvents were ethanol and methanol,[59] while acetone is another alternative.[60] The antioxidant activity of methanolic and aqueous-methanolic leaves extract of *O. sanctum, O. americanum* (syn. *Ocimum canum*) and *O. gratissimum* have shown antioxidant activity by scavenging free radicals; the first plant showing the lowest IC_{50} by the DPPH assay (35.2 μg/ml).[62–64,68] Regarding essential oils, those from *O. basilicum*, containing linalool as main compound (56.7–60.6%), and *O. gratissimum* leaves, rich in methyl cinnamate (48.3%) and γ-terpinene (26%), showed high antioxidant activity through β-carotene-linoleic acid bleaching assay and DPPH assay, with IC_{50} values <0.007 μL/ml (or <6.7 μg/ml) and 5.5 μl/ml, respectively.[65,66] Alternatively, slight antioxidant activity has been reported for *O. forskolei* leaves essential oil rich in endo-fenchol (31.1%) (DPPH assay, IC_{50} of 31.6 μl/ml) and *O. campechianum* leaves/stem essential oil (<40%) rich in methyleugenol (up to 87%).[41,45] In addition to species, cultivar and chemotype, the maturity of the plant at the harvest time also affects the antioxidant activity and phytochemical profile.[67]

Moreover, *ex vivo* studies on rats' pancreas and heart homogenates have shown inhibition of Fe^{2+} and sodium nitroprusside-induced lipid peroxidation by essential oil from *O. basilicum* rich in limonene (47.4%).[69] *In vivo* studies have shown that *O. basilicum* (methanolic-aqueous extract) reduced the brain acetylcholinesterase activity and oxidative stress, which was related to the anti-amnesic and neuroprotective activities and attributed to the presence of phenolic compounds.[68] *O. basilicum* callus extract was also able to limit the deleterious effects of UV-induced oxidative stress, radical production, and membrane integrity in yeast cell culture.[70] In another work, *O. gratissimum* aqueous extract also efficiently inhibit CCl_4-induced liver injuries in rats, which was associated to its antioxidant and anti-inflammatory activities in livers of rats after CCl_4-induced liver damage.[71] Its essential oil has also shown antioxidant activity *in vivo*.[72] Moreover, the methanolic leaves extract of *O. americanum* reverses alterations in oxidative stress markers occasioned by the diabetic

conditions,[64] and *O. sanctum* exerted oxidative stress reduction along with better seizure control, memory retention, and neuronal structure preservation in animal models.[73] Thus, the *in vitro* antioxidant potential can be associated to these antioxidant properties evidenced *in vivo*.

Some novel improvements include encapsulation *via* nanoemulsion of *O. basilicum* essential oil with enhanced antioxidant properties,[35] and the use of LED-based light to manipulate *Ocimum* plants. It enabled to improve commercial production of *O. basilicum* through increasing the volatile content that affects sensory quality, mass, and antioxidant capacity.[74] The use of elicitors reduced stress effect on growth and also increased antioxidant properties of *Ocimum* plants.[75,76]

Antimicrobial and antioxidant activity of *Ocimum* spp. in food systems: use as preservatives

Spoilage microorganisms are responsible for the deterioration and eventual spoilage of food products leading to a reduction in quality and economic value. The biodeterioration of food either on the field or during storage generates post harvest losses. Majority of food products are perishable in nature, hence there is a need to protect them from spoilage microorganisms and ensure the quality of these food products is sustained by extending their shelf life. Various methods of preservation of food products had been devised over the years to ensure that the quality of food products is prolonged after harvesting. The different food preservation techniques such as drying, heat treatment, cold storage, smooking and use of preservatives, including antioxidants and antimicrobials, reduce the risk of food poisoning and preserve food quality. In this context, the application of the extracts and essential oils from different plant sources in food preservation is receiving attention as a more natural alternative.[57]

Table 1. *Ocimum* plants and constituents applied in food preservation.

Ocimum plant	Component	Food	Incorporation	Effect	Main constituent	Ref.
Antimicrobial preservative						
Ocimum basilicum	Essential oil (leaves)	Beef burger	Addition (0.125–0.25%, v/w)		Estragole (85.2%)	[78]
Ocimum basilicum	Essential oil (aerial parts)	Chicken meat	Soaking (0.25–0.5%, w/v; 15 min)			[79]
Ocimum basilicum	Essential oil (aerial parts)	Ewe's cheese	0.025%, w/w, in milk		Estragole (58.2%), linalool (11.2%)	[80]
Ocimum sanctum	Commercial leaves extract	Chicken sausage	Addition (0.03%, w/w)			[81]
Ocimum sanctum	Leaves solution	Indian mackerel	Soaking (up to 30%, 30 min)			[82]
Ocimum sanctum	Essential oil	Fermented dairy products (dahi and yoghurt)	Addition (0.05–0.1%, v/v)	[83]		
Ocimum	*gratissimum*	Ethanol and hexane extracts (leaves)	Cucumber cuts		Soaking (0.05%)	
γ-Terpinene (17.2%), phenolic	compounds (5–11 mg/100 g)	[84]				
Antioxidant preservative						
Ocimum basilicum	Essential oil (leaves)	Beef burger	Addition (0.125–0.25%, v/w)	x	Estragole (85.2%)	[78]
Ocimum basilicum	Essential oil (leaves)	Beef meat	Addition (2–4%)		Estragole (41.4%) and linalool (26.5%)	[8]
Ocimum basilicum	Extract	Pork meat	Addition (0.03%, w/w)			[85]
Ocimum basilicum	Dried leaves and branches	Fesh buffalo cheese	Addition (0.25–0.5%, w/w)		Phenolic compounds (mainly, rosmarinic acid, 0.18%)	[86]
Ocimum sanctum	Aqueous extract (leaves)	Tofu	Addition (3%, w/v)			[87]

Application of Ocimum as an antimicrobial agent in food products

In recent times plant antimicrobials have also been applied to food preservation by keeping food products safe from spoilage microorganisms over a long period of time.[77] The bioactive compounds present in the plant materials determine their suitability as an antimicrobial agent. In particular, in the previous section it was evidenced the antimicrobial properties of *Ocimum* extracts and essential oils, including against foodborne pathogens, such as *Salmonella* spp., *B. cereus, E. coli., L. monocytogenes* and *V. parahaemolyticus*, and food spoilage fungi species, including *Fusarium* spp., *B. cinerea, A. flavus*, and *Alternaria* spp. In this section, some applications are reviewed (Table 1).

Preservation of meat and fish products with Ocimum

The applications of *O. basilicum* essential oils in the preservation of meat[78] and fish products[88] have been investigated. As an example, it was able to decrease the growth rate of *S. aureus* in beef burger (added at 0.125%) with a good acceptability value after cooking.[78] Also, *O. basilicum* essential oil was able to reduce the number of bacterial pathogens and *Salmonella enteritidis* in raw meat. It exhibited a stabilizing effect to lipid oxidation, reduced cooking loss and did not cause any notable quality changes in chicken meat after being soaked in 2.5 and 5.0 mg/ml solutions of the essential oil for 15 min.[79]

It has been observed that the action of essential oils against spoilage microorganisms are limited and affected by the fat content in the food. This might be due to the dissolution of the essential oils in the lipid phase of the food thereby making less essential oil available to act on bacteria present.[88] Spreading of these oils improved their potency against the spoilage microorganisms inherent in fish and shrimps.[89] Another alternative could be the use of bioactive edible films as coating. For example, microencapsulated essential oils of *O. basilicum* (rich in linalool) and *Lippia graveolens* Kunth was applied to obtain bioactive edible film that enables an increase in the shelf life of refrigerated pork meat pieces, exhibiting the lowest concentration of 2-thiobarbituric acid reacting substances and natural microbiota growth, while favorable sensory properties were obtained.[90] In this sense, microencapsulation may reduce odor and obtain higher aqueous solubility than free oils, facilitating their incorporation into polymers.[90]

In addition, a commercial extract from *O. sanctum* leaves has also been tested as preservative in chicken sausages during refrigerated storage (incorporated at 0.03%), being able to reduce values for total plate count, psychrophilic count and yeast and mould count, while favored several sensory parameters.[81] Applied to Indian mackerel fish by soaking (up to 30%, soaking time 30 min), leaves solution was able to extend shelf life until the 13th day with amount of bacteria 6.9×10^7 CFU/g during low-temperature storage.[82]

Preservation of dairy products with Ocimum

Essential oils from plants exhibited antibacterial activity against some spoilage microorganisms of dairy products.[91] The application of *O. sanctum* essential oil (0.5–1.0 μL mL^{-1}) to preserve dairy products have also been reported,[83] as well as either as powder (up to 10:1000, g/g) or as water extract (100:1000, w/w) *O. bassilicum* can increase sensory scores.[92] This latter work showed that the use of basil enhanced the volatile composition of yogurt, being enriched in linalool. A recent work showed that *O. basilicum* at 0.025% (w/w), added to milk before cheese-making process, displays excellent activity to combat microorganisms like clostridia and *E. coli* that may cause late cheese blowing before and after inoculation. The effects on normal cheese flora were slight and intermediate between the effects of *Melissa officinalis* and *Thymus vulgaris* essential oils. Moreover, the main components transferred to milk, cheese and whey were estragole, linalool and 1,8 cineol.[80]

However, the antibacterial activity of plant extracts against microorganisms in dairy products can be limited by the reaction between some phenolic components of this plant extracts and proteins.[93] As earlier reported with other food products, the presence of fat in dairy products reduced the potency of essential oils against spoilage microorganisms. This is thought to be brought about by the shielding of the microorganisms from the antimicrobial action of the bioactive compounds. Therefore, higher

concentrations of essential oils are needed in food matrices compared with those used in *in vitro* assays.[80]

Preservation of plant foods with Ocimum

It has been reported that most of these essential oils and their components are active effective against the spoilage microorganisms inherent in fruits and are able to extend their shelf-life.[94,95] Moreover, as shown in the sections above, *O. bassilicum* essential oils was active against plant pathogens *in vitro*.

In particular, the use of *Ocimum* plants and their extracts in the preservation of food products has been established. Lopez et al. (2008) reported the antimicrobial action of *O. basilicum* against stored rice pests (*Sitophilus oryzae, Rhyzopertha dominica* and *Cryptolestes pusillus*).[96] In another work, fresh cuts of *Cucumis sativus* (cucumber) dipped into *O. gratissimum* ethanol and hexane extracts solutions (0.05%), rich in γ-terpinene, had lower moisture content, pH, total soluble solids, and total load of microbes than untreated ones. However, ascorbic acid, phenolic and carotenoids contents were also low for the former.[84] Ethanolic extracts of leaves from this plant have also been effective against postharvest pathogens of avocado pear (*Persea americana* Mill.).[97]

Application of Ocimum as an antioxidant agent in food products

The essential oils and extracts of *O. bassilicum* leaves have also been applied against oxidation in meat and meat products.[8,78] However, some results have not been satisfactory in all cases, e.g. essential oil rich in estragole at 0.25% was not able to decrease lipid oxidation in raw beef burger at 4°C compared to the untreated control.[78] Alternatively, an essential oil rich in estragole and linalool, added at higher concentrations (2% and 4%), was able to improve color and lipid oxidative stability of refrigerated minced beef samples.[8] Similarly, the inclusion of a commercial basil leaf extract in minced pork at 0.03% has been reported to lower the microbial population and oxidative deterioration, while it improved the sensory quality compared to the control after 5 days of cold storage at 1°C.[85] Furthermore, buffalo fresh cheese with 2.5 and 5.0 g dried basil/kg cheese showed high acceptability by consumers, with additional benefits such as improved functional characteristics, including antioxidant activity and total phenolic content. It also changed hardness and chewiness, while cohesiveness and springiness were not influenced.[86]

O. sanctum extracts have been added to meat, plant and dairy products, e.g., chicken sausages (300 mg/kg), tofu (3%, w/v) and ghee, with or without refrigeration, to increase their oxidative stability by lowering thiobarbituric acid reactive substances, bacteria, and/or free fatty acid.[81,87,98] As an example, aqueous extract of *O. sanctum* (3%, w/v) added during the preparation and storage of tofu was also able to prolong its shelf life up to eight days compared to the control, without requiring refrigeration. The organoleptic characteristics were good with less lipid-peroxidation and less protease activity.[87] Moreover, its mixture with other essentials oils (clove oil, 40%; thyme oil, 40%) in emulsion based chicken sausages (0.25%) enhanced shelf life and storage stability at 4°C.[99]

In another context, the use of *O. sanctum* and *O. basilicum* leaves extracts contributed to improve the antioxidant system in rice seedlings and arsenic toxicity alleviation[100] and to increase the antibacterial and antioxidant properties of ZnO nanoparticles, suggesting a potential for green synthesis of nanoparticles.[101] Potential uses of *O. gratissimum* essential oil in aquiculture include its uses as antiparasitic agent against the parasite *Gyrodactylus* sp. and it also prevented the lipid peroxidation and increased the antioxidant status of fish tissues.[72]

Current challenges of Ocimum plants in food preservation

Despite the acceptability and approval of the use of *Ocimum* and its essential oils as flavorings and in protecting food products from spoilage by some of the regulatory agencies (European Commission, The United States Food and Drug Administration), there is a constraint of the acceptable daily intake of these oils in food, although their toxicity could be low.[65,102] Notwithstanding the several reports *in vitro* and

in vivo, their application in food preservation requires high concentrations in some cases (up to 4% for addition), which might be higher than the tolerable limits accepted/approved by regulatory agencies. Furthermore, the effectiveness of the essential oils against microorganisms can be impaired in food products rich in fats, starch,[103] and proteins,[104] as commented before. The resulting high concentration of these essential oils may lead to the rejection of such food products by consumers. Notably, in the aforementioned studies on *Ocimum*, the organoleptic characteristics of the food were acceptable. Other factors that influence the effectiveness of essential oils against spoilage microorganisms include: pH,[105] the degree of contamination by microorganisms[106] and temperature.[107] When essential oils and plant extracts are added to a fermented product, the inhibitory effects on desirable flora should be negligible to consider their suitability for this matrix.[80] These factors make the practical use of plant essential oils, and their components, including those from *Ocimum* spp., challenging in the preservation of food products. In any case, some of these challenges can be circumvented by microencapsulation and/or incorporating these oils into the material used in the packaging of the food products, e.g., as sachets containing essential oils. The oils can also be immobilized in polymers of packages of the food products.[90,105,108] Besides these preservatives properties, the selection of the sensory characteristics that pair with the food should be also considered since *Ocimum* spp. can be grouped based on anise, citrus aroma, and/or spice-like aroma depending on their phytochemical composition.[109]

Moreover, other *Ocimum* plants, such as *O. campechianum, O. kilimandscharicum* and *O. americanum*, were reported to have antimicrobial and antioxidant activity in the previous sections, and thus more work is required to test it in food systems. Mixtures of essential oils from different plants can be tested to improve their potency, but it should be verified to avoid antagonistic effect among the active ingredients.[90] In this sense, Sharma and coworkers[99] investigated several blends of essential oils including *O. sanctum*. Their results showed that blends with clove oil, *O. sanctum*, and cassia oil or thyme oil at 40%, 20%, 40%, respectively, showed the lowest microbial count, while clove oil, *O. sanctum*, cassia oil, thyme oil, ajowan oil, and betel oil at 25%, 20%, 20%, 15%, 10%, 10%, respectively, showed the highest sensory scores. Alternatively, the combination of rosemary and basil essential oils has no preservative effect against spoilage microorganisms, while individual essential oils were effective.[79] Another key issue is the requirement of standardization to establish the dosage more accurately and to choose the best chemotype and collection time since the phytochemical composition and bioactivity vary,[67,84,110–112] as shown in the sections below.

