

Editorial

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Coenzyme Q10, Glucose Homeostasis and the Probable Mediating Role of Adipokines

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Coenzyme Q10 is one of the most popular nutritional supplements, which has been discovered in 1955. It is also known as ubiquinone, Q10, CoQ and vitamin Q10. This coenzyme has two isoforms; the oxidized form, ubiquinone, is an electron carrier in mitochondrial respiratory chain and the reduced form, ubiquinol, acts as an antioxidant.^{1,2} Studies reported its beneficial effects in some diseases such as diabetes, heart failure, hypertension, and Parkinson disease.^{3,4} Q10 has also been proposed to be helpful in prevention and treatment of neurodegenerative and mitochondrial related diseases.⁵ Q10 could potentially be effective on metabolic disorders including lipid profile, blood pressure, glycemic control and insulin resistance in different diseases.⁶⁻⁸

Many diseases are accompanied with impaired glycemic control and insulin resistance.⁹ Phosphorylation of Insulin Receptor Substrates (IRS) is crucial for insulin signalling cascade, which in turn activates the mitogen-activated protein kinase (MAP-Kinase) with major mitogenic effects and phosphatidylinositol-3-Kinase (PI-3K) with prominent metabolic properties including appropriate cellular glucose distribution.¹⁰ Coenzyme Q10 might induce the tyrosine kinase and phosphatidylinositol 3 kinase (PI3k) activity in liver. These enzymes are involved in improving insulin cascade and increasing GLUT2 and tyrosine phosphorylation of IRS-1, which could in turn enhance glucose uptake and inhibit gluconeogenesis in liver.¹¹ This antioxidant has been shown to reduce HbA1C levels in experimental and clinical studies and to improve long term glycemic control.^{6,7,12,13} It could also increase insulin production and secretion probably by stimulating ATP generation in pancreatic beta cells.¹⁴ Other proposed mechanisms include regulation of insulin receptors, glucose transporters, lipid profile, redox system, and receptors of advanced glycated end products.¹⁵

Obesity, the major growing health problem worldwide, is one the most important contributors of initiation and progression of insulin resistance.¹⁶ The potential mechanisms include higher production of fatty acids, activation of Toll-like receptor 4 and the innate immune system, alterations in endocrine and inflammatory mediators and activation of nuclear factor- κ B (NF- κ B).¹⁷

Recently the metabolic functions of adipose derived peptides, adipokines, have been investigated progressively in different disorders. The changes in the secretion of adipokines in obesity could inhibit insulin signalling through increasing inflammatory adipocytokines and other mediators interfering the IRS phosphorylation and integrity.¹⁷ The relationship between the major adipokines, leptin, adiponectin, resistin and visfatin with glucose homeostasis has previously been demonstrated.^{18,19} Leptin could contribute to glucose homeostasis through direct and indirect actions on peripheral tissues. Direct leptin actions might inhibit insulin and glucagon secretion from pancreatic cells. Moreover, leptin could potentially affect insulin signaling in adipocytes, liver and skeletal muscles. Central leptin actions on glucose homeostasis might be mediated through both the sympathetic nervous system and the parasympathetic nervous system in different tissues.²⁰ Resistin has primarily been known as an adipokine with adverse effects on insulin sensitivity. Resistin could activate NF- κ B and induce the secretion of pro-inflammatory

factors, which could be potentially involved in insulin resistance.¹⁹ Visfatin has similar inflammatory characteristics; however, regardless of some controversies, it is proposed to have favourable effects on glucose metabolism.²¹ Moreover, the reduction in adiponectin levels would be associated with insulin resistance, dyslipidemia, metabolic syndrome and atherosclerosis.¹⁸ Modulating fatty acid oxidation, reducing hepatic gluconeogenesis and hepatic glucose production are among the proposed mechanisms.²² Adiponectin could also activate adenosine monophosphate dependent kinase and peroxisome proliferator-activated receptor- α pathways.¹⁸ There are also recently recognized adipokines with insulin sensitizing features like adipolin (CTRP12).²³ Adipolin improves insulin actions by suppressing the gluconeogenesis via PI3K-Akt pathway and improving glucose uptake of adipocytes and hepatocytes. It increases phosphorylation of IRS-1 and Akt in adipose tissue and liver while this effect is not observed in muscle cells.²³ Adipolin might also have anti-inflammatory effects. Adipolin administration have decreased macrophages accumulation and the gene expression of proinflammatory cytokines in experimental studies.²⁴

There are obvious commonalities between the mechanisms of modulating glucose metabolism by adipokines and Q10. Nevertheless, despite the available data on the functions of adipokines on insulin signalling, there are few studies investigated the probable role of these peptides in mediating the beneficial effects of dietary supplements such as coenzyme Q10 on glucose homeostasis and insulin resistance. In a recent study, the possible underlying mechanisms of coenzyme Q10 supplementation were assessed in diabetic rats. Regardless of previously documented mechanisms, an increase in adiponectin receptors and levels, and a decrease in visfatin levels were observed.¹⁵ Recently, we examined the effects of Q10 on serum adipolin levels and glycemic control of diabetic patients. We observed interesting and unexpected results that will be published soon. These kinds of studies could provide new insights into the possible role of adipocytokines in improving insulin signalling by coenzyme Q10 as a potential adjuvant treatment for conventional anti-diabetic therapies. Further studies investigating the unrecognized mechanisms of the interaction between coenzyme Q10 and adipokines in modulating glucose homeostasis are warranted.

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CONFLICTS OF INTEREST

Dr. Hosseinzadeh-Attar has nothing to disclose.

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