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# Anticancer and Cardioprotective Properties of Medicinal Mushrooms: Current Evidence and Future Prospects

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## ABSTRACT

**Introduction:** Cardiotoxicity is an undesirable side effect of chemotherapy that limits the effectiveness of cancer treatment. Almost all cardiotoxic agents cause cardiovascular complications, leading to oxidative stress and other pathological conditions. The search for bioactive compounds that mitigate chemotherapy-induced cardiotoxicity is a priority in integrative cardiooncology.

**Content:** The administration of anthracycline derivatives, particularly Doxorubicin (DOX) and Adriamycin, is limited due to the risk of development of heart failure. These drugs promote apoptosis and oxidative stress, decrease the activity of antioxidant enzymes, and increase the production of proinflammatory cytokines. The combination of DOX and natural cardioprotective agents has been shown to be an effective therapeutic strategy for improving the outcomes of cancer treatment. Mushrooms, as producers of pharmacologically active compounds with significant cardioprotective effects, have been shown to prevent DOX-induced cardiotoxicity in in vivo models, restoring cell viability, reducing oxidative stress via mitochondria-dependent apoptotic pathways, and improving myocardial function. Therefore, mushroom-derived products may be effective against chemotherapy-induced cardiotoxicity. This review discusses progress in integrative cardiooncology aimed at elucidating the cardioprotective potential of mushrooms as a preventive strategy against cardiotoxicity associated with antitumor treatment.

**Outlook:** Further preclinical and clinical studies are needed to elucidate the antioxidant and antiinflammatory potential of mushrooms and their use as dietary supplements, given the synergistic effects of all bioactive molecules, supporting the prospect of developing clinically effective anticancer and cardioprotective agents.

## 1 | Introduction

Mushrooms or macrofungi taxonomically belong to classes Agaricomycetes and Pezizomycetes of the phyla Basidiomycota and Ascomycota, respectively. They contain minerals, proteins, unsaturated fatty acids, and vitamins, as well as various bioactive compounds (polysaccharides, phenolics, terpenoids, etc.) with therapeutic effects (antioxidant, antiinflammatory, cardioprotective, immunomodulatory, neuroprotective, etc.). Recent studies have proven significant potential of mushrooms to develop healthy food products and pharmaceuticals with high economic and environmental importance (Saltarelli et al. 2015;

**Abbreviations:** ADR, Adriamycin; CAT, catalase; CK, creatinine kinase; CK-MB, creatinine kinase-myoglobin; CPE, cardioprotective effect; cTnI, cardiac troponin I; CVD, cardiovascular diseases; DAVA, Davallialactone; DOX, Doxorubicin; GPx, glutathione peroxidase; GSH, glutathione; HCC, hepatocellular carcinoma; HUVEC, human umbilical vascular endothelial cell; LDH, lactate dehydrogenase; LPO, lipid peroxidation; LVEF, left ventricular ejection fraction; MDA, malondialdehyde; MDBC, mushroom-derived bioactive compounds; MDBP, mushroom-derived biotech products; p-AKT, phosphorylated AKT; PI3K, phosphoinositide 3-kinase; ROS, reactive oxygen species; SOD, superoxide dismutase; TCM, traditional Chinese medicine; VEGF, vascular endothelial growth factor.

Souilem et al. 2017; Pandya et al. 2019; Badalyan and Rapior 2021; Chaudhuri and Datta 2021; Badalyan et al. 2019, 2023; Badalyan, Barkhudaryan et al. 2026; Badalyan, Iotti et al. 2026; Roszczenko et al. 2024; Zade et al. 2025; Buttacavoli et al. 2026; Pozzobon et al. 2026).

Several edible and medicinal mushrooms, such as *Agaricus bisporus*, *A. subrufescens* (= *A. blazei* Murill), *Cordyceps militaris*, *Fomes fomentarius*, *Ganoderma lucidum*, *Grifola frondosa*, *Hericium erinaceus*, *Inonotus obliquus*, *I. xeranticus*, *Laricifomes officinalis*, *Lentinula edodes*, *Morchella esculenta*, *Ophiocordyceps sinensis*, *Taiwanofungus camphoratus*, *Trametes sanguinea*, *T. versicolor*, *Tropicoporus* (= *Phellinus*) *linteus*, and *Vanderbylia* (= *Trametes*) *robiniophila*, are widely used in traditional and Ayurvedic medicines for centuries (Veena and Janardhanan 2017; Szychowski et al. 2018; Thammavong et al. 2020; Al-Tuwaijri et al. 2021; Veena et al. 2021; Zhao and Zheng 2021; Skrzydlewski and Twarużek 2024; Tee et al. 2024; Gafforov et al. 2025; Wang et al. 2025; Mahajon et al. 2026). Among these species, *T. versicolor* (Turkey tail), *H. erinaceus* (Lion's mane), *I. obliquus* (Chaga), *G. lucidum* (Reishi or Lingzhi), *L. edodes* (Shiitake), *G. frondosa* (Maitake), and *Cordyceps* spp. (caterpillar fungi) are well-known medicinal mushrooms (Figure 1).

Recent mycopharmacological studies have examined mushroom-derived bioactive compounds (MDBC) and innovative mushroom-derived biotech products (MDBP) for the treatment of oxidative stress–related diseases, including cardiovascular disease (CVD) (Badalyan et al. 2021; Ma et al. 2024; Martinez-Burgos et al. 2024; Gafforov et al. 2026). Other therapeutic effects of mushrooms were also reported (Badalyan and Zambonelli 2019, 2023; Lee et al. 2019; Niego et al. 2021; Romano et al. 2024; Jafari et al. 2025; Kim et al. 2025; Mishra and Shankar 2025; Badalyan, Barkhudaryan et al. 2026; Badalyan, Iotti et al. 2026; Kirdeeva et al. 2026; Quarcoo et al. 2026).


**FIGURE 1** | The medicinal mushrooms used against chemotherapy-induced cardiotoxicity: (a) *Trametes versicolor*, (b) *Fomes fomentarius*, (c) *Ganoderma lucidum*, (d) *Vanderbylia* (= *Trametes*) *robiniophila*, (e) *Inonotus obliquus*, (f) *I. xeranticus*, (g) *T. sanguinea*, (h) *Agaricus subrufescens* (= *A. blazei*), (i) *Lentinula edodes*, (j) *Grifola frondosa*, (k) *Tropicoporus* (= *Phellinus*) *linteus*, (l) *Morchella esculenta*, and (m) *Cordyceps militaris*. Photo credit: (a) Alisa Atamanchuk (Ukraine) and (b–m) i-Naturalist (https://www.inaturalist.org/; accessed on 16 February, 2026; the images are used under the license Attribution Non-Commercial-No Derivs 4.0).

Due to increased demand for MDBP, progress has been made in cultivating mycelium and producing fruiting bodies of medicinal and edible mushrooms. Various cultivation techniques have been explored to obtain an ecologically safe and standardized mycelial biomass of selected species belonging to different taxonomic and ecological groups, with the aim of supporting the development of mushroom cultivation on a global scale (Badalyan and Zambonelli 2019, 2023; Tee et al. 2024; Mishra and Shankar 2025; Badalyan, Iotti et al. 2026; Dong et al. 2026).

