

New Dietary Supplements from Medicinal Mushrooms: Dr Myko San—A Registration Report

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ABSTRACT: In December 2010 the Ministry of Health and Social Welfare of the Republic of Croatia registered tablet preparations AGARIKON.1 and MYKOPROTECT.1, developed by Dr Myko San—Health From Mushrooms Co., as dietary supplements. This may be the first time for a European manufacturer to successfully register its own medicinal mushroom products in a European country. As a product with a very broad spectrum of action, officially described as a preparation for immunity strengthening and general health improvement, AGARIKON.1 is a result of 20 years of research and practice, and is based on the formulation that has achieved the best tumor growth inhibition rates—above 90% on tumor cell lines of mouse squamous cell carcinoma and fibrosarcoma.

Since the usage of massive dosages of proprietary blended liquid mushroom extracts in patients with breast, colorectal, lung, and other cancers significantly improved their survival rates, alleviated side effects of standard oncological therapies, improved their quality of life, and resulted in life prolongation—the very idea is that scientifically verified medicinal mushroom products can be used as powerful biological weapons to fight human malignancies. If progressive modern medicine were redefined in a more effective and humane way, cancer mycotherapy should be a part of a broad concept of biological prevention and therapy of cancer. Also, with a very broad spectrum of action, generally formulated as “to strengthen immunity,” MYKOPROTECT.1 is intended as an important element in the prevention and fighting of serious viral infections, whether they are caused by well-known viruses (hepatitis, HIV, etc.) or newly emerging ones.

KEY WORDS: medicinal mushrooms, dietary supplements, nutraceuticals, mycotherapy, cancer, antitumor effects, tumor prevention, viral infections, antiviral effects, hepatitis, HIV, AIDS, AGARIKON.1, MYKOPROTECT.1

I. INTRODUCTION

On December 7, 2010, the Ministry of Health and Social Welfare of the Republic of Croatia approved the issuance of registration numbers to Dr Myko San—Health from Mushrooms Co., Zagreb, Croatia, for medicinal mushroom tablet products AGARIKON.1 and MYKOPROTECT.1, registered as dietary supplements. This may be the first time for a European manufacturer to successfully register its own medicinal mushroom products in a European country.

Medicinal properties and effects of many medicinal mushroom species have been investigated thoroughly during the last decades worldwide.^{1–8} Various good or high-quality products derived from medicinal mushrooms are therefore scientifically based and their presence on the market as dietary supplements (or more accurately, as nutraceuticals), at least, is legitimate. Moreover, scientifically verified medicinal mushroom products should be included on the official lists of pharmaceutical drugs without artificial restrictions, while progressive efforts

for the redefinition of contemporary medicine in a more effective and humane way (biological therapies, molecular medicine, evidence-based medicine, holistic approach, healthy nutrition, etc.) should be made. That very idea has been recommended, for many years, by the World Health Organization, to use other (expertly and scientifically) proven experiences and methods from various civilizations for the preservation of human health, in addition to official Western medicine.

II. MULTIFUNCTIONAL NUTRACEUTICAL AND MYCOTHERAPY OF CANCER

AGARIKON.1 is intended to strengthen immunity and improve general health. As a high dosage proprietary blend of mushroom extracts this product is suitable in cancer prevention efforts and can be used in a broader biological approach of cancer therapy. The preparation is made from *Lentinus edodes*, *Ganoderma lucidum*, *Agaricus brasiliensis*, *Grifola frondosa*, and *Pleurotus ostreatus*, with 750 mg of mushroom

polysaccharides per tablet and a prescribed standard daily dosage of one tablet taken three times a day. It is safe and recommended to double the dosage or increase it even more for cancer patients.

Proven multifunctional activity of each mushroom species used in AGARIKON.1 formula (and even that of certain compounds present) makes it possible to use this nutraceutical very extensively—from immunostimulation and immunomodulation to improvement of performance status and general health. This includes the preservation of healthy functioning, slowing or stopping the development and/or progression of various pathological alterations, and active treatment of pathological processes and changes in immune, circulatory, digestive, respiratory, endocrine, nervous, etc., subsystems and in the living human (and mammalian in general) organism as a whole. The extensive scientific evidence demonstrates the dialectical connections between medicinal mushroom effects on the cell, tissue, organ, and system levels.

