

# The Role of Cortisol Excess and Deficiency in Metabolic Syndrome

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**Keywords:** Diabetes mellitus, Cortisol, Blood, Hemoglobin

## Abstract

Cushing disease is characterized for the overproduction of endogenous glucocorticoids. In 2012, Feelders, et al, carried out a literature review from 2000 to 2012. This study found that at the time of diagnosis, 58-85% of patients have hypertension, 32-41% are obese, 20-47% have diabetes mellitus, and 38-71% have dyslipidemia. Polyphenol-rich herbs have shown clinically meaningful benefits on fasting serum glucose reduction, anti-inflammation properties and anti-oxidation in type 2 diabetes mellitus patients.

Recent reviews have listed numerous herbs that have been clinically tested and showed various degrees of effectiveness in preventing and managing Type 2 diabetes mellitus. This commentary will examine whether some herbs can reduce both cortisol and hyperglycemia.

Tetrahydrocannabinol (THC) has showed blunted increases of cortisol relative to healthy controls which demonstrates a suppressing effect. Studies have also shown decreased fasting plasma glucose and improved pancreatic  $\beta$ -cell function, adiponectin, and apolipoprotein after THC intake.

Tribulus terrestris has been tested in rats and found that treatment of rats during overtraining lead to a significant decrease in the serum level of corticosterone. Other studies showed a significant blood glucose-lowering effect in diabetic patients compared to placebo.

Urtica dioica (common nettle) was experimented on dexamethasone induced diabetic mice which revealed significantly reduced hyperglycemia and plasma corticosterone. A separate study using fish exhibited a decrease in plasma cortisol levels after administration of urtica dioica. It also has been shown to lower the blood levels of fasting glucose, 2 hours postprandial glucose, and Hemoglobin A1c significantly.

Momordica Charantia (Bitter melon) has been tested on albino rats and was found to attenuate the chronic unpredictable stress induced changes in the levels of plasma corticosterone in a dose- dependent manner. Momordica has also caused a reduction in hemoglobin A1C and 2 hour glucose after administration.

Tarragon (*Artemisia drancunculus*) has a high concentration of eugenol which was studied in yellow

European eels and reduced the release of plasma cortisol during anesthesia. It has also been evaluated in rats which revealed that Eugenol pretreatment for 7 days decreased the plasma corticosterone levels. Tarragon has also caused significant decrease in hemoglobin A1C, area under the curve of insulin and total insulin secretion in other studies.

Coccinia indica has a high concentration of Beta Sitosterol which has a cortisol lowering effect. Coccinia showed marked improvement in patients for their glucose tolerance and other studies exhibited a significant decrease in the fasting, postprandial blood glucose and hemoglobin A1C of the experimental group compared with that of the placebo group.

Salvia Officinalis has a high concentration of linalool which has shown cortisol level reduction in studies reversing the behavioral alterations observed following rapid eye movement-sleep deprivation in mice. Consumption of Salvia has also exhibited a significant decrease in the 2 hour post-prandial blood sugar levels compared to the control group.

Artichoke has a high concentration of a prebiotic called inulin which has been found to inhibit Corticosterone. It has been tested on brain cells and found that an inulin type hexa-saccharide protected the cells from the lesion induced by corticosterone. Artichoke has shown significant decreases fasting blood glucose, glycosylated hemoglobin and A1C –derived average glucose in studies.

Chamomile has been examined in stressed bovines who were administered Matricaria Chamomilla and cortisol levels were significantly lower in these animals. Chamomile tea has been shown to significantly decreased concentration of hemoglobin A1C, serum insulin levels and insulin resistance.

Sumac bran has a high concentration of myricetin which has been found to reduce corticosterone. Myricetin has shown decreased plasma corticosterone levels in mice subjected to repeated restraint stress. In other studies sumac powder has revealed significant decreases in serum glucose and hemoglobin A1C.

Citrullus Colocynthis has a high concentration of Cucurbitacin R which has shown a cortisol reducing have

effect. Rats injected with cucurbitacin R glucoside and exposed to immobilization stress showed that the level of corticosterone in the adrenal cortex and blood plasma was not increased. Citrullus has shown a significant decrease in hemoglobin A1C and fasting blood glucose levels in *C. colocynthis* treated patients in other studies.

Cardamom has been evaluated on dexamethasone-induced hyperglycemia in albino rats and was found to be useful in fasting hyperglycemia due to glucocorticoids excess. In other studies insulin sensitivity has increased with cardamom.

Chicory has a high concentration of inulin which has a cortisol lowering effect. Hemoglobin A1c was found to decrease by ingesting chicory root extract. Furthermore, substitution of glycemic sugars by inulin or oligo-fructose from chicory has been found to be an effective strategy to reduce the postprandial blood glucose response to foods.

Schisandra has been investigated in terms of the function of the pituitary-adrenal cortex and carbohydrate metabolism in male rats undergoing experimental chronic psychological stress and both the glucose and corticosterone levels were significantly reduced in the Schisandra group. Schisandra has also been investigated in rats after strenuous navigation and exercise where it reduced serum corticosterone and blood glucose levels. Studies in obese patients tended to show a greater decrease fasting blood glucose compared to the placebo group.

Carob has a high concentration of inositol which has a cortisol reducing effect. Subjects who consumed carob pod inositol enriched beverage in studies exhibited a significant decrease in insulin and glucose improvement after postprandial and fasting nocturnal compared with the control group.

In terms of Cushing disease there seems to be a causal relationship between increased cortisol levels and insulin resistance. In addition to endogenous glucocorticoids overproduction in Cushing disease causing insulin resistance we must also examine exogenous glucocorticoids as well. Studies have revealed that the odds ratio for new-onset diabetes mellitus in patients treated with glucocorticoids ranges from approximately 1.5 to 2.5. Other studies showed that the odds ratio for development of new-onset diabetes mellitus has been reported to be 1.36 to 2.31 in patients undergoing glucocorticoid treatment. Finally, there have been studies which found that the rate at which patients developed glucocorticoid-induced hyperglycemia or diabetes was 32.3%. Similarly, there seems to be a correlation between exogenous glucocorticoids and blood pressure as well. Studies have showed increased blood pressure and weight gain in patients treated with glucocorticoids. Further studies evaluating the causal relationship between hypercortisolemia and metabolic syndrome are warranted.