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Review article

A review on comparative study of some pigmented and non-pigmented flower having anti-diabetic activity

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Key words: Diabetes Mellitus, Non-communicable Diseases, flower, pigmented, Non-pigmented, anti-diabetic

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Abstract

Flowers are the aesthetic part of the plant. In addition to having an ornamental value flowers also show, medicinal value. As per World Health Organization, presently around 80% of people worldwide rely on herbal medicines. To reduce the side effects herbal medicines are now in great demand for primary health care. Changes in the lifestyle and unhygienic environment are the main causes of non-infectious chronic diseases. Diabetes Mellitus is one of the gravest non-communicable diseases. The situation is becoming worse day by day. According to the survey, in 2008, 63% deaths were mainly due to non-communicable diseases, and the percentage is even increasing day by day. As per the statics of 2014, 8.5% of adults aged 18 and above have raised blood glucose level. The review encloses information about pigmented and non-pigmented flowers which show anti-diabetic activity. This review article focuses on a comparative study of pigmented and non-pigmented flower with their medicinal activity having anti-diabetic effect. One of the important aspects is to study that whether the anti-diabetic activity of the flowering plant mentioned is associated with the pigmentation or not.

Introduction

Today's fast lifestyle and unhealthy eating habits invites a lot of diseases. Changes in the lifestyle and unhygienic environment are the main cause of non-infectious and chronic diseases. Diabetic mellitus is one of those chronic diseases. Diabetes mellitus (DM) is mainly known for its chronic hyperglycemia and impaired carbohydrates, lipids, and proteins metabolism which is caused by incomplete or insufficient secretion of insulin secretion or improper insulin action. There are two forms of diabetes namely: 1. Insulin-dependent diabetes mellitus (type 1-diabetes mellitus) and 2. Non-insulin-dependent diabetes mellitus (type 2-diabetes mellitus). Type-2 diabetes mellitus accounts for about 90% to 95% of all diabetic patients. Type-2 Diabetes Mellitus mostly results from the interaction among genetics, environmental and other risk factors [1].

Therefore, deficiency or defect in insulin or the insensitivity of its receptors leads to sugar build up in the blood. Hence, though glucose is produced in the body, but in Diabetic patients, the body does not properly process food for use as energy due to the lack of activity of insulin [2].

The roots of botanical medicines are present in every culture throughout the world. Although for hundreds of years, it has been practiced but in present times, the screening of natural products from the biodiversity and finding out their therapeutic activity has become an increasing matter of concern to benefit ourselves with medicines that are efficient in curing the diseases with lesser or minimal side effects. As per World Health Organization, presently around 80% of people worldwide rely on herbal medicines. To reduce the side effects herbal medicines are now in great demand for primary health care. The main reason for this is that they are less

expensive and are more compatible with the human body than conventional medicine [3].

Flowers are the ornamental and aesthetic part of the plant. While going through various journals, it has been found that flowers have a lot of medicinal and therapeutic importance but a lot many works has to be done on them to achieve their physical use. The above study reviews the anti-diabetic activity of pigmented flower and its comparative study with the anti-diabetic activity of non-pigmented flowers. The aim of the review lies in revealing the actual reason behind the anti-diabetic activity of the flowering plants, i.e. whether the pigments or some other phytoconstituents are responsible for the anti-diabetic effect of the above plants.

Overview of diabetes mellitus

Diabetes Mellitus (DM) is a metabolic disorder in which there is an occurrence of chronic hyperglycemia in association with carbohydrates, proteins and lipid metabolism impairment. Diabetes Mellitus, being one of the oldest diseases were initially found in the manuscript of Egypt about almost 3000 years ago [4]. The etiology as well as origin of DM can vary largely but always the basis remains the same. The basis problems in Diabetes Mellitus include defects in either secretion of insulin or its response or in both in due course of the disease.

History

Symptoms of diabetes were observed from back 400BC. Sushruta said that diabetes is characterized by honeyed urine. Von Mering discovered that diabetes is a pancreatic disorder. In 1921, first insulin was used to treat diabetes in a human. First major 'replacement' therapy as well as the hormone to be produced by genetic engineering which was used for the treatment of diabetes was insulin [5].

Statistical scenario of diabetes mellitus

As, shown in table1 the number of people suffering from Diabetes Mellitus in India has to increase from 31.7 to 79.4 million in within just 30 years. These statistics has been highest for the India in comparison to many other countries like China, Indonesia, Japan, Brazil etc.

As per assumption of World Health Organization 180 million people around the globe are suffering from diabetes, and the worst part of the story is that by 2030 the number may increase to more than double. As per statistical analysis, half of the diabetes death occurs in people below 70 years of age, and this death is more than 55% in women. In 2005, about death of 1.1 million people occurred from diabetes. The number of people with diabetes are projected to be 366 million by 2030 [7-8] (Table 1) (Figure 1, 2, 3).

