

Chemical composition, antimicrobial, antioxidant, and toxicity of essential oils as food preservatives

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ABSTRACT: Owing to the toxicity of chemical food preservatives, essential oils have gained significant attention in the food industry. Because they can be toxic at certain concentrations, their toxicity must be carefully considered. This study is a systematic review based on 312 references to ensure accuracy. The databases WOS, PubMed, Embase, Scopus, and Google Scholar are utilized to gather relevant information. Various combinations of the following keywords are employed: essential oil, food preservative, antimicrobial, toxicity, and MIC. The inclusion and exclusion criteria and quality assessment of the included studies led to the formation of a search strategy flowchart. Data were tabulated showing the names of the plants containing volatile oil, the major ingredients of essential oils, their antimicrobial, antioxidant, and anti-aflatoxin effects, oral toxicity, and Minimum Inhibitory Concentration (MIC) of volatile oils against pathogens. The acute, sub-acute, and chronic toxicities of volatile oils are also discussed and investigated. In addition, the toxicity of the essential oils and their MIC were compared. Additionally, the MIC of the effective antibiotics against pathogenic microorganisms were compared with those of the volatile oils. Several figures have been prepared that show the relative frequencies of the data obtained from the tables. These results suggest that essential oils have great potential for use in the food industry. However, only a few studies have been conducted to determine their toxicity. Thus, further investigation is required.

KEYWORDS: Essential oil; food preservative; antimicrobial; toxicity; MIC.

1. INTRODUCTION

Food safety is a vital factor in determining the quality of food and nutrients. It should be carefully considered during food preparation, distribution, and consumption. Contaminated foods are reservoirs of various diseases and infections, leading to diminished food quality and harm to human health.[1,2] Food spoilage occurs due to diverse factors, including food characteristics, storage methods and conditions, environmental factors (light, temperature, and pH), and microbial activities. Bacteria, yeasts, molds, and fungi play an important role in contamination. [1,2] Several preservation methods, including canning, drying, freezing, smoking, pasteurizing, and antimicrobial peptides (AMPs), have been utilized to prolong shelf life and maintain food quality. [1-3]

Preservatives are pivotal in preventing microbial growth and maintaining food durability and stability. Preservatives are divided into three main classes: antimicrobials, antioxidants, and anti-enzymatic. Preservatives can be used either separately or simultaneously. While traditional preservatives, as indicated in Table 1, such as organic acids, nitrates, nitrites, sulfites (sodium and potassium), SO₂, and several polypeptides such as Natamycin and Nisin [4,5] are effective, but they still pose a concern about potential adverse health effects and toxicity, including allergic reactions, headaches, and gastrointestinal issues (e.g., gastric cancer).

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Table 1. Some compounds used as food preservatives

Preservatives	Usage and function
Organic acids (such as acetic acid, benzoic acid, etc.)	Preparing foods with low pH
Nitrates and Nitrites	Inhibition of bacterial proliferation in raw meat
SO ₂ and Sulfites	Preventing the growth of microorganisms inside dried fruits
Natamycin and Nisin	Inhibition of bacterial growth in meat and dairy products

Many people may not consider chemical preservatives disadvantageous; however, some are toxic, and others can indirectly lead to health-threatening harm. For instance, sulfite preservatives may cause headaches, heart palpitations, and allergies, whereas nitrates or nitrites play a fundamental role in the development of gastric cancer. Asthma, Dermatitis, and Hypertension are other diseases caused by chemical preservation. Therefore, chemical types are no longer considered safe for food preparation. Consequently, it is better to examine the application of safer compounds with fewer side effects. An appropriate option is to use pure herbal compounds, extracts, and essential oils as preservatives.[5-7]

Herbal essential oils can be used alone or in combination with other materials as preservatives in the food industry. These essential oils contain various compounds, including monoterpenes and sesquiterpenes. Owing to these compounds and their mutual effects, they exhibit antioxidant, antifungal, and antibacterial properties. Like other preservatives besides their benefits, other preservatives also have side effects. For instance, at high concentrations, they can cause changes in the organoleptic properties of foods.[8,9] Numerous studies have reported that the improper use of essential oils could lead to toxicity. When used at high concentrations, phenolic compounds of essential oils, such as Morin and Cinnamic acid, may cause skin inflammation and dermatitis. The monoterpenes present in essential oils have various biological and health activities. However, further studies have uncovered their neurotoxic, allergenic, and genotoxic effects, as well as their vast fetotoxic effects in pregnancy. These compounds can also disturb the membrane function, DNA structure, and enzyme function.[10,11]

Although volatile oils are widely used in various industries, such as the food industry, their toxicity is underestimated. To the best of our knowledge, no study has explored the toxicity of essential oils as food preservatives. Thus, this study aimed to investigate the main essential oils that have the potential to be used in the food industry. The second aim of this study was to identify the dominant phytochemicals in essential oils. Third, the biological activities of essential oils, including antimicrobial, MIC, antioxidant, and anti-aflatoxin effects, were investigated. Fourth, the oral toxicities of the volatile oils were tabulated.

2. RESULTS

Our primary objective was to identify essential oils with significant antimicrobial activity and understand their chemical composition. To achieve this, we extensively researched the plant sources of these oils and their chemical makeup, as detailed in the Table 2.

Table 2. Essential oils' major effective compounds and their biological effect

Plant name (Effective part)	Common name	Family of the plant	Major effective compounds	Biological effect	R*
<i>Acorus calamus</i> (Rhizomes)	Sweet flag	Acoraceae	β-Aasarone (82.42 %)	Antimicrobial Antioxidant Antifungal Antiaflatoxigenic	[12,13]
<i>Ageratum conyzoides</i> (Flowers and stems)	Billygoat weed	Asteraceae	Precocene I (flower: 58.8%, stem: 76.5%), β-Caryophyllene (flower: 15.2%, stem: 8.1%)	Antibacterial Antioxidant Antifungal	[14,15]
<i>Allium sativum</i> (Bulbs)	Garlic	Alliaceae	Diallyl trisulfide (16.8%-33.4%), Diallyl disulfide (20.8%-27.9%), Allyl methyl trisulfide (19.2%)	Antibacterial Antifungal	[16,17]
<i>Alpinia galanga</i> (Rhizomes)	Siamese ginger	Zingiberaceae	Ethyl cinnamate (37.559 %), Methyl cinnamate (19.993 %), n-Pentadecane (14.614 %)	Antibacterial Antioxidant	[18]

<i>Alpinia zerumbet</i> (Leaves)	Shell ginger	Zingiberaceae	γ -Terpinene (14.5%), Cineole (13.8%), p-Cymene (13.5%), Sabinene (12.5%),	Antimicrobial Antioxidant	[19,20] [21]
<i>Anethum graveolens</i> (Fruits)	Dill	Apiaceae	Carvone (58%), D-Limonene (37%)	Antimicrobial Antioxidant Antifungal	[22,23]
<i>Artemisia absinthium</i> (Aerial parts)	Wormwood	Asteraceae	Sabinene (30.1%), Myrcene (38.9%), 1,8-Cineole (18%)	Antibacterial Antifungal	[24,25]
<i>Artemisia campestris</i> (Aerial parts)	Field wormwood	Asteraceae	α -Pinene (18.65%), β -Pinene (16.78%), β -Myrcene (17.34%), Germacrene D (10.34%)	Antimicrobial Antioxidant Antifungal	[26,27]
<i>Artemisia herba-alba</i> (Aerial parts)	White wormwood	Asteraceae	α/β -thujone (57%), Camphor (24%)	Antimicrobial Antioxidant	[22,28]
<i>Boswellia papyrifera</i> (Leaves)	Sudanese frankincense	Bruceraceae	Octyl acetate (49.5%-81.0%), Diterpenoids (6.6%-32.7%) Octanol (6.5%-13.7%),	Antimicrobial Antifungal	[29,30]
<i>Bunium persicum</i> (Aerial parts)	Black Cumin	Apiaceae	Caryophyllene (27.81%), γ -Terpinene (15.19%), Cumyl acetate (14.67%)	Antimicrobial Antioxidant	[31,32]
<i>Calendula officinalis</i> (Flowers and leaves)	Pot marigold	Asteraceae	α -Cadinol (32.3%), δ -Cadinene (11.8%), τ -Muurolol (8.5%)	Antimicrobial Antioxidant Antifungal	[33]
<i>Carum carvi</i> (Seeds)	Meridian fennel, Persian cumin	Apiaceae	γ -Terpinene (31.03%), β -Pinene (18.77%), p-Cymene (17.16%), Carvone (12.20%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[34,35]
<i>Cedrus deodara</i> (Leaves and peels)	Deodar cedar	Pinaceae	α -terpineol (30.2%), linalool (24.47%), limonene (17.01 %), Anethole (14.57%)	Antimicrobial Antioxidant	[36]
<i>Chenopodium ambrosioides</i> (Leaves, flowers, and stems)	Mexican tea	Amaranthaceae	α -Terpinene (51.3%), p-Cymene (23.4%), p-Mentha-1,8-diène (15.3%)	Antimicrobial Antioxidant Antifungal	[37,38]
<i>Cinnamomum camphora</i> (Leaves)	Camphor tree	Lauraceae	Camphor (93.1%)	Antimicrobial Antifungal	[39]
<i>Cinnamomum cassia</i> (Bark)	Chinese cinnamon	Lauraceae	cis-2-Methoxycinnamic acid (43.06%), Cinnamaldehyde (42.37%)	Antimicrobial Antioxidant Antiaflatoxicogenic	[40,41] [42]
<i>Citrus aurantifolia</i> (Leaves)	Lime	Rutaceae	Limonene (77.5 %), Linalool (20.1 %), Citronellal (14.5 %)	Antioxidant Antifungal Antibacterial Antiparasitic	[43,44] [45]
<i>Citrus aurantium</i> (Flowers)	Sour orange	Rutaceae	Limonene (27.5%), (E)-Nerolidol (17.5%), α -Terpineol (14.0%) α -Terpinol acetate (11.7%)	Antimicrobial Antioxidant	[46]
<i>Citrus grandis</i> (Peels)	Pomelo	Rutaceae	Limonene (63.7%), β -pinene (6.09%)	Antimicrobial Antioxidant Antifungal	[47,48]

<i>Citrus hystrix</i> (Peels and leaves)	Kaffir lime	Rutaceae	Citronellol (10.7%), Limonene (7.3%)	Antibacterial Antioxidant Antiaflatoxicogenic	[17,49,
<i>Citrus reticulata</i> (Peels and leaves)	Mandarin orange	Rutaceae	Limonene (83.67%), γ -Terpinene (6.09%)	Antimicrobial Antioxidant Antifungal	[47,51]
<i>Citrus sinensis</i> (Fruits)	Sweet orange	Rutaceae	Limonene (77.37%), β -pinene (3.45%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[47,52] [53]
<i>Clausena lansium</i> (Leaves)	Wampee	Rutaceae	α -Santalol (31.7%), α -Santalane (19.5%)	Antimicrobial Antioxidant Antifungal	[54,55]
<i>Cleistocalyx operculatus</i> (Leaves)	Voi, Shui weng	Myrtaceae	Myrcene (69.7%), (E)- β -Ocimene (12.24%)	Antimicrobial Antioxidant	[56,57]
<i>Coriandrum sativum</i> (Leaves and seeds)	Cilantro	Apiaceae	Linalool (76.41%), γ -terpinene (5.35%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[34,58] [35]
<i>Croton argyrophylloides</i> (Leaves)	Croton	Euphorbiaceae	Spathulenol (26.7%), Caryophyllene oxide (13.1%), β -Elemene (12.2%)	Antibacterial Antioxidant Antifungal	[19,59,
<i>Croton zehntneri</i> (Leaves)	—	Euphorbiaceae	Estragole (46%), trans-Anethole (42.1%)	Antimicrobial Antifungal Cytotoxic	[19,60,
<i>Cuminum cyminum</i> (Seeds)	Cumin	Apiaceae	Cumin aldehyde (29%), α -Terpinen-7-al (20.7%), γ -Terpinene (12.9%), Terpinolene (52.88%), α -Phellandrene (21.13%)	Antibacterial Antifungal Antiaflatoxicogenic	[17,62]
<i>Curcuma longa</i> (Leaves)	Turmeric	Zingiberaceae	Terpinolene (52.88%), α -Phellandrene (21.13%)	Antimicrobial Antioxidant	[63,64]
<i>Cymbopogon citratus</i> (Leaves)	Lemongrass	Poaceae	Geraniol (55.2%), Neral (44.7 %)	Antibacterial Antifungal Antioxidant Antiaflatoxicogenic	[65,66]
<i>Cymbopogon giganteus</i> (Leaves)	—	Poaceae	cis-p-Mentha-1(7),8-dien-2-ol (19.4%), trans-p-Mentha-2,8-dien-1-ol (16.4%), Limonene (13.7%).	Antimicrobial, Antifungal	[67]
<i>Cymbopogon martini</i> (Leaves)	Ginger grass	Poaceae	Geraniol (40.89%), Cyclofenchene (13.91%), Myrcene (9.34%)	Antimicrobial Antioxidant Antifungal	[68,69] [70,71]
<i>Cymbopogon schoenanthus</i> (Aerial parts)	Camel grass	Poaceae	Piperitone (63.35%), β -Eudesmol (9.305%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[66,72]
<i>Cymbopogon winterianus</i> (Leaves and stems)	Java citronella	Poaceae	Citronellal (27.00%), trans.-Geraniol (22.78%), Citronellol (10.09%)	Antibacterial Antioxidant	[73,74]
<i>Cyperus rotundus</i> (Tubers)	Purple nutsedge	Cyperaceae	Cyperene (16.9%), Caryophyllene oxide (8.9%), α -Longipinane (8.4%)	Antibacterial Antioxidant	[75]
<i>Daucus carota</i> (Seeds and leaves)	Wild carrot	Apiaceae	α -Pinene (27.44%), Sabinene (25.34 %), Germacrene D (16.33 %)	Antimicrobial Antioxidant	[76,77]
<i>Eucalyptus camaldulensis</i>	River red	Myrtaceae	1,8-cineole (16.2%),	Antimicrobial	[78,79]

