



# HerbClip™

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**File: ■ Licorice (*Glycyrrhiza glabra*, Fabaceae)  
■ Gastroesophageal Reflux**

**HC 032541-759**

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## **RE: A Proprietary Licorice Root Extract May Improve Gastroesophageal Reflux Symptoms in Adults**

Raj JP, Saxena U, Belhekar MN, Mamde A, Darak H, Pawar S. Efficacy and safety of GutGard® in managing gastroesophageal reflux-related symptoms: A phases III, single-centre, double-blind, randomized placebo-controlled trial. *Complement Med Res*. February 10, 2025;1-11. doi: 10.1159/000543367.

Licorice (*Glycyrrhiza glabra*, Fabaceae) has been used for centuries in several countries for gastrointestinal and respiratory problems. GutGard® (GG; Natural Remedies; Bengaluru, Karnataka, India), a proprietary licorice root extract, has > 3.3% glabridin, > 10% flavonoids, and ≤ 0.03% glycyrrhizin, a triterpenoid saponin that causes adverse effects (AEs) with long-term use. GG enhanced gut motility, integrity, and immunity, and demonstrated anti-ulcer activity in preclinical studies. Gastroesophageal reflux (GER) is affected by delayed gastric emptying, impaired lower esophageal sphincter function, and other conditions. Main treatments for GER involve acid reduction. Long-term acid suppression raises risks of several serious conditions.

The authors conducted a single-center, parallel group, double-blind, placebo-controlled randomized, controlled clinical trial (RCT) of the efficacy and safety of GG use for GER at Seth GS Medical College and KEM Hospital (Mumbai, Maharashtra, India) from October 11, 2019 – May 24, 2022.\* Adults aged 18-60 years with confirmed GER symptoms for > one month with > two symptom days in the week before randomization, not using proton pump inhibitors, and willing to stop other medicines or supplements for GER were eligible. Exclusion criteria were dyspepsia, severe GER disease (GERD) affecting daily life, pregnancy/lactation, unwillingness to use contraception, allergies to study agents, uncontrolled diabetes, abnormal liver/kidney function, HIV or hepatitis B/C infection, or inability to follow the protocol.

Patients were recruited at outpatient clinics and via a door-to-door community survey. A total of 200 were enrolled and evenly randomized to the GG or placebo group. After screening, participants had a basic physical examination. Blood and urine were collected and analyzed. Electrocardiograms were used to rule out myocardial ischemia. With normal results, solid meal scintigraphy (SMS) was scheduled, followed by liquid meal scintigraphy (LMS) in those with abnormal SMS results. SMS was conducted after > 4 h fasting and eating a radio-labeled meal of idlis (steamed cakes made with batter of a ground, fermented rice [*Oryza sativa*, Poaceae] and lentils [*Vicia lens*, Fabaceae]). Images were collected at 1 min. and 1 and 2 h after meal ingestion to determine the percentage of retention. LMS, if needed, was conducted after > 4 h fasting and intake of radio-labeled orange (*Citrus × sinensis*,

Rutaceae) juice. Baseline measures included the GERD Symptom Assessment Scale (GSAS), GERD-Health-Related Quality of Life (GERD-HRQL), and Global Assessment Questionnaire (GAQ) for quality of life (QoL).

Participants were instructed to take either 150 mg/d GG in a divided dose of two 75 mg capsules of licorice extract and excipients or placebo capsules with a similar appearance that contained only excipients. A two-wk. supply of study agents was dispensed on Day 0. Compliance was verified via pill counts at in-person study visits. Rescue medication was famotidine 20 mg  $\leq$  two tablets/12 h. Telephone visits on Day 7 revisited GSAS scores and queried AEs/serious AEs (SAEs). On Day 14, in-person visits reevaluated GSAS, queried AEs/SAEs and use of rescue medications, collected/counted empty capsule bottles, and issued another two-wk. supply. Blood and urine sampling was repeated. Patients who had LMS at Day 0 repeated S/LMS at d 27, and all repeated one or both procedures on Day 28. After stopping the intervention on Day 28, patients returned on Day 35 to assess rebound symptoms, GSAS, and rescue medications used. Those with persistent symptoms on Day 35 were given an eight-wk. course of pantoprazole 40 mg/d. Plans to assess lower esophageal sphincter pressure and 24-h gastric pH in 10% of study participants were dropped due to restrictions during the Covid-19 pandemic.

Modified intention-to-treat analyses were performed for efficacy and safety. Mean age of participants was  $36.94 \pm 7.03$  years, and  $> 75\%$  identified as male. At baseline, there were no significant between group demographic or clinical differences. A total of 78 in GG and 87 in placebo completed the RCT ( $T = 165$ ). On Day 28, there were significantly lower GERD-HRQ scores for GG vs. placebo ( $P = 0.014$ ), including for heartburn when lying down ( $P = 0.048$ ), heartburn when standing ( $P < 0.001$ ), heartburn after meals ( $P = 0.012$ ), pain when swallowing ( $P = 0.038$ ), use of medicines affecting daily activities ( $P = 0.040$ ), and regurgitation when standing ( $P = 0.098$ ) and after meals ( $P = 0.019$ ).

Baseline-adjusted GSAS scores were significantly improved on Days 14 and 28 for overall symptom frequency, severity, and patient distress with GG vs. placebo ( $P < 0.05$  for all) but no significant decrease in total number of symptoms. By Day 28, there was a trend to significantly fewer symptoms with GG. There were significant reductions with GG vs. placebo in frequency of stomach noises and regurgitation ( $P = 0.025$ ;  $0.023$ , respectively) from Day 7; heartburn ( $P = 0.017$ ), from Day 14; and flatulence and early satiety ( $P = 0.036$ ;  $0.024$ , respectively), on Day 28. GSAS scores for severity and distress from those symptoms also improved significantly with GG vs. placebo during the RCT. GAQ scores were significantly higher for GG vs. placebo for day and night symptoms ( $P = 0.03$  for both).

There were no significant between-group differences in number of rescue medications used, protocol adherence, number of AEs, or laboratory results at any data point. There were no SAEs. The GG group reported significantly better satisfaction vs. placebo at Day 28, with earlier and better symptom resolution. There were no rebound effects in either group.

The authors declare no conflicts of interest.

—Mariann Garner-Wizard

\*The RCT was paused for ~ six months starting in March 2020 with the advent of Covid-19.

Referenced article can be accessed at <https://karger.com/cmr/article/32/1/26/920395/Efficacy-and-Safety-of-GutGardR-in-Managing>.