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Impact Of Using Allopathic Medicine And Herbal Drugs For Diabetes Mellitus

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Abstract
Diabetes Mellitus (DM) is a group of diseases, in which the pancreatic cell doesn't produce sufficient insulin production (or) does not effectively use insulin, which leads to an increase in the glucose level. Obesity and lack of physical activity are the major reasons for DM.WHO estimates that 8.7% of the population in India has diabetes, especially in the age group between 20-70 years. Asia is the leading continent in the world with a large number of populations with diabetes. In the modern days, people go with Allopathic drugs; also we have traditional plant-based drugs, which also effectively control the blood glucose level in the body. In Allopathic, various routes of drug administration are available they are oral, parenteral & Transdermal patches. Oral route metformin is the first-line therapy for type 2 diabetes. Transdermal patches are also an effective way to administer the drug. It reduces patient compliance (reduces pain, and GI disturbance), and administration of patches is also an easy method it doesn't require any special technique. Patches are removed when the skin get irritated. Traditional plant-based drugs are garlic, ginseng, etc. A combination of metformin with ginseng shows better control of blood glucose levels without showing any side effects.

Keywords: Diabetes, Metformin, Ginseng, Glucose level.

INTRODUCTION

Diabetes is a collection of metabolic disorders. It occurs due to a deficiency in insulin production or insulin action or a combination of both (1). Asia is the leading continent in the world which has the highest number of population with diabetes (2). In India diabetes is the summit of the population whose age ranges between 60 -69. In China diabetes is summit at the age of 70-79. In India, impaired glucose activities are seen in more middle-aged people than in Chinese people. It is

generally due to genetically and environmental factors. Also, type 2 diabetes rapidly increases in children. Before 1997, the American Diabetes Association and World Health Organization set the values for Diagnoses of diabetes (fasting plasma glucose level between 140 mg/dl) but later ADA & WHO reduced the fasting plasma glucose level to 126 mg/dl(3). There are several routes used for the treatment of diabetes mellitus (Oral, parenteral, and Transdermal routes).In oral (Hypoglycemic agents) metformin is the most commonly used drug. Metformin shows a positive report on the patient's weight (16).In transdermal patches drug is administered through the skin (No pain), which helps in improving patient compliance (22). Herbal medicine is also used to treat DM, Ginseng is the widely used herbal drug to treat diabetes. It is mainly used for the treatment of diabetes and also for sleeping disorders, and pulmonary problems (61).

Types of Diabetes Mellitus

- Type 1. Insulin-dependent diabetes Mellitus
- Type 2. Insulin-independent Diabetes Mellitus
- Gestational diabetes Mellitus
- Monogenic Types (4)

Clinical practice
(5)

Major Diagnostic Criteria for Diabetes and Pre diabetic or At-Risk States.				
Measure	American Diabetes Association		World Health Organization	
	Diabetes	Pre-diabetes	Diabetes	Impaired Glucose Regulation
Fasting plasma glucose	$\geq$ 126mg/dl	100 -125 mg/dl	$\geq$ 126 mg/dl	110-125 mg/dl
2Hr plasma glucose[during an OGTT with a loading dose of 75g]	$\geq$ 200 mg /dl	140-199 mg/dl	$\geq$ 200 mg/dl	140-199 mg/dl
Casual [or random] plasma glucose	$\geq$ 200 mg /dl	-	$\geq$ 200 mg/dl	-
Glycated Hemoglobin	$\geq$ 6.5%	5.7 - 6.4%	$\geq$ 6.5%	-

1. Type -1 (Insulin-dependent diabetes Mellitus)

The pancreas contains beta cells .Loss of beta cells (In autoimmune condition), leads to Type-1 Diabetes mellitus. Scientifically postulated that loss of beta cells in autoimmune conditions is due to environmental factors .Which could occur over months to years before the initial stage of diabetes.
Signs and symptoms:

- The major symptoms
- Polydipsia
- Polyuria
- Polyphagia
- Dyspenia

2. TYPE- 2(Diabetes Insulin independent)

Type 2 diabetes, which has become currently a worldwide pandemic, has the characteristics of Impaired insulin secretion. Signs and symptoms

Signs and symptoms

- Obesity
- Sedentary lifestyle
- Elderly people are the major cause of symptoms of type 2 diabetes(6)

3. Gestational diabetes is a special condition

It occurs during the pregnancy period which is mostly the second and third trimester region. The other name is transient diabetes mellitus .Which is cured after the child's birth. However controlling this condition is important because it increases the chance of fetus infection, and birth weight increases.

