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A review of the antifungal activities of mint plant extracts against fungal isolates.

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Abstract

Mint an aromatic plant is rich in essential oil and widely used for its condiment in foods. It has medicinal potential in traditional medicine. Fungi infection and its management can be challenging due to the adverse effect of presently available drugs. This paper discusses the potential of mint as an antifungal agent. A literature search using PubMed and the keywords that relates to "Mentha" "mint" "antifungal activity", among others was carried out and data obtained was analyzed using a bibliometric tool. Relevant articles included in our studies were restricted to mint family, fungi of clinical importance, assessment and extraction methods, among others. Here, analysis shows *Candida albicans* is the must studied appearing in 39 studies, followed by *Candida glabrata* (12 times). *Aspergillus niger* and *Aspergillus flavus* appeared in 9 and 8 studies, respectively. *Mentha piperita* was the most abundant mint species used in 28 studies tested against *Candida albicans*. Other mint, *Mentha longifolia*, *Mentha spicata*, and *Mentha pulegium*, among other were identified. Antifungal susceptibility measurement with the highest zone of inhibition was 90 mm from *M. piperita* exerted on *C. albicans* growth. Also, zone of inhibition measured at 10 mm was exerted by *M. pulegium*, *Lavandula stoechas. ssp. stoechas*, *Nepeta cataria* oil extract against *Candida spp*., and *Aspergillus spp.* at MIC values of 0.25mg/ml and 125µg/ml. The MIC value of 0.001 to 0.06 mg/ml *M. piperita* inhibit growth of *Candida species*. With respect to percentile inhibition *Mentha piperita* and *Origanum vulgare* demonstrated anti-fungal activity at 70 to 100% on various fungi species, suggesting these mint species to be an effective source of fungicidal agents. *Mentha piperita* and other mint species extracts show a wide range of inhibitory activities against fungi growth, the various identified extracts and their antimicrobial activity were compared for different solvents, and are then so discussed.

Keywords: Antifungal, Agar-disc diffusion, Microdilution, mint, Fungi, Plant extract

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INTRODUCTION

Mint is an aromatic plant in the *Lamiaceae* family; rich in essential oils and commonly used as herbal tea and food condiment (Raja, 2012). There are 250 genera and over 7000 species in this *Lamiaceae* family (Stankovic, 2020). *Mentha piperita* L. (Peppermint), *Mentha spicata* L. (Spearmint), *Mentha arvensis* (Japanese mint), *Mentha longifolia* L. (Ahmad et al., 2020), and *Origanum vulgare* L. (Alekseeva *et al*., 2020) are just a few of the significant species in this family (see Table 1). The mint plants are characterized by squared-off stem cross-sections, albeit their inflorescences differ (Chaker *et al*., 2011). While the presence of lacunar parenchyma tissues in every section is a distinctive characteristic of some species (Figure 1).

Table 1: List of some *Mentha species* form *Lamiaceae* family and their common names [Adapted from: (Naureen *et al*., 2022).

Mint Species	Common name
Mentha. aquatica L.	Water mint
M. piperita 'Lavandula'	Lavender mint
M. arvensis L.	Corn mint, field mint, ginger mint, wild mint
M. canadensis L.	American wild mint, Canada mint, Chinese mint, East Asian wild mint, Japanese mint, Sakhalin mint
M. longifolia L.	Himalayan silver mint, horsemint
M. piperita L.	Peppermint
M. piperita f. citrate	Bergamot mint, eau de cologne mint, orange mint
M. pulegium M	Mosquito plant, pennyroyal mint, Pennyrile, pudding grass, squaw mint
M. spicata L.	Garden mint, homegrown mint, lamb mint, mackerel mint, spearmint
M. suaveolens	Apple mint, pineapple mint, round-leafed mint, woolly mint
M. suaveolens 'Variegata'	Pineapple mint
M. x piperita f. citrate 'Chocolate'	Chocolate mint

Figure 1: Mint species from Lamiaceae family. **A**. *Mentha piperita* (Shutterstock Images, 2023) **B**. *Mentha longifolia*; primarily a temperate biome, but grown in some Africa region (Plants of the World Online, 2023), **C**. *Origanum vulgare*; a herbaceous and broad-leaved plant, with buds wintering at ground level (Bissanti, 2022) and **D**. *Mentha pulegium* (Jacinto, 2012), one of the mint species with lacunar parenchyma tissues.

Study has demonstrated that plants in this family (*Lamiaceae*) have therapeutic benefits (Uritu *et al*., 2018), including potential antifungal activities (Skendi *et al*., 2020). Additionally, because of its distinctive aroma, which sooth individuals, this plant is frequently used as a raw material in the food, beverage, and pharmaceutical industries as an antiseptic drug, reducing digestive disorders and headaches, wind oil, balm, toothpaste ingredients, perfumes, cosmetics, candies, among others (Hasanah *et al*., 2019).

Fungus, exist either as saprophytic or facultative parasite and may live a symbiotic life in some of its hosts. Fungi are of public health importance, where its chronic infection is characterized with reproductive, renal, oral and skin dysfunctions (Denning and Hope, 2010; Gladiator *et al*., 2013; Marciano *et al*., 2015); while opportunists fungal infection such as *Candida species* is common in metabolic diseases such as found in diabetic patients (Lim *et al*., 2020) and in HIV-infected individuals (Nittayananta, 2016). When not properly treated, fungi may occupy substantial parts of the body especially in immune compromised individuals, that can result in blindness, chronic pulmonary aspergillosis, cryptococcal meningitis, invasive candidiasis, *Pneumocystis jirovecii* pneumonia, invasive aspergillosis, disseminated histoplasmosis, fungal asthma and fungal keratitis, among others (Bongomin *et al*., 2017). Several antifungal properties have been employed in the management of fungi infections, although limited to three major parent compounds namely: polyenes, azoles, and echinocandins (Roemer and Krysan, 2014), yet the use of these antifungal agents are associated with certain challenges. Available antifungal therapies are known for their drug toxicity, drug interactions, and drug resistance (Nami *et al*., 2019). Here, the toxicity is attributed to many similarities between fungal and the human-host cells, thus, leading to few targets for drug development (Denning and Hope, 2010; Scorzoni *et al*., 2017; Silva *et al*., 2019). In addition, fungi possess the ability to synthesize variety of metabolic enzymes and secondary metabolites and pathways to evade host defense mechanisms, thus making them resistant to chemotherapy. For instance, fungi develops resistance through the mechanism of overexpression of efflux pump proteins and biofilm formation, making the once efficient strategies, now infective (Scorzoni *et al*., 2017). Therefore, there is the need to develop novel antifungal agents that are effective with low human-host toxicity and minimal side effects. Recently, plant based product for drug discovery has been adopted as the new approach for developing new chemotherapy against microbial infections and other diseases (Katiyar *et al*., 2012; Potterat and Hamburger, 2008); since their structural analogues can be optimized and processed into new drugs (Ugboko *et al*., 2020). Additionally, medicinal plants are cost effective, have fewer adverse side effects, drug resistance is minimal, stabilizes hormones and metabolism, strengthens immune system, among others (Traditional Medicine, 2019). Importantly, medicinal plant product has benefit in handling some diseases of public health importance (Ekor, 2014). There have been various attempt by scientists to scout for herbal plants with antifungal properties (Nittayananta, 2016), one of such plant is the mint (Bayan and Küsek, 2018; Wenji *et al*., 2019). However, the variety of natural chemical diversity of mint (Rao *et al*., 2015; Rattray and Van Wyk, 2021; Rodríguez-López *et al*., 2022) like in other plants, it has made it difficult to establish an efficient approach for isolating and identifying the pharmacological properties of different medicinal plant extracts, making it difficult to determine their therapeutic potential (Lautié *et al*., 2020). Thus, the need to identify and compare standard methods that will provide detailed information for therapeutic measurements.

There is lack in standard methods for the extraction and assay of bioactive plant constituents (Pandey and Tripathi, 2014; Stéphane *et al*., 2021), when it is applicable to variety of plant species in the same family such as mint. Since extraction is premier and is a crucial step in the preparation for evaluating the pharmacological potential of any medicinal plant, it is important to identify the distinct extraction method for the antifungal potential of mint plants and their methodologies for the antifungal bioassay. Here, we evaluated through a survey of the bibliographic database, various approaches and specific materials used to measure the antifungal activities of mints.

MATERIALS AND METHODS

Data collection and selection

A systematic bibliography literature search was carried out on the National Centre for

Biotechnology Information (NCBI) sites using the advance search options. From NCBI site, a survey of the bibliographic database, PubMed (www.ncbi.nlm.nih.gov/pubmed) search of journal articles describing studies on antifungal activities of mint (*Lamiaceae*) plants was conducted using the keyword search term for mint antifungal determinations (e.g., mint plant; *Lamiaceae* plants; extraction methods; *in vitro* antifungal studies; antifungal activity; biological activity; plant extract; antifungal properties of plant; mint herbal products; mint plant extract). In addition, keyword search for current strategies and standard methodology to determine antifungal activity of plant extract was used. The number of data hits were downloaded by choosing the "Save / Export" option to collect the data into a text file.

