Egypt. J. Chem. **Vol. 65**, No. 6. pp. 447 - 452 (2022)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Cinnamon *Zeylanicum* Aqueous Improves Some Oxidative Stress Biomarkers in Diabetic Type 2 Induced By Streptozotocin in Adult Male Albino Mice

Oras Khalis Yaseen[*1],Mustafa Taha Mohammed[*2]

[1]*Medical Laboratory Department, Baquba Technical Institute, Middle Technical University, Baquba, Iraq.*

[2] *Chemistry Department, College of Science, Mustansiriyah University, Baghdad, Iraq*.

Abstract

Background: the diabetic type 2 population development in the world wide. Its risk describe through the long term complication that provide in destroyed the variety tissues in organs as liver and blood vessels. Cinnamon *zeylanicum* classes as famous medicinal herb , contain large numbers of antioxidant phytochemical compounds: (cinnamaldehyde ,eugenol ,Gallic acid, rutin) and others phenolic compounds and vitamins as(A,K,E,D_3,K,C,B_1,B_2) ,also researches indicated that cinnamon contain interesting minerals like (zinc, copper, Iron, cobalt).therefor cinnamon have capacity to treated T_2DM . Aim: present study aimed to investigation in vitro and in vivo antioxidant effect of aqueous bark extract of *C. zeylanicum*on oxidative stress in T_2DM induce by Streptozotocin (STZ) in mice .Methodology: DPPH free radical scavenging use to evaluated antioxidant activity in vitro. In vivo: Eighty adult male, albino mice were be used and divided into four (n=20).group (A) normal healthy control mice. Group (B) received (200mg/kg) cinnamon aqueous bark extract only. Group (C)mice fed with high fat diet for three weeks and received with (40 mg /kg) STZ injection (diabetic mice group).group (D) firstly treated by the same condition of group (C) and after (10 days) of STZ injunction the diabetic mice treated with (200 mg /kg) of cinnamon extract . Hyperglycemia was investigation by FBS and oxidative stress was investigation by permeant ROS, MDA, TOS and the total antioxidant capacity TAC in serum. Rustle: cinnamon *zeylanicum* extract showed effective DPPH free radical. Control group(A) compared T_2DM group (C) and treatment group (D), herb caused a significant ($p \leq 0.001$) reduction in ROS,MDA,TOS, and a significant increase in total antioxidant capacity TAC also showed significant improvement in FBS and serum insulin. Conclusion: cinnamon *zeylanicum* a protective effect against oxidative stress in diabetic mice due to its antioxidant characters.

Keywords: cinnamon *zeylanicum*,Streptozotocin, oxidative stress, antioxidant capacity.

Introduction

Diabetes type 2 is the most public form of diabetes, occurs with people after 30 age[1] .T2D results from insulin secretory defect from β-cell or reduced sensitivity of a target cell to insulin lead to insulin resistant [2].hyperglycemia is main indicator on diabetes that lead to disturbances in metabolism of macronutrients in body[3]. Metabolism disturbances contribute to start the oxidative stress and progression the complications of diabetes[4]. During high level of glucose cells will be injury and reactive oxygen species will be synthesize [5].organism have antioxidant endogenous enzymatic defect system to scavenger free radical and keep the balanceoxidative and antioxidant[6].Cinnamon *zeylanicum* (*C. zeylanicum*) is the important plant in the Lauraceae family[7]. traditional vital spices used by the peoples in all over the world[8]. bark of the cinnamon consists the various phytocmpounds like

*Corresponding author e-mail: oraschem80@mtu.edu.iq.; (OrasKhalisYaseen).
DOI: 10.21608/EJCHEM.2022.113701.5165

cinnamaldehyde, eugenol[9], led to antioxidant properties of cinnamon bark can use the aqueous extract in alternative medicine [10]. Study below aims: Detecting the efficacy of the antioxidant activity of aqueous extracts of *C. zeylanicum*bark in *vivo* models.

Experimental:

Plant extraction

Preparation of the water extract: fresh bark powder (50gm) collected and dissolvent by (500ml) distil water (at ratio 1:10), the extract put in shaker for (6h) at (37C°),then filtered by (Whatman No.1)filter paper and the supernatant concentrated in rotary evaporator for (2h) .Extract concentrated to dryness at(40C) in oven for (2h) and storied in dark place at (15C) until use in study[11][12].