(Leaves)	gum		α -pinene (15.6%), α -phellandrene (10.0%)	Antifungal	
<i>Eucalyptus globulus</i> (Leaves)	Tasmanian bluegum	Myrtaceae	1,8-Cineole (55.29%), Spathulenol (7.44%)	Antimicrobial Antioxidant	[80]
<i>Eugenia florida</i> (Leaves)	Rainforest cherry	Myrtaceae	seline-3,11-dien-6- α -ol (12.93%), Eremoligenol (11%), γ -Elemene (10.70%)	Antibacterial Antioxidant Antifungal	[81,82]
<i>Eupatorium adenophorum</i> (Inflorescences and roots)	Crofton weed	Asteraceae	γ -Cadinene (18.4 %), γ -muurolene (11.7 %)	Antimicrobial Antioxidant	[83,84]
<i>Ferula assa-foetida</i> (Oleo-gum-resins)	Devil's dung	Umbelliferae	(E)-1-Propenyl sec-butyl disulf (23.9%), 10-epi- γ -Eudesmol (15.1 %)	Antimicrobial Antioxidant Antifungal	[85]
<i>Ferula macrocolea</i> (Aerial parts)	—	Apiaceae	Terpinolene (77.72%), n-Nonanal (4.47%), Linalool (4.35%),	Antibacterial Antifungal	[86]
<i>Foeniculum vulgare</i> (Seeds)	Fennel	Apiaceae	trans-Anethole (75.8%), Estragole (4.6%)	Antimicrobial Antioxidant Antiaflatoxicogenic	[19,87] [88]
<i>Gnaphalium affine</i> (Aerial parts)	Cotton weed	Asteraceae	Eugenol (18.2%), Linalool (10.6%)	Antimicrobial Antioxidant	[17,89]
<i>Hedychium spicatum</i> (Rhizomes)	Spiked ginger lily	Zingiberaceae	Curzerene (14.7 %), Coronar E (13.3 %), Curdione (10.2 %)	Antimicrobial Antioxidant Antifungal	[90]
<i>Heracleum sphondylium</i> (Aerial parts)	Common hogweed	Apiaceae	Curcumene (13.42%), β -Sesquiphellandrene (11.91%), β -Bisabolene (10.11%)	Antimicrobial Antioxidant	[91]
<i>Hyptis suaveolens</i> (Leaves)	Pignut	Lamiaceae	Sabinene (7.3-31.3%), Eucalyptol (14.0-24.6%), β -Caryophyllene (6.9-12.7%), 1, 8-Cineole (11.5%), β -Phellandrene (10.2%)	Antimicrobial Antioxidant Antiaflatoxicogenic	[92,93] [94]
<i>Juniperus communis</i> (Cones and leaves)	Common juniper	Cupressaceae	α -Pinene (51.4%), Myrcene (8.3%)	Antimicrobial Antioxidant Antifungal	[95,96] [97]
<i>Lavandula angustifolia</i> (Leaves and flowers)	English lavender	Lamiaceae	Eucalyptol (52.36%), Camphor (11.91%), δ -Terpinene (8.775%)	Antimicrobial Antifungal	[98,99]
<i>Lippia gracilis</i> (Leaves)	—	Verbenaceae	Thymol (70.3%), p-Cymene (9.2%)	Antimicrobial Antioxidant Antifungal	[100,101]
<i>Lippia origanoides</i> (Stems)	Mexican oregano	Verbenaceae	Carvacrol (29.00%), o-Cymene (25.57%), Thymol methyl ether (11.50%)	Antimicrobial Antioxidant	[102,103]
<i>Litsea elliptica</i> (Leaves)	Medang, Perawas	Lauraceae	α -Terpineol (34.54%), 9-Decen-2-ol (25.09%), p-Menthan-8-ol, (18.57%), 7-Decen-2-one (10.62%)	Antimicrobial Antioxidant	[104,105]
<i>Matricaria chamomilla</i> (Flowers)	Chamomile	Asteraceae	β -Farnesene (29.8 %), α -Bisabolol (15.7 %)	Antimicrobial Antioxidant	[106]
<i>Melaleuca alternifolia</i> (Leaves)	Tea tree	Myrtaceae	Terpinen-4-ol (38.6%), γ -Terpinene (21.7%)	Antifungal Antimicrobial	[107,108]
<i>Melaleuca leucadendron</i> (Leaves)	Weeping paperbark	Myrtaceae	Eugenol methyl ether (95.4 %)	Antimicrobial Antioxidant	[109]

<i>Melissa officinalis</i> (Leaves)	lemon balm	Lamiaceae	Ggeranial (44.20 %), Neral (30.20 %) Citronellal (6.30 %)	Antifungal Antimicrobial Antioxidant Antiaflatoxicogenic	[110,11]
<i>Mentha longifolia</i> (Flowers, leaves, and stems)	Menthol	Lamiaceae	Piperitenone oxide (70.0%), Piperitenone (18.7%)	Antimicrobial Antioxidant Antiaflatoxicogenic	[17,112 [113]
<i>Mentha mozaaffarianii</i> (Leaves and fruits)	Pooneh koohi	Lamiaceae	Piperitenone (59.5 %), cis-liperitenone epoxide (14.9 %), Pulegone (8.5 %)	Antimicrobial Antifungal	[114]
<i>Mentha piperita</i> (Leaves)	Peppermint	Lamiaceae	Menthone (30.63 %), Menthol (25.16 %)	Antimicrobial Antimicrobial Antiaflatoxicogenic	[107,11 [116]
<i>Mentha pulegium</i> (Aerial parts)	Pennyroyal	Lamiaceae	Menthone (35.9%), Pulegone (23.2%),	Antimicrobial Antioxidant	[117]
<i>Monarda citriodora</i> (Flowers)	Lemon mint	Lamiaceae	Thymol (79.7%), p-Cymene (7.7%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[118,11]
<i>Monodora myristica</i> (Seeds)	Calabash nutmeg	Annonaceae	p-Cymene (50.58%), α -Phellandrene (32.09%)	Antibacterial Antioxidant	[120]
<i>Myrtus communis</i> (Aerial parts)	Myrtle	Myrtaceae	1,8-cineole (13.5–19.6%), linalool (7.7–15.8%)	Antimicrobial Antioxidant	[121]
<i>Nardostachys jatamansi</i> (Roots)	Indian spikenard	Caprifoliaceae	Guaia-6,9-diene (11.96 %), Calarene (10.44 %)	Antimicrobial Antioxidant	[122]
<i>Nepeta faassenii</i> (Flowers, leaves, and stems)	Catmint	Lamiaceae	4a α ,7 α ,7 α β -Nepetalactone (34.12%), Elemol (23.23%), spiro (5,6) Dodecane (13.73%)	Antimicrobial Antioxidant	[123]
<i>Nepeta sintenisii</i> (Aerial parts)	—	Lamiaceae	4a α ,7 α ,7 α β -Nepetalactone (51.74%), β -Farnesene (12.26%)	Antimicrobial Antioxidant	[124]
<i>Ocimum basilicum</i> (Aerial parts)	Common basil	Lamiaceae	Estragole (80%), Linalool (16.12%)	Antimicrobial Antioxidant Antifungal	[125,12]
<i>Ocimum gratissimum</i> (Leaves)	Basil, Basil-clove, Alfavaca	Lamiaceae	Eugenol (68.8%), Methyl eugenol (13.21%), cis-Ocimene (7.47%)	Antimicrobial Antifungal	[127,12]
<i>Origanum compactum</i> (Leaves)	Oregano	Lamiaceae	Carvacrol (36.5%), Thymol (29.7%), p-Cymene (24.3%)	Antibacterial Antioxidant	[17]
<i>Origanum vulgare</i> (Leaves)	Oregano	Lamiaceae	Carvacrol (58.30%), Linalool (9.09%),	Antibacterial Antioxidant Antiaflatoxicogenic	[9] [129,13 [131]
<i>Rosa damascena</i> (Petals)	Damask rose	Rosaceae	β -citronellol (14.5-47.5%), Nonadecane (10.5-40.5%), Geraniol (5.5-18%)	Antibacterial Antifungal	[25,132]
<i>Rosmarinus officinalis</i> (Leaves)	Rosemary	Lamiaceae	1,8-Cineole (eucalyptol, 52.2%), Camphor (15.2%), α -Pinene (12.4%)	Antibacterial Antioxidant Cytotoxic Antiaflatoxicogenic	[133] [134]
<i>Satureja hortensis</i> (Flowers and leaves)	Summer savory	Lamiaceae	Thymol (41.28%), γ -Terpinene (37.63%), p-Cymene (12.2%)	Antimicrobial Antioxidant Antifungal	[135,13 [137]

<i>Satureja khuzestanica</i> (Aerial parts)	Marzeh khuzestani	Lamiaceae	Carvacrol (64.4%)	Antiaflatoxicogenic Antimicrobial Antioxidant	[138,13]
<i>Satureja montana</i> (Aerial parts)	Savory	Lamiaceae	Thymol (24.69%), linalool (15.38%)	Antimicrobial Antioxidant	[140]
<i>Syzygium aromaticum</i> (Flowers)	Clove	Myrtaceae	β -Caryophyllene (5-14%), Eugenol (75-88%), Eugenol acetate (4-15%)	Antimicrobial Antioxidant Antifungal	[107,14]
<i>Tagetes elliptica</i> (Leaves)	Chincho	Asteraceae	cis-Tagetenone (37.27%), trans-Tagetenone (18.84%), Dihydrotagetone (14.38%),	Antibacterial Antioxidant	[142]
<i>Tagetes erecta</i> (Leaves and flowers)	African Marigold	Asteraceae	Piperitone (35.9%), Terpinolene (22.2%)	Antimicrobial Antioxidant	[143,14]
<i>Tanacetum parthenium</i> (Flowers and leaves)	Feverfew	Asteraceae	Camphor (45.47%), trans-Chrisantenyl acetate (21.65%), Camphene (9.48%)	Antimicrobial Antioxidant Antifungal	[145]
<i>Thymus schimperi</i> (Flowers and leaves)	Tosign	Lamiaceae	Thymol (49.6 %), Carvacrol (36.3%)	Antimicrobial Antioxidant Antifungal	[146,14]
<i>Thymus vulgaris</i> (Leaves and flowers)	Thyme	Lamiaceae	Thymol (47.59%), γ -Terpinene (30.90%), p-Cymene (8.41%)	Antibacterial Antifungal Antiviral Antioxidant Antiaflatoxicogenic	[148,14] [150]
<i>Trachyspermum ammi</i> (Fruits)	Ajwain	Apiaceae	Thymol (67.4%), p-Cymene (17.9%), γ -Terpinene (11.3%)	Antimicrobial Antioxidant Antifungal	[151]
<i>Vitex agnus</i> (Leaves)	Chaste tree	Lamiaceae	α -Pinene (14.83%), Limonene (10.29%), β -Caryophyllene (6.9%)	Antimicrobial Antioxidant Antifungal	[152,15]
<i>Vitex negundo</i> (Leaves)	Chinese chaste tree	Lamiaceae	2R-acetoxymethyl-1,3,3-trimethyl-4T- (3-methyl-2-buten-1-yl)- 1tcyclohexano (27.198%), Nerolidol (14.61%), β -Caryophyllene (11.949%),	Antimicrobial Antioxidant	[154]
<i>Zingiber officinale</i> (Rhizomes)	Common ginger	Zingiberaceae	Citral (17.25%), δ -Citral (10.25%), Camphene (9.55%)	Antimicrobial Antioxidant Antifungal Antiaflatoxicogenic	[155,15] [157]

