Review Article

An Overview on Medicinal Plants with Antidiabetic Potential

MD. Gulshan*, N. Rama Rao
Department of Pharmaceutics including Industrial Pharmacy, Chalapathi Institute of Pharmaceutical Sciences, Guntur, AP, India.
***Corresponding author's E-mail:** gulshan.md210@gmail.com

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ABSTRACT

Diabetes is a metabolic disorder suffered by both the people of developed and developing countries. To improve human health and to satisfy people's desires for health care without intake of pharmaceuticals, there is a growing need to develop integrated approaches toward management and prevention of diabetes mellitus. In Indian traditional system plant extracts are considered as drug of choice as they are of lesser side effects compared to other type of medicines. So far, 800 species of plants have been identified to possess antidiabetic effect. The present review emphasizes on herbal plants in alphabetical order A-Z which possess antidiabetic potential. From the review it is concluded that most of the herbal plant can be able to reduce the blood glucose level by stimulating the insulin secretion from pancreatic beta–cells of islets of langerhans and the animal models used for testing antidiabetic activity are mostly alloxan and streptozotocin induced ones.

Keywords: Diabetes mellitus, Antidiabetic, Insulin, Hypoglycemic activity, Blood Glucose, Pancreas.

INTRODUCTION

The use of medicinal plants in the treatment of diabetes is an old practice. Recently, herbal medicines gained much attraction for the treatment of various metabolic diseases including diabetes, adiposity and cardiovascular complications. The increasing worldwide incidence of diabetes mellitus in adults constitutes a global public health burden. It is predicted that by 2030, India, China and United States will have the largest number of people with diabetes. By definition, diabetes mellitus is categorized as a metabolic disease characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The vast majority of cases of diabetes fall into two broad etiopathogenic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin-secretary response (American Diabetes Association, 2005). Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Many of them have a number of serious adverse effects; therefore, the search for more effective and safer hypoglycemic agents is one of the most important areas of investigation. In diabetes, hyperglycemia generates reactive oxygen species(ROS), which in turn cause lipid peroxidation and membrane damage and these free radicals play an important role in the production of secondary complications in diabetes mellitus(kidney, eye, blood vessel, and nerve damage). Antioxidants have been shown to prevent the destruction of ß- cells by inhibiting the peroxidation chain reaction and thus they may provide protection against the development of diabetes. Plants contain natural antioxidants (tannins, flavonoids, vitamins C and E, etc.) that can preserve ß- cell function and prevent diabetes induced ROS formation. In this present review article an attempt was made to list out the herbal plants possessing antidiabetic activity by one or the other possible mechanisms.

Table 1: List of herbal plants with antidiabetic effect

Botanical Name	Extract, Part	Drug induced diabetes-animal model	Mechanism of action
Acacia auriculiformis (Leguminosae)[1]	Acetone, bark, pods	Alloxan - rat	↑ insulin secretion
Amaranthus viridis (Amaranthaceae)[2]	MeOH, whole plant	Alloxan - rat	↓ in blood glucose and lipid profile
Acacia Arabica (Leguminosae)[3]	Chloroform, bark	Alloxan - rat	↑ insulin secretion
Aegle marmelos (Rutaceae)[4]	AE, leaves	STZ - rat	Direct stimulation of glucose uptake by insulin secretion
Agrimony eupatoria (Rosaceae)[5]	AE, plant	STZ - mice	Stimulation of insulin secretion BRIN-BD11 pancreatic beta cell line *in vitro*
Alangium salvifolium (Alangiacea)[6]	MeOH, leaves	Dexamethasone - rat	Insulinotropic effect
Allium sativum (Alliacea) [7]	Ethyl, ether, EtOH	Alloxan- rat	↑ insulin secretion
Aloe vera (Lilaceae) [8]	EtOH, leaves	STZ- rat	↑ insulin secretion

