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Mini review

Current knowledge on alleviating *Helicobacter pylori* infections through the use of some commonly known natural products: bench to bedside

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ABSTRACT

Helicobacter pylori, a spiral-shaped Gram-negative bacterium, has been classified as a class I carcinogen by the World Health Organization and recognized as the causative agent for peptic ulcers, duodenal ulcer, gastritis, mucosa-associated lymphoid tissue lymphomas, and gastric cancer. Owing to their alarming rate of drug resistance, eradication of *H. pylori* remains a global challenge. Triple therapy consisting of a proton pump inhibitor, clarithromycin, and either amoxicillin or metronidazole, is generally the recommended standard for the treatment of *H. pylori* infection. Complementary and alternative medicines have a long history in the treatment of gastrointestinal ailments and various compounds has been tested for anti-*H. pylori* activity both *in vitro* and *in vivo*; however, their successful use in human clinical trials is sporadic. Hence, the aim of this review is to analyze the role of some well-known natural products that have been tested in clinical trials in preventing, altering, or treating *H. pylori* infections. Whereas some *in vitro* and *in vivo* studies in the literature have demonstrated the successful use of a few potential natural products for the treatment of *H. pylori*-related infections, others indicate a need to consider natural products, with or without triple therapy, as a useful alternative in treating *H. pylori*-related infections. Thus, the reported mechanisms include killing of *H. pylori* urease inhibition, induction of bacterial cell damage, and immunomodulatory effect on the host immune system. Furthermore, both *in vitro* and *in vivo* studies have demonstrated the successful use of some potential natural products for the treatment of *H. pylori*-related infections. Nevertheless, the routine prescription of potential complementary and alternative medicines continues to be restrained, and evidence on the safety and efficacy of the active compounds remains a subject of ongoing debate.

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1. Introduction

The relationship between *Helicobacter pylori* and gastric pathology was described about 30 years ago by Warren and Marshall.[1] Since then, *H. pylori* has been recognized as the causative agent for peptic ulcers, duodenal ulcer, gastritis, dyspepsia, mucosa-associated lymphoid tissue lymphomas, and gastric cancer. Although numerous natural products are used in traditional medicine for the treatment of bacterial infections, the first report on the anti-*H. pylori* activity of plant products was published only 8 years after its discovery.[2] Since then, the anti-*H. pylori* activity of different plant products or extracts has been rigorously tested both *in vitro* and *in vivo* in animal models. Triple therapy, which comprises two antibiotics and a proton pump inhibitor, is a conventionally effective treatment for *H. pylori* infections. However, the prolonged use of these antibiotics can lead to antibiotic resistance in the infectious organisms and also alter the normal biota of the gastrointestinal system. Use of alternative medicines has been reported to alleviate the problems of antibiotic resistance while effectively eliminating the pathogens. There are several available reports on the anti-*H. pylori* activity of natural products in certain databases of academic journals such as PubMed and Scopus, but paradoxically only a few articles are available based on the clinical reports. On mining the list of available clinical reports, it was surprising to observe that most of the natural products that have been extensively reported in *in vitro* or *in vivo* systems were not scaled up to clinical trials and offered no clue on their safety profiles. Although natural products are generally considered safe under some permitted dosage rates, their use can be considered as a dietary supplement or an additive therapy. This review was undertaken to assess several selected natural products (Fig. 1) exhibiting anti-*H. pylori* activity, which have been tested in preclinical and clinical trials.

Table 1 – PubMed

Keywords used for search with article type as clinical trial	Number of articles
(*Helicobacter pylori*)	2935
(*Helicobacter pylori*) AND herb	1
(*Helicobacter pylori*) AND plant	45
(*Helicobacter pylori*) AND extract	9
(*Helicobacter pylori*) AND (complementary medicine)	27
(*Helicobacter pylori*) AND (traditional medicine)	12
(*Helicobacter pylori*) AND (folk medicine)	12
(*Helicobacter pylori*) AND (oriental medicine)	3
(*Helicobacter pylori*) AND [herb OR plant OR extract OR (complementary medicine) OR (traditional medicine) OR (folk medicine) OR (oriental medicine)]	68

2. Search strategy

Because our focus for this review article is to look for the natural products that were tested at clinical settings for anti-*H. pylori* activity, our initial search was made in the PubMed and Scopus databases and restricted to "clinical trials" alone. While searching in the PubMed, we included the option "clinical trial" in the search as PubMed allows restricting the search based on article types. However, this option is not available with Scopus, and hence the term "clinical trial" was included in the keyword. The search was done considering the different terminologies that have been used in the literature for the study on natural products, and the details of search criteria and the outcome of the search in PubMed and Scopus databases are summarized in Tables 1 and 2, respectively. On careful analysis of the "clinical trial" report in both PubMed and Scopus databases, we found that only olive oil, *Nigella sativa* or caraway, mastic gum, broccoli, cranberry, *Prunus mume*, cinnamon, propolis, and curcumin were suitable for this review as these were tested at *in vitro* or *in vivo* level and

Fig. 1 – Commonly known natural products – bench to bedside.