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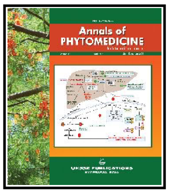

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A comprehensive review on antidiabetic potential of weeds

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Abstract

Diabetes mellitus (DM) is a chronic metabolic disorder with significant health implications worldwide. The search for effective and accessible treatment options has led to the exploration of various medicinal plants, including weed plants, for their potential pharmaceutical activities in managing diabetes mellitus. This review endeavours to provide an overview of the pharmaceutical activities of different weed plants and their constituents in the context of managing diabetes mellitus. For this, a plethora of weed species have been investigated for their antidiabetic properties. Among them, few are roadside weeds (*Parthenium hysterophorus*, *Taraxacum officinale*), other garden weeds (*Cynodon dactylon*, *Portulaca oleracea* and *Amaranthus spinosus*) or certain weeds inhabiting the field during the cropping seasons (*Sinapsis arvensis* and *Amaranthus spinosus*). While most of the antidiabetic medications like biguanides, insulin, sulphony-lureas, *etc*., have adverse effect on the human body such as diarrhoea, cramps, weight loss or weight gain, *etc*. Nowadays, there have been a greater focus on the use of herbal products as they are safe for human use, with minimal to no side-effects. However, a holistic approach to tackle DM should be adopted which integrates allelopathic medicines with herbal products for sustainable disease management and will also reduce the dependence on chemicals. Furthermore, systematic studies need to be undertaken so as to evaluate the future feasibility or effectiveness of extracts obtained from various weed species and their utility in DM management. Based on the pharmacological activities of some of the weeds, there is a new ray for better protocol for future treatment of DM and its related complications.

1. Introduction

Diabetes mellitus is a very common metabolic condition marked by the high blood glucose level (hyperglycemia) as a result of inadequate insulin synthesis from the pancreatic beta cells or insensitive body cells to the insulin. Glucose is a necessary part of our daily functions. Our body utilize it for energy and for that a hormone called insulin produced by the pancreas is required. From the blood, glucose is taken up by insulin and directed towards our cells where it is converted into energy. Globally, numerous people have diabetes and further number is escalating at an alarming rate. According to the WHO, diabetes a prominent cause of death worldwide, kills 1.5 million people every year (Siddiqui *et al*., 2020). Its prevalence in 2010 was approximate at 285 million, accounting for 6.4% of the globe's population and is projected to increase to 7.7% by affecting 438 million adults by 2030.

In 2019, diabetes caused 1.5 million death, and about 48% of all deaths were due to diabetes occurs before the age of 70 years. Additionally, 4,60,000 kidney diseases death were caused by diabetes, and increase blood glucose causes about 20% of cardiovascular death (Anonymous, 2023). Diabetes may also cause permanent vision loss as a result of blood vessel damage in the eyes, foot ulcers and may lead to amputation due to damage of nerves and poor blood flow.

According to International Diabetes Federation (IDF) Atlas (2021), 10.5% of the adult population between the age of 20-79 has diabetes. About half of them are unaware that they are living with this disease. Approximately 90% of diabetic people have type 2 diabetes. This disease may be due to environmental, demographic, socio-economic and genetic factor (Anonymous, 2023).

2. Types and treatment of diabetes

Diabetes is a chronic medical condition which is characterized by elevated blood glucose level.

There are four types of diabetes, *viz*., type 1 diabetes, type 2 diabetes, gestational diabetes and IGT/IFG, each with distinct causes and characteristics as shown in Figure 1.

Gestational diabetes manifests during pregnancy with blood glucose levels exceeding normal yet falling below the diagnostic threshold for diabetes. These women and possibly their children are also at higher risk of type 2 diabetes in future.

Formerly referred to as non-insulin dependent or adult-onset diabetes, this form of the condition hinders the body's effective utilization of insulin, potentially resulting in elevated blood sugar level if left untreated.

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previously known as insulin dependent, juvenile or childhood onset, characterized by deficient insulin production and requires daily administration of insulin.

Impaired glucose tolerance (IGT) and impaired fasting glycaemia (IFG) represent intermediary stages in the progression from normalcy to diabetes. Individuals with IGT or IFG face an elevated risk of developing type 2 diabetes.