Phytochemicals in *Ocimum* and mode of action as preservatives

The main active phytochemicals present in *Ocimum* plants are broadly classified as terpenes (including terpenoids) and phenolic compounds. Some phenolic compounds, such as eugenol, are classified in the terpene group owing to their structure and presence in the volatile fraction and essential oils of medicinal plants.

Terpenes: composition and mode of action

Composition

The essential oils of *Ocimum* are made up terpenes and terpenoids which are active against spoilage microorganisms. These bioactive compounds are hydrocarbons synthesized in the cytoplasm of plant cells using acetyl-CoA as a starting material in the pathway. The rearrangement of the carbon backbone of terpenes may give rise to a single or double cyclic structures.[113] Moreover, terpenoids are products of enzymatic and biochemical modifications of terpenes,[113] which may contain, e.g., some oxygen functionality. Figure 2 shows the structure of the main terpenes found in *Ocimum* plants.

The chemical composition of *Ocimum* essential oil varies depending on the species, cultivar (and even chemotype) and season.[66,110–112] In general, *O. basilicum* essentials contain mainly oxygenated monoterpenes (up to 68.9%). Sesquiterpenes, diterpenes, and hydrocarbons may also appear. Linalool was the main constituent of essential oils (56.7%–60.6%) in some cases, while hydrodistilled essential

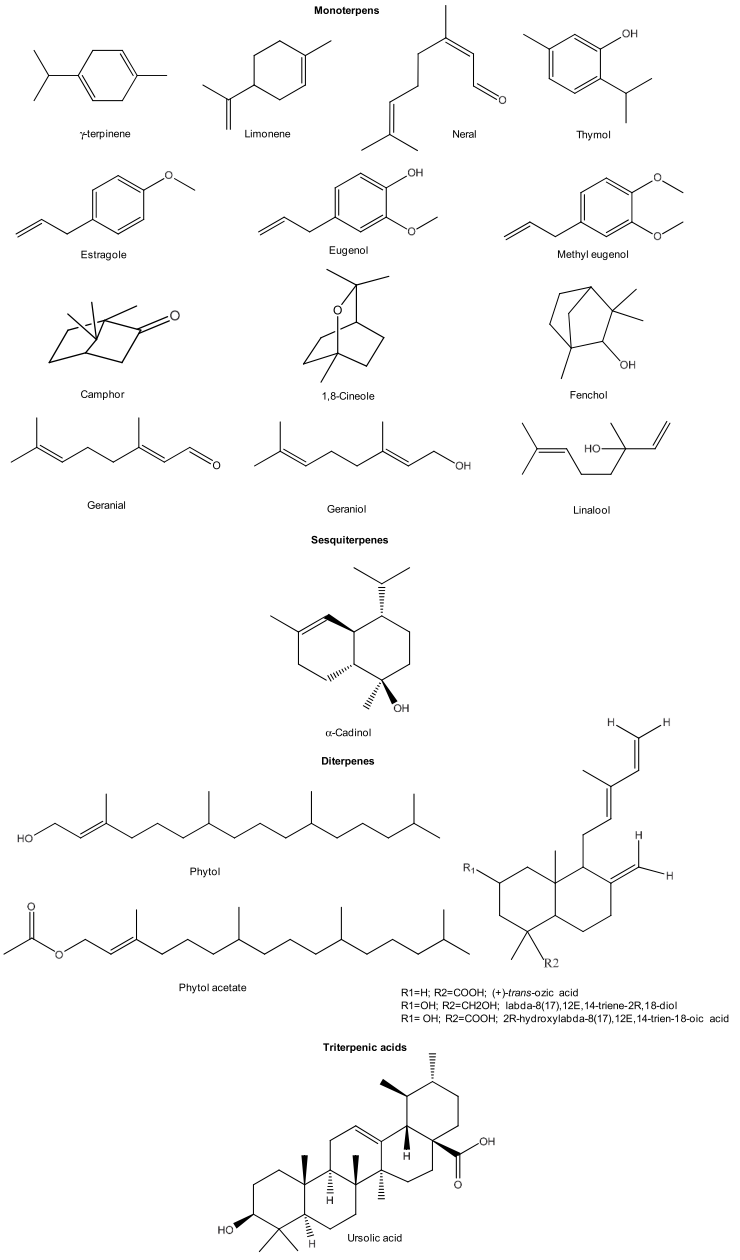

Figure 2. Chemical structure of main terpenoids found in *Ocimum* plants.

oil from Iranian and South Africa *O. basilicum* leaves presented estragole (or methyl chavicol) (41.4%-85.19%) as major compound (Table 2).[8,78,110,111] In this regard, a cluster analysis of 179 essential oil compositions of *O. basilicum* revealed six major chemotypes: linalool, eugenol, estragole, methyl eugenol, 1,8-cineole, and geraniol.[116,117] Another two chemotypes are (*E*)-methyl cinnamate (cinnamic derivative, and so phenolic compounds) and mixed type having both linalool and estragole.[112] Further, Maggio et al.[110] evaluated the chemical profiles of 21 cultivars of *O. basilicum* belonging to Genovese, Napoletano, and Purple types. While estragole occurred in Napoletano type, it was not

Table 2. Content (%) of the main volatile compounds found in essential oils from several *Ocimum* species.[8,65,78,110,112,114,115].

Volatile compound	OB leaf South Africa	OB leaf Iran	OB leaf Italy (Genovese type)	OB leaf Italy (Napoletano type)	OB aerial part India (6 varieties[b], 24 accessions)	OB leaf Italy (Purple type)	OS leaf India	OG aerial part India (11 accessions)	OG leaf Brazil	OK aerial part India
Linalool	26.5	1.0	0.7–17.2	1.8–12.0	0.3–69.7	13.2	44.3	ND-t	0.3	9.7
Estragole[a]	41.4	85.2	ND	ND-18.2	ND-90.7	-	-	-	-	2.3
Eugenol	0.4	0.7	39.3–75.0	27.0–52.4	ND-2.0	38.8	4.4	38.6–79.2	74.8	-
Methyl eugenol	-	0.3	ND-34.2	ND-43.3	ND-16.6	24.4	6.3	-	-	-
1,8-cineole	-	4.0	ND-7.3	ND-2.3	ND-7.2	1.3	21.7	ND-t	15.2	14.4
Geraniol	-	-	ND-0.1	ND-0.2	ND-1.6	0.3	-	-	-	3.7
(*E*)-methyl cinnamate	-	-	-	-	-	-	-	-	-	ND-50.5
α-Cadinol	-	0.2	1.4–36.8	4.3–21	ND-18.0	3.2	-	-	-	-
Phytol acetate	-	-	ND-0.6	ND	-	-	-	-	-	-
Thymol	-	-	ND-1.6	ND	-	-	-	47.6–50.7	-	-
Camphor	-	-	ND-1.2	ND	ND-1.9	t	-	-	0.7	43.21

ND, not detected; t, traces; OB, Ocimum bassilicum; OG, Ocimum gratissimum; OK, Ocimum kilimandscharicum; OS, Ocimum sanctum.
[a]Or methyl chavicol.
[b]Var. difforme, purpurascens, basilicum, glabratum, pilosum, and thyrsiflora.

present in Genovese and Purple basil types. Alternatively, a high presence of eugenol (25–76%), methyl eugenol (0–34.2%), and linalool (0–21.8%) was observed in the majority of Genovese and Napoletano cultivars. α-Cadinol (up to 36.8%), (*E*)-phytol (up to 26.8%) and phytol acetate (up to 26.8%) were high in some particular cultivars.

Eugenol (e.g. 61.30%), estragole (e.g. 44.63%) and/or linalool (e.g. 21.84%) are also some of the major compounds of *O. sanctum* essential oils.[102,114,115] Chemical profiling of *O. gratissimum* essentials oils from aerial parts showed that eugenol (38.6–79.2%) and thymol (47.6–50.7%) were the major components.[102] A recent study on several *Ocimum* species has found that they can be classified into different chemotypes: *Ocimum* × *citriodorum* were rich in geranial/neral and estragole, *O. kilimandscharicum* in camphor (43.21%), and *O. viride* in eugenol (77.86%). γ-Terpinene was found as main compound in hexane extract of *O. gratissimum* leaves[84] and in its essential oil along with methyl cinnamate,[65] as commented before.

In addition, labdane-type diterpenes ((+)-trans-ozic acid, labda-8(17),12E,14-triene-2 R,18-diol, and 2 R-hydroxylabda-8(17),12E,14-trien-18-oic acid) have been isolated in *Ocimum labiatum* (N.E. Br.) A.J.Paton leaves extract obtained by ethanol and ethyl acetate extraction.[118,119] The triterpenic acid ursolic acid has been detected in ethanolic and methanolic extracts of *O. basilicum, O. sanctum, O. gratissimum, O. americanum, O. selloi* and *O. micranthum*, with contents between 0.27% (*O. basilicum*) and 2.02% (*O. sanctum*) in dried leaves.[120]

Mode of action

The functional groups of the terpenoids have been reported to be responsible for their antimicrobial activity, including linalool, eugenol, estragole, and thymol.[57,121] Furthermore, studies have shown that the presence of delocalized electrons is important for antimicrobial activity.[113] The mode of action of terpenes against microbes is by disrupting their membranes that alter the microorganism's ability to effectively carry out osmoregulation and affect the cell permeability resulting in cell collapse.[90] Terpenes alter the detoxification mechanism of the microorganisms through their outer membrane[122] and their physiological processes.[77]

In addition, some *Ocimum* terpenoids are able to inhibit aflatoxin production, which is desirable for the use of essential oils as food preservative,[65,102] as well as to reduce the amount of ergosterol in

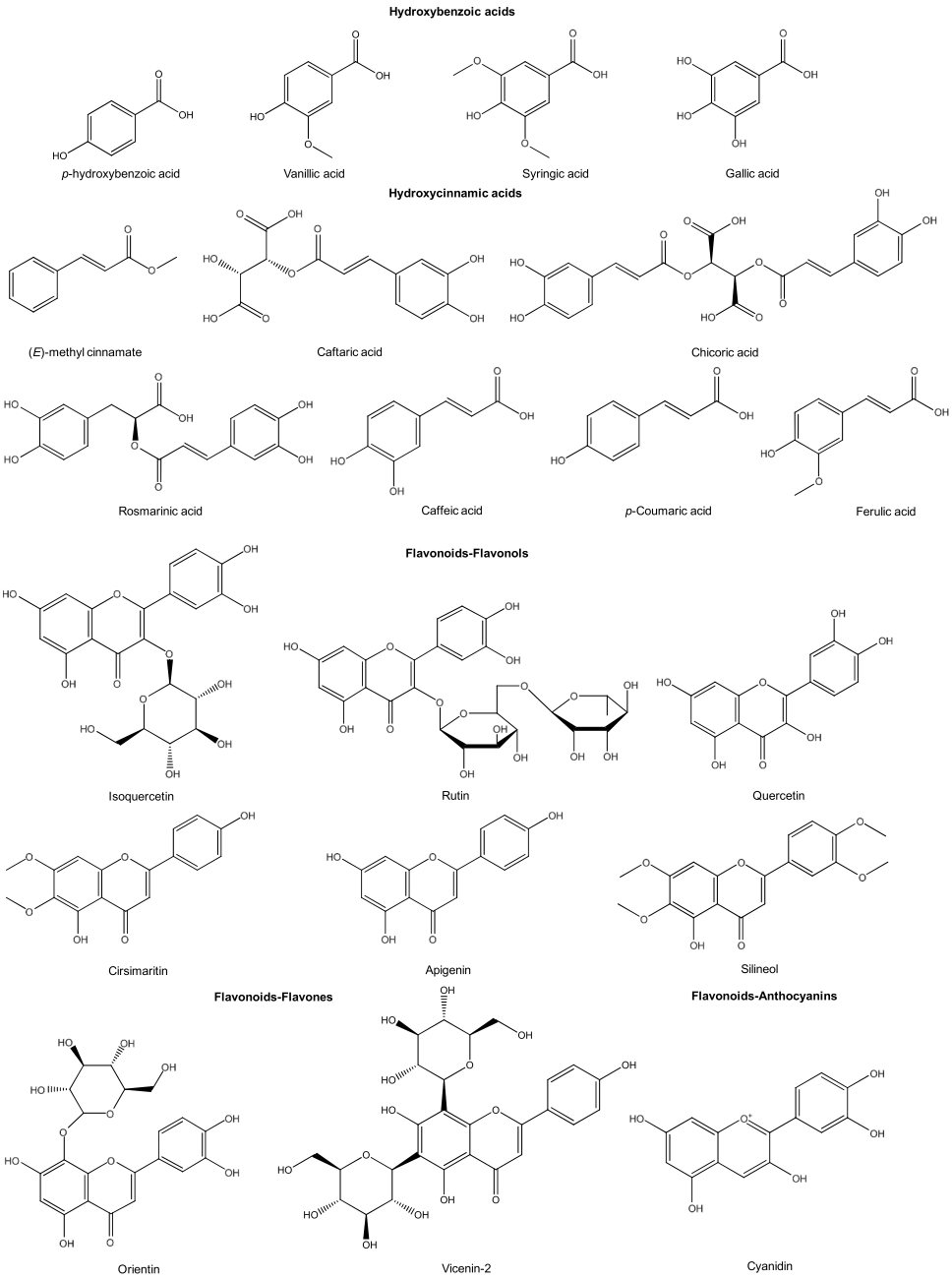

Figure 3. Chemical structure of main phenolic compounds found in *Ocimum* plants.

fungi, which is a membrane sterol essential for growth and normal membrane functions.[114] Thymol also interferes with the starting phases of adherence and with biofilms of some microorganisms.[57]

Furthermore, *Ocimum* terpenes are able to donate electrons to scavenge free radicals involved in the propagation step of autoxidation and other radicals and they have protective effects against prooxidants like iron.[8] For example, eugenol is a potent antioxidant compound and thus it can enhance the shelf life of food products by controlling not only microorganism growth but also free radical scavenging and oxidation of unsaturated lipids.[102] Linalool also showed antioxidant activity

Table 3. Content (mg/g dry matter) of main phenolic compounds found in several *Ocimum* species.[67,123,124,126–128].

Phenolic compound	OB leaf[a] Italy, 3 purple types×5 sampling days	OB aerial parts[a] Italy, different shading conditions	OB leaf[b] Thailand	OS leaf[b] Thailand	OB whole plant[a] India	OB plant material[c] India	OS whole plant[a] India, white type	OS whole plant[a] India, black type	OS plant material[b] India, different accesions	OK plant material[b] India	OG leaf[d] Brazil
Caftaric acid	0.07–1.14	2.89–5.60	-	-	-	-	-	-	-	-	Approx. 20
Chicoric acid	0.12–4.52	3.19–6.03	-	-	-	-	-	-	-	-	Approx. 70
Rosmarinic acid	0.79–22.77	0.78–7.93	-	-	-	0.23	-	-	0.80–6.70	0.48	Approx. 10
Caffeic acid	0.03–0.24	0.53–1.01	0.77	1.34	0.08	-	0.05	0.09	-	-	<10
p-Coumaric acid	0.02–0.58	0.15–0.22	1.23	11.61	0.02	-	0.01	0.06	-	-	-
Gentisic acid	0.30–2.61	-	-	-	-	-	-	-	-	-	-
Rutin	-	0.09–0.18	-	-	-	-	-	-	-	-	-
Isoquercetin	-	up to 0.56	-	-	-	-	-	-	-	-	-

Approx., approximately; ND, not detected; OB, *Ocimum bassilicum*; OG, *Ocimum gratissimum*; OK, *Ocimum kilimandscharicum*; OS, *Ocimum sanctum*; t, traces.
[a]80% methanol extract.
[b]Water extract.
[c]Methanol extract.
[d]Water extract further purified.

in vitro but synergistic interaction of the essential oil constituents can explain the better antioxidant properties of the whole essential oils.[66]

Phenolic compounds: composition and mode of action

Composition. The phenolic content and composition depend on the extraction method and the species.[84] The chemical structure of main phenolic compounds found in *Ocimum* plants are shown in Fig. 3, which can be classified into: hydroxybenzoic acids, hydroxycinnamic acids, and flavonoids (flavonols, anthocyanins, and flavones).

