https://doi.org/10.47183/mes.2025-250

APPLICATION PROSPECTS OF PLANT AND FUNGAL COMPOUNDS IN ANTITUMOR THERAPY

Tatiana V. Gasanova✉, Maria N. Repina, Peter A. Ivanov
Lomonosov Moscow State University, Moscow, Russia

Introduction. Anticancer inhibitors of plant and fungal origin (IPFOs) represent a promising direction in antitumor therapy, offering a variety of mechanisms of action, in most cases different from conventional chemotherapeutic drugs. As a rule, IPFOs simultaneously affect several metabolic pathways, exerting a combined effect on different targets in the cancer cell and reducing the risk of drug resistance development.
Objective. To study promising directions in the development of new antitumor drugs, to generalize current data on the IPFO mechanism of action in the context of a combined approach to cancer treatment.
Discussion. Compounds exhibiting antitumor activity are increasingly attracting the research attention. Due to their diverse mechanisms of action, anticancer IPFOs represent a promising direction in cancer treatment. A large number of conventional chemotherapy drugs, although being of plant origin, demonstrate high effectiveness, which confirms the relevance of searching for new anticancer IPFO compounds. Solid tumors exhibit a pronounced ability to both proliferate and induce angiogenesis, which justifies the current active search for new plant-derived compounds with antiangiogenic properties, along with other IPFOs. As a rule, anticancer IPFOs simultaneously affect several metabolic pathways, exerting a combined effect on different targets in the cancer cell and reducing the risk of drug resistance.
Conclusions. This review has examined the molecular mechanisms of IPFO action, including suppression of angiogenesis and cancer cells proliferation, apoptosis induction, cell cycle modulation, and direct cytotoxic effect by stimulating the activity of $CD8^+$ T lymphocytes, NK cells, and macrophages.

Keywords: antitumor therapy; plant- and fungus-derived tumor inhibitors; apoptosis; programmed cell death; angiogenesis; autophagy; ferroptosis; cell cycle regulation

For citation: Gasanova T.V., Repina M.N., Ivanov P.A. Application prospects of plant and fungal compounds in antitumor therapy. *Extreme Medicine.* 2025;27(3):309–319. https://doi.org/10.47183/mes.2025-250

Funding: the research was carried out within the state assignment (theme No. 121032500078-5 of 2021–2025).

Potential conflict of interest: the authors declare no conflict of interest.

✉ Tatiana V. Gasanova tv.gasanova@gmail.com

Received: 13 Jan. 2025 **Revised:** 01 Apr. 2025 **Accepted:** 28 Apr. 2025 **Online first:** 20 Aug. 2025

УДК 615.3

ПЕРСПЕКТИВЫ ПРИМЕНЕНИЯ СОЕДИНЕНИЙ РАСТИТЕЛЬНОГО И ГРИБНОГО ПРОИСХОЖДЕНИЯ В ПРОТИВООПУХОЛЕВОЙ ТЕРАПИИ

Т.В. Гасанова✉, М.Н. Репина, П.А. Иванов

Московский государственный университет им. М.В. Ломоносова, Москва, Россия

Введение. Ингибиторы растительного и грибного происхождения (ИРГП) представляют собой перспективное направление в противоопухолевой терапии, предлагая разнообразные механизмы действия, в большинстве случаев отличающиеся от традиционных химиотерапевтических препаратов. Как правило, ИРГП одновременно влияют на несколько метаболических путей, что снижает вероятность развития резистентности, оказывая комбинированный эффект на разные мишени в раковой клетке.
Цель. Изучить перспективные направления в создании новых противоопухолевых препаратов для последующего лечения, обобщить современные данные о механизмах действия ИРГП в контексте комплексного подхода к лечению злокачественных опухолей.
Обсуждение. В настоящее время усиленно проводится поиск новых соединений с противоопухолевым потенциалом. ИРГП представляют собой перспективное направление в противоопухолевой терапии, предлагая разнообразные механизмы действия. Многие традиционные химиотерапевтические препараты также имеют растительное происхождение и обладают хорошей эффективностью, что подтверждает актуальность изучения данной тематики. Солидные опухоли обладают повышенной способностью к активной пролиферации и ангиогенезу, что объясняет неизменный интерес к активному поиску новых соединений растительного происхождения с антиангиогенными свойствами, наряду с исследованиями других ИРГП. Как правило, ИРГП одновременно влияют на несколько метаболических путей, что снижает вероятность развития резистентности, оказывая комбинированный эффект на разные мишени в раковой клетке.
Выводы. В обзоре рассмотрены молекулярные механизмы действия ИРГП, включающие в себя подавление ангиогенеза и пролиферации раковых клеток, индукцию апоптоза, модуляцию клеточного цикла, а также прямой цитотоксический эффект путем стимуляции активности $CD8^+$ Т-лимфоцитов, NK-клеток и макрофагов.

Ключевые слова: противоопухолевая терапия; растительные и грибные ингибиторы опухолей; апоптоз; запрограммированная клеточная смерть; ангиогенез; аутофагия; ферроптоз; регуляция клеточного цикла

Для цитирования: Гасанова Т.В., Репина М.Н., Иванов П.А. Перспективы применения соединений растительного и грибного происхождения в противоопухолевой терапии. *Медицина экстремальных ситуаций.* 2025;27(3):309–319. https://doi.org/10.47183/mes.2025-250

Финансирование: исследование выполнено в рамках государственного задания № 121032500078-5 от 2021–2025 гг. ФГБУ «МГУ имени М.В. Ломоносова».

Потенциальный конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

✉ Гасанова Татьяна Владимировна tv.gasanova@gmail.com

Статья поступила: 13.01.2025 **После доработки:** 01.04.2025 **Принята к публикации:** 28.04.2025 **Online first:** 20.08.2025

INTRODUCTION

Although a wide range of effective antitumor drugs have been developed to date, this field continues to remain relevant due to the search for optimal drug combinations with the least number of side effects. In this connection, plant- and fungus-derived compounds are attracting particular attention [1]. The available data suggest that natural compounds affecting autophagic and apoptotic pathways are effective mediators of cancer therapy with specificity for target cancer cells. The multidirectional antitumor effect of natural compounds in combination with their low toxicity are significant prerequisites for the development of drugs for cancer prevention and cancer treatment [1].

