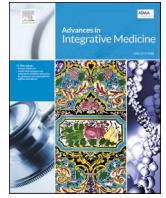


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Effects of ginger supplementation on quality of life in patients with functional dyspepsia: An open-label, clinical trial

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ABSTRACT

Background and purpose: Functional dyspepsia (FD) is a prevalent gastrointestinal disorder, often marked by persistent discomfort and negatively impacting patients' quality of life. Despite various treatment approaches, many patients continue to experience symptoms. Ginger has been suggested as a potential natural remedy for dyspepsia due to its anti-inflammatory and prokinetic properties. While previous studies have focused on ginger's ability to alleviate dyspeptic symptoms, its impact on QoL in FD patients remains unclear. This study aimed to assess the effects of ginger supplementation on QoL in patients with FD.

Materials and methods: This open-label clinical trial enrolled adult FD patients who met the Rome IV criteria. A total of 62 patients were enrolled, and 51 completed the study. Participants received a standardized ginger supplement of 540 mg twice daily for eight weeks. Quality of life was assessed at baseline and post-intervention using a validated questionnaire, Nepean Dyspepsia Index (NDI). Secondary outcomes were also evaluated.

Results: After eight weeks of ginger supplementation, there was a significant improvement in QoL, as indicated by a decrease in NDI scores (mean change \pm SD: 9.97 ± 16.20 , $p = 0.039$). This demonstrates a notable enhancement in the participants' QoL, particularly in terms of interference, eating and improved day-to-day activity. Secondary outcomes also showed favorable changes.

Conclusion: Ginger supplementation may offer a beneficial adjunct therapy for patients with FD, improving both symptom management and overall QoL. Future studies with larger sample sizes and randomized controls are warranted to confirm these findings and explore the mechanisms involved.

1. Introduction

Functional dyspepsia poses a considerable burden on patients' quality of life, characterized by symptoms such as epigastric pain, bloating, nausea, and early satiety. Dyspepsia is a complex disease caused by multiple pathophysiological mechanisms, such as genetic, impaired gastric emptying, visceral hypersensitivity, infectious and psychosocial factors that induce episodic or persistent abdominal pain or discomfort of the upper gastrointestinal tract. The most common form of dyspepsia is functional dyspepsia, characterized by functional abnormalities that can worsen over time [1]. Based on Rome criteria functional dyspepsia is classified into two main categories: (i) postprandial distress syndrome (PDS) characterized by early satiety and postprandial fullness induced by food ingestion; (ii) Epigastric pain syndrome (EPS) characterized by pain and or burning in the epigastrium after meal or

fasting [2].

Epidemiological data obtained over the course of years indicate that levels of functional dyspepsia vary considerably around the world, with high statistics overall (10–40 %) in Western countries and the lowest numbers (5–30 %) being found in Asia. Women are more likely than men to experience functional dyspepsia [3]. Some of the known risk factors for the development of functional dyspepsia are gastrointestinal infections (primarily caused by *Helicobacter pylori*), traveler's diarrhea, antibiotic use, non-steroidal anti-inflammatory drug (NSAID) consumption, early environmental microbiological exposure, smoking, overweight and obesity, and stress perceived as psychosocial states [4]. In light of the above, it is clear that functional dyspepsia is a problem for society, both in terms of healthcare costs and deterioration in quality of life. For patients with dyspepsia, the first intervention is typically to lead a healthy lifestyle and adhere to dietary guidelines, which include

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avoiding: (i) the use of foods high in fat, alcohol and large quantities of coffee, (ii) smoking and (iii) the intake of NSAIDs [5]. Pharmacological remedies are usually represented by antacid drugs, prokinetics, H2 pump antagonists, proton pump inhibitors, and antibiotics. Satisfactory accounts of their effectiveness are still pending, and effective pharmacological treatments available on the market remain limited [6]. In addition, drug therapies are also known to increase the likelihood of potentially serious adverse events including cardiac toxicity (especially prokinetic and antiemetic agents [7,8]).

