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Cordyceps sinensis: Peculiar caterpillar mushroom, salutary in its medicinal and restorative capabilities

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Abstract
This review mainly focuses on the medicinal value of the *Cordyceps sinensis*. Interestingly, *Cordyceps* spp. contains different compounds with the ability to strengthen the response of the immune system and also to control its exacerbated response. Most of the information on the effect of *Cordyceps* on the immune system derives from studies in cancer. Upholding immunity and strong immune system are prime concern especially during microbial infections as in the case of current COVID-19 pandemic. This is a mushroom that is only found in cohabitation with the larvae of an insect, and it is this unique growth parameter that has made it challenging to produce *Cordyceps* spp. in artificial cultivation. Further complicating this cultivation issue is the rarefied atmosphere, mineral-rich soil, and low temperature in which *Cordyceps* naturally grows, resulting in a unique profile of secondary metabolites possessing interesting biological potential for medical exploitation, but which are not readily reproduced in normal laboratory cultivation. In this article, we attempt to unravel many of the mysteries of *Cordyceps* spp., with special attention to *C. sinensis*, the world's most costly medicinal mushroom.

Keywords: *Cordyceps sinensis*, caterpillar mushroom, immuno-booster, medicinal properties, nutritional composition

Introduction
Mushrooms have been used diversely since 5000BC as food, poison, medicine, and as a part of religious rituals (Winkler, 2008) [93]. Mushrooms are often referred to as functional food, which supply diverse health benefits far beyond the traditional nutrients they hold (Cheung *et al*. 2008) [18]. The edible mushrooms are healthy food and amazing nutrient sources because of their various beneficial components, which include protein, carbohydrates, vitamins and minerals, dietary fibre protein lesser number of calories, fats and toxic metals (Wang *et al*. 2014; Kozarski *et al*. 2015) [92, 48]. Fungi is the best source of medicine other than plants and bacteria. They have the potential in production of various novel compounds that are very important in medicine (Hilszczańska, 2012) [33]. Medicinal mushrooms have been studied since ancient times for their bio-metabolites and are eminent for the treatment of several diseases (Tuli *et al*. 2014) [85]. One of the mostly sought out medicinal mushroom belongs to class ascomycetes is *Cordyceps*, which is a precious reservoir of diverse natural products along with various biological activities. *Cordyceps* is entomopathogenic in nature and exists as a growth from the body of the infected insect (Chakraborty *et al*. 2014) [10]. *Cordyceps* is endemic to the grasslands and shrubs of Central Asia and grows at the elevations of 3500-4500m in a frosty and arid environment conditions (Ali, 2012; Baral, 2017) [3, 7].
Cordyceps sinensis, (=*Ophiocordyceps sinensis*) commonly known as cordyceps mushroom/caterpillar fungus. The fungus Cordyceps spp. belongs to Tibetan medicine and consumers describe it as an important source of energy. Cordyceps spp. belongs to Ascomycota, Pyrenomycetes, Hypocreales, and Clavicepitaceae, and at least 700 species are known (Das *et al*. 2021). The name *Cordyceps* is derived from the Latin words 'cord' and 'ceps' meaning 'club' and 'head' respectively. Though these words only describe the outer appearance of the fungus (Holliday *et al*. 2005) [35]. The British Mycologist named Berkely first described this fungus as *Sphaeria sinensis* Berk in 1843. Saccardo, later in 1878, renamed it as *Cordyceps sinensis*. *Cordyceps sinensis*, the accepted scientific name is referred to the final form which is the fruiting body of the fungus coming out of the mummified body of a caterpillar (Devkota, 2006) [22].
The fungus *Cordyceps sinensis* is a well-renowned medicinal mushroom (Arora *et al*. 2008) [4, 6]. Usage of *Cordyceps* as medicines is as old as the Qing Dynasty in China and this

