ORIGINAL ARTICLE

BITTER COFFEE FOR SWEET DIABETES: A RANDOMIZED CONTROLLED TRIAL FOR TREATMENT OF TYPE 2 DIABETES WITH BLACK COFFEE IN BALB C ALBINO MICE

Jawaria Iftikhar, Uzma Naeem*, Sadia Lodhi, Aamna Khokhar***, Abdul Azeem, Mehwish Tayyab*,**

Department Pharmacology, Watim Medical and Dental College, Rawat, Rawalpindi, *Islamic International Medical College, Rawalpindi, **Shifa College of Medicine, Islamabad, ***Islamabad Medical and Dental College, Rawalpindi, Pakistan

Background: Diabetes Mellitus is a chronic metabolic ailment which slowly but surely harms the human body if left untreated. The objective of this study was to determine the effect of black coffee on HbA_{1C}, fasting and postprandial blood sugar levels in mice model of type 2 diabetes mellitus. **Methods:** This was an experimental, randomized control study performed at the Pharmacology Laboratory, Multidisciplinary Research Laboratory at Islamic International Medical College and National Institute of Health (NIH) Islamabad Pakistan. The study comprised a total of 30 male Balb/c albino mice and diabetes was induced in experimental group (n=20) by using low dose streptozotocin (40 mg/Kg). After confirmation, diabetic mice were further divided into two groups of 10 each. Group 2 was diabetic control and Group 3 was treated with black coffee for 45 days. Blood samples were taken from lateral tail vein for fasting and post prandial blood sugar levels and by intracardiac puncture for HbA1c. Statistical analysis was done on SPSS-21. Comparisons between the groups were analyzed using one way ANOVA (post hoc tuckey test), and $p<0.05$ was considered significant. **Results:** Black coffee treated mice (Group 3) had significantly decreased serum HbA_{1C} levels (6.02±0.29) fasting (116.8±4.92) and postprandial (173.6±18.3) blood glucose levels in comparison with those found in diabetic control mice (Group 2). **Conclusion:** Black coffee significantly decreases serum HbA_{1C}, fasting and postprandial blood glucose levels in diabetic mice.

Keywords: Black Coffee, Diabetes, HbA_{1C}, Pancreatic islets cells

Pak J Physiol 2021;17(1):15–8

INTRODUCTION

Diabetes mellitus is a complicated, multifactorial global health burden that has achieved pandemic extents, fuelled by collaborations between several environmental and social components. It is a chronic catabolic disease that is host to many devastating complications. Type 2 Diabetes is the most widely recognized type of Diabetes represented by hyperglycaemia, insulin resistance, and relative insulin insufficiency.[1–3]

The International Diabetes Federation (IDF) data delivered an estimate of 381.8 million adults in 219 nations and regions with diabetes for 2013; and anticipated the number to ascend to 591.9 million in 2035. Conferring to report of International Diabetes Federation (IDF) in 2015, in Pakistan 7 million individuals were diabetics.[4,5]

With change in lifestyle patterns and lack of physical activity, type 2 diabetes mellitus is becoming the foremost type of diabetes which is estimated to affect 642 people by the year 2040. Among the many risk factors, obesity has become the major culprit to cause type 2 diabetes.[6] Type 2 diabetes is increasing at alarming rate despairingly the incidence is stirring up at earlier age in both adults and children.[7] Diabetes related complications, especially cardiovascular impairment, have become the chief basis of morbidity and mortality.[8] Every 6 seconds a diabetic patient pays the penalty of this disease with his life.[9] Nearly 5 million deaths were prompted by type 2 diabetes in year 2017.[10]

The distinctive treatment option of oral hypoglycaemic agents, however offer great glycemic control, yet over a long course of time, somehow fails to halt the progression of complications eventually. Plant materials which are being utilized as customary medication for the treatment of diabetes for quite a long time are considered to turn into the great choices as new treatment innovations.[11] To alleviate this well-being liability, there is an urgent and immediate need to use effective therapies.[12]

A couple of agents used in our routine diet, like black coffee can ensure a magnificent effort in lowering the glucose levels of diabetic patients. Black coffee, being the rich source of antioxidants, fights with the oxidative stress which is believed to be one of the underlying mechanisms in pathogenesis of complications imparted by diabetes.[13]

Long-term coffee consumption is associated with increase in insulin sensitivity and decrease in risk of diabetes. Many investigators have established an inverse relationship between coffee intake and development of type 2 diabetes.[14,15]

Although there are numerous studies done to highlight the eloquent role of black coffee on development of diabetes, yet very scanty data is

available about black coffee as treatment option of type 2 diabetes. In this randomized control trial, the effects of black coffee in Balb/c albino diabetic mice are seen on fasting blood glucose, postprandial blood glucose and serum HbA_{1C}.