Title and abstract selection of articles downloaded were carried out using a modified approach as described by Riordan *et al* (2018). Articles that evaluated mint/Lamiaceae antifungal validity was used as requirement for inclusion in our review. In the case of any uncertainty regarding inclusion of an article, the full text was retrieved and reviewed. Any article considered for inclusion must be peer-reviewed in a scientific journal, not limited to a certain region of the world, and focus on the antifungal activity of the mint plant. Therefore, studies were excluded if they were reported on other antimicrobial activity without antifungal activities. Also, studies had to be conducted on medically important fungus either on human host or other domestic or farm animals.

Data virtualization and analysis

The bibliometric analysis was done using VOSviewer (www.vosviewer.com), a software tool for constructing and visualizing bibliometric networks, to show the development of studies involving mints and its antifungal activity. This was carried out by use of VOSviewer's (Version 1.6.15) text mining functionality for constructing co-occurrence networks of important terms extracted from the downloaded PubMed related scientific journal publications (van Eck and Waltman, 2010). This would help to get an overview of the research studies on mint plants related to its antifungal properties, its different methodology employed and their interconnections. The "choose threshold" selected for the minimum number of occurrences of a term was five (5). Search terms relevant to the study clustered by the VOSviewer were chosen from the "Verify selected term" for the data extraction protocol (See Figure 2). Terms that connote same idea were grouped and treated as one, such as "antifungal properties or antifungal agent"; "analytical method or analytical procedure" and "pharmacological activity and pharmacological property", among others.

Data extraction and characteristic assessment

Extracting of items by manual curation was done by sighting the following: study design, mint *(Lamiaceae*) species, specie of fungi involved, methods of extraction, type of solvent used, list of instruments used, statistical assessment used, among others. Just like in the work of Riordan *et al* (2018), the quality of article to be included in the assessment was not chosen as a criterion. However, the item to be included for the analysis such as, instrument or type of solvent used, must be mentioned by more than two studies.

RESULTS

A PubMed search returned 1,794 published articles (as of 03 March 2022) using the search term: ("Mentha"[Mesh]) OR (((mint herbal products) OR (mint plant extract)) AND ((((((mint plant) OR (Lamiaceae plants)) OR ((extraction methods) OR (in vitro antifungal studies))) OR ((antifungal activity) OR (biological activity))) OR ((plant extract) OR (antifungal properties of plants))) OR (current strategies and standard methodology to determine antifungal activity of plant extract))). These downloaded PubMed file of the 1,794 mints related publications were used as input to the VOSviewer to illustrate the progressions of research involving mint. This would help to get an overview on mint study, its different subfield and their interconnections.

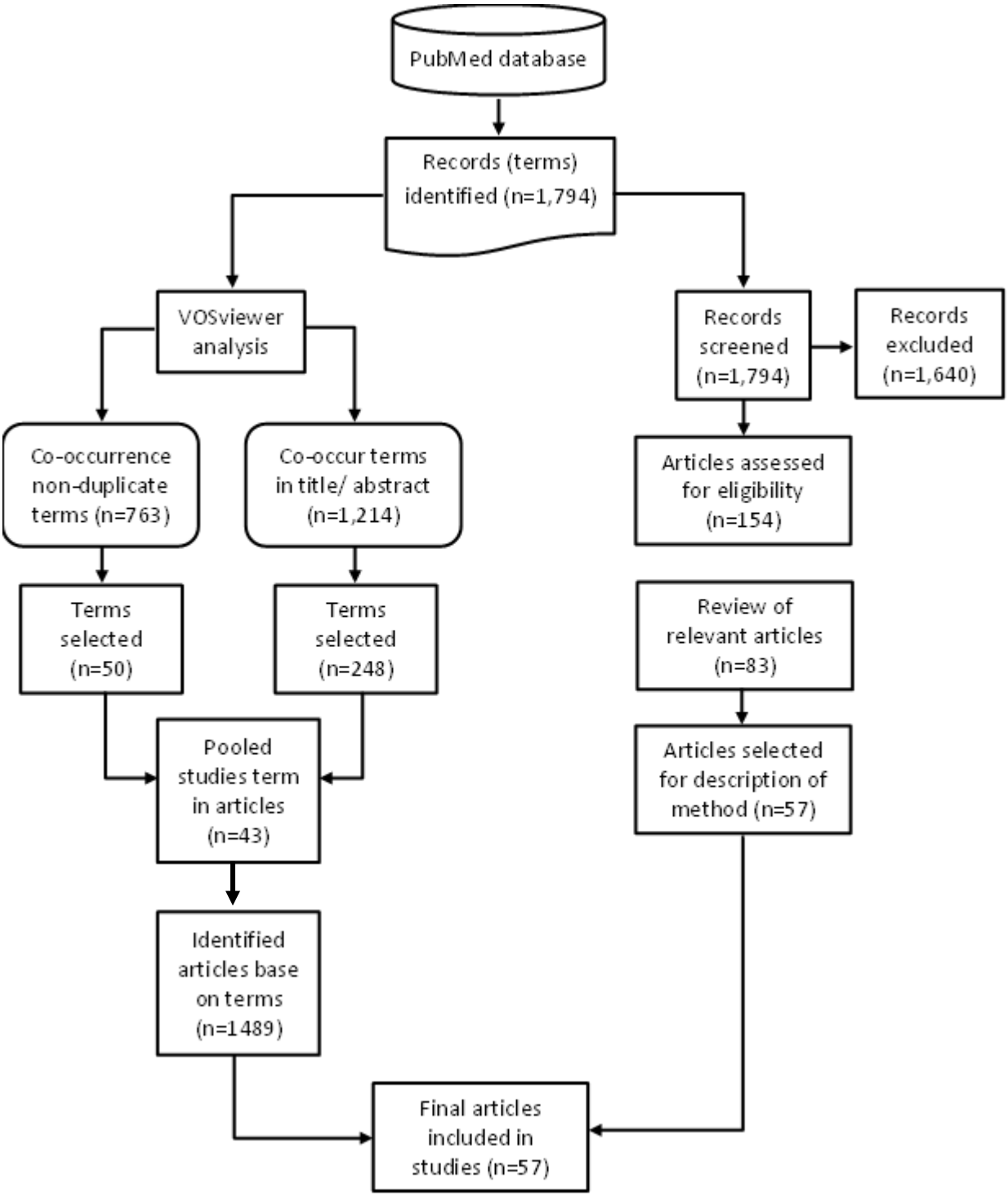


Figure 2: Flow-chart showing study selection process for the review.

The network visualization presented in Figures 3A and B were based on bibliometric data, analyzing all keywords co-occurrence with full count options. Each circle represents a term, the size of a circle designates the number of articles that have the corresponding term in the bibliographic database file. Terms that co-occur extensively tend to be grouped close to each other. Here, the tool VOSviewer grouped the terms into eight clusters, from 763 items with

30485 coupling links between publications, and all of the major cluster are of significant size (Figure 3A). The blue cluster, positioned in the center right area in the network, is the largest and predominantly consist of '*Mentha piperita*' related terms. The blue cluster is linked to the second largest group which is red and purple clusters, located in center left and lower midway areas in the visualization, respectively. The red clusters cover terms related to 'Mentha' a genus of the mint family; while the purple cluster cover terms related to 'plant extract'. Overlapping the blue and red cluster below is the brown cluster, consisting of 'oil, volatile' related terms. Other clusters such as the green, lemon-green and orange clusters overlays among other clusters and other terms are distributed across the network. However, exploring the VOSviewer 'main panel' of the network visualization reveal terms that were underlay in the various clusters, such include terms related to 'antifungal agent', 'fungi', 'microbial sensitivity test', 'dermatitis, allergic contact', 'gas chromatography-mass spectr', 'chromatography, gas', 'peppermint', '*Candida albicans*', and 'anti-infective agent', among others. Some of these terms and their occurrences are shown in supplementary Table 1. The VOSviewer "density visualization" (Figure 3B) feature was used to assess how nodes are distributed in the two-dimensional space underlying the visualization. The density visualization allows identification of dense areas where many nodes are located close to each other; such nodes for mints centered around the terms describing '*Mentha piperita*', 'plant extract', 'microbial sensitivity test', 'spore fungal' and 'statistic, nonparametric', among others.

In the network visualization based on 'Text data', from publications that have corresponding terms in the title and abstract fields, it shows the sizes of the circles, depending on the extensive co-occur terms. Like the bibliography data full count, the occurrence of terms in the title and abstract fields yielded eight (8) non-overlapping clusters (Figure 4A-B) from 1,214 items. These items were selected by the VOSviewer tool from a minimum of five (5) occurrence of terms, and linked to 58,884 co-occurrence terms. Here, the co-occur terms are located close to each other in the visualization. The green cluster, located below the right area in the visualization, is the largest and chiefly consist of 'peppermint oil' related terms. The red cluster, located far left area, is the second largest and covers the terms related to '*spicata*' a specie in the *Mentha* genus. The third (lemon-green) and fourth (purple) clusters located at the center and upper left consist of 'rat' and 'metabolite' related terms, respectively. Overlapping the red cluster is the blue and orange clusters, consisting of 'dpph (2,2-diphenyl-1-picrylhydrazyl)', 'synthesis' related terms, respectively. In the upper right area of the visualization, the brown cluster consist of terms related to biomarker, depression and *Angelica sinensis* and other terms related to pathophysiology. The "density visualization" (Figure 4B) relays terms describing subjects associated with mint study, namely 'biomass', 'substrate', '*Mentha aquatica*', '*longifolium*', 'antimicrobial activity', 'antibiotics', 'separation' 'traditional Chinese medicine', 'therapy', 'safety', 'clinical trials', and 'intervention', among others.

