IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Phytochemical And Pharmacological Investigation On *Glinus Oppositifolius* Linn And *Mollugo Oppositifolia* Linn.

For Anti-Diabetic Activity

Mr.Datir Mahendra Baban[1], Dr. Bharat W Tekade[2]

[1]Research Scholar Department of Pharmacy SunRise University Alwar (RJ)

[2] Professor Department of Pharmacy SunRise University Alwar (RJ)

Abstract

In the analysis of its potential to prevent diabetes, the effects of petroleum ether, chloroform and methanol, fa st blood glucose and blood biochemical analyzes in streptozotocin diabetic rats were investigated. Of all thre e extracts, oral administration of 500 mg/kg of methanol extract significantly reduced glucose overload and s treptozotocin in normal, normal rats after 15 days of treatment. Petroleum ether and chloroform extract did n ot show any significant effect on three groups of rats at an oral dose of 500 mg/kg. Simultaneous histological studies on the pancreas of these animals first demonstrated the comparative regenerative capacity of methan ol extracts necrotic by streptozotocin. The results showed that it had a positive effect on diabetes in the exper imental diabetes model. The plant material were collected dried and extracted. Among these ethanolic extract of *Mollugo oppositifolius linn,*and hydro-alcoholic extract of *Glinus oppositifolius linn,* were taken for studies. *Glinus oppositifolius linn* was examined for its anti-inflammatory activity also. The in-vitro analysis of both extracts were carried out and compared with standard drug. After screening the anti- diabetic property was confirmed by in- vivo methods. Both the plant extracts found to have a moderate to high capacity to regulate the hyperglycemia and associated complications.

Keywords: Glinus oppositifolius,oral glucose, Hypoglycemic, Streptozotocin

INTRODUCTION

As the old adage goes, if you only have one disease, make it diabetes because it is the only one over which you have control. "Diabetes is a terrific illustration of how, by providing the patient the tools, you could manage yourself very well," Clayton M. Christensen stated. The statement "eradicating the excess" is thought to date back to 1500BC in the Egyptian writings Ebers Papyrus. Around the same time, Indian physicians recognised the condition and classified it as madhumeha, or "honey urine," since the urine attracted ants. Sushruta and Charaka, two Indian physicians, defined two forms of diabetes for the first time in 400–500 CE, one of which was linked to age and the other to being overweight[2]. Despite the fact that modern medicine and therapeutic agent development have progressed a long way from insulin therapy to stem cell therapy or various oral antihyperglycaemic drugs such as insulin secretagogues to the recently introduced incretins, the World Health Organization still lists diabetes as one of the top ten causes of death worldwide [3-4].

According to the World Health Organization, over 422 million people worldwide have diabetes, with the majority living in low and middle income countries. Diabetes is directly responsible for 1.6 million deaths per year.[5] According to the International Diabetes Federation, the number of cases and prevalence of diabetes have consistently increased in most countries over the last several decades, to the point that by 2045, the total number of diabetics could reach 700 million [6]. Though diabetes is becoming more common worldwide, the greatest increase is expected in India, where the numbers of diabetics will increase from 41 million in 2009 to 70 million by 2040. As a result, India is known as the world's diabetic capital. According to WHO, India will have the biggest rise (48 percent) in diabetics in the entire population by 2040 [7, 8]. A big contributor to the increase is the constant growth in body weight & obesity throughout many parts of the world. Economic prosperity & technological growth encourage obesity in European and South Asian countries. Environmental factors, as well as social trends toward higher energy use and lower energy expenditure, play a role.[9]

