SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Effects of Ginger Supplementation on Functional Dyspepsia Symptoms and Fat Loss among Patients with Functional Dyspepsia

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1. INTRODUCTION

1.1 Background of the study

Functional dyspepsia (FD) is a common gastrointestinal (GI) disorder characterized by persistent or recurrent pain or discomfort centered in the upper abdomen without an identifiable organic cause based on the Rome IV criteria. It substantially impairs quality of life, often leading to dietary restrictions, nutritional deficiencies, and psychological distress, while also placing a considerable burden on healthcare systems. Although conventional treatments, such as proton pump inhibitors (PPIs) and prokinetics, are frequently used, they often provide only partial symptom relief and adverse effects may restrict long-term use. This highlights the need for safer, more sustainable food-based alternatives. Nutrition plays a pivotal role in the management of FD, as dietary factors significantly influence symptom severity and digestive function. Consequently, there is growing interest in the use of dietary interventions, particularly functional foods and medicinal plants, as promising, food-based strategies for alleviating FD symptoms.

Ginger (Zingiber officinale) has been widely recognized for its dietary and medicinal benefits, particularly in gastrointestinal health. It contains bioactive compounds such as gingerols and shogaols, which exhibit anti-inflammatory, antioxidant, and gastroprotective properties. Studies have shown that ginger can enhance gastric motility, reduce gastric emptying time, and alleviate dyspeptic symptoms by stimulating digestive enzyme secretion and reducing oxidative stress in the gastrointestinal. These properties suggest that dietary ginger supplementation could serve as a natural and effective alternative for managing FD symptoms.

In addition to its gastrointestinal benefits, ginger has been associated with improvements in metabolic health, including weight management and fat loss. Research indicates that ginger supplementation can enhance thermogenesis, increase lipid metabolism, and improve insulin sensitivity, contributing to fat loss. Since most FD patients experience metabolic imbalances, including unintentional weight changes, investigating the potential dual benefits of ginger in both symptom relief and fat loss is particularly relevant. This study aims to explore whether ginger supplementation can serve as a holistic dietary intervention for FD patients, addressing both digestive discomfort and metabolic health. Existing research often focuses on either gastrointestinal benefits or weight management separately, leaving a gap in understanding how ginger might simultaneously influence both factors. By addressing this research gap, the study aims to provide scientific evidence supporting the role of ginger as a multifunctional dietary supplement for FD management.

From a public health and clinical nutrition perspective, identifying cost-effective and accessible dietary interventions is essential for improving patient outcomes. If proven effective, ginger supplementation could offer a nutritional and natural alternative to pharmacological treatments, reducing healthcare costs and improving overall well-being. As dietary approaches gain prominence in disease prevention and management, this study contributes to the growing body of research on functional nutrition and its role in gastrointestinal health.

1.2. Epidemiology and Risk Factors of Functional Dyspepsia

FD affects approximately 10-40% of the global population, with a higher incidence observed in women and individuals under the age of 50. The Rome IV criteria classify FD into two subtypes: postprandial distress syndrome (PDS) and epigastric pain syndrome (EPS), both of which exhibit overlapping symptoms and are associated with multifactorial etiologies, including delayed gastric emptying, visceral hypersensitivity, psychosocial stressors, and overweight.

1.2.1 Pathogenic aspects of Functional Dyspepsia

Functional dyspepsia is a multifactorial gastrointestinal disorder with a complex pathogenesis involving several interrelated mechanisms. One of the most studied aspects is delayed gastric emptying**,** present in approximately 30–40% of FD patients, which leads to symptoms such as postprandial fullness, nausea, and bloating due to prolonged retention of food in the stomach. Another key factor is impaired gastric accommodation, where the stomach fails to relax properly in response to a meal, contributing to early satiety and postprandial distress, particularly in patients with the postprandial distress syndrome (PDS) subtype. Visceral hypersensitivity**,** characterized by heightened sensory responses to normal gastric stimuli, is also commonly observed in FD, particularly in those with epigastric pain syndrome (EPS), and is believed to result from peripheral or central sensitization.

Additionally**,** *Helicobacter pylori* infection has been implicated in a subset of FD cases. While its role is not universal, some patients show symptomatic improvement following eradication therapy, suggesting a possible pathogenic link through mucosal inflammation or altered gastric physiology. Abnormal gastric motility and dysrhythmias**,** including disrupted slow-wave activity and coordination of peristalsis, may also impair gastric processing and contribute to dyspeptic symptoms.

Moreover, psychosocial factors**,** including anxiety, depression, and stress, have a strong association with FD, and dysregulation of the brain-gut axis is believed to mediate the influence of these psychological states on gastrointestinal function. Emerging evidence also points to alterations in gut microbiota**,** or symbiosis, as a potential contributor to FD pathogenesis, with changes in microbial composition influencing inflammation, motility, and mucosal integrity. Overall, these mechanisms suggest that functional dyspepsia arises from an interplay of gastrointestinal dysfunction, immune responses, neuropsychological influences, and microbial factors, underscoring the need for a personalized and multidisciplinary approach to diagnosis and management like nutritional supplements.

Notably, women are more likely than men to develop FD and obesity has been consistently identified as a significant risk factor. Multiple studies have established a strong link between high body mass index and gastrointestinal symptoms, including upper abdominal pain, bloating, and diarrhea. A recent large-scale study further confirmed that elevated BMI is significantly associated with increased risk of FD in females.

This association may be explained by the role of visceral adipose tissue, which is metabolically active and contributes to systemic inflammation by secreting inflammatory cytokines. Visceral fat

also increases intra-abdominal pressure, potentially exacerbating FD symptoms. Obesity, characterized by excessive accumulation of body fat, not only predisposes individuals to FD but also worsens its clinical manifestations and complicates management strategies. Consequently, interventions aimed at alleviating FD symptoms while concurrently addressing excess body fat may offer a more integrated and effective treatment approach.

1.3. Management of functional dyspepsia

The management of functional dyspepsia remains a significant clinical challenge, primarily due to the disorder's heterogeneous symptoms, multifactorial pathophysiology, and the absence of clear structural abnormalities. Current therapeutic strategies are aimed at symptom relief and improving patients' quality of life and can be broadly classified into pharmacological and non-pharmacological approaches. Pharmacological treatments include proton pump inhibitors (PPIs), prokinetics, and antidepressants. However, their efficacy is often modest, with many patients experiencing only partial symptom relief or adverse side effects. Non-pharmacological strategies, such as dietary modifications, have shown some promise but are not universally effective.

In recent years, increasing attention has been directed toward natural remedies, notably ginger (Zingiber officinale), for its potential gastrointestinal benefits. Traditionally used across cultures for digestive ailments, ginger contains active compounds like gingerols and shogaols that exert antiemetic, prokinetic, anti-inflammatory, and antioxidant effects. Additionally, ginger may aid in fat loss through mechanisms involving enhanced thermogenesis, improved lipid metabolism, and modulation of adipogenesis, offering a multifaceted approach to symptom management in FD.

