

Natural effect of Oregano essential oils on the survival of *Helicobacter pylori*: A new therapeutic approach.

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Abstract

Helicobacter pylori is an extremely common infection worldwide: more than two thirds of the world's population suffer from it. H. pylori is a bacterium that infects the mucous membrane of the wall of the human stomach. This is often the cause of chronic type B gastritis, gastric ulcers, and gastric cancers. The eradication of this bacterium as a means of prevention and treatment of ulcers and certain stomach cancers is now a solution that natural medicine can implement through a proven phytotherapeutic protocol. And this is an area where essential oils can make a difference. The consequences of this infection depend on the complex interactions that occur between the person who suffers from it and the bacteria: It all depends on the virulence of the bacteria, the genetic constitution of the person, about his age, of a whole set of environmental factors and his eating habits. At present, more or less invasive treatments are content with a very symptomatic and localized approach. Studies have shown that to combat Helicobacter pylori and relieve the symptoms associated with it, it is recommended to ingest natural antibiotic, probiotic and a proton-pump inhibitors (PPIs) treatment. Other studies rather rare propose an approach to stimulate the immunity of the patient and experiment a nutritional approach compatible with the management of the infection and thus better manage the inflammation. Our opinion, which only focuses on recent publications in journals with high-impact, suggests the impact of oregano oil (*Origanum compactum*) that fight infection with Helicobacter pylori. Findings presented herein could be used to develop novel and alternative preventive and therapeutic strategies aimed to fight Helicobacter pylori infection.

Keywords: Essential oils, Helicobacter pylori, Oregano oil, Phytotherapy, naturals substances.

Introduction

The genus *Helicobacter* were first detected by J. Robin Warren in 1979 in stomach biopsies from ulcer patients [1]. *Helicobacter pylori* (*H. pylori*) is a curved, gram-negative rod, with its characteristic strong urealytic ability, is the gastric helicobacter of humans and is found almost exclusively in the human stomach, which provides the reservoir of infection [2]. Marshall and Warren first proposed the association of *H. pylori* with gastric or peptic ulcer disease [3]. Gastritis is experienced as sharp or burning pain emanating from the abdomen. Gastric or peptic ulcers are actual lesions in either the mucosa of the stomach (gastric ulcers) or in the uppermost portion of the small intestine (duodenal ulcers) [4]. Severe ulcers can be accompanied by vomiting, bloody stools, or both. The symptoms are worse at night, after eating, or under psychological stress conditions. The second most common cancer in the world is stomach cancer, and most findings suggest that long-term infection with *H. pylori* is a major contributing factor [5]. The same applies to gastric MALT lymphoma, a

rare stomach cancer, is caused by *H. pylori* infection and is the only cancer which can possibly be cured by antibiotics [6]. The pathogenic properties of *this* bacterium are due to the ability to survive in the acidic gastric juice and multiply within the mucus, to colonize the gastric mucosa and persist as an extracellular bacterium for several years despite the strong immune responses they trigger [7]. Another protective adaptation of the bacterium is the formation of urease, an enzyme that converts urea into ammonium and bicarbonate, both compounds that can participate in the neutralization of gastric juice. Prominent mucosal inflammation is often evident in the antrum, predisposing patients to hyperacidity and duodenal ulcer disease. Before the bacterium was discovered, psychological stress, spicy foods and high-sugar diets, were considered to be the cause of gastritis and ulcers. Now it appears that these factors merely aggravate the underlying infection [8]. *Helicobacter* has been in human stomachs for at least 100,000 years. The bacterium is present in the stomachs of more than 60% of adults over 60 years of age and 25% of healthy middle-age adults [9]. These percentages may

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vary depending on whether one is talking about developed or developing countries. In developing countries, infection occurs early in life; most children are infected by the age of 10, and prevalence remains high (up to 90%) for all adult age groups. In contrast, in developed countries, a progressive increase in prevalence is observed, from a low percentage of infection in those born after 1980 to 40 to 50% infection rates in the older age groups [10]. The modes and routes of transmission of *H. pylori* from person to person remain to be definitely proven. In the infectious diseases affecting the gastrointestinal tract (chapter 22) of the book " Microbiology: A systemic approach" edition 2018, the authors describe the "family transfer" in helicobacter bacteria as epidemiological evidence for both oral-oral and fecal-oral transmission, with the latter being more likely in developing countries, where sanitation and contaminated water supplies may pose a greater risk [11]. In diagnosis, the urea breath test is a non-invasive method that is sometimes used.