*References

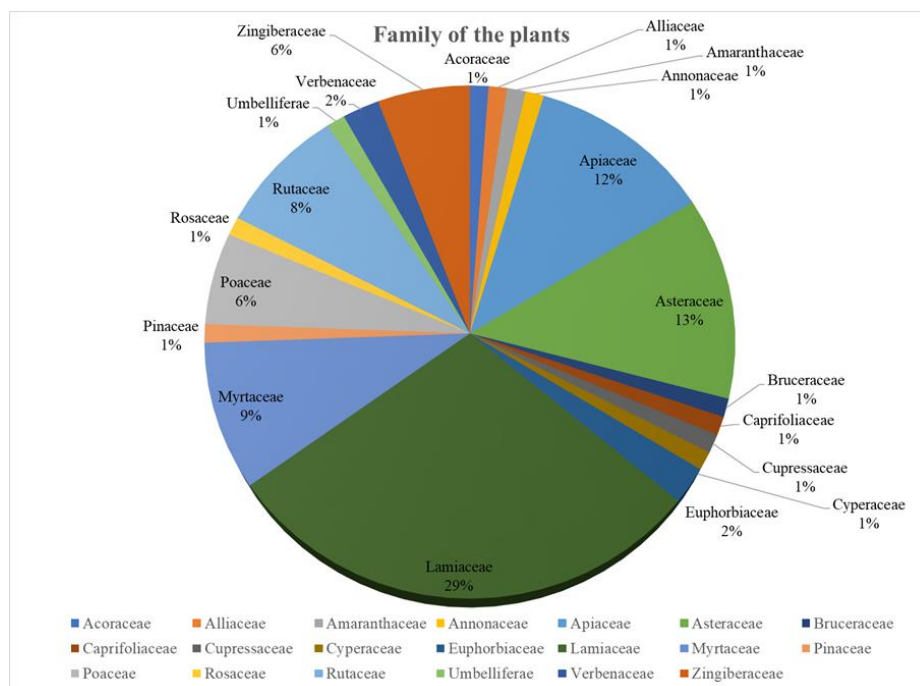


Figure 1. Dominant families tabulated in Table 2

Based on the information gathered in Table 2, the top five most frequently mentioned families were Lamiaceae 25 times, Asteraceae 11 times, Apiaceae 10 times, Myrtaceae 8 times, and Rutaceae 7 times. Figure 1 illustrates the leading plant families. Out of the 107 chemical compositions listed in Table 2, the most mentioned chemicals were limonene 10 times, p-cymene 10 times, gamma-terpinene 10 times, linalool 9 times, thymol 9 times, caryophyllene 8 times, 1,8-cineole 7 times, eugenol 6 times, alpha-pinene 6 times, camphor, carvacrol, myrcene, and piperitenone 5 times each; the abundance of chemical compounds is shown in Figure 2. Different parts of plants show biological effects, such as leaves, stems, and flowers. Figure 3 shows the abundance of the biologically active plant parts.

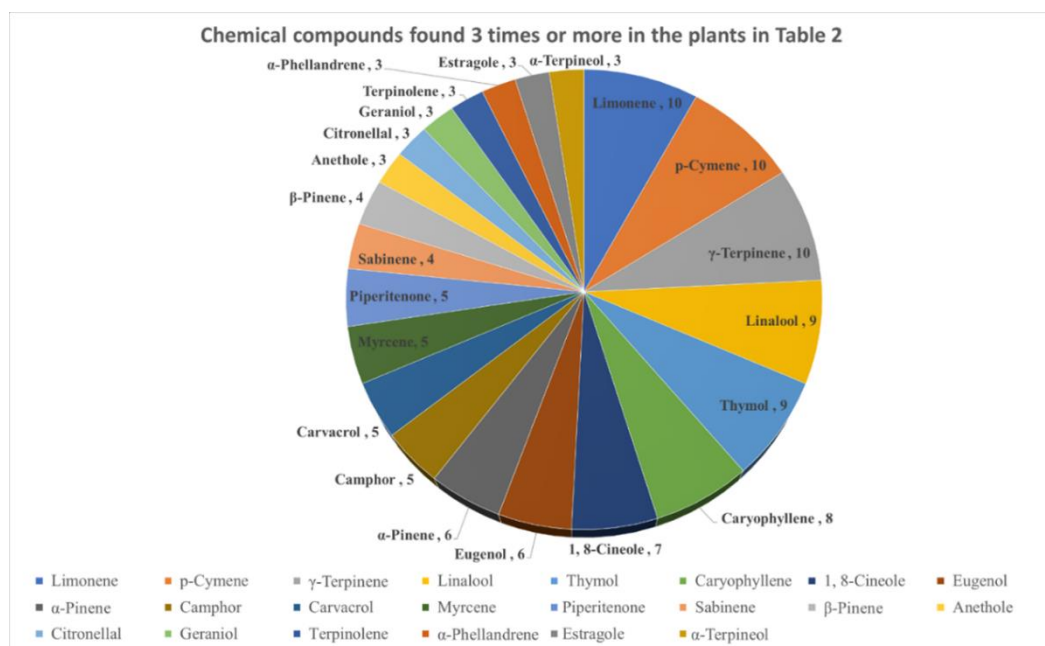


Figure 2. Chemical compounds found 3 times or more in the plants in Table 2

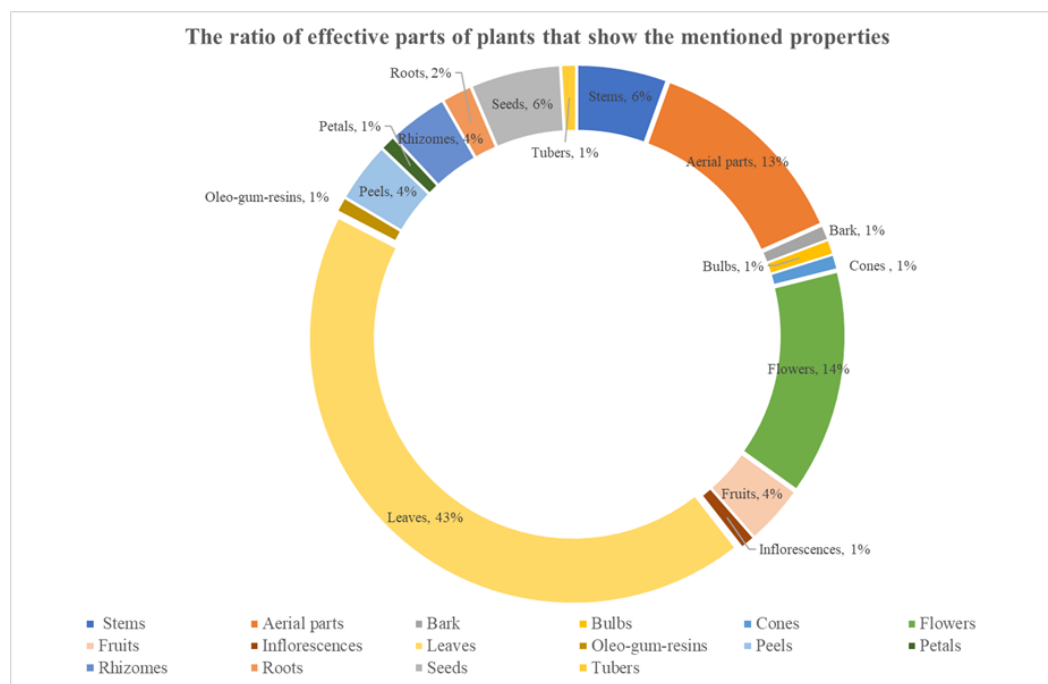


Figure 3. The ratio of effective parts of plants that show the mentioned properties

One of the factors investigated was the anti-aflatoxin activity. *Acorus calamus*, *Carum carvi*, *Cinnamomum cassia*, *Citrus hystrix*, *Citrus sinensis*, *Coriandrum sativum*, *Cuminum cyminum*, *Cymbopogon citratus*, *Cymbopogon schoenanthus*, *Foeniculum vulgare*, *Hyptis suaveolens*, *Melissa officinalis*, *Mentha longifolia*, *Mentha piperita*, *Monarda citriodora*, *Origanum vulgare*, *Rosmarinus officinalis*, *Satureja hortensis*, *Thymus vulgaris*, and *Thymus vulgaris* have shown this property. Subsequently, we conducted a rigorous evaluation of the antimicrobial activity of the essential oils. Assessing antimicrobial activity involved determining the MIC against various microorganisms. Similarly, we meticulously assessed the toxicity, including acute, sub-acute, and chronic, and compiled the data in Table 3.

Table 3. Acute,sub-acute,chronic oral toxicity and MIC of essential oils

Plant name (Effective part)	Acute toxicity (LD ₅₀)	Sub-acute toxicity	Chronic toxicity	MIC*	R**
<i>Acorus calamus</i> (Rhizomes)	350 mg/kg (rats)	-	-	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>B. subtilis</i> (0.25 mg/ml) <i>E. coli</i> (0.5 mg/ml)	[158,159]
<i>Ageratum conyzoides</i> (Flowers and leaves)	Female: 1247.88 mg/kg Male: 1674.57 mg/kg (mice)	100 mg/kg: Decrease in kidney and heart weight, increase in creatinine, decrease erythrocyte, haemoglobin and haematocrit (mice - 28days)	-	<i>S. aureus</i> (64 µg/ml) <i>E. faecalis</i> (256 µg/ml) <i>S. aureus</i> (256 µg/ml) <i>E. coli</i> (256 µg/ml) <i>E. aerogenes</i> (512 µg/ml)	[14,160]
<i>Allium sativum</i> (Bulbs)	4472 mg/kg (mice)	15,25 mg/kg: No significant changes 50 mg/kg: Mild changes in glucose level (mice - 28days)	-	<i>C. albicans</i> (470–940 µg/ml) <i>E. coli</i> (15–15000 µg/mL or 3.95% v/v) <i>L. monocytogenes</i> (8.8% v/v) <i>Salmonella typhi</i> (7% v/v) <i>S. aureus</i> (12–15000 µg/mL or 5% v/v)	[17,161] [162]
<i>Alpinia galanga</i> (Rhizomes)	-	-	-	<i>E. coli</i> (15 µl/ml) <i>P. vulgaris</i> (20 µl/ml) <i>S. enteritidis</i> (10 µl/ml) <i>B. subtilis</i> (2.5 µl/ml) <i>S. aureus</i> (2.5 µl/ml)	[163]

<i>Alpinia zerumbet</i> (Leaves)	2500 mg/kg (rats)	-	-	<i>S. feacalis</i> (5 µl/ml) <i>S. cerevisiae</i> (15 µl/ml) -	[164]
<i>Anethum graveolens</i> (Seeds)	-	-	-	<i>S.aureus</i> (0.62 mg/ml) <i>V.cholerae</i> (0.7 mg/ml)	[165]
<i>Artemisia absinthium</i> (Leaves)	5700 mg/kg (mice)	-	-	<i>Streptococcus mutans</i> (250 µg/ml) <i>Streptococcus mitis</i> (62.5 µg/ml)	[166,167]
<i>Artemisia campestris</i> (Leaves)	>2 g/kg (mice)	-	-	<i>Fusarium graminearum</i> (1.25 µl/ml) <i>F. moniliforme</i> , <i>F. culmorum</i> , <i>P. expansum</i> , <i>A. flavus</i> , <i>A. ochraceus</i> , and, <i>A. parasiticus</i> (2.5 µl/ml) <i>P. viridicatum</i> and, <i>A. niger</i> (10 µl/ml)	[27,168]
<i>Artemisia herba-alba</i> (Aerial parts)	2000 mg/kg (rats)	50, 100, 200 mg/kg: No significant changes (rats - 28days)	-	<i>Klebsiella oxytoca</i> (5-10 mg/ml) <i>Acinetobacter baumannii</i> (10-20 mg/ml)	[28,169]
<i>Boswellia papyrifera</i> (Branches)	-	-	-	<i>Bacillus cereus</i> (4 µg/ml) <i>Enterococcus faecalis</i> (2 µg/ml) <i>Escherichia coli</i> (4 µg/ml) <i>Listeria innocua</i> (4 µg/ml) <i>Proteus mirabilis</i> (16 µg/ml) <i>Salmonella enterica</i> (4 µg/ml) <i>Shigella dysenteriae</i> (8 µg/ml) <i>Staphylococcus aureus</i> (4 µg/ml) <i>Staphylococcus camorum</i> (4 µg/ml)	[170]
<i>Bunium persicum</i> (Seeds)	>4000 mg/kg (rats)	250,500,1000 mg/kg: Changes in the blood parameters happen, attenuated histopathological changes in lung, liver, kidney, testes and spleen tissues (rats - 14days)	-	<i>E.aerogenes</i> (0.125 µg/ml) <i>S.enterica</i> (0.125 µg/ml) <i>B.cereus</i> (0.5 µg/ml) <i>S.aureus</i> (0.25 µg/ml)	[171,172]
<i>Calendula officinalis</i> (Flowers)	20 ml/kg (rats)	-	2.5, 5, 10 ml/kg: nontoxic behaviours were observed (rats - 90days)	-	[173]
<i>Carum carvi</i> (Seeds)	2.62 ml/kg (mice)	-	-	<i>Bacillus cereus</i> (0.5 µl/ml) <i>Escherichia coli</i> (2 µl/ml) <i>Micrococcus luteus</i> (1 µl/ml) <i>Proteus mirabilis</i> (2 µl/ml) <i>Pseudomonas tolaasii</i> (4 µl/ml) <i>Salmonella enteritidis</i> (0.25 µl/ml) <i>Staphylococcus aureus</i> (0.1 µl/ml)	[174,175]
<i>Cedrus deodara</i> (Leaves and peels)	34.4 mg/kg (rats)	-	-	<i>E. coli</i> (1.56 µg/ml) <i>S. aureus</i> (0.78 µg/ml) <i>B. subtilis</i> (0.39 µg/ml) <i>B. cereus</i> (0.78 µg/ml) <i>S. cerevisiae</i> (0.39 µg/ml) <i>A. niger</i> (0.78 µg/ml) <i>P. citrinum</i> (0.39 µg/ml) <i>R. oryzae</i> (0.20 µg/ml) <i>A. flavus</i> (0.20 µg/ml)	[36,176]
<i>Chenopodium ambrosioides</i>	100 mg/kg (mice)	3,7,10,25,40 mg/kg: Increase in liver index, a	-	<i>C. albicans</i> (1 mg/ml) <i>C. albicans</i> (2 mg/ml)	[38,177] [178]

