

Anticancer Compounds From Nine Commercially Grown and Wild Philippine Mushrooms

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ABSTRACT

This paper is a review on the chemical constituents and biological activities of the fruiting bodies of seven edible and two inedible mushrooms with reported anticancer properties found in the Philippines. We previously reported the chemical constituents of the dichloromethane extracts of the fruiting bodies of these mushrooms, which were cultured at Central Luzon State University, bought from the Mushroom Burger and Metro Manila supermarkets, and collected from Mt. Makiling. These studies yielded ergosterol (**1**) ergosterol peroxide (**2**) cerevisterol, dilinoleoyloleoylglycerol, and a mixture of linoleic acid (**3**) palmitic acid, stearic acid and oleic acid from *Pleurotus florida*; **1**, triacylglycerols (**4**) and fatty acid methyl esters from *Pleurotus djamor*; **1** and **4** from *Flammulina velutipes*; **1** and trilinolein (**5**) from *Pleurotus eryngii* and *Lentinula edodes*; **1**, **3**, **5** and brassicasterol from *Agaricus bisporus*; **2** from *Auricularia auricula-judae*; **2-4** and 3 β -linoleoyloxyergosta-7,22-diene from *Coprinopsis lagopus*; and **2** and **4** from *Phellinus gilvus* (Schwein.) Pat. Compounds **1-5** were reported to exhibit anticancer properties, which may contribute to the anticancer activities of these mushrooms. Other studies revealed that the anticancer principles of some of these mushrooms are polysaccharides and proteins.

Keywords: *Pleurotus florida*, *Pleurotus djamor*, *Flammulina velutipes*, *Pleurotus eryngii*, *Lentinula edodes*, *Coprinopsis lagopus*, *Phellinus gilvus*, *Agaricus bisporus*, *Auricularia auricula-judae*

INTRODUCTION

This paper is a review on the chemical constituents and biological activities of seven edible and two inedible mushrooms found in the Philippines. In our previous studies, the edible mushrooms *Pleurotus florida* and *Pleurotus djamor* were cultured at Central Luzon State University; *Lentinula edodes* was bought from Mushroom Burger; *Pleurotus eryngii*, *Flammulina velutipes*, and *Agaricus bisporus* were bought from Metro Manila supermarkets; and *Auricularia auricula-judae* was collected from Mt. Makiling. The inedible mushrooms *Coprinopsis lagopus* and *Phellinus gilvus* (Schwein.) Pat. were also collected from Mt. Makiling.

Pleurotus

The genus *Pleurotus* is composed of a group of edible mushrooms with medicinal properties, such as hematological, antiviral, antitumor, antibiotic, antibacterial, hypocholesterolic, and immunomodulating activities. Recently, the cultivation of these edible *Pleurotus* species has expanded due to their importance in the food industry. Mushrooms are rich in protein, fiber, carbohydrates, vitamins, and minerals (Cohen, Persky, & Hadar, 2002).

Pleurotus florida

P. florida is widely cultivated in the Philippines as the commercial oyster mushroom. Several studies have been conducted on the biological activities, nutritional values, and chemical constituents of this oyster mushroom. The methanol extract of *P. florida* showed significant activity in ameliorating acute and chronic inflammation and exhibited significant platelet aggregation inhibiting activity (Jose & Janardhanan, 2000). This extract also inhibited the growth of a solid tumor induced by EAC cell line (Rahman, Rahaman, Nahar, Uddin, Basunia, & Hossain,



Figure 1: A photo of *Pleurotus florida*

2013). Furthermore, the ethanol extract of *P. florida* was reported to possess antioxidant and antimicrobial activities (Muthulingam, Savio, Seeli, Indra, & Sethupathy, 2010), while the aqueous extract revealed an antihepatotoxic action (Muthulingam, Savio, Seeli, Indra, & Sethupathy, 2010). Our earlier study on the dichloromethane extract of the fruiting bodies of *P. florida* cultured at the Central Luzon State University afforded ergosterol, (1) ergosterol peroxide, (2) cerevisterol, dilinoleoyloleoylglycerol, and a mixture of linoleic acid, (3) palmitic acid, stearic acid, and oleic acid (Ragasa, Ebajo Jr., Reyes, Brkljača, & Urban, 2015). Another study reported that *P. florida* yielded 113 μg ergosterol per gram of the mushroom (Raina, Sodhi, & Sethi, 2014).

