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Role of Heteropolysaccharides in Chemoprevention and Carcinogenesis

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Abstract

Our aging, heredity, lifestyle, race, regular consumption of over processed foods grown on farmland soil depleted of minerals and soil microorganisms rich in nitrate fertilizers and pesticides, irradiated food, industrial toxins (fluoridated drinking water), smoking, viral infections, etc, are directly connected to DNA destabilization by breakage of hydrogen bonds between the base pairs of DNA causing abnormal accelerated replication of open strands to the development and expression of many negative and even fatal processes, such as carcinogenesis. The consequence of so much toxicity is humankind's real and dramatic increase in rates of cancer, autoimmune diseases, toxic metal syndrome and much more.

During the last two decades there has been an increasing recognition of the importance of the human immune system for maintaining good health. Carcinogenesis is process which normally takes several years during which progressive genetic changes occur leading to malignant transformation. With recent advances in technology, biotechnology, information technology a new class of pharmacologically active water soluble heteropolysaccharide immunomodulators emerged from selected medicinal mushrooms found in the fruiting bodies, cultured mycelia, and culture broth. With the help of advanced techniques in biotechnology and information technology, scientists have been able to extract and purify these pharmacologically active compounds, elucidate their chemical structures, and study their potential therapeutic effects. Very few of immunologically active polysaccharides from medicinal mushrooms are pure (1-3)- (1-6)- beta-D-glucans, most are heteroglucans containing other sugar molecules, such as galactose, xylose or mannose.

Keywords: Medicinal Mushrooms, Anticancer Effects, Coriolus Versicolor, PSK (Polysaccharide-K) and PSP (Polysaccharide peptide), Chemoprevention, Adhesion, Invasion, Motility, Metastatic Growth, Cancer Research UK, Pre-Clinical Models, Clinical Trials, Mushroom Polysaccharide compounds.

Introduction

The recognition of Medicinal Mushrooms by Scientists

Scientists of world's premier cancer centers are recognizing medicinal mushrooms for their anticancer effects:

The University of Texas MD Anderson Cancer Center gave scientific review of Coriolus Versicolor (PSK and PSP) as promising candidate for chemoprevention due to the multiple effects on the malignant process by inhibiting adhesion, invasion, motility, and metastatic growth of tumor cells [1].

Here are some details about the effects of PSK and PSP on tumor cells:

- **Inhibition of adhesion:** Tumor cells often exhibit increased adhesion capabilities, allowing them to attach to other cells or tissues and invade them. PSK and PSP have been reported to inhibit the adhesion of tumor cells, which may help prevent their spread.
- **Inhibition of invasion:** Cancer cells need to invade surrounding tissues to establish secondary tumors or metastasize to distant sites. Research suggests that PSK and PSP can suppress the invasive behavior of tumor cells, potentially impeding their ability to spread.
- **Inhibition of motility:** The motility of cancer cells refers to their ability to move and migrate within the body. PSK and PSP have been found to reduce the motility of tumor

cells, limiting their ability to migrate and invade neighboring tissues.

- **Inhibition of metastatic growth:** Metastasis is the process by which cancer cells spread from the primary tumor to other parts of the body. PSK and PSP have shown the potential to inhibit the growth of metastatic tumors, potentially reducing the overall progression of cancer.

PSK may have immunomodulatory effects specifically in situations where the immune system is compromised due to factors such as the presence of tumors or the administration of chemotherapy. In these circumstances, PSK has shown the ability to restore immune function to a more optimal state.

Cancer Research UK wrote: Mushroom-derived polysaccharides have shown anti-tumor activities in both pre-clinical models and in clinical trials [2].

Memorial Sloan Kettering Cancer Center — the world's oldest and largest private cancer center wrote: Lentinan, a polysaccharide, derived from the mycelium of the shiitake mushroom is classified as an antineoplastic polysaccharide and is available for clinical use. Heteroglucans from mushrooms produce their anti-tumor effects in two ways, by activating many kinds of immune cells of innate and acquired immunity that are important for the maintenance of homeostasis, (such as macrophages, monocytes, neutrophils, natural killer cells, dendritic cells) and chemical messengers (cytokines such as interleukins, interferon, colony stimulating factors), triggering complement and by direct cytotoxic effect by triggering apoptosis in mitochondria of cancer cells or interfering with DNA replication such as Cordycepin that have the ability to interfere with DNA replication specifically in tumor cells and virally infected cells [3, 4].

