Review Article

องค์ประกอบทางเคมีและฤทธิ์ทางเภสัชวิทยาของเห็ดกระด้าง

นิรามัย ฝางกระโทก[1]*

[1]ปร.ด. อาจารย์ คณะเทคโนโลยีการเกษตร มหาวิทยาลัยบูรพา วิทยาเขตสระแก้ว จ. สระแก้ว 27160

***ติดต่อผู้นิพนธ์:** นิรามัย ฝางกระโทก คณะเทคโนโลยีการเกษตร มหาวิทยาลัยบูรพา วิทยาเขตสระแก้ว จ.สระแก้ว 27160

โทรศัพท์ 0831477567 อีเมลล์ niramai@buu.ac.th

บทคัดย่อ

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นิรามัย ฝางกระโทก[1]*

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เห็ดเป็นแหล่งของสารอาหารและยาจากธรรมชาติซึ่งช่วยในการส่งเสริมสุขภาพของมนุษย์ เห็ดกระด้าง หรืออาจเรียกว่า เห็ดบด หรือเห็ดลม (*Lentinus polychous* Lév.) เป็นเห็ดพื้นเมืองที่กินได้อยู่ในวงศ์ Polyporaceae เป็นเห็ดที่มีคุณค่าทางโภชนาการและสรรพคุณทางยา โดยทั้งดอกเห็ดและเส้นใยจากเห็ดกระด้างมีสารสำคัญที่เป็นองค์ประกอบหลายชนิดได้แก่ สารกลุ่มฟีนอลิค สารกลุ่มเออร์โกสเตอรอล สารกลุ่มโพลีแซคคาไรด์และโปรตีนต่าง ๆ เห็ดกระด้างมีฤทธิ์ทางเภสัชวิทยาหลายอย่าง ได้แก่ ฤทธิ์ต้านอนุมูลอิสระ ฤทธิ์ต้านการอักเสบ ฤทธิ์ต้านมะเร็ง ฤทธิ์ต้านเอสโตรเจน ฤทธิ์ต้านเอนไซม์แอนจิโอเทนซินวัน-คอนเวอร์ติง และฤทธิ์ปรับภูมิคุ้มกัน นอกจากนี้ ยังมีรายงานว่าสารสกัดหยาบของโพลีแซคคาไรด์จากดอกเห็ดและเส้นใยเห็ดกระด้างมีความปลอดภัยในระดับสัตว์ทดลองอีกด้วย บทความทางวิชาการฉบับนี้ได้รวบรวมและสรุปผลการศึกษาทางวิทยาศาสตร์เกี่ยวกับองค์ประกอบทางเคมีและฤทธิ์ทางเภสัชวิทยาของเห็ดกระด้าง ซึ่งข้อมูลดังกล่าวได้แสดงให้เห็นถึงศักยภาพของเห็ดกระด้างในการพัฒนาโภชนเภสัชภัณฑ์หรืออาหารฟังก์ชัน

คำสำคัญ: เห็ดกระด้าง, องค์ประกอบทางเคมี, ฤทธิ์ทางเภสัชวิทยา

Chemical Constituents and Pharmacological Activities of *Lentinus polychrous* Lév

Niramai Fangkrathok[1]*

[1]Faculty of Agricultural Technology, Burapha University Sakaeo Campus, Sa Kaeo, 27160, Thailand

***Corresponding Author:** niramai@buu.ac.th

Abstract

Chemical Constituents and Pharmacological Activities of *Lentinus polychrous* Lév

Niramai Fangkrathok[1]*

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Mushrooms is a source of nutritional and medicinal natural products in promoting human health. *Lentinus polychous* Lév., a local edible mushroom in family Polyporaceae, has nutritional and medicinal values. Its fruiting bodies and mycelia contain several phenolic compounds, ergosterols, polysaccharides and proteins. The mushroom showed pharmacological properties including anti- oxidant, anti- inflammatory, anti- cancer, anti- estrogenic, anti- angiotensin I- converting enzyme and immunomodulatory activities. In addition, crude polysaccharides from *L. polychrous* fruiting bodies and mycelia were also reported its safety in *in vivo*. Scientific studies of *L. polychrous* chemical composition and pharmacological activities are summarized in this review which suggesting that *L. polychrous* has an efficacy for further nutraceutical or functional food product development.