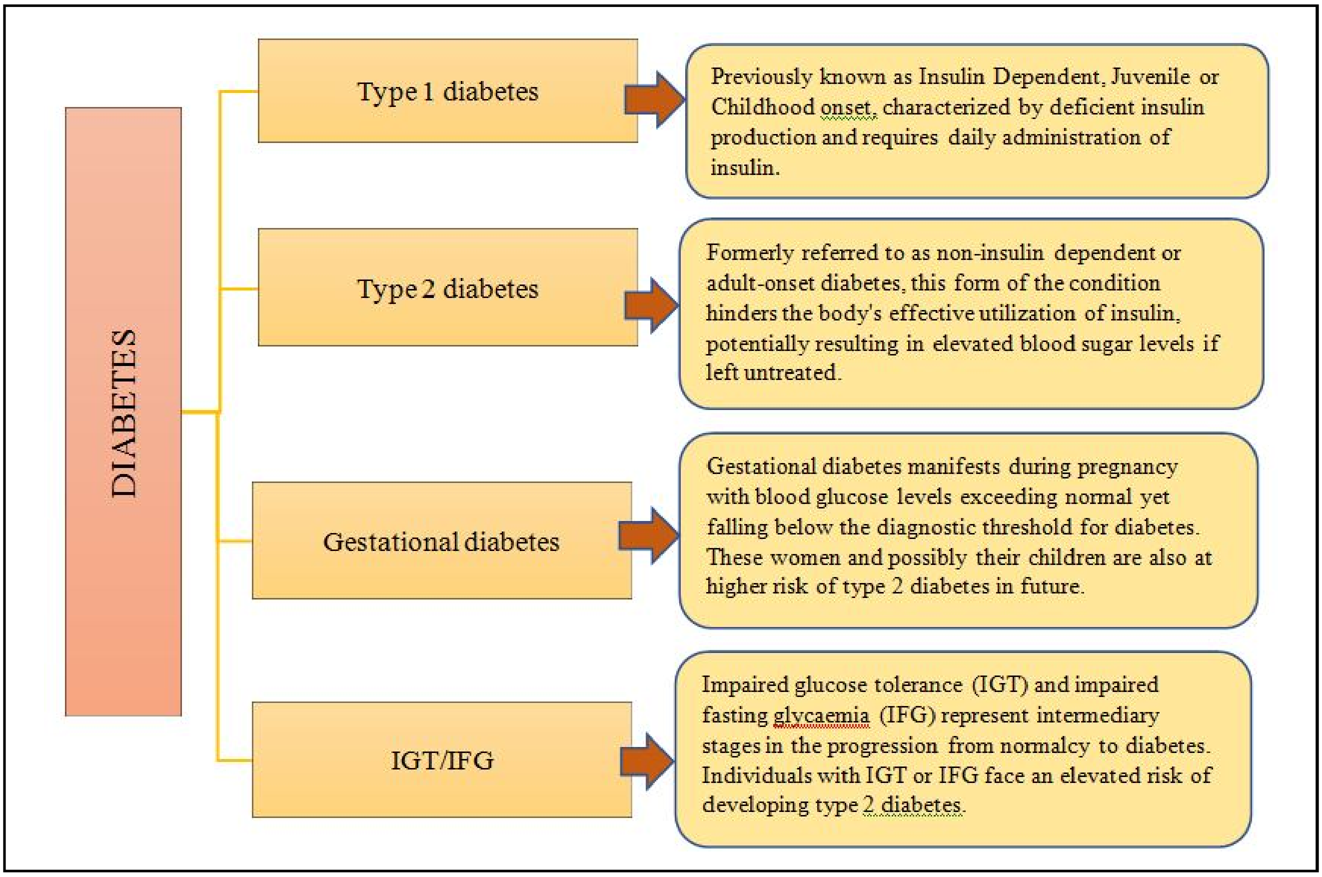

Figure 1: Types of diabetes.

The main treatment for diabetes mellitus (DM) includes chemically synthesized oral antidiabetic drugs. The first choice for the treatment of diabetes among these drugs is metformin. If, the level of glucose is still high, there is recommendation for insulin injections. In addition to metformin and insulin, there are several other antidiabetic medications are also available, modes of their action and adverse effects are tabulated in Table 1.