Pharmacological therapies are the most commonly used interventions, particularly in patients presenting with moderate to severe symptoms. Proton pump inhibitors (PPIs), such as omeprazole and esomeprazole, are frequently prescribed for the epigastric pain syndrome (EPS) subtype of FD. They function by reducing gastric acid secretion and have demonstrated modest efficacy in symptom relief. However, a significant proportion of patients either do not respond or experience only partial relief. Prokinetic agents like domperidone, metoclopramide, and itopride are recommended for the postprandial distress syndrome (PDS) subtype due to their ability to enhance gastric motility and accelerate gastric emptying. Nevertheless, the clinical use of prokinetics is often limited by their side effect profiles, including extrapyramidal symptoms and cardiac concerns, particularly with long-term use. H2-receptor antagonists (e.g., ranitidine) are sometimes used as alternatives to PPIs, especially in patients with mild symptoms, but their efficacy is generally inferior and they are subject to tachyphylaxis with continued use.

In addition to acid suppression and prokinetic therapy, low-dose tricyclic antidepressants (e.g., amitriptyline) and selective serotonin reuptake inhibitors (SSRIs) are employed in patients with overlapping psychological symptoms such as anxiety and depression. These agents may exert their effect through modulation of visceral hypersensitivity and gut-brain axis dysregulation. Another important pharmacological strategy involves the eradication of *Helicobacter pylori*, which has been shown to produce symptom improvement in a subset of FD patients. However, the response is variable, and eradication does not consistently translate into long-term symptom resolution.

Non-pharmacological interventions are increasingly being recognized for their role in managing FD, particularly in patients who are unresponsive to or intolerant of drug therapies. Dietary modifications, such as consuming smaller, more frequent meals and avoiding high-fat, spicy, or fermentable foods, are commonly recommended, though robust evidence supporting specific dietary patterns is lacking. Psychological therapies, including cognitive behavioral therapy (CBT), hypnotherapy, and relaxation techniques, have shown efficacy in improving symptoms, especially in patients with significant psychological comorbidities. These approaches may act by reducing stress and visceral hypersensitivity, which are thought to play roles in FD pathogenesis.

Complementary and alternative medicine (CAM), including herbal remedies, acupuncture, and probiotics, is widely used by patients with FD. Among these, ginger (*Zingiber officinale*) has received considerable attention for its potential gastroprotective, prokinetic, antiemetic, and anti-inflammatory effects. Several small-scale studies and clinical trials have reported beneficial effects of ginger in alleviating dyspeptic symptoms, though heterogeneity in formulations and study designs limits the generalizability of findings. Despite growing interest in CAM, evidence supporting their routine clinical use is still limited, necessitating further rigorous clinical trials.

Despite the availability of various treatment modalities, several limitations remain. One of the primary challenges in managing FD is the heterogeneity in symptom presentation and underlying mechanisms, resulting in varied and often unpredictable treatment responses. This necessitates a trial-and-error approach that can be frustrating for both patients and clinicians. Moreover, many pharmacologic agents, particularly prokinetics and antidepressants, are associated with adverse effects that limit their long-term use and patient adherence. Symptom recurrence is also common, highlighting the chronic and relapsing nature of the disorder. Importantly, most current treatments are palliative rather than curative, as they address symptoms without fully resolving the underlying causes of FD. In conclusion, while both pharmacological and non-pharmacological strategies provide varying degrees of symptom relief in FD, their limitations underscore the need for novel and well-tolerated alternatives.

1.4 Ginger's nutritional and Bioactive components

Ginger (*Zingiber officinale*), a widely used functional food and medicinal herb, has been traditionally valued for its nutritional and therapeutic benefits. Rich in bioactive compounds such as gingerols, shogaols, and paradols, ginger exerts potent anti-inflammatory, antioxidant, and gastroprotective effects.

1.5 Ginger and Functional Dyspepsia

Regarding gastrointestinal health, ginger has long been utilized across the globe. Experimental studies suggest that the nutritive and bioactive compounds in it enhance gastrointestinal motility, modulate serotonin receptors, and possess antiemetic and anti-inflammatory effects. For instance, a randomized controlled trial by Wu et al., demonstrated that ginger significantly increased antral contractions and accelerated gastric emptying in healthy adults. Similarly Hu et al. observed notable improvements in bloating and early satiety among patients with functional dyspepsia following ginger supplementation.

Evidence indicates that ginger may alleviate hallmark symptoms of FD, such as delayed gastric emptying, bloating, and nausea, by improving gastric motility. It is also commonly recommended for various gastrointestinal complaints, including flatulence, abdominal cramps, diarrhea, and spastic colon, as well as for non-gastrointestinal conditions such as headaches, nausea, and motion sickness. Ginger root is rich in a variety of nutrients, including para-aminobenzoic acid, manganese, choline, folic acid, inositol, B vitamins, vitamin C, and essential oils. Nevertheless, systematic reviews have highlighted significant heterogeneity in clinical trial designs, ginger dosages, and outcome measures, underscoring the need for more standardized and methodologically rigorous research.

1.6 Ginger on Fat Loss and Anthropometric Parameters

Beyond its role in gastrointestinal health, ginger has been recognized for its metabolic-enhancing and fat-reducing properties. The co-occurrence of functional dyspepsia (FD) and obesity presents a complex clinical scenario, characterized by overlapping symptoms and shared underlying mechanisms. While ginger supplementation has shown promise in managing FD symptoms and modulating body composition in others, the impact of ginger on body fat content in patients with FD remains inadequately explored.

Several studies have suggested that ginger consumption may aid in weight management by promoting thermogenesis, enhancing lipid metabolism, and regulating appetite hormones. Since excess adiposity is associated with increased FD symptom severity and systemic inflammation, dietary ginger supplementation may offer a dual benefit: symptom relief and improved body composition, making it a valuable nutritional intervention for patients with FD. Although FD is not directly categorized under metabolic disorders, emerging evidence suggests that excess body fat, particularly visceral adiposity, may exacerbate dyspeptic symptoms through both mechanical and hormonal pathways. These findings have led to growing interest in exploring interventions that may concurrently alleviate gastrointestinal symptoms and contribute to body fat reduction. Ginger has been widely used in traditional medicine for its therapeutic properties. It contains several biologically active compounds, notably gingerols, shogaols, and paradols, which exhibit anti-inflammatory, antioxidant, antiemetic, and prokinetic effects. These compounds are known to enhance gastric emptying, stimulate digestive enzymes, and regulate gut motility functions that are particularly relevant for patients with FD. Studies have demonstrated that ginger has a positive impact on gastrointestinal motility and dyspeptic symptoms. For example, Wu et al., found that ginger significantly accelerated gastric emptying and reduced sensations of fullness in healthy individuals. Similarly, Borrelli et al. reported improvements in gastrointestinal discomfort and motility in FD patients after ginger supplementation.

Recent clinical interest has also focused on ginger's role in weight management and body fat reduction. Several randomized controlled trials and meta-analyses have shown that ginger supplementation can result in modest but statistically significant decreases in body weight, BMI, waist circumference, and overall fat mass among overweight or obese individuals. The proposed mechanisms include increased thermogenesis, enhanced lipolysis, improved insulin sensitivity, and appetite regulation. In one meta-analysis, ginger intake ranging from 1 to 3 grams per day over 8 -12 weeks was found to significantly reduce adiposity indicators and improve metabolic

parameters. These effects are particularly promising given the rising prevalence of obesity-related gastrointestinal complaints.