Botanical Name	Extract, Part	Drug induced diabetes-animal model	Mechanism of action
Annona squamosa (Annonaceae) [9]	AE, EtOH, leaves	STZ - rat	↑ insulin secretion, increasing utilization of glucose in muscle and inhibiting the glucose output from liver
Asparagus racemosus (Liliaceae) [10]	EtOH, hexane, chloroform and ethyl acetate root	Isolated perfused rat pancreas	Insulinotropic activity
Achyranthes rubrofusca (Amaranthaceae)[11]	AE, EtOH, leaves	Alloxan - rat	Pancreatic enzymes such as superoxide dismutase (SOD), catalase (CAT) and glutathione level were significantly ↑
Andrographis paniculata (Acanthaceae)[12]	EtOH, plant	Alloxan - albino rat	TG, TC, phospholipids, glycosylated haemoglobin, alanine transaminase (ALT), aspartate transaminase (AST), acid phosphatase (ACP) and alkaline phosphatase(ALP) level
Argyriea cuneata (Convolvulaceae)[13]	EtOH , leaves	Alloxan - rat	Lipid ↓ potential.
Barleria prionitis (Acanthacae)[14]	AAE, leaves and root	Alloxan - rat	↓ blood glucose and glycosylated hemoglobin level
Bauhinia variegate (Caesalpiniaceae) [15]	EtOH, leaves	Insulin – secreting cell line INS-1	(6S,7E,9R)-9-hydroxymegastigma-4, 7-dien-3-one-beta-glycopyraroside(roseoside) have insulinotropic activity
Berberine (Ranunculaceae)[16, 17]	-	Sprague – Dawley Rat pancreatic islets	Glucose – stimulated insulin release, insulin sensitizing and insulinotropic agent
Biophytum sensitivum (Oxalidaceae) [4, 18]	AE, Leaves	Alloxan- rabbits	Stimulates pancreatic beta cells to release insulin
Boerhaavia diffusa (Nyctaginacea) [4, 9]	Chloroform, leaves	Alloxan - rat	↑ insulin sensitivity
Bougainvillea spectabilis (Nyctaginaceae) [9]	EtOH, leaves	STZ - albino rat	↑ glycogenesis in the liver due to ↑ insulin sensitivity
Brassica nigra (Cruciferae) [19]	AE, seed	STZ - rat	Release of insulin
Bryophyllum pinnatum (Crassulaceae)[20]	AE, leaves	STZ - rat	↑ insulin sensitivity
Bauhinia forficate (Fabacea) [21]	dried AE, leaves	STZ- male wistar rat	Acting at multiple sites of glucose regulatory pathways, e.g. glucose tolerance, lipid profile, glycogen biosynthesis, glucose uptake and insulin release
Capparis deciduas (Capparaceae) [22]	AE and EtOH, Fruits	Alloxan - rat	↓ blood glucose level,
Cassia grandis (Leguminosae) [23]	AE and EtOH, Stem	Alloxan - rat	↓ blood glucose, TG, and TC level
Cerios decendra (Rhizophoraceae) [24]	EtOH, leaves	Alloxan - rat	↓ blood glucose level
Colocasia esculenta (Araceae)[25]	EtOH, leaves	Alloxan - rat	↓ blood glucose level and prevented loss of body weight
Costus igneus (Costaceae) [26]	EtOH, leaves	STZ-albino rat	↓ of blood glucose level and prevented body weight loss
Cinnamon zeyalnicum (Lauraceae) [27]	Chloroform, bark	STZ –rats	Insulinotropic effect of cinnamaldehyde,↑in the glucose uptake through glucose transporter (GLUT4) translocation in peripheral tissues
Caesalpinia bonducella (Cesalpinaceae) [4]	AE, seeds	Alloxan - rats	↑ secretion of insulin in isolated islets
Caffeine [28]	Caffeine	Pancreatectomized rats	↓ body weight, fats, and ↓ insulin resistance, enhanced glucose – stimulated first – and second – phase insulin secretion and beta – cell hyperplasia
Camellia sininsis (Theaceae) [4, 29, 35]	Green tea	STZ –rat	Epigallocatechin gallate increases insulin activity
Capsicum frutescens (Solanaceae) [30]	Red chilli	STZ – Sprague Dawley rat	Insulinotropic
Catharanthus roseus (Apocynacea) [38]	Dichloromethane – EtOH leaves and twigs	STZ - rat	Enhance secretion of insulin
Citrullus colocynthis (Cucurbitaceae) [31]	pulp	Alloxan - rat	↑Insulin release
Coccinia indica (cucurbitacea) [8]	EtOH, Leaves	STZ – male rats	Insulin secreting effect or through influence of enzymes involved in glucose metabolism
Cornus officinalis (Cornaceae)[32]	MeOH, fruits	Alloxan, STZ - rats	GLUT4 mRNA and its protein expression in NIDDM rat by promoting proliferation of pancreatic islets and by ↑ postprandial secretion of insulin and therefore accelerating the glucose transport
Caesalpinia digyna (Leguminosae)[33]	AAE roots	STZ - nicotinamide rat	Bergenin protect beta – cell against toxic challenge
Callistemon lanceolatus (Myrtaceae)[34]	EtOH, leaves	STZ -rat	Flavones 5, 7-dihydroxy-6, 8-dimethyl - 4' – methoxy flavone and 8-(2-hydroxypropan-2-yl)-5-hydroxy-7-methoxy-6-methyl-4' –methoxy flavone which possess anti diabetic activity, regeneration of pancreatic islets and ↑ the insulin release

Botanical Name	Extract, Part	Drug induced diabetes-animal model	Mechanism of action
Caralluma sinaica (Asclepiadaceae)[36]	EtOH, leaves	STZ - diabetic rabbits	↓ plasma glucose levels
Caralluma tuberculata (Asclepiadaceae) [37]	MeOH, leaves	STZ – induced diabetic rat	Stimulation of insulin release, inhibition of G-6-Pase activity, enhancement of glucose utilization and inhibition of glucose absorption
Cistus laurifolius (Cistaceae)[39]	AE and EtOH leaves	STZ induced diabetic rat	Potent inhibitor of α- amylase and α-glucosidase due to polyphenolic compounds present in it
Clausena lansium (Rutaceae)[40]	MeOH, Stem bark	Alloxan - rats	Imperatorin, chalepin -↑ *in vitro* insulin release
Cucumis trigonus (Cucurbitaceae) [41]	AE fruit	STZ induced diabetic rat	↓ the elevated blood glucose level and lipid profile
Cuminum cyminum (Apiaceae)[42]	AE, Seeds	Alloxan - rat	↑haemoglobin, glycosylated haemoglobin, prevented decrease in body weight, ↓ plasma and tissue cholesterol, phospholipids, free fatty acids and triglycerides
Cynodon datylon (Poaceae) [43]	AE, Leaves	STZ - rat	↓ urine sugar level, TC, LDL, TG
Diospyros peregrine (Ebenaceae)[44]	AE, Fruit	STZ-nicotinamide rat	Polyphenolics and flavonoids act as antioxidants
Elephantopus scaber (Asteraceae) [45, 50]	acetone, Plant	STZ – rat	↑ insulin sensitivity, augmenting glucose dependent insulin secretion and stimulating the regeneration of islets of langerhans in pancreas due to a steroid called 28Nor-22(R)With a 2, 6, 23-trienolide
Enicostemma littorale (Gentianaceae) [46]	AE, Plant	Alloxan - rat	Potentiation of glucose – induced insulin release through K+ - ATP channel dependent pathway.
Ephedra distachya (Ephedraceae) [7]	Aqueous MeOH, AE, Crude drug	Alloxan - mice	Regeneration and restoration of atrophied pancreatic islets that induces the secretion of insulin.
Eriobotrya japonica (Rosaceae) [47]	AE, leaves	Alloxan, rats	Cinchonain Ib, procyanidin B-2, chlorogenic acid and epicatechin, were tested for insulin secretory activity in INS-1 cells, showed significant increase of insulin secretion from INS-1 cells
Eucalyptus globules (Myrtacea) [8]	AE, Leaves	STZ - mice	↑ insulin secretion from the clonal pancreatic beta cell
Eugenia jambolana (Myrtaceae) [8, 47, 48]	AE, EtOH, seeds	STZ - rabbit	Inhibited insulinase activity, enhances insulin secretion from cells
Eucalyptus citriodora (Myrtaceae)[49]	AE, leaves	Alloxan - rat	↓ the blood glucose level
Emblica officinalis (Euphorbiaceae)[51]	Hydro MeOH, Seed	STZ- Wistar rat	Increase insulin level, antioxidant activity
Ficus bengalensis ss(Moraceae)[52]	AE, bark	STZ - rat	↓ the plasma glucose and serum lipids level
Fermented unsalted soybeans[53]	Fermented product	Pancreatectomized -rat	Isoflavonoid aglycones and small peptides improved insulinotropic action
Ficus amplissima (Moraceae) [54]	MeOH, bark	STZ- rat	Regenerative effect of the on the ß-cells of diabetic rat
Ficus religosa (Moraceae) [55]	AE, bark	STZ- rat	↑ the serum insulin
Genistein[56]	Genistein	STZ- Sprague Dawley rat	Genistein directly acts on pancreatic beta-cells, leading to activation of the cAMP, PKA signaling cascade to exert an insulinotropic effect.
Ginkgo biloba (Ginkgoaceae) [5]	AE, plant	STZ - male wistar rat	↑ insulin release
Genista tenera (Leguminosae)[57]	*n*-butanol, Plant	STZ - rat	21 monoglycosyl and 12diglycosyl flavanoids ↓ blood glucose level
Gymnema sylvestre (Asclepiadaceae) [45]	AAE, AE leaves	Alloxan - rat	↑ insulin release
Gymnema montanum (Asclepiadaceae) [58, 59]	AAE, stem	STZ - rat	↑ plasma insulin levels and significant ↑in hexokinase, glucose-6-phosphate dehydrogenase
Helicteres isora (Sterculiaceae) [4]	Butanol, root	glucose loaded rat	Insulin – sensitizing activity
Hibiscus rosa sinensis (Malvaceae) [60]	EtOH, leaves	Alloxan - rats	↑ Insulin release
Hordeum vulgare (Graminae)[7]	Hydralcoholic extract of seeds	STZ - rat	Mobilization of insulin release
Heinsia crinata (Rubiaceae)[61]	EtOH, leaves	Alloxan - rat	↓ fasting blood glucose levels
Hunteria umbellate (Apocynaceae)[62]	AE, seed	Alloxan, dexamethasone, high fructose induced hyperglycemic rat	↑ peripheral glucose uptake and improvement in insulin resistance
Hypoxis hemerocallidea (Hypoxidaceae)[63]	AE, plant	STZ –mice, rat	↓ the blood glucose level