Cancer inhibitors of plant and fungal origin (IPFOs) have slightly different mechanisms of action in antitumor therapy. The plant-derived cancer inhibitors mainly affect the cellular signaling pathways of carcinogenesis, while exhibiting an anti-inflammatory effect. The fungus-derived cancer inhibitors are capable of stimulating the immune response with subsequent tumor recognition or preventing cancer cell division. An important advantage of IPFOs as candidate substances consists in the presence of properties essential for all drug medications, such as gastrointestinal absorption and metabolism action. In addition, IPFOs demonstrate a high chemical diversity necessary to study correlations between activity and structure [2]. Some first plant-derived drugs (paclitaxel, vinblastine, vincristine, topotecan, irinotecan, and teniposide), have been extensively studied, partially modified, and approved by the U.S. Food and Drug Administration (FDA, USA). These medicines are not the subject of this review [3].

In this study, we analyze promising directions in the development of anticancer drugs, review the current data on the mechanisms of IPFO action in the context of a combined approach to cancer treatment.

MATERIALS AND METHODS

In addition to the Google Scholar and PubMed search system, the Naturally Occurring Plant-based Anti-cancerous Compound-Activity-Target Database (NPACT, http://crdd.osdd.net/raghava/npact/) was used. NPACT features about 1980 experimentally confirmed interactions of compounds and targets. The search queries included the following keywords: anticancer therapy; plant and fungal cancer inhibitors; apoptosis; programmed cell death; angiogenesis; autophagy; ferroptosis; cell cycle regulation (in Russian and English). The search depth was 10 years. The inclusion criteria were the relevance and practical significance of the publications, as well as the availability of preclinical and clinical trial data.

RESULTS AND DISCUSSION

The search for compounds with antitumor potential is currently underway. Anticancer IPFOs represent a promising direction in cancer treatment, offering a variety of mechanisms of action. There is a large number of conventional chemotherapy drugs with high effectiveness, which are also of plant origin. This circumstance justifies the relevance of searching for new compounds. Solid tumors exhibit a pronounced ability to both proliferate and induce angiogenesis, driving the need to develop new plant-derived compounds with antiangiogenic properties, along with the investigation of other IPFOs. As a rule, anticancer IPFOs affect several metabolic pathways simultaneously, exerting a combined effect on different targets in the cancer cell and reducing the risk of drug resistance development.

Among the main methods used to identify compounds with a certain activity are gene cloning, DNA and RNA sequencing, studying the compounds effect on the enzymes activity involved in the relevant metabolic pathways, evaluating differential gene expression using microarrays, flow cytometry, the use of various cell cultures, including those of tumor origin, the use of animal models to assess the systemic effect of the compound, as well as its pharmacokinetics and pharmacodynamics, multidimensional statistical analysis to assess the reliability of the results obtained. The largest amount of information on natural anticancer compounds in NPACT concerns those derived from plants [4]. Many anticancer IPFO have been isolated from herbs used in traditional Chinese medicine [5]. However, it should be noted that not only plant-derived, but also fungus-derived, medications have been found to possess anticancer potential. The key classes of inhibitory compounds for plants and fungi are phenolic compounds and terpenoids. At the same time, in plants, it is alkaloids, flavonoids, and coumarins that demonstrate similar anticancer properties, while in fungi, these are polysaccharides, glucans, steroids, cerebrosides, and proteins. The diverse mechanisms of action of such compounds include apoptosis induction, inhibition of angiogenesis and the cell cycle, immunomodulation, reprogramming of cellular signaling pathways involved in carcinogenesis, as well as various antioxidant and anti-inflammatory effects (Table 1).

Induction of programmed cell death

Apoptosis

Apoptosis, i.e., programmed cell death, occupies a special place among various processes associated with cell cycle regulation, correct functioning of the immune system, hormone-dependent atrophy, and embryo development [9]. The ability of chemical compounds to induce apoptosis determines their significant

Table 1. Classes of inhibitor compounds and their mechanisms of action

Plants	Fungi
Inhibitory compound classes	
alkaloids	polysaccharides
phenolic compounds (polyphenols)	
flavonoids	glucans
terpenoids	
coumarins	steroids
	cerebrosides
	proteins
Mechanisms of action	
induction of cancer cell apoptosis (programmed cell death)	
angiogenesis inhibition (formation of new blood vessels feeding the tumor)	
Modulation of cellular signaling pathways involved in cancer development	Immunomodulation: Some fungus-derived compounds can stimulate the immune system to recognize and attack tumor cells. This includes increased activity of natural killer cells (NK), T lymphocytes, and macrophages
Antioxidant and anti-inflammatory effects	Cell cycle inhibition: other drugs affect the most important proteins and processes involved in cytokinesis, preventing tumor cell reproduction

Table prepared by the authors using data from the references [1–3, 5, 6–8]

therapeutic potential. The following IPFOs can serve as such examples.

Icaritin induces programmed cell death of ovarian cancer cells by activating the apoptosis pathway through p53 and inhibiting the Akt/mTOR signaling pathway [10]. The curcumin anticancer activity may directly depend on the effect on the p53 pathway in human osteosarcoma (HOS) cells [11]. The triggering of internal and external apoptosis pathways is also responsible for the curcumin anticancer effects in monocytic leukemia (SHI-1) cells [12]. It was shown that matrine is capable of stimulating the main apoptotic cascades by increasing the accumulation of Fas and FasL, Bax proteins, while reducing the amount of Bcl-2 apoptosis regulator, which leads to activation of caspases-3, -8, and -9 in human osteosarcoma MG-63 cells, as well as U-2OS, Saos-2, and MNNG/HOS [6, 13]. The molecular mechanism of action of tetrandrine in cancer cells is aimed at increasing the number of Bax, Bak, Bad, and Apaf-1 apoptotic proteins, while the number of Bcl-2 and Bcl-xl antiapoptotic proteins in the cell decreases with the release of cytochrome *c* (cyt *c*) and activation of caspase-3 and caspase-9 in the mitochondrial pathway of apoptosis [14, 15].

