



Effects of cinnamon extract on complications of treatment and eradication of *Helicobacter pylori* in infected people

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ABSTRACT

Introduction: Treatment of *Helicobacter pylori* has various side effects like antibiotic resistance. The purpose of this study was to evaluate the effects of cinnamon extract on complications of treatment and eradication of *H. pylori* in infected people.

Methods: In this randomized clinical trial, a total of 98 eligible healthy and *H. pylori*-infected patients approved by esophageal endoscopy were selected. The cinnamon group received multi-drug treatment including clarithromycin, amoxicillin and pantoprazole as well as a cinnamon extract capsule. The control group received multi-drug treatment and a 40 mg starch capsule. In order to analyze the cinnamon extract efficacy, the urea breath test (UBT) was performed 3 months after the start of treatment. Clinical symptoms were evaluated by a questionnaire at the beginning (day of 0), 7 days and 14 days after starting treatment.

Results: The clinical symptoms such as nausea, vomiting, diarrhea, constipation, blurred vision, headache, metallic flavor, epigastric pain, burp, and appetite were significantly reduced in cinnamon group ($P < 0.05$). The odds ratio exhibited a higher eradication rate of *H. pylori* in cinnamon group (73.47% in cinnamon group compared to 53.06% in the control group) ($P = 0.036$).

Conclusion: Cinnamon as assisted therapy is able to alleviate the disease and reduce the complications of *H. pylori* treatment.

Implication for health policy/practice/research/medical education:

The use of assisted therapy such as cinnamon increases *H. pylori* eradication rate and reduces the related side effects. The cinnamon extract might be recommended to physicians as adjunctive therapy for treatment of *H. pylori* infection.

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Introduction

Gastritis or stomach inflammation is a common digestive disorder caused by destruction of gastric mucosal layer (1). *Helicobacter pylori* infection and non-steroidal anti-inflammatory drugs are known as two important causes of mucosal lesions in the stomach and duodenum (2). *H. pylori* infection is considered as one of the most commonly occurring infectious diseases in humans (3). The prevalence of *H. pylori* infection has been reported 80% and 30%-40% in developing and developed countries, respectively, and 68.3% in Iran (4). Eventually, this type

of infection leads to chronic gastritis, peptic ulcer, and gastric cancer (5). One of the non-invasive diagnostic methods in *H. Pylori* infection is urea breath test (UBT) (6). Due to the increased resistance to antibiotics, the therapeutic regimen for the treatment of *H. pylori* is always determined as a multi-drug strategy. The usual treatment for 90% eradication of *H. pylori* is a triple-treatment or standard treatment of clarithromycin, metronidazole or amoxicillin, and a proton pump inhibitor for over 2 weeks administration (7). Multidisciplinary therapies have several side effects, such as oral metallic taste,

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increased light sensitivity, constipation, diarrhea, seizure, and polyneuropathy. *H. pylori* easily become resistant to clarithromycin and metronidazole. On the other hand, these antibiotics cannot be used again after a course of treatment (8). Due to antibacterial and anti-inflammatory properties, cinnamon is used as complementary medicine besides the multi-drug treatment. In recent years, much attention has been paid to herbal remedies in treatment of *H. pylori*. The antimicrobial effects of many plant species on *H. pylori* have been studied, including green tea, black tea, thymes (9), *Origanum majorana*, garlic (10), *Glycyrrhiza glabra* (11), *Salvia officinalis*, *Myrtus*, wormwood, *Mentha*, *Achillea millefolium*, *Chamomile* and *Rosemary* (3,12). Cinnamon is the dried skin of different species of *Cinnamomum* and a member of Lauraceae family. Cinnamon contains 0.5%-2.5% essential oil and nutritional components like cinnamoyl amonic acid, eugenol, transaminase, and polyethylene compounds including hydroxycinnamic aldehyde, ortho-tetracycline aldehyde, cinnamyl alcohol and acetate, and also terpene compounds such as limonene, alfatripenols, tannins, and oligomeric svidinids such as tinan cyanine and even mucilage derivatives (glucan) such as synizilanol (13). Cinnamon has acceptable antimicrobial and antifungal effects due to the presence of ortho-methoxy cinamine aldehyde (3,13). According to drug resistance and side effects of multi-drug therapy as well as anti-bacterial and anti-inflammatory effects of cinnamon (14,15), this study was designed to evaluate the effects of cinnamon extract on treatment of *H. pylori* infection.