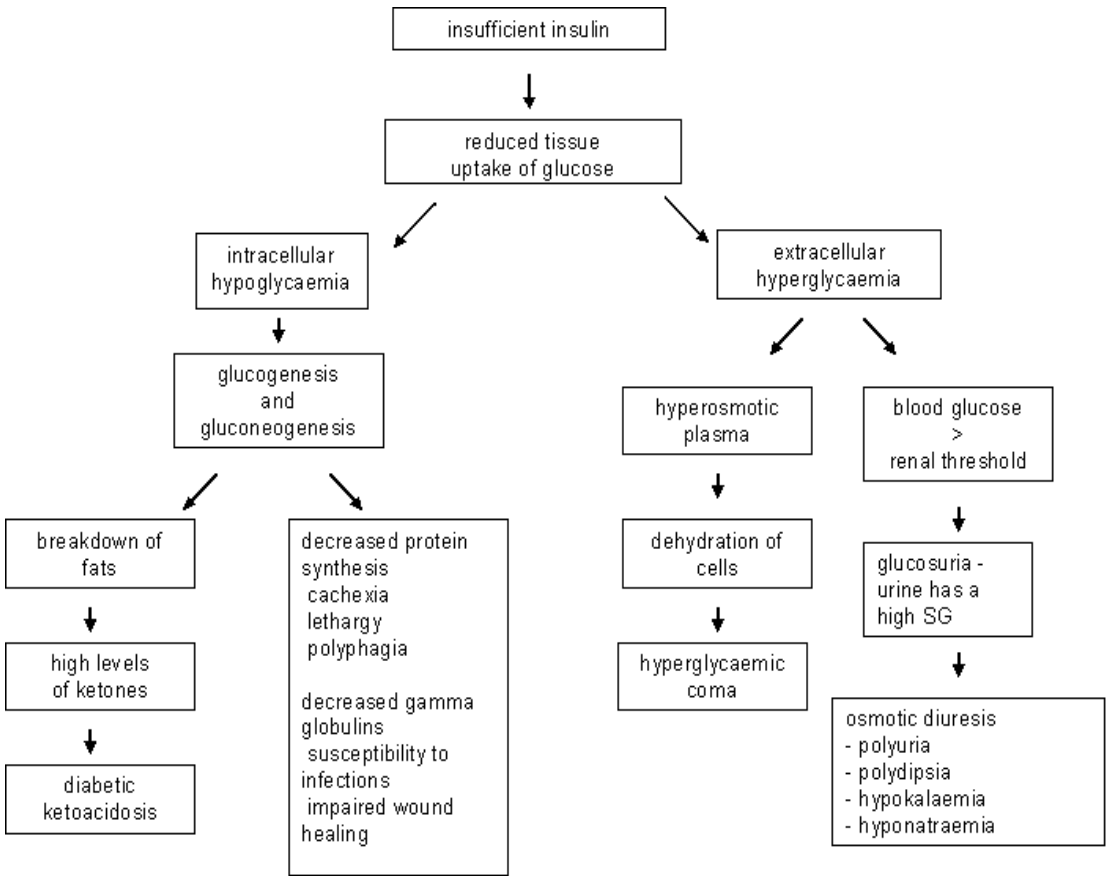


Figure 1. Physiology of Diabetes Mellitus.

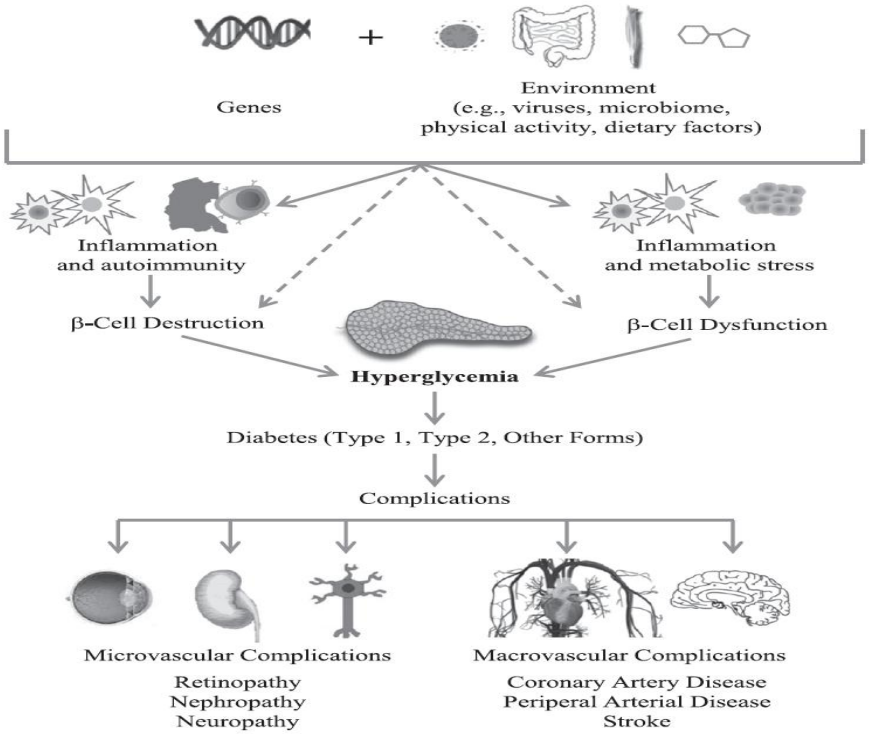


Figure 2. The above diagram shows the pathophysiology with its complications [10].