A number of studies on animal models showed that epigallocatechin gallate (EGCG) can inhibit the growth of malignant cells and induce apoptosis even in cancer cell lines resistant to CD95-mediated apoptosis [16]. Saikosaponin A has proapoptotic activity, namely, it positively regulates the pathway mediated by Bax/Bcl-2/caspase-9/caspase-7/PARP [17], causing apoptosis of human colon cancer cells SW480 and SW620 (colon cancer cell lines derived from primary tumors and lymph node metastases, respectively) in a dose-dependent manner, which is obviously related to the inhibition of the PI3K/Akt/mTOR signaling pathway [18]. Bavachinin can influence the expression of Bcl-2, Bax, caspase-3/9, and the peroxisome proliferator γ (PPARγ) receptor. The bavachinin-induced generation of reactive oxygen species (ROS) depends on the PPARγ activation, which is capable of inducing A549 cell death. The effect caused by an increase in the level of reactive oxygen species (ROS) highlights the potential role of bavachinin as a chemotherapeutic agent against non-small cell lung cancer [19]. Gossypol can interact with the BH3 domain binding groove of the Bcl-xL and Bcl-2 antiapoptotic proteins. Simultaneous incubation of non-Hodgkin's lymphoma Ramos cells with gossypol and etoposide enhances

apoptosis due to the intensive release of cytosolic cyt *c* and activation of caspase-3 signaling depending on time intervals. These results are the basis for future preclinical and clinical studies of gossypol in the treatment of non-Hodgkin's lymphoma [20]. It was shown that the action mechanism of resveratrol involves the blocking of certain transcription factors, such as B cell nuclear factor (NF-kB), AP-1 and Egr-1, as well as a decrease in the expression of antiapoptotic genes and activation of caspases. Its ability to influence the immune response mediated by B cells and increase the serum level of antibodies, exerting an antitumor effect, was previously revealed [21].

Autophagy and ferroptosis

Autophagy is a cellular degradation process leading to the removal of improperly folded or aggregated proteins, as well as the degradation of damaged organelles such as mitochondria, endoplasmic reticulum (EPR), and peroxisomes [22]. Autophagy can inhibit the growth and progression of malignant tumors, since the removal of damaged or non-functioning organelles prevents oncogenesis. At the same time, stimulation of autophagy remains an effective approach in antitumor therapy.

The mammalian target of rapamycin, mTOR, which has the properties of a modulator of cell growth and proliferation, and AMP-activated protein kinase (AMPK), responsible for signal conversion in response to various metabolic stresses, are regulators of autophagy initiation [23]. This process prevents tumor development only provided the possibility of selective autophagy, targeting certain cell organelles [24]. In cases where a tumor has already formed, autophagy suppression often leads to the development of less aggressive cancer forms [25]. It was shown that synthetic quinine analogues — chloroquine (CQ), isolated from the cinchona bark (*Cinchona officinalis*), and hydroxychloroquine (HCQ) — are the most common drugs used to treat acute and chronic inflammatory diseases. These drugs are also used in cancer treatment based on autophagy inhibition mechanisms, which consist in interrupting the fusion of autophagosomes and lysosomes [26].

According to Solomko et al., matrine-induced signals in tumor cells can lead to ferroptosis (has a protective effect against cervical cancer) [6, 13]. Matrine exhibits considerable antitumor activity both *in vitro* and *in vivo*, along with other beneficial properties, e.g., antianxiety and antidepressive effects, relieving neuroinflammation in the brain caused by severe diseases. The mechanism of action of this compound is based on the suppression of cell proliferation and apoptosis induction, e.g., the highly metastatic breast cancer cell line MDA-MB-231 uses the VEGF-Akt-NF-kB signaling pathway. Unfortunately, numerous anticancer drugs (such as etoposide, tyrosine kinase inhibitors, arsenic trioxide, 5-fluorouracil) that cause ferroptosis are cardiotoxic [27]. To address this issue, non-toxic cardioprotective antitumor plant-derived medications with anticancer activity, such as berberine, epigallocatechin gallate, and resveratrol, have been developed and are used in combination with conventional chemotherapeutic agents [16, 21, 28].

Angiogenesis inhibition

Tumors induce the growth of new blood vessels due to releasing various growth factors, including vascular endothelial growth factor (VEGF). This results in the formation of blood capillaries inside the tumor. Protein Kinase G (PKG) regulates beta-catenin levels in healthy cells, promoting angiogenesis. Angiogenesis, in turn, is an important factor in the spread of tumor metastases. Fennel extracts — *Trianthema portulacastrum* and *Spatholobus suberectus* — inhibit tumor growth and angiogenesis, as well as alter the expression of HSP90 heat shock protein and its co-chaperone interactions in mouse models of breast cancer. These findings on the role of HSP90 in breast cancer biology and therapy are consistent with the effects described in the current literature. In fact, tumor growth and angiogenesis decrease when HSP90 is suppressed by the interaction of the KU-32 inhibitor with the C-terminal domain of this chaperone in trastuzumab-resistant HER2-positive breast cancer cells [29]. Morelloflavone blocks injury-induced neointimal hyperplasia by inhibiting vascular smooth muscle cell migration without causing apoptosis or cell cycle arrest [30]. Thus, the use of certain compounds of natural origin suppresses the formation of new blood vessels that require a significant amount of oxygen and nutrients for their growth, which can increase the antitumor effect [7].

Modulation of cellular signaling pathways

MAPK paths. Phytochemicals can affect both the cascade pathway kinase regulated by extracellular signals (ERK) and mitogen-activated protein kinases (MAPK) regulating cell growth and cell survival. Phytochemicals such as ursolic acid, kaempferol, resveratrol, gingerol, sulforaphane, genistein, and isothiocyanates have been reported to induce cancer cell apoptosis through the MAPK and ERK pathways [31]. It was shown that curcumin exerts the anticancer effect on retinoblastoma cells (RB, Y79) by activating exclusively the MAPK pathway.

Akt signaling pathways. The Act/PI3 signaling pathway plays an important role in cancer development. Epidermal growth factor (EGF) regulates a number of molecular mechanisms, including NF-kB activation and Akt phosphorylation. This promotes resistance to apoptosis and uncontrolled cell proliferation, which in turn leads to effects on caspases, Bcl-2 and glycogen synthase 3-β (GSK3b) kinases, as well as mTOR. Alkaloids and phenolic compounds make a significant contribution to the control over the expression of these factors. Resveratrol, curcumin, luteolin, flavone, and sulforaphane

exhibit anticancer properties by ceasing the cell cycle and apoptosis, interfering with Akt/PI3K signaling [32]. In addition, Saikosaponin A inhibits the invasion and migration of SK-N-AS cells (human neuroblastoma cells) by regulating the angiogenesis-associated VEGFR2/Src/Akt pathway and protein expression associated with epithelial-mesenchymal transition (EMT) [17].

JAK/STAT signal transmission paths. By inhibiting the activity of JAK/STAT signaling and activating apoptotic cascades, the curcumin, resveratrol, and EGCG phytochemical compounds inhibit the translocation and collection of β-catenin in the nucleus by stimulating glycogen synthase kinase 3 (GSK3), which can lead to cell death in some forms of cancer [33].