Materials and Methods

Study group

This simple double-blind clinical trial study was conducted at the gastrointestinal department of Shahid Beheshti hospital, Hamadan, Iran in 2019. The *H. pylori*-infected patients' age ranged from 18 to 80 years. The sample size was 49 patients for each cinnamon and control groups (totally 98 cases). *H. pylori* infection was confirmed by endoscopy and biopsy procedures.

Inclusion and exclusion criteria and data collection

The presence of clinical symptoms such as dyspepsia, nausea, vomiting and heartburn, and the absence of drug sensitivity, pregnancy and lactation were considered as inclusion criteria. Exclusion criteria were considered the presence of possible side effects, intolerance to the treatment, and incidence of pregnancy during the study. The demographic data were collected by clinical information questionnaire.

Experimental treatments

Patients were under treat with multiple drug medication, including clarithromycin 500 mg, amoxicillin 1 g, and pantoprazole 20 mg. In addition to the previous drugs, the

cinnamon extract was given in the form of 40 mg capsule for cinnamon group and 40 mg starch capsule for the control group. All medications were administrated twice daily. The UBT was hired three months after treatment in order to assess the efficacy of cinnamon extract application. Complications such as nausea, vomiting, diarrhea, constipation, blurred vision, headache, metallic flavor, epigastric pain, heartburn, skin rash, flatus, burp, and reduced appetite were studied at 0, 7 and 14 days after treatment.

Statistical analysis

Data were analyzed by chi-square, Fisher exact, *t* test, and reduction rate tests using SPSS software (version 23). $P < 0.05$ was considered as statistically significant.

Results

According to the demographic information presented in Table 1, the highest age (≥ 50) was observed in both groups of cinnamon (28.5%) and control (34.8%) groups. The percentage of female subjects existed in two groups of cinnamon and control groups were 57.2% and 59.2%, respectively. The highest level of education in two groups was diploma (38.8% in cinnamon group and 42.8% in the control group). People with height of 169-160 cm included the largest number of people available in this investigation (36.8% in cinnamon group and 42.8% in the control group). The highest weight of patients in cinnamon group was ≥ 80 kg and comprised 28.8% of the population. Also, the highest weight in the control group was 60-69 kg and comprised 34.7% of the population. The highest scale of body mass index (BMI) in both groups was 20-25 kg/m² which included 42.8% and 40.8% of population in cinnamon and control groups, respectively. The most common blood type was O⁺ in cinnamon group (59.1%) and control group (57.1%). In the 81.6% of cinnamon group and 83.7% of members in the control group, the experience of smoking was not recorded. Also the experience of ulcer was found 79.6% and 77.5% in cinnamon and control groups, respectively.

The results also showed that the frequency and percentage of treatment complications in eradication rate of *H. pylori* in both groups of cinnamon and control were decreased significantly at the days of 0, 7 and at the end of the study (day 14) including nausea ($P=0.032$), vomiting ($P=0.049$), blurred vision ($P=0.03$), metallic flavor ($P=0.01$), heartburn ($P=0.045$), epigastric pain ($P=0.02$), flatus ($P=0.047$), and also appetite loss ($P=0.01$) (Table 2).

Negative test for UBT *H. pylori* was 73.47% in the cinnamon group and 53.06% in the control group ($P=0.036$) (Table 3).

Discussion

The study aimed to evaluate the effects of cinnamon extract as an adjuvant on *H. pylori* eradication. In this

Table 1. Demographic information at the beginning of the study

Demographic information		Cinnamon group		Control group		P value ^a
		No.	%	No.	%	
Age	<20	4	8.2	4	8.2	0.742
	20-29	10	20.4	7	14.3	
	30-39	10	20.4	9	18.3	
	40-49	11	22.5	12	24.4	
	≥50	14	28.5	17	34.8	
Sex	Male	21	42.8	20	40.8	0.981
	Female	28	57.2	29	59.1	
Education	Illiterate	11	22.5	13	26.5	0.538
	Under diploma	10	20.4	8	16.3	
	Diploma	19	38.8	21	42.8	
	Academic	9	18.4	7	14.4	
Height	<160	9	18.4	6	12.2	0.821
	160-169	18	36.8	21	42.8	
	170-179	15	30.6	16	32.7	
	≥180	7	14.3	6	12.2	
Weight	<60	9	18.4	8	16.3	0.753
	60-69	14	28.6	17	34.7	
	70-79	12	24.4	11	22.4	
	≥80	14	28.6	13	26.5	
BMI	>20	6	12.2	8	16.3	0.468
	20-25	21	42.8	20	40.8	
	26-30	19	38.8	18	36.8	
	>30	3	6.2	3	6.2	
Blood group	O+	29	59.1	28	57.1	0.990
	O-	4	8.2	4	8.2	
	A+	5	10.2	6	12.2	
	B+	7	14.3	8	16.3	
	AB+	4	8.2	3	6.2	
Smoking	Yes	9	18.4	8	16.3	0.234
	No	41	81.6	41	81.6	
Type of ulcer	Gastric ulcer	39	79.6	38	77.5	0.753
	Duodenal ulcer	9	18.4	11	22.5	
	Both	1	2	0	0	