Despite separate streams of evidence demonstrating ginger's efficacy in treating dyspeptic symptoms and in reducing body fat, studies that specifically examine its impact on body fat loss among patients with functional dyspepsia remain scarce. This represents a significant gap in the literature, as individuals with FD may exhibit altered satiety signaling and digestive function, potentially influencing their body composition and response to dietary interventions. Given that visceral fat contributes to gastrointestinal dysmotility and increases inflammatory mediators that can worsen FD symptoms, targeting fat loss through ginger supplementation may provide dual therapeutic benefits. Preliminary results from a clinical trial conducted by Aregawi et al., showed that ginger improved quality of life and symptom scores in FD patients. Although changes in body composition were not the primary outcome, the findings suggested a trend toward improved metabolic markers, supporting the rationale for further investigation.

1.7 Ginger's Mechanism of Action

Ginger exerts its beneficial effects on FD and body fat management through multiple mechanisms

1.7.1 Ginger's Mechanisms of Action in FD

A. Prokinetic Effects: Enhancing Gastric Motility

Gingerols and shogaols stimulate antral contractions and accelerate gastric emptying, thereby alleviating postprandial distress. Additionally, ginger modulates cholinergic and serotonergic pathways, both of which play crucial roles in gastric motility regulation. By enhancing these pathways, ginger improves gastric motility and reduces symptoms associated with delayed gastric emptying.

B. Anti-Inflammatory and Antioxidant Properties

Gingerols and shogaols exhibit anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as TNF-α, IL-6, and COX-2, thus reducing gastric mucosal inflammation[45]. Furthermore, ginger's potent antioxidant properties help lower oxidative stress, which is a contributing factor in gastric mucosal damage and FD symptoms.

C. Reduction of Visceral Hypersensitivity and Pain

Ginger interacts with transient receptor potential vanilloid 1 (TRPV1) channels, which are involved in gastric hypersensitivity and pain perception. This interaction helps in reducing gastric pain and discomfort commonly experienced in FD. Clinical studies further confirm that ginger supplementation is associated with a significant reduction in epigastric pain and postprandial distress.

D. Stimulation of Digestive Enzyme Secretion

Ginger enhances the secretion of digestive enzymes such as amylase, lipase, and protease, which improve digestion and facilitate nutrient absorption[28]. Additionally, ginger promotes bile acid secretion, aiding in fat digestion and reducing bloating, a common symptom in FD patients [49].

E. Anti-Nausea and Carminative Properties

Ginger has been found to act as a 5-HT3 receptor antagonist, thereby reducing nausea and vomiting, which are frequently associated with FD. Additionally, ginger possesses carminative properties, preventing excessive gas accumulation in the intestines and helping alleviate bloating and discomfort.

1.7.2 Ginger's Mechanisms of Action in Fat Loss and obesity

Fat loss interventions often target energy balance, metabolic rate, appetite regulation, and hormonal control. Ginger has been identified as a natural agent with multifactorial benefits.

A. Thermogenesis and Lipolysis

Ginger enhances thermogenesis by increasing norepinephrine levels and stimulating β-adrenergic receptors, promoting lipolysis. Ginger activates AMPK (AMP-activated protein kinase), a key regulator of fat metabolism, promoting fatty acid oxidation and inhibiting lipogenesis. It has been shown to increase energy expenditure and fat oxidation. Mansour et al. reported that ginger supplementation elevated resting metabolic rate (RMR) in overweight individuals.

B. Appetite Regulation and Satiety

Ginger increases satiety and reduces hunger scores, likely by enhancing levels of GLP-1 and peptide YY, while suppressing ghrelin. This leads to reduced calorie intake, promoting gradual fat loss. Ginger may modulate appetite hormones such as leptin and ghrelin, promoting satiety and reducing calorie intake.

C. Insulin Sensitivity and Glucose Regulation

Insulin resistance is a risk factor for obesity, and ginger has been found to enhance glucose metabolism, potentially aiding in weight management among FD patients. Ginger reduces fasting blood glucose, improves insulin sensitivity, and increases adiponectin levels. These actions support weight loss by improving glucose utilization and reducing fat storage.

D. Anti-Inflammatory Action in Obesity

Obesity is associated with chronic low-grade inflammation. Ginger reduces CRP, IL-6, and TNF-α, creating a more favorable metabolic environment for fat loss.

E. Inhibition of Fat Absorption

Some ginger compounds (e.g., 6-gingerol) have been shown in vitro to inhibit pancreatic lipase, reducing the digestion and absorption of dietary fat. A meta-analysis by Mozaffari-Khosravi et al. , concluded that ginger supplementation significantly reduced body weight, waist-to-hip ratio, and body fat percentage in overweight and obese individuals.

1.8 Tolerability and Safety of Ginger Supplementation

Ginger is generally regarded as safe by the U.S. Food and Drug Administration (FDA) and clinical trials report few adverse effects, most of which are mild and transient, such as gastrointestinal irritation or heartburn. Studies involving daily doses ranging from 1 to 2 grams have shown high compliance and minimal dropouts due to side effects. Nevertheless, evaluating adverse effects and tolerability in a specific patient group, such as those with FD, remains essential for clinical recommendations. Despite its long-standing traditional use, the clinical evidence regarding ginger's effectiveness and safety in FD management remains limited and inconclusive. Moreover, few studies have explored its potential to reduce body fat or documented adverse effects and tolerability in patients with FD. This study aims to assess the effects of dietary ginger supplementation on dyspeptic symptoms, fat loss, and the safety profile of ginger supplementation in FD patients.

1.9 Rationale of the Study

Functional dyspepsia (FD) is a common gastrointestinal disorder that significantly impairs quality of life and affects up to 40% of the global population. Conventional pharmacological treatments often have limited effectiveness and may cause adverse effects, prompting increased interest in dietary and natural alternatives.

Ginger (*Zingiber officinale*), a nutrient-rich root, contains bioactive compounds such as gingerols and shogaols, which have demonstrated anti-inflammatory, antioxidant, and gastroprotective effects. These compounds are known to enhance gastric emptying and reduce visceral hypersensitivity, thereby potentially alleviating dyspeptic symptoms. In addition to its digestive benefits, ginger may aid in fat metabolism and weight loss by influencing thermogenesis and lipid oxidation. This is particularly relevant for FD patients, as abdominal adiposity has been associated with worsened gastrointestinal symptoms and reduced treatment response.

Improving both gastrointestinal symptoms and metabolic outcomes may lead to enhanced quality of life, an essential aspect of holistic FD management. However, clinical data evaluating the efficacy and safety of ginger supplementation in FD patients are limited. This study, therefore, aims to assess the effects of dietary ginger supplementation on functional dyspepsia symptoms, fat loss, safety, and quality of life, contributing to the evidence for ginger as a safe and functional dietary intervention in FD management.

2. STUDY OBJECTIVES

The main aim of this study was to evaluate the effects of dietary ginger supplementation on functional dyspepsia symptoms and fat loss among patients with functional dyspepsia. To address the aim, the following objectives were set:

- To assess the impact of dietary ginger supplementation on the severity and frequency of functional dyspepsia symptoms
- To evaluate changes in quality of life following dietary ginger supplementation in patients with functional dyspepsia
- To determine the effect of dietary ginger supplementation on body composition, particularly fat loss, in patients with functional dyspepsia.
- To assess the tolerability and potential side effects of dietary ginger supplementation in patients with functional dyspepsia.

RESEARCH QUESTIONS

The main research questions that guided this study were:

1. Does dietary ginger supplementation reduce the severity and frequency of functional dyspepsia symptoms?
2. How does ginger supplementation influence the quality of life of patients with functional dyspepsia?
3. What is the effect of dietary ginger supplementation on body fat composition in patients with functional dyspepsia?
4. Is dietary ginger supplementation well-tolerated, and what are the potential side effects?