Botanical Name	Extract, Part	Drug induced diabetes-animal model	Mechanism of action
Ipomoea reniformis (Convolvulus) [64]	EtOH, AE, stem	Alloxan - rat	↓ the blood glucose and lipid level
Juglans regia (Juglandaceae) [65]	MeOH, leaves	male wistar rat	↓ the blood glucose level
Lepechinia caulescens (Lamiaceae) [5]	AE, flowers	Alloxan - mice	↓ glucose tolerance, insulinomimetic activity
Lantana aculeate (Verbenaceae)[66]	EtOH, mature roots	Alloxan - rat	↓ the blood glucose, triglyceride, total cholesterol and ↑ the insulin and glycogen
Limonia acidissima (Rutaceae) [67]	AAE, AE, stem bark	Alloxan - rat	↓ the blood glucose and malondialdehyde, antioxidant enzymes were ↑
Luffa aegyptiaca (Cucubitaceae) [68]	AAE, AE, fruits	Alloxan - rat	Decrease the blood glucose
Medicago sativa (Fabaceae) [5]	AE, plant	STZ - mice	Stimulation of insulin secretion from the BRIN-BD11 pancreatic beta cell
Momordica charantia (Cucurbitacea) [69, 70]	fruit juice	Alloxan - rat	Momrdicin, charantin, and a few compounds such as galactose-binding lectin and insulin like protein isolated from various parts of the plant possess insulinomimetic activity
Mucuna pruriens (leguminosae) [4, 60]	EtOH, seeds	Alloxan - rat	Insulin – like action
Mukia madeaspatana (Cucuerbitaceae)[71]	MeOH, root	Alloxan - rat	↓ blood glucose level
Musanga cecropioides (Moraceae)[72]	EtOH, stem bark	Alloxan - rat	↓ fasting plasma glucose level
Nymphaea pubescens (Nymphaeaeae)[73]	EtOH, plant	Alloxan -rat	Regenerative potential
Nigella sativa oil (Ranunculaceae) [74]	Oil	STZ-nicotinamide hamster rat	Insulinotropic property
Nervilia plicata (Orchidaceae)[75]	AAE, stem	STZ – nicotinamide	Decrease in blood glucose levels
Ocimum gratissimum (Lamiaceae)[76]	AE, Leaves	Alloxan – Wistar rat	↓ blood glucose levels
Panax ginseng (Araliacea) [5]	AEE, berry	Obese mice	Stimulated insulin secretion
Pandanus odorus (Pandanaceae) [5]	AE, root	STZ - rat	4-hydroxybenzoic acid possess insulin secretory activity
Parinari excels (Chrysobalanaceae) [45]	AE, bark	Alloxan - rat	Insulin secretory activity
Prunella vulgaris(Labiatae) [7]	AE, plant	STZ - rat	Jiangtangsu repairs cells of pancreatic islet to release insulin
Piper betle (Piperaceae)[100]	AE, EtOH, Leaves	STZ - rat	↓ glycosylated hemoglobin
Psidium guajava (Myrtaceae) [7]	AE, Leaves	STZ - rat	Strictinin, isostrictinin, edunculagin improved sensitivity of insulin
Pterocarpus marsupium (Fabaceae) [69]	AAE, bark	Alloxan - rat	Pancreatic beta cell regranulation and insulinogenic activity due to epicatehin present in the bark
Paspalum scrobiculatum (Poaceae)[77]	AE, EtOH, plant	Alloxan - wistar rat	Decrease in glycated haemoglobin level
Phoenix dactylifera (Arecaceae)[78]	AE, leaves	Alloxan - Wistar rat	↑ plasma insulin level
Phyllanthus niruri (Euphorbiaceae)[79]	MeOH aerial parts	Alloxan – rats	Cell regenerative power
Phyllanthus simplex (Euphorbiaceae)[80]	Pet ether, ethyl acetate, EtOH, water, plant	Alloxan –rats	Normalized the anti oxidant enzymes of liver and kidney
Pongamia pinnata (Fabaceae)[81]	EtOH, leaves	Alloxan – rats	↓ blood glucose levels and prevented body weight loss
Radix rehmanniae (Scrophulariaceae) [7]	EtOH, rhizome	STZ - mice	↑ insulin secretion' ↓ the glycogen content
Rehmania glutinosa (Scrophulariaceae) [5]	EtOH, rhizome	Alloxan - rat	↑ insulin secretion, ↓ the glycogen content
Ricinus communis (Euphorbiaceae) [45]	EtOH, root	STZ - rat	↑ insulin secretion
Rosmarinus officinalis (Lamiaceae) [86]	EtOH, leaves	Alloxan- rat	↑ insulin secretion
Syzygium cumini (Rutaceae) [60]	EtOH, Fruit	STZ-mice	Insulin secretion and inhibited insulinase activity
Saliva lavandifolia (Lamiacea) [5]	AE, plant	Alloxan - rat	Insulin release
Sarcopoterium spinosum (Rosaceae) [45, 87]	AE, plant	KK-A^y mice	↑ insulin secretion
Selaginella tamariscina (Selaginellaceae) [5]	AE, EtOH, Plant	STZ - rat	Repairing injured pancreatic islet beta cells
Semen coicis (Gramineae) [7]	seeds	Alloxan- rat	Prevention of pancreatic beta – cells injury
Smallanthus sonchifolius (Asteraceae) [82]	Organic solvents, leaves	STZ - rat	↑ synthesis and secretion of insulin
Stevia rebaudiana (Asteraceae) [83]	AE, Leaves	Goto-Kakizak (GK) rats, Wistar rats	Stevioside possess insulinotropic and glucagonostatic action
Swertia chirayita (Gentianaceae) [5]	Hexane, plant	Glucose loaded - Male Albino rats	Blood sugar lowering poperty
Swertia punicea (Gentianaceae) [45]	EtOAc, plant	STZ -rat	Improves insulin resistance
Solanum nigrum (Solanaceae)[84]	AE, leaves	Alloxan - rats	↓ blood sugar levels
Sphenostylis stenocarp (Leguminosae)[85]	MeOH seeds	Alloxan – rat	↓ blood by blood glucose levles