information has been mentioned in Ben-Cao-Cong-Xin (New Compilation of Materia Medica) written by Wu-Yiluo in around 1757 (Singh *et al*. 2008) [81]. It is also known by many names in the interior mountain areas such as its local name 'Yarsha Gamboo', 'Keera jhar' and 'Keera ghas'. The name 'Yarsha Gamboo' means 'summer-grass winter -worm'. In many literatures, 'Gonba' or 'Gumba' or 'Gunba' have also been used instead of 'Gamboo' (Arora,2008) [4, 6]. In Himalayan regions of India and Nepal it is termed as Keera ghaas (insect herb) (Holliday *et al*. 2005; Singh *et al*. 2005) [35]. This term has been said to describe its life stages. Tibetans have been found to believe that during winter season it lives as a worm and later on it undergoes metamorphosis at the start of spring season, in which the worm starts to transform into a kind of grass. Two distinct phases are seen in the whole transformation process. The grass starts growing from the head of the larva first in which a grass-like or blade-like part emerges out of the larval head of the insect. In this particular stage, the larva appears white and can be seen moving. The blade-like part of the larva can be seen protruding out from the insect head resembling a tiny horn which continues to grow further. Ultimately, the host dies and transforms into a brownish-yellow colored 'root' like structure of the grass which is the fruiting body of this particular caterpillar mushroom (Singh *et al*. 2008) [81]. This review discusses about the immense potential of *C. sinensis* in medical purposes.

Fig 1: A fresh specimen of *Cordyceps sinensis* (Shrestha, 2011) [79]

Fig 2: A fresh specimen of *Cordyceps sinensis* surface along with slight damage by insect (Holliday and Cleaver, 2008) [36]

Morphology

Cordyceps sinensis has been found to parasitize the larvae of *Thitarodes* (*Hepialus*) moths (Winkler, 2008) [93]. It consists of fruiting body and the host caterpillar (Yuan et. al 2007) [105]. The fruiting body or the ascocarp of the mushroom arises from the basal part of the insect larval host (*Hepialus* moth) and terminates at the club-like cap which includes the stipe and stroma (Holliday and Cleaver, 2004) [36]. The stroma is seen to be two times as long as the caterpillar when it is fresh (Winkler, 2004). The fruit body or the head of *Cordyceps sinensis* is dark brown-black whereas the root which is the larval body is occupied by the mushroom's mycelium (Garbyal *et al*. 2004) [24] appears yellowish to brown in colour (Holliday and Cleaver, 2004) [36]. The fruiting bodies of *C. sinensis* ranged 4-7 cm long over the corpse of the caterpillar ranging 3-4 cm in size. The fruiting body is mostly erect, little bit swollen at the tip, stalked, emerged singly or upto three from the head of the larvae (Arora *et al*. 2013) [5].

Life Cycle

Cordyceps sinensis is a mushroom that grows on a larva of a lepidopteran insect mainly ghost moth. It releases millions of ascospores in the air during the summer and early autumn seasons, which invades the larval soft skin and initiates germination inside of the larval body. Larval skin can be seen to shed in this particular time. After a certain time, the self-defence mechanism of the larva gets fragile and the fungal cells disperse throughout the body via the circulatory system. The larva which is subterranean in nature continues boring into the soil and enters inside from its back part in a vertical manner. This is the main reason why the host larva of *Cordyceps sinensis* is always in a vertical position whereas the herb can be seen growing from the head part of the larva.

Amidst the winter season, the fungal cells can be seen spreading swiftly inside the larval body and devouring all the internal organs of the larva with a exception of its exoskeleton. The fungal cells inside of the body of the larva form a compact white mass which is known as endosclerotium. This is the dormant stage of *Cordyceps sinensis* fungus which can resist harsh and severe environmental situations mainly freezing cold.

During spring when the outer temperature starts to rise up gradually, the endosclerotium initiates germination and extrudes through the head part and ultimately it protrudes out through the soil. This part that protrudes out from the host larva is known as stroma. The mature stroma consists of two parts. The basal part is known as stalk or stipe and the apical part is often referred to as head or the fertile part. The head or the fertile part starts producing ascospores when it gets fully matured in summer. These produced ascospores will infect the larva later on in those regions. Therefore, it requires a whole year to complete its life cycle (Shrestha,2011) [79].

