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# Hesperidin as a Promising Anti-Diabetic Flavonoid: the Underlying Molecular Mechanism

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## Editorial

Diabetes mellitus is a worldwide metabolic disorder with a rapidly increasing incidence. The International Diabetes Federation (IDF) has estimated the number of patients with diabetes to be 415 million in 2015. The IDF also expected that the number of diabetic patients will increase to 642 million by 2040[1]. The currently used therapeutic options for the management of diabetes has their own limitations. Therefore, there is a greater need for safe and effective alternative anti-diabetic agents[1].

Flavonoids are a diverse group of polyphenolic compounds present in fruits, flowers and leaves of plants. This class of natural compounds is known to have potential benefits in human health[12]. Flavonoids act by modulating oxidative stress and inflammation. We carried out several studies in our laboratory to examine the antioxidant, anti-inflammatory, anti-diabetic and hepatoprotective activities of specific flavonoids[3-9].

Hesperidin is aninexpensive flavone glycoside (Figure 1) abundant in citrus fruits and isolated from the ordinary orange *Citrus aurantium* L. and other plants of the Family *Rutaceae*[10]. Numerous *in vitro* and *in vivo* studies provide evidence that hesperidin possesses beneficial effects for the prevention and treatment of diabetes. In this context, we have reported the potential anti-diabetic effects of hesperidin both *in vitro*[8] and *in vivo*[4]. Hesperidin supplementation potentially regulated the activities of glycolytic and gluconeogenic enzymes and attenuated hyperglycemia in *db/db* C57BL6 mice[11] and high fat diet/streptozotocin (HFD/STZ)-induced diabetic rats[4]. This compound has been reported to up-regulate peroxisome proliferator activated receptor gamma (PPARγ), hepatic glucokinase and adipocyte glucose transporter 4 (GLUT4)[7,8,12,13].

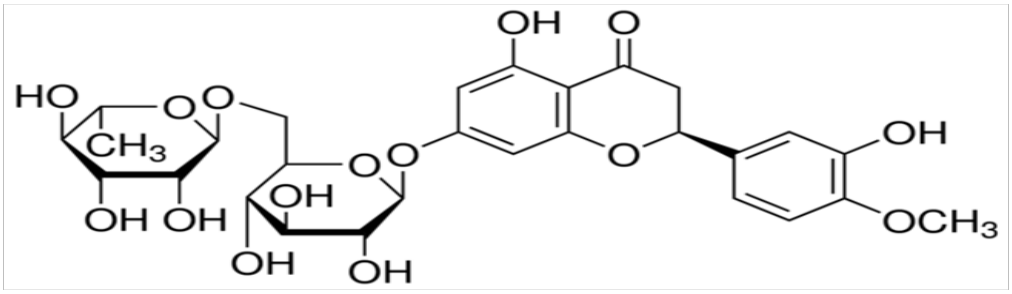


Figure 1: Chemical structure of hesperidin

In HFD-STZ-induced type 2 diabetic rats, we have demonstrated the ability of hesperidin to improve blood glucose levels through attenuation of oxidative stress and production of pro-inflammatory cytokines[4]. In combination with insulin, hesperidin reversed hyperglycemia and down-regulated the generation of free radicals and pro-inflammatory cytokines in experimental diabetic neuropathy[14]. Hesperidin also showed cardioprotective effects in diabetic rats through reducing oxidative stress and apoptosis and improving the PPARγ pathway[15]. In a model of STZ-nicotinamide induced myocardial infarction diabetes, hesperidin decreased the levels of blood glucose, glycosylated hemoglobin (HbA1c), lipids and blood pressure[16]. In addition, it decreased lipid peroxidation and enhanced the antioxidant defenses in both STZ[17] and HFD/STD-induced diabetic rats[4].

Regarding its lipid-lowering tendency, hesperidin reduced circulating and hepatocyte cholesterol levels partially by suppressing hepatic 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, resulting in attenuatedhypercholesterolemia and atherosclerosis[18]. It has also been reported to increase the fecal cholesterol and triglycerides excretion, and impede glucose-6-phosphate dehydrogenase (G6PDH) and fatty acid synthase[12]. Recently, we demonstrated that hesperidin can decrease intestinal glucose and cholesterol absorption, suppress hepatic glucose production and increase insulin sensitivity and peripheral glucose uptake[8].

