**Original Review Article**

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**AN OVERVIEW OF THE TYPES AND QUALITY OF CURRENTLY PRACTICING  
IN VITRO ANTI-GLYCEMIC ACTIVITY OF INDIAN AVAILABLE MEDICINAL  
PLANT EXTRACTS AND PLANT-DERIVED PRODUCTS****D. Durai<sup>1</sup>, J. Annamalai<sup>1</sup>, R. Sundaram<sup>2\*</sup>**

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**ABSTRACT:** Diabetic Mellitus (DM) is a chronic illness caused by the abnormal secretion of insulin by pancreatic cells. Type 2 DM is the most common threat for people nowadays due to changes in lifestyle, food, etc. Since there are no synthetic drugs developed to treat DM in modern science without any adverse side effects, medicinal plants are preferred to replace these drugs. About 1200 plants are reported to have an antidiabetic effect with few or no side effects. The phytochemical constituents, like alkaloids, flavonoids, steroids, terpenoids, etc., present in plants were considered one of the reasons behind anti-glycemic activity. This review article summarises studies that have employed herbal plants and examined their in vitro anti-hypoglycemic effects. Alpha-amylase inhibitory, alpha-glycosidase inhibitory, glucose uptake, DPP IV inhibitory, glucose adsorption capacity, glucose diffusion, and aldose reductase assays were commonly used to analyse the antidiabetic activity of herbal plants. Among them, alpha-amylase inhibitory assay and alpha-glycosidase inhibitory assay were preferred by most of the researchers since they have high precision, sensitivity, and efficacy that are comparable to in vivo approaches.

**Keywords:** Diabetes Mellitus, medicinal plants, phytochemical constituents, *in vitro* antidiabetic assays.

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## 1.INTRODUCTION

Diabetes is an acute illness that is illustrated by impaired insulin resistance, where various parts of the body are apathetic to insulin during the food intake process [1-3]. The flow of glucose in the blood stream is supererogatory and leads to a high level of blood dextrose. Due to an inappropriate glycolytic pathway, unstable molecules (free radicals) are produced, which sabotage cells and cause unusual growth and premature ageing [4,5]. A Greek physician, Aretaeus of Cappadocia, diagnosed the illness as diabainein, which means “to have an increased amount of sugar in the blood and urine”. Thomas Willis, an English physician in the 17th century, diagnosed sugar disease in his patients by analysing their excretion of liquid waste from the body, which contained rich sweetener, and it was named "Honeyed diabetes". Bouchardat and Lancereaux differentiated diabetes grass-tout from diabetes maize in 1880 [6]. In 1921, Frederick Banting and Charles Best used a crude "canine pancreatic extract" to cure a diabetic dog, and they also used a highly refined crude canine pancreatic extract to save the life of a young diabetic child [7]. Later, a new solution for this disease was introduced and named insulin through the collaboration of Banting and Best for treating diabetic patients. Based on the level of insulin, Roger Hinsworth (1935) distinguished between type I and type II diabetes, saying that type I diabetes was determined to be insulin-responsive, whereas type II diabetes was determined to be insulin-insensitive. This finding enabled him to establish a source of new approaches for treating diabetes mellitus. Because of this key finding in diabetic research, insulin has become an active and significant lifesaving source for humans affected by diabetes [6,7]. In accordance with WHO (2019), this NCD (non-communicable disease) (Diabetes Mellitus) caused more than 160,000 fatalities, which turned into the 9th highest rate of death all around the world [8]. It is estimated that by 2035, 592 million people will be severely affected by type 2 diabetes, which has ever since expanded throughout the globe and is now the leading cause of disease in young age groups [9,10]. The impact of DM is soaring and escalating widely, especially in developing countries like India, and is mainly fostered by the elevated universality of stout, obese, and unfit lifestyles. Since India is a democratic country with a highly dense population, the people there live a modern, cultural lifestyle. An estimation in 2019 revealed that 77 million people in the nation had DM, and it could be expected to reach over 134 million by 2045. Among those, 57% of these peoples are left uncharted [11,12]. The majority of people suffer from type 2 DM, which can lead to Multiple Organ Dysfunction Syndrome (MODS). Currently, about 70 percent of healthcare in our nation is still being catered by long-established systems of medicine (i.e., the traditional medicine system). Ayurveda, which is highly dependent on natural resources and offers completely herbal-based pharmaceutical therapies for eliminating illness by studying the anatomy of patients, also aims to create a healthy society. In recent years, the medical and research communities have been constantly scouting for advanced natural agents, and the pharmaceutical industries are also interested in

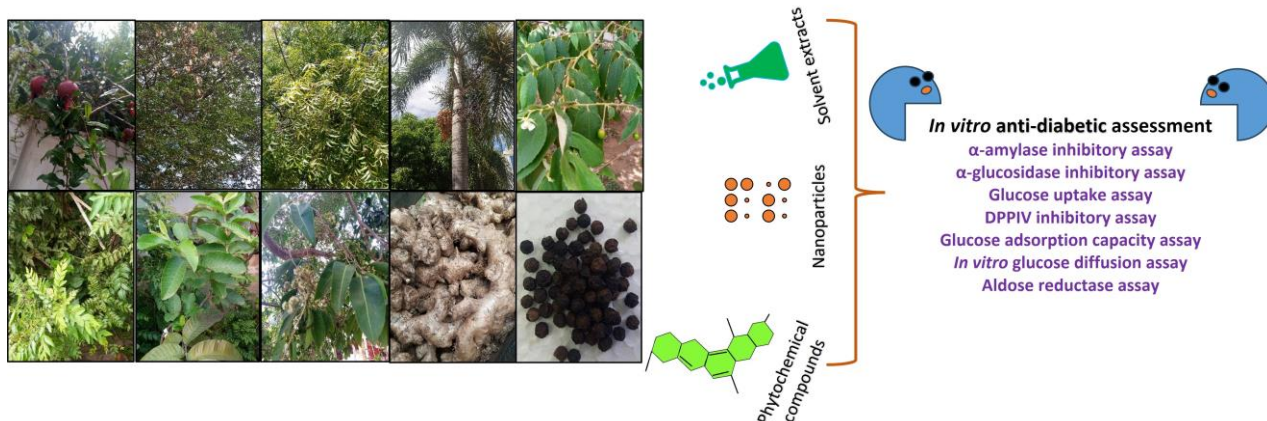
investing a lot of money in research and development programmed for the discovery of natural drugs that have been attributed to possess antimicrobial, anti-diabetic, anti-cancer properties, etc. [12].

Floral species are highly crucial for mankind because they have a rich potential source to produce natural, low-risk tablets, powders, and syrups to keep patients' physical and mental health in check.

