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Advances in anticancer activity of natural products from fungi

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Abstract: **The species and structure of active natural products from fungi are rich and diverse, which can affect many physiological and biochemical processes and are an important source of clinical antitumor drugs. In this paper, the origin, activity and mechanism of antifungal natural products are reviewed, and their future applications are prospected.**

Keywords: fungus; anticancer activity; natural product

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1. Introduction

Cancer is a major disease that seriously endangers human life and health. Chemotherapy is still an important way to treat cancer in clinic.At present, the important sources of chemotherapeutic drugs are artificial synthesis or extraction from microbial fermentation products including medicinal plants and medicinal fungi. Fungi have the characteristics of wide sources, easy culture, fast growth, easy control of fermentation conditions, and large-scale factory production, so that people can quickly, in large quantities, and efficiently obtain natural products with anticancer activity. At present, the main ways to extract anticancer active products from fungi are high yield or new structure modification mining. According to the currently identified anti-cancer active substances, genome mining and other methods are used to search for producing fungi or new active skeleton compounds that can produce the product and its analogues. OSMAC and other strategies were used to explore new skeleton compounds in fungi from various sources and predict and verify their anticancer activity in vitro and in vivo by using molecular docking.

It has been found that the anticancer active products of fungi mainly include polysaccharides, proteins, nucleic acids, esters, sphingolipid complexes, terpenoids, phenolic acids, alkaloids, organic acids and other components. Due to the diversity of various fungal species, growth and metabolism process, culture environment, etc., the types, structures and yields of active products produced by fungi from different sources are also quite different.

2. The main active natural products from fungi

2.1 Fungal polysaccharides

Fungal polysaccharides were mostly isolated from the fruited bodies of fungi, mycelia and fermentation broth. There are many monosaccharides and small molecular weight in polysaccharide structure, including heteropoly and homopolysaccharide structure. Fungal polysaccharides is mainly composed of -1, 3 and -1, 6 glycosidic bonds, and is a natural substance with strong anticancer activity [1]. The IOPS was extracted by Cai et al. from inonotus obliquus showed significant anti-liver cancer activity. Combined application of IOPS with cyclophosphamide (CTX) can enhance its anti-cancer effect and reduce its damage to the normal body [2]. Meng et al. [3] prepared polysaccharide capsules extracted from Mulberry yellow with good anticancer effect on mouse sarcoma S180 and liver cancer H22, and proved that polysaccharide capsules of mulberry yellow are actually non-toxic substances through experiments. Usui et al. [4] isolated a glucan from the fruiting body of phyllostachys citron, and the inhibition rate of mice tumor S180 reached 100%. Zhang [5] polysaccharides extracted from Antrodia Camphorata showed strong inhibitory activity on A431, Hela, S180 and H22 cells.

2.2 Proteins and peptides

As a high molecular compound, protein also has significant anticancer effects. Zhang [6] et al. extracted glycoprotein GLIS from the fruited body of Ganoderma lucidum with concentration dependence, which has significant inhibitory effect on mouse S180 tumor. Liang et al. [7] isolated linear peptide from Simplicillium Obclavatum EIODSF 020E has

significant inhibitory effect on human leukemia HL-60 and K652 cells. The IC50 values of metafamin E isolated from Tamarii against McF-7 A549 of tumor cells were 0.65 and 2.42mmol/L, respectively, showing high anticancer activity and weak anticancer activity against HepG2 cells [8]. At present, studies on the anticancer activity of proteins are still very rare, but the anticancer value and other efficacy of proteins have great potential for development.