Given its regulatory effect on glucose transporters, insulin secretion and sensitivity, oxidative stress, inflammation, peripheral glucose uptake, intestinal glucose absorption and hepatic glucose production, hesperidin can play a promising role in treating diabetes and its complications. Therefore, additional studies are required to determine the exact mechanistic pathways and the beneficial effects of hesperidin for diabetic patients.

## References


1. International Diabetes Federation (IDF). IDF Diabetes Atlas. 7th ed. Brussels, Belgium: (2015) International Diabetes Federation.
2. Barnes, S., Prasain, J. Current progress in the use of traditional medicines and nutraceuticals. (2005) Curr Opin Plant Biol 8(3): 324-328.
3. Mahmoud, A.M. Influence of rutin on biochemical alterations in hyperammonemia in rats. (2012) Exp Toxicol Pathol 64(7-8): 783-789.
4. Mahmoud, A.M., Ashour, M.B., Abdel-Moneim, A., et al. Hesperidin and naringin attenuate hyperglycemia-mediated oxidative stress and proinflammatory cytokine production in high fat fed/streptozotocin-induced type 2 diabetic rats. (2012) J Diabetes Complications 26(6): 483-490.
5. Mahmoud AM, Soliman AS. Rutin attenuates hyperlipidemia and cardiac oxidative stress in diabetic rats. (2013) Egypt J Med Sci 34: 287-302.
6. Mahmoud, A.M. Hematological alterations in diabetic rats - role of adipocytokines and effect of citrus flavonoids. (2013) EXCLI J 12: 647-657.
7. Mahmoud, A.M. Hesperidin protects against cyclophosphamide-induced hepatotoxicity by upregulation of PPARγ and abrogation of oxidative stress and inflammation. (2014) Can J PhysiolPharmacol 92(9): 717-724.
8. Mahmoud, A.M., Ahmed, O.M., Ashour, M.B., et al. In vivo and in vitro antidiabetic effects of citrus flavonoids; a study on the mechanism of action. (2015) Int J Diabetes Dev Ctries 35(3): 250-263.
9. Kamel, E.M., Mahmoud, A.M., Ahmed, S.A., et al. A phytochemical and computational study on flavonoids isolated from Trifoliumresupinatum L. and their novel hepatoprotective activity. (2016) Food Funct 7(4): 2094-2106.
10. Kawaguchi, K., Mizuno, T., Aida, K., et al. Hesperidin as an inhibitor of lipases from porcine pancreas and *Pseudomonas*. (1997) Biosci Biotechnol Biochem 61(1): 102-104.
11. Jung, U.J., Lee, M.K., Jeong, K.S., et al. The hypoglycemic effects of hesperidin and naringin are partly mediated by hepatic glucose-regulating enzymes in C57BL/KsJ-db/db mice. (2004) J Nutr 134(10): 2499-2503.
12. Jung, U.J., Lee, M.K., Park, Y.B., et al. Effect of citrus flavonoids on lipid metabolism and glucose-regulating enzyme mRNA levels in type-2 diabetic mice. (2006) Int J Biochem Cell Biol 38(7): 1134-1145.
13. Agrawal YO, Sharma PK, Shrivastava B, Ojha S, Upadhya HM, Arya DS, Goyal SN. Hesperidin produces cardioprotective activity via PPAR-γ pathway in ischemic heart disease model in diabetic rats. (2014) PLos One 9(11): e111212.
14. Visnagri, A., Kandhare, A.D., Chakravarty, S., et al. Hesperidin, a flavanoglycone attenuates experimental diabetic neuropathy via modulation of cellular and biochemical marker to improve nerve functions. (2014) Pharm Biol 52(7): 814-828.
15. Agrawal, Y.O., Sharma, P.K., Shrivastava, B., et al. Hesperidin produces cardioprotective activity via PPAR-γ pathway in ischemic heart disease model in diabetic rats. (2014) PLos One 9: e111212.
16. Kakadiya, J., Mulani, H., Shah, N. Protective effect of hesperidin on cardiovascular complication in experimentally induced myocardial infarction in diabetes in rats. (2010) J Basic Clin Pharm 1(2): 85-91.
17. Ashafaq, M., Varshney, L., Khan, M.H., et al. Neuromodulatory effects of hesperidin in mitigating oxidative stress in streptozotocin induced diabetes. (2014) Biomed Res Int 2014: 249031.
18. Ahmed, O.M., Mahmoud, A.M., Abdel-Moneim, A., et al. Antidiabetic effects of hesperidin and naringin in type 2 diabetic rats. (2012) Diabetol Croat 41(2): 53-67.



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