More specifically, this nutraceutical can be used to boost general immune function, especially on the cellular level, which imparts the preventive strengthening of resistance to tumor development; fungal, viral, bacterial, and parasitic infection/infestation; as well as various other harmful biological, chemical, and physical agents from the environment. If pathological aberrations have already occurred, the stronger immunity entails a better ability to efficiently fight cancer, infections, and other pathologic disorders. This effect is also present in children and seniors, and particularly in immunocompromised people and those with chronic illnesses. However, immunomodulating properties of some mushroom species can correct immunity imbalances by harmonizing many immunological mechanisms and reactions, offering significant benefits for people suffering from allergies and other autoimmune disorders.

Due to its complex blending of medicinally multifunctional mushroom species, AGARIKON.1 is additionally helpful in the regulation of blood pressure, cholesterol and other lipid levels, and blood sugar. Therefore, it can assist in slowing atherosclerosis and consequent development of cardiovascular disorders, as well as help in the faster and more complete recovery after their worst attacks. To complete the review of the multifunctional action of this nutraceutical, its hepatoprotective,

urinary, and reproductive system tonic and nerve tonic potentials should also be added.

The improvement of the above-mentioned vital functions leads to increased resistance to a number of physical and mental causes of stress, improving stress tolerance. Adaptogenic properties of some medicinal mushrooms include enhanced ability to adapt to new biological challenges that people today must face (primarily through water, food, and air and brought on by modern civilization), to which we are not evolutionarily adapted. This product can also increase physical strength and endurance, raise the pain threshold, and alleviate existing pain. The composition of this nutraceutical helps to reduce fatigue and aids in achieving deeper and healthier sleep, particularly in overworked or overstressed people. Anti-aging properties of some mushroom species that were included in the preparation contribute to postponing and slowing down of the aging process, thus enabling healthier aging.

The specific intention for developing AGARIKON.1 was to develop an efficient additional biological weapon in fighting cancer. Thus, it is based on a specific mushroom extract blend formulation and has been additionally tested within the scientific and technological project “Medicinal effects of mushrooms.” This project was done in cooperation between the Rudjer Boskovic Institute—Department for Molecular Medicine (Zagreb, Croatia) and Dr Myko San Co., with financial support from the Croatian Ministry of Science and Education and co-financed by Dr Myko San Co. Aside from testing for antitumor activity of 20 single mushroom species extracts prepared by Dr Myko San Co., several special proprietary extract blends were tested as well. AGARIKON.1 is based on the formulation that achieved the best tumor growth inhibition rates—above 90% on tumor cell lines of mouse squamous cell carcinoma (SCCVII) and fibrosarcoma (FsaR). During the process of AGARIKON.1 tablet development more than 50 single mushroom species extracts were tested in cooperation with the Laboratory for Carbohydrate Technology of the Faculty for Food and Biotechnology (University of Zagreb, Croatia).

III. DR MYKO SAN IN CANCER RESEARCH

Antitumor effects of medicinal mushrooms and their compounds have been extensively researched

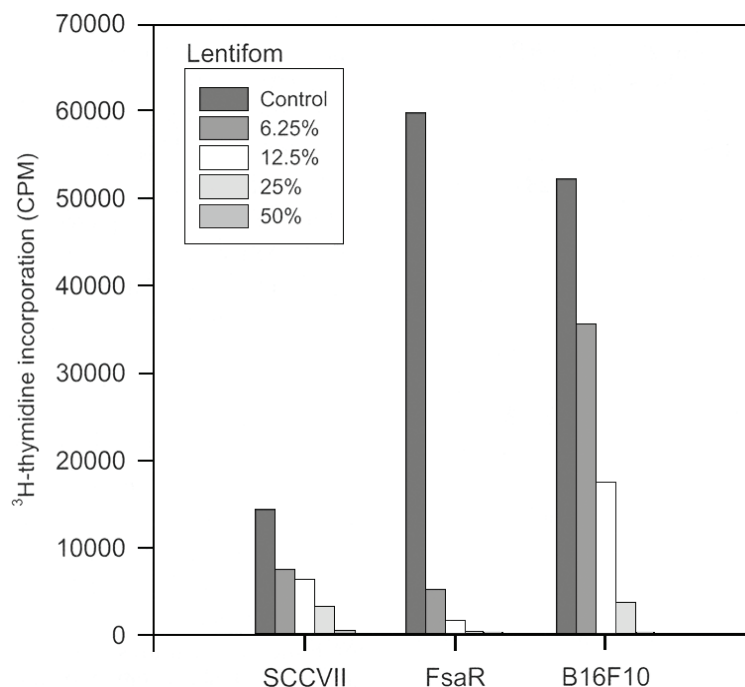


FIGURE 1. Effect of individual doses of the medicinal mushroom preparation LENTIFOM on the incorporation of radioactive thymidine into squamous cell carcinoma (SCCVII), fibrosarcoma (FsaR), and melanoma (B16F10) cells ($*p < 0.01$).⁹

