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Review Article

A comprehensive review of the sedative-hypnotic mechanisms of edible fungi

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Abstract: Edibles are the source of life, providing the body with essential nutrients to maintain physiological functions. As far back as ancient times, people have used edibles to treat diseases, also known as dietary therapy. Edible fungi, as favored foods, not only have rich nutritional value but also have various pharmacological effects and have a significant role in the treatment of insomnia. This review delves into the potential mechanisms of edible fungi in the sedative-hypnotic effect, focusing on several species of edible fungi with remarkable sleep-improving effects including *Cordyceps militaris*, *Ganoderma lucidum*, *Poria cocos*, *Hericium erinaceus* and *Armillaria mellea*. The modulatory effects of active ingredients, including polysaccharides, triterpenes, and nucleosides, found in edible fungi, on the neurotransmitter system, antioxidant, anti-inflammatory pathways, gut microflora homeostasis, and immune function are reviewed. For instance, *C. militaris* reduces excitatory neurotransmitters like glutamate and acetylcholine. *P. cocos* polysaccharides regulate gut flora to positively influence sleep. *G. lucidum* enhances γ-aminobutyric acid (GABA) and serotonin expression, boosts antioxidant activity, and reduces inflammatory mediators, collectively improving sleep quality. In addition to the aforementioned improvements on insomnia by the active components in edible fungi, they also exert sedative and hypnotic effects through other mechanisms. This review summarizes the sedative and hypnotic mechanisms of these edible fungi, providing new perspectives and methodologies for the research on the sedative and hypnotic activity of Changbai Mountain *C. militaris* and other edible fungi, which is conducive to exploring and utilizing more edible fungal resources from the Changbai Mountain with such activities.

Keywords: edible fungi; *Cordyceps militaris*; mechanism of action; sedation-hypnosis effects

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1 Introduction

Insomnia is a frequently occurring sleep disorder. It has been demonstrated to impact an individual's daily functioning, including their capacity for concentration, memory, and productivity. Furthermore, evidence suggests that insomnia may be causally linked to chronic health problems, including cardiovascular disease, mood disorders, and diabetes mellitus[1]. The molecular mechanisms of insomnia involve changes in the levels of various neurotransmitters and hormones in the brain. For instance, when there is an imbalance between the excitatory neurotransmitter glutamate (Glu) and the inhibitory neurotransmitter γ-aminobutyric acid (GABA), it can lead to the occurrence of insomnia[2,3]. When the hypothalamic-pituitary-adrenal (HPA) axis is activated, the level of the stress hormone cortisol in the brain increases, exacerbating the occurrence of insomnia[4]. These changes in neurotransmitter and hormone levels ultimately affect sleep quality. Inflammation is closely linked to insomnia, with cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) being key enzymes in the inflammatory response. Under conditions of inflammation, the upregulation of COX-2 and iNOS leads to increased production of the inflammatory mediator nitric oxide (NO), thereby promoting the inflammatory process. Interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) are two pivotal pro-inflammatory cytokines that regulate sleep through their interactions with the brain and effects on the immune system[5,6]. Furthermore, alterations in metabolites, changes in neurotransmitter receptor sensitivity, genetic factors, modifications in neuroplasticity, and gut flora-brain axis interactions[7] all contribute to the molecular level of insomnia. Collectively, these factors form a complex network in sleep disorders. Clinical chemicals for insomnia such as benzodiazepines, non-benzodiazepines, and melatonin receptor agonists, although sedative and hypnotic in the short term, have

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disadvantages in terms of dependence, cognitive impairment, and potential cardiovascular risks[8].

