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Efficacy of *Mentha pulegium* extract in the treatment of functional dyspepsia: A randomized double-blind placebo-controlled clinical trial

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ABSTRACT

Ethnopharmacological evidence: *Mentha pulegium* L. leaves are used in the Iranian traditional medicine for the treatment of functional dyspepsia. *Aim of study:* To study the efficacy and safety of *M. pulegium* in the treatment of functional dyspepsia patients fulfilling the Rome III criteria.
Materials and methods: The efficacy and safety of a standardized *Mentha pulegium* leaf extract (drug extract ratio: 15.9:1, extraction solvent: 70% v/v aqueous ethanol) (330 mg three times daily taken for 2 months) as add-on to one famotidine 40 mg tablet per day in the treatment of 50 functional dyspepsia patients were compared with those of a parallel placebo group (n =50).
Results: The extract significantly decreased the total dyspepsia score measured by the Hong Kong dyspepsia index compared to the placebo and baseline (P=0.011 and $P < 0.001$ respectively). The stomach pain, upper abdominal bloating, upper abdominal dull ache, belching and total dyspepsia scores were decreased from baseline in the extract group significantly compared to the placebo ($P < 0.001$, $P < 0.001$, P=0.003, $P < 0.001$ and $P < 0.001$ respectively). However, the decreases of other dyspepsia symptoms scores from baseline in the extract group were not significant compared to the placebo ($P > 0.05$). The extract improved the quality of life measured by the SF-36 questionnaire significantly compared to the placebo and baseline (P=0.003 and $P < 0.001$ respectively). Moreover, the extract lowered the rate of *H. pylori* infection determined by the urease test significantly compared to the placebo and baseline (P=0.001 and $P < 0.001$ respectively). The extract did not significantly affect the complete blood count and liver and kidney function tests ($P > 0.05$). The patients did not experience any adverse drug effect.
Conclusions: *M. pulegium* extract (genuine drug extract ratio: 19.4:1; extraction solvent: 70% v/v aqueous ethanol) 270 mg three times daily taken for 2 months as adjunct to one famotidine 40 mg tablet per day seems safe, improves dyspeptic symptoms and quality of life and eradicates *H. pylori* in functional dyspepsia patients.

1. Introduction

Functional dyspepsia is a common disorder of the upper gastrointestinal system affecting up to 40% of the population (Mahadeva and Ford, 2016). Rome III criteria define functional dyspepsia as the presence of symptoms thought to originate in the gastroduodenal region (early satiation, post-prandial fullness, epigastric pain or burning) in the absence of any organic, systemic or metabolic disease likely to explain the symptoms. Although, functional dyspepsia is a non-life-threatening disorder, it markedly reduces patients' quality of life. Economic costs of functional dyspepsia are considerable and caused by lost productivity and cost of diagnosis and treatment (Talley et al., 2016). The treatment of functional dyspepsia can be confusing to the healthcare practitioners because no agent is approved for the treatment. Effective therapies for functional dyspepsia are limited although H_2 blockers, proton pump inhibitors, prokinetics, tricyclic antidepressants and mirtazapine may provide some symptom relief in selected patients. The treatment of functional dyspepsia remains unsatisfactory for many patients. Development of more effective and specific treatments for functional dyspepsia is warranted (Talley, 2016). Phytotherapeutic agents have a long history of use in the treatment of dyspeptic symptoms, possibly due to constituents such as essential oils having spasmolytic, carminative and local anesthetic actions (Saller et al., 2001). Alternative and innovative

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functional dyspepsia therapies which have desirable efficacy and safety may be developed from medicinal plants (Holtmann and Talley, 2015).

Mentha pulegium L. (*M. pulegium*) (pennyroyal) (Labiatae) leaves are used in the Iranian traditional medicine to treat gastrointestinal disorders including dyspepsia, nausea, vomiting, bloating, stomachache, infections and diarrhea. The dosage of the plant dry leaves is 1–4 g as decoction up to three times daily (Zargari, 1996). Smooth muscle relaxant (Estrada-Soto et al., 2010; Soares et al., 2005), smooth muscle spasmolytic (Estrada-Soto et al., 2010), calcium antagonist (Estrada-Soto et al., 2010), anti-inflammatory (Kogiannou et al., 2013; Moussaid et al., 2011), anti-oxidative (Kogiannou et al., 2013; Moussaid et al., 2011), antigenotoxic (Romero-Jiménez et al., 2005), antibacterial (Ibrahim, 2013; Mahboubi and Haghi, 2008), neuroprotective (López et al., 2010), acaricidal (Rim and Jee, 2006), larvicidal (Cetin et al., 2006) and nematicidal (Ntalli et al., 2010) effects of *M. pulegium* have been demonstrated. There has been no study evaluating the effects of *M. pulegium* in the treatment of functional dyspepsia.

