REVIEW ARTICLE

A C G publications

Rec. Nat. Prod. 9:4 (2015) 456-483

records of natural products

Biologically Active Terpenoids from Mushroom origin: A Review

Mehmet E. Duru* **and Gülsen Tel Çayan**

Muğla Sıtkı Koçman University, Faculty of Science, Department of Chemistry

48121 Kötekli Muğla, Türkiye

(Received December 25, 2014; Revised April 06, 2015; Accepted April 07, 2015)

Abstract: Mushrooms are very important sources of drugs for modern medicine. Phyotherapeutic efficiency of terpenes from mushrooms has been proved. Lanostane type triterpenoids having potentials for cancer disease treatments are rich source of mushrooms. Therefore, the demand of isolation of bioactive compounds from the mushroom species has been increasing due to their medicinal importance. The paper reviewed isolation and biological activities such as antibacterial, anticancer, anticandidal, anticholinesterase, anti-compliment, antileishmanial, anti-inflammatory, anti-invasive, antimalarial, antioxidant, antitubercular, antitumor, antiviral, and cytotoxic activities of terpenoids from mushroom origin in the last two decades.

Keywords: Monoterpenoids; Sesquiterpenoids; Diterpenoids; Triterpenoids; Biological Activities; Mushrooms. .

1. Introduction

Mushrooms are used by the local people as food as well as medicines, particularly in the Asian countries such as, China, Japan, Korea as well as in some part of Africa. Mushrooms have attracted increasing attention as a source of bioactive secondary metabolites for the development of nutraceuticals and drugs [1]. Mushrooms are especially used as immunomodulator and anti-tumour agents. Generally, mushrooms are thought that they are natural foods and are produced or naturally grow all over the world [2]. Up to date, polysaccharides, terpenoids, steroids, alkaloids, phenolic structured compounds indicating anticancer, antioxidant, anti-tumour, antiviral, antibacterial, anticholinesterase, antifungal, anti-inflammatory, anti-immunomodulatory activities were isolated from various mushroom species [2-10].

Terpenoids isolated from mushrooms have been associated with various pharmacological activities like anticancer [1, 11-14], antimalarial [15], anticholinesterase [8], antiviral [16], antibacterial [14, 17] and anti-inflammatory activities [18]. For example, oleanolic acid, which is the principal constituent of the triterpenoid portion of the drug, was reported for anti-inflammatory, antihyperlipidemic and antitumor effects [19].

This review presents terpenoids isolated from mushroom species, studied for their chemistry and biological activities in last two decades. Totally, 285 terpenoids (mono-, sesqui-, di-, tri-) together with their biological activities i.e. antibacterial, anticancer, anticandidal, anticholinesterase, anti-compliment, antileishmanial, anti-inflammatory, anti-invasive, antimalarial, antioxidant, antitubercular, antitumor, antiviral, and cytotoxic were investigated.

* Corresponding author: E-Mail: eminduru@mu.edu.tr; Phone: +90-252-2111494 *Fax:* +90-252-2111472

The article was published by Academy of Chemistry of Globe Publications
www.acgpubs.org/RNP © Published 06/01/2015 EISSN:1307-6167

2. Bioactive terpenoids

2.1. Monoterpenoids

Monoterpenoids (**1**-**5**) isolated from mushroom species and their activities are showed in Table 1. In a recent study by Wang *et al.* [1] five monoterpenoids (**1**−**5)** were isolated from *Pleurotus cornucopiae* mushroom fermented on rice. Compounds **1**−**5** were tested inhibitory activity against NO production in lipopolysaccharide- activated macrophage RAW 264.7 and cytotoxicity against HeLa and HepG2 cells by the MTT assay. Compounds **1**−**5** exhibited moderate inhibitory activity with IC_{50} (the half maximal inhibitory concentration) values in the range of 60−90 μM against nitric oxide production in lipopolysaccaride-activated macrophages [1].

Table 1. Bioactive Monoterpenoids and Their Activities.

Compounds	Mushrooms	Bioactivity	Ref.
1 **2** **3** **4** **5**	*P. cornucopiae*	• NO production inhibitory	[1]

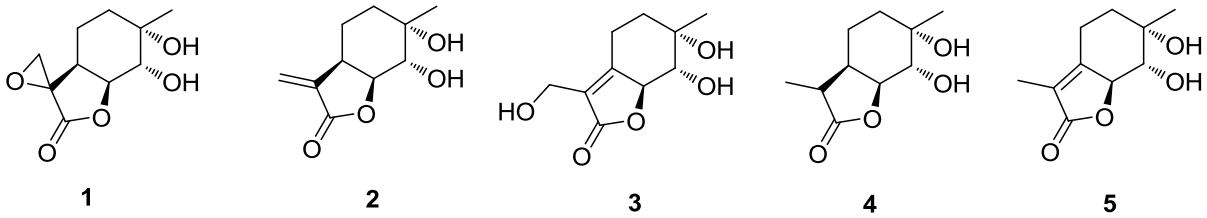


Figure 1. Chemical structure of monoterpenoids.

2.2. Sesquiterpenoids

Sequiterpenoids including aristolane, bisabolane, cuparene, drimane, fomannosane, lactarane, nordasinane, spiro, sterpurane type isolated from mushrooms have been reported. Sesquiterpenoids (**6**-**75**) isolated from mushroom species and their activities are showed in Table 2. From *Stereum hirsutum* used as folk medicine in China and Korea for the treatment of cancer, three new sesquiterpenoids (**6**-**8**) have been isolated. Compounds (**6**-**8**) were screened for their antimicrobial and antioxidant activities while compound **6** was tested for NO inhibitory activity and cytotoxicity. These sesquiterpenoids showed no antimicrobial activity and weak antioxidant activity in DPPH assay. Compound **6** showed strong NO inhibitory activity in the LPS-induced macrophage indicating 15.44±1.07 μM IC_{50} value and cytotoxicity against HepG2 and A549 cell lines with IC_{50} in the range of 10-50 μM [20].

From the fermentation broth of *Stereum hirsutum* afforded three new tricyclic sesquiterpenoids. These sesquiterpenoids identified as hirsutenols A (**9**), B (**10**) and C (**11**). Hirsutenols **9**-**11** exhibited moderate antimicrobial activity against *Escherichia coli* while none of them showed inhibitory activity against *Bacillus subtilis*, *Candida albicans*, *Staphylococcus aureus*, *Aspergillus* spp., *Salmonella typhimurium*, and *Chlorella regularis* [21].

In a recent study by Chen *et al.* [22] inonotic acid A (**12**), 3-O-formyl inonotic acid A (**13**), inonotic acid B (**14**), three new bisabolane sesquiterpenoids, and 3α,6α-hydroxycinnamolide (**15**) were isolated from *Inonotus rickii*. These compounds were investigated for their cytotoxicities against five human cell lines, namely; human myeloid leukemia HL-60, hepatocellular carcinoma SMMC-7721, lung cancer A-549, breast cancer MCF-7, and human colon cancer SW480 cells by using MTT

method. Interestingly, compound (**15**) demonstrated moderate cytotoxic activity against SW480 with IC_{50} value of 20.4 μM [22].

Pleurospiroketals A−E (**16**−**20**) and (6*S*,7*S*)-6,7-dihydroxy-3,6-dimethyl-2-isovaleroyl-4,5,6,7-tetrahydrobenzofuran (**21**) have been isolated from *Pleurotus cornucopiae* (Paulet) Rolland (Pleurotaceae). Pleurospiroketals A−E (**16**−**20**) have a unique benzannulated 5,5-spiroketal skeleton and rare natural sesquiterpenoids. Compounds **16**−**18** exhibited NO inhibitory activity indicating 6.8 μM, 12.6 μM, and 20.8 μM IC_{50} values, respectively. In addition, compounds **16**−**18** exhibited cytotoxic activity against the HeLa cancer cell line by demonstrating IC_{50} of 20.6, 32.8, and 18.8 μM, respectively [12].

Three sesquiterpenoid (**22-24**) have been isolated from *Pleurotus cornucopiae* mushroom fermented on rice. Isolated compounds (**22-24)** were tested inhibitory activity against NO production in lipopolysaccharide- activated macrophage RAW 264.7 and cytotoxicity against HeLa and HepG2 cells by the MTT assay. Compounds **23** and **24** exhibited moderate inhibitory activity with IC_{50} values of 76.5, 72.4 μM against nitric oxide production in lipopolysaccaride-activated macrophages. Compounds **22** and **23** showed weak cytotoxicity against HepG2 (IC_{50}: 76.8 and 68.6 μM) and HeLa cells (IC_{50}: 70.6 and 36.0 μM) [1].

Anthracophyllic acid (**25**), a novel spiro-sesquiterpene, and anthracophyllone (**26**), a new aristolane sesquiterpene have been isolated from *Anthracophyllum* sp. BCC18695 [23]. The compounds were screened for their antibacterial property against *Bacillus cereus*, antimalarial activity against *Plasmodium falciparum* K1 strain, and cytotoxicity against MCF-7, NCI-H187, KB and Vero cells. Biological activity results showed that Anthracophyllic acid (**25**) were inactive against all cell lines at the tested maximum concentrations. Anthracophyllone (**26**) showed moderate cytotoxicity against MCF-7, NCI-H187, KB and Vero cells with IC_{50} values of 32.97, 15.17, 18.02 and 18.06 μM, respectively [23].

Flammulina velutipes cultivated on cooked rice have yielded enokipodins E-J (**27-32**), six new cuparene sesquiterpenes, and sterpurols A (**33**) and B (**34**), two new sterpurane sesquiterpenes, together with four known sesquiterpenes, 2,5-cuparadiene-1,4-dione (**35**), enokipodins B (**36**) and D (**37**), and sterpuric acid (**38**). Bioactivity results showed that compounds **32**, **35-37** indicated both moderate cytotoxicity against HepG2, MCF-7, SGC7901, and A549 with the IC_{50} of in the range of 20-100 μM and antioxidant activity in DPPH scavenging assay with IC_{50} of 78.6 ± 8.2, 80.7 ± 5.2, 154.2 ± 6.2, and 116.5 ± 4.5 μM, respectively. However, the other compounds showed no cytotoxic and antioxidant activities at 200 μM concentration. As for, antibacterial and antifungal assays, compounds **28**, **29** and **31** showed weak antifungal activity against *A. fumigatus* with IC_{50} values of 229.1 ± 3.6, 233.4 ± 3.8, and 235.1 ± 4.2 μM, respectively and compound **32**, **35-37** also exhibited weak antibacterial activity against *B. subtilis* with IC_{50} values of 164.3 ± 6.2, 151.2 ± 4.5, 140.5 ± 6.2, 167.6 ± 7.1, and 154.6 ± 6.8 μM, respectively. The other compounds exhibited no activity against *S. aureus* (MRSA), *E. coli*, *P. aeruginosa* and *C. albicans* SC5314 [24].

The same group studied same mushroom species *Flammulina velutipes* and reported that this mushroom possessed flammulinol A (**39**), flammulinolides A-G (**40-46**). Compounds **40-46** were screened for their cytotoxicity against three tumor cell lines namely; HepG2, HeLa, and KB. Flammulinolides A (**40**), B (**41**), and F (**45**) exhibited strong cytotoxicity against KB cell line showing IC_{50} of 3.9, 3.6, and 4.7 mM, respectively. Compound **40** exhibited moderate cytotoxicity (IC_{50}: 34.7 mM) against HepG2 cell line. Flammulinolide C (**42**) indicated strong cytotoxicity (IC_{50}: 3.0 mM) against Hela cell line and also moderate cytotoxicity (IC_{50} of 12.4 mM) against KB cell line while compound **43** exhibited weak cytotoxicity against all three cell lines. Compounds **44** and **46** showed moderate cytotoxicity against (IC_{50}: 25.8 and 59.5 mM, respectively) Hela cell line. Compounds **39-46** were also tested for their antibacterial activity against meticillin-resistant *Staphylococcus aureus* and *Bacillus subtilis*. All tested compounds showed weak antibacterial activity with IC_{50} value larger than 250 mM [25].

Enokipodins C (**47**) and D (**37**), two new cuparene type sesquiterpenes, together with enokipodins A (**48**) and B (**36**) have been isolated from *Flammulina velutipes*. All isolated compounds were investigated for their antimicrobial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas fluorescens*. All isolated compounds (**36**, **37**, **47**, **48**) were inactive

against gram negative bacteria *Escherichia coli* and *Pseudomonas fluorescens* but were active against gram positive bacteria *Bacillus subtilis* and *Staphylococcus aureus* [6].

From the culture broth of the mushroom *Agrocybe salicacola*, two novel fomannosane-type sesquiterpenoids, agrocybins H (**49**) and I (**50**), along with a known compound illudosin (**51**) have been isolated. Compounds **49**-**51** were screened for their cytotoxicity against MCF-7, HL-60, A-549, SMMC-7712, and SW480 human cancer cell lines by using MTT method. Compounds **49**-**51** showed no cytotoxicity at 40 μM concentrations [26].

Nambinones A-C (**52**-**54**) and 1-epi-nambinone B (**55**), nambinone D (**56**) were isolated from *Neonothopanus nambi* luminescent mushroom. Compounds **54** exhibited cytotoxicity (IC_{50}: 16.42 mM) against NCI-H187 cell line [27].

The ten sesquiterpenoids **57**-**66**, including nordosinanes (**58** and **59**) and aristolanes type sesquiterpenoids (**57**, **60**-**66**) isolated from extract of *Russula lepida* and *Russula amarissima* [28]. The names of the isolated compounds are aristola-1(10), 8-dien (**57**), rulepidiene B (**58**), rulepidanol (**59**), (+)-aristolone (**60**), rulepidol (**61**), rulepidadiol B (**62**), rulepidadiol C (**63**), rulepidatriol B (**64**), rulepidatriol C (**65**), rulepidatriol B (**66**). Compounds **62** and **63** were investigated for their inhibitory activity on the proliferation of WISH, CAKI 1 and A549 cells [28].

From the organic extract of fruiting bodies of the *Strobilurus ohshimae* edible mushroom, four sesquiterpenoids; namely, strobilols A (**67**), B (**68**), C (**69**) and D (**70**) have been isolated. Compounds were tested for their antimicrobial activity against *Staphylococcus aureus* NBRC 13276, *Candida albicans*, and *Pseudomonas aeruginosa*. Strobilols A-D (**67**-**70**) exhibited no antimicrobial activity. Strobilol A (**67**) only showed moderate activity against brine shrimp *Artemia salina* [29].

1,2-dehydrolactarolide A (**71**), a new lactarane sesquiterpene, was obtained from *Lactarius vellereus* together with lactarorufin A (**72**), 3-O-ethyl-lactarolide (**73**) and 3-O-ethyllactarolide B (**74**). Additionally lactarorufin A (**72**) and lactarolide A (**75**), two lactarane sesquiterpenes, were isolated from *L. subpiperatus*. Compound **72**-**75** exhibited no promotional activity against radicle elongation in lettuce seedlings, while compound **71** showed moderate promotional activities of 119%, 152% and 162% at 3.6 μM, 3.6 x 10^1 μM, 3.6 x 10^2 μM, respectively [30].

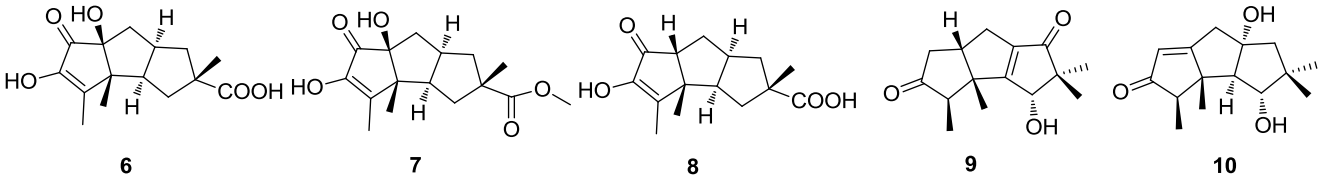
Table 2. Bioactive Sesquiterpenoids and Their Activities.

