ejpmr, 2016,3(9), 388-394.

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 3294-3211

EJPMR

COMBINED EFFICACY OF ALOE VERA AND TURMERIC ON LIPID PROFILE OF STREPTOZOTOCIN INDUCED ALBINO RATS

[1]*Dr. Shruti Agrawal and [2]Dr. Pratiti Ghosh

[1]Assistant Professor & Head, Department of Food & Nutrition, Budge Budge College, Kolkata.
[2]Professor & Head, Department of Physiology, West Bengal State University, Barasat.

***Correspondence for Author: Dr. Shruti Agrawal**

Assistant Professor & Head, Department of Food & Nutrition, Budge Budge College, Kolkata.

Article Received on 05/07/2016 **Article Revised on 25/07/2016** **Article Accepted on 15/08/2016**

ABSTRACT

WHO revealed that 422 million people are living with diabetes mellitus and it is the seventh leading cause of death in the world. While the ratio of men-to-women afflicted with diabetes is roughly equal, women are uniquely and often more severely, affected by the complications of diabetes. One in every 11 individual is a diabetic patient. Various medications are generally recommended as the first line of treatment for type II diabetes as there is fair evidence that they decrease mortality, but there are various side effects. Hence, present research work aimed to experimentally develop a home based low cost concoction to reduce the blood sugar level using aloe vera and turmeric in various proportions and to find the effect of its various doses on the lipid profile of experimental female albino rats. It has been found that high dose showed a rapid hypoglycemic effect, thus necessitating further examination to confirm the ill or good effect of high dose. This concoction was found to lower raised glucose, triglyceride, VLDL and total cholesterol levels and is significant on .01 and .05 level. Hence, aloe vera & turmeric combination in high proportion showed effective results which were consistent with the previous studies done with aloe vera or turmeric singly.

KEYWORDS: hyperglycemia, hyper-triglyceridemia, aloe vera, curcumin.

1. INTRODUCTION

The global prevalence of diabetes among adults over 18 years of age has risen from 108 million (4.7%) in 1980 to 422 million (8.5%) in 2014.[1] Its incidence is escalating rapidly so WHO projects that diabetes will be the 7th leading cause of death in 2030.[2] About 422 million people worldwide suffer from diabetes, 149 million of whom are women. While the ratio of men-to-women afflicted with diabetes is roughly equal, women are uniquely and often more severely, affected by the complications of diabetes. One in every 11 individual is a diabetic patient. International Diabetes Federation Atlas 2015 revealed that every seven second a person dies from diabetes and about 4.9 million deaths are attributed to diabetes in 2014. In India, the average age for onset of diabetes is around 40 whereas in other countries, it is around 55. The prevalence of diabetes mellitus in West Bengal (among all aged people) was found to be higher among males than females when assessed in rural, industrial and urban habitats.[3] 90% of all the diabetic cases are accounted by Type II diabetes mellitus(T2DM) among adults worldwide. In general, as countries become richer, people consume more of sugar-fat-rich diet and are less physical active and the incidence of diabetes rises.

Despite diabetes being a life-long disorder, expensive to manage and afflicts larger masses among developing societies, there is lack of data on its economic burden upon India. The expenses needed for India to treat type II diabetes mellitus is estimated to be around 2.2 billion USD. In India, the direct medical cost to identify one subject with insulin glucose tolerance is INR 5,278.[4] The cost of insulin amounts to 16,000 Indian Rupees per year, while medication for non-insulin-requiring patients costs about 70.00 USD or 4200 Indian Rupees annually.[5] In the Indian context, these costs are prohibitive: 75.5% of the Indian population is earning less than Rs.120 per day and 41.6% less than Rs.107 per day.[6]

Various medications such as metformin, sulfonylurea, biguanides, thiazolidinedione, secretagogues are generally recommended as the first line of treatment for type II diabetes as there is fair evidence that they decrease mortality. Insulin is also used but it leads to various adverse effects including flatulence, bloating and other gastrointestinal (GI) complaints. It is not recommended in patients with inflammatory bowel disease, colonic ulceration, partial intestinal obstruction or chronic intestinal disease associated with disorders of digestion or absorption. Sometimes complications such as hypoglycemia, weight gain, allergic reactions,

pruritus, rash, hepatotoxicity, nausea, diarrhea, flatulence, lactic acidosis, etc. may also occur.

