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Effect of Curcumin Extracts on the Islets of Langerhans Cells of Diabetic White Rats Induced by Alloxan: A Histological Study

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Abstract **Background:** Diabetes mellitus is an unpredictable issue that is portrayed by hyperglycemia coming about because of breakdown in insulin discharge and activity. As of late curcumin extract have been reported to be useful in treatment of type II diabetes. **Aim of the work:** In this research curcumin extract was used instead of chemical drugs for the treatment of diabetes mellitus. **Material and methods:** 30 male adult albino rats aged 5-7 months and their average weight was 150-200 grams were divided into three groups. The first one (n=10) control group, the second group (n=10) was injected with a single dose of alloxan (42 mg/kg). The third group (n=10) was injected with alloxan and after 3 days was received curcumin extract orally 80mg/kgm daily for one month. The rats were scarified after the last dose of the drug and their pancreases were removed, fixed and different sections were prepared and stained for light microscope study. **Results:** After induction of diabetes the islets of Langerhans revealed architectural disarray. The islets cells showed atrophy in size with cellular necrobiosis associated with cystic dilatation and luminal eosinophilic casts. The intensity anti-insulin antibody reaction was decreased. So donation of curcumin extract reduced the islets cells damage and increase in the intensity of anti-insulin antibody reaction. **Conclusion:** The present study revealed that curcumin extract has potential effect in treatment of type II diabetes.

Keywords: *pancreas, islets of Langerhans, diabetes mellitus, Alloxan, curcumin extract, white rats*

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1. Introduction

The pancreas is particularly an important organ from the medical point of view because it is commonly subjected to two important diseases: diabetes mellitus and pancreatic cancer [1]. The diabetes is a problem of morbidity and it is one of the five leading causes of death in the world [2]. Several investigations in human and animal models have demonstrated changes in the cell antioxidant status in diabetes.

The unsettling influences in the defense system in different tissues from animal models were accounted for. There was evidence that elevation in glucose concentration may depress natural antioxidants defense agents such as vitamin C and glutathione [3]. On the other hand, oxidative stress causes type I diabetes especially through apoptosis of pancreatic B-cells and insulin resistance in type Π diabetes [4,5,6].

Alloxan causes diabetes in animals through its ability to destroy the insulin-producing B-cells of the pancreas [7]. Recently, overproduction of reactive oxygen and nitrogen species, lowered antioxidant defense in humans were associated with diabetes mellitus. Also the antioxidants help in neutralization of the effects of free radicals formed when body cells burn oxygen [8].

The employ of medicinal plants or their active ingredients has become a progressively more used for treatment of various pancreatic disorders including diabetes mellitus. One of these medicinal plants is Curcumin (Diferuloyl methane), a polyphenol derived from the herbal remedy and dietary spice turmeric, [9,10]. It had a long history of restorative uses in India and Southeast Asia was known to display an assortment of pharmacological impacts including calming, hostile to tumor, against HIV (Human Immunodeficiency Virus) and anti-infectious activities following oral or topical administration, [11]. Curcumin was a strong antioxidant capacity at neutral and acidic pH.It could inhibit different

cell signaling pathways i.e. its effect on cellular enzyme such as cyclooxygenase and glutathione S- transfereses, immune-modulation and effect on angiogenesis and cell-cell adhesion [12].

The use of curcumin extract for treatment of diabetes mellitus still needs further investigation in order to validate its clinical application as remedy for pancreatic β cells damage.

2. Material and Methods

In this work 30 male adult albino rats aged 5-7 months and their average weight was I50-200 grams will be using. They divided into three groups.

Group I: Control and consisted of ten rats (-ve control).

Group II: Experimental and consisted of ten rats and was subjected to the induction of diabetes by receiving intravenous alloxan at a dose of 42 into tail veins(Sigma Co, USA) dissolved in distilled water [13]. Serum glucose levels was checked after 72 hour and the rats with serum glucose level ≥ 200mg/dl or over was considered diabetic and were used for this study [14].

Group III: Experimental and consists of ten rats and were injected with alloxan and after 3 days were received curcumin extract orally 80mg/kgm by gastric tube daily for one month [15].

At the end of the experiment, the fasted rats were sacrificed by decapitation and their pancreatic glands were rapidly excised, rinsed in saline and fixed in I0% formol saline. Their blood samples were collected to determine the blood glucose level.