Table 1: Proximate nutritional composition of natural and artificially cultured *Cordyceps sinensis* (Cao *et al*. 1993)

Components	Natural (*C. sinensis* and other species)	Artificial culture (mycelium)
Cordycepin	0.5%-0.15%	0.17%-0.40%
Protein(N-content)	20-30%	35-45%
Carbohydrates	10-20%	30-35%
Cordycepic acid	4-5%	8-10%
Ash	3-5%	4-6%
Moisture	0.75-0.95%	4-7%
Fat	7-10%	11-15%
Others	25-40%	15-30%

Table 2: Chemical constituents of *Cordyceps sinensis* for medical significance

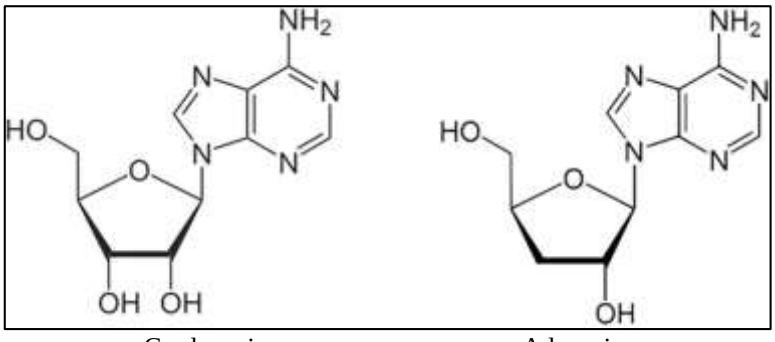
Component	Economic Importance	References
Adenosine	Control of Blood flow in body Anti-inflammatory effect Prevention of cardiac arrythmia	Ding (1987) [23] Berne (1980) [8] Pelleg and Porter (1980)
APS (Acid polysaccharide)	Immunomodulatory effects Antioxidant effects	Shen *et al.* (2011) [77] Li *et al*. (2003) [55] Chen *et al*. (2010) [14, 15] Chen *et al*. (2012) [13]
Cordycepin	Analgesic propertices Improves immunity Antitumor effect Anti-Inflammatory effect Stimulates steroidogenesis Antibacteria, antivirus and pesticidal activities Anti-cancer and anti-metastatic	Yang *et al*. (2010) [99] Paterson (2008) [69] Ikeda *et al*. (2008) [39] Wang *et al*. (2012) [88] Ying *et al.* (2014) [103] Park *et al*. (2014) [68] Qian *et al*. (2012) [72] Pan *et al*. (2011) Pao *et al*. (2012) [67] Leu *et al*. (2011) [52] Zhou *et al*. (2008) [112] Nakamura *et al*. (2015) [62]
Ergosterol	Anti-immunomodulatory and anti-tumor effect Cytotoxicity Antimicrobial activity	Ng and Wang (2005) [63] Seitz (1979) [75] Osswald *et al*. (1986) [65] Kitchawalit *et al.* (2014) [47] Y.H. Li and X.L. Li (1991) [58] Zheng *et al*. (2013) [111] Rajput and Karuppayil (2013) [73]
Cordymin	Anti-diabetic effect	Vestergaard *et al*. (2009) [86] Ahmed *et al*. (2006) [1] Qi *et al*. (2013) [71]
Amino acids, zinc, vitamins also with other trace elements	Improve sexual function by combating sexual weaknesses	Yang *et al*. (1985) [100]
Cordyglucans	Anti-tumor effect	Yalin *et al*. (2005) [98]
Polysaccharides	Hypoglycemic activity	Kiho *et al*. (1999) [45] Li *et al*. (2006) [54]

Chemical Constituents

Cordyceps mushrooms contain many bioactive compounds that have nutritive and medicinal value. *Cordyceps* chemical composition was scouted in 1951. The biochemical components of *C. sinensis* as researched upon and reported by various workers are:

Cordycepin and Cordycepin acid

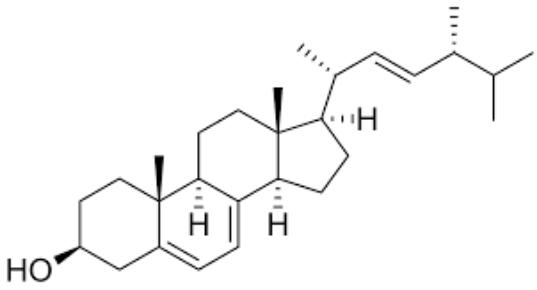
One of the most crucial constituents of the mushroom *C. sinesis* is cordycepin. Cordycepin was first extracted from *C. militaris* (Cunningham, 1951) [19] and its structural formula was confirmed as 3'-deoxyadenosine (Kaczka *et al*. 1964) [41]. Later it was known to be found in *C. sinensis* (Huang *et al*. 2003) [38]. One of the most important medicinal component Cordycepic acid, is and isomer of quinic acid and its chemical structure was confirmed to be 1,3,4-tetrahydroxycyclohexane (Chatterjee *et al*. 1957) [11].