Considering the above data, this study was conducted to evaluate the efficacy and safety of *M. pulegium* in the treatment of patients with functional dyspepsia. Moreover, H_2 blocker is a routine therapy for functional dyspepsia (Talley, 2016), so for ethical reasons, the effects of *M. pulegium* combined with famotidine were examined in the present trial.

2. Materials and methods

2.1. Plant material

M. pulegium was collected from the lands in the Alborz province of Iran in August and a staff botanist visually identified the plant. A voucher specimen of the plant (number 21092) was deposited in the Tehran University Central Herbarium. The leaves were separated from the plant, washed and dried in shade at room temperature. The dry leaves were ground into powder.

2.2. Extraction

The dry leaf powder (70 kg) was extracted with 70% v/v aqueous ethanol as the solvent in a percolator for 72 h, the solvent was completely removed from the extract by a rotary evaporator, toast powder as an excipient was added to and mixed with the extract and the mixture was ground to a powder. The quantity of the dry extract powder produced was 4.4 kg. The excipient constituted 18% of the final extract. Drug extract ratio (DER) and DER native were 15.9:1 and 19.4:1 respectively.

2.3. Preparation of the extract and placebo capsules

The extract powder as the drug and toast powder as the placebo were separately filled into oral gelatin capsules by a hand-operated capsule-filling machine (Scientific Instruments and Technology Corporation, USA). The *M. pulegium* capsules contained 330 mg of the extract powder. To make the placebo capsules smell like the *M. pulegium* capsules, 1 μL of *M. pulegium* essential oil was put in the placebo capsules containers. The *M. pulegium* and placebo capsules were identical in all respects. A sample of the extract and placebo capsules is kept in the Center of Professional Analysis and Processing of Medicinal Plants (Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran).

2.4. Phytochemical analyses of the extract

The antioxidant activity using the DPPH radical scavenging assay and the total flavonoid and phenolic contents were determined by spectrophotometry as described previously (Gutfinger, 1981; Han et al., 2008; Yoo et al., 2008). Moreover, rosmarinic acid, chlorogenic acid and quercetin were quantified in the extract by HPLC according to the methods reported previously (Liu et al., 2013; Verma and Trehan, 2013; Wen et al., 2012). The measurements were done in triplicate. The analyses were performed for standardization of the extract and process control in the Center of Professional Analysis and Processing of Medicinal Plants (Medicinal Plants Research Center, Institute of Medicinal Plants, ACECR, Karaj, Iran). The analytical methods are validated.

2.4.1. Determination of the antioxidant activity

Inhibition of diphenyl-2-picrylhydrazyl (DPPH) radicals by the extract was assayed. A mixture consisting of an extract solution at different concentrations (1.5 mL) and the methanolic solution of the DPPH reagent (1.5 mL) was mixed in a volumetric flask. The mixture was left to stand for 30 min in a dark place, and then the absorption was measured at 517 nm using a spectrophotometer (Human, USA). The radical scavenging activity (RSA) was calculated as a percentage of DPPH discoloration using the equation: RSA (%) =(Ac-As/Ac) ×100.

Abbreviations used in the equation: RSA: radical scavenging activity; Ac: absorbance of the negative control; As: absorbance of the plant sample or ascorbic acid.

Ascorbic acid was used as reference standard. The assay results were expressed as IC50 denoting the antioxidant concentration which reduces the DPPH radicals about 50%.

2.4.2. Determination of the total flavonoid content

The extract (1 mg/mL) or standard was mixed with 4 mL of distilled water and 300 μL of a 5% sodium nitrite solution and after five minutes 300 μL of 10% aluminum chloride solution was added to the mixture. After six minutes, 2 mL of 1 M sodium hydroxide and 3 mL of distilled water were added to the mixture. The solution was properly mixed and absorbance was measured at 510 nm using a spectrophotometer (Human, USA). Rutin (100 μg/mL up to 1200 μg/mL) was used to construct the standard curve and the results were expressed as mg of routine equivalents per capsule.

2.4.3. Determination of the total phenolic content

The total phenolic contents were determined through the Folin-Ciocalteu colorimetric method. In brief, the plant extract solution (1 mL) was mixed with 500 μL of the Folin-Ciocalteu reagent and 5 mL distilled water in a volumetric flask. After five minutes, 1 mL of 15% sodium carbonate solution was added to the mixture and then kept in the dark for 30 min, after which the absorbance was determined at 725 nm using a spectrophotometer (Human, USA). Gallic acid was used to generate the standard curve, and the reduction of the Folin-Ciocalteu reagent by the samples was expressed as mg of gallic acid equivalents per capsule.

