

# Letter: the neglected analgesic properties of red pepper in the clinical management of the irritable bowel syndrome pain - Authors' reply

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## Letter: the neglected analgesic properties of red pepper in the clinical management of the irritable bowel syndrome pain—Authors' reply

EDITORS,

We thank Professor Bortolotti for his interest in our recently published review article.<sup>1,2</sup> We agree that local desensitization techniques using TRP channel agonists hold promise as a treatment for irritable bowel syndrome (IBS). As such, the use of enteric-coated pills containing red pepper has the potential to be efficacious in IBS by ensuring sufficient amounts of capsaicin to be present in the distal intestine for desensitization of the local afferent nerves. Indeed, Bortolotti et al demonstrated a significant decrease in pain scores following 6-week administration of enteric-coated capsules with red pepper, albeit not significantly different when comparing to placebo treatment.<sup>3</sup> Although increased local exposure of the more distal gastrointestinal tract to capsaicin can promote desensitization, it also has the potential to initially elicit a pain response as a result of excitation of TRPV1-positive afferents. As observed in the trial by Bortolotti et al,<sup>3</sup> 14 of 23 patients (61%) receiving enteric-coated capsules with red pepper had to either discontinue treatment due to severe abdominal pain or were required to halve their dose for

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the same reason. Previous studies using an acute challenge with capsaicin in IBS have demonstrated increased perceptive responses,<sup>4</sup> in particular in patients with visceral hypersensitivity.<sup>5</sup> In our opinion, this limits the applicability of encapsulated red pepper for IBS in clinical practice. Using a comparable approach, however, we are currently investigating the efficacy of treatment of IBS symptoms with a novel colon-targeted-delivery capsule containing peppermint oil (Clinicaltrials.gov ID: NCT02716285). Peppermint oil has already shown to be effective in IBS in various small trials and is thought to exert its effects via TRPM8 on sensory afferents.<sup>6</sup> A recent trial using a sustained small-bowel delivery formulation of peppermint oil has also shown promising results after 4 weeks of treatment.<sup>7</sup> Good quality evidence from a large randomized controlled trial is still lacking, however. In addition to filling this gap, we aim to enhance pain reduction by specifically targeting the colon. In our study, we compare the newly formulated peppermint oil capsules, releasing their contents in the colon in a pulsatile fashion, with placebo as well as with the currently marketed enteric-coated capsules that release the

oil in the small intestine. As peppermint oil is assumed to provide antinociceptive effects through activation of TRPM8 and subsequent inhibition of TRPV1 and TRPA1,<sup>8</sup> it is less likely to evoke an initial pain response. Other adverse effects, including peri-anal burning due to local actions of peppermint oil, are expected to be mild. We therefore believe that peppermint oil is the more attractive alternative for desensitization therapy in IBS, as opposed to red pepper.

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The authors' declarations of personal and financial interests are unchanged from those in the original article.<sup>2</sup>

## AUTHORSHIP

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