Many drugs have been withdrawn from the market after such broader usages due to their higher toxicity. Unlike most synthetic drugs that have pure ingredients, such as small molecules or just a single protein, any herb has multiple complex ingredients. Those distinct ingredients in one herb may balance each other, buffer each other or act synergistically to make the systemic effect more powerful. Such combination of herbs takes advantage of the interactions among different ingredients from multiple herbs for more balanced, less toxic and more powerful effects. The complex ingredients in herbal recipes are closer to nature and usually can be absorbed and processed better by the complicated human body. Aloe vera and turmeric are well documented herbs for the treatment of diabetes mellitus.

Aloe vera is a succulent plant species that probably originated in northern Africa. Aloe vera leaves contain phytochemicals such as acetylated mannans, polymannans, anthraquinone C-glycosides, anthrones and anthraquinones including emodin and various lectins which are under study for possible bioactivity. Lophenol, 24-methyl-lophenol, 24-ethyl-lophenol, cycloartanol and 24-methylene-cycloartanol had also been isolated from aloe gel.[7]

Turmeric contains upto 5% essential oils and 5% curcumin, of which curcumin is the active substance. Polyphenol of turmeric and curcumin is known as C.I. 75300 or Natural Yellow 3. The systematic chemical name is (1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione. It can exist in at least two tautomeric forms, keto and enol. The keto form is preferred in solid phase and the enol form in liquid solution. Curcumin is a pH indicator. In acidic solutions (pH <7.4) it turns yellow, whereas in basic (pH > 8.6) solutions, it turns bright red.

Hence, present research work aimed to experimentally develop a home based low cost concoction to reduce the blood sugar level using aloe vera and turmeric in various proportions and to find the effect of its various doses on the lipid profile of experimental female albino rats.

2. METHODOLOGY

2.1. Experimental modeling

Female albino rats, weighing about 100–120 ±10 g, obtained from Bengal Chemicals, Kolkata, were used in this study. The animals were fed with the normal diet (as per ICMR guidelines) for two weeks to allow acclimatization to the experimental conditions before the commencement of the actual study. The experiments were conducted according to the ethical norms approved by Ministry of Social Justices and Empowerment, Government of India and Institutional Animal Ethics Committee Guidelines (IAEC) of West Bengal State University. Four animals were housed in individual polypropylene cages (47cm x 34cm x 20cm), lined with husk with free access to water and food in temperature controlled animal facility under a 12h light–dark cycle at 22±2°C and 55±5% humidity. Care of animals was taken as per guidelines of CPCSEA, Dept. of Animal Welfare, Govt. of India.[8] The project was approved by West Bengal State University, Institutional Animal Ethics Committee meeting held on 24/3/14.

2.2. Preparation of test formulation

Fresh and healthy Aloe vera leaves weighing between 550-650 g with approximate length 50-70 cm were collected from matured healthy plant and washed thoroughly with fresh running tap water. The leaves were dissected longitudinally and fleshy mucilaginous pulp (parenchymatous tissues) was selectively scraped out, leaving behind the thick epidermis layers. The scraped pulp was homogenized in an electrical blender and mixed with water to produce a stock concentration of 0.5mg/ml. It was then diluted with water to obtain the concentrations required for body weight.

Turmeric rhizome was cleaned, peeled, chopped and was grinded to paste to which water was added to obtain a concentration of 1mg/ml and then diluted to for the needed concentration (used as dose according to body weight).[9]

2.3. Induction of experimental diabetes

Streptozotocin (STZ) was used to induce diabetes mellitus in normoglycemic female albino rats. A freshly prepared solution of STZ (40mg/kg body weight) in

0.1M citrate buffer, pH 4.5 was injected intra peritoneal in a volume of 1ml/kg body weight to overnight fasted rats. The animals were considered diabetic when their blood glucose levels were above 250 mg/dl on the 4th day after STZ injection, else, the same dose of STZ was repeated after one week until the levels were above 250 mg/dl.[10]

2.4. Experimental design

Rats were divided into seven groups of four animals (n=4) in each group:

GROUP	DISEASE PREVALENCE	INDUCED TEST FORMULATION
Group –I	Non-diabetic (Negative Control)	N/A
Group –II	Diabetic (Positive Control)	N/A
Group- III	Diabetic	Aloe vera
Group- IV	Diabetic	Turmeric
Group- V	Diabetic	Aloe vera+ Turmeric (low dose)
Group- VI	Diabetic	Aloe vera+Turmeric (medium dose)
Group-VII	Diabetic	Aloe vera+Turmeric (high dose)

2.5. Dose sequence

TREATED GROUPS	DOSE GIVEN FOR TREATMENT	
	TURMERIC(mg/kg)	ALOEVERA(mg/kg)
Group-III: Diabetes + Turmeric	100	_
Group-IV: Diabetes + Aloe vera	_	200
Group-V: Diabetes + Aloe vera+ Turmeric (low dose)	50	100
Group-VI: Diabetes + Aloe vera + Turmeric (medium dose)	100	200
Group-VII : Diabetes + Aloe vera +Turmeric (high dose)	150	300

2.6. Feeding pattern

The dosing schedule was once in 24 hours. The aqueous solution was fed through oral gavages for 30 days experimental period at a fixed time in the morning around 10:30 A.M. Oral gavage was performed using a ball ended feeding needle. The animal was monitored after the procedure to ensure that there were no adverse effects.

2.7. Serum & blood collection

At the end of the experimental period, albino rats were euthanized by diethyl ether and sacrificed by cervical dislocation to determine plasma glucose, haemoglobin and lipid levels from blood samples. After hemoglobin analysis, the blood samples left for 15 minutes at 37°C for serum separation, centrifuged at 3000 rpm for 20 minutes and then stored at -20°C until further analyses.[9]

2.8. Biochemical assay

a) Glucose estimation: Blood sugar was measured by using Glucometer by Contour^{TS} Blood Glucose meter & Contour^{TS} Blood Glucose strip.

b) Lipid profile estimation

Total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) were estimated in a spectrophotometer using commercial kit (Cogent, Span Diagnostic Ltd, India) following standard procedures as given by the manufacturer. Glycerol free triglyceride & VLDL level was calculated from triglycerides (TG) by standardized formula.

2.9. Statistical analysis

The data were presented as mean ±SD. A t-test was done to find out the significance level (p value) using the Statistical Package for Social Science (SPSS) version 22.0.

The work was done in triplicate sets to ensure efficacy of the combined doses.

3. RESULT AND DISCUSSION

Table 1: Blood Glucose Level (mg/dl) Decreases in the Albino Rats after Treatment with the Herbal Concoction Compared to the Control Group

	BEFORE TREATMENT	AFTER TREATMENT
Group-I	115.25±10.22	119.23±13.76
Group –II	267.75±17.34	312.0±10.13
Group-III	283±21.30	240.50±11.44
Group-IV	284±17.60	240.75±6.75
Group-V	245.25±26.42	177.0±17.46
Group-VI	250.75±25.47	119.75±8.53*
Group-VII	268.50±15.78	80.50±9.33

*T –test is significant at 0.01 level

Streptozotocin induced rat showed rapid increase in glucose level. Singly turmeric and aloevera treatment lowered the glucose level and combined supplementation with aloe vera-turmeric, furthered the reduction in blood glucose level. The dose was administered in three different doses among which the medium dose showed good and effective change in the glucose level as high dose showed rapid hypoglycemic effect, which is detrimental to health.

The previous studies[11,12] showed a significant decrease in the plasma glucose when 300 mg/kg body weight and 500 mg/kg body weight of Aloe vera ethanolic extract was administered. Aqueous extracts of Aloe vera leaf possesses the maximum FSG (fasting sugar glucose) lowering capacity.[13] Aloe vera leaf pulp extract showed hypoglycaemic activity on IDDM and NIDDM rats, the effectiveness being enhanced for type II diabetes in comparison with glibenclamide.[14] The high levels of blood and urine glucose in diabetic patients were significantly reduced by administration of Aloe vera. Turmerin present in volatile oils of turmeric inhibited glucosidase enzymes more effectively than the reference standard drug acarbose.[15] Water soluble compounds of turmeric exhibit insulin releasing and mimicking actions within in vitro tissue culture conditions leads to glucose homeostasis.[16] Orally ingested curcumin reverses many of the inflammatory and metabolic derangements associated with obesity and improves glycemic control in mouse models of type 2 diabetes.[17] Prophylactic use of curcumin may effectively rescue islets from damage without affecting the normal function of these cellular structures.[18] Curcuminoids and sesquiterpenoids in turmeric exhibit hypoglycemic effects via PPAR-gamma activation.[19]

