

**AN OPEN LABEL, PHASE II, CLINICAL TRIAL OF CARMINO SOFTGEL CAPSULES IN THE TREATMENT OF PATIENTS WITH ABDOMINAL COLIC AND FLATULENCE.**Tripathi A<sup>1</sup> Joshi Ramchandra<sup>2</sup><sup>1</sup> Consultant, Life Veda Treatment and Research Center, Mumbai - 30. Maharashtra.<sup>2</sup> Consultant Pharmacologist, 14 Shiv Shanti, Juhu Versova Link Road, Andheri (west), Mumbai - 53. Maharashtra**ABSTRACT**

*Abdominal colic is a commonly encountered syndrome of gut and many therapeutic interventions based on 'gut hypotheses have been studied. But, there is no clinically effective and safe medication in the management of abdominal colic and flatulence. This study was planned to evaluate the clinical efficacy and safety of **Carmino softgel capsules** in abdominal colic.*

*All patients of age more than 18 years and suffering from abdominal colic and flatulence were included in the study and patients having severe vomiting and constipation were excluded from the study. All patients were divided into 3 groups: group A included patients with abdominal colic, group B included patients with flatulence and group C included patients with overlapping symptoms of colic and flatulence. All patients were followed up on day 4 and day 6. At each follow-up visit, symptomatic evaluation and clinical examination was done, along with recording the occurrence of any adverse events. The predefined primary end points were rapid symptomatic relief and the predefined secondary endpoints were short- and long-term safety, and overall compliance to the drug treatment.*

*A total of 98 patients were enrolled for the trial and 2 patients were lost to follow-up. There were 35 patients in group A, 30 patients in group B and 31 patients in group C. A significant symptomatic relief from abdominal colic and flatulence was observed in all patients. There were no clinically significant adverse events; either reported or observed during the entire study period. Therefore, it may be concluded that **Carmino softgel capsules** are clinically safe and effective in management of abdominal colic.*

**Key words:** Abdominal colic, Flatulence, Safety and efficacy.

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## INTRODUCTION

Abdominal colic is a commonly encountered syndrome occurring in all age. Severe abdominal pain caused by spasm, obstruction, or distention of any of the hollow viscera, such as the intestines. Chronic abdominal pain is due to various conditions but it is commonly seen due constipation or IBS. Abdominal pain affects 14.7% of the U.S. population,<sup>1</sup> specifically 16% of children<sup>2</sup> and 15 to 50% of the elderly,<sup>3</sup> and it is more common in women than in men.<sup>4</sup> Patients associate abdominal pain and flatulence show several symptoms: infrequent bowel movements, bloating and abdominal discomfort.<sup>5</sup> Health-related quality of life is negatively affected by the presence of chronic flatulence and by its severity. Reduced colonic motility is one of the pathophysiological mechanisms in severe chronic abdominal pain.<sup>5</sup>

There is insufficient evidence from randomized, controlled trials to assess the long-term effectiveness and side-effect profile of laxatives in patients with severe chronic abdominal discomfort.<sup>9,10,11</sup> In recent years, dicycloamine and the nonselective serotonin 5-hydroxytryptamine<sub>4</sub> (5-HT<sub>4</sub>) receptor agonist tegaserod and the chloride-channel activator lubiprostone have been used in the to treat chronic abdominal discomfort and pain.<sup>12,13</sup>

The synthetic drugs results in various adverse effects and in some cases they may lead to habituation therefore, alternative herbal remedies are studied all over the world to explore the better therapeutic efficacy and safety. In this clinical trial we aimed to study the safety and efficacy of Carmino Softgel capsules in abdominal colic and flatulence.

Carmino softgel capsules is a polyherbal formulation.

### Each Soft gelatin capsule contains:

Mentha oil	(Mentha piperata)	100.00 mg
Nutmeg oil	(Myristica fragrans)	10.00 mg
Ajwain oil	(Carum copticum)	5.00 mg
Hing	(Ferula asafoetida)	1.00 mg
Ginger oil	(Zingiber officinale)	0.02 mg

This study was planned to evaluate the clinical efficacy and safety of **Carmino softgel capsules** in abdominal colic.

### Aim of the study

The study was aimed to evaluate the clinical efficacy and safety (short- and long-term) of Carmino softgel capsules in patients suffering from abdominal colic and flatulence.

