

The role of medicinal mushrooms as gastroprotective agents: A short narrative review

Aida PUIA¹, Diana SCHLANGER^{2*}, Ion C. PUIA^{2,3}

¹University of Medicine and Pharmacy Iuliu Hatieganu, Department of Community Medicine, Cluj-Napoca, Romania; draidapuia@gmail.com

²University of Medicine and Pharmacy Iuliu Hatieganu, Department of Surgery, Cluj-Napoca, Romania; schlanger.diana@gmail.com (*corresponding author)

³Regional Institute of Gastroenterology and Hepatology "Octavian Fodor, Surgery Department, Cluj-Napoca, Romania; drpuia@yahoo.fr

Abstract

This review examines the possible clinical uses of extracts from mushrooms with medicinal properties, particularly their role as gastroprotective agents. After conducting a thorough examination of the literature, we identified and chose publications that presented six distinct types of mushroom extracts. These extracts have been experimentally demonstrated to have gastroprotective effects in animal models. Animals like rats or mice were used as subjects in experimental models to generate stomach ulcers through various approaches, such as chemical induction or inducing stress. Studies have shown that mushroom extracts are efficacious in facilitating the healing process of stomach ulcers. Several fundamental modes of action include anti-inflammatory and antioxidant effects, along with enhanced preservation of stomach mucus. No clinical trials pertaining to this topic have been uncovered. However, the initial positive outcomes gained serve as a basis for additional investigation on this subject.

Keywords: gastro protectants; stomach ulcers; therapeutic mushrooms

Introduction

Gastric pathologies related to acid hypersecretion, as well as gastroesophageal reflux disease that can induce gastric or esophageal mucosa disruption are common pathologies, with a significant incidence, probably due to the modern lifestyle habits and the high incidence of obesity, smoking, alcohol consumption and stress. (Delshad *et al.*, 2020; Sipponen and Maaros, 2015).

While conventional medication, like proton pump inhibitors and surgical interventions are currently used in the management of these diseases, they can have important short-term and long-term side effects or complications. On the other hand, there are cases when conventional therapies cannot completely control the symptomatology and therefore, might benefit from adjunctive therapies (Shanika *et al.*, 2023; Slater *et al.*, 2023).

Received: 22 Nov 2023. Received in revised form: 12 Dec 2023. Accepted: 13 Dec 2023. Published online: 19 Dec 2023.

From Volume 49, Issue 1, 2021, Notulae Botanicae Horti Agrobotanici Cluj-Napoca journal uses article numbers in place of the traditional method of continuous pagination through the volume. The journal will continue to appear quarterly, as before, with four annual numbers.

Alternative therapies, and specifically medicinal mushrooms, have proven to be useful in different pathologies and represent a natural therapy that can be successfully used in aiding the management of different diseases (Shang *et al.*, 2021; Wasser, 2014)

The effect of medicinal mushrooms as anti-cancer therapies, in obesity control, in the treatment of cardiovascular disease or diabetes has been largely discussed in multiple studies, but their role in gastroesophageal disease has been less explored. However, we believe that these agents might have important applications and deserve to be analysed. Our study is a literature review that creates a synthesis and in-depth analysis of the current medical literature on the topic.

The progress of the investigation and the aspects followed

In the present narrative literature review, there were analysed studies that respected the following inclusions criteria: original articles referring to medicinal mushrooms with a focus on gastric mucosa protection, gastric acid suppression or treatment of gastritis, gastric ulcer, or gastroesophageal reflux; we chose to focus on papers with direct clinical applications. The reviews and case reports, articles written in other language than English and articles for which full-text was not available were excluded.

The inquiry was conducted by doing a search of the medical literature using the PubMed database. The search terms included “medicinal mushroom”, “medicinal fungi”, “mushroom”, “gastric ulcer”, “gastritis”, “reflux”, “gastroesophageal reflux”, “gastric hypersecretion”, and “gastroprotective”. Following the first search, a curation process was conducted, wherein articles were chosen based on the title and abstract. The complete article was extracted for the remaining investigations; these publications were examined, and a subsequent selection was conducted. The review incorporated the ultimate assortment of articles. There were no limitations on the time for the search.

The investigations of the review articles prioritized the clinically significant ideas and elements offered by the research, rather than focusing on the mechanisms of action. The aim was to contextualize the material within the realm of clinical practice. The extracted data encompassed the study's title and authors, publication year, study design, and the investigation technique specifically centred around the model depicted in Figure 1.