Antioxidants with anti-inflammatory effects

Harmala extract (*Peganum harmala*) can reduce the viability of cervical carcinoma and colon cancer cells due to the action of alkaloids contained in high concentrations therein. In a study aimed at investigating cytotoxicity towards normal and tumor cells, the antioxidant activity of these alkaloids against human breast cancer cells was noted [34]. Three main epigenetic changes occur in tumor cells treated with plant polyphenols, i.e., a change in the structure of chromatin, DNA methylation, and, more importantly, alterations in the microRNAs level. For the same microRNAs, expression is increased in some tumors, while in others, on the contrary, it is reduced. Thus, the expression of the mi-Let-7 cluster increases in breast tumors and, conversely, decreases in lung tumors. Notably, EGCG, curcumin, and resveratrol modulate several classes of microRNAs that are involved in all stages of cancer development and regulate oncogenes or tumor suppressors of various cancers [16, 21]. In particular, tetrandrine was shown to exhibit antiproliferative effects and cytotoxic activity against breast cancer (MDA-MB-231, HCC1937, MCF7) [14, 15].

Cell cycle regulation

The cell cycle is a sequence of intracellular events, leading to cell division. The stages of the cell cycle are mediated by cyclin-dependent kinases (CDK) and their regulatory cyclin subunits [35]. Vindoline and catharanthine have antitumor effects due to their exposure in the M-phase cell cycle. They contribute to the cancer cell death by shortening microtubules and disrupting their function, which leads to the disappearance of mitotic spindle, thereby suppressing cell proliferation [34].

Quercetin can affect the cell cycle at the G1/S and G2/M control points by inducing the CDK p21 inhibitor and reducing the phosphorylation of the key regulatory pRb protein and indirectly blocking E2F, which are important factors of transcription and DNA synthesis [36]. The roscovitin synthetic compound, produced from the natural substance olomucine isolated from the *Raphanus sativus* (*Brassicaceae*) daikon, has passed clinical trials, showing high activity against various types of cancer. This medication is currently at the stage of clinical evaluation of efficacy in the treatment of Cushing's disease and rheumatoid arthritis [37]. This drug is an inhibitor of cyclin-dependent kinases, preventing their activation and DNA repair due to non-homologous end joining (NHEJ). One of the most noticeable effects of the drug is the inhibition of formation of CDK2/cyclin E complexes, which causes a decrease in the pRb phosphorylation level and subsequent inactivation of members of the E2F family, leading to suppression of cyclin transcription and, ultimately, to cell cycle arrest. In this case, cell cycle arrest leads to the initiation of apoptotic death [6]. The modes of flavopiridol action are associated with the phosphorylation of cyclin-dependent kinases that block cell proliferation in G1 and G2 phases, and the apoptosis induction by increasing the level of E2F synthesis and Mcl-1 protein inactivation. A study in which the effect of EGCG on oncogenesis was tested on oral cancer (NOE) cell lines together with curcumin showed the EGCG ability to block cell division in G1, whereas curcumin blocked cell division in S/G2/M phases. The antagonistic interaction between curcumin and etoposide is caused by cell cycle arrest, which gives time for DNA damage to repair and prevents cell death. Another polyphenol, quercetin, may limit the effect of etoposide. Quercetin has a protective effect on HL-60 cells from etoposide, reducing the level of ROS generated in drug-treated cells (Table 2) [38, 39].

Fungus-derived compounds

Cancer fungotherapy and the search for new anticancer agents are not limited to such fungi species as *Fomitopsis pinicola*, *Hericium erinaceus*, *Trametes versicolor*, and *Inonotus obliquus* from the *Basidiomycota* class. However, these four species can serve as typical representatives of medicinal fungi, which are widely used both in conventional medicine and in modern biomedical research. They belong to three different groups and are a rich source of bioactive compounds such as polyphenols, polysaccharides, glucans, terpenoids, steroids, cerebrosides, and proteins that show potential for treating various types of cancer [8]. Ergosterol is an active *Fomitopsis pinicola* fungus-derived compound, which is the main component affecting SW-480 cells and causing their apoptosis. Interestingly, the use of this extract in combination with cisplatin, a common chemotherapeutic agent, in mice showed their synergistic effect of impeding tumor growth. Taken together, these results provide solid evidence that, in addition to nonspecific cytotoxic compounds, *F. pinicola* contains substances with a specific antioncogenic potential, probably acting through the induction of apoptosis [48].

Krestin, isolated from the mycelium of the *Trametes versicolor* wood fungus, belongs to the class of polysaccharides. This compound shows significant

Table 2. Antitumor inhibitors of plant and fungal origin

Title	Compound class	Extracted from	Mechanism	Cell lines	Literature source
Compounds of plant origin					
Vindoline and catharanthine	Alkaloid	*Vinca rosea*	Effect on the cell in the M-phase of cell cycle; shortening of microtubules, disruption of their function, which leads to the mitotic spindle disappearance, thereby suppressing cell proliferation	Kaposi's sarcoma, melanoma, nasopharyngeal cancer, breast cancer, kidney, bladder, breast cells, prostate, cervix (MCF-7, PC3-1C, HeLa)	[6]; [34]
Matrine	Alkaloid	*Sophora flavescens*	Stimulation of the main apoptotic cascades by accumulating Fas/FasL, Fas and reducing Bcl-2 levels, which leads to activation of caspase-3, -8 and -9	Human osteosarcoma cells (MG-63, U2OS, Saos-2 and NG/HAS)	[6]; [13]
Tetrandrine	Alkaloid	*Stephania tetrandra*	Positive regulation of the Bax, Bak, Bad, and apaf-1 pathways; reduction of Bcl-2 and Bcl-xl levels; release of cytochrome *c* and activation of caspase-3 and -9	Breast cancer cells (MDA-MB-231, HCC1937, MCF7)	[14]; [15]
Epigallocatechin gallate	Polyphenol	Green Tea, *Camellia sinensis*	Induction of apoptosis, arrest of cell growth by changing the expression of regulatory proteins of the cell cycle; activation of killer caspases and suppression of NFkB activation; inhibition of Bcl-2 and Bcl-XL expression, as well as induction of Bax, Bak, Bcl-XS and PUMA expression	*In vitro* model: esophagus; oral cavity; prostate; mammary gland; urinary tract; lungs; colon; leukemia; lymphoma. *In vivo* model: cancer of the skin, prostate, colon and uterus; cancer of the stomach, pancreas and oral cavity in humans	[16]; [21]
Curcumin	Polyphenol	Rhizome, *Curcuma longa*	Effects on the p53 pathway, activation of the MAPK pathway, an increase in the Bax:Bcl-2 ratio and the release of cytochrome *c*, the second mitochondrial activator of caspases/direct binding protein IAP	Human osteosarcoma cells (HAS), retinoblastoma cells (RB Y79), monocytic leukemia cells (SHI-1)	[11]; [12]; [38]; [40]
Resveratrol	Polyphenol	A component of white hellebore roots, *Veratrum grandiflorum*	Blocking of certain transcription factors such as NF kB, AP-1, and Egr-1; decreased expression of antiapoptotic genes and activation of caspases	Squamous cell carcinoma of the human esophagus	[6]; [21]; [31]; [32]
Gossypol	Polyphenolic aldehyde	Cotton plant, *Gossypium sp., Malvaceae*	Binding of antiapoptotic proteins Bcl-xL and Bcl-2 to the groove of the BH3 domain; enhancement of apoptosis due to the release of cytosolic cytochrome *c* and activation of caspase-3 signaling	Non-Hodgkin's lymphoma cells	[20]
Saikosaponin a	Terpenoid	*Radix Bupleuri,* root	Activation of the Bax/Bcl 2 cascade and caspase-9, caspase-3, associated with inhibition of the PI3K/Akt/mTOR signaling pathway	Human neuroblastoma cells (SK-N-AS), Human colon cancer cells (SW480, SW60)	[17]; [18]

