RESEARCH ARTICLE

In Vitro, Effect of Ellagic Acid on Glucose and Albumin Levels for Diabetics Type 1 in Al-Muthanna Province

Ali Tariq Hadi[1], Nabil Sabri Al-Habib[1], Riyadh Jaleel Nahi[1]

Department of Chemistry, College of Science, Al-Muthanna University, Samawah, Iraq

Received: 05th July, 19; Revised: 06th August, 19, Accepted: 05th September, 19; Available Online: 25th September, 2019

ABSTRACT

The current study is interested in the study of the effect of ellagic acid on levels of glucose and albumin for people with diabetes of type 1. The target blood samples were collected from 52 diabetics' type 1 (female and male). For each collected sample, the levels of glucose and albumin were firstly measured, and the obtained read was recorded as a control read. A solution of ellagic acid (45 µL) was then added, and the resulting solution was then incubated at 37°C for 45, followed by measuring the levels of glucose and albumin. The same sample was then incubated again at 37°C for a further 45 minutes, and the levels of glucose and albumin were then measured. For both incubation times, the obtained results showed that the addition of ellagic acid reduced the levels of glucose and albumin. Furthermore, varietal differences were observed in the levels of glucose and albumin, depending on the incubation time. Also, all obtained reads were studied statistically as a function for some risk factors such as age, weight, and gender.

Keywords: Diabetics Type 1, Ellagic Acid, Levels of Albumin, Levels of Glucose.

International Journal of Pharmaceutical Quality Assurance (2019); DOI: 10.25258/ijpqa.10.3.19

How to cite this article: Hadi, A.T., Al-Habib, N.S. and Nahi, R.J. (2019). Biosynthesis and Characterization of Gold Nanoparticles by Using Local *Serratia* spp. Isolate. International Journal of Pharmaceutical Quality Assurance 10(3): 43-49.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous metabolic disorder identified by the presence of hyperglycemia due to a lack of insulin secretion or defective insulin action.[1] Insulin is a protein made up of beta cells in the pancreas with a high molecular weight of about 5.8 kDa.[2] Functionally, insulin plays a crucial role in glucose regulations and controls on the uptake of glucose into the cells within the body.[3] Thus, a high level of glucose in the blood represents a signal that the body is ready to infect with diabetes disease. Commonly, there are two main types of diabetes mellitus, which are type 1 and type 2.[4] In general, untreated diabetics can cause many complications to include diabetic ketoacidosis and non-ketotic hyperosmolar coma.[5] Furthermore, serious long term complications include stroke, heart disease, kidney failure, damage to the eyes, and foot ulcers.[6,7] In type 1, the pancreas does not produce insulin or mutated unusable insulin; thereby, the body cannot overcome an increase in levels of glucose sugar.[8] Normally, the concentration of glucose in the blood is below 7.8 mmol/L; however, it typically falls between 4.0–6.0 mmol/L during fasting time.[9,10] In diabetes, glucose, with its biological half-life of 90 minutes, is a perfect indicator of a diabetic's status over the preceding few hours.[11] The main complicated that is associated with high concentrations of glucose is glycation end products.[12] This process is promoted by the presence of elevated blood glucose concentrations in diabetes and occurs with various proteins that include human serum albumin (HAS).[13] Human serum albumin is the most abundant circulating protein found in human blood plasma and constitutes about 50 % of serum protein with a concentration of 3.5–5.5 g/dL under physiological conditions.[14] The HAS is a multifunctional negatively charged protein synthesized in the liver with molecular weight 66.5 kDa consists of 585 amino acids constructed in similar sequence among many veterinary species.[15] The main functions of albumin are regulation of plasma oncotic pressure, maintenance of acid-base balancehe, and acts as an antioxidant system.[16] In the current study, it was interested in the investigation of ellagic acid on the levels of glucose and albumin of diabetics' type 1. Ellagic acid (EA) is also known as 2,3,7,8-tetrahydroxy-chromeno-[5,4,3-cde]-chromene-5,10-dione a polyphenol molecule (Figure 1) with a molecular weight of 302 g/mol with molecular formula

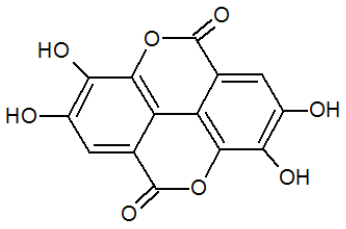

Figure 1: Structure of Ellagic acid.

