Biodiversity as an Ally: Evidence on the Benefits of Mushroom Use during Chemotherapy and Its Translation into Public-Friendly Materials via Generative AI

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1. Introduction

Cancer remains one of the major global public health challenges, representing a leading cause of mortality and significantly reducing both quality of life and life expectancy. In Brazil, an estimated 704,000 new cases are expected between 2023 and 2025. Oncological treatment in the country relies mainly on surgery, chemotherapy, and radiotherapy. However, between 2000 and 2019, the use of surgery and chemotherapy increased, while radiotherapy declined[1].

Chemotherapeutic agents are anticancer drugs that halt cell proliferation through DNA damage, inhibition of replication, and disruption of cell division, including alkylating agents, antimetabolites, antitumor antibiotics, topoisomerase inhibitors, and mitotic inhibitors[2]. However, these drugs also affect healthy cells, including those of the immune system, leading to immunosuppression[3] and negatively impacting the quality of life of cancer patients, with symptoms such as insomnia, nausea, fatigue, loss of appetite, and alopecia[4].

Supportive care during chemotherapy is encouraged to mitigate immunosuppressive effects and improve patients' overall well-being. Among these interventions, supplementation plays an important role in preventing complications and enhancing treatment efficacy, thereby contributing to patient improvement[3]. In this context, mushrooms are considered an excellent source of nutrients and bioactive compounds that may help alleviate chemotherapy side effects[5]. Therefore, the present work summarizes the potential benefits of mushroom supplementation during chemotherapy, provides a perspective on Amazonian mushrooms, and creates didactic materials based on the selected articles using a generative Artificial Intelligence (AI) tool.

2. Methodology

This narrative integrative review was conducted by searching Google Scholar, ScienceDirect, and PubMed for articles published in the last five years (2020–2025) using the keywords: mushroom, chemotherapy, and chemotherapeutics. Inclusion criteria covered in vitro and in vivo experimental studies, while reviews and book chapters were excluded. A total of 21 articles were selected, and their findings were analyzed qualitatively and quantitatively to summarize current evidence on the potential benefits of mushrooms during chemotherapy. Additionally, the selected files were processed in NotebookLM, a generative AI platform, to develop didactic materials (video and podcast), which were subsequently integrated into an interactive website created with Google Sites to facilitate public dissemination.

3. Results and Discussion

Among the selected articles, the most investigated genera in the context of chemotherapy were *Ganoderma* and *Lentinula* (19.05% each), followed by *Morchella* and *Pleurotus* (14.29% each). Other genera included *Agaricus*, *Fomes*, *Inonotus*, *Phellinus*, *Trametes*, and *Tricholoma* (9.52% each), while *Cordyceps*, *Cyclocybe*, *Flammulina*, *Lactarius*, and *Ophiocordyceps* appeared less frequently (4.76% each). *Morchella esculenta* was the most

studied species (3 articles, 14.29%), followed by *Ganoderma lucidum* and *Lentinula edodes* (2 articles each), with both genera also recurring in mushroom mixtures[6-26].

Several mechanisms of action were reported (Figure 1), with antitumor effects being the most frequent, including apoptosis/cell death induction in 11 studies (52.38%), followed by growth/proliferation inhibition in 10 articles (47.62%). Other common mechanisms included oxidative stress mitigation with enhanced antioxidant defenses (8 articles, 38.10%) and modulation of specific signaling pathways, such as regulation of pro- and anti-apoptotic proteins (8 articles, 38.10%). Organ protection was also observed, including nephroprotection (3 articles, 14.29%) and cardioprotection (2 articles, 9.52%), as well as mitigation of chemotherapy-induced taste disturbances (1 article, 4.76%)[6-26].

Additional mechanisms investigated in single studies (4.76%) included specific signaling pathways, such as integrin/FAK/Src/Akt, DNA damage response (DDR), stemness suppression, and the miR-224-5p/ABCB1/P-gp axis. Other targeted mechanisms reported in 1-2 studies included DNA damage and repair modulation, inhibition of ribosomal biogenesis and translation, metabolic pathway regulation, acetylcholinesterase inhibition, multidrug resistance reversal, intestinal barrier protection, and prevention of premature ovarian failure[6-26].

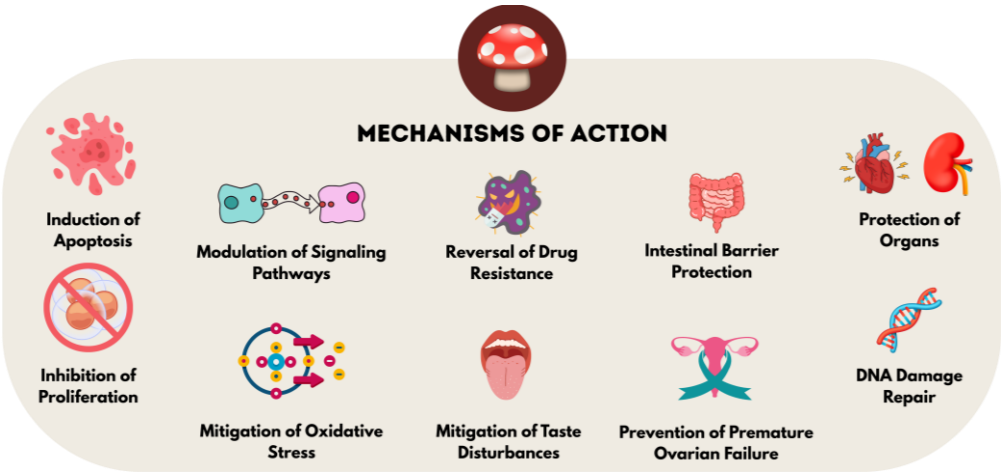

Figure 1. Multifaceted Mechanisms of Action of Mushroom-Derived Products in Conjunction with Chemotherapy.