Cancer and CVD are the most common causes of mortality worldwide. Although these pathologies are considered completely different, they share common risk factors, such as obesity, diabetes mellitus, and chronic inflammation (Kitsis et al. 2018; Di Cesare et al. 2024; Makram et al. 2024; Bonaventura et al. 2025; World Heart Federation and World Heart Report 2025). Furthermore, the chemotherapy used to treat cancer causes cardiotoxicity. Therefore, the development of novel anticancer and cardioprotective agents, as well as the study of their mechanisms of action, is required (Albini et al. 2010; Wu et al. 2017; Gil-Ramirez et al. 2018; Omland et al. 2022; Karunarathna et al. 2025; Yu et al. 2026).

Chemotherapy is administered alone or in combination with surgery or radiotherapy. Among the most effective chemotherapeutic drugs used against various types of tumors, anthracyclines are among the most effective. However, their effective role in improving survival rates for cancer patients is limited by severe cardiotoxicity (Gao et al. 2024; Obeidat et al. 2024; Ciappina et al. 2025). A synergistic effect of natural products used as potential cardioprotective agents has been demonstrated. Preclinical and clinical trials have investigated the cardioprotective potential of products of plant and mushroom origin to prevent chemotherapy-induced cardiotoxicity (Quagliariello et al. 2022; Ali et al. 2024; Firoozbakhsh et al. 2024; Szponar et al. 2024; Das et al. 2025; Shang et al. 2025).

In the present paper, we examined whether the use of MDBP could significantly attenuate chemotherapy-induced cardiotoxicity in cancer patients. We performed extensive research of recent experimental and clinical studies, particularly published from 2020 to 2026 on this topic using the key words "medicinal mushrooms," "cardiotoxicity," "anticancer effect," and "cardio-oncology" from PubMed, Web of Science, SciFinder, BibCNRS, and Research Gate, as well as sent requests directly to the coauthors. This review summarizes progress in investigating the anticancer and cardioprotective potential of mushrooms across different taxonomic groups and outlines prospects for their use in integrative cardiooncology.

## 2 | Cardioprotective Effects of Mushrooms

The risk factors of CVD, such as obesity, diabetes mellitus, hyperlipidemia, and arterial hypertension, are associated with a high mortality rate in humans. The treatment of cardiac diseases leads to adverse effects, and alternative preventive therapies are required (Adhikary et al. 2022; Di Cesare et al. 2024; Chong et al. 2025; World Heart Federation and World Heart Report 2025).

Mushrooms are low-calorie foods with protein, vitamins, and microelement content and have been extensively used in the prevention and treatment of cardiac disorders (Badalyan et al. 2019, 2021, 2023, Badalyan, Iotti et al. 2026; Fitsum et al. 2025; Lakshmaiah and Raghavan 2025; Singh et al. 2025). The cardioprotective potential of *G. lucidum*, *T. versicolor*, and *L. edodes* has been documented in the traditional Chinese medicine (TCM) to manage risk factors for cardiometabolic diseases and promote cardiovascular health. Research data has shown that mushrooms possess antioxidant, cardioprotective, immunomodulatory, and radical scavenging activity due to synthesized bioactive compounds (Badalyan et al. 2019, 2023; Lawal et al. 2025). Terpenoids, isoflavones, lanosterone derivatives and lovastatin extracted from Agaricomycetes species, such as *G. lucidum*, *G. frondosa*, *L. edodes*, and *Pleurotus ostreatus* regulate the lipid metabolism, prevent diabetes mellitus, arterial hypertension, and oxidative stress, therefore the development of CVD (Francia et al. 1999; Chen et al. 2017; Shibu et al. 2017; Singh et al. 2017; Badalyan et al. 2019, 2021, 2023; Chan et al. 2021; Yang et al. 2022; Lakshmaiah and Raghavan 2025; Lawal et al. 2025; Hu et al. 2026).

Preclinical studies have shown that dietary MDBP intake may be considered an alternative natural agent for regulating risk factors for cardiac disease (Shibu et al. 2017). Cardioprotective MDBP obtained from mycelia, fruiting bodies, and spore powder allowed for clinical use may contain acidic polysaccharides (*Auricularia auricula-judae*), grifolan (*G. frondosa*), lovastatin [*Lentinus* (= *Pleurotus*) *sajor-caju*], lectins (*A. bisporus*), cordycepin (*O. sinensis*), eritadenine (*L. edodes*), camphoratins and antrodins (*T. camphoratus*), inotodiol, betulinic and trametenolic acids (*I. obliquus*), hispidin, inotilone, and phellilane (*T. linteus*) (Aras et al. 2018; Badalyan et al. 2023; Tee et al. 2024). Mushroom additives can also improve the aroma and nutritional value of food products, such as bread, yogurt, and pasta (Badalyan and Zambonelli 2023; Badalyan, Iotti et al. 2026).

Among the biomolecules widely used in complementary and alternative medicines, including integrative cardiooncology, are (1→3)-, (1→4)-, and (1→6)-β-D-glucans with significant cardioprotective effects (CPE) found in cereals and fungi or produced by microbial fermentation. They prevent the progression of atherosclerosis, leading to various diseases, such as arterial hypertension, dyslipidemia, hyperglycemia, obesity, and stroke, due to their hypoglycemic, hypocholesterolemic, and hypotensive effects, as well as their prebiotic properties that regulate the gut microbiome (Edo et al. 2025; Li et al. 2025; McCarthy and Papada 2025; Wu et al. 2025). Thus, the consumption of fungal β-glucans reduces the risk of CVD and may be considered a promising alternative for maintaining a healthy heart. However, further studies are required to understand all the physicochemical properties, molecular interactions, and biological properties of these biopolymers (Wouk et al. 2021; Caseiro et al. 2022; Zhong et al. 2023).

It was reported that hypoxia/reoxygenation-induced injury of H9c2 cardiomyocytes reduced their viability up to 54.68 ± 2.14% ($p < 0.001$, vs. the control group). *P. linteus*-derived polysaccharides protected against injury restored the viability of H9c2 cells at 10 μg/mL (69.81 ± 3.67%, $p < 0.001$), 20 μg/mL (77.14 ± 5.56%, $p < 0.001$), and 40 μg/mL (88.32 ± 5.6%,

$p < 0.001$). The polysaccharides influence superoxide dismutase (SOD) activity and the expression level of the key protein B-cell lymphoma 2 (Bcl-2), thereby inhibiting apoptosis by regulating mitochondrial membrane permeability and promoting cell survival (Ren et al. 2025). The treatment also reversed the oxidative imbalance induced by injury in H9c2 cells. However, the optimal was 40 μg/mL which decreased the lactate dehydrogenase (LDH) level to $18.37 \pm 2.93$ U/mg protein ($p < 0.001$), normalized malondialdehyde (MDA) content to near-control levels $330.21 \pm 108.43$ nmol/mg protein ($p < 0.001$), and recovered SOD activity to $1.73 \pm 0.16$ U/mg protein ($p < 0.001$), as well as attenuated of injury-induced reactive oxygen species (ROS) overproduction. The injury resulted in a significant increase in mRNA expression of the proapoptotic protein Bax ($2.38 \pm 0.26$ vs. $1.02 \pm 0.18$ for the control; $p < 0.01$) and a decrease in mRNA expression of the anti-apoptotic protein Bcl-2 ($0.48 \pm 0.08$ vs. $1.11 \pm 0.15$; $p < 0.01$), without significant changes in PI3K ($0.76 \pm 0.21$) or AKT ($1.23 \pm 0.22$) mRNA levels. *P. linteus* polysaccharides at 40 μg/mL effectively suppressed kinase activation (p-PI3K, 1.39-fold, $p < 0.05$; p-AKT, 1.97-fold, $p < 0.001$) while restoring apoptotic balance through 2.45-fold reduction in Bax expression (vs. injured group, $p < 0.001$) and 1.58-fold upregulation of Bcl-2 (vs. injured group, $p < 0.05$), ultimately achieving a 3.88-fold decrease in Bax/Bcl-2 ratio ($p < 0.05$). Thus, *P. linteus* polysaccharides could improve injury in H9c2 cells by a 3.9-fold down-regulation of the Bax/Bcl-2 ratio via the PI3K-AKT pathway (Ren et al. 2025).