The related terms occurrences from the text and abstract fields and their relevance scores were used to further filter the article to be selected for inclusion in the study (Supplementary Table 2). A total of 298 terms occurrences were identified with relevance score of ~0.30 to 2.50 across the map (Figure 4A and Supplementary Table 2). The relevance scores with high value are used to select terms that represent the study topics covered by the text data, while terms with a low relevance score where ignored, since they tend to be general in nature and tend not to be representative of any specific topic. Thus, the selected relevance terms serve as the query for data extraction procedure in the PubMed files.Removing irrelevant hits from the downloaded 1,794 published articles, using co-occurrence terms that were not related to the study, reduced the number of articles to 1,489. Similarly, cross checking relevant articles to be inclusive in our study, we screened articles with description methods and 83 articles were identified. Close screening of the title and abstract and full text review, 57 research articles were retained. Of the articles retained, 37 provided a detailed description on antifungal studies. Twenty-six and 17 articles describe studies relating to *Aspergillus* and *Candida* species respectively. In total, the 57 articles were comprised of the assessment and extraction method, fungi and plant species, and the antifungal activities of plant extract, among others (Table 2).

Tested microorganism with mint extracts

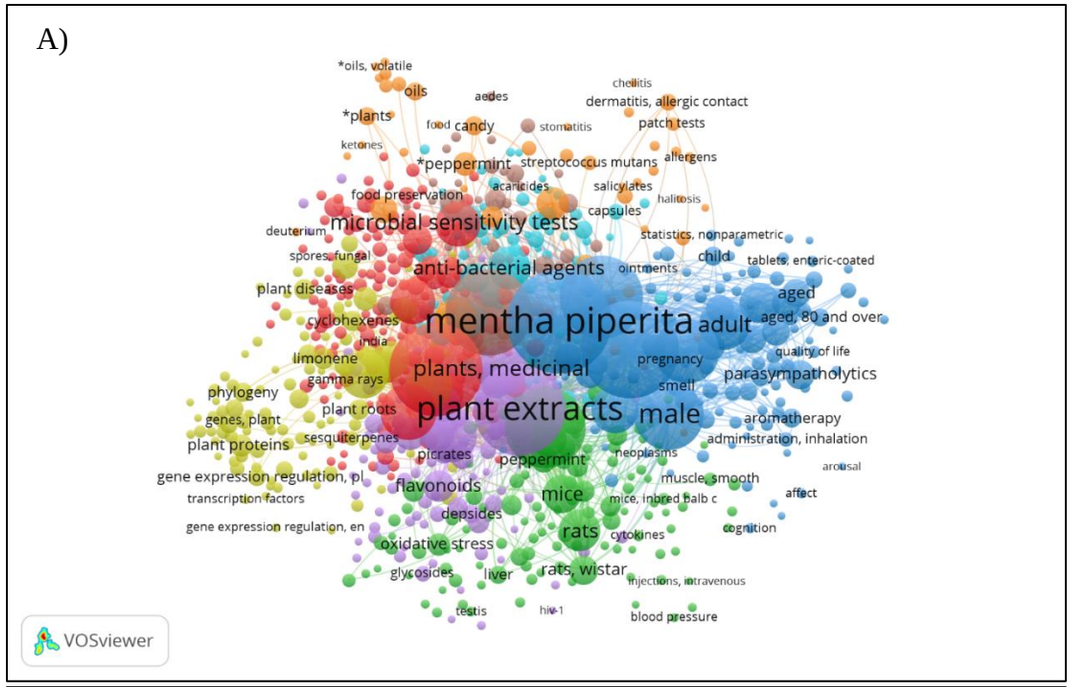
In this review, 62 species and strains of fungi have been tested with various mint extract for *in-vitro* studies. Some species of the fungi were repeatedly tested in several studies and appear more than once. These include fungi from *Aspergillus sp*., *Candida sp*., *Fusarium sp*., *Penicillium sp*., and *Trichophyton sp*., (Table 2). The most studied fungi, is the yeast is *Candida sp*. with *Candida albicans* appearing 39 in the several studies, followed by *Candida glabrata* (12), *Candida tropicalis* (9), and *Candida krusei* (6) and *Candida parapsilosis* and *Candida perfringens* occurring in various studies. Similarly, *Aspergillus niger* and *Aspergillus flavus* (occurring in 9 and 8 articles) are the next most studied among the *Aspergillus sp*., alongside *Aspergillus ochraceus*, *Aspergillus fumigatus* and *Aspergillus parasiticus* were identified in various studies. Other important fungi such as *Fusarium sp*., *Epidermophyton sp*., *Saccharomyces sp*., *Penicillium sp*. and *Trichophyton sp*., were used in the various *in-vitro* studied.

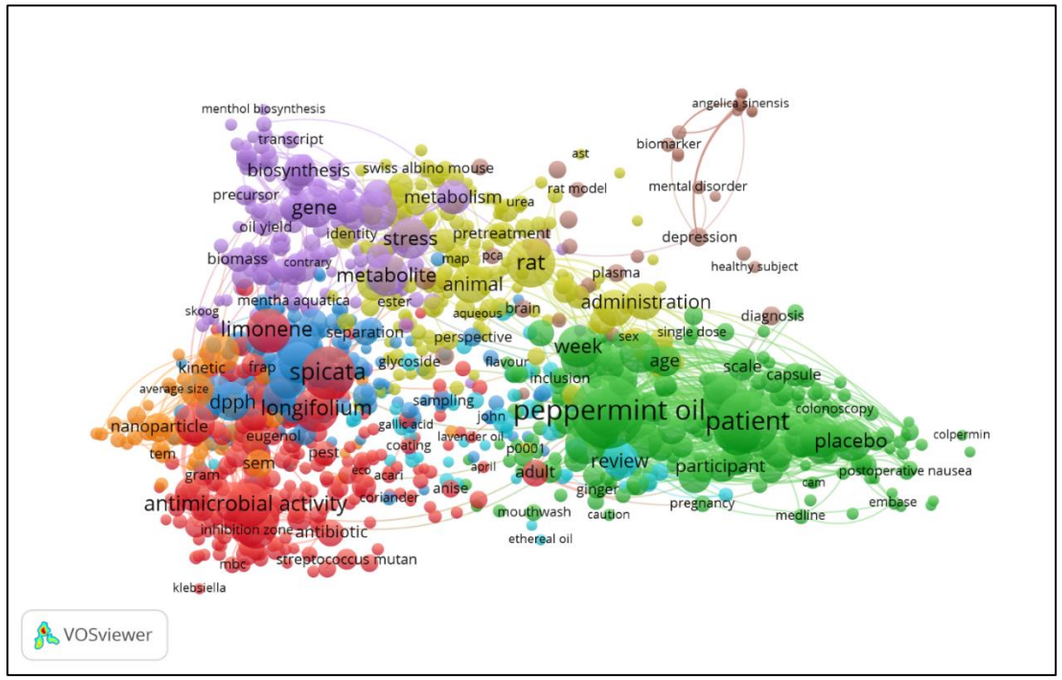
The inhibitory response of each fungal species is relative to the type of mint species extract administered and its responding concentration used. For instance, in a study conducted by Santos *et al*. (2012) where they targeted three *Candida species* (*C. albicans*, *C. tropicalis*, and *C. krusei*) using *Mentha arvensis* and *Turnera ulmifolia* shows that these plants extract has effect on the fugal species even at MIC concentration of 1024 lg/mL. However, *C. tropicalis*. *M. arvensis* and *T. ulmifolia* shows a remarkable inhibitory response to these plant extract at the same concentration. Similarly, Raghavan *et al*. (2018) and Al-Bayati (2009) in their studies used *Candida albicans* utilizing *Mentha piperita* and *Mentha longifolia* leaf extracts respectively. Here the *Candida albicans* in both studies shows a marked sensitivity to both plant extracts (Table 2).

