Original Research Article   **Volume 4, Issue 9 -2018**

Anti-Diabetic Evaluation of Siddha Formulation *Perungaya Chooranam* on Streptozotocin (STZ) Induced Type 2 diabetes mellitus in Wistar rats

K.Nithya*[1], A.Dhivyabharathi[2], N. Anbu[3], K.Kanakavalli[4]

[*1&2] P.G.Scholar, Government Siddha Medical College, Arumbakkam, Chennai 600106, Tamil Nadu, India.
[3]HOD, PG Department of Maruthuvam, Government Siddha Medical College, Arumbakkam, Chennai 600106, Tamil Nadu, India.
[4] Principal, Government Siddha Medical College,Arumbakkam, Chennai 600106, Tamil Nadu, India.
*Corresponding Author: Dr. K.Nithya, P.G.Scholar, Government Siddha Medical College, 6 Anna Arch Road, NSK Nagar, Arumbakkam, Chennai 600106, Tamil Nadu, India.

Abstract

Diabetes mellitus is a metabolic disorder characterized by loss of glucose homeostasis occurring due to defects in insulin secretion or insulin action resulting from impaired metabolism of glucose, lipids and other energy yielding fuels such as lipids and proteins. It is a major endocrine disorder affecting nearly 10 % population all over the world. Globally diabetes has shadowed the spread of modern lifestyle and it can be linked to an increase in overweight and sedentary population. Despite the great strides that have been made in the understanding and management of diabetes, the disease and its related complications are increasing at an alarming rate. Currently, several oral diabetic medicines with different pharmacological actions, for examples, biguanides involving suppression of glucose generation and appetite, -glucosidase inhibitors involving blocking intestinal glucose absorption, and sulfonylureas involving enhancement of insulin secretion, have been used.

Thus, adverse effect of these medicines including impairment of gastrointestinal function, hypoglycemia, and liver dysfunction. The usage of traditional Siddha medicines still an essential part of public healthcare. *Perungaya chooranam* (PC) is a traditional Siddha formulation has a claim of reducing blood sugar level in Siddha literature. Hence the main aim of the present research work is to evaluate the anti-diabetic potential of the Siddha drug PC in rat model. Type 2 diabetes mellitus (T2DM) in rats were induced with Streptozotocin (STZ) is a known inducer of T2DM in rats. The result of the study clearly shows that there was a significant reduction in the level of blood glucose level in rats treated with PC at the dose of 200 and 400 mg/kg. In conclusion Siddha medicines like PC has gaining much attention towards clinical management of T2DM due to increasing adverse event caused by conventional medication upon chronic usage in patients with T2DM.

Keywords: Diabetes mellitus, Siddha medicines, Streptozotocin, Perungaya chooranam, Blood glucose.

1. Introduction

Diabetes mellitus is a complex metabolic disorder resulting from either insulin insufficiency or insulin dysfunction. Type I diabetes (insulin dependent) is caused due to insulin insufficiency because of lack of functional beta cells. Patients suffering from this are therefore totally dependent on exogenous source of insulin while patients suffering from Type II diabetes (insulin independent) are unable to respond to insulin and can be treated with dietary changes, exercise and medication. Type II diabetes is the more common form of diabetes constituting 90% of the diabetic population. Symptoms for both diabetic conditions may include: (i) high levels of sugar in the blood; (ii) unusual thirst; (iii) frequent urination; (iv) extreme hunger and loss of weight; (v) blurred vision; (vi) nausea and vomiting; (vii) extreme weakness and tiredness; (viii) irritability, mood changes etc [1].

Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease [2,3]. In 2000, India (31.7 million) topped the world with the highest number of people with diabetes mellitus followed by China (20.8 million) with the United States (17.7 million) in second and third place respectively. According to survey the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India. It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease [4,5].India currently faces an uncertain future in relation to the potential burden that diabetes may impose upon the country.