Pleurotus djamor

P. djamor, also known as the pink oyster mushroom, is a commercial edible mushroom. Our earlier study on the fruiting bodies of *P. djamor* cultured at the Central Luzon State University yielded ergosterol,



Figure 2: A photo of *Pleurotus djamor*

(1) triacylglycerols, (4) and fatty acid methyl esters (Ragasa, Tan, Ting, Reyes, Brkljača, & Urban, 2016). Another study reported the protein, ash, and fat contents of *P. djamor* (Leal, Mendez, Castro, & Zapata, 2010). Qualitative analysis of *P. djamor* extract indicated the presence of anthroquinones, flavonoids, phenols, saponins, tannins, and terpenoids and the absence of cardiac glycosides and steroids. The antioxidant property of this extract was attributed to the presence of phenols and flavonoids (Sasidhara & Thirunalasundari, 2014). In another study, the *P. djamor* extract showed antibacterial properties against *Pseudomonas aeruginosa* and *Escherichia coli*. This extract contained protein, glucose, and amino acids (Dharmaraj, Kuberan, & Mahalakshmi, 2014). *P. djamor* protein extracts exhibited cytotoxic activities against human hepatoma HepG2 cells, human breast cancer MCF-7 cells, and human lung adenocarcinoma A-549 cells (*Pleurotus djamor*, 2013). Another study reported the antioxidant activity of the ethanol extract of *P. djamor*, and 13 sterols from this extract were identified by GC-MS (Guzman, Zuniga, Santafe, Torres, & Angulo, 2009).

Pleurotus eryngii

P. eryngii, commonly known as the king oyster mushroom is sold in supermarkets in

the Philippines. A number of studies have been conducted on the chemical constituents and biological activities of the king oyster mushroom. Our earlier study on the fruiting bodies of *P. eryngii* bought from a Metro Manila supermarket afforded ergosterol (1) and trilinolein (5) (Ragasa, Tan, Brkljača, & Urban, 2016). Another study reported that the ethanol extract of the king oyster mushroom yielded ergosterol peroxide, which is an inhibitor of osteoclast differentiation (Yokoyama, Bang, Shimizu, & Kondo, 2012). Activity-guided fractionations led to the isolation of an antitumor compound, ergosterol peroxide from the fruiting body of the king oyster mushroom (Lee, Park, Lee, Cho, Choi, & Gal, 2006). Furthermore, the isolation of 5 α ,9 α -epidioxy-8 α ,14 α -epoxy-(22*E*)-ergosta-6,22-dien-3 β -ol,3 β ,5 α -dihydroxyergost-7-en-6-one, 6 β -acetoxy(22*E*)-ergosta-7,22-diene-3 β ,5 α -diol, 3 β ,5 α -dihydroxy (22*E*)-ergosta-7,22-dien-6-one, ergosterol peroxide, 2 α ,5 α ,9 α -epidioxy-(22*E*)-ergosta-7,22-diene-3 β ,6 β -diol, 5 α ,9 α -epidioxy-3 β -hydroxy-(22*E*)-ergosta-7,22-dien-6-one, and 3 β ,5 α ,9 α -trihydroxy-(22*E*)-ergosta-7,22-dien-6-one from the king oyster mushroom have been reported (Yaoita, Yoshihara, Kakuda, Machida, & Kikuchi, 2002). The king oyster mushroom also yielded pleurone, ergosterol, (24*E*)-3 β -hydroxycucurbita-5,24-diene-26-oic acid, and nicotinic acid (Lee, Ryoo, Kwon, Ahn, & Yoo, 2011).



