Scientific Research Publishing

Open Journal of Gastroenterology, 2026, 16(3), 111-122
https://www.scirp.org/journal/ojgas
ISSN Online: 2163-9469
ISSN Print: 2163-9450

Effects of a Polyphenol Nutraceutical Containing Hesperidin, Noni, Dandelion and *Atractylodes macrocephala* Extracts on GERD Symptoms: A Retrospective Chart Analysis

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How to cite this paper: Brown, K., Owen, P., Cook, A. and Burnett, B.P. (2026) Effects of a Polyphenol Nutraceutical Containing Hesperidin, Noni, Dandelion and *Atractylodes macrocephala* Extracts on GERD Symptoms: A Retrospective Chart Analysis. *Open Journal of Gastroenterology*, **16**, 111-122.
https://doi.org/10.4236/ojgas.2026.163012

Received: February 21, 2026
Accepted: March 14, 2026
Published: March 17, 2026

Abstract

Background: Gastroesophageal reflux disease (GERD) is a chronic condition with substantial morbidity and reliance on proton pump inhibitors (PPIs). Long-term adverse effects of PPIs, including enteric infection, nutrient malabsorption, kidney disease, and dementia, increase interest in alternative therapies. A novel over-the-counter polyphenol-based nutraceutical containing hesperidin, Noni fruit, dandelion root, and *Atractylodes macrocephala* defined extracts were taken by patients with chronic GERD for its potential effect on reflux symptoms and compared to patients on usual care. **Methods:** A retrospective analysis was performed using patient chart data of convenience cohorts from a community gastroenterology practice. All patients had confirmed chronic GERD by esophagogastroduodenoscopy. Patients choosing to take the nutraceutical (n = 47) discontinued PPIs and H2-receptor antagonists prior to receiving 2 capsules BID before meals for 4 weeks, while other patients (n = 25) continued usual care, including PPIs. Overall symptom improvement was evaluated using frequency and severity reports from structured clinical notes with a 5-point scale. **Results:** In the nutraceutical group, 81% (38/47) patients reported 100% resolution of their GERD symptoms compared to 16% (4/25) in the usual care group [risk difference (RD): 0.649 (95% CI: 0.476 - 0.822)]. Clinically meaningful improvement of ≥75% for symptoms was 91.5% (43/47) for the nutraceutical vs 24.0% (6/25) in the usual care group [RD: 0.675 (0.520 - 0.830)]. All 32 patients who reported bloating prior to the nutraceutical stated they had less bloating by week 4. The nutraceutical group also had reduced reflux frequency, severity, improved symptoms and decreased reliance on pharmaceutical drugs. There were a few non-serious side effects in the group

taking the nutraceutical. **Conclusion:** This is the first retrospective analysis of combined hesperidin/Noni/dandelion root/*Atractylodes* extracts showing reflux symptom improvement and favorable tolerability. Care must be taken when interpreting these results, however, as GERD symptoms can wax and wane, the sample size was small, adherence to therapy was not recorded and this was not a placebo-controlled study. A larger, well-controlled study is needed to confirm these results.

Keywords

Hesperidin, Noni, Dandelion Root, *Atractylodes*, GERD

1. Introduction

Gastrointestinal (GI) esophageal reflux disease (GERD) affects upwards of 20% of adults in Western countries, with increasing prevalence globally [1]. A recent survey of patients, however, finds that over 40% of patients have experienced chronic symptoms associated with GERD, with over 30% having experienced GERD symptoms in the past week [2].

The exact cause of GERD is unknown, though the risk is higher in individuals who are obese, older, and pregnant, and tends to be more common in men [3] [4]. The primary contributing factor is transient relaxation or dysfunction of the lower esophageal sphincter (LES), allowing acid reflux into the esophagus [5]. Other contributing factors include hiatal hernia, delayed gastric emptying, and impaired esophageal clearance [6]. Obesity can also increase exposure of the esophagus to stomach acid, leading to a higher risk of developing GERD [7]. Typical symptoms of GERD include pyrosis and epigastric pain, which can mimic chest discomfort [8]. These primary symptoms are sometimes accompanied by nausea and regurgitation. Atypical symptoms of GERD can be chronic cough, laryngitis, asthma-like symptoms, and dental erosion, which occur less regularly in patients with GERD but are highly prevalent in over 40% of patients with non-erosive esophageal reflux disease (NERD) [9].

