

Review Article

Alternative Therapeutic Approaches in the Irritable Bowel Syndrome: Use of Probiotics and Medicinal Plants

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Received: 21/01/2016

Revised: 18/02/2016

Accepted: 23/02/2016

ABSTRACT

Background: Irritable Bowel Syndrome (IBS) is the most common gastrointestinal disorder worldwide. It is considered a chronic, multifactorial, relapsing functional bowel disorder normally related to modifications in the motility, secretion and sensitivity of gastrointestinal system.

Objective: This review aimed to study the effects of the use of probiotics and medicinal plants to treat IBS.

Results: Some are the possibilities of treatment for IBD but only a few are effective options. Probiotics have effects against pathogenic bacteria, normalize bowel movements, and reduce visceral hypersensitivity. For example, Bifidobacterium infantis, bifid bacterium lactis, Lactobacillus acidophilus and Lactobacillus caseiShirota are related to decrease pain, bloating and defecation difficulty, improvement in bowel function, stool habit. Medicinal plants may exhibit benefic effects as anti-inflammatory, pro-secretory activity, and affecting gastrointestinal motility. Most common plants used are the rhizomes of Zingiber Officinalis Roscoe and Menthapiperita.

Conclusion: There are several studies showing beneficial effects of probiotics on IBS patients but many controversial effects on the use of medicinal plants to treat the symptoms of this disease.

Key words: Irritable Bowel Disease, probiotics, medicinal plants.

INTRODUCTION

Disruption in the homeostasis of the gastrointestinal tract is related to different diseases, as Irritable Bowel Syndrome (IBS) which is one of the most common gastrointestinal disorders. It may be accompanied by modifications in the motility, secretion and sensitivity of gastrointestinal system, changes in bowel habits, abdominal discomfort, and abdominal pain; bloating, distention; straining, gas and urgency are major

symptoms. Epidemiological data estimate that IBS prevalence is around 10% to 15% in United States and Europe and in the general population it ranges from 5 to 20%. [1-4]

This disorder leads to a significant health care burden and can severely interfere in the quality of life. Its etiology is poorly understood and many factors are involved. However it is known that psychological and psychiatric co-morbidity is often associated to IBS patients. [5-11]

Rome Criteria is well accepted to define IBS. According to Rome III Diagnostic Criteria, IBS is a characterized by recurrent abdominal pain or discomfort that manifest at least 3 days per month over a 3 month span. [4, 12,13] Other symptoms related by IBS

patients include diarrhea, constipation, alternating diarrhea and constipation, dyspepsia, bloating and gas. [14-16] Table 1 shows some aspects of Rome Criteria. [5, 12, 17-20]

Table 1: ROME I, II AND III criteria for IBS diagnosis

Criteria	Parameters	Year of publication	Reference
Rome I	Abdominal discomfort and/or pain and relieve after defecation, Modifications in stool consistence and frequency, Association of item <i>a</i> and <i>b</i> and at least 2 of the following points at least 25% of occurrence or days for 3 months: modification in stool dorm, frequency or passage; bloating/gas and presence of mucus.	1990	Whitehead [17], Spiller et al [18], LekhaSeha [5]
Rome II	Abdominal discomfort and/or pain and relieve after defecation, Association of item <i>a</i> and 2 or 3 features for year associated to relieve after defecation, modifications in form and frequency of stools.	1999	Whitehead [17], Lekha Seha [5]
Rome III	Recurrent abdominal pain or discomfort that manifest at least 3 days per month over a 3 month span, Association of item <i>a</i> with at least, 2 of the following: improvement after defecation, onset associated to modifications in form or frequency of stool.	2006	Quigley et al [12], Goshal et al [19], Occhipinti, Smith [20], Lekha, Seha [5]

IBS: Irritable Bowel Disease

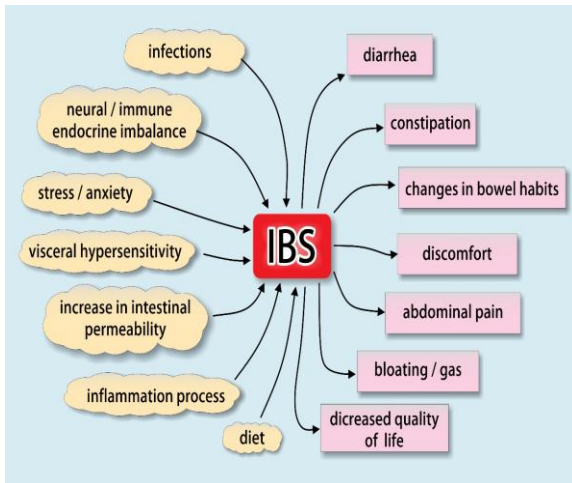


Figure 1: Triggering factors for IBS and main symptoms related by the patients

The peristaltic reflex and sensory in the gut are mainly regulated by 5-hydroxytryptamine (5-HT) that is related to the motility, secretion and sensation in the gut. Authors have shown that the release of this hormone seems to be decreased in patients with constipation-predominant IBS (IBS-C) and increased in diarrhea-predominant IBS (IBS-D). [4, 21-24]