Edibles, as an important source of nutrition, has a profound impact on human health and the progression of diseases. Recently, dietary interventions have emerged as promising adjunctive treatment strategies, applicable not only to cancer but also to metabolic disorders, autoimmune diseases, neurodegenerative diseases, and cardiovascular conditions[9]. Edible fungi are essential in human dietary culture owing to their unique flavor and nutritional value. They are not only rich in proteins, vitamins, and minerals, but also contain biologically active components such as polysaccharides and triterpenoids, which provide a variety of health benefits, including immune-boosting, lipid-regulating, antioxidant, and anti-inflammatory properties. In traditional medicine, especially in Chinese medicine, edible fungi such as *Ganoderma lucidum* and *Lentinus edodes* are commonly consumed for their reputed properties of nourishing and strengthening the body and prolonging life[10]. The use of edible fungi in the treatment of insomnia has a long historical precedent. As early as the Eastern Han Dynasty, "*Shennong's Herbal*" classified *G. lucidum* as a superior product, known for its effects in nourishing the heart and calming the mind. Modern pharmacological research has found that *G. lucidum* extracts, polysaccharides, and triterpenoids all exhibit significant sedative and hypnotic effects. Furthermore, in the 1990s, it was discovered that *Cordyceps militaris* decoction, cordycepin, and adenosine could improve the structure of sleep, shorten the sleep latency period, and extend sleep duration. Consequently, the utilization of edible fungi for the treatment of insomnia is not only a practice with a long historical precedent but also one that is supported by scientific evidence. Changbai Mountain is situated in the southeastern part of Jilin Province, China, providing an ideal growing environment for edible fungi, with a cool and humid climate, fertile soil, and rich vegetation. Among them, *L. edodes* and *Pleurotus citrinopileatus* are particularly renowned and markedly distinct from edible fungi in other regions in terms of their nutritional value and flavor. *C. militaris*, which thrives in the northeastern region, particularly around Changbai Mountain, the wild *C. militaris* from Changbai Mountain has various medicinal values and nourishing functions, comparable to *Panax ginseng* and *Cervi Cornu Pantotrichum*, and is listed as one of the iconic local products of Jilin Province, China[11]. Exploring the pharmacological effects of *C. militaris* deeply holds significant scientific value and practical significance. Although current research on its anti-inflammatory properties and therapeutic effects on diabetes is extensive, discussions on its sedative-hypnotic effects are relatively limited, and the depth of research requires further enhancement[12,13]. With the continuous advancement of modern research, the potential benefits of other edible fungi in sedative-hypnotic and nervous system regulation functions are gradually being recognized and verified. These research findings not only provide new ideas for the study of the sedative-hypnotic effects of *C. militaris* but also offer a natural and healthy treatment option for modern people.

This review provides an in-depth analysis and synthesis of the existing literature on the sedative-hypnotic effects of edible fungi and systematically summarizes the active components and mechanisms of action of these fungi. These findings not only offer new perspectives and ideas for the study of the sedative and hypnotic activities of *C. militaris* from Changbai Mountain but also lay the groundwork for further exploration and exploitation of other potential sedative-hypnotic effects of edible fungal resources in the Changbai Mountain region.

2 The mechanism of sedative-hypnotic effects of *C. militaris*

C. militaris belongs to the kingdom of Fungi, the phylum Ascomycota, the class Sordariomycetes, the order Clavicipitales, the family Clavicipitaceae, and the genus *Cordyceps*. *C. militaris* is a medicinal and dietary fungi with a high nutritional value and is enriched with proteins, polysaccharides, nucleosides, sterols, fatty acids, and a variety of vitamins and minerals. It has been shown to possess anti-inflammatory, antitumor, antioxidant, hypoglycemic, hypolipidemic, and sedative-hypnotic effects[14]. In 1997, Chen *et al.*[15] discovered that a suspension prepared with *C. militaris* powder significantly reduced the spontaneous activity of mice, alleviated convulsions induced by pentylenetetrazole, and to some extent synergized with pentobarbital sodium to induce sleep in mice. These results suggest that *C. militaris* possesses sedative and hypnotic effects. Subsequently, Xu *et al.*[16] found that *C. militaris* has inhibitory effects on the central nervous system. Fan *et al.*[17] discovered that *C. militaris* can improve the sleep of cancer patients. Furthermore, Chen *et al.*[18] found that N6-(2-hydroxyethyl) adenosine (HEA), extracted and purified from *C. militaris* using a water extraction and alcohol precipitation method, could reduce the spontaneous activity of mice (Fig. 1). Compared to the blank group, the medium- and high-dose groups of HEA significantly increased the sleep rate (Fig. 1) and shortened the sleep latency(Fig. 1) induced by subthreshold doses of pentobarbital sodium, the high-dose group significantly increased the duration of pentobarbital sodium-induced sleep in mice (Fig. 1)[18]. Chen *et al.*[19], Nie *et al.*[20], and Pei *et al.*[21] obtained the same results in their studies and found that this may be a sedative-hypnotic effect by increasing the expression of γ-aminobutyric acid type A receptor ($GABA_A$) α1 and 5-hydroxytryptamine receptor 1A (5-HT1A) genes. In addition, Sun *et al.*[22] extracted *C. militaris* polysaccharides (CMP) and total flavonoids from *C. militaris* (CMF). The study results showed that CMP and CMF could reduce spontaneous activity in mice, shorten sleep latency, and prolong sleep duration. It was also found that this might be achieved by regulating the levels of neurotransmitters in the brain, such as reducing the levels of Glu and acetylcholine (ACh), and increasing the level of 5-hydroxytryptamine (5-HT), thereby exerting their sedative and hypnotic effects. Hu *et al.*[23] have found that cordycepin from *C. militaris* also has a sedative-hypnotic effect, and the results of this study suggest that cordycepin may enhance the θ waves power density during non-rapid eye movement (NREM) sleep via nonspecific adenosine receptors to achieve sleep promotion.