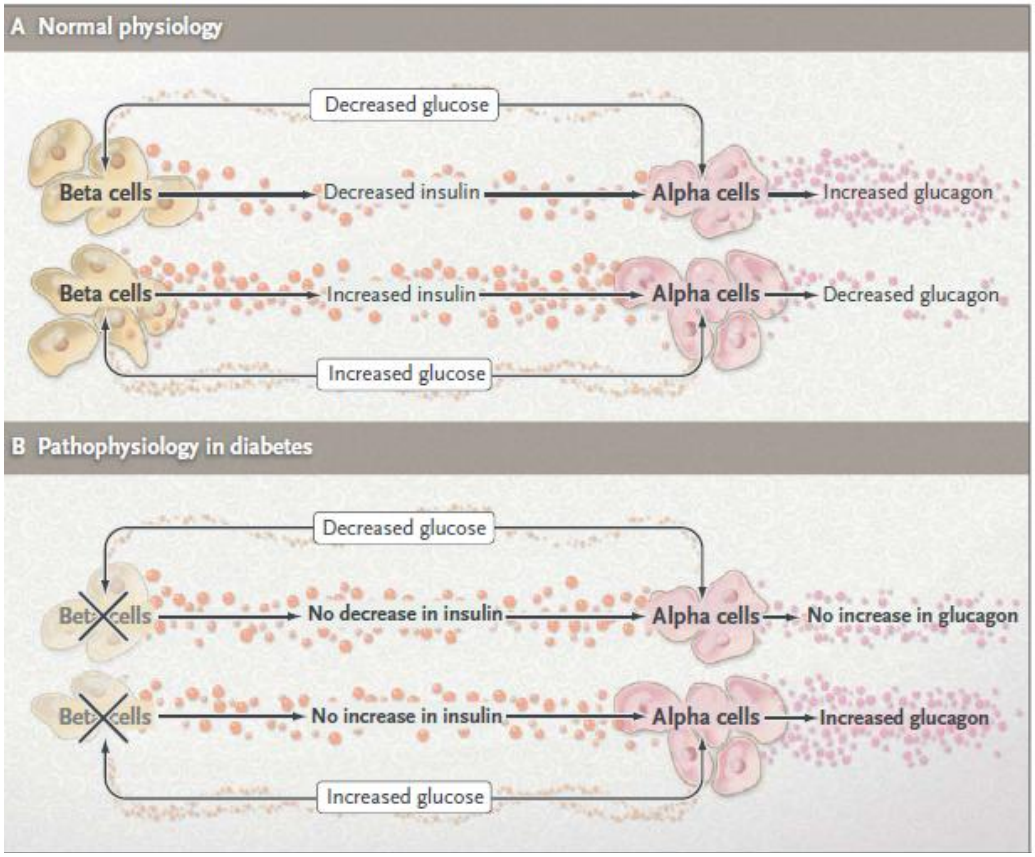


Figure 3. Comparative diagram showing change in physiology of insulin preparation during normal condition and diabetic condition. The first part of the figure shows the physiological decrease in insulin production in association with a low glucose concentration which stimulates alpha-cell for secretion of glucagon. On the other hand, Panel B shows failure of beta-cell in diabetic condition and its pathophysiological effect. Thus, results in the loss of a decrease in secretion of insulin and loss of increased alpha-cell glucagon secretion, despite of the presence of low glucose concentration [11].

Classification of diabetes mellitus

There are various types of Diabetes Mellitus which can be classified based on their etiology of glucose tolerance that a person develops when one is suffering from Diabetes mellitus [12]. Various types of Diabetes Mellitus are mentioned in (Table 2).

Type-1 diabetes mellitus

Pathophysiology

Type 1 Diabetes Mellitus is known as juvenile diabetes as well. Juvenile diabetes is basically known by the destruction of beta cell caused by an autoimmune process. The destruction of beta cell leads to absolute deficiency of insulin. Type 1 DM is usually characterized by the presence of anti–glutamic acid decarboxylase, islet cell or insulin antibodies which determines the autoimmune processes that cause beta cell destruction. Eventually with increase in time, all type-1 diabetic patients require insulin therapy to maintain normal glucose level, i.e. Normoglycemia [13]. The complete pathophysiology of type 1 Diabetes Mellitus has been mentioned in (Figure 4) [14].

Table 1. List of countries with estimated diabetes cases from 2000 to 2030 [6].

	2000		2030	
	Country	**People with diabetes (millions)**	**Country**	**People with diabetes (millions)**
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S.	17.7	U.S.	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Japan	13.9
6	Pakistan	5.2	Pakistan	11.3
7	Russian Federation	4.6	Russian Federation	11.1
8	Brazil	4.6	Brazil	8.9
9	Italy	4.3	Italy	7.8
10	Bangladesh	3.2	Bangladesh	6.7

Statistical scenario of diabetes mellitus

Table 2. Types of diabetes mellitus [12].