Figure 3: A photo of *Pleurotus eryngii*

Flammulina velutipes



Figure 4: A photo of *Flammulina velutipes*

F. velutipes, also known as the Enoki mushroom, is sold in supermarkets in the Philippines. Several studies were conducted on the chemical constituents of this mushroom. Our earlier study on the fruiting bodies of *F. velutipes* bought from a Metro Manila supermarket afforded ergosterol (1) and triacylglycerols (4) (Ragasa, Tan, Brkljača, & Urban, 2016). Another study reported that D-arabinitol, oleic acid, linoleic acid, ergosta-5,7,22-trien-3 β -ol, 5 α ,8 α -epidioxy-ergosta-6,22-dien-3 β -ol, 3 β ,5 α ,9 α -trihydroxy-ergosta-7,22-dien-6-one, 5-hydroxymethyl-2-(1-methylethenyl)-1-cyclohexanol, 1,3-dilinolein, and hemisceramide were isolated from Enoki mushroom (Cai, Liu, Chen, Liao, & Zou, 2013). Moreover, 5 α ,8 α -epidioxy-(22*E*,24*R*)ergost-6,22-dien-3 β -ol, ergosta-4,6,8(14), 22-tetraen-3-one, sterpuric acid, mannitol, and ribitol were obtained from this mushroom (Kang & Chen, 2005). In another study, *F. velutipes* sterols, which mainly consisted of ergosterol, 22,23-dihydroergosterol, and ergost-8(14)-ene-3 β -ol, were reported to exhibit cytotoxicity against U251 cells (Yi, Sun, Tong, Cao, Feng, Firemping, Jiang, Xu, & Yu, 2013).

Lentinula edodes



Figure 5: A photo of *Lentinula edodes*

L. edodes, also known as the shiitake mushroom, is native to East Asia (Cassileth, 2011). It is commercially cultivated for food and health benefits. The shiitake mushroom is used for the treatment of depressed immune function, cancer, allergies, infection, flu, colds, inflammation, heart disease, hyperlipidemia, hypertension, infectious disease, diabetes, and hepatitis and regulating urinary inconsistencies. It is the source of several pharmacological preparations, containing lentinan, eritadenine, shiitake mushroom mycelium, and culture media extracts (Bisen, Baghel, Sanodiya, Thakur, & Prasad, 2010). A polysaccharide, lentinan from *L. edodes*, exhibited anticancer effects in colon cancer cells (Ng & Yap, 2002) and suppressed cytochrome P450 1A enzymes which metabolize procarcinogens to active forms (Okamoto, Kodoi, & Nonaka, 2004). A protein, lentin from shiitake, exhibited antifungal properties, inhibited proliferation of leukemic cells, and suppressed the activity of HIV-1 reverse transcriptase (Ngai & Ng, 2003). Studies of shiitake extracts

showed antiproliferative (Israilides, Kletsas, & Arapoglou, 2008), immunostimulatory (Israilides, Kletsas, & Arapoglou, 2008), hepatoprotective (Akamatsu, Watanabe, & Tamesada, 2004), antimutagenic (de Lima, Delmanto, & Sugui, 2001), and anticaries (Shouji, Takada, Fukushima, & Hirasawa, 2000) effects in mice. Furthermore, the polysaccharide fractions from *L. edodes* exhibited antitumor activities against Sarcoma 180 (S-180) and human colorectal cancer cell lines (HT-29 and HCT-116) *in vitro* (Zheng, Hao, Nan, Jeff, Zhou, & Gao, 2015).

Our earlier study on the fruiting bodies of *L. edodes* bought from Mushroom Burger in Tagaytay afforded ergosterol (1) and trilinolein (5) (Resurreccion, Shen, & Ragasa, 2016). A powder formulation of *L. edodes* which contained proteins, carbohydrates, unsaturated fatty acids, tocopherols and phenolic compounds showed high antioxidant activity (Carneiro, Ferreira, Dueñas, Barros, da Silva, Gomes, & Santos-Buelg, 2013). Another study reported that shiitake mushroom contains polysaccharides, terpenoids, sterols and lipids which are effective in treating various tumors and infections, among others (Wang & Zhang, 2009). The ethanolic extract of shiitake mushroom yielded ergosterol, ergosterol peroxide, (22*E*)-ergosta-5,7,9(11),22-tetraen-3 β -ol, (22*E*)-ergosta-7,9(11),22-trien-3 β -ol, (22*E*)-ergosta-6,8,22-trien-3 β -ol, (22*E*)-norerghosta-5,7,9,22-tetraen-3 β -ol, 3 β ,5 α -dihydroxy-(22*E*)-ergosta-7,22-dien-6-one, (22*E*)-ergosta-4,6,8(14), 22-tetraen-3-one and (22*E*)-ergosta-6,22-diene-3,5 α ,8 α -triol (Rivera, Benavides, & Rios-Motta, 2009). The lipids of the fruiting bodies of *L. edodes* contain high levels of C16:0 and C16:1 fatty acids, high monoglyceride and free fatty acid content and a low triglyceride level (Nikitina, Tsivileva, Pankratov, & Bychkov, 2007). A review on the nutritional compounds and pharmacological properties of *L. edodes* has been provided (Finimundy, Dillon, Henriques, & Ely, 2014).

