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Review

# Dietary amelioration of *Helicobacter* infection

Jed W. Fahey[a,b,*], Katherine K. Stephenson[a], Alison J. Wallace[c]

[a] Lewis B. and Dorothy Cullman Chemoprotection Center, Department of Pharmacology & Molecular Sciences, School of Medicine, Johns Hopkins University, Baltimore, MD, USA

[b] Center for Human Nutrition, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA

[c] New Zealand Institute for Plant and Food Research Limited, Lincoln, New Zealand

ARTICLE INFO

*Article history:*
Received 12 December 2014
Revised 1 March 2015
Accepted 2 March 2015

*Keywords:*
Anti-inflammatory
Cancer
Gastric
*Helicobacter*
*H pylori*
Stomach
Ulcer

ABSTRACT

We review herein the basis for using dietary components to treat and/or prevent *Helicobacter pylori* infection, with emphasis on (*a*) work reported in the last decade, (*b*) dietary components for which there is mechanism-based plausibility, and (*c*) components for which clinical results on *H pylori* amelioration are available. There is evidence that a diet-based treatment may reduce the levels and/or the virulence of *H pylori* colonization without completely eradicating the organism in treated individuals. This concept was endorsed a decade ago by the participants in a small international consensus conference held in Honolulu, Hawaii, USA, and interest in such a diet-based approach has increased dramatically since then. This approach is attractive in terms of cost, treatment, tolerability, and cultural acceptability. This review, therefore, highlights specific foods, food components, and food products, grouped as follows: bee products (eg, honey and propolis); probiotics; dairy products; vegetables; fruits; oils; essential oils; and herbs, spices, and other plants. A discussion of the small number of clinical studies that are available is supplemented by supportive in vitro and animal studies. This very large body of in vitro and preclinical evidence must now be followed up with rationally designed, unambiguous human trials.



## 1. Introduction

Major cancer burdens in humans, especially cancers of the liver, uterus cervix, and stomach, are caused by infectious agents. Infections of the human gut with the bacterium *Helicobacter pylori* have only been recognized for about 3 decades and have achieved widespread acceptance only over the past 2 decades [1]. Clinical studies and basic research on the organism and its close relatives [2] have now so thoroughly validated its discovery and the public health importance of that discovery, for which a Nobel Prize was awarded, that it put the word "Helicobacter" on the tips of

*Abbreviations:* UBT, urea breath test.

* *Corresponding author at:* Department of Pharmacology & Molecular Sciences, Johns Hopkins School of Medicine, 855 N. Wolfe St, Suite 625 Rangos Bldg, Baltimore, MD, 21205. Tel.: +1 410 614 2607.
E-mail address: jfahey@jhmi.edu (J.W. Fahey).

http://dx.doi.org/10.1016/j.nutres.2015.03.001
0271-5317/

tongues worldwide [3]. Alongside a dramatically increased awareness of this infectious agent, there has been a proliferation of strategies for cures, some real and many imagined, to eradicate *H pylori* infection.

### 1.1. *Approach and scope of literature reviewed*

We have reviewed herein the basis for using dietary components or ingredients (food) to treat and/or prevent *H pylori* infection, with emphasis on work reported since the comprehensive review of Mahady 10 years ago [4] and with emphasis on components for which there is mechanism-based plausibility and there have been published clinical results. For this purpose, the PubMed, Scopus, and ClinicalTrials.gov databases were searched for relevant studies using keywords related to *Helicobacter* through February 2015, without restrictions, and by reviewing the reference lists from retrieved articles. Focusing upon the components illuminated by this strategy resulted in an examination of bee products (eg, honey and propolis), probiotics and dairy products, vegetables, fruits, oils, essential oils, herbs, and spices and other plants. We have highlighted the work done with these dietary compounds, following a critical examination of the assumption that the only good *H pylori* is a dead *H pylori* (eg, that complete eradication is necessary) (Section 2) and that foods present an alternative to pharmaceuticals for a variety of sound scientific reasons (Section 3).