Table 1: Antidiabetic medication for the treatment of diabetes (DM)

Antidiabetic medications	Action	Adverse effects	References
Biguanides (Metformin)	Decrease the absorption of glucose from the intestine and reduce the amount of glucose production by liver.	Diarrhoea, cramps, nausea, vomiting and decreased absorption of vitamin B12	Sanchez-Rangel and Inzucchi, 2017
Sulphonylureas	Stimulate the pancreas with the help of beta cells and cause body to make more insulin.	Weight gain, stomach upset, dizziness, sweating, confusion and nervousness	Sola *et al.*, 2015
Meglitinides	Stimulate beta cells to produce more insulin.	Hypoglycemia, weight gain	Ross, 2022
Thiazolidinediones	Increase sensitivity of cells to insulin and decrease glucose production by retarding gluconeogenesis	Edema, weight gain, macular edema, heart failure	Santwana *et al.*, 2020
α-glucosidase inhibitors (Acarbose, Miglitol, Glyset)	Reduce postprandial hyperglycemia	Bloating, gastrointestinal irritation	Derosa and Maffioli, 2012
DPP-4 inhibitors	Reduce blood sugar without causing hypo-glycemia andhelp to produce more insulin by pancreas.	Gastrointestinal problems, skin reactions and increased risk of pancreatitis	Anonymous, 2023

SGLT-2 inhibitors	Work by preventing the kidney from holding on to glucose and help to remove glucose through urine.	Nausea, fatigue, polyuria, polydipsia and xerostomia	Pittampalli, 2018
Glucagon-like peptide (GLP-1analogue)	Increase the use of insulin by body and growth of pancreatic β-cells.	Diarrhoea, nausea, vomiting, indigestion and loss of appetite	Holst, 2019
Dopamine-2 agonist (Bromocriptine)	Reduce blood sugar by reducing glucose production by the liver and increasing insulin sensitivity.	Nausea, vomiting, weakness and lack of energy, low blood pressure	Anonymous, 2022
Insulin	Activate insulin receptors, decrease glucose disposal, increase hepatic glucose production.	Hypoglycemia, mitogenetic effect, weight gain, injectable	Babiker and Dubayee, 2017

Thus, it is a challenge in the management of DM using the chemically synthesised drugs without causing any side effects. However, herbal medicines based on plant formulation can be an alternative option as these have low cost, negligible side effects and easy accessibility (Munish *et al.*, 2022).

India is the largest producer of medicinal herbs. Based on research conducted by the World Health Organization, approximately 70-80 percent of the world's population predominantly relies on modern medicine, with a significant emphasis on herbal and natural remedies for primary healthcare (Rani *et al.*, 2023). Plants possessing a traditional pharmacological background are currently undergoing screening. They represent an outstanding reservoir of natural antioxidants, with the potential to serve as potent medications in contemporary biomedicine (Malik *et al.*, 2020). About 2/3 of world's population is dependent on approximately 700 herbal recipes for the treatment of DM by using around 400 plants (Jwala *et al.*, 2015). Bioactive compounds like saponins, phenols, tannins, alkaloids, terpenoids, flavonoids, *etc.,* are the key factors for medicinal properties of these plants. The mode of action of some hypoglycemic plants varies. Some plants decrease the production of glucose, some stimulate the pancreas to secrete insulin and few reduce the rate of digestion and absorption of starches (Chinaka and Edeh, 2015).

The objective of this review paper was to collect data on Pharmacological activities of some antidiabetic weeds.

3. Pharmacological activities of some antidiabetic weeds

The medicinal characteristics of plants have been recognized for an extended period. The pharmacological properties of plants have been known for a long time. Herbal remedies have been used by indigenous cultures for thousands of years to treat various ailments (Srinivasan and Murali, 2022). Indian medicinal plants have been known for their therapeutic importance in diabetes (Singh and Singh, 2021).

Achyranthes aspera L. (Amaranthaceae)

This invasive weed thrives in wastelands and along roadsides throughout a wide range of countries, including India, Nepal, Sikkim, Sri Lanka, Bangladesh, Bhutan, Myanmar, Cambodia, Laos, Malaysia, Thailand, Vietnam, China, Taiwan, Indonesia, and the Philippines (Wiart, 2020). It is commonly known as prickly chaff flower, devil's horsewhip and chaff flower.