Though FD is not a life-threatening condition, it is accompanied by poor quality of life and experience with various medications and herbs like ginger [9]. While conventional treatments offer symptom relief, complementary approaches like ginger supplementation have gained attention for their potential benefits in managing dyspeptic symptoms. The ginger rhizome, *Zingiber officinale* Roscoe, in the Zingiberaceae family, is one of the most widely used medicinal plants in the world. It has long been used as a remedy for different diseases including GI ailments like belching, bloating, vomiting, indigestion and constipation [10,11]. While conventional treatments offer symptom relief, complementary approaches like ginger supplementation have gained attention for their potential benefits in managing dyspeptic symptoms. This study aims to explore the impact of ginger supplementation on the quality of life of patients with functional dyspepsia.

2. Methods and materials

2.1. Study design

A single-center, open-label, clinical trial with pre and post-intervention assessments for eight weeks. The study was conducted among patients diagnosed with functional dyspepsia attending the University of Debrecen, Internal Medicine Outpatient Department, Debrecen, Hungary. All patients met the criteria of Rome IV for Functional Dyspepsia [12].

2.2. Study participants

A total of 62 patients with functional dyspepsia were enrolled and 51 completed the study. Patient data were collected through a self-completed questionnaire during hospital visits at two study time points, before and after eight weeks of ginger supplementation. Patients were included based on functional dyspepsia symptoms reported during the initial visit. Participation was voluntary and all the participants signed a written informed consent.

2.2.1. Inclusion criteria

- Adult patients aged 18–72 years.
- Diagnosed with functional dyspepsia based on Rome IV criteria.
- Symptomatic for at least 3 months prior to the study.
- Not on any conflicting medications (such as proton pump inhibitors or H2 receptor antagonists) that may interfere with the trial outcomes.

2.2.2. Exclusion criteria

- Patients with organic gastrointestinal disorders (e.g., peptic ulcer disease, GERD, or malignancy).
- Pregnant or breastfeeding women.
- History of allergic reactions to ginger or related supplements.
- Patients taking medications known to interact with ginger (e.g., anticoagulants).

2.3. Randomization and masking

A single-center, Open-label clinical trial, since our study was a single-

group clinical study, to minimize bias and ensure validity, where there's only one treatment group (in our case, patients received ginger supplementation), the conventional randomization to allocate participants to different treatment arms and masking to conceal the treatment assignment from participants and researchers might not be applicable in the traditional sense. However, we applied some measures to minimize bias and enhance the rigor in this study: - A. Randomization of Treatment Timing: While all participants received ginger supplementation, we randomized the timing of when they started receiving the supplementation. This could help control for any temporal effects or other confounding factors. B. Standardized Procedures: The procedures for data collection, assessment, and analysis were standardized across all participants and could help minimize bias and enhance our study's reliability. While these measures cannot fully replicate the rigor of the trial with masking, they can still strengthen the internal validity of our study and provide valuable insights into the effects of ginger supplementation on quality of life in patients with functional dyspepsia.

2.4. Procedures

2.4.1. Intervention

Supplementing with ginger is provided following the established protocol. Patients in this trial were given Swanson 540 mg ginger root extract, Budapest, Hungary, a ready-made product of ginger capsule supplement. For eight weeks, the patients who were enrolled were instructed to take two capsules, each containing 540 mg, one half an hour before lunch and the other before dinner. Before the trial began and for the full eight weeks that they were taking ginger supplements, all patients were asked not to take prokinetic and anti-secretory medications. Participants in the study were advised to carry on with their regular activities and daily eating routines throughout the investigation.

2.4.1.1. Swanson Ginger Root 540 mg supplement. Swanson Ginger Root 540 mg sounds like a comprehensive supplement for digestive health and overall wellness. Below is a breakdown of its main features:

2.4.1.1.1. Main ingredient. Ginger root (*Zingiber officinale*) powder, standardized to contain a minimum of 4 % volatile oils. Ginger has been traditionally used for its various health benefits, particularly for digestive support and anti-inflammatory properties.

2.4.1.1.2. Dosage. Each capsule contains 540 mg of ginger root powder, equivalent to 1.35 g of fresh ginger root. The supplement dosage was two capsules per day taken with water, preferably with a meal. This dosage provides flexibility for users to adjust according to their needs.

