

ORIGINAL ARTICLE

Efficacy of a new nutraceutical formulation: L-tryptophan, probiotics, charcoal, chamomile, mint, and licorice (COLONIR®) in the improvement of gastrointestinal symptoms in subjects with irritable bowel syndrome

Giulia FIORINI ¹, Ilaria M. SARACINO ², Matteo PAVONI ², Bruno NIPOTE ³, Raffaele COLUCCI ⁴, Pietro CAPONE ⁵, Angela SANNINO ⁶, Fabrizio FORTE ⁷, Emiliano DE VERGORI ⁸, Mario BRANCACCIO ⁹, Maurizio CESAREO ¹⁰, Giovanni CASELLA ¹¹, Gaetano C. MORREALE ¹², Leonilde BONFRATE ¹³, Piero PORTINCASA ¹³, Massimo VINCENZI ¹⁴, Carmelo COTTONE ¹⁵, Vittorio M. ORMANDO ¹⁶, Natale SCALISE ¹⁷, Paulin F. LAWSON ¹⁸, Osvaldo BURATTINI ¹⁹, Amedeo MONTALE ²⁰, Francesco LUZZA ²¹, Mauro ROSSI ²², Riccardo VANNI ²³, Rosamaria BOZZI ²⁴, Giuseppina VINCOLI ²⁵, Nicoletta STEFANI ²⁶, Claudio BORGHI ², Dino VAIRA ^{2 *}

¹IRCCS University Hospital of Bologna, Bologna, Italy; ²Department of Surgical and Medical Sciences, University of Bologna, Bologna, Italy; ³Unit of Surgery, Lagonegro Hospital, AOR S. Carlo, Potenza, Italy; ⁴SC Foligno Hospital, USL Umbria 2, Foligno, Perugia, Italy; ⁵Unit of Gastroenterology and Digestive Endoscopy, Maresca Hospital, Torre del Greco, Naples, Italy; ⁶Unit of Gastroenterology and Digestive Endoscopy, Santa Maria della Pietà Hospital, Nola, Naples, Italy; ⁷UOSD of Interventional Gastroenterology, Madonna delle Grazie Hospital, Matera, Italy; ⁸Unit of Gastroenterology and Digestive Endoscopy, G.B. Morgagni – L. Pierantoni Hospital, Forlì, Forlì-Cesena, Italy; ⁹Unit of Gastroenterology and Digestive Endoscopy, S. Maria delle Croci Hospital, Ravenna, Italy; ¹⁰Unit of Gastroenterology, Tirrenia Hospital, Belvedere Marittimo, Cosenza, Italy; ¹¹Private Practitioner in General Medicine – Gastroenterology, Monza, Monza-Brianza, Italy; ¹²Unit of Gastroenterology, Ospedali Riuniti S. Elia/Raimondi, Caltanissetta, Italy; ¹³Department of Biomedical Sciences and Human Oncology, University of Bari Aldo Moro, Bari, Italy; ¹⁴Unit of Gastroenterology and Digestive Endoscopy, S. Pier Damiano Hospital, Faenza, Ravenna, Italy; ¹⁵Private Practitioner in General Medicine – Gastroenterology, Palermo, Italy; ¹⁶Unit of Gastroenterology, San Giuseppe Moscati Hospital, Avellino, Italy; ¹⁷Department of Digestive Endoscopy, ANMI Rossano Center, Cosenza, Italy; ¹⁸Unit of Gastroenterology and Digestive Endoscopy, Beato Matteo Clinical Institute, Vigevano, Pavia, Italy; ¹⁹Unit of Gastroenterology II, IRCCS Saverio De Bellis, Castellana Grotte, Bari, Italy; ²⁰Unit of Gastroenterology and Digestive Endoscopy, E.O. Ospedali Galliera, Genoa, Italy; ²¹Unit of Pathophysiology of the Digestive System, Mater Domini Germaneto, Catanzaro, Italy; ²²Unit of Surgical Digestive Endoscopy, Civil Hospital of Avezzano, L'Aquila, Italy; ²³Section of Gastroenterology and Digestive Endoscopy, Michele e Pietro Ferrero Hospital, Cuneo, Italy; ²⁴Unit of Gastroenterology and Digestive Endoscopy, ASL Benevento, Benevento, Italy; ²⁵U.O.S.D Gastroenterology, San Camillo de Lellis Civil Hospital, Rieti, Italy; ²⁶Section of Gastroenterology, A.S.U. Giuliano Isontina, Trieste, Italy