Three sterols—phellinols A, B, and F—isolated from *Phellinus igniarius* exhibited a CPE against injury induced by oxygen and glucose deprivation followed by reoxygenation in H9c2 cells at a concentration of 20 μM (Li et al. 2021).

The dietary products obtained from *A. bisporus*, *A. subrufescens*, *G. lucidum*, *G. frondosa*, *H. erinaceus*, *Leccinum scabrum*, *P. linteus*, and *Pleurotus* spp. may prevent progression of metabolic syndrome including insulin resistance and obesity (Corrêa et al. 2016; Rubel et al. 2018; Badalyan et al. 2021, 2023; Chan et al. 2021; Badalyan and Zambonelli 2023; Nikolic et al. 2023; Ferraro et al. 2024).

Eritadenine, extracted from *L. edodes*, has been shown to be an antiatherogenic agent with angiotensin-converting enzyme inhibitory activity (Abdullah et al. 2012; Afrin et al. 2016). About 300 bioactive compounds (polysaccharides, proteins, steroids, sterols, triterpenoids, fatty acids, etc.) with therapeutic effects (analgesic, antiangiogenic, antiatherogenic, anticancer, antiinflammatory, antioxidant, cardioprotective, hypolipidemic, immunomodulatory, etc.) were detected in *Ganoderma* spp. (Fernandes et al. 2015; Ferreira et al. 2015; Saltarelli et al. 2015; Meng et al. 2016; Rubel et al. 2018; Badalyan et al. 2019, 2023; Badalyan, Barkhudaryan et al. 2026; Badalyan, Iotti et al. 2026; Chaudhuri and Datta 2021; Cadar et al. 2023; Wu et al. 2024; Karunarathna et al. 2025; Schlosserova et al. 2026). The lanostane triterpenoids isolated from *G. lucidum* and *G. weberianum* have been proposed for the treatment of hyperglycemia and hyperlipidemia (Chen et al. 2017; Yang et al. 2022; Hu et al. 2026) and used in TCM for centuries to prevent cardiovascular disorders (Adhikary et al. 2022).

Currently, various biotech products are being developed from *Ganoderma* spp. mycelia, fruiting bodies, and spores. However, future preclinical and clinical trials are warranted to confirm their efficacy and safety (Ahmad 2018; Wang et al. 2025). Pretreatment of rats with isoproterenol-induced heart failure by *G. lucidum* showed significant CPE (Seiiedy et al. 2023) which, however, needs to be further elucidated in large-scale controlled studies (Chan et al. 2021; Karunarathna et al. 2025).

The CPE of *Trametes versicolor*-derived heteropolysaccharides was studied in Wistar rats with metabolic syndrome after per os administration in 100, 200, and 300 mg/kg (Table 1). The results revealed a significant increase in antioxidant activity, a decrease in blood pressure, an improvement in glucose homeostasis, left ventricular ejection fraction (LVEF), lipid profile, and insulin levels in animals compared to controls ($p < 0.05$). Thus, *T. versicolor* may be considered a cardioprotective agent for the treatment of metabolic disorders (Nikolic et al. 2023).

Species of Ascomycetous genera *Cordyceps* and *Ophiocordyceps* have been used in Ayurvedic and traditional medicine in China, Japan, and Korea as anticancer, antioxidant, and immunomodulatory agents (Das et al. 2021). The *Cordyceps* are used as an adjunct to conventional treatments for arrhythmias; however, their clinical efficacy and antiarrhythmic mechanisms have not been sufficiently investigated (Wang et al. 2022). The treatment of arrhythmia with *Cordyceps* additives was evaluated in randomized controlled trials involving 918 patients. The fungal product significantly improved overall efficacy in both arrhythmia types (tachycardia and bradycardia) in patients without major adverse effects, modulating adrenergic and PI3K-Akt signaling pathways in cardiomyocytes. However, additional recommendations regarding this treatment should be provided (Wang et al. 2022).

Ischemic cardiocerebrovascular diseases (CCVD) are major contributors to disability and mortality in humans. The mechanisms by which *Cordyceps* attenuates ischemic CCVD have recently been reported (Li et al. 2024). In particular, *Cordyceps*-derived bioactive compounds, including cordycepin, protect against CCVD by improving blood perfusion, mitigating ROS damage, suppressing inflammation, preventing cellular apoptosis, and promoting tissue regeneration ($p < 0.01$). *Cordyceps* reduces excitatory neurotoxicity and blood–brain barrier damage induced by cerebral ischemia, improves cardiac energy metabolism, and prevents calcium overload caused by myocardial ischemia. It also exerts a preventive or curative effect on factors causing cardiocerebral ischemia, including arterial hypertension, thrombosis, atherosclerosis, and arrhythmias offering new perspectives for CCVD management (Li et al. 2024).

Medicinal fungus *Cordyceps militaris* contains bioactive cordycepic acid, galactomannans, ergosterol, β-sitosterol, proteins, minerals (Ca, Fe, K, Mg, Na, Se, and Zn) and vitamins ($B_1$, $B_2$, $B_{12}$, E, and K). The use of *C. militaris*-derived products is increasing due to their significant health benefits; however, the mechanism underlying their immunomodulatory effects remains unclear. A randomized controlled trial to study the immunomodulatory effect of a beverage produced by submerged fermentation of *C. militaris* in healthy male and female populations in Thailand provides information to develop