Cordycepin Adenosine

Sterols

Cordyceps contains a number of sterol-type compounds as mentioned by many workers: Delta-3 ergosterol, ergosterol, ergosterol peroxide, 3-sitosterol, Daucosterol, Campesterol, Cerevisterol, α-sitosterol, Fungisterol, Ergosterol peroxide, Ergosteryl-3-*O*-α-D-glucopyranoside, Stigmasterol, 3-*O*-ferulylcycloartenol, Stigmasterol 3-*O*-acetate, Chloresterol, Dihydro brassicasterol (Kadota *et al*. 1986; Zhou *et al*. 1998; Bok *et al*. 1999; Li *et al*. 2003; Yang *et al*. 2011) [42, 9, 55, 101].



Ergosterol

Polysachharides

Cordyceps contain an array of polysachharides such as D-glucan, Mannoglucan, D-mannitol, Cordysinocan and Galactomannan (Kiho *et al*. 1996; Yalin *et al*. 2006; Wu *et al*. 2007; Cheung *et al*. 2009) [97, 94, 17].

Proteins and related compounds

Some proteins and other related compounds of *Cordyceps* are Spermidine, Putrescine, Flazin, Cadaverine, Cordymin, Perlolyrine and L-tryptophan have been identified. (Holliday and Cleaver, 2008; Yang *et al* 2011; Qian *et al* 2012; Zhang et. al 1991) [37, 101, 72, 108].

1. Metals and Vitamins

The vitamins present in *Cordyceps* are B1, B2, B12, E and K and some of the other inorganic elements such as Ca, Na, K, Mg, Cu, Mn, Zn, Pi, Se, Al, Ni, Si, Ga, Sr, Cr and Fe to name a few (Zhu et. al 1998) [114].

2. Nucleotides and Nucleosides

Cordyceps comprise of mainly guanosine, adenine, uracil, uridine, thymidine, deoxyuridine, coerdycepin and guanine (Xiao,1983; Zhu *et al*. 1998; Sharma, 2004) [96, 114, 76].

3. Fatty acids and other organic acids

Twenty-eight saturated and unsaturated fatty acids have been isolated and reported from *C. sinensis* (Zhu *et al*. 1998) [114]. Some fatty acids and other organic acids present in *Cordyceps* are mainly Oleic acid, Stearic acid, Linoleic acid, Lauric acid, Myristic acid, Palmitoleic acid, Lignoceric acid, Penta decanoic acid, Palmitic acid, Docosanoic acid, Succinic acid (Li *et al*. 2003; Yang *et al*. 2009; Yang *et al*. 2011) [55, 101]

Pharmacological or Medicinal importance of *Cordyceps sinensis*

Cordyceps sinensis is a world renowned Traditional Chinese Medicine (TCM) and it has been used in treating many respiratory, pulmonary, liver, renal and cardiovascular diseases along with hyposexuality and hyperlipidaemia to name a few. Also, it has been widely used to treat immune diseases and in modern cancer therapies. It has also been highly advertised as an aphrodisiac that helps in the treatment of impotence in both men and women by increasing sexual prowess. In TCM it has been used for treating a huge array of diseases ranging from aches and pains, along with several respiratory ailments such as cough and phlegm, bronchitis, shortness of breath and asthma (Zhu *et al*. 1998) [114]. Not only in Chinese but also in western medicine *Cordyceps, has* been found to have antibacterial functions, can lower blood pressure, reduction of asthma and strengthening of the heart beat (Mizuno,1999; Ng and Wang, 2005; Paterson and Russel, 2008) [63, 69]. *Cordyceps* has many bioactive chemical compounds (Table 2) that help in controlling of the diseases.