Some phenolic derivatives are found in essential oils, as commented before, such as eugenol, methyl eugenol, thymol, and (*E*)-methyl cinnamate.[112] Hydroxycinnamic acids, such as caftaric (0.08–0.85 mg/g DW), chicoric (0.13–3.55 mg/g DW), and rosmarinic (1.31–21.31 mg/g) acids, as well as anthocyanins (2.07–9.72 mg/g) have been reported in leaves of *O. basilicum* after methanolic extraction. These were the mean values for three type of purple basil.[67] Moreover, among this group, four anthocyanins were tentatively assigned as cyanidin conjugated with *p*-coumaric and/or caffeic acid. Higher contents of caftaric acid were found in other *O. basilicum* samples (up to 5.6 mg/g) obtained after extraction with methanolic extraction, along with chlorogenic acid (up to 0.7 mg/g), caffeic acid (1 mg/g), *p*-coumaric acid (0.3 mg/g), chicoric acid (up to 6 mg/g), and rosmarinic acid (up to 8 mg/g). The flavonols isoquercetin and rutin (up to 0.2 mg/g) were also detected (up to 0.6 mg/g). It depended on the shading treatment type.[123] Other study has also found *p*-hydroxybenzoic acid, vanillic acid, and ferulic acid in *O. basilicum*.[124] The presence of caffeic, *p*-coumaric, and rosmarinic acids in aqueous and ethanolic extracts of this plant was also reported.[125,126] As an example, Table 3 depicts the content of some main phenolic compounds found in *Ocimum*.

Rutin was the main flavonoid identified in ethanol extracts of *O. sanctum*, while it also contained quercetin and the flavones luteolin and apigenin.[129] Acetone extract of *O. sanctum* contained eugenol, cirsimaritin, apigenin, silineol, and rosmarinic acid.[130] In addition, the *C*-glycoside flavones orientin and vicenin have been isolated from aqueous extracts of leaves of *O. sanctum*,[131] while gallic acid was found also in methanolic extracts, together with chlorogenic acid, *p*-hydroxybenzoic acid, caffeic acid, vanillic acid, syringic acid, *p*-coumaric acid and ferulic acid.[124] Hydroxycinnamic acids,

including rosmarinic acid and eugenol, were found in methanolic extracts of *O. kilimandscharicum* and *O. americanum*.[124,127]

Among all these compounds, caftaric acid, chicoric acid, and vicenin-2 have also been identified in *O. gratissimum* leaves,[128] while caffeic acid and rutin (major peak) in their aqueous extract.[132]

Mode of action. Phenolic compounds are innate antioxidants, which can be employed in the preservation of food products. It is due to their unique ring structure that confers the ability to chelate metal ions, prevents lipid peroxidation and free radical scavenging properties.[124] *Ocimum* phenolic compounds are well-recognized for its antioxidant effects, conferred through its high radical scavenging activity,[124,130,133] although the potency depends on their structure.[124] Those with the ortho-dihydroxyl groups (see Fig. 3) possess the capacity to suppress hydroxyl radicals by the inhibition of $HO^{\bullet}$ production.[134] Furthermore, the position and degree of hydroxyl groups on B ring of flavonoids influence its stability and reactivity hence their antioxidant activities (Fig. 3).[135] In particular, the individual phenolic acid composition is an important factor influencing the antioxidant capacity. Although rosmarinic acid is generally one of the major phenolic acids and active components of some *Ocimum* extracts,[127] chicoric acid and caffeic acid are also important contributors to the antioxidant activity.[136] Moreover, flavones like orientin and vicenin isolated from *O. sanctum* provided antioxidant properties *in vitro* and *in vivo* against radiation-induced lipid peroxidation in mouse liver through radical scavenging. The inhibitory effect of orientin on hydrogen peroxide-induced β-galactosidase also supports its antioxidant properties.[137,138]

Moreover, the hydroxyl groups in the structure of phenols have also been reported to be responsible for their activity against spoilage microorganisms.[139] The action of this plant against spoilage microorganisms is also determined by the presence of other groups, like alkyl, acetate, and with the elevation of their lipophilic character.[140] Membrane disruption mainly explains the antimicrobial activity of most phenolic compounds, but there other non-membrane mechanisms of action that can occur.[141] A recent study on phenolic acids has shown that the antimicrobial activity against food borne bacteria could be mainly due to the effect of the undissociated forms, except for chlorogenic and gallic acids, for which the antimicrobial activity is mainly due to a decrease in extracellular pH. Moreover, the dissociated forms of *p*-coumaric and ferulic acids also exhibited inhibitory activity.[142] Orientin has also revealed potent antiviral effects,[143,144] being effective against HSV type 2 of different viral titre on Hep-2 cells.[145] Therefore, besides rosmarinic acid, which is one of the main antimicrobial components of *Ocimum* extracts, all these components can contribute. Bear in mind that the concentration of rosmarinic acid is highly variable and cannot account for all the bioactivity of the extracts, e.g., Domlur Thyagaraj et al.[127] reported the following values: *O. basilicum* (0.023%), *O. sanctum* (0.084–0.426%), *O. americanum* (0.501%), and *O. kilimandscharicum* (0.048%). The same occurs with eugenol (0.005% in *O. americanum*-1.230% in *O. sanctum*).

Synergism can also occur in active *Ocimum* extracts containing phenolic compounds. For instance, the combination of flavonoids from *O. sanctum* (orientin and vicenin) synergistically inhibited the growth of different bacterial strains, such *as E. coli, S. aureus, S. cohnii, K. pneumoniae*, and *Proteus*, while the individual flavonoids were found to be less effective.[131]

Other biological properties with interest for promoting functional foods

In this section other biological properties of *Ocimum* extracts are reviewed since they could have interest in functional food and phytopharmacy sectors for more personalized diets. Figure 1 summarizes the *Ocimum* species object of study and their properties.

Anti-inflammatory and immunomodulatory activity

Plants from *Ocimum* genus are used in folk medicine for treating various diseases, including those of inflammatory nature and immune-related.[146,147] Experimental animal studies and controlled trials in

healthy volunteers have clearly shown the immunomodulatory effects of *O. sanctum* seed oil, leaves ethanolic and aqueous extracts.[148–150] The anti-inflammatory activity of *O. sanctum's* methanol extract (500 mg) was also reported in rats. Fixed oil and linolenic acid present in tulsi have the ability to block cyclooxygenase (COX) and lipoxygenase (LOX) pathways of arachidonic acid metabolism. *O. sanctum* show anti-inflammatory effects against prostaglandin E2 (PGE2) and leukotrienes-induce edema in rats.[151] Similarly, Mrutyunjay reported that *O. sanctum* aqueous extract (200–400 mg/kg) exerted anti-inflammatory effect in rats with carrageenan-induced paw edema through inducing edema reduction, better than that of indomethacin, a standard anti-inflammatory drug.[152]

Aqueous and ethanol leaf extracts of *Ocimum suave* Wild and *Ocimum lamiifolium* Hochst. ex Benth. have shown anti-inflammatory activities in mice (400–800 mg/kg)[146,147]; with a low toxicity (LD_{50} > 8 g/kg). These studies suggest that the highest dose of the extracts, 800 mg/kg, in mice corresponds to intake of around 4 g of the extract for 60 kg adult human, which is lower than the human equivalent LD_{50} (>38.9 g). In all cases, the specific active constituent needs to be investigated.

The suppression of interleukin (IL)-10, IL-2, IL-4, IL-6, IL-17A and tumor necrosis factor (TNF)-α by *O. labiatum* ethanolic extract and a isolated labdane diterpenoid (labda-8(17),12E,14-triene-2 R,18-diol) (structure in Fig. 2) can be of general therapeutic significance.[118] The over expression of these cytokines has been linked to certain autoimmune diseases, as well as activation of pathogenic inflammation.[153,154]

Cardioprotective Activity

O. basilicum is used in traditional Asian medicine to treat cardiovascular diseases, including hypertension and coronary heart disease. Previous studies have demonstrated platelet aggregation inhibitory activity of aqueous extract of *O. basilicum*, implying that it possesses antithrombotic effect *in vitro* and *in vivo* (15–375 mg/kg).[155] This is particularly important because thrombosis contribute to the development of many cardiovascular diseases. Furthermore, other reports show that aqueous extract *O. basilicum* possess hypolipidemic effect (0.5 g/100 g body weight), lowering total cholesterol, triglycerides and LDL-cholesterol levels, and reduces cholesterol synthesis *in vivo*.[156,157] Umar and coworkers demonstrated the antihypertensive effects of aqueous extract *O. basilicum* (leaves and stalks) (100–400 mg/kg) on blood pressure using the renovascular model of hypertension in rats.[158] Interestingly, the beneficial effect of *O. basilicum* ethanolic extract (leaves) (40 mg/kg) on heart was demonstrated in an experimental myocardial infarction model induced by isoproterenol. The study concluded that the cardioprotective effects *O. basilicum* may be through enhanced antioxidant defenses.[125] This is because *O. basilicum* extract markedly improved fibrosis and myocardial necrosis, suppressed left ventricular contractility, significantly increased left ventricular end-diastolic pressure and reduced the raise of malondialdehyde levels both in myocardium and serum. Moreover, *O. basilicum* aqueous and ethanol extracts were also reported to produce cardiotonic effect demonstrated by a significant reduction in membrane Mg^{2+}ATPase and increase in $Ca^{2+}$and Na^{+}/K^{+} ATPase) and ß-adrenergic effects, respectively.[159] In most of these studies phytochemicals were not characterized, while Fathiazad and coworkers[125] showed that the content of rosmarinic acid was 157.4 mg/g in the ethanolic extract of *O. basilicum*. As commented before, this is one of the major phenolic compounds of *Ocimum* plants.

Similarly, *O. sanctum* prevented myocardial infarction and chronic-resistant stress in rats by preventing rise in cAMP level, myocardial superoxide dismutase and catalase activities and lactate dehydrogenase levels.[160,161]

Recently, the ACE inhibition activity *in vitro* and also in spontaneously hypertensive rats (100–500 mg/kg) has been reported for *O. gratissimum* water extract (from whole dried plant), which was attributed to its main phenolic compound, rutin. Caffeic acid was also detected.[132] Other studies carried out in ra-ts showed that leaf methanolic extract of *O. suave* lowered total lipids concentration.[162]

Anti-diabetic Activity

The genus *Ocimum* includes some species ethnopharmacologically used to treat diabetes mellitus in Africa and Asia.[14] Their hypoglycemic effects have been demonstrated *in vitro*, which was enhanced using silver nanoparticles,[163] and in various *in vivo* studies[164,165] for *O. basilicum, O. gratissimum* and *O. americanum* methanolic and aqueous extracts. It is noteworthy that the major phenolic substances from *O. basilicum* and *O. gratissimum*, namely, caffeic acid and its derivatives caftaric, chicoric, and rosmarinic acids, and also the flavonoid vicenin-2, seem to possess short- and long-term beneficial effects on glucose-stimulated insulin secretion. Among them, chicoric acid (3 mg/kg) reduced significantly the glycemic levels of diabetic mice by 53% after 120 min.[128] This further reinforces the potential of *O. basilicum* and *O. gratissimum* as antidiabetic agents. In addition, the antidiabetic properties of a dichloromethane:methanol extract from *O. basilicum* (100–400 mg/kg) were suggested to be due to its ability to suppress endogenous glucose release, inhibit glycogenolysis and/or stimulate glycogenesis. It was able to inhibit α-glucosidase (35.7–100%) and also α-amylase (23.6–81.5%) *in vitro*. In this case, the HPLC peaks were determined but not characterized.[166]

The anti-diabetic potential of *O. gratissimum* on type-2 diabetes was examined by Okoduwa et al.,[15] who found that specific biomarkers, such as aspartate aminotransferase (AST) and alanine aminotransferase (ALT), are responsible for liver damage. These biomarkers are responsible for amino acids dissociation to alpha-keto, metabolized through Krebs cycle and electron transport chain before its transportation into the blood stream. Their study validated that hepatic cells injury leads to damage to its cell membrane allowing permeability of cytoplasmic enzymes into the blood stream, hence it led to an increase in serum activities. All these resulted in liver impairment. However, in diabetic rats their investigation showed that the treatment with *n*-butanol fraction from methanolic *O. gratissimum* leaves extract (250 mg/kg) had the most active liver reduced serum enzyme activities and proved the hepatoprotective effect of *O. gratissimum.*

O. sanctum has been reported to possess great anti-diabetic effects due to the ability of the leaves to reduce blood glucose when administered in diabetic rats. For example, *O. sanctum* treatment (4.45 g/kg/day of dried leaf powder) improved insulin resistance in diabetic rats.[167] Moreover, aqueous extract of *O. sanctum* whole plant (200 mg/kg, 60 days) delayed the development of insulin resistance in rats, preventing hyperglycemia, hypertriglyceridemia, hyperinsulinemia.[168] Gholap and Kar demonstrated that the anti-diabetic effects of *O. sanctum* may be through corticosteroid-dependent pathway.[169] The hypoglycaemic ability was also noticed in rats fed with *O. sanctum* ethanolic extract (200 mg/kg) in a long-term study in alloxanized diabetic rats.[170] In a similar study noticeable insulin-secretory effects were noticed in the rat pancreas perfused with the extract and three partition fractions of *O. sanctum* and related effects were noticed in acute insulin-release studies using isolated rat islets.[171]

Furthermore, the anti-diabetic activity of alcoholic leaf extracts from *O. sanctum, O. gratissimum*, and *O. americanum* against diabetes in rats was significant, being even more potent than metformin but at higher doses (up 800 mg/kg). This is in line with the anti-diabetic and anti-hyperlipidemic activities of hydroethanolic extract of *O. sanctum* against streptozotocin (STZ)- and nicotinamide-induced diabetes in rats, which was found to be comparable with glibenclamide at 250 and 500 mg/kg.[64,172,173] All results suggest that *O. sanctum* could be used as an adjuvant therapy for treating diabetic patients, but characterization studies were lacking. However, this may be because of the active phytoconstituents of *O. sanctum*, such as rosmarinic acid. Other compounds that could participate are ursolic acid, eugenol, linalool, estragole, apigenin and cirsimaritin (see structures in Figs. 2 and Fig. 3).[172]

Hepato-renal protective activity

Ocimum extracts are also effective in decreasing the pathological changes in liver and kidney. As an example, *O. basilicum* treatment ameliorated acetaminophen-induced hepato-renal damage by decreasing serum markers and MDA in both organs and by increasing SOD and CAT activities.