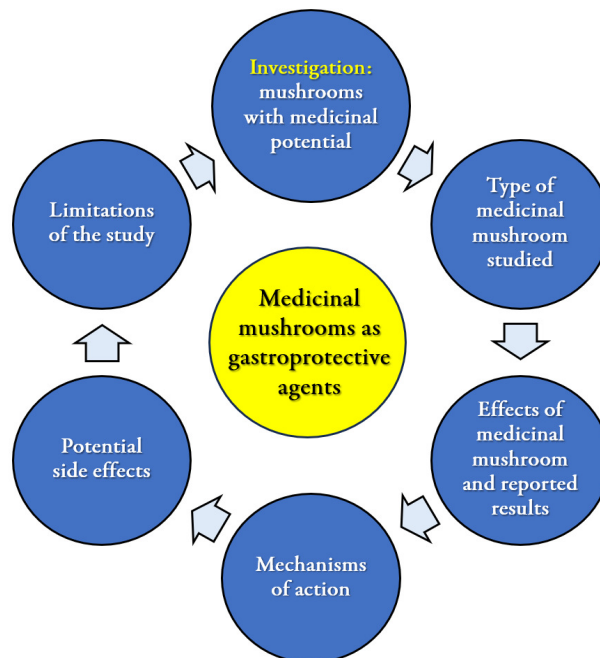


Figure 1. The development of the investigation and the aspects that were subsequently followed

Collecting and organizing the information obtained from the investigations

After the initial search, a total number of 61 articles were retrieved. The initial phase excluded a number of 44 records (out of which 8 reviews and 34 articles that did not refer to the targeted topic, 2 article were written in other languages than English). Seventeen papers were analysed based on the full-text article. After the exclusion of 10 more articles due to having other topics of interest than the investigated one, a number of 7 records were included in the analysis.

All seven studies selected for the review focused on gastroprotective effects of medicinal mushrooms, in the treatment of gastric ulcer. No studies referring to other diseases related to gastric hypersecretion, like gastritis or gastroesophageal reflux were identified. All included studies were experimental studies, performed on rats or mice, using this animal model to induce gastric ulcers and test the gastroprotective effects of different medicinal mushroom extracts.

Regarding the methodology of the studies, different methods for inducing gastric ulcers were used: most studies induced gastric ulcerations through ethanol administration, while other methods used were administration of indomethacin, acetic-acid, or stress-induced ulcers. All studies used a positive control group, where the experimental animals were administered medications known to have a role in the treatment of gastric ulcer. Table 1 presents information on the medicinal mushroom species that underwent research and the approach used in the included studies. All studies used different concentrations of mushroom extract, to determine a comparative analysis as well; furthermore, Padilha *et al.* (2009) analysed comparatively the use of an alkaline or aqueous solutions at different concentrations, so different methods of extraction as well. The timing of the administration of the mushroom extract also varied significantly: from administration of the solution before the ulcer-inducing substance, for different treatment durations, to the administration after the delivery of the ulcer-inducing substance.

Table 1. Medicinal mushroom species and methodology of included studies

Medicinal mushroom (species)	Experimental model	Positive control	Timing of administration of mushroom extract	Source
<i>Amauroderma rugosum</i>	Ethanol-induced ulcer Indomethacin-induced ulcer	Lansoprazole	Pre-treatment (7-day period)	Mai <i>et al.</i> (2022)
<i>Agaricus blazei</i>	Ethanol-induced ulcer	NAC	Pre-treatment (1h before)	Câmara Neto <i>et al.</i> (2022)
<i>Ganoderma lucidum</i>	Acetic acid-induced ulcer	Atropine sulfate	After the administration of ulcer inducing agent (after 1h)	Gao <i>et al.</i> (2004)
<i>Armillariella tabescens</i>	Ethanol-induced ulcer	Ranitidine	-	Lee <i>et al.</i> (2018)
<i>Termitomyces eurhizus</i>	Indomethacin-induced ulcer	Omeprazole	After the administration of ulcer inducing agent (after 6h)	Chatterjee <i>et al.</i> (2013)
<i>Hericium erinaceus</i>	Ethanol-induced ulcer	Omeprazole	Pre-treatment (1h before)	Wong <i>et al.</i> (2013)
<i>Agaricus blazei</i>	Stress-induced ulcer	Cimetidine	Pre-treatment (15-day period)	Padilha <i>et al.</i> (2009)

All studies reported favourable results, but dose-dependent variations of the effect can be observed. The main objective that we looked for was the reduction of the ulceration area or the ulcer healing effect of the mushroom solutions. The main reported results, as well as a comparison between the efficacy of the medicinal

mushroom solution and the negative control group, respectively the positive control group, are presented in Table 2.