DPPH (radical scavenging activity) of cinnamon extracts

DPPH activity regarding the extract of barks from *C. zeylanicum*has been measured base on a previous approach conducted via Blois's method [13]and with a few modifications.[14]

Assessment of the biochemical parameters

Reactive oxygen species (ROS), were determinate using ELISA method by standard kits (Sunlong, China).The malondialdehyde (MDA) concentration was assayed for lipid peroxidation, MDA reacts with thiobarbituric acid to give MDA- TBA pink complex ,MDA assessment spectrophotometrically[15]. Total antioxidant (TAC) and Total oxidant stress (TOS) were determine by Erel method[16][17].

Animals

Adult male albino mic ,age between 6-8 weeks, their weight ranging between 25-30gm and they were left for three days in the lab room before the experiment for adaptation. . Type 2 diabetes was induced according to the method of Reed et.al[18] andBrian L. Furman[19]. Themic in control groupfeded with standard pellet diet and water. Whereas the mic in T_2DM group were are fed with high–fat diet for three weeks. On 22 day all mic diabetic weigh and were treated with streptozotocin (STZ; Direvo, Germany). A single dose of STZ (40 mg/kg, dissolved in 0.1Msodium citrate buffer at pH 4.4). Blood glucose was tested after 5 days STZ administration.

The animals are divided into four groups with ten mic each as following:

Group A: control group (healthy mice).

Group B: Normal mic are fed with *C. zeylanicum*extract for 30 days (200 mg/kg b.w)

Group C: Diabetic control mic (high fat diet+ STZ induced as 40 mg/kg b.w).

Group D: Diabetic induced animals are fed with *C. zeylanicum*extract for 30 days (200 mg/kg b.w).

Statistical analysis

The data throughout this work was reported in the form of (mean ± the standard deviation (SD). Data were analysis by SPSS version 26 and Excel 2010 (One-Way ANOVA followed by Duncan test), the significant level is considered when ($p<0.05$).

Results and Discussion

The results obtained are listed from different concentrations of extract of *C.zeylanicum* and standard vitamin C and the effect of scavenging free radicals as indicated by table (1). *C.zeylanicum* extract scavenged the DPPH stable free radicals in a concentration of 12.50, 25, 50, 100 and 200µg/mL, the extract showed percentage inhibition comparison with the vitamin C that has been utilized as a reference[14][20]. These results evidence of the extract's ability to fight free radicals [21].

Table (1): DPPH free radical scavenging activities of *C.zeylanicum* extract.

Concentration (µg/mL)	200	150	100	50	25
Number of values	3	3	3	3	3
Scavenging Activity (%) Vitamin C	92.2	86	77.8	63	48.7
Scavenging Activity (%) Extract	75.7	66.1	54.2	46	33.16

Table (2): **Effect of cinnamon aqueous extract on serum glucose and insulin in type2 diabetic mice**

parameters		Control (A)	Cn(200mg/kg) (B)	T_2DM (STZ40mg/kg) (c)	STZ+Cn (D)	*P*-value
Glucose(mg/dl)	Mean	110	91	250	140	0.001
	SD	2.23	1.88	2.31	1.56	
Insulin(IU/ml)	Mean	16.24	13.43	8.25	10.38	0.001
	SD	1.33	1.78	2.69	1.47	

The result were obtained (Table2) in a significant increase in glucose levels no a decrease in insulin level in diabetic group ,when treatment with (200mg /kg) cinnamon extract the result noted that level of insulin increase but not returned to control group , and significant decrease in blood glucose level in group D [22].

Table (3): **Effect of cinnamon aqueous extract on ROS, MDA, TOS and TAC in type2 diabetic mice**.