### Study design

The study was an open, non-randomized and non-comparative, phase II clinical trial, conducted at Life Veda Treatment and Research Center, Mumbai.

## MATERIALS AND METHODS

### Inclusion criteria

Patients of both sex and age more than 18 years, suffering from abdominal colic with associated spasmodic abdominal pain and gripping, bloating of abdomen were included in the study.

### Exclusion criteria

Patients having severe vomiting and severe constipation, and those suffering with severe systemic disease were excluded from the study.

### Study procedure

The patients were informed about the study drug, its effects, patient's duration of stay in the trial and overall plan of the study. The history was noted by interviewing the patients. Thorough clinical examination was carried out and the details were noted down in the CRF. All the patients were divided into 3 groups: group A included patients with abdominal colic, group B included patients with flatulence and group C included all other remaining patients with overlapping symptoms of colic and flatulence. The stool sample collected from each patient was examined for routine and microscopic laboratory examination. Patients were advised to administer the drug in the following dosage: 2 Capsule twice a day just before meals.

All patients were followed up on day 4 and day 6. At each follow-up visit, symptomatic evaluation and clinical examination was done, alongwith recording the occurrence of any adverse events (either reported or observed).

**Primary and secondary endpoints**

The predefined primary end points were rapid symptomatic relief from abdominal colic and flatulence. The predefined secondary endpoints were short- and long-term safety, and overall compliance to the drug treatment.

**Adverse events**

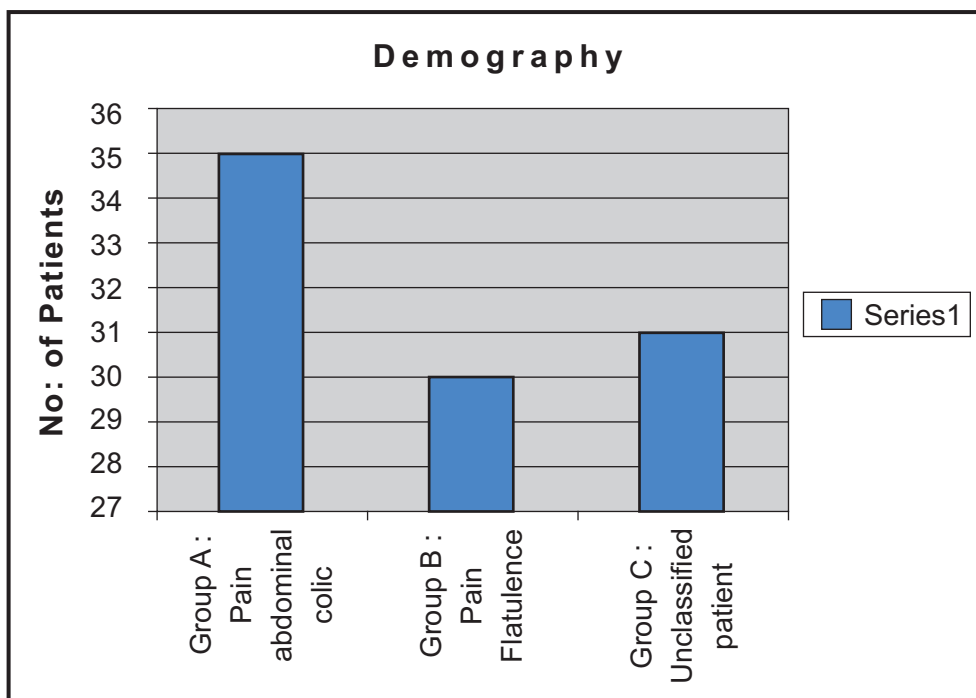
All adverse events, either reported or observed were recorded in the CRF with information about severity, onset, duration and action taken regarding the study drug. Relation of adverse events to the study medication was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), “Possible” (follows a known response pattern

to the suspected drug, but could have been produced by the patient's clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient's clinical state). Patients were allowed to voluntarily withdraw from the study, if they experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for non-compliance were noted.