Ethanolic extract of *A. aspera* root showed reduced level of blood glucose and increased level of serum insulin in diabetic rats (Mishra and Singh, 2011). Lakshmi *et al.* (2018) observed that ursolic and oleolic acid of *A.aspera* leaf has antidiabetic effect against diabetic rats induced by streptozotocin. Ethanol extract of *A. aspera* seeds (Vijayaraj, 2018) showed antidiabetic activity more in acute model as compare to standard glibenclamide. The hypoglycemic effect of this plant may be due to inhibition or reduction of amylase in test animals. This alpha amylase inhibition activity of this plant may be due to occurrence of various phytochemicals like flavonoid, terpenoid and tannins (Muhammad *et al.*, 2022).

Ageratum conyzoides L. (Asteraceae)

Ageratum conyzoides L., also known by the names such as goat weed, chick weed, billygoat weed, white weed and mentrasto. The recognition of *A. conyzoides* as a problematic weed became evident during the period spanning from 1960 to 1980. Numerous reports indicate its extensive presence in multiple regions across Asia, Africa, Australia, and the Americas. In the Asian context, its invasive spread has been documented in countries such as India, Malaysia, the Philippines, Malawi, Cambodia, Thailand, Vietnam, Bangladesh, Pakistan, Sri Lanka, Indonesia, China, and Japan (Kaur *et al.*, 2023)

Nyunaï *et al.* (2009) observed that aqueous extract of *A. conyzoids* leaves reduced the blood glucose level in STZ induced diabetic and normal rats as compared to the initial blood glucose level. This might be due to stimulation of residual pancreatic beta cell function that causes hypoglycemic condition due to increasing pancreatic utilization of glucose. A significant increase in serum insulin was observed in diabetic rats at doses 200, 300 mg/kg of leaf extract of *A. conyzoides* and with glibenclamide (10 mg/kg) after 3 weeks of treatment as compared to diabetic control (Nyunaï *et al.*, 2015). Ojewale *et al.* (2019) observed that root extract of *A. conyzoids* also produced an antihyperglycemic effect by showing a substantial reduction in blood glucose levels.

Amaranthus spinosus L. (Amaranthaceae)

Amaranthus spinosus L. is probably native to the lowlands of the tropics of America, from the United States to Argentina. It is a cosmopolitan weed, mainly distributed in the tropics, but also in temperate regions elsewhere in America, south of Europe, tropical Asia, and Africa (Bayón, 2022). *A. spinosus* is commonly known as needle burr, spiny amaranth, spiny pigweed. Kumar *et al.* (2015) demonstrated that *A. spinosus* root aqueous extract produced a marked decrease in blood glucose levels in rats with alloxan-induced diabetes. Inhibition of α amylase activity and enhancement of insulin from pancreatic α-cells were observed with *A. spinosus* leaf extract (Hasan and Sultana, 2018). Bavarva and Narasimhacharya (2013) observed a significant difference between the diabetic control group and the diabetic rats treated with *A. spinosus* leaf extract (ASLEt). The diabetic controls exhibited elevated levels of urea and creatinine, while the diabetic rats that received ASLEt treatment showed substantial reductions in both urea and creatinine levels. This decline in levels could be linked to enhanced renal function, likely due to the observed decrease in blood glucose concentrations in both groups of diabetic rats receiving ASLEt treatment.

***Boerhaavia diffusa* L. (Nyctaginaceae)**

Boerhaavia diffusa L. exhibits a broad distribution, being found across India, the Pacific region, and the southern United States. It is commonly recognized by the names hogweed, pig weed and spreading hogweed.

Pari and Satheesh (2004) conducted a study to explore the impact of a daily oral intake of an aqueous solution containing *B. diffusa* leaf extract (BLEt) at a dosage of 200 mg/kg over a span of four weeks. Their research focused on evaluating how this treatment affected the concentration of blood glucose and hepatic enzymes in both normal and alloxan-induced diabetic rats. The results of their study indicated a notable reduction in blood glucose levels and a significant increase in plasma insulin concentrations among both the normal and diabetic rats who received the BLEt treatment. Methanolic extract of *B. diffusa* demonstrated antidiabetic effect in wistar rats due to its free radical scavenging and antioxidant activity (Alam *et al.,* 2018). Similarly, Mini *et al.* (2020) observed the antidiabetic effect of methanolic extract of *B. diffusa* roots in dexamethasone-induced insulin-resistant animals.

