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Research Progress on *Auricularia delicata*

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Authors' contributions

This work was carried out in collaboration among all authors. Author LX designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors MSJ, ZB and XA managed the analyses of the study. Authors LX and MSJ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To describe the current status of *A. delicata* emphasizing on the key parameters; occurrence, classification, molecular studies, nutritional and medicinal benefits, cultivation status, and future development perspective.
Place and Duration of Study: China–Zambia Agricultural demonstration center and Engineering Research Center of Chinese Ministry of Education for Edible and Medicinal Fungi, Jilin Agricultural University, China between July 2019 and June 2020.
Methodology: In this study, various literatures were reviewed for each parameter studied. Findings were deduced from current literatures and discussed.
Results: The screening of bioactive contents of *A. delicata* revealed the presence of phenolic compounds; chlorogenic, flavonoids, and ethyl acetate, polysaccharides; Chitosan, fibers, β-glucans, mannans, chitin, and melanin. These substances exhibit hepatoprotective effects, antioxidant activities and antimicrobial activities against some microbes like *Candida albicans, Bacillus subtilis, Enterococcus faecium, Streptococcus aureus, Bacillus cereus, Salmonella typhi*

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and Escherichia coli. A. delicata also contains several nutrients namely; protein, vitamin B2, vitamin C, and minerals; Potassium, Calcium, Iron, Magnesium, Zinc, Manganese, that play a vital role in human growth and development. Moreover, its cultivation using various technologies provides an opportunity for high yield production. *A. delicata* was recently studied at Jilin Agricultural University and domesticated in Heilongjiang province in the northeastern part of China. Due to the similarity of its fruiting body with the structure of the deer tripe, it was assigned a common name as "Deer tripe mushroom". *A. delicata* mycelia are capable of growing on several culture media with different nutritional profiles, optimal temperatures and pH values. It is cultivated under tropic temperatures ranging from 25°C-30°C, optimal pH of 6.5, and humidity 80-90%. The commonly used media include; Potato Dextrose Agar (PDA), Yeast Extract Agar (YEA) and Malt Extract Agar (MEA).

Conclusion: Therefore the above mentioned significant properties (occurrence, nutritional, medicinal, and cultivation) provide a foundation for further research on the development and utilization of *A. delicata.*

Keywords: Edible mushrooms; bioactive compounds; deer tripe mushroom.

1. INTRODUCTION

A. delicata is a delicious edible mushroom utilized as a potential nutritious food source and traditional medicine with dominance in some regions of Africa and Eastern Asia, particularly China and India [1-3]. In the past mushrooms were used as a local food resource [3]. Due to the advancement in mushroom research, many benefits of mushrooms are currently revealed and the perception of mushroom has changed from a local food to a functional food with significant medicinal values [1, 4-5]. Numerous studies on *A. delicata* revealed various biological properties of vital importance for human health [2, 6-7].

The chemical analysis of *A. delicata* fruiting body has identified numerous nutritional and bioactive substances useful for human health. The nutritional contents of *A. delicata* include; proteins, saccharides, vitamins, minerals and low cholesterol content that exhibit various health promoting effects in humans. Besides its nutritional significance, *A. delicata* can be exploited as a functional food (medicinal resource) for the production of novel therapeutic drugs against various human diseases [8-12]. The bioactive compounds of *A. delicata* which include phenolic compounds (ethyl acetate, methanol, chlorogenic acid, and flavonoids), polysaccharides (glucans, chitosans, tannins, sulfated polysaccharides) have the potential to reduce cholesterol, promote immunomodulatory activities, hepatoprotective, anticancer, antioxidant, anti-coagulant, and anti-microbial activities [11, 13, 14].

Similar to *Ganoderma lucidum* (King of medicinal mushrooms) [15], *A. delicata* has demonstrated medicinal properties against various health impairments such as microbial infection, hepatic disorders, cardiovascular disorders [16, 17]. The antioxidant capacity of phenolic compounds coupled with the activity of antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase, and reduced glutathione) ensures efficient free radical scavenging ability by promoting their decomposition [18]. Due to unhealthy eating, poor hygiene, environmental pollution and change in lifestyle, many people are exposed to different health disorders including cardiac disease, lung infection, liver toxicity, tumor, diabetes and many other [19]. This increment in global health challenges coincide with the tremendous increase in consumption of synthetic drugs [20]. Currently, synthetic drugs have been alleged to cause serious side effects to human health such as heart attack, intoxication, and tissue damage [21]. The prolonged administration of some drugs induce oxidative stress in the human body resulting in toxicity in numerous tissues and organ systems, including liver, kidney, lungs, cardiovascular and nervous systems [20]. Immunomodulatory drugs such as; Azidothymidine (an antiretroviral drug), and cisplastin (an anticancer drug) produces several side effects including mitochondrial dysfunction, liver toxicity, nephrotoxicity, cardiac toxicity and skeletal myopathy and apoptosis [20-21]. Similarly the disproportionate use of paracetamol and chlorpromazine leads to hepatotoxicity and dermal toxicity respectively. As a result, this phenomenon has necessitated the need for natural, non-toxic substances as a remedy [21]. Previous studies have mentioned the potent medicinal values of *A. delicata*, suggesting that medicinal compounds extracted from *A. delicata* can be administered as a remedy in pace of these synthetic drugs [21]. Due to its occurrence in a tropical and subtopic areas (from Africa, Europe, America, and Asia) it is evident that *A. delicata* can grow well in tropics with temperatures ranging from 25°C-30°C, .0-6.5 pH, and 80-90% humidity [Fig. 1]. Besides, its mycelia are capable of growing on different culture media (PDA, MEA and YEA), and the fruiting body is capable of growing on different tropical woody logs suggesting that woody and agricultural residues can be used as substrates for the cultivation of *A. delicata*. [22]. The classification based on morphological features and limited molecular studies suggests the need for further exploration on some key features such as internal structures, enzymatic activities, and gene expression [23-25]. The present study aims at introducing and unveiling the potentials of *A. delicata* exploring the current status of the key parameters; occurrence, classification, molecular studies, nutritional and medicinal benefits, cultivation status, and future development perspective [25].