Hence, *O. basilicum* aqueous extract (400 mg/kg b.w.) may act as a natural antioxidant against acetaminophen-induced acute hepato-renal toxicity when used as a post-treatment.[174]

In human liver cells, Chiu and coworker[175] validated the beneficial effect of *O. gratissimum* aqueous extract through its antioxidant and cytoprotective activities. Liver cells exposure to oxidative stress lead to hepatic cell death. However, with *O. gratissimum* aqueous extract administration, hepatic apoptosis and damage was reduced significantly by retaining the phase I and II and antioxidant enzymes activities. Flavonoids and non-flavonoids were present in *O. gratissimum* aqueous extract, with caffeic acid being detected and considered an important component. *In vivo* the hepatoprotective properties of *O. gratissimum* extracts (water, ethanol and methanol extracts) have been shown in several studies, with doses highly variable (0.2 mg/kg-1.6 g/kg). *In vivo*, Chiu et al.[71] validated the significant effect of *O. gratissimum* aqueous extract (0.2 mg/kg b.w.) on acute liver injury induced on male Wistar rats using CCl_4. The hepatoprotective effect was visible through the significant increase in serum catalase (CAT) and DPPH levels, leading to reduced hepatic damage markers, such as HSP70 and iNOS. Furthermore, their study attested that the hepatoprotective activity of *O. gratissimum* aqueous extract was possible through the increase in antioxidant enzymes activities and reduction of stress-related proteins levels, as well as MMP9 activity through ERK and NF-κB signaling pathways. The effects were similar to that of silymarin. In another work, Ighodaro and Omole[176] probed that the co-administration of *O. gratissimum* aqueous extract (0.2–0.4 mg/kg b.w.) and ethanol improved ethanol-induced hepatotoxicity and AST and ALT levels were reduced. Similar effects were found by Ezeonwu et al.[177] for *O. gratissimum* aqueous extract but at higher doses (80 mg/kg b.w.). Moreover, the hepatoprotective effect of *O. gratissimum* ethanolic extracts (100 and 200 mg/kg/, p.o., for 14 days) have also been assessed in a similar manner.[178] In another work, Prabhu and colleagues[179] validated that administration of *O. gratissimum* ethanol extract at various doses had various levels of hepato-protective effect on hepatocytes: at a dose of 0.8 g/kg, there was a reduction in hepatocytic edema with slight widened sinusoidal spaces; at 1.6 g/kg of *O. gratissimum* ethanol extract, the normal physiology of the liver was established, indicating a dose-dependent hepatoprotective activity and displaying an important role in restoring the normal physiological function of liver cells. Awogbindin et al. assessed the hepatoprotective effect of *O. gratissimum* methanol extract. Similarly to the aforementioned extracts, ALT and AST activities were reduced.[180]

Besides other studies on the positive effects of *O. gratissimum* extracts on CCl_4-induced hepatotoxicity,[181–183] this plant also showed hepatoprotective potential against: 2-acetylaminoflour-ene-induced damage injuries,[184] the exposure to petrochemicals,[185] increased AST and ALT levels induced by rifampicin-isoniazid[186] or paracetamol-induced hepatotoxicity.[187] In the latter work, other mechanism proposed was: the activation of constitutive androstane receptor (CAR) regarded as an important regulator of bilirubin in liver. Akpan et al.[188] also validated the hepatoprotective activity of *O. gratissimum* on derangement in serum and biliary bilirubin, cholesterol and electrolytes in STZ-induced diabetic rats. Their study revealed that *O. gratissimum* was associated with hepatoprotective and neuroprotective properties. The reduction of serum and biliary cholesterol levels was associated with enhanced pancreatic exocrine activity, as a result of increased pancreatic amylase and lipase secretion. Generally, phenolic compounds have been proposed as the main contributors to the hepatoprotective effects of *O. gratissimum*.[178,183]

Furthermore, *O. gratissimum* leaves aqueous extract (100–400 mg/kg) could ameliorate gentamicin and mercuric chloride-induced kidney injury through improving antioxidant enzymes, total protein and urea concentrations, and thereby improving renal function.[189,190]

The hepato-protective effects of ethanol extract from *O. sanctum* leaves (200 mg/kg) are also associated with reduced serum ALP, AST and ALT levels and increased albumin:globulin ratio was observed. As before, these effects may be due to the antioxidant properties of its constituents, but the extract was neither characterized nor standardized.[191,192]

Anticancer activity

Aqueous leaves extracts of *O. basilicum* and *O. gratissimum* have been tested for their cytotoxic, cytostatic and anti-proliferative properties against the human breast cancer cell line MCF-7. Both extracts presented cytostatic effects, but only the first species promoted cytotoxic effects and affected the cell proliferation and metabolism. The enzyme AMPK and the protein mammalian Target of Rapamycin (mTOR) signaling were activated by *O. basilicum*.[193] The anticancer effects of *O. basilicum* and *O. sanctum* extracts were also studied by Nakamura and co-authors, [60,194] and the chemopreventive properties was attributed to the high abundance of phenolic compounds, of which rosmarinic acid was the main compound.

O. sanctum extract trigger a reduction in tumor cell size and an increase in lifespan in mice with tumors.[194] Close results were gotten in a similar experiment where the leaf aqueous-ethanolic extract (200 mg/kg, p.o.) led to a rapid reduction in tumor mass, body weight increase, and improve in survival rate of mice.[195] The effect of other *Ocimum* species (*O. gratissimum, O. basilicum, O. americanum*, and *O. kilimandscharicum*), alone or in combination with radiotherapy, was determined on the basis of tumor volume, body weight, and survival rate of animals. All of them showed positive results as well as they presented modulatory influence against lethal irradiation doses of γ-radiation in terms of radiation-induced chromosomal damage and increased the reduced glutathione level and glutathione S-transferase activity.

Besides the former studies, a recent chapter also suggests that *O. sanctum* can be useful in cancer prevention based on *in vitro* and *in vivo* studies. The mechanisms behind this bioactivity involved: induction of apoptosis mediated by activating the release of cytochrome C enzymes and mitochondrial translocation of Bak and Bax apoptogenic proteins, p53, TNF-α and caspases, Apaf-1, and Bcl-2 family proteins, decreasing the expression of vascular endothelial growth factor (VEGF) protein, maintaining educed glutathione levels, reducing the cell invasion, among others.[196]

Clinical trials

Consulting "ClinicalTrials.gov", seven clinical trials have been performed using *Ocimum* plants, alone or mixed with other herbs. In particular, it has been studied the effects of *O. sanctum* in oral hygiene and gingivitis (NCT02681939; NCT03287011), obesity (NCT02681939), anxiety and stress (NCT03184909), *O. basili*cum in male infertility (NCT01895816) and *O. sanctum*/*O. basilicum* mixed with other herbs in asthma (NCT02428322), fasting glucose (NCT02146157), and vascular health (NCT03064958). With the exception of the two first studies (mouthrinse), capsules, coated tablets or softgels were used as administration way or spices (2–6 g) were consumed during the meal. Although most of these studies are completed, results have not been posted. Moreover, a recent review has been performed considering clinical studies on *O. sanctum* and *O. gratissimum*. It showed that administration doses were highly variable, 300 mg-14 g aqueous extracts (1–3 times), 300 mg-1 g (1–2 times) ethanolic extracts and as tincture solution 30 drops a day, with or without combination with other herbs. No adverse events were observed, while occasional nausea was observed in one case. Among other effects, the treatments lowered blood glucose, improved lipid profile, reduced blood pressure, enhanced immune response, improved mood and/or cognitive functions.[9] These results are in line with the aforementioned *in vitro* and *in vivo* properties, which were mainly performed using aqueous or ethanolic extracts.

Conclusions

The anti-spoilage activities of *Ocimum* plants against many storage and field microorganisms have been established as well as their antioxidant properties. This can explain the interest in using *Ocimum* essential oils and extracts in food preservation. In most cases the sensory properties of foods treated

with *O. basilicum* and *O. sanctum* essential oils and extracts were acceptable and it enabled a reduction of the microbial load and/or an increase of the oxidative stability. While terpenes could be the active compounds of essential oils, aqueous and alcoholic extracts contain phenolic compounds, such as hydroxybenzoic acids, hydroxycinnamic acids and flavonoids.

Moreover, the application of *Ocimum* extracts and essential oils has also shown several health beneficial properties that can be the driver for the formulation of functional ingredients with interest in the food and phytopharmacy sectors.

Some challenges still include the selection of the best extraction conditions (with water or using solvents) and standardization of the extracts and essential oils is a requisite due to intra-species variation and potential impact in the sensory properties. This can help to establish adequate dosages for further clinical studies or food uses. For example, *in vivo* doses in animal models varied between 0.2 mg/kg and 5 g/kg, while in foods dosage were up to 4%, depending on the study. Even, more work will enable to evaluate if these essential oils and extracts can lead to formulate multifunctional ingredients for both preservation and health promotion since current studies have only been focused in one of these targets.

Acknowledgments

M.d.M. Contreras thanks the FEDER UJA project 1260905 funded by "Programa Operativo FEDER 2014-2020" and "Consejería de Economía y Conocimiento de la Junta de Andalucía". N. Martins would like to thank the Portuguese Foundation for Science and Technology (FCT-Portugal) for the Strategic project ref. UID/BIM/04293/2013 and "NORTE2020 - Northern Regional Operational Program" (NORTE-01-0145-FEDER-000012).

ORCID

Javad Sharifi-Rad http://orcid.org/0000-0002-7301-8151
Natália Cruz-Martins http://orcid.org/0000-0002-5934-5201
María del Mar Contreras http://orcid.org/0000-0002-3407-0088

Declaration of interest statement

The authors declare no conflict of interest.

References

[1] Sharifi-Rad, M.; Nazaruk, J.; Polito, L.; Morais-Braga, M. F. B.; Rocha, J. E.; Coutinho, H. D. M.; Salehi, B.; Tabanelli, G.; Montanari, C.; Contreras, M. D. M.;, et al. *Matricaria* Genus as a Source of Antimicrobial Agents: From Farm to Pharmacy and Food Applications. *Microbiol. Res.* 2018, *215*, 76–88. DOI: 10.1016/j.micres.2018.06.010.

[2] Sharifi-Rad, M.; Ozcelik, B.; Altın, G.; Daşkaya-Dikmen, C.; Martorell, M.; Ramírez-Alarcón, K.; Alarcón-Zapata, P.; Flaviana, M.; Morais-Braga, B.; Carneiro, J. N. P.;, et al. *Salvia* Spp. Plants-from Farm to Food Applications and Phytopharmacotherapy. *Trends Food Sci. Technol.* 2018, *80*, 242–263. DOI: 10.1016/j.tifs.2018.08.008.

[3] Sharifi-Rad, M.; Roberts, T. H.; Matthews, K. R.; Bezerra, C. F.; Morais-Braga, M. F. B.; Coutinho, H. D. M.; Sharopov, F.; Salehi, B.; Yousaf, Z.; Sharifi-Rad, M.;, et al. Ethnobotany of the Genus *Taraxacum*—Phytochemicals and Antimicrobial Activity. *Phytother. Res.* 2018, *32*(11), 2131–2145. DOI: 10.1002/ptr.6157.

[4] Prasad, M. P.; Jayalakshmi, K.; Rindhe, G. G. Antibacterial Activity of *Ocimum* Species and Their Phytochemical and Antioxidant Potential. *Int. J. Microbiol. Res.* 2012, *4*(8), 302–307. DOI: 10.9735/0975-5276.4.8.302-307.

[5] The Plant List. Available online: http://www.theplantlist.org/tpl1.1/search?q=ocimum (accessed April 01, 2020).

[6] Chowdhury, T.; Mandal, A.; Roy, S. C.; De Sarker, D. Diversity of the Genus *Ocimum* (Lamiaceae) through Morpho-molecular (RAPD) and Chemical (GC–MS) Analysis. *J. Genet. Eng. Biotechnol.* 2017, *15*(1), 125–286. DOI: 10.1016/j.jgeb.2016.12.004.

[7] Okoli, C. O.; Ezike, A. C.; Agwagah, O. C.; Akah, P. A. Anticonvulsant and Anxiolytic Evaluation of Leaf Extracts of *Ocimum Gratissimum*, a Culinary Herb. *Pharmacognosy Res.* 2010, *2*(1), 36–40. DOI: 10.4103/0974-8490.60580.

[8] Falowo, A. B.; Mukumbo, F. E.; Idamokoro, E. M.; Afolayan, A. J.; Muchenje, V. Phytochemical Constituents and Antioxidant Activity of Sweet Basil (*Ocimum Basilicum* L.) Essential Oil on Ground Beef from Boran and Nguni Cattle. *Int. J. Food Sci.* 2019, *2019*, 2628747. DOI: 10.1155/2019/2628747.
[9] Jamshidi, N.; Cohen, M. M. The Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature. *Evidence-based Complement. Altern. Med.* 2017, *2017*. DOI: 10.1155/2017/9217567.
[10] Adam, Z. A.; Omer, A. A. Antibacterial Activity of *Ocimum Basilicum* (Rehan) Leaf Extract against Bacterial Pathogens in Sudan. *Am. J. Res. Commun.* 2015, *3*, 94–99.
[11] Hadush, G.; Bachetti, R. K.; Dekebo, A. Chemical Composition and Antimicrobial Activities of Leaves of Sweet Basil (*Ocimum Basilicum* L.) Herb. *Int. J. Basic Clin. Pharmacol.* 2015, *4*, 869–875. DOI: 10.18203/2319-2003.ijbcp20150858.
[12] Al Abbasy, D. W.; Pathare, N.; Al-Sabahi, J. N.; Khan, S. A. Chemical Composition and Antibacterial Activity of Essential Oil Isolated from Omani Basil (*Ocimum Basilicum* Linn.). *Asian Pac. J. Trop. Dis.* 2015, *5*(8), 645–649. DOI: 10.1016/S2222-1808(15)60905-7.
[13] Vieira, R. F.; Simon, J. E. Caracterizaçao Química De Basil (*Ocimum* Spp.) encontrados Em Mercados E Usados Na Medicina Popular No. *Econ. Bot.* 2000, *54*(2), 207–216. DOI: 10.1007/BF02907824.
[14] Keter, L. K.; Mutiso, P. C. J. Ethnobotanical Studies of Medicinal Plants Used by Traditional Health Practitioners in the Management of Diabetes in Lower Eastern Province, Kenya. *J. Ethnopharmacol.* 2012, *139*(1), 74–80. DOI: 10.1016/j.jep.2011.10.014.
[15] Okoduwa, S.; Umar, I.; James, D.; Inuwa, H. Anti-diabetic Potential of *Ocimum Gratissimum* Leaf Fractions in Fortified Diet-fed Streptozotocin Treated Rat Model of Type-2 Diabetes. *Medicines*. 2017, *4*(4), 73. DOI: 10.3390/medicines4040073.
[16] Bragaa, F. G.; Bouzadab, M. L. M.; Fabrib, R. L.; de Matosa, M.; Moreiraa, F. O.; Sciob, E.; Coimbraa, E. S. Antileishmanial and Antifungal Activity of Plants Used in Traditional Medicine in Brazil. *J. Ethnopharmacol.* 2006, *111*(2), 396–402. DOI: 10.1016/j.jep.2006.12.006.
[17] Murbach Freire, C. M.; Marques, M. O. M.; Costa, M. Effects of Seasonal Variation on the Central Nervous System Activity of *Ocimum Gratissimum* L. Essential Oil. *J. Ethnopharmacol.* 2006, *105*(1–2), 161–166. DOI: 10.1016/j.jep.2005.10.013.
[18] Silva, V. A.; Sousa, J. P.; Guerra, F. Q. S.; Pessôa, H. L. F.; Freitas, A. F. R.; Alves, L. B. N.; Lima, E. O. Antibacterial Activity of *Ocimum Basilicum* Essential Oil and Linalool on Bacterial Isolates of Clinical Importance. *Int. J. Pharmacogn. Phytochem.* 2015, *7*, 1066–1071.
[19] Singh, V.; Krishan, P.; Shri, R. *Ocimum Kilimand Scharicum* Guerke: Phytochemical and Pharmacological Aspects: A Review. *Res. Rev. J. Pharmacogn. Phytochem.* 2014, *2*(3), 1–11.
[20] Taechowisan, T.; Jakkrit, J.; Nutthapol, M.; Waya, S. P. Major Compounds from *Ocimum Basilicum* L. And Their Antimicrobial Activity against Methicillin-resistant *Staphylococcus Aureus*. *Biomed. J. Sci. Tech Res.* 2018, *3*, 1–9. DOI: 10.26717/BJSTR.2018.03.000910.
[21] Khalil, A.;. Antimicrobial Activity of Ethanolic Extracts of *Ocimum Basilicum* Leaf from Saudi Arabia. *Biotechnol.* 2013, *12*(1), 61–64. DOI: 10.3923/biotech.2013.61.64.
[22] Kaya, I.; Yiğit, N.; Benli, M. Antimicrobial Activity of Various Extracts of *Ocimum Basilicum* L. And Observation of the Inhibition Effect on Bacterial Cells by Use of Scanning Electron Microscopy. *Afr. J. Tradit. Complement. Altern. Med.* 2008, *5*(4), 363–369. DOI: 10.4314/ajtcam.v5i4.31291.
[23] Shiju, M.;. An Evaluation of the Antimicrobial Activity of Various Concentrations of *Ocimum Sanctum* against Various Species of Bacteria: An in Vitro Study. *Int. J. Adv. Appl. Sci.* 2014, *3*, 33–36. DOI: 10.11591/ijaas.v3.i1.pp33-36.
[24] Seleman, N. S.; Amri, E. Antibacterial Activity of Aqueous, Ethanol and Acetone Extracts of *Ocimum Sanctum* Linn. *Am. J. Biosci.* 2015, *3*(6), 256–261. DOI: 10.11648/j.ajbio.20150306.18.
[25] Jothi, K. R.; Vijayalakshmi, K.; Tamilarasi, L.; Ezhilarasi, B. Antibacterial Activity of Leaf Extracts of Aloe Vera. *Ocimum Sanctum* and *Sesbania Grandiflora* against the Gram Positive Bacteria. *Asian J. Biomed. Pharm. Sci.* 2014, *4*(35), 60–63. DOI: 10.15272/ajbps.v4i35.564.
[26] Saurabh, G.; Komal, S. Comparative Characterization for Antimicrobial Activity and Bioactive Compounds Present in Leaf Extract of *Ocimum Sanctum*. *J. Food Ind. Microbiol.* 2017, *3*, 1–5. DOI: 10.4172/2572-4134.1000121.
[27] Pawar, B. T.; Pandit, B. D. Antibacterial Activity of Leaf Extracts of *Ocimum Sanctum* L. Against *Xanthomonas Campestris* Pv. *Mangiferaeindicae. Res. J. Recent Sci.* 2014, *3*, 291–294.
[28] Londhe, A. M.; Kulkarni, A. S.; Lawand, R. V. In-vitro Comparative Study of Antibacterial and Antifungal Activities: A Case Study of *Ocimum Kilimandscharicum, Ocimum Tenuiflorum* and *Ocimum Gratissimum*. *Int. J. Pharmacogn. Phytochem. Res.* 2015, *7*, 104–110.
[29] Ba-Hamdan, A. H. A.; Aly, M. M.; Bafeel, S. O. Antimicrobial Activities and Phytochemical Analysis of the Essential Oil of *Ocimum Basilicum*, Collected from Jeddah Region, Saudi Arabia. *J. Microbiol. Res.* 2014, *4*, 1–9. DOI: 10.5923/s.microbiology.201401.01.
[30] Mishra, P.; Mishra, S. Study of Antibacterial Activity of *Ocimum Sanctum* Extract against Gram Positive and Gram Negative Bacteria. *Am. J. Food Technol.* 2011, *6*(4), 336–341. DOI: 10.3923/ajft.2011.336.341.

