

**Reviewed by 02441672**

This study is relevant, interesting, is written in suitable English, and has a correct methodological design. It is important to emphasize the contribution that this study provides for integration between western and eastern medicine, which is fundamental to the advancement of modern science. I suggest that could be added to introduction one or two paragraphs about the effects of prokinetic consolidated in gastroenterology clinic daily.

Response) We added the effects of prokinetic consolidated in gastroenterology clinic daily in Introduction Part.

Prokinetic agents are medications that enhance coordinated GI motility and the transit of content in the GI tract mainly by amplifying and coordinating the GI muscular contractions. In addition, prokinetic therapy should be considered as a means to improve gastric emptying and symptoms of gastroparesis, balancing the benefits and risks of treatment<sup>[4]</sup>. Recently, prokinetic therapy has been shown to improve the symptoms and quality of life in patients with GI motility disorders<sup>[5]</sup>. Therefore, there has been an increasing need to develop safer and more effective gastroprokinetic agents.

In the discussion, I also consider that it's necessary to compare the results of this study those with the known effects of the prokinetics used in western medicine .

Response) We added the explanations in Discussion Part.

Prokinetic drugs, which enhance GI motor function by acting on a variety of neurotransmitter receptors, have been used to treat patients with GI motility disorders<sup>[30]</sup>, and are regarded as one of the most efficacious therapeutics for this disorder<sup>[31,32]</sup>. Cholinergic agonists, the original promotility agents, stimulated muscarinic M<sub>2</sub>-type receptors on the smooth muscle cells, but their effectiveness in motility disorders is inconsistent<sup>[33]</sup>. Metoclopramide and domperidone, dopamine antagonists, have been the most widely used as prokinetic agents<sup>[34]</sup>, but their long-term use has been complicated by a trend toward tolerance and a significant incidence of central nervous system (CNS) side effects<sup>[35]</sup>. Cisapride was shown to promote esophageal peristalsis, augment lower esophageal sphincter pressure and accelerate gastric emptying<sup>[36]</sup>. However, the use of this drug is now restricted due to serious cardiac arrhythmias related to prolonged QT interval<sup>[37]</sup>. Mosapride, a selective 5-HT<sub>4</sub> agonist, is available as a prokinetic agent in a number of Asian countries, but the efficacy data are contradictory<sup>[38]</sup>. Itopride is a dopamine D<sub>2</sub> antagonist with prokinetic effects that is devoid of CNS or cardiovascular side effects and causes minimal elevations of prolactin levels<sup>[39]</sup>. In this study, we did not directly compare the GE and intestine motility rates with these prokinetics agents. However, in a previous study, we showed that the Lizhong Tang depolarized the pacemaker potentials through G-protein, PLC and Ca<sup>2+</sup> dependent pathways. Moreover, the nonselective cationic cation channel was involved in these effects<sup>[6]</sup>. Therefore, we believe that Lizhong Tang might mimic the major excitatory neurotransmitters of the GI tract and act as a gastroprokinetic agent. Additionally, herbal products may be an attractive alternative based on the perception of their 'natural' approach and their low risk of side effects<sup>[40]</sup>. Therefore, we believe that Lizhong Tang may be a good gastroprokinetic agent, and in the future, we should compare the experimental results with those of known prokinetics and analyze the side effects.

**Reviewed by 03474649**

Generally, the manuscript is interesting and handling important topic. The English level is quite well. Briefly, the authors should avoid self plagiarism especially in method section.

Response) We checked by native and *CrossCheck* analysis and corrected. Also, we rechecked the method section.

The discussion section is inadequate and should be written again. The authors should focus more on

its findings not previous report so much. It should be discussed in more detail with the published literature and other proposed substances.

Response) We wrote again and added in more detail with the published literature and other proposed substances in the Discussion Part.

**Reviewed by editor**

[A1] Please provide the grant application form(s). If you can't provide it, please delete this part.

Response) We attached the grant application form.

[A2] Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s). For manuscripts supported by various foundations (i.e., charitable, not-for-profit organizations), the authors should provide a copy of the full approved grant application form(s) or funding agency copy of any approval document(s)/letter(s), consisting of the information section and body section in PDF format. The approved grant application form(s) or funding agency copy of any approval document(s)/letter(s) will be released online together with the manuscript in order for readers to obtain more information about the study and to increase the likelihood of subsequent citation.

Response) We attached the grant application form.

[A3] Please write the COMMENTS section at here. See the format in the Format.

Response) We checked the COMMENTS section.

[A4] An informative, structured abstracts of no less than 200 words should accompany each manuscript. Abstracts for original contributions should be structured into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim as the form of "To investigate/study/..."; METHODS (no less than 140 words); RESULTS (no less than 150 words): You should present  $P$  value where necessary and must provide relevant data to illustrate how it is obtained, e.g.  $6.92 \pm 3.86$  vs  $3.61 \pm 1.67$ ,  $P < 0.001$ ; CONCLUSION (no more than 26 words, in a definite, conclusive, and short statement, not indefinite, vague, or suggestive sentences).

Response) We wrote again the Abstract Part.