**TABLE 1** | The anticancer and cardioprotective properties of several medicinal mushrooms.

| Species | Bioactive agent | Study model | Chemotherapy | Therapeutic effect | References |
|---|---|---|---|---|---|
| *Cordyceps militaris* | Mycelium extract, *per os* administration | Male Wistar rats | Doxorubicin | CPE, antioxidant, induces regression of necrosis and hypertrophy in cardiomyocytes, decreases CK and LDH levels, upregulates mitochondrial electron transport chain activity | Veena et al. (2021) |
| *Ganoderma adspersum* | Mycelium ethanolic extract | Human renal cancer (Caki-1, 786-O, RCC-Shaw) and nontumor HK-2 cells | — | Antiproliferative, induces apoptosis in renal tumor cells via A3 receptors | Schlosserova et al. (2026) |
| *Ganoderma applanatum* | Water-alcohol extract, IP administration | Swiss albino mice with Dalton lymphoma ascites | Doxorubicin | Anticancer, antioxidant, effectively attenuated DOX-induced toxicity | Varghese et al. (2023) |
| *Ganoderma atrum* | Polysaccharide PSG-1 | Kunming mice | Doxorubicin | Decreases cardiotoxicity by regulation of apoptotic pathway in mitochondria | Li et al. (2018) |
| *Ganoderma lucidum* | Ethanolic extract | Male Wistar rats | Adriamycin | Decreases free radicals, rises GSH content | Rajasekaran and Kalaimagal (2012) |
| *G. lucidum* | Hydroethanolic extract | Male Wistar rats | Doxorubicin | Restores CK and LDH, increases SOD activity, decreases lipid peroxidation | Veena and Janardhanan (2017), Veena et al. (2022) |
| *G. lucidum* | Triterpenes | Wistar rats | Doxorubicin | Decreases the activity of cardiac injury markers (CK-MB, LDH, cTnI); increases SOD, CAT, GPx levels; reduces GSH; attenuates lipid peroxidation | Veena and Janardhanan (2022a) |
| *G. lucidum* | Polysaccharide–protein complex | Male Swiss albino mice | Doxorubicin | Reduces the activity of cardiac biomarkers (CK-MB, LDH, cTnI), increases the activity of antioxidants (SOD, CAT, GPx), reduces GSH, attenuates lipid peroxidation | Veena and Janardhanan (2022b) |
| *G. lucidum* | Aqueous solution, per os | Male albino rats | 5-Fluorouracil | CPE, antioxidant, antiinflammatory, cardiopreventive | Ali et al. (2024) |
| *G. lucidum* | *G. lucidum* polysaccharides | Rat H9c2 cardiomyocytes | Doxorubicin | Decreases LDH, CK, and AST levels; inhibits Cul3-mediated K48-linked polyubiquitination of Nrf2; decreases the expression of P53 and p-P6; and increases MDM2 and HO-1 | Hu et al. (2026) |
| Combination of *G. lucidum* and plants | Aqueous extracts | Female C57Bl/6 mice | Doxorubicin | Improves LVEF and radial/longitudinal deformation | Quagliariello et al. (2022) |
| *Inonotus xeranticus* | Davallialactone (DAVA) | In vivo mouse model, H9c2 cells | Adriamycin | Increases the viability of H9c2 cells, reduces ROS production and apoptosis, decreases the expression of ADR-activated proteins | Arunachalam et al. (2012) |

(Continues)

**TABLE 1** | (Continued)

| Species | Bioactive agent | Study model | Chemotherapy | Therapeutic effect | References |
|---|---|---|---|---|---|
| *Lentinula edodes* | Lentinan | Patients with lung, gastric, and colorectal cancers | — | Anticancer, reduces response rate 1-year survival, improves quality of life, prevents radiotherapy and chemotherapy-induced toxicity | Antonelli et al. (2021) |
| *Morchella conica* | Neutral *M. conica* polysaccharides-2 (NMCP-2) | Rat H9c2 cardiomyoblasts | Doxorubicin | Decreases apoptosis and myocardial oxidative stress, increases viability of H9c2 cells | Xu et al. (2021) |
| *M. conica* | Neutral *M. conica* polysaccharides-2 (NMCP-2) | Female BALB/c mice | Doxorubicin | Protects NMCP-2 against $H_2O_2$-induced injury in HEK 293T cells | Xu et al. (2018) |
| *Morchella esculenta* | Methanolic extract | Rat H9c2 cardiomyoblasts | Doxorubicin | Attenuates oxidative stress leading to myocardial injury | Das et al. (2022) |
| *M. esculenta* | Methanolic extract | Rat H9c2 cardiomyoblasts | Doxorubicin | Decreases cardiac biomarkers | Das et al. (2025) |
| *M. esculenta* | Methanolic extract | Male Swiss albino mice | Cyclophosphamide | Improves mitochondrial function, attenuates cardiotoxicity by modulating KEAP1/NRF2 and proinflammatory gene expression | Das et al. (2025) |
| *Phellinus* (= *Tropicoporus*) *linteus* | *P. linteus* polysaccharides | Rat H9c2 cardiomyocytes | — | CPE against ischemia–reperfusion injury | Ren et al. (2025) |
| *P. igniarius* | 22-Hydroxylanostane triterpenoids phellinols A, B, F | Rat H9c2 cardiomyocytes | — | CPE, against oxygen-glucose deprivation and reoxygenation injury | Li et al. (2021) |
| *P. igniarius*, *P. linteus*, *P. nigricans* | Ethanolic extract | Cholangiocarcinoma cell lines (KKU-100, KKU-213A) | — | Strong cytotoxic and antioxidant activity | Thammavong et al. (2020) |
| *Thelephora terrestris* | Vialinin A (*p*-terphenyl) | Human umbilical vascular endothelial cell (HUVEC) | — | Antioxidant and antiinflammatory, prevents HUVEC neovascularization in vitro and in vivo and VEGF-induced HUVEC cell growth in a dose-dependent manner | Himangshu et al. (2018) |
| *T. vialis* | Vialinin A (*p*-terphenyl) | SW480 and Caco-2 cells | — | CPE, antioxidant, antiinflammatory, anticancer, preventing chemotherapy-induced toxicity | Lahori et al. (2025) |
| *Trametes sanguinea* | *T. sanguinea* fermented crude polysaccharide (TSLFACP) | Rat H9c2 cells, human embryonic myocardial cells CCC-HEH-2, male BALB/c mice | Doxorubicin | CPE, inhibits the apoptosis of cardiomyocytes | Shen et al. (2023) |

(Continues)

**TABLE 1** | (Continued)

| Species | Bioactive agent | Study model | Chemotherapy | Therapeutic effect | References |
|---|---|---|---|---|---|
| *T. versicolor* | Heteropolysaccharides, per os | Male Wistar albino rats with metabolic syndrome | — | CPE, increases antioxidant activity, reduces arterial pressure, improves glucose homeostasis and LVEF | Nikolic et al. (2023) |
| *Vanderbylia* (= *Trametes*) *robiniophila* | Huaier polysaccharide | Rat H9c2 cardiomyoblasts | Doxorubicin | Increases cell viability and GPx expression, decreases cardiac biomarker levels (cTnI, LDH), attenuates acute cardiotoxicity by regulating ferroptosis | Ma et al. (2022) |

immune-boosting beverages without side effects or toxicity (Ontawong et al. 2024).

## 3 | Anticancer Effects of Mushrooms

Chemotherapy, radiotherapy, and surgery are the primary treatments for cancer; they effectively reduce tumor progression and the rate of metastasis. However, the side effects of these treatments (alopecia, vomiting, physical discomfort, and sleep disturbances) significantly impair patients' quality of life. Consequently, cardioprotective agents of major clinical importance are needed during cancer treatment.

Recent research has intensified the exploration of MDBC for the development of anticancer adjuvants, given their preventive and therapeutic potential, low toxicity, and limited side effects. Currently, the therapeutic potential of edible and medicinal mushrooms of different taxonomic and ecological groups is widely used in complementary cancer therapy (Nandi et al. 2024; Tsado et al. 2025). Although preclinical studies have demonstrated their cardioprotective, anticancer, and cytotoxic activities, the clinical use of mushrooms remains poorly understood (Wasser 2017; Hetland et al. 2020).

