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Editorial

Bergenin and Diabetes Mellitus: State of the Art

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Received: November 08, 2022; **Published:** November 10, 2022

Bergenin (Figure 1), also know as cuscutin, is a naturally occurring C-glucoside of 4-O-methylgallic acid that is present in a variety of plant species. In the literature, a number of therapeutic uses for bergenin have been suggested, e.g. anti-ulcerative [1], hepatoprotective [2], anticancer [3], neuroprotective [4,5], antidiabetic [6], anti-inflammatory [4,7], antinociceptive [8], and antioxidant [4,9]. Diabetes is a crippling metabolic illness that can cause a number of consequences that have an impact on individuals' lives as well as society at large [10].

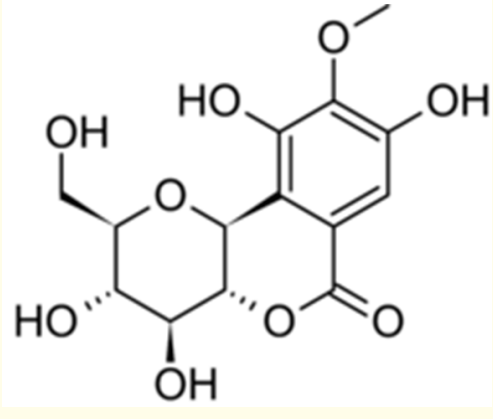

Figure 1: *Bergenin: chemical structure.*

In type 2 diabetic rats, bergenin from *C. digyna* exhibits strong antidiabetic, hypolipidemic, and antioxidant activities [11]. Reduced renal inflammation and blockade of the TGF-β 1 Smads pathway are the underlying mechanisms by which bergenin effectively protects against kidney damage in diabetic rats [12]. The primary chemical component of plants in the genus Bergenia that are utilized in traditional remedies is bergenin [13]. A highly reactive dicarbonyl molecule called methylglyoxal (MG) serves as the main precursor for the creation of advanced glycation end products (AGEs) [13]. Through the prevention of mitochondrial membrane potential dissipation, loss of adenosine triphosphate and decreased adenosine monophosphate-activated protein kinase, pretreatment with bergenin before MG exposure reduced MG-induced mitochondrial dysfunction [13]. These findings show that bergenin may stop the onset of diabetic osteopathy [13]. Significant increases in intracellular calcium concentration, mitochondrial mass, mitochondrial membrane potential and glyoxalase I decreased by MG were seen after bergenin administration [14]. Bergenin also reduced the amount of MG-induced mitochondrial superoxide that formed [14]. Patients with diabetes who have bone problems may find success in MG detoxification by bergenin [14].

Through modulating spermatogenic events and germ cell proliferation, restoring sperm quality, decreasing sperm DNA damage, balancing the levels of antioxidant enzymes and improving histopathological and histomorphometric manifestations, bergenin supplementation significantly improved the physiological and metabolic processes and reversed diabetic testicular dysfunction [15].

Bergenin may be a candidate therapy for the prevention and treatment of diabetic nephropathy since it can reduce oxidative stress via the mTOR/β-TrcP/Nrf2 pathway, which in turn inhibits glucose-induced extracellular matrix synthesis in glomerular mesangial cells [16]. Nitric oxide (NO) production *in vitro* and malondialdehyde (MDA)/nitrite levels *in vivo* were both decreased by bergenin [17]. Inducible nitric oxide synthase (iNOS) is downregulated, and glutathione peroxidase and Nrf2 are upregulated, in the nervous system, which modulates gene expression to provide these antioxidant effects [17]. Additionally, neuropathic mice who were given bergenin had their production of pro- and anti-inflammatory cytokines altered [17]. In neuropathic mice, bergenin produced a long-lasting antinociceptive effect that was accompanied by an increase in antioxidant pathways and a shift in the cytokine balance toward an anti-inflammatory predominance, which favored the restoration of redox and immunological homeostasis in the nervous system [17]. These findings suggest that bergenin has the ability to alleviate the discomfort associated with diabetic neuropathy [17]. Due to its anti-inflammatory, antioxidant and anti-apoptotic characteristics, bergenin shielded beta cells from cytokine-induced apoptosis and restored insulin secretory activity [18]. Therefore, the data point to bergenin as a promising anti-apoptotic substance in the setting of diabetes [18].

Diabetic retinopathy is brought on by the high amounts of oxidative stress that occur in people with diabetes [19]. Bergenin functions as an antioxidant, immunosuppressant, anti-inflammatory, and anticarcinogenic against hepatocarcinoma in addition to being an antioxidant [19]. Streptozotocin (STZ), an intraperitoneal diabetes-inducing agent, was used to study the effects of Bergenin on diabetic retinopathy in rats. It was found that Bergenin significantly prevented STZ-induced diabetic retinopathy in rats [19]. In particular, it has been demonstrated that, in STZ-induced diabetic retinopathy rats, bergenin considerably increases levels of HDL and antioxidant enzymes while significantly decreasing levels of pro-inflammatory cytokines, cholesterol, TG, LDL, AI, MMP-9, VEGF and MCP-1 [19]. Bergenin significantly reduced diabetic retinopathy along with raising antioxidant levels, lowering retinal thickness and increasing cell counts [19].

Bergenin has recently been shown to have the potential to cure type 2 Diabetes Mellitus by reducing inflammation in pancreatic beta cells that is caused by the NOD-like receptor family-pyrin domain containing 3 (NLRP3) inflammasome [20]. As evidenced by the downregulation of NLRP3, apoptosis-associated speck-like protein (ASC), cleaved caspase-1, and gasdermin-D (GSDMD)-N, as well as the reduced release of the cytokines interleukin (IL)-6, tumor necrosis factor (TNF)-α, IL-1β and IL-18, bergenin indeed inhibited NLRP3 inflammasome [20].

In conclusion, several studies suggest that bergenin has a promising pharmacological profile for use as a therapeutic candidate to treat type 2 diabetes mellitus and its complications.

Disclosure Statement

The authors declare that there are no conflicts of interest.

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Volume 6 Issue 2 October 2022