Keywords: *Lentinus polychous* Lév., chemical constituents, pharmacological activities

1. Introduction

Lentinus polychrous Lév. is an edible mushroom in order Polyporales and family Polyporaceae (Chandrasrikul *et al*., 2011). Although it has been found in every regions of Thailand, popularly eaten by people in northeastern and northern Thailand (Chandrasrikul, 1996). Fruiting bodies of *L. polychrous* are sticky depending on cultivate ages (Petcharat, 1995). A mushroom cap is broadly funnel-shaped with diameter of 5-15 cm. Its whitish cap can change to pale brownish when it becomes older age (Figure 1). The cap is covered with short brown hair and recurved fibrous square scales especially at the center. The margin of cap is incurved and then split along the margin in older age. Grills of this mushroom are deep, narrow, crowded, edge finely saw- liked and pale brown. When older age the gills are changed from grayish brown to reddish brown and tinted with purple. Its stalk is cylindrical shape with size of 0.5-2.5 × 0.5-1.4 cm. The stalk is at the center or off-center, solid, whitish and changed to brown color. The flesh of this mushroom is whitish tough. Its spores are smooth ellipsoid with size of 6-9 × 2.7-3.3 μm, often slightly curved, thin walled and whitish spore print. The mushroom grows single or in groups on logs of deciduous trees as their natural habitat (Chandrasrikul *et al*., 2008). Recently, a biology of *L. polychrous* varieties in some provinces in Thailand (13 varieties) and Laos (10 varieties) has been reported. Its cap, gills, scales, stalk, color and size are different in each variety. Season also affects to the scales on caps. Cap skin is smooth in rainy season while in winter season the cap skin is scabbed and scattered. However, *L. polychrous* in Thailand and Laos are almost similar (Rattanamalee and

Rattanamalee, 2012). This mushroom has been popularly consumed because of its good taste and nutrients. In recent report, *L. polychrous* contains moisture content, protein, fat, carbohydrate, fiber and important elements such as sodium, potassium, calcium, iron, magnesium and zinc (Thongekkeaw, 2009). Moreover, *L. polychrous* has been used in the treatment of dyspepsia and fever from adder envenomation (Klinhom and Klinhom, 2006). Therefore, this mushroom may have an interesting chemical composition leading to nutritional and medicinal values. Aim of this review is to aggregate knowledge of *L. polychous* in pharmacological and chemical properties as well as biotechnological application.

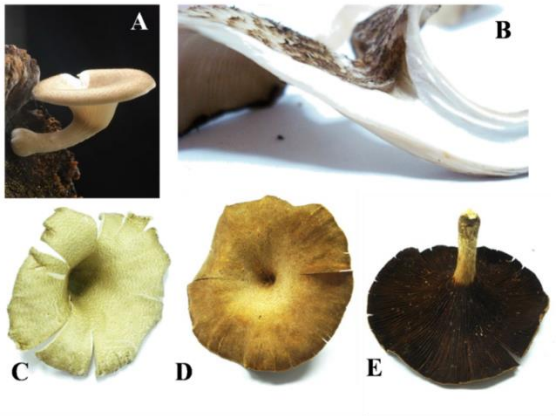

Figure 1. The fruiting bodies of *L. polychrous* Lèv. A) natural fruiting body, B) torn fruiting body, C) cultivated fruiting body, C) dried old fruiting body and D) spores of dried old fruiting body.