This test is usually recommended when verifying that the organism was eradicated by treatment. Other immunoenzymatic assay and molecular tests on the stool are also available [12, 13]. About one-half of the world's population is colonized by *H. pylori*. It's not known what makes some people feel symptoms and get sick, and others do not feel it. It should also not surprise us that the absence of colonization by the bacteria over a short period cannot lead to imbalances and health consequences [14]. Today, there is no treatment to avoid colonization and no effective vaccine for *Helicobacter* [15]. For symptomatic infection, the best treatment is tetracycline plus metronidazole. Currently, these therapies have numerous drawbacks, mostly due to increasing prevalence of antibiotic resistant strains [16, 17]. Given the very limited action of this treatment, eradication of this bacterium as a means of prevention and treatment of ulcers and certain stomach cancers is now a solution that natural medicine can implement through a proven phytotherapeutic protocol. Hence the interest of to develop novel therapeutic agents against *H. pylori* infections. A safe and effective method of treatment is the use of essential oils [18, 19]. They fight against infection and relapse. Here are some essential oils that fight the bacteria *H. pylori*. five plants with maximum effectiveness to know: *Origanum vulgare* (Oregano oil), *Thymus vulgaris* (thyme oil), *Melaleuca alternifolia* (tea tree oil), *Cinnamomum zeylanicum* (cinnamon oil) and *Eugenia caryophyllata* (clove oil). We focus in this mini review on the oregano essential oils known as the best remedy against *H. pylori* infections.

Oregano essential oil (OEO) is considered to be the most effective natural antimicrobial and antioxidant agents [20].

Recent studies have also shown that the OEO is effective as an antioxidant, flavoring agent [21] and retarding the oxidation of lipids [22]; which makes oregano a source of essential oil the most used in the food industry. There are different types of oregano from the genus *Origanum*: *O. vulgare*, *O. onites* L, *O. virens*, *O. majorana* L and *O. viride* representing the Mediterranean region. Carvacrol and thymol are the main antimicrobial, anti-fungal and antioxidant monoterpene phenolic compounds, which account for approximately 85% of OEO [23, 24]. The antimicrobial activity of these compounds is attributed to their lipophilic character. These compounds act as antioxidant agents, retarding lipid oxidation [25]. The antioxidant properties of oregano have been proved to be effective in retarding the process of lipid peroxidation in fatty foods [26]. In addition to the antioxidant and antimicrobial properties of OEO, carvacrol and thymol provide the characteristic flavor and odor. Carvacrol has been found as a potent anti-cancer compound inducing apoptosis in human colon cancer cells [27] and growth inhibition in human cervical cancer cells. Thymol is one of the phenolic compounds of oregano that has a repertoire of pharmacological activities, including anti-inflammatory, anticancer, antioxidant and antimicrobial effects. Recent studies have shown that thymol is responsible for inducing apoptosis in gastric carcinoma cells [28, 29]. There have been reports that toxicity of the OEO constituents were found to be much higher than their therapeutic doses. Although the number of studies on genotoxic effects of OEO constituents is still limited. In bacteria (Table 1), EO and their components perform a variety of mechanisms targeting different pathways, in particular on the cell membrane [30]. Thymol and carvacrol, active ingredients of *oregano*, are able to disintegrate the outer membrane of *H. pylori*, releasing the lipopolysaccharide components, and changing the passive permeability of the cell [31,32].

In a study published in "phytotherapy research", the author emphasizes that the essential oils examined showed different degrees of antimicrobial activity against the strain *H. pylori* SS1. He later ascertains that the EOs of *S. hortensis*, *O. vulgare subsp. vulgare* and *O. vulgare subsp. hirtum* are the most active. despite the significantly low phenol content of the latter. The combination of EO from of *S. hortensis* and *O. vulgare subsp. hirtum* in volume ratio 2:1 showed stronger antimicrobial activity against *H. pylori* [33]. The extracts of *Origanum vulgare*, *Cerastium candidissimum*, *Chamomilla recutita*, *Conyza albida*, *Dittrichia viscosa*, *Anthemis melanolepis* and *Stachys alopecuroides* have been proved active against 15 clinical isolates of *H. pylori* [34]. According to GC- MS, oils in the mixture were characterized by high content of phenols, with carvacrol as the main carrier of antimicrobial activity.

Table 1: Oregano Oil essential and its antibacterial activity related to chemical constituents.

OE	Main constituents	Effective against	Test method	References
O. vulgare	Carvacrol, Thymol, Cymenol, Cymene, alpha-Pinene	<i>H. pylori</i> , <i>S. enteritidis</i> , <i>B. cereus</i> , <i>E. coli</i> , <i>L. monocytogenes</i> , <i>P. aeruginosa</i> , <i>C. albicans</i> , <i>B. subtilis</i> , <i>B. pumilis</i> , <i>S. poona</i> and <i>S. aureus</i>	Broth microdilution method, Checkerboard method, Diffusion method, Resazurin microtitre assays, Germ tube inhibition	Stamatis et al. 2003; Lesjak et al. 2016; Govaris et al., 2010; Gutierrez et al., 2008; Dimitrijevic et al., 2007; Rosato et al., 2009; Hussain et al., 2011; Pozzatti et al., 2010

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Conclusion

About half of the world's population is colonized by *H. pylori*. Oregano essential oils remain an effective alternative to fight against this bacterium. Its action is much greater when it is mixed with other oils rich in phenolic compounds such as *S. hortensis*, cranberry, basil (*Ocimum basilicum*) (Shetty and Labbe 1998) or other. It remains to identify the combination that gives the best synergic effect against *H. pylori*.

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