

## The Potential Gastrointestinal Health Benefits of Thymus Vulgaris Essential Oil: A Review

Abdulaziz Almanea<sup>1\*</sup>, Gamal S. Abd El-Aziz<sup>2</sup> and Mohamed Morsi M. Ahmed<sup>1,3</sup>

<sup>1</sup>Department of Biological Sciences, Faculty of Science,  
King Abdulaziz University, Jeddah, Saudi Arabia.

<sup>2</sup>Department of Anatomy, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia.

<sup>3</sup>Nucleic Acids Research Department, Genetic Engineering and Biotechnology Research Institute (GEBRI), City for Scientific Research and Technological Applications, Alexandria, Egypt.

\*Corresponding author E-mail: azooz040@hotmail.com

<http://dx.doi.org/10.13005/bpj/1810>

(Received: 21 October 2019; accepted: 02 December 2019)

In recent times, medicinal plants have received great attention worldwide due to their effective pharmacological properties and therapeutic benefits. Numerous chemical compounds extracted from various medicinal plants have manifold biological activities. *Thymus vulgaris* (TV) is a flowering plant with an aromatic odor that has been broadly applied in conventional medicine, food additives, and phyto-pharmaceutical preparations. It is recognized to have promising therapeutic potential for curing various types of diseases. The essential oil extracted from TV, which contains a high quantity of flavonoids, possess antioxidant and antimicrobial activities. Consequently, it could be utilized as a good source in developing novel natural antioxidants and antibiotics. This review explores some of the potential health benefits of TV essential oil (TVEO) on the gastrointestinal tract.

**Keywords:** *Thymus Vulgaris*, health benefits, gastrointestinal tract.

*Thymus vulgaris* (TV) or “thyme” is considered as a famous species of the genus “*Thymus*” (family Lamiaceae), which represents one of the distinguishable plants in many parts of the world, especially throughout the Mediterranean area, North Africa, Asia and Europe.<sup>1,2</sup> *Thymus* family is well known for its biological and natural activities like a food additive and its usage in the traditional medicine and pharmaceutical preparations.<sup>3,4,5</sup>

The TV is recognized as common thyme, which perhaps originated from its utility as incense, has been used for centuries as spice, home remedy, drug, perfume, and insecticide. It is considered one of the most eminent herbs based on its history,

aromatic and medicinal properties. In ancient times, Thyme was used by the Sumerian and Egyptian peoples for various medical purposes to save the people from death. Romans overcooked thyme not only to keep the dangerous animals away but also to give the cheese its flavor. Furthermore, TV has been utilized for several years as a treatment for various diseases such as dental plaque, dermatophyte poisons, pneumonia, anti-inflammatory and intestinal disorders.<sup>6,7,8,9,10</sup>

WHO<sup>11</sup> has indicated that the therapeutic features of TV can be attributed to its essential oil, which is utilized in foods for the flavor, aroma, and preservation and additionally in folk medicine. Moreover, essential oil is one of the

most commonly used essential oils in the food industry and in cosmetics as preservatives and antioxidants.<sup>12,13,14,15</sup>

Numerous studies have been done for exploring the biological activities of the essential oil.<sup>16,17,18,19</sup> Based on these studies, this review was designed to explore some of the potential health benefits of TV essential oil (TVEO) in particular on the gastrointestinal tract.

#### **Origin and history of TV**

Approximately, 300 varieties of aromatic herbs and shrubs are included in the genus *Thymus*; they are found in several parts of the world such as countries with a coastline on the Mediterranean Sea, Asia, Southern Europe, and North Africa. The name of TV belongs to the family "*Lamiaceae*". *Thymoma* is an old Greek expression for enraging that was offered to gods in temples because of its aroma.<sup>2</sup> From ancient times, *Thymus* species have been used as medicinal plants due to their pharmacological and biological features, where their leaves have been broadly utilized as herbal tea, stimulant, antifatulent, cough depressant, treatment of common cold and antibacterial agent.<sup>20</sup> In the Yemeni traditional prescription, the fresh and dehydrated leaves of TV can be utilized as dry particles in warm milk or sesame oil to help in the treatment of various diseases such as gastritis, tonsillitis, pharyngitis and renal colic.<sup>21</sup>