and are abundantly documented worldwide. Dr Myko San Co. has also initiated and participated in several research projects on antitumor effects of mushrooms, and has accumulated a significant experience in developing, producing, and using six proprietary antitumor liquid mushroom nutraceutical extracts during its 20 years of operation. The first research project on antitumor effects of mushrooms in Croatia was initiated and financed by Dr Myko San Co. in 1999 and performed in cooperation with Rudjer Boskovic Institute—Department for Molecular Medicine. *In vitro* studies on mouse squamous cell carcinoma (SCCVII), fibrosarcoma (FsaR), and melanoma (B16F10) demonstrated very significant tumor growth inhibition rates of some single-mushroom extracts and some proprietary blends of mushroom extracts (see Fig. 1).⁹

In vivo studies showed a significant lifespan prolongation in mice with transplanted squamous cell carcinoma, fibrosarcoma, and melanoma, corresponding to months and years of human life prolongation (see Fig. 2).⁹

Some promising results were also obtained in the scientific and technological project “Medicinal properties of mushrooms,” initiated by Dr Myko San Co. and sponsored by the Croatian Ministry of

Science and Education, which was performed by the same research team. A significant number of liquid medicinal mushroom extracts of single mushroom species exhibited strong antitumor activity, with a couple of exceptional results (see Fig. 3).

The liquid extracts of *Ganoderma lucidum* and *Agaricus brasiliensis* in specific concentrations and dosages completely blocked tumor cell division in both tumor cell lines tested—squamous cell carcinoma and fibrosarcoma. Proprietary liquid mushroom extract blend AGARIKON also exhibited very high tumor growth inhibition rates on four mouse tumor cell lines (see Fig. 4).

A more serious and progressive medical science and medicinal practice would include all professionally verified case reports and scientific analyses of professionally verified and collected medical records. Such an “evidence-based medicine” approach regarding the practical use of medicinal mushroom products would compensate, to some extent, for the current lack of officially controlled clinical studies, which in the Western world is caused primarily by various artificial restrictions and blockades. These analyses of professionally collected representative data conclusively establish that massive dosages of high-quality

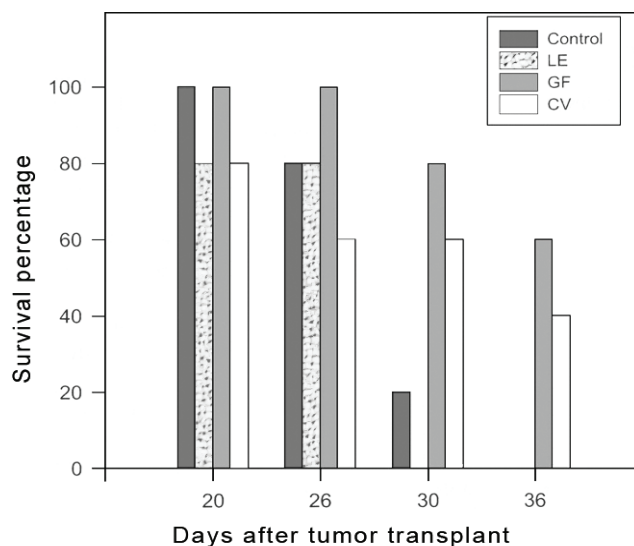


FIGURE 2. Survival rates of mice (C3H/HZgr) with tumors after being injected with squamous cell carcinoma cells. After 7 d, when the tumors have already grown to 5–7 mm in diameter, the mice were treated with preparations from the mushrooms *Trametes (=Coriolus) versicolor*, *Grifola frondosa*, or *Lentinus edodes*. The applied dosage was 0.2 g per 1 mL of saline solution, using a stomach probe, for 10 consecutive days. The control group was treated in the same manner with 1 mL saline solution (* $p < 0.05$).⁹

mushroom extract blends, taken regularly for a longer period of time, used together with standard oncologic therapies, strongly improve short-term and long-term outcomes, compared with standard oncological therapies alone. An analysis of 51 colorectal cancer patients, mainly with advanced and metastatic cancers (29.4% and 60.8% of total sample, respectively), and 105 breast cancer patients (53.7% of total sample with metastatic or recurrent cancer), clearly demonstrates the benefits of treating human cancers with medicinal mushroom products. Patients have taken massive dosages of proprietary liquid mushroom extract blends for 40–80 days on average, within a period from January 2004 to June 2007. Higher short-term and middle-term survival (62.7% with colorectal and