3 The mechanism of sedative-hypnotic effects of *G. lucidum*

G. lucidum belongs to the kingdom of Fungi, the division Basidiomycota, the class Agaricomycetes, the order Polyporales, the family Ganodermataceae, and the genus *Ganoderma*. Known for its rich bioactive components such as triterpenoids and polysaccharides, it is also rich in other components including proteins, sesquiterpenes, glycoproteins, polyunsaturated fatty acids, benzoic acid, phenolic compounds, nucleotides, vitamins, and trace elements[24]. *G. lucidum*, known for its recognized therapeutic properties, is one of the most extensively studied mushrooms in the fields of chemoprevention and functional food[25]. Moreover, its clinical effects, such as antioxidant[26], anti-inflammatory[27], hypoglycemic[28], and sedative-hypnotic effects,

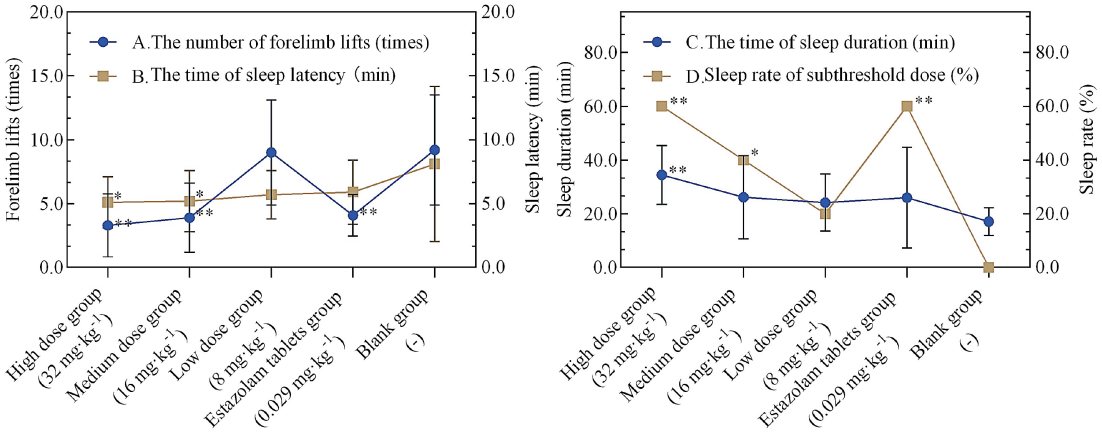

Figure 1 Sleep assay results after HEA treatment (n = 10) in mice. Compared with the blank group, $^{**}P < 0.01$, $^{*}P < 0.05$. The figure was created using GraphPad Prism 9 based on the data from reference[18].