Fig. 1. An overview of significant properties of *A. delicata*, showing its occurrence, classification, cultivation, nutritional values, medicinal values, and molecular studies

2. OCCURRENCE

Varieties of *Auricularia* mushrooms flourish in tropics and subtropics [26]. These mushrooms mostly inhabit warm and moist forests and woodlands [27]. For instance *A. heimuer* is found in Eastern Russia and the northeastern part of China [28]. *Auricularia auricula-judae* is distributed in central Europe and northeastern China [29-30]. *A. thailandica* was initially identified in Chiangmai-Thailand and is also common in southern China, and Philippines [31, 32]. *Auricularia auricular* is distributed in the wet forests of Pak Thong Chai district, Thailand [33, 34]. Additionally, taxonomists described the occurrence of *Auricularia cornea* in different localities like wood forests of Congo Democratic Republic, west Africa including Nigeria, Cameroon, Ghana, and Coted' Ivoire), and Northeast of China, Yunnan province of China [35,36]. Correspondingly, recent studies have successfully described the occurrence of *A. delicata* in different parts of the world, mostly along the equator [37]. The distribution of *A. delicata* is evident in different areas including Australia, Argentina, Mexico, Brazil, Southern-China, Bandundu forests of Congo Democratic Republic, Costa Rica, Panama, Colombia, Northern parts of Zambia, Benin, Miombo woodlands of Tanzania, Ecuador, Honduras, Vietnam, and Malaysia. Recent taxonomic studies showed that *A. delicata* is a wild edible fungus that occurs naturally in the forests and grows typically in clusters on decaying wood [38, 39]. Its fruiting body is thick soft rubbery gelatinous, semicircular in shape, a smooth, hairy upper surface, and a reticulate trip like lower surface, pale cream to pinkish color. Moreover, *A. delicata* exhibits morphological changes when exposed to different weather conditions; it swells in wet weather and it shrinks, turns pale to dark brown when in dry environment [40,41]. These named features attributes to its adaptability to survive in tropical and subtropical regions where the weather condition is usually warm [25,40-42]. Therefore, the above observation suggests that *A. delicata* can be preferably cultivated as a new edible mushroom that grows in the tropical climate and provides a potential basis for further research on cultivation conditions, adaptability, and factors influencing habitat preference of *A. delicata.*

3. CLASSIFICATION

For the first time, a prominent German mycologist and founder of mushroom studies known as (Paul Christoph Hennings) discovered the species *A. delicata* (Fr.) Henn in the year 1893. His endless efforts on the collection of mushrooms between 1884-1887 on the Islands of Porto Rico paved the way for the successful discovery of *A. delicata* [23, 37, 43].

Taxonomic studies by Lowy [23] elaborated a key to the classification of species of *Auricularia,* emphasizing more on the internal structures of the fruiting body than the external features, which are highly variable under the environmental influence [23]. *A. delicata* possesses numerous morphological features including possession of a translucent, soft gelatinous fruiting body, reniform to semicircular structure with maximum 80 mm diameter,1-2 mm thick, pileus glabrous made up of highly compacted gelatinized hyphae and fine hyaline hairs, meruloid to porose reticulate hymenium with pale color, and growing in clusters [23]. The morphological variability observed, particularly the appearance of the hymenial surface that can be ridiculed to reticulate, exclusively suggests that the specimen studied could constitute a complex of species [37]. Thus *A. delicata* can be taxonomically recognized by its distinct merulioid to porous reticulate hymenium with pale veins. Referring to the features mentioned above, taxonomists have classified *A. delicata* into *Auricularia*, Auriculariaceae, Auriculariales, Basidiomycota [Fig. 1]. Boulet [44] classified species of *Auricularia* based on ecological features (ability to colonize wood) and morphological features (size of basidiome). However, Duncan and McDonald [45] discovered that morphological features (i.e size of basidiome) are highly variable due to some influential factors such as exposure to sunlight, moisture condition, and the age of the specimen. Thus, suggesting further investigations beyond morphological and ecological features as the key parameters for classifying *A. delicata.*

4. MOLECULAR STUDIES

Molecular analysis of the fungi genome is essential for the development of the mushroom production industry [46]. Despite the little information reported on the molecular studies of *A. delicata*, studies of DNA structure, gene expression, and enzymatic activities of *A. delicata* are significant for understanding various physiological and biochemical processes influenced by different molecules [46]. Scientific investigations have reported a remarkable variation in the color of fruit bodies of *A. delicata* ranging from pale cream, brown to purple. Henceforth the molecular studies would provide explicit details to account for such observations [37].