^a Chi-square test.

study, there were no significant differences among the two groups regarding the demographic variables (age, sex, height, weight, BMI, smoking, blood type, and type of ulcer). Perri et al indicating that age and smoking were recognized as risk factors leading to *H. pylori* treatment failure (16). Also, the study of Homayoni showed that with age, the frequency of positive cases enhances. In the Homayoni investigation, the smoking was recognized as an interfering factor in the ulcer treatment, but the results of the present study showed no significant statically alteration (17). In the study of Camargo et al smoking failed the treatment of *H. pylori* infection, and the smoking cessation enhanced the treatment process (18). In the study of Silva et al no significant relation was reported between gender and smoking status. However, there was a significant failure in the treatment of older patients (19).

The obtained results from the present study indicated a significant reduction of therapeutic complications in cinnamon and control groups; such as nausea, vomiting,

blurred vision, metallic flavor, heartburn, epigastric pain, flatus, and also appetite loss. The results of this study and the study of Nair et al showed that cinnamon consumption had fewer side effects (20). Unlike to this study, the Homayoni study reported that post-treatment complications were significantly similar in both groups, although the frequency of complications in the cinnamon group was less in comparison with the control group. In this study, the epigastric pain was seen as the most common factor in both groups, and also the frequency of diarrhea in the cinnamon group was lower than the control group (17). Medications with anti-inflammatory and antibacterial effects can employ as a supplement therapy in the treatment of *H. pylori*. Cinnamon with antibacterial and anti-inflammatory properties can be used as assisted therapy of *H. pylori* (21,22). Hong et al in an *in vivo* study investigated the anti-inflammatory activity of cinnamon juice extract as well as *in vitro* models. They showed that cinnamon had a variety of pharmacological activities

Table 2. Comparison of treatment complications in cinnamon and control groups

Complications of treatment	Groups	Frequency (percent) at the beginning of the study	Frequency (percent) at the end of 7 th days	Frequency (percent) at the end of 14 th days	Frequency (percent) reduction rate (between the beginning of the study and end of 14 th days)	P value
Nausea	Cinnamon	15 (30.6)	12 (24.48)	4 (8.16)	11 (73)	0.032
	Control	17 (34.69)	11 (22.44)	11 (22.44)	6 (35)	
Vomiting	Cinnamon	7 (14.9)	3 (6.12)	1 (2)	6 (85)	0.049
	Control	9 (18.36)	5 (10.20)	5 (10.20)	4 (44)	
Diarrhea	Cinnamon	8 (16.32)	3 (6.12)	4 (8.16)	4 (50)	0.06
	Control	10 (20.40)	4 (8.16)	1 (2)	9 (90)	
Constipation	Cinnamon	11 (22.44)	8 (16.32)	6 (12.24)	5 (45)	0.1
	Control	18 (36.73)	18 (36.73)	15 (30.16)	3 (16)	
Blurred vision	Cinnamon	13 (26.53)	5 (10.20)	4 (8.16)	2 (96)	0.03
	Control	9 (18.36)	12 (24.48)	7 (14.28)	2 (22)	
Headache	Cinnamon	20 (40.81)	9 (18.36)	6 (12.24)	4 (20)	0.24
	Control	22 (44.89)	16 (32.65)	14 (28.57)	6 (83)	
Metallic flavor	Cinnamon	22 (44.89)	15 (30.6)	6 (12.24)	16 (73)	0.01
	Control	19 (38.77)	23 (46.93)	26 (53)	-7 (23)	
Epigastric pain	Cinnamon	39 (79.59)	22 (44.89)	12 (24.48)	27 (69)	0.02
	Control	43 (87.75)	29 (59.18)	24 (48.97)	19 (44)	
Heartburn	Cinnamon	32 (65.30)	11 (22.44)	8 (16.32)	24 (75)	0.045
	Control	34 (69.38)	19 (32.65)	15 (26.53)	19 (60)	
Skin rash	Cinnamon	9 (18.36)	1 (2)	1 (2)	8 (88)	0.87
	Control	15 (30.6)	2 (4)	2 (4)	13 (86)	
Flatus	Cinnamon	27 (55.10)	20 (40.81)	13 (26.53)	14 (52)	0.047
	Control	31 (63.26)	23 (46.93)	20 (40.81)	11 (35)	
Burp	Cinnamon	27 (55.10)	14 (28.57)	11 (22.44)	16 (59)	0.09
	Control	32 (65.30)	23 (46.93)	20 (40.81)	12 (37)	
Reduced appetite	Cinnamon	16 (32.65)	11 (22.44)	9 (18.36)	7 (43)	0.01
	Control	17 (34.69)	16 (32.65)	16 (32.65)	1 (1)	