Type 2 diabetes is increasing in prevalence worldwide [6], and it is strongly associated with obesity and insulin resistance [7], as well as defects in pancreatic -cell function and mass [8]. These metabolic disorders impede the critical regulatory influence of insulin on glucose, lipid and protein metabolism, thus precipitating a disease characterized by impairments in these physiological processes. However, it takes years to develop frank diabetes. Patients developing type 2diabetes have often gone through a state of obesity associated with reduced insulin sensitivity along with an activated -cell compensatory mechanism, such as excess basal insulin secretion and hyperproinsulinemia, as a part of their metabolic profile [9]. These pathological conditions occur early in the disease progression of type 2 diabetes [10], and before the -cells severely fail in late stage (insulin-dependent) type 2 diabetes[11-13].

There are several types of glucose-lowering drugs that exert anti-diabetic effects through different mechanisms. These mechanisms include stimulation of insulin secretion by sulfonylurea and meglitinides drugs, increasing of peripheral absorption of glucose by biguanides and thiazolidinediones [14], delay in the absorption of carbohydrates from the intestine by alpha-glucosidase, and reduction of hepatic gluconeogenesis by biguanides [15]. In the past three decades, despite the significant progress made in the treatment of diabetes, the results of treatment in patients is still far from perfect. These treatments have some disadvantages, including drugresistance (reduction of efficiency), side effects, and even toxicity. For example, sulfonylureas lose their effectiveness after 6 years of treatment in 44% of patients. It is also said that the glucose-lowering drugs are not able to control hyperlipidemia [16]. In addition, the side effects of medicines and their interactions with each other in vitro must be considered by medical staff. Today, many treatments that involve the use of medicinal plants are recommended [17]. Most plants contain carotenoids, flavonoids, terpenoids, alkaloids, glycosides and can often have anti-diabetic effects [18]. The anti-hyperglycemic effect that results from treatment with plants are often due to their ability to improve the performance of pancreatic tissue, which is done by increasing insulin secretions or reducing the intestinal absorption of glucose.

The most common herbal active ingredients used in treating diabetes are flavonoids, tannins, phenolic, and alkaloids [19]. The existence of these compounds implies the importance of the

anti-diabetic properties of these plants [20]. For example, tannin improves the function of pancreatic Beta-cells and increases insulin secretion. In fact, the mechanisms of actions for hypoglycemic plants include: increasing of insulin secretion, increasing of glucoses absorption by muscle and fat tissues, prevention of glucose absorption from the intestine, and prevention of glucose production from liver cells [21]. These factors are mostly responsible for the reduction or elimination of diabetes complications.

In diabetes, some herbal alternatives are proven to provide symptomatic relief and assist in the prevention of the secondary complication of the disease. Some herbs have also been proven to help in regeneration of ß-cells and in overcoming resistance. In addition to maintaining normal blood sugar level, some herbs are also reported to possess antioxidant activity and cholesterol lowering action. The management of type 2 diabetes mellitus is possible with drug that can lower the blood sugar level in one hand and restore the liver glycogen level on the other hand. In modern system of medicine, there is no drug, which is reported to possess both of the properties [21]. *Perungaya chooranam* (PC) is a traditional siddha formulation has a claim of reducing blood sugar level in siddha literature. Hence the main aim of the present research work is to evaluate the anti-diabetic potential of the siddha drug PC in rat model.

2. Materials and Methods

2.1. Source of raw drugs:

The Required raw materials were procured from a well reputed indigenous drug shop from, Chennai, Tamil Nadu, India .All raw drugs were authenticated by respective authorities before utilizing the same for the preparing the formulation.

2.2. Ingredients

The siddha formulation *Perungaya Chooranam* comprises of the following ingredients

Ferula asafoetida   - 4.2gm
Rock salt   - 8.4gm
Cuminum cyminum
Acorus calamus
Zingiber officinale
Terminalia chebula   - 12.6gm
Plumbago zeylanica
Costus speciosus

2.3. Formulation of Trial drug *Perungaya Chooranam* [22]

The above ingredients are made into fine powder separately and sieved using cloth. Fine powdered drugs were mixed together according to the proportions as directed in the literature. The final formulation was preserved in air tight container.