Agaricus bisporus



Figure 6: A photo of *Agaricus bisporus*

The common edible button mushroom, *A. bisporus* has two strains – white and brown. The white button mushroom is the more common strain sold in supermarkets, while the brown strain is marketed as “crimini” and “portabello” mushrooms (Kuo, 2004)

There are many studies on the biological activities and chemical constituents of *A. bisporus*. White button mushroom lowers blood glucose and cholesterol levels (Jeong, Jeong, Yang, Islam, Koyyalamudi, Pang, Cho, & Song, 2010), while the polysaccharide of brown button mushroom possessed strong immunostimulatory and anti-tumor bioactivity (Zhang, Ma, Fang, & Wang, 2014). Furthermore, the white button mushroom is protective against hepatic steatosis and nonalcoholic fatty liver disease (Kanaya, Kubo, Liu, Chu, Wang, & Chen, 2011). The exopolysaccharides from *A. bisporus* exhibited antioxidant (Ghahremani-Majd & Dashti, 2015); Mao, Mao, & Meng, 2013) and anti-diabetic properties (Ndungutse, Mereddy, & Sultanbawa, 2015), while the extracts showed antibacterial property (Çaglarırmak, 2009). Our earlier study on the fruiting bodies of *A. bisporus* bought from a Metro Manila supermarket yielded ergosterol, (1) linoleic acid (3) trilinolein, (5) and brassicasterol, (Ragasa, Reyes, Tan, Brkljača, & Urban, 2016).

In another study, ergosterol was isolated in both white and brown button mushrooms where its concentration was higher in early growth stages and accumulated more in the caps after maturation (Asic, Besic, Muhovic, Dogan, & Turan, 2015). The button mushroom was also reported to contain β -glucosidase (Asic, Besic, Muhovic, Dogan, & Turan, 2015), phenolics, ergothioneine and minerals (Ndungutse, Mereddy, & Sultanbawa, 2015). Furthermore, the volatile components of the button mushroom were found to be 18- or 16-carbon compounds, such as octadecanoic acid, hexadecanoic acid derivatives, and other volatiles such as dl-limonene, n-nonane, benzendicarboxylic acid, and cis-linoleic acid esters (Çaglarırmak, 2009). Another study reported that the button mushroom contained the fatty acids, linoleic, palmitic, and stearic acids (Shao, Hernandez, Kramer, Rinker, & Tsao, 2010), while the most abundant vitamins are niacin and riboflavin and the minor vitamins are vitamin B1, vitamin B3, L-ascorbic acid and α -tocopherol (Bernas & Jaworska, 2016).

Auricularia auricula-judae



Figure 7: A photo of *Auricularia auricula-judae*

A. auricula-judae Schrot., also known as Judas's ear and locally known as taingan-daga

is an edible saprophytic fungus, growing in tree stumps in damp moist forests throughout the Philippines (Stuart Jr., 2015). A number of studies have been conducted on the medicinal properties of *A. auricula-judae*. The dichloromethane extract of Judas's ear inhibited lipopolysaccharide (LPS)-induced nitric oxide (NO) production significantly in a dose-dependent manner in the concentration $\geq 10 \mu\text{g/ml}$ ($p < 0.05$) (Damte, Reza, Lee, Jo, & Park, 2011). The extract also markedly reduced the expressions of inflammatory cytokines (IL-6, TNF- α and IL-1 β) mRNA in LPS-treated murine RAW 264.7 macrophages (Damte, Reza, Lee, Jo, & Park, 2011). The polysaccharide extract of *A. auricula-judae* exhibited hypoglycemic (Yuan, He, Cui, & Takeuchi, 1998), hypocholesteremic (Chen, Luo, Li, Guo, Li, Su, & Xiao, 2008), anticomplement (Jeong, Cho, Yang, Gu, Jang, Huh, & Song, 2004), antioxidant (Quel Kho, Vikineswary, Abdullah, Kuppusamy, & Oh, 2009; Fan, Zhang, Yu, & Ma, 2007; Luo, Xiao, Wang, Li, & Ji, 2011), antitumor (Misaki, Kakuta, Sasaki, Tanaka, & Miyaji, 1981; Reza, Jo, & Park, 2012); Reza, Hossain, Lee, Yohannes, Damte, Rhee, & Jo, 2014), hypolipidemic and anti-inflammatory (Jeong, Yang, Jeong, Kim, Jeong, Kim, Mehta, & Song, 2007), antithrombotic (Qiao, Hu, Hui, & Chin, 2009), and wound healing (Khamlue, Naksupan, Ounaron, & Saelim, 2012) properties.