In the past three decades, the popularity of herbal products has grown significantly [13]. Indians have known about the therapeutic properties and values of many herbs since ancient times. With the abundance of the floral population and the advance of science, much of the folklore medicine addressed in traditional systems has been explored scientifically [14]. Traditional herbal plants are chief constituents of molecules with remedial characteristics because of the natural compounds present in them. These traditional herbal plants are useful for healing anthropogenic diseases (human illness) because of the presence of phytonutrient compounds like alkaloids, flavonoids, saponins, steroids, tannins, terpenoids, quinones, sulphur-containing compounds, allied phenolic and polyphenolic compounds, etc. [15]. According to recent survey reports, in the world of herbal science, 1,700 plants are utilized as ayurvedic medicine in India. From this, 700 are vegetable-based medicines, and 800 species are believed to have antidiabetic properties [12,16,17]. The most popular approaches to the control of plasma sugar levels are the blocking of key enzymes [18] i.e.,  $\alpha$ -Glucosidase and  $\alpha$ -amylase. These two are starch digestive stimulants, which can cause increased postprandial hyperglycemia (PPHG); thus, their hindrance plays a vital role in managing PPHG in affected patients with type 2 (insulin resistance) DM. Suppression of  $\alpha$ -glucosidase causes depletion of dextrin hydrolysis, and inhibition of  $\alpha$ -amylase interrupts the disintegration of carbohydrates into simple sugars. Some of the compounds are used in the medical field, and the outcomes have shown a significant diminution in glucose levels in affected people [19,20]. The most important complication associated with the Food and Drug Administration (FDA) approved anti-insulin resistance (type 2) DM drugs, such as voglibose, acarbose, miglitol, sulphonylureas, and thiazolidine, is gastrointestinal (GI) issues like swelling, abdominal distraction, diarrhoea, and meteorism, which require high monitoring and examination of various medicinal agents with fewer side effects are in heavy demand [21-23].

Nowadays, a great interest has evolved in exploring beneficial herbs as an innovative strategy for bio-catalyst (enzyme) suppressors, natural radical scavenging particles, and therapies for numerous illnesses, including DM [24]. Researchers are utilising a secure and profitable scheme regarding the preference of therapeutic herbs by learning their cultural myth, which has been accompanied by *in vitro* and *in vivo* assays or biotic recognition that leads to the finding of innovative plant-derived bioactive molecules. These molecules are investigated and altered to be used as components in pharmaceuticals [25]. This study engaged in reviewing the *in vitro* hypoglycemic exploit of different species of Indian herbs (foretold in lore) with both indigenous and exotic origins that could further progress into herbal drugs. By describing the *in vitro* anti-diabetic functioning technique in depth

and suggesting which activity might be carried out to achieve the greatest outcomes, this review was created in the hopes of supporting future research seekers. It also outlines the benefits and drawbacks of currently practicing *in vitro* anti-diabetic assays.



**Figure 1: Shows reviewed medicinal plant derivatives and the types of *in vitro* anti-diabetic assessment methods used**

## 2. MATERIALS AND METHODS

A thorough search and selection of the scientific literature was made by taking into account all pertinent reports on the aimed topic. Google Scholar, Science Direct, Elsevier, Scopus, and Pubmed were used as information sources to collect relevant articles by using the key words, including DM, medicinal plants, phytochemical constituents, and *in vitro* antidiabetic assays. Overall, more than 100 research articles were collected and segregated based on need, and the redundant articles were rejected. The data obtained from the research articles were credible and assessed for applicability, and then the review was concluded by analysing the significance and outcome of each and every article included.

### 2.1 ANTI-DIABETIC ASSAYS

#### 2.1.1 $\alpha$ -Amylase Inhibitory Activity

In human beings, the digestion of glucose includes different steps. On the first stage, predigestion by ptyalin (salivary amylase) results in the breakdown of the polymer substrate into a short oligopeptide. Then, they are further hydrolyzed in the gut by amylopsin (pancreatic  $\alpha$ -amylase) into maltose, maltotriose, and small malto-oligosaccharides. The dietary starch (maltose) is hydrolyzed by the digestive enzyme ( $\alpha$ -amylase), which is then degraded into glucose and absorbed. Retardation of 1,4- $\alpha$ -D-Glucan glucanohydrolase (alpha-amylase) results in a lowering of PPGH in DM conditions. The activity of the ptyalin *in vitro* enzyme can be calculated by the hydrolysis of glycogen. The alpha-amylase enzyme process was quantified by the use of iodine (I), which indicates a blue colour with glucose. The high tint of blue indicates the  $\alpha$ -amylase suppression activity in the sample, while the low tint of blue represents the catalysis-influenced hydrolysis of

starch or carbs into simple saccharides. i.e., the intensity of the sample is directly proportional to the ptyalin-inhibiting effect [26].

### 2.1.1.a Steps to follow

Mix the extract with different concentrations of  $\alpha$ -amylase (50–200 $\mu$ g/ml) in a test tube and add 0.5 % of starch to it. Then incubate it at 37°C for 5 min and add 2 ml of DNS (3, 5-dinitrosalicylic acid) reagent to it. Keep the test tubes in a water bath for 15 minutes at 100°C, and add 10 ml of distilled water to an ice bath for the dilution of the sample (Miller 1959). Read the solutions at 540 nm under a UV spectrophotometer [27].

Estimate the  $\alpha$ -amylase inhibitory activity by using the following formula:

$$\% \text{ Inhibition} = \left[ \frac{\text{Abs Control} - \text{Abs Samples}}{\text{Abs Control}} \right] \times 100$$

### 2.1.2 $\alpha$ -Glucosidase Inhibitory Activity

Alpha-glucosidase is a membrane-confined enzyme positioned on the outer layer of the small bowel (small intestine) that induces the breakdown of disaccharides to form glucose. Interference with  $\alpha$ -glucosidase can delay the assimilation of dietary saccharides and repress PPGH. Hence, the inhibition of acid maltase ( $\alpha$ -glucosidase) was considered the most efficacious method to treat DM [28]. This enzyme plays an important role in the glycoprotein (GP) and glycolipid (GL) processes and is required in the disintegration of carbohydrates. Alpha glucosidase is the target for the antiviral agents that hinder the initiation of important GP, which is necessary in viral assembly, production, and foreign contamination. Estimation of  $\alpha$ -glucosidase can be done by determining the generation of a colorimetric (405 nm) product that results from hydrolysing the p-nitrophenyl- $\alpha$ -D-glucopyranoside by  $\alpha$ -glucosidase and this action is correlated to the contemporary  $\alpha$ -glucosidase activity. The quantity of  $\alpha$ -glucosidase enzyme instigates the hydrolysis of reactant 1.0  $\mu$  mole per 60 seconds (pH 7.0) is considered one unit of  $\alpha$ -glucosidase [26].

### 2.1.2.a Steps to follow

Mix  $\alpha$ -glucosidase (0.075 units) with an extract at different concentration (50–200 $\mu$ g/ml) in a test tube and add 3 mM p-nitrophenyl glucopyranoside (pNPG) into it (Miller 1959). Then incubate it at 37°C for 30 min, and add 2 ml of Na<sub>2</sub>CO<sub>3</sub>. Read the test tubes at 400 nm under a UV spectrophotometer [27].

Estimate the  $\alpha$ -glucosidase inhibitory activity by using the following formula:

$$\% \text{ Inhibition} = \left[ \frac{\text{Abs Control} - \text{Abs Samples}}{\text{Abs Control}} \right] \times 100$$

### 2.1.3 Glucose Uptake Assay

The Dulbecco's Modified Eagle's Medium (DMEM) is used for the culture of 3T3-adipocyte cells, where 10 % of fetal calf serum is added for their supplementation and then sown into a 96-well plate.