2.4.Animal

Healthy adult Wistar albino rats were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air. A 12 light / dark cycle were maintained .Room temperature was maintained between 22 ± 2^0 Cand relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water *ad libitum*. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of C.L.Baid Metha College of Pharmacy, Chennai, Tamil Nadu, India.XLVIII/07/CLBMCP/2016

2.4.Induction of diabetes by STZ in Rats [23]

Diabetes was induced in Wistar Albino rats aged 2–3 months (180–200 g body weight) by intraperitoneal administration of STZ (single dose of 55 mg/kg b.w) dissolved in freshly prepared 0.01 M citrate buffer, pH 4.5. After injection the animals had food and water *ad libitum*and were given 5% glucose in their drinking water for the first 24 hours to counter any initial hypoglycemia. The development of diabetes was confirmed after 72 hours of the Streptozotocin injection. After 72 hrs of STZ injection under mild anesthesia the blood was withdrawn from the tip of the tail of each rat and the blood glucose level was analyzed.

Animals with more than 250 mg/dl was considered as diabetic and was included in the study.

2.5. Grouping

The animals were divided into 5 groups each constituting 6 rats. Group I were normal rats, Group II were STZ (55 mg/kg b.w., i.p) induced diabetic rats. Group III STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with Glibenclamide 5mg/kg b.w/p.o Group IV STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with *Perungaya Chooranam* 200mg/kg b.w/ p.o Group V STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with *Perungaya Chooranam* 400mg/kg b w/p.o for 28 days. Fasting blood glucose levels was measured before the administration of extracts. The blood glucose levels were checked on 0th, 7th, 14th, and 21st day of the treatment period. Blood was collected from snipping of the rat tail. Blood glucose levels were measured.

| Groups	Treatment
Group I	Normal Control
Group II	Diabetic control- STZ (55 mg/kg)
Group III	Diabetic control- Glibenclamide (5 mg/kg)
Group IV	Diabetic control- PC 200mg/kg
Group V	Diabetic control- PC 400mg/kg

3. Results

3.1. Effect of *Perungaya Chooranam* on Blood glucose profile of STZ induced diabetic rats

Results of the present investigation had clearly shown that treatment with STZ has significantly increased the blood sugar level of about 295 mg/dl measure on 28th day of post induction. Treatment with test drug PC at the dose of 200 and 400 mg/kg has remarkable action on reducing blood sugar of about 128 mg/dl on low dose and 114 mg/dl on high dose. Further standard drug glibenclamide possess similar reduction in blood glucose 104 mg/dl at the dose of 5mg/kg.

Table 1: Effect of *Perungaya Chooranam* on Blood glucose profile of STZ induced diabetic rats

Group	Blood glucose (mg/dl)				
	Day – 0	Day – 7	Day – 14	Day – 21	Day – 28
I	90.40±1.13	88.23±1.328	92.45±2.78	87.13±2.43	93.60±2.18
II	104.22±1.14	244.9±1.66	276.3±1.46	290.8±1.33	295.4±1.22
III	103.5±1.46	152.0±1.32	142.05±1.30	116.3±1.48	104.3±1.46
IV	99.13±1.22	221.5±1.24	191.2±2.27	161.8±1.26	128.5±1.44
V	94.23±1.38	179.8±1.34	158.04±1.98	131.03±1.76	114.8±1.84
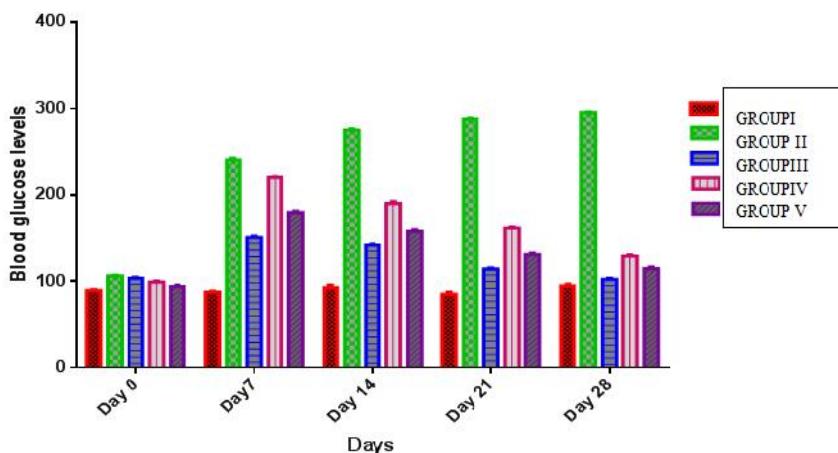
Figure 1: Blood glucose level of *Perungaya Chooranam* and standard drug treated diabetic rats