#### **Plant description of TV**

The TV is a small, evergreen shrub growing to 0.2 m at a medium rate, with a groundcover that can be about 40 cm tall.<sup>22</sup> Its stem becomes woody with the age. The leaves are tiny, approximately 2.5 to 5 mm long and differ considerably in the form and hair covering (Figure 1). The leaves are characterized by ovoid to quadrilateral shape and slightly fleshy aerial constituents are utilized for producing oil, primarily by condensation process. Thyme can grow throughout sunny weather. In addition,<sup>23</sup> and<sup>24</sup> demonstrated that thyme needs well-drained soils and 5 – 8pH to grow.

#### **Chemical composition of TVEO**

Different thyme plants contain about 0.5 to 2.5% oil, which is made up of 45–47% thymol, 32–34% p-cymene, 4–5% carvacrol,  $\alpha$ -terpinene, linalool, and  $\alpha$ -pinene.<sup>25</sup> However, the oil extracted from certain species of thyme may contain up to 60% carvacrol.<sup>26</sup> Thymol and carvacrol (phenolic

compounds) are important ingredients with strong antiseptic properties.<sup>25</sup> Also, the essential oil from TV was investigated by *Al-Maqtari et al.*<sup>21</sup> who reported that it contains 56.53% monoterpenes, 28.69% monoterpene hydrocarbons, 5.04% sesquiterpene hydrocarbons and 1.84% oxygenated sesquiterpenes. It was reported that TV essential oil is a rich source of flavonoid phenolic antioxidants such as zeaxanthin, apigenin, lutein, luteolin and thymine.<sup>27</sup>

Furthermore, thyme and its oil are also a good source of some vitamins. They are chiefly rich in Vitamin A and Vitamin C. Vitamin A is necessary for maintaining healthy mucus membranes and skin as well as good vision. Vitamin C provides resistance against microbial infections and combats the harmful pro-inflammatory free radicals. In addition, it is a good source of Vitamin B6 or pyridoxine, which assists in maintaining GABA levels in the brain and acts as a stress buster. Other vitamins found in this herb include Vitamin K, Vitamin E and folic acid.<sup>28,29</sup> In addition, thyme and its oil are considered excellent sources of some important minerals, which are vital for optimal health e.g. potassium, being an important component of cells and body fluids, controls heart rate and blood pressure, manganese is a co-factor for the antioxidant enzyme superoxide dismutase and iron is involved in red blood cell formation.<sup>30</sup>

#### **Antimicrobial activity of TVEO**

Essential oil extracted from TV and its principle component thymol possess a wide range of activity against different types of bacteria and fungi compared with the other oils both in vitro and in vivo studies.<sup>31,32,33,34</sup> Several studies had indicated that thyme and thymol have strong antimicrobial activities against various types of bacteria such



**Fig. 1.** *Thymus vulgaris*

as *Helicobacter pylori*, *Salmonella typhimurium*, *Staphylococcus aureus*, *Selenomonasartemidis*, *Porphyromonasgingivalis*, *Streptococcus mutans* and *Streptococcus sobrinus*.<sup>35,36</sup> The antimicrobial effect was related to the ability of thyme to penetrate the bacterial plasma membrane; causing efflux of intracellular constituents and hence leads to cell death. Likewise, other studies reported a strong antibacterial activity of thymol against certain types of fungi and yeast such as *Aspergillusflavus*, *Aspergillusparasiticus* and *Candida albicans*.<sup>37,38</sup>

Moreover, *Marino et al.*<sup>39</sup> analyzed the thyme oils for their growth inhibition properties against certain strains of both Gram-negative and Gram-positive bacteria. It was observed that all examined thyme essential oils had a strong antimicrobial effect against both types of bacteria. The TV essential oil is considered highly effective in inhibiting the growth of various species of bacteria. An additional study conducted by *Nolkemper et al.*<sup>40</sup> demonstrated that this oil exhibited inhibitory effect against various types of viruses such as Herpes simplex virus type 1 (HSV-1) and an acyclovir-resistant strain of HSV-1.