Botanical Name	Extract, Part	Drug induced diabetes-animal model	Mechanism of action
Solanum xanthocarpum (Solanaceae)[88]	AE, leaves	Alloxan – rat, mice	Insulin like activity
Tabernanthe iboga (Apocynaceae) [89]	AE, Plant	rats pancreatic islets of langerhans	Insulin release involving the closure of K+ - ATP and the intensification of calcium influx through voltage – sensitive Ca2+ channels
Teucrium polium (Lamiaceae) [90]	MeOH, AE	STZ- rat	Apigenin possess insulinotropic properties
Tinospora crispa (Menispermaceae) [5, 91]	AE, stem	Alloxan - rat	Insulin release *via* modulation of beta- cell Ca2+ concentration
Tribuluks terrestris (Zygophyllaceae) [7]	Saponin from decoction of plant	Alloxan - mice	Increases serum insulin release
Trigonella foenum-graecum (Leguminosae) [60]	AE, seeds	Alloxan - rat	4-hydroxyleucine ↑ glucose stimulated insulin release
Tephrosia villosa (Leguminosae) [92]	EtOH, leaves	Alloxan - rat	↓ the blood glucose level
Tirum fetta rhomboidea (Poaceae)[93]	EtOH	Alloxan -wistar rats	↓ the blood glucose level
Terminalia superb (Combretaceae)[99]	MeOH, $CH_2 CL_2$, stem barks	STZ -rat	↓ blood glucose levels
Vaccinium arctostaphylos (Ericaceae)[94]	EtOH, fruit	Alloxan -wistar rats	↑ expression of GLUT – 4 and ↓ the triglyceride levels
Vernonia amygdalina (Asteraceae)[95]	AE, leaves	STZ - rats	Antioxidant activity, ↓ triglyceride levels
Zaleya decandra (Aizoaceae)[96]	EtOH, roots	Alloxan - rats	Restored the antioxidant enzymes, glucose, urea, creatinine, total cholesterol, triglycride, High density lipoprotein, low density lipo protein,
Zizyphus mauritiana (Rhamnaceae)[97]	Petroleum ether, AE, seed	Alloxan - mice	Restored the elevated biochemical parameters like glucose, urea, creatinine, total cholesterol, triglycride, High density lipoprotein, low density lipo protein, hemoglobin and glycosylated hemoglobin
Zizyphus spina- Christi (Rhamnaceae) [98]	Butanol, leaves	STZ - rat	Christinin A ↑ glucose – induced insulin release

AE – Aqueous extract, AAE – Alcoholic extract, MtOH – methanolic extract, EtOH – Ethanolic extract, STZ- Streptozotocin, $CH_2 Cl_2$ - Methylene chloride, ↑ - increase, ↓ - decrease

DISCUSSION AND CONCLUSION

Though the medicinal herbal extracts showed significant hypoglycemic properties, in most of the cases the underlying molecular mechanism and the target of action is still unknown. Most of the plant's antidiabetic effect was studied in laboratory animals with limited on human beings. People living in remote areas, poor people and people of developing countries still rely on herbal plants for medicinal purposes as they cannot afford allopathic medicines. As most of the plants are parts of daily dietary supplements and few of them are cost effective, still much of the research has to be done in bringing out the herbal drugs as antidiabetic ones to circumvent the side effects of existing allopathic medicines.