Parameters		Control (A)	Cn(200mg/kg) (B)	T_2DM (STZ40mg/kg) (c)	STZ+Cn (D)	*P*-value
ROS (pg/mL)	Mean	156.70	153.55	452.85	247.30	0.001
	SD	16.15	13.71	16.21	9.80	
MDA (µmol/L)	Mean	1.97	0.70	4.83	1.56	0.001
	SD	0.85	0.08	1.24	0.35	
TOS (µmol/L)	Mean	2.07	1.22	4.23	2.27	0.001
	SD	0.66	0.09	0.48	0.58	
TAC (µmol/L)	Mean	1.27	1.57	0.94	1.32	0.001
	SD	0.18	0.08	0.16	0.07	

Table 3 shows the mean± SD values of four groups of serum ROS, MDA, and TOS .through the table (3) the ROS and MDA ,TOS decrease significantly ($p \leq 0.001$) in group B (cinnamon only)when compared to control group(A) . And significantly increase in group C (T_2DM) when compared to control group ,and results showed a significant decrease($p \leq 0.001$) in ROS, MDA, and TOS (mice with T_2DM treated with cinnamon) group D when compared to group C (T_2DM) and control group. the current research has coincided with anther research that indicated the fact that the ROS level in diabetics were higher than control[23] . The cinnamon treated group(D) exhibited better recoveries restoring back to control, a significant ($p \leq 0.001$) decrease in ROS activity has been noticed in the cinnamon treated group compared to T_2DM group (c) ,although subjected to the same conditions of oxidative stress (Table3) indicating the protective activity of the extract against oxidative stress. And this result is consistent with another study[24] showed that treatment by *C. zeylanicum*extract reducing levels the ROS activity in oxidative stress conditions(figure1).The anti-oxidant effect of *C. zeylanicum*that can be possibly a result of the direct ROS scavenging by the constituents of the extract. *C. zeylanicum*reduce the effect of oxidative stress because presence of rich combination of antioxidant phytochemicals that were stated to possess antioxidant, and anti-inflammatory activities.[9] Also from result can be seen that the MDA levels in group C have been considerably ($p \leq 0.001$) higher compared to it in controls and group B, but when treated with cinnamon a result showed interesting decrease in MDA serum value[25]. Based on this study results(figure2), it has been a clear balance between the oxidant and the antioxidant bio-markers in the blood serum following the treatment by cinnamon[26], such balance has been ensured by significant ($p \leq 0.001$) decrease in the concentration of the TOS in group (D) . This result is consistent with a previous studies indicated that antioxidant activity of *C. zeylanicum*are mediate through elevating antioxidant factors and decreasing lipid peroxidation with impaired glucose oxidation in T_2DM[27].

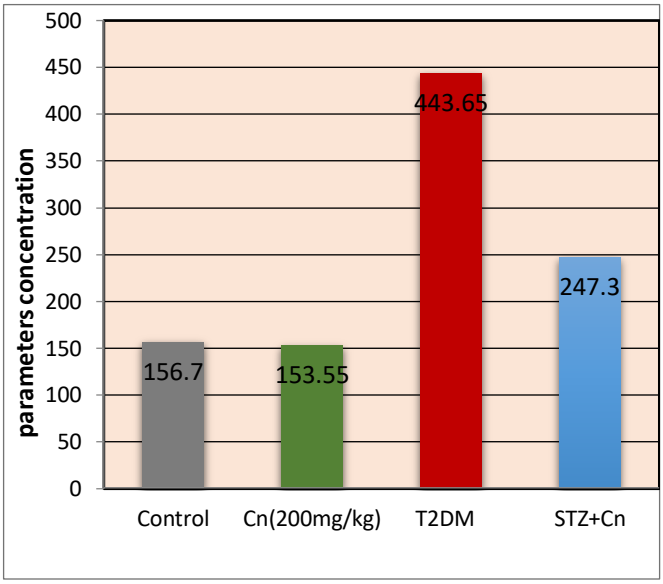

Figure1: Levels ROS in group A (control), group B (Cinnamon 200m/kg), group C (STZ 40mg/kg) and Group D (T_2DM +cinnamon treated) in mice