**RESULTS**

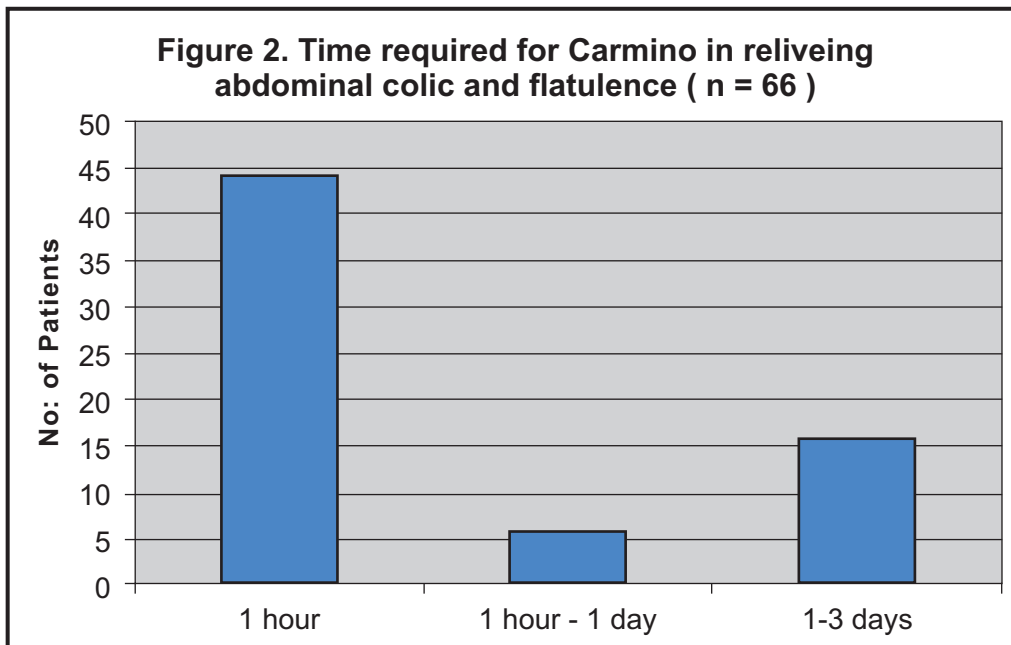
A total of 98 patients were enrolled for the trial and 2 patients were lost to follow-up. There were thirty six percent (36%) patients in group A, thirty one percent (31%) patients in group B and Thirty three percent (33 %) patients in group C. (Figure 1).

**Figure 1: Distribution of patients in different groups**



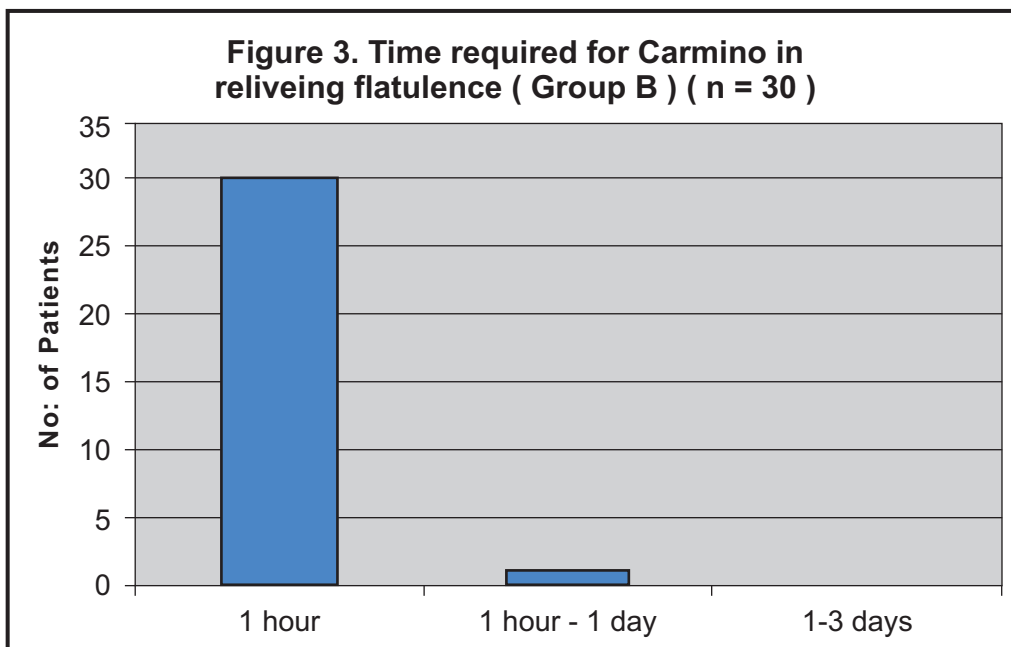
In 44 patients, the symptomatic relief was evident in less than an hour, in 7 patients, the relief was within a day and in 16 patients the relief was recorded within 3 days (Figure 2).