Table 2: Serum Triglyceride (mg/dl) Decreases in the Albino Rats after Treatment with the Herbal Concoction Compared to the Control Group

	BEFORE TREATMENT	AFTER TREATMENT
Group-I	58.25±5.18	57.39±5.09
Group-II	68.75±8.18	76.03±1.67
Group-III	71.13±3.02	64.14±0.64
Group-IV	69.24±5.09	58.51±0.57
Group-V	69.97±6.23	57.93±0.74*
Group-VI	68.73±8.03	57.71±0.88*
Group-VII	68.73±4.82	55.38±0.26*

* T –test is significant at 0.01 level.

Streptozotocin induced rat showed rapid increase in triglyceride level which was reversed by turmeric and aloe vera treatment. High dose showed a noticeable decrease in the TG level, which may be considered effective in lowering its level.

Oral administration of aloe vera gel extract caused a significant decrease in the elevated levels of serum total cholesterol and triacylglycerols[20-22] by 31% and 20.61% respectively as compared to untreated diabetic group. Treatment with Dihar (100 mg/kg) for 6 weeks, in which turmeric was main ingredient, produced decrease in STZ induced lipids levels as compared to control[23,24] showed lipid-lowering effect of *Curcuma longa* in diabetic rats.

Table 3: Very Low Density Lipoprotein (VLDL) Level (mg/dl) Decreases in the Albino Rats after Treatment with the Herbal Concoction Compared to the Control

	BEFORE TREATMENT	AFTER TREATMENT
Group-I	11.65±1.04	11.48±1.02
Group -II	13.75±1.64	15.21±0.17
Group-III	14.23±0.60	12.83±0.13
Group-IV	13.85±1.02	11.70±0.11
Group-V	14.00±1.25	11.59±0.15
Group-VI	13.75±1.60	11.54±0.17
Group-VII	13.75±0.97	11.08±0.49

Streptozotocin induced rat showed rapid increase in VLDL level. Turmeric and aloe vera treated rats also showed lower VLDL level, but when the rats were given combined supplementation of aloevera & turmeric, the level improves. The dose was administered in three different doses among which the high dose shows a noticeable change in the VLDL level. Thus it can be said that the high dose was effective in lowering VLDL level.

Previous study showed that oral administration of aloe vera gel extract caused a significant decrease in the elevated levels of VLDL.[20,21]

Table 4: Total cholesterol Level (mg/dl) Decreases in the Albino Rats after Treatment with the Herbal Concoction Compared to the Control

	BEFORE TREATMENT	AFTER TREATMENT
Group-I	85±4.22	85±5.10
Group -II	122.70±20.68	137.30±19.0
Group-III	83.05±6.61	80.00±8.83
Group-IV	128.55±8.71	125.00±8.52*
Group-V	61.70±16.43	57.78±15.63
Group-VI	61.00±3.56	55.00±3.74
Group-VII	60.90±7.04	53.09±6.66**

*T –test is significant at 0.01 level, ** T –test is significant at 0.05 level.

Present result revealed that the high dose is effective in reducing increased cholesterol level and is highly significant at .05 level. Aloe gel may be a safe anti-hypercholesterolemic agent for hyperlipidemic type 2 diabetic patients.[30] Oral administration of aloe vera gel extract (300 mg/kg bodyweight) for 21 days resulted in a significant reduction in plasma cholesterol.[21] Curcumin has the ability to lower blood cholesterol levels has been explained.[26]

Table 5: High Density Lipoprotein (HDL) (mg/dl) Decreases in the Albino Rats after Treatment with the Herbal Concoction Compared to the Control

	BEFORE TREATMENT	AFTER TREATMENT
Group-I	24.19±1.23	24.27±1.49
Group -II	19.44±2.19	12.64±1.91
Group-III	20.00±1.83	16.24±1.56
Group-IV	20.28±0.57	24.25±0.87
Group-V	20.37±0.52	27.41±1.26*
Group-VI	22.28±0.74	31.67±0.90*
Group-VII	22.37±0.70	32.30±1.08**

*T –test is significant at 0.01 level, ** T –test is significant at 0.05 level.