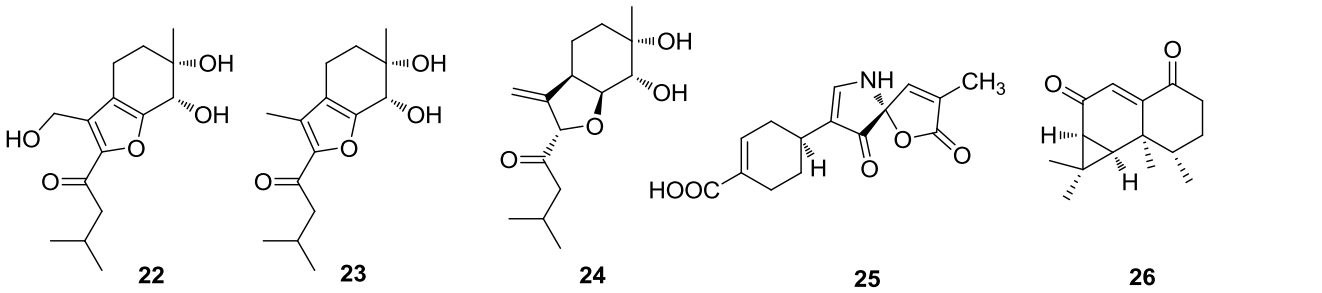
Compounds	Mushrooms	Bioactivity	Ref.
6	*S. hirsutum*	• Antioxidant • Antimicrobial^{NA}	[20]
7	*S. hirsutum*	• Antioxidant • Antimicrobial^{NA} • NO production inhibitory • Cytotoxic	[20]
8	*S. hirsutum*	• Antioxidant • Antimicrobial^{NA}	[20]
Hirsutenol A (**9**) Hirsutenol B (**10**) Hirsutenol C (**11**)	*S. hirsutum*	• Antimicrobial against *Escherichia coli*	[21]
Inonotic acid A (**12**) 3-*O*-formyl inonotic acid A (**13**) Inonotic acid A (**14**) 3*α*,6*α*-Hydroxycinnamolide (**15**)	*I. rickii*	• Cytotoxic	[22]
Pleurospiroketal A (**16**) Pleurospiroketal B (**17**) Pleurospiroketal C (**18**)	*P. cornucopiae*	• NO production inhibitory • Cytotoxic	[12]
Pleurospiroketal D (**19**) Pleurospiroketal E (**20**) (6S,7S)-6,7-dihydroxy-3,6-dimethyl-2-isovaleroyl-4,5,6,7-tetrahydrobenzofuran **(21)**	*P. cornucopiae*	• NO production inhibitory ^{NT} • Cytotoxic ^{NT}	[12]

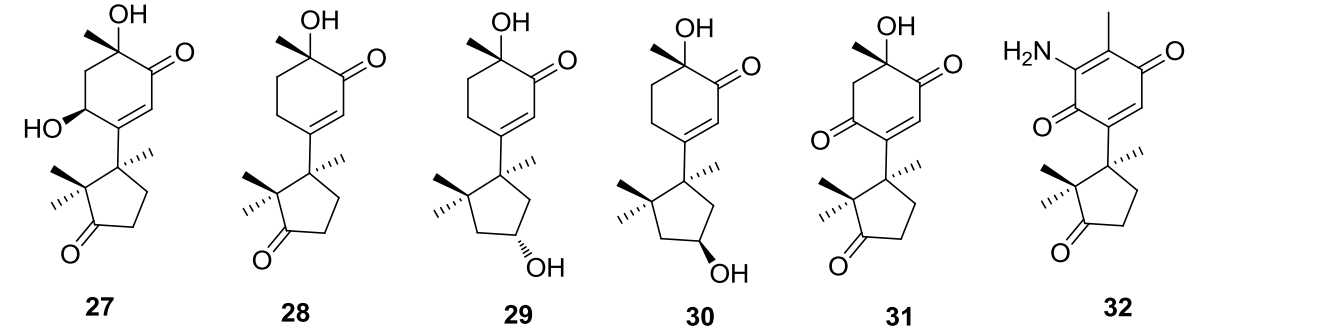
22	*P. cornucopiae*	• NO production inhibitory • Cytotoxic	[1]
23	*P. cornucopiae*	• NO production inhibitory • Cytotoxic	[1]
24	*P. cornucopiae*	• NO production inhibitory • Cytotoxic [NA]	[1]
Anthracophyllic acid (**25**) Anthracophyllone (**26**)	Anthracophyllum sp. BCC18695	• Antimalarial • Antibacterial • Cytotoxic	[23]
Enokipodin E (**27**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA]	[24]
Enokipodin F (**28**) Enokipodin G (**29**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA] • Antifungal	[24]
Enokipodin H (**30**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA]	[24]
Enokipodin I (**31**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA] • Antifungal	[24]
Enokipodin J (**32**)	*F. velutipes*	• Cytotoxic • Antioxidant • Antibacterial	[24]
Sterpurol A (**33**) Sterpurol B (**34**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA]	[24]
2,5-Cuparadiene-1,4-dione (**35**)	*F. velutipes*	• Cytotoxic • Antioxidant • Antibacterial	[24]
Enokipodin B (**36**) Enokipodin D (**37**)	*F. velutipes*	• Antimicrobial • Cytotoxic • Antioxidant • Antibacterial	[6] [24]
Sterpuric acid (**38**)	*F. velutipes*	• Cytotoxic [NA] • Antioxidant [NA] • Antibacterial [NA]	[24]
Flammulinol A (**39**)	*F. velutipes*	• Antibacterial	[25]
Flammulinolide A (**40**) Flammulinolide B (**41**) Flammulinolide C (**42**) Flammulinolide D (**43**) Flammulinolide E (**44**)	*F. velutipes*	• Cytotoxic • Antibacterial	[25]
Flammulinolide F (**45**) Flammulinolide G (**46**)	*F. velutipes*	• Cytotoxic • Antibacterial	[25]
Enokipodin C (**47**) Enokipodin A (**48**)	*F. velutipes*	• Antimicrobial	[6]
Agrocybin H (**49**) Agrocybin I (**50**) Illudosin (**51**)	*A. salicacola*	• Cytotoxic	[26]
Nambinone A (**52**)	*N. nambi*	• Antimalarial • Antitubercular • Cytotoxic	[27]
Nambinone B (**53**)	*N. nambi*	• Antitubercular • Cytotoxic	[27]
Nambinone C (**54**) 1-*epi*-nambinone B (**55**)	*N. nambi*	• Antimalarial • Antitubercular • Cytotoxic	[27] [27]

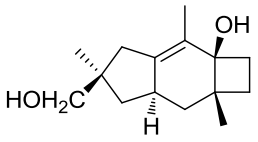
Nambinone D (**56**)	*N. nambi*	• Antitubercular • Cytotoxic	[27]
Aristola-1(10), 8-dien (**57**) Rulepidiene B (**58**) Rulepidanol (**59**) (+)-Aristolone (**60**) Rulepidol (**61**)	*Russula lepida* and *R. amarissima*	NT	[28]
Rulepidadiol B (**62**) Rulepidadiol C (**63**)	*Russula lepida* and *R. amarissima*	• Cytotoxic	[28]
Rulepidatriol B (**64**) Rulepidatriol C (**65**) Rulepidatriol B (**66**)	*Russula lepida* and *R. amarissima*	NT	[28]
Strobilol A (**67**)	*S. ohshimae*	• Brine shrimp toxicity • Antimicrobial	[29]
Strobilol B (**68**) Strobilol C (**69**) Strobilol D (**70**)	*S. ohshimae*	• Antimicrobial	[29]
1,2-Dehydrolactarolide A (**71**)	*L. vellereus*	• Promotional	[30]
Lactarorufin A (**72**) 3-O-ethyl-lactarolide (**73**) 3-O-ethyllactarolide B (**74**)	*L. vellereus*	• Promotional NA	[30]
Lactarolide A (**75**)	*L. subpiperatus*	• Promotional NA	[30]

NA: not active; NT: not tested

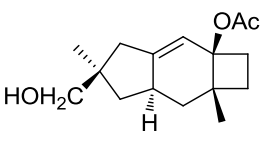




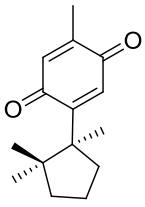




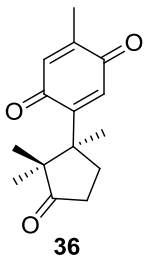
33



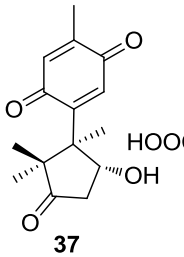
34



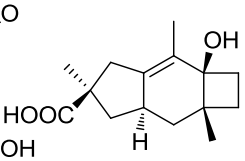
35



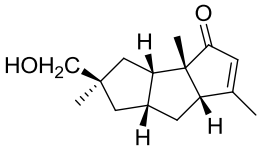
36



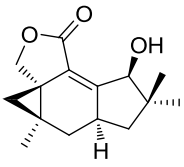
37



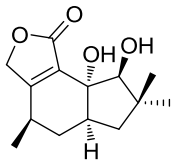
38



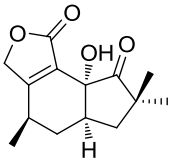
39



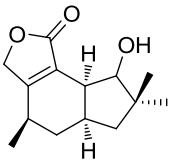
40



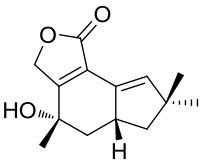
41



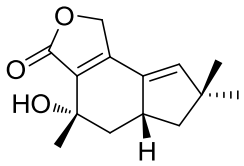
42



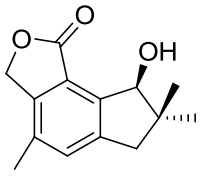
43



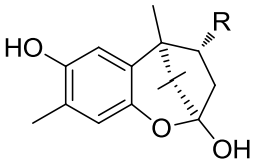
44



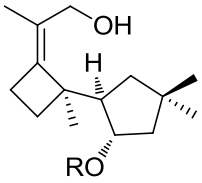
45



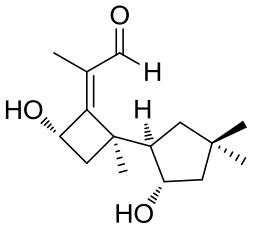
46



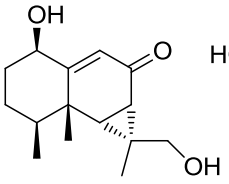
47 R= OH
48 R= H



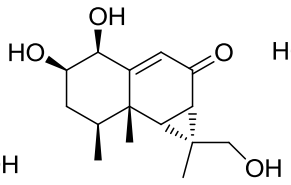
49 R= H
50 R= CHO



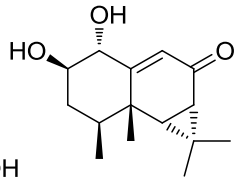
51



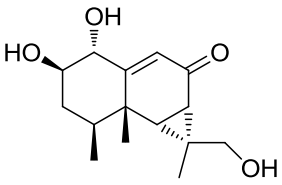
52



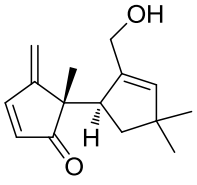
53



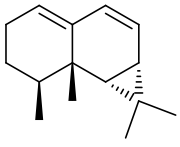
54



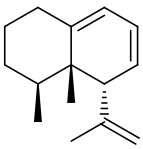
55



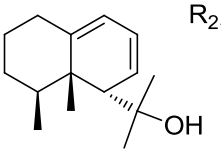
56



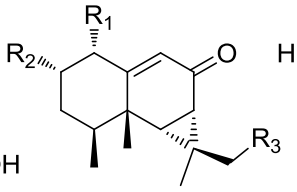
57



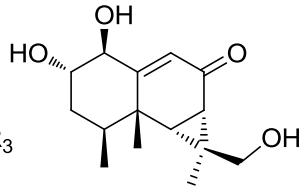
58



59



60 R_1 = H; R_2 = H; R_3 = H
61 R_1 = H; R_2 = OH; R_3 = H
62 R_1 = OH; R_2 = OH; R_3 = H
63 R_1 = H; R_2 = OH; R_3 = OH
64 R_1 = OH; R_2 = OH; R_3 = OH



65

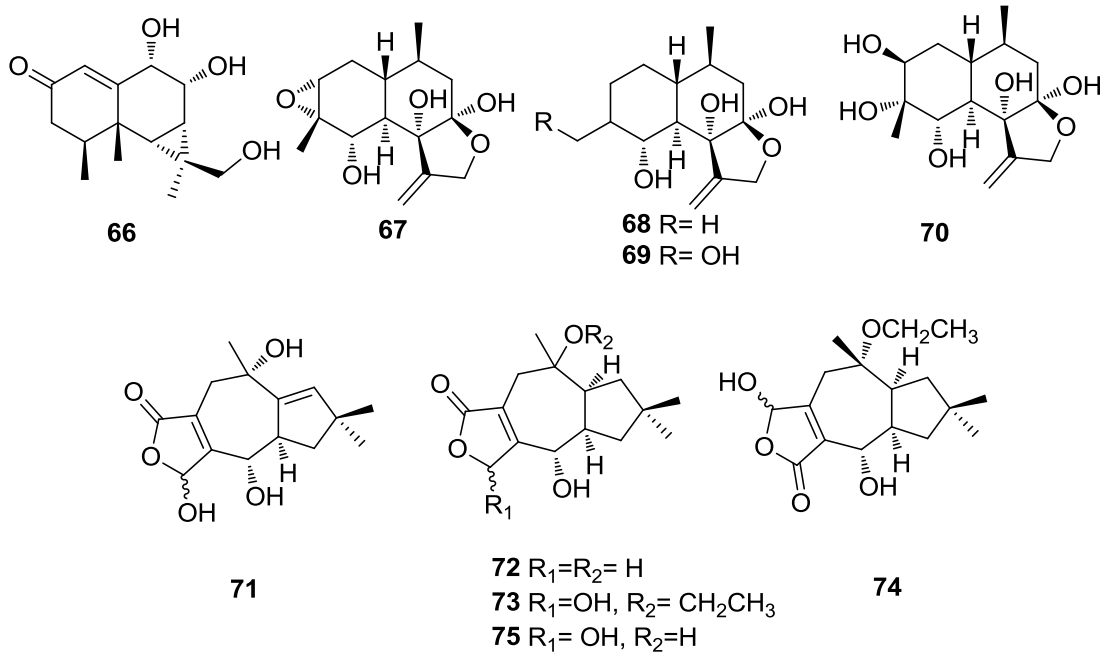


Figure 2. Chemical structure of sesquiterpenoids.

2.3. Diterpenoids

Diterpenoids (**76-119**) isolated from mushroom species and their activities are showed in Table 3. From the medicinal fungus *Cyathus africanus* cyathins D–H (**76**–**80**), neosarcodonin O (**81**), cyathatriol (**82**), and 11-*O*-acetylcyathatriol (**83**) were isolated [7]. The isolated compounds (**81**, **76-83**) were screened for their NO production inhibitory activities from lipopolysaccharide-activated macrophage RAW 264.7 and antitumour activity against HeLa and K562 cell lines [7]. Compounds **76**, **80**, **81** and **83** showed effective inhibitory activity against NO production in lipopolysaccaride-activated macrophages indicating 2.57, 1.45, 12.0, 10.73, and 9.45 μM IC_{50} values, respectively. Compounds **81** and **83** showed strong cytotoxic activity against K562 and Hela lines with IC_{50} values less than 10 μM. Compound **80**, however, showed only mild cytotoxic activity on both cell lines with IC_{50} values of 23.72 and 39.46 μM, respectively [7].

A cyathane-xyloside type diterpene erinacine A (**84**) having effective stimulating activity on the NGF synthesis was isolated from *Hericium erinaceum* which is called edible medicinal lion's mane mushroom. Erinacine A (**84**) is known as antibacterial agent particularly against methicillin-resistant *S. aureus* [31-32].

Eryngiolide A (**85**), the first member of C20 diterpenoids and having two γ-lactone units, was obtained from *Pleurotus eryngii* [13]. Compounds **85-87** were screened for their cytotoxic effects against Hela and HepG2 human cancer cell lines by using MTT assay. Only, **85** showed cytotoxicity against both cell lines, indicating 20.6 and 28.6 μM IC_{50} values, respectively. In contrast, **86** and **87** exhibited no inhibitory activity [13].