Causes for Gestational diabetes mellitus

- Overweight or obesity
- Non-white ancestry
- Family history of type 2 diabetes mellitus
- Parity (number of pregnancies >20 weeks)
- Multiple pregnancies
- Genetic factors
- Cigarette smoking
- Psychosocial factors: depression in
- pregnancy
- Unhealthy dietary factors before pregnancy
- Physically inactive lifestyle before and during pregnancy (7).

4. Monogenic Types

It commonly occurs in mutation in the single gene or impaired insulin secretion in the beta cells of the pancreas. The majority of the patients with monogenic with are not treated or mistakenly identified as type 1 or type 2 diabetes (8).

MODY (MATURITY-ONSET DIABETES OF THE YOUNG)

In 1975, it was described that diabetes occurs before the age of 25 with autosomal dominant inheritance as a result of intrinsic beta cell defect (9).

PATHOGENESIS AND PATHOPHYSIOLOGY OF DIABETES MELLITUS

When the body has more glucose level than the normal level brain recognizes it and sends the message to the pancreas via nerve impulses.Type-1 diabetes is caused by autoimmune conditions, CD4, CD8, and macrophages destroy the insulin production in the pancreas (10). In type 2 diabetes, the feedback mechanism of insulin's secretion and insulin's action is changed which causes abnormal glucose levels in the blood (11). Gestational diabetes occurs due to the abnormal function of the beta cell on the condition of long-term insulin resistance during the gravid period (12).

TREATMENT (PHARMACOLOGICAL MANAGEMENT)

Drugs Used In Allopathic

There are eight various types of Oral Hypoglycemic Agents (non-insulin glucose lowering), they are

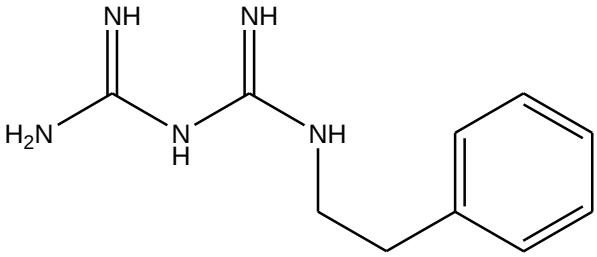
BIGUANIDES

Drugs such as

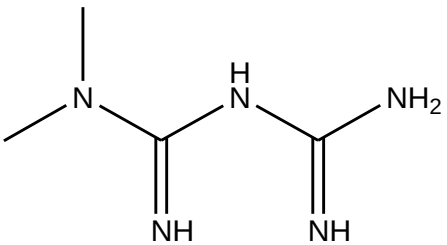
- Metformin
- Phenformin

These drugs are used for the treatment of Type 2 diabetes. Out of these, Metformin is the most widely

used drug (14). Metformin is the first line for the Type 2 diabetes mellitus (15). It is artificially obtained from galegine which is obtained from the natural product Galega officinalis. Galegine itself is obtained from guanidine. Metformin was first used in the year of 1957(16). Metformin can be given carefully to a patient who has a chronic kidney disease because it may cause lactic acidosis (17). It reduces the gluconeogenesis in the liver (20).The combination of metformin and glimepiride shows good effect in patients with uncontrolled Type 2 diabetes mellitus (59). Phenformin was widely used in many countries before it was banned because it causes lactic acidosis (18).