#### **Antioxidant and anti-inflammatory effects of TVEO**

In animal models and *in vitro* studies, thyme oil and thymol have been shown to exhibit strong antioxidant activities. Moreover, the contained flavonoids were shown to prevent the release of superoxide anion and to protect erythrocytes from oxidative stress. Thymol and carvacole also exerted anti-inflammatory effects by inhibiting the synthesis of prostaglandin.<sup>41, 42, 43, 44</sup>

#### **Gastrointestinal effects of TVEO**

Several studies have demonstrated that thyme and its oil are active in both gastric and intestinal environments. A previous study conducted by *Mossaet al.*<sup>45</sup> suggested that thyme extract could be administered orally to treat indigestion. Individual thyme constituents also affect gut health *in vivo*. It was demonstrated that feeding an equal amount of thymol and carvacrol to animals led to the increase in activities of intestinal and pancreatic trypsin, lipase and protease. They may also improve liver function and act as an appetite stimulant.<sup>46,47,14</sup>

Also, as indicated previously by *Höferlet al.*<sup>48</sup>, thymol and carvacrol have spasmolytic effects. In experimental animal models, *Van*

*den Broucke and Lemli*<sup>49</sup> and *Van den Broucke*<sup>50</sup> demonstrated that flavonoids in thyme could relax smooth muscles of ileum by blocking the histamine and acetylcholine receptors, and/or antagonism of the calcium channel.

TVEO is incredibly useful in cases of intestinal infections and infestations like hookworms, ascarids, gram-positive and gram-negative bacteria, fungi and yeasts such as *Candida albicans*. Its active constituent, thymol, is active against enterobacteria and coccid bacteria. It was speculated that thyme oil may improve intestinal health even without substantially improving the population of beneficial gut microbes.<sup>36</sup> Although it appears to have no major effects on gut microbes, the effect of thyme on the gut microflora needs to be better characterized, particularly in light of the growing importance of the gut microbiome as a factor modifying risk for infectious and chronic diseases that impact human health.<sup>51,52</sup>

In the stomach, thyme oil constituents demonstrated beneficial effects. Compared to controls, carvacrol administered orally (10 ml/kg of 8.3-33.3 mm solutions) to rats prior to induction of acute gastric lesions inhibited damage to the gastric epithelium.<sup>53</sup> This protection was evident even when different methods of inducing gastric damage were used. Carvacrol significantly increased gastric mucus content but did not alter the gastric juice volume or total acidity. Also, carvacrol given at oral doses of 25-100 mg/kg, decreased the severity of chemically induced gastric damages in rodents after 14 days of treatment, compared to controls.<sup>54</sup> Similarly, alpha-terpineol was gastroprotective, when administered orally (10 to 50 mg/kg) prior to dosing with ulcer-inducing agents. This effect apparently was not mediated by inhibition of gastric acid secretion or changes in prostaglandin synthesis.<sup>55</sup>

Another study carried out by *Silvia and collaborators*<sup>54</sup> assessed the anti-ulcer and anti-inflammatory actions of carvacrol. It was reported that carvacrol at concentration 50 mg/kg decreased the edema in numerous types of inflammation. Additionally, it was found that after 14 days of treatment, carvacrol exhibited curative effect on the gastric lesions caused by acetic acid.

Moreover, Carvacrol exhibited very low toxicity in experimental rats and is known as the most common food additive and flavoring

agent in drinks.<sup>[56]</sup> An *in vitro* study carried out by Landaet *al.*<sup>57</sup> indicated that carvacrol displays anti-inflammatory activity, antinociceptive and antioxidant actions.<sup>58</sup>

It was observed that acetic acid-caused impairment in the human gastric mucosa leading to gastric ulcer disease, and the degree of injury is controlled by numerous aspects, such as prostaglandins and cytokines.<sup>59,60</sup> Moreover, Shahin *et al.*<sup>61</sup> have reported that carvacrol doses of 25, 50, and 100 mg/kg, exhibited curative effect on the gastric lesions caused by acetic acid by 60%, 91%, and 81%, respectively. They add that this effect of carvacrol may result from the suppression of inflammatory response.

