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Chemical and immunological effects of coffee peels and beans in diabetic rats

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ABSTRACT

Coffee contains chlorogenic acid, caffeine, and other polyphenols that exhibit immunomodulatory effects, enhancing immune function and potentially reducing the risk of autoimmune diseases. Aim: This study aims to examine the important chemical compounds of coffee and evaluate their impacts on the immune system in rats with hyperglycemia. Materials and Methods: Thirty-six male Sprague Dawley rats were divided into normal (n=6) and diabetic (n=30). The second group was injected with streptozotocin (at a dose of 75 mg/ kg intraperitoneally), and those with blood glucose concentrations more than 250 mg/dL were classified as diabetic. Rats were divided into six groups, (1) non-diabetic group (n=6) received distilled water (2 mL/ day); (2) diabetic control group (n=6) received distilled water (2 mL/ day); (3) diabetic group (n=6) received basal diet +5% coffee peels; (4) diabetic group (n=6) received basal diet +10% coffee peels ; (5) diabetic group (n=6) received basal diet +5% coffee beans.; (6) diabetic group (n=6) received a basal diet +10% coffee beans. After 28 days, blood was collected, and serum was extracted to determine immunity function, WBC (White Blood Cell), LYM (Lymphocytes), MID (Middle Cell), RBC (Red Blood Cell), Hgb (Hemoglobin), HCT (Hematocrit),MCV (Mean Corpuscular Volume), MCH (Mean Corpuscular Hemoglobin), MCHC (Mean Corpuscular Hemoglobin Concentration), RDW (Red Cell Distribution Width, PLT (Platelet), MPV (Mean Platelet Volume). Results: The results show a significant increase in fiber in coffee peels compared to coffee beans. It was also found that the carbohydrate content in coffee beans is higher than in coffee peels, and the protein content in coffee beans is also higher than in coffee peels. The best group for WBC, LYM, Mid-size cells (MID), and Granulocytes (GRAN) was that of the group 5 (5% coffee peels). While the best group for Mean Platelet Volume(MPV), and Platelets (PLT) was that of group 4(10% coffee beans). Coffee peels and beans demonstrate significant potential in supporting immune function and reducing inflammation, highlighting their promising role in health applications.

KEYWORDS: Immunological studies - therapeutic nutrition - Coffee -Diabetic rats.

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INTRODUCTION

Immunity is the body's defense system that protects it from diseases caused by foreign invaders like bacteria and viruses. This resistance can be innate, a natural, pre-programmed defense, or adaptive, a learned response developed after encountering an infection or through vaccination. Adaptive immunity relies on special white blood cells that "remember" previous threats, allowing for a faster and more effective response to future exposures. **(Haile *et al.*, 2022).** Coffee is a plant species within the genus Coffea of the Rubiaceae family. Though the identification of numerous coffee variations globally, Coffea arabica, frequently denoted to as Arabica coffee, & Coffea canephora, known as Robusta coffee, are the economically significant alternations grown most extensively worldwide **(Lachine *et al* ., 2019).** Though certain investigations relate consumption of caffeine and coffee to health problems, recent investigation illustrates that coffee significantly strengthening the immunimmuity & protects the body against the possibility of obesity, neurological illness, T2DM, pancreatic tumor, as well as osteoporosis, due to its components like chlorogenic a`, caffeine, kahweol, cafestol, as well as micronutrients (potassium, magnesium, vitamin E, and niacin) **(Abouzid *et al.*, 2022).** Moreover, currently, coffee is recognized as a functional food because of its abundant antioxidant and other advantageous biological features. It was reported that coffee consumption diminishes inflammatory indicators whereas elevating anti-inflammatory indicators **(Al Amri et al ., 2020).** The activation of adenylyl cyclase and the conversion of ATP to cyclic adenosine monophosphate (cAMP) come about as a result of caffeine's interaction with the A2A receptor receptor. Inhibition of phosphodiesterase (PDE) is the mechanism by which this effect brings about an intracellular chain of signaling activities that are driven by an increase in cAMP overexpression. Therefore, the second messenger cAMP is responsible for reinforcing the intracellular nature of the extracellular binding of caffeine. Protein kinase A (PKA) is activated when there is an elevated level of cAMP, which also inhibits the production of proinflammatory cytokines. Through the