3. MATERIALS AND METHODS

3.1 Study design

Pre and post-intervention evaluations were carried out over an eight-week period in this single-center, open-label clinical experiment. Patients having a diagnosis of functional dyspepsia at the University of Debrecen's Internal Medicine Outpatient Department in Debrecen, Hungary, participated in the study. All participants were diagnosed based on the Rome IV criteria for Functional Dyspepsia.

The reason for the choice of an open-label design instead of a randomized controlled trial (RCT) with a placebo group was particularly due to the onset of the COVID-19 pandemic at the start of our study**.** The pandemic posed significant challenges related to participant recruitment, safety protocols, resource allocation and the procurement of placebo materials, all of which made it unfeasible to implement a double-blind, placebo-controlled design during that period. Conducting a randomized controlled trial with a placebo group would have required additional time, funding and material to develop, produce and validate a suitable placebo that closely mimics the appearance, taste, and smell of ginger. Given the pandemics the limited time and resources available during the study period, an open-label design was the most feasible approach to initiate clinical investigation. While we recognize the limitations associated with the lack of blinding, especially the potential for placebo effects in a condition like Functional Dyspepsia, we sought to mitigate bias through the use of validated outcome measures and consistent follow-up procedures. This design allowed us to conduct a preliminary evaluation of ginger supplementation under constrained conditions. Moving forward, we recommend for a randomized, double-blind, placebo-controlled trial to strengthen the evidence and validate our findings under more controlled circumstances.

3.2 Study Participants

The study involved the recruitment of 62 participants with functional dyspepsia, 51 of whom completed the study. Prior to and after eight weeks of ginger administration, a self-administered questionnaire was used to gather data during hospital visits. Based on the existence of functional dyspepsia symptoms reported at the initial appointment, eligibility for inclusion was determined. Written informed consent was given by each subject, and participation was completely voluntary.

3.2.1 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.
- Stable weight for the past three months (± 2 kg)
- Not taking any drugs that could affect the trial's results, such as proton pump inhibitors or H2 receptor antagonists.

3.2.2 Exclusion Criteria:

- Individuals suffering from organic gastrointestinal conditions (such as with malignancy, GERD, or peptic ulcer disease).
- Women who are nursing or pregnant
- A history of allergic responses to supplements containing ginger.
- Individuals who are on weight loss or drugs that have been shown to interact with ginger, such as anticoagulants.
- Use of weight-loss medications or supplements
- Severe dyspeptic symptoms requiring immediate pharmacological intervention

3.3 Randomization and masking

This single-center, open-label clinical trial involved a single arm treatment group receiving ginger supplementation. Given the study's single arm design, traditional methods such as randomization into multiple treatment arms and blinding were not applicable. However, to enhance validity and reduce potential bias, we implemented specific measures: (A) Randomization of Treatment Timing: Although ginger supplements were given to all subjects, we varied when they began taking them. This could assist in adjusting for any confounding variables or temporal effects. To minimize potential confounding factors, we took some steps to ensure that participants' lifestyle habits, particularly diet and physical activity, remained stable throughout the study period.

At baseline, participants were instructed to maintain their usual dietary patterns and levels of physical activity during the 8-week intervention. This instruction was emphasized both verbally and in writing during the enrollment process and reinforced at each follow-up visit. Throughout the study, we conducted regular weekly follow-up contacts by phone, during which participants were asked about any significant changes to their diet, exercise routines, or the use of new supplements or medications. Any reported deviations were documented and monitored closely. Participants were also reminded during each contact to avoid making lifestyle changes that could influence the study outcomes. While we did not implement objective measures (e.g., food diaries or activity trackers), these consistent reminders and monitoring efforts were intended to support compliance and reduce variability related to lifestyle factors.

3.4 Procedures

3.4.1 Intervention

A ready-made Swanson 540 mg ginger root extract capsule, Budapest, Hungary, was used, following the established protocol. Swanson 1080 mg/day, twice day, which is 540 mg of ginger root extract, Budapest, Hungary, a ready-made ginger capsule supplement, was administered to the trial participants. The patients who were enrolled were told to take two 540 mg capsules for eight weeks, one half an hour before lunch and one before dinner. All patients were instructed to refrain from taking prokinetic and anti-secretory drugs for the entire eight weeks that they were taking ginger supplements prior to the start of the experiment. Throughout the study period, study participants were encouraged to continue their typical food and activity habits.

Swanson Ginger Root 540 mg supplement

The ginger supplement we used in our study was commercially available standardized Swanson Ginger Root capsule (Swanson Health Products, Budapest, Hungary).

Formulation: Each capsule contained 540 mg of dried ginger root powder (*Zingiber officinale*).

Type: Whole-root powdered form, not a concentrated extract

Solubility: As a dried powder, ginger is partially water-soluble, but active components such as gingerols and shogaols are more soluble in ethanol or lipids.

Dose Administered: Participants received 2 capsules of each 540 mg per day, corresponding to a total daily dose of 1,080 mg.

Composition (Based on Manufacturer):- The composition of the Swanson ginger root capsules, based on manufacturer information, typically includes 6-gingerol (0.5–1.5%), 6-shogaol (0.1–0.5%), essential oils (1.0–3.0%), trace amounts of zingerone (up to 0.1%), with fiber and starch as the major bulk components, along with other phenolic compounds present in minor amounts.

Material for Capsules: Gelatin obtained from cows is used to make the capsules. Most people tolerate gelatin capsules well, and they are frequently seen in dietary supplements. But it's crucial to remember for people who have religious convictions that exclude consuming goods made from cows or who adhere to particular dietary restrictions.

Free of Common Allergens: Those who prefer natural supplements can use this product because it is devoid of artificial colors, flavors, and preservatives. For those who have dietary sensitivities or allergies, it is also devoid of common allergens like wheat, peanuts, eggs, fish, tree nuts, soy, milk, and shellfish.

3.4.2 The Nepean Dyspepsia Index (NDI)

It has been demonstrated that the Nepean Dyspepsia Index (NDI), which was created in the late 1990s to gauge the impact of functional dyspepsia on quality of life, has clinical significance. It assesses the entire impact of dyspepsia on patients' well-being, taking into account elements such as the intensity of symptoms, emotional state, disruption of daily activities, and general health satisfaction. It stems from the Nepean Dyspepsia Index and is designed to assess the quality of life in functional dyspepsia. A 5-point Likert scale, ranging from 1 ('not at all' or 'not applicable') to 5 ('very'), is used to rate each item. Each subscale's individual item scores are added together to provide a total score that ranges from 10 (lowest) to 100 (highest). According to the tool's developers, a higher SF-NDI score denotes a lower quality of life, with values above >15 indicating a markedly lower health-related quality of life. Numerous studies and populations have used the NDI extensively, proving its validity and reliability in determining how dyspepsia affects quality of life.

3.4.3 The IN-Body 720 Body Composition Analyzer

In this study body composition was analyzed using the INBODY 720. The In-body 720 is a body composition analyzer that utilizes bioelectrical impedance analysis (BIA) technology to measure various components of body composition. It offers detailed insights into body fat, muscle mass, water distribution, and more. It is widely used in clinical settings, fitness centers, sports medicine,

and research. It helps professionals track patients' or clients' body composition changes over time, especially in programs related to weight management, muscle development, or chronic disease management. The measurement process is non-invasive, quick (typically under a minute), and does not require the patient to undress, making it convenient for repeated use over time. Due to its high precision and segmental analysis capabilities, the In-Body 720 is considered one of the more advanced tools available for body composition analysis, particularly useful in clinical trials or research involving changes in body composition.