2.3 Fungal alkaloids

Alkaloids are organic compounds containing nitrogen and alkaloids extracted from plants. It have antibacterial, anti-inflammatory and anti-tumor effects. Camptothecin, as a potent anti-tumor natural active substance, was first extracted by Wall et al. [9]. The alkaloid showed strong inhibitory activity against Hela cells and L1010 cells in vitro. In 2006, it was the first report that Entrophospora infrequens of an endophytic fungus was frequens capable of producing CPT, and Amna et al. study showed that this endophytic fungus was a potential alternative microbial source for CPT by frequens suspended culture E.Frequens [10, 11]. A new alkaloid chaetomugilide A showed inhibitory effect on HepG2 cells [12]. Zhang et al. work [13] showed significant cytotoxic activity against tumor cell LNCap on alkaloid Cytoglobosins I extracted from Marine fungus Chaetomium Globosum, with IC50 of 9.25 mol/L. Mishra also found an alkaloid PM181110 in endophytic fungi [14].

2.4 Ketone

Ma et al. [15] isolated flavonoids from the fruited body of mulberry. Sang et al. isolated and identified Phomone D from Phoma spyn2-p-3, and showed inhibitory effect on hl-60 pc-3 hpct-116 cells [16-18]. Lee et al. isolated five ketones from Marine fungus Phoma sp NTOU4195 [19]. Acremoxanthone was isolated from Acremonium Camptosporum by Melendez Gonzalez et al. [20]. Prabukumar Seetharaman et al. [21] isolated CHR, a flavonoid from A. Acternata KT380662 strain, and made detailed studies on its activity and mechanism.

2.5 Terpenoids

2.5.1 single terpenoids

Wu et al. [22] isolated two monoterpenoids from Pestalotiopsis SP DO14 and measured their structures (4S,6S)-6-[(1S,2R)-4-hydroxy-tetrahydro-2h -pyrano-2-ketone and (6S,2E) -6-hydroxy-3-methoxy5-oxygen-oxy-2-caprylic acid. Experiments showed that these two substances had significant cytotoxic activities against MKN45, LOVO, A549 and HL-60 cancer cell lines.

2.5.2 Sesquiterpenoids

Sesquiterpenes, as the most common kind of terpenes, can be divided into sesquiterpenes alcohols, sesquiterpenes aldehydes and sesquiterpenes lactones according to the difference of their oxygen groups. Zheng[23] et al. isolated two sesquiterpenes 4- (2, 3-dihydroxy-3-methyl-butyroxy) -phenylacetic acid and a new sesquiterpene from Penicillium sp FJ-1.S. Choodej et al. [24, 25] isolated two new chamomile sesquiterpenes from the culture of mangrove basidiomycete X G8D, both of which showed high anti-tumor activity against Kato3 cells. Phenylphenol A and B, which significantly inhibited the activation of NF-KB in A dose-dependent manner, while phenylphenol B had A moderate inhibitory effect on the transcriptional activity of NF-KB.

2.5.3 Diterpenes

Diterpenes have large molecular weight and mostly exist in nature in the form of resins, lactones and glycosides. Paclitaxel, as one of the strongest and most broad-spectrum diterpenoids with anticancer activity, was originally isolated from the stem bark of Pacific Yew by Wan i[26] et al. Stierle et al. [27] found the first taxomycete producing fungus, Taxomyces Andreanae. Xu et al. [28] discussed the strain improvement and optimization of the culture medium of Fusarium oxysporum, a taxol-producing fungus, which will provide a feasible way and more infinite possibilities for the mass production of paclitaxel. The discovery of taxol-producing microbes will greatly reduce people's dependence on taxus chinensis and other taxus-producing plants in nature, and also increase the species diversity and richness of taxus-producing plants. Zhang[29] et al. studied diterpenes named (9R, 10R) -dihydro-resinone from the mangrove fungus Trichoderma sp. Xy24, which showed strong anticancer activity against HeLa and McF-7 cells.

2.5.4 triterpene

Triterpenes are lanoidane derivatives with molecular weight of 400 -- 600. At present, triterpenes are known to have 7 different parent nucleus structures. There are a number of different substituents on the mother nucleus, the common ones are methyl hydroxyl carboxyl ketone acetyl group and methoxy group, etc. According to different functional groups in structure, they can be divided into ganoderma acid ganoderma spore acid Ganoderma lactone ganoderma alcohol ganoderma aldehyde gibberelline acid gibberelline ketone, etc. [30]. The triterpenoids were extracted from the fruiting bodies of Ganoderma Hao [31] had certain inhibitory effects on K562, SW620 and L1210 cells. Liu [32] et al. extracted a novel triterpenoid GL22 from Ganoderma lucidum showed a strong inhibitory

effect on hepatocellular carcinoma cell, with IC50 value of 8.9 mol/L.