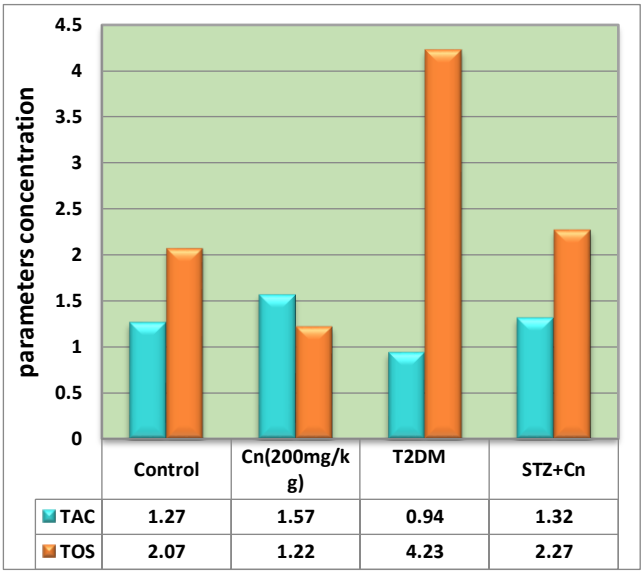

Figure 2: Levels TAC and TOS in group A (control), group B (Cinnamon 200m/kg), group C (STZ 40mg/kg) and group D (T_2DM +cinnamon treated) in mice

Conclusion

when hyperglycemia occur due to increased glucose autoxidation and leading to increase NADH and $FADH_2$ generation that used as a key in electron transport chain in mitochondria[30] . Over production of NADH can produce more proton gradient and increased transferred electrons to oxygen due to produce higher superoxide via the electron transport chain in mitochondria[31].However at the steady state superoxide radical played role in derived other free radical such mainly hydrogen peroxide and hydroxyl radicals[32] .O_2,$H_2O_2$and OH considered important factors of the ROS caused oxidative stress and cellular damage[33], and T_2DM can characterized by oxidative stress because the generation of ROS has a major role in DM complication [34].

In T_2DM free radicals attack membrane phospholipids causing lipid peroxidation[35] and the high level of MDA in serum reflect the increase in lipid peroxidation in diabetics our study are in accordance with previous studies that hyperglycemia increases lipid peroxidation from overproduction of free radicals in diabetics[36]. In hyperglycemia uncontrolled or over production of reactive oxygen species is harmful[9]. and weak defense system of the organism all these factors lead to absence the ability to counteract on ROS generation ,and imbalance between ROS and their protection not occurs ,as a result oxidative stress happened and act as a mediator of insulin resistance and installation a complications of diabetes mellitus[37]. Cinnamon potent antioxidant herb includes Terpenes scavenger ROS has protected role against diabetes and reduces H_2O_2[38]. Flavonoids have attracted positive effect influencing scavenging lethal radicals and Pero oxidant property [39]coumarins, saponin, glycoside, terpenes, and resins are prevent lipid peroxidation as well as enhance the same antioxidant enzyme activity[40].Phenols in cinnamon protective agent capable for preventing molecules oxidation by donation hydrogen atom to free radicals[41]. Gallic acid, and rutin, kampferol, quercetin, lignin and pyrogallol) also cinnamaldehyde and eugenol the highest concentration in the water bark extract [42] there enhance defense against ROS contributed hyperglycemia and protect cells by reduce lipid peroxidation [38].Also vitamins (E and C) that cinnamon contain improved inflammation in diabetic[43] and reduced lipid peroxidation in membrane[44] . [45] B_2 in cinnamon aqueous extract and act by reduced MDA level in diabetic disease. All these antioxidant compound provided cinnamon as an interesting natural source by introducing therapy antioxidant compounds act different strategies for preventing or treating oxidative stress and increase total antioxidant capacity .

Reference

[1] S. E. Kahn, M. E. Cooper, and S. Del Prato, "Pathophysiology and treatment of type 2 diabetes: Perspectives on the past, present, and future," *Lancet*, vol. 383, no. 9922, pp. 1068–1083, 2014, doi: 10.1016/S0140-6736(13)62154-6.

[2] D. Of and D. Mellitus, "Diagnosis and classification of diabetes mellitus," *Diabetes Care*, vol. 37, no. SUPPL.1, pp. 81–90, 2014, doi: 10.2337/dc14-S081.

[3] U. Asmat, K. Abad, and K. Ismail, "Diabetes mellitus and oxidative stress—A concise review," *Saudi Pharm. J.*, vol. 24, no. 5, pp. 547–553, 2016, doi: 10.1016/j.jsps.2015.03.013.

