

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2021 December 7; 27(45): 7739-7865



**EDITORIAL**

- 7739 Orosomuroid in liver diseases  
*Elpek GO*

**FRONTIER**

- 7748 Novel frontiers of agents for bowel cleansing for colonoscopy  
*Di Leo M, Iannone A, Arena M, Losurdo G, Palamara MA, Iabichino G, Consolo P, Rendina M, Luigiano C, Di Leo A*
- 7771 Chronic rejection after liver transplantation: Opening the Pandora's box  
*Angelico R, Sensi B, Manzia TM, Tisone G, Grassi G, Signorello A, Milana M, Lenci I, Baiocchi L*

**OPINION REVIEW**

- 7784 Humans have intestinal bacteria that degrade the plant cell walls in herbivores  
*Fujimori S*

**MINIREVIEWS**

- 7792 Gut microbiome in allogeneic hematopoietic stem cell transplantation and specific changes associated with acute graft *vs* host disease  
*Le Bastard Q, Chevallier P, Montassier E*

**ORIGINAL ARTICLE****Clinical and Translational Research**

- 7801 MicroRNAs expression influence in ulcerative colitis and Crohn's disease: A pilot study for the identification of diagnostic biomarkers  
*Quaglio AEV, Santaella FJ, Rodrigues MAM, Sasaki LY, Di Stasi LC*

**Observational Study**

- 7813 Multimodality management of gallbladder cancer can lead to a better outcome: Experience from a tertiary care oncology centre in North India  
*Goel S, Aggarwal A, Iqbal A, Talwar V, Mitra S, Singh S*
- 7831 In-hospital mortality of hepatorenal syndrome in the United States: Nationwide inpatient sample  
*Kaewput W, Thongprayoon C, Dumancas CY, Kanduri SR, Kovvuru K, Kaewput C, Pattharanitima P, Petnak T, Lertjitbanjong P, Boonpheng B, Wijarnpreecha K, Zabala Genovez JL, Vallabhajosyula S, Jadowiec CC, Qureshi F, Cheungpasitporn W*

**CASE REPORT**

- 7844** Clinical presentation of gastric Burkitt lymphoma presenting with paraplegia and acute pancreatitis: A case report

*Lin Y, Pan YH, Li MK, Zong XD, Pan XM, Tan SY, Guo YW*

**LETTER TO THE EDITOR**

- 7855** SARS-CoV-2 infection in people with pre-existing liver disease: Further research is warranted

*Verma HK, Bhaskar L*

- 7859** Therapeutic potentials of fasudil in liver fibrosis

*Xi Y, Xu PF*

- 7862** Diagnostic biomarkers for pancreatic cancer: An update

*Yang M, Zhang CY*

**ABOUT COVER**

Editorial Board Member of *World Journal of Gastroenterology*, Oscar Teramoto-Matsubara, MD, AGAF, FACG, FACP, Associate Specialist, Department of Gastroenterology, ABC Medical Center, Mexico City 11000, Mexico. teramotomd@prodigy.net.mx

**AIMS AND SCOPE**

The primary aim of *World Journal of Gastroenterology* (WJG, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

**INDEXING/ABSTRACTING**

The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Report® cites the 2020 impact factor (IF) for WJG as 5.742; Journal Citation Indicator: 0.79; IF without journal self cites: 5.590; 5-year IF: 5.044; Ranking: 28 among 92 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2020 is 6.9 and Scopus CiteScore rank 2020: Gastroenterology is 19/136.

**RESPONSIBLE EDITORS FOR THIS ISSUE**

Production Editor: *Ying-Yi Yuan*; Production Department Director: *Xiang Li*; Editorial Office Director: *Ze-Mao Gong*.

**NAME OF JOURNAL**

*World Journal of Gastroenterology*

**ISSN**

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

**LAUNCH DATE**

October 1, 1995

**FREQUENCY**

Weekly

**EDITORS-IN-CHIEF**

Andrzej S Tarnawski, Subrata Ghosh

**EDITORIAL BOARD MEMBERS**

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

**PUBLICATION DATE**

December 7, 2021

**COPYRIGHT**

© 2021 Baishideng Publishing Group Inc

**INSTRUCTIONS TO AUTHORS**

<https://www.wjgnet.com/bpg/gerinfo/204>

**GUIDELINES FOR ETHICS DOCUMENTS**

<https://www.wjgnet.com/bpg/GerInfo/287>

**GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH**

<https://www.wjgnet.com/bpg/gerinfo/240>

**PUBLICATION ETHICS**

<https://www.wjgnet.com/bpg/GerInfo/288>

**PUBLICATION MISCONDUCT**

<https://www.wjgnet.com/bpg/gerinfo/208>

**ARTICLE PROCESSING CHARGE**

<https://www.wjgnet.com/bpg/gerinfo/242>

**STEPS FOR SUBMITTING MANUSCRIPTS**

<https://www.wjgnet.com/bpg/GerInfo/239>

**ONLINE SUBMISSION**

<https://www.f6publishing.com>

## Therapeutic potentials of fasudil in liver fibrosis

Yue Xi, Peng-Fei Xu

**ORCID number:** Yue Xi [0000-0003-1265-6624](https://orcid.org/0000-0003-1265-6624); Peng-Fei Xu [0000-0001-6854-6040](https://orcid.org/0000-0001-6854-6040).