The pathophysiological mechanisms related to IBS are not completely understood and may be related to genetic factors, neural immune endocrine imbalance, visceral hypersensitivity, psychological factors, diet, higher microbial intestinal permeability, inflammation,

previous infections, visceral hypersensitivity and overgrowth. When there is an imbalance in mucosal entero-endocrine system and immune system, an inflammatory biochemical cascade is activated leading to abnormal functional responses in enteric and sensory nerves with a disruption in the integrity of the intestinal barrier. There is also increase in pro-inflammatory cytokines synthesis, as Tumor Necrosis Factor- α (TNF- α), Interleucin-1 β (IL-1 β), IL-6, IL-8. [4, 16, 25-28]

It is possible to find some possibilities for treatment of IBS patients but not many have been implemented and only a few are effective options. This leads to an urgent necessity of a multidisciplinary approach for IBS prevention and treatment. [10]

This review aimed to study the effects of the use of probiotics and medicinal plants to treat IBS.

MATERIALS AND METHODS

This review was based on a survey of articles using databases as: Pubmed, PMC, Medline, Scielo, Scopus and Lilacs. A retrospective search was carried out to identify relevant clinical trials and reviews involving humans and animal models.

Probiotics: Therapeutic Approach for IBS Patients?

The use of probiotics is a common strategy used by the IBS patients but their roles remain uncertain mainly because of the limited number of clinical trials about this therapeutic strategy. [29,30] Table 2 shows some studies regarding to the use of these substances.

The use of probiotics implies in the intake of single bacterial strains or combinations of bacterial strains in order to modify or influence the commensal gut micro biota. The probiotic may be defined as a “living microbial food supplement” which exhibit potential effects on human health and improve the host by improvement of the intestinal balance when the intake is sufficient to influence the micro biota. The use of these components in gastrointestinal diseases (as in symptoms such as diarrhea and constipation) is very common nowadays. They may influence other symptoms as bloating, distension abdominal pain, flatulence, altered bowel movements, and gut micro biota. One important meta-analysis showed that there

are significant effects of probiotics on global IBS symptom rating for 24 mono-strain preparations pooled; but *Lactobacilli* and *Bifidobacteria* was only efficient when used separately. Other meta-analysis postulated that probiotics may exhibit positive effects only in abdominal pain. [1, 31-35]

Probiotics may exert benefits in intestinal function protecting against pathogenic bacteria. They have the ability to amplify intestinal tight junctions and stabilize the permeability and promote stimulation of goblet cells to produce mucus which improve intestinal barrier, normalize bowel movements, and reduce visceral hypersensitivity. [1, 36-38]

Table 2 associates the use of probiotics and IBS. [38, 41-53]

There are a number of studies using probiotics in IBS patients and many different results can be found, possibly due to the heterogeneity of probiotics. Different dosages as well as the bacterial strains and mixtures of these may contribute to this heterogeneity. [54]

Table 2: Effects of some probiotics in patients with Irritable Bowel Disease

Probiotic	Effects	Reference
Bifidobacterium infantis 35624	Decrease in pain, and defecation difficulty; Downregulation inflammation.	Brener et al [39], Whorwell et al [40], Guglielmetti et al [41], Ford et al [35], Lacy, Chey, Lembo [29]
Bifidobacterium lactis DN-173 010	Increase gastrointestinal transit, decrease stool frequency;	Hussain, Quigley [42]; Brener et al [39]
Lactobacillus acidophilus-SDC	Improvement pain	Sin et al [43]
Bifidobacterium lactisDN-173010	Improvement distention and pain.	Agrawal et al [44]
Bifidobacterium bifidum MIMBb75	Improvement in quality of life, bloating and flatulence.	Guglielmetti [41]
Escherichia coli Nissle and VSL#3*	Improvement in intestinal barrier.	Kruis et al [45], Michail, Kenche [46]
Lactobacillus plantarum299v (DSM 9843)	Improvement of pain and bloating.	Ducrotte et al [47]
Saccharomycescerevisiae (S. boulardii)	Improvementofpain.	De Chambrum et al [48], Palma et al [49]
Lactobacillus GG	Decrease of pain, improvement in the functional scale;	Kianifar et al [50]
Lactobacillus casei Shirota	Improvement after 16 weeks.	Thijssen et al [51]
Mixture VSL#3	Improvement of general symptoms.	Rohatgi et al [52]
Probiotic mixture Lactobacillus acidophilus, L. rhamnosus, Bifidobacterium breve, B. actis, B. longum, and Streptococcus thermophiles	Symptom relief in diarrhea.	Yoon et al [53]

*VSL#3: a high-concentration probiotic preparation.