2.4.4. Determination of the rosmarinic acid content

A Knauer HPLC (Germany) was used with pump K1001 and UV detector K2501 (Germany). The analytical column was Phenomenex NX-C18 (diameter 4.6 mm, length 250 mm). Analysis was repeated with added standards in order to ensure the results. All reagents were of analytical reagent grade and purchased from Merck (Germany). The analysis of rosmarinic acid was carried out by HPLC. 330 nm was selected as the wavelength for UV detection. Elution was carried out at a flow rate of 1.0 mL/min at 25 °C. Two mobile phases, A and B were used. Mobile phase A was 0.1% (v/v) formic acid solution in water, while mobile phase B was acetonitrile. A ratio of 88% A and 12% B was applied in the first 30 min. After 30 min, a ratio of 80% A and 20% B was used for the next 15 min. Finally, 70% A and 30% B were used after 45 min for an additional 15 min.

2.4.5. Determination of the chlorogenic acid content

A Knauer HPLC (Germany) was used with pump K1001 and UV detector K2501 (Germany). The mobile phase was acetonitrile and 0.5% aqueous phosphoric acid (11.5:88.5 v/v); the flow rate of 1.0 mL/

min and determination wavelength of 327 nm and analytical column was Phenomenex NX-C18 (diameter 4.6 mm, length 250 mm). Analysis was repeated with added standards in order to ensure the results. All reagents were of analytical reagent grade and purchased from Merck (Germany).

2.4.6. Determination of the quercetin content

The chromatographic separations were achieved using a YMC triart C_{18} column (250 mm×4.6 mm , 5 μm). A reverse phase HPLC assay was carried out using an isocratic elution with a flow rate of 1 mL/minutes, a mobile phase of 35 : 65 (acetonitrile : 0.2 phosphoric acid) and a detection wavelength of 360 nm. The injection volume was 50 μL of each solution. The total run time was 16 min for each injection. The solvents and distilled water were prior filtered through a PTF membrane using a set of glass bottles with the aid of a vacuum pump. The result was expressed as mg of quercetin per capsule.

2.5. The trial protocol

A 2-arm, randomized, double-blind, placebo controlled parallel-group trial was performed in the Baqiyatallah Hospital (Tehran, Iran). The trial was conducted from December 21, 2015 to March 19, 2016. Inclusion criteria: patients aged 20–80; patients fulfilling Rome III criteria for functional dyspepsia. Exclusion criteria: patients with peptic ulcer disease, inflammatory bowel disease, irritable bowel syndrome, pure gastro-esophageal reflux disease, biliary motility disorder and any organic gastrointestinal disease; patients with a history of *Helicobacter pylori* (*H. pylori*) infection eradicating drugs use within the past 3 months; patients with a history of gastrointestinal system surgery; patients with background systemic diseases such as diabetes mellitus, heart failure, hepatic failure, renal failure, asthma, chronic obstructive pulmonary disease, neoplasms and severe psychiatric diseases; patients addicted to alcohol and opium; patients using cardiac, antihypertensive, antipsychotic, antianxiety, antibiotic and corticosteroid drugs and iron and calcium; patients with a history of discontinuing prescribed pharmacotherapy and incomplete treatment; pregnant women; women planning pregnancy; breast-feeding women. Five hundred and seventy six patients were screened. The enrolled patients were equally randomized to the extract and placebo groups. Block randomization with computer generated random number table and sequentially numbered containers each representing a block consisting of two patients was used for the treatment allocation. The patients were instructed to take one extract or placebo capsule three times a day besides daily intake of one famotidine 40 mg tablet for 2 months. The extract dosage regimen was determined empirically. The outcome measures were dyspepsia severity, quality of life, infection with *H. pylori*, complete blood cell count and the blood levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, blood urea nitrogen and creatinine. The dyspepsia severity was the primary outcome measure and the other parameters were secondary outcome measures. The parameters were evaluated at the beginning of the trial and after 2, 4 and 8 weeks of intervention. The dyspepsia severity, quality of life, infection with *H. pylori* and blood parameters were evaluated by the Hong Kong dyspepsia index (a validated symptom severity questionnaire for dyspepsia patients) (Hu et al., 2002), SF-36 (Short-Form 36 Item Health Survey) questionnaire, urease test and an auto-analyzer (Hitachi 917, Japan) respectively. Three different persons generated the random allocation sequence, enrolled the patients and assigned them to interventions. These persons, care-providers and patients were blinded to interventions. Compliance was measured by counting returned drugs and asking how many doses of the drugs were (or were not) taken. The clinicians treating the patients were gastroenterologist, internist or resident of internal medicine; were licensed in Tehran, Iran; had been practicing medicine for an average of 17 years; and had expertise in herbal medicine. Fifty patients in each group was the sample size calculated to detect 3.8 difference of dyspepsia severity score between the groups, considering type I error =0.05% and 80% power. The chi-squared and paired and independent samples *t*-tests were used for data analyses and $P < 0.05$ was considered as significant. The data were analyzed by the intention-to-treat approach. The protocol was approved by the ethics committee of the Baqiyatallah University of Medical Sciences (approval number: IR.BMSU.REC.1394.149). The trial was performed in accordance with the revised Declaration of Helsinki 2013. Written informed consent was obtained from the patients. The trial is registered with the Iranian Registry of Clinical Trials, number IRCT201602172288N9.