suppression of inflammation, the activity of numerous immunological actors is reduced. These immune players include the proliferation of T and B cells, the cytotoxicity of natural killer (NK) cells, macrophages, and the creation of antibodies. In addition to this, it has the ability to alter the levels of expression of major histocompatibility class I molecules and toll-like receptors (TLRs). **(Al-Brakati *et al* ., 2020)**. Splenocytes of mice were incubated for twenty-four hours with freeze-dried 0.1 milligram per milliliter instant coffee or arabinogalactan. As an outcome, significant rise has been found in anti-inflammatory cytokine (interleukin-2) concentrations in the monocytes of mice. **(Ali *et al.,* 2020).** Another investigation indicated that caffeine supplementatio in rats diminished the expression of inflammatory cytokines (TNF-α, IL-6) in monocytes and PBMC, that are immune system cells . A further investigation demonstrated that mRNA concentrations of TNF-α and interleukin-6 have been inhibited in the murine macrophage-like cell line RAW 264.7 cells managed with lipopolysaccharides (LPS) of coffee. A negative association has been identified among intake of coffee extract & the concentration of inflammatory cytokines (**Ansley *et al.,* 2013)**. Another research investigated that coffee consumption significantly promoted the migration of RAW 246.7 hepatic macrophage cells & macrophage, while also elevating the expression of numerous cytokines (iNOS, tumor necrosis factor alpha, as well as IL-6) at the mRNA level in RAW 246.7 & hepatic macrophage cell lysates **(Chung *et al.,* 2016).** The research investigating the influence of caffeine on the innate immune system indicated that caffeine intake enhanced the activity of natural killer cells, that are recognized for their cytotoxic role in defeating pathogens, in contrast, it has been stated that the influence in question is reversed in cases of high intake of caffeine (eighteen milligrams per kilogram per day) (**Dewidar *et al.,* 2020).** Recent reports indicate that moderate coffee consumption (three to four cups per daily) is beneficial for human health (**Vieira** et al ., **2020).**

AIM OF STUDY: -

The objective of this investigation is to investigate the essential chemical compounds of coffee and assess their effects on the immune system in rats had hyperglycemia.

MATERIALS AND METHODS: -

A- Source of coffee beans and peels: Coffee beans and peels were purchased from Al-Baha City, KSA, local market, washed, cleaned, blended, & ground into fine powder utilizing an electric grinder. To reduce oxidation, they were stored in dark-stoppered glass bottles until ready to be used. according to **(Russo, 2001).**

B-Rats: Thirty-six male Sprague Dawley rats (*n*=36) weighing 150-170 g were obtained from Egypt's Ministry of Health's Animal Unit at Helwan Farm. For two weeks, the rats were housed in individual plastic cages under controlled conditions, with a temperature of 22°C and a 12-hour light/dark cycle at the Faculty of Home Economics, Menoufia University, Egypt. The rats had unrestricted access to food and water. All experiments followed the National Institute of Health's Guiding Principles for Animal Care and Use. Rats were weighed after two weeks of acclimatization and randomly allocated to one of two groups: diabetic (30 rats) and normal (6 rats)

C- Induction of Diabetes (T1DM): After two weeks of acclimatization of rats, type 1 diabetes mellitus was induced by intraperitoneal injections of Streptozotocin (STZ) as described previously. The rats were injected with a dose of 75 mg/kg intraperitoneally of Streptozotocin (STZ) (Sigma-Aldrich, St. Louis, MO, USA). Following this, all rats fasted for 8 hr, then blood samples were taken from the retro-orbital veins to determine blood glucose concentrations. The study included diabetic rats with blood glucose concentrations more than 250 mg/dL. Following the exclusion of rats with blood glucose concentrations below 250 mg/dL and deceased rats, 24 rats were included in the study and subsequently developed diabetes. In addition, diabetic rats

D- Diets:

- Basal diet: The basal diet comprises protein (10%), corn oil (10%), choline chloride (0.2%), cellulose (5%), combination of vitamin (1%), salt combination (4%) **(Hegested et al., 1941),** & corn starch (to one hundred percent). in accordance with **AIN (1993)**

E- Experimental Design

The study included all normal (6 rats) and diabetic (30 rats). In addition to the experimental procedure, all rats involved in this investigation were fed the standard diet. The proposed interventions were orally administered once per day. **AIN., (1993).** The weights of the rats were also recorded, and diabetic rats have divided into experimental groups accordingly. The following were the experimental groups:

1- The non-diabetic group (ND-Gr) consisted of six normal rats that received a daily 2 mL of distilled water orally per rat once daily.
2- The diabetic control group (DC-Gr) consisted of six diabetic rats that received a daily 2 mL of distilled water orally per rat once daily
3- The diabetic group (DC-Gr), consisting of six rats, received basal diet + 5% coffee beans
4- The diabetic group (DC-Gr), consisting of six rats, received basal diet + 10% coffee beans
5- The diabetic group (DC-Gr), consisting of six rats, received basal diet + 5% coffee peels
6- The diabetic group (DC-Gr), consisting of six rats, received basal diet + 10% coffee peels

F- Blood sampling: Initially, blood samples have been collected from the retro-orbital vein following a fasting period of twelve hours, while at the end of each experiment, they have been collected from the hepatic portal vein. Blood samples have been gathered into clean, dry centrifuge glass tubes and permitted to clot in a water bath at thirty-seven degrees Celsius for twenty-eight minutes. The serum was subsequently separated by centrifuging the tubes at four thousand revolutions per minute for ten minutes. The serum has been cautiously aspirated and transferred to a clean Eppendorf tube, where it was kept at minus twenty degrees Celsius until analysis. This method was labeled by **(Schermer,1967).**

G- **Complete blood count (CBC) test**

The test is included WBC count, HB, RBC count, WBC& Platelet count. The results of CBC are generated by highly automated electronic and pneumatic analyzers based on aperture- impedance and\or laser beam cell sizing and counting according to **Jacobs et al., (2001).**

H- Statistical analysis:

The student-Newman-Keuls test has been utilized to separate the means after a significant main effect has been discovered. The data was examined via an entirely randomized factorial design [SAS, 1988]. Treatment variances (P value less than 0.05) have been deemed significant by the Costat Program. Analyses of biological outcomes were conducted using one-way ANOVA.

- **Ethical Approval**

The study was approved by Al-Baha University's Research Ethics Committee (Ref. No. 46123022), Approval date 17 April 2025.

RESULTS AND DISCUSSION

4.1. Chemical composition of coffee peels and beans:

Table 1 illustrates the chemical composition of coffee peels and beans. The results indicate that coffee peels include ash, carbohydrates, fat, moisture, fiber, protein, and energy value. The dry weight (D/W) was 9.5, 32.3, 1.95, 7.18, 39.3, 9.77, and 185.63 kilocalories per one hundred grams, correspondingly.

coffee beans contain ash, carbohydrates, fat, moisture, fiber, protein, and energy value. The dry weight was 5.9, 42.9, 12.9, 9.9, 13.2, 15.2, and 348.5 kilocalories per 100 grams, respectively

Table (1): Chemical composition of coffee peels and beans

Constitutes (%)	coffee peels	coffee beans
Ash	9.5	5.9
Carbohydrates	32.3	42.9
Fat	1.95	12.9
Moisture	7.18	9.9
Fiber	39.3	13.2
Protein	9.77	15.2
Energy value (Kcal/l00g)	185.63	348.5

DW= Dry weight

RESULTS

4.2. Immunological results.

Blood Parameters

Table (2) illustrates the influence of various levels of coffee peels and beans on RBC, Hgb, MCV, RDW, HCT, MCH, and MCHC in diabetic rats.

As demonstrated the mean value of RBC of control +ve was significantly lower (p under 0.05) than control negative, which were 1.10±0.18 and 5.30±0.15 m/ul, correspondingly. In contrast, the value of all groups was significantly higher than control (+) by a mean of 1.31±0.01, 1.22±0.03; 1.80±0.06, and 1.51±0.04m/ul, correspondingly.

