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ANTI-TUMOUR POTENTIAL OF ACTIVE COMPOUNDS (POLYSACCHARIDES) OF WILD MUSHROOMS FROM RAJOURI DIST. OF JAMMU & KASHMIR, INDIA

Nidhi Anand* and P.N. Chowdhry

National Centre of Fungal Taxonomy (NCFT), New Delhi, India

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Correspondence to Author:

Nidhi Anand

National Centre of Fungal Taxonomy (NCFT), New Delhi, India

E-mail: anand.nidhi608@gmail.com

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ABSTRACT: Natural products have been closely linked through the use of traditional medicines and natural poisons. Mushrooms have an established history of use in traditional oriental medicine, where most medicinal mushroom preparations are regarded as a tonic, that is, they have beneficial health effects without known negative side-effects and can be moderately used on a regular basis without harm. Mushrooms comprise a vast and yet largely untapped source of powerful new pharmaceutical products. In particular, and most importantly for modern medicine, they represent an unlimited source of compounds which are modulators of tumour cell growth. Furthermore, they may have potential as functional foods and sources of novel molecules. In the present study, we have reviewed the compounds with anti-tumor potential in some of the new wild varieties of mushroom of Rajouri Dist. of Jammu and Kashmir region. The main anti-tumor compounds prominent in such species comprises low-molecular-weight compounds viz. quinones, cerebrosides, isoflavones, catechols, amines, triacylglycerols, sesquiterpenes, steroids, organic germanium and selenium) and high-molecular-weight compounds viz. homo and heteroglucans, glycans, glycoproteins, glycopeptides, proteoglycans, proteins and RNA-protein complexes). Amongst all, the polysaccharides in mushroom species also showed potent antitumour activity against sarcoma 180, mammary adenocarcinoma 755, leukemia L-1210 and a host of other tumors.

INTRODUCTION: The state, Jammu and Kashmir in India is rich in macro fungal diversity due to wide agro-climatic variations diverse physiographic and undulating topography, but understanding of the macro-fungal flora of the Kashmir is still in an exploratory stage and undoubtfully there are many more species to be recorded [1].

Jammu and Kashmir State is stretched between 32°17'-37°03' N latitude and 72°03'-80°20' E longitude, and covers a total area of 222,235 km², with an average annual rainfall between 60-80 cm. It is bordered to the north and east by the main Himalayan ranges and Punjab plains to the south.

The state exhibits varied climatic and topographic conditions and provide pleasant environment for the lavish growth of diverse group of plants. However, information on the species of wild mushrooms from this state is limited. In this backdrop, a systematic study of wild mushroom diversity from various locations of Jammu and Kashmir was undertaken.

The number of mushroom species on earth is estimated to be 140,000, suggesting that only 10% are already known. Assuming that the proportion of useful mushrooms among the undiscovered and unexamined mushrooms will be only 5% (a small logical %), this implies 7,000 yet undiscovered species of possible benefit to mankind [2].

The higher Basidiomycetes include about 10,000 species from 550 genera and 80 families in the Basidiomycetes class with macroscopic fruiting bodies. Furthermore, approximately 700 species of higher Basidiomycetes have been found to possess significant pharmacological activities [3-5]. The macro fungi have been divided into four groups: edible flesh, medicinal, poisonous and miscellaneous, where the properties are less well defined [6].

It is not surprising that mushrooms are a source of many biologically active compounds. Mushrooms manage to grow in darkness and dampness in highly competitive environments and protect themselves from hordes of attacking microbes by developing natural protective substances. Modern scientific studies on the above called "medicinal mushrooms" have expanded exponentially during the last two decades and scientific explanation to show how compounds derived from mushrooms function in humans are increasingly being established [7].

Fungal fruiting bodies, fungal mycelium or the culture fluid in which the mycelium has been cultivated may all be explored for biological activity. More recently, some species of edible higher Basidiomycetes have been found to markedly inhibit the growth of different tumor cell lines. There are approximately two hundred species of higher Basidiomycetes that were found to have this activity [8]. Additionally, both cellular components and secondary metabolites of a large number of mushrooms have been shown to affect the immune system and therefore might be used to treat a variety of diseases [9].

Mushrooms which appear to enhance or potentiate resistance to disease states are being sought for the treatment of cancer, immunodeficiency diseases (including AIDS) or generalized immunosuppression after drug treatment [10, 11]. The present review thus aims in describing the descriptive information of some of the predominant anti-cancerous polysaccharides in 06 newly identified species of macro fungi belonging to different genus reported for the first time from Rajouri Dist. of J&K, India [12].

The mushrooms collected were taxonomically and morphologically identified and were deposited as record specimens in NCFT, New Delhi, India. The 06 new species of mushrooms identified and deposited via accession no. were *Scleroderma citrinum* (NCFT5674.12), *Lepiota trachoma* (NCFT4375.12), *Psilocybe subtropicalis* (NCFT 5611.12), *Ganoderma applanatum* (NCFT 5671.12), *Cyptotrama asprata* (NCFT5237.12) and *Entoloma serrulatum* (NCFT4571.12)

Mushrooms as Anticarcinogenic Agents: Carcino-genesis is a process which normally takes several years during which progressive genetic changes leading to malignant transformation. Cancer prevention is the best intervention in this process before invasive disease develops. Over the last half century, our understanding of carcinogenesis has grown enormously, owing largely to recent technology, allowing exploration of molecular pathways, cancer-associated genes and tissue architecture. This knowledge provided the basis for most cancer-preventive intervention strategies and particularly for one of the strategies for chemoprevention – the use of drugs, biologicals and nutrients to prevent the development of cancer (i.e. to inhibit, delay or reverse carcinogenesis) [13].