Streptozotocin induced rat showed rapid increase in total cholesterol and HDL-C level. Turmeric and aloe vera treated rats showed lowered total cholesterol and HDL-C level, where the maximal decrease was observed with combined high dose of aloevera & turmeric. and is also found to be highly significant.

Some previous study showed treatment with *A. greatheadii* moderately increased HDL-C levels and significantly decreased TC: HDL-C ratios.[27] HDL value in groups given aloe vera aqueous extract (150 and 200mg/kg of body weight respectively) were significantly increased, compared with those given 100mg/kg of body weight.[28] In another study, the decreased plasma levels of high-density lipoprotein–cholesterol in diabetic rats were restored to near normal levels following treatment with the extract of aloe vera.[21]

4. CONCLUSION

Previous studies showed that aloe vera and turmeric were helpful in reducing blood glucose level but moderately high combined dose of aloe vera and turmeric (200mg/kg and 100mg/kg body weight respectively) showed significantly noticeable decrease in blood glucose level. High dose (aloe vera and turmeric in the ratio of 300 mg/kg body weight and 150mg/kg body weight respectively) showed a rapid hypoglycemic effect, thus necessitating further examination to confirm the ill or good effect of high dose. This concoction was found to lower raised glucose, triglyceride, VLDL and total cholesterol levels. Hence, aloe vera & turmeric combination in high proportion showed effective results which were consistent with the previous studies done with aloe vera or turmeric singly.

5. ACKNOWLEDGEMENT

We owe sincere thanks to UGC for funding this project (Letter no. F.PSW-183/11-12).

