Journal of Diabetes and Metabolism
ISSN: 2155-6156

Babu et al., J Diabetes Metab 2012, 3:7
DOI: 10.4172/2155-6156.1000e110

Editorial Open Access

Herbs in the Management of Hyperglycemia in Diabetes. Importance of Screening Methods in the Identification of Phyto Anti-Hyperglycemic Principles

Bassa V. Babu[1]*, Vipin Kumar Chaturvedi[1] and Rao M. Uppu[1,2]

[1]*Laboratory of Autoimmunity, Torrey Pines Institute for Molecular Studies, San Diego, CA 92121, USA*
[2]*Department of Environmental Toxicology and the Health Research Center, Southern University and A&M College, USA*

It is common knowledge that normal glucose regulation is impaired in diabetes mellitus. The two major classes are type 1 or insulin dependent, and type 2 or non-insulin dependent diabetes mellitus. Where in type 1 diabetes there is almost complete destruction/loss of insulin producing cells resulting in glucose starvation in skeletal muscle, in type 2 diabetes the major manifestations are insensitivity of the pancreatic beta cells to glucose stimulated insulin release and the impairment of skeletal muscle cells to insulin stimulated glucose entry (insulin resistance).

Over the years many natural products, especially plant derived have been used in the traditional medicine for the treatment of diabetes. Apart from their empirical value, the scientific basis for investigating the Nature's inventory of chemical compounds for an anti-diabetic principle forms an interesting inquiry. Insulin is released from the beta cells of pancreas in response to rising glucose in the bloodstream. Interestingly, although glucose is a potent natural stimulator of insulin release from the pancreatic beta cells, there is no evidence to show that primitive man consumed bolus meals comprising of carbohydrates in abundant quantities, to raise the blood glucose levels high enough (180 mg/dL) to stimulate insulin release from the pancreas. Furthermore, nature is also rich in chemical compounds that are structurally similar to glucose. The insulino tropic activities of sulfonylureas which have structural similarities with glucose support this line of thinking. Of late, incretins and incretin mimetics have been used for the treatment of diabetes. Incretins like glucagon like peptie-1 (GLP-1) and gastric inhibitory polypeptide (GIP) are gut hormones released in response to ingestion of food. These are short lived as they are immediately acted upon by dipeptidyl peptidase-4 (DPP-4). Apart from modifying the peptide for a longer duration of action, inhibitors of DPP-4 are in clinical use as antidiabetics. The search for natural inhibitors of DPP-4 in some of the plants and their products used for glycemic control therefore would merit attention.

Among plant based antidiabetic principles, *Panax ginseng*, the Asian vegetable bitter melon, *Gymnema sylvestre*, Fenugreek and Tian Hua Fen (trichosanthes root) are known to contain factors that lower blood sugar levels in diabetics. Interestingly, the parent compound of biguanides used in the treatment of insulin resistance was originally isolated from a plant source (French lilac) [1].

Lately, several laboratories across the world are engaged in the screening of herbs for their antidiabetic properties using modern methods of detection [2-6]. Animal models of both type 1 diabetes with chemically ablated pancreas (using alloxan, or streptozotocin) and models of type 2 diabetes like Ob/Ob mouse, Zucker diabetic rats, and in vitro cultures of pancreatic beta cells are used in the bioassay for anti-hyperglycemic activity. Since widely varying physiological mechanisms can produce hyperglycemia as an end result, proper selection of screening methods are critical in identifying and purifying naturally occurring antidiabetic principles. One bioassay developed by us involved alloxan-recovered rabbits. Rabbits are susceptible to alloxan to varying degrees and some of them quickly recover after initially exhibiting fasting hyperglycemia in the days following the administration of alloxan (Figures 1A and 1B). These animals designated as alloxan-recovered rabbits still remain less tolerant to glucose. Thus oral glucose (3 g/kg bdwt) tolerance tests in these animals provide a wide range of peak values to use as a sensitive test for the identification of hypoglycemic properties present in the herbal extracts [7] (Figures 1A and 1B). Cultures of immortalized pancreatic beta cells (e.g., Hit T-15) currently available through the ATCC are ideal in identifying insulino tropic compounds. Interestingly, one partially purified herbal extract that dramatically improved glucose tolerance in alloxan-recovered rabbits, strongly inhibited insulin secretion in the *in vitro* cultures of pancreatic beta cells [2] (Figure 1C). This observation underscores the importance of employing more than one test method in the screening of herbal extracts for their anti-hyperglycemic activity. Therefore it is very important to design studies that combine *in vivo* methods with *in vitro* techniques for gaining a better insight into the actions of naturally occurring anti-hyperglycemic compounds.

Acknowledgment

This publication was supported in part by National Institutes of Health (NIH) grant No. P20RR16456 and US Department of Education (ED) grant PO31B040030. The contents of this publication are solely the responsibility of authors and do not necessarily represent the official views of the NIH or USED.