***Calotropis gigantea* L. (Asclepiadaceae)**

Calotropis gigantea L. is commonly known as crown flower and giant milkweed. It is prevalent weed in arid regions and has its origins in India (Negi and Bisht, 2021). Gupta and Chaphalkar (2016) conducted research focusing on antidiabetic effect of *C. gigantea* flowers. Their study demonstrated that when human diabetic samples were exposed to proteases of *C. gigantea* flowers, an increase in the count of granulocytes was observed compared to the control group. Interestingly, the levels of monocytes remained consistent with those of the control group in the presence of proteases. White flower extract of *C. gigantea* also showed a significant hypoglycemic activity in alloxan-induced diabetic rat model. Moreover, biochemical investigations (Manivannan and Shopna, 2017) have clearly explained the mechanism of its action that will be beneficial to use this plant extracts as a therapeutic target in diabetes research. Kumar *et al.* (2022) showed experimentally the nephroprotective effect of stem bark extract of *C. gigantea* in artificially induced type II diabetes in rats.

***Cynodon dactylon* (L.) Pers (Poaceae)**

Cynodon dactylon (L.) Pers is native to Europe, Africa, Australia and much of Asia, commonly known as couch grass, bermuda grass, quick grass and twitch grass. The pharmacological experiment of *C. dactylon* on standard drug tolbutamide showed almost the same blood glucose level at an interval of 1 h, 3 h, 5 h and 7^{th} day, respectively (Kumar *et al.,* 2011). The leaf extract of *C. dactylon* (Karthik and Ravikumar, 2011) was discovered to mitigate the risks of hyperglycemia and hyperlipidemia, while also diminishing oxidative stress in diabetic rats. Notably, a substantial rise in HDL levels and a reduction in cholesterol, triglyceride, LDL, and VLDL levels were observed after a 15-day treatment period. Aqueous extract of *C. dactylon* (whole plant and leaves) possesses antidiabetic potential as it markedly decreased the blood glucose level in rats with alloxan-induced diabetes. However, Ramya *et al.* (2014) observed that chloroform and ethanolic extract of *C. dactylon* roots outperforme the aqueous extract in reducing elevated blood glucose levels in rats with alloxan-induced diabetes.

***Euphorbia hirta* (L.) Millsp. (Euphorbiaceae)**

It is distributed throughout the temperate or tropical parts of India, Asia, Australia, and Africa, often found in lowland, paddy fields, gardens, waste places, and in the roadsides (Gosh *et al.*, 2019). Common names of *E. hirta* are dove milk, garden spurge, hairy spurge, pillpod sandmat, pillpod spurge, snakeweed, sneeze weed and red euphorbia. The ethanolic extract (250 and 500 mg/kg) of flower, stem and leaves of *E. hirta* were used by Kunal *et al.* (2010) to evaluate the antidiabetic activity against normal and STZ induced diabetic mice. It was observed that leaf extract (500 mg/kg) caused maximum reduction of blood glucose level. Similarly, Goldie *et al.* (2012) demonstrated the antidiabetic properties of *E. hirta* ethanolic extract using various doses; namely, 100, 200, 400, and 800 mg/kg, in alloxan treated rats. However, the most significant decrease in blood glucose occurred at the dosage of 800 mg/kg. *In vitro* study by Shilpa *et al.* (2020) reported significant inhibitory effect of methanolic extract of *E. hirta* whole plant on the enzyme alpha amylase in a concentration dependent manner comparable to that of the drug metformin.

***Evolvulus alsinoides* L. (Convolvulaceae)**

This common weed is known as slender dwarf morning glory which thrives in open grassy areas across India and subtropical regions worldwide. It holds significant medicinal value and has been traditionally used in India to address various health concerns (Yadav *et al*., 2016). The levels of glycoproteins in the tissues of kidney and liver of diabetic rats were restored after administration of *E. alsinoides* whole plant extract for 45 days (Duraisamy *et al.*, 2013). *E. alsinoid* plant extract caused significantly rise in the insulin level and inhibition of lipid peroxidation (Gomathi *et al.*, 2013a). The experimental studies (Gomathi *et al.*, 2013b) prove that *E. alsinoides* is beneficial in normalizing glucose homeostasis and in restoring glycoprotein levels in STZ-induced diabetic rats.

***Lantana camara* L. (Verbenaceae)**

This plant commonly known as indradhanu and lantana has successfully naturalized in over 60 countries, where it is recognized as a highly invasive and detrimental weed. It is classified among the top hundred most destructive invasive alien species globally (Noguchi and Kurniadie, 2021).