Common pharmaceutical interventions include proton pump inhibitors (PPIs), H2-receptor antagonists (H2Ra), antacids, and prokinetics. PPIs are the first-line treatments due to their superior acid suppression and symptom relief, but up to 45% of patients on these drugs experience refractory symptoms [10]. H2Ra are recommended for mild symptoms or as adjuncts to PPIs, antacids can provide quick, short-term relief for occasional symptoms and prokinetics are sometimes used to enhance gastric emptying, though less commonly prescribed due to side effects [11]. Despite proven pharmaceutical interventions that are relatively safe and effective, patients still search for complementary and alternative therapies to relieve GERD symptoms.

Typical complementary and alternative therapies include lifestyle and dietary modifications, such as anti-inflammatory diets, avoiding trigger foods that are acidic

or fatty, weight loss, and meal timing adjustments, which can significantly reduce GERD symptoms [12]. In addition, brain-gut behavioral therapies, techniques like diaphragmatic breathing, may reduce reflux episodes [11]. Finally, case reports of osteopathic manipulative treatment (OMT), a manual therapy targeting the diaphragm and thoracic spine, may alleviate reflux symptoms by improving visceral function but require more extensive study [13]. These therapies are often considered for patients who are refractory to PPIs, wish to avoid long-term medication, or are not ideal candidates for surgery. Other GERD patients seek out nutraceuticals and dietary supplements, which may decrease symptoms.

The aim of this retrospective chart analysis was to assess a polyphenol-based nutraceutical formulation composed of hesperidin, Noni fruit (*Morinda citrifolia*), dandelion root (*Taraxacum officinale*) and *Atractylodes macrocephala* (also known as Baizhu) extracts taken by chronic GERD patients in a community gastroenterology practice compared to patients with chronic GERD who did not respond to diet, lifestyle or conventional pharmaceutical intervention.

2. Methods

2.1. Study Design

This retrospective chart analysis identified convenience cohorts from a single community gastroenterology practice: one chose to take an over-the-counter polyphenol-based nutraceutical (n = 47; 2 capsules twice daily) and another was managed with contemporaneous usual care (n = 25). Outcomes in these cohorts were evaluated using the same standardized patient-reported symptom assessment framework used in this gastroenterology practice, obtaining data using structured clinical notes from patient charts.

2.2. Inclusion and Exclusion Criteria

Consecutive charts were screened between May 2024 and January 2025 to identify adults with chronic GERD who had complete baseline and 4-week follow-up documentation. Chronic GERD was defined as the presence of typical reflux symptoms (pyrosis, epigastric pain, and/or regurgitation) persisting for more than 3 months, in combination with esophagogastroduodenoscopy (EGD) findings consistent with GERD when present, including Los Angeles (LA)-graded esophagitis, hiatal hernia, irregular Z line, or Barrett's esophagus. Inclusion criteria were: age ≥ 18 years, documented chronic GERD of at least 3 months duration, completion of the practice's structured GERD intake questionnaire, availability of baseline and 4-week follow-up symptom assessments, and receipt of either the polyphenol nutraceutical or usual care during the defined period. Patients were excluded if key outcome data at 4 weeks were missing and thus insufficient to judge overall symptoms.

2.3. Ethics

Under a revision of the US Code of Federal Regulations, 45 CFR 46, also known

as the "Revised Common Rule", data that is recorded by a physician for a retrospective chart review in a de-identified manner so that once the analysis of the data cannot link back to patients is exempt from IRB or ethics committee review under exemption category 4[1]. The polyphenol-based over-the-counter nutraceutical was available in the gastroenterology practice to patients who chose to take the formulation after failing to respond to lifestyle modification and other treatments. Each participant consented in writing to have their data retrospectively analyzed from patient charts and to the publication of the resulting data.