The mechanism of gastro-protective effects of carvacrol in various rat models was evaluated by Silva and collaborators<sup>54</sup> and it was revealed that 25 mg/kg of carvacrol exhibited gastro-protective effects that were facilitated by endogenous prostaglandins and increased mucus production. It was also demonstrated that carvacrol inhibited the COX-2 antioxidant activity and pro-inflammatory cytokine TNF- $\alpha$  production.<sup>58,62</sup>

An obvious application for the use of thyme oil for curing of ulcerative colitis and Crohn's disease has been submitted in the European. In a study involving young pigs, thymol was orally administered (50 mg/kg) after the morning meal.<sup>63</sup> At 12-hour post-dosing, tissue samples from the oxyntic gland and pyloric mucosa of the stomach were collected. RNA was then isolated and changes in gene expression were determined by microarray analysis. The outcome was that acute thymol dosing activates genes associated with mitosis, regulation of cell division and the digestive function of the stomach.

## CONCLUSION

In conclusion, *Thymus vulgaris* is an important medicinal and aromatic plant that has been used for centuries in phytopharmaceutical preparations, food preservatives and as an aromatic ingredient. Its essential oil contains bioactive monoterpenes such as thymol, carvacrol, and linalool, which have antioxidative, anti-inflammatory, antibacterial and antifungal effects. Thyme essential oil showed antibacterial and antifungal activity.

## REFERENCES

1. Zaidi M. A and Crow Jr S. A. Biologically active traditional medicinal herbs from Balochistan, Pakistan. *Journal of ethnopharmacology*, **96** (1-2): 331-334 (2005).
2. Maksimoviæ Z, Stojanoviæ D, Šoštariæ I, Dajiæ Z and Ristiæ M. Composition and radical scavenging activity of *Thymus glabrescens* Willd. (Lamiaceae) essential oil. *Journal of the Science of Food and Agriculture*, **88** (11): 2036-2041 (2008).
3. Simandi B, Hajdu V, Peredi K, Czukor B, Nobik-Kovacs A and Kery A. Antioxidant activity of pilot plant alcoholic and supercritical carbon dioxide extracts of thyme. *European journal of lipid science and technology*, **103** (6): 355-358 (2001).
4. Sokoviæ M, Glamoëlija J, Aëiriæ A, Kataranovski D, Marin P. D, Vukojeviæ J and Brkiæ D. Antifungal activity of the essential oil of *Thymus vulgaris* L. and thymol on experimentally induced dermatomycoses. *Drug development and industrial pharmacy*, **34**(12): 1388-1393 (2008).
5. Sokoviæ M, Vukojeviæ J, Marin P, Brkiæ D, Vajs V and Van Griensven L. Chemical composition of essential oils of thymus and mentha species and their antifungal activities. *Molecules*, **14**(1): 238-249 (2009).
6. Basch E, Ulbricht C, Hammerness P, Bevins A and Sollars D. Thyme (*Thymus vulgaris* L.), thymol. *Journal of herbal pharmacotherapy*, **4**(1): 49-67 (2004).
7. Aygun O, Aslantas O and Oner S. A survey on the microbiological quality of Carra, a traditional Turkish cheese. *Journal of Food Engineering*, **66**(3): 401-404 (2005).
8. Martínez-Francés V and Ríos S. Lesser known herbal spirits of the Valencia and Alicante provinces East-Southern Spain. *Industrial Crops and Rural Development. Villalobos*; MAJ: 417-426 (2005).
9. Karabegoviæ I. T, Vukosavljeviæ P. V, Novakoviæ M. M, Gorjanoviæ S. Ž, Džamiæ A. M and Lazjiæ M. L. Influence of The storage on bioactive compounds and sensory attributes of Herbal liqueur. *Digest Journal of Nanomaterials & Biostructures (DJNB)*, **7**(4) (2012).
10. Satyal P, Murray B, McFeeters R and Setzer W. Essential oil characterization of *Thymus vulgaris* from various geographical locations. *Foods*, **5**(4): 70 (2016).
11. Organización Mundial de la Salud, WHO, World Health Organization. WHO monographs on selected medicinal plants. World Health Organization (1999).