At the same time Hgb of control +ve group was significantly lower (p-value below 0.05) as than control (-) rats, being 10.10±0.37 and 15.52±0.50 g/dl, respectively. In addition, the value of all groups was significantly elevated than control (+) rats by means of 14.98±0.97,15.38±0.45; 15.79±0.71, and 16.25±0.66g/dl, correspondingly.

Table (2) illustrates that the mean MCV value of the positive control group has significantly been raised (p-value below 0.05) than the negative control group, with values of 65.96±4.61 & 58.62±3.16 fl, respectively. The values of all groups have substantially been diminished than the +ve control, which was 40.95±3.00, 53.84±3.41, and 51.35±2.90 fl, correspondingly.

As illustrated in table (2) the mean value of RDW of control +ve rats was significantly elevated (p-value less than 0.05) when compared to control -ve 20.42±0.52 and 13.22±0.69 %, respectively. Moreover, the value of all groups was significantly declined when compared to the control (+) being 12.20±0.72, 11.80±9.47, 12.02±0.55, and 11.20±0.48 %, respectively.

As demonstrated in table (1) results, the mean value of HCT of control +ve rats was significantly lower (p-value less than 0.05) when compared to the control (-) group, 17.00±0.53 & 30.40±1.51 %, respectively. Additionally, the value of all groups was significantly elevated when compared to the control (+) group, which were 26.82±1.73, 28.00±1.25, 23.00±1.78, and 25.00±1.13 %, respectively.

The mean value of MCH of control positive was significantly lower (p under 0.05) when compared to control (-), which were 9.10±0.29 and 17.20±0.22 pg, correspondingly. Moreover, the value of all groups was significantly higher when compared to control (+) which were 13.78±0.23, 14.80±0.10, 15.00±0.39, and 17.28±0.59pg, respectively.

As illustrated in table (2) the mean value of MCHC of control +ve was significantly lower (p under 0.05) than control -ve rats which were 6.40±1.22 and 12.50±0.70 g/dl, respectively. whereas, the value of all groups was significantly higher than control positive by mean 11.28±0.59, 13.00±1.00; 13.00±1.00, and 13.22±0.70g/dl, correspondingly. It could be noticed (Table 2) that the best results of RBC, Hgb, HCT and MCH were found in group 3 (5%) green fenugreek powde. This is likely because of the

high nutritional content of green fenugreek powder, which is rich in vital minerals and vitamins like vitamin C, folic acid, and iron. These nutrients are crucial for the production and health of red blood cells, directly influencing variables like hemoglobin (Hgb), MCV, MCH, RDW (red cell distribution width), HCT (hematocrit), The 5% concentration may provide an optimal balance, enhancing these blood markers

Table (2): Influence of numerous degrees of coffee beans and peels on RBC, Hgb, MCV, RDW, HCT, MCH and MCHC in diabetic rats

Group Parameter	Control negative	Control positive	Five percent Coffee beans	Ten percent Coffee beans	Five percent Coffee peels	Ten percent Coffee peels
RBC (m/ul)	5.301±0.15	1.101±0.18	1.311±0.01	1.221±0.03	1.801±0.06	1.511±0.04
Hgb (g/dl)	15.521±0.50	10.101±0.37	14.981±0.97	15.381±0.45	15.791±0.71	16.251±0.66
MCV(fl)	58.621±3.16	65.961±4.61	57.841±2.68	56.751±2.82	55.38±1.51	52.92±2.60
RDW(%)	13.221±0.69	20.421±0.52	12.20±0.72	11.801±0.47	12.021±0.55	11.201±0.48
HCT(%)	30.401±1.51	17.001±0.53	26.821±1.73	28.001±1.25	23.001±1.78	25.00±1.13
MCH(pg)	17.201±0.22	9.101±0.29	13.781±0.23	14.801±0.10	15.001±0.39	17.28±0.59
MCHC(g/dl)	12.501±0.70	6.401±1.22	11.281±0.59	13.001±1.00	13.001±1.00	13.221±0.70

Distinction is significant at 5 % (P-value under 0.05). Control positive: Diabetic mice fed on a stander diet. Control negative: Mice fed on standard diet.