Scabronine M (**88**), a novel cyathane diterpenoid, and sarcodonin I (**89**) was obtained from *Sarcodon scabrosus* [33]. The compounds (**88**–**89**) were tested for their effects of nerve growth factor (NGF)-induced neurite outgrowth on PC12 cell line. Scabronine M (**88**) only exhibited inhibitory activity [33].

In another study, *Sarcodon scabrosus* also gave cyathane type diterpenoids; namely, scabronines K (**90**) and L (**91**), sarcodonin G (**92**), sarcodonin A (**93**), sarcodonin M (**94**), and scabronine H (**95**) by *Shi et al.* [34]. In addition, the synthetic compound 19-*O*-acetylsarcodonin G (**96**) was obtained by acetylation of **92** [34]. The isolated compounds (**87-91**) were screened for their NGF-induced neurite outgrowth on PC12 cell line at 25 μM. After 24 h treatment only sarcodonin G (**92**) and sarcodonin A (**93**) showed neurite outgrowth promoting activity in the presence of 20 ng/mL NGF [34]. Sarcodonin

G (**92**) was investigated for its antibacterial activity against *Bacillus subtilis* and *Staphylococcus aureus*, and weak antibacterial activity was observed [17]. In addition, Sarcodonin G (**92**) also exhibited anti-proliferative activity against HOC-21, HEC-1, U251-SP, MM-1CB and HMV-1 human cancer cell lines [35].

Literature shows that *Sarcodon scabrosus* mushroom is rich in cyathane diterpenes. *Kamo et al.* [18] isolated four natural cyathane diterpenes (**81**, **93**, **99-100**); namely, sarcodonin A (**93**), neosarcodonin O (**81**), allocyathin B_2 (**100**), and neosarcodonin A (**101**) from the mushroom *Sarcodon scabrosus* and the anti-inflammatory activity of them were also evaluated by the mouse ear inflammatory test. The authors also prepared derivatives (**97-99** and **102-106**) from the compound **93** [18]. The derivatives (**97-99** and **102-106**) exhibited anti-inflammatory activity between 43-78%. At the same conditions, natural diterpenoid **93**, however, demonstrated 75% activity. Other natural diterpenoids **81** and **99** indicated weak activities which are lower than 40% [18].

The compounds sarcodonin A (**93**) and allocyathin B_2 (**100**) were also investigated for their antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis*, and weak antibacterial activity was observed [17]. *Shibata et al.* [17] isolated sarcodonin M (**94**) from the mushroom *Sarcodon scabrosus* and also prepared a derivative, sarcodonin L (**107**) by oxidation by using Jones reagent. Both **94** and **107** exhibited good antibacterial activity [17]. *Shi et al.* [36] also isolated secoscabronine M (**108**) which is a hemiacetal cyathane diterpenoid, and scabronine A (**109**) from *Sarcodon scabrosus* (Fr.) Karst [36].

The other source of diterpenes is *Sarcodon cyrneus* mushroom from which four cyathane diterpenes, cyrneines A (**110**), B (**111**), C (**113**) and D (**114**) were isolated along with glaucopine C (**112**). Effects of the cyrneines (**110-111**, **113-114**) and glaucopine C (**112**) on the nerve growth factor (NGF) gene expression in human astrocytoma (1321N1) cells and on neurite outgrowth on pheochromocytoma (PC12) cells were investigated [37]. While, cyrneine B (**111**) ingenerated the strongest NGF expression (7.3-fold at 200 μM concentration), cyrneine A (**110**), cyrneine C (**113**), cyrneine D (**114**) and glaucopine C (**112**) inspired NGF expression level by 3.8-fold, 2.7-fold, 1.3-fold and 3.5-fold, respectively. These results mean that cyrneine A (**110**), cyrneine B (**111**) and glaucopine C (**112**) induce neurite outgrowth on PC12 cells and also they stimulated NGF gene expression on 1321N1 cells [37]. In another study by same group, cyrneine A (**110**), B (**111**), C (**113**), D (**114**) and glaucopine C (**112**) were also isolated from same mushroom. Cyrneines and gloucopine C were tested for their NGF gene expression effect in 1321N1 cells and neurite outgrowth effect on PC12 cells. Among them, cyrneine B caused the strongest NGF expression (7.3-fold at 200 μM). Glaucopine C (**112**) exhibited anti-inflammotory activity lower than that of the reference NSAID indomethacin [38].

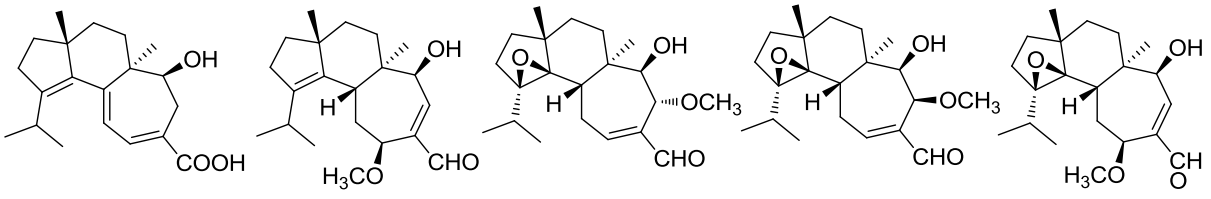
Tricholomalides A (**115**), B (**116**), and C (**117**), neurotrophic diterpenes, were isolated from the mushroom *Tricholoma* sp for the first time. The trichoaurantianolides B (**118**) and C (**119**) which are the metabolites of *T. aurantium*, were also isolated in this study by *Tsukamoto et al.* [39]. To determine potential bioactivity the isolated compounds were subjected to neurite outgrowth assay and cytotoxicity test against HeLa cell lines. Tricholomalides A (**115**), B (**116**), and C (**117**) induced neurite outgrowth in rat PC-12 cells at 100 μM concentrations [40].

Table 3. Bioactive Diterpenoids and Their Activities.

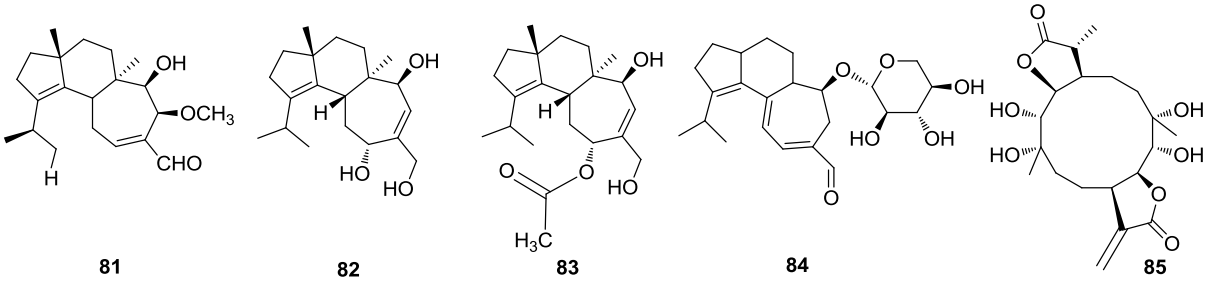
Componunds	Mushrooms	Bioactivity	Ref.
Cyathin D (**76**) Cyathin E (**77**) Cyathin F (**78**) Cyathin G (**79**) Cyathin H (**80**)	*C. africanus*	• NO production inhibitory • Cytotoxic	[7]
Neosarcodonin O (**81**)	*C. africanus*	• Cytotoxic	[7]
	S. scabrosus	• Anti-inflammatory • NO production inhibitory	[18]
Cyathatriol (**82**) 11-*O*-acetylcyathatriol (**83**)	*C. africanus*	• NO production inhibitory • Cytotoxic	[7]
Erinacine A (**84**)	*H.erinaceum*	• Antibacterial	[31] [32]
Eryngiolide A (**85**) **86**, **87**	*P. eryngii*	• Cytotoxic	[13]

Scabronine M (**88**) Sarcodonin I (**89**)	*S. scabrosus*	• Cytotoxic	[33]
Scabronine K (**90**) Scabronine L (**91**)	*S. scabrosus*	• Cytotoxic	[34]
Sarcodonin G (**92**)	*S. scabrosus*	• Antibacterial • Cytotoxic	[17] [34, 35]
Sarcodonin A (**93**)	*S. scabrosus*	• Antibacterial • Cytotoxic	[17] [34]
Sarcodonin M (**94**)	*S. scabrosus*	• Antibacterial	[17]
Scabronine H (**95**)	*S. scabrosus*	• Cytotoxic	[34]
19-*O*-acetylsarcodonin G (**96**)	*S. scabrosus*	• Cytotoxic	[34]
19-O-linoleoyl sarcodonin A (**97**) 19-O-Oleoyl sarcodonin A (**98**) 19-O-Steroyl sarcodonin A (**99**) Allocyathin B_2 (**100**) Neosarcodonin A (**101**) 19-O-Octanoyl sarcodonin A (**102**) 19-O-Butryl sarcodonin A (**103**)	*S. scabrosus*	• Anti-inflammatory	[18]
19-O-Acetyl sarcodonin A (**104**) 19-O-Benzoyl sarcodonin A (**105**) 19-O-Pivaloyl sarcodonin A (**106**)	*S. scabrosus*	• Anti-inflammatory	[18]
Sarcodonin L (**107**)	*S. scabrosus*	• Antibacterial	[17]
Secoscabronine M (**108**) Scabronine A (**109**)	*S. scabrosus*	NT	[36]
Cyrneine A (**110**) Cyrneine B (**111**)	*S. cyrneus*	• NGF gene expression	[37]
Glaucopine C (**112**)	*S. cyrneus*	• NGF gene expression • Anti-inflammatory	[37] [38]
Cyrneine C (**113**) Cyrneine D (**114**)	*S. cyrneus*	• NGF gene expression	[37]
Tricholomalide A (**115**) Tricholomalide B (**116**) Tricholomalide C (**117**)	*Tricholoma* sp.	• Cytotoxic	[39]
Trichoaurantianolide B (**118**) Trichoaurantianolide C (**119**)	*T. aurantium*	NT	[39]

NT: not tested



76 **77** **78** **79** **80**



81 **82** **83** **84** **85**

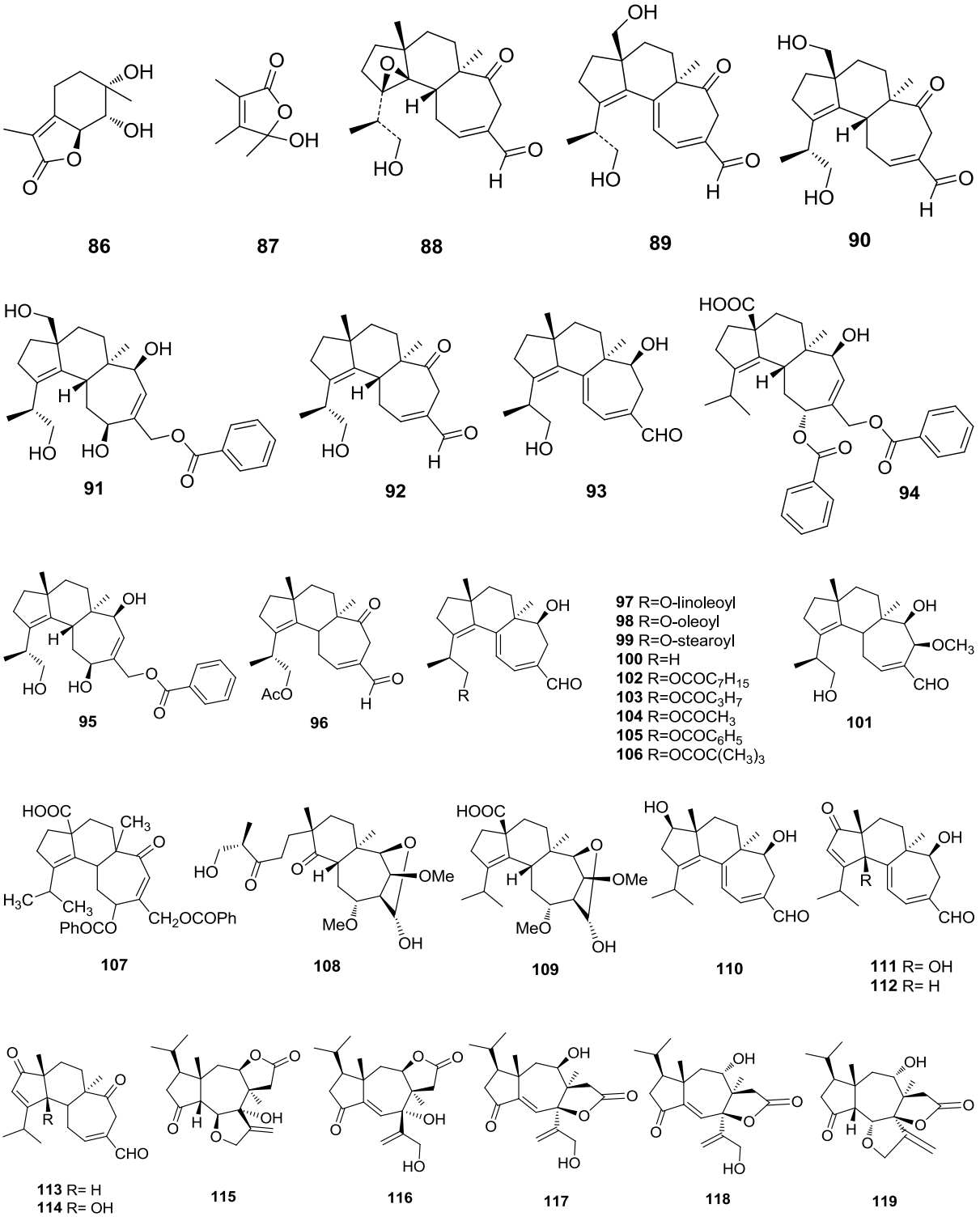


Figure 3. Chemical structure of diterpenoids.

2.4. Triterpenoids

Most of the triterpenoid compounds isolated from mushrooms are the lanostane type triterpenoids. Many lanostane triterpenes have been reported as potential anticancer agents [1, 11-14]. The biologically active triterpenoids (**120**-**285**) isolated from mushroom species and their activities are showed in Table 4.

Ganoboninketals A−C (**120-122**), three new nortriterpenes, were isolated from the medicinal mushroom *Ganoderma boninense*. Ganoboninketals A−C (**120-122**) were tested for their antiplasmodial activity against *Plasmodium falciparum*, NO inhibitory activity in the LPS-induced macrophages and cytotoxicity against A549 and HeLa cells. Compounds **120**−**122** showed antiplasmodial activity indicating 4.0, 7.9, and 1.7 μM IC_{50} values, respectively. Compounds **120** and **122** exhibited weak cytotoxicity against A549 cell line with IC_{50} values of 47.6 and 35.8 μM, respectively while compound **121** showed weak cytotoxicity toward HeLa cell line with IC_{50} value of 65.5 μM. Compounds **120-122** also exhibited NO inhibitory activity indicating 98.3, 24.3, and 60.9 μM IC_{50} values, respectively [40].

Seven novel lanostane type triterpenoids, named; ganorbiformins A, B, C, D, E, F and G (**123-129**) and twelve known triterpenoids (**130-141**) were isolated from cultured mushroom *Ganoderma orbiforme* BCC 22324 [15]. Compounds **123**, **126-129**, **134-135**, **137**, **139** and **141** were investigated for cytotoxicity against three cancer cell-lines (NCIH187, MCF-7 and KB) and nonmalignant Vero cells. The antimalarial activity against *Plasmodium falciparum* K1, and antitubercular activity against *Mycobacterium tuberculosis* H37Ra were also evaluated [15]. Compounds **123**, **126-129, 134**, **139** and **141** demonstrated no activity or weak activities in these three assays. However, in contrast, ganoderic acid T (**137**) and its C-3 epimer compound (**135**) exhibited all of the tested activities. Compound **135** indicated potent antitubercular activity (MIC 1.3 μM) and demonstrated weak cytotoxicity to noncancerous Vero cells (IC_{50} 16 μM) [15].