12. Bendahou M, Muselli A, Grignon-Dubois M, Benyoucef M, Desjobert J. M, Bernardini A. F and Costa J. Antimicrobial activity and chemical composition of *Origanum glandulosum* Desf. Essential oil and extract obtained by microwave extraction: Comparison with hydrodistillation. *Food Chemistry*, **106** (1): 132-139 (2008).
13. Prasanth Reddy V, Ravi Vital K, Varsha P. V and Satyam S. Review on *Thymus vulgaris* traditional uses and pharmacological properties. *Med. Aromat Plants*, **3**: 164 (2014).
14. Hosseinzadeh S, Kukhdan A. J, Hosseini A and Armand R. The application of *Thymus vulgaris* in traditional and modern medicine: a review. *Global J Pharmacol*, **9**: 260-6 (2015).
15. Dauqan E. M and Abdullah A. Medicinal and functional values of thyme (*Thymus vulgaris* L.) herb. *Journal of Applied Biology & Biotechnology*, **5**(02): 017-22 (2017).
16. Stahl-Biskup E. Essential oil chemistry of the genus *Thymus*—a global view. *Thyme: the genus Thymus*, 75-124 (2002).
17. Burt S. Essential oils: their antibacterial properties and potential applications in foods—a review. *International journal of food microbiology*, **94**(3): 223-253 (2004).
18. Shin S and Kim J. H. In vitro inhibitory activities of essential oils from two Korean *Thymus* species against antibiotic-resistant pathogens. *Archives of pharmacol research*, **28**(8): 897 (2005).
19. Politeo O, Juki M and Milos M. Chemical composition and antioxidant capacity of free volatile aglycones from basil (*Ocimum basilicum* L.) compared with its essential oil. *Food Chemistry*, **101**(1): 379-385 (2007).
20. Rota M. C, Herrera A, Martínez R. M, Sotomayor J. A and Jordán M. J. Antimicrobial activity and chemical composition of *Thymus vulgaris*, *Thymus zygis* and *Thymus hyemalis* essential oils. *Food control*, **19**(7): 681-687 (2008).
21. Al Maqtari M. A, Alghalibi S. M and Alhamzy E. H. Chemical composition and antimicrobial activity of essential oil of *Thymus vulgaris* from Yemen. *Turkish J. Biochem*, **36**: 342-349 (2011).
22. Al-Rawi H. L. Chakravarty. Medicinal plants of Iraq, Ministry of Agriculture and irrigation, State Board for Agricultural and Water Resources Research. National Herbarium of Iraq, Baghdad, **93** (1988).
23. Huang J, Huang C and Liebman M. Oxalate contents of commonly used Chinese medicinal herbs. *Journal of Traditional Chinese Medicine*, **35**(5): 594-599 (2015).
24. Prasanth Reddy V, Ravi Vital K, Varsha P. V and Satyam S. Review on *Thymus vulgaris* traditional uses and pharmacological properties. *Med. Aromat Plants*, **3**: 164 (2014).
25. Bagamboula C. F, Uyttendaele M and Debevere J. Inhibitory effect of thyme and basil essential oils, carvacrol, thymol, estragol, linalool and p-cymene towards *Shigella sonnei* and *S. flexneri*. *Food microbiology*, **21**(1): 33-42 (2004).
26. Azaz A. D, Irtem H. A, Kurkcuoğlu M and Baser K. H. C. Composition and the in vitro antimicrobial activities of the essential oils of some *Thymus* species. *Zeitschrift für Naturforschung C*, **59**(1-2): 75-80 (2004).
27. AgroWeb. Thyme- The timeless herb of albania. 2016; <http://agroweb.org/article.html?id=thymethe-timeless-herb-of-albania>
28. Dauqan E. M and Abdullah A. Medicinal and functional values of thyme (*Thymus vulgaris* L.) herb. *Journal of Applied Biology & Biotechnology*, **5**(02): 017-22 (2017).
29. National Institutes of Health. 2016. Vitamin B6. U.S. Department of Health & Human Services. <https://ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/>
30. Sharangi A. B and Guha S. Wonders of leafy spices: Medicinal properties ensuring Human Health. *Science International*, **1**(9): 312-317 (2013).
31. Lai P. K and Roy J. Antimicrobial and chemopreventive properties of herbs and spices. *Current medicinal chemistry*, **11**(11): 1451-1460 (2004).
32. Mitsch P, Zitterl-Eglseer K, Köhler B, Gabler C, Losa R and Zimpernik I. The effect of two different blends of essential oil components on the proliferation of *Clostridium perfringens* in the intestines of broiler chickens. *Poultry science*, **83**(4): 669-675 (2004).
33. Penalver P, Huerta B, Borge C, Astorga R, Romero R and Perea A. Antimicrobial activity of five essential oils against origin strains of the Enterobacteriaceae family. *Apmis*, **113**(1): 1-6 (2005).
34. Al-Bayati F. A. Synergistic antibacterial activity between *Thymus vulgaris* and *Pimpinella anisum* essential oils and methanol extracts. *Journal of ethnopharmacology*, **116**(3): 403-406 (2008).
35. Manou I, Bouillard L, Devleeschouwer M. J and Barel A. O. Evaluation of the preservative properties of *Thymus vulgaris* essential oil in topically applied formulations under a challenge test. *Journal of Applied Microbiology*, **84**(3): 368-376 (1998).
36. Ceyhan N and Ugur A. Investigation of in vitro antimicrobial activity of honey. *Rivista di biologia*, **94**(2): 363-371 (2001).
37. Arras G and Usai M. Fungitoxic activity of 12 essential oils against four postharvest citrus

