Pilot Study to Investigate the Changes in Metabolic and Physiological Parameters using Cordyceps sinensis supplementation (3 grams per day) in a double blind, randomized format

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Background

Cordyceps sinensis is a fungus that has been used in traditional Chinese medicine for hundreds of years to treat asthma, tuberculosis, chronic bronchitis and renal failure (Pegler et al, 1994). It is also used as a tonic to relieve exhaustion and fatigue, maintain health and to regain "energy status" following illness (Bok et al, 1999; Pegler et al, 1994).

Wild Cordyceps sinensis is rare, and artificial cultivation now dominates production. This confers the advantage that the product is not contaminated by bacteria, other fungi and heavy metals. It is now possible to purchase tablets and capsules containing various strains of Cordyceps sinensis from a large number of companies over the internet and in health food stores.

The pharmacologically active components of Cordyceps sinensis are still unresolved. Cordycepin and cordycepic acid have been proposed as important active constituents (Pegler et al, 1994; Zhu et al, 1998a), and it is now believed that cordycepic acid is, in fact, d-mannitol, and that cordycepin is 3'-deoxyadenosine (Zhu et al, 1998a). It seems unlikely however that either, or both, of these simple compounds could be responsible for the varied and complex reported physiological actions of Cordyceps sinensis. Kiho et al (1986, 1993, 1996, 1999) have conducted a series of experiments in which they have extracted a number of polysaccharides from Cordyceps sinensis, which they reported to exhibit hypoglycaemic effects in normal and diabetic mice. Other researchers have also succeeded in extracting active components from Cordyceps sinensis, which are claimed to inhibit the proliferation of human mesangial cells in vitro and inhibit autoimmune disease progression in lupus model mice (Lin et al, 1999).

Well designed, pre-clinical, animal based studies have indicated that Cordyceps sinensis has numerous metabolic and physiological actions. For example, Cordyceps sinensis increased intra-tracheal secretion in rats, and hence may facilitate expectoration, which could account for the effectiveness of this supplement in treating cough in asthmatic patients when taken as an adjunct to conventional therapy (Qiuo & Ma, 1993). Furthermore, Kiho et al (1996) administered an extract of Cordyceps sinensis by intraperitoneal injection (50mg/kg) to normal and streptozotocin-induced diabetic mice, and demonstrated a lowering of plasma triglyceride levels at 3 and 6 hours post-administration. A related study, to determine the mechanism behind this hypolipidaemic action, showed that 14 C incorporation into newly synthesised cholesterol was significantly reduced following subcutaneous injection of Cordyceps sinensis extract in mice (Li et al, 1992). It has also been demonstrated that an extract from natural Cordyceps sinensis increased the number of T-helper cells in mice following intraperitoneal administration over three days (0.2g/day), while the number of T-suppressor cells was unchanged (Chen et al, 1987).

Studies published to date aimed at investigating the metabolic and physiological effects of Cordyceps sinensis in vivo in groups of healthy volunteers and patients have reported effects on cardiovascular (Chen, 1995), immune (Liang et al, 1997), skeletal muscle (Xiao et al, 1999) and respiratory (Zhu et al, 1998) function, and glucose (Guo & Zhang, 1995) and lipid (Shao et al, 1990) metabolism. These studies have, however, generally been semi-quantitative in nature and/or poorly designed.

In view of the sparcity of quantitative data from studies involving human volunteers, the aim of this experiment will be to investigate the effect of 4 weeks of placebo or Cordyceps sinensis dietary supplementation on resting heart rate and blood pressure, fasted blood glucose and lipid concentrations, white cell count, and respiratory and muscle function in young healthy volunteers.

Protocol

Eighteen (18), young, healthy subjects (between the age of 19 to 22) were recruited to take part in the experiment. Following completion of a routine health screening questionnaire, subjects were familiarised with the exercise procedures to be conducted over the course of the study and were told in detail about all procedures to be performed.

Following this, subjects reported to the laboratory following an overnight fast and a 10 ml venous blood sample was obtained by veneputure to determine blood glucose concentration, white cell count, and plasma triglyceride and cholesterol concentrations. In addition, resting heart rate and blood pressure, vital capacity and forced expiratory volume, and handgrip strength and endurance were measured after collection of the blood sample. The respiratory function measurements were conducted in the presence and absence of increased airways resistance, by attaching variable width tubing to the spirometer inlet. All of these procedures are painless, non-invasive and are used routinely in the Human Studies Laboratory, School of Biomedical Sciences (University of Nottingham-Queens´ Medical Centre).

Subjects were then be randomly assigned to 2 experimental groups, who were be asked to ingest Cordyceps sinensis or taste matched placebo tablets, at a dose of 3 g per day, in a double-blind manner for 4 weeks (2 x 500 mg tablets, 3 times per day). The experimental procedures executed prior to supplementation were repeated after 2 and 4 weeks of supplementation. Thus, ~ 30 mls of blood (less than a quarter of a cup) was be taken over a 4 week period.