3. Results

3.1. Phytochemical analyses

The IC_{50} of the extract was 63.60 ± 0.01 μg/mL, whereas the IC_{50} of ascorbic acid was 5.71 ± 0.001 μg/mL in the DPPH assay. The total flavonoid content as milligrams of rutin equivalents per capsule was 14.29 ± 0.11. The total phenolic content of the extract as milligrams of gallic acid per capsule was 36.42 ± 1.06. Moreover, the amount of rosmarinic acid, chlorogenic acid and quercetin in the extract capsule were 4.80 ± 0. 13 mg, 0.11 ± 0.005 mg and 0.06 ± 0.002 mg respectively (Figs. 1–6). The values are expressed as mean ± standard deviation.

3.2. Clinical trial

One hundred and three patients entered the study. Fifty patients in each of the *M. pulegium* extract and placebo groups completed the trial. The CONSORT flow diagram of the trial is shown in the Fig. 7. The patients fully complied with the protocol. Demographic data of the patients in the extract and placebo groups did not differ significantly (Table 1). There was no significant difference between the extract and placebo groups in terms of the baseline values of the outcome variables. The extract significantly decreased the total dyspepsia score compared

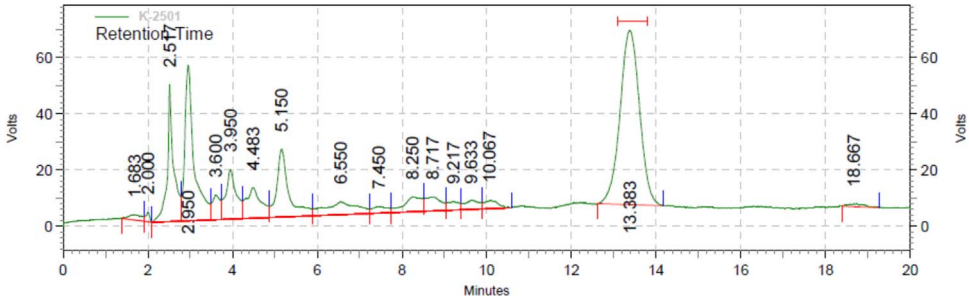

Fig. 1. HPLC chromatogram of the test sample rosmarinic acid.

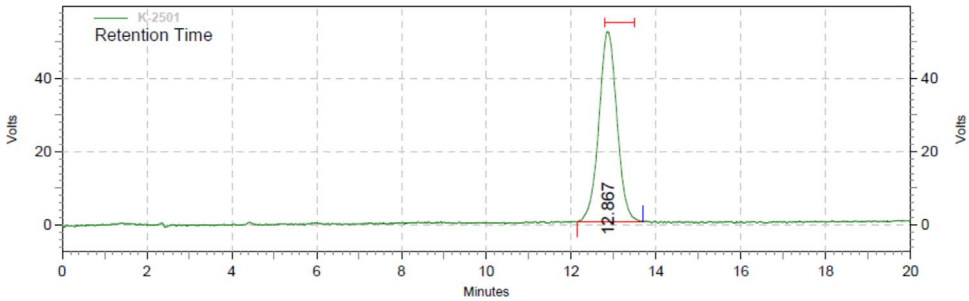

Fig. 2. HPLC chromatogram of the standard rosmarinic acid.