2.4. Nutraceutical

The nutraceutical polyphenol formulation per capsule was composed of defined extracts of hesperidin 90% (HPLC) (50 mg), Noni fruit (*Morinda citrifolia*) extract 5:1 (200 mg), Dandelion root (*Taraxacum officinale*) extract 10:1 (125 mg), and *Atractylodes macrocephala* extract (Baizhu extract) 10:1 (225 mg).

2.5. Participants

Patients are from a single community gastroenterology practice. All patients are routinely evaluated for their primary symptoms and response to conventional pharmaceutical therapy (*i.e.*, PPIs, H2Ra) when entering the practice for treatment. In addition, patients fill out a GERD intake questionnaire prior to any therapy, evaluating their GERD-related symptoms, treatment history, lifestyle issues, and general medical history. All participants are also evaluated by EGD to confirm GERD as part of normal clinical practice. Patients are asked before taking any treatment about symptoms which include pyrosis, epigastric pain, regurgitation, bloating and nocturnal symptoms using a 5-point scoring scale created by the practice as part of normal clinic practice.

2.6. Outcomes

All data were extracted from the electronic medical record by the treating gastroenterologist using a standardized data collection form developed specifically for this retrospective analysis. The form captured demographics, body mass index, endoscopic findings, prior and current GERD treatments, and patient-reported symptom changes at approximately 4 weeks after treatment initiation. Because this was a single-investigator chart review, blinding of the extractor to treatment group was not feasible.

Overall symptom improvement was categorized using a 5-point scale (0%, 25%, 50%, 75%, 100%) that is routinely used in this practice. Assignment to each category was based on a combination of structured clinical note entries describing changes in symptom frequency and severity, as well as documented changes in reliance on acid-suppressive medications. A rating of 100% improvement was assigned when notes indicated complete resolution of reflux-related symptoms and

[1]U.S. Department of Health and Human Services (2018). *Federal Policy for the Protection of Human Subjects*, 45 C.F.R. § 46.104(d)(4).

discontinuation of acid-suppressive medications. A rating of ≥75% resulted in clinically meaningful improvement reflected near-complete relief with only rare, mild breakthrough symptoms and/or substantial reductions in both symptom burden and medication use. A rating of 50% improvement corresponded to clear but partial symptom relief with ongoing, though reduced, dependence on medications. A rating of 25% indicated only mild change from baseline, and 0% indicated no improvement or worsening of symptoms.

2.7. Statistical Analysis

Categorical outcomes were compared using risk differences (RDs), risk ratios (RRs), and odds ratios (ORs) with 95% confidence intervals (CIs) calculated using Wald methods. Ordinal outcomes were converted to numeric scores (0 - 4) and analyzed using Cliff's delta (δ) to quantify the probability that a randomly selected participant from the nutraceutical group would have a better outcome than one from the usual care group. Confidence intervals not crossing the null were interpreted as statistically meaningful. To address baseline differences between groups, a multivariable logistic regression model was used to estimate adjusted treatment effects. LA grade was included as a categorical variable (A, B, C). Additional covariates included Barrett's esophagus, gastritis, and irregular Z-line. Adjusted odds ratios (aORs) with 95% confidence intervals were calculated for two prespecified outcomes: complete resolution (100% improvement) and clinically meaningful improvement (≥75% improvement). Model fit and multicollinearity were assessed and found acceptable. All analyses were two-sided.

3. Results

The patient group choosing to consume the polyphenol-based nutraceutical (n = 47) had a higher percentage of women (76.6%) with a mean age of 48.2 (15.0) years, with all having pyrosis, epigastric pain and bloating (Table 1). The usual care group (n = 25) not taking the nutraceutical had slightly fewer women (64.0%) with a similar age and symptoms. Both groups were slightly overweight with a similar percentage of obese individuals.

Table 1. Demographics and characteristics of convenience cohorts.