Methyl ganoderate A acetonide (**142**) and *n*-butyl ganoderate H (**143**), methyl ganoderate A (**144**), ganoderic acid B (**145**), ganoderic acid E (**146**), ganolucidic acid A (**147**), ganodermadiol (**148**), ganoderic acid Y (**149**), ganoderiol F (**150**), lucidumol B (**151**), ganodermanondiol (**152**), ganodermanontriol (**153**), lucidadiol (**154**), lucidenic acid N (**155**), lucidenic acid A (**156**), methyl lucidenate E_2 (**157**), *n*-butyl lucidenate N (**158**), and *n*-butyl lucidenate A (**159**) were obtained from *Ganoderma lucidum* [8].The isolated compounds **142**–**159** were tested for their anticholinesterase activity by the spectrophotometric Ellman method. All compounds gave moderate inhibition to acetylcholinesterase enzyme, with IC_{50} values in the range of 9.40 to 31.03 μM. *n*-butyl ganoderate H (**143**), *n*-butyl lucidenate N (**158**) and *n*-butyl lucidenate A (**159**) showed superior activity against acetylcholinesterase indicating 9.40 ± 0.88, 11.58 ± 0.36, and 12.26 ± 0.68 μM IC_{50} values, respectively. In contrast, all the compounds except lucidadiol (**154**) and lucidenic acid N (**155**) displayed no butyrylcholinesterase inhibitory activity. These results exhibit that lanostane triterpenes show potential as drug candidates for acetylcholinesterase inhibition. [8].

Previous studies of the same group on *Ganoderma lucidum*, called reishi, provided information on eighteen triterpenoids namely; butyl ganoderate A (**160**), butyl ganoderate B (**161**), *n*-butyl lucidenate N (**158**), and *n*-butyl lucidenate A (**159**), ganoderic acid A (**162**), methyl ganoderate A (**144**), ganoderic acid B (**145**), methyl ganoderate B (**163**), methyl ganoderate D (**164**), ganoderic acid E (**146**), methyl ganoderate E (**165**), ganolucidic acid A (**147**), methyl ganoderate H (**166**), lucidenic acid N (**155**), methyl lucidenate A (**167**), methyl lucidenate P (**168**), methyl lucidenate E_2 (**157**), and methyl lucidenate F (**169**) [41]. The inhibitory effect of isolated compounds (**144-145**, **147**, **155**, **157**, **159-169**) was studied on adipocyte differentiation in 3T3-L1 cells [41]. When compared with the non-treated control, nearly all of the compounds at 40 μg/mL concentration showed inhibition between 22% and 56% of lipid deposit, indicative of 3T3-L1 cell differentiation. Butyl lucidenate N (**158**) indicated the highest inhibition of lipid droplet formation (56%) among the others. The treatment of *n*-butyl lucidenate N (**158**) in a dose-dependent manner reduced the accumulation of lipid droplets in the cells. Compound **158** also suppressed GPDH activity effectively to lipid accumulation. As known, in the triglyceride synthesis pathway, the cytosolic enzyme GPDH plays a central role [41].

In a previous study, five triterpenoids (**144**, **156**, **162**, **170-171**); namely, ganoderic acid Sz (**170**), ganoderic acid C1 (**171**), ganoderic acid A (**162**), methyl ganoderate A (**144**), and lucidenic acid A (**156**) were isolated from *Ganoderma lucidum* [42]. The anticomplement activity of **144**, **156**, **162**, **170-171** against the classical pathway of the complement system was examined. Compound **169** was found to be potent anticomplement indicating 44.6 μM IC_{50} value, whereas compounds **144**, **156**, **162**, **171** were determined to be inactive [42].

From *Ganoderma lucidum* strain (YK-02), lucidenic acid N (**155**), lucidenic acid A (**166**), lucidenic acid B (**172**), and lucidenic acid C (**173**) were isolated [44]. Compounds (**155-156**, **172-173**) were screened for their anti-invasive effect against HepG2 cells. The interesting study was done based on the treatment of the lucidenic acids (almost 50 μM) with 200 nM phorbol 12-myristate 13-acetate (PMA). After 24 h incubation of this mixture, the anti-invasive effect against HepG2 cells was observed. According to *Weng et al.* [43] the lucidenic acids (**155-156**, **172-173**) have anti-invasive activity on hepatoma cells [43].

Two new lanostanoids; namely, 7-oxo-ganoderic acid Z (**174**), 15-hydroxy-ganoderic acid S (**175**), together with ganoderiol F (**150**) and ganodermic acid Q (**176**) yielded lipophilic extract of *Ganoderma lucidum* [44]. Compounds **174** and **175** showed inhibition activity against the HMG-CoA reductase indicating 22.3 and 21.7 μM IC_{50} values, respectively, and against acyl CoA acyltransferase indicating 5.5 and 47.3 μM IC_{50} values, respectively [44].

The fruiting bodies of *Ganoderma lucidum* was also studied by *Gao et al.* [45]. Ten lanostante-type triterpenes including three new lanostane aldehydes; namely lucialdehydes A (**177**), B (**178**), and C (**179**), along with ganodermanonol (**180**), ganodermadiol (**148**), ganodermanondiol (**152**), ganodermanontriol (**153**), ganoderic acid A (**162**), ganoderic acid B (**145**), and ganoderic acid C1 (**171**) have been isolated [45]. The compounds were tested for their cytotoxicity against Lewis lung carcinoma (LLC), T-47D (high PR expression of breast cancer cell lines), Meth-A (murine sarcoma), and Sarcoma 180, tumour cell lines. Among the compounds, lucialdehydes B (**178**), C (**179**), ganodermanonol (**180**) and ganodermanondiol (**152**) were found to be exhibit cytotoxic effects on T-47D, LLC, Meth-A, and Sarcoma 180 tumour cells, of particular importance is lucialdehyde C (**179**) which demonstrated the highest cytotoxicity against tested tumour cell lines with ED_{50} values of 10.7, 4.7, 3.8 and 7.1μg/mL, respectively. Ganodermanonol (**180**), however, only exhibited good cytotoxicity against Meth-A cells [45].

From the basidiomycetes of *Ganoderma amboinense* sixteen lanostane triterpenes, one of which is new and was identified as ganodermacetal (**181**) were isolated [46]. Other isolated triterpenoids were identified as methyl ganoderate C (**182**), ganoderic acid C (**183**), ganoderic acid F (**184**), lanosta-7,9(11), 24-trien-3β,15α, 22-triacetoxy-26-oic acid (**185**), ganodermatriol (**186**), ganoderic acid D (**187**), ganoderic acid DM (**188**), 15-hydroxy-ganoderic acid S (**175**), methyl ganoderate E (**165**), ganodermanontriol (**153**), ganoderiol F (**150**), methyl ganoderate B (**163**), ganoderic acid P (**189**) and ganoderic acid H (**190**), ganoderic acid N (**191**) [46].The *in vitro* toxicity of compounds **150**, **153**, **181**, **182**, **184**, and **185** were studied against brine shrimps (*Artemia salina*) larvae by comparing with chaetomugilin A as a positive reference compound isolated from an endophyte *Chaetomium globosum*. The four compounds **150**, **153**, **181** and **182** were found to present remarkable toxicity with lethality rates of 91.5%, 81.8%, 70.3% and 75.8%, respectively. At the same conditions, the positive reference chaetomugilin A demonstrated 78.3% lethality rate [46].

Wu et al. [47] purchased ganoderic acid DM (**188**), known as *Ganoderma lucidum* triterpenoid, and **188** was tested its cytotoxicity against cell proliferation and colony formation in MCF-7 human breast cancer cells. Compound **188** mediated G1 cell cycle arrest both concentration and time dependently. It also significantly decreased the protein level of CDK2, CDK6, p-Rb, cycle D1 and c-Myc in MCF-7 cells [47].

Ganoderic acid X (**192**), which has been reported to inhibit various cancer cell lines growth, is a lanastanoid type triterpenoid and has been isolated with other anticancer triterpenoids from *Ganoderma amboinense* by *Li et al*. [48]. Some of these triterpenoids also showed inhibitory activity against topoisomerases I and II *α in vitro* [48]. Since ganoderic acid X (**192**) inhibited both the topoisomerase I and IIα as well as sensitized the cancer cells and thereby promoted apoptosis. Compound (**192**) shows potential as a therapeutic agent for cancer therapy [48].

From *Ganoderma colossum*, colossolactone V (**193**), colossolactone VI (**194**), colossolactone VII (**195**), and colossolactone VIII (**196**), colossolactone E (**197**) and colossolactone A (**198**) were isolated. HIV-1 protease inhibitory activity of compounds **193-197** together with schisanlactone A (**198**) and colossolactone G (**199**) which were previously isolated compounds by *Salah et al.* [49] from the same mushroom were also evaluated. Schisanlactone A (**198**), colossolactone E (**197**), colossolactone V (**193**), and colossolactone VII (**195**) were found to be active against HIV-1 protease with IC_{50} values of 5.0, 8.0, 9.0 and 13.8 μg/mL, respectively [50].

Three of these were the novel triterpenes (lucialdehyde D, **201**; ganoderone A, **202**; and ganoderone C, **203**), seven triterpenes (**201-207**) were isolated from *Ganoderma pfeifferi*. Previously isolated triterpenes examined i.e. lucialdehyde B (**204**), ganoderol A (**205**), ganoderal A (ganoderol B) (**206**), applanoxidic acid G (**207**), and ganoderone B (lucidadiol) (**154**) [9]. Triterpenoids (**202-206**) were tested antiviral activity against influenza A and herpes simplex type I (HSV) viruses. Remarkable activity was observed for lucialdehyde B (**204**) against herpes simplex virus (IC_{50}: 0.075 μg/mL), followed by ganoderal A (ganoderol B) (**206**), and ganoderone A (**202**) with IC_{50} values of 0.03 and 0.3 μg/mL, respectively. In contrast, applanoxidic acid G (**207**) and ganoderone B (lucidadiol) (**154**) did not show antiviral activity. Likewise, ganoderone A (**203**), lucialdehyde B (**204**), ganoderol A (**205**), and applanoxidic acid G (**207**) exhibited no antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, and *Candida maltose* [9].

Ganodermadiol (**148**), lucidadiol (**154**) and applanoxidic acid G (**207**) were also isolated from *Ganoderma pfeifferi* by the same group [16]. Antiviral activity of the compounds were also tested against influenza virus type A and HSV type 1. All compounds demonstrated activity against both virus types [16].

Two 3,4-seco-25,26,27-trinorlanostane type triterpeniod; namely, fornicatin A (**208**) and fornicatin B (**209**) together with methyl lucidenate H (**210**) were obtained from *Ganoderma fornicatum* [51]. The inhibitory effects of **208** and **210** on PAF-induced (Platelet-activating factor), ADP-induced (Adenosine diphosphate), and AA-induced (Arachidonic acid) rabbit platelet aggregation were tested. The results indicated that both compounds **208** and **209** were potent inhibitors on PAF-induced platelet aggregation. Compound **209** also showed mild inhibitory activity against ADP-induced platelet aggregation [51].

From *Ganoderma concinna* yielded twelve compounds, 5*α*-lanosta-7,9(11),24-triene-3*β*-hydroxy-26-al (**211**), 5*α*-lanosta-7,9(11),24-triene-15*α*-26-dihydroxy-3-one (**212**) and 8*α*,9*α*-epoxy-4,4,14*α*-trimethyl-3,7,11,15,20-pentaoxo-5α-pregrane (**213**) [52]. The nine previously identified triterpenoids were; namely, ganoderal A^3 (**214**), ganodermenonol (**215**), ganodermadiol (**148**), ganoderic acid Y (**149**), ganoderiol F (**150**), ganodermatriol (**186**), ganodermanontriol (**153**), ganoderiol A (**216**), ganoderiol B (**217**) [52]. *Gonzalez et al.* [52] investigated biological activity of only the three new compounds and the results indicated that **211**, **212**, and **213** induced apoptosis in human promyelocyticleukemia HL-60 cells [52].

Tsugaric acid A (**218**), B (**219**), and tsugarioside A (**220**) were identified from the *Ganoderma tsugae* Murr. together with 3*β*-hydroxy-5*α*-lanosta-8, 24-dien-21-oic acid (**221**), 3-oxo-5*α*-lanosta-8, 24-dien-21-oic acid (**222**) [10, 53]. Continuous studies with the same mushroom of same group gave other lanostanoids; namely, tsugaric acid C (**223**), tsugariosides B (**224**) and C (**225**) [10]. The cytotoxic activity of compounds **225, 218-221** were investigated against CaSKi, HT-3, PLC/PRF/5, SiHa, T-24, and 212 cell lines. Compound **220** indicated noteworthy activity against T-24 cell line, while **218** and **221**, however, exhibited noteworthy activity against HT-3, T-24, and CaSKi cell lines [54].

Fifteen lanostane triterpenoids (**226-240**) have been recently isolated from *Naematoloma fasciculare* mushroom by *Kim et al.* [11]. All of these isolated lanostane triterpenoids (**226-240**)were tested antiproliferative activity against four human cancer cell lines i.e. colon adenocarcinoma (HCT-15), ovary malignant ascites (SK-OV-3), skin melanoma (SK-MEL-2), and non-small cell lung adenocarcinoma (A549) using the Sulforhodamine B (SRB) assay. Almost all compounds except compounds **226** and **227** indicated cytotoxicity against the above human cancer cells demonstrating IC_{50} values between 2.29 μM and 28.48 μM concentrations [11]. In addition, Compounds **228** and **229** indicated important cytotoxicity. Compound **228** showed 6.59, 7.08, 8.26, and 8.53 μM IC_{50} values, against HCT-15, A549, SK-MEL-2, SK-OV-3, respectively. Compound **229**, however, demonstrated IC_{50} values of 3.99, 7.36, 4.77, and 8.50 μM, against same cancer cell lines, respectively. Moreover, compounds **236**, **237**, and **238** exhibited moderate cytotoxicity against same cancer cell lines. IC_{50} values of compound (**235**) found to be 7.85, 8.53, 5.17, and 8.22 μM, IC_{50} values of compound (**236**) were 2.37, 2.82, 2.29, and 3.06 μM, and IC_{50} values of compound (**236**) were 4.47, 3.29, 4.54, and 7.71 μM, respectively [11]. Interestingly, triterpenes **230**, **231**, **234**, and **235**, have a side chain of *N*-

glycyl-3-hydroxy-3-methylglutaryl group in C-2 and C-3 positions. These compounds exhibited significant selective cytotoxic activity against human melanoma (SK-MEL-2) cell line with IC_{50} values of 8.60 μM, 9.06 μM, 9.16 μM, and 5.73 μM [11]. The position of side chain in the triterpenoid sometimes affects the cytotoxic activity. The compounds **226** and **232** or **227** and **233** were the examples of this theory. The difference between compounds **226** and **232** or compounds **227** and **233** is the position of the 3-hydroxy-3-methylglutaryl group. As mentioned in the paper by *Kim et al.*[11] if 3-hydroxy-3-methylglutaryl group bonded at C-3 position such as in compounds **226** and **227** it reduced the activity substantially. In contrast, like in compounds **232** and **233**, when bonded at C-2 position the cytotoxic activity increased [11].Compounds **238** and **239** having ketone functionalities at C-12 have demonstrated selective cytotoxicity with IC_{50} values of 9.86 and 7.98 μM against the SK-OV-3 cell line [11].

Five lanostane type triterpenes, astraodorol (**241**), and astraodoric acids A−D (**242**-**245**) by *Arpha et al.* [14] were isolated from the *Astraeus odoratus*. The compounds (**241**-**245**) were investigated for their antitubercular activity against *Mycobacterium tuberculosis* H37Ra, and the cytotoxicity against KB, NCI-H187, and MCF-7 cancerous cell lines [14]. Astraodoric acids A (**242**) and B (**243**) exhibited moderate antitubercular activity indicating 50 and 25 μg/mL MIC values, respectively. The same compounds also showed cytotoxic activities with IC_{50} values of 34.69 and 18.57 μg/mL against KB cancer cell line, respectively. Against NCI-H187 cell line, however, **242** and **243** exhibited 19.99 and 48.35 μg/mL IC_{50} values. Although, astraodoric acid D (**245**) had no activity against *M. tuberculosis* H37Ra; but, it was found to be slightly cytotoxic against KB, NCI-H187, and MCF-7 cancer cell lines with IC_{50} values of 31.55, 34.15, and 40.15 μg/mL, respectively [14].