Incubate this for 24 hours. After incubation, wash the cells and add them to serum-free DMEM for attaining serum deprived state. Restore the medium using 20 µl of a 2-deoxyglucose mix that contains 130 µl of glucose-free DMEM. Add the sample to the well plates, triplicate them, and incubate them for 5 hours. After the incubation, view the well plate under a microscope. The supernatant free lysed cells are used to analyse the glucose content by using the DNAS method. Read the well plate at 570 nm. The readings of the samples will be compared with the control. The optical density (OD) of the zero control is 100% viable. The viability percentage of the extract is determined in comparison with the control [29].

#### 2.1.4 DPP IV Inhibitory Assay

Dipeptidyl peptidase-4 inhibitors are a group of anti-diabetic drugs used to manage type 2 DM. Univariate analysis and multivariate logistic regression analysis revealed that DPP IV inhibitors are associated with an increase in BP, which causes the risk factors in diabetic patients that lead to cardiac failure, stroke, and many other cardiovascular conditions [30].

##### 2.1.4.a Steps to follow

Take the extract in a 96-well plate at various concentrations and add p-nitroaniline solution to it. Then prepare Dipeptidyl Peptidase Enzyme Solution in various concentrations, and after that, add 0.1 mL of Gly-Pro-pNA solution to the plate. Incubate the plate at 37°C for 15 minutes, and then read the absorbance at 405 nm in a microplate reader [31].

#### 2.1.5 Glucose adsorption capacity Assay

The samples were determined by the method of Ou *et al.* Add 25 ml of glucose solution to 1% of plant extract, mix the solution thoroughly, and maintain it at 37°C for 6 hours in a water bath. Then centrifuge the solution at 4800 rpm for 20 minutes, and determine the amount of glucose in the supernatant solution. Estimate the concentration of glucose by using the following formula:

$$\text{Glucose bound} = G1 - G6 / \text{weight of sample} \times \text{volume of solution}$$

Where G1 is the glucose concentration of the original solution. G6 is the glucose concentration after 6 hours [32]

#### 2.1.6 *In vitro* glucose diffusion Assay

This assay was done according to the method of Ahmed *et al.* Add 25 ml of glucose solution and 1% of plant extracts in a dialysis bag against 200 ml of distilled water and place it in a water bath (37°C). Estimate the amount of glucose in the dialysate at 30, 60, 120, and 180 minutes using a glucose oxidase peroxidase diagnostic kit [32]. The glucose dialysis retardation index (GDRI) will be determined by using the following formula:

$$\text{GDRI}\% = \frac{\text{Glucose content with addition of sample (mg/dL)}}{\text{Glucose content of the control}} \times 100$$

### 2.1.7 Aldose reductase assay

#### 2.1.7.a Preparation of Aldose Reductase:

Homogenize 1g of eye lenses in 12 volumes of 135 mM sodium phosphate buffer (pH 7.0), which contains 0.5 mM phenylmethyl sulfonyl fluoride and 10 mM 2-mercaptoethanol. Maintain 4°C throughout the procedure. Centrifuge the homogenate mixture at 10,000 rpm for 30 minutes, and restore the supernatant in a separate test tube, which is the final product of the aldose reduction enzyme preparation. Determine the activity of this preparation by measuring the amount of NADP released per unit time at 37°C and pH 7.0. One unit (U) of activity is defined as the amount of enzyme that catalyse the oxidation of 1µmol of NADPH per minute under the experimental conditions [33]. The activity of aldose reductase will be determined by using the following formula:

$$\text{Activity} \frac{U}{mL} = \text{Change in OD of test/ min} \times \text{Total volume of the assay 6.2} \\ \times \text{Volume of enzyme taken for analysis}$$

Where 6.2 = micromolar extinction coefficient of NADPH at 340 nm

#### 2.1.7.b Steps to follow

Measure the aldose reductase activity by the photometric method. [34] Add 50 µL of drug solution and 50 µL of NADPH (0.04 mM) in a 96-well plate. Add 100 µL of prepared aldose reductase enzyme into the well plate. Initiate the enzymatic activity by adding 75 µL of substrate, DL-glyceraldehyde ( $5 \times 10^{-4}$  M), into it. Record the absorbance every minute for a duration of 20 minutes at 340 nm. The reduction in the absorbance due to the oxidation of NADPH to NADP is observed at different time points. The concentrations of the suppressors producing 50% inhibition of the enzyme activity ( $IC_{50}$ ) will be determined from the % of inhibition [34].

### 3. DISCUSSION

DM is currently described as one of the most endemic disorders of the ductless gland (endocrine) all over the world [35]. DM has elevated due to expeditious cultural and social evolutions: demographic ageing, increase in population, nutritional changes, lowering of physical activity, and unhealthy practices in many countries [36]. Adult-onset diabetes (Type 2) is a prevalent condition and a serious international health problem. Risk factors for developing type 2 DM are highly interconnected with overweight and the pedigree tree of diabetes [37]. To attain better blood glucose control, antihypoglycemic drugs are used as single agents and also in combination with some other medicinal drugs. All oral antidiabetic agents have adverse side effects with long-term blood glucose control, [38-40] so plant-based drugs are considered a choice since they are secure and economical, and they play a vital role in manage DM [41-43]. WHO had approved the assessment of historical plants as an antidiabetic remedy because of their efficacy, being harmless with low or no side effects, and being considered a treasure trove of resources for the examination of diabetic agents. Various scientific investigations were carried out by researchers to provide research-based proof of the

medicinal use of traditional plants and their various parts [44,45]. The phytochemical constituents, like alkaloids, flavonoids, steroids, terpenoids, etc., present in plants were considered the reasons behind anti-glycemic activity and some particular compounds, such as 7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4H-chromen-4-one, (S)-2-(3,4-dihydroxyphenyl)-7,8-dihydroxychroman-4-one, and 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one, which stimulate the antidiabetic activity.

