P6

Alternative Therapies for Type-2 Diabetes

A review into the Present and Potential Prescription and Non-Prescription Oral Therapies for Type-2 Diabetes.



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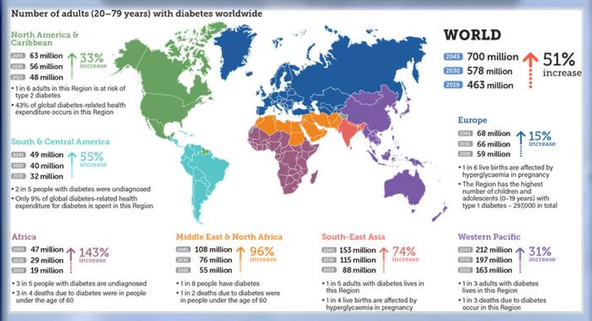
ABSTRACT



IDF Diabetes Atlas- 9th Edition (2019) Retrieved from https://diabetesatlas.org/en/

It is estimated that there is world prevalence of 425 million people diagnosed with Diabetes mellitus (DM) and as such, it remains ranked as one of the top 4 Non-Communicable diseases. Apart from diet and exercise, the prescribed use of different families of xenobiotic compounds for the restoration of euglycemic levels in the body is well known. Such compounds include both Allopathic and Phyto-therapeutic medicines, with the latter being widely taunted due to the lack of supporting clinical evidence of their efficacies. Inspired by these controversies, we have seen it fit to do a comprehensive review of the subclasses and species of the respective categories, and weigh them against each other. Further to this, because of the lack of knowledge of research drugs that are presently being investigated for DM therapy, we found it necessary to include these in our review. Our overall aim was to provide a holistic report that would better educate the public on the present and potential medicines that are available to treat this disease.

METHODOLOGY

Present medicinal therapies for Type-2 Diabetes (T2D) can be classified into 3 categories:

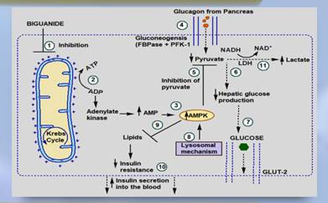
1) Allopathic Therapies
2) Phyto-Therapies
3) Coordination Complexes (Research Drugs)

- In the first category, the six (6) main classes of FDA approved pharmacological drugs (Biguanides, Sulfonylureas, Meglitinides, Alpha-Glucosidase inhibitors, DPP-4 inhibitors and Thiazolidinediones) are examined and discussed.
  - For each family of these compounds, we have described their nomenclatures, mechanisms of action and patient-reported side effects.
- In the second category we present a list of some herbal sources, from which our review showed the greatest amount of supporting scientific evidence of *in vivo* anti-diabetic activity.
- Finally, we report here a few Coordination Complexes, which from our review, have shown to be most successful in the attenuation of hyperglycemic levels in biological systems.

ALLOPATHIC THERAPIES (PRESCRIPTION DRUGS)

BIGUANIDES

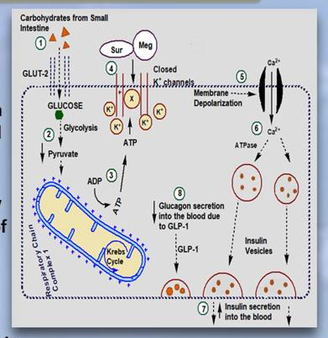
Biguanides belong to a group of oral T2D drugs that improves insulin sensitivity in the liver. It acts by decreasing hepatic glucose production and intestinal absorption of glucose, while increasing peripheral glucose uptake and utilization.



SULFONYLUREAS & MEGLITINIDES

These two groups of oral T2D drugs work in the pancreas.

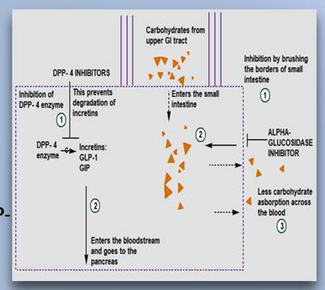
- Sulfonylureas stimulate the release of calcium ions. This stimulates insulin production and thereby decreases blood glucose levels.
- Meglitinides are similar to Sulfonylureas, meaning they have the same mechanism of action in the pancreas. However, Meglitinides are short-acting anti-diabetic agents, with a half-life of approximately one hour. Their fast activity is compromised by their much shorter duration of action.



ALPHA-GLUCOSIDASE & DPP-4 INHIBITORS

Both of these suppressing-based therapies target the small intestine.

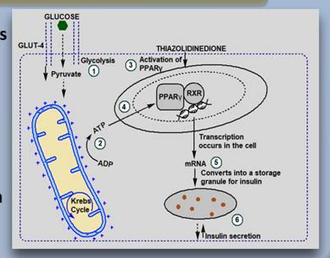
- Alpha-Glucosidase inhibitors inhibit the activity of the enzyme Alpha-Glucosidase, and thereby inhibit the absorption of carbohydrates.
- Dipeptidyl-Peptidase IV inhibitors, also known as DPP-4 inhibitors, block the enzymatic activity of DPP-4 , which degrades incretins.



THIAZOLIDINEDIONES

Thiazolidinediones is a new class of antidiabetic drugs.

- They promote insulin sensitivity in the adipose tissue and muscles by stimulating the Peroxisome Proliferator Activated Receptor (PPAR) gene, which in turn improves insulin sensitization.



