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Research Note

The Medicinal Fungus *Cordyceps militaris*: Academia to Industry in Thailand

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Abstract

The medicinal mushroom (*Cordyceps* species) is a highly valued source of useful natural products having diverse biological activities. *Cordyceps militaris* (commonly known as orange caterpillar fungus), a kind of herbal drug and food additive mushroom, were used as a tonic food in Asia from ancient times. Their products have been developed from cultivated fruit bodies and fermented mycelia of *C. militaris*. Various studies of culture techniques will be expected to reduce contamination. A traditional methodology (autoclave) to sterilize culture media was compared with a protocol that included hydrogen peroxide to sterilize culture media (without autoclaving and inoculating cultures without the laminar airflow cabinet) for growing *C. militaris* CMRU strain. The results showed that the two methods had no significant differences in cordycepin production and biomass production. Production of *C. militaris* products is now becoming a large industry in Thailand.

Keywords: Cordyceps, knowledge transfer, academia to industry

Main Body

Medicinal mushrooms (*Cordyceps* species) have received attention from the world because of their biological activities. *Cordyceps* species belong to Ascomycota, Pyrenomycetes, Hypocreales, and Clavicipitaceae, and at least 700 species are known (Das *et al*., 2021). Cordyceps are specific macrofungi due to their characteristic parasite habit on larvae and insect pupae (Liu et al., 2015).

Cordyceps militaris belonging to the class Ascomycetes, have been used widely as a raw drug and a folk tonic food in Asia. It contains many types of active compounds (such as cordycepin, adenosine, polysaccharides, ergosterol, mannitol, etc.). Cordycepin is a unique active substance of Cordyceps, and its production in *C. militaris* is higher than that of other Cordyceps species. The production of cordycepin from *C. militaris* fruiting bodies can be enhanced by artificial cultivation (Lin et al., 2022).

Cordyceps militaris have beneficial properties such as pro-sexual, anti-inflammatory, antioxidant, anti-ageing, anti-tumour/anticancer/antileukemic, anti-proliferative, anti-metastatic, immunomodulatory, anti-microbial, anti-bacterial, anti-viral, anti-fungal, anti-protozoal, insecticidal, larvicidal, anti-fibrotic, steroidogenic, hypoglycemic, hypolipidaemic, antiangiogenetic, anti-diabetic, anti-HIV, anti-malarial, anti-fatigue, neuroprotective, liver-protective, reno-protective and pneumo-protective (Das et al., 2010). *Cordyceps militaris* helps in the improvement of learning and memory impairment in patients with Alzheimer's disease (Thakur et al., 2022). *Cordyceps militaris* extract has the potential to promote eye healthcare, especially for high-acuity vision healthcare (Chen et al., 2022).

The cultivation of *C. militaris* can be divided into 2 methods: insects and artificial media.

Insects: Artificial growth and stroma production of *C. militaris* have been studied in the laboratory on various insect pupae and larvae, most commonly on the silkworm *Bombyx mori*. Other insects used for artificial stroma production are *Antherea pernyi*, *Mamestra brassicae*, *Tenebrio molitor*, *Ostrinia nubilalis*, *Heliothis virescens*, *H. zea* and *Spodoptera frugiperda*, *Andraca bipunctata*, *Philosamia cynthia*, *Spodoptera litura* (reviewed by Shrestha *et al*., 2012). Chen and Ichida (2002) found a higher rate of infection and stroma formation in silkworm pupae compared with silkworm larvae.

Artificial media: Since insects can be difficult to handle and therefore prone to microbial contamination, alternative artificial media have been tested for commercial production of *C. militaris* fruiting bodies. *Cordyceps militaris* was grown in liquid media for mycelium harvesting and in solid media for fruiting-bodies induction. Many types of natural organic substrates can be used as artificial media. Cereals (such as rice, barley, millet, corn grain, etc.) with the addition of some organic substances turned out to be good substitutes for insects. In our laboratory, rice mixed with silkworm pupa powder has proven to be superior to other substrates and is now routinely used. The fruiting bodies of *C. militaris* have been successfully grown on a large scale. Yields were found less on insects than on cereals in cultivation (Xie et al., 2009a, b).

Not only media, but successful cultivation also requires appropriate control of temperature, humidity, and light. Some experiments have already demonstrated that the chemical components of natural and cultured *C. militaris* are similar (Jiang and Sun, 1999).

Links between universities and industries (University-Industry Linkages: UIL) are one way to develop technology and innovation to create competitiveness in the industry. There are many forms of UIL, ranging from linkage by market forces to institutional linkages. From research on UIL in the past, most of them found that institutional linkages are a more effective form of generating and transferring knowledge and technology. However, there are relatively few institutionalized UIL models in Thailand. This is due to the limitations in the technological capacity gap between universities and industry, lack of mutual trust, and policy problems at both the government and university levels. Resolving these issues is necessary if institutional linkages between universities and industry are seen as important.

Links between industry and universities found in Thailand, most of them are limited to links by market mechanisms. Market-coordinated linkages such as consulting, technical services, sale of products, and licensing. These activities will mainly focus on buying and selling knowledge and academic services. Long-term institutional linkages, such as joint labs at a company/university, joint patenting and joint research publication (joint publication), are a minority. A survey of 136 UIL projects of UIL activities in Thailand found that the major patterns of UIL were in the areas of consulting, technical services, innovation and invention trading, and licensing activities accounting for 49, 35, 17 and 8 percent, respectively (Schiller, 2006).

Cordyceps militaris were known to Thai people no more than 15 years ago, but before that, few Thai people only knew *Ophiocordyceps sinensis* (Tibetan cordyceps mushrooms). *Ophiocordyceps sinensis* is expensive, therefore, only the rich can consume it. *Cordyceps militaris* contains similar secondary metabolites in its fruiting bodies as *O. sinensis*. Therefore, *C. militaris* has been widely regarded as a substitute for *O. sinensis*. In 2010, Tapingkae *et al*. studied the effect of a cultivation method on yield and cordycepin production of *C. militaris*. A traditional methodology (autoclave) to sterilize culture media was compared with a protocol that

included hydrogen peroxide to sterilize culture media (without autoclaving and inoculating cultures without the laminar airflow cabinet) for growing *C. militaris*. The results showed that the two methods had no significant differences in cordycepin production and biomass production. *Cordyceps militaris* is suitable for production in the industrial system because the trend of the world is concerned about health. Nowadays, Thailand has entered an ageing society. Quite a several people are turning to take care of their health more and see the importance of nutritional supplements. The food supplement is a huge market, and its value is constantly increasing. *Cordyceps militaris* are used as dietary supplements in humans and animals. There are many forms such as capsules, tablets, water extracts, and cosmetics can be mixed with a variety of food. However, there is very little medical research on *C. militaris* in Thailand. Most medical information is derived from research abroad.

Successful knowledge transfer can be achieved if universities do not expect too much commercial interest in their research. The training course was one of the methods that saw clear results as in the case of *C. militaris* mushroom. Many people had benefited from the research. Research related to medicinal plants or mushrooms is needed by industry. People prefer to use medical herbs rather than synthetic ones.

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