Nowadays, herbal plants play a vital role in the treatment of a variety of diseases. We reviewed the *in vitro* antidiabetic activity of different herbal plants available in India. About 45,000 species of plants have been found in India; among them, more than a thousand possess medicinal properties, and about 1200 plants are reported in ethnomedicine to have an antidiabetic effect with few or no side effects [46]. Using *in vitro* testing as a research technique is simple. Compared to trials involving animals or people, researchers may carry out more in-depth analyses and assess biological impacts on a larger number of *in vitro* assays [47]. The results obtained in this review on *in vitro* antidiabetic activity showed efficiency for the treatment of type 2 diabetes. The studies included in this review are given below (Table.1). *In vitro* study focused on the effectiveness of  $\alpha$ -amylase inhibitory and  $\alpha$ -glucosidase inhibitory assays were done by Priyamvada *et al.* (2021) in methanolic and petroleum ether extracts of *Achyranthes aspera* and showed dose-dependent antidiabetic activity [48]. Nirmali Wickramaratne *et al.* (2016) have done the  $\alpha$ -amylase inhibitory assay on aqueous, ethyl acetate, methanolic, and petroleum ether extracts of *Adenantha pavonine* [49].  $\alpha$ -amylase inhibitory and  $\alpha$ -glucosidase inhibitory assays on methanolic extracts of *Albizia lebeck* were performed by Danish Ahmed *et al.* (2014), and  $\alpha$ -amylase inhibitory assay performed using NiO NPs from extracts of *Areca catechu* were carried out by Shwetha *et al.* (2021) [50,51]. An *in vitro* study (Megha *et al.*, 2013) on *Bauhinia purpurea* extracts with different solvents (hexane and petroleum ether) followed the  $\alpha$ -amylase inhibitory, glucose uptake by yeast cells, and non-enzymatic glycosylation of haemoglobin assays [54]. The investigation of  $\alpha$ -amylase inhibitory assay on chloroform extract and St NPs of *Gymnema sylvestre* was done by Vishnupriyan Varadharaj *et al.* (2014) and Harshad *et al.* 2019 [58,66]. The alpha-amylase inhibitory assay in aqueous extract and ZnO NPs and the  $\alpha$ -glucosidase inhibitory assay in aqueous, chloroform, and methanolic extracts and ZnO NPs of *Moringa oleifera* were processed by Harshad *et al.*, 2019 [58]. The  $\alpha$ -amylase inhibitory assay in aqueous extract and Au NPs of *Physalis minima* was examined by Velmurugan Sekar *et al.* (2022) [70]. In 2012, Vishal Jain *et al.* carried out an experimental study of  $\alpha$ -amylase inhibitory assay and the aldose reductase inhibition assay in methanol and valoneic acid dilactone extracts of *Punica granatum* [74]. The *Swertia chirayita* plant (methanol and hot water extracts) was chosen, and its hypoglycemic effect was checked using  $\alpha$ -amylase inhibitory assay carried out by Priyanka Roy *et al.* (2015) [79]. ZnO NPs of *Tamarindus indica* extracts were tested for their anti-diabetic activity by employing  $\alpha$ -amylase inhibitory and  $\alpha$ -glucosidase inhibitory



assays, as experimented by Dilaveez Rehana *et al.* (2017) [53]. Aqueous extract of *Terminalia paniculate* was used for the examination of  $\alpha$ -amylase,  $\alpha$ -glucosidase inhibitory, and glucose uptake assays (L6 Rat Skeletal Muscle Cell) by Subramaniam Ramachandran *et al.* (2013); cell glucose uptake assays (rat cell line 3T3 F442A (3T3-Adipocyte) cell) were carried out in methanolic extract of *Withania somnifera* by Shah *et al.* (2021) [83,29]. The ethyl acetate extract and Ag NPs of *Zingiber officinale* were experimentally studied for their hypoglycemic activity by applying amylase inhibitory, glucosidase inhibitory assays and Cell glucose uptake assay Sathak Sameer Shaik Mohammed *et al.* (2020) and Priya Rani *et al.* (2011) [64,84]. From the research investigations, it could be seen that  $\alpha$ -amylase inhibitory and  $\alpha$ -glucosidase inhibitory assays were preferred by most of the researchers since they have high precision, sensitivity, and efficacy comparable to *in vivo* approaches. Assays based on cell culture have a high chance of contamination, and in aldose reductase assays, denature of enzymes may occur, so they are considered a drawback for use. Both  $\alpha$ -amylase inhibitory and  $\alpha$ -glucosidase inhibitory assays showed a dose-dependent effect on the activity, but the efficiency differs by plant species. In the  $\alpha$ -amylase inhibitory assay, aqueous, methanolic, and hexane extracts showed the most effective results, followed by methanol and ethyl acetate in  $\alpha$ -glucosidase inhibitory assay, and all solvents tested demonstrated moderate anti-diabetic effects in the glucose uptake and glucose adsorption capacity assays. *Stachys japonica* methanolic fruit extract demonstrated the strongest anti-diabetic effect of all the extracts included in this study, i.e., an  $IC_{50}$  of  $400.6 \pm 2.48$   $\mu\text{g/ml}$  using  $\alpha$ -amylase inhibitory activity, and *Caesalpinia digyna* methanolic root extract showed an  $IC_{50}$  value of  $402.23 \pm 10.14$   $\mu\text{g/ml}$  on  $\alpha$ -glucosidase inhibitory activity when compared with other studied *in vitro* assays.

**TABLE 1: A LIST OF INDIAN AVAILABLE MEDICINAL PLANTS AND THE IN VITRO ASSAYS USED TO EVALUATE THEIR ANTI-DIABETIC EFFECT**

S. No	Name of the plant	Parts Used	Extract Used	Assays	Result	Reference
1	<i>Achyranthes aspera</i>	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	<i>Achyranthes aspera</i> showed dose dependent increase in percentage inhibitory activity against $\alpha$ -amylase. It has greater inhibitory	[48]

					activity than petroleum extract	
				Alpha-glucosidase inhibitory assay	<i>Achyranthes aspera</i> showed dose dependent increase in percentage inhibitory activity against $\alpha$ -amylase. It has greater inhibitory activity than petroleum extract	
			Petroleum Ether Extract	Alpha-amylase inhibitory assay	<i>Achyranthes aspera</i> showed dose dependent increase in percentage inhibitory activity against $\alpha$ -amylase	
				Alpha-glucosidase inhibitory assay	<i>Achyranthes aspera</i> showed dose dependent increase in percentage inhibitory activity against $\alpha$ -amylase	

2	<i>Adenantha pavonina</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the aqueous extract was found to be 214.85 ± 9.72µg/ml	[49]
			Ethyl Acetate Extract		The IC <sub>50</sub> value of the EtOAc extract was found to be 59.93 ± 0.25µg/ml	
			Methanolic Extract		The IC <sub>50</sub> value of the crude MeOH extract was found to be 16.16 ± 2.23µg/ml	
			Petroleum Ether Extract		The IC <sub>50</sub> value of the petroleum ether extract was found to be 145.49 ± 4.86µg/ml	
3	<i>Albizzia lebeck Benth</i>	Bark	Methanolic Extract (7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-4H-chromen-4-one)	Alpha-amylase inhibitory assay	The % inhibition of α-Amylase from <i>Bacillus subtilis</i> was found to be 93.98 ± 1.02 µg/ml	[50]

			Alpha-glucosidase inhibitory assay	The % inhibition of $\alpha$ -Glucosidase from <i>Saccharomyces cerevisiae</i> was found to be $93.91 \pm 1.21 \mu\text{g/ml}$
	Methanolic Extract ((S)-2-(3,4-dihydroxyphenyl)-7,8-dihydroxychroman-4-one)		Alpha-amylase inhibitory assay	The % inhibition of $\alpha$ -Amylase from <i>Bacillus subtilis</i> was found to be $84.36 \pm 0.60 \mu\text{g/ml}$
			Alpha-glucosidase inhibitory assay	The % inhibition of $\alpha$ -Glucosidase from <i>Saccharomyces cerevisiae</i> was found to be $73.14 \pm 1.30 \mu\text{g/ml}$
	Methanolic Extract (2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-chromen-4-one)		Alpha-amylase inhibitory assay	The % inhibition of $\alpha$ -Amylase from <i>Bacillus subtilis</i> was found to be $90.10 \pm 0.58 \mu\text{g/ml}$
			Alpha-glucosidase inhibitory assay	The % inhibition of $\alpha$ -Glucosidase from <i>Saccharomyces</i>

