



## AURICULARIA: A REVIEW OF PHARMACOLOGICAL STUDIES

**Suci Rahma, Ega Putri Rhena, Evita Amalia Putri Adindika, Fitri Widiyani, Gheriya Zahira,  
Gusti Ayu Putu Purnama Dewi Saraswati, Hemalia Putri, Indah Marliana, Jordan Saputra,  
Nabila Putri Pramesti, Ricky Rianto, Theresia Anastasya Sriyanti Silaen, Vasgherina Ramadhaniawianto,  
Yoga Sukmana, Yulistia Afta Nurhamidah and Maulana Yusuf Alkandahri\***

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.



\*Corresponding Author: Maulana Yusuf Alkandahri

Faculty of Pharmacy, Universitas Buana Perjuangan Karawang, Karawang, West Java, Indonesia.

Article Received on 16/11/2024

Article Revised on 05/12/2024

Article Accepted on 26/12/2024

### ABSTRACT

*Auricularia* is one of the jelly fungi groups that belongs to the Basidiomycota class and has a unique jelly texture. Fungi that belong to this class are generally macroscopic or easily seen with the naked eye. Currently, there have been many studies that prove that fungi from the genus *Auricularia* have several pharmacological activities, including antibacterial, antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, antinephritic, and antihyperlipidemic. Currently, there has been no detailed evaluation report on the potential that shows the effectiveness of fungi from the genus *Auricularia*, therefore this review article will discuss the potential pharmacological activity of fungi from the genus *Auricularia*.

**KEYWORDS:** *Auricularia*, Antibacterial, Antioxidant, Anti-inflammatory, Hepatoprotective, Antidiabetic, Antinephritic, Antihyperlipidemic.

### INTRODUCTION

Eukaryotic organisms constituting the kingdom fungi have long been of interest to pharmaceuticals and industries as they serve as a natural source of important bioactive secondary metabolites. Compared with other plant-derived active products, the biochemistry of fungi is an underexplored resource despite their historical contribution to the discovery of antibiotics (penicillins, cephalosporins, etc.), immunosuppressants (including cyclosporine, mycophenolic acid), antifungal drugs (griseofulvin, echinocandins), cholesterol-lowering statins, antimigraine ergot alkaloids, etc. Despite their proven potential as a source of pharmaceuticals, only a small fraction of the described fungal species have been screened for drugs. Edible and medicinal mushrooms are among the most studied fungi due to their biologically active compounds.<sup>[1]</sup> One of the species of fungi reported to have various pharmacological activities is *Auricularia*, including as antibacterial, antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, antinephritic, antihyperlipidemic. Currently, there is no detailed evaluation report on the potential that shows the effectiveness of *Auricularia* fungi, therefore this review article will discuss the potential pharmacological activities of fungi of the genus *Auricularia*.

### PHARMACOLOGICAL STUDIES

#### Antibacterial

The increasing resistance to antibiotics and the complexity of defeating multidrug-resistant bacteria have led to an increased search for new and effective antimicrobials from various plants. Natural products with higher levels of plants can provide a source of new antimicrobial agents with possible novel mechanisms of action.<sup>[2]</sup> The administration of *Auricularia auricula-judae* mushroom extract has been reported to inhibit the growth of *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* bacteria with minimum inhibitory concentrations of 5 µg/mL.<sup>[3]</sup>

#### Antioxidant

Free radicals are molecules that lose electrons so that the molecule becomes unstable so that it tries to return electrons from other molecules or cells.<sup>[4,5]</sup> Antioxidants are compounds that can protect cells from damage caused by free radicals. Antioxidants will interact by stabilizing free radicals to prevent damage caused by possible free radicals.<sup>[6]</sup> Administration of *Auricularia* spp extract has been reported to have potent antioxidant activity with an IC<sub>50</sub> of 40 µg/mL in the DPPH model.<sup>[7]</sup>