2.4.1.1.3. Capsule material. The capsules are made from gelatin derived from bovine sources. Gelatin capsules are commonly used in dietary supplements and are generally well-tolerated by most individuals. However, it's important to note for those who follow specific dietary restrictions or have religious beliefs that prohibit the consumption of bovine-derived products. The choice behind Gelatin capsules is crucial for several reasons:

2.4.1.1.4. Bioavailability and stability. Gelatin capsules are widely used because they offer good stability and can protect sensitive contents from light and oxygen, which can degrade the active compounds in ginger. This ensures that the active ingredients remain effective when they reach the digestive system.

2.4.1.1.5. Controlled release. Gelatin capsules dissolve quickly once ingested, releasing the ginger supplement contents directly into the stomach. This is ideal for studies on dyspepsia since it ensures that ginger is absorbed and active in the gastrointestinal tract, where it can exert its intended effects.

2.4.1.1.6. Digestibility and safety. Gelatin is derived from animal sources, and it is easily digestible, which is important for patient tolerance and compliance. Gelatin capsules are well tolerated by most patients, which can help maintain consistency in the study results without

introducing adverse effects related to the capsule material itself.

2.4.1.1.7. Cost-effectiveness and availability. Gelatin capsules are relatively affordable and widely available, making them practical for clinical trials. This helps in maintaining the study within budget constraints, while still ensuring a high-quality delivery mechanism for the ginger supplement.

2.4.1.1.8. Minimizing interference. Gelatin capsules are inert, meaning they do not interfere with the ginger's properties or effectiveness, nor do they react in ways that might influence body fat measurement or digestion, ensuring that any observed effects can be attributed to the ginger itself. Selecting gelatin capsules for this study, therefore, supports a more controlled, safe, and effective means of administering ginger, helping to yield reliable, interpretable data on body fat loss and the management of functional dyspepsia.

2.4.1.1.9. Free from common allergens. The product is free from artificial colors, flavors, and preservatives, making it suitable for those who prefer natural supplements. Additionally, it is free from common allergens such as wheat, peanuts, eggs, fish, tree nuts, soy, milk, and shellfish, which is beneficial for individuals with food sensitivities or allergies.

2.4.2. The short-form nepean dyspepsia index (SF-NDI)

The Nepean Dyspepsia Index (NDI) was developed in the late 1990s to measure the quality of life impact of functional dyspepsia and it has been shown to have a clinical relevance [13,14]. It evaluates how dyspepsia affects patients' overall well-being, encompassing factors like symptom severity, emotional state, interference with daily tasks, and overall satisfaction with health. The SF-NDI, a questionnaire with ten items, breaks down into five subscales of two items each, focusing on the impact of dyspepsia on different aspects of patients' quality of life. These include tension/anxiety, disruption of eating/drinking habits, understanding and management of symptoms, and interference with work/-study [13]. It stems from the Nepean Dyspepsia Index (NDI) and is designed to assess the quality of life in functional dyspepsia [14]. Each item is rated on a 5-point Likert scale from 1 ('not at all' or 'not applicable') to 5 ('extremely'). Scores from individual items within each subscale are summed up to yield a total score ranging from 10 (lowest) to 100 (highest). A higher SF-NDI score indicates a poorer quality of life, with scores exceeding > 15 signifying significantly reduced health-related quality of life, as determined by the creators of the tool. The NDI has been widely employed in various studies and populations, demonstrating its validity and reliability in assessing the impact of dyspepsia on quality of life [15,16].

2.5. The outcome of the study

The primary outcome measure was the change in quality of life (QoL) as assessed by the Short-Form NDI questionnaire. The questionnaire was administered at baseline and the end of the eight-week study period. The Short-Form NDI consists of 10 items scored on a 5-point Likert scale, with higher scores indicating worse QoL. Total scores range from 0 to 50, with higher scores indicating greater impairment in QoL. Secondary outcome measures included changes in the frequency of dyspeptic episodes and symptom severity of the disease.