					<i>cerevisiae</i> was found to be 92.59 ± 1.36 µg/ml	
4	<i>Areca catechu</i>	Leaves	Aqueous Extract (NiO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 268.13µg/mL, whereas the IC <sub>50</sub> value of metformin was observed to be 232.12µg/mL. It showed greater inhibition.	[51]
5	<i>Asystasia gangetica</i>	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	The 50 % inhibitory concentration of methanolic extract was found to be 3.75 µg/ml	[52]
				Alpha-glucosidase inhibitory assay	The 50 % inhibitory concentration of methanolic extract of <i>Asystasia gangetica</i> was found to be 325	

					µg/ml	
6	<i>Azadirachta indica</i>	Leaves	Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 60.41 µg/ml	[53]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 38.62 µg/ml	
7	<i>Bauhinia purpurea</i>	Trunk	Hexane Extract	Alpha-amylase inhibitory assay	At a concentration of 100 µg/ml of <i>B. purpurea</i> hexane extract showed a percentage inhibition was 93.5%	[54]
				Glucose uptake Assay by yeast cells	The glucose uptake was found to increase in a dose dependent manner hexane extract	
				Non-enzymatic glycosylation of	Hexane extract <i>Bauhinia purpurea</i> exhibited higher	

haemoglobin  
assay

inhibition of  
glycosylation as  
compared with  
the standard drug

Petroleum Ether  
Extract

Alpha-  
amylase  
inhibitory  
assay

At a  
concentration of  
100 µg/ml of *B.  
purpurea*  
petroleum ether  
extract showed a  
percentage  
inhibition was  
93.0%

Glucose  
uptake Assay  
by yeast cells

The glucose  
uptake was found  
to increase in a  
dose dependent  
manner in  
petroleum ether  
extract

Non-  
enzymatic  
glycosylation  
of  
haemoglobin  
assay

Petroleum extract  
of *Bauhinia  
purpurea*  
exhibited higher  
inhibition of  
glycosylation as  
compared with  
hexane extract

8	<i>Bixa orellana</i>	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	The methanol extract of <i>B. orellana</i> showed 0.04 mg ml <sup>-1</sup> inhibition	[55]
9	<i>Bruguiera cylindrica</i>	Leaves	Ethanollic Extract	Glucose uptake Assay by yeast cells	The glucose uptake was found in the presence of 25 mM glucose. It showed the maximum increase (83.33%) in the presence of at 25 mM glucose.	[56]
10	<i>Caesalpina digyna</i>	Root	Methanolic Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value was found to be 686.94 ± 3.98 µg/ml	[5]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value was found to be 402.23±10.14 µg/ml	
11	<i>Callistephus chinensis</i>	Flower Waste	Ethanollic Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value was found to be 1.37 µg/ml	[57]



				Glucose uptake Assay by yeast cells	Maximum uptake of glucose (96.875%) was observed in presence of 0.5mg/ml extract.	
12	<i>Calophyllum tomentosum</i>	Leaves	Aqueous Extract (Ag NPs)	Alpha-amylase inhibitory assay	<i>Calophyllum tomentosum</i> has potentially inhibited the activity of $\alpha$ -amylase	[31]
				Beta-glucosidase inhibitory assay	Beta-glucosidase is greatly inhibited by Ag NPs compared to $\alpha$ -amylase	
				Dipeptidyl peptidase IV (DPPIV)	DPPIV is greatly inhibited by Ag NPs compared to $\alpha$ -amylase and showed slightly higher inhibition than $\beta$ -glucosidase	
13	<i>Carissa carandas</i>	Stem	Methanolic Extract	Alpha-amylase	<i>Carissa carandas</i> showed	[58]

				inhibitory assay	46.95±0.46% inhibition at 500 µg/mL concentration	
			Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum inhibition of <i>Carissa carandas</i> was found to be 61.08±0.40% at a concentration of 1000µg/ml	
14	<i>Cassia fistula</i>		Aqueous Extract	Alpha-amylase inhibitory assay	A maximum inhibition of <i>Cassia fistula</i> was found to be 88.65% at a concentration of 1000µg/ml	[59]
15	<i>Cassia tora</i>	Root	Aqueous Extract	Alpha-amylase inhibitory assay	<i>Cassia tora</i> showed 44.95±0.69% inhibition at 500 µg/mL concentration	[58]

16	<i>Centratherum anthelminticum</i>	Leaves	Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum inhibition of <i>Centratherum anthelminticum</i> was found to be 77.84±0.35% at a concentration of 500µg/ml	[58]
			Chloroform Extract		The maximum inhibition of <i>Centratherum anthelminticum</i> was found to be 72.94±0.25% at a concentration of 1000µg/ml	
			Methanolic Extract		The maximum inhibition of <i>Centratherum anthelminticum</i> was found to be 63.56±0.36% at a concentration of 1000µg/ml	
17	<i>Cinnamomum tamala</i>	Bark	Aqueous Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract in % inhibition was found to be 93.78%	[60]

			Methanolic Extract			
18	<i>Cinnamomum verum</i>	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract in % inhibition was found to be 97.49%	[55]
19	<i>Cissampelous pairera</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	The highest inhibition of aqueous leaf extract at 100µg/ml concentration was 82%	[61]
			Aqueous Extract (Ag NPs)		The highest inhibition of Ag NPs of leaf extract at 100µg/ml concentration were found to be 92%.	

20	<i>Citrus hystrix</i>	Fruit	Fruit Juice Extract	Alpha-amylase inhibitory assay	The $\alpha$ -amylase inhibition activity of <i>C. hystrix</i> was observed as 75.55%	[62]
				Alpha-glucosidase inhibitory assay	The $\alpha$ -glucosidase inhibition activity of <i>C. hystrix</i> was observed as 70.68%	
21	<i>Citrus maxima</i>	Fruit	Fruit Juice (Red) Extract	Alpha-amylase inhibitory assay	The $\alpha$ -amylase inhibition activity of <i>C. maxima</i> (Red) was observed as 79.75%	[62]
				Alpha-glucosidase inhibitory assay	The $\alpha$ -glucosidase inhibition activity of <i>C. maxima</i> (Red) was observed as 72.83%	
			Fruit Juice (White) Extract	Alpha-amylase inhibitory	The $\alpha$ -amylase inhibition activity of <i>C. maxima</i>	

				assay	(White) was greater than $\alpha$ -glucosidase inhibition activity	
				Alpha-glucosidase inhibitory assay	The $\alpha$ -glucosidase inhibition activity of <i>C. maxima</i> (White) was observed as 71.88%	
22	<i>Costus igneus</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	<i>Costus igneus</i> has potentially inhibited the activity of $\alpha$ -amylase	[63]
				Alpha-glucosidase inhibitory assay	The inhibition rate for $\alpha$ -glucosidase was higher than that for $\alpha$ -amylase	
			Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The percentage of inhibition ranged between 20 % (20 $\mu$ g/ml) to 74 % (100 $\mu$ g/ml) for $\alpha$ -amylase	

					inhibitory assay	
					Alpha-glucosidase inhibitory assay	The percentage of inhibition ranged between 36 % (20 µg/ml) to 82% (100 µg/ml) for α-glucosidase inhibitory assay
23	<i>Curcuma amada</i>	Sprouts	Aqueous Extract (Ag NPs)	Alpha-amylase inhibitory assay	<i>C. amada</i> Ag NPs at a concentration of 200 µg/mL displayed maximum α-amylase inhibition of 65.40% with an IC <sub>50</sub> value of 139.29 µg/ml	[64]
				Alpha-glucosidase inhibitory assay	<i>C. amada</i> Ag NPs provided a maximum α-glucosidase inhibitory activity of 68.78% at 200 µg/mL concentration respectively; with an IC <sub>50</sub> value of	