The role of molecular markers to efficiently describe this species may also be explored to account for the genetic variation within species with the potential to enhance the identification of novel strains [47]. An intra-genomic dichotomy occurred in the *A. delicata* strains based on the genetic distance of the ITS locus and nLSU gene sequences [47].

5. MEDICINAL/THERAPEUTIC VALUES

Studies on pharmacological properties of *Auricularia* mushrooms have identified numerous bioactive compounds of medicinal importance from a wide variety of species of the genus *Auricularia* [48-51]. Most *Auricularia* species (*A. delicata, A. cornea, A. auricula-judae, A. thailandica A. heimuer*), exhibit numerous therapeutically applicable properties including antitumour, antioxidant, antimicrobial, antifungal, anti-inflammatory response, immunomodulatory reaction, hypoglycemic potential, reducing gastrointestinal discomfort (diarrhea, constipation and indigestion) [51-55].

5.1 Antimicrobial Activity

For decades mushrooms have been used as a potential source of traditional medicine among local communities of Asia, Africa, some parts of Europe and America [55]. The discovery of new research methods has facilitated the effective extraction of bioactive substances of pharmaceutical importance from mushrooms [56]. This achievement has fostered the transformation of mushrooms from being merely used as traditional herbs into commercialized functional foods [57]. Various researches have explicitly revealed the strong antimicrobial properties of mushrooms [58-63]. Nwachukwu and Uzoeto [64] discovered that the phenolic compounds (ethanolic extracts) of *A. auricular* demonstrated high antimicrobial response against *E. coli, S. typhi,* and *C. albicans*. Studies on medicinal values of *A. auricula-judae* and *A. auricular* showed the high antimicrobial activity of chitosans against *E. coli* and *S. aureus* while the sulfated polysaccharide extracts of *A. auricular* revealed antiviral activity against Newcastle Disease virus in chicken [65]. Melanin extracted from *A. auricular* demonstrates anti-microbial properties by inhibiting the activity of *E. coli, Pseudomonas aeruginosa* and *Pseudomonas fluorescens*. Moreover, the sulfate anions in sulfated polysaccharides are capable of suppressing the multiplication of HIV-1 by inhibiting it from binding to the CD4 receptors [66-69].

Additionally, through a series of scientific investigations, researchers have reported that *A. delicata* contains some bioactive substances such as ethyl acetate, methanol, and chloroform that exhibit antimicrobial activities [70-72]. These three extracts of *A. delicata* demonstrated an inhibitory response on the growth of some microbes, namely: *Bacillus subtilis, Enterococcus faecium, Streptococcus aureus, Bacillus cereus, and Escherichia coli,* and *Candida albicans* [9, 73]. This observation reveals the potential uses of *A. delicata* extracts as a substitute for some antibiotics [15,74]. Moreover, the application of phenolic extracts of *A. delicata* as an alternative microbial therapy may lower the risks of developing antimicrobial resistance and aid in averting the health complications resulting from excessive consumption of antibiotics [75-77]. Extensive research on pharmaceutically bioactive substances of *A. delicata* has a potential implication in eliciting insights into the identification and application of bioactive substances (polysaccharides, amino acids, organic acids, and phenolic compounds) for suppressing various microbial infections.

5.2 Hepatoprotective Activity

The liver is among the most vital organs in the human body. Its primary functions include; detoxification of metabolic waste products such as ammonia, breakdown and elimination of hazardous drugs, recycling of dead red blood cells, metabolism of macronutrients (protein, carbohydrates and lipid), secretion of bile, and regulation of blood glucose level through glycogenesis, glycogenolysis and gluconeogenesis reactions [78, 79]. Liver damage results in complications such as chronic hepatitis, cirrhosis, fibrosis, and hepatic carcinoma, interfering with the normal functions of other body systems [80, 81]. Numerous studies have revealed that toxins and drugs lead to increased generation of reactive oxygen species such as superoxides, hydroxyl radicals, and hydrogen peroxide in liver cells [82-84]. Reactive oxygen species accelerate cellular oxidative damage accompanied by adverse cellular injuries, neurodegeneration, tumor growth, inflammation, and cardiovascular disorders (hypertension, heart attack, and heart failure) [84-87]. Superoxide anions ($O2^-$) are capable of producing hydroxyl radicals that exert hazardous effects in the human body by accelerating the destruction of proteins, carbohydrates, lipids, nucleic acids, and amino acids, resulting in severe tissue damage [88-90]. Consequently, the protection of liver cells against hepatotoxic substances is inevitable for its proper functioning [91, 92].