**Author for Correspondence: riaydhnahi@yahoo.com; sajadayad1975@gmail.com*

$C_{14}H_6O_8$.[17] Structurally, it has four fused rings contain four hydroxyl groups attached to the main rings to represent the lipophilic and two lactones groups, which can act as hydrogen-forming sides and electron acceptors, respectively, and represent the hydrophilic domain.[18]

Naturally, EA is found in various fruits and vegetables, including strawberries, blackberries, raspberries, walnuts, pecans, pomegranates, and wolfberry.[19] Ellagic acid possesses antioxidant, anti-mutagenic, and anticancer properties.[20] Furthermore, it has beneficial effects in acute pancreatitis, specially, in reducing the levels of pancreatic inflammation and fibrosis.[21] Recently, ellagic acid has been receiving attention as an agent that may have potential bioactivities preventing chronic diseases such as DM and reducing glycation formation products.[22,23]

EXPERIMENTAL

Chemicals and Instruments

All materials that were used in the current study were purchased from commercially available sources. In this study, In this study, powder of ellagic acid was used and operating solutions for the Cubas (C 111). These operating solutions include cleaner solution, deproteinized solution, solution of activator, albumin kit, and glucose kit that which manufactured by the German company Roche. The main instrument used in this study is the Cubas (C 111), the cubas (C 111) is fully automatic instrument analyzer intended for the in vitro determination of clinical chemistry and it was used to measure concentrations of glucose and albumin in the serum of human. This instrument found in the Center for Endocrinology and Diabetes in Muthanna Governorate in the Division of Chemistry of Laboratory.

Blood Samples Collection

Blood samples were collected from 52 people with diabetes of type 1(male and female). The collected samples were kept in vacuum collection tubes with gel. The serum was then separated by the centrifuge (3000 rpm for 5 mins) and was placed in a fridge at 4ºC to be used in the next step.

Preparation of Ellagic Acid Solution

Ellagic acid powder (8.5 mg, 0.0085 mmole) was dissolved in distilled water (10 mL). The resulting solution was then centrifuged (3000 rpm for 5 min) to check if there any remaining insoluble amount of ellagic acid.

Measurement of Concentration of Glucose and Albumin

The serum sample was spun down using a centrifuge for 5 minutes, and (300 µL) of the target sample was then placed in Cubas cup at a sample area. The concentration of both glucose and albumin was then measured using the Cubas (C 111) system as control reads. To this sample, a solution of ellagic acid (45 µL) was added, and the resulted solution was then incubated at 37 °C for 45 minutes, followed by measuring the concentration of glucose and albumin. The obtained reads were recorded as reads for incubation for 45 minutes. The same solution was then incubated again for a further 45 minutes at 37°C, followed by measuring the concentrations of glucose and albumin as and recorded as reads for incubation after 90 minutes. This process was repeated for all collected samples.

Statistical Analysis

This study designed by a completely randomized design (CRD) that was used in the statistical analysis for data by using a one-way ANOVA test, LSD (Least significant difference), and independent *t*-test at a 5% level of significance. The controls data that recorded before treatment of the target samples with ellagic acid and the reads that were recorded after incubation the target samples with ellagic acid for 45 and 90 minutes were investigated statistically between by Pearson correlation coefficient test. Data were processed and analyzed by using Statistical Program Social Science (SPSS 22) and the results were expressed as mean ± SD.