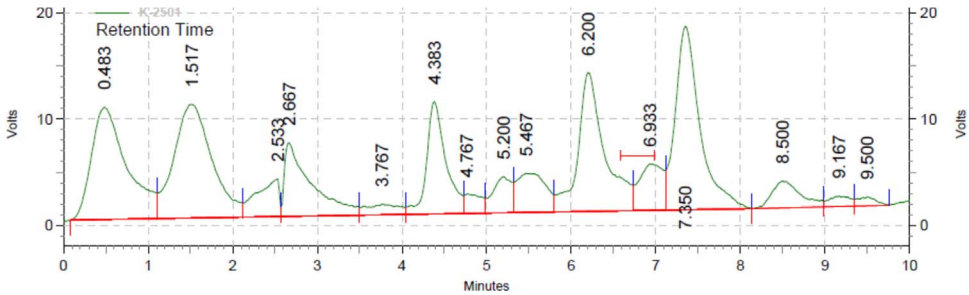

Fig. 3. HPLC chromatogram of the test sample chlorogenic acid.

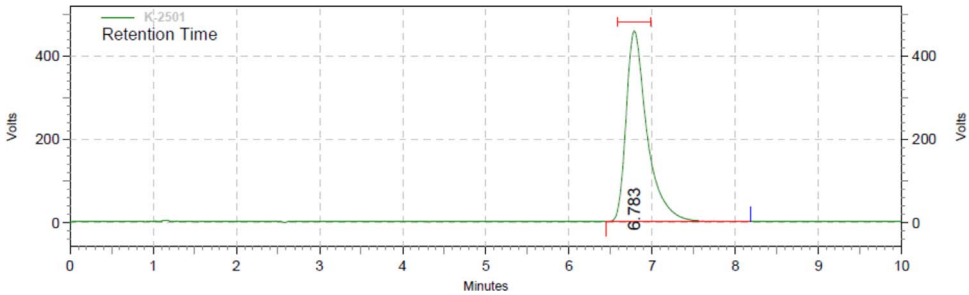

Fig. 4. HPLC chromatogram of the standard chlorogenic acid.

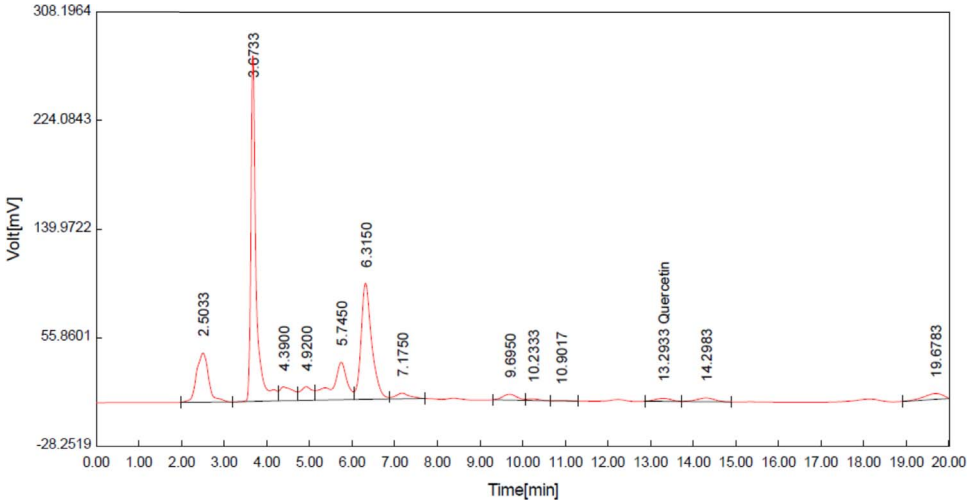

Fig. 5. HPLC chromatogram of the test sample quercetin.

to the placebo and baseline at the endpoint ($P = 0.011$ and $P < 0.001$ respectively) (Table 2). The stomach pain, upper abdominal bloating, upper abdominal dull ache, belching and total dyspepsia scores were decreased from baseline in the extract group significantly compared to the placebo at the endpoint ($P < 0.001$, $P < 0.001$, $P = 0.003$, $P < 0.001$ and $P < 0.001$ respectively) (Table 3). However, the decreases of other dyspepsia symptoms scores from baseline in the extract group were not significant compared to the placebo at the endpoint ($P > 0.05$) (Table 3). The extract improved the quality of life significantly compared to the placebo and baseline at the endpoint ($P = 0.003$ and $P < 0.001$ respectively) (Table 4). Moreover, the extract lowered the rate of the *H. pylori* infection significantly compared to the placebo and baseline at the endpoint ($P = 0.001$ and $P < 0.001$ respectively) (Table 5). The extract did not significantly affect the values of the