Table 2. Anti-ulcerous effect of medicinal mushroom extract

Effect on extension of ulcers	Comparative results of mushroom extract		Source
	Negative control	Positive control	
Reduction of the ulcerated area by 80% (dose 100 mg/kg) – ethanol-induced Reduction of the ulcerated area by 86% (dose 50 mg/kg) – indomethacin-induced	Superiority	Inferiority	Mai <i>et al.</i> (2022)
Decreased ulcerative lesions by 75-88% (solutions of 25 mg/kg and 50 mg/kg)	Superiority	Inferiority	Câmara Neto <i>et al.</i> (2022)
Acceleration of gastric ulcer healing by 55.9% (dose 1 g/kg)	Superiority	Inferiority	Gao <i>et al.</i> (2004)
Reduced formation of ulcer (doses 100 mg/kg and 200 mg/kg)	Superiority	Equivalent	Lee <i>et al.</i> (2018)
Reduced ulcer damage scores and increased healing effect (solution 20 mg/kg)	Superiority	Superiority	Chatterjee <i>et al.</i> (2013)
Decreased ulceration area – inhibition percentage of ulcer area by 72.97% (solution 400 mg/kg)	Superiority	Superiority	Wong <i>et al.</i> (2013)
Decreased ulceration index by 21.88% and 28.63% (aqueous and respective alkaline extracts - 400 mg/kg)	Superiority	Inferiority	Padilha <i>et al.</i> (2009)

Although with variability between reports, the included studies mentioned other additional parameters that might influence the gastric ulcer healing effect of the medicinal mushroom extracts. The most relevant results are gathered in Table 3.

Table 3. Additional effects of medicinal mushroom extracts

Anti-inflammatory effects	Gastric acid secretion	Gastric mucus production	Source
Anti-inflammatory effects (inflammatory cytokine production)	No effect on Ph-normalization	-	Mai <i>et al.</i> (2022)
Antioxidant effect (free radical formation), mast cell expression	-	-	Câmara Neto <i>et al.</i> (2022)
-	-	Restored the decreased gastric mucus levels	(Gao <i>et al.</i> (2004)
Anti-inflammatory effects (cytokine expression and macrophage involvement)	-	-	Lee <i>et al.</i> (2018)
Reduce number of inflammatory cells and mucosal congestion	-	Increased mucin content	Chatterjee <i>et al.</i> (2013)
Antioxidative effects (influence on reactive oxygen species)	-	Increased mucus production Increased alcian blue binding capacity of gastric mucus	Wong <i>et al.</i> (2013)
-	-	-	Padilha <i>et al.</i> (2009)

General considerations based on the investigation

Diseases related to gastric acid hypersecretion are one of the most prevalent pathologies in the world, constituting an important burden for modern society. Although, there are several available conventional therapies, the need for long-term treatments, incomplete control of the disease and associated adverse effects keep the optimal treatment of gastric ulcer and gastroesophageal reflux disease as a current issue in medicine (Kamada *et al.*, 2021; Katelaris *et al.*, 2023).

Our study intended to perform an extensive literature review on the subject of alternative treatments for diseases related to gastric acid hypersecretion, with the focus on the role of medicinal mushroom and possible clinical practice applications. We have ultimately identified seven papers that discussed the use of medicinal mushroom extracts in the treatment of gastric ulcer disease; unfortunately, there are no reports regarding the treatment of other pathologies, like gastritis or gastroesophageal reflux. All studies were experimental animal studies, and although the investigated mushrooms are considered edible mushrooms, there were no clinical reports.

In the seven included studies, six different types of medicinal mushroom extracts were analysed, showing clearly the high heterogeneity of the included studies. Furthermore, there has also been observed heterogeneity in the experimental model, both in the timing of administration of the extract and the method of inducing the gastric ulcers. This idea should be taken into consideration in further research studies, since the pathophysiology of gastric ulcer formation might influence the efficacy of a certain substance in the treatment of the disease. The variability in posology should also be addressed; once again, the time of the administration of the investigated substance might influence its action, just like in conventional medical therapies.

All studies had a comparative study design, analysing in parallel a negative control group (without administering any treatments), a positive control group (treated with conventional therapies), and experimental groups (treated with diverse doses of the investigated mushroom extract, therefore offering the opportunity to investigate a dose-dependent effects as well). The choice of treatment for the positive control group varied between studies, only three studies (Chatterjee *et al.*, 2013; Mai *et al.*, 2022; Wong *et al.*, 2013) choosing a proton pump inhibitor, which is the current gold standard treatment and due to these reasons, might be the best option for an accurate comparison.