2.6. Safety

The ginger supplement under investigation is allowed by food regulations and is regarded as safe. Ginger is generally considered safe when consumed in moderate amounts as a spice or dietary supplement. It is recognized by the U.S. Food and Drug Administration (FDA) as a food additive that is "generally recognized as safe." However, high doses of ginger may cause gastrointestinal side effects such as heartburn, diarrhea, and stomach discomfort in some individuals. Furthermore, individuals taking anticoagulant medications should exercise caution when consuming ginger, as it may increase the risk of bleeding [17].

Although no adverse events linked to the intake of the supplement were foreseen, the subjects were continuously monitored.

2.7. Data analysis

Statistical analysis was performed by SPSS version 26.0 (IBM, Armonk, NY, USA). Descriptive statistics were used to describe demographic and clinical characteristics. Data are presented using percentages, mean and standard deviation. The paired *t*-test or Wilcoxon signed-rank test was used for comparing scores before and eight weeks after taking ginger supplementation. A *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics of study participants

In this study, 124 patients with functional dyspepsia were screened for eligibility, of whom 62 were enrolled and 51 completed the eight weeks of ginger supplementation Fig. 1. The mean age of the study subjects was 49.74 ± 16.38 years and 78.4 % were females. The baseline characteristics of the study subjects are described in Table 1.

The impact of ginger supplementation on the quality of life in patients with functional dyspepsia was assessed using the NDI (Nepean Dyspepsia Index) questionnaire. Before the intervention, participants completed the NDI-SF questionnaire to assess their baseline level of dyspeptic symptoms and quality of life. Following the intervention period, participants completed the NDI-SF questionnaire again to evaluate any changes in their symptoms and quality of life after receiving ginger supplementation. The results from this study showed a statistically significant improvement from baseline to post-intervention assessment.

Primary outcomes: Following the eight weeks of ginger supplementation, participants with functional dyspepsia experienced a statistically significant improvement in Nepean Dyspepsia Index (NDI) scores (mean change \pm SD: 9.97 ± 16.20 , $p = 0.039$) Table 2, indicating enhanced quality of life.

Secondary outcomes: Frequency of dyspeptic episodes and severity of pain, demonstrated favorable changes post-supplementation Fig. 2. No significant adverse events related to ginger supplementation were reported during the study period. Compliance with the ginger supplementation regimen was good, with 82 % of participants completing the intervention as prescribed.

4. Discussion

The findings from this study indicate that ginger supplementation may have a positive impact on the quality of life of patients with functional dyspepsia. Functional dyspepsia is a common gastrointestinal disorder characterized by symptoms such as epigastric pain or discomfort, postprandial fullness, early satiety, and bloating, which significantly impact patients' quality of life [12]. Despite the prevalence of functional dyspepsia, treatment options remain limited, often focusing on symptom management rather than addressing the underlying pathophysiology[18]. Herbal supplements, such as ginger, have gained attention for their potential therapeutic effects on gastrointestinal symptoms due to their anti-inflammatory, anti-nausea, and prokinetic properties [19,20].

In this study, we investigated the effects of ginger supplementation on quality of life in patients with functional dyspepsia using the Nepean Dyspepsia Index (NDI) as a primary outcome measure. The findings indicated a significant improvement in quality of life among participants following eight weeks of ginger supplementation. In the Nepean Dyspepsia Index (NDI) Scores following eight weeks of ginger supplementation, there was a statistically significant improvement as compared to baseline (mean change \pm SD: 9.97 ± 16.20 , $p = 0.039$)