Our earlier study on the fruiting bodies of *A. auricula-judae* collected from Mt. Makiling afforded a major sterol, ergosterol peroxide (**2**) (Ragasa, Tan, De Castro, & Shen, 2016). A recent study on Judas's ear identified thirty-six volatile compounds and ergosterin andergost-5,8-dien-3 β -ol from the dichloromethane extract, while the diethyl ether extract afforded twenty-six volatile compounds, ergosterin and linoleic acid (Sun, Zhang, Ding, Zhao, Lei, Liu, & Huang, 2015).

Coprinopsis lagopus

Figure 8: A photo of *Coprinopsis lagopus*

C. lagopus Fries is commonly known as harefoot mushroom due to its vague resemblance to the paw of a white rabbit (Crosier, Patrick, Heit, & McSwain, 1949). *Coprinus lagopus* is the name of this mushroom until 2001 when it was named *Coprinopsis lagopus* (Fries) Redhead, Vilgalys, & Moncalvo (*Coprinopsis lagopus*, 2016). The harefoot mushroom is widely distributed throughout the world and grows on wood chips, compost heaps and vegetable refuse. It is a gray to beige inedible mushroom that grows up to less than 5 cm (*Coprinopsis lagopus* mushroom, 2016). Our earlier study on the fruiting bodies of *C. lagopus* collected from Mt. Makiling yielded ergosterol peroxide, (2) linoleic acid, (3) triacylglycerols, (4) and 3 β -linoleoyloxyergosta-7,22-diene (Ragasa, Tan, De Castro, Perez, & Shen, 2016). Another study reported the isolation of the quinones, lagopodin A and lagopodin B from the harefoot mushroom (Progress in the Chemistry of Organic Natural Products, 2012). The isolation of ergosterol and 22-dihydroergosterol from the carpophores of this mushroom were also reported (Defago, Fazeli, & Schweizer, 1971).

Phellinus gilvus

Figure 9: A photo of *Phellinus gilvus*

P. gilvus is a plant pathogenic fungus having a wide host range worldwide (Gautam, 2014). Several studies have been conducted on the chemical constituents and biological activities of *P. gilvus*. Our earlier study on the fruiting bodies of *P. gilvus* collected from Mt. Makiling yielded ergosterol peroxide (2) and triacylglycerols (4) (Ragasa, Tan, De Castro, & van Altena, 2016). Another study reported the isolation of the steroids gilvsins A–D, 24-methylenelanost-8-ene-3 β ,22-diol and 5 α -ergosta-7,22-diene-3-one from this mushroom (Liu, Tsai, Chang, Chou, & Lin, 2009). The organic extract of the fruiting bodies of *P. gilvus* exhibited biphasic vasodilator activity on rat aorta with endothelium. The major constituents of this extract were trametenolic acid B and eburicoic acid which exhibited a moderate vasorelaxant effect on rat aorta (Hosoe, Iizuka, Chiba, Itabashi, Morita, Ishizaki, & Kawai, 2006). The polysaccharides isolated from *P. gilvus* significantly inhibited melanoma growth in mice by significantly increasing the melanoma apoptosis rate (Bae, Jang, Yim, & Jin, 2005); enhanced wound repair in diabetic impaired healing (Bae, Jang, & Jin, 2005); and inhibited BaP-induced forestomach carcinogenesis in mice by down-regulating mutant p53 expression (Bae, Jang, Yim, Park, & Jin, 2005). The extract of this mushroom may be useful in preventing acute

pulmonary inflammation in human diseases (Jang, Kim, Bae, Rhee, Jang, Song, Kwon, & Park, 2004).

