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A Review on Study Efficiency of Thymus Vulgaris L Plant Extract on Multidrug Resistance Bacteria

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Abstract

Since fewer or occasionally no antimicrobial agents are effective against such bacteria, the global rise of multi-drug resistant bacteria has turned into a health crisis. The objective of the presented work is to determine the antibacterial efficacy of Thymus vulgaris extracts against bacteria that have developed multidrug resistance, including staphylococcus, E. coli, and Klebsiella. T. vulgaris, a prominent aromatic plant with around 100 species worldwide, is frequently utilized both for culinary and medicinal purposes. Becaise of the numerous therapeutic benefits of its essential oils, commonly referred to as thyme oil, the genus Thymus contains significant medicinal herbs that come highly recommended. Because of their biological and pharmacological characteristics, thymus species are regarded as medicinal plants. Its primary ingredients, carvacrol and thymol, are responsible for its characteristics. Among all herbs, fresh thyme possesses the most antioxidants. Thymus vulgaris L. is frequently utilized in folk medicine for treating a wide range of illnesses, including gastro enteric and bronchopulmonary disorders. In vitro tests against Staphylococcus sp., E. coli strains, and Streptococcus pp. revealed antimicrobial activity of thyme essential oil and the compound thymol. Strongest antimicrobial effects have been observed in thyme essential oil.

Keywords:- Thymus vulgaris L plant , Medicinal Application of thyme plant , Antibacterial activity

Introduction

Antimicrobial drug resistance is a global issue that affects both developing and developed nations, hospitals, and the general public (1). The WHO launched the first international policy to combat this phenomenon; one of the references of such strategy is monitoring trends in the antimicrobial resistance with the use of standardized microbiological techniques.

Infections with resistant bacteria have a negative impact on treatment outcomes, illness duration, costs, and disease spread. Multidrug-resistant (MDR) bacteria are a serious warning to all areas of medical science since they can lead to treatment failure, which poses serious risks, especially when it comes to critically ill patients [2,3]. The most difficult organisms to treat include those that are extensively drug-resistant (XDR), such as Pseudomonas aeruginosa, Acienetobacter baumannii, Escherichia coli, Mycobacterium tuberculosis, Klebsiella pneumonia, and methicillin-resistant Staphylococcus aureus (MRSA) carrying NDM-1 (New Delhi metallo-beta-lactamase-1) vancomycin resistant MRSA and vancomycin resistant enterococci (VRE) [4]. According to renowned microbiologist A. Fleming, "There is potentially no chemotherapy drug to which the bacteria cannot react by somehow acquiring fastness under suitable circumstances." As a result, there is a good risk that the organism might later acquire a resistance to newly developed medications. Those drugs are also quite expensive. The strongest antimicrobial activities were discovered in thyme essential oils [2]. They appear to have a wide range of antibiotic activity against the microflora which causes hospital acquired infections in various cases. Essential oils could be a valuable weapon against MDR bacteria due to their wide-ranging and complicated activity and their synergistic effects. Additionally, there is no evidence of the development of resistant bacteria following their use, which is extremely encouraging for the human disease's treatment [5].

Multidrug Resistance (MDR) bacteria

The WHO today views antimicrobial resistance as one of the main dangers to the public health all over the world, particularly in light of the expansion of MDR bacterial pathogens worldwide. As a result of the exposure to such medications, the MDR pathogens could develop resistance to various antimicrobials through horizontal gene transfer and gene mutation. The spread and emergence of MDR bacteria throughout the world was caused by insufficient surveillance, antibiotics' misuse, and badly controlled antibiotics regulation in the clinical medicine and livestock industry, despite the fact that resistance acquisition is a natural process [7]. No less than 23,000 deaths each year in the US alone and no less than 33,000 in Europe are directly attributable to resistance to antibiotics, which is a serious health issue [8]. Even though estimates are complicated to make in this subject, it is expected that the number of deaths would rise from the current frightening level to no less than 10 million by the year 2050 [9].