2.6 Steroids

Steroidal compounds in natural products is one of the most popular material frequency, the biosynthesis of almost all organisms can steroidal compounds natural steroidal phyletic and various complex number extensive biological activities. It is a kind of important natural organic compounds, the extraction and separation of the steroidal compounds synthesis and application research has become very active field of drug development. Steroid compounds widely exists in fungus, ergot steroid structure as the main existence form, has many characteristics, such as content of great variety. The compounds is a key part of the fungus contains chemical composition, is a key part of the biological activities. Five ergosteroidal compounds were isolated from Ganoderma flavum by Su [33] et al. and identified as :5,8 -peroxyergosteroidal 6, 22-diene-3 -alcohol 5,8 -peroxyergosteroidal 6,9, 22-triene-3 -alcohol ergosteroidal 7, 22-diene-3 -alcohol ergosteroidal 7, 22-diene-3-ketone. The IC50 values of these steroids were 76.93mol/L, 37.19mol/L, 13.02mol/L, 48.19mol/L and 1.25 mol/L, respectively.

Table 1 Anticancer active substances and their sources

Structure type	Compound	Corresponding tumor cell line	Producing strain	References
Polysacc-haride	IOPS	HepG2, MCF-7	Inonotus.obliquus (Fr) Pilát	[2]
	Phellinus linteus polysaccharides	S180, HepG2	Phellinus igniarius (L. ex Fr.) Quel	[3]
	glucan	S180	Fomitopsis pinicola	[4]
	Cinnamomum camphora polysaccharide	A431, Hela, S180, H22	Antrodia cinnamomea	[5]
Protein	Glycoprotein GLIS	S180	Ganoderma lucidum	[6]
	inear peptide	HL-60, K652	Simplicillium obclavatum	[7]
	MetforminE	MCF-7, A549	Aspergillus tamarii	[8]
Alkaloid	Camptothecin	Hela, L1010	Entrophospora infrequens	[10]
	chaetomugilide A	HepG2	Chaetomium globosum TY1	[12]
	Cytoglobosins I	LNCap	Chaetomium globosum	[13]
Ketone	Phomone D	HL-60, PC-3, HCT-116	Phoma sp. YN02-P-3	[16][17][18]
	acremoxanthone E	U251, PC-3, HCT-15,	Acremonium camptosporum	[20]
	CHR	MCF-7, SKLU-1	A. alternata KT380662	[21]
Terpenoi-ds	4 S , 6 S) - 6 - [(1 S , 2R)-1,2-]-4-hydroxy-4-Methoxy	MKN45, Lovo, A549, HL-60	Pestalotiopsis sp. DO14	[22]
	4- (2, 3-dihydroxy-3-methyl-butoxyl) -phenylacetic acid	Tca8113, MG-63	Penicillium sp. FJ-1	[23]

	Benzodiazepines A	KATO-3	XG8D	[24]
	Benzodiazepines B			
	Paclitaxel	Hela, MCF-7, A549	Taxomyces andreanae	[27]
	(9R,10R)-dihydro-resinone	Hela, MCF-7	Trichoderma sp. Xy24	[29]
	GL22	Huh.7.5	Ganoderma mushrooms	[32]
Sterides	5α，8α-Peroxyergosterone-6，22-diene-3β- alcohol	CT26	G. luteomarginatum	[33]
	5α，8α-Peroxyergosterone-6，9，22-triene-3β- alcohol Peroxyergosterone			
	Ergot steroid-7，22-diene-3β-alcohol			
	Ergot steroid-7，22-diene-3-ketone			

3. Mechanism of action of antitumor active products from main fungal sources

At present, there are abundant studies on the mechanism of natural active products of fungi at home and abroad. In this paper, the mechanism of action of polysaccharides, terpenes, alkaloids, steroids and other substances will be described and summarized.