ANTICANCER STEROLS AND LIPIDS

The compounds which we isolated from local collections of the seven edible and two inedible Philippine mushrooms were sterols and lipids with reported anticancer properties. Ergosterol (**1**) was isolated from *Pleurotus florida*, *Pleurotus djamor*, *Pleurotus eryngii*,

Lentinula edodes, *Agaricus bisporus*, and *Flammulina velutipes*. Ergosterol peroxide (**2**) was obtained from *P. florida*, *Auricularia auricula-judae*, *Coprinopsis lagopus*, and *Phellinus gilvus*. The omega-6 fatty acid, linoleic acid (**3**) was afforded by *P. florida* and *A. bisporus*. Triacylglycerols (**4**) were provided by *P. djamor*, *F. velutipes*, *C. lagopus*, and *P. gilvus*, while trilinolein (**5**) was isolated from *P. eryngii*, *L. edodes*, and *A. bisporus*. The chemical structures of **1-5** are presented in Fig. 10.

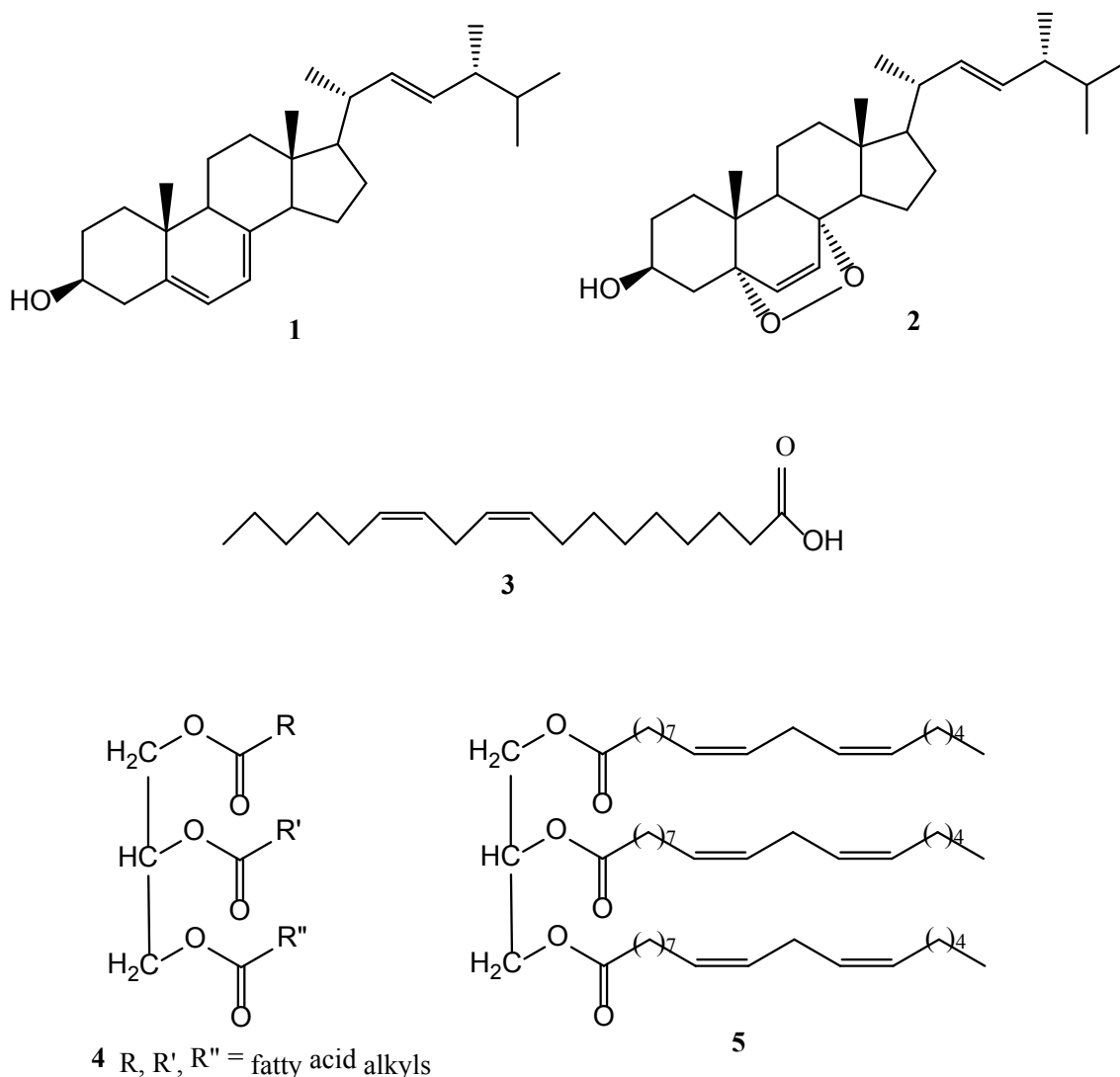


Figure 10: Chemical structures of ergosterol (**1**), ergosterol peroxide (**2**), linoleic acid (**3**), triacylglycerols (**4**) and trilinolein (**5**) isolated from Philippine mushrooms.

ERGOSTEROL (1)

Several studies were reported on the biological activities of ergosterol (1). A study reported that **1** provided significant protection against the promotion of bladder tumor induced by many types of promoters in the environment (Yazawa, Yokota, & Sugiyama, 2000). Moreover, the ergosterol content of brown and white button mushrooms correlated with their antioxidant activities (Shao, Hernandez, Kramer, Rinker, & Tsao, 2010). In another study, **1** was reported to have the capability to inhibit lipid peroxidation (Dissanayake, Abeytunga, Vasudewa, & Ratnasooriya, 2009).

ERGOSTEROL PEROXIDE (2)

Many studies have been reported on the biological activities of ergosterol peroxide (2). Compound **2** showed strong trypanocidal activity on the intracellular form of *T. cruzi* (Ramos-Ligonio, López-Monteon, & Trigos, 2012); suppressed inflammatory response in RAW 264.7 macrophages and growth of HT29 colon adenocarcinoma cells (Kobori, Yoshida, Ohnishi-Kameyama, & Shinmoto, 2007); exhibited anti-tumor