The "ESKAPE" pathogens, which include *S. aureus*, *Enterococcus faecium, K. pneumoniae, P. aeruginosa*, *Acinetobacter baumannii, and Enterobacter spp*., were first mentioned in [10] and are the six most common MDR bacterial pathogens. Other opportunistic pathogens that can develop MDR strains and produce serious infections include *E. coli, Burkholderia cepacia and Enterococcus faecalis*.

Three distinct but connected mechanisms—tolerance, resistance, and persistence—allow bacteria to circumvent the antimicrobial effects of antibiotics [11]. Inherited mutations that impair the effux pumps, drug target, or actual antibiotic molecule are the root cause of resistance, which is the capacity of bacteria to grow in presence of high quantities of some antibiotic. [12] There are resistant populations in all kinds of habitats, including animals, water, inanimate surfaces, people, food, and plants. [13] A considerable increase in the minimal inhibitory concentration (MIC) of antibiotics is needed to efficiently kill resistant bacteria because they might grow when antibiotic pressure is applied, their resistant phenotype is inheritable, and they could grow under antibiotic pressure [14].

Medical plant

In various nations, medicinal plants are employed instead of manufactured drugs. As a result of the growth in bacterial resistance to antibiotics, which has become one of the major global health concerns, scientists are currently focusing on herbal extracts' potential to serve as microbial agents. Different spices, herbs, and extracts are used to flavor food, preserve it, and in the past, a lot of them were also utilized medicinally [15]. Herbal remedies are a rich natural source of both the chemical components of modern medications and the medicinal goods utilized in conventional therapy. All segments of the population use medicinal plants extensively, either directly (in home treatments) or indirectly (in contemporary medicines) [16] . In addition to being

commercially significant, aromatic and medicinal plants have been essential in easing human suffering. [17] . In addition to providing vegetables and fruits, fodder for cattle, and fuel, medicinal plants are also used economically. The primary reason why medicinal plants are employed in medicines is because they include combinations that work synergistically and/or to neutralize negative effects [18]. Medicinal plants are the best source of a wide range of medications, according to the WHO. Compounds from herbal plants are used in conventional treatments that 80% of the populace of developed nations uses [19]. Early 19th-century opium morphine separation sparked the recent discovery of useful chemicals from plants utilized in medicine [20] .

***Thymus vulgaris L* plant**

Thymus vulgaris (Thyme) is a little perennial medicinal plant that is a member of the Lamiaceae family, one of the largest and most well-known flowering plant families, with over 4000 species 220 and genera all over the world. It also goes by the name "common thyme" and is native to the Mediterranean region, North Africa, some regions of Asia, and a few other carefully chosen regions of the entire world, typically grow as a subshrub between 5cm and 30cm tall, with a fibrous ligneous root and small, greenish-grey leaves with narrow edges [21] . It blooms from May to September and has multiple stiff, branched stems that are 10 to 20 cm tall. The flowers are white or purple in color and have a distinct aroma (Figure 1). It is extensively grown as a culinary herb because to its potent scent, which is caused by thymol.

Figure (1)-*Thymus Vulgaris* plant

Chemical Compostopn of Thyme Essentioal Oil

Oils are extremely complex natural mixtures that can include between 30 and 60 different components at wildly varying amounts. The biological qualities of the essential oils are typically determined by these key elements [22]. There are at least six chemotypes of Thymus vulgaris that produce essential oils with various chemical compositions; nevertheless, only the 'thymol'-type, in which thymol is the major constituent, satisfies the definition in the European Pharmacopoeia. Up to 2.5% of the dried herb's composition is essential oil, which mostly consists of thymol, p-cymene, carvacrol, linalool, β-myrcene, γ-terpinene, and terpinen-4-ol. A few substances are glycosides to some extent, the chemical composition of more significant compounds. Figure 2 displays p-cymene, thymol, and carvacrol [23] .