3.5 Outcome Measures

The study assessed multiple outcomes to evaluate the impact and safety of the intervention over an eight-week period. Quality of life related to dyspeptic symptoms was measured using the Short-Form Nepean Dyspepsia Index (NDI) questionnaire, administered at both baseline and at the end of the intervention. This tool includes 10 items rated on a 5-point Likert scale, where higher scores reflect greater impairment in quality of life. The total score ranges from 0 to 50.

In addition to quality of life, the study evaluated physiological and symptomatic changes. These included body fat percentage, assessed via bioelectrical impedance analysis (BIA), as well as body weight and waist-to-hip ratio (WHR). Changes in the frequency and severity of dyspeptic episodes were also tracked, using the NDI to capture symptom improvement. All measurements were recorded at baseline and repeated after the eight-week intervention period.

Furthermore, adverse events and tolerability were systematically monitored throughout the study. Participants were asked to report any side effects or unusual symptoms during scheduled follow-up visits and via direct contact when necessary. The nature, frequency, and severity of any reported adverse events were recorded and evaluated to assess the safety and tolerability of the intervention.

A. Improvement in Functional Dyspepsia (FD) Symptoms and Quality of Life (QoL): Assessed using the Nepean Dyspepsia Index (NDI) at baseline and post intervention. Reduction in symptom severity scores, including postprandial fullness, early satiety, bloating, and epigastric pain.
B. Fat Loss and Body Composition Changes: Measured at baseline and post-intervention. Body Mass Index (BMI, kg/m^2), Waist circumference (cm) and Body fat percentage (%), assessed using bioelectrical impedance analysis (BIA), the IN-Body 720 Body composition analyzer.
C. Adverse Events and Tolerability: Assessed at baseline and post-intervention with close follow-ups. Frequency and type of reported side effects (dyspepsia symptoms and allergic reactions). Compliance rate with ginger supplementation measured via pill count

3.6 Ethical clearance

This study was conducted in full compliance with the ethical principles outlined in the Declaration of Helsinki. The study protocol was reviewed and approved by the University of Debrecen, registry reference number: DE RKEB/IKEB 5622-2020 and registered in clinicaltrials.gov, NCT06313814. Prior to being included in the study, each participant gave written informed consent attesting to their voluntary involvement and comprehension of the goals, methods, risks, and advantages of the research. The freedom to leave the study at any time without facing any

repercussions was guaranteed to the participants. All personal data was anonymized, and research records were safely kept to preserve their privacy. The participants were given a thorough explanation of any small hazards related to taking ginger supplements. Any unanticipated problems were resolved immediately to guarantee participant safety, and no negative effects beyond those typically linked to ginger use were anticipated. This study aimed to contribute to the growing body of knowledge regarding the use of herbal supplements in improving the quality of life in patients with functional dyspepsia while maintaining a high standard of ethical conduct throughout the research process.

3.7 Data analysis

All statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were employed to summarize baseline demographic and clinical characteristics, as well as adherence rates to ginger supplementation. Continuous variables, such as age, BMI, symptom severity, and body fat percentage, were presented using mean, median, standard deviation, and range. Categorical variables, including gender distribution, anthropometric and clinical symptoms were summarized using frequencies proportions and percentages.

To assess the effectiveness of the intervention, both descriptive and inferential statistical methods were utilized. Changes in outcomes, such as quality of life scores, symptom severity, body fat percentage, and other physiological indicators, were analyzed by comparing pre- and post-intervention values. For normally distributed data, the paired t-test was applied, while the Wilcoxon signed-rank test was used for non-normally distributed data. A p-value of less than 0.05 was considered statistically significant.

Adverse events and tolerability data were analyzed descriptively. The frequency and type of reported side effects were summarized using counts and percentages. Participant-reported tolerability was categorized as good, moderate, or poor based on self-reports and study monitoring.

4. RESULTS

4.1. Socio-demographic and Baseline Characteristics of Study Subjects

A total of 62 participants with functional dyspepsia were enrolled in the study. Of these, 51 participants completed the 8-week intervention with daily dietary ginger supplementation (1.080 grams/day). Eleven patients were lost to follow-up due to non-compliance and unrelated health issues. The mean age of participants was 49.74 ± 16.4 years and the mean BMI was 25.66 ± 4.9 kg/m² at baseline. The baseline characteristics of the study participants are shown. Data analysis was performed on the 51 participants who completed the study.

4.2. Effects of Ginger on Functional Dyspepsia Symptoms and Quality of Life

The influence of ginger supplementation on the quality of life in patients diagnosed with functional dyspepsia was evaluated using the Nepean Dyspepsia Index (NDI) questionnaire. At baseline, participants completed the NDI-SF to establish initial measures of dyspeptic symptoms and quality of life. Following an 8-week intervention period, the same questionnaire was administered to assess post-intervention outcomes. Quality of life, assessed using the Nepean Dyspepsia Index (NDI), improved following the intervention. Mean total NDI score improved from 19.07 ± 23.2 at baseline to 9.10 ±19.3 at week 8 ($p < 0.05$), indicating enhanced daily functioning and reduced symptom-related distress. Subscales reflecting interference, eating and drinking habits, and daily activity impact (work) showed statistically significant improvements ($p< 0.05$ for all domains). The analysis revealed a statistically significant improvement in both dyspeptic symptoms and quality of life from baseline to the 8-week follow-up.

4.3. Effects of Ginger on Fat Loss and Anthropometric Parameters

In our study, the Body Composition Analyzer (IN Body 720) provided a measurement of a wide range of body composition parameters. These included total body weight, fat mass, skeletal muscle mass (SMM), percent body fat (%BF), visceral fat level, body mass index (BMI), waist-hip ratio (WHR), body water (BW), basal metabolic rate (BMR), and segmental analysis of fat and lean mass in each limb and the trunk.

Ginger supplementation may influence some of these parameters, primarily through its thermogenic, anti-inflammatory, and digestive properties. For example, ginger has been shown to promote fat metabolism and appetite regulation, which can lead to reductions in fat mass, percent body fat, and visceral fat levels. Its anti-inflammatory effects may contribute to improvements in the body water ratio, especially in individuals with fluid retention or low-grade inflammation. Additionally, ginger may modestly enhance energy expenditure, potentially reflected as a slight increase in BMR. However, significant changes in muscle mass or total body weight are less likely unless combined with dietary or physical activity interventions.

Although the In-Body 720 provides a wide range of body composition parameters, in our study, we recorded all available parameters but focused our analysis on specific ones relevant to the research objectives. These included body weight (wt)**,** body mass index (BMI)**,** waist-hip ratio (WHR)**,** percent body fat (%BF)**,** and body fat mass. These parameters were selected to evaluate

the potential effect of ginger supplementation on body composition indicators and body fat distribution.