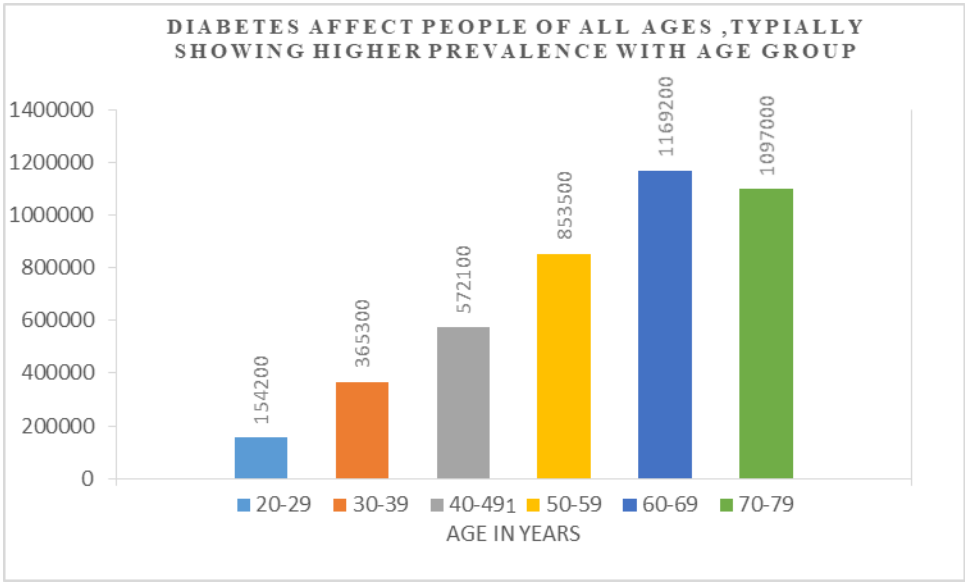

Figure 0. Statistical report on Deaths attributable to diabetes [10]

Diabetes Mellitus, also known as Type II Diabetes, is characterised by hyperglycemia as a result of impaired glucose absorption, dietary nutrient metabolism (carbohydrates, proteins, and lipids) as a result of insulin secretion abnormalities, or both. These metabolic changes contribute to the development of macro and micro vascular disorders such retinopathy, nephropathy, neuropathy, and coronary heart disease over time. Symptoms of diabetes include increased appetite (polyphagia), increased urination (polyuria), increased thirst (polydypsia), weight loss, lethargy, decreased vision, fatigue, nocturia, nausea, headache, mood swings, and irritability [11]. **1.2 Classification of diabetes mellitus and other categories of glucose regulation:**

The type of diabetes that a person has is typically determined by the conditions that exist at the time of diagnosis, and many diabetics do not simply fit into a single category.[9]

1.Type 1 Diabetes Immune-Mediated Diabetes

Insulin deficiency and hyperglycemia are hallmarks of type 1 diabetes, a chronic autoimmune disease. Despite the fact that the disorder has a significant genetic component, which would be inherited primarily through the HLA complex, the elements that allow clinical disease to emerge remain unknown. Even while symptoms are more common in childhood and adolescence, they can occur at any age. T1DM pathogenesis is thought to also include T cell-mediated apoptosis of -cells, despite the fact that the disease's cause is unknown.[11]

2 Type 2 Diabetes

Diabetes mellitus is a chronic disease characterised by hyperglycemia and the late onset of vascular and neuropathy complications. The pathophysiology of type 2 diabetes is complex, with many different elements interacting to cause the illness to develop. In both type 1 and type 2 diabetes, fasting hyperglycemia is produced by a disruption to normal in hepatic glucose production. The rapid mobilisation of fat storage raises fasting free fatty acid levels in diabetes, in addition to hyperglycemia. According to research, hyperglycemia-induced intracellular overproduction of reactive oxygen species may be the common trigger for a variety of pathways linked to diabetes-related cell damage. Microvascular and neuropathy complications of diabetes have a complicated and poorly understood pathophysiology. [12-13]

Materials and Methods

Plant Material

.1 Introduction to Molluago oppositifolia linn.- **Mollugenacae**

Figure2: Molluago oppositifolia linn

Mollugo cerviana is a warm temperate to tropical annual blooming plant native to southern and south-eastern Europe, Africa, Asia, and Australia. It grows in practically all sections of India, but is most commonly found as a weed in the sandy and arid ponds of southern India. [62]

Common name: Slender carpet weed

Vernacular name:

Sanskrit: Grishma sundara, Phanya

Hindi: Taph-jhad

Malayalm/Kannada: Parpadaka

Telugu/Tamil: Parpadagum

Bengal: Ghima sak

Maharashtra: Pada

Taxonomy

Kingdom: Plantae

Clade: Angiospermae

Order: Caryophyllales

Family: Mollugenacace

Genus: Mollugenacae

Species: Molluago oppositifolia linn

2.Introduction of Glinus oppsitifolia linn-Mollugenace

Figure3: Glinus oppsitifolia linn

Glinus Lotoides is a prostrate annual or short-lived perennial herb that can be found across the tropics and subtropics, but especially in Africa, Asia, Australia, and South Europe. It can be found up to a height of 800 metres in India's warmer plains and highlands. The sensitive young leaves are used for both eating and fishing.