[31] Rathnayaka, R. M.;. Antibacterial Activity of *Ocimum Sanctum* Extracts against Four Food-borne Microbial Pathogens. *Sch. J. App. Med. Sci.* 2013, *1*, 774–777.
[32] Yamani, H. A.; Pang, E. C.; Mantri, N.; Deighton, M. A. Antimicrobial Activity of Tulsi (*Ocimum Tenuiflorum*) Essential Oil and Their Major Constituents against Three Species of Bacteria. *Front. Microbiol.* 2016, *7*, 681. DOI: 10.3389/fmicb.2016.00681.
[33] Moghaddam, A. M. D.; Shayegh, J.; Mikaili, P.; Sharaf, J. D. Antimicrobial Activity of Essential Oil Extract of *Ocimum Basilicum* L. Leaves on a Variety of Pathogenic Bacteria. *J. Med. Plant. Res.* 2011, *5*, 3453–3456.
[34] Silva, V. A.; da Sousa, J. P.; Pessôa, H. L. F.; de Freitas, A. F. R.; Coutinho, H. D. M.; Alves, L. B. N.; Lima, E. O. *Ocimum Basilicum* : Antibacterial Activity and Association Study with Antibiotics against Bacteria of Clinical Importance. *Pharm. Biol.* 2016, *54*(5), 863–867. DOI: 10.3109/13880209.2015.1088551.
[35] Balasubramani, S.; Moola, A. K.; Vivek, K.; Kumari, B. D. R. Formulation of Nanoemulsion from Leaves Essential Oil of *Ocimum Basilicum* L. And Its Antibacterial, Antioxidant and Larvicidal Activities (*Culex Quinquefasciatus*). *Microb. Pathog.* 2018, *125*, 475–485. DOI: 10.1016/j.micpath.2018.10.017.
[36] Gupta, D.; Bhaskar, D. J.; Gupta, R. K.; Karim, B.; Jain, A.; Singh, R.; Karim, W. A Randomized Controlled Clinical Trial of *Ocimum Sanctum* and Chlorhexidine Mouthwash on Dental Plaque and Gingival Inflammation. *J. Ayurveda Integr. Med.* 2014, *5*(2), 109–116. DOI: 10.4103/0975-9476.131727.
[37] Penmetsa, G. S.; Pitta, S. R. Efficacy of *Ocimum Sanctum*, Aloe Vera and Chlorhexidine Mouthwash on Gingivitis: A Randomized Controlled Comparative Clinical Study. *Ayu*. 2019, *40*(1), 23–26. DOI: 10.4103/ayu.AYU_212_18.
[38] Jakowienko, P.; Wójcik-Stopczyńska, B.; Jadczak, D. Antifungal Activity of Essential Oils from Two Varieties of Sweet Basil (*Ocimum Basilicum* L.). *Veg. Crop. Res. Bull.* 2011, *74*, 97–106. DOI: 10.2478/v10032-011-0008-4.
[39] Sethi, S.; Prakash, O.; Chandra, M.; Punetha, H.; Pant, A. K. Antifungal Activity of Essential Oils of Some Ocimum Species Collected from Different Locations of Uttarakhand. *Indian J. Nat. Prod. Resour.* 2013, *4*, 392–397.
[40] Abou El-Soud, N. H.; Deabes, M.; El-Kassem, L. A.; Khalil, M. Chemical Composition and Antifungal Activity of *Ocimum Basilicum* L. Essential OiL. *Open Access Maced. J. Med. Sci.* 2015, *3*, 374–379. DOI: 10.3889/oamjms.2015.082.
[41] Ali, N. A. A.; Chhetri, B. K.; Dosoky, N.; Shari, K.; Al-Fahad, A. J. A.; Wessjohann, L.; Setzer, W. N. Antimicrobial, Antioxidant, and Cytotoxic Activities of *Ocimum Forskolei* and *Teucrium Yemense* (Lamiaceae) Essential Oils. *Medicines*. 2017, *4*(2), 17. DOI: 10.3390/medicines4020017.
[42] Kocić-Tanackov, S.; Dimić, G.; Lević, J.; Tanackov, I.; Tuco, D. Antifungal Activities of Basil (*Ocimum Basilicum* L.) Extract on *Fusarium* Species. *Afr. J. Biotechnol.* 2011, *10*(50), 10188–10195. DOI: 10.5897/AJB11.1330.
[43] Balakumar, S.; Rajan, S.; Thirunalasundari, T.; Jeeva, S. Antifungal Activity of*Ocimum sanctum* Linn. (Lamiaceae) on clinically isolated dermatophytic fungi. *Asian Pac. J. Trop. Biomed.* 2011, 4(8), 654–657. DOI: 10.1016/S1995-7645(11)60166-1.
[44] Mohr, F. B. M.; Lermen, C.; Gazim, Z. C.; Gonçalves, J. E.; Alberton, O. Antifungal Activity, Yield, and Composition of *Ocimum Gratissimum* Essential Oil. *Genet. Mol. Res.* 2017, *16*(1), 1–10. DOI: 10.4238/gmr16019542.
[45] Figueiredo, P. L. B.; Silva, S. G.; Nascimento, L. D.; Ramos, A. R.; Setzer, W. N.; Da Silva, J. K. R.; Andrade, E. H. A. Seasonal Study of Methyleugenol Chemotype of *Ocimum Campechianum* Essential Oil and Its Fungicidal and Antioxidant Activities. *Nat. Prod. Commun.* 2018, *13*, 1055–1058. DOI: 10.1177/1934578x1801300833.
[46] Yucharoen, R.; Anuchapreeda, S.; Tragoolpua, R. Anti-herpes Simplex Virus Activity of Extracts from the Culinary Herbs *Ocimum Sanctum* L., *Ocimum Basilicum* L. And *Ocimum Americanum* L. *Afr. J. Biotechnol.* 2011, *10*, 860–866.
[47] Al-Amri, S. A. H.; Odisho, S. M.; Ibrahem, O. M. S. In Vitro Antiviral Potential of *Ocimum Basilicum* and *Olea Europaea* Leaves Extract against Newcastle Disease Virus of Poultry. *Iraqi J. Vet. Med.* 2015, *39*(1), 94–99. DOI: 10.30539/iraqijvm.v39i1.204.
[48] Chiang, L.; Cheng, P. W.; Lin, C. C.; Lin, C. C. Antiviral Activities of Extracts and Selected Pure Constituents of *Ocimum Basilicum*. *Clin. Exp. Pharmacol. Physiol.* 2005, *32*(10), 811–816. DOI: 10.1111/j.1440-1681.2005.04270.x.
[49] Ghoke, S. S.; Sood, R.; Kumar, N.; Pateriya, A. K.; Bhatia, S.; Mishra, A.; Dixit, R.; Singh, V. K.; Desai, D. N.; Kulkarni, D. D.;, et al. Evaluation of Antiviral Activity of *Ocimum Sanctum* and *Acacia Arabica* Leaves Extracts against H9N2 Virus Using Embryonated Chicken Egg Model. *BMC Complement. Altern. Med.* 2018, *18*(1), 174. DOI: 10.1186/s12906-018-2238-1.
[50] Jayati, I.; Bhatia, A. K.; Kumar, A.; Goel, A.; Gupta, S.; Rahal, A. In Vitro Antiviral Potential of *Ocimum Sanctum* Leaves Extract against New Castle Disease Virus of Poultry. *Int. J. Microbiol. Immunol. Res.* 2013, *2*, 051–055.
[51] Varshney, P.; Dash, S. K.; Bhatia, A. K. In Vitro and in Vivo Antiviral Potential of Hot Aqueous Extract of *Ocimum Sanctum* and Argemone Mexicana Leaves. *Med. Plant. Res.* 2013, *3*, 78–86. DOI: 10.5376/mpr.2013.03.0011.
[52] Patil, R.; Patil, R.; Ahirwar, B.; Ahirwar, D. Isolation and Characterization of Anti-diabetic Component (Bioactivity—guided Fractionation) from *Ocimum Sanctum* L. (Lamiaceae) Aerial Part. *Asian. Pac. J. Trop. Med.* 2011, *4*(4), 278–282. DOI: 10.1016/S1995-7645(11)60086-2.
[53] Huang, D.; Ou, B.; Prior, R. L. The Chemistry behind Antioxidant Capacity Assays. *J. Agric. Food Chem.* 1841–1856, *2005*(53). DOI: 10.1021/jf030723c.

[54] Mishra, A. P.; Sharifi-Rad, M.; Shariati, M. A.; Mabkhot, Y. N.; Al-Showiman, S. S.; Rauf, A.; Salehi, B.; Župunski, M.; Sharifi-Rad, M.; Gusain, P.;, et al. Bioactive Compounds and Health Benefits of Edible *Rumex* species-A Review. *Cell. Mol. Biol.* 2018, *64*(8), 27–34. DOI: 10.14715/cmb/2018.64.8.5.

[55] Salehi, B.; Martorell, M.; Arbiser, J. L.; Sureda, A.; Martins, N.; Maurya, P. K.; Sharifi-Rad, M.; Kumar, P.; Sharifi-Rad, J. Antioxidants: Positive or Negative Actors? *Biomolecules*. 2018, *8*(4), E124. DOI: 10.3390/biom8040124.

[56] Sharma, P.; Jha, A. B.; Dubey, R. S.; Pessarakli, M. Reactive Oxygen Species, Oxidative Damage, and Antioxidative Defense Mechanism in Plants under Stressful Conditions. *J. Bot.* 2012, *2012*, 217037. DOI: 10.1155/2012/217037.

[57] Salehi, B.; Mishra, A. P.; Shukla, I.; Sharifi-Rad, M.; Contreras, M. D. M.; Segura-Carretero, A.; Fathi, H.; Nasrabadi, N. N.; Kobarfard, F.; Sharifi-Rad, J. Thymol, Thyme, and Other Plant Sources: Health and Potential Uses. *Phytother. Res.* 2018, *32*(9), 1688–1706. DOI: 10.1002/ptr.6109.

[58] Salehi, B.; Valussi, M.; Jugran, A. K.; Martorell, M.; Ramírez-Alarcón, K.; Stojanović-Radić, Z. Z.; Antolak, H.; Kręgiel, D.; Ksenija, S. M.; Sharifi-Rad, M.;, et al. *Nepeta* Species: From Farm to Food Applications and Phytotherapy. *Trends Food Sci. Technol.* 2018, *80*, 104–122. DOI: 10.1016/j.tifs.2018.07.030.

[59] Teofilović, B.; Grujić-Letić, N.; Goločorbin-Kon, S.; Stojanović, S.; Vastag, G.; Gadžurić, S. Experimental and Chemometric Study of Antioxidant Capacity of Basil (*Ocimum Basilicum*) Extracts. *Ind. Crops Prod.* 2017, *100*, 176–182. DOI: 10.1016/j.indcrop.2017.02.039.

[60] Złotek, U.; Mikulska, S.; Nagajek, M.; Swieca, M. The Effect of Different Solvents and Number of Extraction Steps on the Polyphenol Content and Antioxidant Capacity of Basil Leaves (*Ocimum Basilicum* L.) Extracts. *Saudi J. Biol. Sci.* 2016, *23*(5), 628–633. DOI: 10.1016/j.sjbs.2015.08.002.

[61] Tenore, G. C.; Campiglia, P.; Ciampaglia, R.; Izzo, L.; Novellino, E. Antioxidant and Antimicrobial Properties of Traditional Green and Purple "Napoletano" Basil Cultivars (*Ocimum Basilicum* L.) From Campania Region (Italy). *Nat. Prod. Res.* 2017, *31*(17), 2067–2071.

[62] Kapepula, P. M.; Mbombo Mungitshi, P.; Franck, T.; Mouithys-Mickalad, A.; Mumba Ngoyi, D.; Kalenda, P. D. T.; Kabamba Ngombe, N.; Serteyn, D.; Tits, M.; Frédérich, M.; et al. Antioxidant Potentiality of Three Herbal Teas Consumed in Bandundu Rural Areas of Congo. *Nat. Prod. Res.* 2017, *31*(16), 1940–1943. DOI: 10.1080/14786419.2016.1263844.

[63] Islam, G. M.; Akter, S. S.; Hoque, M. D. M. Traditional Foods for Health: In Vitro Screening for Antioxidant Capacity of Popular Traditional Tribal Foods in the Sylhet Territory in Bangladesh—focusing on Total Phenolic and Tannin Contents. *J. Food Meas. Charact.* 2018, *12*(3), 2087–2093. DOI: 10.1007/s11694-018-9823-3.

[64] Ononamadu, C. J.; Alhassan, A. J.; Imam, A. A.; Ibrahim, A.; Ihegboro, G. O.; Owolarafe, A. T.; Sule, M. S. In Vitro and in Vivo Anti-diabetic and Anti-oxidant Activities of Methanolic Leaf Extracts of *Ocimum Canum*. *Casp. J. Intern. Med.* 2019, *10*, 162–175. DOI: 10.22088/cjim.10.2.162.