All the analysed mushroom extracts showed superiority compared to the negative control, proving a gastroprotective effect of the investigated substance. On the other hand, the positive control was more effective in some cases, showing the superiority of conventional therapy. This fact is not a negative result on its own, since in clinical practice, association of treatments can be beneficial, and the cumulative effect of these therapies can be investigated.

A strong dose-dependent effect was observed throughout studies, the best effect being observed usually at the highest tested dose. This is however not universally true, since we can observe in Table 3, in the study reported by Mai *et al.* (2022) the best gastric ulcer effect for ethanol induced ulcers at the medium tested dose (100 mg/kg), and the best effect for indomethacin induced ulcers at the lowest tested dose (50 mg/kg). This underlines once again the importance of further investigating and determining the correct posology even for these alternative therapies.

Decreasing the ulcer area and enhancing the healing of gastric ulcers is the main objective of these alternative therapies, but the underlying mechanisms are also very important, but incompletely elucidated. Several studies have addressed this issue, analysing the effect on the dynamic of inflammatory cytokines, prostaglandins, oxidative stress and even gene expression. These results show the richness of underlying mechanisms that work towards the enhancing of the healing process in gastric ulcers (an overview of the main findings is reported in Table 3). Interestingly, only one study (Mai *et al.*, 2022) analysed the effect of medicinal mushroom extract on gastric acid suppression – no effect was seen, the gastroprotective action being owed to other physiological pathways. Important findings were made regarding the effect on gastric mucus secretion,

showing that the medicinal mushroom extract is truly involved in increasing the protective mechanisms of the gastric mucosa.

The current limitations of existing studies and the potential for future research advancements

The objective of this narrative review was to compile the existing material from the medical literature regarding the given issue. The primary constraint of the findings is from the data obtained during the literature inquiry: the sample size of the incorporated research is small, and all investigations were carried out in controlled experimental settings. Hence, despite the presence of encouraging findings, it is imperative to exercise caution when interpreting them, while also considering their primary clinical implications. Exploring new and innovative treatments for prevalent illnesses, including stomach ulcer disease, is a compelling topic that merits increased focus. We assert that increased research is necessary to go deeper into this matter.

Various extracts derived from medicinal mushrooms demonstrate encouraging gastroprotective effects in experimental mice. Despite the absence of clinical investigations, the encouraging outcomes shown in experimental conditions need additional scrutiny.

Authors' Contributions

Conceptualization: AP, DS, ICP; Data curation: AP; Investigation: DS; Methodology: DS, ICP; Supervision: ICP; Writing - original draft: AP, DS; Writing - review and editing: ICP. All authors read and approved the final manuscript.

Ethical approval (for researches involving animals or humans)

Not applicable.

Acknowledgements

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interests

The authors declare that there are no conflicts of interest related to this article.