*Corresponding author: Dino Vaira, Department of Surgical and Medical Sciences, University of Bologna, via Massarenti 9, 40138 Bologna, Italy. E-mail: berardino.vaira@unibo.it

ABSTRACT

BACKGROUND: Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders. IBS is characterized by recurrent chronic abdominal pain and altered bowel habits in the absence of organic damage. Although there are reviews and guidelines for treating IBS, the complexity and diversity of IBS presentation make treatment difficult. Treatment of IBS focuses on relieving symptoms as mild signs and symptoms can often be controlled by

managing stress and by making changes in diet and lifestyle. The use of nutraceutical compounds has been advocated as a possible alternative treatment in patients with IBS. COLONIR[®] (Omega Pharma Srl, Milan, Italy) may be an alternative or adjuvant treatment in patients with gastrointestinal symptoms. This study aimed to evaluate the effect of this new nutraceutical formulation in inducing symptoms remission and improve gastrointestinal habits.

METHODS: An initial cohort of 1004 consecutive patients referred to 25 different Units of Internal Medicine a/o Gastroenterology in Italy to perform colonoscopy for intestinal symptoms was asked to participate. Patients were treated for 2 months with two doses of nutraceuticals/day during meals namely COLONIR[®]. Patients were assessed at baseline and after 2 months to evaluate the frequency and severity of gastrointestinal symptoms in the past seven days with a questionnaire based on ROMA IV criteria.

RESULTS: After 2 months, 899 patients completed the follow-up. COLONIR[®] achieved a statistically significant reduction of severity of symptoms in the study population without any documented side effects.

CONCLUSIONS: These promising results, here reported, need to be confirmed, valuating the efficacy of COLONIR[®] in relieving gastrointestinal symptoms in IBS patients in further studies.

(Cite this article as: Fiorini G, Saracino IM, Pavoni M, Nipote B, Colucci R, Capone P, *et al.* Efficacy of a new nutraceutical formulation: L-tryptophan, probiotics, charcoal, chamomile, mint, and licorice (COLONIR[®]) in the improvement of gastrointestinal symptoms in subjects with irritable bowel syndrome. *Minerva Gastroenterol* 2023;69:123-7. DOI: 10.23736/S2724-5985.22.03282-X)

KEY WORDS: Irritable bowel syndrome; Gastroenterology; Dietary supplements.

Irritable bowel syndrome (IBS) is one of the most common functional gastrointestinal disorders which affects 10-25% of the general adult population.¹ IBS is characterized by recurrent chronic abdominal pain and altered bowel habits in the absence of organic damage.² The pathophysiology of IBS is not clear, and many theories have been put forward. According to the ROME IV criteria, IBS is a clinical diagnosis and presents as one of the three predominant subtypes: 1) IBS with constipation (IBS-C); 2) IBS with diarrhea (IBS-D); and 3) mixed IBS (IBS-M). Furthermore, former ROME definitions refer to IBS-M as alternating IBS (IBS-A).³ Across the IBS subtypes, the presentation of symptoms may vary among patients: abdominal pain, straining, myalgias, urgency, bloating and fatigue.⁴ Although there are reviews and guidelines for treating IBS, the complexity and diversity of IBS presentation makes treatment difficult. The American College of Gastroenterology Functional GI Disorders Task Force stated that the current data do not support extensive testing in IBS patients if no alarming findings exist such as weight loss, hematochezia, iron deficiency.⁵ Whereas, if symptoms are not typical or alarm features are present, testing should be performed including complete blood test and specific tests for predominant symptoms (*e.g.*, diarrhea or constipation). Invasive test such as colonoscopy is acceptable in patients with alarm symptoms and/or family history of inflammatory bowel disease, colon cancer, he-