Astrakurkurol (**246**) and astrakurkurone (**247**), two new lanostane-type triterpenes, were isolated from *Astraeus hygrometricus*. Antifungal activity against *Candida albicans* and leishmanicidal activity against *Leishmania donovani* of these compounds were also evaluated [55]. The agar disc diffusion method was chosen to perform the anticandidal activity of the compounds against *Candida albicans* MTCC 183. As known, *C. albicans* is a virulent strain, and resistant to nystatin (20 μg/disc), fluconazole (10 μg/disc) and amphotericin-B (20 μg/disc) which are the antifungal agents used in pharmaceuticals [55].The compounds (**246**) and (**247**) demonstrated strong activity against *C. albicans* which presented MIC values between 0.25 and 0.20 μg/disc.

The truffle-mimiking mushroom *Astraeus pteridis*, gave five lanostane type triterpenoids; namely, 3-*epi*-astrahygrol (**248**), astrahygrone (**249**), astrapteridone (**250**), astrapteridiol (**251**), and 3-*epi*-astrapteridiol (**252**) [56].The compounds (**249**-**252**) were tested for their antitubercular activity against *Mycobacterium tuberculosis*. Although compounds **248** and **249** showed mild activity, demonstrating MIC values of 34.0, and 58.0 μg/mL respectively, **250** and **251** showed almost no activity indicating more than 64 μg/mL MIC values. Additionally these compounds exhibited no cytotoxic activity to non-malignant/non-cancerous Vero cells (African green monkey kidney fibroblasts) at concentrations up to 100 μg/mL [56].

Antrodia camphorata has been used as a chemopreventive agent in Asian folk medicine in Taiwan. *Du et al.* [57] studied the triterpenoid-rich fraction of the mushroom. Five triterpenoids, antcin K (**253**), antcin C (**254**), zhankuic acid C (**255**), zhankuic acid A (**256**), and dehydroeburicoic acid (**257**) were elucidated. The cytotoxic activity of these triterpenoids (**253**–**257**) was also investigated by the same group. The most potent cytotoxic component was found to be dehydroeburicoic acid (**257**). In HL 60 cells dehydroeburicoic acid (**257**) induced G2/M phase arrest dose dependently. Compound (**257**) was also showed the activities which its extract also demonstrated [57].

Two triterpenoids (**258**-**259**) and two seco-cucurbitane triterpene acid (**260**-**261**) isolated from extract of *Russula lepida* and *Russula amarissima* [28]. The names of the isolated compounds are lepida acid A (**258**), rosacea acid B (**259**), 3,4–secocucurbita–4,24*E*–diene–3,26-dioic acid (**260**), cucurbitane hydroxyl acid (**261**) [29]. Compounds **260**-**261** were investigated for their inhibitory activity on the proliferation of WISH, CAKI 1 and A549 cells. Cucurbitane hydroxyl acid (**261**) showed only moderate activity among them. The IC_{50} values were 72, 85.4, and 90.3, μM, respectively. The situated bioactivity of seco-cucurbitane **261** indicates that **261** may lead to further specific assays to be tested [28].

Lanosta-8(9), 24(28)-diene-3*β*-ol (**262**), eburicoic acid (**263**), spongiporic acid A (**264**) and spongiporic acid B (**265**) were isolated and identified from *Spongiporus leucomallellus*. Antibacterial and antifungal activities of spongiporic acid A (**264**) was assessed [58]. It was determined that although, it showed weak activity at 10 µg/disc dose against *Proteus vulgaris*, *Bacillus subtilis* and *Bacillus brevis*, it exhibited activity at 50 µg/disc against *Proteus vulgaris* and clear inhibition zones against *B. subtilis*, *B. brevis* and the fungus *Paecilomyces variotii* [58].

Bioactive triterpene cucurbitacin B (**266**) and its esters 16-oleyl, 16-linoleyl, and 16-palmityl (**267a-c**), together with two novel cucurbitane triterpenoids, namely, leucopaxillones A (**268**) and B (**269**) have been obtained from the mushroom *Leucopaxillus gentianeus* (syn. *Leucopaxillus amarus*) [59]. The MTT assay was used to assess the growth inhibitory effects of compounds **268**-**269**, **266, 267a-c** on proliferation of four different human tumour cell lines such as, MCF-7, HepG2, kidney carcinoma CAKI-1 and A549. Cucurbitacin B (**266**) exhibited the best activity against all tested cell lines. Leucopaxillone A (**274**), however, showed a specific growth inhibitory activity on the MCF-7 cell line [59].

Although compounds **266**, **268**-**270** were isolated from both cultivated mycelia and the fruiting body of the same mushroom; alternatively, compound **271** and a fatty acid ester mixtures of **267** were absent in the mycelia. Likely, 18-deoxyleucopaxillone A (**271**), was isolated from the mycelia, though it was not detected in the mushroom bodies. Compounds (**266**-**272**) were screened for their antiproliferative activity against the NCI-H460 human tumour cell line [60]. The IC_{50} value of cucurbitacin B (**266**) the most active one among the studied triterpenoids (**266**-**272**). When the cucurbitacin B (**266**) (IC_{50}: 0.011 µg/mL) and cucurbitacin D (**270**) (IC_{50}: 0.12 µg/mL) compared, role of acetylation at the OH-25 position at C-25 became important. Among the leucopaxillones (**268**, **269**, and **272**) leucopaxillone B (**269**) was moderately active. As for 16-deoxy cucurbitacin B (**271**), it exhibited lesser active than **266** [60].

24(*E*)-3*β*-hydroxylanosta-8,24-dien-26-al-21-oic acid (**273**) having cytotoxicity on several cancer cell lines was isolated from the mushroom *Hebeloma versipelle*. Compound **273** was investigated cytotoxic activity against HL60, Bel-7402, SGC-7901 and A549 tumour cell lines. It was showed good activity IC_{50} values of 11.2, 20.9, 22.6 and 25.0 µg/mL, respectively [61].

Saponaceols A (**274**), B (**275**), and C (**276**) three triterpene curustulinol esters were isolated from *Tricholoma saponaceum* [62]. The inhibitory effect of saponaceol A (**274**) on cell growth was evaluated in HL-60 human leukemia cells and it was found moderately active with an IC_{50} of 8.9 µM [62].

Elfvingic acid A (**277**), elfvingic acid B (**278**), elfvingic acid C (**279**), elfvingic acid D (**280**), elfvingic acid E (**281**), elfvingic acid F (**282**), elfvingic acid G (**283**), elfvingic acid H (**284**), and the methyl ester of elfvingic acid H (**285**) were isolated from *Elfvingia applanata* [63]. Compounds **277**-**280** and **285** were assayed for their cytotoxicity against Ehlrich cells and Kato III. While only compound **285** exhibited cytotoxicity (IC_{50}: 1.1 µg/mL for both Ehlrich cells and Kato III cells), in the same conditions the positive control, hinokitiol, indicated 0.6 µg/mL [63].

Table 4. Bioactive Triterpenoids and Their Activities.

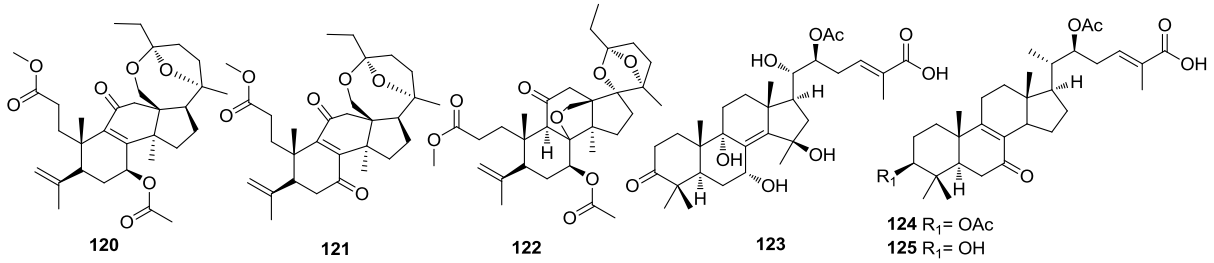
Compounds	Mushrooms	Bioactivity	Ref.
Ganoboninketal A (**120**) Ganoboninketal B (**121**) Ganoboninketal C (**122**)	*G. boninense*	• Antiplasmodial • NO inhibition • Cytotoxic	[40]
Ganorbiformin A (**123**)	*G. orbiforme*	• Antitubercular • Antimalarial • Cytotoxic	[15]
Ganorbiformin B (**124**)	*G. orbiforme*	NT	[15]
Ganorbiformin C (**125**)	*G. orbiforme*	NT	[15]
Ganorbiformin D (**126**) Ganorbiformin E (**127**) Ganorbiformin F (**128**) Ganorbiformin G (**129**)	*G. orbiforme*	• Antitubercular • Antimalarial • Cytotoxic	[15]

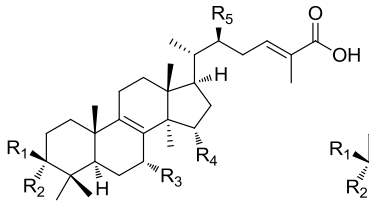
Ganoderic acid V (**130**) 7-O-methyl-ganoderic acid O (**131**) **132**, **133**, **136** Ganoderic acid R (**138**) (**140**)	*G. orbiforme*	NT	[15]
The C-3 epimer of ganoderic acid T (**135**) Ganoderic acid T (**137**), **134**, **139** Ganoderic acid S (**141**)	*G. orbiforme*	• Antitubercular • Antimalarial • Cytotoxic	[15]
Methyl ganoderate A acetonide (**142**) *n*-Butyl ganoderate H (**143**) Methyl ganoderate A (**144**) Ganoderic acid B (**145**) Ganoderic acid E (**146**) Ganolucidic acid A (**147**) Ganodermadiol (**148**) Ganoderic acid Y (**149**) Ganoderiol F (**150**) Lucidumol B (**151**) Ganodermanondiol (**152**) Ganodermanontriol (**153**) Lucidadiol (**154**)	*G. lucidum*	• Anticholinesterase	[8] [8]
Lucidenic acid N (**155**)	*G. lucidum*	• Anticholinesterase • Anti-invasive	[8] [43]
Lucidenic acid A (**156**)	*G. lucidum*	• Anticholinesterase • Anti-invasive	[8] [43]
Methyl lucidenate E_2 (**157**)	*G. lucidum* *G. pfeifferi*	• Anticholinesterase • Antiviral	[8] [16]
n-Butyl lucidenate N (**158**) *n*-Butyl lucidenate A (**159**)	*G. lucidum*	• Anticholinesterase • Effect of on adipocyte differentiation in 3T3-L1 cells	[8] [41]
Butyl ganoderate A (**160**) Butyl ganoderate B (**161**) Ganoderic acid A (**162**) Methyl ganoderate B (**163**) Methyl ganoderate D (**164**) Methyl ganoderate E (**165**) Methyl ganoderate H (**166**) Methyl lucidenate A (**167**) Methyl lucidenate P (**168**) Methyl lucidenate F (**169**)	*G. lucidum*	• Effect of on adipocyte differentiation in 3T3-L1 cells	[41]
Ganoderic acid Sz (**170**) Ganoderic acid C1 (**171**)	*G. lucidum*	• Anticomplement	[42]
Lucidenic acid B (**172**) Lucidenic acid C (**173**)	*G. lucidum*	• Anti-invasive	[43]
7-Oxo-ganoderic acid Z (**174**) 15-Hydroxy-ganoderic acid S (**175**)	*G. lucidum*	• Inhibitory activity against HMG-CoA reductase and acyl CoA acyltransferase	[44]
Ganodermic acid Q (**176**)	*G. lucidum*	NT	[44]
Lucialdehyde A (**177**) Lucialdehyde B (**178**) Lucialdehyde C (**179**) Ganodermanonol (**180**)	*G. lucidum*	• Cytotoxic	[45]
Ganodermacetal (**181**) Methyl ganoderate C (**182**)	*G. amboinenese*	• Toxic activity against brine shrimp larvae	[46]
Ganoderic acid C (**183**)	*G. amboinenese*	NT	[46]
Ganoderic acid F (**184**)	*G. amboinenese*	• Toxic activity against	[46]

Lanosta-7,9(11), 24-trien-3*β*,15*α*, 22-triacetoxy-26-oic acid (**185**)		brine shrimp larvae	[46]
Ganodermatriol (**186**) Ganoderic acid D (**187**)	*G. amboinenese*	NT	[46]
Ganoderic acid DM (**188**)	*G. lucidum*	• Cytotoxic	[47]
Ganoderic acid P (**189**) Ganoderic acid H (**190**) Ganoderic acid N (**191**)	*G. amboinenese*	NT	[46]
Ganoderic acid X (**192**)	*G. amboinenese*	• Cytotoxic	[50]
Colossolactone V (**193**) Colossolactone VI (**194**) Colossolactone VII (**195**) Colossolactone VIII (**196**) Colossolactone E (**197**) Schisanlactone A (**198**) Colossolactone G (**199**) Colossolactone A (**200**)	*G. colossum*	• Anti-HIV-1 Protease	[50] [50]
Lucialdehyde D (**201**) Ganoderone A (**202**)	*G. pfeifferi*	• Antiviral	[9]
Ganoderone C (**203**) Lucialdehyde B (**204**) Ganoderol A (**205**) Ganoderal A (Ganoderol B) (**206**)	*G. pfeifferi*	• Antiviral	[9]
Applanoxidic acid G (**207**)	*G. pfeifferi*	• Antiviral	[16]
Fornicatin A (**208**) Fornicatin B (**209**) Methyl lucidenate (**210**)	*G. fornicatum*	• The inhibitory effects of on PAF-induced, ADP-induced, and AA-induced rabbit platelet aggregation	[51]
5*α*-Lanosta-7,9(11),24-triene-3*β*-hydroxy-26-al (**211**) 5*α*-Lanosta-7,9(11),24-triene-15*α*-26-dihydroxy-3-one (**212**) 8*α*,9*α*-Epoxy-4,4,14*α*-trimethyl-3,7,11,15,20-pentaoxo-5α-pregrane (**213**)	*G. concinna*	• Cytotoxic	[52]
Ganoderal A[3](**214**) Ganodermenonol (**215**) Ganoderiol A (**216**) Ganoderiol B (**217**)	*G. concinna*	NT	[52]
Tsugaric acid A (**218**) Tsugaric acid B (**219**) Tsugarioside A (**220**) 3*β*-Hydroxy-5*α*-lanosta-8, 24-dien-21-oic acid (**221**) 3-Oxo-5*α*-lanosta-8, 24-dien-21-oic acid (**222**)	*G. tsuage*	• Cytotoxic	[54]
Tsugaric acid C (**223**) Tsugarioside B (**224**)	*G. tsuage*	NT	[52]
Tsugarioside C (**225**)	*G. tsuage*	• Cytotoxic	[54]
Fusciculol J (**226**) Fusciculol K (**227**) Fusciculol L (**228**) Fusciculol M (**229**) Fusciculol G (**230**) **231** **232** **233** **234** **235** **236** Fusciculol C (**237**) **238**	*N. fasciculare*	• Cytotoxic	[11]
Astraodorol (**241**) Astraodoric acid A (**242**) Astraodoric acid B (**243**) Astraodoric acid C (**244**)	*A. odoratus*	• Antitubercular • Cytotoxic	[14]