The antitumor effects of several medicinal mushrooms (*Agaricus subrufescens*, *A. sylvaticus*, *Antrodia cinnamomea*, *G. lucidum*, *I. obliquus*, and *Trametes versicolor*) in cancer patients during and/or after treatment have recently been reported (Wasser 2017; Hetland et al. 2020; Zhao and Zheng 2021; Nandi et al. 2024; Tsado et al. 2025). In particular, a previous study demonstrated the antitumor potential of medicinal mushrooms in patients with advanced lung cancer, with disease stabilization in 35% of patients (vs. 22% in controls), accompanied by an increased NK-cell activity, reduced treatment-related side effects, and improved quality of life, revealed by improved Karnofsky performance status in 50% of patients (vs. 14% in controls). However, some patients developed gastrointestinal disturbances and thrombocytopenia during treatment (Jeitler et al. 2020). Further clinical studies are required to evaluate the safety and therapeutic value of MDBP in cancer treatment protocols.

Mushroom-derived β-glucans, such as krestin, as well as glycoproteins, lipopolysaccharides, and proteins, have notably been identified as effective immunomodulators to prevent oncogenesis in several types of cancer by inducing cell apoptosis in the host (Guggenheim et al. 2014; Kozarski et al. 2014; Tsai et al. 2016; Pandya et al. 2019).

It was reported that the immunomodulatory effects of mushrooms (*A. subrufescens*, *G. lucidum*, *G. frondosa*, *O. sinensis*, and *T. versicolor*) contribute to cytokine induction and cytotoxic effects on cancer cells (Tsai et al. 2016). However, collaboration between mycologists, pharmacologists, clinicians, and oncologists is essential to adapt treatment protocols to the individual needs of cancer patients. Further studies of different approaches in mushroom-based cancer therapy will support the development of new treatment strategies aimed at reducing long-term complications, improving quality of life and survival of patients (Tsai et al. 2016).

Colorectal cancer poses a significant risk to human health due to its high incidence and mortality rate. The genetic predisposition, inflammation, and oxidative stress are key factors in the pathogenesis of this disease. Meanwhile, disease incidence is rising among young people, underscoring the importance of implementing preventive strategies. Available chemotherapeutic drugs, such as anthracyclines, often cause serious side effects, including cardiotoxicity.

Vialinin A (*p*-terphenyl), isolated from the edible Agaricomycetes mushroom *Thelephora vialis*, possesses antiinflammatory and antioxidant effects and inhibits neovascularization in human umbilical vein endothelial cells (HUVEC) in vitro and in vivo. Pretreatment of HUVEC with vialinin A prevents vascular endothelial growth factor (VEGF)–induced HUVEC growth, ROS and MDA generation, NF-κB nuclear translocation, and DNA-binding activity. Vialinin A also prevents angiogenesis and the expression of platelet endothelial cell adhesion molecule-1 and von Willebrand factor (Himangshu et al. 2018). Thus, the anticancer effects of vialinin A seem to be mediated by its antioxidant and antiangiogenic properties.

In vivo study of CPE of vialinin A in the chemotherapy-induced toxicity against human colorectal cancer cells SW480 and Caco-2 showed a dose-dependent anticancer effect by suppression of ROS generation, activation of caspase-3, and modulation of the expression of apoptotic and inflammatory markers in cancer cells. The elucidation of the molecular mechanisms of the anticolorectal cancer effect of vialinin A is in progress (Lahori et al. 2025).

The polypore species *Vanderbylia* (= *Trametes*) *robiniophila*, known as Huaier and documented in TCM, contains bioactive molecules (polysaccharides, alkaloids, ketones, minerals, and proteins) which regulate oxaliplatin resistance in HCT-8 cells by modulating autophagy and inhibiting the Wnt/β-catenin signaling pathway in patients with breast, colorectal, liver, and stomach cancers (Feng et al. 2024). The use of *V. robiniophila*-derived polysaccharide granules is recommended in clinical guidelines for patients with hepatocellular carcinoma (HCC). The product showed a weaker in vitro inhibitory effect on proliferation in nude mice and human HCC cells but exhibited significant anti-HCC effects in animal models. The anticancer mechanism of this product remains poorly understood. Furthermore, 16S rRNA gene sequencing and analysis revealed that *V. robiniophila*-derived polysaccharide altered the gut microbiome (Li et al. 2025). Thus, *V. robiniophila* exacerbates autoimmunity in cancer patients, improving their survival rate and quality of life (Ji et al. 2024). Further large-scale clinical trials of *V. robiniophila* have demonstrated its anticancer effect, as a natural adjuvant agent (Xie et al. 2024; He et al. 2026).

A polyphenol isolated from the hymenochaetoid fungus *Phellinus baumii* has shown antitumor activity in colorectal cancer, with low toxicity and fewer side effects than radiotherapy and chemotherapy. It inhibited the proliferation of human HCT116 cells and induced apoptosis and cell cycle arrest, increased ROS levels by about twofold, and depolarized mitochondrial membrane potential by about 40%–60% in cancer cells. As an alternative therapeutic strategy, this polyphenolic compound can be considered a potential replacement anticancer drug. However, further studies are required to evaluate its anticancer effects and elucidate the in vivo mechanisms underlying early colorectal cancer prevention in animal models (Liu et al. 2023).

Polysaccharides, polyphenols, and triterpenoids with anticancer, antiinflammatory, and antioxidant properties have been detected in *P. linteus* (Sanghuang mushroom). This fungus may be considered a potential adjuvant to cancer treatment (Wu et al. 2022). A preparation based on *P. linteus* mycelium extract was suggested as a supplementary medicine to alleviate the toxic effects associated with adjuvant chemotherapy in patients with pancreatic cancer after radical pancreatectomy (Figueiredo and Régis 2017; Lee et al. 2019).

An analysis of recent data of 407 patients with pancreatic cancer after curative resection and adjuvant chemotherapy, among which 103 patients received per os Mesima (*P. linteus* mycelium extract) before chemotherapy and 304 patients were in the control group, showed that the median overall survival was longer in the group that received the tested extract (Kim et al. 2025). No significant benefit in terms of overall survival or recurrence-free survival was observed in the mushroom group; patients in this group received FOLFIRINOX, a combination of oxaliplatin, irinotecan, 5-fluorouracil, and folinic acid. However, among patients treated with non-FOLFIRINOX regimens, such as gemcitabine, *P. linteus* use was associated with improved overall survival. In particular, the mushroom/gemcitabine combination resulted in greater cancer cell death than gemcitabine alone, due to the antiinflammatory and immunomodulatory effects of *P. linteus*. Thus, the perioperative use of *P. linteus* in patients with resected pancreatic cancer was associated with a 34.3% increase in median overall survival (47.0 vs. 35.0 months). Consequently, this fungus, as a potential adjuvant, may improve the patient's survival (Kim et al. 2025).