Common name: Lotus sweet juice

Vernacular names

Bengali. Duserasag

Hindi: Gandibudi

Marathi: Kothuk, Bhisata

Oriya/Punjabi: Gandhibuti

Telugu: Chandrasi koora

Taxonomy

Kingdom: Plantae

Clade: Angiospermae

Order: Caryophyllales

Family: Molluginaceae

Genus: Glinus

Species: oppsitifolia

Binomial name: Glinus oppsitifolia linn.

Extraction of Plant Material

Phytochemical Evaluation of Plant Extracts

Preliminary Phytochemical screening

The results of preliminary phytochemical screening are depicted

Drugs and chemicals

The following drugs and chemicals were used with their sources: streptozotocin Sigma-Aldrich Co.USA,, glucose kit Ranbaxy Diagnostics, India,, Gliclazide Sun Pharma, India, ,petroleum ether SD Fine, Mumbai,, chloroform SD Fine, Mumbai, and methanol SD Fine, Mumbai,.

Table1: Phytochemical Evaluation of Plant Extracts:

Phytochemical Constituent	*Mollugo oppositifolius linn*,. (Ethanolic extract)		*Glinus oppositifolius linn*, (Hydro--Alcoholic Extract)	
	Pet ether Extract	Pet ether Extract	Hydro--alcoholic extract	Ethanolic extract
Carbohydrates	++	++	++	++
Proteins	++	++	++	++
Alkaloids	--	--	--	++
Tannins	--	--	--	++
Phenols	++	--	--	++
Flavonoids	--	--	++	++
Saponins	--	--	++	++
Glycosides	--	++	++	++
Terpenoides	--	--	--	++
Steroids	++	++	--	++

(++) Present; (--) Absent

.

The phyto-constituents in the petroleum ether extracts of both plants were lower. The ethanolic extract of Mollugo cerviana was found to contain the highest concentration of powerful phyto components such as alkaloids, flavanoids, steroid glysosides, while hydro-alocholic extract of *Glinus oppositifolius linn,* was found to contain mostly flavanoids and saponins

Effect of different solvent extract of Glinus oppositifo- lius on oral glucose tolerance :

To perform glucose tolerance test, overnight fasted rats were used. Rats were divided into five groups, each of six animals. Group I was kept as control which re- ceived 1 mL of 2.5% Tween 80 per oral and Group V received gliclazide 25 mg/kg, per oral sus- pended in vehicle. A dose 500 mg/kg a petroleum ether, chloroform, methanolic extracts of Glinus oppositi- folius suspended in vehicle was administered orally, to the Groups II, III and IV respectively. All the animals were given glucose 3 g/kg orally, 30 min after dosing. Blood was

collected by retro-orbital puncture for glucose estimation 0 min and at 30, 90 and 150 min after drug administration.

Effect of different solvent extract of Glinus oppositifo- lius on blood glucose level in normal fasted rats 11: Overnight fasted rats were divided into five groups of six rats of each. Group I received only vehicle Tween 80 in distilled water 2.5 % v/v, per oral. Group V re- ceived gliclazide 25 mg/kg per oral,. Group II, III and IV received dose 500 mg/kg petroleum ether, chloro- form, methanolic extracts of Glinus oppositifolius sus- pended in vehicle was administered to the animals. Blood was collected by retro-orbital puncture for glucose estimation just prior to and at 1, 2, and 3 hours after dos.

Effect of different solvent extract of Glinus oppositifo- lius on streptozotocin-induced diabetes in rats 9: Diabetes was induced in night fasted rats by intraperi- tonial injection of streptozotocin 50 mg/kg, i.p., dissolved in 0.1M citrate buffer, pH 4.5. One group of 6 identical rats was kept without streptozotocin administration as normal control, Group I,. Forty eight hours after strepto- zotocin administration blood samples were drawn by retro orbital puncture and glucose levels determined to confirm diabetes. The diabetic rats exhibiting blood glu- cose levels in the range of 200 and 300 mg/100 mL were selected for the studies. These diabetic rats were sub- divided into 5 groups as follows: Group II, untreated rats, given 0.5 mL of 5%Tween 80; Group III, diabetic rats given 500 mg/kg,Glinus oppositifoliusL, petroleum ether extract in 0.5 mL 5%Tween 80; Group IV, diabetic rats given 500 mg/kg,Glinus oppositifolius chloroform ex- tract in 0.5 mL 5% Tween 80; Group V diabetic rats given