MATERIAL AND METHODS

This comparative randomized control experimental study was carried out at Pharmacology Laboratory, Multidisciplinary Research Laboratory at Islamic International Medical College and National Institute of Health (NIH) Islamabad Pakistan. Before starting the study, a formal approval by the Ethics Review Committee of Islamic International Medical College, Riphah International University, was obtained. The duration of this study was 12 months (April 2017 to April 2018). A total of 30 healthy, 6–8 weeks old male, weighing 30–50 g albino Balb/c mice, having normal baseline parameters were included in the study.

All the mice were accommodated in standard cages made up of plastic and placed on metallic racks, at the Animal House of NIH, Islamabad. The mice had free access to tap water through the inverted bottles fixed on top of the cages. Animal house atmosphere was maintained at 20±2 °C with relative humidity of 50–70% and a light and dark cycle of 12 hours each. After the acclimatization for 1 week, the mice were randomly divided into two groups, 10 mice were allocated to Group 1 and 20 mice were allocated to the experimental Group. Group 1 was labelled as Normal Control and was given normal diet for 5 days whereas the Experimental group was given normal diet plus streptozotocin (40 mg/Kg/day)[16] intraperitoneally for consecutive 5 days. After 5 days, confirmation of diabetes was done in experimental group by measuring fasting blood glucose levels. Experimental group was later on divided into two groups, i.e., Group 2 and 3. Group 2 mice were labelled as Diabetic Control and were given normal standard diet only. Group 3 mice were given normal diet mixed with Black Coffee (5 g/Kg/day)[17] orally for 45 days.

A mid cycle sampling was done after 20 days to see the progress of drugs on fasting and postprandial blood glucose levels. After 45 days of treatment, final sampling of the experiment was done from lateral tail vein in all groups which included fasting and postprandial blood glucose levels, and HbA_{1C} by cardiac puncture.

Statistical analysis was done using SPSS-21. Results were documented as Mean±SEM. Comparisons of quantitative parameters among the three groups were analysed by using the one way ANOVA (post hoc tuckey test), and $p<0.05$ was considered significant.

RESULTS

Table-1 shows the comparison of Mean±SEM of all the groups. The results of group 3 are comparable to group 2. The diabetic control and significant value of $p<0.05$ is seen.

In the below mentioned table, the significant results are verified which are certainly comparable with the disease control group. In black coffee treated group, there was a substantial drop in hyperglycaemia which displays the positive effect of black coffee as a treatment tool for type 2 diabetes.

Table-1: Comparison of Mean±SEM in all groups

		Group 1 Normal control		Group 2 Diabetic control		Group 3 Black coffee treated		
Sampling	**Variables**	**Mean**	**SEM**	**Mean**	**SEM**	**Mean**	**SEM**	***P***
Initial sampling (day 15)	Fasting (mg/dl)	91.9	3.61	371.4	38.6	305.5	32.6	0.61
Mid-term Sampling (day 36)	Fasting (mg/dl)	81.0	4.07	337.6	35.3	116.8	4.92	0.000
	Random (mg/dl)	107.1	2.23	374.6	23.4	265.1	21.2	0.000
Terminal Sampling (day 61)	Fasting (mg/dl)	81.0	4.07	337.6	35.3	116.8	4.92	0.000
	Random (mg/dl)	139.1	7.35	443.8	21.5	173.6	18.3	0.000
	HbA_{1C} (%)	4.75	0.13	7.82	0.11	6.02	0.29	0.000

$p<0.05$=statistically significant

DISCUSSION

The results of present study confirm that hyperglycaemia induced by streptozotocin, is ameliorated by black coffee. In present study, the anti-diabetic effect of black coffee is seen in group 3.