Table 2 (continued)

Title	Compound class	Extracted from	Mechanism	Cell lines	Literature source
Bavachinin	Flavonoid	*Psoralea corylifolia,* legume family	PPARγ activation leading to ROS generation	Non-small cell lung cancer (A549)	[19]
Icaritin	Flavonoid	Traditional Chinese herb, *Epimedium Genus*	Activation of apoptosis via p53 and inhibition of the Akt/mTOR pathway	Ovarian cancer, leukemia, lymphoma and multiple myeloma	[10]; [41]; [42];
Quercetin	Flavonoid	Larch, *Larix*	Generation of free radicals that lead to oxidative damage of nucleic acids, lipid peroxidation and cell death; possibility to cause apoptosis through the AMPK-α or COX-2 signaling pathway	Human hepatocyte cells, epithelial cell lines, prostate cancer	[14]; [36]; [38]; [39]
Morelloflavone	Flavonoid	Seeds, *Garcinia morella*	Inhibition of activation of RhoA and Rac1 GTPases with insignificant effect on Cdc42 GTPase activation. Inhibition of phosphorylation and kinase activation of the Raf/MEK/ERK pathway, without affecting VEGFR2 activity	U87 glioma cells and C6 rat glioma cells	[30]; [43]; [44]
Fungus-derived compounds					
Krestin	Polysaccharide	Mycelium of wood, *Trametes versicolor*	The ligand for TLR4 receptors leads to the induction of inflammatory cytokines TNF-alpha and IL-6	Allogeneic and syngeneic tumors of animals	[45]; [46]
Lentinan	Polysaccharide	Wood fungus, *Lentinus edodes*	Stimulation of T-lymphocytes, induction of interleukins 1 and 3, as well as the production of nitric oxide by immune cells, leading to an increase in the level of colony-stimulating factor and the level of proteins of the acute phase of inflammation	Tumors of the stomach, bones and breast	[47]
Ergosterol	Polysaccharide	*Fomitopsis pinicola*	Induction of apoptosis: increased levels of pro-apoptotic proteins such as BAX, caspase-7 and PARP, and decreased amounts of anti-apoptotic proteins BCL-2 and STAT-3	Breast cancer cell lines	[48]; [49]
Aqueous extract		*Hericium erinaceus*	Suppression of antiapoptotic proteins (Bcl-2, Bcl-xL(S), XIAP and cIAPs) in the absence of increased proapoptotic proteins	Various cancer cell lines and tumors associated with the digestive tract	[50]; [51];

Table prepared by the authors using data from the references [6, 10–21, 46–49, 31, 32, 34, 36, 38–50]

antitumor activity against allogeneic and syngeneic animal tumors [45].

Polysaccharide-K (PSK) demonstrates a similar activity in various types of cancer, especially in gastrointestinal cancer. This medicine has been approved in Japan and China for use in cancer treatment [49]. Lentinan (isolated from *Lentinus edodes*) also belongs to the class of polysaccharides. This compound prevents neoplastic transformations caused by chemical carcinogens and viruses, while also suppressing the development of allogeneic and some syngeneic tumors. This polysaccharide is most often used in the treatment of tumors of the stomach, bones, and breast. The action mechanism of lentinan involves stimulation of $CD8^+$ T lymphocytes, induction of interleukins 1 and 3, as well as the production of nitric oxide by immune cells. This leads to an increase in the synthesis of colony-stimulating factor (CSF) and the accumulation of proteins of the inflammation acute phase in combination with direct and indirect (through T lymphocytes) effects on macrophages. Lentinan showed clinical efficacy in various types of cancer, including stomach and lung cancer [47]. Another study by the same scientific group was devoted to the use of conk extracts from the *Hericium erinaceus* fungus with various solvents and testing for cytotoxicity against human monocytic leukemia U937 cells. The results showed that both aqueous and ethyl extracts can induce apoptosis. The suggested mechanism of action is through the suppression of anti-apoptotic factors (Bcl-2, Bcl-xL(S), XIAP and cIAPs) in combination with the absence of an increase in the level of pro-apoptotic proteins.

Erinacin A, a mycelial derivative of *H. erinaceus*, demonstrates activity that suppresses the growth of various gastrointestinal tumor lines [50]. Extracts of *H. erinaceus* or their fractions/components were shown to exhibit immunostimulating activity; antimetastatic activity by inhibiting matrix metalloproteinases; activity promoting the growth of probiotic intestinal flora; antioxidant potential; proapoptotic activity; and angiogenesis inhibition. This range of anticancer properties is provided by various compounds, including polysaccharides, lipids, terpenoids (unique erinacins), and even proteins. Thus, there are two possible strategies for the investigation of *H. erinaceus* anticancer effects, such as studying the complex effects of extracts with their further use as preventive dietary supplements and a detailed study of the mechanisms of individual fungus-derived compounds for use in targeted personalized anticancer therapy [51]. The anticancer potential of the *Inonotus obliquus* fungus is represented by several groups of components. Unique triterpenoids such as lanostane, inotodiol, and inonotsuoxides act *in vivo* on preparations of mouse skin and tumors of mouse xenografts derived from human chronic lymphocytic leukemia. Low molecular weight polyphenolic compounds of this fungus can inhibit topoisomerase II, which leads to a decrease in the growth of cultured HCT116 human colon carcinoma cells. Similar to *H. erinaceus*, cinder conk (*Inonotus obliquus*) is extremely rich in polysaccharides, which can perform immunomodulatory functions and inhibit oncogenesis [52].