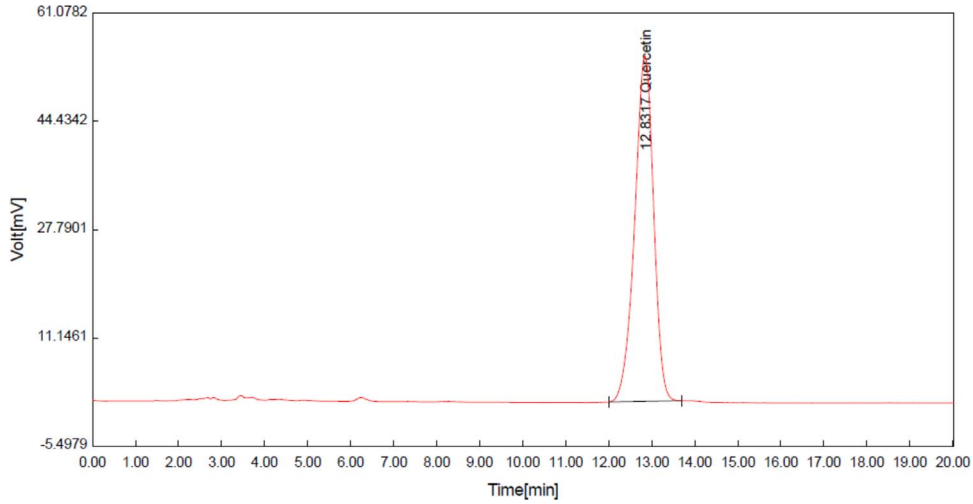

Fig. 6. HPLC chromatogram of the standard quercetin.