Two-way Analysis of Variance for Repeated Measures was used to detect statistical differences within and between treatment groups in the paramaters measured. When significant, a Least-Squares Difference post-hoc test was used to locate differences.

Safety and Toxicity

There is abundant animal based literature to show that Cordyceps sinensis is a very safe product (Huang et al, 1987; Lin et al, 1999, Wang & Zhao, 1987; Zhu et al, 1998b, Manabe et al, 2000). There have been very few reports of adverse reactions to Cordyceps sinensis in humans, and it is freely available to the general public as a dietary supplement. The recommended daily dose of Cordyceps sinensis for ingestion in adults is most commonly 1 g, 3 times a day (China-guide, 2000), which was employed in the present study. This investigator could find only two reports of adverse effects of supplementation in humans (Shao et al, 1990; Xu, 1992), which were reports of nausea, dry mouth and stomach discomfort. It should be noted however that these reported adverse reactions are extremely low in number and any subject experiencing any adverse effect would be withdrawn from the study. The Cordyceps sinensis and placebo tablets used in the present study will be provided free of charge by Mycology Research Laboratories Ltd. and produced to GMP standards (licence no. ML1032).

Results

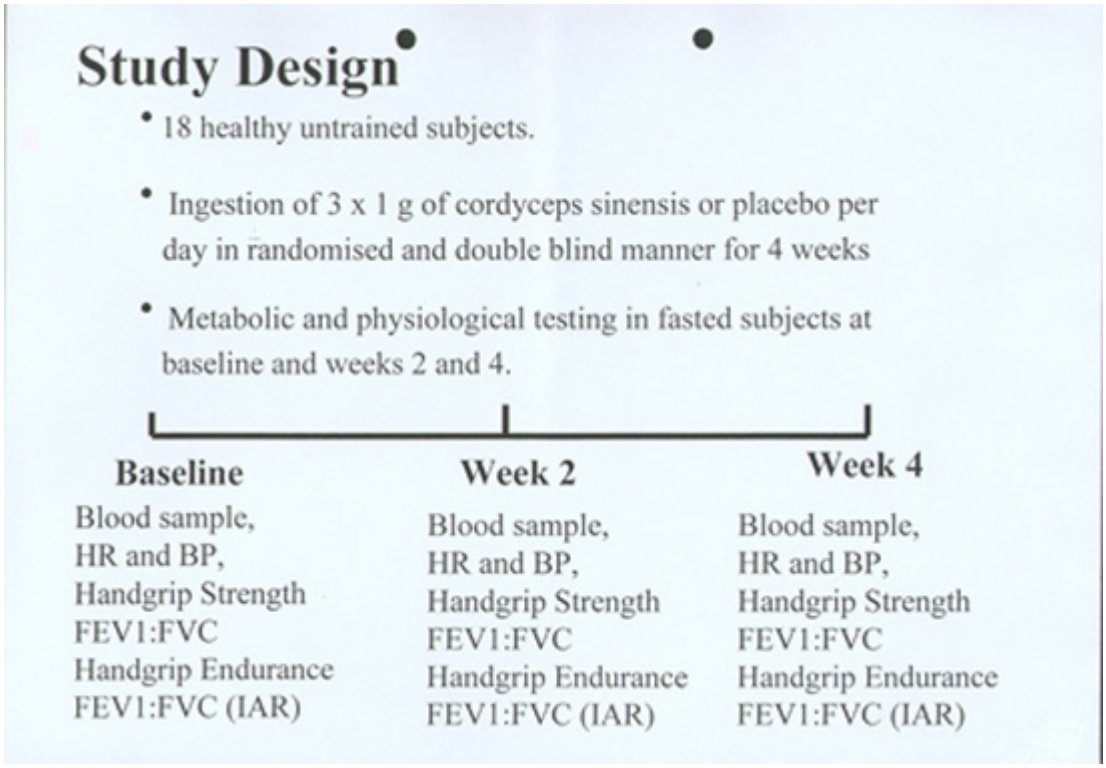


Table 1: Subjects' demographic characteristics

Characteristic	Placebo (n = 9)	Cordyceps (n = 8)
Mean (range) age (years)	21.1 (19-22)	21.3 (20-22)
Mean (range) height (cm)	172.8 (157.5-186.0)	166.8 (155.9 – 180.7)
Mean (range) weight (kg)	68.9 (54.4 – 87.5)	64.7 (50.8 – 81.0)
Male (%)	44	38