3.1 Activity mechanism of fungal polysaccharides

The pharmacological activity of polysaccharides depends on the 1, 3-glycoside bonds in the structure of polysaccharides. Cai et al. [2] confirmed that there are three main anticarcinogenic mechanisms of polysaccharide IOPS extracted from Oboronophila through studies: one is the block cancer cell proliferation in G0 / G1 phase and induce cell apoptosis and differentiation, then it is directly by apoptosis signaling pathways guide, finaly it is indirectly by stimulating the immune system which plays a role of anti-cancer. The polysaccharide from Agaricus matsutake extracted by Ning plays an immunomodulatory role mainly by stimulating the body to produce specific and non-specific immunity. It also has an inhibitory and preventive effect on tumors by inhibiting the metastasis of cancer cells, resisting mutations or reducing the activity of drug metabolizing enzymes in liver mitochondria. In addition, the polysaccharide can destroy the formation of cell wall at different stages of the cell cycle, thus directly killing tumor cells and inhibiting and killing cancer cells [34]. Li et al. extracted polysaccharide -D-glucan from Ganoderma lucidum with serum specific protein or leukocyte surface binding, can activate macrophages natural killer cells T helper cells and other effector cells to produce interleukin-interferon tumor necrosis factor NO and antibody, thus playing an anti-tumor role.

3.2 Activity mechanism of terpenes

Triterpenoids extracted by Jinrida in Betulinus obfuscatus can inhibit tumor growth by making cell proliferation stay in GO/G1 phase. Diterpenoids paclitaxel, on the one hand, can assemble microtubules in cells, so that cancer cells cannot form spindles and spindles, and cell division stays in the late G2 and M stages, inhibiting cell mitosis and inducing cell apoptosis, thus inhibiting the proliferation of tumor cells [36]. On the other hand, paclitaxel can also directly induce cell senescence and apoptosis [37]. The anticancer mechanism of paclitaxel is as follows [38], Figure 1.

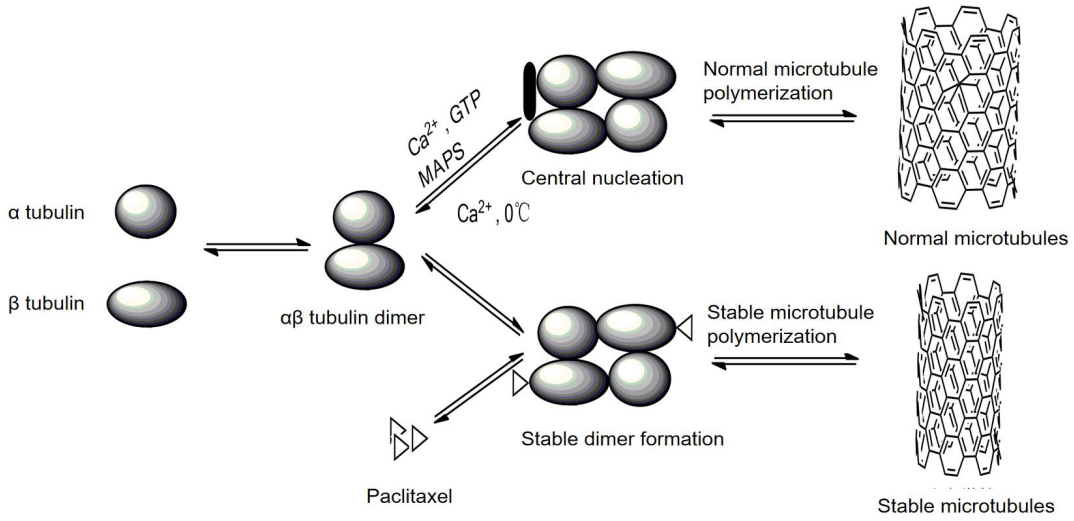

Figure 1. Mechanism of taxol action.