Previous research has demonstrated that most hepatotoxic agents display hazardous oxidative stress in the human body [92]. However, human antioxidant enzymes can play a significant role in suppressing the oxidative effect [93]. Studies have identified three main antioxidant enzymes in the human body including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [86, 93, 94]. SOD provides defense against oxygen-derived free radicals by catalyzing the dismutation of superoxide anion ($O2^-$) into hydrogen peroxide. Catalase catalyzes the lysis of hydrogen peroxide into water (H2O) and oxygen (O2). Glutathione reduces hydroperoxides and peroxides through oxidation of glutathione [94-96]. Previous investigations reported that polysaccharides and triterpenoids extracts of *G. lucidum* demonstrated strong capacity in suppressing the toxic effects of carbon tetrachloride and the hepatitis B virus in liver cells [97, 98]. Moreover, ganoderic acid promotes the activities of SOD and glutathione while lowering the levels of biomarkers of hepatic injury including serum aminotransferases, β-glucuronidase, and malondialdehyde [78, 99, 100].

Mycelial polysaccharides of *P. ostreatus* demonstrated the ability to inhibit lipid peroxidation and nitric acid synthesis in the liver cells while polysaccharide extracts of *A. auricular*, *L. edodes* and *G. frondosa* showed hepatoprotective effects against paracetamol-induced liver injury in mice by lowering the levels of aspartate and alanine aminotransferases [92, 101-103]. Recent studies on liver toxicity have revealed that excessive alcohol intake can trigger the secretion of pro-inflammatory cytokines, including tumor necrosis factor, interleukin-6, and interleukin 1β. Inflammatory cytokines are capable of initiating inflammatory reactions, eventually resulting in hepatic cell death [73, 85, 104-108]. (1→3)- and (1→6)-β-D-glucan-containing polysaccharides extracted from *A. cornea* exhibit antioxidant and hepatoprotective effects against ethanol-induced liver damage. *A. cornea* polysaccharides inhibit the activities of pro-inflammatory cytokines hence protecting the liver cells against damage [85, 109, 110]. Correspondingly, experimental studies on the antioxidant potential of *A. delicata* extracts revealed the presence of antioxidant compounds such as ethyl acetate and methanol [76]. Acetyl acetate and methanolic extracts of *A. delicata* have been identified as the hepatoprotective candidates for protecting the liver against paracetamol-induced liver intoxication [76, 111, 112]. In vivo studies by Kabuyi et al. [70] using mouse as animal model demonstrated that when acetyl acetate and methanol extracts were administered to a mouse with paracetamol-induced liver injury, the toxic levels of paracetamol in liver cells diminished[70, 92, 111, 112]. Analysis of ethanolic extracts of *A. delicata* revealed the presence of an essential phenolic compound named chlorogenic acid, which acts as a hepatoprotective agent [113]. Chlorogenic acid stimulates the proper functioning of bile ducts, preventing bile stagnation by enhancing its smooth flow, and reducing the likelihood of developing gallstones [21, 114, 115]. Furthermore, research reports on the antioxidant potential of *A. delicata* showed that the application of methanol extracts to the rats raised the level of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and reduced glutathione [19, 95, 104, 116, 117]. Antioxidant enzymes catalyze detoxification reactions by breaking down the hazardous reactive oxygen species like superoxide anion into less harmful compounds such as water and oxygen. Consequently, the antioxidant properties of ethyl acetate and methanolic extracts of *A. delicata* are a suitable natural remedy against hepatic disorders [111, 118-119]. Previous studies have shown that Auricularia extracts have been used in the Chinese traditional medicine since ancient times [113, 115]. Recent advancement in research has aided the recognition of the traditional medicine into the pharmaceutical industry. *Auricularia* extracts are utilized as potential resources for the production of hepatoprotective, anticancer, antimicrobial, hypoglycemic, and immunomodulatory drugs [119]. These extracts are currently processed in the pharmaceutical industry, commercialized and made available in various markets in China. Therefore, there is an unveiled potential for mushroom scholars to investigate on various hepatoprotective extracts of *A. delicata,* such as amino acids, polysaccharides, as well as chlorogenic acid, which can facilitate the alleviation of liver ailments [102, 119, 120].

5.3 Antioxidant Activity

Fruiting bodies and mycelial extracts of *Auricularia* mushrooms are rich in varieties of bioactive metabolites [120]. Recent studies on the pharmacological potential of *Auricularia* polysaccharides elucidated their potent antioxidant activity against numerous free radical molecules [121]. The polysaccharide extracts from *A. auricula, A. heimuer,* and *A. cornea* coincide with 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, superoxide radical scavenging activity, and hydroxyl radical scavenging activity [122,123]. Superoxides are hazardous substances formed by photochemical reactions whose effect may result in the formation of more reactive oxygen species such as singlet oxygen and hydroxyl radicals that accelerate oxidative damage [123]. Reactive oxygen species destroy the membrane lipids through peroxidation reactions resulting in increased membrane permeability, cellular contents leakage, severe cell damage, and eventually leading to cell death [122,124,125]. However, *Auricularia* mushrooms have demonstrated potent antioxidant abilities against the above mentioned free radicals [125]. Polysaccharides possess some properties that account for its potent free radical scavenging activity. These prominent features include; the polysaccharide's ability to degrade the superoxide anions, the effective inhibition of hydroxyl radicals formation and decomposition of hydroperoxides [61, 126].