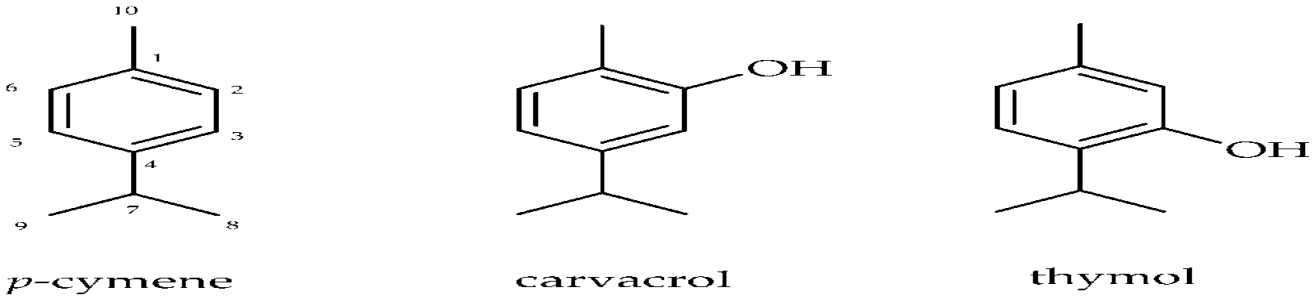

Figure (2): The chemical structure of Thymol, carvacrol and p-cymen.

Medicinal Application of thyme plant

Thymol, the primary component in thyme essential oil, is effective against the bacteria Staphylococcus and Salmonella. Thyme's antiseptic and tonic qualities make it a valuable immune system booster in long-term infections, particularly fungal ones, along with a potent treatment for chest infections like whooping cough, bronchitis, and pleurisy [24]. Thyme and thyme oil were employed as antiseptics, mouthwashes, disinfectants, and fumigants. For small chest and throat infections, the pleasant-tasting infusion can be swallowed, and sore throats could be soothed by chewing on the fresh leaves. Thyme is frequently used to cure children's worms as well as asthma, hay fever, and other herbal conditions. Thyme was touted as an antimicrobial, an antiseptic, an anthelmintic, an astringent, a disinfectant, a carminative, a tonic, and a medicinal drug [25] . In situations of various intestinal illnesses and infestations, such as the ascarids, hookworms, gram-negative and gram-positive bacteria, fungi, and yeasts such as Candida albicans, thyme is tremendously helpful. Thymol, the substance that makes it active, is effective against enterobacteria and coccid bacteria. Additionally, thyme could enhance liver performance and stimulate hunger. It will be utilized for treating infections of the bronchi, urinary tract, and cartilaginous tubes [26] . Thyme is effective in treating laryngitis and inflammation. Thymol, the primary ingredient in thyme's volatile oil, has anti-enterobacterial properties [26] . It is utilized to treat skin conditions such as dermatitis, acne, sciatica, oily skin, and bug bites. White Thyme oil, a rectified product that is kinder to the skin, is also employed. Thyme can be applied to the skin to treat neuralgia, rheumatic pain, and stings and bites [25] .

Antibacterial activity of *Thymus vulgaris* L plant

The chemical components of thyme, notably thyme essential oil, determine its antimicrobial activity [27] , proven the ability of thyme essential oil to combat food-related fungus and bacteria. The presence of terpene hydrocarbons (γ-terpinene) and phenolic compounds (thymol) in thyme essential oil is associated to its antimicrobial ability [28]. When combined with γ-terpinene and thymol, p-Cymene, the third major component of thyme, exhibits synergistic antibacterial effect [29] . Thymol and carvacrol have antifungal and antimicrobial properties [28] . Additionally, the antimicrobial properties of thymol and carvacrol are based on their capacity to disintegrate bacterial outer membranes, which alters pH homeostasis and the equilibrium of inorganic ions, releasing lipopolysaccharides, and increasing the cytoplasmic membrane's permeability to ATP12 [30] .