Medicinal Plants: Therapeutic Approach for IBS Patients?

Plants have been used over the years to the discovery of several pharmacological

products and there are a huge diversity of herbs with remarkable medicinal applications and pharmacological potential. [55]

Probably the most common medicinal plant used to treat IBS is ginger which root is the rhizome of *Zingiber officinalis Roscoe*. Some studies show that ginger effectively treats gastrointestinal symptoms; work as antiemetic and in pain relieving. [56-60]

Menthapiperita is another plant recommended to treat IBS symptoms. Its oil

has been recommended for the treatment of IBS by the National Institute for Health and Clinical Excellence Guidelines [61] and widely prescribed as an enteric-coated peppermint oil tablet that exhibit antispasmodic effects. [62-65]

Table 3 summarizes some studies of medicinal plants and their effects on the IBS in humans and animal models. [62, 66-81]

Table 3: Effects of some plants or their components or mixture of plants in the Irritable Bowel Disease

Plant or isolated component	Effects	Model	Reference
Eugenol (<i>Eugenia caryophyllata</i>)	Reduction of restraint stress-induced development of IBS*-like gastrointestinal dysfunction.	Rats	Garabadu et al [66]
Zingerone	Reduction of colonic transit, fecal output, neutrophil infiltration, and lipid peroxide formation. Lead to a marked improvement in stress induced-irritable bowel disorder.	IBS patients	Banji et al [67]
<i>Menthapiperita</i> , <i>Melissa officinalis</i> , <i>Coriandrumsativum</i>	Exhibit antibacterial activity and have the ability to work on intestinal dysbiosis and improve IBS symptoms.	IBS patients	Thompson et al [62]
Phytoestrogen-rich soy germ fermented ingredient	Inhibition of elevation of faecal proteolytic activity; improved occluding expression, and decreased colonic mast cell density; prevented the stress-induced hyperpermeability and visceral hypersensitivity.	Cyclic rats	Moussa et al [68]
<i>Curcuma longa</i>	Reduction in abdominal pain and discomfort (2/3 of the related improvement in IBS symptoms).	IBS patients	Gupta et al [69]; Bundy et al [70]
Acacia fiber	Improvement in bowel habit relief and overall IBS symptoms.	IBS patients	Min et al [71]
<i>Linunusitatissimum</i>	Role in relief of IBS symptoms.	IBS patients	Cockerell et al [72]
<i>Curcuma xanthorrhiza</i> and <i>Fumaria officinalis</i>	No benefits.	IBS patients	Rahimi, Abdollahi [73]; Brinkhaus et al [74]
Iridoidfrom <i>Valerianajatamansi</i>	Increase in the content of 5-HT* in colon and serum.	IBS patients	Yan et al [75]
Red pepper powder	Decrease in the intensity of abdominal pain and bloating.	IBS patients	Bortolotti, Porta [76]
<i>Coptischinensis</i> rhizomes	Reduction of visceral pain.	IBS patients	Tjong et al [77]
<i>Actinidiadeliciosa</i>	Increase defecation frequency in IBS-C† patients and shortens colon transit time.	IBS patients	Chang et al [78]
Enzyme-treated rice fiber	Reduction of restraint stress-induced development of IBS-like gastrointestinal dysfunction (attenuation of urgent fecal excretion, hyperalgesiaand colonic mucosal 5-HT secretion).	IBS patients	Kanauchi et al [79]
<i>Aloe vera</i>	No benefits.	IBS patients	Davis et al [80]
<i>Cynarascolymus</i>	Reduction of the severity of symptoms.	IBS patients	Walker, Middleton [81]

*IBS: Irritable Bowel Syndrome; †IBS-C: patients with constipation-predominant; *5-HT: 5-hydroxytryptamine.

Table 4: Products manufactured with plants and their effects on the IBS

Products	Effects	Models	Reference
Caricol®	Improvement of constipation and bloating.	IBS patients	Muss et al [82]
Carmint®	Reduction of abdominal pain, bloating.	IBS patients	Vejdani et al [83]; Thompson et al [62]
Iberogast® (or STW-5)	Reduction in pain and bloating; improvement in bowel habit and dyspepsia.	IBS patients	Simmen et al [85]; Thompson et al [62]
DA-IBS formula®	Reduction of pain, bloating, and flatulence	IBS-D† and alternating bowel habits	Hu et al [84]
STW 5-II®	Improvement in IBS symptoms and abdominal pain.	IBS patients	Madish et al [86]
Padma Lax®	Improvement in constipation, severity of abdominal pain and bloating.	IBS patients	Sallon et al [87]

*IBS: Irritable Bowel Disease; †IBS-D: Irritable Bowel Disease predominant Diarrhea.