Chlorogenic acid extracted from *A. delicata* has demonstrated the antioxidant capacity against paracetamol-induced liver injury [71,113,127]. It promotes the initiation of a protective response on the hepatocyte membranes, maintaining optimally reduced glutathione (GSH) levels, and scavenging free radicals resulting from paracetamol metabolism [128, 129]. Chlorogenic acid counteracts the liver damage by preventing cell death and destruction from the oxidative effect of acetaminophen toxins [44,130,131].

The detoxification role of chlorogenic acid against acetaminophen-induced liver injury is enhanced by the promoter effects of Toll-like receptor ¾ and the induced nuclear factor k-B signaling pathway, which activates the mechanism for preventing hepatic inflammation [130,132,133]. Scientific studies on the analyses of selenium content of *A. delicata* revealed its content of selenium minerals (3.3 mg/g), which are essential for the proper functioning of the thyroid gland and act as an enzyme co-factor in antioxidant defense [18,44]. Moreover, phytochemical screening of *A. delicata* demonstrated that *A. delicata* contains high levels of phenolic compounds (47.9 mg/g) and flavonoids (4.38 mg/g). These compounds are capable of scavenging free radicals; such nutraceutical significance might be accredited with their potential to confine free radicals by donating a hydrogen atom [70, 134-138]. Despite these efforts in exploring the medicinal values of *A. delicata,* some medicinal properties have not been precisely investigated, including antitumor activity, cardiac protective activity, as well as the immunomodulatory mechanism [67, 135]. Therefore, research emphasis on the antioxidant potential of *A. delicata* will pave the way for furthering our understanding of the mechanism of action of numerous bioactive contents of *A. delicata* that are currently unknown, with their pharmacological role in improving human health [136-138].

6. NUTRITIONAL VALUES

Edible mushrooms contain many nutritious compounds that vary from one species to another due to some factors such as species diversity, cultivation methods, age, and storage methods such as drying [139]. *A. delicata* contains protein, carbohydrates, low fat, melanin, vitamins, and mineral elements [Fig. 1], [140]. The monosaccharides of *A. delicata* provide the flavor of the mushroom, whereas the polysaccharides are reported to have significant medicinal properties such as antimicrobial, anticancer, antitumor, antifungal, hypoglycemic, immunomodulatory activity, antioxidant, and hepatoprotective activity. Moreover, the macro and microelements such as Zinc, Magnesium, Calcium, and Potassium are essential for the physiological activities of body cells [140].

6.1 Vitamins and Minerals

Varieties of mushrooms contain vitamins and mineral elements that are useful for improving human health [141-142]. The macroelements such as; K, Na, Mg, P, Ca, Zn play a crucial role in enhancing physiological processes at the cellular level including ionic balance, enzymatic reactions, and impulse transmission. Vitamins nourish and promote the proper functioning of different body tissues and organs [143-146]. The analysis of experimental results on mineral elements of *A. cornea* and *A. delicata* revealed the presence of 3.84% potassium minerals in *A. delicata* and 2.16% in *A. cornea.* However, the content of calcium was 0.55% and 1.79% in *A. delicata* and *A. cornea,* respectively. Additionally, the content of Silica determined was 3.15% in *A. delicata* and 23% dry weight in *A. cornea* [147].

A. delicata contains some micronutrients such as Zinc, Calcium, vitamin B2, and vitamin C that are required for proper functioning of body cells [6, 8, 139]. While comparing the nutritional analyses of three cultivated *Auricularia* mushrooms (*A. delicata, A. auricula-judae,* and *A. cornea*), the content of the named micronutrients was significantly higher in *A. delicata* than the other mushrooms studied [10,148,149]. Therefore the inclusion of supplementary materials with proper substrate formulation will increase the abundance of micronutrients in *A. delicata* fruiting body [143,150,151].

6.2 Proteins

Proteins are among the most abundant compounds in mushrooms [5]. Mushroom proteins are predominantly higher than vegetable proteins [13]. Thus it can be recommended for nutritional enhancement [3,5,13]. Fruiting bodies of *A. delicata* contain proteins useful in daily diets, as protein supplements from fish and beef are expensive among rural communities due to low household income. Most rural residents experience difficulties in accessing other sources of protein [13,152,153]. The analysis of protein content of *A. auricula-judae* showed that it contains 8.36% of protein and 33% of total proteins are made of amino acid chains [63]. Proteins extracts of *A. cornea* are reported to have functional properties and are referred to as bioactive peptides. These bioactive protein compounds have the ability to stimulate the immune system [63]. In addition, the protein content of *A. delicata* was 116 g/kg [10], and the essential amino acids are higher and close to the need of the human body [2,11]. *A. delicata* proteins are reported to play vital roles in the human body including enhancing the proper functions of membrane transporters, activation of immune system, and development of body tissues [63]. Therefore *A. delicata* can be processed and consumed as a functional food for combating nutritional deficiency in the human body.