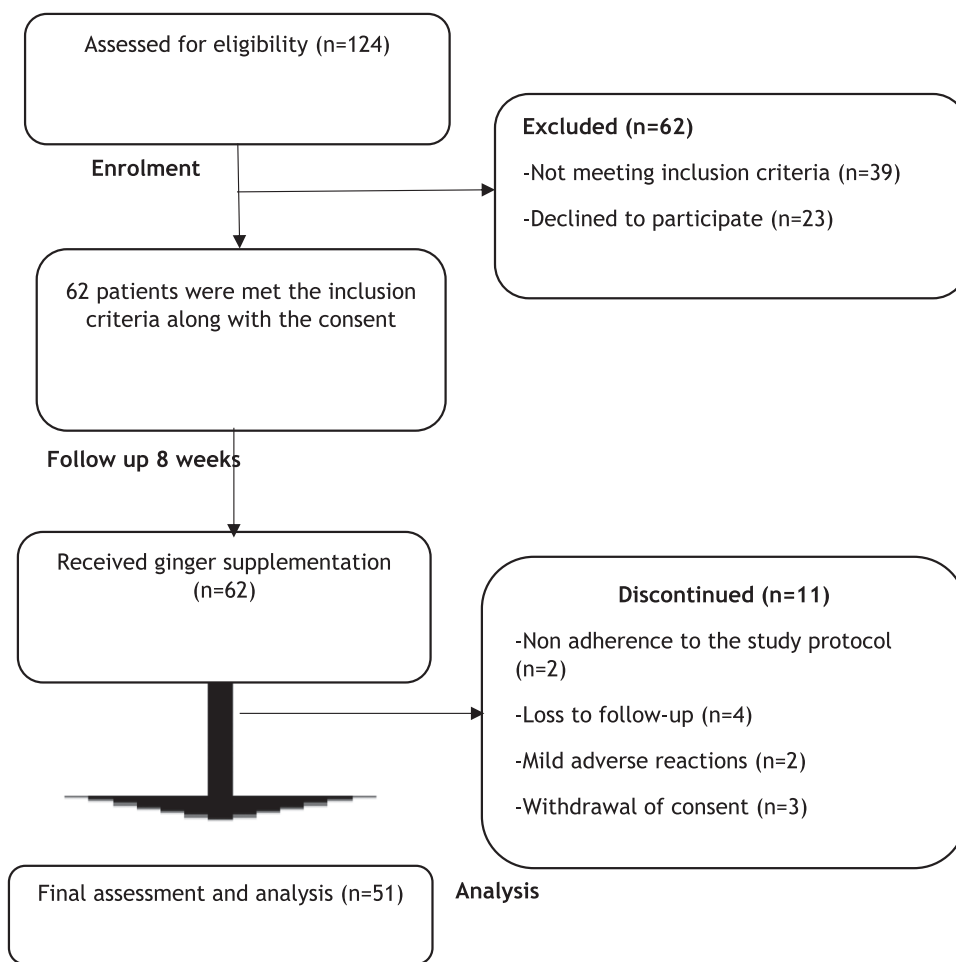


Fig. 1. Flow diagram of study subjects.

Table 1
Baseline characteristics of enrolled subjects (n = 51).

Parameters		
Gender	Male	11(21.6 %)
	Female	40(78.4 %)
Age (years)		49.74± 16.38
BMI (Kg/m ²)		25.66± 4.90
PDS (n/%)		29(57.0 %)
EPS (n/%)		33(64.7 %)

BMI-Body Mass Index, PDS- Postprandial Distress Syndrome, EPS-Epigastric Pain Syndrome Sex, PDS and EPS are presented as number (N) and percentage (%) and Age and BMI are presented as mean and standard deviation.

Table 2
Nepean Dyspepsia Index (NDI) scores at baseline and eight weeks of ginger supplementation.

NDI parameters	Baseline (mean ±SD)	At 8weeks (mean± SD)	Change in score	p-value
Tension	9.20 (22.6)	7.1(16.7)	-2.1(30.95)	0.670
Interference	14.5 (24.7)	6.7(20.2)	-7.8(22.45)	0.020 *
Eat/drink	15.1(25.3)	7.4(16.1)	-7.7(20.70)	0.013 *
Knowledge	5.70(21.4)	2.7(15.4)	-3.0(18.40)	0.524
Work	12.7(24.5)	5.4(19.8)	-7.3(22.15)	0.010 *
Total	19.07(23.2)	9.10(19.3)	-9.97(16.20)	0.039 *

NDI – Nepean dyspepsia Index SD; standard deviation

Values are presented as mean ± SD

*P < 0.05 considered statistically significant

Table 2. This improvement indicates a clinically meaningful enhancement in the quality of life among participants with functional dyspepsia and it suggests that ginger supplementation may provide meaningful relief from the symptoms of functional dyspepsia, leading to enhanced overall well-being and improved daily functioning. The observed reduction in the frequency of dyspeptic episodes and severity of symptoms further supports the notion that ginger supplementation has beneficial effects on gastrointestinal symptoms in patients with functional dyspepsia.