RESULTS AND DISCUSSION

In the current study, the amount of ellagic acid (8.5 mg, 0.0085 mmol) was chosen according to the solubility of ellagic acid in the water, and the volume of addition (45 µl) was chosen based on the standard dose of the ellagic that allowed giving to the body. In general, the current study revealed interesting results for both glucose and albumin levels. For glucose level, it was found a significant difference between the control reads the corresponding reads that were recorded after incubation with ellagic acid for 45 minutes ($p < 0.05$, $p = 0.038$) as shown in Table 1 and Figure 1. In contrast, the incubation of the treated samples for 90 minutes did not display a significant

Table 1: Comparison of glucose and albumin means between the control reads and the reads that were recorded after incubation with ellagic acid for 45 and 90 min for diabetics type 1.

Parameter	*Control reads*	*Incubation for 45 min*	*Incubation for 90 min*	*p value*
Glucose con.(mg/dL)	343.7 ± 142.7	291 ± 118	299.8 ± 122.7	a- 0.084 b- 0.038* c- 0.083 d- 0.730
Albumin con.(g/L)	48.6 ± 4	42.4 ± 3.3	43.9 ± 3.3	a- 0.000* b- 0.000* c- 0.000* d- 0.039*

*represents a significant difference at $p \leq 0.05$. Letters (a,b.c.d) represent type of the statistical analysis: a- Represent the comparison among the control reads and the reads that were recorded after incubation with ellagic acid for 45 and 90 min. b- Represent the comparison between control reads and after incubation for 45 minutes. C- Represent the comparison between control reads and after incubation for 90 min. d- Represent the comparison between reads after incubation for 45 minutes and 90 mintues.

difference ($p > 0.05$, $p = 0.083$) comparison to the control reads or with each other as shown in Table 1 and Figure 1. While for albumin levels, it was observed that both incubation times (45 and 90 minutes) indicated an interesting difference in albumin concentrations comparison to the control or with each other ($p < 0.05$) as shown in Table 1 and Figure 2.

Also, the relationship between the controls reads and their corresponding reads that were recorded after incubation for 45 and 90 minutes for both glucose and albumin were also studied statistically. For glucose levels, it was found there is a strong positive correlation ($r = 0.951$ and $r = 0.948$) between the control and that read that was recorded after incubation with ellagic acid for 45 and 90 minutes, respectively as shown in Table 2. These relationships indicate a proportionate relationship increased with a higher value of glucose levels as shown in Figures 3 and 4.

For albumin, it was also found a strong positive correlation; $r = 0.902$ and $r = 0.896$ between the control reads and their corresponding reads that were recorded after incubation with ellagic acid for 45 and 90 minutes, respectively as shown in Table 3. This means the effect of ellagic acid is increased with increasing value of albumin, regardless of the incubation time, whether 45 minutes or 90 minutes, as shown in Figures 5 and 6. For more investigations, the effect of ellagic acid on levels

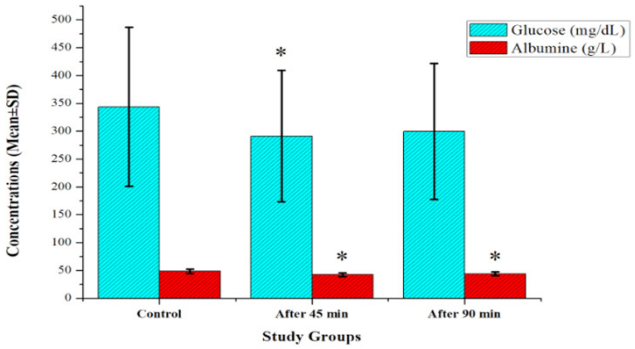

Figure 2: Effect of ellagic acid on glucose and albumin levels for diabetic's type 1.*represents a significant difference at $p \leq 0.05$ for the comparison among the control reads and the reads that were recorded after incubation with ellagic acid for 45 and 90 minutes.