Carcinogenesis has traditionally been under- stood as having three stages: initiation, promotion, and progression. Although more recently carcinogenesis has not been described in those terms, but rather as a malignant transformation as a whole, we hereby refer to the literature in which such divisions of the stages of carcinogenesis were made. It has been described that the modulation of the human immune system, attributed to mushrooms, particularly to various mushroom polysaccharides, was likely to affect primarily the promotion and progression stages, according to the referred model of carcinogenesis.

Nonetheless, other substances contained in mushrooms were described as possibly being able to interfere with the referred tumor initiation process, through a variety of mechanisms such as enhancing the antioxidant capacity of cells or up regulating phase I and II enzymes involved in the metabolic transformation and detoxification of mutagenic compounds.

Additionally, other mushroom constituents have been described as being able to inhibit what was considered to be the promotion or progression stages of carcinogenesis, by exerting direct cytotoxicity against tumor cells, interfering with tumor angiogenesis, or up regulating other no immune tumor-suppressive mechanisms [14].

Many species of Fungi from the division Basidiomycetes (mushrooms) have been found to contain medicinally active compounds, which has been of great recent interest [15-20]. There are advantages of using mushrooms as sources of bioactive compounds, rather than plants. For example, the fruiting body can be produced in much less time and the mycelium may also be rapidly produced (in a liquid culture that can be manipulated to produce optimal quantities of active products, or from mycelial biomass and supernatant of submerged cultures using bioreactors) [21-25].

Antitumor Polysaccharides of mushrooms: Polysaccharides are polymers of sugars (monosaccharide) joined to each other by glycosidic linkages. These are very complex molecules because sometimes covalent bonds occur between many pairs of carbon atoms. Consequently one sugar unit can be joined to more than two other sugars, which results in the formation of highly branched enormous macromolecules. Polysaccharides are a structurally diverse class of macromolecules able to offer the highest capacity for carrying biological information due to a high potential for structural variability [5].

Whereas the nucleotides and amino acids in nucleic acids and proteins effectively, interconnect in only one way, the monosaccharide units in polysaccharides can interconnect at several points to form a wide variety of branched or linear structures [26]. This high potential for structural variability in polysaccharides gives the necessary flexibility to the precise regulatory mechanisms of various cell-cell interactions in higher organisms. The polysaccharides of mushrooms occur mostly as glucans.

Some of which are linked by β (1-3), (1-6) glycosidic bonds and α-(1-3) glycosidic bonds but many are true heteroglucans. Most often there is a main chain, which is either β (1-3), β (1-4) or mixed β (1-3), β (1-4) with β (1-6) side chains. Hetero-β-D-glucans, which are linear polymers of glucose with other D-monosaccharide, can have anticancer activity but α-D-glucans from mushroom usually lack anticancer activity[5]. Heteroglucan side chains contain glucuronic acid, galactose, mannose, arabinose or xylose as a main component or in different combinations. Glycans are polysaccharides containing units other than glucose in their backbone.

A wide range of antitumor or immuno-stimulating polysaccharides of different chemical structure from higher Basidiomyces mushrooms has been investigated [5]. Some correlation has been drawn between the chemical structure and antitumor activities of mushroom polysaccharides. A wide range of glycans extending from homopolymers to highly complex heteropolymers [27] exhibits antitumor activity. Differences in activity can all be correlated with ability of the polysaccharide molecule to solubilize in water, size of the molecules, branching rate and form.

Such structural features as β-(1-3) linkages in the backbone (main chain) of the glucan and additional β-(1-6)-branch points are needed for antitumour activity[5]. β -glucans with only (1-6) glycosidic linkages have little or no activity. Higher molecular weight glucans are more effective than those of low molecular weight against tumors [28, 29]. There is a broad similarity in the various methods that have been developed for extraction of anti-cancer polysaccharides from mushrooms. Usually dried mushroom in powdered form is heated in 80% ethanol to eliminate low molecular weight substances.

Crude fractions are obtained from the remaining ethanol extracts by further extraction with water, 1% ammonium oxalate and 5% sodium hydroxide. The polysaccharides are then fractionally purified by a combination of techniques, including ethanol concentration, fractional precipitation, ion-exchange chromatography, gel filtration and affinity chromatography. A study [30] has established a more efficient procedure for the extraction of β-glucan from mushroom. The β-glucan is isolated through ethanol precipitation and freeze-dried in liquid nitrogen. Purity testing using a carbohydrate analysis column produced 87.65% purity.

CONCLUSION: Mushroom polysaccharides offers a lot of hope for cancer patients and sufferers of many devastating diseases. A fundamental principle in oriental medicine is to regulate homeostasis of the whole body and to bring the disease person to his or her normal state [31]. A variety of polysaccharides from a number of mushroom varieties have been demonstrated to enhance the immune system. All of these have shown significant antitumour activity as a result of their ability to activate the host immune system rather than direct cytotoxicity.

The mushroom polysaccharides appear to be well tolerated and compatible with chemotherapy and radiation therapy. There may be a possibility that plolysaccharide content and its potency may varies in mushrooms according to the temperature and geographical conditions. This article may also found to be a stepping stone to explore this area of research too on the other hand. Further studies are needed to describe the molecular mechanisms that occur in specific immuno-modulation by mushroom polysaccharides

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