[4] E. F. F. Silva, C. M. M. Ferreira, and L. De Pinho, "Risk factors and complications in type 2 diabetes outpatients," *Rev. Assoc. Med. Bras.*, vol. 63, no. 7, pp. 621–627, 2017, doi: 10.1590/1806-9282.63.07.621.

[5] V. Bellou, L. Belbasis, I. Tzoulaki, and E. Evangelou, "Risk factors for type 2 diabetes mellitus: An exposure-wide umbrella review of meta-analyses," *PLoS One*, vol. 13, no. 3, pp. 1–27, 2018, doi: 10.1371/journal.pone.0194127.

[6] P. Zhang, T. Li, X. Wu, E. C. Nice, C. Huang, and Y. Zhang, "Oxidative stress and diabetes: antioxidative strategies," *Front. Med.*, vol. 14, no. 5, pp. 583–600, 2020, doi: 10.1007/s11684-019-0729-1.

[7] P. Ranasinghe, S. Pigera, G. S. Premakumara, P. Galappaththy, G. R. Constantine, and P. Katulanda, "Medicinal properties of 'true' cinnamon (Cinnamomum zeylanicum): A systematic review," *BMC Complement. Altern. Med.*, vol. 13, no. 1, p. 1, 2013, doi: 10.1186/1472-6882-13-275.

[8] Y. Shen, L. N. Jia, N. Honma, T. Hosono, T. Ariga, and T. Seki, "Beneficial effects of cinnamon on the metabolic syndrome, inflammation, and pain, and mechanisms underlying these effects-a review," *J. Tradit. Complement. Med.*, vol. 2, no. 1, pp. 27–32, 2012, doi: 10.1016/S2225-4110(16)30067-0.

[9] O. K. Yaseen and M. T. Mohammed, "Effects of cinnamon and their beneficial content on treatment of oxidative stress," *Syst. Rev. Pharm.*, vol. 11, no. 9, pp. 847–850, 2020, doi: 10.31838/srp.2020.9.121.

[10] P. Subash-Babu, A. A. Alshatwi, and S. Ignacimuthu, "Beneficial antioxidative and antiperoxidative effect of cinnamaldehyde protect streptozotocin-induced pancreatic β-cells damage in wistar rats," *Biomol. Ther.*, vol. 22, no. 1, pp. 47–54, 2014, doi: 10.4062/biomolther.2013.100.

[11] L. Jiao *et al.*, "Proanthocyanidins are the major anti-diabetic components of cinnamon water extract," *Food Chem. Toxicol.*, vol. 56, pp. 398–405, 2013, doi: 10.1016/j.fct.2013.02.049.

[12] A. Rajendran, M. Rafiqkhan, D. Selvam, and V. Thangaraj, "Pharmacognostic Profile and Phytochemical Analysis of Cinnamonum Zeylanicum Bark Extracts," *33 Res. Artic.*, vol. 5, no. 1, pp. 33–39, 2017.

[13] I. Gulcin *et al.*, "Anticholinergic, antidiabetic and antioxidant activities of cinnamon (cinnamomum verum) bark extracts: polyphenol contents analysis by LC-MS/MS," *Int. J. Food Prop.*, vol. 22, no. 1, pp. 1511–1526, 2019, doi: 10.1080/10942912.2019.1656232.

[14] P. R. E. Ribeiro *et al.*, "Chemical composition and antioxidant activity in the essential oil of Cinnamomum zeylanicum Nees with medicinal interest," *J. Med. Plants Res.*, vol. 14, no. 7, pp. 326–330, 2020, doi: 10.5897/jmpr2020.6966.

[15] F. Haidari, M. Mohammadshahi, B. Abiri, M. Zarei, and M. Fathi, "Cinnamon extract supplementation improves inflammation and oxidative stress induced by acrylamide: An experimental animal study.," *Avicenna J. phytomedicine*, vol. 10, no. 3, pp. 243–252, 2020, doi: 10.22038/ajp.2019.13899.

[16] O. Erel, "A novel automated method to measure total antioxidant response against potent free radical reactions," *Clin. Biochem.*, vol. 37, no. 2, pp. 112–119, 2004, doi: 10.1016/j.clinbiochem.2003.10.014.