3.3 Alkaloid activity mechanism

The main anti-tumor mechanism of camptothecin is the inhibition of topoisomerase 1, an intraruclear enzyme required for DNA replication, which significantly inhibits the DNA synthesis of tumor cells, leading to DNA fragmentation and tumor cell death [39]. Vinblastine and vincristine are antitumor drugs used to treat lymphoma and leukemia. Both alkaloids prevent metaphase mitosis and bind to tubulin, preventing the cell from producing the spindles it needs to divide. They bind to tubulin in cells, which then lyses and blocks cell division during mitosis, thereby inhibiting tumor growth [40].

3.4 Steroidal activity mechanism

Wu [41] et al. extracted ergosterol peroxide (EP) from Phoma SP belongs to steroid compounds. Its anticancer mechanism is described from the following aspects: 1. According to the current literature, the expression of P53 tumor suppressor gene is directly proportional to the degree of DNA damage, while EP can promote the high expression of P53 tumor suppressor gene, resulting in mitochondrial damage, the release of apoptosis factor CYT C, and the activation of downstream apoptosis executor Caspase-3, promoting the apoptosis of A549 cells. The production of reactive oxygen species (ROS) is usually considered as the cytotoxicity and apoptosis inducer of cancer cells, which is usually formed in the maladjusted mitochondria. EP can increase the intracellular ROS level, which can cause oxidative stress, damage the cellular components such as lipids and DNA, and induce cell growth inhibition and apoptosis. EP can reduce the expression of NLRP3 inflammatome in cells, thereby inhibiting the proliferation and migration of A549 cells. EP can also promote the expression of LC3-2, and the formation of autophagosome in cells can promote the death of A549 cells through autophagy, thus achieving an anti-tumor effect. The specific mechanism is as follows, Figure 2.

4. Existing problem

4.1 Immature artificial culture technology

The technology of large scale directional culture of single flora is lagging behind and the lack of experience is the main obstacle to the development of natural products of fungi into pharmaceutical industry. At present, most of the medicinal fungi in China are wild bacteria or strains obtained in some laboratories within a short time. However, there is no large-scale fungal culture base in China, so the lack of culture technology is an important factor restricting the pharmaceutical industry chain.

4.2 Low purity

The process complexity is an important challenge for clinical application in this field. At present, the application of natural anti-cancer products of fungi in the market is limited to adjutant drugs combined with chemoradiotherapy, which has a great relationship with the backward extraction technology, few purified substances, and the difficulty in achieving medical drug standards. To optimize the process and improve the purification rate has become a hot topic for many scholars.