Table 2

Effects of *Glinus oppositifolius* on blood glucose level of streptozotocin-induced diabetic rats					
Group	Blood glucose mg/dl, concentration at different time day,				
	0	4	7	10	15
Vehicle	243.92±1.56	247.18±2.48	243.01±0.61	219.37±3.15	221.26±2.40
Ether extract 500 mg/kg	216.48±3.08	208.34±1.93	228.07±3.27	207.19±2.74	214.73±1.09
Chloroform ract 500 mg/kg	224.59±2.73	237.18±2.64	207.05±3.52	213.81±2.81	207.43±1.67
Methanol ract 500 mg/kg	227.06±2.54	176.31±3.43*	162.94±3.73**	136.47±3.19**	99.06±2.97**
Gliclazide 25 mg/kg	228.68±2.56	173.04±3.09	158.73±3.26**	107.31±2.18**	87.42±3.73**
n = 6; *, ** Values are statistically significant compared to normal Group at $p < 0.05$, $p < 0.01$ respectively					

Table 3

Effects of *Glinus oppositifolius* on oral glucose tolerance test on rats					
Group	Blood glucose mg/dl, concentration at different time min,				
	0	30	60	90	120
Vehicle	87.61±3.58	145.63±2.37	138.28±2.73	125.84±2.94	119.80±3.42
Ether extract	86.23±2.43	143.56±4.19	137.25±3.19	127.59±3.53	118.23±2.18
Chloroform	87.57±2.06	142.72±2.53	128.58±3.26	124.23±3.07	117.23±2.45
Methanol	86.48±2.48	128.75±3.75*	117.29±3.09**	104.96±3.16**	97.23±3.47**
Gliclazide	87.13±2.16	114.56±3.15**	104.27±2.43**	94.61±2.37**	84.62±3.61**
n = 6; *, ** Values are statistically significant compared to normal Group at $p < 0.05$, $p < 0.01$ respectively					

Table 4

Effects of *Glinus oppositifolius* on blood glucose level in normal fasted rats				
Group	Blood glucose mg/dl, concentration at different time hour,			
	0	1	2	3
Vehicle	73.25±2.53	80.19±2.09	82.73±3.45	73.81±2.68
Ether extract 500 mg/kg	75.61±2.06	74.53±3.46	72.19±3.19	76.93±2.47
rm extract500 mg/kg	80.13±3.17	76.18±2.39	72.49±2.58	78.26±2.83
Methanol extract500 mg/kg	73.20±2.29	71.39±2.41	62.57±2.32*	56.38±2.95*
Gliclazide 25 mg/kg	73.25±2.46	61.75±2.38*	23.64±2.42*	46.16±2.73*
n = 6; * Values are statistically significant compared to normal Group at p < 0.01 respectively				

Effect of extracts on estimation of blood glucose in normal and experimental rats

Values are expressed as the mean ± S.D; Statistical significance (p)calculated by one way ANOVA followed by dunnett's $^{***}P< 0.001$, $^{**}P < 0.01$,$^{*}P < 0.05$ calculated by comparing treated group with CONTROL group.