REFERENCES

1. Arumugam sathy, Perumal Siddhuraju, Protetive effect of bark and empty pod extracts from *acacia auriculiformis* against paracetamol intoxicated liver injury and alloxan induced type II diabetes, Food and tocicology, 56, 2013, 162-170.
2. B,S,Ashok Kumar, Antidiabetic, antihyperlipidemic and antioxidant activities of methanolic extract of *amaranthus viridis Linn* in alloxan induced diabetic rats, Experimental and toxicologic pathology, 64, 2012, 75-779.
3. Patil RN, Patil RY, Ahirwar A, Ahirwar D, Evaluation of antidiabetic and related actions of some Indian medicinal plants in diabetic rats, Asian Pac J Trop Med, 4, 2011, 20-23.
4. Ayodhya S, Kusum S, Anjali S, Hypoglycemic activity of different extracts of various herbal plants Singh, *Int J Ayurveda Res Pharm,* 1(1), 2010, 212-224.
5. Bnouham M, Ziyyat A, Mekhfi H, Tahri A, Legsyer A, Medicinal plants with potential antidiabetic activity- a review of ten years of herbal medicine research, (1990-2000), Int J Diabetes metab, 14, 2006, 1-25.
6. K shirsagar RP, Darade SS, Takale V, Effect of *Alangium salvifolium (Alangiaceae)* on dexamethasone induced insulin resistance in rats, J Pharm Res, 3(11), 2010, 271-276.
7. Chauhan A, Sharma PK, Srinivastava P, Kumar N, Duehe R, Plants having potential antidiabetic activity, A review, Der pharm let, 2(3), 2010, 2(3), 369-387.
8. Singh LW, Traditional medicinal plants of Manipur as anti-diabetics, J Med Plant Res, 5(5), 2011, 677-687.
9. Malviya N, Jain S, Malviya S, Antidiabetic potential of medicinal plants, Acta Pol Pharm, 67(2), 2010, 113-118.
10. Hannan JM, Marenah L, Ali L, Rokeya B, Flatt PR, Abdel- wahab YH, Insulin secretory actions of extracts of *Aspargus racemosus* root in perfused pancreas, isolated islets and clonal pancreatic beta – cells, J Endocrinol, 192(1), 2007, 159-168.
11. Geetha G, kalavalarasariel Gopinathapillai P, Sankar V, Antidiabetic effect of *Achyranthes rubrofusca* leaves extracts on alloxan induced diabetic rats, Pak J Pharm sci, 24, 2001, 193-19.
12. Ravikumar R, Krishnamoorthy P, Kalidoss A, Antidiabetic and antioxidant efficacy of *Andrographis paniculata* in alloxanized albino rats, Int J Pharm Technol, 2, 2010, 1016-1027.
13. Biradar SM, Rangani AT, kulkarni VH, Joshi H, Habbu PV, Smita DM, Prevention of onset of hyperglycemia by extracts of *Argyriea cuneata* on alloxan - induced diabetic rats, J Pharm Res, 3, 2010, 2186-2187.
14. Dheer R, Bhatnagar P, A study of the antidiabetic activity of *Barleria prionitis* Linn, Indian J Pharmacol, 42, 2010, 70-73.
15. Frankish N, de Sousa Meneezes F, Mills c, Sheridan H, Enhancement of insulin release from the beta- cell line INS-1 by an

ethanolic extract of *Bauhinia variegate* and its major constituent roseoside, Planta Med, 76(10), 2010, 995-997.