Table 2: Mean fasting plasma glucose and lipid concentrations in placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment Group	Time		
		0 Weeks	2 Weeks	4 Weeks
Glucose (mmol/L)	Placebo	4.95±0.69	4.58±0.29	4.77±0.36
	Cordyceps	4.43±0.38	4.69±0.55	4.58±0.32
Total : HDL cholesterol ratio	Placebo	2.49±0.60	2.84±1.00	2.66±0.60
	Cordyceps	2.65±0.95	2.98±0.87	3.11±1.12
Total Cholesterol (mmol/L)	Placebo	4.33±0.82	4.10±0.54	4.19±0.61
	Cordyceps	4.74±1.17	4.76±1.16	4.53±1.07
HDL Cholesterol (mmol/L)	Placebo	1.84±0.57	1.57±0.47	1.70±0.49
	Cordyceps	1.84±0.33	1.66±0.34	1.53±0.21
LDL Cholesterol (mmol/L)	Placebo	1.96±0.40	1.96±0.34	1.94±0.39
	Cordyceps	2.26±1.07	2.56±1.14	2.39±1.05
Triglycerides (mmol/L)	Placebo	1.16±0.35	1.27±0.50	1.27±0.31
	Cordyceps	1.41±0.78	1.23±0.48	1.46±1.12

HDL: high density lipoprotein
LDL: low density lipoprotein

Table 3: Mean haematological parameters in placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment Group	Time		
		0 Weeks	2 Weeks	4 Weeks
Haemoglobin (g/dl)	Placebo	14.2±1.2	13.8±1.2	13.9±1.1
	Cordyceps	13.9±1.5	14.1±1.0	13.9±1.3
Platelets ($x10^9/l$)	Placebo	254.1±49.3	273.7±52.3	256.3±43.7
	Cordyceps	240.4±51.6	250.3±61.7	243.1±42.7
MCV (fl)	Placebo	90.6±2.8	90.1±3.2	91.6±3.8
	Cordyceps	91.8±4.5	91.6±4.0	92.6±4.2
RBC ($x10^{12}/l$)	Placebo	4.8±0.4	4.7±0.4	4.7±0.3
	Cordyceps	4.6±0.4	4.7±0.4	4.6±0.4
PCV	Placebo	0.43±0.03	0.42±0.03	0.43±0.03
	Cordyceps	0.42±0.04	0.43±0.03	0.42±0.04

MCV: mean cell volume
RBC: red blood cell count
PCV: packed cell volume

Table 4: Mean biochemical parameters in placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment Group	Time		
		0 Weeks	2 Weeks	4 Weeks
Electrolytes				
Sodium (mmol/L)	Placebo	141.1 ± 1.3	140.9 ± 1.6	140.0 ± 1.8
	Cordyceps	141.1 ± 1.6	140.6 ± 2.1	140.1 ± 1.7
Potassium (mmol/L)	Placebo	4.3 ± 0.2	4.3 ± 0.1	4.4 ± 0.3
	Cordyceps	4.3 ± 0.2	4.4 ± 0.2	4.3 ± 0.2
Indices of renal function				
Urea (mmol/L)	Placebo	4.1 ± 0.9	3.6 ± 1.0	4.2 ± 1.0
	Cordyceps	4.4 ± 1.2	4.2 ± 1.7	4.6 ± 1.4
Creatinine (µmol/L)	Placebo	76.4 ± 12.0	75.8 ± 11.3	75.7 ± 10.4
	Cordyceps	79.4 ± 14.4	79.6 ± 15.1	79.4 ± 15.1
Indices of hepatic function				
Gamma GT (U/L)	Placebo	22.0 ± 8.8	23.9 ± 10.6	22.2 ± 8.2
	Cordyceps	29.9 ± 12.2	27.8 ± 13.1	26.4 ± 10.5
Alk.Phos. (U/L)	Placebo	65.0 ± 13.0	63.2 ± 9.9	63.0 ± 12.6
	Cordyceps	59.9 ± 11.4	59.5 ± 12.0	60.1 ± 13.1
ALT (U/L)	Placebo	25.6 ± 11.7	55.8 ± 105.6	23.9 ± 10.8
	Cordyceps	31.1 ± 8.4	28.3 ± 8.4	30.0 ± 12.0
Bilirubin (µmol/L)	Placebo	11.3 ± 8.1	11.3 ± 7.2	9.9 ± 6.4
	Cordyceps	12.4 ± 5.9	11.5 ± 5.9	11.0 ± 6.9
Albumin (g/L)	Placebo	42.1 ± 1.8	42.7 ± 1.9	42.2± 3.1
	Cordyceps	40.5 ± 3.7	43.3 ± 2.7	41.4 ± 2.9

Gamma GT: gamma glutamyl transpeptidase
Alk. Phos.: alkaline phosphatase
ALT: alanine transaminase