Ginger supplementation showed minimal changes in body composition. The average body fat percentage decreased slightly from 26.8 ± 3.4 at baseline to 25.9 ± 3.1 after 8 weeks; however, this difference was not statistically significant ($p = 0.173$). Likewise, there were no significant changes in body weight or BMI over the 8-week period (mean change: 0.5 ± 1.1 kg, $p = 0.24$)

4.4. Detailed Body Composition Metrics (IN-Body 720)

Body composition was analyzed a lot of parameters. Following 8 weeks of daily ginger supplementation (1.080 g/day), no significant changes were observed in body composition metrics. Although minor variations were noted in weight, body fat percentage, and skeletal muscle mass, none reached statistical significance ($p > 0.05$)

4.5 Segmental Fat and Lean Mass Analysis

Segmental analysis of body composition showed minimal reductions in regional fat mass across limbs and trunk. Lean mass remained stable, and all observed differences were statistically non-significant ($p > 0.3$). This supports the conclusion that ginger supplementation had no significant effect on localized fat or muscle mass

4.6. Overall Changes in Body Composition

After 8 weeks of ginger supplementation, no statistically significant changes were observed in body composition. BMI slightly increased from 25.66 ± 4.90 to 26.15 ± 5.10 kg/m² ($p = 0.240$). BF% decreased from 26.8 ± 3.4% to 25.9 ± 3.1% ($p = 0.173$), while fat mass decreased from 27.6 ± 2.6 kg to 27.01 ± 2.1 kg ($p = 0.324$). WHR also decreased slightly (from 0.92 ± 0.82 to 0.91 ± 0.73), but the change was not significant ($p = 0.410$).

4.7. Subgroup Comparisons

The main influencing factors that could affect the effectiveness of ginger supplementation on the analyzed body composition parameters in our study include age, BMI, Body fat percentage, and duration of intervention. Age plays a role, as older adults may gain more benefits from ginger's anti-inflammatory and digestive properties. Body mass index (BMI) and overall body weight are also important, with individuals having a higher BMI potentially experiencing more significant reductions in fat mass and appetite regulation. A higher body fat percentage offers more room for fat reduction, making such individuals more responsive. Similarly, those with elevated visceral fat levels may exhibit greater improvements due to ginger’s thermogenic and fat metabolism-enhancing effects. Gender differences may influence the response due to variations in fat distribution and hormonal regulation. Another one could be duration of supplementation, longer durations may tend to produce greater and more sustained improvements in the measured body composition parameters.

4.7.1. Comparison by sex

At baseline, female participants had a significantly higher body fat percentage and BMI compared to males ($p < 0.05$). After 8 weeks, both sexes experienced modest and statistically non-significant changes in body composition. Females showed an average reduction in BF% of $–0.8 \pm 2.1\%$, while males demonstrated a slightly greater decrease of $–1.1 \pm 2.9\%$ ($p = 0.622$ for between-group comparison). Changes in BMI and WHR were comparable between groups, with no significant differences observed.

4.7.2. Comparison by age group

Participants were stratified into two groups: those under 50 years ($n = 26$) and those aged 50 years or older ($n = 25$). Younger participants had a slightly greater reduction in BF% ($–1.0 \pm 2.3\%$) compared to older participants ($–0.7 \pm 2.5\%$), but the difference was not statistically significant ($p = 0.648$). Changes in BMI, WHR, and body fat mass were similarly non-significant between the age groups.

4.7.3 Comparison by BMI Category

Participants were categorized based on baseline BMI as: Normal weight (18.5–24.9 kg/m²): $n = 24$ and Overweight/Obese (≥25 kg/m²): $n = 27$. No statistically significant differences were found between BMI categories. However, overweight/obese participants showed slightly greater reductions in BF% and fat mass, though these did not reach significance.

4.8. Reported adverse effects and Tolerability

Ginger supplementation was generally well tolerated by participants. Mild gastrointestinal side effects were mostly observed during the first week of the intervention and resolved on their own without the need for medical treatment. No serious adverse events occurred throughout the study. The most frequently reported side effects included mild bloating (14.9%), heartburn (12.8%), and diarrhea (10.6%), all of which were temporary and self-limiting. Importantly, no participants discontinued the ginger supplementation due to these effects. Additionally, one participant experienced a mild headache that subsided without any intervention.

5. DISCUSSION

This study investigated the effects of dietary ginger supplementation on functional dyspepsia symptoms, quality of life, fat loss, and adverse effects among patients with FD. The outcomes provide promising evidence that ginger supplementation over an 8-week period significantly improves both dyspeptic symptoms and patients' quality of life, with high tolerability and minimal adverse effects.

5.1 Ginger's Impact on Functional Dyspepsia Symptoms and Quality of Life

The results demonstrated a significant improvement in functional dyspepsia symptoms and associated quality of life, as measured by the Nepean Dyspepsia Index (NDI). Total NDI scores improved markedly from baseline to the 8-week follow-up (mean change: -9.97, $p = 0.039$), reflecting enhanced daily functioning and reduced dyspeptic symptom-related distress. Notably, statistically significant improvements were observed in the subdomains of interference ($p = 0.020$), eating and drinking habits ($p = 0.013$), and work-related impacts ($p = 0.010$), which are core components affecting patients' daily experiences with FD. The observed improvements in symptom frequency and severity, further support ginger's potential as an effective natural therapy in managing FD.

These results align with previous clinical and preclinical studies suggesting that ginger possesses prokinetic, antiemetic, and anti-inflammatory properties that may contribute to symptom relief in functional gastrointestinal disorders. A comprehensive review and meta-analysis demonstrated that dyspeptic patients who consumed ginger showed a significant improvement in gastric emptying compared to those in the placebo group [5]. Additionally, ginger extract was found to enhance stomach emptying in healthy individuals, although this effect was observed only at higher doses. Other studies have also explored ginger's potential impact on dyspepsia. In one double-blind, randomized trial, ginger significantly alleviated dyspeptic symptoms. Furthermore, another randomized controlled study reported that a combination of ginger and artichoke extract markedly reduced dyspepsia symptoms compared to a placebo.

The benefits of ginger may be attributed to its anti-inflammatory, antioxidant, and antiemetic properties. These characteristics likely aid in relieving gastrointestinal inflammation, promoting healthy gastric motility, and alleviating symptoms of functional dyspepsia. Compounds such as gingerols found in ginger have been shown to suppress the production of pro-inflammatory cytokines and enzymes that drive inflammation, thereby helping to reduce irritation in the stomach lining. Research indicates that ginger's anti-inflammatory effects on the gastrointestinal system could be valuable in managing conditions like inflammatory bowel disease, gastritis, and gastric ulcers. Its ability to inhibit the synthesis of pro-inflammatory cytokines, including TNF-alpha and IL-1 beta, as well as enzymes like COX-2, is believed to underlie its anti-inflammatory action. Additionally, ginger constituents such as shogaols and gingerols exhibit both antioxidant and anti-inflammatory activities, which may offer protection against oxidative stress and inflammation within the digestive tract.

Ginger promotes the secretion of mucus, creating a protective layer in the stomach, and boosts the activity of antioxidant enzymes, helping to counteract oxidative stress. Additionally, ginger has

been shown to inhibit the growth of H. pylori, a major contributor to stomach ulcers, potentially aiding in the elimination of the infection. Research has demonstrated that ginger extract can suppress COX-2 and NF-κB activity, along with reducing the production of IL-1β, IL-6, IL-8, and TNF-α in LPS-stimulated human peripheral blood mononuclear cells. Further studies have found that ginger and its active components inhibit prostaglandin production by blocking COX-1 and COX-2, as well as leukotriene synthesis by inhibiting 5-LOX. Moreover, ginger has been shown to reduce NF-κB expression and decrease levels of pro-inflammatory cytokines, such as TNF-α, IL-1β, IL-6, and interferon-γ. Ginger's ability to regulate gastric motility and enhance gastric emptying may also explain the observed reductions in symptom severity and frequency. In vivo experiments have indicated that hydromethanolic extracts of dried ginger effectively counteract spasmogenic effects.