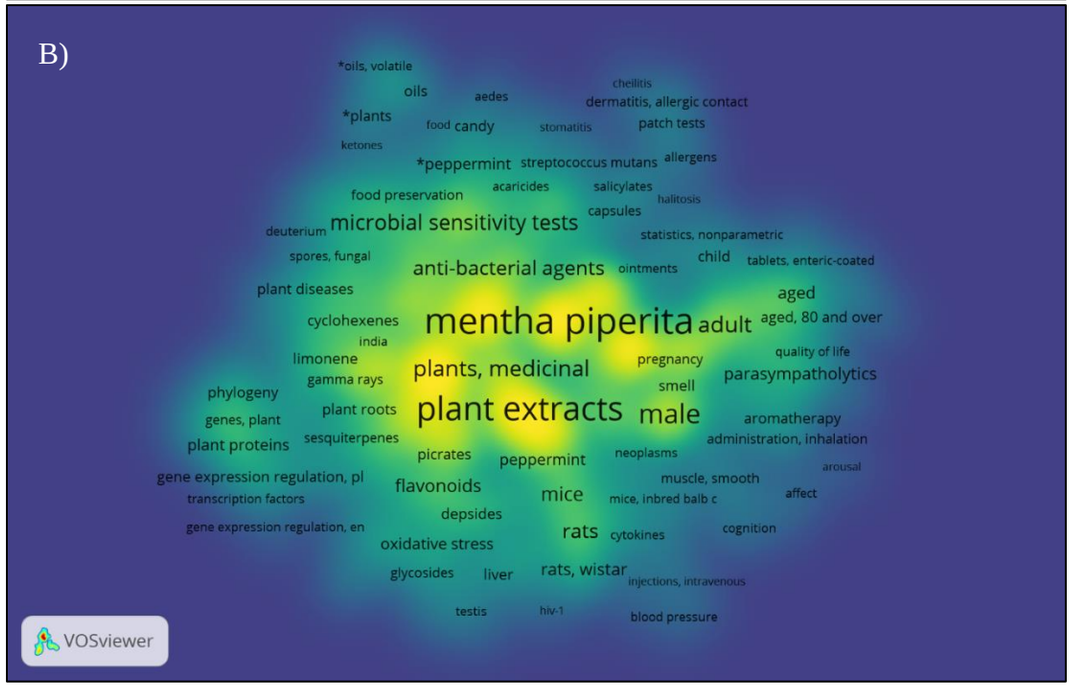
Aspergillus niger were identified to be sensitive to *Mentha suaveolens* Ehrh, and *Mentha spicata L., and Mentha piperita L* even at a lower concentration in studies carried out by El-Sayeda *et al*. (2012) and Soković *et al*. (2009). The inhibitory effect exacted by the essential oils of these plants yielded antifungal activities on *Aspergillus niger* with MICs 6.8 µg/ml to as low 1.0 µL/mL respectively. Other species of fungi that infect human superficial skin *Trichophyton rubrum* among others were shown to be sensitive to *Mentha spicata L* (Piras *et al.*, 2021; Soković *et al*., 2009). There susceptibility to the mint plant when compare with other studies is so significant that at MIC of 0.5 to 0.32 a strong growth of *Trichophyton rubrum* is inhibited.

Mint Species tested for antifungal growth

A number of mint species (28) were identified in the 57 studies selected (Table 2). In terms of plant extracts used, *Mentha piperita* was most abundant studied mint species utilized in 28 studies and tested mainly against *Candida albicans*. Other notable *Mentha species* identified include; *Mentha longifolia* and *Mentha spicata* occurring in 8 studies, *Mentha pulegium* occurring in six studies, *Mentha suaveolens* and *Mentha arvensis* appears in five and four studies, respectively. Similarly, other mint plant species tested in the antifungal assay were *Origanum vulgare* (appearing in 4 studies), *Mentha cervina*, *Nepeta cataria* and *Rosmarinus officinalis* appearing twice in the studies respectively. In addition, *Mentha viridis, Calamintha nepeta ssp. glandulosa*, *Lavandula stoechas. ssp. stoechas*, *Salvia fruticosa*, *Salvia macrosiphon Boiss*, *Salvia ofcinalis*, *Salvia tomentosa*, *Satureja hortensis* and *Ziziphora tenuior* appear once in the identified mint species. *Mentha piperita*, the most abundant mint species present in different studies gave a positive result in the antifungal activities depending on plant part, type of solvent and concentration of plant extract used. For instance, the plant part readily used here is the mint leaves followed by the whole and aerial plant. Interestingly, the leaf of *Mentha piperita* shows variation of responses in the identified studies on fungi (Table 2), where in studies like that of Bluma *et al*. (2008) up to 90% inhibition were observed, while in van Vuuren *et al*. (2009) studies shown an efficacy of MIC values of 6mg ml^{-1} against fungi pathogen, and as low as 0.25 µL/ml MIC value was obtained on tested microorganism in dos Santos *et al*. (2021) studies. However, in the case of *Mentha longifolia* the plant used is either leaf or the aerial parts of the plant. Both plant part used shows remarkable effect on the tested microorganism (Table 2).







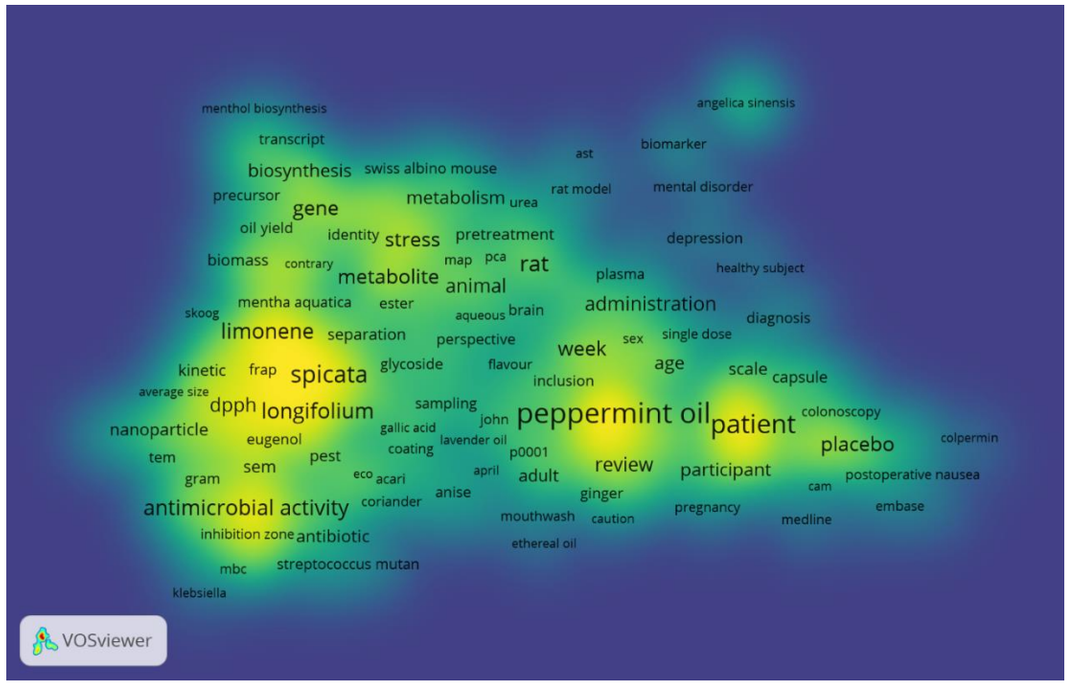


Figure 3: VOSviewer visualization of a term co-occurrence network for antifungal properties of mint plants using current strategies and standard methodology. A: Each term identified being represented by circle. The size of each circle shows number of publications related to the term. B: The density visualization provides identification of dense area where various nodes are identified close to each other.

Figure 4: VOSviewer visualization for text occurrences for antifungal properties of mint plants using current strategies and standard methodology. A: Each circle shows each text/term identified. The size of each circle shows number of publications related to the text. B: The density visualization provides identification of dense area where various nodes are identified close to each other.

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Khanzada *et al*., 2021)	*Fusarium solani* *Aspergillus niger* *Aspergillus flavus* *Mucor Spp*	0.02% v/v	*Mentha piperita*	Whole plant	Ethanol	10.275		disc diffusion	10.0 ± 0.1 mm 6.0 ± 0.1 mm - -	24–48 h; 28ºC	HPLC	Mean, Standard Deviation
(Tyagi and Malik, 2010)	*Candida albicans*	10^6 cfu/ml	*Mentha piperita*		Oils in liquid phase			Agar plate dilution Broth dilution, 96-well microplate	1.125 mg/ml 1.125 mg/ml 1.125 mg/ml	12 - 48 h; 30°C	GC, GC-MS	ANOVA
(Mehta, 2020)	*Candida albicans*	50 µl/well	*Mentha sp.*	NA	Oils	NA		96 well ELISA plate	~70%	72 h; 25°C		Mean and SD; one-way ANOVA; Kolmogorov Smirov test
(Song *et al*., 2019)	*Candida albicans*	10^5 cfu/ml	*Mentha piperita*	NA	Bacterial exopolysaccharides (EPS-PO) Peppermint oil Peppermint oil (PO) emulsion			double dilution	4.0 mg/mL, 16.0 mg/mL	24 h; 37 °C		Mean and SD
(Córdoba *et al*., 2019)	*Candida albicans* *Candida parapsilosis* *Candida glabrata* *Candida kruse*	1–5 x 10^6 cfu/ml	*Mentha piperita*		Oil extraction by hydro-distillation				0.8 to 800 mg l^{-1}	24 h; 30º C2039	GC	NA
(Rajkowska, Kunicka-Styczyńska, *et al*., 2017)	*Candida albicans* *Candida tropicali* *Candida glabrata* *Candida lusitaniae*	10^6 cfu/ml	*Mentha piperita*		Oil		0.1 % (v/v)	broth macrodilution	0.03-8.0% v/v	24– 48 h; 35ºC 2039	GC-MSFID	principal component analysis (PCA); Hierarchical cluster analysis
(Carvalhinho *et al*., 2012)	*Candida albicans* *Candida parapsilosis*		*Mentha piperita*	Leaves	Oil			disk diffusion (DD)	~17mm	24–48 h2039; 36 ± 1ºC		nonparametric Kruskal–Wallis and Mann–Whitney's
(Sharma *et al*., 2017)	*Fusarium oxysporum f. sp. lycopersici*	5 x 10^5 cfu/ml	*Mentha piperita*		Oil			broth microdilution	125 ppm	48 h; 28ºC	GC-MS, scanning Electron microscopy (SEM), Atomic force microscopy (AFM)	ANOVA; Duncan multiple range tests