Cancer chemoprevention refers to the use of natural or synthetic substances to prevent, delay, or inhibit the development of cancer by targeting specific molecular pathways or risk factors associated with cancer development. The study published in the International Journal of Cancer in 2008, compared women with histologically confirmed breast cancer to an equal number of women without breast cancer. The study specifically looked at the relationship between mushroom consumption and breast cancer risk in Korean women. According to the study, there was a strong inverse correlation between mushroom consumption and breast cancer risk [5, 6].

From clinical practice and various clinical trials, the use of PSK (Polysaccharide-K) has shown positive outcomes in certain cancer types: Colorectal Carcinoma: In clinical trials involving colorectal carcinoma, the use of PSK after surgery and chemotherapy has been associated with extended survival rates. Specifically, it has been reported that PSK extended 5-year and 8-year survival in patients with colorectal carcinoma. In lung cancer stages I-III the administration of PSK has been found to significantly extend 5-year survival rates. In fact, the survival rate has been reported to increase by 2-4 times compared to standard treatment alone. In patients with advanced stomach cancer and metastasis PSK given alongside surgery and chemotherapy at 3-6g/day doubled 2-year and 5-year survival and extended 15-year survival. In stage III of cervical and uterine cancer in combination with radiotherapy PSK given at (3-6g/day) enhanced survival and increased sensitivity of the cancers to radiotherapy. Analyzing the efficacy of Coriolus extracts on survival of cancer patients from 13 randomized, placebo-controlled clinical trials, Coriolus was found to result in a significant survival advantage compared with standard conventional anti-cancer treatment alone. Many of the mushroom polysaccharide compounds have proceeded through to Phases I, II and III clinical trials. Mushroom chemicals have been studied for their potential role in an integrative approach to managing cancer patients. These chemicals have been found to target multiple biochemical and physiological signaling pathways involved in tumor growth and the tumor microenvironment [7].

Here are some specific pathways that mushroom chemicals may affect: VEGF/MMPs/PDGF/EGF/mTOR

- **Vascular Endothelial Growth Factor (VEGF):** VEGF is a signaling protein involved in the formation of new blood vessels (angiogenesis) that supply nutrients to tumors. Mushroom chemicals may help inhibit the activity of VEGF, thereby reducing angiogenesis and potentially limiting tumor growth.
- **Matrix Metalloproteinases (MMPs):** MMPs are enzymes involved in the breakdown of extracellular matrix, which allows cancer cells to invade and spread. Mushroom chemicals may have inhibitory effects on MMPs, thereby potentially reducing the invasive behavior of tumor cells [9-11].
- **Platelet-Derived Growth Factor (PDGF):** PDGF is a protein that plays a role in cell growth and division. It is also involved in angiogenesis and the recruitment of cells to the tumor microenvironment. Mushroom chemicals may interfere with PDGF signaling, potentially disrupting tumor growth and the supportive microenvironment.
- **Epidermal Growth Factor (EGF):** EGF is a protein that promotes cell growth and division. Abnormal EGF signaling can contribute to the development and progression of cancer.
- Mushroom chemicals may modulate EGF signaling, potentially inhibiting tumor growth.
- **Mammalian Target of Rapamycin (mTOR):** mTOR is a protein kinase involved in regulating cell growth, proliferation, and survival. Dysregulation of the mTOR pathway can contribute to tumor development. Mushroom chemicals may have an impact on mTOR signaling, potentially inhibiting tumor cell growth [12].

Overall, the goal of both cancer prevention and treatment is to minimize the impact of cancer on individuals and improve their overall health. People are considered “healthy” until they show symptoms! So, if we’ve been harboring a malignancy for 20 years we may feel all right, but we haven’t been. If one day we start preventing cancer, we may, at that very moment, be treating it as well not even knowing.

Conclusion

Therefore: cancer prevention and treatment may sometimes be the same thing!

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