2. Chemical properties

Mushrooms are good sources of bioactive compounds which exhibit pharmacological activities leading to health benefit. The fungal bioactive metabolites can be obtained from many origins including wild or cultivated fruiting bodies, spores, mycelial biomass and supernatant of submerged cultures. Cultivation technologies in production of fruiting bodies, spores and cultivated mycelia biomass provide unlimited sources of bioactive compounds. There were several studies on chemical composition from fruiting bodies and mycelia of *L. polychrous*. Several phenolic compounds in its fruiting bodies and mycelia including catechin, tannic acid, gallic acid, quercetin, isoquercitin, eriodictyol and kaempferol were reported (Amassa *et al.*, 2009; Attarat and Phermthai, 2015; Attarat and Thamisak 2014; Sirival, 2010). These bioactive constituents play an important role in several pharmacological activities providing a health benefit.

Mushroom is a natural source of phytosterol-like structures such as ergosterol, fungisterol and many other derivatives. Many bioactive compounds were isolated from *L. polychrous* mycelia including a new polyhydroxyoctane, 6-Methylheptane-1,2,3,4,5-pentaol (**1**), and five ergostanoids i.e. (22*E*,24*R*)-ergosta-7, 22-dien-3β, 5α, 6β-triol (**2**), 3β, 5α-dihydroxy-(22*E*, 24*R*)-ergosta-7, 22-dien-6-one (**3**), ergosta-4, 6, 8(14), 22-tetraen-3-one (**4**), (3β, 5α, 8α, 22E)-5, 8-diepoxy-ergosta-6, 22-dien-3-ol (**5**) and 5, 8-epidioxy-(3β, 5α, 8α, 22E)-ergosta-6, 9(11), 22-trien-3-ol (**6**) (Fangkrathok *et al.*, 2013b) (Figure 2). All these compounds showed anti-oxidant, anti-inflammatory and immuno-modulatory effects (Fangkrathok *et al.*, 2013a; 2014a; 2014b).

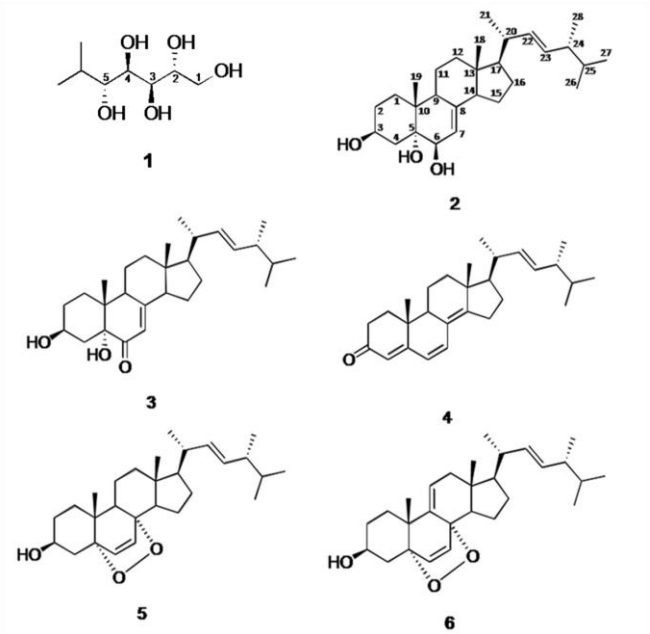

Figure 2. Structures of isolates (**1-6**) from *L. polychrous* mycelia extract (Fangkrathok *et al.*, 2013b)

Polysaccharides such as chitin, cellulose, (1,3)-β-glucans, (1,6)-β-glucans, (1,3)-α-glucans and polysaccharide-protein complexes are composited in

