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Case Series

Efficacy and safety of Neemint capsules in an open label single arm trial of patients with gastrointestinal disorders

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ABSTRACT

Anti-inflammatory drugs which are commonly used medication in gastrointestinal (GI) disorder worsen symptoms and increasing impend need of better treatment method for the disease. Neemint capsules composed of polyherbal formulation of neem oil and peppermint oil. We conducted this study to assess the efficacy and safety of Neemint capsules in patients with gastrointestinal disorders including irritable bowel syndrome. We conducted an open label clinical study of 15 patients (mean age, 35.2±14.26 years; 86.6% males) with two or more GI symptoms. Patients were given Neemint capsule of 500 mg (350 mg of neem oil+150 mg of peppermint oil) as per each schedule visit. The primary endpoint was change in gastrointestinal symptom rating scale (GSRS-IBS). Secondary endpoints included monitoring of AE and SAE, IBS-quality of life questionnaire and change in subject's global assessment of symptoms. The overall GSRS score improvement was found to be 64.23%. The IBS-QOL scores also indicated 57.2% increase in the quality of life of the study subject. The mean global assessment of symptoms (diarrhoea, constipation, abdominal pain, nausea vomiting and bloating) score recorded was 0. All results were significant at $p<0.05$. In this study we found that Neemint capsules is highly efficacious in the treatment of IBS and GI symptoms and it is also well-tolerated and safe in study subjects (n=15) having complaints of IBS and GI disturbances.

Keywords: Gastrointestinal disorder, Treatment, Open label, IBS

INTRODUCTION

A GI disorder is a condition/disease that occurs within gastrointestinal tract. GI tract has two major functions: serves as barrier to outside environment and allows nutrients to enter into the tract. Diseases attack GI tract are constipation, IBS, nausea, lactose intolerance, gas, bloating, gastro oesophageal 20 reflux disease, haemorrhoids, food poisoning, celiac disease.[1] IBS is the most common functional disease of GI tract.[2] It shows the symptoms of abdominal discomfort, pain, feelings of serious illness, stool irregularity, myalgias, urgency bloating.[3,4] Pain and pressure are the most frequent symptoms in both gastric and intestinal disease.[5] Dietary habits and nutrients uptake has a great importance in gastrointestinal diseases. Eating habits, severity of symptoms, disease progression reported a strong correlation in IBS.[6] Fermentable oligo-, di- and mono-saccharides polyols (FODMAPs) consider as the source for aggravating the symptoms in IBS/IBD as it is poorly absorbed into the intestine.[7] Abstaining triggered foods, excessive alcohol, caffeine intake and taking small meals are some of the recommendation of diet from UK's National institute of health and care excellence (NICE) for the patients suffering from Irritable bowel syndrome. Drugs are in use for treating IBS are Mebeverine and hyoscine as antispasmodic drugs, antidepressants, rifaximin and probiotics which has low efficacy and several side effects.[8,9] Chemical based treatments has some limitations due to negative side-effects such as insomnia,

nausea, heart burn, constipation, dry mouth and effect the overall health pattern. Therefore, herbs have been indicated for usefulness in treatment of IBS. Now a day's herbal treatment are using by 50% of the Western population.[10] Peppermint oil has been evaluated for its efficacy and tolerability in GI conditions, including non-serious constipation or diarrhoea associated with IBS to reduce global symptoms of pain and bloating.[11,12] Neem have therapeutic properties due to the presence of rich amount of antioxidants and other valuable components such as azadirachtin, nimbolinin, nimbin, nimibidol, salanin and quercitin.[13] Various health benefits are reported from the neem extract.[14] There is an unmet need for the development of formulation comprising herbal ingredients for the treatment of irritable bowels syndrome which if taken orally gives magical results. So, in this study the use of Neemint capsule constituted of neem extract and peppermint oil was tested in GI patients. Together effect of both neem and peppermint oil is also reported in the study of *Agrotis ipsilon*.[15] Neemint capsule is enteric coated which is to be taken orally by the patients. If direct oral consumption of neem oil or mint oil is taken, it leads to degradation of the same in stomach, causing gas formation and other undesirable effects, rendering the formulation less useful. HPMC based capsule are widely used in pharmaceutical and food industries.[16] Putting the formulation enteric coated HPMC based capsule and this drug delivery mechanism results in enhancing the efficacy of the formulation as enteric coating permits transit through the stomach to the small intestine before the medication is released. Most of the prior studies disclose the utilization of formulations in the form of tablets or capsules comprising peppermint oil for the treatment of gastrointestinal disorders including irritable bowel syndrome. But the present study comprises of enteric coated HPMC based capsule with a blend of both neem seed oil and peppermint oil for the treatment of irritable bowel syndrome, which is not disclosed in any of the prior art studies. The capsule disclosed in present invention basically provides effect of both neem seed oil and peppermint oil together in single formulation for relief in IBS associated diarrhoea, constipation and other associated fifteen symptoms with the almost no side effects.