Platelets

Table (3) demonstrates the influence of numerous levels of coffee peels and beans on PLT and MPV in diabetic rats. As demonstrates in this table, the mean value of PLT of control positive was elevated than control negative, which were 367.10±11.19 and 110.50±3.50 k/ul, correspondingly. Additionally, the value of all groups were significantly lower (p under 0.05) when compared to control (+), via mean 118.20±2.77, 116.20 ±2.96; 85.00±3.46 and 80.20±2.90 k/ul, consistently.

As for MPV, the mean value of control +ve has been reduced than control -ve, which were 2.00±0.20 and 3.85±0.13 fl, correspondingly, as well as Also, the value of all groups has been elevated than control positive, by mean 2.94±0.02, 3.19±0.10 and 3.92±0.02. fl, respectively. It is evident that the PLT raised while MPV decreased by hyperglycemia, while feeding with experimental diets showed the reverse. The best group was recorded was group 4 (10%) Coffee beans.

Table (3): Influence of numerous degrees of coffee beans and peels on PLT and MPV in diabetic rats.

Group Parameter	Control positive	Control positive	Five percent Coffee beans	Ten percent Coffee beans	Five percent Coffee peels	Ten percent Coffee peels
PLT(k/ul)	110.50±3.50	367.10±11.19	118.20±2.77	116.20±2.96	85.001±3.46	80.20±2.90
MPV(fl)	3.85±0.13	2.00±0.20	3.001±0.08	3.281±0.07	2.941±0.05	2.981±0.08

Control +Ve: Diabetic rats fed on a basal diet. Control -Ve: Rats fed on basal diet.

Cells related to immunity-

Table (4) illustrates the influence of several levels of coffee peels and beans on WBC, LYM, MID and GRAN in rats pretreated with Alloxan. The mean value of WBC of control +ve was significantly reduced (p under 0.05) than control negative, which were 5.30±0.26 & 6.13±0.06 k/ul, correspondingly. Furthermore, the value of all groups was significantly elevated than control (+) by means 8.06±0.15, 9.50±0.21; 7.50±0.28, 9.34 ±0.09k/ul, consistently.

As for LYM, the mean value of control (+) has been reduced than control (-), which were 3.94±0.15 and 5.00±0.17 %L, consistently. Whereas. The value of all groups was greater than control (+) which were 5.40±0.10, 8.10±0.21; 5.32±0.16, and 6.32±0.31 %L respectively.

The same table demonstrated that the mean value of MID of control (+) was significantly lower (p under 0.05) than control -ve, which were 0.52±0.017 and 0.70±0.010 % M, respectively. The value of all groups was greater than the control positive, which were 1.36±0.053, 1.72±0.024, 1.28±0.029, and 1.32±0.017% M, correspondingly.

As for Granulocytes GRAN, it was observed that the mean value of control +ve was significantly less (p-value less than 0.05) compared to control negative, with the former being 0.29±0.019 %G and the latter being 0.42±0.013 %G. Additionally, it is worth noting that the values of all groups was found to be higher than the control positive, with the mean values being 0.58±0.018, 0.60±0.021, 0.52±0.022, and 0.60±0.018% G each. It was clear that the group consisting of five (five percent) coffee peels was the most effective group for WBC, LYM, MID, and GRAN.

Table (4): Influence of different degrees of coffee beans & peels on WBC, LYM, MiD and GRAN in diabetic rats.