mushroom cell wall (Yap and Ng, 2001). Fungal β-glucans showed immunostimulatory, anti-tumor and cholesterol lowering activities (Nicolosi *et al.*, 1999; Sima *et al.*, 2018; Vannucci *et al.*, 2013). Similarly, fruiting bodies of *L. polychrous* contain polysaccharides and 70 kDa polysaccharopeptides (PSP) (0.41 ± 0.03 mg/g protein) which has immunological and anti-tumor properties (Attarat and Phermthai, 2015; Attarat and Thamisak 2014; Parris, 2000). The ethanolic precipitation from *L. polychrous* hot water extract showed the highest concentration of β-1,3-1,6-glucan (1.21 mg/ml). And this β-glucans were heterogeneous non-starch polysaccharides which found in the cell wall of several microorganisms and grains. (Inpad *et al.*, 2015). In addition, Mongkontanawat and Wongekalak (2015) could increase the content of total glucan, α-glucan and β-glucan, in *L. polychrous* by blanching the mushrooms. Since heating in blanching process can affect the content of glucan in mushroom (Manzi *et al.*, 2004), Therefore, blanching process may help to increase the health beneficial property of mushroom.

Mushrooms contain abundance of ligninolytic enzymes for lignin degradation. Laccase, lignin peroxidase and manganese peroxidase are main ligninolytic enzymes found in mushroom. *L. poluchrous* mycelia can also produce several ligninolytic enzymes such as laccase, xylanase, manganese peroxidases, β-galactosidase and cellulase in both liquid and solid media (Budda *et al.*, 2012; Petchluan *et al.*, 2014; Petre and Teodorescu, 2011; Pukahuta *et al.*, 2004). And this laccase production could be induced by using $CuSO_4$ as a laccase inducer (Khammuang *et al.*, 2013). There were several studies using ligninolytic enzyme production from *L. polychrous* mycelia in the biotechnological application on waste degradation (Nitayapat *et al.*, 2015). Interestingly, the degradation activity of *L. polychrous* mycelia on biomass could also increase nutritional properties (Nitayapat *et al.*, 2015). These ligninolytic enzymes from the mushroom fruiting bodies and spent compost from mushroom cultivation are useful for waste management especially textile industry (Law *et al.*, 2003; Trejo-Hernandez *et al.*, 2001). The structurally different synthetic dyes including Indigo Carmine (indigoid dye), Remazol brilliant blue R (anthraquinone dye), Bromophenol blue (triarylmethane dye) and Methyl red (azo dye) were decolorized by using this mushroom crude enzyme (Khammuang and Sarnthima, 2007; Sarnthima *et al.*, 2009). Moreover, Wangpradit and Chitprasert (2014) developed chitosan-coated *L. polychrous* mycelia for biosorption and biodegradation of anionic reactive dyes resulting in improvement of dye adsorption capacity. This decolorizing property of ligninolytic enzymes from mushroom is also useful in cosmetic application. For example, crude laccase from *L. polychrous* mycelia could decolorize the synthetic melanin in the absence and presence of selected redox mediators especially vanillin (Khammuang and Sarnthima, 2013). This result may lead to the further development of skin-whitening products from the mushroom extracts.

3. Pharmacological properties

Mushrooms contain high nutritional and medicine values, therefore, they are consumed as a food, dietary supplement and for treatment. Mushrooms can be considered as a medicinal food or nutritional food called a functional food. Although such functional or medicinal foods should not be claimed to cure the diseases, there are accumulating of scientific studies that strongly support some functional food property from mushroom in disease prevention and treatment. Several medicinal effects of mushroom and mushroom-derived substances were reported such as anti-cancer, anti-tumor, anti-microbial, anti-viral, anti-allergic, immunomodulating, anti-inflammatory, anti-atherogenic, anti-oxidative, anti-mutagenicity, hypoglycemia, hepatoprotective and psychoactive activities (Fan *et al.*, 2006; Lindequist *et al.*, 2005; Ruimi *et al.*, 2011).

3.1. Anti-oxidant activity

L. polychrous fruiting bodies and mycelia showed high anti-oxidant activity and contained several phenolic compounds as described above (Amassa *et al.*, 2009; Attarat and Phermthai, 2015; Attarat and Thamisak 2014; Sirival, 2010;). The methanolic extract and crude polysaccharides from this mushroom fruiting bodies and mycelia were also reported to have anti-oxidant activity (Thetsrimuang *et al.*, 2011a; Thetsrimuang *et al.*, 2011b). In

addition, the mushroom β-glucan also exhibited high anti-oxidant activity (Inpad *et al.*, 2015). This anti-oxidant activity may relate to anti-inflammatory activity and other pharmacological properties of mushroom leading to health benefits.