Types	Subtypes	Etiology of Glucose Intolerance
1. Type 1*	Insulin deficiency is caused from Beta cell Destruction A. Immune mediated B. Idiopathic	The auto immune destruction of beta cells is unknown
2. Type 2*	In this type, insulin resistance is with relative insulin deficiency to a predominantly secretary defect with insulin resistance.	
3. Other specific types	A. Genetic defects in beta cell function, e.g. glucokinase	Regulates insulin secretion due to defect in glucokinase generation
	B. Genetic defects in insulin action, e.g. leprechaunism	Pediatric syndromes that have mutations in insulin receptors
	C. Endocrine disorders, e.g. Acromegaly, Crushing syndrome	Diabetogenic effects of excess hormones level
	D. Diseases of Exocrine pancreas, e.g. pancreatitis, neoplasm	Loss or destruction of insulin producing beta cells
	F. Infections, e.g. congenital rubella	Beta cell injury followed by autoimmune response
Gestational diabetes mellitus (GDM)	Any degree of glucose intolerance with onset or first recognition during pregnancy	Combination of insulin resistance and impaired insulin secretion.

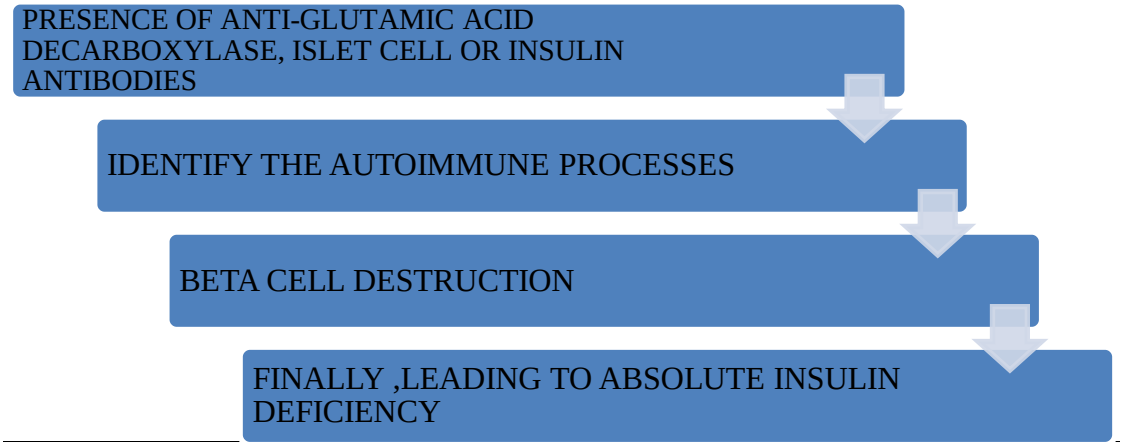


Figure 4. Pathophysiology of Type 1 Diabetes Mellitus [13].

Demographics

The overall age-adjusted incidence of insulin-requiring diabetes was 17.5 per 100,000 person-years in men and 13.6 per 100,000 person-years in women in European countries. In men, the incidence was twice as high in blacks as in whites [15]. A 2011 Centre for Disease Control and Prevention (CDC) report estimates that DM affects about 25.8 million people in the US (7.8% of the population) in 2010 [16]. The South-East Asia Region (SEAR) has a high prevalence of T1DM in children, with an estimated 77,900 children affected [17].

Epidemiology

Type-1 Diabetes Mellitus approximately accounts for 5 to 10% of all diagnosed diabetes. About 40 to 60% of persons with this type of Diabetes Mellitus are Juvenile. The Juveniles with Diabetes Mellitus is usually younger than 20 years of age at onset, thus for them diabetes turn out to be one of the most common severe chronic diseases of childhood affecting about 0.3% of the general population by the age of 20 years as well as 0.5 to 1% during the lifespan [18]. The worldwide prevalence of T1DM is 0.1 to 0.3%, with 78,000 new cases every year, especially among young individuals (<5 years). Some 79,100 children below the age of 15 years are predicted to suffer from T1DM annually all over the world [19].

Causes

There is a strong relation between Type 1 DM and other endocrine autoimmunity. There are three types of autoantibodies known to be associated with Type 1 DM.

i) **Islet cell surface antibodies (ICSA):** Auto antibodies generated against Islets cell surface antigens (ICSA) have also been defined in as many as 80% of Type 1 Diabetes.

ii) **Islet cell cytoplasmic antibodies (ICCA)**: The major antibodies found in 90% of Type 1 Diabetics are against the proteins from islet cell cytoplasm.

iii) **Specific Antigenic Targets of Islet Cells**: Antibodies against (GAD) Glutamic Acid Decarboxylase has been identified over 80% patient newly diagnosed with Type I DM. The presence of anti-GAD antibodies is an indicator to the future development of Type 1 DM in a high-risk population [20].

The tendency to develop autoimmune diseases, including type 1 diabetes mellitus can be passed down through family linage [21].

Type-2 diabetes mellitus

Pathophysiology

Type 2 DM is known for its insulin resistance. Insulin resistance is caused by insulin insensitivity. This results in decline in insulin production which eventually leads pancreatic beta-cell damage. This pancreatic beta-cell failure becomes the reason for decreased transport of glucose into the liver, fat cells, and muscle cells. With hyperglycemia, there is an increased breakdown of fat. In recent studies it has also been found that the pathophysiology of type 2 diabetes mellitus also involves impaired functioning of alpha-cell [13]. The pathophysiology of type- 2 Diabetes Mellitus is shown in figure 5.