	Nutraceutical (n = 47)	Usual Care (n = 25)
Sex [n (%)]		
Male	11 (23.4%)	9 (36.0%)
Female	36 (76.6%)	16 (64.0%)
Age Mean (SD) [years]	48.2 (15.0)	45.2 (16.9)
Age Range [years]	20 - 71	20 - 78
Body Mass Index Mean (SD)	26.5 (6.2)	25.7 (3.9)
Obese [n (%)]	12 (25.5%)	6 (24.0%)
Alcohol Use	32 (68.1%)	17 (68.0%)

Continued

Gastrointestinal Comorbidities		
LA Grade A Esophagitis [n (%)]	19 (40.4%)	5 (20.0%)
LA Grade B Esophagitis [n (%)]	7 (14.9%)	4 (16.0%)
LA Grade C [n (%)]	2 (4.3%)	3 (12.0%)
Irregular Z Line	19 (40.4%)	12 (48.0%)
Hiatal Hernia [n (%)]	15 (31.9%)	14 (56%)
Barrett's Esophagus [n (%)]	2 (4.3%)	1 (4.0%)
Gastritis [n (%)]	9 (19.2%)	4 (16.0%)
Infection (*H. pylori*) [n (%)]	1 (2.1%)	1 (4.0%)
Small Intestinal Bacterial Overgrowth [n (%)]	6 (12.8%)	5 (20%)
Inflammatory Bowel Disease [n (%)]	3 (6.4%)	0
Proctitis [n (%)]	1 (2.1%)	0
Primary Symptoms		
Pyrosis [n (%)]	47 (100%)	15 (60.0%)
Epigastric Pain [n (%)]	16 (34.0%)	14 (56%)
Bloating [n (%)]	32 (68.1%)	13 (52.0%)
Constipation [n (%)]	2 (4.3%)	0
Dysphagia	0	1 (4.0%)
Nausea [n (%)]	0	1 (4.0%)
Diarrhea [n (%)]	1 (2.1%)	0

LA, Los Angeles; SD, Standard deviation.

The nutraceutical group had twice as many patients with LA Grade A esophagitis [19 (40.4%) vs 5 (20.0%)], relatively equivalent LA Grade B esophagitis [7 (14.9%) vs 4 (16.0%)] and a lower percentage of patients with LA Grade C esophagitis [2 (4.3%) vs 3 (12.0%)]. Irregular Z line findings in each group [19 (40.4%) vs 12 (48.0%)] were similar. There were 2 patients in the nutraceutical group and 1 patient in the usual care group diagnosed with Barrett's esophagus. Gastritis [9 (19.2%) vs 4 (16.0%)] was roughly equivalent in both groups.

For patients in the nutraceutical cohort who were taking PPIs at baseline, a standardized weaning protocol was employed. Patients were instructed to take their PPI every other day for approximately 5 days, after which the PPI was discontinued, and the nutraceutical was initiated at a dose of 2 capsules twice daily before meals. Any H2Ra therapy was discontinued at the time of nutraceutical initiation without a separate washout period. In the usual care cohort, management followed the treating physician's standard practice. Usual care consisted of GERD-focused lifestyle and dietary counseling, typically including recommendations to reduce alcohol and coffee intake, avoid late-evening meals, and pursue weight reduction when appropriate, combined with pharmacologic therapy as indicated. Most patients were

treated with once-daily prescription-strength PPIs, with some receiving lower-dose over-the-counter PPI preparations, H2Ra, and/or antacids at the clinician's discretion.

A majority of patients in the nutraceutical group [28 (59.6%)] reported previous failure to control their symptoms with PPI use, one patient failed on famotidine [1 (2.1%)], and 18 patients [18 (38.3%)] were untreated by pharmaceutical intervention but had ongoing symptoms after trying diet and lifestyle modification (*i.e.*, reduced alcohol and coffee consumption, not eating late, weight loss encouragement). In the usual care group, 9 (36.0%) reported previous failure to control symptoms with PPIs, one patient failed with famotidine 1 (4.0%) and 15 (60.0%) were untreated but trying to control GERD symptoms by diet and lifestyle modification. Patients in both groups reported no or 0% resolution of their symptoms on these therapies or lifestyle modifications upon entry to the practice.

The nutraceutical group demonstrated substantially higher rates of symptom improvement across all categories compared with usual care (Table 2).

Table 2. Symptom improvement distribution by treatment group.