6.3 Carbohydrates

Mushrooms contain sugars of different types based on their structural and chemical properties [14]. Numerous researches have reported the presence of monosaccharides, disaccharides, and polysaccharides in different mushroom species [141]. Recently, researchers have developed a great interest in mushroom polysaccharides due to their potential pharmacological values [14,141]. *A. delicata* contains glucose, a reducing sugar that plays a significant role as a readily available source of energy in the human body. Moreover, the dietary fibers contained in *A. delicata* include both soluble and insoluble polysaccharides, which are essential components of the chitinous cell walls [5,154]. Dietary fibers stimulate vital physiological processes, particularly enhancing body relaxation, preventing constipation by improving bowel movements and increasing the surface area for smooth digestion of food substances in the digestive track, reducing excessive blood sugar, and cholesterol [14,141,155,156]. The beta-glucans found in the mushroom cell walls are reported to activate the immune system against cancer cells and tumors [136]. The dietary fibers from *A. delicata* are believed to improve the absorption of some mineral elements such as Ca and Mg in the digestive track [10,157,158]. Henceforth a continuous investigation on *A. delicata* saccharides will facilitate the discovery of valuable bioactive substances that are significant in human nutrition and medicine.

7. CULTIVATION

Mushroom farming is principally carried out via a series of interdependent activities that must be accomplished accurately in the sterile environment [152,162]. However, the process of tissue culture, substrate preparation, inoculation, incubation, and other growing conditions depends on a particular species cultivated [163,164]. The quality of spawn and its preparation in a sterile condition are fundamental parameters for the efficiency of mushroom production [4,164-167]. Similarly, for the cultivation of *A. delicata,* the named parameters are highly contemplated [167].

Table 1. A comparative study of bioactivity of *A. delicata* relative to other edible and medicinal mushrooms

Species	Category	Biomaterial source	Bioactive Metabolite	Bioactivity	Biomedical application	References
Auricularia delicata	Polysaccharides Phenolic compounds Flavonoids	Fruiting body, Mycelium	Chitosan, fibers, β-glucans, mannans, chitin, melanin Chlorogenic acid Ethyl acetate. Epicatechin, rutin, naringin	Antimicrobial against: *S. aureus,* B. cereus, *E. coli,* S. typhi, C. albicans Antitumor Hepatoprotective Antioxidant Immunomodulatory.	Synthesis of antimicrobial, hepatoprotective, antioxidant , immunomodulatory drugs	[11,133]
Auricularia auricula-judae	Polysaccharides Phenolic compounds	Fruiting body, Mycelium	Chitosan, fibers, β-glucans, mannans, chitin, pectin	Anticancer/ Antitumor Immunomodulatory Antimicrobial against *S. aureus, E. coli, E. aerogenes*	Production of antitumor drugs against varieties of cancer. Production of immunomodulatory drugs, antimicrobial drugs.	[59,67,77]
Auricularia polytricha	Polysaccharides Phenolic compounds	Fruiting body	β-glucans, mannans, Ascorbic acid, Ethylene diaminate traacetic acid	Antidiabetic Antimicrobial Hypolipidemic Antioxidant: activates serum aspartate, aminotransferases, superoxide dismutase SOD.	Production of Antidiabetic drugs, Antimicrobial drugs, hypolipidemic drugs.	[17,68]

Table 1 continues…

Species	Category	Biomaterial source	Bioactive Metabolite	Bioactivity	Biomedical application	References
Ganoderma lucidum	Polysaccharides	Fruiting body, Mycelium	α-glucans, β-glucans,	Immunomodulatory effect: activates macrophages, induce synthesis of IFN-y-cytokines.	Synthesisof Immmunom odulatory drugs	[97,138,159]
	Terpenoids		Ganolucidoid A, Ganolucidoid B	Anti-inflammatory	Synthesis of Inflammatory drugs	
	Flavonoids		Quercetin Kaempferol	Antioxidant Antimicrobial	Synthesis of antioxidant and antimicrobial drugs	
	Phenolic compounds		Ganoderic acid, Ganomycin, β-Ganoderma nontriol, Ganolucidic acid A, Lucidumol Ethyl acetate	Antiviral: Inhibit HIV-1 viral replication by deactivating HIV-1 protease Antibacterial against: *S. aureus,* B. cereus, S. typhimurium	Synthesis of Antiretroviral drugs.	
Lentinula edodes	Polysaccharides	Fruiting body, Mycelium	Lentinan	Immunomodulatory effects: Activates T cells (immune cells)	Production of Immunomodulatory drugs.	[70,115]
	Phenolic compounds		Gallic acid			
	Flavonoids		Protocatechuic acid, catechin, tocopherols			