[17] O. Erel, "A new automated colorimetric method for measuring total oxidant status," *Clin. Biochem.*, vol. 38, no. 12, pp. 1103–1111, 2005, doi: 10.1016/j.clinbiochem.2005.08.008.

[18] M. J. Reed *et al.*, "A new rat model of type 2 diabetes: The fat-fed, streptozotocin-treated rat," *Metabolism.*, vol. 49, no. 11, pp. 1390–1394, 2000, doi: 10.1053/meta.2000.17721.

[19] B. L. Furman, "Streptozotocin-Induced Diabetic Models in Mice and Rats," *Curr. Protoc. Pharmacol.*, vol. 70, no. 1, pp. 5.47.1-5.47.20, 2015, doi: 10.1002/0471141755.ph0547s70.

[20] S. Mathew and T. E. Abraham, "Studies on the antioxidant activities of cinnamon (Cinnamomum verum) bark extracts, through various in vitro models," *Food Chem.*, vol. 94, no. 4, pp. 520–528, 2006, doi: 10.1016/j.foodchem.2004.11.043.

[21] S. Preethi, R. Gayathri, and V. V. Priya, "Phytochemical screening , antioxidant activity , and total phenolic content of crude ethanolic extract of Cinnamomum verum – An in vitro study," vol. 13, no. 5, pp. 3–6, 2020.

[22] M. Al-Qulaly, M. Okasha, and M. Hassan, "Effect of Ginger and Cinnamon on Induced Diabetes Mellitus in Adult Male Albino Rats," *Bull. Egypt. Soc. Physiol. Sci.*, vol. 0, no. 0, pp. 373–388, 2021, doi: 10.21608/besps.2020.45577.1078.

[23] M. Mandal, A. Varghese, V. K. Gaviraju, S. N. Talwar, and S. S. Malini, "Impact of hyperglycaemia on molecular markers of oxidative stress and antioxidants in type 2 diabetes mellitus," *Clin. Diabetol.*, vol. 8, no. 4, pp. 215–222, 2019, doi: 10.5603/DK.2019.0015.

[24] P. Azimi, R. Ghiasvand, A. Feizi, M. Hariri, and B. Abbasi, "O RIGINAL D ATA Oxidative Stress , and Inflammation," *Rev. Diabet. Stud.*, vol. 11, pp. 258–266, 2015, doi: 10.1900/RDS.2014.11.259.

[25] S. Hall Murff, "The Association Between Oxidative Stress, Inflammation and Diabetes," *Am. J. Biomed. Sci. Res.*, vol. 4, no. 1, pp. 38–39, 2019, doi: 10.34297/ajbsr.2019.04.000755.

[26] P. Neha and S. Pandey-Rai, "Biochemical activity and therapeutic role of antioxidants in plants and humans.," *Plants as a source Nat. antioxidants*, no. February 2015, pp. 191–224, 2014, doi: 10.1079/9781780642666.0191.

[27] A. Jamuna Rani and S. V. Mythili, "Study on total antioxidant status in relation to oxidative stress in type 2 diabetes mellitus," *J. Clin. Diagnostic Res.*, vol. 8, no. 3, pp. 108–110, 2014, doi: 10.7860/JCDR/2014/7603.4121.

[28] A. Zeb, "Concept, mechanism, and applications of phenolic antioxidants in foods," *J. Food Biochem.*, vol. 44, no. 9, pp. 1–22, 2020, doi: 10.1111/jfbc.13394.

[29] A. Elbehiry, H. M. Edrees, and Y. M. Elmosaad, "Hypoglycemic and Anti-Inflammatory Effect of Gold Nanoparticles in Streptozotocin-Induced Type 1 Diabetes in Experimental Rats," *Int. J. Diabetes Res.*, vol. 2017, no. 1, pp. 16–23, 2017, doi: 10.5923/j.diabetes.20170601.03.

[30] N. Kaludercic and F. Di Lisa, "Mitochondrial ROS Formation in the Pathogenesis of Diabetic Cardiomyopathy," *Front. Cardiovasc. Med.*, vol. 7, no. February, pp. 1–15, 2020, doi: 10.3389/fcvm.2020.00012.

[31] S. Tangvarasittichai, "Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus," *World J. Diabetes*, vol. 6, no. 3, p. 456, 2015, doi: 10.4239/wjd.v6.i3.456.