					136.47 $\mu\text{g}/\text{m}$	
				Cell glucose uptake assay (Human fibroblast cell line 3T3)	The highest concentration (500 $\mu\text{g}/\text{mL}$ ) showed less glucose uptake (30.20%) in comparison to the lowest concentration (20 $\mu\text{g}/\text{mL}$ ) which displayed higher glucose uptake (64.46%) with an overall $\text{IC}_{50}$ value of 62.62 $\mu\text{g}/\text{ml}$	
24	<i>Curcuma longa</i>	Tuber	Acetone Extract	Alpha-amylase inhibitory assay	The acetone extract of <i>C. longa</i> showed 0.02 $\text{mg mL}^{-1}$ inhibition	[55]
			Methanolic Extract		The methanol extract of <i>C. longa</i> showed 1.5 $\text{mg mL}^{-1}$ inhibition	



25	<i>Emblica officinalis</i>	Fruit	Alcohol maceration	Alpha-glucosidase inhibitory assay	Inhibition of alpha-glucosidase enzyme by Amla fruit extract showed 46.66%	[65]
			Decoction		Inhibition of alpha-glucosidase enzyme by Amla fruit extract showed 30%	
			Ethanollic Extract		Inhibition of alpha-glucosidase enzyme by Amla fruit extract showed 61.66%	
			Water maceration		Inhibition of alpha-glucosidase enzyme by Amla fruit extract showed 20%	
26	<i>Enicostema littorale</i>	Leaves	Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum inhibition was found to be 60.10±0.299% at a concentration of 1000µg/ml	[58]

27	<i>Euphorbia nivulia</i>	Stem	Methanolic Extract	Alpha-amylase inhibitory assay	<i>Euphorbia nivulia</i> showed 48.74±0.58% inhibition at 500 µg/mL concentration	[58]
28	<i>Ficus bengalensis</i>	Bark	Aqueous Extract (Cold Water)	Alpha-amylase inhibitory assay	The aqueous extract of <i>F. bengalensis</i> bark showed 0.38 mg mL <sup>-1</sup> inhibition for cold water	[55]
			Aqueous Extract (Hot Water)		The aqueous extract of <i>F. bengalensis</i> bark showed 0.14 mg mL <sup>-1</sup> inhibition for hot water	
29	<i>Gymnema sylvestre</i>	Leaves	Starch Nanoparticles (St NPs)	Alpha-amylase inhibitory assay	The highest inhibition activity of the St NPs showed 58.56 ± 0.44% at concentration of 100 µg/ml	[66]

			Chloroform Extract		The maximum inhibition was found to be 63.01±0.81% at a concentration of 500µg/ml	[58]
30	<i>Hibiscus rosasinensis</i>	Leaves	Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 38.93µg/ml	[53]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 20.32µg/ml	
31	<i>Lepidium sativum</i>	Seed	Chloroform Extract	Alpha-amylase inhibitory assay	<i>Lepidium sativum</i> showed 57.32±0.69% inhibition at 500 µg/mL concentration	[58]
			Methanolic Extract		The maximum inhibition was found to be 52.40±1.03% at a	

					concentration of 500µg/ml	
			Aqueous Extract	Alpha-glucosidase inhibitory assay	The highest inhibition was found to be 67.13±0.30% at a concentration of 1000µg/ml	
			Methanolic Extract		The maximum inhibition was found to be 66.67±0.29% at a concentration of 1000µg/ml	
32	<i>Melothria scabra</i>	Leaves	Ethanollic Extract	Glucose adsorption capacity	The ethanollic extract showed highest glucose concentration (134.4mg/dl) at 100 mmol/l	[32]
				Glucose Diffusion Inhibitory Assay	The ethanollic extract showed highest inhibition concentration (104.5mg/dl) in 180 minutes	

				Glucose uptake by yeast cells	Increase in glucose uptake was observed as 84.21%	
33	<i>Mirabilis jalapa</i>	Flower	Aqueous Extract	Alpha-amylase inhibitory assay	The aqueous extract showed maximum% inhibition at the concentration of 50µg/ml and the value was found to be 38.36%.	[67]
				Alpha-glucosidase inhibitory assay	The maximum percentage inhibition was exerted by the aqueous extract at the concentration of 50µg/ml (21.48%).	
			Ethanollic Extract	Alpha-amylase inhibitory assay	The ethanol extract showed the maximum% inhibition of alpha-amylase at the concentration	

					of 100µg/mg, value was found to be 38.77%.	
				Alpha-glucosidase inhibitory assay	The maximum percentage inhibition was exerted by the ethanol extract at the concentration of 50µg/ml (26.82%).	
34	<i>Moringa oleifera</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	<i>Moringa oleifera</i> showed 53.86±0.81% inhibition at 500 µg/mL concentration	[58]
			Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum inhibition was found to be 73.81±0.25% at a concentration of 1000µg/ml	
			Chloroform Extract		The highest inhibition was found to be 63.27±0.25% at a	

			Methanolic Extract		concentration of 1000µg/ml  The maximum inhibition was found to be 74.04±0.20% at a concentration of 1000µg/ml	
			Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 35.72µg/ml	[53]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 17.25µg/ml	
35	<i>Muntingia calabura</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	The inhibition concentration curve showed maximum inhibition than chloroform and petroleum ether extract	[68]

	Chloroform Extract		The inhibition concentration curve showed maximum inhibition than petroleum extract
	Methanolic Extract		The inhibition concentration curve showed maximum inhibition than other extract
	Petroleum Ether Extract		The inhibition concentration curve showed minimum inhibition
	Aqueous Extract	Alpha-glucosidase inhibitory assay	Aqueous extract of <i>M. calabura</i> showed maximum inhibition curve than chloroform and petroleum ether extract
	Chloroform Extract		Chloroform extract of <i>M. calabura</i> showed



					maximum inhibition curve than petroleum ether extract	
			Methanolic Extract		Methanol extract of <i>M. calabura</i> showed maximum inhibition curve than other extract	
			Petroleum Ether Extract		Petroleum ether extract of <i>M. calabura</i> showed minimum inhibition curve	
36	<i>Murraya koenigii</i>	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	The methanol extract of <i>M. koenigii</i> showed 0.05 mg mL <sup>-1</sup> inhibition	[55]
			Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 59.9µg/mL	[53]

				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 33.31 µg/mL	
37	<i>Pandanus canaranus</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	The aqueous extract of <i>P. canaranus</i> showed maximum % inhibition (20.16 ± 0.540 µg/ml)	[69]
				Alpha-glucosidase inhibitory assay	The aqueous extract of <i>P. canaranus</i> showed 77.08 ± 1.254 µg/ml % of inhibition	
				Non-Enzymatic antidiabetic activity	The aqueous extract of <i>P. canaranus</i> showed maximum % inhibition (70.83 ± 0.334 µg/ml)	
			Ethyl Acetate Extract	Alpha-amylase inhibitory	<i>P. canaranus</i> showed 48.45 ± 1.985 µg/ml %	

			assay	inhibition activity
			Alpha-glucosidase inhibitory assay	<i>P. canaranus</i> showed maximum % inhibition (90.08 ± 1.002 µg/ml) against antidiabetic activity
			Non-Enzymatic antidiabetic activity	<i>P. canaranus</i> shoeds 62.57 ± 0.43 µg/ml % inhibition activity
		Methanolic Extract	Alpha-amylase inhibitory assay	The inhibitory effect of methanolic extract possessed 16.12 ± 0.591 µg/ml
			Alpha-glucosidase inhibitory assay	The maximum inhibitory effect of methanolic extract possessed 88.38 ± 1.934 µg/ml