Anti-tumor and Anti-cancerous Properties

Plants have been used since centuries for the treatment of cancer. They have been a major source of anticancer agents and it has been found that more than 60% of anticancer agents have been extracted from natural resources in any manner (Hiradeve *et al*. 2010) [34]. Medicinal mushrooms are most propitious for cancer therapy and *Cordyceps* has been used as an anti-tumour medicinal herb in TCM (Ji,1999) [40]. *Coryceps* has been recommended and sought out by many doctors throughout the world as a supplement to chemotherapy, radiation and other cancer treatments. Chemotherapy and radiation treatment of cancer and tumours have been depleting health status of the patients. *Cordyceps* as a natural source has shown promising results in inhibition of the tumour growth and in some cases dissolving them which can help strengthen the body of the patient (Nakamura *et al*. 2003) [61]. Cordyceps species and their compounds have been used in TCM as a remedy for the treatment and prevention of cancer and other diseases (He and Zhang, 2006).

Many bioactive compounds of *Cordyceps* have been found to have anti-tumor activities and are mainly sterols, polysachharides, cordycepin (Table 2) to name a few. There have been many experiments being conducted in animals. Yoshida *et al*. (1989) [104] reported that a water extract of *C. sinensis* raises the median survival time of ICR mice that were inoculated with allogeneic Ehrlich ascites carcinoma cells and BALB/c mice inoculated with syngeneic Meth A fibrosarcoma cells. There are other substances than cordycepin and polysachharides in the methanolic extract of *C. sinensis* that inhibit the growth of K562, Calu-1, Raji, Wish and Vero tumor cells (Kuo *et al*. 1994) [49]. Bok *et al*. (1999) [9] reported that the glycosylated form of ergosterol peroxide from *C. sinensis* is more powerful than its aglycone in inhibiting the spread of Jarkat, HL-60, K 562, WM-1341 and RPMI-8226 tumor cells. Anti-tumor activities was demonstrated in mice inoculated with Sarcoma 180 when they were orally administered with polysachharide fractions CI-P and CI-A, isolated from *C. sinensis* (Ohmori *et al*. 1986) [64]. Impromptu complex of *C. sinensis* and selenium (Se-CS) was produced and experimented in its efficacy in treatment of Uterine cervix cancer (Hao *et al*. 2014) [31].

Fatigue

Cordyceps is used as a tonic for the remedy of weariness and fatigue and for the restoration of depleted energy while recovering from sicknesses (Holliday and Cleaver, 2004) [36]. It has been found to improve shortness in breath along with reduction of fatigue in patients diagnosed with chronic heart failure. So, it was used by competitive sportsmen in order to treat fatigue and weakness with heightened endurance and energy levels (Liu et. al 1997) [59]. Caterpillar fungus is well known for enhancing physical stamina among sportsmen by increasing the production of ATPs (Adenosine Tri-Phosphate) (Dai *et al*. 2001) [20]. A study with the involvement of healthy elderly volunteers of around an average age of 65, examined the performance output along with their oxygen capacity while exercising on stationary bicycles. Some portion of the people consumed *C. sinensis* in their diet whereas the remaining people consumed a placebo. After 6 weeks, the results were demonstrated and it was found that *Cordyceps* had significantly increased the energy levels and oxygen capacity than the placebo (Zhu and Rippe, 2004). *Cordyceps* amplifies cellular energy in the form of ATP and upon hydrolysis of these phosphates from ATP loads of energy is

released which is further utilized by the cell (Dai *et al*. 2001; Siu *et al*. 2004) [20, 82].

Immunomodulatory Properties

Cordyceps fungus extracts are well known for their immune stimulation functions and can both suppress and improve several aspects of the immune system (Kuo *et al*. 1996; Yarnell and Abascal, 2008; Xiao *et al*. 2010) [50, 102, 95]. If *Cordyceps* is administered to a patient in an immune deficient state such as HIV, cancer or hepatitis, the number of white blood cells increase along with its activity. On the contrary if the same *Cordyceps* is administered to a person in a hyper immune state the activity of white blood cells drops whereas the red blood cells increase in their number. Such immunomodulation at the differential level is very intriguing and maybe nature's smart bomb against sickness (Holliday and Cleaver, 2004) [36]. Different components of *Cordyceps* polysachharides improved the immune response, thymus index, spleen index, phagocytic function of monocyte macrophage, cellular immune function in chronic renal failure while also enhancing renal functions (Guan *et al*. 1992; Zhang *et al*. 2011;) [25, 107]. *C. sinensis* exerts a mitogenic action on splenic lymphocytes and also increases interleukin-2 from spleen cells in rats diseased with chronic renal failure (Cheng, 1992) [16].