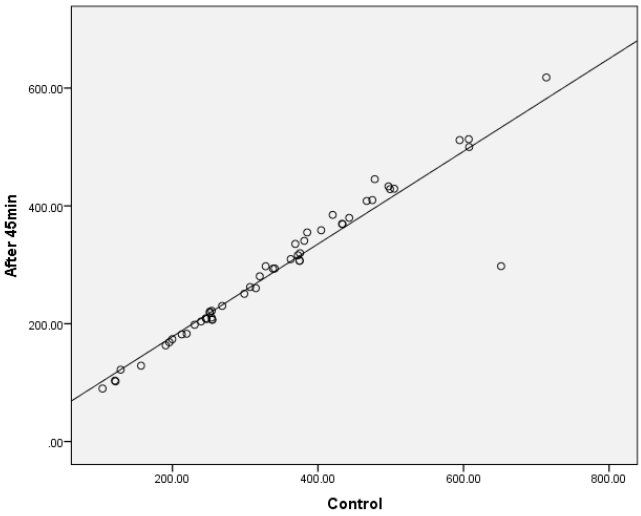

Figure 3: The correlation of glucose level diabetics' type1 after incubation with ellagic acid for 45 min.

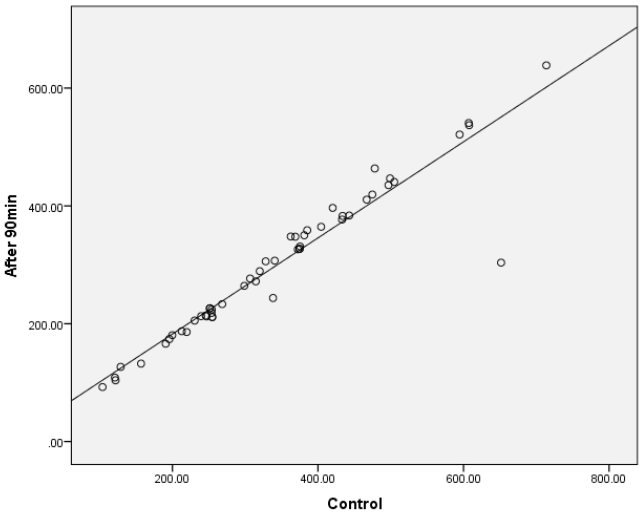

Figure 4: The correlation of glucose level of diabetics' type 1 after incubation with ellagic acid for 90 min.

Table 2: Correlation between the control reads and the reads that were recorded after incubation with ellagic acid of glucose means among patients with type1.

Glucose (mg/dL)	*Mean ± SD*	*r*	*p-value*
Control reads	343.7±142.7	0.951	*0.000**
Incubation for 45 min	291 ± 118		
Control reads	343.7 ± 142.7	0.948	*0.000**
Incubation for 90 min	299.8 ± 122.7		

* represents a significant difference at $p \leq 0.05$. r: represent the correlation coefficient.

Table 3: Correlation between the control reads and the reads that were recorded after incubation with ellagic acid of albumin means among patients with type 1.

Glucose (mg/dL)	*N*	*Mean ± SD*	*r*	*p-value*
Control reads	52	48.6 ± 4	0.902	0.000*
incubation for 45 minutes	52	42.4 ± 3.3		
Control reads	52	48.6 ± 4	0.896	*0.000**
incubation for 90 minutes	52	43.9 ± 3.3		

* represents a significant difference at $p \leq 0.05$. r: represent the correlation coefficient.

of glucose and albumin was studied as a function for some risk factors such as age, gender, and weight of patients was studied statistically. In general, it was indicated that the effect of ellagic acid on the levels of glucose for diabetics type 1 does not depend on these factors age factor for both incubation time (45 and 90 minutes), as shown in Tables 4, 5 and 6.