The chemotherapeutic agents most frequently addressed in the studies were doxorubicin (DOX) and cisplatin (DDP/CisPt/Cis), each appearing in 4 studies (19.05%), followed by paclitaxel (PTX) and cyclophosphamide (CP) in 3 studies each (14.29%), and 5-fluorouracil (5-FU) and oxaliplatin (L-OHP/OXA) in 2 studies each (9.52%). Less frequently studied agents included temozolomide (TMZ) and carboplatin (CB), each in 1 study (4.76%)[6-26].

DOX, although widely used, is limited by dose-dependent cardiotoxicity and neurotoxicity, primarily due to oxidative stress, mitochondrial dysfunction, endoplasmic reticulum stress, ferroptosis, and apoptosis. Mushroom-derived interventions showed protective effects: *Cordyceps militaris* mycelium extract mitigated oxidative stress, improved mitochondrial respiratory chain activity and ATP levels, and inhibited acetylcholinesterase in the brain, reducing neurotoxicity[6]; *Morchella esculenta* methanolic extract attenuated DOX-induced oxidative damage in cardiac cells and tumor-bearing mice without affecting antitumor activity[15,25]; β-(1→6)-D-glucan from *Agaricus bisporus* synergistically enhanced DOX cytotoxicity in triple-negative breast cancer cells, suggesting potential dose reduction[13].

Cisplatin, a key agent for solid tumors, is limited by nephrotoxicity, as well as ototoxicity, neurotoxicity, and hepatotoxicity. Mushroom-based interventions mitigated these

adverse effects through multiple mechanisms: the neutral polysaccharide from *Ophiocordyceps lanpingensis* reduced pro-apoptotic signaling and enhanced anti-apoptotic Bcl-2[10]; *Lentinus squarrosulus* peptide acted as a chemosensitizer in lung cancer cells, enhancing apoptosis and suppressing integrin-mediated survival pathways[12]; methanolic extracts from *Ganoderma tuberculosum* and *G. parvigibbosum* protected renal proximal tubular cells by reducing ROS, β-catenin accumulation, and pro-apoptotic protein expression[18]; and *Flammulina velutipes* extract attenuated cisplatin-induced chronic kidney disease by modulating oxidative stress, inflammation, apoptosis, fibrosis, and organic ion transport pathways[23].

PTX, despite its efficacy, can cause neuropathy, nephrotoxicity, myelotoxicity, and mucositis. Polysaccharides from *Ganoderma lucidum* spores improved PTX-induced intestinal barrier injury, promoted epithelial proliferation, and reduced apoptosis[9]. CP, 5-FU, oxaliplatin, TMZ, and carboplatin also present significant toxicities and limitations, including ovarian failure, multidrug resistance, impaired DNA repair, and reduced chemotherapy efficacy. Mushroom-derived interventions, including extracts from *Morchella esculenta*, *Lentinula edodes*, *Trametes robiniophila*, *Ganoderma lucidum*, and other species, demonstrated organ protection, enhanced chemosensitivity, immunomodulation, and mitigation of chemotherapy-induced side effects. Specific effects included premature ovarian failure prevention, intestinal barrier restoration, cardioprotection, enhanced tumor cell apoptosis, and modulation of signaling pathways associated with tumor survival, stemness, and drug resistance[17,19-21].

Overall, these studies underscore the potential of medicinal mushrooms and their bioactive compounds to enhance the efficacy of chemotherapy, reduce treatment-related toxicity, and overcome drug resistance, providing promising complementary strategies in cancer therapy. In the state of Amazonas, although no studies have yet directly investigated this application, strains of the edible mushrooms *Pleurotus ostreatus* and *Lentinus strigosus*, as well as the medicinal mushroom *Ganoderma* sp., isolated in the region, have shown potential for synthesizing pharmacologically relevant molecules, representing promising candidates for future research as adjuvant and complementary agents[27-29].

Despite the relevance of these studies in advancing new cancer treatment strategies, such information rarely reaches patients, their families, or the general public, although this outreach should also be considered a responsibility of scientists. In this context, generative AI tools can serve as valuable allies, enabling the creation of didactic materials from scientific literature. As an outcome of this work, we developed an interactive website featuring concise text descriptions, a video, a podcast, and full references, aimed at facilitating public dissemination. The website is available at: https://sites.google.com/view/cogumelos-e-quimioterapia/início.

4. Conclusion

Mushrooms offer promising complementary strategies during chemotherapy, enhancing antitumor effects, reducing toxicity, and modulating immune and signaling pathways. Amazonian biodiversity presents untapped potential, as local strains of *Pleurotus*, *Lentinus*, and *Ganoderma* belong to genera already recognized for their therapeutic effects in chemotherapy context. Studies with these strains should be conducted. Furthermore, using a generative AI tool, high-quality didactic materials were produced from the selected articles, maintaining scientific rigor while enabling translation of knowledge to the general public.

Keywords: Micodiversity, Oncology, Chemotherapics, Artificial Intelligence

Acknowledgments

To the Conselho Nacional de Pesquisa e Desenvolvimento (CNPq, Process Number: 141036/2022-2) and Fundação de Amparo à Pesquisa do Estado do Amazonas (Resolution nº

002/2023 – CD/FAPEAM and nº 002/2024 – POSGRAD 2024/2025 - UFAM). The authors are grateful to Canva IA for generating images, NotebookLM for generating audio and video assets, and Google Sites for hosting the website.

Divulgation

The authors and reviewers have not reported any conflicts of interest during the evaluation. Therefore, the Pan-Amazonian Oncology Congress holds the copyright and has the approval and permission from the authors for dissemination of this abstract via electronic means.

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