matocchezia, nocturnal or progressive abdominal pain, weight loss, anemia, elevated inflammatory markers, or electrolyte disturbances, or in patients over 50.⁶ Treatment of IBS focuses on relieving symptoms as mild signs and symptoms can often be controlled by managing stress and by making changes in diet and lifestyle. In addition, based on the onset of symptoms and their impact on patient daily life, medications can be suggested such as fiber supplements, laxatives, anti-diarrheal medications, anticholinergic, antidepressants, antibiotics (*e.g.*, rifaximin) or medications that are able to increase fluid secretion on small intestine (*e.g.*, linaclotide, lubiprostone). Moreover, in the last years, researchers are investigating the role of fecal microbiota transplantation to treat IBS.⁷ The use of nutraceutical compounds has been advocated as a possible alternative treatment in patients with IBS.⁸ COLONIR[®] (Omega Pharma Srl, Milan, Italy), an association of natural active ingredient (L-tryptophan, probiotics, charcoal, chamomile, mint, and licorice) may be an alternative or adjuvant treatment in patients with gastrointestinal symptoms. This study aimed to evaluate the effect of this new nutraceutical formulation in inducing symptoms remission and improve gastrointestinal habits.

Materials and methods

Between March 2021 and March 2022, 1004 consecutive patients referred to 25 different Gas-

troenterology Unit in Italy to perform colonoscopy for intestinal symptoms (abdominal pain, alteration of gut habits etc. lasting for at least 8 weeks with negative upper GI endoscopy and ultrasound) were asked to participate. Flow chart of the study (Figure 1). Exclusion criteria were: presence of pathological findings at colonoscopy (e.g., diverticular disease, polyps, neoplasm); presence of *Helicobacter pylori* infection; concomitant comorbid conditions (i.e. chronic renal failure, liver cirrhosis); active malignant neoplasm; pregnancy or lactation; age <18 or >90. Patients were treated for 2 months with two doses of nutraceuticals/day during meals, COLONIR®. Patients were assessed at baseline and after 2 months to evaluate the frequency and severity of gastrointestinal symptoms in the past seven days with a questionnaire based on ROMA IV criteria.³ The questionnaire is divided into three parts, first part describes smoking and alcohol habits, comorbidity and concomitant drugs assumption; the second part aims to assess bloating, abdominal pain score from 0 (no symptoms) to 100 (severe) and length from 0 (no symptoms) to 10 days (at least once a day); the third part evaluates the presence of 10 symptoms (abdominal pain, nausea, borborygmi, bloating, aerophagia, flatulence, constipation, diarrhea, tenesmus and incomplete emptying) and their level of severity (no symptom, light, tolerable, moderate, quite severe, severe, intolerable). Symptoms' remission was defined as reduction of at least 50% of severity and length of the above-mentioned symptoms. Patients were also asked to report any adverse event.

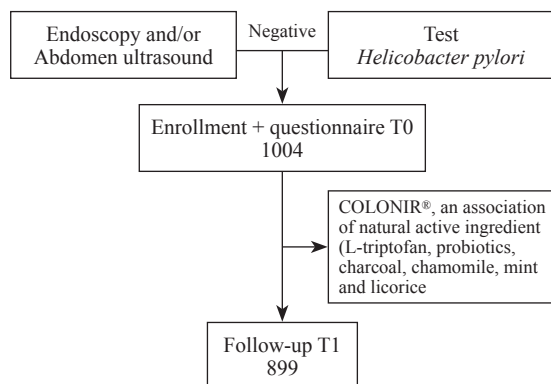


Figure 1.—Flow chart of the study.

Statistical analysis

Frequency, distribution analyses and non-parametric tests were used for the statistical analysis (Medcalc 19.1.3 software; MedCalc Software, Ostend, Belgium) as appropriate on patients that completed 2 months of treatment. Results were considered statistically significant for P values <0.05.

Results

One thousand and four patients (40.9% males; mean age: 56.67 years) were consecutively enrolled. Patient characteristics are summarized in Table I, while Body Mass Index (BMI) and alcohol/smoking habits are reported in Table II, III. Concomitant therapies are reported in Table IV. After 2 month, 899 patients completed the follow-up while 105 were excluded because

TABLE I.—Characteristic of the population.