continue to attract the attention of modern medical researchers. Feng *et al.*[29] investigated the effects of luciden D (LUC), a triterpenoid extracted from *G. lucidum*, on sleep, and found that LUC significantly shortened the sleep latency and prolonged the sleep time, down-regulated the expression levels of COX-2 and iNOS proteins, and inhibit the production of IL-6 and TNF-α as well as the inflammatory mediator NO, thus improving the sleep of rats and showing a sedative-hypnotic effect Yu *et al.*[30] have demonstrated that *G. lucidum* triterpenoids show a significant synergistic effect when combined with both pentobarbital sodium and barbital sodium. This synergism not only facilitates the initiation of sleep but also supports the maintenance of sleep patterns. Similarly, Feng *et al.*[31] have reported that Ganoderma Jujube Seed Capsules are capable of extending sleep duration and reducing sleep latency in mice. Moreover, these capsules exhibit a synergistic hypnotic effect when administered alongside subthreshold doses of barbital sodium. In addition, some studies have shown that *G. lucidum* polysaccharides also have sedative and hypnotic effects. Cui's team[32] found that *G. lucidum* polysaccharides upregulated the TNF-α content of serum and brain tissues, thereby increasing the duration of NREM sleep in rats. Meanwhile, Chu *et al.*[33] showed that *G. lucidum* polysaccharides could enhance the activity of GABAergic neurons and 5-HTergic neurons in the brain of rats, reduce the voluntary activity of rats, shorten the sleep latency period, and increase the length of delta waves during NREM sleep, thus prolonging the duration of sleep. It was also found that *G. lucidum* extracts can exert sedative-hypnotic effects by modulating the richness of the gut microbiota in mice[34,35]. The mechanism of action may involve increasing the abundance of beneficial bacteria (such as *Bifidobacterium* and *Lactobacillus*) and reducing the abundance of potentially harmful bacteria or opportunistic pathogens (such as *Klebsiella*), thereby improving sleep. *G. lucidum* and its extracts have been found to exert sedative-hypnotic effects through different mechanisms in several studies, as summarized in Table 1.

4 The mechanism of sedative-hypnotic effects of *P. cocos*

P. cocos belongs to the kingdom of Fungi, the phylum Basidiomycota, the Class Atheliales, the order Polyporales, the family Polyporaceae, and the genus *Wolfiporia*. *P. cocos*, a medicinal and edible fungi, parasitizes the decaying roots of coniferous trees such as *Pinus densiflora* or *Pinus massoniana*[48]. *P. cocos* has antitumor, antioxidant, hypolipidemic, and sedative-hypnotic activities[49,50]. Wang *et al.*[51] investigated the sedative and hypnotic effects of *P. cocos* aqueous extract in synergy with sub-threshold and supra-threshold doses of pentobarbital sodium. The results indicated that, under the synergistic effect of pentobarbital sodium, the aqueous extract of *P. cocos* could significantly shorten the sleep latency of mice, prolong sleep duration, and increase the sleep rate of mice, demonstrating sedative and hypnotic effects[52]. Zhang *et al.*[53] observed that *P. cocos* acidic polysaccharides not only rectified the dysbiosis of intestinal flora in restless rats, but also exerted a tranquilizing effect, potentially by regulating the metabolism of linoleic acid, taurine, hypotaurine, phenylalanine, and α-linolenic acid, among other pathways. Kim *et al.*[54] administered *P. cocos* extract via gastric gavage and confirmed its effects in reducing sleep latency, increasing sleep duration, enhancing slow-wave sleep under normal conditions, ameliorating sleep disturbances caused by caffeine-induced arousal, and counteracting insomnia induced by the activation of the HPA axis through subcutaneous injection of adrenocorticotropic hormone (ACTH). Dose-dependent administration reduces sleep latency and increases sleep duration. In the ACTH-induced sleep disturbance model, an increase in slow-wave sleep and a decrease in sleep latency were observed. The *P. cocos* extract was demonstrated to improve sleep quality and sleep architecture by inhibiting the $GABA_A$ receptor, a mechanism associated with the suppression of neurotransmission in the superior cervical ganglion neurons. Researchers believe that the extract obtained from *P. cocos* has the potential to become a novel sleep aid in the near future[55]. Shah *et al.*[56] conducted an experiment where rats were orally administered *P. cocos* ethanol extract (PCE) and the active component pachymic acid (PA) 7 days after surgical implantation of a transmitter. Sleep architecture was recorded using telemetric electroencephalography (EEG) following oral drug administration. Both PCE and PA increased the total sleep time and NREM sleep time and reduced the number of sleep/wake cycles recorded by EEG. Furthermore, PCE increased intracellular chloride levels, $GAD_{65/67}$ protein levels, and the α-, β-, and γ-subunits of the $GABA_A$ receptor in primary cultured hypothalamic neurons. These data suggest that PCE modulates the sleep architecture by activating the $GABA_A$ergic system. Additionally, because PA is the active component of PCE, it may have similar pharmacological effects[56]. Further research has indicated that ergosterone in *P. cocos* can promote the secretion of cytokines, IL-1β, and TNF-α, enhancing NREM sleep[57,58]. A summary of the sedative-hypnotic effects of *P. cocos* is shown in Fig. 2.