(Aerial parts)		serum AST and ALT levels, and also induced distinct morphological changes in liver, heart, and kidney (mice - 27days)		<i>C. albicans</i> (1 mg/ml) <i>C. glabrata</i> (0.25 mg/ml) <i>C. guilliermondi</i> (0.25 mg/ml) <i>C. krusei</i> (1 mg/ml) <i>C. lusitaneae</i> (1 mg/ml)	
<i>Cinnamomum camphora</i> (Leaves)	2749 mg/kg (mice)	-	-	<i>Bacillus cereus</i> (625 µg/ml) <i>Propionibacterium acnes</i> (312.5 µg/ml) <i>Pseudomonas aeruginosa</i> (625 µg/ml) <i>Serratia marcescens</i> (625 µg/ml) <i>Staphylococcus aureus</i> (1250 µg/ml) <i>Streptococcus pyogenes</i> (625 µg/ml)	[39,179]
<i>Cinnamomum cassia</i> (Bark)	-	-	-	<i>B. cereus</i> (339 µg/ml) <i>E. coli</i> (2640 µg/ml) <i>L. monocytogenes</i> (2640 µg/ml) <i>S. infantis</i> (2640 µg/ml) <i>S. aureus</i> (1320 µg/ml)	[17]
<i>Citrus aurantifolia</i> (Peels of ripe fruits)	-	100-500 mg/kg: Mild hepatotoxic and nephrotoxic 4 deaths of 60 subjects (rats - 60 days)	-	<i>A. flavus</i> (560 µg/mL) <i>A. parasiticus</i> (1130 µg/mL)	[17,180]
<i>Citrus aurantium</i> (Zest of fruits and leaves)	4360 mg/kg (mice)	-	-	<i>S. aureus</i> (leaves: 1 v/v%) <i>B. subtilis</i> (leaves: 1 v/v% zest; 2 v/v%) <i>E. coli</i> (leaves: 2 v/v%)	[181,182]
<i>Citrus grandis</i> (Peels)	-	-	-	<i>B. subtilis</i> (9.38 µl/ml) <i>S. aureus</i> (9.38 µl/ml) <i>E. coli</i> (37.50 µl/ml) <i>P. chrysogenum</i> (4.69 µl/ml)	[183]
<i>Citrus hystrix</i> (Peels and leaves)	-	-	-	<i>P. gingivalis</i> (1.06 mg/ml) <i>S. sanguinis</i> (2.12 mg/ml) <i>S. mutans</i> (1.06 mg/ml)	[184]
<i>Citrus reticulata</i> (Peels and leaves)	4520 mg/kg (mice)	-	-	-	[182]
<i>Citrus sinensis</i> (Peels)	4040 mg/kg (mice)	-	-	<i>S. aureus</i> , <i>Penicillium chrysogenum</i> , <i>B. subtilis</i> , <i>E. coli</i> , and <i>S. cerevisiae</i> (4.66-18.75 µl/ml)	[182,185]
<i>Clausena lansium</i> (Leaves)	-	-	-	<i>S. aureus</i> (312.5 µg/ml) low antifungal activities in <i>Candida</i> spp.	[55,186]
<i>Cleistocalyx operculatus</i> (Leaves)	-	-	-	<i>B. cereus</i> (1250 µg/ml) <i>S. aureus</i> (625 µg/ml) <i>A. niger</i> (625 µg/ml) <i>C. albicans</i> (2500 µg/ml) <i>Candida</i> spp. (0.05–0.4% v/v)	[187]
<i>Coriandrum sativum</i> (Leaves and fruits)	1.53 ml/kg (mice)	-	-	<i>L. monocytogenes</i> (0.018–0.074% v/v) <i>M. tuberculosis</i> (97 µg/ml) <i>C. albicans</i> (no inhibition) <i>C. tropicalis</i> (no inhibition) <i>M. canis</i> (9 µg/ml)	[17,188]
<i>Croton argyrophylloides</i> (Leaves)	9.84 mg/kg (rats)	-	-	<i>C. albicans</i> (>5000 µg/ml) <i>C. tropicalis</i> (>2500 µg/ml) <i>M. canis</i> (620 µg/ml)	[60,189] [190,191]
<i>Croton zehntneri</i> (Leaves)	2500 mg/kg (rats)	-	250 mg/kg: No death but some changes (rats – 10 weeks)		[60,192] [193]

<i>Cuminum cyminum</i> (Seeds)	0.44 ml/kg (mice)	250,500 mg/kg: No significant changes were observed 1000 mg/kg: Increase of in ALT (rats - 23 and 45days)	-	<i>B. cereus</i> (0.05 µl/ml) <i>B. subtilis</i> (0.05 µl/ml or 1000 µg/ml)	[17,194] [188]
<i>Curcuma longa</i> (Rhizomes and stems)	> 5000 mg/kg (rats)	1000 mg/kg: No significant changes (rats - 28days)	500 mg/kg: No significant changes were observed (rats-13weeks)	<i>Microsporium gypsum</i> (459,6 µg/ml) <i>Epidermophyton floccosum</i> (229,8 µg/ml) <i>Trichophyton mentagrophytes</i> (114.9 µg/ml) <i>Trichophyton rubrum</i> (459.6 µg/ml)	[195,196]
<i>Cymbopogon citratus</i> (Leaves and stalks)	>2000 mg/kg (mice)	2000 mg/kg: Only changes body weights and a few changes in ALT and GI serum activity of GOT v lower (mice-21days)	-	<i>Bacillus subtilis</i> (163.25 µl/ml) <i>Enterococcus faecalis</i> (136.25 µl/ml) <i>Micrococcus luteus</i> (142.11 µl/ml) <i>Staphylococcus aureus</i> (135.42 µl/ml) <i>Pseudomonas aeruginosa</i> (174.18 µl/ml) <i>Yersinia enterocolitica</i> (156.24 µl/ml) <i>Serratia marcescens</i> (181.37 µl/ml) <i>Candida albicans</i> (245.18 µl/ml) <i>Candida krusei</i> (211.36 µl/ml) <i>Candida glabrata</i> (221.32 µl/ml) <i>Candida tropicalis</i> (226.25 µl/ml) <i>Salmonella enteritidis</i> (112.36 µl/ml) <i>Salmonella enteritidis</i> (181.25 µl/ml)	[197]
<i>Cymbopogon giganteus</i> (Leaves)	>2000 mg/kg (rats)	50,500 mg/kg: No toxic effects were observed (rats - 28days)	-	<i>E. faecalis</i> (6.7 mg/ml) <i>S. aureus</i> (2.1 mg/ml) <i>L. monocytogenes</i> (13.3 mg/ml) <i>E. aerogenes</i> (12 mg/ml) <i>E. coli</i> (6.3 mg/ml) <i>P. aeruginosa</i> (70 mg/ml) <i>S. enterica</i> (10 mg/ml) <i>S. typhimurium</i> (8.3 mg/ml) <i>S. dysenteriae</i> (25 mg/ml) <i>Staphylococcus aureus</i> (250 µg/ml) <i>Bacillus subtilis</i> (250 µg/ml) <i>Staphylococcus epidermidis</i> (125 µg/ml) <i>Streptococcus mutans</i> (500 µg/ml) <i>Klebsiella pneumoniae</i> (250 µg/ml) <i>Escherichia coli</i> (500 µg/ml) <i>Salmonella typhimurium</i> (250 µg/ml)	[198,199]
<i>Cymbopogon martini</i> (Leaves)	>5000 mg/kg (mice)	500,1000 mg/kg: No toxicity or mortality (mice-28days)	-	<i>Staphylococcus aureus</i> (250 µg/ml) <i>Bacillus subtilis</i> (250 µg/ml) <i>Staphylococcus epidermidis</i> (125 µg/ml) <i>Streptococcus mutans</i> (500 µg/ml) <i>Klebsiella pneumoniae</i> (250 µg/ml) <i>Escherichia coli</i> (500 µg/ml) <i>Salmonella typhimurium</i> (250 µg/ml) <i>Staphylococcus aureus</i> (2.63 mg/ml) <i>Escherichia coli</i> (2.63 mg/ml)	[68,200]
<i>Cymbopogon schoenanthus</i> (Aerial parts)	>2000 mg/kg (mice)	10, 100, and 200 mg/kg: - Some changes in liver weight Significant changes in urea, glucose, and potassium, at high doses some changes happen the liver and kidney (mice - 28days)	-	<i>Staphylococcus aureus</i> (2.63 mg/ml) <i>Escherichia coli</i> (2.63 mg/ml)	[67,201]
<i>Cymbopogon winterianus</i>	5.81 g/kg (male mice)	-	-	<i>Bacillus cereus</i> (2 µl/ml) <i>Escherichia coli</i> (6 µl/ml)	[174,202]

(Leaves)	17.42 g/kg (female mice)			<i>Micrococcus luteus</i> (2 µl/ml) <i>Proteus mirabilis</i> (6 µl/ml) <i>Salmonella enteritidis</i> (4 µl/ml) <i>Staphylococcus aureus</i> (2 µl/ml)	
<i>Cyperus rotundus</i> (Rhizomes)	5000 mg/kg (mice)	-	-	<i>S. aureus</i> (10 mg/ml) <i>S. epidermidis</i> (20 mg/ml) <i>B. subtilis</i> (10 mg/ml) <i>S. typhimurium</i> (40 mg/ml) <i>E. coli</i> (>40 mg/ml) <i>S. dysenteriae</i> (40 mg/ml)	[203,204]
<i>Daucus carota</i> (Seeds)	-	-	-	Gram-positive (0.32–0.64 µl/ml) <i>Cryptococcus neoformans</i> (0.16 µl/ml) Dermatophytes (0.32–0.64 µl/ml)	[205]
<i>Eucalyptus camaldulensis</i> (Leaves)	-	-	-	<i>S. aureus</i> (1500 ppm) <i>coli</i> (1500 ppm) <i>Acinetobacter baumannii</i> (1000 ppm) <i>Proteus vulgaris</i> (2500 ppm)	[206]
<i>Eucalyptus globulus</i> (Leaves)	1650 mg/kg (mice)	1000 mg/kg: No significant changes were observed (mice - 28days)	-	<i>E. tarda</i> (7,812 µg/ml) <i>V. ichthyenteri</i> (125,000 µg/ml) <i>V. harveyi</i> (7,812 µg/ml) <i>P. damsela</i> (31,248 µg/ml) <i>S. infantis</i> (31,248 µg/ml) <i>S. paratyphus</i> (15,624 µg/ml) <i>L. garosiae</i> (31,248 µg/ml)	[207,208]
<i>Eugenia florida</i> (Leaves)	-	-	-	<i>Candida albicans</i> (500 µg/ml) <i>Candida krusei</i> (500 µg/ml) <i>Candida glabrata</i> (500 µg/ml) <i>Candida parapsilosis</i> (500 µg/ml) <i>Staphylococcus aureus</i> (500 µg/ml) <i>Escherichia coli</i> (1000 µg/ml)	[209]
<i>Eupatorium</i> <i>adenophorum</i> (Aerial parts)	-	-	-	<i>Klebsiella pneumoniae</i> (0.40 µl/ml) <i>Staphylococcus aureus</i> (0.05 µl/ml) <i>Pseudomonas aeruginosa</i> (0.10 µl/ml) <i>Xanthomonas oryzae</i> (0.10 µl/ml) <i>Erwinia chrysanthemi</i> (0.10 µl/ml)	[83]
<i>Ferula assa-foetida</i> (Seeds)	-	-	-	<i>S. typhi</i> (0.093 mg/ml) <i>E. coli</i> (0.111 mg/ml) <i>S. aureus</i> (0.032 mg/ml) <i>B. subtilis</i> (0.027 mg/ml) <i>A. niger</i> (0.036 mg/ml) <i>C. albicans</i> (0.028 mg/ml)	[85]
<i>Ferula macrocarpa</i> (Aerial parts)	1.79 ml/kg (mice)	0.1, 0.2, 0.4, 0.6 ml/kg: No significant change was observed (mice - 28days)	-	<i>C. albicans</i> ATCC 5027 (1.6 µg/ml) <i>C. albicans</i> ATCC 76616 (3.3 µg/ml)	[210,211]
<i>Foeniculum vulgare</i> (Seeds)	1.038 ml/kg (mice)	-	-	<i>E. coli</i> (0.781 µl /ml) <i>P. aeruginosa</i> (25 µl /ml) <i>A. flavus</i> (0.125 µl /ml) <i>A. niger</i> (0.125 µl /ml) <i>M. canis</i> (<0.0625 µl /ml) <i>S.aureus</i> (0.781 µl /ml)	[188,212]
<i>Gnaphalium affine</i> (Aerial parts)	-	-	-	<i>E. coli</i> (1.56 µg/ml) <i>S. aureus</i> (0.39 µg/ml) <i>B. subtilis</i> (0.78 µg/ml) <i>B. cereus</i> (0.78 µg/ml) <i>B. laubach</i> (0.78 µg/ml) <i>S. typhimurium</i> (0.78 µg/ml) <i>S. cerevisiae</i> (0.20 µg/ml) <i>A. niger</i> (0.20 µg/ml) <i>P. citrinum</i> (0.20 µg/ml) <i>R. oryzae</i> (0.20 µg/ml)	[213]