4. Discussion

Diabetes mellitus is one of the most important health issues in Mauritius with a prevalence of 24.5% in 2015 [24]. The International Diabetes Federation reported that in 2015 there were 220,000 cases of diabetes in Mauritius and the number of cases of diabetes in adults that are undiagnosed was found to be 113100. Alterations in carbohydrates, protein, and fat metabolism entail an increase in blood glucose level which causes long-term devastating complications in many organs of the body [25]. Prolonged uncontrolled hyperglycemic level leads to macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and to microvascular complications (diabetic nephropathy, neuropathy, and retinopathy) [26]. Complications related to diabetes are the major cause of disability and mortality among the Mauritian diabetic population.

Type 2 diabetes mellitus (T2DM) is a chronic illness due to endocrine dysfunction. Uncontrolled, diabetes is associated with various acute and chronic comorbidities. T2DM is a rapidly growing health concern in both developed and developing nations. T2DM accounts for over 90% of cases globally [27,28]. According to the World Health Organization (WHO), in 2011, approximately 364 million people globally suffer from diabetes (DM), with projections that DM-related deaths will double from 2005 to 2030 [29]. In 2004, 3.4 million people died directly from the consequences of high blood glucose. The prevalence of DM worldwide was calculated as 2.8% in 2000. This is expected to increase to 4.4% by 2030 [30]. The growing concern is the epidemic growth in obesity and increase in the elderly population, which will continue to increase the prevalence of DM. Another study, using data from 91 countries, estimates that the prevalence can be as high as 7.7% (439 million adults) by 2030. Other estimates include a 70% increase in DM in developing countries and 20% increase in developed nations.

Type 2 diabetes is associated with insulin resistance, and a lack of appropriate compensation by the beta cells leads to a relative insulin deficiency. Insulin resistance can be improved by weight reduction and exercise [31]. If lifestyle intervention fails, there are a variety of drugs available to treat type 2 diabetes [32], which can be divided into five main classes: drugs that stimulate insulin production from the beta cells (e.g. sulphonylureas), drugs that reduce hepatic glucose production (e.g. biguanides), drugs that delay carbohydrate uptake in the gut (e.g. - glucosidase inhibitors), drugs that improve insulin action (e.g. thiazolidinediones) or drugs targeting the GLP-1 axis (e.g. GLP-1 receptor agonists or DPP-4 inhibitors).

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 important areas of investigation[33]. Many oral hypoglycemic agents are currently used in the clinical practices, but these synthetic agents are unsatisfactory in terms of preventing secondary complications and adverse side effects of disease [34,25]. Recently, novel herbal medicines have been recommended as novel anti-diabetic treatments for their efficacy in the human clinical trials with minimal side effects [36,37]. The ethnobotanical information on the potential antidiabetic medicinal plants has been reported for approximately 800 plants [38]. However, only a few have been evaluated scientifically regarding their activities.Results of the present investigation has clearly shown that treatment with STZ has significantly increased the blood sugar level of about 295 mg/dl measure on 28th day of post induction. Treatment with test drug PC at the dose of 200 and 400 mg/kg has remarkable action on reducing blood sugar of about 128 mg/dl on low dose and 114 mg/dl on high dose. Further standard drug glibenclamide

possess similar reduction in blood glucose 104 mg/dl at the dose of 5mg/kg. Alternate therapy is a novel approach for chronic management of diabetes as it render more therapeutic benefits with no side effects and further its much cost effective for affordable for people from lower economic zone.