However, the current study found that there is a relationship between the effect of ellagic acid and the factors on the levels

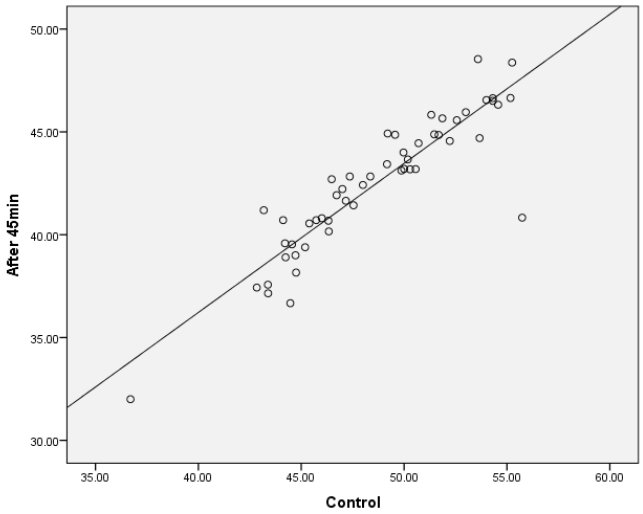

Figure 5: The correlation of albumin level between before and after incubation with ellagic acid for 45 min for diabetics' type 1.

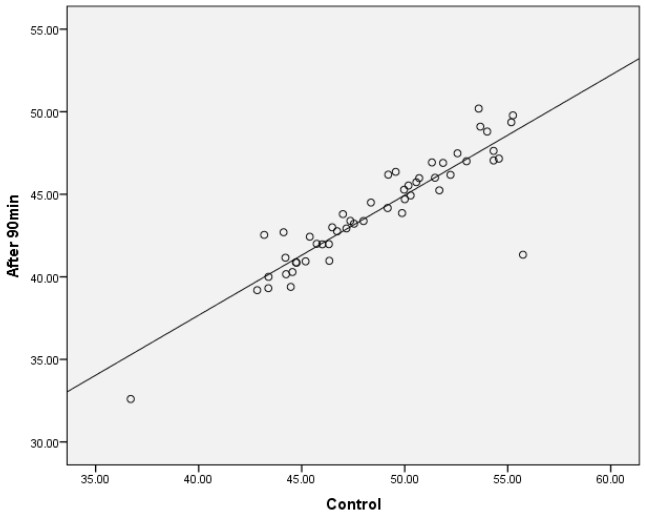

Figure 6: The correlation of albumin level between before and after incubation with ellagic acid for 90 min for diabetics' type 1.

Table 4: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of glucose means according to the age factor for diabetics type 1.

Age	*Control reads*	*Incubation for 45 min*	*Incubation for 90 min*	*p-value*
6-25 years	330 ± 142	280 ± 123 [a]	291.6 ± 132.4 [b]	a-0.348 b-0.482 c-0.608
26-45 years	355.8 ± 156	308.6 ± 135.7 [a]	317 ± 138.8 [b]	a-0.501 b-0.424 c-0.562
46-65 years	331.6 ± 128	272.2 ± 86.6 [a]	276.2 ± 87.4 [b]	a-0.123 b-0.151 c-0.180
66-85 years	394±199	334.9 ± 167 [a]	358.6 ± 177 [b]	a-0.713 b-0.829 c-0.923

Letters (a,b.c.) represent type of the statistical analysis: a-Between control reads and the reads that were recorded after incubation with ellagic acid for 45 minutes, b-Between control reads and after incubation for 90 minutes, c-Among the control reads and the reads that were recorded after incubation for 45 and 90 minutes.

Table 5: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of glucose means according to gender factor for diabetics type 1.

