Hypothesis

A Contemporary Treatment Approach to Both Diabetes and Depression by *Cordyceps sinensis*, Rich in Vanadium

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Diabetes mellitus is accompanied by hormonal and neurochemical changes that can be associated with anxiety and depression. Both diabetes and depression negatively interact, in that depression leads to poor metabolic control and hyperglycemia exacerbates depression. We hypothesize one novel vanadium complex of vanadium-enriched *Cordyceps sinensis* (VECS), which is beneficial in preventing depression in diabetes, and influences the long-term course of glycemic control. Vanadium compounds have the ability to imitate the action of insulin, and this mimicry may have further favorable effects on the level of treatment satisfaction and mood. *C. sinensis* has an antidepressant-like activity, and attenuates the diabetes-induced increase in blood glucose concentrations. We suggest that the VECS may be a potential strategy for contemporary treatment of depression and diabetes through the co-effect of *C. sinensis* and vanadium. The validity of the hypothesis can most simply be tested by examining blood glucose levels, and swimming and climbing behavior in streptozotocin-induced hyperglycemic rats.

Keywords: antidepressants – vanadium enriched *Cordyceps sinensis* – diabetes – depression – high blood sugar-diabetes

Introduction

Diabetes mellitus is accompanied by hormonal and neurochemical changes that can be associated with anxiety and depression (1, 2). The prevalence of depression is ~18% higher in diabetic patients than in the general population, and only 33% of depression cases among diabetic patients are diagnosed and treated (3, 4). These associations may be related to the increased risk of depressive symptoms in individuals with diabetes, increased risk of Type 2 diabetes in individuals with depressive symptoms or both. Growing evidence from clinical studies indicate that diabetic patients with major depression demonstrate poor adherence to antidiabetic regimens,

have poor glycemic control, and are at an increased risk for retinopathy (5) and macrovascular complications (6).

The two processes, diabetes and depression, negatively interact, in that depression leads to poor metabolic control and hyperglycemia exacerbates depression. A contemporary treatment approach advocates an aggressive stance toward both diabetes and depression management to optimize global outcome. However, to our knowledge, an algorithm incorporating the management of both has not been discovered or reported in the literature to date. It is worthwhile to investigate one potential strategy of contemporary treatment toward both diabetes and depression. We hypothesize one novel vanadium complex of vanadium-enriched *Cordyceps sinensis* (VECS), which will be beneficial in preventing depression in diabetes and also influence the long-term course of glycemic control.

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Figure 1. Diagram illustrating processing scheme of contemporary treatment approach of Vanadium and *C. sinensis* toward both diabetes and depression.

Vanadium, glycemic control and depression management

Vanadium, element number 23, atomic weight 50.94, is normally present in very low concentrations ($<10^{-8}$ M) in virtually all the cells in plants and animals. As a potential therapeutic agent, in recent times, it is attracting increasing attention. Vanadium compounds have the ability to imitate the action of insulin (7, 8). Oral administration of inorganic vanadium salts has shown antidiabetic activity *in vitro* (9), *in vivo* (10) and even in patients (11). The improved metabolic control can improve the mood and the insulin mimicry may have further favorable effects on the level of treatment satisfaction and mood (12). Some evidence suggests that patients with adequate glycemic control will have an improved sense of well-being (13, 14).

Cordyceps sinensis, depression management and glycemic control

Mushrooms and primarily basidiomycetous fungi are a popular and valuable food, low in calories and high in minerals, essential amino acids, vitamins and fibers (15, 16). Some of them produce substances, which have potential medical effects, and are called medicinal mushrooms (17–20).

Mushrooms are a low-calorie food with minimal fat and are highly suitable for obese persons. With no starch and low sugars, mushrooms might be considered the ‘delight of diabetics’ (21). *Cordyceps sinensis* is a fungus, and has been known as a traditional medicine in China. Many studies have shown that *C. sinensis* possesses hypoglycemic (22, 23) and vasorelaxant activities (24). *Cordyceps sinensis* has an antidepressant-like activity and some of its constituents might act as adrenoceptor and dopamine D2 receptor agonists or noradrenaline/dopamine reuptake inhibitors (25). Fermented *C. sinensis* improved the diabetes-induced decrease in serum insulin

concentration, and attenuated the diabetes-induced increases in blood glucose concentrations (26).

Vanadium enriched *Cordyceps sinensis*

Using trace elements at lower doses, in combination with fungus have been ascribed as one of the potent ways to reduce trace elements-associated toxicity and maintain their effect (27, 28). An important property of fungus is the ability to take up and accumulate trace metals such as cadmium, lead, arsenic, copper, nickel, silver, chromium, and mercury in the body or mycelium of the fungus (29–31). Taken together, these data suggest that fermented fungus of *C. sinensis* rich in vanadium may be beneficial in preventing depression in diabetes (Fig. 1).

Testing the hypothesis

The validity of the hypothesis can most simply be tested by examining blood glucose levels and the swimming and climbing behavior in streptozotocin-induced hyperglycemic rats following VECS treatment. Streptozotocin inhibits insulin secretion and causes a state of insulin-dependent diabetes mellitus (32). The streptozotocin-induced diabetic rats prematurely and repeatedly present more intense immobility in the forced swimming test, demonstrating their susceptibility to behavioral alterations in this animal model (33).

Conclusions

In this article, we suggest that the VECS may be a potential strategy for contemporary treatment of depression and diabetes through the co-effect of *C. sinensis* and vanadium (Fig. 1). This hypothesis represents a completely novel area of study, which will lead to valuable treatments for psychological disorders as well as physical diseases.

If the hypothesis is supported by further experimentation, it may improve people's quality of life and reduce the medical cost of our healthcare system.

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