**Author contributions:** Xu PF designed the framework and supervised the preparation; both authors have wrote the letter, prepared the figures, read and approved the final letter.

**Conflict-of-interest statement:** The authors declare that they have no conflict of interest.

**Country/Territory of origin:** United States

**Specialty type:** Gastroenterology and hepatology

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review report's scientific quality classification**

Grade A (Excellent): 0  
Grade B (Very good): B  
Grade C (Good): 0  
Grade D (Fair): 0  
Grade E (Poor): 0

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution

**Yue Xi, Peng-Fei Xu**, Center for Pharmacogenetics and Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA 15261, United States

**Corresponding author:** Peng-Fei Xu, PhD, Academic Research, Postdoctoral Fellow, Research Associate, Center for Pharmacogenetics and Department of Pharmaceutical Sciences, University of Pittsburgh, 323 Salk Pavilion, 335 Sutherland Drive, Pittsburgh, PA 15261, United States. [pex9@pitt.edu](mailto:pex9@pitt.edu)

### Abstract

Fasudil has the potential to prevent liver fibrosis by activating natural killer cells and inhibiting the proliferation of hepatic stellate cells. Fasudil may be a promising clinical therapeutic drug for the prevention and treatment of liver fibrosis.

**Key Words:** Fasudil; Liver fibrosis; Natural killer cell; Hepatic stellate cell; Clinical therapeutic drug

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core Tip:** This letter to the editor is to supplement the ongoing discussion on the therapeutic potentials of Fasudil in the treatment of hepatic fibrosis. Fasudil is potential for the treatment of liver fibrosis through activating natural killer cells and inhibiting the proliferation of hepatic stellate cells. Fasudil, a vasodilator used in clinical treatment of cerebral vasospasm, exhibits the protective and therapeutic effect on liver fibrosis.

**Citation:** Xi Y, Xu PF. Therapeutic potentials of fasudil in liver fibrosis. *World J Gastroenterol* 2021; 27(45): 7859-7861

**URL:** <https://www.wjgnet.com/1007-9327/full/v27/i45/7859.htm>

**DOI:** <https://dx.doi.org/10.3748/wjg.v27.i45.7859>

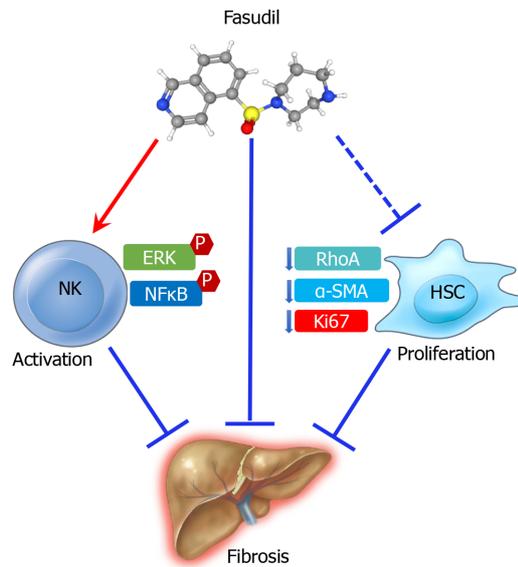
### TO THE EDITOR

We read with great interest the recent basic study by Han *et al*[1], that reported Fasudil, a potent RhoA/ROCK inhibitor and vasodilator, prevents and treats liver fibrosis and liver injury. They found Fasudil alleviates thioacetamide (TAA)-induced liver fibrosis in mice. The anti-fibrotic phenotypic exhibition of Fasudil is impressive.

NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Received:** July 4, 2021  
**Peer-review started:** July 4, 2021  
**First decision:** August 8, 2021  
**Revised:** August 11, 2021  
**Accepted:** November 24, 2021  
**Article in press:** November 24, 2021  
**Published online:** December 7, 2021

**P-Reviewer:** Zhang J  
**S-Editor:** Wang LL  
**L-Editor:** A  
**P-Editor:** Wang LL



**Figure 1** Schematic illustration depicting that fasudil prevents and treats liver fibrosis by activating natural killer cells and inhibiting hepatic stellate cells proliferation. NK: Natural killer; HSCs: Hepatic stellate cells.

Hepatic fibrosis is the formation of scar tissue in response to chronic liver damage, such as chronic hepatitis and hepatic steatosis[2]. Currently, there is no pharmacotherapy available approved by Food and Drug Administration (FDA) in the treatment of liver fibrosis[3]. Fasudil has been approved in Japan and China for the prevention of artery tightening and ischemia caused by cerebral vasospasm and pulmonary hypertension[4]. Due to its safety and efficacy, Fasudil might be a promising clinic agent for the prevention and treatment of liver fibrosis.