64.8% with breast cancer were alive at the time of analysis) was observed. Additionally, at the end of mycotherapy the status of survivors was improved or unchanged in over 90% of colorectal cancer cases and almost 90% of breast cancer cases. This analysis was presented at the 4th International Medicinal Mushroom Conference (Ljubljana, Slovenia) in September 2007.¹⁰ This analysis of the official medical records shows that certain complex medicinal mushroom extracts powerfully inhibit tumor growth and can cause tumor regression in human malignancies, help patients endure aggressive standard cancer therapies, decrease systemic toxicity and other harmful side-effects, while boosting the immunological and performance status of cancer patients, improve their quality of life,

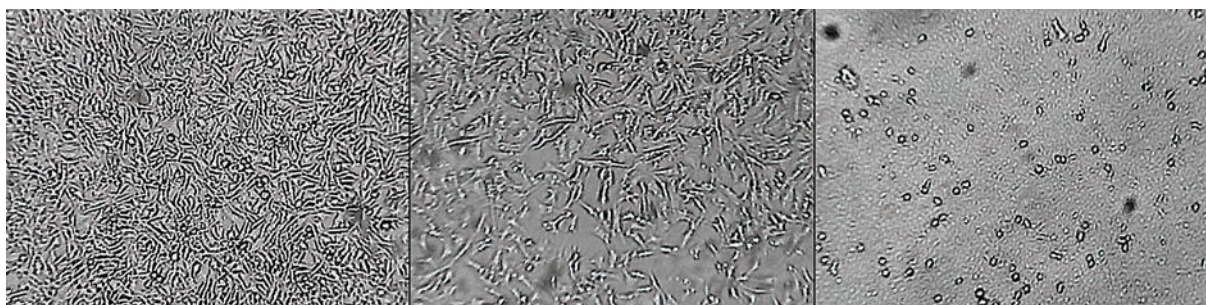


FIGURE 3. This microphotography shows a marked concentration-dependent reduction in squamous cell carcinoma proliferation using *Agaricus brasiliensis* extracts. From left to right the image shows control, 25%, and 50% of original Dr Myko San Co. *A. brasiliensis* extract.

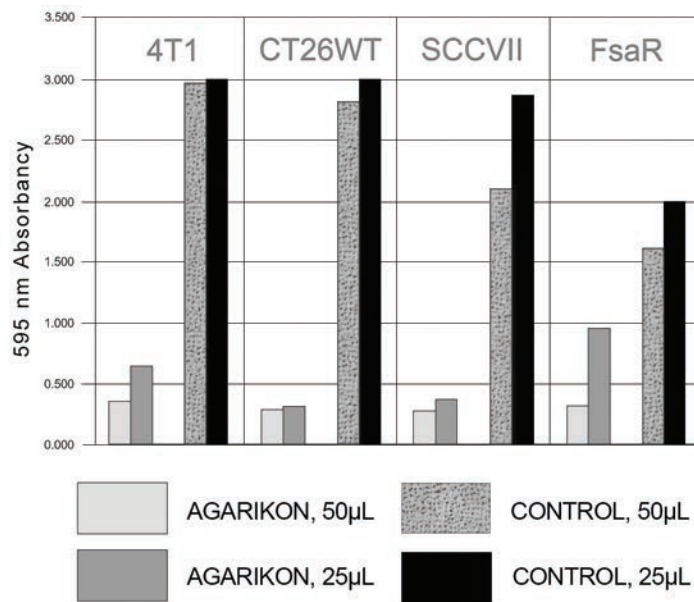


FIGURE 4. The effects of Dr Myko San Co. proprietary liquid preparation AGARIKON on four types of mouse tumors. The 25 and 50 µL doses, shown here compared with control, strongly decrease the growth, and consequently absorbance at 595 nm, of breast adenocarcinoma (4T1), colon adenocarcinoma (CT26WT), squamous cell carcinoma (SCCVII), and fibrosarcoma (FsaR).

and prolong their lives.^{10–11} To complete the same study and ensure new data that will provide deeper insight in long-term survival dynamics, additional analysis on the same cancer patient samples will be performed and presented at the 6th International Medicinal Mushroom Conference.