				Non-Enzymatic antidiabetic activity	The inhibitory effect of methanolic extract possessed $58.20 \pm 0.632$ $\mu\text{g/ml}$	
			Petroleum Ether Extract	Alpha-amylase inhibitory assay	The extract of <i>P. canaranus</i> showed $32.29 \pm 0.9$ $\mu\text{g/ml}$ % inhibition	
				Alpha-glucosidase inhibitory assay	The extract of <i>P. canaranus</i> showed $0.52 \pm 0.027$ $\mu\text{g/ml}$ % inhibition	
				Non-Enzymatic antidiabetic activity	The extract of <i>P. canaranus</i> showed maximum % inhibition ( $33.96 \pm 0.484$ $\mu\text{g/ml}$ )	
38	<i>Pandanus tectorius</i>	Leaves	Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum inhibitory effect of aqueous extract possessed $76.05 \pm 0.30\%$	[58]

39	<i>Physalis minima</i>	Whole Plant	Aqueous Extract	Alpha-amylase inhibitory assay	The aqueous extract suppressed the most alpha amylase enzyme activity higher than AuNPs extract and had a 90–93% anti-diabetic effect	[70]
			Aqueous Extract (Au NPs)		The phyto-fabricated AuNPs suppressed the most alpha amylase enzyme activity and had a 90–93% anti-diabetic effect	
40	<i>Piper nigrum</i>	Leaves	Ethanollic Extract	Alpha-amylase inhibitory assay	<i>Piper nigrum</i> possess significant antidiabetic activity than essential oil extract	[71]

41	<i>Pithecellobium dulce</i>	Bark	Petroleum Ether Extract	Alpha-amylase inhibitory assay	<i>Pithecellobium dulce</i> possess high inhibitory potential against antidiabetic activity	[72]
				Alpha-glucosidase inhibitory assay	<i>Pithecellobium dulce</i> possess good inhibitory potential against antidiabetic activity	
42	<i>Polyalthia longifolia</i>	Leaves	Chloroform Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 180.3±1.35µg/mL	[73]
				Alpha-glucosidase inhibitory assay	The inhibitory effect of chloroform extract was found to be ranging from 5.96±1.40% to 69.99±4.06%	
			Ethanollic Extract	Alpha-amylase inhibitory	The IC <sub>50</sub> value of the extract was found to be	

				assay	154.3±2.42µg/mL	
				Alpha-glucosidase inhibitory assay	The inhibitory effect of chloroform extract was found to be ranging from 9.78±0.85 % to 72.01±2.28 %	
43	<i>Psidium guajava</i>	Leaves	Aqueous Extract	Alpha-amylase inhibitory assay	The maximum inhibitory effect of aqueous extract possessed 72.1%	[74]
				Alpha-glucosidase inhibitory assay	The inhibitory percentage varied from 26.3%-74.8%	
			Ethanollic Extract	Alpha-amylase inhibitory assay	The maximum inhibitory effect of ethanolic extract possessed 97.5%	
				Alpha-glucosidase	The inhibitory effect of ethanolic	

				inhibitory assay	extract varied from 33.6%-91.8%	
			Methanolic Extract	Alpha-amylase inhibitory assay	The methanolic extract showed a percentage inhibition 27.8% at 0.2 ml concentration and 96.3% inhibition at 1.0 ml	[75]
				Alpha-glucosidase inhibitory assay	The methanolic extract showed highest concentration (89.4%) to the lowest concentration (31.7%) from 1.0 ml to 0.2 ml	
44	<i>Pueraria tuberosa</i>	Tuber	Chloroform Extract	Alpha-amylase inhibitory assay	<i>Pueraria tuberosa</i> showed 56.12±0.46% inhibition at 500 µg/mL concentration	[58]
			Aqueous Extract	Alpha-glucosidase inhibitory	The inhibition concentration was found to be	



				assay	70.35±0.39 at a concentration of 1000µg/ml	
			Chloroform Extract		The highest inhibition was found to be 71.68±0.29% at a concentration of 1000µg/ml	
			Methanolic Extract		The maximum inhibition was found to be 76.86±0.39% at a concentration of 1000µg/ml	
45	<i>Punica granatum</i>	Fruit Rind	Methanolic Extract	Alpha-amylase inhibitory assay	Fruit rinds of <i>Punica granatum</i> have significantly and dose dependently inhibited the α-amylase enzyme activity. The IC <sub>50</sub> value of the extract was found to be 1.02 µg/mL	[76]

				Aldose Reductase Inhibition Assay	The IC <sub>50</sub> value of the extract was found to be 2.050 µg/mL	
			Valoneic acid dilactone Extract	Alpha-amylase inhibitory assay	Fruit rinds of <i>Punica granatum</i> have significantly and dose dependently inhibited the α-amylase enzyme activity. The IC <sub>50</sub> value of the extract was found to be 0.284 µg/mL	
				Aldose Reductase Inhibition Assay	The IC <sub>50</sub> value of the extract was found to be 0.788 µg/mL	
46	<i>Salacia oblonga</i>	Stem	Aqueous Extract	Alpha-amylase inhibitory assay	The maximum percentage of inhibition (59.46±0.04%) was obtained at a concentration of 100 mg/mL	[77]

				Alpha-glucosidase inhibitory assay	The maximum percentage of inhibition (68.51±0.01%) was obtained at a concentration of 100mg/mL	
47	<i>Solanum xanthocarpum</i>	Leaves	Aqueous Extract	Alpha-glucosidase inhibitory assay	The maximum percentage of inhibition (79.22±0.35%) was obtained	[58]
			Chloroform Extract		<i>Solanum xanthocarpum</i> showed 75.30±0.29% enzyme inhibitory properties at a concentration of 1000µg/ml	
48	<i>Stachys japonica</i>	Fruit	Methanolic Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 400.6±2.48 µg/mL	[78]

				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 350.8±1.86 µg/mL
			Ethyl acetate fraction	Alpha-amylase inhibitory assay	<i>Stachys japonica</i> showed higher enzyme inhibitory properties than extract (ME) and fractions (HF and MF)
				Alpha-glucosidase inhibitory assay	<i>Stachys japonica</i> showed higher enzyme inhibitory properties than extract (ME) and fractions (HF and MF)
				Cell glucose uptake assay (HepG2)	The treatment of the EAF had increased the glucose uptake in the dose-dependent manner

			Hexane fraction	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 850.36±5.62 µg/mL	
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 723.26±3.05 µg/mL	
			Methanolic fraction	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 250.63±0.89 µg/mL	
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 198.26±0.58 µg/mL	
49	<i>Swertia chirayita</i>	Leaves	Aqueous Extract (Hot Water)	Alpha-amylase inhibitory assay	Very high significant antidiabetic activity was observed	[79]