Group **Parameter**	**Control negative**	**Control postive**	**Ten percent Coffee beans**	**Ten percent Coffee beans**	**Five percent Coffee peels**	**Ten percent Coffee peels**
WBC(k/ul)	6.13±0.06	5.3±00.26	8.061±0.15	9.501±0.21	7.501±0.28	9.341±0.09
LYM(%L)	5.00±0.17	3.941±0.15	5.401±0.10	8.101±0.21	5.321±0.16	6.321±0.31
MID(%M)	0.70±0.010	0.521±0.017	1.36±0.053	1.721±0.024	1.281±0.029	1.321±0.017
GRAN(%G)	0.42±0.013	0.29±0.019	0.581±0.018	0.601±0.021	0.521±0.022	0.601±0.018

DISCUSSION

The goal of these investigations to analyze the crucial chemical compounds of coffee (beans & peels) and assess their influences on the immunity in rats with hyperglycemia. The antioxidant properties of coffee have a significant role in neutralizing free radicals, that could otherwise trigger cellular damage and contribute to chronic illnesses. By reducing oxidative stress, these antioxidants help maintain cellular health and support overall immune system resilience. This protective effect can lead to a lower risk of developing conditions associated with inflammation and oxidative damage **(Alamri et al., 2019).** Indicates a significant reduction in WBC and LYM percentages in diabetic rats treated with coffee extracts, possibly due to its antioxidant properties. (**Farooqui et al., 2019).** Show different effects, such as no significant change in total WBC count or an increase in lymphocytes with some coffee types, suggesting the outcome is dependent on the coffee type (e.g., green vs. roasted), processing, and specific extract used **(Asmamaw *et al.*,2021),** Some studies show that coffee extracts can help reduce total WBC counts in diabetic rats, potentially by acting as an anti-inflammatory agent and improving anemia **(Singh *et al.*,2019)**. Noted a decrease in granulocytes (GRAN) in rats treated with coffee bean extracts, which may be linked to a decrease in inflammatory processes. (**Radosinska *et al.* 2021)**, The RBC count was detected to be higher in the coffee-treated group in comparison with the control group, though the distinction wasn't always statistically significant, and reported a significant increase in Hgb, Hgb, MCV, RDW, HCT, MCH and MCHC in a coffee-treated group. Coffee contains polyphenols and other compounds that act as antioxidants, neutralizing harmful free radicals that cause oxidative stress, which is often elevated in diabetic conditions. **(Priftis *et al.* 2018)**. The concentration of the coffee extract or the dose of the coffee given to the rats can influence the outcome, with higher concentrations potentially having a greater effect. (**Wang *et al.* 2023)**, A statistically significant variance has been found in the RBC variables between type 2 diabetes mellitus cases and the control group. The mean RBC count, hemoglobin, hematocrit (P under 0.001), and MCHC (P equal 0.002) in cases had type II diabetes were significantly reduce compared to those in the control group. The mean red cell distribution width was significantly elevated in the type II diabetic case group than the control group (P under 0.001). The mean count of RBC, hematocrit, and hemoglobin levels in cases with good glycemic control were significantly elevated compared to those with poor glycemic control. A statistically significant negative correlation has been identified among glycemic management and RBC count, hematocrit, hemoglobin as well as concentrations in diabetic cases. **(Liardon *et al.* 2020**). Supplementing diabetic rats with coffee beans and peels shows promise for improving immune function, with green coffee bean extract often being more beneficial than roasted forms due to higher antioxidant content. Investigations demonstrates that these supplements may diminish oxidative stress, enhance antioxidant enzyme activity, and decrease inflammatory markers, which collectively support immune function in diabetic rats. The effectiveness varies by the coffee form (peels vs. beans) and roasting degree, with some research suggesting that coffee peels may have an enhanced therapeutic effect when combined with other herbs. **(Sadiq *et al.* 2019**). Coffee peels show potential for improving the biochemical changes associated with diabetes and enhancing the therapeutic effects of other herbs. By improving antioxidant status and reducing inflammation, coffee bean and peel supplements help to normalize some of the immune-related physiological changes that occur in diabetes. **(Mahmoud *et al.* 2013**).

CONCLUSION

In conclusion, Coffee peels and beans can help stimulate the immune system via increasing the production of cytokines, which are molecules that aid in cell signaling during immune responses. It also enhances the activity of immune cells, like lymphocytes and natural killer cells, which has vital roles in the body defense against infections. Additionally, caffeine's anti-inflammatory properties can aid modulate response of the immunity, potentially diminishing the severity of inflammatory conditions. Coffee peels and beans demonstrate significant potential in supporting immune function and reducing inflammation, highlighting their promising role in health applications

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