The methanolic, ethanolic, and aqueous extracts of wild-grown mushrooms *G. lucidum*, *H. erinaceus*, *L. edodes*, *P. ostreatus*, and *Volvariella volvacea* were screened for their anticancer, anti-α-glucosidase, antithrombotic, and antityrosinase effects (Sharif et al. 2018). The anticancer activity was evaluated on HT-29 colon and H-1299 lung carcinoma cells. Different levels of growth inhibition in HT-29 cells were observed at 200 μg/mL of mushroom extracts: *G. lucidum* induced 29% cell viability, followed by *H. erinaceus* (66%), *L. edodes* (68%), *V. volvacea* (83%), and *P. ostreatus* (84%). In contrast, for H-1299 cells, *G. lucidum* induced 24% cell viability, followed by *P. ostreatus* (61%) and *H. erinaceus* (72%) (Koss-Mikołajczyk et al. 2021).

Lentinan extracted from *L. edodes*, as an adjunct to standard cancer treatment, improves response rates, 1-year survival by attenuating cardiotoxicity induced by radiotherapy and chemotherapy in patients with colorectal, esophageal, gastric, gastrointestinal, and lung cancers (Antonelli et al. 2021).

## 4 | Cardiotoxicity-Attenuating Effects of Mushrooms

Understanding the pathogenesis of cancer and CVD, the mechanism of action of anticancer drugs, and the assessment

of patients' cardiac health and risk factors, as well as regular monitoring, is essential to prevent chemotherapy-induced cardiotoxicity which could limit anticancer drug dosages and reduce the efficacy of tumor elimination. Moreover, chemotherapy-induced cardiotoxicity represents a significant cause of serious cardiac complications in cancer survivors. In particular, up to 20% of adults undergoing cancer treatment experience cardiotoxicity, and among them, approximately 7 to 10% develop heart failure. Therefore, the study of mechanisms and strategies to prevent chemotherapy-induced cardiotoxicity and the search for novel cardioprotective agents remain the focus of integrative cardiooncology (Albini et al. 2010; Koss-Mikołajczyk et al. 2021; Omland et al. 2022; Quagliariello et al. 2022; Cheah et al. 2023; Firoozbakhsh et al. 2024; Gao et al. 2024; Ciappina et al. 2025).

Almost all antitumor drugs, including alkylating agents, anthracyclines, taxanes, and topoisomerase inhibitors, exhibit cardiotoxicity and increase the risk of heart failure, myocarditis, cardiac arrhythmias, arterial hypertension, coronary artery disease, ferroptosis, mitochondrial dysfunction, and oxidative stress. Among these drugs, anthracyclines, particularly doxorubicin (DOX), are particularly cardiotoxic. Additionally, the risk factors for anthracycline-induced cardiotoxicity include preexisting cardiomyopathy, cardiac dysfunction related to prior cancer treatment, and heart failure. Therefore, the cardiotoxicity may develop through oxidative stress, mitochondrial dysfunction, cell apoptosis, and alterations in iron-regulating proteins, as well as calcium imbalance and inflammation (Figure 2).

The implementation of various therapeutic protocols may prevent chemotherapy-induced cardiotoxicity in cancer patients, including early diagnosis and administration of cardioprotective drugs. Several innovative strategies, notably mitochondrial transplantation, have been proposed to attenuate DOX-induced cardiotoxicity in in vivo and in vitro models (Omland et al. 2022; Gao et al. 2024).

Recently, there has been a growing interest in using MDBP, botanicals, herbal preparations, and other natural products in traditional medicine as potentially safe and effective cardioprotecive agents to prevent anthracycline-induced cardiotoxicity during cancer therapy. The dietary supplements may reduce oxidative stress in the myocardium, cardiotoxic effects of antitumor drugs, and the risk of heart failure. However, the interaction between traditional medicine and conventional chemotherapeutic agents needs to be studied in greater detail to prevent adverse synergistic effects (Wang et al. 2025).

These interventions should also target cancer patients with a history of CVD, as they may be at an increased risk of side effects. Thus, preventive strategies using MDBP and other natural agents without side effects are needed to attenuate cardiotoxicity in cancer patients; however, preclinical and clinical trials in this area are scarce, making it difficult to confirm the overall positive impact of such products (Syahputra et al. 2022).

Available natural products may offer CPE against DOX-induced cardiotoxicity in both in vitro and in vivo studies (Szponar et al. 2024). The combination of DOX and natural products may decrease drug concentration in healthy tissues and increase it in cancer cells, thereby enhancing anticancer effects. Progress in preclinical studies using natural preventive agents against DOX-induced cardiotoxicity has not yet translated into clinical implementation due to the low bioavailability of cardioprotective adjuvants in humans and the lack of cardiac biomarkers to detect myocardial injury and cardiotoxicity. Further studies are required to better understand the complex signaling networks that play a key role in cardiomyocyte dysfunction and survival during DOX treatment for cancer (Szponar et al. 2024).

### 4.1 | Doxorubicin-Induced Cardiotoxicity

DOX is a highly effective anthracycline agent used to treat solid tumors, which causes dose-dependent cardiotoxicity during and after several years of treatment. The cumulative toxic dose of DOX is up to 400 mg/m$^2$, which may increase the cardiac toxicity in clinical practice (Wang et al. 2022). The molecular mechanisms underlying DOX-induced cardiomyopathy remain incompletely understood. Several mechanisms, such as oxidative stress,

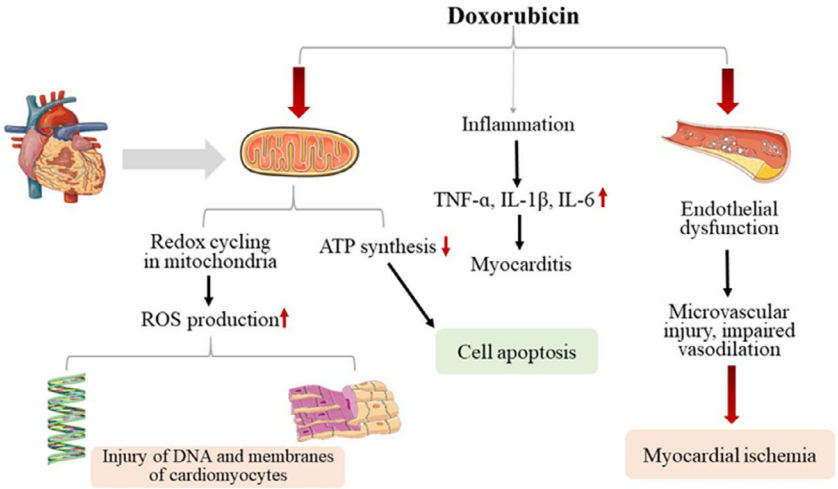


**FIGURE 2** | The mechanism of DOX-induced cardiotoxicity: ATP, adenosine triphosphate; IL-β, interleukin-1β; IL-6, interleukin-6; ROS, reactive oxygen species; TNF-α, tumor necrosis factor-α.

topoisomerase βII inhibition, mitochondrial dysfunction, dysregulation of $Ca^{2+}$ homeostasis, intracellular $Fe^{2+}$ accumulation, resulting in apoptosis and necrosis, autophagy, myofibrillar disarray, and loss of H9c2 cells have been proposed (Syahputra et al. 2022). In DOX-induced cardiotoxicity, the levels of creatinine kinase (CK), LDH, lipid peroxidation (LPO), and advanced oxidation products of proteins significantly increased, while the activities of glutathione (GSH), SOD, glutathione peroxidase (GPx), and catalase (CAT) were reduced. Combining DOX therapy with natural cardioprotective agents could be an effective strategy to enhance its anticancer effect (Biswal et al. 2025) (Table 1).