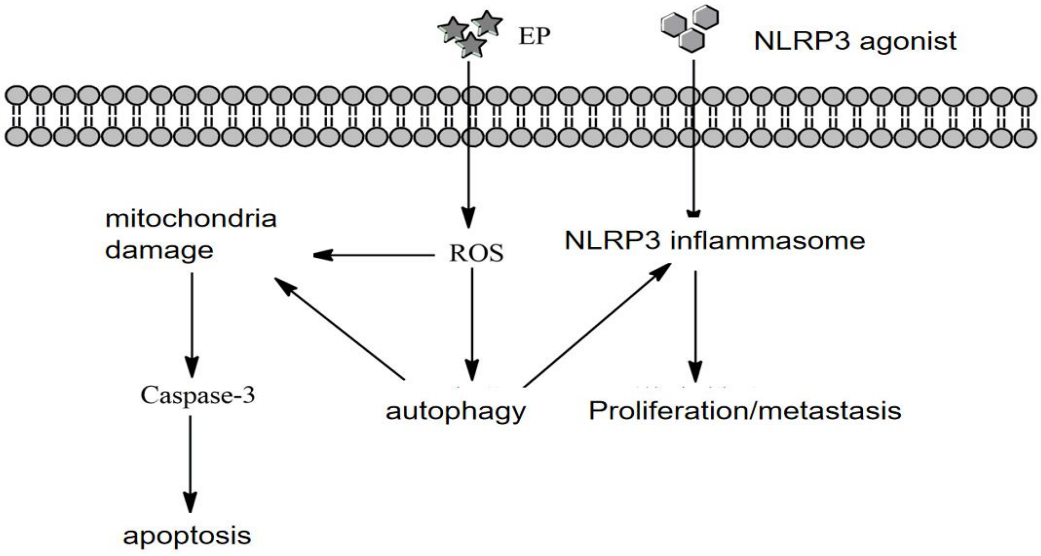

Figure 2. Anti-tumor mechanism of ergosterol peroxide (EP).

4.3 Numerous targets

The complex mechanism is the biggest difficulty for natural products of medicinal fungi to go into clinical practice at present, and many natural products have a time-dependent effect on cancer cells, and the killing effect on cancer cells is also closely related to the immunity of the body, which poses great challenges to drug makers and doctors in terms of dosage and intensity

5. Summary and prospect

Medicinal fungi resources are abundant, sources and the value of natural products is huge, has a broad prospects for development, it is easy to develop fast growth characteristics control, making it possible to quickly a large number of effective anticancer activities of natural products, which the active substances of polysaccharide terpenoids proteins, alkaloids and so on, has its unique anticancer activity and summarizes its mechanism mainly from block cell proliferation cell signaling pathways regulating function of the protein expression enhance cellular immunity and direct toxicology of tumor cells. The review of such mechanisms not only enriches the existing anticancer methods, but also opens up new ideas in clinical medicine.

The natural products of medicinal fungi have shown a broad prospect in the field of anticancer, although the specific toxicology and anti-tumor mechanism of most substances in the natural products of medicinal fungi are still not clear. And the existing industrial techniques for these substances to improve the purity is not up to the medical requirements. Most of the existing research on fungi, plants or land, and the study of marine fungi rare, and many other problems, but neither medicinal fungi, or the product is produced by fungi. Its many advantages such as rapid growth of the wide variety of anti-cancer performance is higher, has showed its huge potential clinical value to us believe in the near future, with the optimization of extraction technology, cultivating technology constantly updated, anti-cancer mechanism unceasing exploration. We can obtain more efficient and more convenient active substances used in the treatment of cancer. At the same time, the production of engineered bacteria by genetic engineering can also play an extremely important role in the development of medicinal fungi.

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References

[1] Guo TL, Yan XJ, Hu XW, et al. Research progress of fungal polysaccharides[J]. Advances in modern biomedical Science, 2013, 13(18):3578-3583.