Table 3. Comparison of treatment efficacy based on urea breath test (UBT) at the study of the effects of cinnamon extract on complications of treatment and eradication of *Helicobacter pylori* in infected people

Variable	Frequency and percentage of UBT ^a	Frequency and percentage of UBT ^a	P value
Cinnamon	36 (73.47%)	13 (26.53%)	0.036
Control	26 (53.06%)	23 (46.94%)	

^a Chi-square test.

including anti-inflammatory, antibacterial, antiviral and anti-cancer properties. In the study of Hang et al, following oral administration of cinnamon to mice, the serum levels of TNF- α and IL-6 were significantly reduced. This anti-inflammatory effect may be due to the presence of polyphenols in the cinnamon extract (23). Durak et al study showed that cinnamon had anti-inflammatory and antioxidant activity and was able to eliminate free radicals and inhibit lipoxigenase activity (14, 24). Zaidi et al investigated the indigenous medicinal plants of Pakistan such as cinnamon can be used to treat peptic ulcer and gastric cancer (25).

The effectiveness of *H. pylori* treatment with UBT is assessed by measuring the odds ratio. The results of this study showed that prescription of 40 mg powder of

cinnamon extract twice a day causes a significant negative UBT in cinnamon group (73.47%) and the control group (53.06%) ($P = 0.036$). The odds ratio of the *H. pylori* symptoms in cinnamon group was 2.45 times higher than the control group. In the study of Homayoni, the fecal antigen test was 67% and 55% negative in cinnamon and control groups, respectively. These results indicated that the consumption of cinnamon powder had therapeutic effects on *H. pylori* infected patients (17). It should be noted that in the Homayoni study the fecal antigen test has been used to evaluate the eradication of *H. pylori* while in the present study, the UBT has been used to evaluate the eradication of *H. pylori*. In the study of Shafaghi-Asl et al with the aim of comparison of the effects of water and ethanol extracts of *Curcuma longa* and cinnamon on the

in-vitro growth of *H. pylori*, showed that both plants had antibacterial properties (26). Pakbaz et al investigated the effects of 10 medicinal herbs, including cinnamon against *H. pylori*. All *H. pylori* isolated strains were sensitive to gentamicin, tetracycline, and ciprofloxacin (27). Ranjbaran et al investigated the antibacterial effect of 4 plant extracts of cinnamon, black cumin, fennel and lemon on *H. pylori* by disc diffusion and flow cytometry techniques. The results indicate that among 14 strains of *H. pylori*, 49.9% of the strains were susceptible to cinnamon extract. In general, the mentioned study showed that all four herbal extracts had antibacterial effects on *H. pylori* (3).

Conclusion

Cinnamon is a medicinal plant with antibacterial and anti-inflammatory effects which can reduce the complications of *H. pylori* treatment and increase the efficacy of antibiotics.

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Authors' contribution

Study design: GhI, MM, ArKh, DD, BI; data collection: GhI, MM, ArKh; data analysis: GhI, MM, ArKh, DD, BI; manuscript preparation: GhI, MM, ArKh, DD, BI; final approval: GhI, MM, ArKh, DD, BI.

Conflict of interests

There was no conflict of interest to declare by the authors.

Ethical considerations

The project was approved by the ethics committee in research with the number of IR.UMSHA.REC.1397.135 and was registered in the Iranian Center for Clinical Trial with the identifier number of IRCT20121114011469N3.

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