References

- Câmara Neto JF, Campelo M da S, Cerqueira GS, de Miranda JAL, Guedes JAC, de Almeida RR, ... Ribeiro MENP (2022). Gastroprotective effect of hydroalcoholic extract from *Agaricus blazei* Murill against ethanol-induced gastric ulcer in mice. *Journal of Ethnopharmacology*, 292, 115191. <https://doi.org/10.1016/j.jep.2022.115191>
- Chatterjee A, Khatua S, Chatterjee S, Mukherjee S, Mukherjee A, Paloi S, Acharya K, Bandyopadhyay SK (2013). Polysaccharide-rich fraction of *Termitomyces eurbizus* accelerate healing of indomethacin induced gastric ulcer in mice. *Glycoconjugate Journal* 30(8):759-768. <https://doi.org/10.1007/s10719-013-9479-5>
- Delshad SD, Almario CV, Chey WD, Spiegel BMR (2020). Prevalence of gastroesophageal reflux disease and proton pump inhibitor-refractory symptoms. *Gastroenterology* 158(5):1250-1261.e2. <https://doi.org/10.1053/j.gastro.2019.12.014>
- Gao Y, Tang W, Gao H, Chan E, Lan J, Zhou S (2004). *Ganoderma lucidum* Polysaccharide fractions accelerate healing of acetic acid-induced ulcers in rats. *Journal of Medicinal Food* 7(4):417-421. <https://doi.org/10.1089/jmf.2004.7.417>
- Kamada T, Satoh K, Itoh T, Ito M, Iwamoto J, Okimoto T, ... Koike K (2021). Evidence-based clinical practice guidelines for peptic ulcer disease 2020. *Journal of Gastroenterology* 56(4):303-322. <https://doi.org/10.1007/s00535-021-01769-0>
- Katellaris P, Hunt R, Bazzoli F, Cohen H, Fock KM, Gemilyan M, ... Melberg J (2023). *Helicobacter pylori* world gastroenterology organization global guideline. *Journal of Clinical Gastroenterology* 57(2):111-126. <https://doi.org/10.1097/MCG.0000000000001719>
- Lee S, Lee D, Park JY, Seok S, Jang TS, Park HB, ... Kim KH (2018). Antigastritis effects of *Armillariella tabescens* (Scop.) Sing. and the identification of its anti-inflammatory metabolites. *Journal of Pharmacy and Pharmacology* 70(3):404-412. <https://doi.org/10.1111/jph.12871>
- Mai Y, Xu S, Shen R, Feng B, He H, Xu Y (2022). Gastroprotective effects of water extract of domesticated *Amauroderma rugosum* against several gastric ulcer models in rats. *Pharmaceutical Biology* 60(1):600-608. <https://doi.org/10.1080/13880209.2022.2047210>
- Padilha MM, Avila AAL, Sousa PJC, Cardoso LGV, Perazzo FF, Carvalho JCT (2009). Anti-inflammatory activity of aqueous and alkaline extracts from mushrooms (*Agaricus blazei* Murill). *Journal of Medicinal Food* 12(2):359-364. <https://doi.org/10.1089/jmf.2008.0177>
- Shang A, Gan R-Y, Xu X-Y, Mao Q-Q, Zhang P-Z, Li H-B (2021). Effects and mechanisms of edible and medicinal plants on obesity: an updated review. *Critical Reviews in Food Science and Nutrition* 61(12):2061-2077. <https://doi.org/10.1080/10408398.2020.1769548>
- Shanika LGT, Reynolds A, Pattison S, Braund R (2023). Proton pump inhibitor use: systematic review of global trends and practices. *European Journal of Clinical Pharmacology* 79(9):1159-1172. <https://doi.org/10.1007/s00228-023-03534-z>
- Sipponen P, Maarros H-I (2015). Chronic gastritis. *Scandinavian Journal of Gastroenterology* 50(6):657-667. <https://doi.org/10.3109/00365521.2015.1019918>
- Slater BJ, Collings A, Dirks R, Gould JC, Qureshi AP, Juza R, ... Marks JM (2023). Multi-society consensus conference and guideline on the treatment of gastroesophageal reflux disease (GERD). *Surgical Endoscopy* 37(2):781-806. <https://doi.org/10.1007/s00464-022-09817-3>
- Wasser S (2014). Medicinal mushroom science: Current perspectives, advances, evidences, and challenges. *Biomedical Journal* 37(6):345. <https://doi.org/10.4103/2319-4170.138318>
- Wong J-Y, Abdulla MA, Raman J, Phan C-W, Kuppasamy UR, Golbabapour S, Sabaratnam V (2013). Gastroprotective effects of lion's mane mushroom *Hericium erinaceus* (Bull.:Fr.) Pers. (Aphyllophoromycetidae) extract against

ethanol-induced ulcer in rats. Evidence-Based Complementary and Alternative Medicine 2013:1-9.
<https://doi.org/10.1155/2013/492976>



The journal offers free, immediate, and unrestricted access to peer-reviewed research and scholarly work. Users are allowed to read, download, copy, distribute, print, search, or link to the full texts of the articles, or use them for any other lawful purpose, without asking prior permission from the publisher or the author.



License - Articles published in *Notulae Botanicae Horti Agrobotanici Cluj-Napoca* are Open-Access, distributed under the terms and conditions of the Creative Commons Attribution (CC BY 4.0) License.

© Articles by the authors; Licensee UASVM and SHST, Cluj-Napoca, Romania. The journal allows the author(s) to hold the copyright/to retain publishing rights without restriction.

Notes:

- **Material disclaimer:** The authors are fully responsible for their work and they hold sole responsibility for the articles published in the journal.
- **Maps and affiliations:** The publisher stay neutral with regard to jurisdictional claims in published maps and institutional affiliations.
- **Responsibilities:** The editors, editorial board and publisher do not assume any responsibility for the article's contents and for the authors' views expressed in their contributions. The statements and opinions published represent the views of the authors or persons to whom they are credited. Publication of research information does not constitute a recommendation or endorsement of products involved.