[2] Cai L. In vitro and in vivo study on anticancer activity of Polysaccharides from Fuscum obliquus[D]. Chongqing University of Technology, 2017.
[3] Meng QL. Pharmacological effects of fermentation products of Mulberry Yellow fungus[D]. Jilin Agricultural University, 2011.
[4] Mizuno T, Iwasaki Y, Satoh H, et al. Studies on the Host-mediated Antitumor Polysaccharides. Part V: Chemical Structure and Antitumor Activity of A Water-soluble Glucan isolated from Tsugasarunokoshikake, the Fruit Body of Fomitopsis pinicola[J]. Bulletin of the Faculty of Agriculture Shizuoka University, 1981, 32:29-40.
[5] Zhaoli M, Xiaoni Q I, Jing Z, et al. Affinity screening and analysis of active components interacted with cancer cells at simulating the in vivo micro-environment from traditional Chinese medicines[J]. Entia Sinica(Chimica), 2014.
[6] Zhang J, Tang Q, Zhou C, et al. GLIS, a bioactive proteoglycan fraction from Ganoderma lucidum, displays anti-tumour activity by increasing both humoral and cellular immune response[J]. Life Sci, 2010, 87(19-22):628-637.
[7] Liang X, Zhang X, Nong X, et al. Eight linear peptides from the deep-sea-derived fungus Simplicillium obclavatum EIODSF 020[J]. Tetrahedron, 2016,72(22):3092-3097.
[8] Ma YM, Liang XA, Zhang HC, et al. Cytotoxic and Antibiotic Cyclic Pentapeptide from an Endophytic Aspergillus tamarii of Ficus carica[J]. J Agric Food Chem, 2016, 64(19):3789-3793.
[9] Wall ME, Wani MC, Cook CE, et al. Plant Antitumor Agents. I. The Isolation and Structure of Camptothecin, a Novel Alkaloidal Leukemia and Tumor Inhibitor from Camptotheca acuminata1,2[J]. Journal of the American Chemical Society, 1966, 88(16):3888-3890.
[10] Amna T, Puri SC, Verma V, et al. Bioreactor studies on the endophytic fungus Entrophospora infrequens for the production of an anticancer alkaloid camptothecin[J]. Canadian Journal of Microbiology, 2006, 52(3):189-196.
[11] Puri SC, Verma V, Amna T, et al. An Endophytic Fungus from Nothapodytes f oetida that Produces Camptothecin[J]. Journal of Natural Products, 2006, 68(12):1717-1719.
[12] Li X, Tian Y, Yang SX, et al. Cytotoxic azaphilone alkaloids from Chaetomium globosum TY1[J]. Bioorganic & Medicinal Chemistry Letters, 2013, 23(10):2945-2947.
[13] Zhang Z, Min X, Huang J, et al. Cytoglobosins H and I, New Antiproliferative Cytochalasans from Deep-Sea-Derived Fungus Chaetomium globosum[J]. Marine Drugs, 2016, 14(12):233.
[14] Verekar SA, Mishra PD, Sreekumar ES, et al. Anticancer activity of new depsipeptide compound isolated from an endophytic fungus[J]. Journal of Antibiotics, 2014, 67(10):697-701.
[15] Ma XK, Zhang H. Synthesis of functional polysaccharides and flavones from Mulberry yellow, an endangered medicinal fungus: The academic Annual Meeting of Chinese Mycelium Society 2018, Tai 'an, Shandong, China, 2018[C].
[16] Sang X, Chen S, Tang M, et al. α-Pyrone derivatives with cytotoxic activities, from the endophytic fungus Phoma sp. YN02-P-3[J]. Bioorganic & Medicinal Chemistry Letters, 2017:S960894X-S17306935X.
[17] Sang XN, Chen SF, Chen G, et al. Phomeketales A–F, six unique metabolites from the endophytic fungus Phoma sp. YN02-P-3[J]. Rsc Advances, 2016, 6(69):64890-64894.
[18] Sang XN, Chen SF, An X, et al. A novel 3,4-dihydronaphthalen-1(2H)-one with spiro-butyrolactone and a new isocoumarin isolated from the endophytic fungus Phoma sp. YN02-P-3[J]. Journal of Asian Natural Products Research, 2016.
[19] Lee MS, Wang SW, Wang GJ, et al. Angiogenesis Inhibitors and Anti-Inflammatory Agents from Phoma sp. NTOU4195[J]. J Nat Prod, 2016, 79(12):2983-2990.
[20] Meléndez-González C, Murià-González MJ, Anaya AL, et al. Acremoxanthone E, a Novel Member of Heterodimeric Polyketides with a Bicyclo[3.2.2]nonene Ring, Produced by Acremonium camptosporum W. Gams (Clavicipitaceae) Endophytic Fungus[J]. Chemistry & Biodiversity, 2015, 12(1):133-147.
[21] Seetharaman P, Gnanasekar S, Chandrasekaran R, et al. Isolation and characterization of anticancer flavone chrysin (5,7-dihydroxy flavone)-producing endophytic fungi from Passiflora incarnata L. leaves[J]. Annals of Microbiology, 2017, 67(4):321-331.
[22] Wu L S, Jia M, Chen L, et al. Cytotoxic and Antifungal Constituents Isolated from the Metabolites of Endophytic Fungus DO14