<i>Hedychium spicatum</i> (Rhizomes)	-	-	-	<i>A. flavus</i> (0.20 µg/ml) <i>Staphylococcus aureus</i> (15.6 µl/ml) [214] <i>Pasteurella multocida</i> (31.3 µl/ml) <i>Escherichia coli</i> (15.6 µl/ml) <i>Salmonella enterica</i> (7.8 µl/ml)
<i>Heracleum sphondylium</i> (Aerial parts)	-	-	-	<i>E. coli</i> (>44.8 mg/ml) [91] <i>P. aeruginosa</i> (22.4 mg/ml) <i>S. enteritidis</i> (>44.8 mg/ml) <i>Bacillus cereus</i> (1.39 mg/ml) <i>L. monocytogenes</i> (11.2 mg/ml) <i>S. aureus</i> (11.2 mg/ml) <i>C. albicans</i> (22.4 mg/ml)
<i>Hyptis suaveolens</i> (Leaves)	-	-	-	<i>S. aureus</i> (3.12 mg/ml) [215] <i>P. aeruginosa</i> (12.5 mg/ml)
<i>Juniperus communis</i> (Cones and leaves)	-	-	-	<i>Staphylococcus aureus</i> (125 µl/ml) [97,216] <i>Streptococcus pyogenes</i> (125 µl/ml) <i>Streptococcus agalactiae</i> , <i>Haemophilus influenzae</i> , <i>Corynebacterium spp.</i> <i>Campylobacter jejuni</i> (>500 µl/ml)
<i>Lavandula angustifolia</i> (Flowers and leaves)	>2 g/kg (mice)	2000 mg/kg: No significant changes were observed (mice – 21days)	-	<i>Bacillus cereus</i> (3 mg/ml) [217,218] <i>Enterococcus faecalis</i> (2 mg/ml) <i>Listeria monocytogenes</i> (1 mg/ml) <i>Staphylococcus aureus</i> (2 mg/ml) <i>Streptococcus pyogenes</i> (1 mg/ml) <i>Escherichia coli</i> (1 mg/ml) <i>Klebsiella pneumoniae</i> (1.5 mg/ml) <i>Proteus mirabilis</i> (2 mg/ml) <i>Pseudomonas aeruginosa</i> (0.5 mg/ml) <i>Salmonella enteritidis</i> (1.5 mg/ml) <i>Candida albicans</i> (0.75 mg/ml) <i>Cryptococcus neoformans</i> (0.75 mg/ml) <i>Microsporium canis</i> (0.5 mg/ml) <i>Microsporium gypseum</i> (0.25 mg/ml) <i>Trichophyton mentagrophytes</i> (0.5 mg/ml) <i>Trichophyton rubrum</i> (0.5 mg/ml) <i>Aspergillus fumigatus</i> (1 mg/ml) <i>Aspergillus niger</i> (2 mg/ml) <i>Fusarium oxysporum</i> (1 mg/ml) <i>Penicillium citrinum</i> (1 mg/ml)
<i>Lippia gracilis</i> (Leaves)	4000 mg/kg (mice)	-	-	<i>F. oxysporum</i> (0.625 mg/ml) [101,219] <i>F. solani</i> (0.625 mg/ml) <i>C. gloeosporioides</i> (0.31 mg/ml) <i>C. lindemuthianum</i> (0.31 mg/ml)
<i>Lippia origanoides</i> (Leaves and stems)	3500 mg/kg (mice)	120 mg/kg: No detectable toxic effects a significant char in mean corpuscular volume (MCV) (rats - days)	-	<i>E. coli</i> (5.263 mg/ml) [220] <i>S. aureus</i> (1.316 mg/ml) [102,221] <i>P. aeruginosa</i> (5.263 mg/ml) <i>C. albicans</i> (2.631 mg/ml) <i>C. parapsilosis</i> (2.631 mg/ml)
<i>Litsea elliptica</i> (Leaves)	3488.86 mg/kg (rats)	125, 250, 500 mg/kg: No significant change was observed (rats-28days)	-	- [222]
<i>Matricaria chamomilla</i> (Leaves)	-	-	-	<i>B. cereus</i> (4 µg/ml) [223] <i>E. faecalis</i> (4 µg/ml) <i>E. coli</i> (4 µg/ml) <i>L. innocua</i> (2 µg/ml)

				<i>S. enterica</i> (2 µg/ml) <i>S. dysenteriae</i> (1 µg/ml) <i>S. aureus</i> (2 µg/ml) <i>S. camorum</i> (2 µg/ml) <i>P. mirabilis</i> (4 µg/ml) <i>Bacillus subtilis</i> (18.36 µg/ml) [224,225] <i>Enterococcus faecalis</i> (18.45 µg/ml) <i>Micrococcus luteus</i> (18.68 µg/ml) <i>Staphylococcus aureus</i> (14.26 µg/ml) <i>Pseudomonas aeruginosa</i> (12.32 µg/ml) <i>Yersinia enterocolitica</i> (15.46 µg/ml) <i>Salmonella enterica</i> (16.36 µg/ml) <i>Serratia marcescens</i> (16.24 µg/ml) <i>Pseudomonas fluorescens</i> (28.5 µg/ml) 9 <i>Salmonella enterica</i> (25.43 µg/ml) <i>Candida albicans</i> (26.76 µg/ml) <i>Candida glabrata</i> (29.85 µg/ml) <i>Candida krusei</i> (26.32 µg/ml) <i>Candida tropicalis</i> (27.46 µg/ml)
<i>Melaleuca alternifolia</i> (Leaves)	1.9–2.6 ml/kg (rats)	-	-	
<i>Melaleuca leucadendron</i> (Twigs and flowers)	-	-	-	<i>B. spizizenii</i> (4 µg/ml) [109] <i>S. aureus</i> (8 µg/ml) <i>E. aerogenes</i> (4 µg/ml) <i>E. coli</i> (4 µg/ml) <i>K. pneumoniae</i> (4 µg/ml) <i>P. aeruginosa</i> (8 µg/ml) <i>S. enterica</i> (8 µg/ml)
<i>Melissa officinalis</i> (Leaves)	>2000 mg/kg (mice)	-	100,200mg/kg The kidney has modifications, decrease in glucose, increase in urea in high doses (mice-3month)	<i>S. aureus</i> (3 µl/ml) [110,226] <i>B. subtilis</i> (2 µl/ml) <i>P. aeruginosa</i> (2 µl/ml) <i>E. coli</i> (2 µl/ml) <i>S. enterica</i> (5 µl/ml) <i>C. albicans</i> (3 µl/ml)
<i>Mentha longifolia</i> (Flowers, leaves, and stems)	470 mg/kg (rats)	-	-	<i>Salmonella typhimurium</i> [17,227] (1560 µg/ml) <i>E. coli</i> (780 µg/ml) <i>Micrococcus luteus</i> (190 µg/ml) <i>S. aureus</i> (780 µg/ml)
<i>Mentha mozaffarianii</i> (Leaves and fruits)	>2000 mg/kg (mice and rats)	100 mg/kg: Significant increases in blood glucose, cholesterol, ALT, AST, ALP, and TSH microscopic lesions in some organs were observed 200 mg/kg: Some of the animals died on the 5th day (rats - 28days)	-	<i>Bacillus subtilis</i> (1.87 mg/ml) [114,228] <i>B. pumilus</i> (1.87 mg/ml) <i>Enterococcus faecalis</i> (15 mg/ml) <i>Staphylococcus aureus</i> (7.5 mg/ml) <i>Staphylococcus epidermidis</i> (7.5 mg/ml) <i>Escherichia coli</i> (15 mg/ml) <i>Candida albicans</i> (10 mg/ml)
<i>Mentha piperita</i> (Aerial parts)	1612.45 mg/kg (mice)	-	-	<i>S. aureus</i> (1 µl/ml) [229,230] <i>S. epidermidis</i> (1 µl/ml) <i>S. saprophyticus</i> (1 µl/ml) <i>S. pneumoniae</i> (1 µl/ml) <i>E. coli</i> (1 µl/ml)

<i>Mentha pulegium</i> (Aerial parts)	>5000 mg/kg (rats)	-	-	<i>E. aerogenes</i> (0.25 µl/ml) <i>C. albicans</i> (0.125 µl/ml) <i>Salmonella typhimurium</i> (3.8 mg/ml) [117,231] <i>Escherichia coli</i> (3.2 mg/ml) <i>Listeria innocua</i> (1.8 mg/ml) <i>Listeria monocytogenes</i> (2.6 mg/ml) <i>Brochothrix thermosphacta</i> (0.8 mg/ml) <i>Pseudomonas putida</i> (1.3 mg/ml) <i>Enterococcus faecalis</i> (0.25% v/v) [232] <i>Escherichia coli</i> (0.06% v/v) <i>Streptococcus pyogenes</i> (0.06% v/v) <i>Klebsiella pneumoniae</i> (0.06% v/v) <i>Staphylococcus aureus</i> (0.125% v/v) <i>Pseudomonas aeruginosa</i> (0.25% v/v) <i>Candida albicans</i> (1 % v/v) <i>Meyerozyma caribbica</i> (0.125% v/v) <i>Saccharomyces cerevisiae</i> (0.125% v/v)
<i>Monarda citriodora</i> (Aerial parts)	-	-	-	<i>S. aureus</i> (3.0 mg/ml) [233,234] <i>E. coli</i> (3.5 mg/ml) <i>K. pneumonia</i> (2.5 mg/ml) <i>S. typhi</i> (3.0 mg/ml) <i>Staphylococcus aureus</i> (1.32 mg/ml) [235,236] <i>Acinetobacter baumannii</i> (2.64 mg/ml) <i>Staphylococcus epidermis</i> (6.6 mg/ml)
<i>Monodora myristica</i> (Seeds)	316 mg/kg (mice)	-	-	<i>M.luteus</i> (2000 µg/ml) [122,237] <i>E.coli</i> (1500 µg/ml) <i>S.aureus</i> (3100 µg/ml) <i>B.subtilis</i> (1600 µg/ml) <i>P.neumnae</i> (2500 µg/ml)
<i>Myrtus communis</i> (Leaves)	1000 mg/kg (mice)	-	-	<i>Streptococcus mutans</i> (5 mg/ml) [123] <i>Streptococcus pyogenes</i> (5 mg/ml) <i>Staphylococcus aureus</i> (10 mg/ml) <i>Enterococcus faecalis</i> (10 mg/ml) <i>Escherichia coli</i> (10 mg/ml) <i>Klebsiella pneumoniae</i> (10 mg/ml) <i>Salmonella enterica</i> (10 mg/ml) <i>Shigella flexneri</i> (10 mg/ml) <i>Pseudomonas aeruginosa</i> (10 mg/ml) <i>Candida albicans</i> (5 mg/ml) <i>Candida parapsilosis</i> (5 mg/ml) [124] <i>Bacillus cereus</i> (5.62 µg/ml) <i>Bacillus subtilis</i> (1.40 µg/ml) <i>Listeria monocytogenes</i> (5.62 µg/ml) <i>Staphylococcus aureus</i> (1.40 µg/ml) <i>Staphylococcus epidermidis</i> (11.25 µg/ml) <i>Lactobacillus plantarum</i> (1.40 µg/ml) <i>Lactobacillus sakei</i> (1.40 µg/ml) <i>Micrococcus luteus</i> (1.40 µg/ml)
<i>Nardostachys jatamansi</i> (Roots)	>3160 mg/kg (mice)	-	-	
<i>Nepeta faassenii</i> (Flowers, leaves, and stems)	-	-	-	
<i>Nepeta sintenisii</i> (Aerial parts)	-	-	-	