[65] Prakash, B.; Shukla, R.; Singh, P.; Mishra, P. K.; Dubey, N. K.; Kharwar, R. N. Efficacy of Chemically Characterized *Ocimum Gratissimum* L. Essential Oil as an Antioxidant and a Safe Plant Based Antimicrobial against Fungal and Aflatoxin B1 Contamination of Spices. *Food Res. Int.* 2011, *44*(1), 385–390. DOI: 10.1016/j.foodres.2010.10.002.

[66] Hussain, A. I.; Anwar, F.; Hussain Sherazi, S. T.; Przybylski, R. Chemical Composition, Antioxidant and Antimicrobial Activities of Basil (*Ocimum Basilicum*) Essential Oils Depends on Seasonal Variations. *Food Chem.* 2008, *108*(3), 986–995. DOI: 10.1016/j.foodchem.2007.12.010.

[67] McCance, K. R.; Flanigan, P. M.; Quick, M. M.; Niemeyer, E. D. Influence of Plant Maturity on Anthocyanin Concentrations, Phenolic Composition, and Antioxidant Properties of 3 Purple Basil (Ocimum Basilicum L.) Cultivars. *J. Food Compos. Anal.* 2016, *53*, 30–39. DOI: 10.1016/j.jfca.2016.08.009.

[68] Singh, V.; Kahol, A.; Singh, I. P.; Saraf, I.; Shri, R. Evaluation of Anti-amnesic Effect of Extracts of Selected *Ocimum* Species Using In-vitro and In-vivo Models. *J. Ethnopharmacol.* 2016, *193*, 490–499. DOI: 10.1016/j.jep.2016.10.026.

[69] Ademiluyi, A. O.; Oyeleye, S. I.; Oboh, G. Biological Activities, Antioxidant Properties and Phytoconstituents of Essential Oil from Sweet Basil (*Ocimum Basilicum* L.) Leaves. *Comp. Clin. Path.* 2016, *25*(1), 169–176. DOI: 10.1007/s00580-015-2163-3.

[70] Nazir, M.; Tungmunnithum, D.; Bose, S.; Drouet, S.; Garros, L.; Giglioli-Guivarc'h, N.; Abbasi, B. H.; Hano, C. Differential Production of Phenylpropanoid Metabolites in Callus Cultures of *Ocimum Basilicum* L. With Distinct in Vitro Antioxidant Activities and in Vivo Protective Effects against UV Stress. *J. Agric. Food Chem.* 1847–1859, *2019*(67). DOI: 10.1021/acs.jafc.8b05647.

[71] Chiu, C.; Huang, C.; Chen, T.; Kao, H.; Liu, J.; Wang, Y.; Tzang, B.-S.; Hsu, T. Beneficial Effects of *Ocimum Gratissimum* Aqueous Extract on Rats with CCl_4-Induced Acute Liver Injury. *Evid.-Based Complementary Altern. Med.* 2012, *2012*, 736752. DOI: 10.1155/2012/736752.

[72] BandeiraJr, G.; Pês, T. S.; Saccol, E. M. H.; Sutili, F. J.; Rossi Jr, W.; Murari, A. L.; Heinzmann, B. M.; Pavanato, M. A.; de Vargas, A. C.; Silva, L. D. L.; et al. Potential Uses of *Ocimum Gratissimum* and *Hesperozygis Ringens* Essential Oils in Aquaculture. *Ind. Crop. Prod.* 2017, *97*, 484–491. DOI: 10.1016/j.indcrop.2016.12.040.

[73] Sarangi, S. C.; Pattnaik, S. S.; Katyal, J.; Kaleekal, T.; Dinda, A. K. An Interaction Study of *Ocimum Sanctum* L. And Levetiracetam in Pentylenetetrazole Kindling Model of Epilepsy. *J. Ethnopharmacol.* 2020, *249*, 112389. DOI: 10.1016/j.jep.2019.112389.
[74] Carvalho, S. D.; Schwieterman, M. L.; Abrahan, C. E.; Colquhoun, T. A.; Folta, K. M. Light Quality Dependent Changes in Morphology, Antioxidant Capacity, and Volatile Production in Sweet Basil (*Ocimum Basilicum*). *Front. Plant Sci.* 2016, *7*, 1–14. DOI: 10.3389/fpls.2016.01328.
[75] Ghasemi Pirbaloutia, A.; Malekpoor, F.; Salimi, A.; Golparvard, A. Exogenous Application of Chitosan on Biochemical and Physiologicalcharacteristics, Phenolic Content and Antioxidant Activity of Twospecies of Basil (*Ocimum Ciliatum* and *Ocimum Basilicum*) Underreduced Irrigation. *Sci. Hortic.* 2017, *217*, 114–122. DOI: 10.1016/j.scienta.2017.01.031.
[76] Bahcesular, B.; Yildirim, E. D.; Karaçocuk, M.; Kulak, M.; Karaman, S. Seed Priming with Melatonin Effects on Growth, Essential Oil Compounds and Antioxidant Activity of Basil (*Ocimum Basilicum* L.) Under Salinity Stress. *Ind. Crops Prod.* 2020, *146*, 112165. DOI: 10.1016/j.indcrop.2020.112165.
[77] Magiatis, P.; Skaltsounis, A. L.; Chinou, I.; Haroutounian, S. A. Chemical Composition And In-Vitro Antimicrobial Activity Of The Essential Oils Of Three Greek *Achillea* Species. *Z. Naturforsch.* 2002, *57*(3–4), 287–290. DOI: 10.1515/znc-2002-3-415.
[78] Sharafati-Chaleshtori, R.; Rokni, N.; Rafieian-Kopaei, M.; Drees, F.; Salehi, E. Antioxidant and Antibacterial Activity of Basil (*Ocimum Basilicum* L.) Essential Oil in Beef Burger. *J. Agric. Sci. Technol.* 2015, *17*, 817–826.
[79] Stojanović-Radić, Z.; Pejčić, M.; Joković, N.; Jokanović, M.; Ivić, M.; Šojić, B.; Škaljac, S.; Stojanović, P.; Mihajilov-Krstev, T. Inhibition of *Salmonella* Enteritidis Growth and Storage Stability in Chicken Meat Treated with Basil and Rosemary Essential Oils Alone or in Combination. *Food Control.* 2018, *90*, 332–343. DOI: 10.1016/j.foodcont.2018.03.013.
[80] Licon, C. C.; Moro, A.; Librán, C. M.; Molina, A. M.; Zalacain, A.; Berruga, M. I.; Carmona, M. Volatile Transference and Antimicrobial Activity of Cheeses Made with Ewes' Milk Fortified with Essential Oils. *Foods*. 2020, *9*(1), 35. DOI: 10.3390/foods9010035.
[81] Bhat, Z. F.; Kumar, S.; Kumar, L. Effect of *Ocimum Sanctum* Linn (Tulsi) on the Oxidative Stability and Storage Quality of Chicken Sausages. *Nutr. Food Sci.* 2015, *45*(4), 510–523. DOI: 10.1108/NFS-01-2015-0002.
[82] Riady, M. H.; Rostini, I.; Andriani, Y.; Pratama, R. I. Effectiveness of the Ruku-ruku Leaf Solution (*Ocimum Sanctum*) as a Natural Preservative in Indian Mackerel (Rastrelliger Sp.) During Low-temperature Storage. *Asian Food Sci. J.* 2019, *12*, 1–13. DOI: 10.9734/afsj/2019/v12i330084.
[83] Anand, S.; Grover, C. R.; Beniwal, A. Evaluation of *Ocimum Sanctum* Essential Oil as Potential Preservative for Fermented Dairy Products. *J. Pure Appl. Microbiol.* 2016, *10*(4), 2763–2771. DOI: 10.22207/JPAM.10.4.35.
[84] Adeogun, O. O.; Maroyi, A.; Afolayan, A. J. Effects of Leaf Extracts of *Ocimum Gratissimum* L. On Quality of Fresh Cut *Cucumis Sativus* L. *Asian J. Plant Pathol.* 2017, *11*(4), 174–184. DOI: 10.3923/ajppaj.2017.174.184.
[85] Kuzelov, A.; Andronikov, D.; Taskov, N.; Sofijanova, E.; Saneva, D. Oxidative Stability Effect of Basil, Garlic and Muscat Blossom Extracts on Lipids and Microbiology of Minced Meat. *Comptes Rendus L'Academie Bulg. Des Sci.* 2017, *70*, 1227–1236.
[86] Ribas, J. C. R.; Matumoto-Pintro, P. T.; Vital, A. C. P.; Saraiva, B. R.; Anjo, F. A.; Alves, R. L. B.; Santos, N. W.; Machado, E.; Agustinho, B. C.; Zeoula, L. M. Influence of Basil (*Ocimum Basilicum* Lamiaceae) Addition on Functional, Technological and Sensorial Characteristics of Fresh Cheeses Made with Organic Buffalo Milk. *J. Food Sci. Technol.* 2019, *56*(12), 5214–5224. DOI: 10.1007/s13197-019-03990-5.
[87] Anbarasu, K.; Vijayalakshmi, G. Improved Shelf Life of Protein-rich Tofu Using *Ocimum Sanctum* (Tulsi) Extracts to Benefit Indian Rural Population. *J. Food Sci.* 2007, *72*(8), 300–305. DOI: 10.1111/j.1750-3841.2007.00487.x.
[88] Mejlholm, O.; Dalgaard, P. Antimicrobial Effect of Essential Oils on the Seafood Spoilage Micro-organism *Photobacterium Phosphoreum* in Liquid Media and Fish Products. *Lett. Appl. Microbiol.* 2002, *34*, 27–31. DOI: 10.1046/j.1472-765x.2002.01033.x.
[89] Harpaz, S.; Glatman, L.; Drabkin, V.; Gelman, A. Effects of Herbal Essential Oils Used to Extend the Shelf Life of Freshwater-reared Asian Sea Bass Fish (*Lates Calcarifer*). *J. Food Prot.* 2003, *66*(3), 410–417. DOI: 10.4315/0362-028x-66.3.410.
[90] Hernández-Hernández, E.; Castillo-Hernández, G.; González-Gutiérrez, C. J.; Silva-Dávila, A. J.; Gracida-Rodríguez, J. N.; García-Almendárez, B. E.; Di Pierro, P.; Vázquez-Landaverde, P.; Regalado-González, C. Microbiological and Physicochemical Properties of Meat Coated with Microencapsulated Mexican Oregano (*Lippia Graveolens* Kunth) and Basil (*Ocimum Basilicum* L.) Essential Oils Mixture. *Coatings*. 2019, *9*(7), 414. DOI: 10.3390/COATINGS9070414.
[91] Smith-Palmer, A.; Stewart, J.; Fyfe, L. The Potential Application of Plant Essential Oils as Natural Food Preservatives in Soft Cheese. *Food Microbiol.* 2001, *18*(4), 463–470. DOI: 10.1006/fmic.2001.0415.
[92] Gurkan, H.; Hayaloglu, A. A. Volatiles and Sensory Characteristics of Yogurt Manufactured by Incorporating Basil (*Ocimum Basilicum* L.). *Int. J. Food Prop.* 2017, *20*(sup1), S779–S789. DOI: 10.1080/10942912.2017.1311344.

[93] Pol, I. E.; Mastwijk, H. C.; Slump, R. A.; Popa, M. E.; Smid, E. J.; Popa, M. E.; Smid, E. J.; Smid, E. J. Bioenergetic Consequences of Nisin Combined with Carvacrol Towards *Bacillus Cereus*. *Innov. Food Sci. Emerg. Technol.* 2001, *3*(1), 55–61. DOI: 10.4315/0362-028x-64.7.1012.
[94] Roller, S.; Seedhar, P. Carvacrol and Cinnamic Acid Inhibit Microbial Growth in Fresh-cut Melon and Kiwifruit at 4 Degrees and 8 Degrees C. *Lett. Appl. Microbiol.* 2002, *35*(4), 390–394. DOI: 10.1046/j.1472-765x.2002.01209.x.
[95] Serrano, M.; Martinez-Romero, D.; Castillo, S.; Guillen, F.; Valero, D. The Use of the Natural Antifungal Compounds Improves the Beneficial Effect of MAP in Sweet Cherry Storage. *Innov. Food Sci. Emerg.* 2005, *6* (1), 115–123. DOI: 10.1016/j.ifset.2004.09.001.
[96] Lopez, M. D.; Jordan, M. J.; Pascual-Villalobos, M. J. Toxic Compounds in Essential Oils of Coriander, Caraway and Basil Active against Stored Rice Pests. *J. Stored Prod. Res.* 2008, *44*(3), 273–278. DOI: 10.1016/j.jspr.2008.02.005.
[97] Onaebi, C.; Onyeke, C.; Osibe, D.; Ugwuja, F.; Okoro, A.; Onyegirim, P. Antimicrobial Activity of *Ocimum Gratissimum* L. And *Carica Papaya* L. Against Postharvest Pathogens of Avocado Pear (*Persea Americana* MilL.). *J. Plant Pathol.* 2019, *102*(2), 319–325. DOI: 10.1007/s42161-019-00420-5.
[98] El-Sayed, S. M.; Youssef, A. M. Potential Application of Herbs and Spices and Their Effects in Functional Dairy Products. *Heliyon*. 2019, *5*(6), e01989. DOI: 10.1016/j.heliyon.2019.e01989.
[99] Sharma, H.; Mendiratta, S. K.; Agarwal, R. K.; Gurunathan, K. Bio-preservative Effect of Blends of Essential Oils: Natural Anti-oxidant and Anti-microbial Agents for the Shelf Life Enhancement of Emulsion Based Chicken Sausages. *J. Food Sci. Technol.* 2020, *57*(8), 3040–3050. DOI: 10.1007/s13197-020-04337-1.
[100] Gautam, A.; Pandey, A. K.; Dubey, R. S. Azadirachta Indica and *Ocimum Sanctum* Leaf Extracts Alleviate Arsenic Toxicity by Reducing Arsenic Uptake and Improving Antioxidant System in Rice Seedlings. *Physiol. Mol. Biol. Plants*. 2020, *26*(1), 63–81. DOI: 10.1007/s12298-019-00730-z.
[101] Stan, M.; Popa, A.; Toloman, D.; Silipas, T. D.; Vodnar, D. C. Antibacterial and Antioxidant Activities of ZnO Nanoparticles Synthesized Using Extracts of *Allium Sativum, Rosmarinus Officinalis* and *Ocimum Basilicum*. *Acta Metall. Sin.* 2016, *29*(3), 228–236. *(English Lett.)*. DOI: 10.1007/s40195-016-0380-7.
[102] Kumar, A.; Shukla, R.; Singh, P.; Dubey, N. K. Chemical Composition, Antifungal and Antiaflatoxigenic Activities of *Ocimum Sanctum* L. Essential Oil and Its Safety Assessment as Plant Based Antimicrobial. *Food Chem. Toxicol.* 2010, *48*(2), 539–543. DOI: 10.1016/j.fct.2009.11.028.
[103] Gutierrez, J.; Barry-Ryan, C.; Bourke, P. The Antimicrobial Efficacy of Plant Essential Oil Combinations and Interactions with Food Ingredients. *Int. J. Food Microbiol.* 2008, *124*(1), 91–97. DOI: 10.1016/j.ijfoodmicro.2008.02.028.
[104] Li, K.; Zhang, M.; Bhandari, B.; Xu, J.; Yang, C. Improving Storage Quality of Refrigerated Steamed Buns by Mung Bean Starch Composite Coating Enriched with Nano-emulsified Essential Oils. *J. Food Process Eng.* 2020, *43*(9), e13475. DOI: 10.1111/jfpe.13475.
[105] Ribeiro-Santos, R.; Andrade, M.; Ramos de Melo, N.; Sanches-Silva, A. Use of Essential Oils in Active Food Packaging: Recent Advances and Future Trends. *Trends Food Sci. Technol.* 2017, *61*, 132–140. DOI: 10.1016/j.tifs.2016.11.021.
[106] Somolinos, M.; García, D.; Condón, S.; Mackey, B.; Pagán, R. Inactivation of *Escherichia Coli* by Citral. *J. Appl. Microbiol.* 2010, *108*(6), 1928–1939. DOI: 10.1111/j.1365-2672.2009.04597.x.
[107] Rattanachaikunsopon, P.; Phumkhachorn, P. Assessment of Factors Influencing Antimicrobial Activity of Carvacrol and Cymene against *Vibrio Cholerae* in Food. *J. Biosci. Bioeng.* 2010, *110*(5), 614–619. DOI: 10.1016/j.jbiosc.2010.06.010.
[108] Syafiq, R.; Sapuan, S. M.; Zuhri, M. Y. M.; Ilyas, R. A.; Nazrin, A.; Sherwani, S. F. K.; Khalina, A. Antimicrobial Activities of Starch-based Biopolymers and Biocomposites Incorporated with Plant Essential Oils: A Review. *Polymers*. 2020, *12*(10), 2403. DOI: 10.3390/polym12102403.
[109] Tangpao, T.; Chung, H. H.; Sommano, S. R. Aromatic Profiles of Essential Oils from Five Commonly Used Thai Basils. *Foods*. 2018, *7*(11), 1–13. DOI: 10.3390/foods7110175.
[110] Maggio, A.; Roscigno, G.; Bruno, M.; De Falco, E.; Senatore, F. Essential-Oil Variability in a Collection of *Ocimum Basilicum* L. (Basil) Cultivars. *Chem. Biodivers.* 2016, *13*(10), 1357–1368. DOI: 10.1002/cbdv.201600069.
[111] Chávez-González, M. L.; Rodríguez-Herrera, R.; Aguilar, C. N. Essential Oils: A Natural Alternative to Combat Antibiotics Resistance. A Natural Alternative to Combat Antibiotics Resistance. *Antibiot. Resist. Mech. New Antimicrob. Approaches*. 2016, 227–237. DOI: 10.1016/B978-0-12-803642-6.00011-3.
[112] Raina, A. P.; Gupta, V. Chemotypic Characterization of Diversity in Essential Oil Composition of Ocimum Species and Varieties from India. *J. Essent. Oil Res.* 2018, *30*(6), 444–456. DOI: 10.1080/10412905.2018.1495109.
[113] Soltanin, J.;. Secondary Metabolite Diversity of the Genus Aspergillus: Recent Advances. In *New and Future Developments in Microbial Biotechnology and Bioengineering*; Gupta, V., Ed.; Elsevier: Amsterdam, 2016; pp 275–292.
[114] Khan, A.; Ahmad, A.; Manzoor, N.; Khan, L. A. Antifungal Activities of *Ocimum Sanctum* Essential Oil and Its Lead Molecules. *Nat. Prod. Commun.* 2010, *5*(2), 345–349.

