

The Medicinal Efficacies of *Cordyceps Militaris* (L.) Link

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Abstract

Cordyceps militaris is the representative species of *Ascomycete* genus *Cordyceps* and can be found throughout most of the Northern Hemisphere as a pathogen of lepidopteran insect pupae. Mycelia or fruit bodies of *C. militaris*, traditionally used as an herbal cure and a tonic food in East Asia, are studied in the West recently because of its various pharmacological capabilities. Various types of extracts prepared from mycelia or bodies of *C. militaris* are found to exhibit a variety of anti-cancer efficacies in colon cancer, lung cancer and skin cancer etc. Besides, *C. militaris* extracts are found to exhibit active alleviation toward type I hypersensitivity, so called allergy, in activated mast cells and irritated mice. They are also shown to ameliorate the inflammatory responses in evoked cells and mice. The mycelia or bodies of *C. militaris* may confer a complementary/integrative resource to cure or prevent allergy or tumors.

Keywords: *Cordyceps militaris*; type I hypersensitivity; allergy; cancer

Introduction

Cordyceps militaris is the representative species of *Ascomycete* genus *Cordyceps* and can be found throughout most of the Northern Hemisphere as a pathogen of lepidopteran insect pupae [1]. *C. militaris* is easily recognized by the sexual fruit bodies protruding from the inside of fungi-infected lepidopteran insect pupae. The fruit body structure gives the fungus its common name of 'pupa grass' in China and Taiwan. The sexual fruit bodies of *C. militaris* and *C. sinensis* are well-known for being used as a traditional Chinese medicine. In recent years, this ancient eastern elixir is getting more attention from western researchers and clinic practitioners as a research topic and an alternative way of medication respectively [2].

Anti-cancer activities

C. militaris has been investigated for its various pharmacological activities. Various kinds of extracts prepared from *C. militaris* mycelia or fruit bodies are found to exhibit a variety of anti-cancer efficacies based upon the cell-based or animal models. Mollah *et al.* (2012) showed that butanol extract of *C. militaris* mycelia grown on germinated soybean evokes G₂/M cell cycle arrest of human colon cancer HT-29 cells through down-regulation of cycl in B1 and cdc25c [3]. Results collected from the examination of water extract of *C. militaris* mycelia indicate that the extract treatment can induce death receptor- and mitochondria-mediated apoptosis in lung carcinoma A549 cell via up-regulation of Bax/Bcl-2 ratio and caspase-8/caspase-3 activation and also can diminish telomerase activity [4]. Using cell and xenografted animal model, Park *et al.* (2009) showed that treatment of the extract prepared from silkworm pupae grown *C. militaris*

fruit bodies can inhibit VEGF-A and -B synthesis in human MM cells [5], suggesting that the extract incubation can retard angiogenesis. Angiogenesis inhibition is related to GSK 3 α /3 β , PI3K and Akt1. They also demonstrate that treatment with *C. militaris* extract can inhibit growth of subcutaneously xenografted melanomas.

Anti-allergy and anti-inflammatory activities

A previous finding has showed that the ethylacetate (EtOAc) layer of methanol extract of germinated soybean grown *Cordyceps militaris* fruit bodies (GSCM) can inhibit both the β -hexosaminidase release (degranulation marker) in activated mast cells and the signaling pathway evoked by Fc ϵ R (IgE antibody receptor) cross-linking by allergen. EtOAc extract also can alleviate passive cutaneous anaphylaxis in mice [6]. The aforementioned observation implies that the components existing in EtOAc extract possess the inhibitory ability against type I hypersensitivity so called allergy. An anti-allergic compound called genistein 4'-O- β -D-glucoside 4''-O-methylate is further purified from the methanol extract of GSCM [7]. The anti-allergic capability of methyl-glycoside on β -hexosaminidase release is better than genistein or genistin, both of which are major isoflavones in most soy products and participate in the regulation of immune response. It also can inhibit the expression of IL-4 as well as TNF- α and Fc ϵ R-provoked signaling cascade. In addition to anti-allergic effectiveness, a study in 70% ethanol extract (CME) of cultured *C. militaris* mycelia showed that CME treatment can scavenge DPPH, suggesting it possesses anti-oxidation capability. CME showed anti-inflammatory activity in the croton oil-induced ear edema and carrageen in-induced edema in mice [8]. Recently Hwang *et al.* (2016) reported that WIB801C, the cordycepin standardized extract of *C. militaris*, can reduce post-ischemia inflammation and improve neurological deficit. WIB801C treatment also can increase survival rate of rats with cerebral ischemic stroke via decreased infiltration of microglia/inflammatory cells, reduced infarct volume/cerebral edema and dwindled blood-brain barrier damages [9].

Conclusion

The incidences of allergy are steadily increasing in many developed countries in the past decades. Most of the existing therapies for allergic diseases will lead to uncomfortable side effects. Thus mycelia or fruit bodies of *C. militaris* may confer a resource for finding a target drug

to cure or alleviate allergy. Although great efforts have been spent on finding a better way to cure or prevent cancers in the past century, it is still a long way to go. *C. militaris* may at the same time offer a complementary/integrative therapeutic source to prevent or treat various tumors.

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