2.1. Tissue Preparation for Structural Study

Specimens from pancreas of each group were removed at the end of experiment and after fixation in I0% formol saline for 24 hours. The tissues were processed according [16].

2.2. Immunohis to Chemical Study

For immunohis to chemistry study the paraffin pancreatic sections were de-waxed in xylene and then rehydrated. The slides were prepared according [17].

3. Results

• Histological results:

Group I:

The islets of Langerhans appeared to be ellipsoid or spherical structures of varying sizes and were unevenly scattered between the pancreatic acini. Each islet was consisted of epithelial cells which form trabecular structures separated by a dense network of anastomosing capillaries. The epithelial cells were round or oval in shape with central rounded nuclei, surrounded with a delicate cellular membrane, filled with a fine granular cytoplasm and form tube like structures around central capillary (Figure 2, Figure 3).

Group II:

The islets of Langerhans revealed significant architectural disarray. They were damaged and shrunken in size. The islets cells showed atrophy in size with cellular necrobiosis associated with cystic dilatation with luminal eosinophilic casts in the duct system (Figure 4, Figure 5).

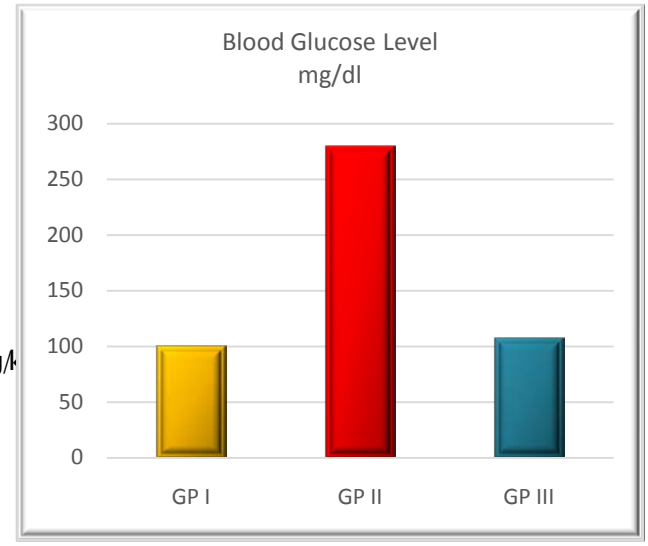

Figure 1. Comparison between average value of fasting blood glucose levels of group I, II and III

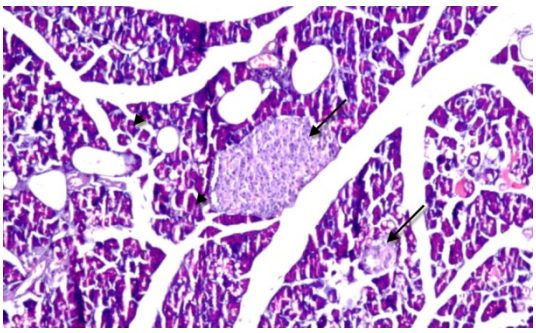

Figure 2. A photomicrograph of a section of pancreasof groupI showing that the islets of Langerhans are ellipsoid or spherical structures (arrows)(endocrine portion) and are unevenly scattered between the pancreatic acini(arrow heads) with duct system(exocrine portion) (H & E X I00)

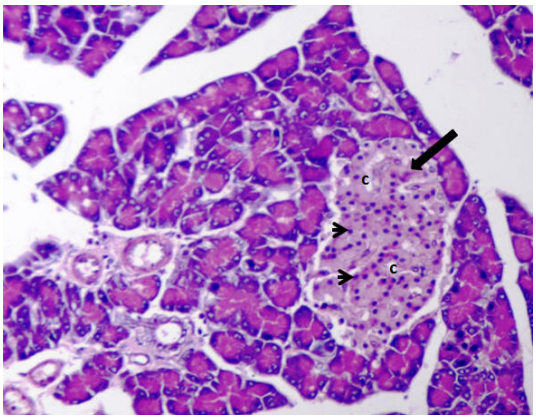

Figure 3. A photomicrograph of a section of pancreas of group I showing that an islet (arrow) is consists of epithelial cells separated by a dense network of anastomosing capillaries(C). The epithelial cells are round or oval in shape with central rounded nuclei (arrowheads). (H&E; X 400)