CASE SERIES

This study was an open label clinical trial conducted at Rajalakshmi hospital, Bangalore on 15 patients from 26 April 2021 to 6 June 2021. The subjects were included based on the following criteria during screening and the study: age group of 18-65 years (Inclusive of both genders); diagnosed with 2 or more symptoms like indigestion, abdominal pain or cramps, nausea, vomiting, bloating, constipation, diarrhoea, changes in bowel habits, loss of appetite. The exclusion criteria were based on presence of any cardiovascular, renal, respiratory or any other chronic illness; pregnant or lactating females; allergy to test product; subject participating in a similar clinical study, currently or during the previous 90 days. Voluntary informed consent was obtained from all the participants for enrolment. After completing the screening based on inclusion and exclusion criteria, 15 subjects were taken for the test product of Neemint capsules of 500 mg which comprises of 350 mg of neem oil and 150 mg of peppermint oil as per each schedule visit (visit 1: day-7 to 0, visit 2: day 7±2, visit 3: day 14±2, visit 4: day 28±2).[17,18] No concomitant treatments were given along with study product.

Patient disposition, demographics and baseline characteristics

Total fifteen subjects were enrolled in the study and received treatments. Most of the subjects in this were males (86.6%), having the mean age of 35.2±14.2 years. All the subjects (100%) were having Asian ethnicity. The mean height and weight of the patients was 168.46±4.631 cm and 67.3±6.46 kg respectively. Among the total subjects 66.66% were married and 86.66% were living with family. The 33.3 percenatges and 13.33 percenatges of subjects were having the habit of smoking and drinking alcohol respectively. The 60% of the total subjects were degree holders where as 40% of the total subjects were having income more than one lakh and 53.3% of total subjects belonged to business class as shown in Table 1.

Vital signs of the subjects at the screening

The mean values of the vital signs at the time of screening were recorded. The mean temperature of the study participants at the time of screen was 36.92±0.38 °C, the mean blood pressure at screening visit was 127.2/81.3 mmHg, the mean respiratory rate and mean pulse rate at screening visit was 81.6±4.55 CPM and 18.2±0.54 bpm respectively.

Laboratory tests values at the screening

The mean laboratory values of the study subjects were recorded at the time of screening visit. All the mean baseline laboratory data was found to be normal (haemoglobin (g/dl)-13.87, neutrophil (%)-56.53, lymphocyte (%)-34.1, eosinophil (%)-4.13, monocytes (%)-5.4, RBC count (million/cumm)-4.64, platelet count (lakhs/cumm)-2.53, MCV (FL)-82.6, SGOT (U/l)-28.9, SGPT (U/l)-34, creatinine (mg/dl)-1.06, ESR (mm/hr)-24.2). No clinically significant differences were reported in analysis of laboratory values, vital signs and physical examination. Only the baseline sodium (134.3±0.37 mmol/l) and potassium (3.3±0.37 mmol/l) was found low (not clinically significant), which reached to the normal levels after the treatment course, and that was (137.5±1.70 mmol/l) as well as (4.06±0.31 mmol/l), respectively.

Primary outcome

There is 25.18, 45.32 and 65.46% decline in GI symptom (GSRS total score) after 1, 2 and 4 weeks of treatment period with Neemint capsules. The change in decline in GSRS scores was highly statistically significant ($p<0.00001$) at week 1, week 2 and week 4. The Table 2 represents the percentage decline in the mean GSRS variable scores of study subjects after the treatment with Neemint capsules for 4 weeks. The lowest percentage improvement is in the GSRS variable, passing of gas (50%), whereas the highest percentage improvement is in the GSRS variable, feeling full even long after you have stopped eating (73.02%). A significant decline in the mean GSRS score is seen in each evaluation visit which represents the overall effectiveness of the treatment of symptoms of IBS shown in Figure 1.