### Anti-inflammatory

Inflammation is a disorder involving localized increase in the number of leukocytes and various complex mediator molecules. The inflammatory response plays a central role in the pathogenesis of many diseases, initiated by pathogen invasion or by tissue injury caused by free radicals, followed by a series of vascular and cellular reactions. Among leukocytes, macrophages are key players in the inflammatory response and are also the main source of pro-inflammatory cytokines and enzymes including tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukins (ILs), cyclooxygenase (COX), and inducible nitric oxide synthase (iNOS).<sup>[8]</sup> Existing synthetic molecules such as nonsteroidal anti-inflammatory drugs (NSAIDs) and selective COX-2 inhibitors are known to have side effects that increase the incidence of adverse cardiovascular thrombosis.<sup>[9]</sup> Alternative therapies with minimal side effects from natural plant extracts should be the focus of scientific research. Administration of *Auricularia auricula-judae* extract at concentrations of 10, 30, and 100  $\mu\text{g}/\text{mL}$  was reported to inhibit nitric oxide (NO) production and reduce the expression of inflammatory cytokines (IL-6, TNF- $\alpha$  and IL-1 $\beta$ ) mRNA in murine RAW 264.7 macrophages induced by lipopolysaccharide (LPS) *in vitro*.<sup>[10]</sup>

### Hepatoprotective

The liver is a vital organ that plays a major role in metabolism, detoxification and elimination of toxic substances and liver disease is still a major health problem.<sup>[11]</sup> Free radicals are a major risk factor for liver disease.<sup>[12]</sup> Synthetic drugs used in the treatment of liver disease are inadequate and can sometimes cause serious side effects.<sup>[13]</sup> Therefore, alternative treatments are needed as hepatoprotectors, one of which is from medicinal plants. Oral administration of *Auricularia cornea* extract at doses of 200 and 400 mg/kg has been reported to protect the liver by increasing antioxidant activity, reducing lipid peroxidation, increasing alcohol metabolism, inhibiting the level of inflammatory mediator expression, and preventing histopathological changes in mice induced by 50% alcohol solution.<sup>[14]</sup>

### Antidiabetic

Diabetes is a common, multietiological, and hereditary endocrine and metabolic disorder,<sup>[15]</sup> which has now become the third major threat to human health. The number of people with diabetes mellitus II (DM II) reaches around 90% of all types of diabetes.<sup>[16]</sup> Currently, clinical treatment of type II diabetes is mainly in the form of insulin injection, oral sulfonylurea, and BIS guanidine as hypoglycemic drugs to achieve the goal of lowering blood sugar. These drugs have strong and rapid effects, but all have different levels of toxicity and side effects.<sup>[15]</sup> Therefore, it is necessary to find new and safe hypoglycemic active ingredients, which have become a hot spot in biology and medicine. Oral administration of *Auricularia cornea* extract at doses of 100 and 400 mg/kg has been reported to reduce blood glucose levels in mice induced by streptozotocin.<sup>[17]</sup>

### Antinephritic

Long-term hyperglycemia can lead to secondary complications such as kidney damage.<sup>[18]</sup> Diabetic nephropathy is a major cause of end-stage renal disease and cardiovascular disease,<sup>[19]</sup> characterized by an increased lipid profile and increased oxidative stress.<sup>[20]</sup> Diabetic nephropathy affects approximately 30% of patients with type 1 diabetes and 25% of patients with type 2 diabetes, showing excessive morbidity and mortality.<sup>[19]</sup> Hyperglycemia causes excessive mitochondrial superoxide production and directly causes excessive reactive oxygen species (ROS) production, which can lead to tubulointerstitial fibrosis and inflammatory cell infiltration.<sup>[21]</sup> Accumulation of inflammatory cells in the glomerulus of diabetic nephropathy stimulates the secretion of cytokines and chemokines, which transfer inflammatory cells to the damaged area.<sup>[22]</sup> Oral administration of *Auricularia cornea* extract at doses of 0.1 and 0.4 g/kg was reported to reduce high levels of NAG in urine, renal MAU/ALB levels, and renal 6-keto-PGF1 $\alpha$  levels, as well as increase serum levels of G-CSF and renal MMP-9 in mice in a diabetic nephropathy model.<sup>[23]</sup>