Demographics

In the U.S., people suffering from type 2 Diabetes Mellitus are quite high. About 95% of 30 million people living in U.S. is suffering from Diabetic Mellitus that to with type 2 diabetes mellitus. Moreover, statistics says about 86 million people suffering from pre-diabetes which means that people have a high risk for developing type 2 diabetes [22]. Irrespective of all the associations established demographically, one of the main reasons of type-2 diabetes mellitus is low socio-economic status. People at higher age group are closely related with the risk of developing type-2 Diabetes Mellitus. There is variability to a larger extent for the prevalence of type 2 diabetes worldwide.

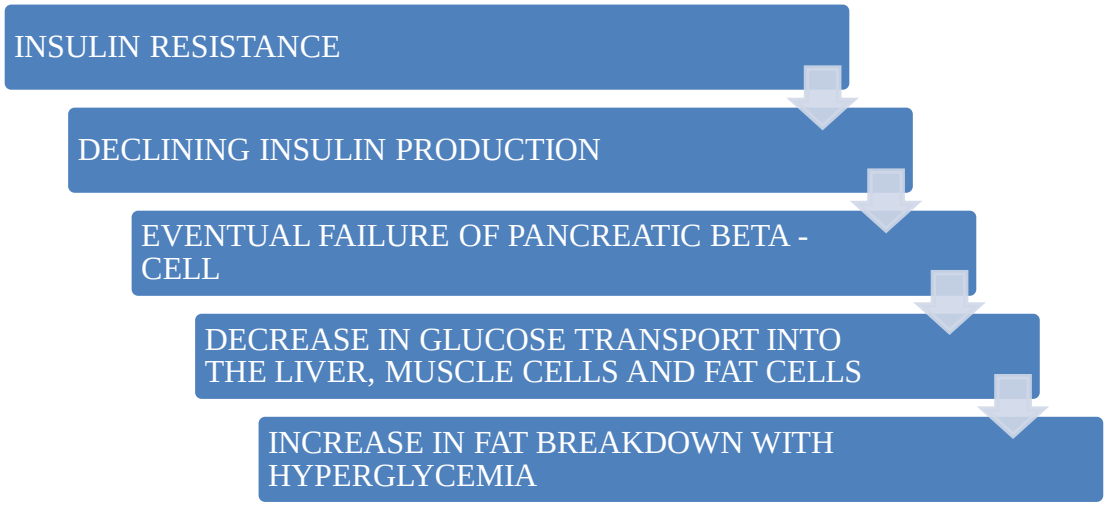


Figure 5. Pathophysiology of Type 2 Diabetes Mellitus [10].

Epidemiology

An estimation states that in 2011, 366 million people was suffering from Diabetes Mellitus and the statistics would probably hit to 552 million by 2030, [23].People suffering from type-2 DM is increasing. Nearly about 80% of Diabetic people are living in a low socio-economic and belong to middle-income countries. In 2011, Diabetes Mellitus caused about 4.6 million deaths. [24] The occurrence of type-2 Diabetes Mellitus varies from one geographical region to the other substantially with changing environmental conditions as well as risk factors related to lifestyle [25].

Causes

Type-2 Diabetes Mellitus is basically a lifestyle disease. Type 2 DM mainly and primarily because of genetics and lifestyle factors. Lifestyle factors which lead to the development of type 2 DM includes physical inactivity, cigarette smoking, sedentary lifestyle and generous alcohol consumption [26]. Obesity gives 55% contribution to most of the cases of development of type 2 Diabetes Mellitus [27].

The future challenge will include cataloguing and determining various genetic risk factors. Understanding the interaction between the risk factor with the known environment and lifestyle risk factors increase the propensity to type 2 Diabetes.

i) **Cytokines, Adipokines and Inflammation:** Insulin stimulated Glucose uptake into muscle cells and adipocytes majorly depend upon GLUT4 (Glucose Transporter). Insulin resistance and obesity is mainly associated with the down regulation of GLUT 4. RBP4 protein may also have some relation with Type II DM as RBP4 protein levels were found to be elevated in Insulin-resistant mice.

ii) **Endoplasmic Reticulum Stress Response and Diabetes:** ER stress pathway is active in the Liver, and adipose tissue from an obese mouse resulting in increased activation of C-jun N terminal Kinase (JNK) which brings about the phosphorylation of IRS-1 on serine residue thus suppressing insulin action and downstream signaling pathway.

iii) **Mitochondria and Reactive Oxygen Species:** ROS has some role to play in Insulin resistance. Obesity usually elevates ROS production resulting in enhanced activation of inflammatory pathway which results in decreased Insulin Sensitivity.

iv) **Oxidative Metabolism and the Pancreatic β- cell:** Oxidative mitochondrial metabolism, and ATP regulation is essential for Glucose stimulated insulin secretion. Maintenance of ATP/ADP ratio is imperative for proper Insulin transport. Inhibition of ATP/ADP regulated potassium channel encoded by KCNJII and ABCC8 results in depolarization of Plasma membrane, opening of Voltage-gated Calcium channel, Calcium influx and binding and transport of insulin granules to cell surface. But the ATP/ADP ratio is altered by UCP2, an integral mitochondrial protein. UCP2 expression negatively regulates glucose-stimulated insulin secretion [28].