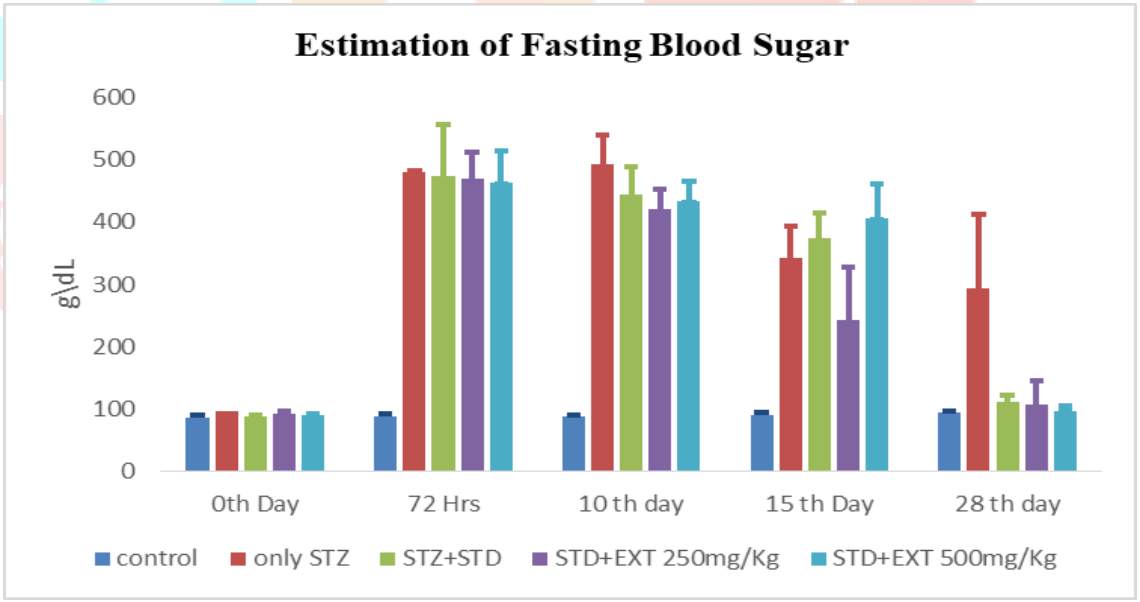

Figure:4 Analysis of *Mollugo oppositifolius linn*,on fasting blood sugar level

Table 5

Fasting blood sugar level on diabetes animals with standard and extract

Group	Before Induction of STZ		After Induction of STZ	Fasting blood sugar level on diabetes animals with standard and extract	
	Initial fasting blood sugar	Fasting blood sugar on 72 hr	Fasting blood sugar on 10th day	Fasting blood sugar on 15th day	Fasting blood sugar on 28th day
Control	86.5±3.95	88.5±4.05	88±3.63	90.5±4.11	94.5±2.63
ONLY ST	97±3.14ns	480±45.5***	493±49.9***	343±119ns	293±101
STZ+STD	89.3±1.89ns	473±82.6***	345±44.3***	135±39.3*	113±8.54
STZ + *Mollugo oppositifolius linn,* **EXT 250mg/kg**	93.5±3.62ns	470±41.4***	320±33.4***	243±84.6ns	118±36.8
STZ + *Mollugo oppositifolius linn,***EXT 500mg/kg**	90.8±2.39ns	463±51.1***	333±33.3***	175±56.8*	97.5±37.1
STZ + *Glinus oppositifolius linn,* **EXT 250mg/kg**	92.5±2.09ns	474±11.04***	332±2.4***	163±11.66ns	116±43.4
STZ + *Glinus oppositifolius linn,* **EXT 500mg/kg**	89.8±3.12ns	465±17.21***	253±24.5***	140±16.6*	109±31.9

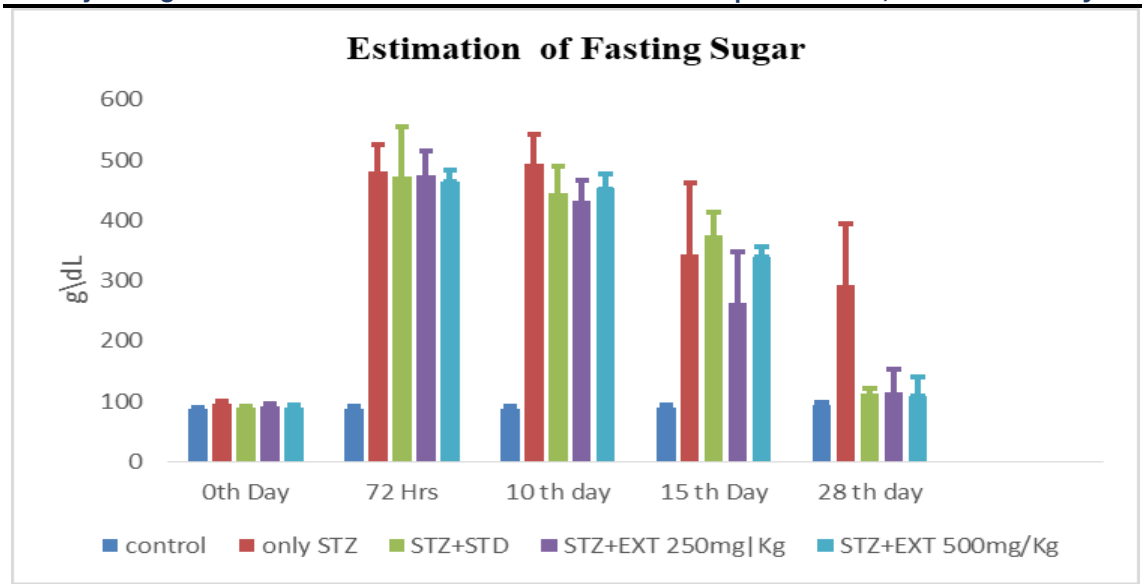

Figure:6 Analysis of *Glinus oppositifolius linn* extract on fasting blood sugar level