### 1.2. *Helicobacter infection*

*H pylori* is recognized by the World Health Organization as a class I human carcinogen. Infection with *H pylori* is implicated causally in development of chronic gastritis and in peptic ulcer disease. The pathophysiology of infection has been exhaustively reviewed by others, notably by Kusters et al [5]. Briefly, this gram-negative, flagellated, spirilliform (rapidly motile) bacterium (order Campylobacterales) uses the enzyme urease (not present in mammalian tissues) to convert urea in the stomach to carbon dioxide and ammonia, thus elevating the highly acidic pH of the gastric lumen and allowing it to survive an otherwise exceedingly hostile environment. *H pylori* "tunnels" into the mucus layer covering the gastric epithelium and may persist for decades where it can deliver a highly immunogenic protein dubbed "CagA" and/or a vacuolization-inducing protein dubbed "VacA" to epithelial cells (these are strain dependent), thus activating both immune and inflammatory responses.

*H pylori* infection is an important factor leading to a progression through acute or chronic inflammation of the gastric mucosa and peptic ulcer disease. This gastritis, if persistent, can lead to duodenal ulcers and to mucosa-associated lymphoid tissue lymphoma. If atrophic, it can lead to gastric ulcers and to metaplasia, dysplasia, and gastric cancer. *H pylori* infection results in a 3- to 6-fold increase in the relative risk for developing gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma. Although more than half of the world's population is infected with *H pylori* (usually in childhood), most infected individuals never develop gastric cancer. For those individuals who are infected, attributable risk estimates range from 50% to 73%, such that approximately half a million new cases of gastric cancer yearly (approximately 55% of the total number of cases) are directly attributable to infection with *H pylori* [6]. Societal costs, not only of these cancers but of gastric and duodenal ulcers, are enormous.

### 1.3. *Gastric cancer*

Stomach cancer and gastritis, gastric ulcers, and duodenal ulcers are diseases of both the industrialized and the developing world. In many developing countries, more than 90% of the population is infected with *H. pylori*, but not all developing countries have a high incidence of gastric cancer. Many African countries were originally reported to have an extremely low incidence of gastric cancer and very high rates of *H pylori* infection [7], leading to examination of factors such as bacterial virulence genotype, dietary factors, and host (human) genetic polymorphism to help explain the gastric cancer incidence in this region [8-11]. Although infection with *H pylori* is rapidly declining in Western nations, 50% to 80% of adults in Asia and 70% to 90% of adults in South and Central America are colonized [12]. Globally, gastric cancer is the third leading cause of cancer mortality of both sexes, with more than 951 000 cases worldwide and approximately 723 000 deaths [13], and it is still a leading cause of cancer death in many countries.

### 1.4. *Treatment of Helicobacter infection*

The development or identification of ways in which to lower the prevalence of *H pylori* infection and the consequent risk of cancer is of compelling importance because infection can result in gastritis, gastric and duodenal ulcers, and perhaps other sequelae [14,15]. There are currently no vaccines against this infection, and expectations for their future development are generally negative [16,17]. Combinations consisting of twice daily treatment for 7 to 14 days, with (1) a proton pump inhibitor such as omeprazole or lansoprazole and the antibiotics (2) amoxicillin and (3) clarithromycin or metronidazole (dubbed "triple therapy") [18,19], are generally effective therapies for those who can afford them (eg, residents of industrialized countries). However, antibiotic therapy for infected individuals in most of the developing world is impractical due to complex economic, social, and logistic considerations. There are other problems with antibiotic treatment in that the development of antibiotic resistance is of considerable concern (discussed in more detail later in this review), and eradication rates in many studies are as low as 70%. This bodes poorly for a strategy of treating entire populations with antibiotics.

However, complete eradication of *H pylori* in symptom-free people might not be prudent due to the intriguing but not yet proven possibilities of adverse side effects. These may include such things as an increased risk of lower esophageal adenocarcinoma and an exaggeration of gastroesophageal reflux symptoms [20,21]. The concept that a diet-based treatment could reduce levels of *H pylori* colonization or virulence, mitigate gastritis, inhibit progression of corpus atrophy, and perhaps eventually delay or prevent development of gastric cancer—without completely eradicating the