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Magro *et al*., 2006)	*Aspergillus candidus* *Aspergillus niger* *Penicillium sp.* *Fusarium culmorum*		*Mentha piperita L*	Leaves	Aqueous		1-1.50 g/ml	Disc	4.46 and 2.30 cm 7.93 and 5.93 cm 1.70 and 0.96 cm 1.06 and 0.50 cm	48 h; 28 °C		F-test / Fcrit; regression analysis
(Soliman and Badeaa, 2002)	*Aspergillus flavus* *Aspergillus parasiticus* *Aspergillus ochraceus* *Fusarium moniliforme*		*Mentha viridis*		Oil		3000 ppm	Disc	3000 ppm/ 100% reduction	7–14 days; 28ºC 2040	HPLC	Correlation
(Abbas *et al*., 2021)	*Fusarium brachygibbosum*		*Salvia macrosiphon Boiss*		Methanol, Butanol, Water				11 ±0.67mm		colorimeter	Mean, SD
(El-Naghy *et al*., 1992)	*Candida albicans* *Candida tropicalis* *Aspergillus flavus* *Aspergillus niger* *Aspergillus ochraceus* *Penicillium rubrum* *Penicillium Chrysogenum* *Penicillium. purpurogenum*		*Peppermint*		Oil		1%	Disc	~8.5cm	12 d; 30°C		
(Agarwal *et al*., 2008)	*Candida albicans*	50 µL, 5 x 10^8 cfu/ml	*Mentha piperita*				0.03–5% v/v	disc diffusion assay	22.2 mm	48 h; 30ºC	Scanning electron microscopy (SEM)	Mean, SD; Student's t-test
(Doddanna *et al*., 2013)	*Candida albicans*		*Mentha piperita* *Mentha arvensis*	Leaves	Aqueous Ethyl alcohol		10 mg/ml	wells	- 13 mm	72 h; 25°C		Mean, SD; ANOVA
(Höfling *et al*., 2010)	*Candida albicans* *Candida dubliniensis* *Candida parapsilosis* *Candida tropicalis* *Candida guilliermondii* *Candida utilis* *Candida krusei* *Candida lusitaniae* *Candida glabrata* *Candida rugosa*	5 × 10^3 cfu/ml	*Mentha piperita*	Leaves	Dichloromethane*/ Methanol		1 to 0.001 mg/m	microplates (96 wells)	R*/ 0.06 to 0.001 mg/mL	48 h; 37ºC	Thin Layer Chromatography	

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Duarte *et al*., 2005)	*Candida albicans*	10^4 cfu/ml	*Mentha arvensis svar. piperita,* *Mentha piperita,* *Mentha pulegium,* *Mentha spicata*	Leaves	Oils/ water-distillation and Ethanol	0.26 and 29.60 0.80 and 26.80 0.42 and 32.00 0.21 and 43.60	2–0.03 mg mL^{-1}	tissue culture test plate (96 wells)	1.1 mg/ml 0.6 mg/ml 0.74 mg/ml	48 h; 36ºC	GC; GC-MS	
(Tampieri *et al*., 2005)	*Candida albicans*		*Origanum vulgare* *Mentha piperita*	whole plant whole plant	Hydrodistillation		Oil	Semisolid agar antifungal susceptibility	500 ppm 500 ppm	7 days; 25ºC	GC-MS	
(Yiğit *et al*., 2009)	*Candida albicans* *Candida tropicalis* *Candida glabrata*	10^6 cfu/ml	*Mentha longifolia L.,* *Mentha piperita L. Hudson*	Aerial parts	Methanol/Chlo-roform*	30 mg/ml	2.5 mg/ml 1.25mg/ml	Disc diffusion	10.2mm/R* 12.3mm/R* No activity/*	48 h; 30ºC	Soxhlet apparatus	Mean; Correlation
(Bluma *et al*., 2008)	*Aspergillus parasiticus* *Aspergillus flavus*		*Mentha piperita,* *Origanum vulgare* *Minthosthachys verticillata*	Leaves, stems	Oil/hydrodistilla-tion		500 mg/kg	Agar discs	85-90%			Mean; F-value
(Gursoy *et al*., 2009)	*Candida perfringens* *Candida albicans* *Candida krusei*	10^6 cfu/ml	*Mentha longifolia ssp. typhoides var. typhoides*	Aerial parts	Methanol	4.30% (w/w).	10 mg/ml	Agar well diffusion	13mm;36.0 0 mg/mL 13mm;36.0 0 mg/mL 15mm;18.0 0 mg/mL	24 h; 37ºC	Soxhlet	Mean; SD
(Petretto *et al*., 2014)	*Saccharomyces cerevisiae* *Tetrapisispora phaffii* *Metschnikowia pulcherrima* *Candida zemplinina*		*Mentha suaveolens spp*	Aerial parts	Oil	0.22% (v/w)		Agar diffusion test	9.45 ± 0.4 mm 12.10 ± 0.2 mm 11.55 ± 0.4 mm 10.00 ± 0.3 mm	24 and 48 h; 25ºC	Clevenger type apparatus; GC; GC-MS	Mean; SE; ANOVA
(van Vuuren *et al*., 2009)	*Candida albicans*	10^6 cfu/ml	*Mentha piperita* *Rosmarinus officinalis L.*		Oil		128 mg/ml		6 mg/ml 6 mg/ml	48 h; 37ºC		Mean

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Vasudeva *et al*., 2014)	*Aspergillus niger*		*Origanum vulgare*	Leaves	Chloroform Volatile oil	12.5 g 1.66% v/w			100%; 0.07800 mg/ml 100%; 0.00970 mg/ml		Clevenger's apparatus; Thin Layer Chromatography (TLC); GC-MS	Mean; SE
(D. C. dos Santos *et al*., 2021)	*Candida albicans*	2×10^6 ufc/ml	*Mentha piperita*	Aerial parts	Oil Ethanol (70% v/v)		0.5%	96-well microplates	0.25 µL/ml	48 h	Clevenger type apparatus; GC-MS	ANOVA
(Helal *et al*., 2019)	*Candida albicans*	5×10^6 cfu/ml	*Mentha cervina* *Ocimum basilicum* *Origanum vulgare* *Mentha pulegium* *Salvia ofcinalis*	Ariel parts	Oil		12µl	Disc-Difusion	43±2.83mm; 0.4 mg/ml 45±1.41mm; 25 mg/ml 42±1.83mm; 25 mg/ml 39±0.82 mm 0±0.0 mm	48 h; 35ºC	Clevenger-type apparatus; GC-MS	Mean; SD
(Sarac and Ugur, 2009)	*Candida albicans*	10^6 yeast/mL	*Mentha longifolia ssp. longifolia,* *Mentha longifolia ssp. typhoides var. typhoides* *Mentha pulegium,* *Salvia fruticosa* *Salvia tomentosa* *Calamintha nepeta ssp. glandulosa* *Nepeta cadmea* *Lavandula stoechas. ssp. stoechas,* *Ziziphora tenuior*	Aerial parts	Oil hydrodistillation		20 µl	disc diffusion	16 mm 15mm 18mm - 8mm 14mm 12mm 10mm 20mm	48 h; 30ºC	Clevenger type apparatus	
(Henley-Smith *et al*., 2014)	*Candida albicans*	4×10^7 cfu/ml	*Mentha piperita*	Aerial parts	Oil; Ethanol		1.6×10^{-5} to 1.25% (v/v)	96-well microtiter-plate	0.10%	48 h; 37ºC	Genevac	SE; Regression
(Zomorodian *et al*., 2013)	*Candida albicans* *Candida dubliniensis* *Candida tropicalis* *Candida krusei* *Candida glabrata*	1-5 × 10^6 cells/ml	*Nepeta cataria L*	Aerial parts	Oil/hydro-distillated	0.9		96-well microtitre	0.125-0.5 µL/mL	24-48 h; 30°C	Clevenger-type, GC-MS	