It is deemed appropriate to highlight the fact that the caterpillar fungus (*Cordyceps sinensis*) is also obsessed with prospective competence to boost immunity. Previous study highlighted that cordycepin, the active compound found in this fungus can inhibit lipopolysaccharide (LPS)-induced inflammation through the suppression of NF-κB in macrophage cells (Kim *et al*. 2006) [46]. The effect of cordycepin on immune cells could be a novel target for development of immune modulators. It has been reported that during the 2003 outbreak of severe acute respiratory syndrome in china the Yartsa gunbu's value have established huge attention (Chen *et al*. 2013) [12]. *C. sinensis* might be used for the treatment of the COVID-19 for reducing inflammation and fibrosis, increasing immune response and antiviral effect. It may be a better option to use anciently known and well-studied agents rather than discovering new ones to find a rapid treatment for COVID-19 in these pandemic times (Kaymakci and Guler, 2020; Salvia and Singh, 2021) [74].

Anti-bacterial activity

Cordyceps sinensis possesses antibacterial properties. CSAP (Cordyceps sinensis Antibacterial Protein) an antibacterial protein isolated form *C. sinensis* cultured mycelia inhibited the growth of both gram-positive and gram-negative bacteria but had no significant effect against fungi and yeast (Zheng *et al*. 2006) [110]. Fermentation broth of *C. sinensis* showed antibacterial activity strongly against *Staphylococcus aureus* and *E. coli* and also on *Bacillus subtilis*, *Bacillus thuringenesis* (Li *et al*. 2002) [56, 57]. Cordycepin inhibits the growth of *Clostridium paraputrificum* and *Clostridium perfringens* but doesn't show effects on *Lactobacillus spp.* and *Bifidobacterium* spp. (Ahn *et al*. 2000) [2].

Aphrodisiac and Sexual Stimulator

In Traditional Chinese medicine *C. sinensis* has been used since centuries in order to treat both male and female sexual problems mainly hypolibidinism and impotence. It has been a promising herb in increasing sex drive, increasing sperm count and checking infertility (Guo,1986; Chen and Huang, 2010) [29, 15]. A study reported that *C. sinensis* supplement administered to 22 males showed increased sperm count (33 %) and reduction in incidence of sperm malformities (29%) (Guo,1986) [29]. Another study was done with the involvement of both men and women including 189 patients with decreased libido. After administration of *C. sinensis* their desire improved by 66% (Wan et. al 1998) [90].

Anti-diabetic properties

Diabetes is a very serious disease throughout the world. Many research activities have been conducted on the salutary effects of *Cordyceps sinensis* in its potential as a blood sugar regulator. The caterpillar fungus has been shown to decrease the blood sugar levels by improving glucose metabolism and through the conservation of hepatic glycogen (Zhao *et al*. 2002) [109]. It has an antidepressant-like activity which helps to prevent diabetes induced higher blood glucose concentrations. Extracts of the caterpillar fungus has been found to inhibit the diabetes in rats (Shi *et al*. 2009) [78]. Researchers have also demonstrated the anti-diabetic effect on alloxan-diabetic, normal and streptozotocin-diabetic rats. They claimed that polysachharides of *C. sinensis* must be responsible for it (Li *et al*. 2006; Wang and Shiao, 2000) [54, 101]. *Cordyceps* improves blood glucose metabolism also while augmenting insulin sensitivity in animals (Zhao *et al*. 2002) [89]. In a human trial, 95% of the patients administered with 3grams per day of *C. sinensis* showed improvement in their blood sugar levels while other treatment methods showed about 54% improvement only (Guo and Zhang, 1995) [27]. In a nutshell, *Cordyceps* can be beneficial in the control of diabetes in diabetic patients, either singly or in conjunction with other medicines (Holliday and Cleaver, 2004) [36].