The *Cordyceps militaris* fungus showed promising results in preclinical studies of antiproliferative and antimetastatic effects against various types of cancer. *Ganoderma lucidum*, known as reishi, contains ganoderic acids, which have antitumor and immunomodulatory properties. *Grifola frondosa*, also known as maitake, contains such compounds as maitake polysaccharides, which demonstrated anticancer activity in preclinical studies [53].

CONCLUSION

Plants contain a diverse range of biologically active compounds, including alkaloids, flavonoids, terpenoids, and polyphenols, which have been traditionally used in medical practice. Despite promising laboratory results in suppressing tumor growth and metastasis, many plant compounds require further study and clinical trials to confirm their effectiveness and safety. Among the anticancer IPFOs analyzed in this review, which are not a substitute for conventional drugs but are promising for concomitant therapy, matrine, etoposide, resveratrol, and ergosterol have attracted the greatest research interest [39, 30, 48]. Establishing optimal dosages and compositions of potential drugs is essential for assessing the prospects for their practical use, taking into account possible interactions with other medicinal products. Sustainable cultivation and harvesting of plant sources should be ensured.

It is important to note that treatment methods based on promising plant-derived medicines do not replace conventional approaches in cancer treatment. In general, a comprehensive approach to assessing the therapeutic potential of plant-derived cancer inhibitors is required. Fungi are a vast and diverse group of organisms known for their complex chemistry and unique biological activity. Their potential to produce powerful anticancer compounds has been known for decades, leading to significant research efforts aimed at identifying and characterizing cancer inhibitors of fungal origin. On the other hand, some fungus-derived compounds can be toxic to healthy cells. Similar to plant-derived compounds, fungus-derived medicines require optimization to ensure safe and effective dosage, as well as targeted delivery. Currently, clinical trials face a number of issues associated with underfunding and regulatory obstacles. The development of safe and effective drugs based on compounds of fungal origin requires complex purification methods and the creation of appropriate formulations, as well as the introduction of innovative achievements to solve these problems. Further research is needed to elucidate the action mechanisms of these compounds and identify targeted therapeutic strategies, similar to plant-derived preparations.