### Antihyperlipidemic

Hyperlipidemia is an important risk factor in the initiation and development of atherosclerosis. The main manifestations of this disorder include increased plasma concentrations of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and low concentrations of high-density lipoprotein cholesterol (HDL-C).<sup>[24]</sup> Administration of *Auricularia polytricha* extract at a dose of 3.6 grams/200 grams was reported to significantly reduce total cholesterol levels in a rat model of hyperlipidemia induced by used cooking oil.<sup>[25]</sup>

### CONCLUSION

The use of herbal medicines is currently growing, including in pharmacological practices that can prevent and treat diseases. Through the exploration of plant biopharmaceuticals and nutraceuticals, herbal medicines have reached the international market. It is seen that some fungi of the genus *Auricularia* are versatile plants through a number of pharmacological activities. Information on fungi of the genus *Auricularia* that currently exists can be used as basic data for further research, to find the active compounds contained and newer and more complete pharmacological activities.

### REFERENCES

1. Fasinu PS, Okoye FBC, Abiodun OO, Kamdem RST, Ogbole OO. Editorial: Fungal bioactive metabolites of pharmacological relevance. *Front Pharmacol*, 2022; 13: 912068.
2. Bhalodia NR, Shukla VJ. Antibacterial and antifungal activities from leaf extracts of *Cassia fistula* L.: An ethnomedicinal plant. *J Adv Pharm Technol Res*, 2011; 2(2): 104-109.
3. Oli AN, Edeh PA, Al-Mosawi RM, Mbachu NA, Al-