These findings align with previous studies demonstrating ginger’s therapeutic potential in managing gastrointestinal disorders. A comprehensive review and meta-analysis revealed that, compared to patients in a placebo group, patients with dyspepsia who consumed ginger experienced a substantial increase in stomach emptying [21]. Ginger extract improved stomach emptying in healthy volunteers, but only when it was used in large amounts [22]. Similar studies have investigated the possible effects of ginger on dyspepsia. In a study, ginger was proven to reduce dyspepsia symptoms in a double-blind, randomized study considerably and compared to a placebo, a combination of ginger and artichoke extract dramatically reduced dyspepsia symptoms according to randomized controlled research [23].

This could be due to the anti-inflammatory, antioxidant, and anti-emetic properties of ginger. These properties may contribute to the therapeutic effects of ginger in alleviating gastrointestinal inflammation, regulating gastric motility, and reducing symptoms associated with functional dyspepsia. Gingerols and other compounds in ginger have been shown to inhibit the production of pro-inflammatory cytokines and enzymes involved in the inflammatory response, thus reducing

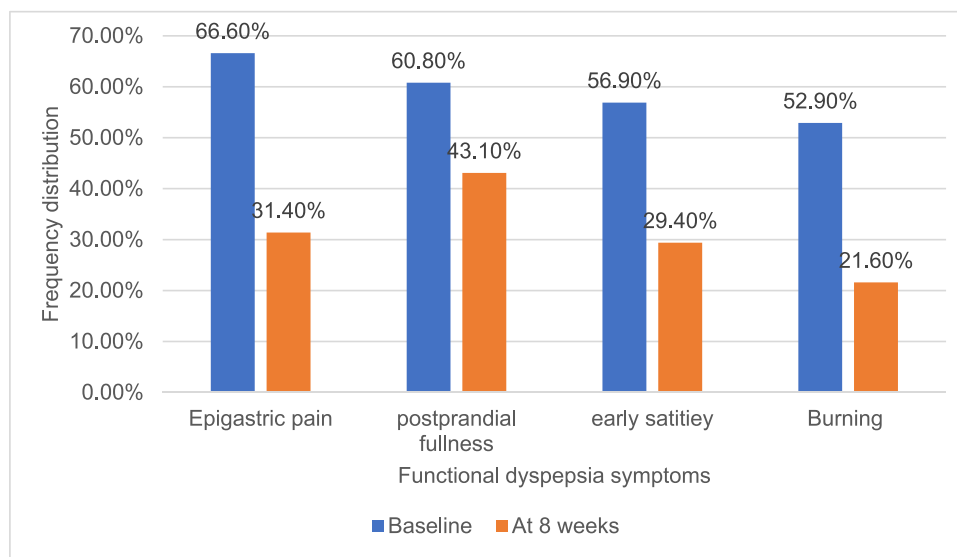


Fig. 2. Frequency distribution of dyspeptic symptoms at baseline and eight weeks of ginger supplementation.

inflammation in the stomach lining. Studies suggest that ginger has anti-inflammatory effects on the gastrointestinal tract, which could be beneficial for treating conditions such as inflammatory bowel disease, gastritis and gastric ulcers. The capacity of ginger to prevent the synthesis of proinflammatory cytokines like TNF-alpha and IL-1 beta as well as enzymes like COX-2 that are involved in inflammation is assumed to be the source of ginger's anti-inflammatory qualities. Furthermore, substances found in ginger termed shogaols and gingerols have been demonstrated to have anti-inflammatory and antioxidant properties. These compounds may also help to protect against oxidative damage and inflammation in the gastrointestinal tract [23,24].