Balti *et al.* (2020) observed that leaf extract of *L. camara* caused lowering of blood glucose. The diabetic controlling characteristics of this plant may be due to enhancement of insulin and diminished absorption of glucose from the intestines (Pandeya *et al.,* 2022). Methanol extract of *L. camara* leaves (400 mg/kg body weight) when administered orally to rats with alloxan induced diabetes, which led to a reduction in blood glucose levels to 121.94 mg/dl (Ganesh *et al.*, 2010). Venka Tachalam *et al.* (2011) explored the potential for reducing blood sugar activity of *L. camara* fruits on the basis of body weight, histological studies and HbAIc profile in experimental diabetic rats.

***Mimosa pudica* L. (Fabaceae)**

Mimosa pudica L. is also known by the names sensitive plant, touch-me-not, chui-mui and lajwanti. It is a prevalent weed often found along roadsides. Its extensive and tenacious root system can harm crops, making it difficult to eradicate once established. Interestingly, in countries such as Bangladesh, India, Thailand, and the Philippines, it is employed as an antidiabetic remedy (Uddin° and Sarker. 2014).

Seeds of *M. pudica* possess antioxidant properties and also exert antidiabetic effect (Sunday *et al.,* 2020) through the augmentation of pancreatic insulin secretion and alpha-amylase activity. Hence, the seeds of this plant could be employed to avert hepatic damage linked to diabetes. Sutar *et al.* (2009) demonstrated that ethanolic extract of *M. pudica* leaves lowered the glucose levels in rats with diabetes (Albino rats) to 50.35% as compared to metformin drug which was 62.44% on the 7th day.

***Oxalis corniculata* L. (Oxalidaceae)**

Oxalis corniculate L. is commonly known as changeri, ambati, creeping wood sorrel and creeping oxalis. It exhibits a broad distribution across Asia and holds significance as a weed of importance in nations including India and China (Groom *et al.,* 2019). Dutta *et al.* (2016) substantiated the diabetes fighting potential of the ethanolic extract of *Oxalis corniculata* in STZ-induced diabetic rats. Methanol extract and fraction of methanol extract (OCMF-3) of *O. corniculata* whole plant demonstrated antihyperglycemic effects in animals with diabetes induced by STZ (Mekap *et al.,* 2016) and this activity was comparable to standard drug**.**

***Parthenium hysterophorus* L. (Asteraceae)**

Parthenium hysterophorus L. popularly known as carrot grass, congress grass is an invasive weed ranked as the seventh most dangerous globally. Originally native to the Americas, it has subsequently spread to Africa, Australia, and Asia (Kaur *et al*., 2021). Aqueous extract of *P. hysterophorus* showed strong hypoglycemic action by reducing the fasting glucose level within 2 h in alloxan induced diabetic rats (Khaket *et al.,* 2015). Makhdoom *et al.* (2022) demonstrated the impact of the methanolic extract of *P. hysterophorus* (MEPH) on diabetes reduction in alloxan-induced diabetic rabbits studied through histological analysis. It was observed that 100 mg/kg of MEPH repaired the alloxan-induced pancreatic damage effectively.

***Portulaca oleracea* L. (Portulacaceae)**

Portulaca oleraceae L. is the eighth most widespread weed found across temperate, subtropical, and tropical regions worldwide. This plant is commonly known by names segan, purslane and pussley, has its origins in India and Persia, but it has also naturalized in America, where it is commonly encountered as a garden weed (Syed *et al*., 2016). The term "Global Panacea" has been given to this plant as it is the most used medicinal plant listed by World Health Organization. So, this plant is treated as pharmacological agent to be used for medicine and food for human and animals. *P. oleracea* has hypoglycemic activity as observed in alloxan induced diabetic rats. The plant led to the enhancement of disrupted glucose metabolism and elevated insulin secretion by restoring the functionality of impaired pancreatic beta cells. (Chugh *et al.,* 2019).