6. REFERENCES

1. Global report on diabetes. World Health Organization, Geneva, 2016.
2. Mathers CD, Loncar D. (2006) "Projections of global mortality and burden of disease from 2002 to 2030". *PLoS Med*, 3(11): e442.
3. Das S, Maji D, Majumder PP. "Prevalence of diabetes in various habitats of West Bengal", Indian J Indian Med Assoc. 2005; 103(11): 580-4.
4. Ramachandran A. "Socio-Economic Burden of Diabetes in India". Journal of Association of Physicians of India, 2007; 55: 9-12.
5. Shobhana R, P Rama Rao, Lavanya A, Williams R, Vijay V, Ramachandran A. Expenditure on health care incurred by diabetic subjects in a developing country: A study from southern India". Diabetes Research and Clinical Practice, 2000; 48: 37-42.
6. Prabhakaran D, Ajay V. "Non-communicable Disease in India: A perspective". Centre for Chronic Disease Control discussion report for the WHO 2009, New Delhi, India.
7. Tanaka M, Misawa E, Ito Y, Habara N et al. "Identification of five phytosterols from Aloe vera gel as anti-diabetic compounds." Biol Pharm Bull, 2006; 29(7): 1418-22.
8. Palanisamy M, GAnnesan K, Murugan Rajadurai. "Antidiabetic Efficacy of Ellagic Acid in Strteptozotocin Induced Diabetes Mellitus in Albino Wistar Rats" Asian Journal of Pharm & Clinical Research, 2011; 4(3).
9. Hussein M.A., Jamil, K. and Rao, M. "Hypoglycemic, hypolipidemic and antioxidant properties of tulsi (Ocimum sanctum Linn) on streptozotocin induced diabetes in rats". 2002; Ind. J. clin. Biochem. 16(2): 190-194.
10. Sweety Lanjhiyana, Debapriya Garabadu." Antihyperglycemic potential of Aloe vera gel in Experimental Animal Model" Annals of Biological Research, 2011; 2(1): 17-31.
11. Ravi Naik Mude, Swapna Rekha Somesula, Pradeepkiran Jangampalli Adi, Bhaskar Matcha. "Diabetic Regulation Through Blood Constituents' Modulations On Treatment With Aloe vera In Alloxan Induced Diabetic Rats" Digest Journal Of Nanomaterials And Biostructures, 2012; 7(2): 649–655.
12. Vanitha M.N, Vasudha K.C et al. "Serum Adenosine DeaminaseActivity in Type 2 Diabetes Mellitus Patients" Int J Diabetes Dev Ctries, 2012 doi 10.1007/s3410-012-0087-x.
13. Deepak Kumar, Versha Parcha, Alok Maithani and Ishan Dhulia. "Effect and evaluation of antihyperlipidemic activity guided isolated fraction from total methanol extract of *Salvadora oleoides (Decne.)* in Triton WR-1339 Induced hyperlipidemic rats" Pharmacogn Mag. 2012; 8(32): 314–318.
14. Okyar A, Can A, Akev N, Baktir G, Sütlüpinar N. "Effect of Aloe vera leaves on blood glucose level in type I and type II diabetic rat models." Phytother Res. 2001 Mar; 15(2): 157-61.
15. Lekshmi PC, Arimboor R, Indulekha PS, Menon AN. Turmeric (Curcuma longa L.) volatile oil inhibits key enzymes linked to type 2 diabetes. Int J Food Sci Nutr. 2012; 63(7): 832-4.
16. Suresh kumar, Mohan kumar, James R. McFarlane "An aqueous extract of *Curcuma longa* (turmeric) rhizomes stimulates insulin release and mimics insulin action on tissues involved in glucose homeostasis *in vitro". Phytotherapy Research. 2011*; 25(3): 396–401.
17. Stuart P. Weisberg, Rudolph Leibel, Drew V. Tortoriello. "Dietary Curcumin Significantly Improves Obesity-Associated Inflammation and Diabetes in Mouse Models" Diabetes Endocrinology. 2008; 149(7): 3549–3558.
18. Kanitkar Meghana, Galande Sanjeev, Bhonde Ramesh "Curcumin prevents streptozotocin-induced islet damage by scavenging free radicals: a prophylactic and protective role"*Eur J Pharmacol, 2007; 577(1-3): 183-91.*
19. Nishiyama T, Mae T, Kishida H, Tsukagawa M, Mimaki et al."Curcuminoids and sesquiterpenoids in turmeric (Curcuma longa L.) suppress an increase in blood glucose level in type 2 diabetic KK-Ay mice". J Agric Food Chem. 2005; 23; 53(4): 959-63.
20. Enas Ali Kamel Mohamed. "Antidiabetic, Antihypercholestermic and Antioxidative Effect of Aloe vera Gel Extract in Alloxan Induced Diabetic Rats" Australian Journal of Basic and Applied Sciences, 2011; 5(11): 1321-1327.
21. Rajasekaran S, Sivagnanam K, Ravi K and Subramanian S. "Beneficial effects of aloe vera gel extract on lipid profile status in rats with streptozotocin diabetes." Clin. Exp. Pharmacol. Physiol, 2006; 33(3): 232-237.
22. Kim SJ, Nian C, Doudet DJ, McIntosh CH."Dipeptidyl peptidase IV inhibition with MK0431 improves islet graft survival in diabetic NOD mice partially via T-cell modulation". Diabetes. 2009; 58(3): 641-51.
23. Patel SS, Shah RS, Goyal RK. "Antihyperglycemic, antihyperlipidemic and antioxidant effects of Dihar, a polyherbal ayurvedic formulation in streptozotocin induced diabetic rats." Indian J Exp Biol. 2009; 47(7): 564-70.
24. Aggarwal BB, Harikumar KB "Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases." Int J Biochem Cell Biol. 2009; 41(1): 40-59.
25. Husini HF, Kianbakht S and Hajiaqhaee R et al. "Anti-hyperglycemic and Anti-hypercholesterolemic Effects of Aloe vera Leaf Gel in Hyperlipidemic Type 2 Diabetic Patients: A Randomized Double-

Blind Placebo-Controlled Clinical Trial" Planta Medica. 2012; 78(4): 311-6.
26. Suresh Babu, P. and Srinivasan, K. "Amelioration of renal lesions associated with diabetes by dietary curcumin in streptozotocin diabetic rats". Mol. Cell. Biochem. 1998; 181: 87-96.
27. Du Toit Loots, Marlien Pieters, Md Shahidul Islam, Lisa Botes "Antidiabetic effects of Aloe ferox and Aloe greatheadii var. davyana leaf gel extracts in a low-dose streptozotocin diabetes rat model" South African Journal of Science, 2011; 1-6.
28. Akram Ahangarpour, Maryam Mohammadian, and Mahin Dianat "Antidiabetic Effect of Hydroalcholic *Urtica dioica* Leaf Extract in Male Rats with Fructose-Induced Insulin Resistance" Iran J Med Sci. 2012; 37(3): 181–186.