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Bardaweel *et al*., 2018)	*Candida glabrata*	1×10^5 cfu/ml	*Mentha spicata L*	Aerial parts	Oil/ hydrodistillation	1.04 ml/100 g		96 flat bottom microtiter plates	256 µg/mL	48 h; 33 °C	Clevenger; GC-MS	Mean; SD; Student's t-test
(Spadaccino *et al*., 2021)	*Candida albicans* *Aspergillus flavus* *Fusarium oxysporum* *Fusarium solani* *Fusarium tabacinum* *Penicillum spp* *Trichophyton rubrum* *Trichophyton mentagrophytes*	10^4-10^6 cfu/ml	*Nepeta cataria*	Leaves	Oil; ethanolic	0.74% v/w -	30 mg/m	Disk-diffusion assay	10mm/125µg/ml and ND 39mm/~16µg/ml and 16mm/~63µg/ml 17mm/125µg/ml and ND 35mm/~16µg/ml and 14mm/125µg/ml 35mm/~16µg/ml and 15mm/~63µg/ml 27mm/~63µg/ml and ND 18mm/125µg/ml and ND 35mm/~16µg/ml and 16mm/~63µg/ml	48-72 h; 37ºC	Soxhlet extractor; Clevenger-type; GC-MS	Mean; SD
(Emre *et al*., 2021)	*Candida albicans* *Candida glabrata* *Trichophyton sp.* *Epidermophyton sp*	10^4 cells/mL	*Satureja hortensis* *Mentha spicata L. subsp. spicata*	Seeds	Hexane; Isopropanol			Well agar	23/24mm ~18/18mm 23/24mm 21/18mm	72 h; 25 ± 0.1 °C	Centrifuged, rotary evaporator	Mean; SD
(Hamoud *et al*., 2012)	*Candida albicans* *Candida parapsilosis* *Candida glabrata*	10^5 cfu/ml	*Peppermint*		Oil			96 well plates	0.3 mg/ml 0.6 mg/ml 0.6 mg/ml	48 h; 25ºC	GLC-MS	Mean
(Hussain *et al*., 2010)	*Aspergillus flavus* *Aspergillus niger* *Rhizopus spp*	10^4 spores/ml	*Mentha. Arvensis* *Mentha piperita* *Mentha longifolia* *Mentha spicata*	Leaves	Oil/ hydrodistillation	7.00 - 17.0 g kg^{-1} (w/w)		Disc diffusion	14–33 and 16–30 mm 20.0–330.3 and 56.2–139.0 µg/ml	48 h; 30ºC	Clevenger-type apparatus; GC; GC-MS	Mean; SD; ANOVA
(Ibrahim, 2013)	*Aspergillus fumigatus*		*Mentha pulegium L*	Leaves	Chloroform; Methanol	78.1 g 20 g						

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extrac t Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Kasrati *et al*., 2013)	*Candida glabrata*		*Mentha suaveolens subsp. timija*	Aerial part	Oil	1.0 % and 0.9 % (v/w)			6.73–30.0 mm 0.15 and 0.23 mg/ml		GC-MS	
(Mahboubi and Haghi, 2008)	*Aspergillus niger* *Candida albicans*	10^6 cfu/ml	*Mentha pulegium*	Aerial parts	Oil/hydrodistilla-tion	0.27% (v/w)	0.012 5 µl/ml	Disc	10 mm/0.25 µg/ml 16mm/1 µg/ml	48 h; 37ºC	GC-MS	
(Rajkowska, Otlewska, *et al*., 2017)	*Candida albicans*	300 cells/mL	*Mentha piperita*		Oil		≥1.0 % v/v		0.0075% v/v; 0.5× MIC	14days; 37ºC	GC-MS-FID	similarity coefficient
(Valková *et al*., 2021)	*Penicillium crustosum* *Penicillium citrinum* *Penicillium expansum* *Candida glabrata* *Candida albicans* *Candida krusei* *Candida tropicalis*	1×10^6 cell/ml	*Mentha x piperita L* *Rosmarinus officinalis*		Oil		125, 250, and 500 µl/L	Agar disc	6.67 ± 0.58 mm; 9.00 ± 1.00 mm resp; 87.91 ± 1.06% and 90.19 ± 2.99%, 89.38 ± 2.05%, 86.12 ± 3.04%, resp 9.66 ± 0.58 mm 6.67 ± 0.58 mm 9.67 ± 0.58 mm	5days; 25◦C	GC-MS; GC-FID	Mean; ANOVA; Tukey's test
(Madhavan and Sreedevi, 2018)	*Candida albicans*	Not given	*Mentha piperita*	Leaves	Cold water			Disk diffusion method	28.75 ± 2.57mm	48 hrs	Digital Vernier caliper	
(K. K. A. Santos *et al*., 2012)	*Candida albicans* *Candida tropicalis* *Candida krusei* *C. tropicalis, M. arvensis, T. ulmifolia*	10^5 cfu/ml	*Mentha arvensis*	Leaves	Maceration/Etha nol	0.008-0.1024 %		Microdilution method	≥1024 µg/ml	24hrs		
(Al-Bayati, 2009)	*Candida albicans*	2×10^7 cells/ml	*Mentha longifolia L.*	Leaves	Steam distillation			Disc diffusion and Microdilution method	125.0 µg/ml	48hrs		
(Piras *et al*., 2021)	*Cryptococcus neoformans,* *Trichophyton rubrum* *Trichophyton verrucosum*		*Mentha spicata L.*						(0.32 µL/mL			
(El-Kashoury *et al*., 2012)	*Candida albicans* *Saccharomyces cerevisiae* *Aspergillus niger*		*Mentha suaveolens Ehrh*	Aerial parts	Hydrodistillation	0.60%		broth microdilution method	4 µg/ml, 5.2 µg/ml, 6.8 µg/ ml			student's t-test

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Soković *et al*., 2009)	*Aspergillus niger* *Aspergillus ochraceus* *Aspergillus versicolor* *Aspergillus flavus* *Aspergillus terreus,* *Alternaria alternata,* *Penicillium ochrochloron* *Penicillium funiculosum* *Cladosporium cladosporioides* *Trichoderma virid* *Fusarium tricinctum,* *Phomopsis helianthi* *Microsporum canis,* *Epidermophyton floccosum* *Trichophyton rubrum* *Trichophyton mentagrophytes* *Trichophyton tonsurans*		*Mentha spicata L.* *Mentha piperita L.*	Dry plant material	Hydrodistillation			macro- and microdilution method	0.25- 1.5 µL/mL	72hrs		
(Moghaddam *et al*., 2013)	*Dreschlera spicifera* *Fusarium oxysporum f.sp. ciceris* *Macrophomina phaseolina.*		*Mentha piperita*	Leaves	Hydrodistillation	1.38 %			3.9±0.78 mm 3.4±0.73 mm 10.8±1.72 mm	48hrs		
(Houicher *et al*., 2016)	*Fusarium graminearum* *Fusarium moniliforme* *Penicillium*		*Mentha spicata*						2.5 µL mL-1			
(Samber *et al*., 2015)	*Candida albicans* *Candida tropicalis* *Candida glabrata*		*Mentha piperita L.*					broth dilution method	225 ug/ml.	3 days		

Table 2: Summary of selected studies that investigated the antifungal activities of mint plant on various species of fungi (continued)

Author/Study	Targeted Fungi	Inoculate Conc.	Mint Species	Plant Part Used	Extraction Method/Solvent	Extract yield (%)	Extract Conc. Used	Antifungal method of assessment	Zone of Inhibition (mm)/ Antifungal activity	Incubation period	Instrument(s) used	Statistical Test
(Gonçalves *et al*., 2007)	*Candida albicans* *Candida tropicalis* *Candida parapsilosis* *Cryptococcus neoformans* *Epidermophyton floccosum* *Trichophyton mentagrophytes* *Microsporum canis* *Trichophyton rubrum* *M. gypseum* *Aspergillus flavus* *Aspergillus niger* *Aspergillus fumigatus*	1.2 x10 ^{3} cells/mL for yeasts; 1.2 x10^{4} cells/ mL for filamentous fungi.	*Mentha cervina*	Aerial parts	Hydrodistillation			Macrodistillation	0.64- 5µL mL-1	48 hrs to 3-7 days		
(Oumzil *et al*., 2002)	*Candida albicans* *Candida glabrata*	10 ^{4} cfu/ml	*Mentha suaveolens*	Aerial parts	steam distillation	0.012.		Agar diffusion; Micro titration	0.69 -1.38 ppm	24hrs		
(Tullio *et al*., 2019)	*Candida spp* *Cryptococcus neoformans* *Trichophyton mentagrophytes*		*Mentha x piperita*	Whole plants	Steam distillation				0.125-0.5%v/v	72hrs		
(Mishra *et al*., 2016)	*Candida albicans*		*Mentha spicata L.* var. viridis		Steam distillation			agar well	18.67 ± 0.88 mm	3 days		
(Ceyhan-Güvensen and Keskin, 2016)	Yeast strain		*Mentha pulegium*	Leaves				disc diffusion				
(Pietrella *et al*., 2011)	*Candida albicans*	2.5 × 10^{3} cells/ml	*Mentha suaveolens*	Leaves	Hydrodistillation			micro-broth dilution method	0.39-0.78	24hrs		Student t test
(Bakht *et al*., 2014)	*Candida albicans*		*Mentha longifolia*	Aerial parts				disc diffusion method				
(Yadegarinia *et al*., 2006)	*Candida albicans*	10^{7} cfu/ml	*Mentha piperita L.*		Steam distillation			broth dilution method	90mm	48hrs		
(Mimica-Dukic *al*., 2003)	*Trichophyton tonsurans* *Candida albicans*	10^{5} cells/100 µl	*Mentha aquatica L.* *Mentha longifolia L.* *Mentha piperita L.*	Aerial parts	Hydrodistillation	0.69, 3.73, 3.21		Micro dilution technique	8-10 µl/ml	72 hrs		
(Işcan *et al*., 2002)	*Candida albicans*	10^{5} cells/ml	*Mentha piperita L*					Micro-Dilution Broth Method	0.625mg/ml	24hrs		

Another notable mint *Origanum vulgare* shows their plant extract used in the identified studies to have a more significant inhibitory effect when compared to other mint species (Table 2). Here, either whole or leaves of plant part used yielded between 90 to 100% inhibition in the tested microorganism as reported by Bluma *et al*. (2008) and Vasudeva *et al*. (2014), respectively. Separately, Tampieri *et al*. (2005), Vasudeva *et al*. (2014) and Helal *et al*. (2019) show *Origanum vulgare* plant extracts can inhibit microorganism pathogen at MIC values of 500ppm, ~0.08 mg/ml and 25 mg/ml respectively. All these observable variation between species may have risen due to differences in the phytochemical composition of the mint species and their biological activities against microorganism tested.