In vitro, thyme essential oil has the capacity to stop E. coli growth [31]. Other researchers discovered that thymol inhibits the growth of *E. coli and S. typhimurium* [32] . Thymol, the main component in thyme essential oil, has antimicrobial activity, according to a paper [29] . The strongest effect against microorganisms was discovered by [33] to be shared by essential oils of *T. serpyllum and T. vulgaris*, which correlate directly with their thymol level. Additionally, several varieties of thyme's essential oils are utilized in vaporizers to combat a variety of yeasts as well as human pathogenic Gram-negative and Gram-positive bacteria.

Thyme Essential Oil

There are currently 928 species of genus Thymus in Northern Africa, Europe, Southern America, Asia, and Australia. Thyme is a member of the Lamiaceae family. There is growing economic interest in this aromatic and medicinal plant, which includes the species *T. vulgaris* (common thyme) and *T. serpyllum* (wild thyme) [34] . Other

species with a large distribution in Mediterranean basin include *T. Willkomii, T. Satureioides (Morocco), T. Moroderi (Spain), T. Carnosus (Iberian), T. Grandulosus (North Africa and Spain), T. Capitellatus, T. Villosus, T. Camphoratus (Portugal), T. Longicaulis, T. Poulegioides (Italy), T. lotocephalus, and T. herba-barona.* The essential oil from T. vulgaris could include up to 30 monoterpenes, giving the oils from same species' plants a variable chemical makeup and resulting in various chemotypes. For instance, the species T. vulgaris has oil chemotypes in Southern France where the predominant components are geraniol, alpha-terpineol, thuyanol-4, carvacrol, linalool, and thymol, while there is a record of a chemotype with 1,8-cineol as the primary component in Spain. [35] . Thyme oil is one of the top 10 most popular oils worldwide, because it is utilized as a natural food preservative, has powerful antibacterial, antioxidant, and antifungal properties, and adds flavor to a wide range of meals and beverages, along with cosmetics and personal care goods (cosmetics soaps, perfumes, and oral solutions) [36] [37].

Antibacterial activity of *Thymus Vulgaris L*

The inclusion of thymol and carvacrol, two of the thyme essential oils' phenolic components, is thought to be responsible for their potent antibacterial properties. Thymol and carvacrol were the two compounds that exhibited the strongest anti-*Listeria monocytogenes* effects in a study by [38]. The strongest antibacterial efficacy against E. coli O157:H7 and S. aureus was observed in a study involving essential oils of thyme [39].

Utilizing natural antimicrobial agents, like plant essential oils as well as their components, is one of the alternate methods for getting rid of antibiotic-resistant bacteria [40] . Comparing such plants' antibacterial effects, is crucial for selecting the best ones. The effects of thyme oils were evaluated and compared in this work against several pathogenic and resistant bacteria. Results of the current investigation suggest that certain pathogenic bacteria are sensitive to the antimicrobial properties of thyme oil. Thyme has long been utilized for treating a variety of medical conditions, including UTIs, dyspepsia, dysmenorrhea, upper respiratory congestion, coughing, bronchitis, gastritis, sprains, spasms, dysmenorrhea, and stomach cramps, figure (3. 1). Thymus vulgaris could have considerable antimicrobial activity due to its component (Carvacrol 2-11%, Thymol 10-64%, p-Cymene 10-56%, and g-Terpinene 2-31%), as demonstrated in this work. It seems sense that thyme oil's mode of action could be comparable to that of other phenolic compounds, which is widely thought to involve disruption of cytoplasmic membrane, proton motive force (PMF), electron flow, active transport, and cell content coagulation [41].