3.2. Anti-inflammatory activity

Traditionally, the hot water extract from the fruiting body of *L. polychrous* has been used as a tonic and medicine in the treatments of dyspepsia and fever from snake or scorpion envenomation (Klinhom and Klinhom, 2006). This traditional use may involve with anti-inflammatory activity of this mushroom. The extract from *L. polychrous* mycelia showed anti-inflammatory activity in both *in vitro* and *in vivo*. The extract suppressed the production of nitric oxide (NO) and gene expression of inducible nitric oxide synthase (iNOS), interleukin (IL) -1β, IL-6, tumor necrosis factor (TNF) -α and cyclooxygenase (COX) -2 from lipopolysaccharide (LPS) -induced RAW264.7 cells. Moreover, the extract significantly reduced carageenan-induced paw edema in rats (Fangkrathok *et al.*, 2013a). Five ergostanoids isolated from *L. polychrous* (Figure 2) suppressed the production of NO and reactive oxygen species (ROS) from LPS-induced RAW264.7 cells especially compounds **5** and **6** which showed stronger activity (Fangkrathok *et al.*, 2014b). Compound **5** or ergosterol peroxide was reported to possess anti-inflammatory activity by decreasing TNF-α, IL-6, NO and prostaglandin E2 (PGE2) secretions and also reducing gene expressions of iNOS and COX-2 from LPS-induced inflammatory responses of RAW264.7 cells (Chao *et al.*, 2010; Kobori *et al.*, 2007; Tewtrakul *et al.*, 2010). Moreover, compound **1** also showed anti-inflammatory activity against macrophages via suppression of pro-inflammatory mediator mRNA expressions including iNOS, TNF-α, IL-1β, IL-6, COX-1 and COX-2 (Fangkrathok *et al.*, 2014a). These evidences indicate that *L. polychrous* can be a good functional food with anti-inflammatory property.

3.3. Anticancer activity

The methanolic extract and crude polysaccharides from this mushroom fruiting bodies and mycelia exhibited mild inhibitory effect on cell proliferations of breast cancer cell lines, MCF-7 (Amassa *et al.*, 2009; Thetsrimuang *et al.*, 2011a). Attarat and Thamisak (2014) reported their previous study that ethanolic extract of this mushroom showed slightly inhibitory effect on the proliferation of cholangiocarcinoma cell line, M213, and human hepatocellular liver carcinoma cell line, HepG2.

3.4. Immunomodulatory activity

The ethanolic extract from *L. polychrous* mycelia stimulated the proliferation of mitogen-induced T-cells via induction of IL-2 production. However, the extract decreased Th1 differentiation by reducing the production of Th1 cytokine, interferon-γ (IFN-γ) (Fangkrathok and Sripanidkulchai, 2016). This extract also showed immunorestoration effect on T- and B-cells isolated from cyclophosphamide-induced immunocompromised mice by enhancing the mitogenic-inducted cell proliferation ability (Fangrathok and Sripanidkulchai, 2012). In addition, five ergostanoids isolated from *L. polychrous* especially compounds **5** and **6** showed immunosuppressive effect by suppressing the production of NO and ROS from LPS-induced RAW264.7 cells and the mitogenic-induced splenocyte proliferation in both T- and B-cells (Fangkrathok *et al.*, 2014b). These immunosuppressive effect may involve with peroxide in their structure. Moreover, compound **1** also suppressed the proliferation of mitogen-induced T- and B-cells isolated from murine splenocytes (Fangkrathok *et al.*, 2014a). This immunosuppressive effect of both crude extract and compound **1** correlated with anti-inflammatory activity. These evidences indicate an efficacy of *L. polychrous* on immunomodulation especially suppressive effect on immunity, therefore, this mushroom can be further developed to functional food or supplement for autoimmune disease patients.