The inhibitory response of each fungal species is relative to the type of mint species extract administered and its responding concentration used. For instance, in a study conducted by Santos *et al*. (2012) where they targeted three *Candida species* (*C. albicans*, *C. tropicalis*, and *C. krusei*) using *Mentha arvensis* and *Turnera ulmifolia* shows that these plants extract has effect on the fugal species even at MIC concentration of 1024 lg/mL. However, *C. tropicalis*. *M. arvensis* and *T. ulmifolia* shows a remarkable inhibitory response to these plant extract at the same concentration. Similarly, Raghavan *et al*. (2018) and Al-Bayati (2009) in their studies used *Candida albicans* utilizing *Mentha piperita* and *Mentha longifolia* leaf extracts respectively. Here the *Candida albicans* in both studies shows a marked sensitivity to both plant extracts (Table 2).

Aspergillus niger were identified to be sensitive to *Mentha suaveolens* Ehrh, and *Mentha spicata L., and Mentha piperita L* even at a lower concentration in studies carried out by El-Sayeda *et al*. (2012) and Soković *et al*. (2009). The inhibitory effect exacted by the essential oils of these plants yielded antifungal activities on *Aspergillus niger* with MICs 6.8 µg/ml to as low 1.0 µL/mL respectively. Other species of fungi that infect human superficial skin *Trichophyton rubrum* among others were shown to be sensitive to *Mentha spicata L* (Piras *et al.*, 2021; Soković *et al*., 2009). There susceptibility to the mint plant when compare with other studies is so significant that at MIC of 0.5 to 0.32 a strong growth of *Trichophyton rubrum* is inhibited.

Mint Species tested for antifungal growth

A number of mint species (28) were identified in the 57 studies selected (Table 2). In terms of plant extracts used, *Mentha piperita* was most abundant studied mint species utilized in 28 studies and tested mainly against *Candida albicans*. Other notable *Mentha species* identified include; *Mentha longifolia* and *Mentha spicata* occurring in 8 studies, *Mentha pulegium* occurring in six studies, *Mentha suaveolens* and *Mentha arvensis* appears in five and four studies, respectively. Similarly, other mint plant species tested in the antifungal assay were *Origanum vulgare* (appearing in 4 studies), *Mentha cervina*, *Nepeta cataria* and *Rosmarinus officinalis* appearing twice in the studies respectively. In addition, *Mentha viridis, Calamintha nepeta ssp. glandulosa*, *Lavandula stoechas. ssp. stoechas*, *Salvia fruticosa*, *Salvia macrosiphon Boiss*, *Salvia ofcinalis*, *Salvia tomentosa*, *Satureja hortensis* and *Ziziphora tenuior* appear once in the identified mint species.

Mentha piperita, the most abundant mint species present in different studies gave a positive result in the antifungal activities depending on plant part, type of solvent and concentration of plant extract used. For instance, the plant part readily used here is the mint leaves followed by the whole and aerial plant. Interestingly, the leaf of *Mentha piperita* shows variation of responses in the identified studies on fungi (Table 2), where in studies like that of Bluma *et al*. (2008) up to 90% inhibition were observed, while in van Vuuren *et al*. (2009) studies shown an efficacy of MIC values of 6mg ml^{-1} against fungi pathogen, and as low as 0.25 µL/ml MIC value was obtained on tested microorganism in dos Santos *et al*. (2021) studies. However, in the case of *Mentha longifolia* the plant used is either leaf or the aerial parts of the plant. Both plant part used shows remarkable effect on the tested microorganism (Table 2). Another notable mint *Origanum vulgare* shows their plant extract used in the identified studies to have a more significant inhibitory effect when compared to other mint species (Table 2). Here, either whole or leaves of plant part used yielded between 90 to 100% inhibition in the tested microorganism as reported by Bluma *et al*. (2008) and Vasudeva *et al*. (2014), respectively. Separately, Tampieri *et al*. (2005), Vasudeva *et al*. (2014) and Helal *et al*. (2019) show *Origanum vulgare* plant extracts can inhibit microorganism pathogen at MIC values of 500ppm, ~0.08 mg/ml

and 25 mg/ml respectively. All these observable variation between species may have risen due to differences in the phytochemical composition of the mint species and their biological activities against microorganism tested.

Antifungal assessment methods

The *in-vitro* assessment of the antifungal activities of the various species of mint employed hydro distillation approach for the extraction of bioactive compounds. Essential oils where mainly the forms of the end product of the extraction process with 0.22 to 1.66% yield across the identified articles. This depends on the starting size of the sample mint, as in one study up to 7 – 17g/Kg (w/w) was obtained as the yield across four different species of *Menthas* (Hussain *et al*., 2010). Other solvents such as chloroform, ethanol and methanol were used in various studies for the extraction of the bioactive component of the plants.

In-vitro antifungal activity test was carried out using mainly four formats of assessment. Sixteen studies used disc diffusion method for assessing the antifungal sensitivity test, nine studies used '96-well microtiter plates' method of assessment. Eight studies used the 'broth dilution' method, also in a different study, 8 articles used the 'agar well diffusion' assessment method. In another study, the combination of two format of assessment was used, this include 'disc diffusion' and 'microdilution' method (Al-Bayati, 2009). Also, macro- and microdilution method was employed for the assessment (Soković *et al*., 2009), which involved large number of fungal species in the sensitivity test. However, disc and well diffusion method were mainly the method for administering the mint extract in the microbial growth environment, with 15 studies utilizing disc method, and 12 studies using the well approach. The concentration used ranges from 0/50 to 5 % (v/v) or 1 to 128 mg/ml of various diluent. The antifungal activities are measured by either zone of inhibition or minimum inhibitory concentration (MIC). Twenty-three studies used MIC as means to determine the antifungal activity, 13 studies use zone of inhibition (ZI), 8 studies used both MIC and ZI, while 5 studies used percentage reduction. Despite the method of measuring the antifungal activity, each tested mint extract shows some degree of effect against the various strains of fungi used in the studies.

Importantly, the exposure of the mint extract to inhibit the fungi growth varies considerably in different studies. Fifteen studies use 48 hours exactly, while 8 studies used between 24 to 48 hours, two studies used 12 hours and five studies used 3 to 14 days for the incubation period. However, the incubation temperature ranges across the studies were between 25 to 37^{o}C.

Solvents used for extraction

From the findings of this review, 4 solvents were mostly used in the studies to extract the bioactive compounds of the selected mint plants (Table 2). They include water, ethanol, chloroform and methanol. Other solvents used include hexane, isopropanol and dichloromethane. These choices depend on the research design, part of plant to be extracted and the polarity of the bioactive compound of interest. From this review a trend in the use of polar solvents for extraction was observed. This could be because of the high extract yield that is obtainable as a result of using highly polar solvent (Nawaz *et al*., 2020). It was also observed that ethanol was the most used solvent in the studies reviewed. This choice may be because of its ability to extract both polar and non-polar compounds which increases the quantity of phytochemical constituents in an extract (Akinmoladun *et al*., 2022).

The extraction method commonly employed in mint studies as identified here, is the hydrodistillation. The hydrodistillation method is identified in 19 studies (Table 2), used for extracting essential oil for the antifungal activity. This method of extraction can be done either by water distillation, water and steam distillation, and straight steam distillation (Aramrueang *et al*., 2019), to isolate volatile compound that will be represented in the oil. In total, twenty-seven (27) mint oil were employed various study here to test the antifungal activity of the mint plant. Selecting the right solvent for extraction in a biological experiment is a key and major step in obtaining a quality research outcome. Here, the isolated essential oil shows various antifungal activities from 1.125 mg/ml (MIC value) for *Mentha piperita* oil on *Candida albicans* in the study of Tyagi and Malik (2010); to 100% inhibition of *Mentha viridis oil* on *Aspergillus flavus*, *Aspergillus parasiticus*, *Aspergillus ochraceus* and *Fusarium moniliforme* growth as studied by Soliman and Badeaa (2002) (Table 2). However, ethanolic extract of the mint plant shows appreciable antifungal activity in two

studies, with a remarkable zone of inhibition. Here, Khanzada *et al.* (2021) shows ethanolic extract of *Mentha piperita* has an effect on *Fusarium solani* with a zone of inhibition of 10.0 ± 0.1 mm; while in the Santos *et al.* (2012) study shows ethanolic extract of *Mentha arvensis* has an inhibitory effect on *Candida albicans*, *Candida tropicalis* and *Candida krusei* at MIC value of ≥1024 µg/ml.

Instruments used for extract validity

Only eight different instruments, among the 22 studies were used to evaluate validity of extracted constituent. Of the research which determined the extract make up and the quantity of each component, 18 studies employed the use of Gas chromatography mass spectrometry (GC-MS), nine studies used Gas chromatography, while eight studies used both GC and GC-MS. Most of the studies that used these instruments use oil extracts from the mint plants as the agent for the antifungal properties. Two studies used HPLC to determine the constituent identity of the ethanolic and oil extract of the mint species; thereby validating antifungal properties of the mint extract. Also, 2 studies used scanning electron microscopy (SEM) to validate the microstructure characteristics and effect of the mint extract on the fungi membrane integrity (Agarwal *et al*., 2008; Sharma *et al*., 2017). Other instrumentation used for validation include TLC for determining the quantity and make-up of a mint extract constituent (Höfling *et al*., 2010; Vasudeva *et al*., 2014), where organic solvent were used in both studies to extract the bioactive components of the mint plant.