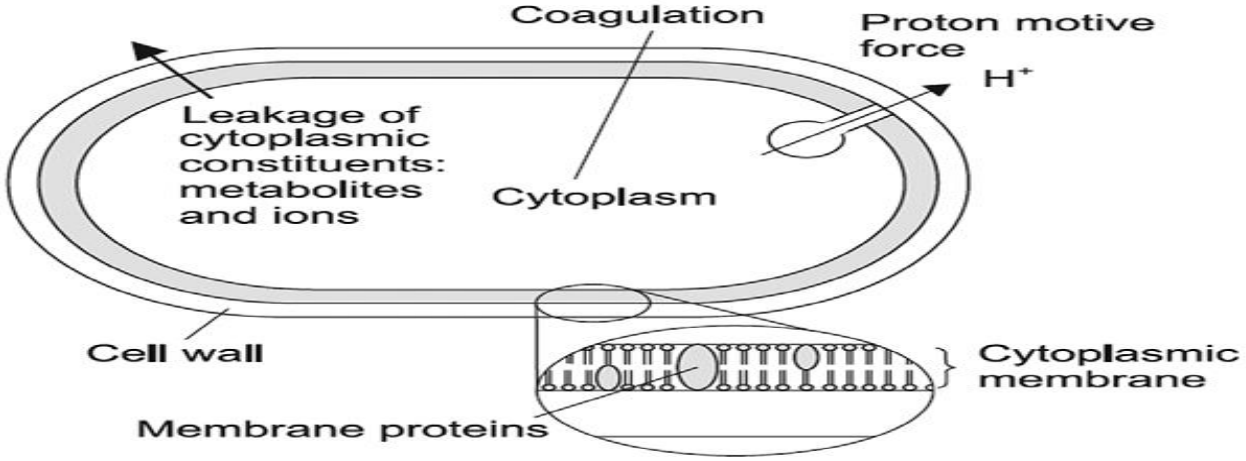

Figure:(3) - Essential oils components effects: cell wall degradation, damage to the cytoplasmic membrane, damage to the membrane proteins, cytoplasm coagulation, leakage of cell contents, and depletion of proton motive force

Conclusion

The results of the current investigation revealed that *T. vulgaris* plant extract has high levels of

flavonoids and essential oil as well as antibacterial and antioxidant properties. More pathological and clinical research is needed to fully understand the unexploited potential of T. vulgaris plant, which could be utilized as an easily accessible source of the natural antioxidants and antibiotics in drugs and food products. Experiments have shown that thyme has the potential to treat a wide range of diseases.