Phenformin



metformin

MOLECULAR FORMULA: C4H11N5 (52)

ROUTE OF ADMINISTRATION: Oral
DOSE: 500mg

METFORMIN FLOATING TABLET COMPOSITION

1. K-Carrageenan
. 2. Guar Gum
3. Magnesium Stearate
4. Talc
5. Metformin HCL
6. HPMC
7. Citric acid
8. Sodium bicarbonate

BIOAVAILABILITY

Metformin also has a low bioavailability. So, metformin is loaded in a hollow core system to form a mold because it is inexpensive (50).Metformin (1,1-dimethylbiguanide hydrochloride) 0.5 to 1mg oral dose. Its Tmax is 2.5hrs and its elimination half-life is 6 hrs. (58) The peak plasma concentration occurs after 2 hrs(60).

ADVERSE EFFECT:

METFORMIN: Diarrhea and Nausea are some adverse effects of the drug METFORMIN and it may also cause gastrointestinal effects (56).

TRANSDERMAL DRUG DELIVERY SYSTEM (TRANSDERMAL PATCH)

Pioglitazone Hcl is an anti-diabetic agent that helps to reduce the glucose level in the body by reducing insulin resistance , this oral hypoglycemic agent has less t-1/2 life, so more than 1 dose is required. To prevent those kinds of difficulties transdermal patches are used. The transdermal route is the easiest way to deliver the drug to the body than the oral /parenteral. Transdermal patches are the adhesive device that contains drug (30). Transdermal patches reduce the undesirable side effects also they help to increase the biological half-life of the drug (22). Delivery of a drug through the skin has more advantages than other routes, it prevents - pain (during injection), first-pass metabolism, GI irritation, multiple doses & side effects. Repaglinide has lower bioavailability and half-life, normal dose for this medicine is 16mg so it requires multiple doses. To prevent multiple doses transdermal patches are prepared and used. (23) Microneedle was first reported as an NDDS in 1998. Intramuscular injection can produce pain and other routes like intranasal have created local effects (28). Microneedle patch**es** are the alternative method for the injection, they help to reduce the pain & it doesn't require any training to administer the patches (25).In TDDS, microneedles are made up of biodegradable polymer or dissolving polymer (29).MN patches are mainly used for T2D therapy(31). Saxagliptin is used for patients with T2D, but it has lower bioavailability so saxagliptin patches are prepared by adding a hydrophilic agent to increase bioavailability and avoid first-pass metabolism. (26) High doses of the drug are prevented and Patch is removed when the skin gets irritated. (27). Also, It avoid hepatic first pass metabolism(24)

ALTERNATIVE MEDICINES

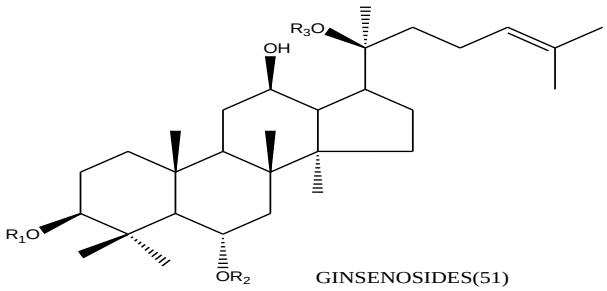
HERBAL DRUGS USED IN DIABETES MELLITUS

- Ginseng

- Allium stadium
- Aloe
- Borbadensis
- Azadirachta indica
- Brassica
- Juncea
- Carica Papaya
- Catharanthus roseus (13)

GINSENG: Ginseng is the most widely used traditional plant in the world. It has been used for many years in Korea, China, and Japan. It is mainly used for the treatment of diabetes and also for sleeping disorders, and pulmonary problems. Ginseng originated from the Chinese word RenShen means "HUMAN PLANT" (42).

Japanese scientists found that ginseng root helps in diabetes treatment (45). It is widely available in 190 countries , root ginseng is available in more than 130 countries(57).