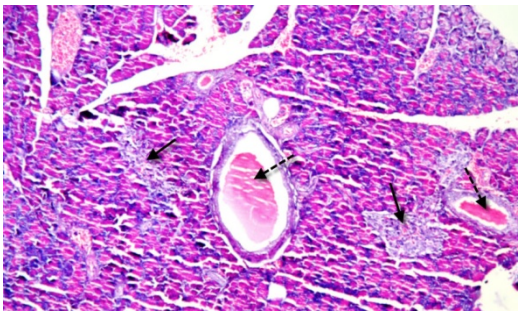

Figure 4. A photomicrograph of a section of pancreas of group II showing that the islets of Langerhans are damage and shrunken in size (arrows) with cystic dilatation with luminal eosinophilic casts in the duct system(intermittent arrows) (H&E; X I00)

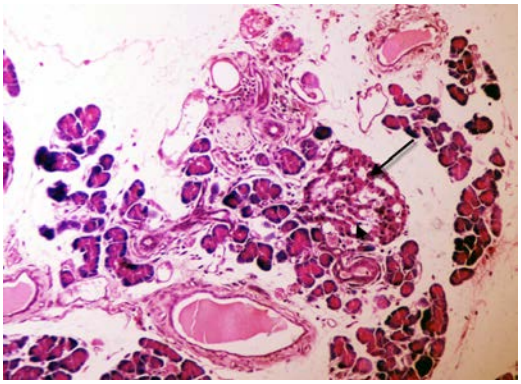

Figure 5. A photomicrograph of a section of pancreas of group II showing that the islet of Langerhans isshrunken(arrow) and islet cells are atrophy in size with cellular necrobiosis (arrow head) (H&E; X 400)

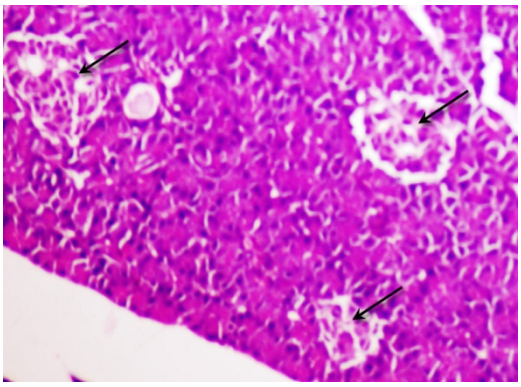

Figure 6. A photomicrograph of a section of pancreas of group III showing that the islets of Langerhans appear with normal size and shape ellipsoid or spherical of varying sizes (arrows) (H&E; X I00)

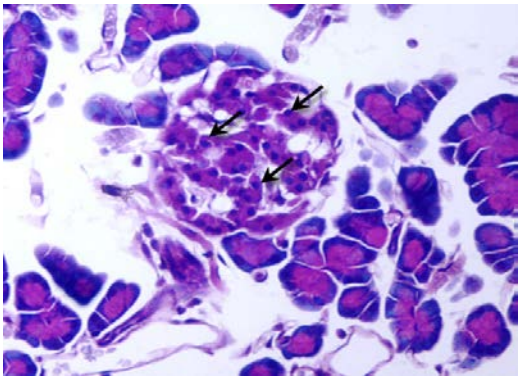

Figure 7. A photomicrograph of a section of pancreas of group III showing that the islets cells appear normal and intact without ductal cystic dilatation in duct system compared with group II(arrows) (H & E; X 400)

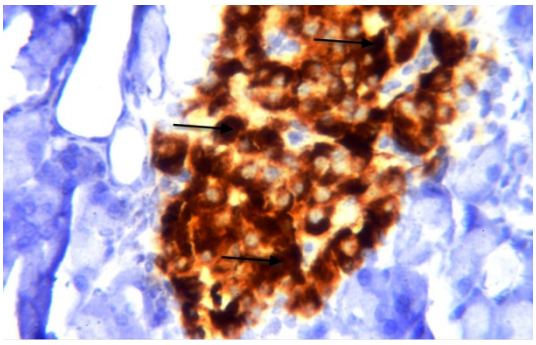

Figure 8. A photomicrograph of a section of pancreas of group I showing an islet (arrows) with a strong immunoreaction for insulin of most B-cells (Anti-insulin antibody reaction; X 400)