activity in multiple myeloma U266 cells, Walker carcinosarcoma, human mammary adenocarcinoma, human gastric tumor (SNU-1), human hepatoma (SUN-354), human colorectal tumor (SUN-C4), and murine sarcoma-180 cell lines (Rhee, Jeong, Lee, & Koh, 2012) and Hep3B (Takei, Yoshida, Ohnishi-Kameyama, & Kobori, 2005); showed an inhibitory effect on androgen-sensitive (LNCaP) and androgen-insensitive (DU-145) human prostate cancer cells (Chen, Kuo, Chiang, Lo, & Sheen, 2009); suppressed cell growth and STAT1 mediated inflammatory responses in HT29 cells (Russo, Cardile, Piovano, Caggia, & Espinoza, 2010); inhibited the growth and induced apoptosis of HL60 human leukaemia cells, inhibited TPA induced

inflammation and tumor promotion in mice and suppressed proliferation of mouse and human lymphocytes stimulated with mitogens (Leon, Brouard, Torres, Quintana, & Rivera, 2008); displayed potent activity against the cancer cell lines MDA-MB435, HCT-8 and SF-295 (Liu, Wang, Shao, Wei, Wang, Sun, Zheng, & Guan, 2009) and induced death of miR-378 cell (Wu, Xie, Deng, Li, & Yang, 2012); exhibited significant inhibitory activities against leishmaniasis, *Mycobacterium tuberculosis* H37Rv and *M. avium* (Correa, Cardona, Quiaones, Torres, & Franco, 2006); inhibited the hemolytic activity of human serum against erythrocytes (Seo, Hung, Na, Jung, & Kim, 2009); blocked MyD88 and VCAM-1 expression, and cytokine production which indicated that it may play an important role in the immunomodulatory activity of GF (Wu, Lu, Lai, & Ng, 2013); and possessed marked activity against PGE2 release and down-regulated mRNA expressions of iNOS and COX2 (Tewtrakul, Tansakul, Daengrot, Ponglimanont, & Karalai, 2010). Furthermore, **2** suppressed LPS-induced DNA binding activity of NF- κ B and C/EBP β ; inhibited the phosphorylation of p38, JNK and ERK MAPKs; down-regulated the expression of low density lipoprotein receptor in RAW264.7 cells; induced the expression of oxidative stress-inducible genes, and the cyclin-dependent kinase inhibitor; and suppressed STAT1 and interferon-inducible genes (Rugutt, & Rugutt, 2012).