Population (total N.)	1004	
Sex		
M	411	40.9 (37.9-44.0)
F	593	59.1 (55.9-62.0)
Average age	56.67	
Standard deviation	15.4922	

TABLE II.—Body Mass Index: scale of values and ranges.

	Cases	BMI range	% (95%CI)
Class			
Severe underweight	7	<16	0.7 (0.3-1.4)
Underweight	30	16-18.5	3.0 (2.1-4.2)
Normal	523	18.5-25	52.1 (49.0-55.1)
Overweight	337	25-30	33.6 (30.7-36.5)
Obese			
Obese class 1	79	30-35	7.9 (6.3-9.7)
Obese class 2	18	35-40	1.8 (1.1-2.8)
Obese class 3	9	>40	0.9 (0.4-1.6)

TABLE III.—Smoking and alcohol habits.

Habit	Cases (N.)	% (95%CI)
Smoke		
Yes (N. 186)		18.56 (16.2-21.0)
No (N. 683)		68.16 (65.1-70.8)
Ex (N. 133)		13.27 (11.3-15.5)
Not declared (N. 2)		0.2 (0.05-0.7)
Alcohol		
Yes (N. 197)		19.74 (17.2-22.2)
No (N. 801)		80.26 (77.1-82.1)
Not declared (N. 6)		0.6 (0.2-1.3)

questionnaires were not fully completed. Based on questionnaire results, COLONIR[®] was able to achieve a statistically significant reduction of symptoms severity at 2 months (P values <0.05). Data are reported in Figure 2.

Discussion

Gastrointestinal conditions are prevalent in the population and account for significant morbidity and health care costs.⁹ There is growing evidence that integrative medicine approaches can improve symptoms and affect physiology and disease course. Recently, several different approaches can allow to improve symptoms, by acting with different mechanisms.¹⁰ However, there are very few studies that assess the effect of nutraceutical compounds in a very large population and in a real clinical practice. Therefore, this study aimed to evaluate the efficacy and safety of 2 months treatment with COLONIR[®] for the management of gastrointestinal symptoms in a large cohort of

IBS patients. The findings show that COLONIR[®] can achieve a statistically significant reduction of severity of symptoms in our population without any documented side effects. These results could be explained by looking at the combination of its components: L-tryptophan improves gastrointestinal peristalsis;¹¹ probiotics and Vitamin B3-B5-B6 help to obtain a balanced microbiota;¹² charcoal reduces bloating;¹³ chamomile and Melissa can reduce nausea;¹⁴ peppermint and licorice act to regulate gastrointestinal motility.¹⁵ The efficacy of COLONIR[®] is also related to its rapidity to obtain benefits and symptoms improvement as patients reported a relief of symptoms after only two months of therapy.

Limitations of the study

Although this study, to our knowledge, represents the first largest Italian IBS survey on more than 1000 consecutive patients which represents the real world and real routine practice of most GI units in Italy, has several limitations: 1) duration lasts only two months; 2) due to its design (prospective, interventional non randomized study), placebo effect need to be taken into account; and 3) there is no comparison with an alternative treatment.

Conclusions

In conclusion, these promising results, here reported, need to be confirmed, valuating the efficacy of COLONIR[®] in relieving gastrointestinal symptoms in IBS patients in further studies.

TABLE IV.—Drugs use.		
Drugs	N.	% (95%CI)
None	621	61.85 (58.8-64.8)
Statins	108	10.76 (8.6-12.4)
Steroid medications	28	2.79 (1.9-4.0)
Antidiabetics	44	4.38 (3.2-5.8)
Immunosuppressive drugs	3	0.30 (0.1-0.8)
NSAIDS	15	1.49 (0.9-2.4)
PPI	107	10.66 (8.9-12.7)
Other	196	19.52 (17.1-22.1)
Two drugs	89	8.86 (7.2-10.7)
Three drugs	26	2.59 (1.7-3.7)
Four or more drugs	2	0.20 (0.05-0.7)