Gender	*Control reads*	*Incubation for 45 minutes*	*Incubation for 90 minutes*	*p-value*
Female [c]	342.5 ± 143.6	287.8 ± 114.4 [a]	295.2 ± 119.7 [b]	a- 0.074 b- 0.121 c- 0.152
Male [c]	346v± 145.2	297.7 ± 128.4 [a]	309.2 ± 132 [b]	a- 0.302 b- 0.431 c- 0.556

Letters (a,b.c.) represent type of the statistical analysis: a- Between control reads and the reads that were recorded after incubation with ellagic acid for 45 minutes, b- Between control reads and after incubation for 90 minutes, c- Among the control reads and the reads that were recorded after incubation for 45 and 90 minutes.

Table 6: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of glucose means according to weight factor for diabetics type 1.

Weight	*Control reads*	*Incubation for 45 min*	*Incubation for 90 min*	*p-value*
≤ 45 kg[c]	312.3 ± 144.2	264.6 ± 126.8 [a]	271.2 ± 130.8 [b]	a- 0.486 b- 0.547 c- 0.747
46-72 kg[c]	360.3 ± 160.2	310.9 ± 138 [a]	321.5 ± 143 [b]	a- 0.271 b- 0.386 c- 0.508
73-99 kg[c]	342.2 ± 135.3	281.6 ± 97 [a]	289 ± 102 [b]	a- 0.104 b- 0.152 c- 0.206
≥ 100 kg[c]	315.2 ± 66	275.8 ± 73.2 [a]	284.6 ± 70 [b]	a- 0.517 b- 0.611 c- 0.778

***** represents a significant difference at p≤0.05. Letters (a,b.c.) represent type of the statistical analysis: a- Between control reads and the reads that were recorded after incubation with ellagic acid for 45 minutes, b- Between control reads and after incubation

of albumin for diabetics' type 1. Generally, except patients over 65 years old, all studied patients with 6-65 years old displayed a relationship between the effect of ellagic acid and the age factor on the albumin levels, as shown in Table 7.

In addition, there is a significant difference in albumin levels for both females and males ($p < 0.05$), as shown in Table 8. This means the gender of the patient has a role in the effect of ellagic acid on the albumin levels of patients with type 1, regardless of the time of incubation time. Furthermore, it was observed that the ellagic acid on albumin changed is affected

Table 7: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of albumin means according to the age factor for diabetics type 1.

Age	*Control reads*	*incubation for 45 min*	*incubation for 90 min*	*p-value*
6-25 years[c]	49.7 ± 3.7	43.3 ± 3[a]	44.8 ± 2.8 [b]	a- 0.000* b- 0.000* c- 0.000*
26-45 years	48.4 ± 4.8	42.6 ± 4.2 [a]	44.1 ± 4.4 [b]	a- 0.000* b- 0.000* c- 0.000*
46-65 years	47.7 ± 3.2	41.5 ± 1.8 [a]	42.9 ± 2 [b]	a- 0.000* b- 0.000* c- 0.000
66-85 years	49.8 ± 5.7	43.1 ± 5.2 [a]	44.6 ± 4 [b]	a- 0.155 b- 0.253 c- 0.304

Letters (a,b.c.) represent type of the statistical analysis: a-Between control reads and the reads that were recorded after incubation with ellagic acid for 45 min, b-Between control reads and after incubation for 90 minutes, c-Among the control reads and the reads that were recorded after incubation for 45 and 90 min.

Table 8: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of albumin means according to gender factor for diabetics type 1.

Gender	*Control reads*	*Incubation for 45 minutes*	*Incubation for 90 minutes*	*p-value*
Female [c]	47.7 ± 3.4	41.7 ± 2.8 [a]	43 ± 2.5 [b]	a- 0.000* b- 0.000* c- 0.000*
Male [c]	50.4 ± 4.7	43.9 ± 3.8 [a]	45.6 ± 4 [b]	a- 0.000* b- 0.002* c- 0.000*

Letters (a,b.c.) represent type of the statistical analysis: a- Between control reads and the reads that were recorded after incubation with ellagic acid for 45 minutes, b- Between control reads and after incubation for 90 minutes, c- Among the control reads and the reads that were recorded after incubation for 45 and 90 minutes.