				<i>Salmonella typhi</i> (1.40 µg/ml) <i>Escherichia coli</i> E. coli (22.50 µg/ml) <i>Candida albicans</i> (<0.35 µg/ml) <i>S.aureus</i> (18 µg/ml) [238,239] <i>B.cereus</i> (18 µg/ml) <i>E.coli</i> (9 µg/ml) <i>P.aeruginosa</i> (9 µg/ml)
<i>Ocimum basilicum</i> (Aerial parts)	3.64 ml/kg (mice)	-	-	<i>Staphylococcus aureus</i> [240,241] (0.75 µg/ml) <i>Shigella flexineri</i> (3 µg/ml) <i>Salmonella enteritidis</i> (3 µg/ml) <i>Escherichia coli</i> (6 µg/ml) <i>Klebsiella sp.</i> (6 µg/ml) <i>Proteus mirabilis</i> (12 µg/ml) <i>Pseudomonas aeruginosa</i> (≥24 µg/ml)
<i>Ocimum gratissimum</i> (Leaves)	intra-peritoneal: 0.27 g/kg (mice) 0.43 g/kg (rats) oral: 1.41 g/kg (mice) 2.29 g/kg (rats)	80, 133, 213 mg/kg: Some significant changes in behaviour, enlargement in some organs, increase in weight, some changes in brain and liver (rats - 30days)	-	<i>P. aeruginosa</i> (1% v/v) [17,242] <i>S. aureus</i> (0.031% v/v) <i>E. coli</i> (0.625 µl/ml) [17,243] <i>P. aeruginosa</i> (1648 µg/ml) <i>S. aureus</i> (0.6 µL/mL or 575 µg/ml) Three <i>Candida</i> spp. (10–20 µl/ml)
<i>Origanum compactum</i> (Aerial parts)	>5000 mg/kg (rats)	-	-	<i>S.aureus</i> (500 µg/ml) [244,245] <i>S.epidermidis</i> (500 µg/ml) <i>B.subtilis</i> (250 µg/ml) <i>Sh.dysenteriae</i> (250 µg/ml) <i>P.aeruginosa</i> (62.5 µg/ml) <i>E.coli</i> (125 µg/ml) <i>C.albicans</i> (500 µg/ml)
<i>Origanum vulgare</i> (Leaves)	-	-	50, 100, 200 mg/kg: Some significant changes (rats - 90days)	<i>C. albicans</i> (10 µg/ml) [17,246] <i>Saccharomyces cerevisiae</i> (5 µg/ml) <i>B. subtilis</i> (10 µg/ml) <i>E. coli</i> (0.1% v/v or 40 µg/ml) <i>S. aureus</i> (0.1% v/v or 20 µg/ml)
<i>Rosa damascena</i> (Flowers)	350 mg/kg (mice)	-	-	<i>K. pneumoniae</i> (12.5 µl/ml) [247] <i>K. oxytoca</i> (3.125 µl/ml) <i>Acinetobacter</i> spp. (0.78 µl/ml) <i>S. aureus</i> (3.125 µl/ml) <i>E. coli</i> (6.25 µl/ml) <i>Staphylococcus</i> spp. (6.25 µl/ml) <i>P. mirabilis</i> , <i>S. pyogenes</i> , <i>Enterobacter</i> spp. And <i>Enterococcus</i> spp. (12.5 µl/ml) <i>P. aeruginosa</i> (50 µl/ml)
<i>Rosmarinus officinalis</i> (Leaves)	>2000 mg/kg (mice)	1000-2000 mg/kg: Only changes in body weights no histopathologic changes (mice - 28days)	-	<i>Escherichia coli</i> (720 µg/ml) [138,248] <i>Klebsiella pneumoniae</i> (540 µg/ml) <i>Salmonella typhimurium</i> (360 µg/ml) <i>Pseudomonas aeroginaosa</i> (1080 µg/ml) <i>Listeria monocytogenes</i> (270 µg/ml) <i>Streptococcus pneumoniae</i> (360 µg/ml) <i>Staphylococcus aureus</i> (360 µg/ml) <i>Bacillus cereus</i> (540 µg/ml) <i>Bacillus subtilis</i> (540 µg/ml) <i>Candida albicans</i> (180 µg/ml) <i>Candida tropicalis</i> (270 µg/ml)
<i>Satureja hortensis</i> (Aerial parts)	-	-	-	
<i>Satureja khuzestanica</i> (Aerial parts)	1.79 ml/kg (mice)	0.2,0.4,0.6 ml/kg: No significant toxicity on the liver and kidney tissues as well as on the haematological parameters in the mice (mice - 28days)	-	

				<i>Rhodotorula rubra</i> (130 µg/ml) <i>Rhodotorula mucilaginosa</i> (90 µg/ml) <i>C. albicans</i> (5 µg/ml) [17] <i>S. cerevisiae</i> (5 µg/ml) <i>E. coli</i> (0.05% v/v or 40 µg/ml) <i>S. Typhimurium</i> (0.05% v/v) <i>S. aureus</i> (0.013% v/v or 5 µg/ml) <i>L. monocytogenes</i> (0.05% v/v)
<i>Satureja montana</i> (Aerial parts)	-	-	-	<i>C. jejuni</i> (0.05% v/v) [17] <i>E. coli</i> (0.04% v/v) <i>L. monocytogenes</i> (0.03% v/v) <i>S. enteritidis</i> (0.04% v/v) <i>S. aureus</i> (0.04% v/v)
<i>Syzygium aromaticum</i> (Flowers)	-	-	-	<i>S. aureus</i> (5.29 µg/ml) [249] <i>E. coli</i> (10.57 µg/ml) <i>S. infantis</i> (10.57 µg/ml)
<i>Tagetes elliptica</i> (Leaves)	-	-	-	<i>S. aureus</i> (20.83 µg/ml) [144] <i>K. pneumonia</i> (41.67 µg/ml) <i>P. aeruginosa</i> (93.33 µg/ml) <i>X. oryzae</i> (83.38 µg/ml)
<i>Tagetes erecta</i> (Leaves and flowers)	-	-	-	<i>Citrobacter amalonaficus</i> (25 µl/ml) [145,250] <i>Proteus vulgaris</i> (20 µl/ml) <i>Serratia marcescens</i> (25 µl/ml) <i>Enterobacter aerogenes</i> (38 µl/ml) <i>Staphylococcus aureus</i> (8 µl/ml) <i>Staphylococcus subtilis</i> (4 µl/ml) <i>Bacillus megaterium</i> (20 µl/ml) <i>Bacillus cereus</i> (16 µl/ml)
<i>Tanacetum parthenium</i> (Flowers and leaves)	2130 mg/kg (rats)	1000 mg/kg: No significant changes (rats-28days)	-	<i>Tricophyton spp.</i> [147,251] <i>Microsporum spp.</i> (0.08 µl/ml to 0.31 µl/ml)
<i>Thymus schimperi</i> (Flowers and leaves)	1284.2 mg/kg (rats)	65, 130,260 mg/kg: A significant decrement WBC counts and a significant increase of MCV in high dose (260 mg/kg) (rats - 28days)	-	<i>C. albicans</i> (1 µg/ml) [17,252] <i>E. coli</i> (0.05% v/v or 2 µg/ml) <i>L. monocytogenes</i> (0.02% v/v) <i>S. aureus</i> (0.02% v/v or 5 µg/ml) <i>C. jejuni</i> (0.04% v/v) <i>B. subtilis</i> (2 µg/ml) <i>S. enteritidis</i> (0.04% v/v)
<i>Thymus vulgaris</i> (Leaves)	2000 mg/kg (rats)	100,250 mg/kg: No significant changes 500 mg/kg: severe changes in the lung (rats - 28days)	-	<i>Bacillus cereus</i> (2 µl/ml) [253,254] <i>Enterococcus faecalis</i> (2 µl/ml) <i>Staphylococcus aureus</i> (0.5 µl/ml) <i>Pseudomonas aeruginosa</i> (4 µl/ml) <i>Escherichia coli</i> (0.5 µl/ml) <i>Candida albicans</i> (0.5 µl/ml) <i>Aspergillus flavus</i> (0.5 µl/ml)
<i>Trachyspermum ammi</i> (Fruits)	2294 mg/kg (rats)	1000 mg/kg: No significant change (rats -23 and -45days)	-	<i>B. subtilis</i> (890 µg/ml) [152,255] <i>S. aureus</i> (219 µg/ml) <i>E. coli</i> (219 µg/ml) <i>S. typhimurium</i> (44.5 µg/ml) <i>B. subtilis</i> (445-890 µg/ml) <i>M. flavus</i> (445 µg/ml) <i>A. alternata</i> (44.5-130 µg/ml) <i>T. viride</i> (219-267 µg/ml)
<i>Vitex agnus</i> (Leaves and fruits)	> 5000 mg/kg (mice)	1000, 2000, 3000,5000 mg/kg: No significant change (mice - 28days)	-	<i>Staphylococcus aureus</i> (>64 µg/ml) [256,257] <i>Escherichia coli</i> (64 µg/ml) <i>Pseudomonas aeruginosa</i> (>64 µg/ml)
<i>Vitex negundo</i> (Leaves)	>2000 mg/kg (rats)	-	250, 500, 1000 mg/kg: No significant change	

			(rats-13weeks)	<i>Streptococcus faecalis</i> (>64 µg/ml) <i>Micrococcus catarrhalis</i> (>64 µg/ml) <i>Candida albicans</i> (4 µg/ml) <i>Cryptococcus neoformans</i> (64 µg/ml) <i>Candida parapsilosis</i> (>64 µg/ml) <i>Candida tropicalis</i> (>64 µg/ml) <i>Trichophyton rubrum</i> (32 µg/ml) <i>Fonsecaea compacta</i> (>64 µg/ml) <i>Microsporium gypseum</i> (64 µg/ml) <i>Aspergillus fumigatus</i> (64 µg/ml) <i>S. aureus</i> (0.25 mg/ml) <i>S. epidermidis</i> (0.5 mg/ml) <i>E. faecalis</i> (1.0 mg/ml)	[162,258]
<i>Zingiber officinale</i> (Rhizomes)	8660 mg/kg (mice)	-	-		

*MIC: Minimum inhibitory concentrations ** Reference

Sub-acute: All data obtained from articles which toxicity researches performed in the range of 20 - 30 days

Chronic: All data obtained from articles which toxicity researches performed in approximately 90 days and more

3. DISCUSSION

Essential oils are natural gifts with various applications in different industries. They are widely used in the food industry due to their biological effects, such as antimicrobial, antioxidant, and anti-aflatoxin properties. The toxicity of essential oils should be thoroughly considered, particularly in relation to their application as food preservatives. The molecular interactions of essential oils with pathogens should be explored to understand the mechanism of action of volatile oils as antimicrobial agents.

3.1 Molecular interaction

Studies on the antimicrobial activity of essential oils indicate that these materials target oxidative pathways in bacteria because, after exposure to bacterial cells, they produce many more oxidative stress-sensitive proteins such as glycyl radical cofactor, catalase-peroxidase, DNA mismatch repair protein, clpB, btpG, and luxS. These changes indicate that oxidative stress in cells is increased, resulting in membrane lipid peroxidation, which leads to cell content leakage and, eventually, the cells' death. In addition, the increase in oxidative stress causes damage to proteins and genetic structures and removes the ability of bacteria to recover. [259] Essential oils have an anti-aflatoxigenic effect by affecting parts of the fungi gene and inhibiting or reducing the gene's transcription. [42,260]

Terpenes such as p-cymene have a hydrocarbon structure without an influential functional group, and when used alone, they have a negligible antimicrobial effect. p-Cymene is one of the most abundant compounds in essential oils. This compound attaches firmly to the membrane, making it uneven and causing a change in its enthalpy and melting temperature. By affecting the membrane potential, it changes the movement of flagellated cells because their movement depends on the membrane potential and protons of the cell.[8,17,25]

The aldehyde group of cinnamaldehyde can covalently bond with DNA proteins and disrupt their normal function, but it has three forms for its antimicrobial effect. At low doses, it interferes with the cell's cytokinesis and with less essential enzymes and disrupts its division. At sublethal doses, it affects ATPase enzymes; at high and lethal doses, it causes damage to the membrane. In fungi, it interferes with division by having a non-competitive inhibitory effect on the enzymes required to build the wall. [8,17,25]

Terpenoids, which have a structure similar to terpenes, have oxygenated and phenolic groups that are essential for their antimicrobial effects. Thymol is a monoterpenoid that interacts with the inner and outer membranes, changes the permeability, and causes ions and cell compounds to leak. Some changes in the membrane lipid profile occur at concentrations that are not immediately lethal to the cell, known as sublethal concentrations. By interacting with the outer membrane proteins, thymol changes its shape. Its effect on citrate metabolism and enzymes involved in ATP production reduces the cell's ability to recover. Interference with the outer membrane causes the release of lipopolysaccharides, which can also cause the growth of gram-negative bacteria. In yeast and fungi, thymol induces cell lysis in proliferating cells and causes Ca²⁺ bursts, similar to those during stress and nutrient starvation. Thymol in yeast causes a disturbance in the pH gradient, regardless of the glucose level and leakage of ions. [8,17,22,25]

3.2 Main compounds of essential oils

Since phytochemicals in essential oils play an important role in their biological effects, we tabulated their dominant ingredients. We extracted the dominant compounds from the plants with MIC values of $\mu\text{g/ml}$. These plants included *Bowsellia papyrifera*, *Bunium persicum*, *Cedrus deodara*, *Matricaria chamomilla*, *Melaleuca altemifolia*, *Melaleuca leucadendron*, *Nepeta sintenisii*, *Ocimum gratissimum*, *Satureja montana*, *Tagetes elliptica*, and *Thymus vulgaris*. The main phytochemicals in the mentioned plants were α -terpineol, β -terpineol, γ -terpineol, and terpene-4-ol.