Table 4 include products of single (Caricol®) and mixture of different plants (Carmint®, Iberogast®(STW-5 and STW-5II), DA-IBS® and Padma Lax). [62, 82-87]

Rahimi and Abdollahi [73] showed that the most effective herbal plant in IBS

patients was seen for *Menthapiperita* essential oil and showed that STW-5 formula is the most studied. They postulate that the results with the plants in the management of IBS symptoms are “different mechanisms of action such as

anti-inflammatory, pro-secretory activity, and affecting gastrointestinal motility". Also, the compound preparations seem to be more efficient than single ones due to the multifactorial nature of the pathophysiology of IBS.

CONCLUSION

There are many studies showing beneficial effects of probiotics on IBS patients. The literature shows many controversial effects on the use of medicinal plants to treat the symptoms of this disease but it is also possible to find several plants with significant potential for improvement of the pain and discomfort. IBS is a multifactorial disease and the therapeutic approach involving a multidisciplinary team and the inclusion of alternative therapies may bring benefits to the patients by improving their quality of life.

Conflict of Interests: Authors declare no conflict of interests.

REFERENCES

1. Didari T, Mozaffari S, Nikfar S, Abdollahi M. Effectiveness of probiotics in irritable bowel syndrome: updated systematic review with meta-analysis. *World J Gastroenterol.* 2015; 21:3072-3084.
2. Ohman L, Isaksson S, Lundgren A, Simrén M, Sjövall H. A controlled study of colonic immune activity and beta7+ blood T lymphocytes in patients with irritable bowel syndrome. *Clin Gastroenterol Hepatol.* 2005; 3:980-986.
3. Saha L. Irritable bowel syndrome: Pathogenesis, diagnosis, treatment, and evidence-based medicine. *World J Gastroenterol.* 2014; 20(22):6759-6773.
4. Lee YJ, Park KS. Irritable bowel syndrome: Emerging paradigm in pathophysiology. *World J Gastroenterol.* 2014; 20(10):2456-2469.
5. Moraes-Filho JP, Quigley EM. The intestinal microbiota and the role of probiotics in irritable bowel syndrome: a review. *ArqGastroenterol.* 2015; 52(4):331-8.
6. Camilleri M, Lasch K, Zhou W. Irritable bowel syndrome: methods, mechanisms, and pathophysiology. The confluence of increased permeability, inflammation, and pain in irritable bowel syndrome. *Am J PhysiolGastrointest Liver Physiol.* 2012; 303: G775-G785.
7. El-Salhy M. Irritable bowel syndrome: diagnosis and pathogenesis. *World J Gastroenterol* 2012; 18: 5151-5163.
8. El-Salhy M. Recent developments in the pathophysiology of irritable bowel syndrome. *World J Gastroenterol.* 2015 July 7; 21(25): 7621-7636. Published online 2015 July 7.
9. Liang WJ, Zhang G, Luo HS, Liang LX, Huang D, Zhang FC. Tryptase and Protease-Activated Receptor 2 Expression Levels in Irritable Bowel Syndrome. *Gut Liver.* 2015.[Epub ahead of print]
10. Mosińska P, Storr M, Fichna J. The role of AST-120 and protein-bound uremic toxins in irritable bowel syndrome: a therapeutic perspective. *Therap Adv Gastroenterol.* 2015; 8(5): 278-84.
11. Drossman DA, Camilleri M, Mayer EA, Whitehead WE. AGA technical review on irritable bowel syndrome. *Gastroenterology.* 2002; 123:2108-31.
12. Quigley EM, Abdel-Hamid H, Barbara G, Boeckxstaens G, De Giorgio R, Delvaux M, Drossman DA, Foxx-Orenstein AE, Guarner Fet al. A global perspective on irritable bowel syndrome: a consensus statement of the World Gastroenterology Organization Summit Task Force on irritable bowel syndrome. *J Clin Gastroenterol.* 2012; 46: 356-366.
13. Longstreth GF, Thompson WG, Chey WD. Functional bowel disorders. *Gastroenterology* 2006; 130:1480-1491.
14. Volz MS, Farmer A, Siegmund B. Reduction of chronic abdominal pain in patients with inflammatory bowel disease via transcranial direct current stimulation: a randomized controlled trial. *Pain.* 2015 Oct 13. [Epub ahead of print]
15. Grinsvall C, Törnblom H, Tack J, Van Oudenhove L, Simrén M. Psychological factors selectively upregulate rectal pain perception in hypersensitive patients with irritable bowel syndrome. *Neurogastroenterol Motil.* 2015; 27(12):1772-82.
16. Barbara G, Cremon C, Carini G, Bellacosa L, Zecchi L, De Giorgio R, Corinaldesi R, Stanghellini V. The immune system in irritable bowel syndrome. *J Neurogastroenterol Motil.* 2011; 17(4):349-59.