[32] R. Alghazeer, N. Alghazir, N. Awayn, O. Ahtiwesh, and S. Elgahmasi, "Biomarkers of oxidative stress and antioxidant defense in patients with type 1 diabetes mellitus," *Ibnosina J. Med. Biomed. Sci.*, vol. 10, no. 6, p. 198, 2018, doi: 10.4103/ijmbs.ijmbs_59_18.

[33] K. Dong, H. Ni, M. Wu, Z. Tang, M. Halim, and D. Shi, "ROS-mediated glucose metabolic reprogram induces insulin resistance in type 2 diabetes," *Biochem. Biophys. Res.*

Commun., vol. 476, no. 4, pp. 204–211, 2016, doi: 10.1016/j.bbrc.2016.05.087.

[34] G. Z. Réus, A. S. Carlessi, R. H. Silva, L. B. Ceretta, and J. Quevedo, "Relationship of oxidative stress as a link between diabetes mellitus and major depressive disorder," *Oxid. Med. Cell. Longev.*, vol. 2019, no. Mdd, 2019, doi: 10.1155/2019/8637970.

[35] O. Khalis and M. T. Mohammed, "HIGHLIGHT ON CRITICAL PHYSIOLOGICAL STRESS PATHWAY IN," vol. 32, no. 3, pp. 12450–12456.

[36] M. Samiei *et al.*, "Investigating the mutagenic effects of three commonly used pulpotomy agents using the ames test," *Adv. Pharm. Bull.*, vol. 5, no. 1, pp. 121–125, 2015, doi: 10.5681/apb.2015.017.

[37] K. Chandra, P. Singh, S. Dwivedi, and S. Jain, "Diabetes Mellitus and Oxidative Stress: A Co-relative and Therapeutic Approach," *J. Clin. Diagnostic Res.*, vol. 2, no. Glut 4, pp. 10–15, 2019, doi: 10.7860/jcdr/2019/40628.12878.

[38] O. Khalisyaseen and M. T. Mohammed, "Identification Of Some Antioxidant Active Compounds In True Cinnamon (Cinnamomm Zeylanicum) Bark Extract," vol. 8, no. 4, pp. 7565–7577, 2021.

[39] M. T. Lee, W. C. Lin, B. Yu, and T. T. Lee, "Antioxidant capacity of phytochemicals and their potential effects on oxidative status in animals - A review," *Asian-Australasian J. Anim. Sci.*, vol. 30, no. 3, pp. 299–308, 2017, doi: 10.5713/ajas.16.0438.

[40] M. A. Mahdi, M. T. Mohammed, A. Mohammed Noori Jassim, and A. I. Mohammed, "Phytochemical content and anti-oxidant activity of hylocereusundatusandstudyoftoxicityandtheability ofwoundtreatment," *Plant Arch.*, vol. 18, no. 2, pp. 2672–2680, 2018.

[41] I. Kallel *et al.*, "Optimization of Cinnamon (Cinnamomum zeylanicum Blume) Essential Oil Extraction: Evaluation of Antioxidant and Antiproliferative Effects," *Evidence-based Complement. Altern. Med.*, vol. 2019, 2019, doi: 10.1155/2019/6498347.

[42] N. Błaszczyk, A. Rosiak, and J. Kałużna-Czaplińska, "The potential role of cinnamon in human health," *Forests*, vol. 12, no. 5, pp. 1–17, 2021, doi: 10.3390/f12050648.

[43] J. Fiedor and K. Burda, "Potential role of carotenoids as antioxidants in human health and disease," *Nutrients*, vol. 6, no. 2, pp. 466–488, 2014, doi: 10.3390/nu6020466.

[44] L. A. Martini, A. S. Catania, and S. R. G. Ferreira, "Role of vitamins and minerals in prevention and management of type 2 diabetes mellitus," *Nutr. Rev.*, vol. 68, no. 6, pp. 341–354, 2010, doi: 10.1111/j.1753-4887.2010.00296.x.

[45] M. Ashoori and A. Saedisomeolia, "Riboflavin (vitamin B2) and oxidative stress: A review," *Br. J. Nutr.*, vol. 111, no. 11, pp. 1985–1991, 2014, doi: 10.1017/S0007114514000178.