GINSENOSIDES(51)

MOLECUAR FORMULA: C30H5202

ROUTE OF ADMINISTRATION: Oral

DOSE: 1-2 gram.

t/2 : <24 hours

CHEWABLE GINSENG TABLET FORMULATION (53)

Saponins are the main active ingredients in ginseng which is known as ginsenosides

1. Ginseng powder 40%
2. mannitol Total 52%-58.5%
3. sorbitol 20.5%
4. magnesium stearate 0.5-2%
5. copovidone 0-5%
6. colloidal silicon dioxide 1%

ADVERSE EFFECTS

GINSENG: Headache, Insomnia, Nausea, Skin eruption, and Diarrhea are some adverse effects of GINSENG (55).

NON- PHARMACOLOGICAL ACTION:

Lifestyles modification in diabetes mellitus

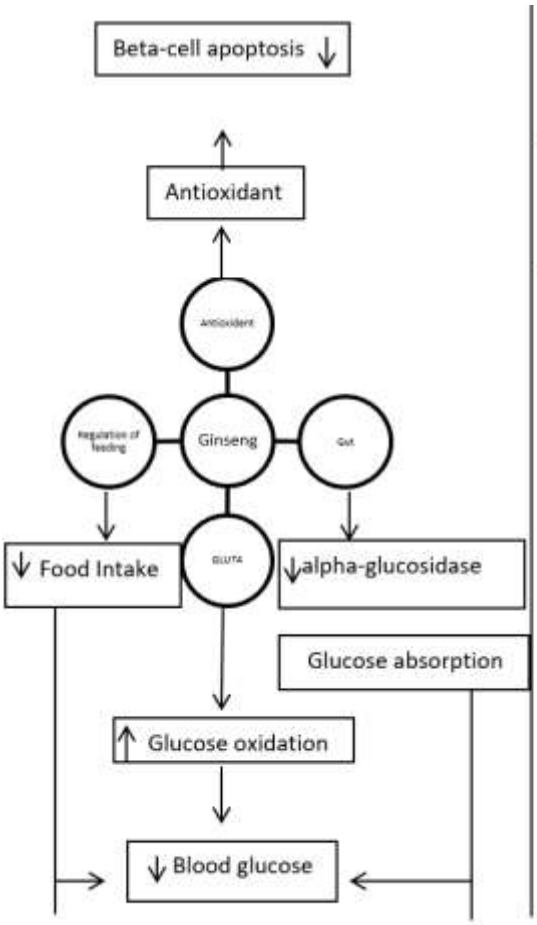
Risk factors for Diabetes Mellitus include obesity, poor diet, smoking, physical inactivity, and elevated blood pressure. Type-2 diabetes can be reduced by consuming low glycemic level containing fruit (Apples) and vegetables (Tomato, Allium Sataivum).Allium Sataivum is the Botanical name of Garlic. It has good hypoglycemic activity. It contains sulfur compounds (36). Garlic helps reduce the fasting blood glucose level (37). Garlic is effectively used as a dietary supplement. It has antioxidant, and hypoglycemic activity (38). Garlic is more effective in the patient with a mild increase in the glucose level (40). Essential components present in the garlic oil are,

- 38.6% DADS,
- 30.8% diallyl trisulfide,
- 10.0% diallyl sulfide, and\
- Small amounts of other volatile compounds (39).