17. Whitehead WE, Drossman DA. Validation of symptombased diagnostic criteria for irritable bowel syndrome: a critical review. *Am J Gastroenterol.* 2010; 105: 814-20.
18. Spiller RC. Effects of serotonin on intestinal secretion and motility. *Curr Opin Gastroenterol.* 2001;17:99-103.
19. Ghoshal UC, Srivastava D, Misra A, Ghoshal U. A proof-of-concept study showing antibiotics to be more effective in irritable bowel syndrome with than without small-intestinal bacterial overgrowth: a randomized, double-blind, placebo-controlled trial. *Eur J Gastroenterol Hepatol.* 2016 Jan 1. [Epub ahead of print]
20. Occhipinti K, Smith JW. Irritable bowel syndrome: a review and update. *Clin Colon Rectal Surg.* 2012; 25: 46-52.
21. Sun J, Wu X, Meng Y, Cheng J, Ning H, Peng Y, Pei L, Zhang W. Electroacupuncture decreases 5-HT, CGRP and increases NPY in the brain-gut axis in two rat models of Diarrhea-predominant irritable bowel syndrome (D-IBS). *BMC Complement Altern Med.* 2015 Sep 29; 15(1):340.
22. Talley NJ. Serotonergic neuroenteric modulators. *Lancet* 2001; 358: 2061-2068.
23. Dunlop SP, Coleman NS, Blackshaw E, Perkins AC, Singh G, Marsden CA, Spiller RC. Abnormalities of 5-hydroxytryptamine metabolism in irritable bowel syndrome. *Clin Gastroenterol Hepatol.* 2005; 3:349-357.
24. Khan WI, Ghia JE. Gut hormones: emerging role in immune activation and inflammation. *ClinExpImmunol.* 2010; 161: 19-27.
25. Jarrett ME, Cain KC, Barney PG, Burr RL, Naliboff BD, Shulman R, Zia J, Heitkemper MM. Balance of Autonomic Nervous System Predicts Who Benefits from a Self-management Intervention Program for Irritable Bowel Syndrome. *J Neurogastroenterol Motil.* 2016; 22(1):102-11.
26. Lembo AJ, Lacy BE, Zuckerman MJ, Schey R, Dove LS, Andrae DA, Davenport JM, McIntyre G, Lopez R, Turner L, Covington PS. Eluxadolone for Irritable Bowel Syndrome with Diarrhea. *N Engl J Med.* 2016; 374(3): 242-253.
27. Jalili M, Vahedi H, Janani L, Poustchi H, Malekzadeh R, Hekmatdoost A. Soy Isoflavones Supplementation for Patients with Irritable Bowel Syndrome: A Randomized Double Blind Clinical Trial. *Middle East J Dig Dis.* 2015; 7:170-6.
28. Gracie DJ, Ford AC. Symbiotics in irritable bowel syndrome--better than probiotics alone? *Curr Opin Clin Nutr Metab Care.* 2011; 18(5):485-9.
29. Lacy BE, Chey WD, Lembo AJ. New and Emerging Treatment Options for Irritable Bowel Syndrome. *Gastroenterol Hepatol (N Y).* 2015; 11(4 Suppl 2):1-19.
30. Alvarez-Calatayud G, Margolles A. Dual-coated lactic acid bacteria: an emerging innovative technology in the field of probiotics. *Future Microbiol.* 2016 Jan 18. [Epub ahead of print]
31. Mazurak N, Broelz E, Storr M, Enck P. Probiotic Therapy of the Irritable Bowel Syndrome: Why Is the Evidence Still Poor and What Can Be Done About It? *J Neurogastroenterol Motil.* 2015; 21(4): 471-85.
32. Kneifel W, Salminen S. Probiotics and health claims. Blackwell Publishing Ltd, 2011.
33. Dai C, Zheng CQ, Jiang M, Ma XY, Jiang LJ. Probiotics and irritable bowel syndrome. *World J Gastroenterol.* 2013; 19:5973-5980.
34. Fuller R. Probiotics in man and animals. *J ApplBacteriol.* 1989; 66:365-378.
35. Ford AC, Quigley EM, Lacy BE, et al. Efficacy of prebiotics, probiotics, and symbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis. *Am J Gastroenterol.* 2014; 109:1547-1561.
36. Gareau MG, Sherman PM, Walker WA. Probiotics and the gut microbiota in intestinal health and disease. *Nat Rev Gastroenterol Hepatol.* 2010;7:503-514.
37. Enck P, Klosterhalfen S, Martens U. Probiotic therapy of the irritable bowel syndrome. *Dtsch Med Wochenschr.* 2011; 136:371-375.
38. Korterink JJ, Ockeloen L, Benninga MA, Tabbers MM, Hilbink M, Deckers-Kocken JM. Probiotics for childhood functional gastrointestinal disorders: a systematic review and meta-analysis. *Acta Paediatr.* 2014; 103:365-372.
39. Brenner DM, Moeller MJ, Chey WD, Schoenfeld PS. The utility of probiotics in the treatment of irritable bowel syndrome:

- a systematic review. *Am J Gastroenterol.* 2009; 104: 1033-149.
40. Whorwell PJ, Altringer L, Morel J, et al. Efficacy of an encapsulated probiotic *Bifidobacterium infantis* 35624 in women with irritable bowel syndrome. *Am J Gastroenterol.* 2006; 101(7):1581–1590.
 41. Guglielmetti S, Mora D, Gschwender M, Popp K. Randomised clinical trial: *bifidobacterium bifidum* MIMBb75 significantly alleviates irritable bowel syndrome and improves quality of life—a double-blind, placebo-controlled study. *Aliment Pharmacol Ther.* 2011; 33(10):1123–1132.
 42. Hussain Z, Quigley EM. Systematic review: Complementary and alternative medicine in the irritable bowel syndrome. *Aliment Pharmacol Ther* 2006; 23: 465-471.
 43. Sinn DH, Song JH, Kim HJ, Lee JH, Son HJ, Chang DK, Kim YH, Kim JJ, Rhee JC, Rhee PL. Therapeutic effect of *Lactobacillus acidophilus*-SDC 2012, 2013 in patients with irritable bowel syndrome. *Dig Dis Sci.* 2008; 53:2714–2718.
 44. Agrawal A, Houghton LA, Morris J, Reilly B, Guyonnet D, Goupil-Feuillerat N, Schlumberger A, Jakob S, Whorwell PJ. Clinical trial: the effects of a fermented milk product containing *Bifidobacterium lactis* DN-173 010 on abdominal distension and gastrointestinal transit in irritable bowel syndrome with constipation. *Aliment Pharmacol Ther.* 2009; 29:104–114.
 45. Kruis W, Chrubasik S, Boehm S, Stange C, Schulze J. A double-blind placebo-controlled trial to study therapeutic effects of probiotic *Escherichia coli* Nissle 1917 in subgroups of patients with irritable bowel syndrome. *Int J Colorectal Dis.* 2012; 27:467–474.
 46. Michail S, Kenche H. Gut microbiota is not modified by Randomized, Double-blind, Placebo-controlled Trial of VSL#3 in Diarrhea-predominant Irritable Bowel Syndrome. *Probiotics Antimicrob Proteins.* 2011;3:1–7.
 47. Ducrotté P, Sawant P, Jayanthi V. Clinical trial: *Lactobacillus plantarum* 299v (DSM 9843) improves symptoms of irritable bowel syndrome. *World J Gastroenterol.* 2012;18:4012–4018.
 48. deChambrun GP, Neut C, Chau A, et al. A randomized clinical trial of *Saccharomyces cerevisiae* versus placebo in the irritable bowel syndrome. *Dig Liver Dis.* 2015;47:119-124.
 49. Palma ML, Zamith-Miranda D, Martins FS, Bozza FA, Nimrichter L, Montero-Lomeli M, Marques ET Jr, Douradinha B. Probiotic *Saccharomyces cerevisiae* strains as biotherapeutic tools: is there room for improvement? *Appl Microbiol Biotechnol.* 2015;99(16):6563-70.
 50. Kianifar H, Jafari SA, Kiani M, Ahanchian H, Ghasemi SV, Grover Z, Mahmoodi LZ, Bagherian R, Khalesi M. Probiotic for irritable bowel syndrome in pediatric patients: a randomized controlled clinical trial. *Electron Physician.* 2015; 7(5):1255-60.
 51. Thijssen AY1, Clemens CH, Vankerckhoven V, Goossens H, Jonkers DM, Masclee AA. Efficacy of *Lactobacillus casei* Shirota for patients with irritable bowel syndrome. *Eur J Gastroenterol Hepatol.* 2016;28(1):8-14.
 52. Rohatgi S1, Ahuja V1, Makharia GK1, Rai T1, Das P2, Dattagupta S2, Mishra V1, Garg SK. VSL#3 induces and maintains short-term clinical response in patients with active microscopic colitis: a two-phase randomised clinical trial. *BMJ Open Gastroenterol.* 2015; 2(1): e000018.
 53. Yoon H, Park YS, Lee DH, Seo JG, Shin CM, Kim N. Effect of administering a multi-species probiotic mixture on the changes in fecal microbiota and symptoms of irritable bowel syndrome: a randomized, double-blind, placebo-controlled trial. *J Clin Biochem Nutr.* 2015; 57(2):129-34.
 54. Sitarek P, Skala E, Wysokińska H, Wielanek M, Szemraj J, Toma M, Śliwiński T. The Effect of *Leonurus sibiricus* Plant Extract on Stimulating Repair and Protective Activity against Oxidative DNA Damage in CHO Cells and Content of Phenolic Compounds. *Oxid Med Cell Longev.* 2016; 2016:5738193.
 55. Lima TB, Silva ON, Oliveira JT, Vasconcelos IM, Scalabrin FB, Rocha TL, Grossi-de-Sá MF, Silva LP, Guadagnin RV, Quirino BF, Castro CF, Leonardecz E, Franco OL. Identification of *E. dysenterica* laxative peptide: a novel strategy in the treatment