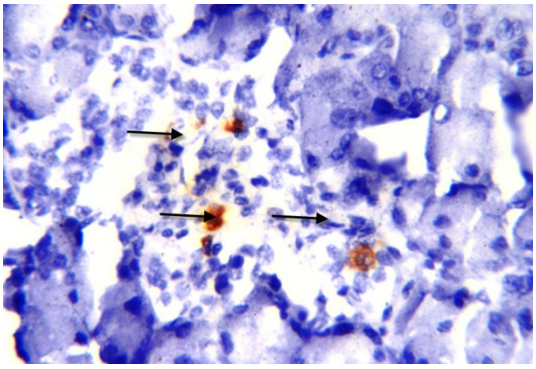

Figure 9. A photomicrograph of a section of the pancreas of group II showing an islet (arrows) with mild to nil immunoreaction for insulin in few B-cells (Anti-insulin antibody reaction; X400)

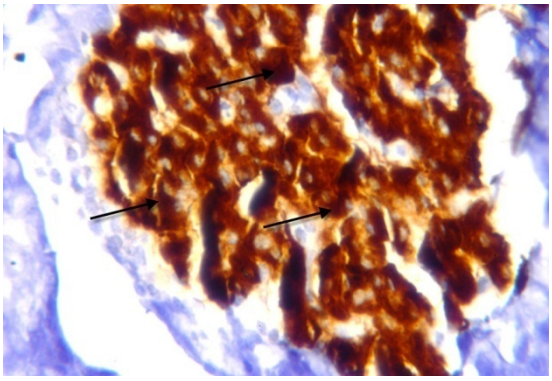

Figure 10. A photomicrograph of a section of the pancreas of group III showing an islet (arrows) with strong immunoreaction for insulin in numerous B-cells (Anti-insulin antibody reaction; X400)

Group III: The islets of Langerhans appeared to restore their size and shape with normal intact cells without ductal cystic dilatation in duct system compared with group II (Figure 6, Figure 7).

- **Immunohistochemical results:**

Group I:

The islets of Langerhans of group I showed sever reaction in almost all of the islet cells (Figure 8) and Table 1.

Group II:

The islets of Langerhans of group I showed no reaction in almost all of the islet cells (Figure 9) and Table 1.

Group III:

The islets of Langerhans of group I showed sever reaction in almost all of the islet cells (Figure 10) and Table 1.

• **Morphometric results:** Morphometric study showed:

Table 1. The quantitative measurements of mean grey of insulin content

Group	I	II	III
Ant insulin antibody	+++	+/-	+++

+++ Strong reaction.++ Moderate reaction. + Mild reaction. - Nil reaction.

• **Blood glucose results:**

Group I: The average value of fasting blood glucose levels was I00.6mg/dl (Figure 1).

Group II: The average value of fasting blood glucose levels was found to be increased to (297.8mg/dl) compared with group I (Figure 1).

Group III: The average value of fasting blood glucose levels was found to be decreased to (I07.II mg/dl) compared with the group II (Figure 1).

4. Discussion

Diabetes mellitus is the most common endocrine disease accompanied with various metabolic disorders [18]. It leads to hyperglycemia, hyperlipidemia, hypertension, atherosclerosis, retinopathy, neuropathy and nephropathy [2,19]. Alloxan is well known for its selective pancreatic islets cells toxicity and has been extensively used in induced diabetes mellitus in animals. It causes diabetes in animals through its ability to destroy the insulin-producing B-cells of the pancreas [20,21]. Also it increases the free radicals production and causes pancreatic tissues injury with consequent increase in lipid peroxidation which contributes to the increased rate of hepatic glucose production. The alloxan is taken up by the B-cells via the glucose transporter GLUTZ and causes alkylation of DNA and reduction of ATP and NAD content [7,22].

The results of the present study revealed that induction of diabetes by alloxan resulted in abnormal histological changes in islets of Langerhans and their cells. They were damaged and shrunken.The islets cells showed atrophy in size with cellular necrobiosis associated with cystic dilatation with luminal eosinophilic casts in the duct system.These findings are in agreement with those described by [7,8,23,24]. They stated that the alloxan oxidizes the pancreatic B-cell glucokinase with concomitant inactivation of the enzyme which couples changes in the serum glucose level that inhibit glucose induced insulin secretion and lead to necrosis of the pancreatic B-cells.

In the present study a significant decrease in insulin contents in diabetic rats was observed. These findings came in accordance with [25] who suggested that one of the causes of diabetes was the impaired insulin response to glucose. [26] Saied that the insulin receptor in pancreatic B-cells created an insulin secretory defect associated with a modest decrease of islet size. [27] Proved that the loss of insulin production was demonstrated as loss of insulin-staining cells of the islets of alloxan treated mice.