Management of diabetes

Diabetes being one of the gravest non-communicable chronic diseases which is a threat to the society. Diabetes Mellitus can be managed by both pharmacological and non-pharmacological methods. Diabetes cannot be cured permanently but definitely they can be managed by following a balanced meal plan and exercising regularly. The person suffering from Diabetes should regularly monitor his blood glucose level. Pharmacologically Diabetes can be controlled by various medications. The pharmacological agents and medications are listed in table 3.

Table 3. Pharmacological method of managing diabetes [12].

Pharmacologic Agent	Daily Dosage (mg)	Duration of action (Hrs)	Dosing Schedule	Mechanism of action
Beta cell stimulators 1. Sulfonylureas (First generation)	100-500	60	1 time/day	Stimulate the release of insulin from beta cells in the pancreas
2. Sulfonylureas (Second generation)	2.5-40	6-24	1-2 times/ day	
3.Nonsulfonylureas	1-8	18-24	1 time/day with first meal.	
Biguanide	500-3000	7-12	1-3 times/day with food	Decreases production and release of glucose by liver
Alpha glucosidase inhibitors	25-300	4-6	1-3 times/ day with or without food	Delays the breakdown and absorption of carbohydrates from intestine.
Thiazolidinediones	4-45	16-24	1-2 times/ day with or without food	Sensitizes body cells to the action of insulin.

Study of pigmented flowers having anti- diabetic activity

Pigmented flowers (Table 4)

1. ***Rhododendron arboretum* Sm.:** Aqueous and methanolic extract of the flower shows inhibitory activity on the rat intestinal α-glucosidase. (α-glucosidase inhibitor-quercetin-3-O-beta-D-galactopyranoside- hyperin is isolated from the flower) [29].
2. ***Cassia auriculate* L.:** Aqueous extract of the flower for 30 days shows significant increase in plasma insulin. (not effective in dose 0.15g/kg and 0.30g/kg but effective at dose 0.45g/kg) [30]. The phytochemistry of aqueous extract as well as water soluble part of ethanol extract of the flowers contains flavonoids, tri terpenoids, anthocyanins and tannins. It was documented that Aqueous extract of the flower has increased plasma insulin and blood glucose level was reduced considerably as per body weight. On the other hand, the water-soluble part of the ethanolic extract also showed the same effect, and this is even more effective than the aqueous extract as per body weight [31].
3. ***Aquilaria agallocha* Roxb.:** Ethanolic extract of the flowers was found to inhibits both alpha-amylase and alpha- glucosidase enzymes efficiently *invitro* in a dose dependent manner. Polyphenolic compounds in the ethanolic extract shows anti-diabetic activity [32].
4. ***Hibiscus rosasinensis* L.:** Ethanolic extract of the flower of *Hibiscus rosasinensis* is of dark brown color. The flower extract is a medicinal tool of which can be used for the treatment of Diabetes Mellitus. It is largely effective in decreasing blood glucose and hike insulin level in the body [38]. These flower extracts reduce blood glucose effectively at the dose of 250 mg/kg as well as 500 mg/kg [32]. In Diabetic state, the extract of these flowers leads to the formation of free radicals which is causes by the auto-oxidation of glucose. This mechanism is highly effective in reducing blood glucose [33].
5. ***Helianthus annuus*** L. is a coarse, stout and an erect plant which is 1-3 meter high. Flowers bearing yellow pigment contain phytoconstituents such as Quercimeritrin, anthocyanin, abundant amount of choline and betaine, triterpene, Saponins. The plant is a remedy for diarrhea, dysentery, epistaxis, flu, fractures, inflammations, splenitis, whitlow and wounds. Studies have revealed that *Helianthus annuus* L. fractions have hypoglycemic effect in Streptozotocin induced diabetic rats. Mechanism of inhibition has been hypothesized to be mediated through increase in insulin secretion, inhibition of gluconeogenesis, protection of pancreatic β-cells from Streptozotocin and glucose induced oxidative stress [43].
6. ***Catharanthus roseus*** L. also known as Madagascar periwinkle, *Vinca rosea*. The two class of active constituents include alkaloid and tannins. The major phytoconstituents like Vinblastine and Vincristine are indispensable drugs for Cancer while other phytoconstituents ajmalicine and Serpentine has hypertensive effect. Studies revealed Vinca rosea exhibit significant antihyperglycemic activities in alloxan- induced hyperglycemic rats. β-cells renewal has been found to occur by the application of methanolic extract [44].
7. ***Anthyllis henoniana*** (Coss.) is a woody Saharan plant appropriate for the rehabilitation of deteriorating area. The flower extracts exhibit potential antidiabetic effects in metabolic disorders in alloxan induced diabetic rats. The flavonoids and glycosides present in plant are majorly responsible for antidiabetic activity. Iso Quercetin has been found to have a potential hypoglycemic effect [45].