- pathogens: chemical analysis of Thymus capitatus oil and its effect in subatmospheric pressure conditions. *Journal of Food Protection*; **64**(7): 1025-1029 (2001).
38. Inouye S, Uchida K and Yamaguchi H. In vitro and in vivo anti Trichophyton activity of essential oils by vapour contact. *Mycoses*, **44**(3 4): 99-107 (2001).
  39. Marino M, Bersani C and Comi G. Antimicrobial activity of the essential oils of Thymus vulgaris L. measured using a bioimpedometric method. *Journal of food protection*, **62**(9): 1017-1023 (1999).
  40. Nolkemper S, Reichling J, Stintzing F. C, Carle R and Schnitzler P. Antiviral effect of aqueous extracts from species of the Lamiaceae family against Herpes simplex virus type 1 and type 2 in vitro. *Plantamedica*, **72**(15): 1378-1382 (2006).
  41. Youdim K. A and Deans S. G. Effect of thyme oil and thymol dietary supplementation on the antioxidant status and fatty acid composition of the ageing rat brain. *British Journal of Nutrition*, **83**(1): 87-93 (2000).
  42. Nickavar B, Mojab F and Dolat-Abadi R. Analysis of the essential oils of two Thymus species from Iran. *Food chemistry*, **90**(4): 609-611 (2005).
  43. El-Nekeety A. A, Mohamed S. R, Hathout A. S, Hassan N. S, Aly S. E and Abdel-Wahhab M. A. Antioxidant properties of Thymus vulgaris oil against aflatoxin-induced oxidative stress in male rats. *Toxicol*, **57**(7-8): 984-991 (2011).
  44. Amiri H. Essential oils composition and antioxidant properties of three thymus species. Evidence-Based Complementary and Alternative Medicine, (2012).
  45. Mossa J. S, Al-Yahya M. A and Al-Meshal I. A. Medicinal Plants of Saudi Arabia, 1987.
  46. Thompson J. D, Chalchat J. C, Michet A, Linhart Y. B and Ehlers B. Qualitative and quantitative variation in monoterpene co-occurrence and composition in the essential oil of Thymus vulgaris chemotypes. *Journal of chemical ecology*, **29**(4): 859-880 (2003).
  47. Hashemipour H, Kermanshahi H, Golian A and Veldkamp T. Effect of thymol and carvacrol feed supplementation on performance, antioxidant enzyme activities, fatty acid composition, digestive enzyme activities, and immune response in broiler chickens. *Poultry science*, **92**(8): 2059-2069.
  48. Höferl M, Buchbauer G, Jirovetz L, Schmidt E, Stoyanova A, Denkova Z and Geissler M. Correlation of antimicrobial activities of various essential oils and their main aromatic volatile constituents. *Journal of Essential Oil Research*, **21**(5): 459-463 (2009).
  49. Van Den Broucke C. O and Lemli J. A. Spasmolytic activity of the flavonoids from Thymus vulgaris. Pharmaceutisch Weekblad, **5**(1): 9-14 (1983).
  50. Vandenbroucke C. Chemical and Pharmacological Investigation on Thymus Herba and Its Liquid Extracts. In: Plantamedica. PO BOX 30 11 20, D-70451 STUTTGART, GERMANY: GEORG THIEME VERLAG, 1980; 253-254.