***Ruellia tuberosa* L. (Acanthaceae)**

Ruellia tuberosa L., commonly known as meadow weed, minnie root, cracker plant and popping pod has originated from America, was introduced to India as a garden plant. It has since become naturalized and thrives as a garden weed. In the folk medicine of Taiwan, it has been utilized for its antidiabetic properties (Bhogaonkar *et al*., 2012). Root extract of *R. tuberosa* have reduced enzymes activities like lipase, protease and amylase on the serum of diabetic rats (Safitri *et al.,* 2019). The mechanism by which *R. tuberosa* showed its hypoglycemic potential is due to inhibition of pancreatic alpha-amylase and it was observed by Wulan *et al.* (2015) *in silico* studies that it acts as non-competitive inhibitor of the alpha amylase. Similarly, stem and leaf extract of this plant alleviated hyperglycemia and increase hepatic antioxidant capacity and reduce the generation of oxidative stress in HFD/STZ induced diabetic rats (Chang *et al.,* 2018).

***Silybum marinum* (L.) Gaertn. (Asteraceae)**

Silybum marinum (L.) Gaertn., also known by names blessed milk thistle, marian thistle, mary thistle, saint mary's thistle, variegated thistle and scotch thistle, has its origins in the Mediterranean region of Europe, is deliberately grown for its medicinal properties in countries like Egypt, Tunisia, China, and Argentina. Nevertheless, its status as an invasive weed has been recorded in various other nations (Lehoczky *et al*., 2018). Silymarin, an active component of fruits and seeds of *Silybum marinum***,** markedly decrease the blood glucose levels and elevate serum insulin levels in diabetic rats induced by streptozotocin (Katiyar *et al.,* 2012). Similarly, Sayyah *et al.* (2020) among individuals diagnosed with type 2 diabetes investigated the antidiabetic activity of this plant.

***Sida acuta* Burm. f. (Malvaceae)**

Originally indigenous to Mexico and Central America, the weed has now expanded its presence globally. *S. acuta* is also known as common wireweed, is frequently found alongside crops within the Indian agricultural sector (Patil, 2014). Arya *et al.* (2012) reported the reduction in blood glucose level after 2 and 4 h of oral administration of alcoholic leaf extract of *S. acuta* in normal rats. *In vitro* study by Dinlakanont *et al.* (2020) demonstrated the inhibitory activity of methanolic extract of root, leaf and stem parts of *S. acuta* on porcine alpha amylase, alpha glucosidase from *saccharomyces cerevisiae*. Leaf extract (Okwuosa *et al.,* 2011) also showed decrease in blood glucose in alloxan induced rabbits and significant tolerance for glucose in glucose fed normal rabbits.

***Sinapis arvensis* L. (Brassicaceae)**

This plant commonly known as wild mustard, field mustard and charlock has its origins in the Mediterranean region and has since become extensively naturalized in Europe, temperate Asia, Pakistan, and North Africa. (Meikeet *et al*., 2010). Wild mustard is a serious weed of cultivated land. *S. arvensis* seed extract (Mohammed *et al.,* 2021) and seed oil (Sarwar *et al.,* 2019) showed antidiabetic potential in experimental diabetic rats. Moreover, the plant's leaf extract also exhibited properties that counteracted diabetes by improving glucose metabolism and increasing insulin sensitivity, and causes reduction in oxidative stress and inflammation in treated rats (Adeyemi *et al.,* 2020).

***Synedrella nodiflora* (L.) Gaertn. (Asteraceae)**

Synedrella nodiflora (L.) Gaertn., native to tropical South America, is an annual herb that has now spread across India. Currently, this exotic weed is encroaching upon crop fields and forests (Ghayal *et al*., 2014). It is also known by the names Cinderella weed, Node weed, pig grass and Synedrella. Hypoglycemic effect (Zahan *et al.,* 2012) of this plant was noted in both normal rats and those with alloxan-induced diabetes. When the plant extract was administered intraperitoneally at doses of 150 mg/kg and 300 mg/kg, it resulted in a decrease in glucose levels by 57.87% and 66.83%, respectively, in alloxan-induced rats. Whereas, the reduction was 72% for metformin after 3 days.

***Taraxacum officinale* L. (Asteraceae)**

Taraxacum officinale L. is commonly known as dandelion and lion's tooth. This plant originates from Eurasia, with its distribution extending into Asia, Europe, and North America, specifically the temperate zone of the Northern Hemisphere (Rasool and Sharma, 2014). *In vitro* antidiabetic studies by Mir *et al.* (2015) showed that methanol and aqueous extract of *T. officinale* possess considerable alpha-amylase and alpha-glucosidase inhibitory activities. Similarly, Choi *et al.* (2018) and Guo *et al.* (2019) investigated the hypoglycemic activity of *T. officinale*, which is due to the suppression of alpha glucosidase and alpha amylase enzyme functions. *In vivo* studies (Juee and Naqishbandi, 2020) of root extracts of *T. officinale* exhibited antidiabetic properties in both normal and alloxan-induced diabetic mice.