Table 1 Summary of the sedative-hypnotic effects mechanisms of *G. lucidum* and its extracts

Active ingredient/complex	Mechanism of action	Reference
	Neurotransmitter regulation	
G. lucidum water extract	Increases GABA and 5-HT levels Decreases Glu and Gln levels	[36]
Compound *G. lucidum*	Increases GABA levels Decreases Glu and Gln levels	[37]
G. lucidum spore powder	Regulates 5-HT and Glu/GABA balance	[38]
G. lucidum compound (*G. lucidum*, *Ostreae Concha*, *Ziziphi Spinosae Semen*)	Increases 5-HT and dopaminelevels Decreases Orexin A, substance P, and NO levels	[39]
G. lucidum fruiting body extract	Increases GABA and 5-HT levels	[40]
	Anti-inflammatory effect	
G. lucidum alcohol extract	Increases TNF-α levels	[32]
Ganoderic acid LUC	Inhibits the production of inflammatory mediator NO, downregulates the expression levels of iNOS and COX-2 proteins, inhibits the production of TNF-α, IL-6	[29]
	Regulation of gut microbiota abundance	
G. lucidum alcohol extract	Regulating gut microbiota Involvement of serotonin pathway	[34]
Ganoderma sessile alcohol extract	Regulates the abundance of *Bacteroidetes*, *Bifidobacterium*, *Lactobacillus*, and *Klebsiella* in the gut	[35]
	Antioxidant effect	
G. lucidum polysaccharides	Mimics superoxide dismutase activity to enhance the clearance of OH^-	[41]
G. lucidum extract	Downregulates MAD levels, improves metabolic conditions	[42]
	Regulates gene expression	
G. lucidum crude polysaccharides	Significantly decreased the mRNA expression of *GABRA1*, *GRIN2A* and *GAD1*, and increased the expression level of *GABRA5*, *MTNR1A*, *HTR1A* and *HTR2A* genes	[43]
G. lucidum polysaccharides	Increased gene expression of $GABA_A$, $5\text{-}HT_{1A}$	[44]
	Others	
G. lucidum spore extract (RGLS)	Improves GABAergic activity Inhibits neuroinflammatory responses in the mPFC	[45]
G. lucidum polysaccharides	Enhances GABAergic and 5-HTergic neurons Increases the duration of δ waves during NREM sleep	[33]
G. lucidum granules	Improves hematopoietic function	[46]
G. lucidum alcohol extract	Reduces the accumulation of *L*-glutamine	[47]
Ganoderma sessile water extract	Alleviates nervous system inflammation, regulates oxidative stress and neurogenesis in the brain	[42]

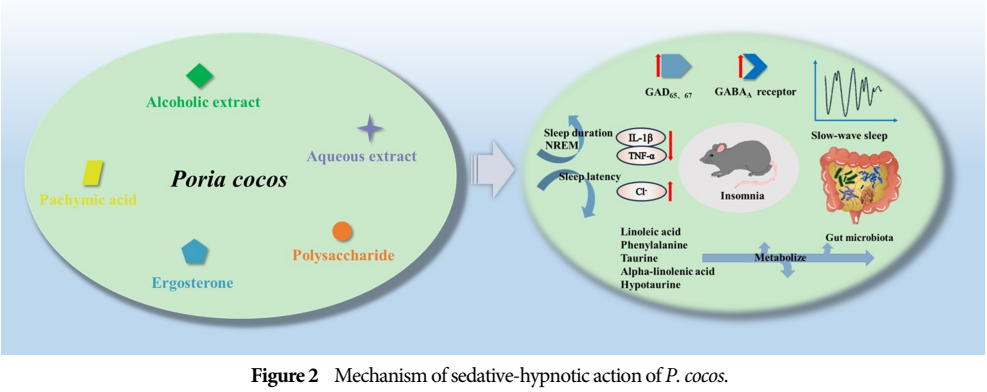

Figure 2 Mechanism of sedative-hypnotic action of *P. cocos*.

5 The mechanism of sedative-hypnotic effects of *Hericium erinaceus*

H. erinaceus belongs to the kingdom of Fungi, the phylum Basidiomycota, the class Atheliales, the order Aphyllophorales, the family Hericaceae, and the genus *Hericium*. *H. erinaceus* is edible and medicinal mushroom, and wild *H. erinaceus* is distributed in Changbai Mountain and Daxinganling area in Northeast China. It is not only rich in nutrition, but also has high medicinal value. Research shows that *H. erinaceus* contains polysaccharides, proteins, terpenes, phenols, and flavonoids active ingredients[59, 60].