5. Conclusion

Diabetes is multifactorial disease that has a significant adverse impact on health and mortality particularly from cardiovascular diseases. Now, a day, herbal drugs are gaining popularity in the treatment of diabetes and its related complications.New drugs or formulations which are devoid of the side effects caused by conventional medication will improve the compliance in type 2 diabetic patients. Our present study results clearly demonstrated that there was a significant reduction in the level of blood glucose level in rats treated with PC at the dose of 200 and 400 mg/kg. From this it was concluded that *Perungaya chooranam* possesses potent antidiabetic action may be due to bioactive components present in the formulation.

Acknowledgements

6. References

1. Manisha Modak. Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes. J Clin Biochem Nutr. 2007 May; 40(3): 163–173.
2. Joshi SR, Parikh RM. India - diabetes capital of the world: now heading towards hypertension. J Assoc Physicians India. 2007;55:323–4.
3. Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues. Australas Med J. 2013;6(10):524–31.
4. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(3):1047–53.
5. Whiting Dr, Guariguata L, Weil C, Shawj. IDF Diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011;94:311–21.
6. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010; 87: 4–14.
7. Unwin N, Gan D, Whiting D. The IDF Diabetes Atlas: providing evidence, raising awareness and promoting action. Diabetes Res Clin Pract 2010; 87: 2–3.
8. Guilherme A, Virbasius J, Vishwajeet P, *et al*. Adipocyte dysfunction linking obesity to insulin resistance and type 2 diabetes. Nat Rev Mol Cell Biol 2008; 9: 367–377.
9. Yoon KH, Lee JH, Kim JW, *et al*. Epidemic obesity and type 2 diabetes in Asia. Lancet 2006; 368: 1681–1688.
10. Bell GI, Polonsky KS. Diabetes mellitus and genetically programmed defects in beta-cell function. Nature 2001; 414: 788–791.
11. Butler AE, Janson J, Bonner-Weir S, *et al*. Beta-cell deficit and increased beta-cell apoptosis in humans with type 2 diabetes. Diabetes 2003; 52: 102–110.
12. Kahn SE, Halban PA. Release of incompletely processed proinsulin is the cause of the disproportionate proinsulinemia of NIDDM. Diabetes 1997; 46: 1725–1732.
13. Tabak AG, Jokela M, Akbaraly TN, *et al*. Trajectories of glycemia, insulin sensitivity and insulin secretion preceeding the diagnosis of type 2 diabetes: The Whitehall II Study. Lancet 2009; 373: 2215–2221.

14. Bathaie S, Mokarizade N, Shirali S. An overview of the mechanisms of plant ingredients in the treatment of diabetes mellitus. J Med Plant. 2012;4(44):1–24.

15. Hui H, Zhao X, Perfetti R. Structure and function studies of glucagon-like peptide-1 (GLP1): the designing of a novel pharmacological agent for the treatment of diabetes. Diabetes Metab Res Rev. 2005;21:313–31.

16. Dey L, Attele AS, Yuan CS. Alternative therapies for type 2 diabetes. Altern Med Rev. 2002;7:45–58.

17. Kooti W, Moradi M, Akbari SA, Sharafi-Ahvazi N, AsadiSamani M, Ashtary-Larky D. Therapeutic and pharmacological potential of Foeniculum vulgare Mill: A review. J HerbMed Pharmacol. 2015;4:1–9.

18. Afrisham R, Aberomand M, Ghaffari MA, Siahpoosh A, Jamalan M. Inhibitory Effect of Heracleum persicum and Ziziphus jujuba on Activity of Alpha-Amylase. Journal of Botany. 2015;2015:1–8.