Improvement of biochemical markers like HbA_{1C}, fasting and postprandial blood glucose levels in this study, is supported by the study of Sasha Jin *et al*[17] who studied the effect of chlorogenic acid (CGA, one of the major phenols present in black coffee) on glucose and lipid metabolism in late diabetic db/db mice for 12 weeks. They established that CGA could reduce the levels of fasting plasma glucose and HbA_{1C} during diabetes and improve kidney fibrosis through the modulation of adiponectin receptor signalling pathways in db/db mice.[17]

The reduction in biochemical and histopathological parameters were found by Kobayashi M *et al*[18] who used black coffee, caffeine extract, decaffeinated coffee against different sets of experiments to analyze the preventive part of black coffee on development of STZ-induced diabetes in male C57 BL/6J mice. They demonstrated that continuous black coffee ingestion prevented the development of STZ-induced diabetes mellitus. Black coffee also

increased pancreatic insulin output and suppressed the STZ-induced decline in pancreatic insulin content.[18]

Hui Cao *et al*[19] endorsed that significant evidence from epidemiological investigations showed that dietary polyphenols manage and prevent type 2 diabetes. Their review summarizes human studies and clinical trials of polyphenols as anti-diabetic agents. In prospective cohort studies, higher coffee consumption has been associated with a lower risk of Type 2 diabetes. It is demonstrated that ingestion of chlorogenic acid could significantly reduce early fasting glucose and insulin responses in overweight men during an oral glucose tolerance test. Polyphenols from different foods like coffee showed anti-diabetic effects in T2D patients through increasing glucose metabolism, improving vascular function as well as reducing insulin resistance and HbA1c level.[19]

Hesti Riany *et al*[20] concluded that different species of coffee (arabica, robusta and liberica) cultivated in Jambi province of Indonesia, have the ability to counter the hyperglycaemia induced by streptozotocin in mice. According to this intervention, the liberica species has offered the most promising results regarding biochemical analysis. There is marked decrease in fasting and postprandial blood glucose levels in streptozotocin induced diabetic mice given liberica species of coffee for 30 days as compared to mice given other species. There is another interesting aspect of this study is that when the histological parameters were examined; the mice treated with arabica species of coffee for 30 days, showed the lowest degenerative changes in liver.[20] That study embarks the finding in accordance with the previous studies.

Sake Juli Martina *et al*[21] determined that the use of Arabica coffee gayo bean and leaf extract showed a greater decrease in blood glucose levels in healthy mice after a glucose challenge. The biochemical parameters, i.e., fasting and postprandial blood glucose levels were markedly reduced to prove the evidence which are consistent with the outcomes of contemporary study. Blood sugar levels can be reduced by using Arabica coffee gayo bean extract as an alternative treatment. Taking coffee on regular basis not only reduces the risk of diabetes mellitus but also has ability to treat it. The components in coffee beans like caffeine stimulate lipolysis in adipose tissue. Arabica coffee gayo beans have ample amount of chlorogenic acid. Chlorogenic acid is a beneficial agent in the treatment of diabetes due to its antioxidant and anti-inflammatory effects which are very favourable in counteracting its effects.[21]

In the present study, improvement in biochemical parameters in Groups 3, which was given black coffee, was observed indicating that black coffee can be used in treatment of type 2 diabetes mellitus.

CONCLUSION

Black coffee significantly lowers HbA_{1C}, fasting and postprandial blood glucose levels in diabetic mice model. Therefore black coffee can be used as adjunct treatment for type 2 diabetes.