16. Wang ZQ, Lu FE, Leng Sh, Fang XS, Chen G, Wang ZS, et al, Facilitating effects of berberine on rat pancreatic islets through modulating hepatic nuclear factor 4 alpha expression and glukokinase activity, World J Gastroenterol, 14(39), 2008, 6004-6011.
17. Ko BS, Choi SB, Parj SK, Jang JS, Kim YE, Park S, Insulin sensitizing and insulinotropic action of berberine from *Cortidis rhizome.* Biol Pharm Bull, 28(8), 2005, 1431-1437.
18. Puri D, The insulinotropic activity of Nepalese medicinal plant *Biophytum sensitivum,* preliminary experimental study, J Ethnopharmacol, 78(1), 2001, 89-93.
19. Anand P, Murali YK, Tandon V, Murthy PS, Chandra R, Insulinotropic effect of aqueous extract of *Brasica nigra* improves glucose homeostasis in streptozotocin induced diabetic rats, Exp Clin Endocrinol Diabetes, 117(6), 2009, 251-256.
20. John A, O,Ojewole, Antinociceptive, anti – inflammatory and antidiabetic effects of *Bryophyllum pinnatum (Crassulaceae)* leaves aqueous extract, Journal of Ethnopharmacoogy, 99, 2005, 13-19.
21. A,M, Da Cunha, S,Menon, R,Menon, A,G, Couto, C,Burger, M,W,Biavatti, Hypoglycemic activity of dried extracts of *Bauhinia forficate* link, Phytomedicine, 17, 2010, 37-41.
22. Rathee S, Mogla OP, Sardana S, Vats M, Rathee P, Antidiabetic activity of *Capparis deciduas* Forsk Edgew, J Pharm Res, 3, 2010, 231-234.
23. Lodha SR, Joshi SV, Vyas BA, Upadhye MC, KIrve MS, Salunke SS, et al, Assessment of the antidiabetic potential of *Cassia grandis* using an *in vivo* model, J Adv pharm Technol Res, 1, 2010, 330-333.
24. Nabeel MA, Kathiresan K, Manivannan S, Antidiabetic activity of the mangrove species *Cerios decendra* in the alloxan – induced diabetic rats, J Diabetes, 2, 2010, 97-103.
25. Kumawat NS, Chaudhari SP, Wani Ns, Deshmukh TA, Patil Vr, Antidiabetic activity of ethanol extract of *Colocasia esculenta* leaves in alloxan induced diabetic rats, Int J Pharm Tech Res, 2, 2010, 1246-1249.
26. Vishnu B, Naveen A, Akshay K, Sikarwar MS, APtil MB, Antidiabetic activity of insulin plant (*Costus igneus*) leaves extract in diabetic rats, J Pharm Res, 3, 2010, 608-611.
27. Anand P, Murali KY, TAndon V, Murthy PS, Chandra R, Insulinotropic effect of cinnamaldehyde on transcriptional regulation of pyruvate kinase, phosphoenolpyruvate carboxykinase, and GLUT4 translocation in experimental diabetic rats, Chem Biol Interact, 186(1), 2010, 72-81.
28. Park S, Jang JS, Hong SM, Long – term consumption of caffeine improves glucose homeostasis by enhancing insulinotropic action through islet insulin/insulin – like growth factor 1 signaling in diabetic rats, Metabolism, 29(1), 2007, 599-607.
29. Islam MS, Choi H, Green tea, anti- diabetic or diabetogenic, a dose response study, Biofactors, 29(1), 2007, 45-53.
30. Islam S, Choi H, Dietary red chilli (*Capsicum frutescns L)* is insulinotropic rather than hypoglycemic in type 2 diabetes model of rats, Phytother Res, 22(8), 2008, 1025-1029.
31. Dallak M, Al- khateeb M, abbas M, Elessa R, al- hashem F, basher N, Et al, *In vivo,* acute, normo – hypoglycemic, antihyperglycemic, insulinotropic actions of orally administered ethanol extract of *citrullus colocynthis(L)* Scharb pulp, Am J BIochem BIotechnol, 5(3), 2009, 119-126.
32. Chen CC, Hsu Cy, Chen CY, Liu HK, *Fructis corni* suppresses hepatic gluconeogensis related gene transcription, enhances glucose responsiveness of pancreatic beta – cells, and prevents toxin induced beta – cells death, J Ethnopharmacol, 117(3), 2008, 483-490.
33. Rajesh kumar, Dinesh K,Patel, Satyendra K, Prasad, Damiki Laloo, Sairam Krishnamurthy, Hemalatha, Type 2 antidiabetic activity of bergenin from the roots of *Caesalpinia digyna* Rottler, Fitoterapia, (83), 2012, 395-401.
34. Syed Nazreen, Gurpreet Kaur, Mohammad mafboob Alam, Syed Shafi, Hinna Hamid, Mohammad Ali, Mohammad Sarwar Alam, New flavones with antidiabetic activity from *Callistemon lanceolatus* DC, Fitoterapia, 83, 2012, 1623-1627.
35. K,R,W, Abeywickrama, W, D, Ratnasooriya, A, M,T Amarakoon, Oral hpoglycaemic and antidiabetic activities of Sri lankan Orange Pekoe Fannings (BOPF) grade black tea(*Camellia sinensis L.*) in rats, Journal of Ethnopharmacology, 135, 2011, 278-286.
36. Mohammed Habibuddin, Hassan Ali Daghiri, Touseef Humaira, Mohammed Saeed Al Qahtani, Ali Al Hasan Hefzi, Antidiabetic effect of alcoholic extract of *Caralluma sinaica* L, on streptozotocin – induce diabetic rabbits, Journal of Ethnopharmacology, 117, 2008, 215-220.
37. Essam A, Abdel – Sattar, Hossam M, Abdallah, Alaa khedr, Ashraf, Abdel – Naim, Ibrahim A, Shehata, Antihyperglycemic activity of *Caralluma tuberculata* in streptozotocin – induced diabetic rats, Food and Chemical Toxicology, 59, 2013, 111-117.
38. Som Nath Singh, Praveen Vats, Shoba Suri, Radhey Shyam, M,M,L,Kumaria, S, Ranganathan, K, Sridharan, Efect of an antidiabetic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats, Journal of Ethopharmacology, 76, 2001, 269-277.
39. Nilufer Orhan, Mustafa Aslan, Murat Sukuroglu, Didem Deliorman Orhan, *In vivo* and *in vitro* antidiabetic effect of *Cistus laurifolius* L, and detection of major phenolic compounds by UPLC-TOF-MS analysis, Journal of Ethnopharmacology, 146, 2013, 859-865.
40. A.C.Adebajo.E.O. Iwalewa, E.M. Obuotor, G.F. Ibikunle, N.O. Omisore, C.O. Adewunmi, O.O. Obaparusi, M.Klaes, G. Adetogun, T.J. Schmidt, E.J. Verspohl, Pharmacological properties of the extract and some isolate compounds of *Clausena lanseum* stem bark, anti-trichomonal, antidiabetic, anti-inflammatory, hepatoprotective and antioxidant effects, Journal of Ethnopharmacology, 12, 2009, 10-19.
41. Md. Salahuddin, Sunil S, Jalalpure, Antidiabetic activity of aqueous fruit extract of *Cucumis trigonus* Roxb, In streptozotocin – induced – diabetic rats, Journal of Ethnopharmacology, 127, 2010, 565-567.
42. Surya Dhandapani, vijayakumar Ramasamy Subramanian, Senthilkumar Rajagopal and Nalini Namasivayam, Hypolipidemic effect of *Cuminum cyminum* L on alloxan – induced diabetic rats, Pharmacological Research, (46), 2002, 3.
43. Santosh Kumar Singh, Achyut Narayan Kesari, Rajesh Kumar gupta, Dolly jaiswal, Geeta Watal, Assessment of antidiabetic potential of *Cyandon dactylon* extract in streptozotocin diabetic rats, Journal of Ethanopharmacology, 114, 2007, 174-179.
44. Saikat Dewanjee, Anup K Das, Ranbir Sahu, Moumita Gangopadhyay, Antidiabetic activity of *Diospyros Peregrina* fruit, Effect on hyperglycemia, hyperlipidemia and augmented oxidative stress in experimental type 2 diabetes, Food and Chemical Toxicology, 47, 2009, 2679-2685.
45. Rao Mu, Sreenivasulu M, Chengaiah B, Reddy KJ, Chetty Cm, Herbal medicines for diabetes mellitus, a review, Int J PharmTech Res, 2(3), 2010, 183-1892.
46. Maroo J, Vasu VT, Aalinkeel R, Gupta S, glucose lowering effect of aqueous extract of *Enicostemma littorale* blume in diabetes, a possible mechanism action, J Ethnopharmacology, 81(3), 2002, 317-320.
47. Qa'dan F, Verspohl EJ, Nahrstedt A, Petereit F, Matalka KZ, Cinchonain Ib isolated from *Eriobotrya japonica* induces insulin

secretion *in vitro* and *in vivo.* J Ethanopharmacol, 124(2), 2009, 224-227.

48. Modak M, Dixit P, Londhe J, Ghaskadbi S, Paul A, Devasagayam T, Indian herbs and herbal drugs used for the treatement of diabetes, J Clin Biochem Nutr, 40(3), 2007, 163-173.

49. Arjyun P, Shivesh J, Sahu An, Antidiabetic activity of aqueous extract of *Eucalyptus citriodora* hook in alloxan induced diabetic rats, Pharmacogn Mag, 5, 2009*, 51-54.*

50. P. Daisy, R. Jasmine, S. Ignacimuthu, E. Murugan, A novel steroid from *Elephantopus scaber* L, An Ethnomediciinal plant with antidiabetic activity, Phytomedicine, 16, 2009, 16, 252-257.

51. Parminder Nain, Vipin Saini, Sunil Sharma, Jaspreet Nain, Antidiabetic and antioxidant potential of *Emblica officinalis* Gaertn, leaves extract in streptozotocin induced type – 2 diabetes mellitus (T2DM) rats, Journal of Ethnopharmacology, 142, 2012, 65-71.