References

1. Okeke, I. N.; Klugman, K. P. and Bhutta, Z. A. (2005). Antimicrobial resistance in developing countries. Part Ii: Strategies for Countainment. J. Lancet. 5,:568-580.
2. Bradley, J. S.; Guidos, R.; Baragona, S.; Bartlett, J. G.; Rubinstein, E.; Zhanel, G. G.; Tino, M. D.; Pompliano, D. L.; Tally, F.; Tipirneni, P.; Tillotson, G. S. and Powers, J. H. (2007). Anti- infective research and development- problems, challenges, and solutions. J. Lan. Infect. Dis.1: 68-78.
3. So, A. D.; Gupta, N.; Brahmachari, S. K.; Chopra, I.; Munos, B.; Nathan, C.; Outterson, K.; Paccaud, J. P.; Payne, D. J.; Peeling, R. W.; Spigelman, M. and Weigelt, J. (2011). Towards new business models for R and D for novel antibiotics. J. Drug Resis. Updat. 14: 88–94.
4. Aruguete, D. M.; Kim, B.; Hochella, M. F.; Jr., M.; Cheng, Y.; Hoegh, A.; Liue, J. and Pruden, A. (2013). Antimicrobial nanotechnology: it is potential for the effective management of microbial drug resistance and implications for research needs in microbial nanotoxicology. J. Env. Sci. Pro. Imp.15: 93-102.
5. Rasooli I, Owlia P (2005) .Chemoprevention by thyme oils of *Aspergillus parasiticus* growth and aflatoxin production. Phytochemistry. 66: 2851–2856.
6. WHO. Worldwide Country Situation Analysis (2015): Response to Antimicrobial Resistance; WHO Library Cataloguing-in-Publication Data;World Health Organization: Geneva, Switzerland .
7. Medina, E.; Pieper, D.H.(2016). Tackling Threats and Future Problems of Multidrug-Resistant Bacteria. Curr. Top. Microbiol. Immunol., 398, 3–33.
8. Cassini, A.; Högberg, D.L.; Plachouras, D.; Quattrocchi, A.; Hoxha, A.; Simonsen, G.N.; Colomb-Cotinat, M.; Kretzschmar, M.E.; Devleesschauwer, B.; Cecchini, M.; *et al*.(2019). Burden of the AMR Collaborative Group. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: A population-level modelling analysis. Lancet Infect. Dis. 2019, 19, 55–56.
9. Abat, C.; Rolain, J.M.; Dubourg, G.; Fournier, P.E.; Chaudet, H.; Raoult, D (2017) . Evaluating the Clinical Burden and Mortality Attributable to Antibiotic Resistance: The Disparity of Empirical Data and Simple Model Estimations. Clin. Infect. Dis. 65, S58–S63.
10. Rice and colleagues (2008) . Federal funding for the study of antimicrobial resistance in nosocomial pathogens: No ESKAPE. J. Infect. Dis. 197, 1079–1081
11. Levin-Reisman, I.; Brauner, A.; Ronin, I.; Balaban, N.Q. (2019) . Epistasis between antibiotic tolerance, persistence, and resistance mutations. Proc. Natl. Acad. Sci. USA, 116, 14734–14739.
12. Brauner, A.; Fridman, O.; Gefen, O.; Balaban, N.Q .(2016) . Distinguishing between resistance, tolerance and persistence to antibiotic treatment. Nat. Rev. Microbiol., 14, 320–330.
13. Tafoukt, R.; Leangapichart, T.; Hadjadj, L.; Bakour, S.; Diene, S.M.; Rolain, J.M.; Touati, A. (2018). Characterisation of blaOXA-538, a new variant of blaOXA-48, in Shewanella xiamenensis isolated from river water in Algeria. J. Glob. Antimicrob. Resist. 13, 70–73.
14. Kim, J.S.; Wood, T.K. (2017) .Tolerant, Growing Cells from Nutrient Shifts Are Not Persister Cells. Mbio 8, e00354-17.