References

1. Amosova EN, Zueva EP, Razina TK, Krylova SG. Medicinal plants as complementary therapies for the treatment of tumors. *The Bulletin of experimental biology and medicine*. 2003;2:24–34 (In Russ.).
EDN: ULASLT
2. Harvey AL. Medicines from nature: are natural products still relevant to drug discovery? *Trends in Pharmacological Science*. 1999;20(5):196–8.
https://doi.org/10.1016/s0165-6147(99)01346-2
3. Prajapati J, Goswami D, Rawal RM. Endophytic fungi: A treasure trove of novel anticancer compounds. *Current Research in Pharmacology and Drug Discovery*. 2021;2:100050.
https://doi.org/10.1016/j.crphar.2021.100050
4. Mangal M, Sagar P, Singh H, Raghava GP, Agarwal SM. NPACT: Naturally Occurring Plant-based Anti-cancer Compound-Activity-Target database. *Nucleic Acids Research*. 2013;41(Database issue):D1124–9.
https://doi.org/10.1093/nar/gks1047
5. Ali M, Wani SU, Salahuddin M, Manjula SN, Mruthunjaya K, Dey T, et al. Recent advance of herbal medicines in cancer- a molecular approach. *Heliyon*. 2023;9(2):e13684.
https://doi.org/10.1016/j.heliyon.2023.e13684
6. Solomko ESh, Stepanova EV, Abramov ME, Baryshnikov AYu, Lichinitser MR. Angiogenesis inhibitors of plant origin: perspective for clinical usage. *Russian Journal of Biotherapeutics*. 2010;9(4):3–10 (In Russ.).
7. Surh YJ, Na HK. NF-kappaB and Nrf2 as prime molecular targets for chemoprevention and cytoprotection with anti-inflammatory and antioxidant phytochemicals. *Genes and Nutrition*. 2008;2(4):313–7.
https://doi.org/10.1007/s12263-007-0063-0
8. Blagodatski A, Yatsunskaya M, Mikhailova V, Tiasto V, Kagansky A, Katanaev VL. Medicinal mushrooms as an attractive new source of natural compounds for future cancer therapy. *Oncotarget.* 2018;9(49):29259–74.
https://doi.org/10.18632/oncotarget.25660
9. Elmore S. Apoptosis: a review of programmed cell death. *Toxicologic Pathology*. 2007;35(4):495–516.
https://doi.org/10.1080/01926230701320337
10. Gao L, Chen M, Ouyang Y, Li R, Zhang X, Gao X, et al. Icaritin induces ovarian cancer cell apoptosis through activation of p53 and inhibition of Akt/mTOR pathway. *Life Sciences*. 2018;202:188–194.
https://doi.org/10.1016/j.lfs.2018.03.059
11. Zahedipour F, Bolourinezhad M, Teng Y, Sahebkar A. The Multifaceted Therapeutic Mechanisms of Curcumin in Osteosarcoma: State-of-the-Art. *Journal of Oncology*. 2021;2021:3006853.
https://doi.org/10.1155/2021/3006853
12. Zhu G, Shen Q, Jiang H, Ji O, Zhu L, Zhang L. Curcumin inhibited the growth and invasion of human monocytic leukaemia SHI-1 cells *in vivo* by altering MAPK and MMP signalling. *Pharmaceutical Biology*. 2020;58(1):25–34.
https://doi.org/10.1080/13880209.2019.1701042
13. Jin J, Fan Z, Long Y, Li Y, He Q, Yang Y, et al. Matrine induces ferroptosis in cervical cancer through activation of piezo1 channel. *Phytomedicine*. 2024;122:155–65.
https://doi.org/10.1016/j.phymed.2023.155165
14. Aung TN, Qu Z, Kortschak RD, Adelson DL. Understanding the Effectiveness of Natural Compound Mixtures in Cancer through Their Molecular Mode of Action. *International Journal of Molecular Sciences*. 2017;18(3):656.
https://doi.org/10.3390/ijms18030656
15. Lima EN, Lamichhane S, Bahadur KCP, Ferreira ES, Koul S, Koul HK. Tetrandrine for Targeting Therapy Resistance in Cancer. *Current Topics in Medicinal Chemistry*. 2024;24(12):1035–49.
https://doi.org/10.2174/0115680266282360240222062032
16. Singh BN, Shankar S, Srivastava RK. Green tea catechin, epigallocatechin-3-gallate (EGCG): mechanisms, perspectives and clinical applications. *Biochemical Pharmacology*. 2011;82(12):1807–21.
https://doi.org/10.1016/j.bcp.2011.07.093
17. Cheng T, Ying M. Antitumor Effect of Saikosaponin A on Human Neuroblastoma Cells. *BioMed Research International*. 2021;2021:5845554.
https://doi.org/10.1155/2021/5845554
18. Zhang X, Liu Z, Chen S, Li H, Dong L, Fu X. A new discovery: Total Bupleurum saponin extracts can inhibit the proliferation and induce apoptosis of colon cancer cells by regulating the PI3K/Akt/mTOR pathway. *Journal of Ethnopharmacology*. 2022;283:114742.
https://doi.org/10.1016/j.jep.2021.114742
19. Ge LN, Yan L, Li C, Cheng K. Bavachinin exhibits antitumor activity against non-small cell lung cancer by targeting PPARγ. *Molecular Medicine Reports*. 2019;20(3):2805–11.
https://doi.org/10.3892/mmr.2019.10485
20. Li ZM, Jiang WQ, Zhu ZY, Zhu XF, Zhou JM, Liu ZC, et al. Synergistic cytotoxicity of Bcl-xL inhibitor, gossypol and chemotherapeutic agents in non-Hodgkin's lymphoma cells. *Cancer Biology and Therapy*. 2008;7(1):51–60.
https://doi.org/10.4161/cbt.7.1.5128
21. Yi J, Li S, Wang C, Cao N, Qu H, Cheng C, et al. Potential applications of polyphenols on main ncRNAs regulations as novel therapeutic strategy for cancer. *Biomedicine and Pharmacotherapy*. 2019;113:108703.
https://doi.org/10.1016/j.biopha.2019.108703
22. Glick D, Barth S, Macleod KF. Autophagy: cellular and molecular mechanisms. *Journal of Pathology*. 2010;221(1):3–12.
https://doi.org/10.1002/path.2697
23. Menendez JA, Vazquez-Martin A, Garcia-Villalba R. tabAnti-HER2 (erbB-2) oncogene effects of phenolic compounds directly isolated from commercial Extra-Virgin Olive Oil (EVOO). *BMC Cancer*. 2008;8(377):1–23.
https://doi.org/10.1186/1471-2407-8-377
24. Miller DR, Thorburn A. Autophagy and organelle homeostasis in cancer. *Developmental Cell*. 2021;56(7):906–18.
https://doi.org/10.1016/j.devcel.2021.02.010
25. Ascenzi F, De Vitis C, Maugeri-Sacca M, Napoli C, Ciliberto G, Mancini R. SCD1, autophagy and cancer: implications for therapy. *Journal of Experimental and Clinical Cancer Research*. 2021;40(1):265.
https://doi.org/10.1186/s13046-021-02067-6
26. Ferreira PMP, Sousa RWR, Ferreira JRO, Militao GCG, Bezerra DP. Chloroquine and hydroxychloroquine in antitumor therapies based on autophagy-related mechanisms. *Pharmacological Research*. 2021;168:105582.
https://doi.org/10.1016/j.phrs.2021.105582
27. Beretta GL. Ferroptosis-induced Cardiotoxicity and Antitumor Drugs. *Current Medicinal Chemistry*. 2024;31(31):4935–57.
https://doi.org/10.2174/0929867331666230719124453