In addition to its sedative-hypnotic effect, *H. erinaceus* possesses a range of biological activities, including antioxidant, antitumor, immunomodulatory, anti-inflammatory, gastrointestinal, anti-fatigue, and neuroprotective effects[61]. Li *et al.*[62] discovered that the mycelium of *H. erinaceus* had a beneficial effect on persistent sleep disorders and exhibited anxiolytic properties by restoring dopamine levels, thereby improving sleep disorders triggered by early anxiety induced by the hanging tail test. Administration of high doses of *H. erinaceus* mycelium extract resulted in an increase in the expression of brain-derived neurotrophic factor (BDNF), which has been identified as an important biomarker for

altered sleep behavior. Furthermore, this study demonstrated for the first time that erinacine A and C may be the primary compounds and active ingredients. A preliminary study by Okamura *et al.*[63] showed that the administration of *H. erinaceus* extract tablets (Amyloban 3399) for 4 weeks to schoolgirls with sleep disorders resulted in elevated salivary levels of free 3-methoxy-4-hydroxyphenylethylene glycol (MHPG, a biologic indicator of anxiety disorders), indicating that *H. erinaceus* can improve anxiety and enhance sleep quality. Another clinical trial showed that *H. erinaceus* extracts increased circulating pro-BDNF levels by circulating pro-BDNF and BDNF as biomarkers, but there was no significant change in circulating levels of BDNF. Oral administration of *H. erinaceus* mycelium for 8 weeks improved mood and sleep disorders, and these effects persisted after 8 weeks, with improvements in mood disorders associated with changes in peripheral pro-BDNF and pro-BDNF/BDNF ratio[64]. In a study conducted by Furuta *et al.*[65], it was demonstrated that an extract of *H. erinaceus*, including water and alcohol extracts, can alter behavioral rhythms in mice. Furthermore, the ingestion of *H. erinaceus* extract resulted in the advancement of the sleep phase in immature mice, while the free-running phase of the suprachiasmatic nucleus (SCN) remained unaffected. Additionally, the study found no impact on photosensitivity. Furthermore, researchers investigated the impact of nerve growth factor (NGF) on clock gene mRNA expression levels and discovered that NGF, a neurotrophic factor that facilitates neuronal differentiation and survival, plays a pivotal role in regulating circadian rhythm activity. They also observed that NGF administration resulted in a phase shift in the circadian rhythms of hamsters, consequently altering their activity patterns. The chemical components of *H. erinaceus*, hericenones, and erinacines, stimulate the synthesis of NGF, Bina *et al.*[66] also reached the same conclusion, so Furuta *et al.*[65] suggested that the alteration of behavioral rhythms after the ingestion of *H. erinaceus* extracts may be related to the increase of NGF in the SCN. The mechanism of action of *H. erinaceus* sedative-hypnotics is summarized in Fig. 3.

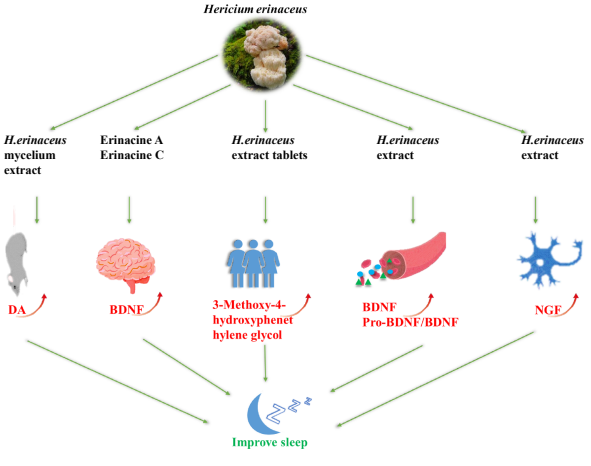

Figure 3 Mechanism of sedative-hypnotic action of *H. erinaceus*.