15. Mousavi, S.M., W. George, R. David, S.S. Mirzargar and R. Omidbaigi., (2011) . Antibacterial activities of a new combination of essential oils against marine bacteria. Aquaculture International, 19(1): 205-214.
16. Srinivasan, D., L.P. Perumalsamy, S. Nathan and T. Sures., (2001) . Antimicrobial activity of certain indian medicinal plants used in folkloric medicine. Journal of Ethnopharmacology, 74(3): 217-222.
17. Baquar, S.R., (2001). Textbook of economic botany. 1ST Edn., Lahore: Published in Pakistan by Ferozsons(Pvt) Ltd.
18. Gilani, A. and H. Atta-ur-Rahman, (2005). Trends in ethnopharmacology. Journal of Ethnopharmacology, 100(1-2): 43-49.
19. Arunkumar, S. and M. Muthuselvam, (2009) .Analysis of phytochemical constituents and antimicrobial activities of aloe veral. Against clinical pathogens. World Journal of Agricultural Sciences, 5: 572-576.
20. Kinghorn, A.D., (2001). Pharmacognosy in the 21st century. Journal of Pharmacy and Pharmacology, 53(2): 135-148.
21. Al-Rawi, A., (1988) . Medicinal plants of iraq. Second Edn.: Baghdad
22. Fatimah AA (2014) . Chemical composition, antioxidant and antitumor activity of Thymus vulgaris L. essential oil. Middle-East Journal of Scientific Research.; 21 (10): 1670-1676.
23. Taheri M, Maleknia L, Alizadeh GhN, Almasian A, Chizarif Agh (2014) . Effect of zirconium dioxide nanoparticlesas A mordant on properties of wool with Thyme: Dyeing, flammability and antibacterial. An International Open Free Access, Peer Reviewed Research Journal.; 31(1):85-96.
24. Marina S, Jasmina G, Petar DM, Dejan B, Leo JLD (2010) . Antibacterial effects of the essential oils of commonly consumed medicinal herbs using an in vitro model. Molecules. 15: 7532-7546. DOI: 10.3390/molecules15117532.
25. Prasanth R, Ravi VK, Varsha PV, Satyam S (2014). Review on Thymus vulgaris traditional uses and pharmacological properties. Med Aromat Plants.; 3 (4):1-3.
26. Saleh H, Azizollah JK, Ahmadreza H, Raham A (2015) . The Application of *Thymus vulgaris* in traditional and modern medicine: A Review. Global Journal of Pharmacology.; 9 (3): 260-266.
27. Boruga O, Jianu C, Mişcă C, Goleţ I, Gruia AT, Horhat FG. (2014). *Thymus vulgaris* essential oil: chemical composition and antimicrobial activity. Journal of Medicine and Life.; 7(3): 56-60 .
28. Rota MC, Herrera A, Martínez RM, Sotomayor JA, Jordán MJ. (2008). Antimicrobial activity and chemical composition of *Thymus vulgaris*, Thymus zygis and *Thymus hyemalis* essential oils. Food Control.; 19(7): 681-687.
29. Dorman, H.J.D. and S.G. Deans, (2000) . Antimicrobial agents from plants: antibacterial activity of plant volatile oils. *J. Appl. Microbiol.*, 88: 308–316
30. Lambert, R.J.W., P.N. Skandamis, P. Coote and G.J n(2000). mode of action of oregano essential oil, thymol and carvacrol. J. Appl.
Microbiol., 91 453–462
31. Marino M, Bersani C, Comi G (1999). Antimicrobial activity of the essential oils of Thymus vulgaris L. measured using a bioimpedometric method. J. Food Prot. 62: 1017-1023.
32. Karapinar M, Aktug SE (1987). Inhibition of food borne pathogens by thymol, eugenol, menthole and anethole. Int. J. Food Microbiol. 4: 161-166.
33. Varga E, Bardocz A, Belák A, Maráz A, Boros B, Felinger A, Böszörményi A, Horváth G (2015). Antimicrobial activity and chemical composition of thyme essential oils and the polyphenolic content of different thymus extracts. Farmacia . 63(3): 357-361. 33-
34. Nadia Z, Rachid M (2013). Antioxidant and antibacterial activities of *Thymus vulgaris L.* J. Medicinal and Aromatic Plant Res. 1: 5-11

35. Ben-Jabeur M, Ghabri E, Myriam M, Hamada W. (2015). Thyme essential oil as a defense inducer of tomato against gray molf and Fusarium wilt. Plant Physiol. Biochem. 94: 35-40.
36. Rasooli I, Owlia P (2005) Chemoprevention by thyme oils of Aspergillus parasiticus growth and aflatoxin production.Phytochemistry. 66: 2851–2856
37. Schulz H, Quilitzsch R, Kruger H. (2003). Rapid evaluation and quantitative analysis of thyme, origano and chamomile essential oils by ATR-IR and NIR spectroscopy. J. Mol. Struct. 661-662: 299-306.
38. Yamazaki K, Yamamoto T, Kawai Y, Inoue N. (2004).
39. Burt S. 2004. Essential oils: their antibacterial properties and potential applications in foods – a review. Int. J. Food Microbiol. 94: 223-253.
40. Magi G, Marini E, Facinelli B (2015) . Antimicrobial activity of essential oils and carvacrol, and synergy of carvacrol and erythromycin, against clinical, erythromycin-resistant Group A Streptococci. Front Microbiol.6:165.
41. Daferera DJ, Ziogas BN, Polissiou MG (2000). GC-MS analysis of essential oils from some Greek aromatic plants and theirfungitoxicity on Penicilliumdigitatum. J Agric Food Chem 2000;48:2576–81.

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