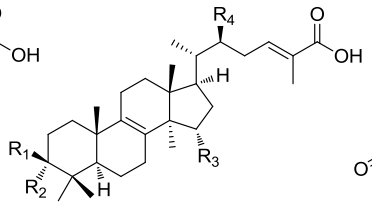
Astraodoric acid C (**245**)	*A. odoratus*	• Antitubercular • Cytotoxic	[14]
Astrakurkurol (**246**) Astrakurkurone (**247**)	*A. hygrometricus*	• Anticandidal	[55]
3-*epi*-astrahygrol (**248**) astrahygrone (**249**) astrapteridone (**250**) astrapteridiol (**251**) 3-*epi*-astrapteridiol (**252**)	*A. pteridis*	• Antitubercular • Cytotoxic	[56]
Antcin K (**253**) Antcin C (**254**) Zhankuic acid C (**255**) Zhankuic acid A (**256**) Dehydroeburicoic acid (**257**)	*A. camphorata*	• Cytotoxic	[57] [57]
Lepida acid A (**258**) Rosacea acid B (**259**)	*R. lepida and* *R. amarissima*	NT	[28]
3,4−Secocucurbita−4,24*E*−diene−3,26-dioic acid (**260**) Cucurbitane hydroxyacid (**261**)	*R. lepida and* *R. amarissima*	• Cytotocic	[28]
Lanosta-8(9), 24(28)-diene-3*β*-ol (**262**) Eburicoic acid (**263**)	*S. leucomallellus*	NT	[58]
Spongiporic acid A (**264**)	*S. leucomallellus*	• Antibacterial	[58]
Spongiporic acid B (**265**)	*S. leucomallellus*	NT	[58]
Cucurbitacin B (**266**) Cucurbitacin B esters (**267**) Leucopaxillone A (**268**) Leucopaxillone B (**269**)	*L. gentianeus*	• Antiproliferative	[60]
Cucurbitacin D (**270**) 16-Deoxycucurbitacin B (**271**) **272**	*L. gentianeus*	• Antiproliferative	[60]
24(*E*)-3*β*-Hydroxylanosta-8,24-dien-26-al-21-oic acid (**273**)	*H. versipelle*	• Cytotoxic	[61]
Saponaceol A (**274**) Saponaceol B (**275**) Saponaceol C (**276**)	*T. saponaceum*	• Cytotoxic	[62]
Elfvingic acid A (**277**) Elfvingic acid B (**278**) Elfvingic acid C (**279**) Elfvingic acid D (**280**) Elfvingic acid E (**281**) Elfvingic acid F (**282**) Elfvingic acid G (**283**) Elfvingic acid H (**284**) The methyl ester of elfvingic acid H (**285**)	*E. applanata*	• Cytotoxic	[63]

NT: not tested

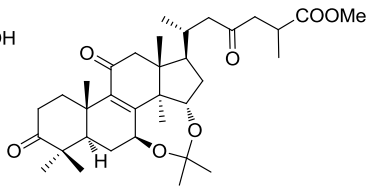




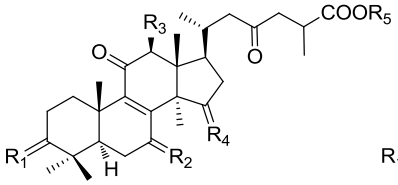
126 R_1, R_2 = O, R_3 = OH, R_4 = OAc, R_5 = OAc
127 R_1, R_2 = O, R_3 = OH, R_4 = H, R_5 = OAc
128 R_1, R_2 = O, R_3 = OCH_3, R_4 = H, R_5 = OAc
130 R_1, R_2 = O, R_3 = OH, R_4 = OAc, R_5 = H
131 R_1 = H, R_2 = OAc, R_3 = OCH_3, R_4 = OAc, R_5 = OAc



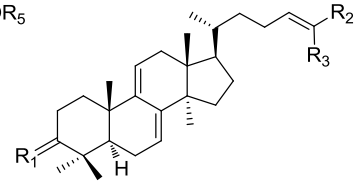
129 R_1, R_2 = O, R_3 = H, R_4 = OAc
132 R_1, R_2 = O, R_3 = OAc, R_4 = OAc
133 R_1, R_2 = O, R_3 = OAc, R_4 = H
134 R_1, R_2 = O, R_3 = OH, R_4 = OAc
135 R_1 = OAc, R_2 = H, R_3 = OAc, R_4 = OAc
136 R_1 = OH, R_2 = H, R_3 = OAc, R_4 = OAc
137 R_1 = H, R_2 = OAc, R_3 = OAc, R_4 = OAc
138 R_1 = H, R_2 = OAc, R_3 = H, R_4 = OAc
139 R_1 = H, R_2 = OH, R_3 = OAc, R_4 = OAc
140 R_1 = H, R_2 = OH, R_3 = OAc, R_4 = H
141 R_1 = H, R_2 = OH, R_3 = H, R_4 = OAc



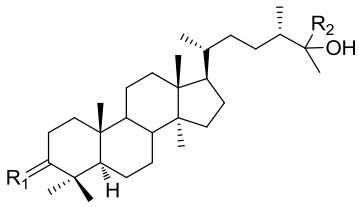
142



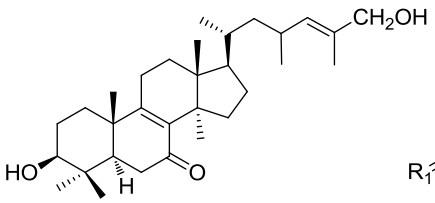
	R_1	R_2	R_3	R_4	R_5
143	αH, βOH	O	OAc	O	Bu
144	O	αH, βOH	H	αOH, βH	Me
145	αH, βOH	αH, βOH	H	O	H
146	O	O	H	O	H
147	O	H_2	H	αOH, βH	H



	R_1	R_2	R_3
148	αH, βOH	CH_2OH	Me
149	αH, βOH	COOH	Me
150	O	CH_2OH	CH_2OH

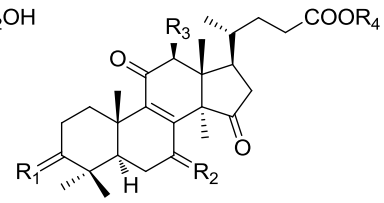


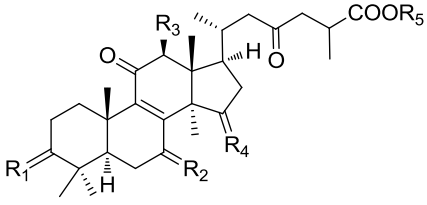
	R_1	R_2
151	αH, βOH	Me
152	O	Me
153	O	CH_2OH



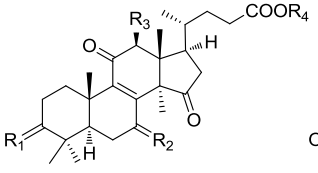
154

	R_1	R_2	R_3	R_4
155	αH, βOH	αH, βOH	H	H
156	O	αH, βOH	H	Me
157	αH, βOH	O	OAc	Me
158	αH, βOH	αH, βOH	H	H
159	O	αH, βOH	H	Me

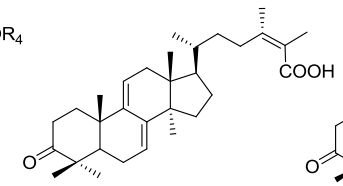




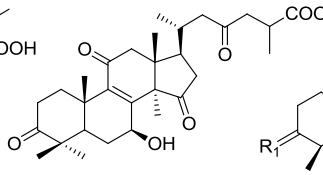
	R_1	R_2	R_3	R_4	R_5
160	O	βOH	H	αOH	Bu
161	βOH	βOH	H	O	Bu
162	O	βOH	H	αOH	H
163	βOH	βOH	H	O	Me
164	O	βOH	H	O	Me
165	O	O	H	O	H
166	βOH	O	OAc	O	Me



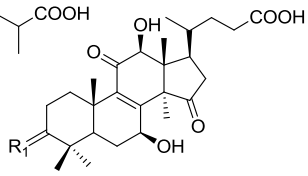
	R_1	R_2	R_3	R_4
167	O	βOH	H	Me
168	βOH	βOH	OAc	Me
169	O	O	H	Me



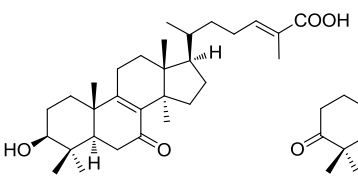
170



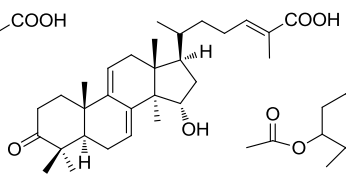
171



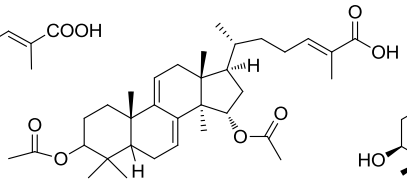
172 R_1= O
173 R_1= β-OH



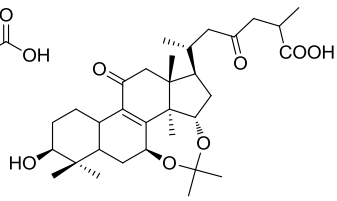
174



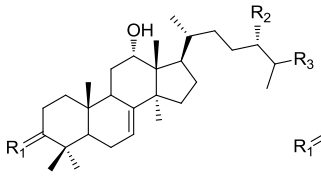
175



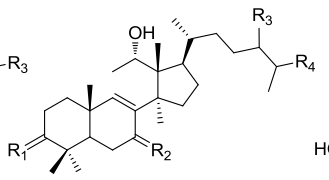
176



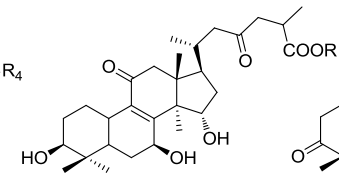
181



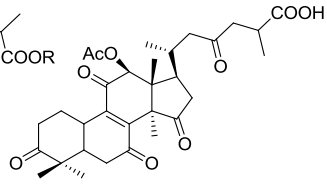
	R_1	R_2	R_3
177		$\Delta^{24,25}$	CHO
180	O	$\Delta^{24,25}$	CH_2OH



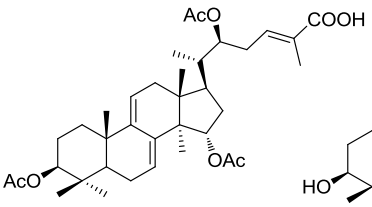
	R_1	R_2	R_6	R_8
178	O	O	$\Delta^{24,25}$	CHO
179		O	$\Delta^{24,25}$	CHO



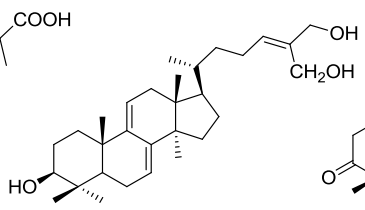
182 R= CH_3
183 R= H



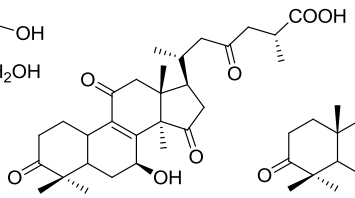
184



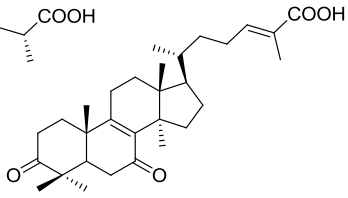
185



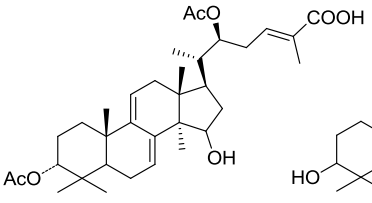
186



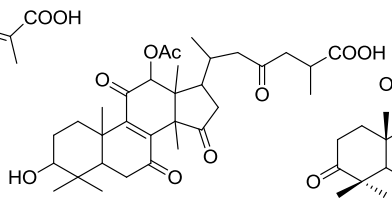
187



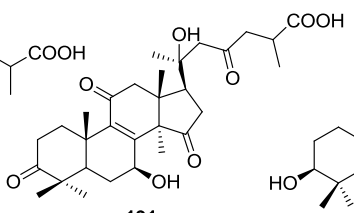
188



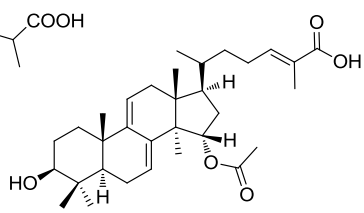
189



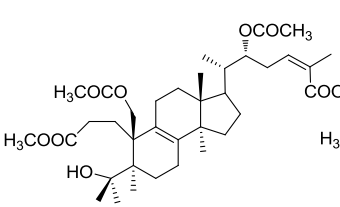
190



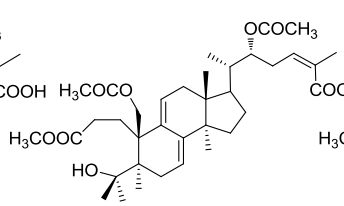
191



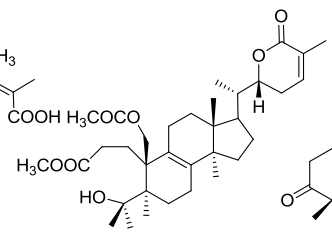
192



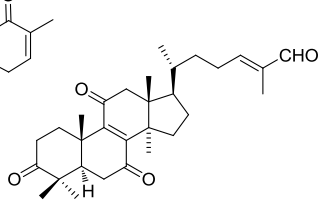
193



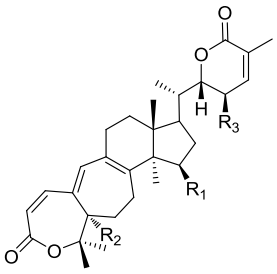
194



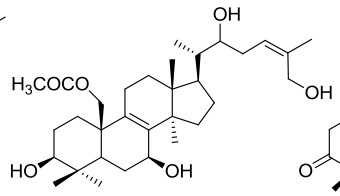
195



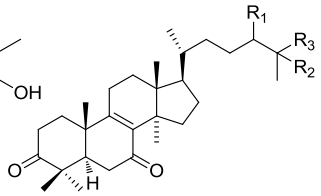
201



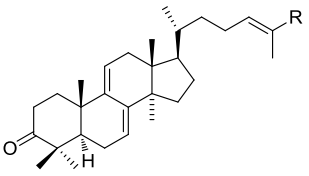
196 R_1= OAc **R_2**= H **R_3**=OH
197 R_1= OAc **R_2**= H **R_3**= H
198 R_1= H **R_2**= H **R_3**=H
199 R_1= OAc **R_2**= OH **R_3**= H



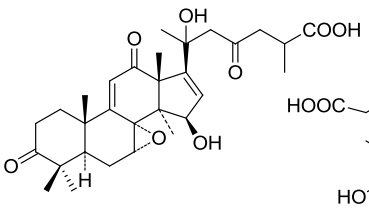
200



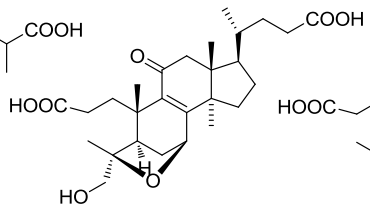
202 R_1= R_2= $\Delta^{24(25)}$, R_3= CH_2OH
203 R_1=R_2= -O- , R_3= CH_2OH
204 R_1=R_2= $\Delta^{24(25)}$, R_3= CHO



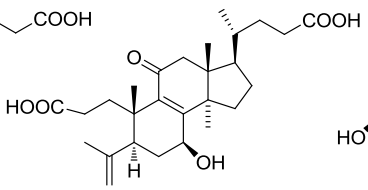
205 R= CH_2OH
206 R= CHO



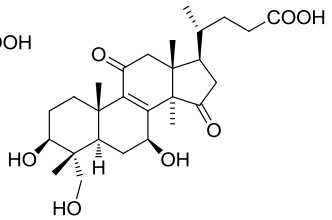
207



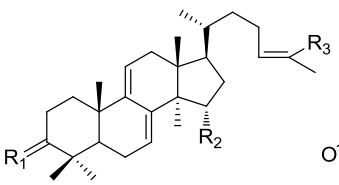
208



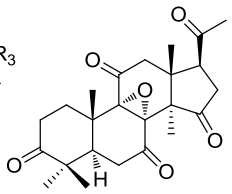
209



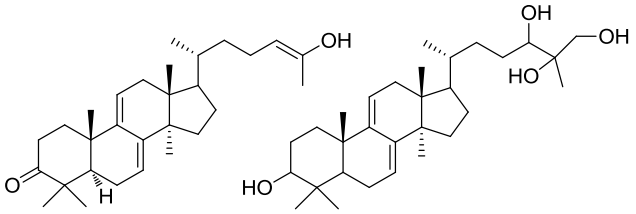
210



211 R_1= β–OH, H; R_2= H; R_3= CHO
212 R_1= O; R_2= α–OH; R_3= CH_2OH
214 R_1= O; R_2= H; R_3= CHO

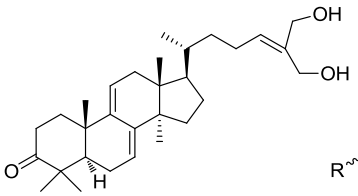


213

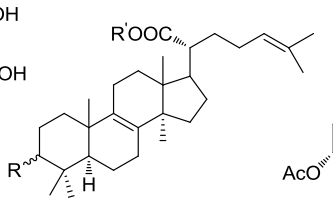


215

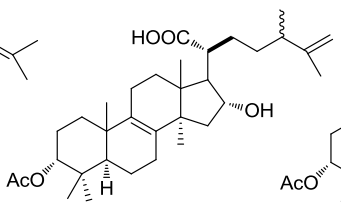
216



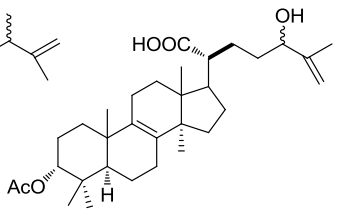
217



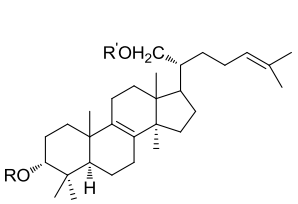
218 R= α–OAc, R'= H
220 R= α–OAc, R'= β–D-glucosyl
221 R= β–OH, R'= H
222 R= O, R'= H