- of chronic constipation and irritable bowel syndrome. *Peptides*. 2010; 31(8):1426-33.
56. van Tilburg MA, Palsson OS, Levy RL, et al. Complementary and alternative medicine use and cost in functional bowel disorders: a six month prospective study in a large HMO. *BMC Complement Altern Med*. 2008; 8:46.
 57. Grzanna R, Lindmark L, Frondoza CG. Ginger--an herbal medicinal product with broad anti-inflammatory actions. *J Med Food*. 2005; 8:125-32.
 58. Ghayur MN, Gilani AH. Pharmacological basis for the medicinal use of ginger in gastrointestinal disorders. *Dig Dis Sci*. 2005;50:1889-97.
 59. Terry R, Posadzki P, Watson LK. The use of ginger (*Zingiber officinale*) for the treatment of pain: a systematic review of clinical trials. *Pain Med*. 2011;12:1808-18.
 60. van Tilburg MA, Palsson OS, Ringel Y, Whitehead WE. Is ginger effective for the treatment of irritable bowel syndrome? A double blind randomized controlled pilot trial. *Complement Ther Med*. 2014;22(1):17-20.
 61. National Institute for Health and Clinical Excellence. Clinical practice guideline. Irritable bowel syndrome in adults: diagnosis and management of irritable bowel syndrome in primary care. 2008. Available from [<http://www.nice.org.uk/nice/media/live/11927/39746/39746.pdf>].
 62. Thompson A, Meah D, Ahmed N, Conniff-Jenkins R, Chileshe E, Phillips CO, Claypole TC, Forman DW, Row PE. Comparison of the antibacterial activity of essential oils and extracts of medicinal and culinary herbs to investigate potential new treatments for irritable bowel syndrome. *BMC Complement Altern Med*. 2013; 13:338.
 63. Grigoleit H-G, Grigoleit P. Peppermint oil in irritable bowel syndrome. *Phytomed*. 2005; 12:601-606.
 64. Allam S, Krueger D, Demir IE, Ceyhan G, Zeller F, Schemann M. Extracts from peppermint leaves, lemon balm leaves and in particular angelica roots mimic the pro-secretory action of the herbal preparation STW 5 in the human intestine. *Phytomedicine*. 2015;22(12): 1063-70.
 65. Somi MH, Bagheri M, Ghojzadeh M. Efficacy of an Iranian herbal preparation (Lax-Asab) in treating functional constipation: A randomized, placebo-controlled clinical trial. *J Tradit Complement Med*. 2015;5(3):153-6.
 66. Garabadu D, Shah A, Singh S, Krishnamurthy S. Protective effect of eugenol against restraint stress-induced gastrointestinal dysfunction: Potential use in irritable bowel syndrome. *Pharm Biol*. 2015;53(7):968-74.
 67. Banji D, Banji OJ, Pavani B, KranthiKumarCh, Annamalai AR. Zingerone regulates intestinal transit, attenuates behavioral and oxidative perturbations in irritable bowel disorder in rats. *Phytomedicine*. 2014 Mar 15;21(4):423-9.
 68. Moussa L, Bézirard V, Salvador-Cartier C, Bacquié V, Houdeau E, Théodorou V. A new soy germ fermented ingredient displays estrogenic and protease inhibitor activities able to prevent irritable bowel syndrome-like symptoms in stressed female rats. *Clin Nutr*. 2013; 32(1):51-8.
 69. Gupta SC, Sung B, Kim JH, Prasad S, Li S, Aggarwal BB. Multitargeting by turmeric, the golden spice: From kitchen to clinic. *Mol Nutr Food Res*. 2013; 57(9):1510-28.
 70. Bundy R, Walker AF, Middleton RW, Booth J. Turmeric extract may improve irritable bowel syndrome symptomology in otherwise healthy adults: a pilot study. *J Altern Complement Med*. 2004; 10(6):1015-8.
 71. Min YW, Park SU, Jang YS, Kim YH, Rhee PL, Ko SH, Joo N, Kim SI, Kim CH, Chang DK. Effect of composite yogurt enriched with acacia fiber and *Bifidobacterium lactis*. *World J Gastroenterol*. 2012; 7; 18(33):4563-9.
 72. Cockerell KM, Watkins AS, Reeves LB, Goddard L, Lomer MC. Effects of linseeds on the symptoms of irritable bowel syndrome: a pilot randomised controlled trial. *J Hum Nutr Diet*. 2012;25(5):435-43.
 73. Rahimi R, Abdollahi M. Herbal medicines for the management of irritable bowel syndrome: a comprehensive review. *World J Gastroenterol*. 2012; 18(7):589-600.
 74. Brinkhaus B, Hentschel C, Von Keudell C, Schindler G, Lindner M, Stützer H, Kohnen R, Willich SN, Lehmacher W, Hahn EG. Herbal medicine with curcuma and fumitory in the treatment of irritable bowel syndrome: a randomized, placebo-controlled, double-