Another study on short-term and long-term effects of large dosages of the same complex mushroom extracts in 65 lung cancer patients, taken regularly for 40–100 days, from January 2004 to June 2007, with results at the end of June 2009, provides essentially similar results. The sample of 65 patients consists of two principally different parts: 13 small-cell lung cancer (SCLC) patients (4 in extensive and 9 in the limited stage) and 52 non-small-cell lung cancer (NSCLC) patients (30 of them in advanced and 20 in metastatic stages). Also based on official medical records analysis, this study gave similar positive results regarding tumor size changes, performance status, and chemotherapy tolerance influenced by the intake of liquid mushroom extracts. But this study also revealed very significant data on long-term survival of mycotherapy users in comparison with official 5-year survival data of patients with standard cancer therapy alone. SCLC patients in extensive stage with standard therapy have a median survival of 7 to 9 months, while those who ad-

ditionally used mycotherapy had a median survival of 27 mos. SCLC patients with limited disease have a median survival of 14 months, while in mycotherapy users it had increased to 37 months. A very significant long-term survival increase was also observed in NSCLC patients who used mycotherapy, e.g., 4-year survival rate of metastatic NSCLC patients (stage IV) is only 2%, while the same stage mycotherapy users had a survival rate of almost 20%.¹² This study was presented at the 5th International Medicinal Mushroom Conference in September 2009 (Nantong, China). It found that mycotherapy with large dosages of complex mushroom extracts, combined with standard oncological therapies, can significantly prolong lung cancer patients' lifespan, strongly inhibit tumor growth, improve the total effectiveness of standard cancer therapies (surgery, radiotherapy, and chemotherapy), while helping the patients to bear aggressive standard cancer therapies, alleviating their side-effects and boosting immunological and performance status of lung cancer patients.¹² To summarize, cancer patients with a high-quality mycotherapy survive more frequently, live longer, and enjoy increased quality of life (see Fig. 5).

Based on the research, studies, and experiences described above—which were fundamental

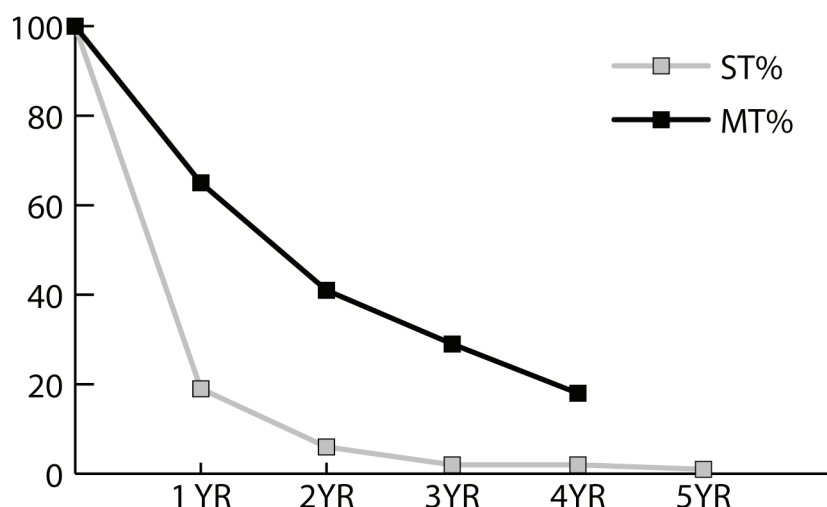


FIGURE 5. The comparison of standard oncological therapy used alone and combined with mycotherapy; effects on human survival rate in stage IV non-small-cell lung carcinoma (NSCLC) cases ([www.mykosan.com/Scientific Research/Lung cancer](http://www.mykosan.com/ScientificResearch/Lung%20cancer)).

for the development of AGARIKON.1 tablets—there is considerable potential in this nutraceutical to become an important part of open-minded concepts and practice of biological cancer prevention and therapy. For cancer suffering patients and their families it is a new mycotherapeutic weapon fighting human malignancies—solid tumors, leukemias, and lymphomas. Used with standard cancer therapies, this product is intended to enhance chemotherapy tolerance and reduce its toxicity and damaging side-effects, especially preventing damage to immunocompetent cells, as well as improving radiation therapy tolerance and reducing its side-effects. Taken early enough prior to surgery, AGARIKON.1 may improve surgery tolerance and accelerate recovery. Physical strength and endurance preservation and improvement, as well as tumor pain alleviation, frequently leading to enhancements in the patient's mental status, is, based on the company's rich experience, expected with significant probability.