Table 9: Distribution of control reads and the reads that were recorded after incubation with ellagic acid of albumin means according to weight factor for diabetics type 1

Weight	*Control reads*	*Incubation for 45 min*	*Incubation for 90 min*	*p-value*
≤ 45 kg [c]	49.6 ± 3.6	43.5 ± 2.8 [a]	44.8 ± 2.6 [b]	a- 0.001* b- 0.005* c- 0.002*
46–72 kg [c]	48.3 ± 4.5	42.2 ± 3.8 [a]	43.7 ± 3.8 [b]	a- 0.000* b- 0.000* c- 0.000*
73–99 kg [c]	48.6	± 4 42.2 ± 3 [a]	43.7 ± 3.3 [b]	a- 0.000* b- 0.000* c- 0.000*
≥ 100 kg [c]	47 ± 3.7	41.9 ± 1 [a]	43.8 ± 1.6 [b]	a- 0.041* b- 0.209 c- 0.101

*represents a significant difference at $p \leq 0.05$. Letters (a,b.c.) represent type of the statistical analysis: a- Between control reads and the reads that were recorded after incubation with ellagic acid for 45 minutes, b- Between control reads and after incubation for 90 minutes, c- Among the control reads and the reads that were recorded after incubation for 45 and 90 minutes.

by the patient's weight for both incubation times, as described in Table 9.

CONCLUSIONS

In this study, it has been concluding that ellagic acid decreased the levels of glucose and albumin for patients of DM of type 1, thereby leading to reduce glycation products that cause further complications for diabetics. The study was also found that the factors of age, gender, and weight did not show a significant relationship with the effect of ellagic acid on the levels of glucose for diabetes' type 1. Nevertheless, these factors displayed a relationship with the effect of ellagic acid on the levels of albumin for diabetics' type 1.