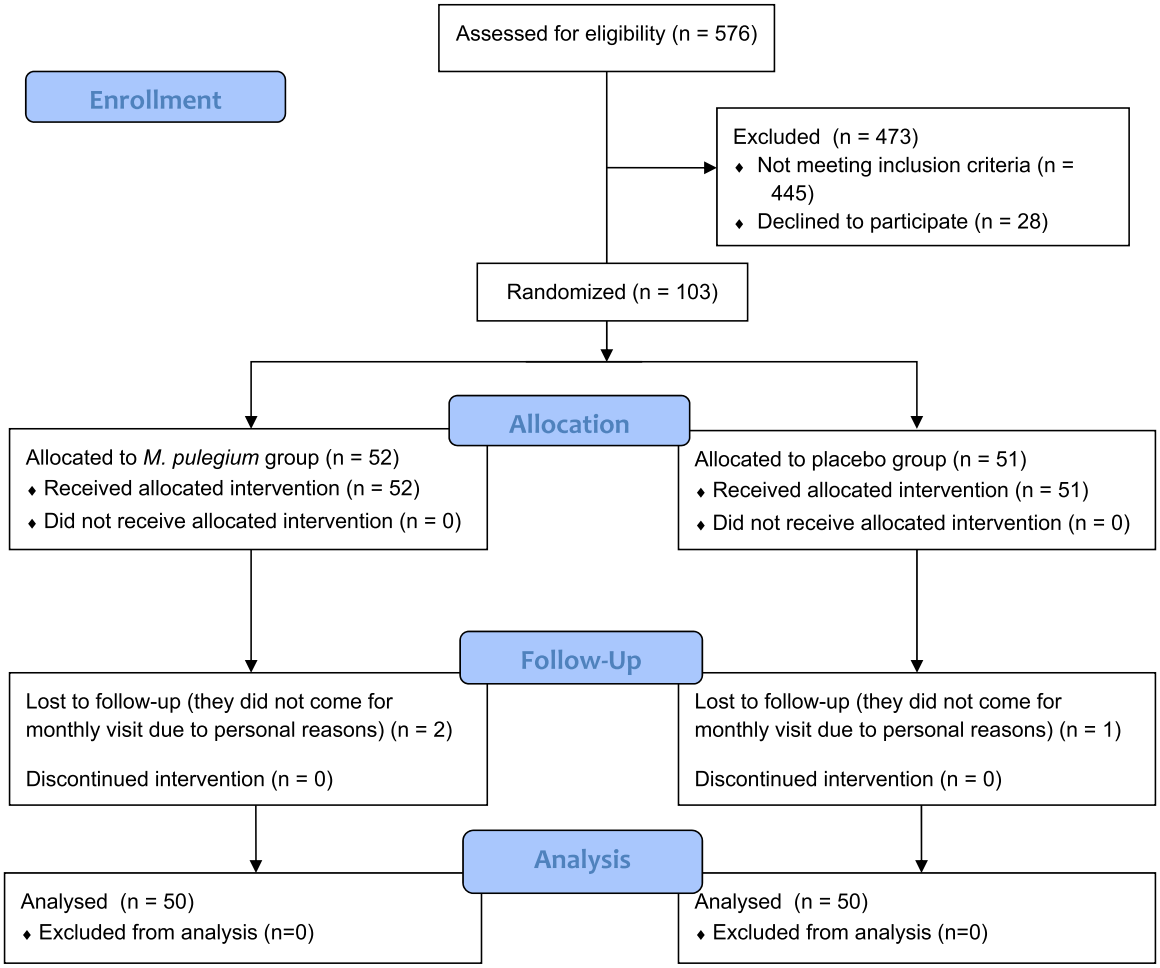

Fig. 7. The CONSORT diagram showing progress of the patients through the trial.

blood parameters ($P > 0.05$). No adverse drug reaction was observed in the patients.

4. Discussion

The results suggest that the *M. pulegium* extract safely improves abdominal pain, bloating, belching, global symptoms and quality of life, and eradicates *H. pylori* infection in functional dyspepsia. Moreover, the results show profound effects of the extract on these parameters. Famotidine is a routine therapy for functional dyspepsia (Talley, 2016), so for ethical reasons, it was given to patients of both the extract and placebo group. Thus, the dyspepsia improvement in the extract group compared to the placebo is caused by the extract. Moreover, it can be concluded that *M. pulegium* monotherapy is effective in functional dyspepsia, although it may be less effective than combination therapy. Pulegone (a component of *M. pulegium*) has been linked to toxicity.

Table 1
Demographic characteristics of the study participants. Where appropriate, values are given as mean ± standard deviation.

Parameter	*M. pulegium* group	Placebo group
Gender	25 males, 25 females	23 males, 27 females
Age (years)	38.31 ± 12.57	42.87 ± 13.33
Number of patients with dyspepsia duration less than 1 year	5	2
Number of patients with dyspepsia duration more than 1 year	45	48
Body mass index (kg/m^2)	27.52 ± 4.45	29.38 ± 4.46

Table 2
The Hong Kong dyspepsia index in the *M. pulegium* and placebo groups before and after 2, 4 and 8 weeks of intervention. The data are expressed as mean ± standard deviation.

	M. pulegium	Placebo
Baseline score	27.79 ± 7.32	24.91 ± 6.10
After 2 weeks	23.0 ± 5.11	23.0 ± 5.32
After 4 weeks	22.39 ± 5.33	22.56 ± 5.32
After 8 weeks	20.89 ± 4.61	22.58 ± 4.20
Within group *P* -value†	< 0.001	0.141
Between groups *P*-value‡	0.011	

† paired *t*-test (0–8 weeks),
‡ Independent samples *t*-test.

Table 3
The dyspepsia symptom score decrease in the *M. pulegium* and placebo groups (endpoint *vs.* baseline). The data are expressed as mean ± standard deviation.

	M. pulegium	Placebo	Between groups *P*-value†
Stomach pain	1.19 ± 1.12	0.20 ± 0.91	< 0.001
Upper abdominal bloating	1.50 ± 1.01	0.18 ± 0.98	< 0.001
Upper abdominal dull ache	0.56 ± 1.10	−0.02 ± 0.72	0.003
Stomach pain before meals	0.40 ± 1.03	0.18 ± 0.81	0.259
Stomach pain when anxious	0. 25 ± 1.12	−0.02 ± 0.75	0.175
Vomiting	0. 15 ± 0.50	0.07 ± 0.25	0.346
Nausea	0. 52 ± 0.81	0.24 ± 0.60	0.065
Belching	1. 52 ± 1.11	0.09 ± 0.80	< 0.001
Acid regurgitation	0. 25 ± 0.90	0.4 ± 0.82	0.418
Heartburn	0. 44 ± 1.13	0.15 ± 0.82	0.120
Feeling of acidity in stomach	0. 56 ± 1.00	0.56 ± 0.91	0.973
Loss of appetite	0. 44 ± 0.92	0.31 ± 0.63	0.453
Total dyspepsia score	6. 89 ± 5.12	2.33 ± 3.43	< 0.001

† Independent samples *t*-test.

Table 4
The SF-36 Health Survey scores in the *M. pulegium* and placebo groups before and after 2, 4 and 8 weeks of intervention. The data are expressed as mean ± standard deviation.