- blind clinical trial. *Scand J Gastroenterol.* 2005 Aug; 40(8):936-43.
75. Yan X, Hong Y, Shi J, Qin Y, Zhang J, Lin Q, Chen Z, Zhao R, Cui X, Gao X. [Influence of iridoid from *Valerianajatanansi* on 5-HT and 5-HIAA in rats with irritable bowel syndrome]. *ZhongguoZhong Yao ZaZhi.* 2011; 36(9):1235-8.
 76. Bortolotti M, Porta S. Effect of red pepper on symptoms of irritable bowel syndrome: preliminary study. *Dig Dis Sci.* 2011; 56(11):3288-95.
 77. Tjong Y, Ip S, Lao L, Fong HH, Sung JJ, Berman B, Che C. Analgesic effect of *Coptischinensis* rhizomes (*CoptidisRhizoma*) extract on rat model of irritable bowel syndrome. *J Ethnopharmacol.* 2011; 135(3):754-61.
 78. Chang CC, Lin YT, Lu YT, Liu YS, Liu JF. Kiwifruit improves bowel function in patients with irritable bowel syndrome with constipation. *AsiaPac J Clin Nutr.* 2010; 19(4):451-7.
 79. Kanauchi O, Mitsuyama K, Komiyama Y, Yagi M, Andoh A, Sata M. Preventive effects of enzyme-treated rice fiber in a restraint stress-induced irritable bowel syndrome model. *Int J Mol Med.* 2010; 25(4):547-55.
 80. Davis K, Philpott S, Kumar D, Mendall M. Randomised double-blind placebo-controlled trial of aloe vera for irritable bowel syndrome. *Int J ClinPract.* 2006; 60(9):1080-6.
 81. Walker AF, Middleton RW, Petrowicz O. Artichoke leaf extract reduces symptoms of irritable bowel syndrome in a post-marketing surveillance study. *Phytother Res.* 2001; 15:58–61.
 82. Muss C, Mosgoeller W, Endler T. Papaya preparation (Caricol®) in digestive disorders. *Neuro Endocrinol Lett.* 2013; 34(1):38-46.
 83. Vejdani R, Shalmani HRM, Mir-Fattahi M, Sajed-Nia F, Abdollahi M, Zali MR, Alizadeh AHM, Bahari A, Amin G. The efficacy of an herbal medicine, carmint, on the relief of abdominal pain and bloating in patients with irritable bowel syndrome: a pilot study. *DigDis Sci.* 2006; 51:1501–1507.
 84. Hu X, Xu D, Zhao Y, Yang X, Meng J, Shen H, Guo J. The Alleviating Pain Effect of Aqueous Extract from Tong-Xie-Yao-Fang, on Experimental Visceral Hypersensitivity and Its Mechanism. *Biol Pharm Bull.* 2009; 32:1075–1079.
 85. Simmen U, Kelber O, Okpanyi SN, Jaeggi R, Bueter B, Weiser D. Binding of STW 5 (Iberogast) and its components to intestinal 5-HT, muscarinic M3, and opioid receptors. *Phytomedicine.* 2006; 13Suppl 5:51–55.
 86. Madisch A, Holtmann G, Plein K, Hotz J. Treatment of irritable bowel syndrome with herbal preparations: results of a double-blind, randomized, placebo-controlled, multi-centre trial. *Aliment Pharmacol Ther.* 2004;19:271–279.
 87. Sallon S, Ben-Arye E, Davidson R, Shapiro H, Ginsberg G, Ligumsky M. A novel treatment for constipation-predominant irritable bowel syndrome using Padma Lax, a Tibetan herbal formula. *Digestion.* 2002; 65:161–171.

How to cite this article: Barbalho SM, Goulart RDA, Alves de Carvalho AC et al. Alternative therapeutic approaches in the irritable bowel syndrome: use of probiotics and medicinal plants. *Int J Health Sci Res.* 2016; 6(3):277-285.