- Dahmoshi HOM, Al-Khafaji NSK, *et al.* Evaluation of the phytoconstituents of *Auricularia auricula-judae* mushroom and antimicrobial activity of its protein extract. *Eur J Integr Med*, 2020; 38: 101176.
4. Tena N, Martin J, Asuero AG. State of the art of anthocyanins: antioxidant activity, sources, bioavailability, and therapeutic effect in human health. *Antioxidants*, 2020; 9(5): 1-28.
  5. Alkandahri MY, Nisriadi L, Salim E. Secondary metabolites and antioxidant activity of methanol extract of *Castanopsis costata* leaves. *Pharmacol Clin Pharm Res*, 2016; 1(3): 98-102.
  6. Lü JM, Lin PH, Yao Q, Chen C. Chemical and molecular mechanisms of antioxidants: experimental approaches and model systems. *J Cell Mol Med*, 2010; 14(4): 840-860.
  7. Gebreyohannes G, Nyerere A, Bii C, Sbhatu DB. Investigation of antioxidant and antimicrobial activities of different extracts of *Auricularia* and *Termitomyces* species of mushrooms. *Scientific World J*, 2019; 2019: 7357048.
  8. Verma N, Tripathi SK, Sahu D, Das HR, Das RH. Evaluation of inhibitory activities of plant extracts on production of LPS-stimulated pro-inflammatory mediators in J774 murine macrophages. *Mol Cell Biochem*, 2010; 336(1-2): 127-135.
  9. Chowdhury MA, Abdellatif KR, Dong Y, Das D, Suresh MR, Knaus EE. Synthesis of celecoxib analogues possessing a N-difluoromethyl-1,2-dihydropyrid-2-one 5-lipoxygenase pharmacophore: biological evaluation as dual inhibitors of cyclooxygenases and 5-lipoxygenase with anti-inflammatory activity. *J Med Chem*, 2009; 52(6): 1525-1529.
  10. Damte D, Reza MA, Lee SJ, Jo WS, Park SC. Anti-inflammatory activity of dichloromethane extract of *Auricularia auricula-judae* in RAW264.7 Cells. *Toxicol Res*, 2011; 27(1): 11-14.
  11. Adewusi EA, Afolayan AJ. A review of natural products with hepatoprotective activity. *J Med Plants Res*, 2010; 4: 1318-1334.
  12. Valko M, Leibfritz D, Moncol J, Cronin M, Mazur M, Telser J, *et al.* Free radicals and antioxidants in normal physiological functions and human disease. *Int J Biochem Cell Biol*, 2007; 39: 44-84.
  13. Prakash T, Fadadu SD, Sharma, UR, Surendra V, Goli D, Stamina P, Kotresha D. Hepatoprotective activity of leaves of *Rhododendron arboreum* in CCl<sub>4</sub> induced hepatotoxicity in rats. *J Med Plants Res*, 2008; 2(11): 315-320.
  14. Wang X, Lan Y, Zhu Y, Li S, Liu M, Song X, *et al.* Hepatoprotective effects of *Auricularia cornea* var. *Li.* polysaccharides against the alcoholic liver diseases through different metabolic pathways. *Sci Rep*, 2018; 8(1): 7574.
  15. Song LZ, Zhu LY, Gao YS, Li SF, Zhang YJ. Structural characteristics and hypoglycemic activity of polysaccharides from green tea leaves. *Food Sci*, 2018; 39: 169-175.
  16. Wang J, Hu W, Li L, Huang X, Liu Y, Wang D, *et al.* Antidiabetic activities of polysaccharides separated from *Inonotus obliquus* via the modulation of oxidative stress in mice with streptozotocin-induced diabetes. *PLoS One*, 2017; 12(6): e0180476.
  17. Fu Y, Wang L, Jiang G, Ren L, Wang L, Liu X. Anti-diabetic activity of polysaccharides from *Auricularia cornea* var. *Li.* *Foods*, 2022; 11(10): 1464.
  18. Foster SR, Dilworth LL, Omoruyi FO, Thompson R, Alexander-Lindo RL. Pancreatic and renal function in streptozotocin-induced type 2 diabetic rats administered combined inositol hexakisphosphate and inositol supplement. *Biomed Pharmacother*, 2017; 96: 72-77.
  19. Yuan D, Liu XM, Fang Z, Du LL, Chang J, Lin SH. Protective effect of resveratrol on kidney in rats with diabetic nephropathy and its effect on endoplasmic reticulum stress. *Eur Rev Med Pharmacol Sci*, 2018; 22(5): 1485-1493.
  20. Cui Y, Shi Y, Bao Y, Wang S, Hua Q, Liu Y. Zingerone attenuates diabetic nephropathy through inhibition of nicotinamide adenine dinucleotide phosphate oxidase 4. *Biomed Pharmacother*, 2018; 99: 422-430.
  21. Krishan P, Singh G, Bedi O. Carbohydrate restriction ameliorates nephropathy by reducing oxidative stress and upregulating HIF-1 $\alpha$  levels in type-1 diabetic rats. *J Diabetes Metab Disord*, 2017; 16: 47.
  22. Hu X, Zhang X, Jin G, Shi Z, Sun W, Chen F. Geniposide reduces development of streptozotocin-induced diabetic nephropathy via regulating nuclear factor-kappa B signaling pathways. *Fundam Clin Pharmacol*, 2017; 31(1): 54-63.
  23. Wang D, Jiang X, Teng S, Zhang Y, Liu Y, Li X, *et al.* The antidiabetic and antinephritic activities of *Auricularia cornea* (an albino mutant strain) via modulation of oxidative stress in the db/db Mice. *Front Immunol*, 2019; 10: 1039.
  24. Alkandahri MY, Kusumiyati K, Renggana H, Arfania M, Frianto D, Wahyuningsih ES, *et al.* Antihyperlipidemic activity of extract and fractions of *Castanopsis costata* leaves on rats fed with high cholesterol diet. *RASĀYAN J Chem*, 2022; 15(4): 2350-2358.
  25. Budinastiti R, Rya HA, Suci NW. The effect of cloud ear fungus (*Auricularia polytricha*) on serum total cholesterol levels on wistar rats induced by reused cooking oil. *Jurnal Kedokteran Diponegoro*, 2016; 5(4): 1576-1586.