

## Ellagic Acid and Type 2 Diabetes



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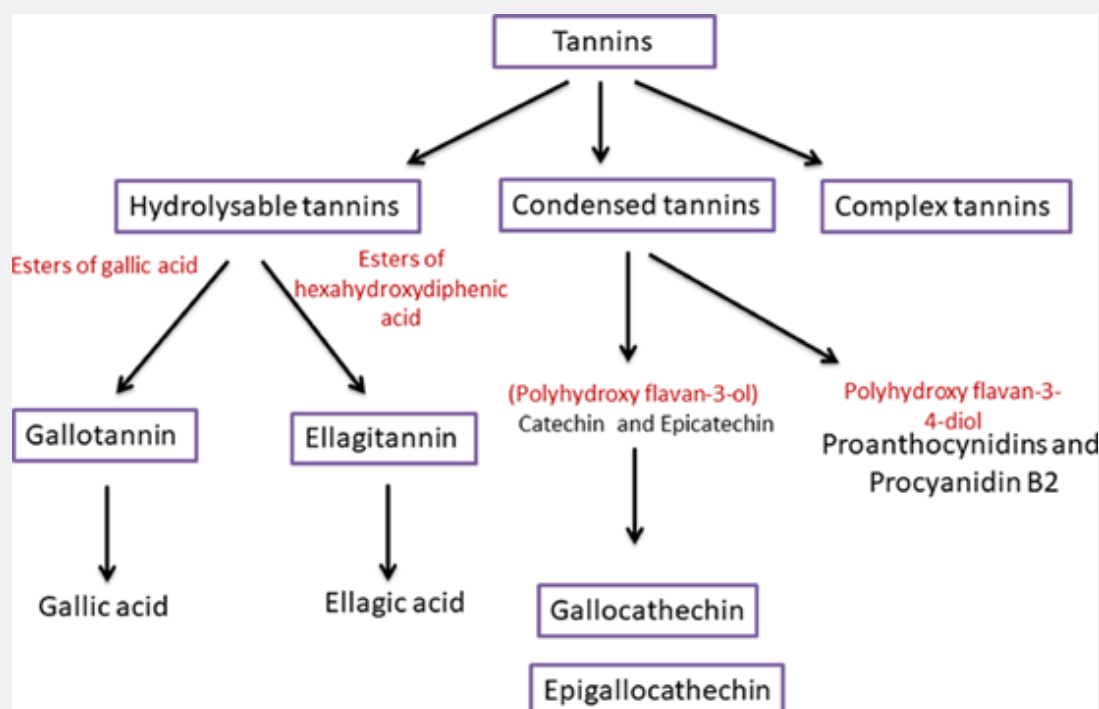
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### Short Communication

Type 2 Diabetes and its associated complications are one of the leading causes of death worldwide. Various natural products such as alkaloids, glycosides, flavonoids, terpenoids and polyphenols are reported for their activity in the management of diabetes and its related diabetic complications. Tannins have been systematically studied by many researchers in recent decades

for their effect on diabetes and its complications (Figure 1) [1]. Ellagic acid (EA) (Figure 2) has been recently complicated with type 2 Diabetes exerting anti-diabetic activity through action on pancreatic  $\beta$ -cells resulting in increased size and number of  $\beta$ -cells, increased antioxidant status, decreased blood glucose and increased serum insulin [2].



**Figure 1:** Tannins categories.

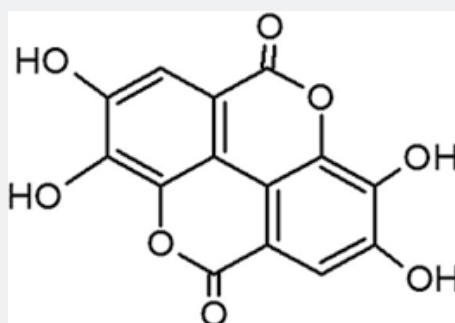


Figure 2: Chemical structure of ellagic acid.

Preclinical studies in streptozotocin- induced diabetic rats have shown that insulin or EA treatment provided protection against severe hyperglycemia lowering blood glucose and significantly suppressed TNF- $\alpha$  and IL-6 levels in both cerebral cortex and hippocampus. EA consumption also increased levels of anti-inflammatory cytokine IL-10 and neurotrophic factors NGF (Nerve Growth Factor), BDNF (Brain Derived Growth Factor), NT-3 (Neurotrophin-3) and Neurotrophin-4/5 (Neurotrophin-4/5) indicating a general neurotrophic action [3]. When streptozotocin-induced diabetic rats were fed with EA, EA suppressed advanced glycation end products (AGE) accumulation in diabetic rat kidney and improved AGE-mediated pathogenesis of Diabetic Nephropathy [4].

In vitro studies have shown that EA ameliorates oxidative stress and insulin resistance via micro-RNA -223-mediated keap1-Nrf2 activation (the major regulator of cytoprotective response to endogenous and exogenous stress caused by reactive oxygen species) in high glucose-induced type 2 Diabetes, HepG2 cells [5]. A clinical study has shown that type 2 diabetic patients who consumed 180 mg per day EA for 8 weeks, had significantly decreased blood glucose, insulin, insulin resistance, hemoglobin A1c, total cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, total antioxidant capacity, malondialdehyde, the activity of glutathione peroxidase and superoxide dismutase, C-reactive protein, TNF- $\alpha$  and interleukin 6 [6].

It is known that elevated blood glucose levels in prolonged diabetes leads to secondary complications of type 2 Diabetes such as retinopathy, neuropathy and kidney disease. Encapsulated ellagic acid (NEA) was synthesized using ZnO nanoparticles. Enzymes,  $\alpha$ -glucosidase (a hydrolase acting on 1,4- $\alpha$  bonds

degrading starch and disaccharides into  $\alpha$ -glucose molecules) and aldose reductase (a reductase responsible for occurrence of secondary complications in diabetics) were significantly inhibited by NEA [7]. EA is a natural compound which can be a potential therapeutic alternative for the treatment of type 2 Diabetes. EA supplementation can be helpful in these patients through improvement in chronic effects of type 2 Diabetes by inhibiting inflammatory signaling pathways.

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