[115] Kumar, A.; Mishra, P.; Rodrigues, V.; Baskaran, K.; Verma, R. S.; Padalia, R. C.; Sundaresan, V. Delineation of *Ocimum Gratissimum* L. Complex Combining Morphological, Molecular and Essential Oils Analysis. *Ind. Crops Prod.* 2019, *139*, 111536. DOI: 10.1016/j.indcrop.2019.111536.
[116] Sharopov, F.; Setzer, W. N. Medicinal Plants of Tajikistan. In *Vegetation of Central Asia and Environs*; Egamberdieva, D., Öztürk, M., Eds.; Springer Nature: Switzerland, 2018; pp 163–210.
[117] Sharopov, F. S.; Satyal, P.; Ali, N. A.; Pokharel, S.; Zhang, H.; Wink, M.; Kukaniev, M. A.; Setzer, W. N. The Essential Oil Compositions of *Ocimum Basilicum* from Three Different Regions: Nepal, Tajikistan, and Yemen. *Chem. Biodiversity*. 2016, *13*(2), 241–248. DOI: 10.1002/cbdv.201500108.
[118] Kapewangolo, P.; Omolo, J. J.; Bruwer, R.; Fonteh, P.; Meyer, D. Antioxidant and Anti-inflammatory Activity of *Ocimum Labiatum* Extract and Isolated Labdane Diterpenoid. *J. Inflamm. Res*. 2015, *12*(1), 4–15. DOI: 10.1186/s12950-015-0049-4.
[119] Hussein, A. A.; Meyer, J. J. M.; Jimeno, M. L.; Rodríguez, B. Bioactive Diterpenes from Orthosiphon Labiatus and Salvia Africana-lutea. *J. Nat. Prod.* 2007, *70*(2), 293–295. DOI: 10.1021/np0680376.
[120] Silva, M. G. V.; Vieira, Í. G. P.; Mendes, F. N. P.; Albuquerque, I. L.; Dos Santos, R. N.; Silva, F. O.; Morais, S. M. Variation of Ursolic Acid Content in Eight *Ocimum* Species from Northeastern Brazil. *Molecules*. 2008, *13*(10), 2482–2487. DOI: 10.3390/molecules13102482.
[121] Nabrdalik, M.; Grata, K. Antibacterial Activity of *Ocimum Basilicum* L. Essential Oil against Gram-negative Bacteria. *Post Fitoter*. 2016, *17*, 80–86.
[122] Ravikumar, P. H. S.; Makari, H. K.; Gurumurthy, H. *In Vitro* Antimicrobial Activity of Ethanol Extracts of *Thevetia Peruviana*. *Biotechnol. Indian J.* 2007, *6*, 2318–2322.
[123] Castronuovo, D.; Russo, D.; Libonati, R.; Faraone, I.; Candido, V.; Picuno, P.; Andrade, P.; Valentao, P.; Milella, L. Influence of Shading Treatment on Yield, Morphological Traits and Phenolic Profile of Sweet Basil (*Ocimum Basilicum* L.). *Sci. Hortic.* 2019, *254*, 91–98. DOI: 10.1016/j.scienta.2019.04.077.
[124] Guleria, S.; Tiku, A. K.; Singh, G.; Koul, A.; Gupta, S.; Rana, S. *In Vitro* Antioxidant Activity and Phenolic Contents in Methanol Extracts from Medicinal Plants. *J. Plant Biochem. Biotechnol.* 2013, *22*(1), 9–15. DOI: 10.1007/s13562-012-0105-6.
[125] Fathiazad, F.; Matlobi, A.; Khorrami, A.; Hamedeyazdan, S.; Soraya, H.; Hammami, M.; Maleki-Dizaji, N.; Garjani, A. Phytochemical Screening and Evaluation of Cardioprotective Activity of Ethanolic Extract of *Ocimum Basilicum* L. (Basil) against Isoproterenol Induced Myocardial Infarction in Rats. *DARU J. Pharm. Sci.* 2012, *20*(1), 87–92. DOI: 10.1186/2008-2231-20-87.
[126] Wongsa, P.; Chaiwarit, J.; Zamaludien, A. In Vitro Screening of Phenolic Compounds, Potential Inhibition against α-amylase and α-glucosidase of Culinary Herbs in Thailand. *Food Chem.* 2012, *131*(3), 964–971. DOI: 10.1016/j.foodchem.2011.09.088.
[127] Domlur Thyagaraj, V.; Koshy, R.; Kachroo, M.; Mayachari, A. S.; Sawant, L. P.; Balasubramanium, M. A Validated RP-HPLC-UV/DAD Method for Simultaneous Quantitative Determination of Rosmarinic Acid and Eugenol in *Ocimum Sanctum* L. *Pharm. Methods*. 2013, *4*(1), 1–5. DOI: 10.1016/j.phme.2013.08.003.
[128] Casanova, L. M.; Gu, W.; Costa, S. S.; Jeppesen, P. B. Phenolic Substances from *Ocimum* Species Enhance Glucose-stimulated Insulin Secretion and Modulate the Expression of Key Insulin Regulatory Genes in Mice Pancreatic Islets. *J. Nat. Prod.* 2017, *80*(12), 3267–3275. DOI: 10.1021/acs.jnatprod.7b00699.
[129] Upadhyay, R.; Nachiappan, G.; Mishra, H. N. Ultrasound-assisted Extraction of Flavonoids and Phenolic Compounds from *Ocimum Tenuiflorum* Leaves. *Food Sci. Biotechnol.* 1951–1958, *2015*(24). DOI: 10.1007/s10068-015-0257-y.
[130] Kelm, M. A.; Nair, M. G.; Strasburg, G. M.; DeWitt, D. L. Antioxidant and Cyclooxygenase Inhibitory Phenolic Compounds from *Ocimum Sanctum* Linn. *Phytomedicine*. 2000, *7*(1), 7–13. DOI: 10.1016/S0944-7113(00)80015-X.
[131] Ali, H.; Dixit, S. In Vitro Antimicrobial Activity of Flavonoids of *Ocimum Sanctum* with Synergistic Effect of Their Combined Form. *Asian Pac. J. Trop. Dis.* 2012, *2*, 396–398. DOI: 10.1016/S2222-1808(12)60189-3.
[132] Shaw, H. M.; Wu, J. L.; Wang, M. S. Antihypertensive Effects of *Ocimum Gratissimum* Extract: Angiotensin-converting Enzyme Inhibitor in Vitro and in Vivo Investigation. *J. Funct. Foods*. 2017, *35*, 68–73. DOI: 10.1016/j.jff.2017.05.033.
[133] Praveena, R.; Sadasivam, K.; Deepha, V.; Sivakumar, R. Antioxidant Potential of Orientin: A Combined Experimental and DFT Approach. *J. Mol. Struct.* 2014, *1061*, 114–123. DOI: 10.1016/j.molstruc.2014.01.002.
[134] Bąkowska-Barczak, A.;. Acylated Anthocyanins as Stable, Natural Food Colorants-a Review. *Pol. J. Food Sci.* 2005, *14*, 107–116.
[135] Sarian, M. N.; Ahmed, Q. U.; Mat So'ad, S. Z.; Alhassan, A. M.; Murugesu, S.; Perumal, V.; Mohamad, S. N. A. S.; Khatib, A.; Antioxidant, L. J. Antidiabetic Effects of Flavonoids: A Structure-Activity Relationship Based Study. *BioMed Res. Int.* 2017, *2017*, 8386065. DOI: 10.1155/2017/8386065.
[136] Kwee, E. M.; Niemeyer, E. D. Variations in Phenolic Composition and Antioxidant Properties among 15 Basil (*Ocimum Basilicum* L.) Cultivars. *Food Chem.* 2011, *128*(4), 1044–1050. DOI: 10.1016/j.foodchem.2011.04.011.
[137] Nayak, V.; Uma Devi, P. Protection of Mouse Bone Marrow against Radiation-induced Chromosome Damage and Stem Cell Death by the *Ocimum* Flavonoids Orientin and Vicenin. *Radiat. Res.* 2005, *163*(2), 165–171. DOI: 10.1667/RR3263.

[138] Uma Devi, P.; Ganasoundari, A.; Vrinda, B.; Srinivasan, K. K.; Unnikrishnan, M. K. Radiation Protection by the *Ocimum* Flavonoids Orientin and Vicenin: Mechanisms of Action. *Radiat. Res.* 2000, *154*(4), 455–460. DOI: 10.1667/0033-7587(2000)154[0455:RPBTOF]2.0.CO;2.
[139] Lima, M. C.; Paiva de Sousa, C.; Fernandez-Prada, C.; Hareld, J.; Dubreuil, J. D.; de Souza, E. L. A Review of the Current Evidence of Fruit Phenolic Compounds as Potential Antimicrobials against Pathogenic Bacteria. *Microb. Pathog.* 2019, *130*, 259–270. DOI: 10.1016/j.micpath.2019.03.025.
[140] Chibane, L. B.; Degraeve, P.; Ferhout, H.; Bouajila, J.; Oulahal, N. Plant Antimicrobial Polyphenols as Potential Natural Food Preservatives. *J. Sci. Food Agric.* 2019, *99*(4), 1457–1474. DOI: 10.1002/jsfa.9357.
[141] Rempe, C. S.; Burris, K. P.; Lenaghan, S. C.; Stewart, C. N. The Potential of Systems Biology to Discover Antibacterial Mechanisms of Plant Phenolics. *Front. Microbiol.* 2017, *8*, 422. DOI: 10.3389/fmicb.2017.00422.
[142] Pernin, A.; Guillier, L.; Dubois-Brissonnet, F. Inhibitory Activity of Phenolic Acids against Listeria Monocytogenes: Deciphering the Mechanisms of Action Using Three Different Models. *Food Microbiol.* 2019, *80*, 18–24. DOI: 10.1016/j.fm.2018.12.010.
[143] Li, Y. L.; Ma, S. C.; Yang, Y. T.; Ye, S. M.; But, P. P. H. Antiviral Activities of Flavonoids and Organic Acid from *Trollius Chinensis* Bunge. *J. Ethnopharmacol.* 2002, *79*(3), 365–368. DOI: 10.1016/S0378-8741(01)00410-X.
[144] Lam, K. Y.; Ling, A. P. K.; Koh, R. Y.; Wong, Y. P.; Say, Y. H. A Review on Medicinal Properties of Orientin. *Adv. Pharmacol. Sci.* 2016, *2016*, 4104595. DOI: 10.1155/2016/4104595.
[145] Boominathan, S. P.; Sarangan, G.; Srikakelapu, S.; Rajesh, S.; Duraipandian, C.; Srikanth, P. Antiviral Activity of Bioassay Guided Fractionation of *Plumbago Zeylanica* Roots against Herpes Simplex Virus Type 2. *World J. Pharm. Res.* 2014, *3*, 1003–1017.
[146] Masresha, B.; Makonnen, E.; Debella, A. *In Vivo* Anti-inflammatory Activities of *Ocimum Suave* in Mice. *J. Ethnopharmacol.* 2012, *142*(1), 201–205. DOI: 10.1016/j.jep.2012.04.041.
[147] Mequanint, W.; Makonnen, E.; Urga, K. In Vivo Anti-inflammatory Activities of Leaf Extracts of Ocimum Lamiifolium in Mice Model. *J. Ethnopharmacol.* 2011, *134*, 32–36. DOI: 10.1016/j.jep.2010.11.051.
[148] Mediratta, P. K.; Sharma, K. K.; Singh, S. Evaluation of Immunomodulatory Potential of *Ocimum Sanctum* Seed Oil and Its Possible Mechanism of Action. *J. Ethnopharmacol.* 2002, *80*(1), 15–20. DOI: 10.1016/s0378-8741(01)00373-7.
[149] Mondal, S.; Varma, S.; Bamola, V. D.; Naik, S. N.; Mirdha, B. R.; Padhi, M. M.; Mehta, N.; Mahapatra, S. C. Double-blinded Randomized Controlled Trial for Immunomodulatory Effects of Tulsi (*Ocimum Sanctum* Linn.) Leaf Extract on Healthy Volunteers. *J. Ethnopharmacol.* 2011, *136*(3), 452–456. DOI: 10.1016/j.jep.2011.05.012.
[150] Mukherjee, R.; Dash, P. K.; Ram, G. C. Immunotherapeutic Potential of *Ocimum Sanctum* (L) in Bovine Subclinical Mastitis. *Res. Vet. Sci.* 2005, *79*(1), 37–43. DOI: 10.1016/j.rvsc.2004.11.001.
[151] Pandey, G.;. Pharmacological Activities of *Osimum Sanctum* (Tulsi): A Review. *Int. J. Pharma. Sci. Rev. Res.* 2010, *5*, 61–66.
[152] Mrutyunjay, M. M.;. Evaluation of the Anti Inflammatory Activity of *Ocimum Sanctum* Linn (Tulsi) in Albino Rats. *Int. J. Curr. Microbiol. Appl. Sci.* 2014, *3*, 198–205.
[153] Krueger, J. G.; Fretzin, S.; Suarez-Farinas, M.; Haslett, P. A.; Phipps, K. M.; Cameron, G. S. IL-17A Is Essential for Cell Activation and Inflammatory Gene Circuits in Subjects with Psoriasis. *J. Allergy Clin. Immunol.* 2012, *130*(1), 145–154. DOI: 10.1016/j.jaci.2012.04.024.
[154] Maruthamuthu, V.; Henry, L. J. K.; Ramar, M. K.; Kandasamy, R. Inhibition of the IL-2-inducible Tyrosine Kinase (Itk) Activity: A New Concept for the Therapy of Inflammatory Skin Diseases. *J. Ethnopharmacol.* 2020, *255*, 112369. DOI: 10.1016/j.jep.2019.112369.
[155] Tohti, I.; Tursun, M.; Umar, A.; Turdi, S.; Imin, H.; Moore, N. Aqueous Extracts of *Ocimum Basilicum* L. (Sweet Basil) Decrease Platelet Aggregation Induced by ADP and Thrombin *in Vitro* and Rats Arterio--venous Shunt Thrombosis *in Vivo*. *Thromb. Res.* 2006, *118*(6), 733–739. DOI: 10.1016/j.thromres.2005.12.011.
[156] Amrani, S.; Harnafi, H.; Bouanani, N. H.; Aziz, M.; Caid, H. S.; Manfredini, S.; Besco, E.; Napolitano, M.; Bravo, E. Hypolipidaemic Activity of Aqueous *Ocimum Basilicum* Extract in Acute Hyperlipidaemia Induced by Triton WR-1339 in Rats and Its Antioxidant Property. *Phytother Res.* 2006, *20*, 1040–1045. DOI: 10.1002/ptr.1961.
[157] Bravo, E.; Amrani, S.; Aziz, M.; Harnafi, H.; Napolitano, M. *Ocimum Basilicum* Ethanolic Extract Decreases Cholesterol Synthesis and Lipid Accumulation in Human Macrophages. *Fitoterapia*. 2008, *79*(7–8), 515–523. DOI: 10.1016/j.fitote.2008.05.002.
[158] Umar, A.; Imam, G.; Yimin, W.; Kerim, P.; Tohti, I.; Berké, B.; Moore, N. Antihypertensive Effects of *Ocimum Basilicum* L. (OBL) on Blood Pressure in Renovascular Hypertensive Rats. *Hypertens. Res.* 2010, *33*(7), 727–730. DOI: 10.1038/hr.2010.64.
[159] Muralidharan, A.; Dhananjayan, R. Cardiac Stimulant Activity of *Ocimum Basilicum* Linn Extracts. *Indian J. Pharmacol.* 2004, *36*, 163–166.
[160] Sood, S.; Narang, D.; Dinda, A. K.; Maulik, S. K. Chronic Oral Administration of *Ocimum Sanctum* Linn. Augments Cardiac Endogenous Antioxidants and Prevents Isoproterenol-induced Myocardial Necrosis in Rats. *J. Pharm. Pharmacol.* 2005, *57*(1), 127–133. DOI: 10.1211/0022357055146.