Table 4. Description of pigmented flowers with their mechanism of action

Name	Picture of flower	Mechanism
Rhododendron arboreum Sm.		Aqueous methanolic extract of the flower was found to show inhibitory activity on the rat intestinal α-glucosidase . (α-glucosidase inhibitor-quercetin-3-O-beta-D-galactopyranoside- hyperin is isolated from the flower) moreover (3b)-stigmast-5-en-3-ol isolated from the flower of *Rhododendron arboreum* Sm. act as anti-diabetic agent regulating the glucose transport. It has the ability to restore the uptake of glucose without stimulation of insulin, hence proved to have an insulin like property [34].
Cassia auriculate L.		Aqueous extract of the flower for 30 days shows significant increase in plasma insulin. (not effective in dose 0.15g/kg and 0.30g/kg but effective at dose 0.45g/kg), β- sitosterol and Xanthophyll from *Cassia auriculate* L. was found to have potential anti diabetic activity.
Aquilaria agallocha Roxb.		Ethanolic extract of the flowers efficiently inhibits both alpha-amylase and alpha- glucosidase enzymes *in vitro* in a dose dependent manner. Polyphenolic compounds in the ethanolic extract shows anti-diabetic activity.
Hibiscus rosasinensis L.		Ethanolic extract of the flower of *Hibiscus rosasinensis* is largely effective in decreasing blood glucose and hike insulin level in the body at the dose of 250mg/kg and 500mg/kg. The extract leads to the formation of free radicals which results in auto-oxidation of glucose. The extract of *Hibiscus rosasinensis* contains polyphenols as well as flavonoids that show anti-oxidative and beta cells regeneration properties. According to the present studies, these properties are responsible for anti-diabetic activity of the flower [40]. Anthocyanin pigments isolated from *Hibiscus rosasinens is* L. was found to reduce hypoglycemia in Alloxan induced mice.

Helianthus annuus L.		Studies have revealed that *Helianthus annuus* L. fractions have hypoglycemic effect in Streptozotocin induced diabetic rats. Mechanism of inhibition has been hypothesized to be mediated through increase in insulin secretion, inhibition of gluconeogenesis, protection of pancreatic β-cells from Streptozotocin and glucose induced oxidative stress.
Catharanthus roseus (L.)		Studies revealed Vinca rosea exhibit significant antihyperglycemic activities in alloxan- induced hyperglycemic rats. β-cells renewal has been found to occur by the application of methanolic extract.
Anthyllis henoniana (Coss.)		The flower extracts exhibit potential antidiabetic effects in metabolic disorders in alloxan induced diabetic rats. The flavonoids and glycosides present in plant are majorly responsible for antidiabetic activity. Iso Quercetin has been found to have a potential hypoglycemic effect.

Study of non-pigmented flowers having anti-diabetic activity

Non- pigmented flowers: (Table 5)

1. ***Syzygium cumini* L.:** Ethanolic extract in diabetic rats shows anti-diabetic activity. Active compound present is – mycaminose which may have potential anti-diabetic activity [34].
2. ***Sesbenia grandiflora* L.*:*** Ethanolic flower extract has tannins, saponins & flavonoids. The flavonoids in 70% alcoholic extract may decrease the high blood glucose levels as well [35]. *Sesbenia grandiflora* shows alpha amylase inhibitory effect. In-vitro inhibitory effect of alpha amylase of the flower shows inhibition of blood glucose upto 81% because of the presence of tripenes, lignin and terpenes majorly [36].
3. ***Bauhinia forficate* L.:** Ethanolic extract of the flower contains active ingredient kaempferol-3-neohesperidoside (insulin mimetic), which shows anti-diabetic activity [34].
4. ***Michelia champaca* (L.) Baill. ex Pierre:** The flower extract shows significant anti-hyperglycemic effect at a dose level of 400mg/kg. The ethanolic extract, crude aqueous extract and extract of petroleum ether, does not give any relevance to hypoglycemic effect but indicates the supportive action towards glucose utilization. This in turn, means that the predicted mechanism of action is similar to that of Biguanides in which insulin secretion is not increased but glucose uptake is promoted. The petroleum extract of the ether contains fats and terpenoids. Ethanolic extract contains flavonoids, carbohydrates, tannins, and alkaloids, and crude aqueous extract contains only saponin in addition [37].
5. ***Plumbago auriculata* (Lam.):** In Ayurveda the whole plant has been described for potential effect against many ailments such as Rheumatic pains, sprain, dysmenorrhea, scabies, leprosy etc. Pharmacological studies depicted antihyperglycemic effect on diabetic induced animals. Plumbagin an active constituent of the plant was found to have effect on GLUT 4 translocation in Streptozotocin induced diabetic rats [46].

6. ***Lilum longiflorum* Thunb**.: The bulb of *Lilium longiflorum* exhibits potential anti-hyperglycemic activity. The anti-hyperglycemic activity was mainly due to the Steroidal glycosides identified by (LC- Q TOF MS/MS). The plant bears desirable potential in glucose metabolism and insulin sensitivity [47].
7. ***Pterospermum acrefolium* (L.)** which is commonly known as Kanakchampa is traditionally used in inflammation, Leprosy, Ulcer, tumor, Laxative etc. Many Phytoconstituents have been reported from this plant. Molecular modelling studies have revealed Quercetin and Apigenin are the major constituents responsible for glucose lowering mechanism by increasing the glucose uptake in peripheral tissues and by inhibition of Gluconeogenesis [48].