3.5. Estrogenic and anti-estrogenic activities

Mushroom is a natural source of phytosterol-like structures such as ergosterol, fungisterol and many other derivatives. Ergosterol is a major fungal sterol and known as vitamin D2 (ergocalciferol) precursor. It is abundant in all mushrooms species because it is a constitutive compound of the hyphae membranes. Vitamin D or calciferol is a fat-soluble vitamin commonly occurring in the D2 or D3

(cholecalciferol) forms and its active form plays a role in maintaining blood levels of phosphorus and calcium, promotes bone mineralization and calcium absorption and can be used in cancer treatment (Mehta and Mehta, 2002). Therefore, the consumption of ergosterol containing mushrooms also give a good benefit for health as well as vitamin D or D3 supplement consumption (Greer and Marshall, 1989; Koyyalamudi *et al.*, 2009). Some phytosterols were reported to show estrogenic activity (Ju *et al.*, 2004; Nakari, 2005), while mycosterol, or ergosterol, isolated from yeast extract was reported to inhibit breast cancer cell proliferation via the anti-estrogenic activity (Subbiah and Abplanalp, 2003). Based on the steroid skeleton of five ergostanoids from *L. polyshrous* mycelia, the estrogenic or anti-estrogenic activities were studied by using human breast cancer cells, T47D. Compound **2-6** showed no estrogenic activity. However, the compounds exhibited anti-estrogenic activity by suppressing estradiol-enhancing cell proliferation. Compound **4** could compete with estradiol to bind the estrogen receptors (ERs) especially ERα (Fangkrathok *et al.*, 2013b). It is possible that compound **4** acts as antagonist by occupation into ligand-binding pocket of ERs to block the binding of estradiol and then inactivate the signaling cascade from ligand-receptor binding and may bind to ERα with more specificity than to ERβ because of the difference between ERα and ERβ binding cavity structures.

3.6. Anti-angiotensin I-converting enzyme activity

Angiotensin I-converting enzyme is an important enzyme in renin angiotensin system and causes blood pressure increasing (Jang *et al.*, 2011). Crude water extract and crude protein extracts from *L. polychrous* fruiting bodies showed inhibitory effect on angiotensin I-converting enzyme activity (Kokram *et al.*, 2016). In addition, the extracts were used as an active ingredient in a healthy drink for helping in lowering blood pressure. Interestingly, this healthy drink product also showed similar inhibitory activity on angiotensin I-converting enzyme (Kokram *et al.*, 2016).

3.8. Safety

Mekjaruskul and colleagues (2015) reported an acute toxicity study of crude polysaccharides from *L. polychrous* fruiting bodies and mycelia in rats. A single-administration of various doses (50, 500 and 2,500 mg/kg BW) were investigated in male and female Wistar rats. After 14 days of observation, there was no significant change in blood biochemical parameters between treated and control groups. Accordingly, the highest dose (2.5 g/kg BW) of both extracts did not cause toxicity, the no observed-adverse-effect level (NOAEL) dose is higher than 2.5 g/kg. Therefore, mushroom extracts from fruiting bodies and mycelia are safe for consumption.

4. Summary

Mushroom fruiting bodies, spores and cultivated mycelia biomass are unlimited sources of bioactive compounds. *L. polychous* is also an edible mushroom that has nutritional and medicinal values from its chemical constituents. Both *L. polychrous* fruiting bodies and mycelia contain a plenty of phenolic compounds, ergosterols, polysaccharides and proteins. These chemical constituents lead to its pharmacological properties including anti-oxidant, anti- inflammatory, anti- cancer, anti- estrogenic, anti-angiotensin I- converting enzyme and immunomodulatory activities. In conclusion, these several medicinal effects and mushroom-derived substances from *L. polychrous* can be further developed into nutraceutical or functional food products. Furthermore, the ligninolytic enzymes from this mushroom can be further used in biotechnological and environmental application.

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