

for prevention and treatment of inflammatory bowel diseases by its down-regulating production and expression of inflammatory mediators ability [25]. In another study, BALB/c mice were induced asthma by intraperitoneal and intranasal ovalbumin. Mice were administered *C. militaris* significantly reduced airway inflammation less effectively than prednisolone or montelukast [26]. Moreover, So-Young Won *et al.*, have studied the anti-inflammatory of the 70% ethanolic extracts of cultured mycelia and fruiting bodies of *C. militaris*. Both extracts exhibited strong topical antiinflammatory activity in the croton oil-induced ear edema in mice. Additionally, cultured mycelia extract can inhibit the acute anti-inflammatory in carrageenin-induced edema mice model. The cultured mycelia extract of *C. militaris* inhibited the NO production and iNOS expression in RAW 264.7 cells stimulated by lipopolysaccharide in a dose-dependent manner [27].

Antibacterial/ Antifungal/ Antiprotozoal/Antiviral

The methanolic extract of *C. militaris* showed strong antibacterial activity against *Bacillus cereus* (MIC- 0.015 mg/ml; MBC- 0.03 mg/ml) and *Pseudomonas aeruginosa* (MIC- 0.015 mg/ml; MBC- 0.03 mg/ml). *Salmonella typhimurium* showed to be resistant with antibacterial effect of the extract (MIC- 3.00 mg/ml; MBC- 6.25 mg/ml). Antibacterial of *C. militaris* was stronger than streptomycine and ampicilline against *Bacillus cereus* and *Pseudomonas aeruginosa* [19].

A cytotoxic antifungal protease protein was isolated from the dried fruiting bodies of *Cordyceps militaris* using anion-exchange chromatography. This protein called *C. militaris* protein (CMP), has shown to inhibit the serine protease. It exerts strong antifungal effect against the growth of the fungus *Fusarium oxysporum*. Furthermore, it showed cytotoxicity against human breast and bladder cancer cells [28]. Cordymin, an antifungal peptide, was purified from the medicinal mushroom *C. militaris*. Cordymin exerts antifungal activity against several fungal species including *B. maydis*, *M. arachidicola* and *R. solani*. It is noted that the antifungal potency of cordymin is higher than that of many antifungal proteins. Cordymin also reduced the proliferation of MCF-7 breast cancer cells. Moreover, cordymin inhibits the activity of HIV-reverse transcriptase IC₅₀ of 55 µM. The mechanism of inhibition probably involves protein–protein interaction [29]. Filipa *et al.*, also have shown the strong antifungal of the methanolic extract of *C. militaris* fruiting body on *Aspergillus fumigatus*, *Aspergillus ochraceus*, *Aspergillus versicolor*, *Aspergillus niger* about (MIC-

0.04 mg/ml); on *Penicillium funiculosum*, *Penicillium ochrochloron* and *Trichoderma viride* (MFC- 0.17 mg/ml). The antifungal activity of *C. militaris* extract was stronger than two drugs used as bifonazole and ketoconazole [19]. Trigg *et al.*, have shown the strong inhibition growth effects of cordycepin on cultures of the erythrocytic stages of *Plasmodium knowlesi* incubated *in vitro*. At very low concentrations (10 µM), cordycepin inhibited the growth *in vitro* of the parasite after incubating for 4 hours. The mechanism may be related to partially prevent by adenosine synthesized and no effect on the host red cell [30].

Hwan Hee Lee showed anti-influenza effects of *Cordyceps* extract using a DBA/2 mouse model. Mice were pretreated with *Cordyceps* extract then intranasally infected with 2009 pandemic influenza H1N1 virus. The DBA/2 mouse was highly susceptible to H1N1 virus infection. They showed that *Cordyceps* extract provided strong an antiinfluenza effect on mice. The mice were treated with extract shown stable body weight and reduced mortality. The antiviral activity of *C. militaris* extract on influenza infection may be mediated by increasing of IL-12 expression and production of NK cells [31]. Other authors have shown that an acidic polysaccharide isolated from the extract of *C. militaris* can inhibit the influenza A virus titers. This acidic polysaccharide was intranasally administered, and is reduced virus titers of mice infected with influenza A virus in the bronchoalveolar lavage fluid and the lung and also enhanced survival rate [23].

Pro-Sexual

Traditional medicine has used *Cordyceps* species for improving the sexual function. Wen-Hung Lin *et al.*, have shown the spermatogenic effect of *C. militaris*. These authors administered the diet supplemented with *C. militaris* mycelium to subfertile boars for 2 months. The sperm production was increased significantly in boars fed with diet contained *C. militaris* extract in both quality of fertile sperm and the quantity of semen volume and total sperm number. They also detected the cordycepin in plasma in boars supplemented with *C. militaris*. More interesting, an amount of motile sperm cells and sperm morphology were also enhanced significantly [32].

Anti-Fatigue

The tonic effect of *C. militaris* has been reported in traditional medicine. Jung *et al.*, investigated the tonic effect of *C. militaris* on the forced swimming capacity and the change of biochemical parameters in mice.

They showed that the mice were fed with *C. militaris* extract had the swimming times to exhaustion longer. These mice also have lower the plasma triglyceride levels [33].

Anti-Diabetic

C. militaris extract also have an antidiabetic effect. Soo Bong Choi *et al.*, have shown the effect of *C. militaris* extract on the insulin secretion and insulin resistance. These authors reported that the extract reduced the fasting serum glucose levels, improved insulin resistance by enhancing glucose utilization in skeletal muscles and increased the insulin secretion in 90% pancreatectomized male Sprague Dawley rats [34].

CONCLUSION

As we have summarized in this review, *C. militaris* has many beneficial pharmacological activities for human health such as anticancer, antitumor, immunomodulatory, antioxidant, anti-pathogenic activities, etc. The bioactive compounds responsible for these pharmacological activities have been identified. They are cordycepin, adenosine, polysaccharides, sterols and other more. It is now very needed to elucidate the chemical structures of the remaining bioactive compounds principles and discovery other pharmacology activity of *C. militaris*.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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