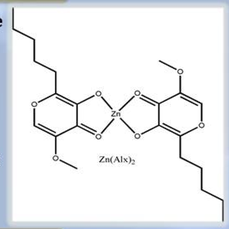
PHYTO-THERAPIES (ETHNOPHARMACOLOGICAL)

BOTANICAL NAME	GENERIC NAME	BIOLOGICAL EVALUATIONS
Momordica charantia (MC) 	Bitter Melon, Carille, Karela	500mg/kg MC extract reduced fasting plasma glucose (FPG) level in STZ-induced rats at 2 hrs. From 0 hrs, FPG: >200 mg/dL to 2 hrs, FPG: <85 mg/dL (Sarkar *et al.*, 1996) DOI: 10.1006/phrs.1996.0001
Zingiber officinale (ZO) 	Ginger, Jengibre,	500mg/kg b.w. daily of ZO aqueous extract reduced the serum glucose levels (SGL) in diabetic rats for 7-weeks (52 % reduction). From 1 wks, SGL: > 4500 mg/l to 7 wks, SGL: < 3000 mg/l (Al-Amin *et al.*, 2006) DOI: 10.1079/bjn20061849
Curcuma longa (CL) 	Turmeric, Saffron (Trinidad)	300mg/kg b.w. CL dose reduced blood glucose levels (BG) in STZ-induced diabetic rats for 8-weeks. From 0 wks, BG: >500 mg/dL to 8 wks, BG: 358.33 ± 33.05 mg/dL (Patumraj *et al.*, 2006) PMID: 17148847
Panax ginseng (PG) 	Asian ginseng, Korean ginseng	200mg/kg dose of PG extracts reduced (>10mmol/l to < 8mmol/l) FBG levels in non-insulin-dependent patients. (Sotaniemi *et al., 1995)* DOI: 10.2337/diacare.18.10.1373
Allium sativum (AS) 	Garlic	0.25g/kg of AS ethyl ether extract reduced BG levels in alloxan-diabetic rabbits. From 0 hr, BG: > 200 mg/ml to < 180 mg/ml. (Jain *et al.*, 1980) DOI: 10.1093/ajcn/28.7.684
Cucumis sativus (CS) 	Cucumber	200mg/kg b.w. of CS extracts reduced FBG levels in diabetic rats to 81.02, 58.65 and 32.61% at 4, 8 and 12 hrs respectively. From 0hr, FBG: 28 mmol/L to 12hr, FBG: 9 mmol/L (Sharmin *et al., 2012*) DOI: 10.3329/jsr.v5i1.10252
Cucurbita pepo (CP) 	Pumpkin, Squash	300 mg/kg b.w. of CP fruit extract reduced PBG levels significantly (P < 0.01)in STZ-induced diabetic rats for 30 days. From 0 day, PBG: >350 mg/dL to 30 days, PBG: < 150 mg/dL (Xia & Wang ,2007*).* DOI: 10.1002/jsfa.2916
Coriandrum sativum (CS) 	Cilantro, Coriander	400 mg/kg of leaf ethanolic extract decreased BG levels in mice with hyperglycemia (BG> 200 mg / dL). From day 0, BGL: 267±60 mg/dL to day 14, BGL: 108±23. *(*Aligita *et al.*, 2018*)* URL: https://eijppr.com/g0YW8P3

COORDINATION COMPLEXES (RESEARCH DRUGS)

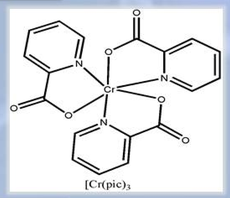
ZINC

It has been found that glycemic control can be enhanced in T1D and T2D by zinc supplementation, but the primary molecular mechanisms have only gradually been clarified. By supporting the signal transduction of insulin and by reducing the production of cytokines, zinc appears to exert insulin-like effects (Jansen *et al.*, 2009). DOI: 10.1016/j.jnutbio.2009.01.009



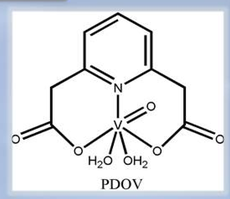
CHROMIUM

Several studies have documented effects of chromium in people with glucose intolerance and diabetes. Improvements in glucose, insulin and related variables in response to chromium supplementation normally occur within a few weeks or less (*Anderson, 2000).* PMID: 10705100



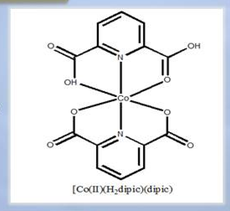
VANADIUM

Studies have demonstrated the potential of vanadium compounds as insulin-mimetic or enhancing agents. The biochemical underpinnings of the insulin-mimetic effects of vanadium salts can be gauged by two fundamental aspects: the enhancement of glucose utilization; and its storage after entering the cell (Rambaran, 2020). DOI:10.1016/j.ica.2020.119448



COBALT

It has been reported that cobalt possesses glucose-lowering properties by increasing GLUT-1 expression and inhibition of gluconeogenesis in STZ-diabetic rats. However, at higher concentrations the results have been shrouded by toxic events, which has made its effects controversial (Clyne et al., 2009). DOI: 10.1080/003655101753267964:



CONCLUSION

- Due to the extensive clinical studies performed on Allopathic medicines, they remain the most trusted and widely used of all oral therapies for T2D.
- Influenced by both cost and custom, Phyto-therapeutic medicines are still being used, especially in underdeveloped countries. Their relative safeties and efficacies still need to be further evaluated by well-designed, controlled clinical studies.
- Short comings, based on insulin dependence, for both Allopathic and Phyto-therapeutic medicines continues to fuel research in Organometallic and Coordination Complex Chemistry for more efficient anti-diabetic medication.