28. Dian L, Xu Z, Sun Y, Li J, Lu H, Zheng M, et al. Berberine alkaloids inhibit the proliferation and metastasis of breast carcinoma cells involving Wnt/β-catenin signaling and EMT. *Phytochemistry*. 2022;200:113217. https://doi.org/10.1016/j.phytochem.2022.113217
29. Zarguan I, Ghoul S, Belayachi L, Benjouad A. Plant-Based HSP90 Inhibitors in Breast Cancer Models: A Systematic Review. *International Journal of Molecular Sciences*. 2024; 25(10):5468. https://doi.org/10.3390/ijms25105468
30. Pinkaew D, Cho SG, Hui DY, Wiktorowicz JE, Hutadilok-Towatana N, Mahabusarakam W, et al. Morelloflavone blocks injury-induced neointimal formation by inhibiting vascular smooth muscle cell migration. *Biochimica et Biophysica Acta*. 2009;1790(1):31–9. https://doi.org/10.1016/j.bbagen.2008.09.006
31. Adachi S, Shimizu M, Shirakami Y, Yamauchi J, Natsume H, Matsushima-Nishiwaki R, et al. (-)-Epigallocatechin gallate downregulates EGF receptor via phosphorylation at Ser1046/1047 by p38 MAPK in colon cancer cells. *Carcinogenesis*. 2009;30(9):1544–52. https://doi.org/10.1093/carcin/bgp166
32. Park CM, Jin KS, Lee YW, Song YS. Luteolin and chicoric acid synergistically inhibited inflammatory responses via inactivation of PI3K-Akt pathway and impairment of NF-κB translocation in LPS stimulated RAW 264.7 cells. *European Journal of Pharmacology*. 2011;660(2-3):454–9. https://doi.org/10.1016/j.ejphar.2011.04.007
33. Tsai JH, Hsu LS, Lin CL, Hong HM, Pan MH, Way TD, et al. 3,5,4'-Trimethoxystilbene, a natural methoxylated analog of resveratrol, inhibits breast cancer cell invasiveness by down-regulation of PI3K/Akt and Wnt/β-catenin signaling cascades and reversal of epithelial-mesenchymal transition. *Toxicology and Applied Pharmacology*. 2013;272(3):746–56. https://doi.org/10.1016/j.taap.2013.07.019
34. Kooti W, Servatyari K, Behzadifar M, Asadi-Samani M, Sadeghi F, Nouri B, et al. Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study. *Journal of Evidence-Based Integrative Medicine*. 2017;22(4):982–95. https://doi.org/10.1177/2156587217696927
35. Wang Z. Cell Cycle Progression and Synchronization: An Overview. *Cell-Cycle Synchronization.* 2022;2579:3–23. https://doi.org/10.1007/978-1-0716-2736-5_1
36. Georgiou N, Kakava MG, Routsi EA, Petsas E, Stavridis N, Freris C, et al. Quercetin: A Potential Polydynamic Drug. *Molecules*. 2023;28(24):8141. https://doi.org/10.3390/molecules28248141
37. Meijer L, Hery-Arnaud G, Leven C, Nowak E, Hillion S, Renaudineau Y, et al. Safety and pharmacokinetics of Roscovitine (Seliciclib) in cystic fibrosis patients chronically infected with Pseudomonas aeruginosa, a randomized, placebo-controlled study. *Journal of Cystic Fibrosis*. 2022; 21(3):529–36. https://doi.org/10.1016/j.jcf.2021.10.013
38. Kluska M, Wozniak K. Natural Polyphenols as Modulators of Etoposide Anti-Cancer Activity. *International Journal of Molecular Science*. 2021;22(12):6602. https://doi.org/10.3390/ijms22126602
39. Ward AB, Mir H, Kapur N, Gales DN, Carriere PP, Singh S. Quercetin inhibits prostate cancer by attenuating cell survival and inhibiting anti-apoptotic pathways. *World Journal of Surgical Oncology*. 2018;16(1):108. https://doi.org/10.1186/s12957-018-1400-z
40. Karmakar S, Banik NL, Patel SJ, Ray SK. Curcumin activated both receptor-mediated and mitochondria-mediated proteolytic pathways for apoptosis in human glioblastoma T98G cells. *Neuroscience Letters*. 2006;407(1):53–8. https://doi.org/10.1016/j.neulet.2006.08.013
41. Yang XJ, Xi YM, Li ZJ. Icaritin: A Novel Natural Candidate for Hematological Malignancies Therapy. *BioMed Research International*. 2019; 2019:4860268. https://doi.org/10.1155/2019/4860268
42. Zhang C, Sui X, Jiang Y, Wang X, Wang S. Antitumor effects of icaritin and the molecular mechanisms. *Discovery Medicine*. 2020;29(156):5–16.
43. Li X, Ai H, Sun D, Wu T, He J, Xu Z, et al. Anti-tumoral activity of native compound morelloflavone in glioma. *Oncology Letters*. 2016; 12(5):3373–7. https://doi.org/10.3892/ol.2016.5094
44. Pang X, Yi T, Yi Z, Cho SG, Qu W, Pinkaew D, et al. Morelloflavone, a biflavonoid, inhibits tumor angiogenesis by targeting rho GTPases and extracellular signal-regulated kinase signaling pathways. *Cancer Research*. 2009;69(2):518–25. https://doi.org/10.1158/0008-5472.can-08-2531
45. Tsukagoshi S, Hashimoto Y, Fujii G, Kobayashi H, Nomoto K, Orita K. Krestin (PSK). *Cancer Treatment Reviews.* 1984; 11(2):131–55. https://doi.org/10.1016/0305-7372(84)90005-7
46. Price LA, Wenner CA, Sloper DT, Slaton JW, Novack JP. Role for toll-like receptor 4 in TNF-alpha secretion by murine macrophages in response to polysaccharide Krestin, a Trametes versicolor mushroom extract. *Fitoterapia*. 2010;81(7):914–9. https://doi.org/10.1016/j.fitote.2010.06.002
47. Xu H, Qi Z, Zhao Q, Xue J, Zhu J, He Y, et al. Lentinan enhances the antitumor effects of Delta-like 1 via neutrophils. *BMC Cancer*. 2022;22(1):918. https://doi.org/10.1186/s12885-022-10011-w
48. Hussein Zaki A, Haiying B, Mohany M, Al-Rejaie SS, Abugammie B. The effect mechanism of ergosterol from the nutritional mushroom Leucocalocybe mongolica in breast cancer cells: Protein expression modulation and metabolomic profiling using UHPLC-ESI-Q. *Saudi Pharmaceutical Journal*. 2024; 32(5):102045. https://doi.org/10.1016/j.jsps.2024.102045
49. Narayanan S, de Mores AR, Cohen L, Anwar MM, Lazar F, Hicklen R, et al. Medicinal Mushroom Supplements in Cancer: A Systematic Review of Clinical Studies. *Current Oncology Reports*. 2023; 25(6):569–87. https://doi.org/10.1007/s11912-023-01408-2
50. Bailly C, Gao JM. Erinacine A and related cyathane diterpenoids: Molecular diversity and mechanisms underlying their neuroprotection and anticancer activities. *Pharmacological Research*. 2020; 159:104953. https://doi.org/10.1016/j.phrs.2020.104953
51. Atmaca H, Camli Pulat C, Ilhan S, Kalyoncu F. Hericium erinaceus Extract Induces Apoptosis via PI3K/AKT and RAS/MAPK Signaling Pathways in Prostate Cancer Cells. *Chemistry and Biodiversity*. 2024;21(12):e202400905. https://doi.org/10.1002/cbdv.202400905
52. Abugomaa A, Elbadawy M, Ishihara Y, Yamamoto H, Kaneda M, Yamawaki H, et al. Anti-cancer activity of Chaga mushroom (Inonotus obliquus) against dog bladder cancer organoids. *Frontiers of Pharmacology*. 2023;14:1159516. https://doi.org/10.3389/fphar.2023.1159516

53. Liu Y, Guo ZJ, Zhou XW. Chinese Cordyceps: Bioactive Components, Antitumor Effects and Underlying Mechanism-A Review. *Molecules*. 2022;27(19):6576. https://doi.org/10.3390/molecules27196576

Authors' contributions. All the authors confirm that they meet the ICMJE criteria for authorship. The most significant contributions were as follows: Tatiana V. Gasanova — scientific substantiation, data analysis, manuscript writing, editing and approval of the final version of the manuscript; Peter A. Ivanov — data analysis and manuscript editing; Maria N. Repina — collection and processing of material, literature search and analysis, writing and editing of the manuscript.

AUTHORS

Tatiana V. Gasanova, Cand. Sci. (Biol.)
https://orcid.org/0000-0001-5086-5254
tv.gasanova@belozersky.msu.ru

Peter A. Ivanov, Cand. Sci. (Biol.)
https://orcid.org/0000-0003-0305-8021
regaflight@gmail.com

Maria N. Repina
https://orcid.org/0009-0005-5644-3438
rep-masha@yandex.ru