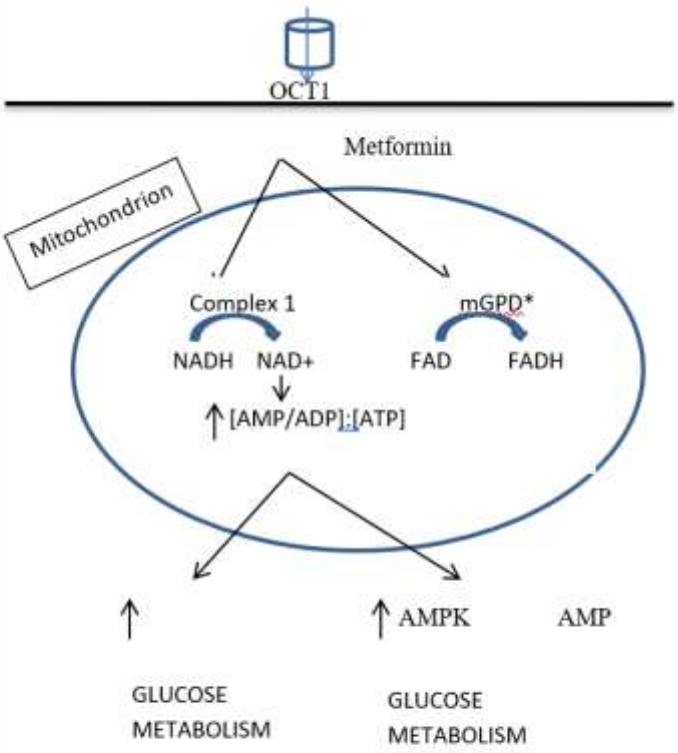
Low-fat milk can reduce the occurrence of diabetes mellitus. Consuming processed foods like Maida, sweets, candies, and soft drinks will increase the risk of diabetes. T2DM can be prevented by doing yoga, physical exercise & meditation. Stress plays a major role in causing diabetes (21). Nopales are used to reduce glucose levels in the body in long-term use, it has hypoglycemic properties and it controls the glycemic level in the body_(32). Lifestyle modification includes maintenance of BMI, dietary pattern maintenance, and to increase physical activity (33).T2DM chances can be controlled by consuming coffee (without sugar) and dark chocolates (34). Physical activities for minimum 30 min can be encouraged in the DM (35).

COMPARISON BETWEEN ALLOPATHY AND GINSENG

WHO predicts that in 2030 the world population will rise to 37%, and the number of people with diabetes also rise to 114%. In Asia China and India are the countries with the highest number of population with diabetes (41). Modern and traditional methods play a major role in the diabetes treatment. Diabetes is known as hyperglycemia (43).The drugs used for Type 2 diabetes have more adverse and toxic effects, so it is important to find the new drug with the same effect and has a low adverse effect. The medicinal plant with the hyperglycemic property is used for the treatment of diabetes (44).Ginseng tablet has a low oral bioavailability because they undergo first-pass metabolism, and mucoadhesive enteric-coating ginsenosides are used (48). But metform=in is the first-line drug used for T2D (49).



MOA OF GINSENG(46)



MOA OF METFORMIN(47)

COMBINATION OF METFORMIN WITH GINSENG

Metformin shows Cardio-vascular complaints and some metabolic disease in DM patients. So, therapeutic outcome of a patient can be improved by the combination of metformin with an herbal drug such as ginseng. Ginseng extract with metformin helps in long-term glycemic control (62).

ANIMAL STUDIES

The first low dose of Streptozotocin was administered to the mice on the first four days there was no increase in the fasting blood glucose level, on the second dose of STZ fasting blood glucose level was increased up to 500mg/dl and it was maintained for more than 1 month. Metformin supplement helps control the fasting blood glucose level for 7 days but with the second dose of STZ administration the value is increased and after 3 weeks of metformin administration value is increased to 300-400mg/dl. Red ginseng extract supplement also shows a similar effect to metformin. However, co-administration of metformin with red ginseng extract maintains the fasting glucose level at 200mg/dl. It shows that metformin alone or RGE has less effect than the combination of both. The co-administration of metformin with RGE doesn't affect the Biological parameters (63).

CONCLUSION

In the modern world, people consuming fast foods and lack of physical activity have increased, which leads to diabetes mellitus. Medicines today for diabetes mellitus contain patient compliance like drug tolerance at multiple doses and accumulation of drugs in long-term medication which causes drug toxicity. Since Metformin is a multi-dose drug for Diabetes Mellitus, therefore we conclude that

combination of Metformin with Ginseng shows the long-term control of glycemic level in the body in mono dose form. In future we recommend to do research study on using ginseng with metformin to find the therapeutic efficacy on diabetes mellitus patients.

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