REFERENCES

1. Olokoba AB, Obateru OA, Olokoba LB. Type 2 diabetes mellitus: a review of current trends. Oman Med J 2012;27(4):269–73.
2. Chen L, Magliano DJ, Zimmet PZ. The worldwide epidemiology of type 2 diabetes mellitus —present and future perspectives. Nat Rev Endocrinol 2011;8(4):228–36.
3. Ighodaro OM. Molecular pathways associated with oxidative stress in diabetes mellitus. Biomed Pharmacother 2018;108:656–62.
4. Zafar J, Bhatti F, Akhtar N, Rasheed U, Bashir R, Humayun S, *et al*. Prevalence and risk factors for diabetes mellitus in a selected urban population of a city in Punjab. J Pak Med Assoc 2011;61(1):40–7.
5. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. J Pak Med Assoc 2016;66(12):1637–42.
6. Abbasi A, Juszczyk D, van Jaarsveld CHM, Gulliford MC. Body Mass Index and incident Type 1 and Type 2 Diabetes in children and young adults: A retrospective cohort study. J Endocr Soc 2017;1(5):524–37.
7. Atlas D. International Diabetes Federation. IDF Diabetes Atlas, (7th ed). Brussels, Belgium: International Diabetes Federation; 2015.
8. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018;14(2):88–98.
9. Basit A, Fawwad A, Qureshi H, Shera A. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. BMJ Open 2018;8(8):e020961.
10. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, *et al*. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018;138:271–81.
11. American Diabetes Association. Standards of medical care in diabetes —2010. Diabetes Care 2010;33(Suppl 1):S11–61.
12. Kleinert M, Clemmensen C, Hofmann SM, Moore MC, Renner S, Woods SC, *et al*. Animal models of obesity and diabetes mellitus. Nat Rev Endocrinol 2018;14(3):140–62.
13. Camandola S, Plick N, Mattson MP. Impact of coffee and cacao purine metabolites on neuroplasticity and neurodegenerative disease. Neurochem Res 2019;44:214–27.
14. Mirmiran P, Carlström M, Bahadoran Z, Azizi F. Long-term effects of coffee and caffeine intake on the risk of pre-diabetes and type 2 diabetes: findings from a population with low coffee consumption. Nutr Metab Cardiovasc Dis 2018;28(12):1261–6.
15. Casal S, Rebelo I. Coffee: a dietary intervention on type 2 diabetes? Curr Med Chem 2017;24(4):376–83.
16. Arulmozhi DK, Kurian R, Bodhankar SL, Veeranjaneyulu A. Metabolic effects of various antidiabetic and hypolipidaemic agents on a high-fat diet and multiple low-dose streptozocin (MLDS) mouse model of diabetes. J Pharm Pharmacol 2008;60(9):1167–73.
17. Jin S, Chang C, Zhang L, Liu Y, Huang X, Chen Z. Chlorogenic acid improves late diabetes through adiponectin receptor signaling pathways in db/db mice. PLoS One 2015;10(4):e0120842.
18. Kobayashi M, Kurata T, Hamana Y, Hiramitsu M, Inoue T, Murai A, *et al*. Coffee ingestion suppresses hyperglycemia in streptozotocin-induced diabetic mice. J Nutr Sci Vitaminol 2017;63(3):200–7.

19. Cao H, Ou J, Chen L, Zhang Y, Szkudelski T, Delmas D, *et al*. Dietary polyphenols and type 2 diabetes: Human study and clinical trial. Crit Rev Food Sci Nutr 2019;59(20):3371–9.
20. Riany H. Effects of coffee consumption in improving hyperglicemia in diabetes-induced mice. Int J Ecophysiol 2019;1(1):72–80.
21. Martina SJ, Govindan PAP, Wahyuni AS. The difference in effect of Arabica coffee gayo beans and leaf (Coffea Arabica Gayo) extract on decreasing blood sugar levels in healthy mice. Open access Maced J Med Sci 2019;7(20):3363–5.

Address for Correspondence:

Dr. Jawaria Iftikhar, Assistant Professor, Department of Pharmacology, Watim Medical and Dental College, Rawalpindi, Pakistan. **Cell:** +92-300-4219529
Email: drjawaria16@hotmail.com

Received: 18 Dec 2020 **Reviewed: 27 Mar 2021** **Accepted: 28 Mar 2021**

Contribution of Authors:

JI: Concept, data acquisition, analysis and manuscript writing
UN: Concept, data acquisition, analysis and manuscript writing
SL: Design, methodology, analysis and manuscript writing
AK: Design, methodology, revision of the project and critical review if intellectual content
AA: Revision of the project and critical review if intellectual content
MT: Revision of the project and critical review if intellectual content

Funding disclosure: None to declare
Conflict of interest: None