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IN PRAISE OF THE HUMBLE MUSHROOM *CORDYCEPS MILITARIS*

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ABSTRACT

Cordyceps militaris is an important medicinal mushroom useful for the extraction of several bio-metabolites for natural drugs to revitalize the various physiological systems of the body from the ancient era. The constituents of *C. militaris* are now using widely in the modern pharmaceutical industries. The active principles of *C. militaris* are beneficial to act principally as pro-sexual, anti-cancer, immunomodulatory, and anti-oxidant agent, let alone its others beneficial activities for most of the systems of the body. In addition, it has lots of clinical applications. The prospects of this novel mushroom could be used not only for modern medicinal manufacturers, but also for the community people for the betterment of their health. The present review highlights the importance of this medicinal mushroom *C. militaris*, also aiming to draw necessary attention of the researchers as a frontier one.

INTRODUCTION: Medicinal mushroom is a field involving the study of their biology, chemistry as well as their practical applications in the field of pharmacology, in order to prepare novel drugs by biotechnological means. This field is becoming more important day by day, and has been widely investigated due to its practical benefits. Synthetic drugs are available in the commercial market and are being used in daily life, but they are not safe enough as they leave some side effects and sometimes harmful for human health. On the other hand, there is still a lack in research on the chemistry and bio-constituents of the medicinal mushrooms those may provide more efficacious and safer drugs having no side effects.

The medicinal mushroom (*Cordyceps* species) is a valuable source of useful natural products having diverse biological activities [1]. *Cordyceps militaris* (an entomopathogenic fungus), is one of the most important medicinal mushrooms, belonging to the class *Ascomycetes*, has been used popularly as a crude drug and a folk tonic food in East Asia [2]. It possesses many kinds of active components (such as cordycepin, polysaccharides, ergosterol, and mannitol), and due to its several physiological activities, it is currently using for multiple medicinal purposes [3, 4, 5]. There are over 2, 500 mushroom varieties are grown in the world today[6]. It is estimated that more than 10 million metric tones of edible and medicinal mushrooms were produced last year in various countries [7]. Therefore, mushroom family has received significant attention from medical and pharmacological researchers as ample source of biologically active compounds [8]. The use of herbal supplements in the Europe including United States is continuously growing and raises concerns about safety, efficacy, and how they affect safe patient care in most of the cases [9]. On this standpoint, the use of natural products including medicinal mushrooms is increasing day by day and the growth of the medicinal mushroom product industry have led to increase concern regarding their safety scale [10].

As the emerging diseases are increasing in number, the modern medicines get tired to fight against and also it is really a time consuming matter to develop a suitable new drug for. On the other hand, as the medicinal mushrooms *Cordyceps militaris* possesses several biological and clinical applications; additionally, it offers preventive cares that could a great help for the human being by strengthening their body defense system by acting passively.

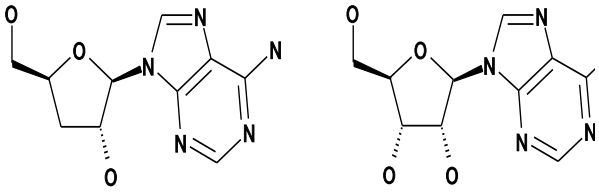
The *Cordyceps militaris* was once used only as a traditional tonic but times have changed: The ancient medicinal fungus *C. militaris*, which has been used as a crude drug for the welfare of mankind in old civilization, is now of a matter of concern due to its unexplored potentials. WHO estimated that about three-quarters of the world's population currently use natural drugs and other forms of traditional medicines like medicinal mushrooms to treat their diseases[11] including breast cancer (12%) [12], liver disease (21%) [13], HIV (22%) [14], asthma (24%) [15] and rheumatological disorders (26%) [16]. The acceptance and recognition of natural medicine has been in part due to the acknowledgement of the value of traditional and indigenous pharmacopoeias, the incorporation of some medicines derived from these sources into pharmaceuticals [17, 18], the need to make health care affordable for the

community people and the perception that pharmaceutical drugs are increasingly over prescribed, expensive and even dangerous. Another important perception fomenting this interest is that natural remedies are somehow safer and more efficacious with least side effects than remedies that are pharmaceutically derived [19, 20].

Simultaneously, the development of modern chemistry permitted the isolation of chemicals from medicinal mushrooms that have served as drugs or starting materials for the synthesis of many important drugs used today. Many more modern drugs have been synthesized as a result of knowledge gained from studies of mechanisms of actions of chemicals first isolated from medicinal mushrooms[8]. Thus, medicinal mushrooms have played a major role in the development of modern medicine and continue to be widely used in their original form [21].

FIG. 1 PHOTOGRAPH OF *CORDYCEPS MILITARIS*

Biological activities of *Cordyceps militaris:* The main active constituent of *C. militaris* fruiting bodies (Fig. 1) is cordycepin, which was first extracted from *C. militaris* and then found to be present in *Cordyceps sinensis* [22] and *Cordyceps kyushuensis*[23]. The cordycepin (3′ -deoxyadenosine, $C_{10}H_{13}N_5O_3$, m. pt. 225 °C, [α] D-47 °C) (Fig. 2), a nucleoside analogue [22, 24], is considered as a nucleic acid antibiotic that might inhibit canceration of cells and thus contribute to the normalization of cancer cells as one of constituents of gene DNA [22].



(A) **(B)**

FIG. 2 CHEMICAL STRUCTURES OF (A) CORDYCEPIN AND (B) ADENOSINE

In addition, it has been reported that the cordycepin is intracellularly converted into its 5′ -mono-, di- and triposphates that inhibit the activity of several enzymes (Fig. 3) in the purine biosynthetic pathway [25].