References

1. Cusi K, DeFronzo RA (1988) Metformin: a review of its metabolic effects. Diabetes Rev 6: 89-131.
2. Babu BV (2003) Antitumor agents. US Patent 6,660, 309.
3. Poudyal H, Campbell F, Brown L (2010) Olive leaf extract attenuates cardiac, hepatic, and metabolic changes in high carbohydrate–high fat-fed rats. J Nutr 140: 946-953.
4. Gireesh G, Thomas SK, Joseph B, Paulose CS (2009) Antihyperglycemic and insulin secretory activity of Costus pictus leaf extract in streptozotocin induced diabetic rats and in *in vitro* pancreatic islet culture. J Ethnopharmacol 123: 470-474.
5. Hannan JM, Marenah L, Ali L, Rokeya B, Flatt PR, et al. (2006) *Ocimum sanctum* leaf extracts stimulate insulin secretion from perfused pancreas, isolated islets and clonal pancreatic beta-cells. J Endocrinol 189: 127-136.
6. El Aoufi S, Gendre P, Sennoune SR, Rigoard P, Maixent JM, et al. (2007) A high calorie diet induces type 2 diabetes in the desert sand rat (*Psammomys obesus*), Cell Mol Biol (Noisy-le-grand) 53: OL943-OL953.
7. (1985) The hypoglycemic activity of Ficusbengalensis.

***Corresponding author:** Bassa V. Babu, Laboratory of Autoimmunity, Torrey Pines Institute for Molecular Studies, San Diego, CA 92121, USA, Tel: +1 619 948 8494; E-mail: bbassa9823@aol.com

Received September 01, 2012; **Accepted** September 10, 2012; **Published** September 15, 2012

Citation: Babu BV, Chaturvedi VK, Uppu RM (2012) Herbs in the Management of Hyperglycemia in Diabetes. Importance of Screening Methods in the Identification of Phyto Anti-Hyperglycemic Principles. J Diabetes Metab 3: e110. doi:10.4172/2155-6156.1000e110

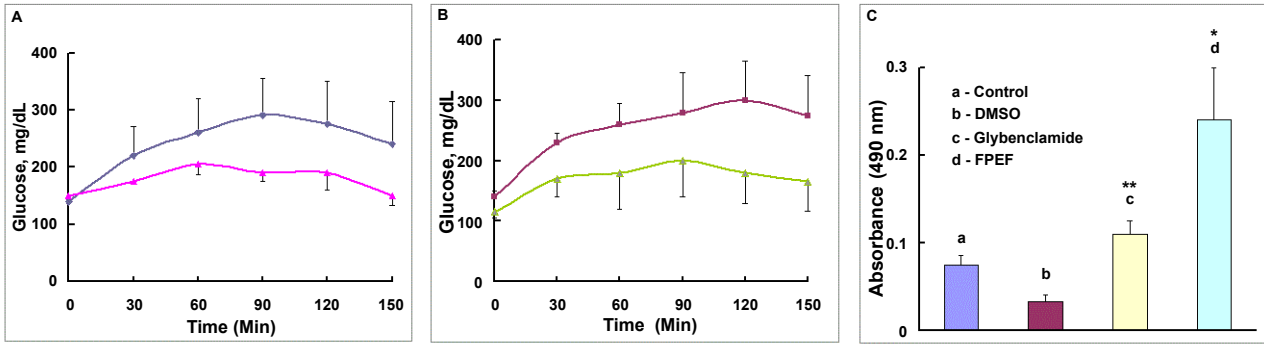

Figure 1: (A) Glucose tolerance in alloxan-recovered rabbits treated with tolbutamide. Alloxan-recovered rabbits, after an overnight fasting, were orally administered tolbutamide (1 g/kg bdwt). Glucose (3 g/kg bdwt) was administered orally 90 min later. Blood samples were drawn from the marginal ear vein at various intervals as shown and serum glucose concentration was determined by a glucose-oxidase method.

(B) Glucose tolerance in alloxan-recovered rabbits treated with the bark extract (silica gel chromatographic fraction) of *Ficus bengalensis*. Alloxan-recovered rabbits, after an overnight fasting, were orally administered with the bark extract (1 g/kg bdwt). Glucose (3 g/kg bdwt) was administered orally 90 min later. Blood samples were drawn and analyzed for serum glucose as described in **A**.

(C) Insulin content of the culture media in which pancreatic beta cells were exposed to: **a:** none (control); **b:** DMSO (10 µL/mL); **c:** glybenclamide (1 mg/mL); and **d:** fenugreek protodioscin enriched fraction (FPEF; 1 mg/mL). Pancreatic beta cells were grown in 12-well cluster dishes to 60% confluence and then treated with various agents **(a-d)** in high glucose DMEM medium for 30 min. The insulin content of the medium was determined using an ELISA kit from Crystal Chem (Downers Grove, IL). Data points in **A-C** represent values of mean ± SEM (**A** and **B**) or mean ± SD (n=3; **C**). In Figure 1C, *p<0.01 and **p<0.05 for DMSO *vs*. glybenclamideand FPEF treatments (respectively). With regard to (**a**) untreated controls, the treatments with (**c**) glybenclamide and (**d**) FPEF are significant at p<0.05.