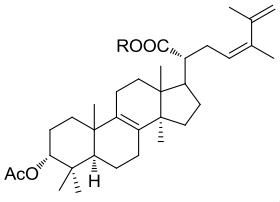
219



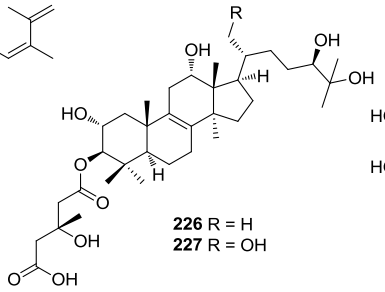
223



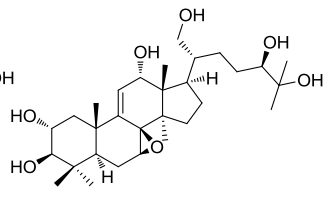
224 R= Ac, R'= β–D-xylosyl



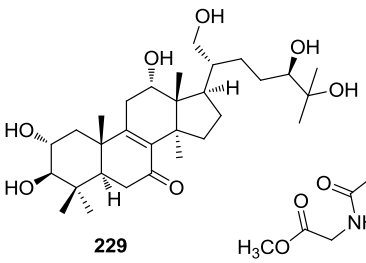
225 R= β–D-xylosyl



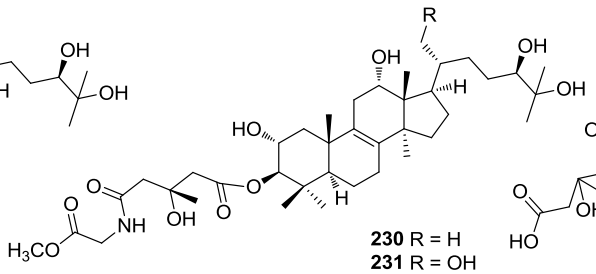
226 R = H
227 R = OH



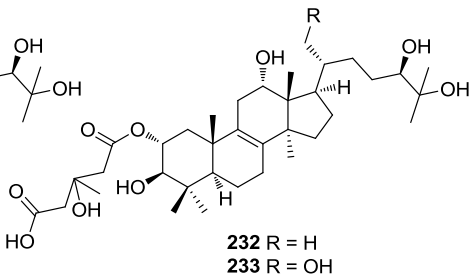
228



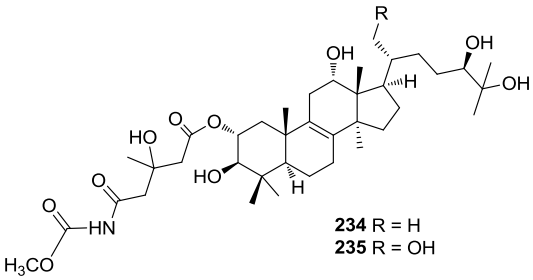
229



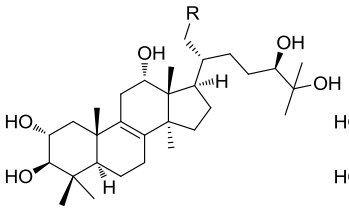
230 R = H
231 R = OH



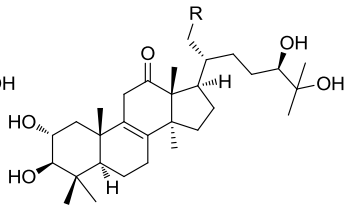
232 R = H
233 R = OH



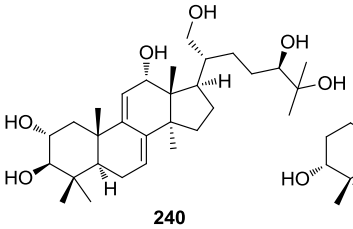
234 R = H
235 R = OH



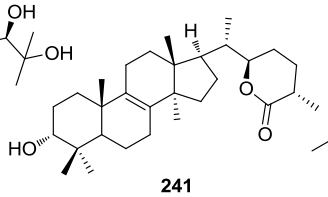
236 R = H
237 R = OH



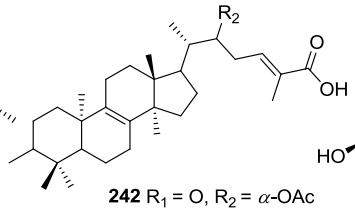
238 R = H
239 R = OH



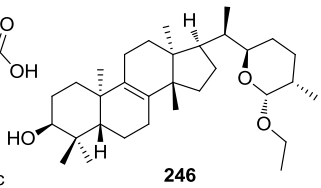
240



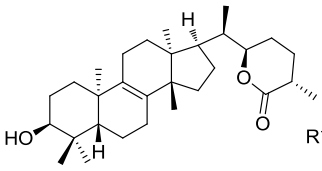
241



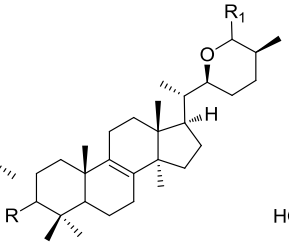
242 R_1 = O, R_2 = α-OAc
243 R_1 = O, R_2 = α-OH
244 R_1 = α-OH, R_2 = α-OH
245 R_1 = α-OH, R_2 = α-OAc



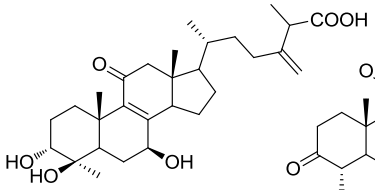
246



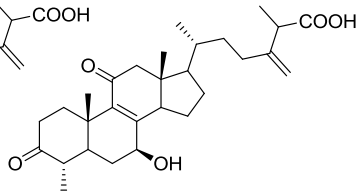
247



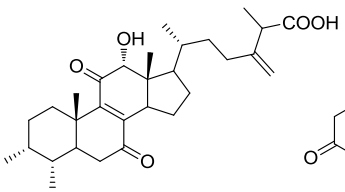
248 R= α-OH **R_1**= O
249 R= **R_1**= O
250 R=O **R_1**= α-OH
251 R= β-OH **R_1**= α-OH
252 R= **R_1**= α-OH



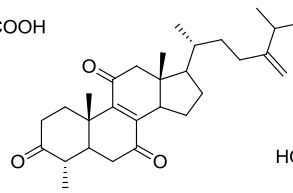
253



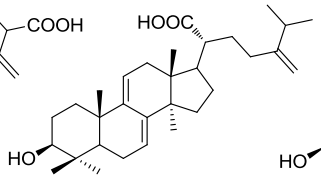
254



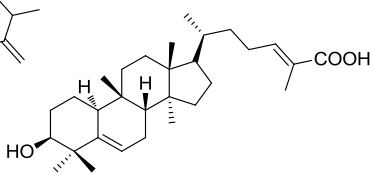
255



256



257



258

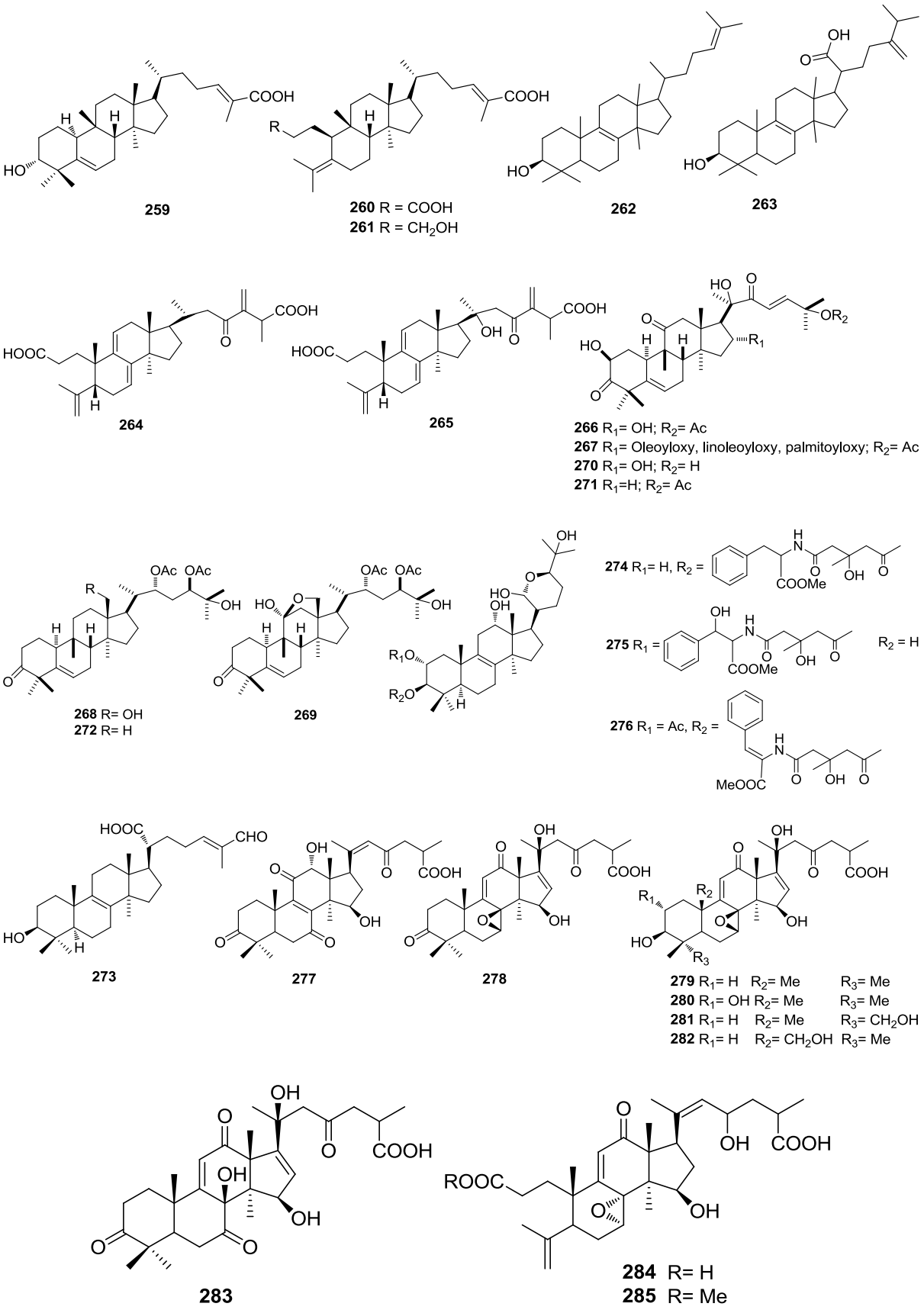


Figure 4. Chemical structure of triterpenoids.

3. Conclusion

This review focused 5 mono-, 70 sesqui-, 44 di-, 166 tri- terpenoids from different mushroom species and their biological activities. Some compounds are exhibited potent bioactivities. For example, sesquiterpenoids flammulinolides A (**40**), B (**41**), C (**42**), F (**45**), and diterpenoids neosarcodonin O (**81**), 11-O-acetylcyathatriol (**83**) exhibited strong cytotoxicity. Diterpenoid erinacine A (**84**) used as antibacterial agent. Triterpenoids lucialdehyde C (**179**), fusciculols L (**228**), M (**229**), G (**230**), and elfvingic acid H (**285**) showed significant cytotoxic activity. The C-3 epimer of gonoderic acid T (**135**) was found potent antitubercular, n-butyl ganoderate H (**143**), n-butyl lucidenate N (**158**), and n-butyl lucidenate A (**159**) indicated superior anticholinesterase activity. Ganoderic acid X (**192**) used as potential therapeutic agent for cancer therapy.

In conclusion, there is important evidence for the pharmacological uses of mushrooms. It seems likely that a number of compounds from mushrooms may provide interesting leads for new bioactive candidates.

Acknowledgments

Authors would like to thank The Scientific and Technological Research Council of Turkey (TUBITAK) for supporting their mushroom studies to the project (TUBITAK-109T933). One of authors would also like to thank to TUBITAK for supporting with the grants; namely, Ph.D Graduate Scholarships for Turkish Citizens (TUBITAK-BIDEB-2211-E).

References

[1] S. Wang, L. Bao, F. Zhao, Q. Wang, S. Li, J. Ren, L. Li, H. Wen, L. Guo and H. Liu (2013). Isolation, identification, and bioactivity of monoterpenoids and sesquiterpenoids from the mycelia of edible mushroom *Pleurotus cornucopiae*, *J. Agric. Food Chem.* **61**, 5122-5129.

[2] M. Zhang, S. W. Cui, P. C. Chueng and K. Q. Wang (2007). Antitumor polysaccharides from mushrooms: a review on their isolation process, structural characteristics and antitumor activity, *Trends in Food Sci. Technol.* **18**, 4-19.

[3] M. F. Moradali, H. Mostafavi, S. Ghods and G. A. Hedjaroude (2007). Immunomodulating and anticancer agents in the realm of macromycetes fungi, *Int. Immunopharm.* **7**, 701-724.

[4] H. Tong, N. Xia, K. Feng, G. Sun, X. Gao, L. Sun, R. Jiang, D. Tian and X. Sun (2009). Structural characterization and in vitro antitumor activity of a novel polysaccharide isolated from the fruiting bodies of *Pleurotus ostreotus*, *Bioresource Technol.* **100**, 1682-1686.

[5] S. Rout and R. Banerjee (2007). Free radical scavenging, anti-glycation and tyrosinase inhibition properties of a polysaccharide fraction isolated from the rind from *Punica granatum*, *Bioresource Technol*. **98**, 3159-3163.

[6] N. K. Ishikawa, Y. Fukushi, K. Yamaji, S. Tahara, and K. Takahashi (2001). Antimicrobial cuparene-type sesquiterpenes, enokipodins C and D, from a mycelial culture of *Flammulina velutipes*, *J. Nat. Prod.* **64**, 932-934.

[7] J. J. Han, Y. H. Chen, L. Bao, X. L. Yang, D. L. Liu, S. J. Li, F. Zhao and H. W. Liu (2013). Anti-inflammatory and cytotoxic cyathane diterpenoids from the medicinal fungus *Cyathus africanus*, *Fitoterapia* **84**, 22-31.

[8] I. S. Lee, B. R. Ahn, J. S. Choi, M. Hattori, B. S. Min and K. H. Bae (2011). Selective cholinesterase inhibition by lanostane triterpenes from fruiting bodies of *Ganoderma lucidum*, *Bioorg. Med. Chem. Lett.* **21**, 6603-6607.

[9] T. H. J. Niedermeyer, U. Lindequist, R. Mentel, D. Gordes, E. Schmidt, K. Thurow and M. Lalk (2005). Antiviral terpenoid constituents of *Ganoderma pfeifferi*, *J. Nat. Prod.* **68**, 1728-1731.