The recent studies have demonstrated that the active principles of the medicinal mushroom *Cordycpes militaris* are practically beneficial to act as pro-sexual [26, 27], anti-inflammatory [28, 29], anti-oxidant/anti-aging [26, 30], anti-tumor/anti-cancer/anti-leukemic [31-35], anti-proliferative [31], anti-metastatic [31, 36], immunomodulatory [36-39], anti-microbial [40], anti-bacterial[41], anti-viral [37, 39, 42, 43], anti-fungal [36, 39], anti-protozoal [44], insecticidal [39, 45], larvicidal [45], anti-fibrotic [46], steroidogenic[36], hypoglacaemic [47, 26], hypolipidaemic [28, 48], anti-angiogenetic [49], anti-diabetic [47], anti-HIV [43], anti-malarial [50], anti-fatigue [51, 3], neuroprotective [1, 52], liver-protective [26, 28, 29, 51], reno- protective [26, 53, 54] as well as pneumo-protective [26], let alone their other synergistic activities, which let it be marketable in the western countries as an alternative medicine.

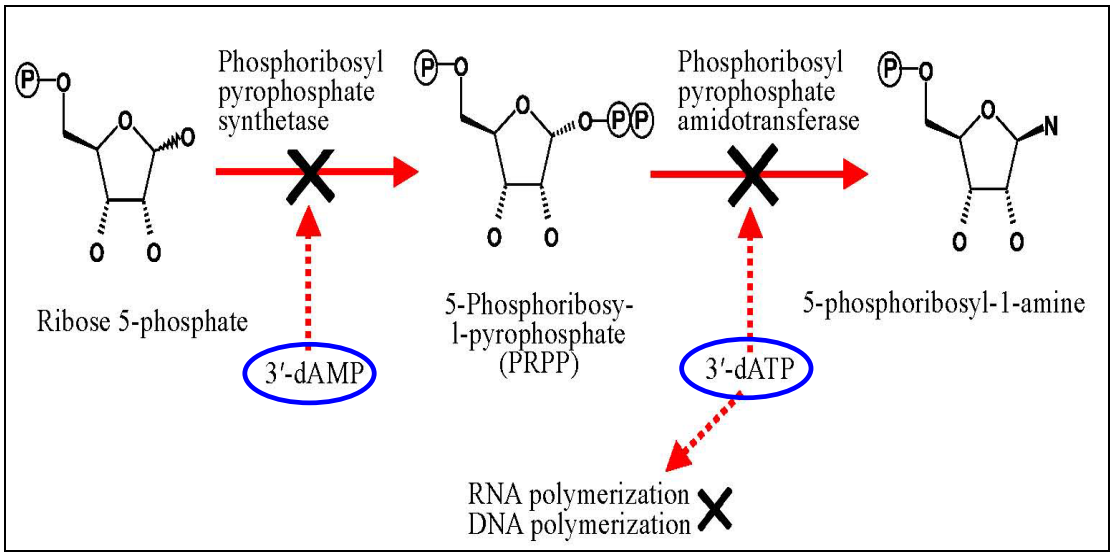


FIG. 3: MECHANISM OF ACTION OF CORDYCEPIN (INHIBITION OF PURINE AND POLYNUCLEOTIDE BIOSYNTHESIS BY CORDYCEPIN)

As *Cordycpes militaris* has an effective immunomodulatory activity, it can be used for the prevention of several diseases. Therefore, the medicinal mushroom *C. militaris* is one of the most important candidates that may be used as the medicinal base in the future.

Clinical applications of C*ordyceps militaris*: Although *Cordyceps sinensis* was used more extensively than *Cordyceps militaris*, their clinical applications are more or less similar. Therefore, the extracts of *Cordyceps militaris* can be used in the cases of insufficient pulmonary function, coughing and sputum, dizziness, memory failure, myodesopsia, vision failure, cold virus, in appetence, night sweat, pale face, pale lips, buzzing in the ears, toothache and loose teeth, insomnia and thirsty, cold or hot limbs, lumbago or pain in knees, nervous prostration, diabetes, night enuresis, sexual impotence, anemia and, slow recovery from illness [3]. There might have some other clinical applications yet to unveil.

Frontier prospects: Nature is the source of all the raw materials that we need. About 2-3 decades ago, most of the drugs were of natural origin. A variety of reasons remain behind why people like to use natural medicines as it is evident that patients are getting even more distressed after using the chemically synthesized drugs, rather than natural means like medicinal mushrooms that can conquer life-claiming diseases, leaving no side effects on human health. To maintain proper growth, the pharmaceutical industries need innovation and access to high output rate on low-cost materials with reasonable safety. The combination of modern chemistry with bio-based starting materials, like bio-metabolites, offers the scope for revolutionizing mushroom based pharmaceutical industries. In the near future, bio-metabolites (cordycepin, polysaccharides etc.) extracted from medicinal mushroom *C. militaris* will have a role that compares with that of oil and gas crackers today.

CONCLUSION: The ancient medicinal mushroom *C. militaris*, which has been used as a tonic drug in the old civilization, is now of a prospective harbor to explore many mysterious potentials. The novel components obtained from *C. militaris* already have more

than 21 clinically approved beneficial effects for human health [3]. Especially, the anti-cancer agent cordycepin from *C. militaris* is expected to play evolutionary roles in the pharmacognosy sector, leading to create a viable base for pharmaceutical industries as some emerging diseases like CANCER, SARS, AIDS, SWINE FLU have no proper remedies yet. In this context, this novel medicinal mushroom *Cordyceps militaris* needs further elaborative study, pharmacological investigations, clinical trials and public awareness.

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