**Figure 2: Time required for Carmino softgel capsules in relieving abdominal colic (Group A) (n=66)**



There was a total relief observed in all patients suffering from flatulence and 30 patients had symptomatic relief in less than an hour, while 1 patient had symptomatic relief in a day's time (Figure 3).

**Figure 3: Time required for Carmino softgel capsules in relieving flatulence (Group B) (n=30)**



There were no clinically significant adverse events; either reported or observed during the entire study period.

## DISCUSSION

Despite years of research, the etiology of abdominal colic still remains unclear. Various researchers have hypothesized different etiologies. The 'gut hypothesis' emphasizes that abdominal colic might be due to some problem with the gut and excessive. Various chemical agents in the tissues activate primary afferent nociceptors like bradykinins, PGs, leukotrienes, histamine, slow-release substance of anaphylaxis, substance P and NO. Simple abdominal colic often results from indigestible material in the alimentary tract leading to spasmodic contractions in the muscular linings. Flatulence and constipation with accumulation of fecal matter may result in abdominal colic. Biliary, renal and uterine colic is caused by the spasmodic contractions of the smooth muscles<sup>14</sup>.

This clinical study observed a significant symptomatic relief from abdominal colic and flatulence in all the patients included in the study. The symptomatic relief was evident in less than an hour in majority patients, while almost all were relieved within a day. Total relief was observed in all patients suffering from bloating. There were no clinically significant adverse events; either reported or observed during the entire study period.

A Carmino softgel capsule has a non-specific antispasmodic activity. Peppermint oil have spasmolytic activity and used in irritable bowel syndrome.<sup>15</sup> It is also having antimicrobial action.<sup>16</sup> Carum copticum shows analgesic, antispasmodic and antioxidant activity.<sup>17</sup> Zingiber officinale credited for antispasmodic, analgesic, antiinflammatory and antioxidant activities. The active ingredients of Zingiber officinale are gingerols and diarylheptanoids<sup>18, 19</sup>. Zingiber officinale is proven to be effective in inhibiting the gastric and intestinal motility and also has been found to inhibit the colonic motility in vitro<sup>20</sup>. Zingiber officinale was proven effective in inhibiting the intestinal, gastric, and colonic motility and the spasmolytic activity of Zingiber officinale might be attributed to gingerol that was found to inhibit PG biosynthesis and serotonergic activity<sup>21</sup>.

Zingiber officinale has inhibitory effects on COX-1 and -2 enzymes<sup>22</sup> and the mechanism of action is hypothesized to be due to the attenuation of COX-1 and -2 (regulated by the eukaryotic transcription factor NF-kappaB) and thromboxane-synthase enzymatic activity<sup>23</sup>. The [6]-gingerol of Zingiber officinale acts by interfering with intracellular signaling cascades, those involving NF-kappaB and mitogen-activated protein kinases<sup>24</sup>. Thomson et al. documented significant inhibitory effects of Zingiber officinale extract on PG-E2 production<sup>25</sup>.

Ahmed et al., observed that the antioxidant effect of Zingiber officinale extract was comparable to ascorbic acid as demonstrated by lowered lipid peroxidation, while maintaining the activities of other antioxidant enzymes (superoxide dismutase, catalase and glutathione peroxidase)<sup>26</sup>. Therefore, the observed clinical benefits of Carmino softgel capsules might be due to the synergistic actions of its ingredients.

Nutmeg acts as antibacterial. Ferula asafoetida gum extract interfere with a variety of muscarinic, adrenergic and histaminic receptor activities or with the mobilisation of calcium ions required for smooth muscle contraction non-specificly. Thus acts as an antispasmodic and anti-inflammatory.

## CONCLUSION

This clinical study observed a significant symptomatic relief from abdominal colic and flatulence in all the patients. The symptomatic relief was evident in less than an hour in majority of the patients, while almost all were relieved within a day. Total relief was observed in all patients suffering from abdominal colic and bloating. There were no clinically significant adverse events; either reported or observed during the entire study period. Therefore, it may be concluded that Carmino softgel capsules is clinically safe and effective in management of abdominal colic and flatulence.

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