Table 5: Mean leukocyte concentrations in the placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment Group	Time		
		0 Weeks	2 Weeks	4 Weeks
WBC ($x10^9/l$)	Placebo	6.30±1.65	6.5±1.49	6.76±2.28
	Cordyceps	5.16±1.02	5.43±1.30	5.86±1.57
Lymphocytes ($x10^9/l$)	Placebo	2.17±0.69	2.28±0.71	2.13±0.63
	Cordyceps	1.93±0.39	2.05±0.48	1.84±0.35
Monocytes ($x10^9/l$)	Placebo	0.60±0.35	0.53±0.13	0.48±0.12
	Cordyceps	0.37±0.15	0.38±0.17	0.39±0.18
Neutrophils ($x10^9/l$)	Placebo	3.36±1.24	3.49±1.98	3.89±2.09
	Cordyceps	2.68±0.72	2.80±0.82	3.37±1.57
Basophils ($x10^9/l$)	Placebo	0.03±0.03	0.03±0.01	0.04±0.02
	Cordyceps	0.04±0.01	0.03±0.01	0.05±0.02
Eosinophils ($x10^9/l$)	Placebo	0.19±0.14	0.16±0.08	0.20±0.06
	Cordyceps	0.15±0.07	0.16±0.07	0.22±0.12

WBC: white blood cell count

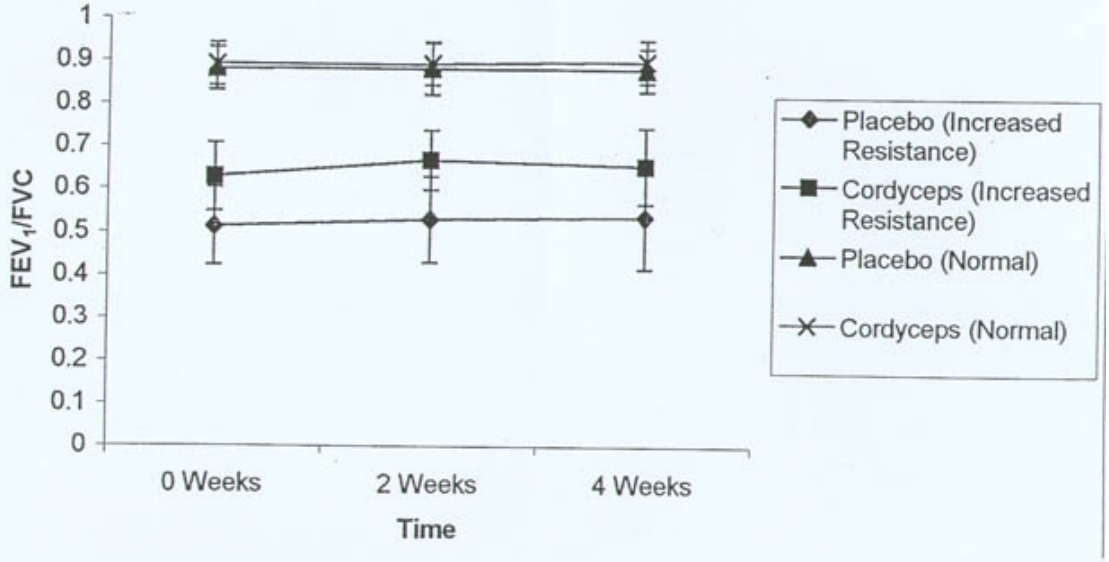
Table 6: Mean resting heart rate and blood pressure in placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment Group	Time		
		0 Weeks	2 Weeks	4 Weeks
Heart Rate (beats/min)	Placebo	67±13	69±11	68±14
	Cordyceps	63±8	65±10	64±8
Diastolic Blood Pressure (mm Hg)	Placebo	65±9	66±6	66±8
	Cordyceps	63±8	64±6	63±4
Systolic Blood Pressure (mm Hg)	Placebo	125±15	125±14	121±13
	Cordyceps	120±14	125±15	123±20

Table 7: Mean maximum hand grip strength and hand grip endurance in placebo and Cordyceps groups over the four-week study period

Measured Parameter	Treatment group	Time		
		0 Weeks	2 Weeks	4 Weeks
Maximum Hand Grip (kg)	Placebo	44.5±13.3	41.4±13.8	46.4±13.2
	Cordyceps	41.2±14.4	41.0±15.4	41.0±14.9
Hand Grip Endurance at 70% of Maximum (s)	Placebo	26±9	21±7	21±5
	Cordyceps	23±5	21±6	24±7

Figure 1: FEV_1/FVC ratio for both treatment groups under conditions of normal and increased airways resistance



Conclusions:

There was no demonstrative impact on both metabolic nor physiological measurements with the application of Cordyceps sinensis supplementation in the eighteen healthy subjects. At the same time, there were no side-effects noted or recorded by the subjects.

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