52. Chaturvedi N, Sharma S, Antidiabetic and antihyoerlipidemic activity of water soluble solid extract of *Ficus bengalensis* Linn, Bark in rats, Biochem cell Arch, 10, 2010, 65-69.

53. Kwon DY, Jang JS, Hong SM, Lee JE, Sung SR, Park HR, et,al, Long-term consumption of fermented soybean-derived Chungkookjang enhances insulinotropic action soybeans in 90% pancreatectomized diabetic rats, Eur J Nutr, 46(1), 2007, 44-52.

54. Karuppusamy Arunachalam, Thangaraj Parimelazhagan, Antidaibetic Activity of *Ficus amplissima* Smith, Bark extract in streptozotocin induced diabetic rats, Journal of Ethnopharmacology, 46(1), 2013, 147, 302-310.

55. Rucha pandit, Ashish Phadke, Aarti Jagtap, Antidiabetic effect of *Ficus religosa* In streptozotocin induced diabetic rats, Journal of Ethnopharmacology, 128, 2010, 462-466.

56. Liu D, Zhen W, Yang Z, Carter JD, Si H, Reynolds KA, Geinstein acutely stimulates insulin secretion in pancreatic beta-cells through a cAmp-dependent protein kinase pathway, Diabetes, 55(4), 2006, 1043-1050.

57. Amelia P, Rauter, Bioactivity studies and chemical profile of the antidiabetic plant *Genista tenera*, Journal of Ethnopharmacology, 122, 2009, 384-393.

58. Kunga Mohan Ramkumar, Pachumuthu Vanitha, Chidambaram Uma, Natarajan Suganya, Elango Bhakkiyalakshmi, Jaiganesh Sujatha, Antidiabetic aactivity of alcoholic stem extract of l *Gymnema montanum* in streptozotocin – induced diabetic rats, Food and Chemical Toxicology, 49, 2011, 3390-3394.

59. R. Ananthan, C. Baskar, V.NarmathaBai, L.Pari, M.Latha, K.M.Ramkumar, Antidiabetic effect of *Gymnema monatanum* leaves, effect on lipid peroxidation induced oxidative stress in experimental diabetes, Pharmacological Research, 48, 2003, 551-556.

60. Grover JK, Yadav S, Vats V, Medicinal plants of India with anti-diabetic potential, J Ethopharmacology, 81(1), 2002, 81-100.

61. Okokon JE, Umoh EE, Etim EI, Jackson CL, Antiplasmodial and antidiabetic activities of ethanolic leaves extract of *Heinsia crinata,* J Me Food, 12, 2009, 131-136.

62. Adejuwon Adewale Adeneyee, Olufunmilayo Olaide Adeyemi, Further evaluation of antihyperglycaemic activity of *Hunteria umbellate*(K,Schum) Hallier f, seed extract in experimental diabetes, Journal of Ethnopharmacology, 126, 2009, 238-243.

63. John A,O. Ojewole, Antinociceptive, and anti-inflammatory and antidiabetic properties of *Hypoxis hemerocallidea* Fisch, & C.A.Mey,(Hypoxidaceae) corm 'African potato' aqueous extract in mice and rats, Journal of Ethnopharmacology, 103, 2006, 126-134.

64. Sangeswaran B, ilango K, Chaurey M, Bhskar VH, Antihyperglycemic and antihyperlipidemic effects of extracts of *Ipomoea reniformis* chois on alloxan induced diabetic rats, Ann Biol Res,1, 2010, 157-163.

65. Teimoori M, Kouhsari MS, Ghafarzadegan R, Hajaghaee R, Antidiabetic effects of *Juglans regia* leaves methanolic extract on alloxan – induced male wistar rats, J Med Plants, 9, 2010, 143-149.

66. Kumar KV, Sharief SD, Rajkumar R, Ilango B, Sukumar E, Antidiabetic potential of *Lantana aculeate* root extract in alloxan induced diabetic rats. Int J Phytomed, 2, 2010, 299-303.

67. Ilango K, Chitra V, antidiabetic and antioxidant activity of *Limonia acidissima* Linn, In aloxan induced diabetic rats, Der Pharmacia letter, 1, 2009, 117-125.

68. Saxena SCRC, Chaurasia ID, Shrivastav R, Antidiabetic activity of *Luffa aegyptiaca (Mill)* in alloxan induced diabetic rats, J Chem Pharm Res, 3, 2011, 522-525.

69. Saxena A, Vikram NK, Role of selected Indian plants in management of type 2 diabetes, a review , J Altern Complemnt Med, 10(2), 2004, 369-378.

70. Kaczmar T, Herbal support for diabetes management, Clin Nutr Insights, 6(8), 1998, 1-4.

71. Wani VK, Dubey RD, Verma S, Sengottuvelu S. Sivakumar T, Antidiabetic activity of methanolix extract of *Mukia maderaspatana* in alloxan induced diabetic rats, Int J Pharm Technol Res,3, 2011, 214-220.

72. A.A.Adneye, O.P. Ajagbonna, O.W.Ayodele, Hypoglycemic and antidiabetic activities on the stem bark aqueous and ethanol extracts of *Nusanga ccropioides* in normal and alloxan – induced diabetic rats, Fitoterapia*,* 78, 2007, 502-505.

73. Sreenathkumar S, Arcot S, Antidiabetic activity of *Nymphaea pubescens* Willd – a plant drug of aquatic flora, J Pharm Res, 3, 2010, 3067-3069.

74. Fararh KM, Atoji Y, shmizu Y, takewaki T, Insulintropic properties of *Nigella sativa* oil in streptozotocin plus nicotinamide diabetic hamster, Res Vet Sci, 73(3), 2002, 279-28.

75. E.K. Dilip Kumar, G.R..Janardhana, Antidiabetic activity of alcoholic stem extract of *Nervilia plicata* in streptozotcin-nicotinamide induced type 2 diabetic rats, J of Ethnopharmacology*,* 133, 2011, 480-483.

76. Bihari CG, Manaswini B, Keshari PS, Kumar Ts, Phytochemical investigation & evaluation for antidiabetic activity of leavesy extracts of various *Ocimum*(Tulsi) species by alloxan induced diabetic model, J Pharm Res, 4, 2011, 2-29.

77. Jain S, Bhatia G, Barik R, Kumar P, Jain A, Dixit VK, Antidiabetic activity of *Paspalum scrobiculatum* Linn, In alloxan induced diabetic rats, J Ethnopharmacology, 127, 2010, 325-328.