Considering the data gathered in Table 2, the efficacy of terpeneol cannot be denied. For instance, in two plants' essential oils, *Myrtus communis* and *Melaleuca leucadendron*, 1,8-cineole was predominant. Still, in *Melaleuca leucadendron*, the second substance was terpeneol, and the MIC value of *Melaleuca leucadendron* was a thousand times less than that of *Myrtus communis*, which shows the efficacy of terpeneol as an antimicrobial substance. Terpeneol is a monoterpeneol, and as discussed in the mechanism of action, the alcohol group of its structure is key to its antimicrobial activity.[17]

Of these 11 plants, β -farnesene was present in two plants, which showed high antimicrobial activity in MIC tests. β -Farnesene belongs to a terpene family named sesquiterpenes, and as stated in the mechanism of action, terpenes show better activity against gram-positive bacteria than against gram-negative bacteria. β -farnesene showed great antimicrobial activity against both, but it had a higher inhibitory activity against gram-positive bacteria.

Satureja montana and *Thymus vulgaris* are two plants whose main compounds are thymol and carvacrol. Both are monoterpeneols with similar structures. They differed only in the location of the alcohol group. Similar to terpeneol, the chemical group is key to its antimicrobial activity. There is a lack of studies on chemicals such as tagetenone, which comprises most essential oils with a high MIC value. Studying their structure and mechanism of action can improve our understanding of the potential antimicrobial activity of essential oils.

Of these 14 essential oils, terpeneol and its isomers were present in seven. As discussed previously, terpeneol shows promise as an antimicrobial agent. However, it was also present in half of the essential oils, which showed some toxicity in the animal tests. This highlights the need for more studies on its possible toxic effects and underscores its potential as a key area for future antimicrobial research.

Three of these essential oils contained p-cymene, all of which showed signs of toxicity. However, a recent study [261] found no adverse toxic effects of p-cymene. This underscores the need for further research on the potentially toxic effects of p-cymene, which could provide valuable insights into the safety of essential oils. Six of these essential oils, either alone or together, contained thymol, carvacrol, menthone, and limonene, which have similar basic structures. This raises the possibility of toxicity, especially because some studies have shown that thymol causes cellular damage. [262]

Among the phytochemicals mentioned above, the toxicity of eugenol has been extensively studied, and studies have indicated the risk of using eugenol. Some health-threatening evidence has been observed in some cases, such as cytotoxicity and genotoxicity. [263]

3.3 Potential toxicity of essential oils

Based on the information presented in Table 3, the essential oils of eight plants, *Acorus calamus*, *Cedrus deodara*, *Chenopodium ambrosioides*, *Cuminum cyminum*, *Foeniculum vulgare*, *Mentha longifolia*, *Monodora myristic* and *Rosa damascena*, had an LD_{50} value of less than 1 g/kg, indicating their potency to be toxic. Those for whom sub-acute toxicity was performed showed the same toxic potency. Several essential oils showed concernable toxicity on subacute tests, which are *Ageratum conyzoides*, *Chenopodium ambrosioides*, *Citrus aurantifolia*, *Thymus vulgaris*, *Bunium persicum*, *Thymus schimperi*, and *Ocimum gratissimum*. However, despite the toxicity, only *Cedrus deodara*, *Thymus vulgaris*, *Bunium persicum*, and *Ocimum gratissimum* showed exceptional MIC values in the range of $\mu\text{g/ml}$, and the MIC values of others were in the range of mg/ml.

3.4 Biologically-active compounds of essential oils

Table 4 shows the dominant components of the essential oils, which could be responsible for their pharmacological activities and toxicity.

Table 4. Biologically active compounds of essential oils

Compound name	Type of the compound	Functional groups	Properties	Toxicity	References
Limonene	Monocyclic monoterpene	Ketone	Antibacterial, antifungal, antiviral, and antioxidant	LD ₅₀ : 5200 mg/kg (Rat) Carcinogenic properties in animals Safe in terms of mutagenicity	[264-267]
p-Cymene	Monocyclic monoterpene Alkyl isoprenoid aromatic	Aromatic	Antimicrobial, antitumor antioxidant, antidiabetic anti-aflatoxin, and anti-inflammatory	LD ₅₀ : 4750 mg/kg (Rat)	[261,268] [269,270]
γ-Terpinene	Aromatic monoterpene	-	Antimicrobial, antioxidant, and anti-inflammatory	LD ₅₀ : >2000 mg/kg (Rat)	[270-272]
Linalool	Alcoholic and aromatic monoterpene	Hydroxyl	Antimicrobial, antioxidant, anti-inflammatory, and antiparasitic feature against Plasmodium and Leishmania	LD ₅₀ : 2790 mg/kg (Rat)	[270,273,274]
Thymol	Monoterpenoid phenol with an alcoholic structure	Aromatic and Hydroxyl	Antibacterial, antifungal, antioxidant, anti-carcinogenesis, anti-aflatoxigenic, and anti-inflammatory	LD ₅₀ : 980 mg/kg (Rat)	[270,275,276]
Caryophyllene	Bicyclic sesquiterpene	-	Antimicrobial, antioxidant, and anti-inflammatory	LD ₅₀ : >5000 mg/kg (Rat)	[277-279]
1,8-Cineole	Saturated monoterpene	Ether	Bactericidal, anti-bacterial, anti-inflammatory, anti-oxidative, and anti-cancer	LD ₅₀ : 2480 mg/kg (Rat)	[280-283]

3.5 Investigating plant families that are abundantly mentioned in Table 2

The plants listed in Tables 2 and 3 belong to different plant families. The Lamiaceae, Asteraceae, Apiaceae, Myrtaceae, and Rutaceae families are seen more frequently than other plant families. We examined these plant families in Table 5.

Table 5. Important plant families, their characteristics, properties, and toxicity

Plants family	Properties	Important plants of mentioned family	Useful characteristics	Toxicity	Reference
Lamiaceae	236 Genera 7,000 species	Basil, mint, sage, savory, oregano, thyme, and lavender	Anti-inflammatory, analgesic, anti-bacterial, antioxidant, antimicrobial, antimalarial, anticancer	Not show much toxicity	[284-286]
Asteraceae	1,500 Genera 20,000 species	Yarrow, chicory, sunflower, st. john's wort, and roman chamomile	Antioxidant, anti-inflammatory, antimicrobial, anti-mutagenic	Not show much toxicity	[287]
Apiaceae	400 Genera 3,700	Carrots, celery,	Anti-tumor,	Not show much	[288,289]

	species	parsley, anise, fennel, dill, cumin, black cumin, and chives	antimicrobial, anti-inflammatory, analgesic, antioxidant, antifungal	toxicity minor changes in chronic and sub-chronic toxicity	
Myrtaceae	150 Genera 5,800 species	Myrtle, eucalyptus, syzygium, eugenia, clove, feijoa, and rainforest cherry	Antioxidants, antiviral, antibacterial, antifungal, anti-inflammatory anticancer	Not show much toxicity more studies suggested	[290,291]
Rutaceae	150 Genera 900 species	Oranges, grapefruits, lemons, and limes	Antimicrobial, antioxidant, anti-inflammatory	Not show much toxicity	[292-294]

3.6. Comparing the toxicity of essential oils that have MIC in range µg/ml

According to the data in Table 3 and as mentioned before, some plants have perfect MICs, which means that plants with a lower concentration can prevent many microorganisms that are harmful to the body. Now, we will explore the toxicity of these plants to see whether or not it is cost-effective to use their essential oils. There is a lack of information on the toxicity of plants such as *Boswellia papyrifera*, *Daucus carota*, *Eupatorium adenophorum*, *Gnaphalium affine*, *Matricaria chamomilla*, *Melaleuca Leucadendron*, *Monarda citriodora*, *Nepeta sintenisii*, and *Syzygium aromaticum*. More studies should be conducted to identify the toxicity status of these plants. If deemed suitable after examining other aspects, the essential oils of these plants could prove to be valuable assets in the industry. *Bunium persicum*, *Carum carvi*, *Cedrus deodara*, *Cuminum cyminum*, *Cymbopogon winterianus*, *Ferula macrecolea*, *Foeniculum vulgare*, *Melissa officinalis*, *Ocimum gratissimum*, *Thymus schimperi*, *Thymus vulgaris*, and *Trachyspermum ammi* are among the plants whose MIC is in the order of mg/l. However, their toxicity is in the range of mg/l, which means there is a large gap between these two properties of the essential oils of these plants. These plants can be effectively used by considering all other aspects and characteristics.

Based on available data, *Mentha piperita*, a widely popular herb, exhibits a significant gap between its MIC and toxicity. This is a promising sign, suggesting that if no other issues or limitations are associated with this plant, it could be a safer and more practical option for industrial use, particularly in the food and pharmaceutical sectors. The names of some plants that can be seen in the tables are not given in this section; this does not mean that they do not have a suitable MIC or have shown high toxicity. It is worth mentioning that it is true that they have not demonstrated excellent MICs, similar to the mentioned plants, but they have shown good MICs in dealing with microbial agents. Changing the composition of these essential oils or other substances or adding another series of compositions can shift the level of toxicity and MIC in a way that favors the MIC.

3.7. Comparing the antimicrobial and antifungal potency of essential oils with antibiotics

A series of antibiotics are used for each microorganism, some of which are first-line drugs. Table 6 compares the MIC levels of common antibiotics for each microorganism with the MIC level of plant essential oils effective against the same microorganism.

Table 6. A comparison of the antimicrobial and antifungal potency of essential oils with antibiotics

Microorganism name	Effective antibiotics and antifungals	MIC*	Most effective essential oils	MIC*	R**
<i>Aspergillus spp.</i>	Caspofungin	0.008 - 0.061 µg/ml	<i>Cedrus deodara</i>	1 - 10 µg/ml	[295]
<i>Bacillus cereus</i>	Imipenem and Levofloxacin Other antibiotics	≤ 5 µg/ml > 10 µg/ml	<i>Matricaria chamomilla</i> , <i>Nepeta sintenisii</i> , <i>Boswellia papyrifera</i> , <i>Cedrus deodara</i> , <i>Bunium persicum</i> <i>Thymus vulgaris</i>	5 µg/ml 5 µg/ml 5 µg/ml < 1 µg/ml < 1 µg/ml 2 µg/ml	[296] [297]
<i>Campylobacter jejuni</i>	Erythromycin Other antibiotics	2 µg/ml > 2 µg/ml			
<i>Candida albicans</i>	Micafungin Other antifungals	0.06 µg/ml 0.06 - 16 µg/ml	<i>Melaleuca altemifolia</i> , <i>Nepeta sintenisii</i>	25 - 30 µg/ml 0.35 µg/ml	[298]
<i>Enterococcus faecalis</i>	Teicoplanin and Amoxicillin/	≤0.25 µg/ml	<i>Boswellia papyrifera</i> , <i>Matricaria chamomilla</i> ,	2 µg/ml 4 µg/ml	[299]

<i>Escherichia coli</i>	Clavulanate		<i>Melaleuca altemifolia</i>	18 µg/ml	
	Other antibiotics	0.25 - 8 µg/ml			
	In sensitive strains:		<i>Boswellia papyrifera, Cedrus deodara, Matricaria chamomilla, Melaleuca leucadendron, Nepeta sintenisii, Satureja montana, Tagetes elliptica, Thymus vulgaris, Ocimum gratissimum</i>		[300]
	Norfloracin and Ciprofloxacin	0.01 - 0.02 µg/ml		1.5 - 40 µg/ml	
<i>Proteus mirabilis</i>	Other antibiotics	1 - 10 µg/ml		and most of them	
	In resistant strains:			4 µg/ml	
	Ceftazidime	7.5 µg/ml			
	Other antibiotics	30 - 240 µg/ml			
<i>Rhizopus oryzae</i>	Ciprofloxacin	2 µg/ml	<i>Boswellia papyrifera, Matricaria chamomilla, Ocimum gratissimum</i>	16 µg/ml	[301]
	Imipenem	4 µg/ml		4 µg/ml	
	Other antibiotics	2 - 256 µg/ml		12 µg/ml	
	Amphotericin B	3 µg/ml	<i>Cedrus deodara</i>	0.2 µg/ml	[295]
<i>Salmonella</i>	Other antifungals	16 µg/ml			
	Ciprofloxacin	0.125 - 4 µg/ml	<i>Nepeta sintenisii</i>	1.4 µg/ml	[302]
	Other antibiotics	>> 4 µg/ml			
	Rifampicin and Gentamycin	0.25 µg/ml	<i>Boswellia papyrifera, Cedrus deodara, Matricaria chamomilla, Melaleuca altemifolia, Melaleuca leucadendron, Nepeta sintenisii, Satureja montana, Tagetes elliptica, Thymus vulgaris, Bunium persicum, Ocimum gratissimum</i>		[303]
<i>Staphylococcus aureus</i>	Quinupristin/Dalfopristin	0.25 µg/ml		0.25 - 15 µg/ml	
	Other antibiotics	0.25 - 32 µg/ml			

*MIC written in the table depending on the type of microorganism varies between antibiotics and antifungal agents.