Hyperglycemia is caused by high rates of glycogenolysis and gluconeogenesis, as well as impaired glucose use by peripheral tissues due to decreased glucose uptake from the circulation. Because carbohydrates cannot be used as fuel in diabetes, the activity of hyperglycemic hormones becomes more prominent due to a shortage of insulin. A high glucagon level lowers the hepatic fructose-2,6 - bisphospate level, lowering glucose consumption. Insulin-dependent enzymes are less active, resulting in glycolysis suppression and gluconeogenesis promotion, resulting in hyperglycemia.

The delivery of STZ+NIC resulted in a 5 times increase in fasting blood sugar level in the current study, as shown in table 5.9. For around three weeks, the hyperglycemic state was maintained. After 28 days of daily treatment with the usual medicine glibenclamide and various doses of Glinus lotoides,mollugo cerviana (250 mg/Kg and 500 mg/Kg), blood sugar levels fell by 23–72 percent in a dose-dependent manner. The depletion was still rapid on the 15th day, and thereafter saw a steady and consistent decline in FBS.

The groups receiving 500mg/Kg weight of ethanolic extract of mollugo cerviana showed the greatest drop in glucose levels. As evidenced by the considerable increase in insulin levels in diabetic rats. Increased pancreatic production of insulin from existing -cells could be one plausible route for antihyperglycemic effect in diabetic rats. Several researchers have observed that using a variety of plants with antihyperglycemic action has a similar stimulatory impact on insulin release.

Conclusion:

The plants that includes in the study are *Glinus oppositifolius linn, Mollugo oppositifolius linn*,Ser, locally referred to as thread stem carpet weed. It is a member of the Molluginaceae family. Both plants are found in marshy wet land as a weed. that both plants has got immense pharmacological properties because of their rich ness in flavonoids class of secondary metabolites. Both the plant materials were reported to have anti-diabetic components in it.

The plant material were collected dried and extracted. Among these ethanolic extract of *Mollugo oppositifolius linn,*and hydro-alcoholic extract of *Glinus oppositifolius linn,* were taken for studies. *Glinus oppositifolius linn* was examined for its anti-inflammatory activity also. The in-vitro analysis of both extracts were carried out and compared with standard drug. After screening the anti- diabetic property was confirmed by in- vivo methods. Both the plant extracts found to have a moderate to high capacity to regulate the hyperglycemia and associated complications.

Then the extract was further purified to isolate the potent molecule with bioactive guided isolation method.

Acknowledgments:

The authors express their gratitude to the authority of SRS University and DNCOP College, facilities and encouragement for carrying out research work.

Reference

1. Loriaux, D Lynn (March 2006). "Diabetes and the Ebers Papyrus: 1552 B.C.". The Endocrinologist. 16 (2): 55–56.

2. Roberts, Jacob (2015). "Sickening sweet". Distillations. Vol. 1 no. 4. pp. 12–15. Retrieved 20 March 2018.

3. Poretsky, Leonid, ed. (2009). Principles of diabetes mellitus (2nd ed.). New York: Springer. p. 3. ISBN 978-0-387-09840-1

4. Regin Elsa George ,Siby Joseph A review of newer treatment approaches for type-2 diabetes: Focusing safety and efficacy of incretin based therapy

5. Ginter E., Simko V. (2013) Global Prevalence and Future of Diabetes Mellitus. In: Ahmad S.I. (eds) Diabetes. Advances in Experimental Medicine and Biology, vol 771. Springer, New York

6. World Health Organization: Diabetes Mellitus: Report of WHO Study Group. Geneva, World Health Org., 1985, (Tech. Rep. Ser., no. 727)

7. Ramachandran A, et al. High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia. 2001 Sep 1; 44(9):1094–101.

8. R. M. Anjana et al Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research–India Dibetes (ICMR–INDIAB) study Diabetes Care 2014 Jan; 37(Supplement 1): S81-S90. *Diabetologia* volume 54, pages3022–3027(2011)

9. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Diabetes Care 1997; 20:1183– 1197 2. Genuth S, Alberti KG, Bennett P, et al.;

10. American Diabetes Association Standards of medical care in diabetes--2014. *Diabetes Care.* 2014;37(3):S14–S80.

11. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes—2020*
American Diabetes Association, Diabetes Care 2020 Jan; 43

12. Pragya Tiwari1, Recent Trends in Therapeutic Approaches for Diabetes Management: A Comprehensive Update, Journal of Diabetes Research, Volume 2015.