	M. pulegium	Placebo
Baseline score	23.79 ± 9.20	20.8 ± 7.81
After 2 weeks	19.01 ± 6.41	19.11 ± 6.10
After 4 weeks	17.17 ± 5.43	19.0 ± 6.31
After 8 weeks	15.92 ± 4.22	18.96 ± 5.60
Within group *P*-value†	< 0.001	0.097
Between groups *P*-value‡	0.003	

† paired *t*-test (0–8 weeks),
‡ Independent samples *t*-test.

Table 5
The rate of *Helicobacter pylori* (*H. pylori*) infection in the *M. pulegium* and placebo groups before and after 8 weeks of intervention.

	M. pulegium	Placebo
Baseline rate	45	40
Endpoint rate	7	39
Within group *P*-value†	< 0.001	0.845
Between groups *P*-value†	0.001	

† Chi-squared test.

However, the pulegone content of the extract used in this trial was not determined. Notably, the complete blood count and liver and kidney function tests did not show any abnormality and also no adverse effect was observed in this trial. Therefore, use of the extract for 2 months seems safe. The anti-dyspeptic effect of *M. pulegium* has been attributed to its cholagogic action (Zargari, 1996). Notably, the Rome III criteria divide functional dyspepsia patients into two subgroups: patients with postprandial distress syndrome characterized by postprandial fullness and early satiation, and patients with epigastric pain syndrome characterized by epigastric pain or burning. However, the subgroups often overlap and many patients do not fit into any of the subgroups (Talley et al., 2016). It should also be noted that the physiopathology of functional dyspepsia is unknown. It is believed that a variety of mechanisms contribute to the disease including gastric accommodation/emptying, gastric acid, diet, infections, genes, cytokines, duodenal eosinophilia, anxiety/depression, brain pain modulating circuits and duodenal sensitivity (Talley, 2016). Short-term treatment and lack of testing for the treatment response by subgroup and identification of the constituents and mechanisms responsible for the extract effects are the limitations of this study. The action mechanisms of the effective drugs in functional dyspepsia are obscure. Theoretically, *M. pulegium* may relieve the functional dyspepsia symptoms through several mechanisms including smooth muscle relaxant effect resulting in gastric fundus relaxation and increased gastric accommodation, reduction of dysmotility and modulation of peripheral or central pain pathways. Additionally, bloating is due to accumulation of excessive gas in the stomach and intestines. Belching is a physiological mechanism that prevents the accumulation of gas in gastrointestinal tract (Kessing et al., 2014). Frequent belching is common in patients with functional dyspepsia with an incidence up to 80% (Camilleri et al., 2005; Lin and Triadafilopoulos, 2003). Patients with functional dyspepsia swallow air more frequently than healthy individuals and have more belches (Conchillo et al., 2007). The excessive air swallowing is possibly a reaction to unpleasant gastrointestinal sensations (Bredenoord, 2010). Therefore, *M. pulegium* may alleviate belching by antifoaming action similar to other herbal carminatives (Grigoleit and Grigoleit, 2005), reduction of air swallows or via other mechanism(s). The anti-bloating effect of *M. pulegium* may be attributed to its carminative or analgesic actions. *H. pylori* infection is causally linked to functional dyspepsia, but only a minority (1 out of 17) will respond to eradication (Talley, 2016). Thus, eradication of the *H. pylori* infection may also somewhat contribute to the *M. pulegium* effects. Phenolics, flavonoids, quercetin, rosmarinic acid, chlorogenic acid and antioxidant activity were quantified in the *M. pulegium* extract. The extract had a considerable amount of the constituents and antioxidant activity. Given the possible involvement of inflammation and oxidative stress in the pathogenesis of functional dyspepsia (Suzuki et al., 2012; Talley, 2016), the anti-inflammatory and antioxidant effects of the *M. pulegium* and specifically the compounds identified in the plant extract (Leyva-López et al., 2016; Li et al., 2016) may play a role in its anti-dyspeptic effects. In conclusion, the findings of this study indicate the value of *M. pulegium* in the treatment of functional dyspepsia. Further studies regarding the effects of *M. pulegium* in the treatment of functional dyspepsia patient subgroups are needed. Moreover, studies

to identify the active compounds and action mechanisms of *M. pulegium* in the functional dyspepsia seem warranted.

5. Conclusions

M. pulegium extract (genuine drug extract ratio: 19.4:1; extraction solvent: 70% v/v aqueous ethanol) 270 mg three times daily taken for 2 months as adjunct to one famotidine 40 mg tablet per day seems safe, improves dyspeptic symptoms and quality of life and eradicates *H. pylori* in functional dyspepsia patients.

Conflict of interest

The authors declare no conflict of interest.

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