6 The mechanism of sedative-hypnotic effects of *Armillaria mellea*

A. mellea belongs to the kingdom of Fungi, the phylum Basidiomycota, the class Agaricomycetes, the order Agaricales, the family Marasmiaceae, and the genus *Armillaria*. *A. mellea* is primarily distributed in Northeast China, particularly in the vicinity of Changbai Mountain and Daxinganling. *A. mellea* is a rich source of fatty acids, indole compounds, sphingolipids, sterols, sesquiterpenes, among other compounds, it possesses a diverse range of biological activities, including hypoglycemic, antioxidant, immunomodulatory, cardiovascular, and neurological circulatory effects[67]. Yuan *et al.*[68] demonstrated that *A. mellea* powder and fermentation solution markedly reduced sleep latency and extended sleep duration in mice, indicating the presence of sedative-hypnotic activity. It was reported that by intraperitoneal injection of preparations of *A. mellea* into mice, it was observed that either the aqueous extract, ethanol extract, or ferment concentrate of *A. mellea* significantly reduced spontaneous activity and enhanced the hypnotic effect of a low dose of sodium pentobarbital in mice. Furthermore, it was observed that the sleep duration of mice induced by either sodium pentobarbital or sodium cyclohexenobarbital was significantly prolonged by the administration of *A. mellea*[69,70], which provides additional evidence that *A. mellea* has a significant sedative-hypnotic effect. Wei *et al.*[71] also found that *A. mellea* extract was able to improve sleep. In their study of the hypnotic activity of *A. mellea*, Liu *et al.*[72] combined their findings with the current state of research on sleep regulation. They concluded that *A. mellea* may improve sleep by selectively increasing slow-wave sleep while ensuring a normal proportion of rapid eye movement sleep. Li *et al.*[73] found that aqueous and alcoholic extracts of *A. mellea* increased NREM and REM sleep during rest. Subsequently, Lyu *et al.*[74] found that *A. mellea* fermentation liquid significantly reduced the spontaneous activity in sleep-deprived mice, indicative of its potential to mitigate the impact of sleep deprivation. Moreover, the fermentation liquid notably decreased the malondialdehyde (MDA) levels, thereby alleviating oxidative stress. These findings imply that *A. mellea* could have sedative and hypnotic effects, potentially through the modulation of oxidative stress[74]. In addition, Wu *et al.*[75] and Zheng *et al.*[76] found that *A. mellea* could also exert sedative-hypnotic effects at the center. Qi and others[77] found that the oral liquid of Naoxin Shu, which is mainly composed of the concentrated fermentation *A. mellea* fermentation liquid (AFL), can regulate the sleep-wake cycle by modulating the expression and enzymatic activity of glutamic acid decarboxylase 67 (GAGB) and glutamic acid decarboxylase (GAD) proteins, as well as maintaining the dynamic balance of neurotransmitters GABA and Glu. Yao *et al.*[78] found that the AFL significantly reduced the number of activities and slower body weight loss in *p*-chlorophenylalanine-induced insomniac rats, decreased sleep latency and increased sleep duration in pentobarbital-treated rats, and showed better sedative effects. The results also showed that AFL increased serum levels of glutathione peroxidase and superoxide dismutase and decreased serum levels of TNF-α, IL-1β, and IL-6 in rats. In addition, AFL alleviated insomnia by increasing 5-hydroxytryptamine levels and 5-HT_{1A} and 5-HT_{2A} receptor expression in rat hippocampus. Meanwhile, AFL also reversed the changes in the gut bacterial community of insomnia model rats and increased the abundance of gut bacterial flora, for example, increasing the relative abundance of Ruminococcaceae, Lachnospiraceae, and Saccharimonadaceae, restoring the altered gut microbial ecosystems in insomniac rats. Yao *et al.* showed that AFL can also exert a sedative-hypnotic effect through the regulation of neurotransmitters, antioxidant, anti-inflammatory, and gut bacterial flora abundance. These studies suggest that the hypnotic mechanism of *A. mellea* is complex, and the specific mechanism is shown in Fig. 4.

Figure 4 Mechanism of sedative-hypnotic action of *A. mellea*.

