A novel *Cordyceps militaris* Ferment Extract with Chinese characteristics targets on well aging

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Introduction:

Cordyceps militaris, a traditional herbal drugs in China, has gained considerable significance in several clinical and biotechnological applications, while it is difficult to be fully extracted the bioactive constituents from *C. militaris* by traditional extraction methods. Generally, bio-fermentation is one innovative technology to extract active substances effectively, especially, probiotics and fermentation by probiotics is famous in food, cosmeitic and pharmaceutical industry.

In order to gain the active substances, we developed the Cordyceps Militaris Ferment Extract (CMF) through fermentation with probiotics as strain, and it have been proved that the active components were increased significantly than common extraction method. Moroever, the potential applications of CMF in cosmetic and medicine industry have been carried out in this studies.

Materials & Methods:

First of all, the Cordyceps Militaris Ferment Extract (CMF) was obtained by high-efficiency fermentation process using highly active *Lactobacillus* as the strain and Cordyceps militaris as the main substrate, and the main active substances were quantitatively detected, such as cordycepin by HPLC method, cordycepic acid through colorimetric method. Then the HIF-1α expression was assessed with Human keratinocytes (HaCaT) cells; Further, the multi-dimensional anti-aging tests have being carried out, for anti-oxidant efficacy, the scavenging rate of hydroxyl free radicals (·OH) and superoxide free radical (ROS) were measured by chemical method and HaCaT-UV damage model (*in-vitro* test) respectively; for anti-inflammatory effect, the expression value of inflammatory factors were monitored in mice macrophages model (*in-vitro* test); moreover, for the well aging, the expression level of collagen I was measured with fibroblast model using immunofluorescence statistics.

Results & Discussion:

Fig.1 Chromatogram of CMF
The content of cordycepin is significantly increased after fermentation and the concentration of cordycepin can reach to 125 ppm.

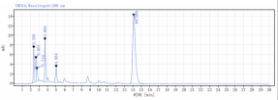

Table 1 content of cordycepin
The content of cordycepic acid in the sample before fermentation is only 5.76 g/L, and the content in CMF is 3.06 times that before fermentation.

Sample name	Cordycepic acid content g/L
Sample 1 (before fermentation)	5.76
Sample 2 (after fermentation, CMF)	17.62

Fig.2 Expression level of HIF-1α in cells
Compared with the control, the expression value of HIF-1α was significantly increased by CMF. When the concentration was 0.1%, the expression level of HIF-1α could reach to 108%, thereby improving skin hypoxia deficiency and cell viability.

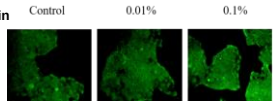

Fig.3 Expression level of collagen I in cells
The expression of Collagen I was up-regulated significantly by 23% with 0.1% CMF, which suggested CMF will play an important role in anti-aging by increasing expression of collagen I.

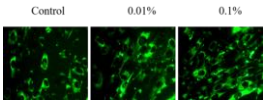

Table 2 Effect of CMF on hydroxyl radical
After fermentation, the ability of scavenging hydroxyl radicals is significantly improved, which is 4.12 times that before fermentation.

（v/v）	Sample1 (before fermentation)	Sample2 (after fermentation, CMF)
20%	45.92%	100%*
10%	33.31%	100%*
5%	27.51%	88.56%*
2%	16.45%	67.80%*

Table 3 Inhibitory effect of CMF on pro-inflammatory factors
1.5% CMF inhibited the release of inflammatory factors IL-6, IL-1β and TNF-α, especially IL-1β with a 100% inhibition rate. Therefore, CMF can effectively reduce skin problems caused by inflammation.

Content	IL-6		IL-1β		TNF-α	
	Content pg/mL	inhibition rate/%	Content pg/mL	inhibition rate/%	Content pg/mL	inhibition rate/%
Normal control group	0	--	0	--	200.4	--
Model group （LPS）	111.55	--	7.48	--	553.17	--
sample 1 （1.5%）	423.11	--	0	100**	663.01	--
1.5% CMF	98.73	11.49*	0	100**	595.25	8.66

Conclusions:

Fermentation by probiotics is an effective manner of active ingredient extraction and enrichment, after fermentation, the value of active ingredients in CMF were greatly increased, especially cordycepin and cordycepic acid, which is the foundation of well aging.

Our findings conclude that CMF can improve skin hypoxia by increasing the expression of HIF-1α, thereby ameliorating the skin aging caused by oxidant damage, inflammatory response and intrinsic aging, thus CMF may consider as a desirable cosmetic ingredient for skin protection and/or preparation of skin care products.

References:

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