Nutraceuticals with mushroom and plant origins, such as extracts of *G. lucidum* with *Arthrospira* (= *Spirulina*) *platensis* and *Moringa oleifera*, are rich in amino acids, polyphenols, polysaccharides, proteins, and terpenoids and have improved LVEF by about 40% and radial/longitudinal deformation of the heart in animals with DOX-induced cardiotoxicity (Quagliariello et al. 2022).

The CPE of ergothioneine, flavonoids, and β-glucans against DOX-induced cardiotoxicity in in vitro and in vivo cell, animal, and human models have been studied (Syahputra et al. 2022; Wang et al. 2022; Cheah et al. 2023; Shang et al. 2025). A dietary ergothioneine accumulates in the cardiac tissue and due to its antioxidant effect protects against mitochondrial damage and chemotherapy-induced cardiac dysfunction. However, further studies are needed to confirm the CPE of ergothioneine (Cheah et al. 2023).

The study of the mechanism of DOX-induced cardiotoxicity in mice has demonstrated that β-glucans can prevent left ventricular dilation and fibrosis, decreasing cardiotoxicity by suppressing oxidative stress and stimulating mitochondrial function. However, further studies are required to define the therapeutic potential of β-glucans in cardiooncology, exploring their mechanisms of action and elucidating their clinical implications as a basis for new strategies (Wang et al. 2022).

Preclinical and clinical studies have revealed the preventive effects of flavonoids against DOX-induced cardiotoxicity, acting as natural antioxidants, anticancer, and cardioprotective agents. Flavonoids (such as apigenin, hesperidin, luteolin, naringenin, quercetin, and rutin), as well as seven flavonoid subclasses comprising more than 49 compounds (18 flavones, 11 flavonols, seven isoflavones, six flavanones, three chalcones, two flavanols, and two anthocyanins), have been described as cardioprotective agents. Among these compounds, quercetin emerges as the most promising agent, consistent with extensive preclinical data demonstrating multiorgan protection without compromising the therapeutic efficacy of DOX (Syahputra et al. 2022; Shang et al. 2025). Further investigation is required to determine the CPE of flavonoid-based natural products against DOX-induced cardiotoxicity in the context of adjuvant cancer therapy.

The hydroethanolic extract of *G. lucidum*, as a natural antioxidant, protected cardiomyocytes against DOX-induced cardiotoxicity; however, the exact mechanism of action deserves further investigation (Veena and Janardhanan 2017). Mycelium extract of *G. lucidum*, as a source of polysaccharides, triterpenes, and polyphenols, significantly increases SOD, GPx, CAT, and GSH activity and decreases LPO level in rats. The extract prevents DOX-induced cardiotoxicity at 18 mg/kg body weight and is administered to animals at 250 and 500 mg/kg body weight daily for 5 days prior to DOX therapy. Histopathological findings, hematology profiles, and electrocardiographic parameters supported the CPE of *G. lucidum* against DOX-induced cardiotoxicity and perspectives of its use in alternative oncotherapy (Veena et al. 2018). *G. lucidum* biomass extract attenuated DOX-induced increases in CK and LDH levels by about 47% and 76%, respectively, as well as oxidative stress in a preclinical model (Veena et al. 2022).

The findings of another study have shown that triterpenes extracted from the fruiting bodies and mycelium of *G. lucidum* improved DOX-induced cardiomyopathy in rats by decreasing the levels of cardiac biomarkers, such as creatinine kinase-myoglobin (CK-MB), LDH, and cardiac troponin (cTnI), restoring the activity of SOD, CAT, GPx, and GSH and reducing LPO in the myocardium. Thus, *G. lucidum*-derived triterpenes prevented DOX-induced oxidative stress and cardiac injury in rats and may serve as a therapeutic agent for cardiomyopathy (Veena and Janardhanan 2022a).

A polysaccharide–protein complex isolated from hydroalcoholic extracts of fruiting bodies and mycelia of *G. lucidum* attenuated DOX-induced cardiomyopathy and enhanced activities of SOD and CAT in Swiss albino mice. The histopathological observations suggest that a polysaccharide–protein complex from *G. lucidum* may be considered a natural agent against DOX-induced cardiotoxicity (Veena and Janardhanan 2022b).

The study of CPE of *G. lucidum* polysaccharides on H9c2 rat cardiomyocytes revealed that pretreatment with polysaccharides significantly decreased LDH, CK, and aspartate aminotransferase (AST) levels and attenuated histopathological changes in cardiac tissue as a result of DOX-induced cardiotoxicity (Xu et al. 2017) (Table 1).

The cardioprotective mechanism of *Ganoderma atrum*-derived polysaccharide in DOX-treated mice was revealed. The polysaccharide attenuated myocardial injury by reducing apoptosis and preserving mitochondrial structure, associated with increased manganese SOD activity, decreased caspase activity, and suppression of DOX-induced mitochondrial dysfunction. The use of *G. atrum* polysaccharide is suggested as an effective preventive strategy against DOX-induced cardiotoxicity (Li et al. 2018) (Table 1).

Antibacterial, anticholinesterase, and antioxidant activities, as well as antiproliferative effects on breast cancer cells, were reported in the ethanolic extract of *Ganoderma adspersum* mycelium (Table 1). The study showed that the extract reduced cell viability by more than 80% in both 786-O and RCC-Shaw human renal cancer cell lines. Mycelium extract at up to 500 μg/mL was well tolerated by nontumor human renal HK-2 cells. Thus, *G. adspersum* is a promising source of antiproliferative compounds for the development of standardized therapeutic agents for adjuvant cancer therapy (Schlosserova et al. 2026).

The intraperitoneal administration of hydroalcoholic extract of *Ganoderma applanatum* to Swiss albino mice with ascites related to Dalton's lymphoma and treated with DOX revealed a dose-dependent attenuation of chemotherapy-induced cardiac and hepatic tissue injuries (Table 1). Therefore, *G. applanatum* may be further tested as a potent candidate for adjuvant chemotherapy against DOX-induced toxicities (Varghese et al. 2023).

A polysaccharide extracted from *V. robiniophila* was used to treat DOX-induced heart injury in mice. In vitro experiments revealed a significant increase in H9c2 cell viability after treatment. The levels of biomarkers cTnI and LDH were lower in the DOX-polysaccharide group than in the DOX group, and structural alterations were detected in cardiac tissue. Moreover, the expression of ferroptosis marker and GPx was increased in the first group (Table 1). Thus, *T. robiniophila* polysaccharide attenuated DOX-induced cardiac damage, probably by regulating ferroptosis (Ma et al. 2022).

The protective effect of a crude polysaccharide, derived from polypore fungus *Trametes sanguinea*, has been shown against in vitro DOX-induced cardiotoxicity using H9c2 cardiomyocytes and CCC-HEH-2 embryonic myocardial cells, as well as an in vivo murine model of DOX-induced cardiac injury (Table 1). A daily pretreatment with a polysaccharide (200 mg/kg) for 6 days attenuated DOX-induced toxicity by decreasing the serum cardiac injury index and improving histopathological morphology. Furthermore, the use of polysaccharides attenuated the expression of LC3-II, Beclin-1, and PRAP. Thus, *T. sanguinea* may protect the heart tissue by inhibiting autophagy and apoptosis (Shen et al. 2023).