Improvement Category	Nutraceutical (n = 47)	Usual Care (n = 25)
100%	38 (80.9%)	4 (16.0%)
75%	5 (10.6%)	2 (8.0%)
50%	4 (8.5%)	0 (0%)
25%	0 (0%)	12 (48.0%)
0%	0 (0%)	7 (28.0%)

After 4 weeks, 80.9% (38/47) of the nutraceutical group compared to 16% (4/25) of the usual care group, showed complete resolution (100%) of symptoms. Clinically meaningful improvement (≥75%) of symptoms was 91.5% (43/47) for the nutraceutical vs 24.0% (6/25) in the usual care group. The between-group effect estimates for complete and clinically meaningful improvement of symptoms are shown in Table 3.

Table 3. Between-group effect estimates.

Outcome	RD (95% CI)	RR (95% CI)	OR (95% CI)
100% Resolution	0.649 (0.476 - 0.822)	5.06 (1.98 - 12.9)	21.6 (6.5 - 71.8)
≥75% Improvement	0.675 (0.520 - 0.830)	3.81 (1.99 - 7.31)	28.7 (9.7 - 84.7)

OR, odds ratio; RD, risk difference; RR, risk reduction.

The calculated Cliff's delta was 0.62, representing a large effect size, indicating an ~81% probability that a randomly selected nutraceutical-treated participant had a better outcome than one receiving usual care.

To account for baseline imbalances in esophagitis severity and other clinical

characteristics, a multivariable logistic regression model was constructed, including treatment group, LA grade (categorical), Barrett's esophagus, gastritis, and irregular Z-line. After adjustment, the nutraceutical intervention remained strongly associated with improved outcomes. For complete symptom resolution, the adjusted odds ratio (aOR) was 18.9 (95% CI: 5.8 - 63.4). For clinically meaningful improvement (≥75%), the aOR was 24.7 (95% CI: 8.4 - 78.1). None of the covariates materially attenuated the treatment effect, and LA Grade C was the only baseline factor associated with reduced odds of improvement. These findings demonstrate that the observed treatment benefit persists even after controlling for baseline clinical differences.

All 32 patients who initially reported bloating in the nutraceutical group were found to have less bloating after 4 weeks. Of the 28 patients on PPIs and 1 patient on famotidine before taking the nutraceutical, 23 (79.3%) stopped taking all acid reflux medications. Twenty-seven (27) of the 47 participants (57.4%) over the 4-week period on nutraceutical proactively requested additional product following completion of the initial trial period.

Among 15 patients in the usual care group who initially had pyrosis, 6 reported no improvement in response to lifestyle modifications and switched to PPIs over 4 weeks. After switching, these 6 patients had substantial improvement in their symptoms, 4 with 100% and 2 with 75% (**Table 2**). Of the remaining 9 patients who initially reported pyrosis and chose to remain on lifestyle modifications, only 3 reported about 25% improvement. For the other 9 patients on PPIs in the usual care group who were also offered lifestyle modification strategies, all showed minimal improvement of about 25% compared to baseline. The remaining patient on famotidine in the usual care group and lifestyle modification showed no improvement after 4 weeks.

In the nutraceutical cohort, side effects were infrequent and non-serious when solicited by the treating physician. Single reports included difficulty swallowing the capsules, mild insomnia, transient headache, a mild increase in anxiety, mild right upper quadrant discomfort, and nausea. One patient experienced an esophageal spasm approximately 2 weeks after starting the nutraceutical, but this event resolved without discontinuation of the product. No serious adverse events were identified in either cohort during the 4-week period.

4. Discussion

The clinical diagnosis of GERD is routine, but the pathogenesis of this condition is multifaceted and complex [14]. Because of the complex pathophysiology of GERD, no one pharmaceutical treatment seems to provide sufficient relief to all patients though PPIs seem to provide satisfactory relief to about 50% of patients [15]. In addition, adherence to pharmaceutical therapy has shown that a little over 50% of patients faithfully take their medication and about 60% report problems adhering to diet and lifestyle modification patients [16]. Procedures and surgery are normally reserved for non-responders to acid suppressive medication or in

patients who present with serious erosive complications from GERD. For these reasons, patients experiencing GERD seek out new solutions in the form of alternative medicine to relieve discomfort and pain. This retrospective patient chart analysis suggests that a novel nutraceutical polyphenol blend of hesperidin/Noni/dandelion root/*Atractylodes* extracts may provide symptomatic relief for patients with GERD.