19. Mamun-or-Rashid A, Hossain MS, Naim Hassan B, Kumar Dash M, Sapon A, Sen MK. A review on medicinal plants with antidiabetic activity. Journal of Pharmacognosy and Phytochemistry. 2014;3(4):149–59.

20. Gupta PD, De A. Diabetes Mellitus and its herbal treatment. International Journal of Research in Pharmaceutical and Biomedical Sciences. 2012;3(2):706–21.

21. Hegazy GA, Alnoury AM, Gad HG. The role of Acacia Arabica extract as an antidiabetic, antihyperlipidemic, and antioxidant in streptozotocin-induced diabetic rats. Saudi medical journal. 2013;34(7):727–33.

22. Sarabenthira Vaithiya Rathna Vali – Page No : 19

23. A. Akbarzadeh. Induction of diabetes by Streptozotocin in rats. Indian J Clin Biochem. 2007 Sep; 22(2): 60–64.

24. International Diabetes Federation. *Mauritius*. Brussels, Belgium: International Diabetes Federation; 2015.

25. Qamar F., Afroz S., Feroz Z., Siddiqui S., Ara A. Evaluation of hypoglycemic effect of *Cassia italic* . *Journal of Basic and Applied Sciences*. 2011;7(1):61–64.

26. Fowler M. J. Microvascular and macrovascular complications of diabetes. *Clinical Diabetes*. 2008;26(2):77–82. doi: 10.2337/diaclin.26.2.77.

27. Zimmet P, Alberti KGMM, Shaw J. Global and societal implications of the diabetes epidemic. *Nature*. 2001;414(6865):782–787.

28. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. *Diabetes Research and Clinical Practice*. 2010;87(1):4–14.

29. World Health Organization. *Diabetes: Key Facts*. Geneva, Switzerland: World Health Organization; 2011.

30. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care*. 2004;27(5):1047–1053.

31. Solomon TP, Sistrun SN, Krishnan RK, Del Aguila LF, Marchetti CM, O'Carroll SM, et al. Exercise and diet enhance fat oxidation and reduce insulin resistance in older obese adults. J Appl Physiol. 2008;104:1313–1319.

32. Krentz AJ, Patel MB, Bailey CJ. New drugs for type 2 diabetes mellitus: what is their place in therapy? Drugs. 2008;68:2131–2162.

33. Saxena A, Vikram NK. Role of selected Indian plants in management of type 2 diabetes: a review. J Altern Complement Med. 2004;10(2):369–378.

34. Vetrichelvan T, Jegadeesan M. Anti-diabetic activity of alcoholic extract of Aerva lanata (L.) Juss. ex Schultes in rats. J Ethnopharmacol. 2002;80:103–107.

35. Westphal SA, Palumbo PJ. Insulin and oral hypoglycemic agents should not be used in combination in the treatment of type 2 diabetes. Arch Intern Med. 2003;163:1783–785.

36. Chien SC, Young PH, Hsu YJ, Chen CH, Tien YJ, Shiu SY, Li TH, Yang CW, Marimuthu P, Tsai LF, Yang WC. Antidiabetic properties of three common Bidens pilosa variants in Taiwan. Phytochemistry. 2009;70:1246–1254.

37. Modak M, Dixit P, Londhe J, Ghaskadbi S, Paul A. Indian herbs and herbal drugs used for the treatment of diabetes. J Clin Biochem Nutr. 2007;40:163–173.
38. Mentreddy SR. Medicinal plant species with potential antidiabetic properties. J Sci Food Agric. 2007;87:743–750.

Access this Article in Online	
 Quick Response Code	Website: www.ijcrims.com
	Subject: Siddha Medicine

How to cite this article:
K.Nithya, A.Dhivyabharathi, N. Anbu, K.Kanakavalli. (2018). Anti-Diabetic Evaluation of Siddha Formulation *Perungaya Chooranam* on Streptozotocin (STZ) Induced Type 2 diabetes mellitus in Wistar rats. Int. J. Curr. Res. Med. Sci. 4(9): 25-32.
DOI: http://dx.doi.org/10.22192/ijcrms.2018.04.09.XXX