***Tribulus terrestris* L. (Zygophyllaceae)**

Tribulus terrestris L. naturally inhabits warm temperate and tropical areas in southern Europe, southern and western Asia, Africa, and Australia. It is dispersed across regions like Africa, Southern Europe, China, Japan, Korea, and the western parts of Asia. Typically, it can be located within cultivated crops, overgrazed pastures, roadsides, lawns, and neglected areas (Hashim *et al.,* 2014). This weed is known by many names, like goat's head, bindii, burra gokharu, small caltrops, cat's head, devil's thorn, puncture vine and tackweed. Its fruit extract (Alkhaldi *et al.,* 2020) demonstrated dose-dependent inhibitory effects on both alpha glucosidase and alpha amylase enzymes. Among the extracts, hexane exhibited the highest alpha glucosidase inhibition activity, followed by acetone and ethanol extracts. Stefanescu *et al.* (2021) observed that plant extract (TT-LPC and TT-HPC) decreased the blood glucose level significantly in 12th week compared with 1st week.

***Tridax procumbens* L. (Asteraceae)**

Tridax procumbens L. also known as tridex daisy, coat buttons and mexican daisy is widespread weed across India. While it originates from tropical America, it has been introduced to various tropical, subtropical, and temperate regions worldwide (Pawar and Patil, 2017). This plant is a traditional Indian therapeutic plant (Kakkar *et al.,* 2022) that has ability to lower the blood glucose as well as curb diabetic neuropathy (DN). Biochemical markers study in streptozotocin (45 mg/kg body weight) induced wistar rats showed a considerable improvement in DN using *T. procumbens* extract (250, 375 and 500 mg/kg). An additive effect in reducing blood glucose was observed with a combination treatment of *T. procumbens* extract (500 mg/kg) and standard drug gabapentin. Sonawane *et al.* (2014) observed that methanolic extract of this plant has potential to reduce postprandial glucose level *via* alpha amylase inhibitory action.

Weeds (Figure 2), commonly considered as nuisances in agriculture and landscaping, exhibit a remarkable array of bioactive compounds, including polyphenols, flavonoids, alkaloids, and more. These compounds have demonstrated antidiabetic properties in preclinical studies, presenting a multifaceted approach to managing diabetes. Notably, weeds may enhance insulin sensitivity, mitigate chronic inflammation linked to insulin resistance and scavenge free radicals, all contributing to improved glucose control. Scientific validation through rigorous clinical trials remains a critical need to establish their efficacy and safety definitively. Determining optimal dosage forms and preparations also requires further exploration. Safety concerns, particularly potential interactions with other medications, must be addressed to ensure responsible usage.

The future of weeds in diabetes management holds promise. Advancements in research methodologies and comprehensive clinical trials can pave the way for their inclusion as valuable components of holistic diabetes care. Identification and isolation of specific bioactive compounds within weeds may lead to the development of novel antidiabetic drugs or dietary supplements. Integrating weed-based remedies with conventional medicine offers a holistic approach, potentially reducing the reliance on synthetic drugs.

Figure 2: Weeds having antidiabetic potentials.

4. Conclusion

From the above discussion, we can conclude that weed is a relative term as what may be weed (wasteful/useless plant) to one may be a medicinal or useful plant to another individual; for example, for some people *Parthenium hysterophorus* might only be a roadside weed, but for diabetic patients, its aqueous extract has strong hypoglycemic properties. Similarly, *Cynodon dactylon, Lantana camara, etc*., all in one form or another have antiglycemic action on the blood glucose level, hence they all have pharmaceutical properties that may be utilized for the management of diabetes mellitus. These plants and their constituents exhibit various mechanisms, such as improving insulin sensitivity, enhancing glucose uptake, and reducing inflammation, which contribute to their antidiabetic effects, however their use should be done only after the consultation or under the supervision of medical professionals. Moreover, integration of herbal products with allelopathic chemical will help in lowering the dependence on chemicals along with providing sustainable disease management. It is important to note that while some studies suggest potential benefits of these plants, but further research is necessary to assess the full potential of these weed plants as a prospective DM management approach.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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