

Plant BRCs for Type 2 Diabetes

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Elevated blood glucose over normal levels leads to a condition called diabetes or hyperglycemia. Among approximately 30 million diabetic patients in USA, 90-95% are suffering from type 2 diabetes, and about 5% are affected by type 1 diabetes. Lack of insulin synthesis and insulin resistance is considered as culprits for type 1 and type 2 diabetes, respectively. Diabetes is triggered by interaction of predisposed genetic makeup of an individual with the environment that is favorable to diabetes [1]. In order to overcome diabetic condition, many people are trying to manipulate their internal body environment by dietary supplements. Approximately 20-30% of diabetic people are using herbal or dietary supplements. Ethnic background appears to play a role while choosing dietary supplements. Hispanics, Native Americans, Asians, and African Americans are inclined to use dietary supplements. Botanicals, one of the major sources of dietary supplements, are commonly used by diabetic patients [1]. The concept of metformin (1,1-dimethylbiguanide), a most common biguanide drug used by diabetic patients now, is originated from guanidine identified in French lilac plant (*Galega officinalis* L.). Several biguanide related compounds (BRCs) are illustrated in Figure 1. People used this herbal medicine during medieval Europe. Blood glucose-lowering (hypoglycemic) activity of French lilac is ascribed to presence of higher levels of guanidine [2]. Similarly, several indigenous herbs are commonly used for the treatment of diabetes in Ayurvedic medicine practiced in India since 6th century BC. Perhaps, about 800 plants are potential source for anti-diabetic compounds in nature [3].



Figure 1: Biguanide and BRCs. Phenformin and metformin are BRC-drugs developed for the treatment of diabetes. Guanidine, galegine, L-arginine, biuret and urea are some of the known BRCs (Modified from [4]).

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Recently, Perla and Jayanty [4] quantified BRCs in fenugreek seeds (*Trigonella foenum-graecum* L.), green curry leaves (*Murraya koenigii* (L.) Sprengel), green bitter gourd (*Momordica charantia Descourt.*), garlic (*Allium sativum* L.), sweet potato (*Ipomea batatas* (L.) Lam.), and potato tubers (*Solanum tuberosum* L.). They have found highest amount of BRCs in curry leaves followed by fenugreek, bitter gourd and potato. Garlic and sweet potato contained very low or negligible amounts of BRCs. In fact, most of these plant products exhibited anti-diabetic activity in laboratory and/or clinical studies [3]. Several BRCs induce various levels of toxicity in animals or humans. Guanidine is more toxic than biguanide. Galegine, a less toxic BRC with anti diabetic property was also isolated from French lilac [2]. Interestingly, galegine also reduce body weight indirectly by inhibiting synthesis and stimulating oxidation of fatty acids [5]. L-arginine is another BRC or a guanidine-containing amino acid known to stimulate the release of insulin, glucagone, prolactine and growth hormone [6]. Structurally, guanidine is close to urea [7], and biguanide is similar to biuret (a byproduct of urea) (Figure 1). Recently, Perla and Jayanty [4] proposed biosynthetic pathways for various BRCs in plants. The future for plant BRCs as herbal remedies for type 2 diabetes is bright and promising, but further testing is required before marketing them as anti-diabetic herbal supplements.

Keywords: Biguanide; Diabetes; Anti diabetic; Functional foods; Plant foods

Abbreviations: BRC: Biguanide Related Compound

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