In the present work, curcumin extract administration reduced markedly the degree of damage produced in the pancreatic islets as a result of induction of diabetes. Curcumin increased islet viability and delayed islet reactive oxygen species (ROS) production, which was mediated through inhibiting poly ADP-ribose polymerase-I activation [28].

Curcumin extract administration to diabetic rats showed improvement in the pancreatic islets cells structure, increase in the number of B-cells as well as increase in islets area compared to diabetic animals. Also significant increase in insulin hormone contents was observed. These findings are in agreement with [29-32] whereas curcumin and its analogues treatments increased the number of small pancreatic islets and decreased lymphocyte infiltration in pancreatic islets and they played antioxidant defense. Thus curcumin as a natural polyphenolic source exerts its beneficial effects by modulating different signaling molecules including transcription factors, chemokines, cytokines, tumor suppressor genes, adhesion molecules, microRNAs.

5. Conclusion

The present study revealed that curcumin extract administrations are effective in protecting the islets of Langerhans against diabetes and considered to be effective in treatment of diabetes.

References

[1] Slack, J. M. W. I995. Developmental biology of the pancreas. Development; 121(6): I569-I580.

[2] Kumar, G. P., Kumar, S. D. and Subremanian, P. S. 2006.Anti-diabetic activity of fruits of Terminalia Chebulaonstreptozotocin induced diabetic rats. J Health Sci. 52: 283-291.

[3] Inouye, M., Mio, T. and Sumino, K. I999. Link between glycogen and lipo- oxidation in red blood cells in diabetes. Clin Chem. Acta; 285: 35-44.

[4] Bonnefont- Rousselot, D., Bastard, J. P. and Delatter, J. 2002. Consequences of the diabetic status on the oxidant/antioxidant balance. Diabetes Metab; 6: 163-76.

[5] Gumieniczek, A., Hopkata, H., Zbigniew, W. and Justyna, N. 2002. Changes in antioxidant status of heart muscle tissue in experimental diabetes in rabbits. Acta Biochemica Polonica; 49(2) 529-535.

[6] Jin, L., Xue, H.Y., Jin, L.J., Li, S.Y. and Xu, Y.P. 2008. Antioxidant and pancreas protective effect of aucubin on rats with streptozotocin-induced.Eur J Pharmacol; 582: I62-I67.

[7] Jakus, V. 2000. The role of free radicals, oxidative stress and antioxidant systems in diabetic vascular disease. BratistLekListy; 101 (10): 541-551.

[8] Somlak, C., Suthee R., Rataya L., Chada P, and Siwanon J. 2012. Curcumin Extract for Prevention of Type 2 Diabetes. Diabetes Care; 35(II): 2121-2127.

[9] Conteas, C.N., Panossian, A.M., Tran, T.T., and Singh, H.M. 2008. Treatment of HIV associated diarrhea with curcumin. Digestive disease and sciences. 45(10): 2188-2191.

[10] Gota, V.S., Maru, G.B., Soni, T.G., et al. 2010. Safety and pharmacokinetics of a solid lipid curcumin particle formulation in osteosarcoma patients and healthy volunteers. Journal of Agricultural and Food Chemistry. 58(4): 2095-2099.

[11] Harish, G, Venkateshappa, C., Mythri, R.B., et al. 2010. Bioconjugates of Curcumin display improved protection against glutathione depletion mediated oxidative stress in a dopaminergic neuronal cell line: implications for Parkinson'sdisease. Bio-organic and Medicinal Chemistry. 18(7): 2631-2638.

[12] Amanda, N.L., Lucas, L. C., and César T. S., 2015. Alloxan-Induced Diabetes Causes Morphological and Ultrastructural Changes in Rat Liver that Resemble the Natural History of Chronic Fatty Liver Disease in Humans.J Diabetes Res. 20I5; 20I5: 494578.

[13] Shabeer, J., Srivastava, R.S., Singh, S.K., 2009. Antidiabetic and antioxidant effect of various fractions of Phyllanthus simplex in alloxan diabetic rats. J. Ethnopharmacology. I24: 34-38.

[14] Arun, N, and Nalini, N. 2002. Efficacy of turmeric on blood sugar and polyol pathway in diabetic albino rats. Plant Foods for Human Nutrition. 57(1): 41-52.