[161] Sood, S.; Narang, D.; Thomas, M. K.; Gupta, Y. K.; Maulik, S. K. Effect of *Ocimum Sanctum* Linn. On Cardiac Changes in Rats Subjected to Chronic Restraint Stress. *J. Ethnopharmacol.* 2006, *108*(3), 423–427. DOI: 10.1016/j.jep.2006.06.010.
[162] Paul, V. T.; Mezui, C.; Enow-Orock, G. E.; Dimo, T.; Nyasse, B. Healing Effect on Chronic Gastric Ulcers and Short Term Toxicity Profile of the Leaf Methanol Extract of *Ocimum Suave* Wild (Lamiaceae) in Rats. *Afr. J. Tradit. Complement. Altern. Med.* 2005, *2*, 312–325. DOI: 10.4314/ajtcam.v2i3.31130.
[163] Malapermal, V.; Botha, I.; Krishna, S. B. N.; Mbatha, J. N. Enhancing Antidiabetic and Antimicrobial Performance of *Ocimum Basilicum*, and *Ocimum Sanctum* (L.) Using Silver Nanoparticles. *Saudi J. Biol. Sci.* 2017, *24*(6), 1294–1305. DOI: 10.1016/j.sjbs.2015.06.026.
[164] Aguiyi, J. C.; Obi, C. I.; Gang, S. S.; Igweh, A. C. Hypoglycaemic Activity of *Ocimum Gratissimum* in Rats. *Fitoterapia*. 2000, *71*(4), 444–446. DOI: 10.1016/S0367-326X(00)00143-X.
[165] Nyarko, A. K.; Asare-Anane, H.; Ofosuhene, M.; Addy, M. E.; Teye, K.; Addo, P. Aqueous Extract of *Ocimum Canum* Decreases Levels of Fasting Blood Glucose and Free Radicals and Increases Antiatherogenic Lipid Levels in Mice. *Vasc. Pharmacol.* 2002, *39*(6), 273–279. DOI: 10.1016/S1537-1891(03)00029-6.
[166] Ezeani, C.; Ezenyi, I.; Okoye, T.; Okoli, C. *Ocimum Basilicum* Extract Exhibits Antidiabetic Effects via Inhibition of Hepatic Glucose Mobilization and Carbohydrate Metabolizing Enzymes. *J. Intercult. Ethnopharmacol.* 2017, *6*(1), 22–28. DOI: 10.5455/jice.20161229054825.
[167] Suanarunsawat, T.; Anantasomboon, G.; Piewbang, C. Anti-diabetic and Anti-oxidative Activity of Fixed Oil Extracted from *Ocimum Sanctum* L. Leaves in Diabetic Rats. *Exp. Ther. Med.* 2016, *11*(3), 832–840. DOI: 10.3892/etm.2016.2991.
[168] Reddy, S. S.; Karuna, R.; Baskar, R.; Saralakumari, D. Prevention of Insulin Resistance by Ingesting Aqueous Extract of *Ocimum Sanctum* to Fructose-fed Rats. *Horm. Metab. Res.* 2008, *40*(1), 44–49. DOI: 10.1055/s-2007-993218.
[169] Gholap, S.; Kar, A. Hypoglycemic Effects of Some Plant Extracts are Possibly Mediated through Inhibition in Corticosteroid Concentration. *Pharmazie*. 2004, *59*(11), 876–878.
[170] Vats, V.; Grover, J. K.; Rathi, S. S. Evaluation of Antihyperglycemic and Hypoglycemic Effect of *T. Foenumgraecum, O. Sanctum* and *P. Marsupium* in Normal and Alloxanized Diabetic Rats. *J. Ethnopharmacol.* 2002, *79*(1), 95–100. DOI: 10.1016/S0378-8741(01)00374-9.
[171] Hannan, J. M. A.; Marenah, L.; Ali, L.; Rokeya, B.; Flatt, P. R.; Abdel-Wahab, Y. H. A. *Ocimum Sanctum* Leaf Extracts Stimulate Insulin Secretion from Perfused Pancreas, Isolated Islets and Clonal Pancreatic β-cells. *J. Endocrinol.* 2006, *189*(1), 127–136. DOI: 10.1677/joe.1.06615.
[172] Parasuraman, S.; Balamurugan, S.; Christapher, P. V.; Petchi, R. R.; Yeng, W. Y.; Sujithra, J.; Vijaya, C. Evaluation of Antidiabetic and Antihyperlipidemic Effects of Hydroalcoholic Extract of Leaves of *Ocimum Tenuiflorum* (Lamiaceae) and Prediction of Biological Activity of Its Phytoconstituents. *Pharmacognosy Research*. 2015, *7*(2), 156–165. DOI: 10.4103/0974-8490.151457.
[173] Onaolapo, A. Y.; Onaolapo, O. J. *Ocimum Gratissimum* Linn Causes Dose Dependent Hepatotoxicity in Streptozotocin-Induced Diabetic Wistar Rats. *Maced. J. Med. Sci.* 2012, *5*(1), 17–25. DOI: 10.3889/MJMS.1857-5773.2011.0206.
[174] Karaali, H. F.; Fahmi, R. R.; Borjac, J. M. Effect of *Ocimum Basilicum* Leaves Extract on Acetaminophen-induced Nephrotoxicity in BALB/c Mice. *J. Complement Integr. Med.* 2018, *16*(2). DOI: 10.1515/jcim-2018-0111.
[175] Chiu, Y. W.; Lo, H. J.; Huang, H. Y.; Chao, P. Y.; Hwang, J. M.; Huang, P. Y.; Huang, S.-J.; Liu, J. Y.; Lai, T. J. The Antioxidant and Cytoprotective Activity of *Ocimum Gratissimum* Extracts against Hydrogen Peroxide-induced Toxicity in Human HepG2 Cells. *J. Food Drug Anal.* 2013, *21*(3), 253–260. DOI: 10.1016/j.jfda.2013.07.002.
[176] Ighodaro, O. M.; Omole, J. O. Ethanol-induced Hepatotoxicity in Male Wistar Rats: Effects of Aqueous Leaf Extract of *Ocimum Gratissimum*. *J. Med. Med. Sci.* 2012, *3*, 499–505.
[177] Ezeonwu, V. U.; Dahiru, D. Protective Effect of Bi-herbal Formulation of *Ocimum Gratissimum* and *Gongronema Latifolium* Aqueous Leaf Extracts on Acetaminophen-induced Hepato-nephrotoxicity in Rats. *Am. J. Biochem.* 2013, *3*, 18–23.
[178] Surana, V.; Jain, D. Protective Effect of *Ocimum Gratissimum* against Carbon Tetrachloride Induced Hepatic Damage in Rats. *Pharmacologyonline*. 2010, *2*, 1111–1119.
[179] Prabhu, K. S.; Lobo, R.; Shirwaikar, A. A.; Shirwaikar, A. *Ocimum Gratissimum*: A Review of Its Chemical, Pharmacological and Ethnomedicinal Properties. *Open Complement. Med. J.* 2009, *1*(1), 1–15. DOI: 10.2174/1876391X00901010001.
[180] Awogbindin, I. O.; Tade, O. G.; Metibemu, S. D.; Olorunsogo, O. O.; Farombi, E. O. Assessment of Flavonoid Content, Free Radical Scavenging and Hepatoprotective Activities of *Ocimum Gratissimum* and *Spondias Mombin* in Rats Treated with Dimethylnitrosamine. *Arch. Bas. App. Med.* 2014, *2*, 45–54.
[181] Iroanya, O.; Okpuzor, J.; Adebesin, O. Hepatoprotective and Antioxidant Properties of a Triherbal Formulation against Carbon Tetrachloride Induced Hepatotoxicity. *J. Pharm.* 2012, *2*, 130–136.
[182] Uhegbu, F. O.; Elekwa, I.; Akubugwo, E. I.; Chinyere, G. C.; Iweala, E. E. J. Analgesic and Hepatoprotective Activity of Methanolic Leaf Extract of *Ocimum Gratissimum* (L.). *Res. J. Med. Plant.* 2012, *6*(1), 108–115. DOI: 10.3923/rjmp.2012.108.115.

[183] Pereira, C.; Barros, L.; Ferreira, C. F. R. I. Extraction, Identification, Fractionation and Isolation of Phenolic Compounds in Plants with Hepatoprotective Effects. *J. Sci. Food Agric.* 2015, *96*(4), 1068–1084. DOI: 10.1002/jsfa.7446.
[184] Adetutu, A.; Olorunnisola, O. S. Hepatoprotective Potential of Some Local Medicinal Plants against 2-acetylaminoflourene-induced Damage in Rat. *J. Toxicol.* 2013, *2013*, 272097.
[185] Ujowundu, C. O.; Nwokedinobi, N.; Kalu, F. N.; Nwaoguikpe, R. N.; Okechukwu, R. I. Chemoprotective Potentials of *Ocimum Gratissimum* in Diesel Petroleum Induced Hepatotoxicity in Albino Wistar Rats. *J. Appl. Pharm. Sci.* 2011, *1*, 56–61.
[186] Thalla, S.; Ramana, V. K.; Delhiraj, N. Hepatoprotective Effect of Hydroalcoholic Extract of Ocimum Gratissimum Leaves on Rifamicin-isoniazid Induced Rats. *Indian J. Res. Pharm. Biotechnol.* 2013, *1*, 649–654.
[187] Chigozie, U. J.; Monanu, M. O.; Patrick, K. C.; Egbachukwu, S. I. Potential Hepatoprotective Effect of Different Solvent Fractions of *Ocimum Gratissimum* (OG) in a Paracetamol - Induced Hepatotoxicity in Wistar Albino Rats. *J. Invest. Biochem.* 2016, *5*(1), 10–16. DOI: 10.5455/jib.20160320033421.
[188] Akpan, A. U.; Ewa, I. D.; Etim, B. E. *Ocimum Gratissimum* Alleviates Derangements in Serum and Biliary Bilirubin, Cholesterol and Electrolytes in Streptozotocin- Induced Diabetic Rats. *Int. J. Biochem. Res. Rev.* 2013, *3* (3), 171–189. DOI: 10.9734/IJBCRR/2013/4258.
[189] Ogundipe, D. J.; Akomolafe, R. O.; Sanusi, A. A.; Imafidon, C. E.; Olukiran, O. S.; Oladele, A. A. *Ocimum Gratissimum* Ameliorates Gentamicin-Induced Kidney Injury but Decreases Creatinine Clearance following Sub-Chronic Administration in Rats. *Evid.-Based Complementary Altern. Med.* 2017, *22*(4), 592–602. DOI: 10.1177/2156587217691891.
[190] Sharma, M. K.; Kumar, M.; Kumar, A. Protection against Mercury-induced Renal Damage in Swiss Albino Mice by *Ocimum Sanctum*. *Environ. Toxicol. Pharmacol.* 2005, *19*(1), 161–167. DOI: 10.1016/j.etap.2004.06.002.
[191] Chattopadhyay, R. R.; Sarkar, S. K.; Ganguly, S.; Medda, C.; Basu, T. K. Hepatoprotective Activity of *Ocimum Sanctum* Leaf Extract against Paracetamol Induced Hepatic Damage in Rats. *Indian J. Pharmacol.* 1992, *24*, 163–165.
[192] Prakash, P.; Gupta, N. Therapeutic uses of *Ocimum Sanctum* Linn (Tulsi) with a Note on Eugenol and Its Pharmacological Actions: A Short Review. *Indian J. Physiol. Pharmacol.* 2005, *49*(2), 125–131.
[193] Torres, R. G.; Casanova, L.; Carvalho, J.; Marcondes, M. C.; Costa, S. S.; Sola-Penna, M.; Zancan, P. *Ocimum Basilicum* but Not *Ocimum Gratissimum* Present Cytotoxic Effects on Human Breast Cancer Cell Line MCF-7, Inducing Apoptosis and Triggering mTOR/Akt/p70S6K Pathway. *J. Bioenerg. Biomembr.* 2018, *50*(2), 93–105. DOI: 10.1007/s10863-018-9750-3.
[194] Karthikeyan, K., Gunasekaran, P., Ramamurthy, N., Govindasamy, S. Anticancer Activity of Ocimum Sanctum. Pharm. Biol. 2011, 37(4), 285-290
[195] Monga, J.; Sharma, M.; Tailor, N.; Ganesh, N. Antimelanoma and Radioprotective Activity of Alcoholic Aqueous Extract of Different Species of *Ocimum* in C 57 BL Mice. *Pharm. Biol.* 2011, *49*(4), 428–436. DOI: 10.3109/13880209.2010.521513.
[196] Kaushal, N.; Rao, S.; Ghanghas, P.; Abraham, S.; George, T.; D'souza, S.; Mathew, J. M.; Chavali, J.; Swamy, M. K.; Baliga, M. S. Usefulness of *Ocimum Sanctum* Linn. In Cancer Prevention: An Update. In *Anticancer Plants: Properties and Application*; Akhtar, M.S., Swamy, M.K., Eds.; Springer: Singapore, 2018; pp 415–429.