Furthermore, research has indicated that ginger's calcium-antagonistic properties contribute to its spasmolytic effects. Enhanced spasmolytic activity helps protect the stomach from injury and ulcer formation by minimizing the exposure time of the mucosa to acidic gastric contents and accelerating gastric emptying. Ginger also stimulates the production and secretion of mucin, which acts as a protective buffer against the damaging effects of hydrochloric acid, particularly at the pyloric end of the stomach. Collectively, these findings suggest that ginger exerts gastroprotective effects by activating muscarinic receptors and inhibiting 5-HT_3 receptors. Although the exact mechanisms of ginger's action and its potential long-term side effects in the management of functional dyspepsia require further investigation, our study contributes to the expanding evidence supporting its role as a complementary treatment for this disorder. These findings may hold significant implications for clinical practice

Regarding clinical implications, the findings of this study demonstrate the potential of ginger as a functional food component in the management of functional dyspepsia. Improvements in NDI scores, particularly in the domains of eating and drinking behaviors, indicate that ginger supplementation may help patients with FD overcome appetite loss and food avoidance associated with gastrointestinal discomfort. From a clinical nutrition perspective, integrating ginger into dietary interventions provides a natural, safe, and low-cost approach to complement conventional therapies. Nutritionists and dietitians are encouraged to consider ginger as part of comprehensive management plans aimed at reducing gastrointestinal symptoms and enhancing patients' quality of life. However, to fully confirm its efficacy and determine appropriate dosing, further large-scale randomized controlled trials are warranted.

5.2 Effects of ginger on Fat Loss and anthropometric Parameters among FD patients

Contrary to expectations from previous metabolic studies on ginger, this study found no statistically significant changes in body fat percentage, BMI, or other anthropometric measurements after 8 weeks of supplementation. While there was a slight reduction in body fat percentage (from 26.8% to 25.9%, $p = 0.173$) and body fat mass (from 27.6 kg to 27.01 kg, $p = 0.324$), these changes were not meaningful from a clinical or statistical standpoint. Although earlier studies have highlighted ginger's thermogenic effects and its role in promoting lipid metabolism and fat loss, our study did not find a significant decrease in body fat following an eight-week intervention. The average baseline body fat percentage (26.8 ± 3.4) remained largely unchanged after supplementation (25.9 ± 3.1, $p = 0.173$). These findings align with other research that has reported mixed results regarding ginger's anti-obesity and lipid-lowering properties. The

absence of notable fat reduction among FD patients could be attributed to several complex factors. One possibility is the relatively short duration of the intervention and the modest ginger dosage used, which may not have been sufficient to produce meaningful changes in body composition. Additionally, while ginger's thermogenic and lipid-lowering effects appear promising. They may be comparatively mild relative to other metabolic boosters and therefore insufficient to achieve significant fat loss in an FD population. Ginger's thermogenic impact might simply be too modest to bring about noticeable changes in body fat among these patients.

Another possible explanation could be FD's complex and multifactorial nature, which involves altered gastrointestinal motility, visceral hypersensitivity, and psychological stress. Since ginger primarily supports digestion, it may not fully address all these underlying mechanisms. As a result, any improvement in symptoms may be limited, preventing broader benefits such as enhanced dietary habits and physical activity, which could influence body fat levels. Moreover, the interaction between appetite regulation and FD symptoms might also reduce the effectiveness of ginger in promoting fat loss. FD patients often suffer from irregular appetites due to issues like early satiety, nausea, and bloating. Although ginger may promote satiety, this could unintentionally disrupt eating patterns. If ginger suppresses appetite without adequately relieving symptoms like nausea or bloating, it could lead to reduced food intake, insufficient nutrient consumption, and metabolic slowdown, ultimately counteracting any potential fat reduction.

5.3. Subgroup Comparisons

This study explored the effects of dietary ginger supplementation on body composition in patients with FD, with additional subgroup analyses by sex, age, and BMI category. While modest reductions in body fat percentage and fat mass were observed after 8 weeks, these changes were not statistically significant across the overall sample or within subgroups. The subgroup results suggest that short-term ginger supplementation at a daily dose of 1.08 grams does not significantly impact BMI, body fat, or WHR in patients with FD. These findings align with previous research indicating inconsistent or limited effects of ginger on anthropometric measures, especially in the absence of additional dietary or lifestyle interventions.

5.3.1. Influence of Sex

Although women had higher baseline body fat levels, the reduction in BF% was similar between sexes. This indicates that the response to ginger was independent of sex in this population. These results are consistent with prior studies reporting non-sex-specific effects of ginger on metabolic and inflammatory markers.

5.3.2. Influence of Age

Participants under 50 years showed slightly greater reductions in BF%, which may reflect better metabolic responsiveness. However, the differences were not statistically significant, and the limited sample size may reduce power to detect such effects.

5.3.3 Influence of BMI

Participants with higher baseline BMI (≥25 kg/m²) showed slightly greater improvements in BF% and fat mass, although the differences did not reach statistical significance. This suggests a possible trend where overweight or obese individuals may derive more benefit in terms of fat reduction. These observations are in line with studies indicating that individuals with higher adiposity may be more responsive to anti-inflammatory or thermogenic properties of ginger.

5.4. Clinical Implications

Although negative outcomes may seem disappointing, they offer valuable insights into the potential limitations of ginger as a therapeutic tool for body fat loss management among FD patients. These findings suggest that ginger's primary benefits are more symptom-targeted, offering relief from FD symptoms rather than exerting significant metabolic or weight-related effects. This underscores the potential need for a combined approach to FD management, integrating ginger with lifestyle interventions such as balanced nutrition, regular exercise, and stress management, for those facing body composition challenges. Moreover, the results emphasize the importance of refining future research designs by incorporating varied dosages, extended intervention periods, adjunctive treatments, and rigorous methodologies (e.g., randomized, double-blind trials) to better assess efficacy and underlying mechanisms. Finally, the lack of fat reduction calls for a reassessment of the assumed metabolic roles of ginger, encouraging further investigation into its effects on biochemical markers like lipid profiles, insulin sensitivity, and inflammatory processes in FD patients.

5.5. Safety and Tolerability

Ginger supplementation was well tolerated, with no serious adverse events reported. A small number of participants experienced mild gastrointestinal discomfort, which was transient and did not lead to study withdrawal. These findings reaffirm ginger's strong safety profile, aligning with prior research. Mild bloating was reported by 14.9% of participants, which is comparable to outcomes from other clinical studies; for instance, a randomized controlled trial found a 12% incidence of bloating during ginger use. This effect is likely linked to ginger's prokinetic properties, which can temporarily disturb gastric motility in sensitive individuals. Similar rates have been observed in past studies, such as one by, which also emphasized the benign and short-lived nature of this symptom.