13. J. B. Buse , "Overview of current therapeutic options in type 2 diabetes. Rationale for combining oral agents with insulin therapy," *Diabetes Care*, vol. 22, pp. 65–70, 1999.

14. Saudek CD, Herman WH, Sacks DB, Bergenstal RM, Edelman D, Davidson MB. A New Look at Screening and Diagnosing Diabetes Mellitus. The Journal of Clinical Endocrinology & Metabolism. 2008 Jul 1;93(7):2447–53.

15. Sheehy AM, Flood GE, Tuan W-J, Liou J, Coursin DB, Smith MA. Analysis of Guidelines for Screening Diabetes Mellitus in an Ambulatory Population. Mayo Clinic Proceedings. 2010 Jan 1;85(1):27–35.

16. Patel P, Macerollo A. Diabetes Mellitus: Diagnosis and Screening. AFP. 2010 Apr 1;81(7):863–70.

17. Wagman, A.S. Nuss, J.M ;Current Therapies and Emerging Targets for the Treatment of Diabetes, Current Pharmaceutical Design, Volume 7, Number 6, 2001, pp.417-450(34) 1.

18. Beverly JK, Budoff MJ. Atherosclerosis: Pathophysiology of insulin resistance, hyperglycemia, hyperlipidemia, and inflammation. Journal of Diabetes. 2020 Feb;12(2):102–4.

19. Skyler JS. Diabetes Mellitus: Pathogenesis and Treatment Strategies. J Med Chem. 2004 Aug 1;47(17):4113–7.

20. Verma PR et al ; Evaluation of antidiabetic antihyperlipidemic and pancreatic regeneration, potential of aerial parts of Clitoria ternatea. Revista Brasileira de Farmacognosia. 2013 Sep;23(5):819–29.

21. Juvekar, A.R. and Bandawane, D.D. (2009), 'Preliminary study on hypoglycemic effect of Alstonia scholaris Linn. in normal and streptozotocin induced diabetic rats', Advances in pharmacology and toxicology 10(3), 89–92.

22. Ashok Kumar, B.S et al (2012), 'Antidiabetic, antihyperlipidemic and antioxidant activities of methanolic extract of Amaranthus viridis Linn in alloxan induced diabetic rats', Experimental and Toxicologic Pathology 64(1-2), 75–79.

23. Pallab Das Gupta and Amartya De. Diabetes mellitus and its herbal treatment. International Journal of research in pharmaceutical and biomedical sciences. 2012; 3(2):706-720.

24. Evans, J.L., Goldfine, I.D., Maddux, B.A. and Grodsky, G.M. (2002), 'Oxidative Stress and Stress-Activated Signalling Pathways: A Unifying Hypothesis of Type 2 Diabetes', Endocrine Reviews 23(5), 599-622.

25. Wajchenberg, B.L. (2007), 'β-Cell Failure in Diabetes and preservation by clinical treatment', Endocrine Reviews 28(2), 187-218

26. Kusminski, C.M et al . (2009), 'Diabetes and apoptosis: lipotoxicity', Apoptosis 14(12), 1484-1495

27. Ullah Asmat et al ;Diabetes mellitus and oxidative stress—A concise review, Saudi Pharmaceutical Journal, Volume 24, Issue 5,2016, Pages 547-553,

28. Bansal and Bilaspuri, 2011 G.S. Bilaspuri, Impacts of oxidative stress and antioxidants on semen functions, Vet. Med. Int. (2011)

29. P.M. Patricia Reactive species and diabetes: counteracting oxidative stress to improve health Curr. Opin. Pharmacology. 9 (2009), pp. 771-779

30. Vincent, A.M. and Feldman, E.L. (2004), 'New insights into the mechanisms of diabetic neuropathy'. Reviews in Endocrine and Metabolic disorders 5(3), 227-236,