REFERENCES

1. A. D. Association, 'Diagnosis and classification of diabetes mellitus', *Diabetes Care*, vol. 32, no. 1, pp. 62–67, 2009.
2. A. J. Krentz, L. Heinemann, and M. Hompesch, 'Assessment of B-cell function', in *Translational Research Methods for Diabetes, Obesity and Cardiometabolic Drug Development: A Focus on Early Phase Clinical Studies*, Springer, pp. 45–70, 2014.
3. Z. Fu, E. R. Gilbert, and D. Liu, 'Regulation of insulin synthesis and secretion and pancreatic beta-cell dysfunction in diabetes', *Curr. Diabetes Rev.*, vol. 9, no. 1, pp. 25–53, 2013.
4. A. D. Association, 'Diagnosis and classification of diabetes mellitus', *Diabetes Care*, vol. 30, no. suppl 1, pp. S42–S47, 2007.
5. G. E. Umpierrez, M. B. Murphy, and A. E. Kitabchi, 'Diabetic ketoacidosis and hyperglycemic hyperosmolar syndrome', *Diabetes Spectr.*, vol. 15, no. 1, pp. 28–36, 2002.
6. A. Chawla, R. Chawla, and S. Jaggi, 'Microvasular and macrovascular complications in diabetes mellitus: Distinct or continuum?', *Indian J. Endocrinol. Metab.*, vol. 20, no. 4, pp. 546–551, 2016.
7. A. Tuttolomondo, C. Maida, and A. Pinto, 'Diabetic foot syndrome as a possible cardiovascular marker in diabetic patients', *J. Diabetes Res.*, p. 12, 2015.
8. J. L. Chiang, M. S. Kirkman, L. M. B. Laffel, and A. L. Peters, 'Type 1 diabetes through the life span: a position statement of the american diabetes association', *Diabetes Care*, vol. 37, no. 7, pp. 2034–2054, 2014.
9. A. Ceriello, S. Colagiuri, J. Gerich, and J. Tuomilehto, 'Guideline for management of postmeal glucose', *Nutr. Metab. Cardiovasc. Dis.*, vol. 18, no. 4, pp. 17–33, 2008.
10. F. Thomas, C. G. Pretty, T. Desaive, and J. G. Chase, 'Blood glucose levels of subelite athletes during 6 days of free living', *J. Diabetes Sci. Technol.*, vol. 10, no. 6, pp. 1335–1343, 2016.
11. K. Pippitt, M. Li, and H. E. Gurgle, 'Diabetes mellitus: screening and diagnosis', *Am. Fam. Physician*, vol. 93, no. 2, pp. 103–109, 2016.
12. V. P. Singh, A. Bali, N. Singh, and A. S. Jaggi, 'Advanced glycation end products and diabetic complications', *Korean J. Physiol. Pharmacol. Off. J. Korean Physiol. Soc. Korean Soc. Pharmacol.*, vol. 18, no. 1, pp. 1–14, 2014.
13. H. Nagayama *et al.*, 'Glycated albumin as an improved indicator of glycemic control in hemodialysis patients with type 2 diabetes based on fasting plasma glucose and oral glucose tolerance test', *Biomed. Pharmacother.*, vol. 63, no. 3, pp. 236–240, 2009.
14. R. Raoufinia, A. Mota, N. Keyhanvar, F. Safari, S. Shamekhi, and J. Abdolalizadeh, 'Overview of albumin and its purification methods', *Adv. Pharm. Bull.*, vol. 6, no. 4, pp. 495–507, 2016.
15. P. Caraceni, M. Tufoni, and M. E. Bonavita, 'Clinical use of albumin', *Blood Transfus.*, vol. 11, no. Suppl 4, pp. 18–25, 2013.
16. H. Birn and E. I. Christensen, 'Renal albumin absorption in physiology and pathology', *Kidney Int.*, vol. 69, no. 3, pp. 440–449, 2006.
17. L. Sepúlveda, A. Ascacio, R. Rodríguez-Herrera, A. Aguilera-Carbó, and C. N. Aguilar, 'Ellagic acid: Biological properties and biotechnological development for production processes', *Afr. J. Biotechnol.*, vol. 10, no. 22, pp. 4518–4523, 2011.
18. S. Muthukumaran, C. Tranchant, J. Shi, X. Ye, and S. J. Xue, 'Ellagic acid in strawberry (Fragaria spp.): Biological, technological, stability, and human health aspects', *Food Qual. Saf.*, vol. 1, no. 4, pp. 227–252, 2017.
19. E. Saldanha *et al.*, 'Polyphenols in the prevention of acute pancreatitis: preclinical observations', in *Polyphenols in human health and disease*, R. R. Watson, V. R. Preedy, and S. Zibadi, Eds. San Diego: Academic Presspp. 427–433, 2014.

20. F. M. Mady and S. R.-M. Ibrahim, 'Cyclodextrin-based nanosponge for improvement of solubility and oral bioavailability of Ellagic acid', *Pak. J. Pharm. Sci*., vol. 31, no. 5, pp. 2069–2076, 2018.
21. A. Masamune, M. Satoh, K. Kikuta, N. Suzuki, K. Satoh, and T. Shimosegawa, 'Ellagic acid blocks activation of pancreatic stellate cells', *Biochem. Pharmacol*., vol. 70, no. 6, pp. 869–878, 2005.
22. G. Raghu, S. Jakhotia, P. Y. Reddy, P. A. Kumar, and G. B. Reddy, 'Ellagic acid inhibits non-enzymatic glycation and prevents proteinuria in diabetic rats', *Food Funct.*, vol. 7, no. 3, pp. 1574–1583, 2016.
23. P. Malini, G. Kanchana, and M. Rajadurai, 'Antibiabetic efficacy of allagic acid instreptozotocin induced diabetes mellitus in albino wistar rats', *Asian J Pharm Clin Res*, vol. 4, pp. 127–128, 2011.