from Dendrobium officinale[J]. 2015.
[23] Zheng C, Chen Y, Jiang LL, et al. Antiproliferative metabolites from the endophytic fungus Penicillium sp. FJ-1 isolated from a mangrove Avicennia marina[J]. Phytochemistry Letters, 2014, 10:272-275.
[24] Siwattra C, Thapong T, Tohru M, et al. Chamigrane Sesquiterpenes from a Basidiomycetous Endophytic Fungus XG8D Associated with Thai Mangrove Xylocarpus granatum[J]. Marine Drugs, 2016, 14(7):132.
[25] Li W, Sun YN, Lee C, et al. Annulohpoxylotol A and B, new sesquiterpenoids from the endophytic fungusAnnulohypoxylon truncatum, are natural NF-κB inhibitors[J]. Archives of Pharmacal Research, 2017, 40(2):152-158.
[26] Wani MC, Taylor HL, Wall ME, et al. Plant antitumor agents. IV. The isolation structure of taxol, a novel antileukemic and antitumor agent from Taxus brevifolia[J]. Journal of the American Chemical Society, 1971, 93(9):2325-2327.
[27] Stierle A, Strobel G, Stierle D. Taxol and taxane production by Taxomyces andreanae, an endophytic fungus of Pacific yew[J]. Ence, 1993, 260(5105):214.
[28] Feng X, Tao W, Long C, et al. Strain improvement and optimization of the media of taxol-producing fungus Fusarium maire[J]. Biochemical Engineering Journal, 2006, 31(1):67-73.
[29] Zhang M, Liu JM, Zhao JL, et al. Two new diterpenoids from the endophytic fungus Trichoderma sp. Xy24 isolated from mangrove plant Xylocarpus granatum[J]. Chinese Chemical Letters, 2016.
[30] Chen H, Yang HL, Liu GQ. Biosynthesis and fermentation regulation of triterpenes from Ganoderma lucidum[J]. Journal of Fungi, 2015, 34(01):1-9.
[31] Hao MM, Wang JY, Feng N, et al. Comparison of anti-tumor and anti-inflammatory activities of triterpenes of different polarity in fruite bodies of Ganoderma lucidum in vitro[J]. Journal of Fungi, 2019, 38(06):917-925.
[32] Ge L, Kai W, Shan K, et al. The natural compound GL22, isolated from Ganoderma mushrooms, suppresses tumor growth by altering lipid metabolism and triggering cell death[J]. Cell Death & Disease, 2018, 9(6):689.
[33] Su HG. Chemical constituents and cytotoxic activity of Huangbian Ganoderma lucidum[D]. Chengdu University of Traditional Chinese Medicine, 2018.
[34] Zhou N. improvement of human health by polysaccharide from agaricus matsutake[J]. Chinese Edible Fungi, 2020, 39(01):38-41.
[35] Li LW, Zhao G. Research progress of antitumor immunobioactivity of medicinal fungal polysaccharides[J]. Chinese Journal of Cancer Prevention and Treatment, 2015, 22(14):1156-1160.
[36] Jin L, Ou WB, Xu XQ. Study on triterpenoids in liquid fermentation of Fusillomonas oryzae inhibiting tumor cell activity [J]. University of South China, 2018.
[37] Shi Q W. History of natural Medicine chemistry: Paclitaxel[J]. Chinese Herbal Medicine, 2011, 42(10):1878-1884.
[38] Chen L, Zhang QY, Jia M, et al. Endophytic fungi with antitumor activities: Their occurrence and anticancer compounds.[J]. Critical Reviews in Microbiology, 2014:1-20.
[39] Chandra S. Endophytic fungi: novel sources of anticancer lead molecules[J]. Applied Microbiology & Biotechnology, 2012, 95(1):47-59.
[40] Wu H, Yang F, Li L, et al. Ergosterol peroxide from marine fungus Phoma sp. induces ROS-dependent apoptosis and autophagy in human lung adenocarcinoma cells[J]. Scientific Reports, 2018, 8(1).