The mycelial extract of *C. militaris* tested against DOX-induced cardiotoxicity in male Wistar rats revealed a decrease in oxidative stress, upregulation of respiratory chain complex activity, and regression of necrosis and hypertrophy in cardiomyocytes, as evidenced by decreased levels of CK and LDH (Table 1). The CPE of *C. militaris* was mediated by the upregulation of activity of mitochondrial dehydrogenases, electron transport chain complex, and adenosine triphosphate (Veena et al. 2021).

The species of the genus *Morchella* (Ascomycota, Pezizomycetes) are used in traditional medicine to treat bronchial asthma, cough, colds, indigestion, excess mucus, and dyspnea (Das et al. 2022). The study of CPE of the methanolic extract of medicinal fungus *Morchella esculenta* against DOX-induced toxicity in vitro on H9c2 cardiomyoblastic cells showed a reduction in cytotoxicity at 150 and 200 µg concentration, a significant decrease in levels of cardiac biomarkers, and a return to near-normal levels of SOD, GPx, and GSH, attenuating the oxidative stress and cardiac tissue injury (Table 1). The potential of *M. esculenta* as a cardioprotective agent in the treatment of cancer patients has been reported (Das et al. 2022). A significant CPE of the methanolic extract of *M. esculenta* in solid tumor-bearing mice, independent of the toxic effect of DOX and cyclophosphamide, has also been demonstrated (Das et al. 2025).

The purified polysaccharides from *Morchella conica* were tested in human embryonic kidney cells (HEK 293T). The results showed that the polysaccharides exerted a pronounced protective and antioxidant effect against damaged HEK 293T cells and could be used as natural antioxidants (Table 1) (Xu et al. 2018). Further study of *M. conica* polysaccharides on DOX-induced cardiotoxicity in H9c2 cells revealed increased myocardial cell viability and reduced LDH levels in mice, improved myocardial tissue histology, and exhibited a significant CPE against cardiac injury, likely by inhibiting oxidative stress and mitochondrial apoptotic pathways. Thus, the *M. conica* extract could be considered a dietary supplement to reduce anthracycline-induced cardiotoxicity (Xu et al. 2021) (Table 1).

Recent data showed that the flavonoids, polyphenols, terpenoids, and quinones, found in mushrooms, may enhance cell viability, attenuate myocardial fibrosis, improve cardiac function, and suppress ferroptosis which plays a vital role in the pathogenesis of DOX-induced cardiotoxicity in vitro and in vivo (Yi et al. 2024). An association between DOX-induced cardiac ferroptosis and key proteins has been described. As potential ferroptosis regulators, natural products are likely to exert therapeutic effects against DOX-induced cardiotoxicity by modulating protein activity (Arunachalam et al. 2012).

### 4.2 | Cardiotoxicity Induced by Other Chemotherapeutic Agents

Adriamycin (ADR) is an anticancer agent that causes cardiotoxicity primarily by inducing oxidative stress. Davallialactone (DAVA), derived from the hymenochaetoid fungus *Inonotus xeranticus* with antiplatelet and antioxidant effects, showed protective effect against ADR-induced cardiomyocyte apoptosis and antioxidant injury compared with the antioxidant N-acetylcysteine (Lee et al. 2006). The CPE of DAVA was tested in a mouse model of ADR-induced acute cardiomyopathy in vivo. DAVA improved the viability of ADR-treated H9c2 cells; reduced ROS production and apoptosis; decreased the expression of activated Cu/Zn SOD, Mn-SOD, c-Jun N-terminal, and extracellular signal-regulated kinases; and prevented free radical generation, proving its beneficial use against ADR-induced cardiomyopathy (Arunachalam et al. 2012) (Table 1).

The CPE of *G. lucidum* extract against ADR-induced cardiotoxicity in Wistar rats led to an increase in serum levels of cardiac enzymes, as well as alanine aminotransferase (ALT), aspartate transaminase (AST), LDH, and CK, exhibiting significant antioxidant properties (Rajasekaran and Kalaimagal 2012) (Table 1). This fungus possesses cardioprotective, antiinflammatory, and antioxidant effects and was used to mitigate 5-fluorouracil (5-FU)-induced cardiotoxicity. The results showed that 5-FU increased the expression levels of heart-type fatty acid-binding protein (h-FABP), cTnI, MDA, TNF-α, and cyclooxygenase-2 (COX-2). *G. lucidum* may be considered a preventive agent against 5-FU-induced cardiotoxicity due to its antioxidant and antiinflammatory properties, as a natural cardioprotectant (Ali et al. 2024).

## 5 | Future Perspectives and Potential Applications

Cancer and CVD are among the leading causes of morbidity and mortality worldwide. In the context of cancer, CVD encompasses

not only the side effects of antitumor treatments but also metabolic disorders induced by oncological diseases. CVDs are considered a leading cause of death among cancer survivors. Research indicates that abnormalities in lipid metabolism play a significant role in the development of cardiac pathologies. Despite progress in this area, there is a lack of drugs targeting dyslipidemia to treat tumors and mitigate cardiac risk. The metabolic profiles and adaptations observed in cancer and CVD are complex and dynamic. The reprogramming of lipid metabolism induced by malignancy can trigger metabolic and inflammatory stress in the heart, highlighting the need to understand the molecular mechanisms of these processes to develop novel therapeutic strategies.

The medications targeting abnormalities of lipid metabolism can also suppress tumor growth. The potential of natural compounds to simultaneously treat CVD and cancer by targeting lipid metabolism represents a promising therapeutic approach. Understanding the mechanisms of action of natural products, particularly those related to the regulation and reprogramming of lipid metabolism, will open a new perspective for the development of innovative treatments for CVD associated with cancer therapy (Zhu et al. 2024).

This review discusses the therapeutic effects of several medicinal mushrooms (*Cordyceps*, *Ganoderma*, *Lentinula*, *Morchella*, *Phellinus*, and *Trametes*) on cardioprotection and anticancer properties and their use to prevent and treat cardiotoxicity in cancer patients undergoing chemotherapy. In vitro and in vivo studies have demonstrated the valuable effect of MDBP on human well-being. However, available research data indicate the cardioprotective potential of mushroom products, but not the mechanisms of their action. Moreover, they are mainly concerned with preclinical rather than clinical trials. Future studies focused on regulatory safety, toxicity, and risks are essential to obtain robust scientific data and practical knowledge to optimize the efficacy of natural compounds and products, including MDBP, while minimizing their adverse effects.

Recent advances in mycopharmacology and integrative cardiooncology will enhance the health benefits of MDBP, making them more accessible to a broader population for cancer treatment. Future preclinical and clinical trials will contribute to understanding the mechanisms underlying the antioxidant and antiinflammatory effects of mushrooms and justify their use as clinically effective anticancer and cardioprotective mycopharmaceuticals based on mushroom-derived bioactive molecules and their synergistic effects.

### Author Contributions

S.B., S.R., and A.B. contributed to the conceptualization and framework of the manuscript. S.B., S.R., and A.B. wrote the manuscript. S.B. and S.R. designed Figure 1, and A.B. created Figure 2. All authors participated in the manuscript revision and read and approved the final submitted version.


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### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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