The validation of bioactive compounds in the essential oil or any of the extract of the mint plant using the above instruments can aid in verifying the potentials of the constituent of the individual mint extract. According to GC-MS study by Rajkowska, *et al*. (2017) reveal that Peppermint oil are predominated by Menthol (43.9%), Menthone (23.1%) and some quantity of 1,8-Cineole (6.6%) and Menthyl acetate (4.9%), among other, both exacting inhibitory activity on fungi species. Whereas GC-MS studies by Petretto *et al.* (2014) shows *Mentha suaveolens* essential oil was dominated by oxygenated compounds (87.13%) which many have contributed in the inhibition of all fungi growth tested. However, HPLC analysis revealed Potent polyphenols *Mentha piperita* with antifungal properties this include ferulic acid (3.01 ± 0.26 µg/mg extract) and caffeic acid (0.43 ± 0.04 µg/mg extract) (Khanzada et al., 2021).

Mode of antifungal susceptibility measurements

At various concentrations, the mint plant presents various susceptibility values depending on the mint species and type of extract used, and targeted fungi species. Considering the mode of evaluation used in different studies, either by measuring the zone of inhibition or reading MIC, *M. piperita* exert the most zone of inhibition tests up to 90 mm against *C. albicans* (Table 2). In another antifungal susceptibility study, *M. piperita* exert a zone of inhibition to a distance of 8.5 cm (85 mm), this sensitivity test was positive for multiple fungal species including *Candida* and *Aspergillus species* (Table 2). Magro *et al*., (2006) studies, shows that *Aspergillus niger* is susceptible to a concentration of 1 and 1.50mg/ml of *M. piperita* aqueous extract affecting fungi growth, by reducing the colonies' diameters to the zone of ~7.9 cm (79mm) and ~5.9 cm (53 mm). Reduction of colonies growth of up to 10 mm was observed with *Lavandula stoechas. ssp. Stoechas* oil against *C. albicans* (Table 2), *Nepeta cataria* ethanolic extract *C. albicans*, *Aspergillus flavus*, *Fusarium spp.*, *Penicillum spp.*, and *Trichophyton species*. Another zone of inhibition measurement at 10 mm was exerted by *M. pulegium* oil against *A. niger* and *C. albicans* even at a concentration of 0.0125µl/ml of 0.27% (v/w) plant extract yield. The least zone of 3.4 mm was exerted by *M. piperita*; however, various zone of inhibition was noted for other mint species ranging from 45 -3.9 mm and 4.46 - 1.06 cm for the evaluation of the antifungal susceptibility testing.

Similarly, the MIC susceptibility measurement provides the lowest concentration at which the growth of fungi species/colonies is completely inhibited by the mint extracts. Here, the lowest MIC value of 0.001 to 0.06 mg/ml is associated with *M. piperita* methanolic extract susceptibility test against *Candida albicans*, *Candida dubliniensis*, *Candida parapsilosis*, *Candida tropicalis*, *Candida guilliermondii*, *Candida utilis*, *Candida krusei*, *Candida lusitaniae*, *Candida glabrata*, *Candida rugosa* (Table 2). The highest MIC identified in this study is 16mg/ml which inhibits the growth of *C. albicans* by the action of *M. piperita* oil extract after 24 hours of exposure

to the mint extract. Also, the MIC susceptibility of *C. albicans* to *M. piperita* performed using Agar plate dilution, Broth dilution, and 96-well microplate, shows that ~1.13 mg/ml (~1130µg/ml) of the mint essential oil is required to exert it anti-fungicidal activity (Table 2). Other studies show that as low as 0.25µL/mL to a concentration up to 1024µg/ml within diverse mint species yield a significant growth inhibition among various fungi species (Table 2). This shows that mint extract has an effect on fungal growth, since various susceptibility measurements demonstrated that there is a significant effect on the inhibition of fungi species growth based on the MIC values presented in Table 2. This is further demonstrated from identified studies that reported relatively to complete growth inhibition at 70 to 100% on various fungi species (Table 2) by the effect of mints such as *Mentha piperita*, *Origanum vulgare*, *Minthosthachys verticillata*, *Rosmarinus officinalis*, and *Mentha viridis*, even at MIC of ~0.01mg/ml and ~0.09mg/ml.

DISCUSSION

The three major assessment methods identified in this study were disc diffusion, broth/agar dilution, and 96-well microtiter-plate which have been used in various antimicrobial susceptibility tests. These methods identified are generic and reproduceable as they give a clear and distinct result area on the antifungal extract's effects on the growth fungi. In addition, they could be reliable assessment methods, where data generated from the observation can easily be compared to the response of the fungi organism from the potential antifungal properties of the plants. These traditional methods take an average of two to three days to carry out the sensitivity test. Other methods not identified in this study include molecular (genotypic), flow cytofluorometric and bioluminescent methods. Recently, more precision assessment methods are advocated, such as the genotypic which will facilitate the identification of antifungal resistance gene, thus, increasing the accuracy of susceptibility test and the specificity of the various testing agents (van Belkum *et al*., 2019; Yee *et al*., 2021).

The antifungal activities of mint plants identified here were dose-dependent on the selected fungi species. For instance, the most inhibitory effect with 100% inhibition of growth is seen in the chloroform and oil extract of *Origanum vulgare* (Vasudeva *et al*., 2014), where the concentration of the extract used is at 10 mg/ml and the minimum inhibitory concentration (MIC) on the tested organism *Aspergillus niger* was 0.07800 and 0.00970 mg/ml for the chloroform and oil extract, respectively. Also in another study, 10 mg/ml of the extract was used but the zone of inhibition identified falls within the range of 13 - 15 mm and the MIC 18 – 36 mg/ml targeted at various *Candida species* using *Mentha longifolia*, *Mentha piperita* and *Mentha arvensis* organic extract instead of the oil (Doddanna *et al*., 2013; Gursoy *et al*., 2009). However, the minimal amount of 12µl of oil on inhibition zone between 39 – 45 mm with MIC 0.4 – 25 mg/ml was identified in another study (Helal *et al*., 2019), these activity was against *Candida albicans* for the following mints *Mentha cervina*, *Ocimum basilicum*, *Origanum vulgare*, *Mentha pulegium* and *Salvia oficinalis*. These variation in the antifungal susceptibility may depend on the biochemical composition of the various extracts. More so, oil or any organic solvent extracts containing phytochemical may exert variety of action against fungi growth either through disrupting the integrity of any molecular component cell, interfering with the cellular metabolic processes, among others (Vasudeva *et al*., 2014). Essential oils from mint plant has been shown to have the capacity of changing fungi morphology, increasing its membrane permeability leading to loss of intercellular electrolyte, macromolecules such as soluble carbohydrates, proteins and nucleic acids (Yan *et al*., 2021). The physiochemical properties of oil extracts, alongside its phytochemical and long use from ancient time (Nazzaro *et al*., 2017), may have informed its repeated use in various studies identified here.

Determining the phytochemical composition of plant extract used in any assessment method requires the use of highly sensitive instrumentation for detecting the bioactive compounds. Interestingly, majority of the instruments used are of the same class and capable of analyzing soluble and volatile compounds imbibed in the assessment discs. Compounds such as phenolics, flavonoids and alkaloids even at very low concentration in the extract can flow from the edge of the agar or paper disc gradually decreasing as the space between the disc and fungi increases, until it defines the inhibitory potential of the extract

(Sandle, 2016; Tenover, 2015). Thus, these bioactive molecules can be screened using chromatographic assay such as GC, GC-MS, HPLC, among others at that very low concentration. These instruments used in this study can aid to correlate the bioactive constituent against the fungi in each assessment methods such as the disc diffusion (Al-Huqail *et al*., 2019; Beniaich *et al*., 2022; Negi *et al*., 2020; Tonea *et al*., 2016).

Therefore, it is important in every assessment method adopted that the constituent composition of the extract and the amount present be evaluated. Generally, the three-assessment methods: 'disc diffusion', 'broth/agar dilution', and '96-well microtiter-plate' can be explored within the mint species against the fungi species for investigating the antifungal potential of the mint extracts.

CONCLUSION

In this review we identified various mint species and the antifungal potential of their extracts on fungal isolated. Various extraction and assessment methods of compared show different effect against fungal pathogens vary according to mint species. According to our findings, we feel that the disc diffusion method be used for any mint plant antifungal assessment potential, not just only because it is the most applied method in this reviewed, but for its distinct and remarkable inhibition values (either measure as MIC or zone of inhibition) against fungal growth. Mints oil should be further explored for its applications as an antifungal agent, since majority of the assessment done in our review shows the mint oil is rich in constituents that can inhibit fungal growth. Therefore, it is important to continue to explored the essential oil of mint plants for their antifungal properties.

Conflict of Interest

We the authors, declare that we have no competing interests in the research.

Author contribution

SA planned and conducted the study, drafted and revised the manuscript. IPE validated the data and reviewed the drafted manuscript. All authors read and approved the final paper

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