Protective effects on kidney

Traditionally people viewed *Cordyceps* mushroom as a tonic that help in strengthening of the kidneys. It has been also known to boost regeneration of tubular cells, protect tubular cells sodium pump activity and in decreasing the calcium content of certain tissues (Li *et al*. 1996; Wang *et al*. 1988) [53, 87]. *Cordyceps sinensis* extract may be one of the peculiar and novel therapeutic drugs for chronic kidney diseases (Song *et al*. 2010) [83]. The kidney enhancing potential of *Cordyceps* is due to its ability to increase 17-hydroxy-corticosteroid and 17-ketosteroid levels in the body (Zhu et. al 1998) [114]. A serious disease that is common with elderly people is chronic renal failure. 51 patients suffering from chronic renal failure were taken for a study. They were administered 3-5 grams of *C. sinensis* per day which showed promising results by hugely improving kidney function and overall immunity in comparison to the untreated control group (Guan *et al*. 1992) [25]. In another human study, 57 patients with gentamicin-induced kidney damage were taken. They were administered 4.5 grams of *Cordyceps* per day or by other treatment methods. The squad which received *Cordyceps* had recovered 89% of normal kidney function whereas other treatment methods only showed 45% recovery (Zhu *et al*. 1998) [114]. A dry powder preparation of *C. sinensis* mycelia, bailing capsule, helps in the prevention of rejection in renal transplants, protects renal function along with reduction in the incidence of infections (Sun *et al*. 2004) [84].

Protective effects on lung

C. sinensis plays a major relaxant role in the bronchi,

increases adrenaline secretion and also has a role in contraction of the trachea caused by histamine. It is also known to be an expectorant and has an anti-asthmatic action while also preventing pulmonary emphysema (Guo and Guo, 2000) [28]. It improves the pulmonary function and is used in the treatment of respiratory diseases such chronic bronchitis, asthma etc. (Kuo *et al*. 2001; Yue *et al*. 2008) [51, 106]. *C. sinensis* extracts have performed inhibition of tracheal contractions which is very essential for asthma patients. Moreover, the anti-inflammatory properties it possesses can bring more relief to the asthma patients (Halpern,1999) [30].

Protective effects on heart

C. sinensis traditionally has been used in the treatment of heart disease. It has many effects on the cardiovascular system that includes decrease of myocardial oxygen consumption, improvement of myocardial ischaemia and anti-platelet aggregation. It also shows inhibitory effects on arrythmia that is induced by aconitine, adrenaline and barium chloride. It also increases myocardial blood flow which improves myocardial ischaemia (Guo and Yang, 1999) [26].

Organ transplant

Tolypocladium inflatum, which is the asexual stage of *Cordyceps* fungus produces cyclosporin which is an antifungal drug. Due to this compound, it was quickly acknowledged that when this drug was used there was a drastic reduction in the possibility of rejection of new organs. Somehow, cyclosporin is acting as an anti-recognition factor. Today it is used as a anti-rejection drug among transplant patients (Holliday and Cleaver, 2004) [36].

Protective effects on liver

Cordyceps has been used as a supplement in the treatment of chronic hepatitis diseases mainly B and C. In a study, *Cordyceps* extract was combined with other medicinal mushroom extracts as an adjunct to lamivudine for the treatment of hepatitis B. It was observed that the groups that had received *Cordyceps* combination in their treatment had a much significant outcome in a short span of time than the control group that were administered lamivudine (Wang *et al*. 2002) [89].

Conclusion

Upholding immunity and strong immune system are major concern especially during microbial infections as in the case of current COVID-19 pandemic. Many questions arise on the need and values of boosting the immunity at this juncture. The caterpillar fungus (*Cordyceps sinensis*) has immune-strengthening actions and may be helpful in a wide range of conditions in which the immune system is weakened. Other potential therapeutic effects such as anticancer may be more difficult to be elucidated in clinical studies and more pre-clinical studies are needed to a better understanding of the mechanisms involved. In conclusion, new future efforts are needed to elucidate the bioactive compounds present in *Cordyceps* genus and its therapeutic potential because it is better to use anciently known and well-studied agents rather than discovering new ones to find a rapid treatment for COVID-19 in these pandemic times.

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