Comparative study of antidiabetic activity of pigmented and non-pigmented flowers:

The comparative study of antidiabetic activity of pigmented and non-pigmented flower is shown in table 6.

Table 5. Description of non-pigmented flowers with their reason of showing anti-diabetic activity.

Name	Picture of the flowers	Reason of showing anti-diabetic action
***Syzygium cumini* L.**		Ethanolic extract in diabetic rats shows anti-diabetic activity. Active compound present is – mycaminose.
***Sesbenia grandiflora* L.**		Ethanolic flower extract has tannins, saponins & flavonoids. Tannins and flavonoids show anti-diabetic activity in other medicinal plants. The flavonoids in 70% alcoholic extract may decrease the high blood glucose levels here as well. In-vitro inhibitory effect of alpha amylase of *Sesbenia grandiflora* diminishes blood glucose level upto 81% mainly due to the presence of tripenes, lignin and terpenes [38].
***Bauhinia forficate* L.**		Ethanolic extract of the flower contains active ingredient kaempferol-3-neohesperidoside (insulin mimetic), which shows anti-diabetic activity.

Michelia champaca **(L.) Baill. ex Pierre**		The ethanolic extract, crude aqueous extract and extract of petroleum ether indicates the supportive action of towards glucose utilization. This in turn, means that the predicted mechanism of action is similar to that of Biguanides in which insulin secretion is not increased but glucose uptake is promoted.
Plumbago autriculata **(Lam.)**		Pharmacological studies depicted antihyperglycemic effect on diabetic induced animals. Plumbagin a active constituent of the plant was found to have effect on GLUT 4 translocation in Streptozotocin induced diabetic rats.
Lilum longiflorum **Thunb**		The anti-hyperglycemic activity was mainly due to the Steroidal glycosides identified by (LC- Q TOF MS/MS). The plant bears desirable potential in glucose metabolism and insulin sensitivity.
Pterospermum acrefolium **(L.)**		Molecular modeling studies have revealed Quercetin and Apigenin are the major constituents responsible for glucose lowering mechanism by increasing the glucose uptake in peripheral tissues and by inhibition of Gluconeogenesis.

Table 6. Comparative study of pigmented and non-pigmented flowers with their active ingredients having anti-diabetic activity.

Anti-diabetic activity of pigmented flowers	
Pigmented flowers	
Flowers	**Constituents responsible**
Rhododendron arboreum Sm.	quercetin-3-O-beta-D-galactopyranoside- hyperin and (3b)-stigmast-5-en-3-ol.
Cassia auriculate L.	Flavonoids, triterpenoids, anthocyanins tannins, β- sitosterol and Xanthophyll.
*Aquilaria agallocha*Roxb.	Polyphenolic compounds
Hibiscus rosasinensis L.	Polyphenols flavonoids and Anthocyanin
Helianthus annuus L	Phytoconstituents having antidiabetic effect yet to be identified.
Catharanthus roseus (L.)	Flavonoids having antidiabetic property
Anthyllis henoniana(Coss.)	Quercetin
Non-pigmented flowers	
Flowers	**Constituents responsible**
Syzygium cumini L.	Mycaminose.
Sesbenia grandiflora L.	Tannins, terpenes, tripenes, lignin and flavonoids.
Bauhinia forficate Link.	Kaempferol-3-neohesperidoside.
Michelia champaca (L.) Baill. ex Pierre	Fats, terpenoids, flavonoids, tannins and other chemical constituents in the extracts may be responsible for showing anti-diabetic activity.
Plumbago autriculata (Lam.)	Plumbagin
Lilum longiflorumThunb	Steroidal Glycosides
Pterospermum acrefolium (L.)	Quercetin

Discussion and conclusion

In most of the plants, we can find that the ethanolic extract of the flowers shows anti-diabetic activity irrespective of its pigmentation and non-pigmentation. In some plants, anthocyanin is a polyphenolic compound that imparts color in the *Hibiscus Rosa-sinensis* which in turn is responsible for the anti-diabetic activity of the flower. But the situation is not same for all the plants. *Rhododendron arboretum* is a flower with shows anti-diabetic activity due to the presence of the substance known as hyperin which is not the same pigment that is responsible for the color of the flower. Similarly, anthocyanins are also present in *Cassia articulate* but its yellow in color not red. On the other hand, in the case of non-pigmented flowers, flavonoids are one of the important compounds for producing anti-diabetic activity but they do not produce any pigment. That means, from the above examples of flowers we can conclude that there might be some cases where the compounds imparting pigments are responsible for showing anti-diabetic activity as well, but the therapeutic activity has nothing to do with the colors of the flowers exclusively. Some non-pigmented flowers are responsible for showing anti-diabetic activity and also bears the coloring pigments, but they are non-pigmented. Thus, the pigmented and non-pigmented property of the flower cannot be co-related as such. Furthermore, studies are to be carried out to establish a co-relation if possible.

Conflict of interest:

There is no potential conflict of interest associated with this review work.

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