LINOLEIC ACID (3)

Linoleic acid (3) belongs to the omega-6 fatty acids. Fatty acid **3** was reported to be a strong anticarcinogen in a number of animal models; reduced risk of colon and breast cancer (Maeda, Sumiyoshi, & Kimura, 2004); and lowered cardiovascular disease risk and inflammations (Chan, Thomas, & Tomlinson, 2002). Furthermore, linolenic acid and **3**

inhibited parasites growth by 70% and 64% respectively, against *P. berghei* using the 4-day suppressive test. The two compounds when used in combination inhibited the parasites by 96% on day 4 of treatment (Whelan, 2008).

TRIACYLGLYCEROLS (4)

Triacylglycerols (4) have been reported to significantly inhibit the tumor growth in the spleen of mice with intrasplenically implanted Lewis lung carcinoma (Melariri, Campbell, Etusim, & Smith, 2012). Lipid 4 exhibited antimicrobial activity against *S. aureus*, *P. aeruginosa*, *B. subtilis*, *C. albicans*, and *T. mentagrophytes* (Ragasa, Lorena, Mandia, Raga, & Shen, 2013).

TRILINOLEIN (5)

Trilinolein (5) exhibited protective effects against cardiovascular disorders, lowered cardiovascular disease risk and inflammations (Chan, Thomas, & Tomlinson 2002), inhibited ischemia-induced ventricular arrhythmias and showed anti-oxidant effect (Chan, Kao, & Tomilson, 2005). Lipid 5 was also reported to inhibit the growth of human non-small cell lung carcinoma A549 and induce apoptosis in a dose- and time- dependent manner (Chou, Huang, Pan, Chien, Chen, Wu, Sheu, & Cheng, 2011).

DISCUSSION

Our studies on the chemical constituents of the dichloromethane extracts of local collections of seven edible and two inedible Philippine mushrooms yielded sterols (1-2) and lipids (3-5) with reported anticancer activities. Among these compounds, ergosterol peroxide (2) was reported as the most active. It is interesting to note that *A. auricula-judae* Schrot., also known as Judas's ear and locally known as taingan-daga contains only ergosterol

peroxide (2) as its major constituent. No minor constituent was isolated from this mushroom. Furthermore, all the edible and inedible mushrooms studied contained ergosterol and/or ergosterol peroxide as their major constituents. Few minor sterols and lipids were isolated from some of the mushrooms.

Other studies reported proteins and polysaccharides as the anticancer principles of mushrooms. *P. djamor* protein extracts exhibited cytotoxic activities against human hepatoma HepG2 cell, human breast cancer MCF-7 cells, and human lung adenocarcinoma A-549 cell (*Pleurotus djamor*, 2013), while a protein from *L. edodes* inhibited proliferation of leukemic cells (Ngai & Ng, 2003). A polysaccharide of *A. bisporus* possessed strong anti-tumor bioactivity (Zhang, Ma, Fang, & Wang, 2014). A polysaccharide from *L. edodes* exhibited anticancer effects in colon cancer cells (Ng & Yap, 2002), while the polysaccharide fractions of this mushroom showed antitumor activities against Sarcoma 180 (S-180) and human colorectal cancer cell lines (HT-29 and HCT-116) *in vitro* (Zheng, Hao, Nan, Jeff, Zhou, & Gao, 2015). The polysaccharide extract of *A. auricula-judae* exhibited antitumor properties (Misaki, Kakuta, Sasaki, Tanaka, & Miyaji, 1981; Reza, Jo, & Park, 2012; Reza, Hossain, Lee, Yohannes, Damte, Rhee, & Jo, 2014), while the polysaccharides from *P. gilvus* significantly inhibited melanoma growth (Bae, Jang, Yim, & Jin, 2005) and BaP-induced stomach carcinogenesis in mice (Bae, Jang, Yim, Park, & Jin, 2005).

CONCLUSION

The reported anticancer constituents of mushrooms are divided into four classes of compounds: polysaccharides, proteins, sterols, and lipids, which are obtained using different extraction procedures due to their different polarities and characteristics. Our studies

on the dichloromethane soluble chemical constituents of Philippine mushrooms employed normal-phase column chromatography for the isolation process. Hence, only the relatively nonpolar compounds (sterols and lipids) were isolated and identified in the local studies. No other classes of secondary metabolites were isolated from the dichloromethane extracts of the fruiting bodies of the seven edible and two inedible Philippine mushrooms.

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