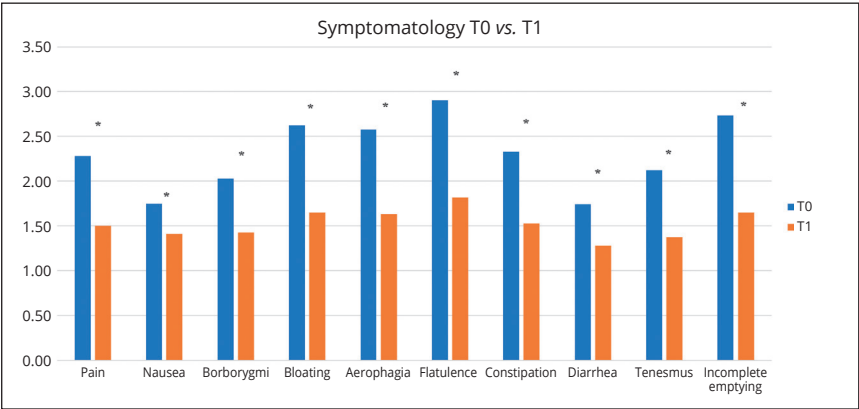


Figure 2.—Efficacy of COLONIR[®] in the reduction of IBS symptoms. T0: time of enrollment; T1: time 1 at two months from the enrollment. *Statistically significant difference.

References

1. Chey WD, Kurlander J, Eswaran S. Irritable bowel syndrome: a clinical review. *JAMA* 2015;313:949–58.
2. Ford AC, Lacy BE, Talley NJ. Irritable Bowel Syndrome. *N Engl J Med* 2017;376:2566–78.
3. Defrees DN, Bailey J. Irritable Bowel Syndrome: Epidemiology, Pathophysiology, Diagnosis, and Treatment. *Prim Care* 2017;44:655–71.
4. Grayson M. Irritable bowel syndrome. *Nature* 2016;533:S101.
5. Moayyedi P, Chey WD, Harris LA, Lacy BE, Saito YA, *et al.*; ACG Task Force on Management of Irritable Bowel Syndrome. American College of Gastroenterology Monograph on Management of Irritable Bowel Syndrome. *Am J Gastroenterol* 2018;113:1–18.
6. Camilleri M. Diagnosis and Treatment of Irritable Bowel Syndrome: A Review. *JAMA* 2021;325:865–77.
7. Raskov H, Burcharth J, Pommegaard HC, Rosenberg J. Irritable bowel syndrome, the microbiota and the gut-brain axis. *Gut Microbes* 2016;7:365–83.
8. di Michele F. Why Use Nutraceutical Strategies for the Irritable Bowel Syndrome? *Curr Med Chem* 2022;29:2075–92.
9. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, *et al.* Worldwide Prevalence and Burden of Functional Gastrointestinal Disorders, Results of Rome Foundation Global Study. *Gastroenterology* 2021;160:99–114.e3.
10. Dossett ML, Cohen EM, Cohen J. Integrative Medicine for Gastrointestinal Disease. *Prim Care* 2017;44:265–80.
11. Brzozowski T, Konturek PC, Konturek SJ, Pajdo R, Bielanski W, Brzozowska I, *et al.* The role of melatonin and L-tryptophan in prevention of acute gastric lesions induced by stress, ethanol, ischemia, and aspirin. *J Pineal Res* 1997;23:79–89.
12. Peterson CT, Rodionov DA, Osterman AL, Peterson SN. B Vitamins and Their Role in Immune Regulation and Cancer. *Nutrients* 2020;12:3380.
13. Senderovich H, Vierhout MJ. Is there a role for charcoal in palliative diarrhea management? *Curr Med Res Opin* 2018;34:1253–9.
14. Srivastava JK, Shankar E, Gupta S. Chamomile: A herbal medicine of the past with bright future. *Mol Med Rep* 2010;3:895–901.
15. Yang R, Yuan BC, Ma YS, Zhou S, Liu Y. The anti-inflammatory activity of licorice, a widely used Chinese herb. *Pharm Biol* 2017;55:5–18. </jrn>

Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—Dino Vaira has given substantial contributions to the study conception; Giulia Fiorini, Ilaria M. Saracino, and Matteo Pavoni contributed to the manuscript draft, all authors included patients in the study and revised it critically. All authors read and approved the final version of the manuscript.

History.—Manuscript accepted: November 29, 2022. - Manuscript received: September 19, 2022.