		Root			Root extract also showed minor antidiabetic activity	
		Stem			High significant antidiabetic activity was observed	
		Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	Very high significant antidiabetic activity was observed	
		Root			Root extract also showed minor antidiabetic activity	
		Stem			High significant antidiabetic activity was observed	
50	<i>Swertia cordata</i>	Leaves	Aqueous Extract (Hot Water)	Alpha-amylase inhibitory assay	Very high significant antidiabetic activity was	[79]

				observed	
	Root			Root extract also showed minor antidiabetic activity	
	Stem			High significant antidiabetic activity was observed	
	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	Very high significant antidiabetic activity was observed	
	Root			Root extract also showed minor antidiabetic activity	
	Stem			High significant antidiabetic activity was observed	

51	<i>Syzygium cumini</i>	Seeds	Aqueous Extract (Cold Water)	Alpha- amylase inhibitory assay	The aqueous extract of <i>S.</i> <i>cumini</i> showed $0.38 \text{ mg mL}^{-1}$ inhibition for cold water	[55]
			Aqueous Extract (Hot Water)		The aqueous extract of <i>S.</i> <i>cumini</i> showed $0.13 \text{ mg mL}^{-1}$ inhibition for hot water	
			Methanolic Extract		<i>Syzygium cumini</i> possess significant antidiabetic activity based on the dosage	[80]
		Leaves	Aqueous Extract	Alpha- amylase inhibitory assay	The significant antidiabetic activity was observed ( $52.93 \pm 0.92\%$ )	[58]
52	<i>Syzygium caryophyllatum</i>	Bark	Methanolic Extract	Alpha- amylase inhibitory assay	The maximum percentage inhibitory activity of $78.03\%$ was	[81]



					showed at concentration of 500 µg/ml bark extract
				Alpha-glucosidase inhibitory assay	The maximum percentage inhibitory activity of 80.9% was showed at concentration of 100 µg/ml bark extract
	Fruit Pulp	Methanolic Extract		Alpha-amylase inhibitory assay	The highest percentage inhibitory activity of 56.9% was showed at concentration of 500 µg/ml fruit pulp extract
				Alpha-glucosidase inhibitory assay	The highest percentage inhibitory activity of 63.35% was showed at concentration of 100 µg/ml fruit pulp extract

	Leaves	Methanolic Extract	Alpha-amylase inhibitory assay	The highest percentage inhibitory activity of 69.4% was showed at concentration of 500 µg/ml leaves extract
			Alpha-glucosidase inhibitory assay	The highest percentage inhibitory activity of 78.2% was showed at concentration of 100 µg/ml leaves extract
	Seeds	Methanolic Extract	Alpha-amylase inhibitory assay	The maximum percentage inhibitory activity of 78.03% was showed at concentration of 500 µg/ml seed extract
			Alpha-glucosidase inhibitory assay	The highest percentage inhibitory activity of 77.59% was showed at concentration of

					100 µg/ml seed extract	
53	<i>Tamarindus indica</i>	Leaves	Aqueous Extract (ZnO NPs)	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be maximum 28.63µg/mL	[53]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be maximum 13.32µg/mL	
54	<i>Tecomella undulata</i>	Bark	Methanolic Extract	Alpha-amylase inhibitory assay	The methanolic extract of <i>T. undulata</i> showed 50.80±0.70 % inhibition	[58]
55	<i>Tephrosia tinctoria</i>	Stem	Aqueous Extract	Alpha-amylase inhibitory assay	<i>Tephrosia tinctoria</i> possess significant antidiabetic activity	[82]

			Alpha-glucosidase inhibitory assay	<i>Tephrosia tinctoria</i> possess significant antidiabetic activity
			Cell glucose uptake assay	At 75µg/ml, glucose uptake assay in crude aqueous extract of TT (2.61±0.07)
		Aqueous Extract (Ag NPs)	Alpha-amylase inhibitory assay	The Ag NPs significantly inhibits carbohydrate digesting enzymes than the crude aqueous extract of <i>T.tinctoria</i>
			Alpha-glucosidase inhibitory assay	The Ag NPs significantly inhibits carbohydrate digesting enzymes than the crude aqueous extract of <i>T.tinctoria</i>

				Cell glucose uptake assay	At 75µg/ml, glucose uptake assay in Ag NPs showed the maximum 3.80±0.028 fold	
56	<i>Terminalia paniculata</i>	Bark	Aqueous Extract	Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found 3.62µg/mL	[83]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 287.10µg/mL	
				Cell glucose uptake assay (L6 Rat Skeletal Muscle Cell)	<i>Terminalia paniculata</i> showed dose-dependent glucose uptake action	
57	<i>Tribulus terrestris</i>	Leaves	Acetone Extract	Alpha-amylase inhibitory assay	The acetone extract of <i>Tribulus terrestris</i> showed 0.02 mg mL <sup>-1</sup> inhibition	[55]

58	<i>Withania somnifera</i>	Leaves	Methanolic Extract	Cell glucose uptake assay (Rat cell line 3T3 F442A (3T3-Adipocyte) cell)	The leaf crude extract showed highest percentage of glucose uptake (108.53%) in Mumbai region sample (WSM-L) when 10 µg/ml of sample was used	[29]
59	<i>Zingiber officinale</i>	Sprouts	Aqueous Extract (Ag NPs)	Alpha-amylase inhibitory assay	<i>Z. officinale</i> Ag NPs at a concentration of 200 µg/mL exhibited maximum α-amylase inhibitory activity of 55.10% with an IC <sub>50</sub> value of 166.83 µg/mL.	[64]
				Alpha-glucosidase inhibitory assay	<i>Z. officinale</i> Ag NPs exhibited a maximum α-glucosidase inhibitory activity of 57.50% at 200 µg/mL concentration	

					respectively; with an IC <sub>50</sub> value 166.30 µg/ mL.	
				Cell glucose uptake assay (cell line 3T3)	The highest concentration (500 µg/mL) showed less glucose uptake (26.77%) in comparison to the lowest concentration (20 µg/ mL) which displayed higher glucose uptake (99.56%) with an overall IC <sub>50</sub> value of 41.22 µg/ mL	
		Ethyl Acetate Extract		Alpha-amylase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 180.13 mg/ml	[84]
				Alpha-glucosidase inhibitory assay	The IC <sub>50</sub> value of the extract was found to be 980.21 mg/ml	

#### 4. CONCLUSION

This review explored *in vitro* antidiabetic assays using medicinal plants that are available in India. *In vitro* antidiabetic assays are preferred by most of the researchers since they are more convenient, simple, and economically viable to use. This review explored the currently performed *in vitro* antidiabetic assays and briefed their methodology. Among the assays used for the activity,  $\alpha$ -amylase

inhibitory and  $\alpha$ -glucosidase inhibitory assays were frequently utilised to establish the effect of antidiabetic activity due to their efficiency.

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#### **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

Not applicable.

#### **HUMAN AND ANIMAL RIGHTS**

No Animals/Humans were used for studies that are base of this research.

#### **CONSENT FOR PUBLICATION**

Not applicable.

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#### **CONFLICT OF INTEREST**

Authors declare that there is no conflict of interest.

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