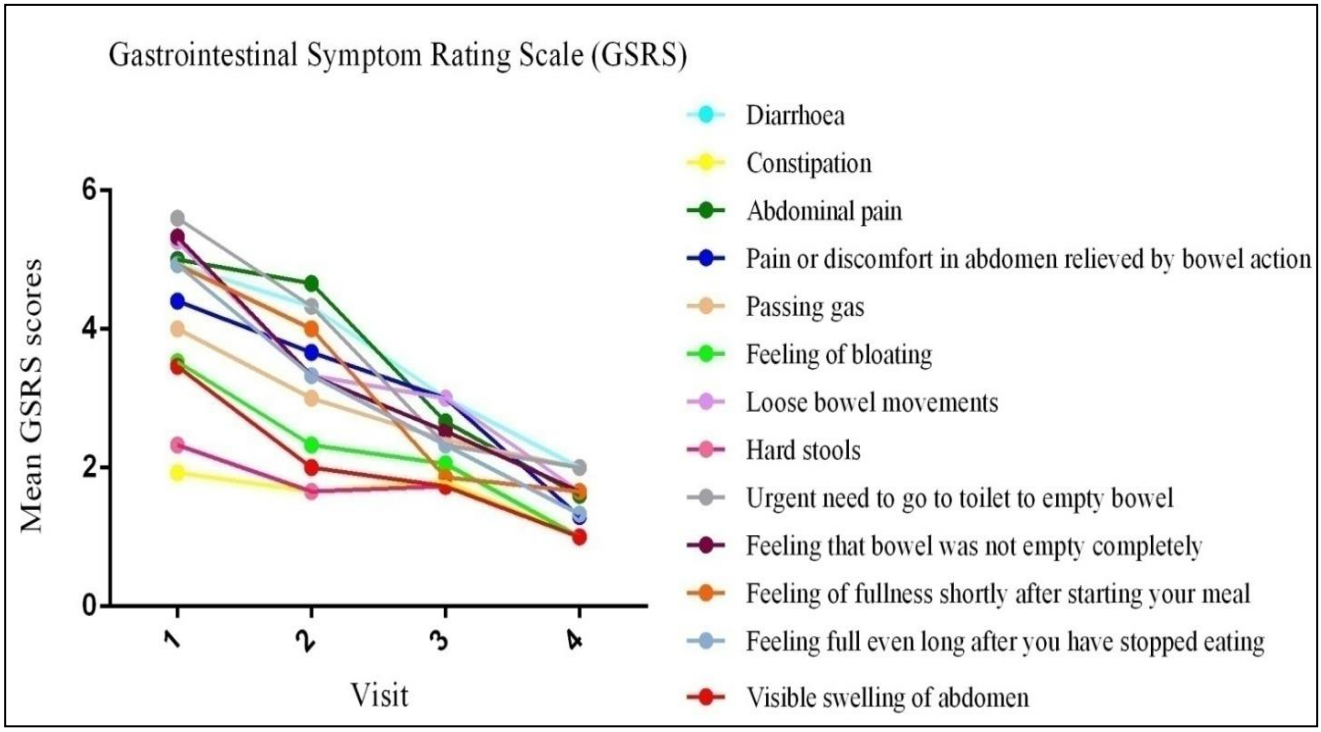

Figure 1: Represents the changes in the specific GSRS score during the course of treatment.