78. Mard SA, jalalvand K, Jafarinejad M, Balochi H, Naseri MKG, Evaluation of the antidiabetic and antilipaemic activities of the hydroalcoholic extract of *Phoenix dactylifera* alm leaves and its factions in alloxan induced diabetic rats, Malaysian J Med Sci, 17, 2010, 4-13.

79. Okoli CO, Ibiam AF, Ezike AC, Akah PA, Okoye TC, Evaluation of antidiabetic potentials of *Phyllanthus niruri* in alloxan diabetic, Afr J Biotechnol, 9, 2010, 248-259.

80. Shabeer J, Srivastava RS, Singh Sk, Antidaibetic and antioxidant effect of various fractions of *Phyllanthus simplex* in alloxan diabetic rats, J Ethnopharmacol, 124, 2009, 34-38.

81. Lanjhiyana S, Garabadu D, Ahirwar D, Bigoniya P, Rana AC, Patra KC, et al, Hypoglycemic activity studies on aerial leaves of *Pongamia pinnta* in alloxan – induced diabetic rats, Der Pharmacia Lettre, 3, 2011, 555-70.

82. Mentreddy SR, Mohamed AI, Rimando Am, Medicinal plants with hypoglycemic /anti-hyperglycemic properties, a review, *Proc Assoc Adv Ind Crop Conf* 2005, 20, 341-353.

83. Jeppesen PB, Gregerrsen S, Alstrup KK, Hermansen K, Stevioside induces antihyperglycemic, insulinotropic and glucagonostatic effects *in vivo,* studies in the diabetic Goto-Kakizak (GK) rats, Phytomedicine, 9(1), 2002, 9-14.

84. Poongothai K, Ahmed KSZ, Ponmurugan P, Jayanthi M, Assessment of antidiabetic and antihyperlipidemic potential of *Solanum nigrum* and *Musa paradisiaca* in aloxan induced diabetic rats, J Pharm Res, 3, 2010, 2203-2205.

85. Ubaka CM, Ukwe CV, Antidiabetic effect of the methanolic seed extract of *Sphenostylis stenocarpa* in rats, J Pharma Res, 3, *2010,* 2192-2194,

86. Tulay Bakirel, Utku Bakirel, Oya Ustuner Keles, Sinem Gunes, Ulgen, Hasret Yardii, *In vivo* assessement of antidiabetic and antioxidant activities of rosemary (*Rosamarinus officinalis)* in alloxan – diabetic rabbits, J Ethnopharmacol, 116, 2008, 64-73,

87. Polina Smirin, Dvir Taler, Guila Abitbol, Tamar Brutman-Barazani, Zohar Kerem, Sanford R, Sampson, Tovit Rosenzweig, *Sarcopoterium spinosum* extract as an antidiabetic agent, *In vitro and in vivo* study, Journal of Ethnopharmacology, 129, 2010, 10-17.

88. D,M, Kar, L, Maharana, S, pattnaik, G,K, Dash, Studies on hypoglycaemic activity of *Solanum xanthocarpum* Schrad, & Wendl,fruit extract in rats, Journal of Ethnopharmacology, 108, 2006, 251-256.

89. Souza A, Mbatchi B, herchuelz A, induction of insulin secretion by an aqueous extract of *Tabernanhte iboga* Bail,(Apocynaceae)in rat pancreatic islets of langerhans, J Ethnopharmacol, 13(3), 2011, 1015-1020.

90. Esmaeli MA, Yazdanparast R, Hypoglycaemic effect of *Tercrium polium,* studies with rat pancreaticislets, J Ethnopharmacol, 95(1), 2004, 27-30.

91. Noor H, Ashcroft SJH, Pharmacological characterization of the anithyperglycemic properties of *Tinospora crispa* extract, J Ethnopharmacol, 62(1), 1998, 7-13.

92. Ahamd A, Balakrishnana BR, Akhtar R, Pimprikar R, antidiabetic activity of leaves of *Tephrosia villosa* pers, In alloxan induced diabetic rats, J Pharm Res, 2, 2009, 528-531.

93. Duganath N, Krishna DR, Reddy GD, Sudheera B, mallikarjun M, Beesetty P, evaluation of anti-diabetic activity of *Triumfetta rhomboidea* in alloxan induced wistar rats, Res J Pharm Biol Chem Sci, 2, 2011, 721-726.

94. Feshani AM, Kouhsari Sm, Mohammadi S, *Vaccinium arctostaphylos,* a commom herbal medicine in Iran, molecular and biochemical study of its antidaibetic effects on alloxan – induce diabetic wistar rats, J Ethnopharmacol, 13, 2011, 67-7.

95. Michael UA, David BU, Theophine CO, Philip Fu, Ogochukwu AM, Benson VA, Antidiabetic effects of combined aqueous leaves extract of *Vernonia amygdalina* and metformin in rats, J Basic Clin Pharm, 1, 2010, 197-202.

96. Meenakshi P, Bhuvaneshwari R, Rathi MA, Thiruoorthi L, Guravaiah DC, Jiji MJ, et al, Antidiabetic activity of ethanolic extract of *Zaleya decandra* in alloxan- induced diabetic rats, Appl Biochem Biotechnol, 162, 2010, 1153-1159.

97. Jarald EE, Joshi SB, Jain DC, Antidiabetic activity of extracts and fraction of *Zizyphus mauritiana.* Pharm Biol, 47, 2009, 328-334.

98. Abdl- zaher Ao, Salim SY, Assaf MH, Abdel- Hady RH, *Teucrium polium* antidiabetic activity and toxicity of *Zizyphus spina – Christi* leaves, J Ethnopharmocolgy, 101(1-3), 2005, 129-138.

99. Kamtchouing, Antidiabetic activity of methanol\methylene chloride stem bark extracts of *Terminalia superb* and *Canarium schweinfurthii* on streptozotocin induced diabetic rats, Journal of Ethnopharmacology*,* 104, 2005, 306-309.

100. Arambewela, LS, Arawwawala, L.D. Ratnasooriya, W.D, Antidiabetic activities of aqueous and ethanolic extracts of *Piper betle* leaves in rats, Journal of Ethnopharmacology, 102, 2005, 239 -245.

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