  51. Rajpal D. K and Brown J. R. Modulating the human gut microbiome as an emerging therapeutic paradigm. *Science progress*, **96**(3): 224-236 (2013).
  52. Joyce S. A and Gahan C. G. The gut microbiota and the metabolic health of the host. *Current opinion in gastroenterology*, **30**(2): 120-127 (2014).
  53. Oliveira I. S, da Silva F. V, Viana A. F. S, dos Santos M. R, Quintans-Júnior L. J, Maria do Carmo C. M and de CM Oliveira R. Gastroprotective activity of carvacrol on experimentally induced gastric lesions in rodents. Naunyn-Schmiedeberg's archives of pharmacology, **385**(9): 899-908 (2012).
  54. Silva F. V, Guimaraes A. G, Silva E. R, Sousa-Neto B. P, Machado, F. D, Quintans-Júnior L. J and Oliveira R. C. Anti-inflammatory and anti-ulcer activities of carvacrol, a monoterpene present in the essential oil of oregano. *Journal of medicinal food*, **15**(11): 984-991 (2012).
  55. Souza R. H. L, Cardoso M. S. P, Menezes C. T, Silva J. P, De Sousa D. P and Batista J. S. Gastroprotective activity of  $\alpha$ -terpineol in two experimental models of gastric ulcer in rats. Daru: journal of Faculty of Pharmacy, *Tehran University of Medical Sciences*, **19**(4): 277 (2011).
  56. Burdock G. A. Fenaroli's handbook of flavor ingredients. CRC press 2016.
  57. Landa P, Kokoska L, Pribylova M, Vanek T and Marsik P. In vitro anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E 2 biosynthesis. *Archives of pharmacol research*, **32**(1): 75-78 (2009).
  58. Guimarães A. G, Oliveira G. F, Melo M. S, Cavalcanti S. C, Antonioli, A. R, Bonjardim L. R and Araújo A. A. Bioassay guided evaluation of antioxidant and antinociceptive activities of carvacrol. *Basic & clinical pharmacology & toxicology*, **107**(6): 949-957 (2010).
  59. Kobayashi T, Ohta Y, Yoshino J and Nakazawa S. Teprenone promotes the healing of acetic acid-induced chronic gastric ulcers in rats by inhibiting neutrophil infiltration and lipid peroxidation in

- ulcerated gastric tissues. *Pharmacological Research*, **43**(1): 23-30 (2001).
60. Okabe S and Amagase K. An Overview of Acetic Acid Ulcer Models-The History and State of the Art of Peptic Ulcer Research - *Biological and Pharmaceutical Bulletin*, **28**(8): 1321-1341 (2005).
61. Shahin M, Konturek J. W, Pohle T, Schuppan D, Herbst H and Domschke W. Remodeling of extracellular matrix in gastric ulceration. *Microscopy research and technique*, **53**(6): 396-408 (2001).
62. Hotta M, Nakata R, Katsukawa M, Hori K, Takahashi S and Inoue H. Carvacrol, a component of thyme oil, activates PPAR $\alpha$  and  $\beta$  and suppresses COX-2 expression. *Journal of lipid research*, **51**(1): 132-139 (2010).
63. Colombo M, Priori D, Gandolfi G, Boatto G, Nieddu M, Bosi P and Trevisi P. Effect of free thymol on differential gene expression in gastric mucosa of the young pig. *Animal*, **8**(5): 786-791 (2014).