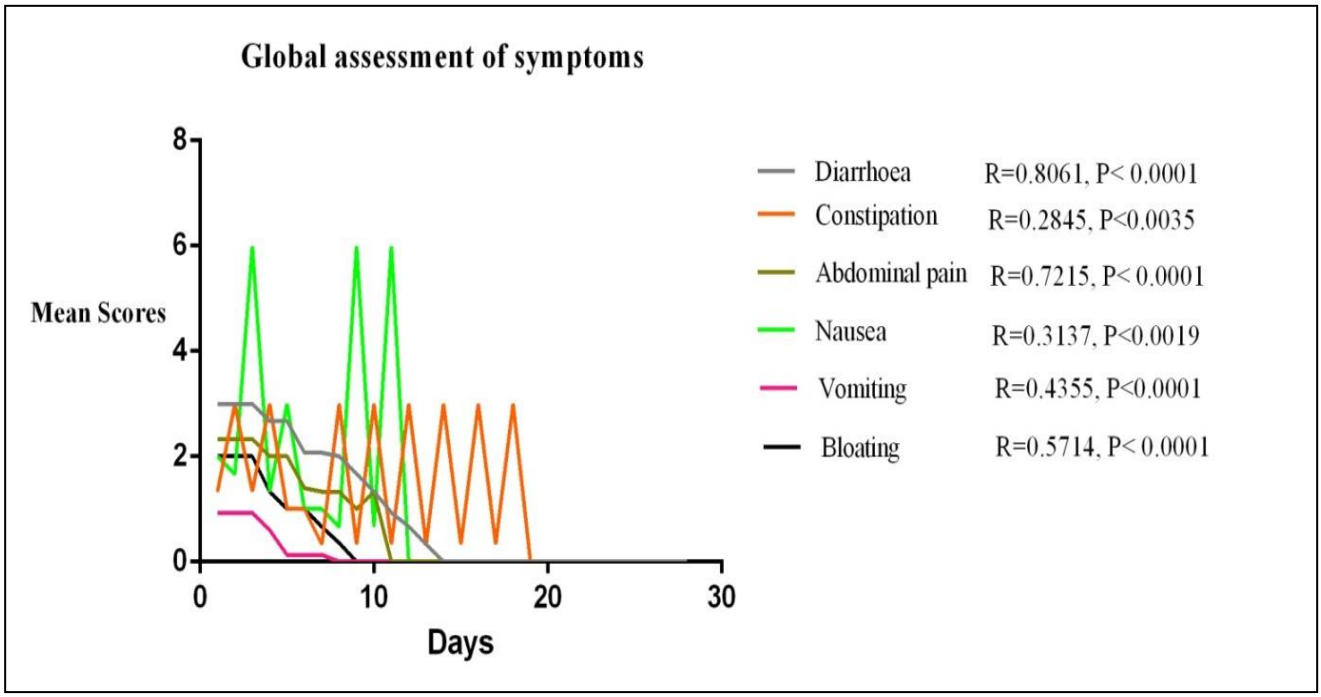

Figure 2: Global assessment of symptom before and after treatment with Neemint capsule for 28 days, (n=15).

Table 1: Baseline demographics details of all the study participants, (n=15).

Parameters	Subjects mean values (%)
Gender	
Male	13 (86.6)
female	5 (13.3)
Age (mean) (years)	35.2±14.2
Ethnicity	Asian (100)
Marriage	
Yes	10 (66.6)
No	5 (33.3)
Living with family	
Yes	13 (86.6)
No	2 (13.3)
Smoker	
Yes	5 (33.3)
No	10 (66.6)
Alcohol abuse	
Yes	2 (13.3)
No	13 (86.6)
Income status (INR)	
0-10000	4 (26.6)
20000-30000	1 (6.66)
30000-40000	1 (6.66)
50000-100000	3 (20)
>100000	6 (40)
Education	
High school	3 (20)
Intermediate	2 (13.3)
Degree	9 (60)
Masters	1 (6.66)
Occupation	
Labourer	1 (6.66)
High school	0 (0)
Intermediate	4 (26.6)
Degree	2 (13.3)
Business	8 (53.3)
Height (cm)	168.46±4.631
Weight (kg)	67.3±6.46
BMI (kg/m^2)	23.7±2.23

Table 2: Percentage improvement in the mean GSRS scores of study subjects after the treatment with Neemint capsules.

GSRS variables	Mean GSRS score at baseline	Mean GSRS score at visit 4	Percentage change in mean GSRS score
Diarrhoea	4.93	2	59.43
Constipation	1.93	1	48.1
Abdominal pain	5	1.6	68
Pain or discomfort in abdomen relieved by bowel action	4.4	1.3	70.45
Passing gas	4	2	50
Feeling of bloating	3.53	1	71.67
Loose bowel movements	5.26	1.66	68.44
Hard stools	2.33	1	57
Urgent need to go to toilet to empty bowel	5.62	2	64.2
Feeling that bowel was not empty completely	5.33	1.66	68.8
Feeling of fullness shortly after starting your	4.93	1.66	66.32

Continued.