Hepatic stellate cells (HSCs) and natural killer (NK) cells play key roles in the pathogenesis of liver fibrosis. They isolated NK cells from mice treated with vehicle, TAA, or TAA and Fasudil and treated the NK-92 cells with different concentrations of Fasudil. These results showed that Fasudil robustly promotes NK cell activation. When discussing the effect of Fasudil on HSCs, they used human stellate cell line LX2 cells and observed that Fasudil directly induces apoptosis and inhibits the proliferation of LX2 cells. LX2 cell is indeed a model for the study of HSC activation. But to investigate HSCs activation, the model of primary HSCs subjected to culture activation and LX2 cells subjected to the stimulation of the potent profibrogenic cytokine transforming growth factor-beta 1 (TGF-β1) and then treated with the drugs under study are more widely accepted. Here, the authors proposed that Fasudil inhibited liver fibrosis by blocking HSCs activation by directly using the LX2 cells treated with Fasudil, which is far-fetched and hard to interpret. As primary HSCs are activated by prolonged culture, HSCs isolated from human or mouse livers and treated with the studied drug may be a more comprehensive approach to evaluate HSC activation.

Other studies also showed that Fasudil has anti-fibrotic phenotypic exhibition in rat models of hepatic fibrosis, such as Fasudil alleviated hepatic fibrosis in type 1 and 2 diabetic rats and carbon tetrachloride (CCl<sub>4</sub>)-induced rat liver injury[5-7]. Combined with these studies, we proposed that Fasudil is potential for the treatment of liver fibrosis through multitargeted effects, as outlined in Figure 1. Taken together, Fasudil is a promising medication for the prevention and treatment of liver fibrosis.

## REFERENCES

- Han QJ**, Mu YL, Zhao HJ, Zhao RR, Guo QJ, Su YH, Zhang J. Fasudil prevents liver fibrosis via activating natural killer cells and suppressing hepatic stellate cells. *World J Gastroenterol* 2021; **27**: 3581-3594 [PMID: 34239271 DOI: 10.3748/wjg.v27.i24.3581]
- Tanwar S**, Rhodes F, Srivastava A, Trembling PM, Rosenberg WM. Inflammation and fibrosis in chronic liver diseases including non-alcoholic fatty liver disease and hepatitis C. *World J Gastroenterol* 2020; **26**: 109-133 [PMID: 31969775 DOI: 10.3748/wjg.v26.i2.109]
- Alukal JJ**, Thuluvath PJ. Reversal of NASH fibrosis with pharmacotherapy. *Hepatol Int* 2019; **13**: 534-545 [PMID: 31363910 DOI: 10.1007/s12072-019-09970-3]

- 4 **Zhao J**, Zhou D, Guo J, Ren Z, Zhou L, Wang S, Xu B, Wang R. Effect of fasudil hydrochloride, a protein kinase inhibitor, on cerebral vasospasm and delayed cerebral ischemic symptoms after aneurysmal subarachnoid hemorrhage. *Neurol Med Chir (Tokyo)* 2006; **46**: 421-428 [PMID: [16998274](#) DOI: [10.2176/nmc.46.421](#)]
- 5 **Xie Y**, Song T, Huo M, Zhang Y, Zhang YY, Ma ZH, Wang N, Zhang JP, Chu L. Fasudil alleviates hepatic fibrosis in type 1 diabetic rats: involvement of the inflammation and RhoA/ROCK pathway. *Eur Rev Med Pharmacol Sci* 2018; **22**: 5665-5677 [PMID: [30229844](#) DOI: [10.26355/eurev\\_201809\\_15834](#)]
- 6 **Zhou H**, Fang C, Zhang L, Deng Y, Wang M, Meng F. Fasudil hydrochloride hydrate, a Rho-kinase inhibitor, ameliorates hepatic fibrosis in rats with type 2 diabetes. *Chin Med J (Engl)* 2014; **127**: 225-231 [PMID: [24438608](#)]
- 7 **Ikeda H**, Kume Y, Tejima K, Tomiya T, Nishikawa T, Watanabe N, Ohtomo N, Arai M, Arai C, Omata M, Fujiwara K, Yatomi Y. Rho-kinase inhibitor prevents hepatocyte damage in acute liver injury induced by carbon tetrachloride in rats. *Am J Physiol Gastrointest Liver Physiol* 2007; **293**: G911-G917 [PMID: [17761835](#) DOI: [10.1152/ajpgi.00210.2007](#)]



Published by **Baishideng Publishing Group Inc**  
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA  
**Telephone:** +1-925-3991568  
**E-mail:** [bpgoffice@wjgnet.com](mailto:bpgoffice@wjgnet.com)  
**Help Desk:** <https://www.f6publishing.com/helpdesk>  
<https://www.wjgnet.com>