Table 1 continues…

Species	Category	Biomaterial source	Bioactive Metabolite	Bioactivity	Biomedical application	References
Pleurotus eryngii	Polysaccharides	Fruiting body	β-glucans	Antioxidant	Synthesis of antioxidant drugs	[71,112, 115]
	Flavonoids		naringin, rutin, kaempferol			
	Phenolic compounds		Gallic acid			
Pleurotus ostreatus	Phenolic compounds	Fruiting body	Gallic acid	Antioxidant	Synthesis of antioxidant drugs	[80,81,112]
Auricularia cornea	Phenolic compounds	Fruiting body	Gallic acid Chlorogenic acid	Antioxidant		[160]
	Flavonoids		Caffeic acid, epicatechin, rutin, naringin	Antioxidant	Synthesis of antioxidant drugs	
Auricularia heimuer	Polysaccharides	Fruiting body, Mycelium	Chitosan, fibers, β-glucans, mannans.	Hypolipidemic, Antioxidant, Antimicrobial, Antitumor.	Synthesis of hypolipidemic, antimicrobial, hepatoprotective, antioxidant , immunomodulatory drugs	[122,160].
	Flavonoids		Epicatechin, rutin, naringin			
Grifola frondosa	Polysaccharides	Fruiting body	α-glucans, β-glucans, Grifolan	Immunomodulatory. Induce synthesis of IFN-y-cytokines. activates macrophages, lymphokines and cytokines (INF-y-, TNF α, IL-I β,IL-6)	Production of Immunomodulatory drugs.	[109,161]

Samuel et al. [168] reported that the use of sawdust as the primary substrate with maize and paddy straw supplements in the cultivation of *Pleurotus ostreatus* showed the fastest rate of mycelial growth about 0.797 and 0.763 cm/day respectively during spawn run. However, the shortest time for pinhead formation was 35 days. Xing et al. [10] asserted that cultivation of *A. delicata* using 68% sawdust supplemented by 7.5% wheat bran, 2% maize powder, 20% cotton-seed hull, and 1% brown sugar resulted to 4.5 mm/day mycelial growth rate which is equivalent to 0.45 cm/day. Moreover, the investigation of biological properties and cultivation of *A. delicata* identified the optimal cultivation conditions in solid culture. Experimental results showed that the optimal cultivation conditions include; pH 6.0 to 6.5, the temperature was 25-30°C, carbon sources were sucrose and starch, while the nitrogen sources were peptone and yeast extract [Fig. 2] [10]. Cultivation under these optimal conditions demonstrated a higher rate of mycelial growth on the substrates [1, 10].

Studies on *P. ostreatus* by Shah et al. [169] showed that at 25°C pinhead appeared 27-34 days after inoculation, whereas Quimio [170], reported that the formation of pinheads was observed 3-4 weeks after inoculation. Nevertheless, Xing et al. [10] revealed that the cultivation of *A. delicata* strains on a solid culture medium (solid fermentation), produced the fruit bodies within 12-15 days after inoculation. However, the total number of days from inoculation to harvest was about 40 to 42 days. The overall yield production of *P. ostreatus* was 646.9 g fresh weight while *A. delicata* productivity was 750 g fresh weight after three consecutive harvests [10, 169]. Numerous studies have demonstrated that both solid and liquid culture media can be used in cultivation of various species of mushrooms [171]. The use of liquid fermentation technology in mushroom cultivation has a potential effect in fastening the rate of mycelial colonization of substrates and shortening the cultivation cycle [159-161]. Furthermore, recent research reports have revealed an increase in the use of the liquid