GSRS variables	Mean GSRS score at baseline	Mean GSRS score at visit 4	Percentage change in mean GSRS score
meal			
Feeling full even long after you have stopped eating	4.93	1.33	73.02
Visible swelling of abdomen	3.46	1	71.09

Table 3: IBS quality of life scores, (n=15).

Subject no.	Total baseline scores	Baseline scores on (0-100) scale	Total scores at visit 4	Scores on (0-100) at visit 4
1	104	48.52941	41	94.85294
2	138	23.52941	44	92.64706
3	138	23.52941	42	94.11765
4	125	33.08824	47	90.44118
5	125	33.08824	47	90.44118
6	134	26.47059	41	94.85294
7	122	35.29412	47	90.44118
8	125	33.08824	47	90.44118
9	104	48.52941	45	91.91176
10	137	24.26471	44	92.64706
11	104	48.52941	41	94.85294
12	138	23.52941	44	92.64706
13	104	48.52941	42	94.11765
14	125	33.08824	47	90.44118
15	104	48.52941	41	94.85294
Mean	121.8	35.44118	44	92.64706

Secondary outcome

IBS-QOL mean data obtained at baseline (visit 1) was 35.41±10.032 and at the last evaluation visit (visit 4) was 92.647±1.8011. It was observed that there was a significant change in the quality of life of all the subjects and the level of significance p<0.00001 with 64.23% score improvement. Individual subjects IBS quality of life scores as shown in Table 3.

Global assessment of symptoms

It was observed that there was a significant decline in the intensity of symptoms (Diarrhoea, constipation, abdominal pain, nausea, vomiting, bloating) at the 4th evaluation visit at the level of significance (p value) when treated with Neemint capsules shown in Figure 2.

Safety evaluation

Adverse event

No serious adverse events reported during whole study.

DISCUSSION

Irritable bowel syndrome is a gastrointestinal disease whose symptom may vary in patients from mild to severe.[19] The disease defined by recurrent attacks of abdominal pain, feelings of distension, and changed bowel habits.[20,21] IBS is highly prevalent in age group of 26-55 years.[22] The treatment for IBS considered in terms of dietary habits and drug therapy.[23] Peppermint oil reported as a safe treatment for relieving the symptoms in IBS due to anti-inflammatory, antimicrobial, antioxidant, anti-spasmotic and anaesthetic properties.[24,25] It is also helpful in patients with function dyspepsia due to anti emetic properties.[26] Neem extract has anti-inflammatory properties and help in relieving stomach infections and other digestive disorders by improving gut flora.[27] Neem shows anti-ulcer effect and is more effective than Ranitidine but less effective than omeprazole.[28] In our study we combine both the therapeutic properties of neem and peppermint oil in form of Neemint capsules for treating gastrointestinal disorders. The study was conducted among 18-45 years of the age group of either gender. Our results demonstrated that Neemint capsules was highly efficacious in the treatment of IBS and GI symptoms and it is also well-tolerated and safe in study subjects (n=15) having complaints of IBS and GI disturbances. The study was conducted over one month. A significant decline was seen in the mean GSRS score in each evaluation visit of study subjects, which was 55.6±5.1 at baseline and reached 19.2±2.48 at the end of the trial. The overall GSRS score improvement was found 64.23%. No serious adverse effects were found. The IBS-QOL scores also indicated remarkable improvement in the quality of life of the study subject. The IBS-QOL scores also indicated remarkable improvement in the quality of life of the study subject.

The baseline IBS-QOL mean scores were 35.41±10.032 whereas, the 4th visit it was observed to be 92.647±1.8011, which indicates that there was an increase of 57.2% in quality of life of the subjects, and the results were significant at $p<0.05$, where, the calculated level of significance was<0.00001. The respective mean of global assessment score at day 1 for diarrhoea, constipation, abdominal pain, nausea vomiting and bloating symptom were 3, 1.33, 2.33, 2, 0.93, and 2. All the symptoms were resolved at day 14 and the mean global assessment score was 0 for all the above-mentioned symptoms at EOT. The present studies showed superior results as compared to the previous studies. And, hence the Neemint capsules can be used as an effective and safer option for the treatment for patients with complaints of inflammatory bowel syndrome and other abdominal distensions.

CONCLUSION

The study accomplished the goal of Neemint capsules which shown huge improvements in subsiding symptoms and proven to be safe and effective as a treatment for gastrointestinal disorder.

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Conflict of interest: None declared
Ethical approval: Not required

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