**References

3.8. The impact of processing and storage on the toxicity of essential oils

Chemical compounds are sensitive to different environmental factors owing to the formation of various materials with different functions and characteristics. These environmental factors include light, oxygen, temperature, humidity, and pH. Light provides the energy needed to excite electrons and causes changes in the molecular structure. However, temperature changes have significant effects on the structure and microbial activities. As a result of pH changes, some compounds change, and the foundations of the substances are changed, which cannot show its effect as before.[304]

During storage and processing, owing to the time-consuming nature of these operations, changes have occurred that facilitate the oxidation process, and the oxidation of the substance is equal to the loss of the property and proper performance of the substance in question and then by turning into radicals. Radicals can cause significant damage to cell structures and various problems, including cancer. For example, essential oils prepared for a long time, especially oxidized terpenoids, cause skin irritation, whereas non-oxidized terpenoid compounds have no or minimal skin irritation effects. The unsaturated parts can react with air and create a variety of harmful substances, including peroxy radicals. These radicals can have various effects and induce a series of reactions. These radicals can also react with each other to form multiple compounds, such as alcohols, aldehydes, and others, which interact with the primary structure. However, some of these interactions remain unclear.[305] Therefore, it is vital to check the toxicity of essential oils in detail, and the changes that occur over time during the processing, storage, and distribution processes are especially worthy of attention.

3.9. Safety data requirement for essential oil as food preservatives

When considering the addition of substances to food, whether as preservatives or additives, it is imperative to conduct comprehensive studies to assess both short- and long-term toxicity in animals. This is crucial for mitigating potential unnecessary and adverse side effects. Preservatives are utilized to prolong the shelf life of foods and prevent spoilage; however, their properties can evolve over time and under varying conditions. Even after assessing their toxicity, further research is necessary to comprehensively understand their evolution and interactions with other substances, preservatives, and additives. This issue is multifaceted, particularly when considering food safety and public health.[305,306]

3.10. Regulatory frameworks for a safe and effective use of essential oils a critical appraisal

Regulations and guidelines play a crucial role in safeguarding the quality and safety of the ingredients used in food and health products. These measures are essential to ensure their appropriate use and to minimize unnecessary side effects, thereby protecting public health. At the international level, the World Health Organization (WHO) plays a key role in setting regulations and guidelines for assessing the quality and safety of materials used in food and health products. It provides comprehensive information about many online materials, which is updated monthly. In addition to the WHO, every country has organizations that monitor and evaluate the quality and safety of objects in the food industry. Even in some countries such as Canada and Japan, the use of essential oils is regulated, and to comply with these regulations, complete information about the source, potency, medicinal ingredients, non-medicinal ingredients, dosage, etc., needs to be presented to the related organization.

The JECFA (Joint FAO/WHO Expert Committee on Food Additives) committee, a joint initiative by the WHO and FAO, has been established to use EOs as preservatives. This committee evaluates the safety of food additives and publishes the findings. Organizations such as FAOLEX also provide information about the regulations and guidelines for foods and herbal ingredients.[307]

3.11. Risk assessment methods for evaluating the toxicity of essential oils

Risk assessment is vital for minimizing negative impacts and health risks associated with various factors. Different methods have been recommended to control and effectively achieve these risks. A common approach involves a four-step process.

3.11.1. Hazard identification:

This step involves evaluating a chemical's potential toxicity and examining documents detailing its effects to assess the health risk assessments of using essential oils in quantitative metrics. This method considers the chronic and sub-chronic risks of using certain chemicals combined in farm animals, which incorporates various toxicological information about the tested animals.[308]

3.11.2. Dose-response analysis:

This is a complex and intellectually stimulating step, as it aims to establish the relationship between a substance's dose and its potential effects. It involves extrapolating results from experimental animals to humans and accounting for individual differences, which can significantly influence the results.

3.11.3. Exposure quantification:

This step involves evaluating the chemical dosage to which different groups will be exposed based on their geographical locations, lifestyles, and other factors. It provides a range of values and identifies vulnerable groups.

3.11.4. Risk characterization:

The final step involves combining the results from the previous three steps to estimate risk. This risk varies among populations. However, it is important to note that risk assessment is often used to protect the group at greatest risk, emphasizing ethical considerations in the process.

It's essential to recognize that risk assessment is a dynamic field that demands continuous feedback and improvement. This ongoing process of feedback and adjustments is not only important but also a shared commitment to refine the process and achieve more accurate risk estimates, considering the various factors that can influence the results.[309] Several tests can be performed to evaluate the risk of using essential oils in different industries, such as other volatile materials. The skin irritation test stands out because of the nature of essential oils and the potential skin exposure to these materials. This test, which can be conducted using methods such as in vivo semi-occlusive single-patch testing and clinical tests in specific numbers and ranges of age, is of paramount importance.[310] Another test is the mucous membrane irritation test, which requires specific attention and comprehensive study because these materials can be exposed after oral usage. A modified HET-CAM assay can be performed at an irritation threshold concentration (ITC).[311]

Another test is the phototoxicity test. Because essential oils are volatile, the skin and eyes can be exposed to the material and become sensitive to light after some changes. Methods such as the 3T3 neutral red uptake phototoxicity test can be used to evaluate this risk. Many toxicology tests, such as acute and subacute toxicity tests, must be performed to assess the materials' severe side effects and prevent them from

occurring. These tests are mainly performed on animals such as rats in the laboratory in specific terms over a particular time range. [171]

Mutagenic tests are of massive importance because their effects occur over the long term, and the source of their impact cannot be diagnosed and related to these effects, which makes them a hidden and dangerous side effect. One of these test methods involves exposing a *Drosophila* larva to essential oil and evaluating the mutagenic effects in the larva.[312] In addition, many analytical methods are required to ensure the safety of these chemicals. Analysis of centrifuged blood serum of the animal test for Haematological and biochemical parameters, analysis of biochemical parameters such as specific amounts of metabolites and electrolyte proteins, and hematology, histology, and tissue embedding analysis are some of the safety assessment processes of using food additives such as essential oils.[180]

3.12. Limitations of the study and suggestions for future research

There is a significant lack of information on the toxicity of plant essential oils, which causes several limitations in the practical and industrial use of these materials. For the effective use of these materials as preservatives, it is crucial to understand the three types of toxicities that may manifest at different time intervals. Regarding the chemical compounds that were discussed and examined, depending on the geographical area, climatic conditions, and many other factors, the percentage of these compounds in essential oil varies. Of course, the main ingredients are, in most cases, the same as the declared compounds, but the percentage of the composition of the substances varies, which requires further investigation into the use of these plants. When used together or in combination with other preservatives, these essential oils present the potential for synergistic effects. Although promising, such effects also pose the risk of unpredictable outcomes. Therefore, further studies, especially in the field of toxicity, are necessary for a more effective and safe use of these essential oils. This call for more research should motivate us to investigate this important study area further.

4. CONCLUSION

Plants' essential oils are one of the most important natural substances with many uses in various industries, especially in the food industry as a preservative. These essential oils have different properties, such as antimicrobial, antioxidant, and anti-aflatoxin activities, which can prevent the growth and activity of many microorganisms inside food. In addition, the chemical structures inside these compounds cause biological effects in essential oils. MIC is one of the parameters that show the level of antimicrobial properties. By examining this factor, essential oils are potentially active compounds in dealing with pathogens, and in some cases, they even work better than antibiotics and antifungals. Despite all these cases, the toxicity of these essential oils remains a problem. In the case of essential oils of some plants, despite their unique and practical properties, due to oral toxicity occurring in small doses, their use in the food industry is limited. Owing to the different characteristics of essential oils, using these plant compounds in the food industry as preservatives should be increased. However, the toxicity of these compounds should also be considered, and further in-depth studies are required.

5. MATERIALS AND METHODS

5.1. Inclusion criteria from databases

In this systematic review, we concentrated on pertinent studies using specific MeSH keywords across databases, such as WOS, Scopus, PubMed, Embase, and Google Scholar. Keywords encompassed essential oil, food preservatives, antimicrobials, toxicity, and MIC. We carefully reviewed the retrieved articles to ensure they met the inclusion criteria. This screening process involved thoroughly examining the titles, abstracts, and keywords. Only articles that directly addressed the intersection of these keywords were included in the dataset. Irrelevant, duplicate, and unpublished references, as well as manuscripts without full text, were excluded.

5.2. Quality Assessment

To preserve the integrity of our research, we implemented stringent quality assessment criteria for the chosen articles. This process involved evaluating the peer-reviewed papers for their methodological robustness, relevance, and reliability.

5.3. Synthesis of Information

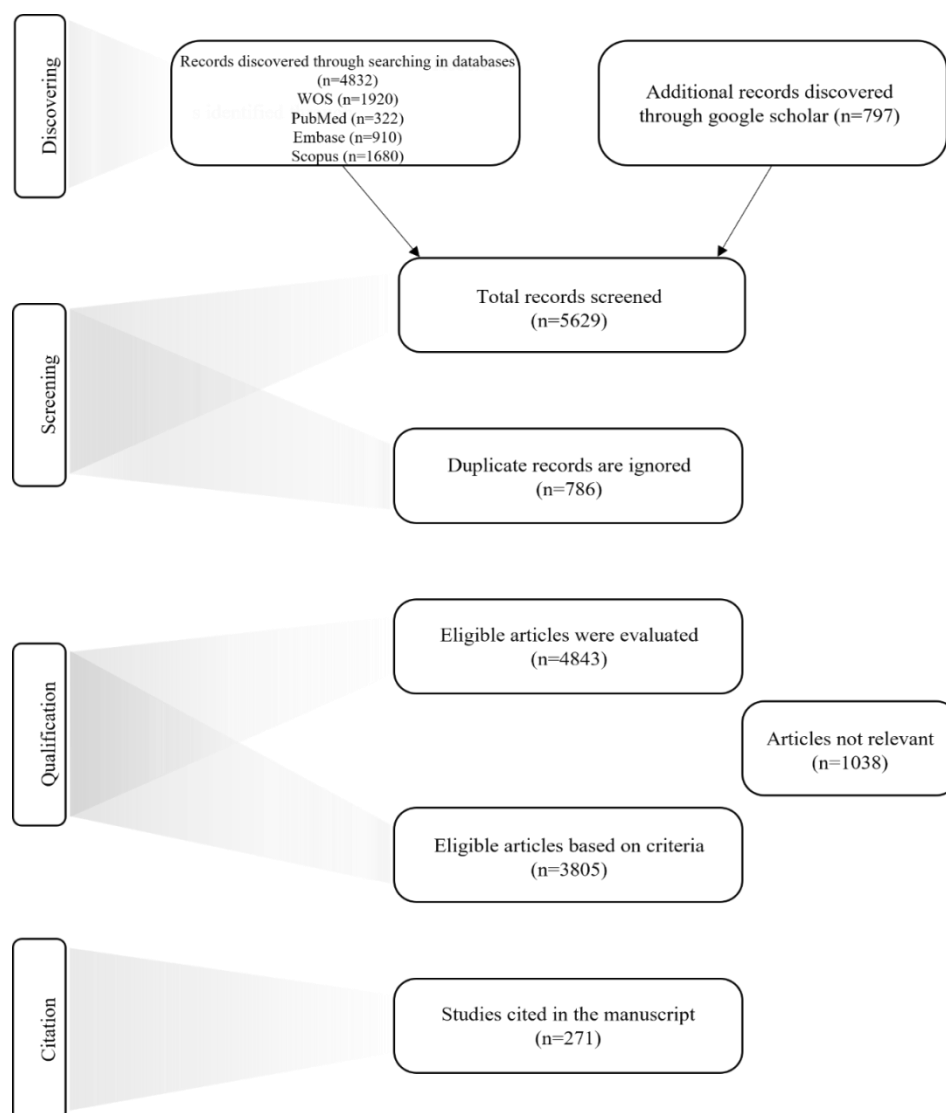


Figure 4. The flow chart of the search strategy

The consolidated data from 312 selected articles was the foundation for our research and analysis. This methodological strategy guaranteed a comprehensive review, enabling us to extract significant insights from the current literature and enhance our understanding of potential keyword interactions. Figure 4 illustrates the search strategy used by the authors.

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