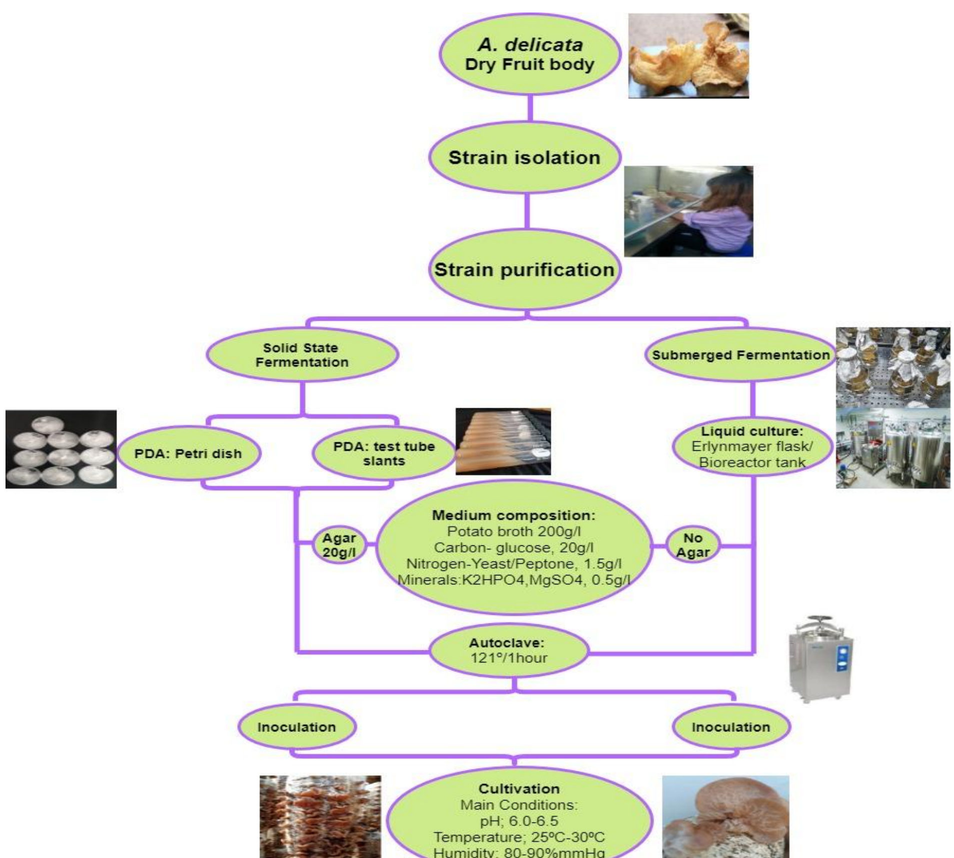

Fig. 2. A schematic view of the cultivation process of *A. delicata*

Table 2. Future development perspective of *A. delicata*

Area of Concern	Key Motives	Opportunity for Improvement
Cultivation	Maximizing production of *A. delicata*	There is a need for increased production to sufficiently meet the growing demand for *A. delicata*. Use of appropriate technology, quality spawn, and advanced management skills
Nutrition	Nutritive potentials; Macronutrients and micronutrients; good taste, delicious, source of protein, saccharides, dietary fibers, vitamins, and minerals	Potential for improving human health, as a functional food can help to combat malnutrition. More research should be done to identify further nutritional elements useful for improving human health.
Medicinal values	Antimicrobial, antioxidant, hepatoprotective, cardiac protection, antitumor, and immunomodulatory activity.	There is a growing demand for natural herbal products to counteract the side effects of synthetic drugs including the development of drug resistance. Hence *A. delicata* can be used as an alternative natural treatment against many health disorders.
Molecular studies	Limited information on molecular studies	Researchers should focus on molecular studies of *A. delicata* analyzing genome, enzyme activities, nucleic acids, and other associated physiochemical processes.
Marketing	Species awareness; limited supply in the market	Community awareness of the species through advertisement. Providing education on its good taste, delicious, nutritional, and medicinal values. Processing *A. delicata* into various products (i.e powder, spice, tea blend, food ingredient) More *A. delicata* mushrooms should be available to a variety of markets.

Fig 3. Cultivated *A. delicata* at different stages of growth (from primordial to mature fruit body)

fermentation technology in commercial farming of a wide variety of mushrooms including *A. heimuer, A. cornea, A. auricula-judae,* and *P. ostreatus* [160]. Consequently, the application of both solid and liquid fermentation is vital for the cultivation of *A. delicata.* However, in order to cope with the increasing demand in the market, large scale productions are highly encouraged.

Thus submerged fermentation is promoted due to its fast rate of mycelial colonization, simplifies the inoculation process, shortening the cultivation cycle, lower risks of contamination and increasing productivity. In addition, the above aspects demonstrate the promising potential of cultivating *A. delicata* as a commercial mushroom crop [172, 173].

8. FUTURE DEVELOPMENT PERSPECTIVE OF *A. delicata*

Current studies on *A. delicata* have been carried out in laboratories of Jilin agricultural university whereby the fruit bodies were collected from Zambia, Africa. This study marked the beginning of domestication of *A. delicata,* due to its external structure and texture resembling the deer tripe it has been assigned a common name as; "Deer tripe mushroom" [37]. The first time large scale cultivation of *A. delicata* has been executed in Heilongjiang province in the northeastern part of China [Fig. 3]. As an emerging edible species, *A. delicata* should be promoted to a global level [38]. Table. 2 highlights the key areas that can be further studied for the prospects of *A. delicata* productivity.

9. CONCLUSION

The discovery of *A. delicata* has been successfully carried out for centuries. Studies on taxonomic characteristics and distribution of *A. delicata* revealed its occurrence in tropical and subtropical climatic conditions; these discoveries pave the way for exploring the adaptability to its habitat and optimal conditions for its domestication. This study has also shown many therapeutic and nutritional benefits of *A. delicata.* Thus extensive research on pharmaceutically bioactive substances of *A. delicata* has a potential implication in eliciting insights into identification and application of polysaccharides, amino acids, organic acids and phenolic compounds for suppressing various health impairments such as; microbial infections, liver ailments, gastrointestinal disorders, tumors, hyperglycemia, hyperlipidemia as well as immunodeficiency.

Additionally, due to its antioxidant, antimicrobial, and hepatoprotective properties, *A. delicata* extracts can be utilized as a nutritional supplement for many human diseases as a means to enhance its nutraceutical importance. Therefore, there is a potential for exploring the appropriate methods of extracting numerous functional compounds of *A. delicata* useful for promoting good health. Researchers on the fungi genome have not explicitly explored the *A delicata* genome. There is a potential for a detailed investigation of the functional genes through comparative genomics. The study on fungi genome will enable the mycologists to clearly describe *A. delicata* and distinguish it from other species based on the genome structure. The genomic study of *A. delicata* will facilitate the establishment of the evolutionary relationship between species of the same genus (*Auricularia)*. However, further research on cultivation technology is crucial for improving the productivity of *A. delicata*. Thus there is a need for extensive investigation on optimization of cultivation conditions, in both solid and submerged culture mediums. The determination of a more effective optimal cultivation formula will fasten the mycelia growth, shorten the cultivation cycle, and eventually improve the yield production of *A. delicata*.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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