Ginger stimulates the secretion of mucus, which forms a protective barrier in the stomach, and enhances the activity of antioxidant enzymes, helping to combat oxidative stress. Moreover, ginger has been found to inhibit the growth of *H. pylori* bacteria, a common cause of stomach ulcers, and may therefore contribute to the eradication of the infection. To fight *H. pylori* infection, ginger extract suppressed the activity of COX-2 and NF-kB as well as the production of IL-1b, IL-6, IL-8, and TNF-a from LPS-stimulated human peripheral blood mononuclear cells [25]. Another study on ginger and its components has revealed that they limit prostaglandin synthesis by inhibiting COX-1 and COX-2 as well as leukotriene biosynthesis by inhibiting 5-LOX [26]. Ginger and its phytochemicals have also revealed that they can lower NF-kB expression and the levels of proinflammatory cytokines (TNF-a, IL-1b, IL-6, and interferon-g) [27]. Additionally, ginger's ability to modulate gastric motility and enhance gastric emptying could contribute to the observed improvements in symptom severity and frequency. The hydro-methanolic extract of dried ginger successfully reverses spasmogenic effects, according to in vivo studies [28].

Moreover, studies have shown that the calcium-antagonistic action of ginger results in spasmolysis. Increased spasmolytic activity protects against potential gastric injury and ulcerogenesis by reducing the time that acidic gastric contents are in contact with the mucosa and decreasing the gastric emptying time. It also promotes the production and release of mucin, a buffer that shields the pyloric end of the stomach's walls from the corrosive effects of hydrochloric acid. Taken together, these findings suggest that ginger has gastro-protective effects through activating muscarinic receptors and blocking 5-HT (3) receptors [29]. While the precise mechanisms underlying ginger's effects and long-term adverse effects on functional dyspepsia require further elucidation, our study adds to the growing body of evidence supporting its use as a complementary therapy for this condition. The findings from this study may have important implications for clinical practice. If

ginger supplementation is indeed found to improve the quality of life in patients with functional dyspepsia, it could offer a relatively inexpensive and accessible adjunctive therapy to conventional treatments. Moreover, understanding which subgroups of patients are most likely to benefit from ginger supplementation could help personalize treatment approaches.

4.1. Limitations of the study

Despite the promising results, some limitations should be acknowledged. The relatively small sample size may influence the generalizability of the findings and the open-label design of the trial introduces the possibility of placebo effects, particularly with regard to subjective symptom improvements. **Placebo Effect:** Since participants are aware they are receiving ginger supplementation, their expectations may influence their perception of symptom improvement, leading to a placebo effect.

4.2. Future directions

While our study provides promising evidence for the potential benefits of ginger supplementation in improving QoL among FD patients, some areas need to be considered in future studies.

Randomized Controlled Trials (RCTs): To strengthen the evidence, future research should include double-blind, placebo-controlled trials to minimize bias and account for potential placebo effects observed in open-label studies. **Larger and More Diverse Populations:** Expanding the study to a larger and more diverse cohort would enhance generalizability and allow for subgroup analyses based on demographics, symptom severity, and dietary habits. **Longer Follow-Up Periods:** Investigating the long-term effects of ginger supplementation beyond eight weeks could provide insights into sustained benefits or potential diminishing effects over time. **Mechanistic Studies:** Exploring the underlying mechanisms by which ginger improves QoL in FD patients through biomarker analysis or physiological assessments would be valuable.

5. Conclusions

Ginger supplementation shows promise in improving the quality of life for patients with functional dyspepsia. The findings from this study suggest that ginger supplementation could be a valuable adjunctive treatment option for patients with FD, particularly for those seeking

symptom relief from non-pharmacological interventions. The significant reduction in symptoms indicates that ginger may play an important role in managing dyspepsia, improving patients' quality of life by reducing discomfort and digestive disturbances.

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CRediT authorship contribution statement

Zoltan Csiki: Writing – review & editing, Visualization, Validation, Supervision, Software, Methodology, Investigation, Data curation, Conceptualization. **Aregawi Lemlem Gebremariam:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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