[15] Banchroft, J.D.; Stevens, A. and Turner, D.R. 1996. Theory and practice of histological techniques.4th ed. Churchil Livingstone, New York, London, San Francisco, Tokyo.

[16] Kanter, M., Uysal, T. and Kara, O. 2006. Depression of glucose levelsand partial restoration of pancreatic B-cell damage by melatonin in streptozotozin-induced diabetic rats. Arch. Toxicol; 80: 362-369.

[17] Patel, D., Gidwani, B., Sarwa, K., Kaur, C.D., Dhongade, H.J., Sahu, P., Sahu, V., 2016. A comprehensive review on the anti-diabetic activity of Momordicacharantia and Syzygiumcumini seeds. Int. J. Biol. Pharm. Allied Sci. 5: 1561-1575.

[18] Anfenan, M. L. K., 2014. Evaluation of nutritional and antidiabetic activity of different forms of Ginger in rats. Middle-East J Scientific Res. 2I: 56-62.

[19] Jorns, A., Mundy, R., Tiedge, M. and Lenzen, S. 1997. Comparabbitive toxicity of alloxan, N-alkylalloxans and ninhydrin to isolated pancreatic islets in vitro. J. of Endocrinology; 155: 283-293.

[20] Wolf, S. P. 1993. Diabetes mellitus and free radicals. Free radicals, transition, metals and oxidative mellitus and complication.Br. Med. Bull; 49: 264-652.

[21] Prasad, S. K., Kulshreshtha, A. and Qureshi, T. N. 2009. Antidiabetic Activity of Some Herbal Plants in Streptozotocin Induced Diabetic Albino Rats. Pakistan Journal of Nutrition; 8 (5): 551-557.

[22] Rohilla, A. and Ali, S., 20I2. Alloxan induced diabetes: mechanisms and effects. Int. J. Res. Pharma. Biomed Sci. 3: 819-823.

[23] Dhanesha, N., Joharapurkar, A., Shah, G., Kshirsagar, S., Patel, V., Patel, K., Jain, M., 20I3. Treatment with exendin-4 improves the antidiabetic efficacy and reverses hepatic steatosis in glucokinase activator treated db/db mice. Eur. J. Pharmacol.714: 188-192.

[24] El-Esawy, B.H., Alghamdy, A.N., El Askary, A., Elsayed, E.M., 20I6. Histopathological evaluation of the pancreas following administration of paricalcitol in alloxan-induced diabetic wistar rats. World. J. Pharm. Pharmac. Sci. 5: 189-198.

[25] El-Esawy, B.H., Alghamdy, A.N., El Askary, A., Elsayed, E.M., 20I6. Histopathological evaluation of the pancreas following administration of paricalcitol in alloxan-induced diabetic wistar rats. World. J. Pharm. Pharmac. Sci. 5: 189-198.

[26] Ho, E., Ning, Q., Yu, H. T., Weimin, L. and Tammy, M. B. 200I. Dietary zinc supplementation inhibits NFkB activation and protects againstchemically induced diabetes in CDI mice. Exp. Bio and Medicine; 226: 103-111.

[27] Meghana K, Sanjeev G, Ramesh B. 2007. Curcumin prevents streptozotocin-induced islet damage by scavenging free radicals: a prophylactic and protective role. European Journal of Pharmacology. 577(1-3): 183-191.

[28] Kanitkar M, Gokhale K, Galande S, Bhonde RR. 2008. Novel role of curcumin in the prevention of cytokine-induced islet death in vitro and diabetogenesis in vivo. British Journal of Pharmacology. I55(5): 702-7I3.

[29] Kanitkar M, Bhonde RR. 2008. Curcumin treatment enhances islet recovery by induction of heat shock response proteins, Hsp70 and heme oxygenase-I, during cryopreservation. Life Sciences. 82(3-4): 182-189.

[30] Zafar KS, Inayat-Hussain SH, Siegel D, Bao A, Shieh B, Ross D. 2006. Overexpression of NQOI protects human SK-N-MC neuroblastoma cells against dopamine-induced cell death. Toxicology Letters. 166(3): 261-267.

[31] Balamurugan AN, Akhov L, Selvaraj G, Pugazhenthi S. 2009. Induction of antioxidant enzymes by curcumin and its analogues in human islets: implications in transplantation. Pancreas. 38(4): 454-460.

[32] Shatadal, G.; Sharmistha, B.; Parames C.S. 20I5. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease. Food and Chemical Toxicology. 83: 111-124.