In a mouse model, hesperidin, a citrus flavonoid, accelerated gastric emptying and increased intestinal transit, both of which also assist in GERD prevention [17]. Noni fruit (*M. citrofolia*) in rat models of acid reflux esophagitis, acute gastritis induced by alcohol and serotonin, and acetic acid-induced gastric ulcer increased gastric emptying, prevented gastric reflux, reduced the formation of gastric lesions, and accelerated the healing of acetic acid-induced chronic gastric ulcers [18]. Dandelion root extracts have shown pharmacological effects in models of dyspepsia, GERD and gastritis [19], as well as prokinetic properties [20]. Finally, *A. macrocephala*, the species of *Atractylodes* in the nutraceutical tested herein, has been used in alternative medicine preparations as "Baizhu" with other herbal extracts to treat irritable bowel syndrome, simple and functional dyspepsia, especially postprandial discomfort, diarrhea peptic ulcers, and chronic enteritis in humans [21].

There are several limitations to this retrospective analysis. First, this was not a controlled study that could differentiate real vs placebo-like effects of the nutraceutical, and all patients were on heterogenous treatment regimens. The administering physician was not blinded to the treatments or to the outcomes collected, which lends itself to bias. Second, the type of patients who enter this gastroenterology practice tend to seek out alternative therapies, so this may also present certain bias in interpretation of the results. Third, the convenience groups compared here were not equivalent with substantial differences in pyrosis prior to receiving treatment, *i.e.*, 100% in the nutraceutical group vs 60% in the usual care group. In addition, the usual care group had worse esophagitis by LA scoring and the percentage of patients with hiatal hernias, suggesting worse disease. Fourth, the case series analysis did not employ validated GERD-specific questionnaires, such as GERD-HRQL and RDQ. Despite adjustment, differential baseline imbalances can influence outcomes (*i.e.*, observed differences in LA Grades as well as smaller imbalances, irregular Z-line, Barrett's esophagus and gastritis). Finally, there were no objective physiologic assessments taken (e.g., pH impedance or repeat endoscopic and pathologic evaluation) before or after treatment.

Other issues could also bias the outcomes of this analysis. Symptoms in esophageal conditions fluctuate over time, even without intervention. If participants in the nutraceutical group entered the study during a symptomatic peak, subsequent improvement could reflect the underlying cyclical nature of the condition rather than a true treatment effect. This phenomenon would tend to inflate observed effect sizes, especially when the usual care group has a more stable or slowly improving baseline trajectory. This symptomatic peak or baseline severity prior to treatment

could also result in the regression to the mean, exaggerating the apparent benefit. This would bias results in favor of the nutraceutical, even in the absence of a true pharmacologic effect. One also cannot discount better adherence in the nutraceutical group to lifestyle and diet modification, which could result in better outcomes. Finally, small sample size and differences in sample size can amplify effects, in this case for the nutraceutical group.

Despite these limitations and biases, to our knowledge, this is the first nutraceutical formulation combining a defined extract of *A. macrocephala* with hesperidin, Noni fruit, and dandelion root, not part of previous alternative medicine formulations, to suggest relief of GERD using multiple analytical approaches. These results provide a rationale for larger, properly controlled studies to evaluate efficacy, durability, and potential disease-modifying effects of this formulation.

Authors' Contributions

K.B. conceived the retrospective analysis, performed the evaluation on all patients, helped interpret the data and contributed to the writing of this article. P.O. and A.C. performed background literature research on the individual components of the nutraceutical and edited the manuscript. B.P.B. helped interpret the data and wrote the initial draft of the manuscript, as well as edited the manuscript for content.

Funding

This study was self-funded. No external grants or institutional funding were received for the conduct of this research or the preparation of this manuscript.

Declaration

Dr. Kenneth Brown discloses that he has an ownership interest in KBS Research Inc., the company that manufactures the nutraceutical product evaluated in this retrospective analysis. Dr. Bruce P. Burnett served as an independent consultant for data interpretation and manuscript preparation and received consulting fees from KBS Research Inc. The authors acknowledge these relationships and affirm that all data collection and analysis were conducted with scientific rigor and transparency.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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