Heartburn was reported by 12.8% of participants, echoing previous research findings. This side effect may stem from ginger's stimulation of gastric acid secretion, driven by compounds like gingerols and shogaols, which can irritate the stomach lining and worsen reflux. Lete and Allué noted that 10–15% of participants experienced heartburn at doses above 1 gram per day, indicating a dose-dependent relationship. A systematic review also identified heartburn as a frequent, dose-related adverse effect. Additionally, ginger's ability to relax the lower esophageal sphincter may contribute to reflux symptoms. However, some evidence suggests that mild heartburn could reflect beneficial changes in gut microbiota.

Diarrhea occurred in 10.6% of participants, a rate consistent with earlier studies but still lower than the side effect rates associated with synthetic prokinetic agents. Zeng et al. observed a similar frequency of diarrhea with high-dose ginger intake (2 grams/day). Other studies have noted

ginger's mild laxative properties as a manageable effect, with individual sensitivity and preparation method potentially influencing its occurrence.

The majority (87.2%) of participants rated ginger supplementation as good or excellent. This aligns with earlier findings showing over 85% of users reporting favorable tolerability despite occasional mild side effects. Lete and Allué, similarly documented high satisfaction rates in their study on ginger for digestive issues. Importantly, no participants rated tolerability as poor or very poor in this study, underscoring its general acceptability. Supporting evidence from additional clinical trials [6, 19] also reported no instances of poor tolerability and found that ginger was often better tolerated than conventional drugs, reinforcing its role as a gentle, natural nutritional therapeutic option.

The findings highlight the potential of dietary ginger as a safe and effective option for managing FD, with significant implications for clinical practice. Clinically, they support the use of ginger as a natural, low-cost alternative or adjunct to conventional therapies for functional dyspepsia, particularly for patients seeking complementary treatment options. The high tolerability and safety of ginger may improve patient adherence and satisfaction with treatment regimens. From a research perspective, these results pave the way for further investigations to confirm the benefits in larger and more diverse populations, optimize dosage, and evaluate long-term safety and efficacy. Public health efforts could leverage ginger's accessibility to improve functional dyspepsia management, especially in resource-limited settings where access to conventional medications may be constrained.

5.6 Strengths and limitations of the study

Strengths: The study presents several notable strengths: Firstly, its clinical relevance stands out, as it addresses functional dyspepsia, a prevalent and burdensome gastrointestinal disorder through a practical and accessible dietary intervention. This aligns well with current trends emphasizing nutritional approaches in medical management. A second strength lies in the standardized dosage used: participants received a commercially available ginger capsule at 1080 mg/day. This ensures consistency and reproducibility, enhancing the applicability of the findings to real-world settings. Furthermore, the study employed the Nepean Dyspepsia Index (NDI), a validated and disease-specific tool, which allowed for comprehensive and accurate assessment of both symptom changes and quality of life. The research also took a holistic approach, evaluating not only symptom severity and QoL but also anthropometric measures and adverse effects. This multi-dimensional analysis offers a broader understanding of ginger's potential impact. Importantly, the intervention demonstrated good tolerability, with no dropouts due to adverse effects, indicating that ginger supplementation is both safe and feasible in clinical and community environments.

Limitations: Despite these strengths, the study has some limitations. The open-label design means that neither participants nor investigators were blinded, which may have introduced placebo effects and observer bias, influencing subjective outcomes. Additionally, the absence of a control or placebo group limits the ability to attribute observed effects specifically to ginger, as other variables, such as diet, psychological state, or the natural fluctuation of symptoms, could have played a role. The relatively short intervention period of eight weeks may not be sufficient to assess long-term efficacy or the development of side effects. Generalizability is another concern, as the

specific sample size and study setting may not reflect broader or more diverse populations. Furthermore, although symptom relief was evident, there were no significant changes in anthropometric measures like body weight or fat mass, which may reduce the relevance of ginger for individuals seeking metabolic benefits.

6. CONCLUSION AND FUTURE DIRECTIONS

This study provides evidence that dietary ginger supplementation may alleviate symptoms of functional dyspepsia (FD) while enhancing patients' quality of life. The intervention demonstrated good tolerability and was associated with minimal adverse effects, underscoring ginger's potential as a safe, natural nutritional therapeutic option. Although no significant changes were observed in anthropometric measures, like fat loss, the noticeable relief of gastrointestinal symptoms suggests improved digestive efficiency and possibly better nutrient assimilation. These findings highlight ginger's potential as a natural, nutrition-based supportive therapy in the management of FD.

Future Research Directions

To further elucidate the therapeutic potential of ginger, future studies should investigate its broader impacts on nutritional status, metabolic health, and gastrointestinal function. A well-designed randomized, double-blind, placebo-controlled trial (RCT) is essential to minimize bias and accurately determine the efficacy of ginger supplementation, with blinding helping to control for placebo effects.

An adequate sample size should be recruited to ensure statistical power, and the intervention period extended to 12–24 weeks to assess sustained benefits, long-term safety, and delayed outcomes, including improvements in quality of life.

Population stratification based on functional dyspepsia (FD) subtype (postprandial distress syndrome vs. epigastric pain syndrome), BMI category (normal vs. overweight/obese), and sex would allow for the examination of subgroup-specific responses and enhance the generalizability of findings.

Furthermore, the inclusion of both subjective outcome measures (validated symptom severity and quality-of-life scales) and objective biochemical markers; such as CRP, IL-6, TNF-α, fasting insulin, lipid profiles, and gut hormones (e.g., ghrelin and leptin) is recommended to explore the underlying mechanistic pathways of ginger's action on metabolic and gastrointestinal health.

7. NEW FINDINGS

Clinical Improvement in FD Symptoms

Ginger supplementation at 540 mg twice daily for 8 weeks significantly improved functional dyspepsia symptoms, as measured by the Nepean Dyspepsia Index (NDI). The total NDI score dropped from 19.07 ± 23.2 to 9.10 ± 19.3 ($p < 0.05$), indicating substantial symptom relief. Improvements were noted across NDI subdomains, especially in eating/drinking comfort, daily functioning, and work performance, confirming ginger's positive impact on health-related quality of life.

No Effect on Body Composition

Despite the theoretical anti-obesity effects of ginger reported in other contexts, no statistically significant changes were observed in BMI, body fat percentage, or waist-hip ratio (WHR) over the 8 weeks. This indicates that short-term ginger supplementation does not promote fat loss in individuals with FD, at least at the studied dose and duration.

High Tolerability with Mild Side Effects

Ginger was well tolerated, with only mild, transient side effects reported: Bloating (14.9%), Heartburn (12.8%) and Diarrhea (10.6%). Importantly, no participants discontinued the intervention due to side effects. A high percentage (87.2%) rated the supplement as good or excellent in tolerability.

Functional Food Potential

The study highlights ginger's role as a safe, effective, evidence-based nutraceutical for the management of FD symptoms, even though it does not support weight management in this population. This supports the growing interest in functional foods as complementary therapies in gastrointestinal care.

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10. LIST OF PUBLICATIONS

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Candidate: Lemlem Gebremariam Aregawi
Doctoral School: Doctoral School of Nutrition and Food Sciences
MTMT ID: 10099904

List of publications related to the dissertation

1. **Aregawi, L. G.**, Csiki, Z.: Effects of ginger supplementation on quality of life in patients with functional dyspepsia: an open-label, clinical trial.
   Advances in Integrative Medicine. [Epub ahead of print], 2025.
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3. **Aregawi, L. G.**, Csiki, Z.: Ginger's nutritional implication on gastrointestinal health.
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   DOI: http://dx.doi.org/10.1371/journal.pone.0213546
   IF: 2.74

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