7 Other edible fungi with sedative-hypnotic effects

Cordyceps sinensis is a valuable medicinal fungi that contains a variety of biologically active components that are beneficial to the human body, such as polysaccharides, nucleosides, amino acids, and trace elements, which have the properties of regulating the immune system, improve heart and liver function, regulate the respiratory system, and regulate blood lipids[79]. Changbai Mountain *C. sinensis* is known as the "Treasure of the Northeast" and is listed alongside *P. ginseng* and *Cornu cervi pantotrichum* as one of the three major tonics[80]. Cao *et al.*[81] found that *C. sinensis* fermentation solution inhibited spontaneous activity, shortened sleep latency, and prolonged sleep duration in mice. Zhao *et al.*[82] found that *C. sinensis* improved sleep quality in premenopausal breast cancer patients due to chemotherapy. Shen *et al.*[83] found that *C. sinensis* polysaccharide liposome oral solution could effectively treat insomnia symptoms in chronic hepatitis B patients. *Tremella fuciformis* Berk is the fruiting body of the fungi *T. fuciformis* of the family Auriculariaceae, which is traditional edible fungi in China and has been enjoyed by the majority of people throughout the ages. *T. fuciformis* Berk is rich in polysaccharides, dietary fiber, and a variety of vitamins and minerals, and has pharmacological effects such as moistening the lungs and nourishing the yin, strengthening the immune system, and beautifying and nourishing the face[84,85]. Li *et al.*[86] found that Chinese herbal preparations containing *T. fuciformis* Berk could effectively alleviate insomnia symptoms in patients with blood deficiency constitutions. In addition, Feng *et al.*[87] listed *T. fuciformis* Berk as a remedy for insomnia, which further proved that *T. fuciformis* Berk has promising therapeutic effects for insomnia. *Isaria cicadae* is medicinal fungi parasitic on cicada larvae, belonging to the same genus *Cordyceps* as *C. sinensis*. This fungi is rich in a variety of bioactive components, including polysaccharides, nucleosides, ergosterol, fatty acids, and thymopeptides. It has been demonstrated to possess a range of pharmacological activities, including immunomodulation, antitumor efficacy, and enhancement of renal function[86]. In 1991, Liu *et al.*[88] showed that the ethanol extract of *I. cicadae* significantly reduced voluntary activity and prolonged pentobarbital-induced sleep in mice. Subsequently, Zhang *et al.*[89] found that *I. cicadae* could be used to treat insomnia by, among other things, stimulating GABA to increase its receptors or synergizing with 5-HT.

8 Conclusions

Edible fungi, as an important part of traditional Chinese medicine, have a long history of use in sedative and hypnotic applications. Modern research continues to reveal their profound mechanisms of action, which not only provides strong support for the modernization of traditional medicines but also offers broad prospects for the development of new natural drugs for the treatment of insomnia. The Changbai Mountain is located in the southeastern part of Jilin Province, China, and is known for its unique temperate monsoon climate, significant vertical climate zones, humid forest environment, and a variety of microclimates, which together form a diverse ecological system, providing ideal growing conditions for the rich wild edible fungi resources, known as the "Cradle of Edible Fungi." The Changbai Mountain *C. militaris*, due to the unique climatic conditions of the Changbai Mountain, have their special quality and efficacy compared with *Cordyceps* from other regions and is one of the geographical indication products of Jilin Province, China, which may become the focus of research and development in the future. Although there is relatively insufficient research on the sedative-hypnotic effects of Changbai Mountain *C. militaris* at present, existing literature on the sedative and hypnotic effects of other edible fungi such as *G. lucidum*, *P. cocos*, *H. erinaceus*, and *A. mellea* provides valuable references. These studies indicate that edible fungi exert sedative and hypnotic effects through mechanisms such as antioxidant activity, modulation of neurotransmitters, and regulation of the gut microbiota balance. These findings not only enrich our understanding of the sedative and hypnotic effects of edible fungi but also provide new perspectives for pharmacological research on the sedative and hypnotic activities of Changbai Mountain *C. militaris*. This will help to further explore and utilize the diversity of the pharmacological activities of edible fungi in the Changbai Mountain region. However, despite the significant therapeutic potential demonstrated by these edible fungi, current research still has its limitations, such as in-depth exploration of mechanisms of action and extensive clinical validation. Future studies need to further optimize extraction processes, clarify the specific pathways of action of active components, and conduct large-scale clinical trials to verify the safety and efficacy of these fungi in the treatment of insomnia. Moreover, considering individual differences and potential interactions, developing personalized treatment plans is also an important direction for future research. In summary, the research and application prospects of edible fungi in the field of sedative-hypnotic effects are broad and promising, offering the potential to provide safer and more effective sleep improvement solutions for modern individuals.

Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

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