IV. THE QUEST FOR NEW POTENT ANTIVIRAL AGENTS

MYKOPROTECT.1 tablet preparation is also intended to strengthen immunity, so most of the basic information on AGARIKON.1 covers this nutraceutical as well. But the intention behind the development of this product was conceptually different—it is planned to be an additional potent biological tool to fight viral infections. As a high-dos-

age proprietary blend of mushroom extracts made from *Lentinus edodes* and *Ganoderma lucidum*, it contains 750 mg of mushroom polysaccharides in a single tablet. With the standard daily dosage of one tablet three times a day, which is safe to double or increase even more for people suffering or directly endangered by extremely dangerous viral infections, such as AIDS, new dangerous influenza virus strains, etc.

Although not as extensively researched as the antitumor effects of mushrooms, antiviral effects of medicinal mushrooms have been thoroughly verified by medicinal mushrooms science.¹⁻⁸ Researching the ancient application practices of traditional medicine, several authors made pioneering verifications of significant inhibiting activities of *Lentinus edodes* against several influenza virus strains, measles, poliomyelitis, herpes simplex, and other viruses.¹³

Special attention has been paid, quite early, to the HIV/AIDS problem. A fundamental study from the Yamaguchi University School of Medicine showed that polysaccharides from medicinal mushrooms *L. edodes*, *Ganoderma lucidum*, and *Trametes (=Coriolus) versicolor* can almost completely block both cell-free and cell-to-cell infection by various HIV strains.¹⁴ Regarding the estimate of immunologist M. Clerici, presented at the World Conference on AIDS in Vancouver (Canada) in 1996, that as many as 30 to 50% of the people who come into contact with HIV do not

become seropositive, due to the strength of their immune system, immunoprevention of HIV infection and/or development of AIDS using medicinal mushroom nutraceuticals opens new prospects.

Viral hepatitis, particularly hepatitis C, is, however, the most common (and still increasing) viral disease in the world. Approximately 30% of those infected become chronic active hepatitis patients, who are at a highly increased risk of developing liver cancer, cirrhosis, or liver failure. In the search for substances that might contribute to immunoprevention, inactivation of serologically active infection, or regression of active illness, medicinal mushrooms possess significant potential. *G. lucidum* has showed positive results in 92.4% of patients.¹⁵ Hepatoprotective action of substances from *L. edodes*, including effects on chronic persistent hepatitis, has also been verified, even in controlled double-blind studies.¹⁶

During its many years of operation, Dr Myko San—Health from Mushrooms Co. has accumulated a large body of experience in treating viral infections, primarily hepatitis C, using blended liquid extracts of several medicinal mushrooms. Although the systematic analysis of collected data has not yet been performed, in a majority of cases, after 2 months of treatment the lowering of viremia (measured by PCR RNA test) and improvement of liver function (measured by liver enzyme testing) was observed. There have also been several documented cases of the complete clearance of virus from the blood “below the level of test sensitivity.”

Considering many other research studies and Dr Myko San’s own experiences in treating viral infections, there is potential for MYKOPROTECT.1 to become an important element in the prevention and treatment of serious viral infections, whether they are caused by well-known viruses or newly emerging ones. This nutraceutical is intended to assist in blocking virus adhesion on the surface of host cells and hinder penetration into attacked cells; it tries to block virus genetic code transcription as well as reduce or stop virus multiplication in attacked and penetrated cells. There is a significant probability of prevention and effective treatment of infections with hepatitis viruses, HIV (particularly high-risk groups, seropositive people, and those with developed AIDS), herpes viruses, influenza viruses, cytomegalovirus, mononucleosis (Epstein-Barr vi-

rus), recurring or particularly resilient flu, and colds caused by parainfluenza or rhinoviruses. Mycotherapy should become a regular practice to prevent viral infections and/or to control infection and accelerate recovery.

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