[10] K. H. Gan, Y. F. Fann, S. H. Hsu, K. W. Kuo and C. N. Lin (1998). Mediation of the cytotoxicity of lanostanoids and steroids of *Ganoderma tsugae* through apoptosis and cell cycle, *J. Nat. Prod.* **61**, 485-487.

[11] K. H. Kim, E. Moon, S. U. Choi, S. Y. Kim and K. R. Lee (2013). Lanostane triterpenoids from the mushroom *Naematoloma fasciculare*, *J. Nat. Prod.* **76**, 845-851.

[12] S. J. Wang, L. Bao, J. J. Han, Q. X. Wang, X. L. Yang, H. A. Wen, L. D. Guo, S. J. Li, F. Zhao and H. W. Liu (2013). Pleurospiroketals A-E, perhydrobenzannulated 5,5-spiroketal sesquiterpenes from the edible mushroom *Pleurotus cornucopiae*, *J. Nat. Prod*. **76**, 45-50.

[13] S. J. Wang, Y. X. Li, L. Bao, J. J. Han, X. J. Yang, H. R. Li, Y. Q. Wang, S. J. Li and H. W. Liu (2012). Eryngiolide A, a cytotoxic macrocyclic diterpenoid with an unusual cyclododecane core skeleton produced by the edible mushroom *Pleurotus eryngii*, *Organ. Lett.* **14**, 3672-3675.

[14] K. Arpha, C. Phosri, N. Suwannasai, W. Mongkolthanaruk and S. Sodngam (2012). Astraodoric acids A-D: new lanostane triterpenes from edible mushroom *Astraeus odoratus* and their anti-*Mycobacterium tuberculosis* H37Ra and cytotoxic activity, *J. Agric. Food Chem.* **60**, 9834-9841.

[15] M. Isaka, P. Chinthanom, S. Kongthong, K. Srichomthong and R. Choeyklin (2013). Lanostane triterpenes from cultures of the basidiomycete *Ganoderma orbiforme* BCC 22324, *Phytochemistry* **87,** 133-139.

[16] R. A. A. Mothana, N. A. A. Ali, R. Jansen, U. Wegner, R. Mentel and U. Lindequist (2003). Antiviral lanostanoid triterpenes from the fungus *Ganoderma pfeifferi*, *Fitoterapia* **74**, 177-180.

[17] H. Shibata, A. Irie and Y. Morita (1998). New antibacterial diterpenoids from the *Sarcodon scabrosus*, *Biosci. Biotech. Biochem.* **62**, 2450-2452.

[18] T. Kamo, Y. Imura, T. Hagio, H. Makabe, H. Shibata and M. Hirota (2004). Anti-inflammatory cyathane diterpenoids from *Sarcodon scabrosus*, *Biosci. Biotech. Biochem.* **68**, 1362-1365.

[19] J. Liu (1995*).* Pharmacology of oleanolic acid and ursolic acid, *J. Ethnopharmacology.* **49**, 57-68.

[20] K. Ma, L. Bao, J. Han, T. Jin, X. Yang, F. Zhao, S. Li, F. Song, M. Liu and H. Liu (2014). New benzoate derivatives and hirsutane type sesquiterpenoids with antimicrobial activity and cytotoxicity from the solid-state fermented rice by the medicinal mushroom *Stereum hirsutum*, *Food Chem.* **143**, 239-245.

[21] B. S. Yun, I. K. Lee, Y. Cho, S. M. Cho, and I. D. Yoo (2002). New tricyclic sesquiterpenes from the fermentation broth of S*tereum hirsutum*, *J. Nat. Prod.* **65**, 786-788.

[22] H. P. Chen, W. B. Dong, T. Feng, X. Yin, Z. H. Li, Z. J. Dong, Y. Li, and J. K Liu (2014). Four new sesquiterpenoids from fruiting bodies of the fungus *Inonotus rickii*, *J. Asian Nat. Prod. Res.* **16**, 581-586.

[23] C. Intaraudom, N. Boonyuen, S. Supothina, P. Tobwor, S. Prabpai, P. Kongsaeree and P. Pittayakhajonwu (2013). Novel spiro-sesquiterpene from the mushroom *Anthracophyllum* sp. BCC18695. *Phytochemistry Lett.* **6**, 345-349.

[24] Y. Wang, L. Bao, X. Yang, L. Li, S. Li, H. Gao, X. S. Yao, H. Wen and H. W Liu (2012). Bioactive sesquiterpenoids from the solid culture of the edible mushroom *Flammulina velutipes* growing on cooked rice, *Food Chem*. **132**, 1346-1353.

[25] Y. Wang, L. Bao, D. Liu, X. Yang, S. Li, H. Gao, X. Yao, H. Wen and H. Liu (2012). Two new sesquiterpenes and six norsesquiterpenes from the solid culture of the edible mushroom *Flammulina velutipes*, *Tetrahedron* **68**, 3012-3018.

[26] L. Y. Liu, Z. H. Li, Z. J. Dong, X. Y. Li, J. Su, Y. Li, and J. K Liu (2012). Two novel fomannosane-type sesquiterpenoids from the culture of the basidiomycete *Agrocybe salicacola*, *Nat. Prod. Bioprospect.* **2**, 130-132.

[27] S. Kanokmedhakul, R. Lekphroma, K. Kanokmedhakul, C. Hahnvajanawong, S. Bua-art, W. Saksirirat, S. Prabpai and P. Kongsaeree (2012). Cytotoxic sesquiterpenes from luminescent mushroom *Neonothopanus nambi*, *Tetrahedron* **68**, 8261-8266.

[28] M. Clericuzio, C. Cassino, F. Corana and G. Vidari (2012). Terpenoids from *Russula lepida* and *R. amarissima* (Basidiomycota, Russulaceae), *Phytochemistry* **84**, 154-159.

[29] F. Hiramatsu, T. Murayama, T. Koseki and Y. Shiono (2007). Strobilols A-D: four cadinane-type sesquiterpenes from the edible mushroom *Strobilurus ohshimae*, *Phytochemistry* **68**, 1267-1271.

[30] T. Kamo, M. Matsue, M. Kashiwabara and M. Hirota (2006). 1,2-Dehydrolactarolide A, a new plant growth regulatory lactarane sesquiterpene from *Lactarius vellereus*, *Biosci. Biotechnol. Biochem.* **70**, 2307-2309.

[31] H. Kawagishi, A. Shimada, R. Shirai, K. Okamoto, F. Ojima, H. Sakamoto, Y. Ishiguro and S. Furukawa (1994). Erinacines A, B and C, strong stimulators of nerve growth factor (NGF)-synthesis, from the mycelia of *Hericium erinaceum*, *Tetrahedron Lett.* **35**, 1569-1572.

[32] H. Kawagishi, A. Masui, S. Tukuyama and T. Nakamura (2006). Erinacines J and K from the mycelia of *Hericium erinaceum*, *Tetrahedron* **62**, 8463-8466.

[33] L. Liu, X. W. Shi, S. C. Zong, J. J. Tang and J. M. Gao (2012). Scabronine M, a novel inhibitor of NGF-induced neurite outgrowth from PC12 cells from the fungus *Sarcodon scabrosus*, *Bioorgan. Med. Chem. Lett.* **22**, 2401-2406.

[34] X. W. Shi, L. Liu, J. M. Gao and A. L. Zhang (2011). Cyathane diterpenes from chinese mushroom *Sarcodon scabrosus* and their neurite outgrowth-promoting activity, *Eur. J. Med. Chem.* **46**, 3112-3117.

[35] M. Dong, S.P. Chen, K. Kita, Y. Ichimura, W.Z. Guo, S. Lu, S. Sugaya, T. Hiwasa, M. Takiguchi, N. Mori, A. Kashima, K. Morimura, M. Hirota and N. Suzuki (2009). Anti-proliferative and apoptosis-inducible activity of sarcodonin G from *Sarcodon scabrosus* in Hela cells, *Int. J. Oncol.* **34**, 201-207.

[36] X. W. Shi, A. L. Zhang, G. Pescitelli and J. M. Gao (2012). Secoscabronine M, a novel diterpenoid from the chinese bitter mushroom *Sarcodon scabrosus*, *Chirality* **24**, 386-390.

[37] M. C. Marcotullio, R. Pagiotti, F. Maltese, G. Norbert, O. M Mwankie, T. Hoshino, Y. Obarac, and N. Nakahata (2007). Cyathane diterpenes from *Sarcodon cyrneus* and evaluation of their activities of neuritegenesis and nerve growth factor production, *Bioorg. Med. Chem.* **15**, 2878-2882.

[38] M. C. Marcotullio, R. Pagiotti, V. Campagna, F. Maltese, G. Fardella, G. Altinier and A. Tubaro (2006). Glaucopine C, a new diterpene from the fruiting bodies of *Sarcodon glaucopus*, *Nat. Prod. Res.* **20**, 917-921.

[39] S. Tsukamoto, A. D. Macabalang, K. Nakatani, Y. Obara, N. Nakahataa and T. Ohta, (2003). Tricholomalides A-C, new neurotrophic diterpenes from the mushroom *Tricholoma* sp., *J. Nat. Prod.* **66**, 1578-1581.

[40] K. Ma, J. Ren, J. Han, L. Bao, L. Li, Y. Yao, C. Sun, B. Zhou, and H. Liu (2014). Ganoboninketals A-C, antiplasmodial 3,4-seco-27-norlanostane triterpenes from *Ganoderma boninense* Pat., *J. Nat. Prod.* **77**, 1847-1852.

[41] I. S. Lee, J. J. Seo, J. P. Kim, H. J. Kim, U. J. Youn, J. S. Lee, H. J. Jung, M. K. Na, M. Hattori, B. S. Min and K. H. Bae (2010). Lanostane triterpenes from the fruiting bodies of *Ganoderma lucidum* and their inhibitory effects on adipocyte differentiation in 3T3-L1 cells, *J. Nat. Prod*. **73**, 172-176.

[42] H. W. Seo, T. M. Hung, M. K. Na, H. J. Jung, J. C. Kim, J. S. Choi, J. H. Kim, H. K. Lee, I. S. Lee, K. H. Bae, M. Hattori and B. S. Min (2009). Steroids and triterpenes from the fruit bodies of *Ganoderma lucidum* and their anti-complement activity, *Arch. Pharm. Res.* **32**, 1573-1579.

[43] C. J. Weng, C. F. Chau, K. D. Chen, D. H. Chen and G. C. Yen (2007). The anti-invasive effect of lucidenic acids isolated from a new *Ganoderma lucidum* strain, *Mol. Nutr. Food Res.* **51**, 1472-1477.

[44] C. Li, Y. Li and H. H. Sun (2006). New ganoderic acids, bioactive triterpenoid metabolites from the mushroom *Ganoderma lucidum*, *Nat. Prod. Res.* **20**, 985-991.

[45] J. J. Gao, B. S. Min, E. M. Ahn, N. Nakamura, H. K. Lee and M. Hattori (2002). New triterpene aldehydes, lucialdehydes A-C, from *Ganoderma lucidum* and their cytotoxicity against murine and human tumor cells, *Chem. Pharm. Bull.* **50**, 837-840.

[46] S. X. Yang, Z. C. Yu, Q. Q. Lu, W. Q. Shi, H. Laatsch and J. M. Gao (2012). Toxic lanostane triterpenes from the basidiomycete *Ganoderma amboinense*, *Phytochemistry Lett.* **5**, 576-580.

[47] G. S. Wu, J. J. Lu, J. J. Guo, Y. B. Li, W. Tan, Y. Y. Dang, Z. F. Zhong, Z. T. Xu, X. P. Chen and Y. T. Wang (2012). Ganoderic acid DM, a natural triterpenoid, induces DNA damage, G1 cell cycle arrest and apoptosis in human breast cancer cells, *Fitoterapia* **83**, 408-414.

[48] C. H. Li, P. Y. Chen, U. M. Chang, L. S. Kan, T. W. H. Fanga, K. S. Tsai and S. B. Lin (2005). Ganoderic acid X, a lanostanoid triterpene, inhibits topoisomerases and induces apoptosis of cancer cells, *Life Sci*. **77**, 252-265.

[49] R. Salah, A. El Halawany, N. Nakamura, C. Ma and M. Hattori (2008). New lanostane triterpene lactones from the Vietnamese mushroom *Ganoderma colossum* (FR.) C. F. Baker, *Chem. Pharm. Bull.* **56**, 642-646.

[50] R. S. El Dine, A. M. El Halawany, C. M. Ma and M. Hattori (2008). Anti-HIV-1 protease activity of lanostane triterpenes from the Vietnamese mushroom *Ganoderma colossum*, *J. Nat. Prod.* **71**, 1022-1026.

[51] X. Niu, M. Qiu, Z. Li, Y. Lu, P. Cao and Q. Zheng (2004). Two novel 3,4-seco-trinorlanostane triterpenoids isolated from *Ganoderma fornicatum*, *Tetrahedron Lett.* **45**, 2989-2993.

[52] A. G. Gonzalez, F. Leon, A. Rivera, J. I. Padron, J. Gonzalez-Plata, J. C. Zuluaga, J. Quintana, F. Estevez and J. Bermejo (2002). New lanostanoids from the fungus *Ganoderma concinna*, *J. Nat. Prod.* **65**, 417-421.

[53] L. J. Lin, M. S. Shiao and S. F. Yeh (1988). Triterpenes from *Ganoderma lucidum*, *Phytochemistry* **27**, 2269-2271.

[54] H. J. Su, Y. F. Fann, M. I. Chung, S. J. Won and C. N. Lin (2000). New lanostanoids of *Ganoderma tsugae*, *J. Nat. Prod.* **63**, 514-516.

[55] T. K. Lai, G. Biswas, S. Chatterjee, A. Dutta, C. Pal, J. Banerji, N. Bhuvanesh, J. H. Reibenspies and K. Acharya (2012). Leishmanicidal and anticandidal activity of constituents of Indian edible mushroom *Astraeus hygrometricus*, *Chem. Biodivers.* **9**, 1517-1524.

[56] R. Stanikunaite, M. M. Radwan, J. M. Trappe, F. Fronczek and S. A. Ross (2008). Lanostane-type triterpenes from the mushroom *Astraeus pteridis* with antituberculosis activity, *J. Nat. Prod.* **71**, 2077-2079.
[57] Y. C. Du, F. R. Chang, T. Y. Wu, Y. M. Hsu, M. El-Shazly, C. F. Chen, P. J. Sung, Y. Y. Lin, Y. H. Lin, Y. C. Wu and M. C. Lu (2012). Antileukemia component, dehydroeburicoic acid from *Antrodia camphorate* induces DNA damage and apoptosis *in vitro* and *in vivo* models, *Phytomedicine* **19**, 788-796.
[58] F. C. Ziegenbein, H. P. Hanssen and W. A. Konig (2006). Secondary metabolites from *Ganoderma lucidum* and *Spongiporus leucomallellus*, *Phytochemistry* **67**, 202-211.
[59] M. Clericuzio, M. Mella, P. Vita-Finzi, M. Zema and G. Vidari (2004). Cucurbitane triterpenes from the fruiting bodies and cultivated mycelia of *Leucopaxillus gentianeus*, *J. Nat. Prod.* **67**, 1823-1828.
[60] M. Clericuzio, S. Tabasso, M. A. Bianco, G. Pratesi, G. Beretta, S. Tinelli, F. Zunino and G. Vidari (2006). Cucurbitane triterpenoids from *Leucopaxillus gentianeus*, *J. Nat. Prod.* **69**, 1796-1799.
[61] H. J. Shao, C. Qing, F. Wang, Y. L. Zhang, D. Q. Luo and J. K. Liu (2005). A new cytotoxic lanostane triterpenoid from the basidiomycete *Hebeloma versipelle*, *J. Antibiot.* **58**, 828-831.
[62] K. Yoshikawa, M. Kuroboshi, S. Ahagon and S. Arihara (2004). Three novel crustulinol esters, saponaceols A-C from *Tricholoma saponaceum*, *Chem. Pharm. Bull.* **52**, 886-888.
[63] K. Yoshikawa, N. Nishimura, S. Bando, S. Arihara, E. Matsumura and S. Katayama (2002). New lanostanoids, elfvingic Acids A-H, from the fruit body of *Elfvingia applanata*, *J. Nat. Prod.* **65**, 548-552.