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Evaluation of Bio-Activity of *Urginea Maritima* Follicle Extract Nanoparticles in Alloxan-Induced Diabetic Rats

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Abstract

THIS study explored the biosynthesis of silver nanoparticles (AgNPs) using *Urginea maritima* follicles extract (UMBE) as a reducing agent, to develop a therapeutic application. Furthermore, the current study represents the clinical application of the UMBE and its prepared nanoparticles and the impact of both factors on the levels of various biomarker parameters (metabolic, antioxidant and oxidant) in the sera of female albino rats with induced diabetes was evaluated. The outcomes indicated that the levels of metabolic biomarkers (glucose and total lipid) were significantly increased in diabetic groups while the total protein level decreased compared to the healthy group. Whereas the antioxidant markers, have shown significantly drop in their sera concentration in diabetic rats compared to the healthy group. Significantly, both UMBSNPs and UMBE demonstrated the ability to enhance the activity of antioxidant enzymes in the diabetic group when compared to the healthy group. Similarly, the oxidant markers increased in diabetic rats compare to healthy ones with a significant change. Based on the latest findings, it is evident that UMBE and UMBSNPs have the potential to enhance antioxidant status and mitigate the oxidative impact associated with diabetes mellitus, suggesting their promise as an alternative treatment.

Keywords: AgNPs, Antioxidant, Diabetes mellitus, Oxidative stress, *Urginea maritima*.

Introduction

Nanotechnology holds great promise to revolutionize both the diagnosis and treatment of a wide variety of diseases. These technologies, which operate at the nanoscale - systems with dimensions around one-thousandth the width of a human hair - have the potential to significantly impact the world's leading causes of illness and death. Nanoscale systems and technologies have been the focus of extensive scientific research and development over the past several decades. This research has led to the approval and introduction of various nano-enabled products by the U.S. Food and Drug Administration, including chemotherapeutic drugs, anesthetics, imaging agents, and nutritional supplements, among others [1]. Silver nanoparticles (AgNPs) are defined as a nanomaterial where all its dimensions fall within the 1-100 nanometer size range. Compared to silver in its bulk, larger form, these silver nanoparticles exhibit a greater capacity and higher surface area-to-volume ratio. At the nanoscale, silver takes on unique electrical, optical, and catalytic properties. These distinctive nanoscale characteristics have prompted the investigation and development of AgNP-based products for targeted drug delivery, diagnosis, detection, and imaging applications [2]. Throughout history, people have turned to medicinal plants to treat a wide range of health conditions. It is widely recognized that plants with long-standing use in traditional medicine exhibit a variety of biological effects [3]. Indeed, these medicinal plants have historically served as safe, effective, and renewable sources of natural antioxidants or free radical scavengers. In particular, they are rich in phenolic compounds, such as phenolic acids, flavonoids, tannins, stilbenes, and anthocyanins, which contribute to their antioxidant properties [4]. The phenolic compounds present in medicinal and food plants are widely recognized as the primary contributors to their antioxidant activity. These phenolics make a significant contribution in the fight against many disease conditions, including cancer, diabetes, aging, cardiovascular disease, and other degenerative disorders [5]. Diabetes mellitus (DM) is a metabolic disorder primarily defined by high blood

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sugar levels (hyperglycemia), excessive thirst (polydipsia), and excessive hunger (polyphagia). DM is one of the most prevalent metabolic conditions, and its incidence is rising at a concerning rate globally [6]. There are primarily four common types of DM. Type 1 DM (T1DM) is caused by the autoimmune destruction of pancreatic beta cells, resulting in a complete lack of insulin production. This form is also known as insulin-dependent diabetes mellitus (IDDM). The most prevalent type is Type 2 DM (T2DM), which is caused by either insufficient insulin production or desensitization of insulin receptors, preventing glucose from entering cells. T2DM accounts for 90-95% of all diabetes cases. Additionally, there is a type called gestational diabetes mellitus (GDM) that occurs only during pregnancy. GDM affects approximately 5-15% of pregnant women, with the prevalence varying based on ethnicity and geographic region [7]. *Urginia maritima* (UM), also known as *Drimia maritima* or *Scilla maritima*, is a species belonging to the Liliaceae family. It is the largest among all Mediterranean geophytes (plants with underground storage organs). UM is a winter-active perennial follicles native to the coastal regions of the Mediterranean. This plant is commonly referred to as white squill, sea squill, or crusader spear [8].

In the traditional Indian medicinal system, UM is renowned for its various therapeutic applications. The follicles of this plant are the most commonly used parts, reportedly employed as cardiotonic agents (supporting heart function). UM has also been used in the treatment of numerous conditions, particularly asthma, edema (dropsy), rheumatism, leprosy, and various skin ailments [9]. In addition to its other medicinal applications, the extract of UM follicles has also been traditionally reported to have hypoglycemic (blood sugar-lowering) properties. The fresh follicles of the plant contain two glycosides, scillarin A and scillarin B. Furthermore, UM follicles are known to comprise flavonoids, carbohydrates, antifungal glycoproteins, steroids, alkaloids, tannins, coumarins, and saponins [10]. Multiple studies have explored the antidiabetic properties of medicinal plants, including UM. In a 2019 study by Yamina Bouatrous, the researchers specifically investigated the antidiabetic effects of UM in an *in vivo* mouse model. The mouse study involved inducing postprandial hyperglycemia, or elevated blood glucose levels after a meal. This allowed the researchers to assess the potential of UM to mitigate the symptoms of diabetes in a controlled experimental setting [11]. To establish a better understanding of the functional roles of the bioactive compounds in UMB as a basis for potential future pharmacological and clinical applications, the current study aims to produce AgNPs using UMBE. Additionally, the study sought to conduct an *in vivo* evaluation of the effects of the UM crude extract and the prepared AgNPs on the levels of oxidants, antioxidants, and metabolic biomarkers in a laboratory animal model of alloxan-induced conditions.

Material and Methods

Urginea maritima crude aqueous extracts

Urginea maritima plant follicles (UMB) were harvested from lawns in Duhok, Iraq, in April 2021. The UMB was washed with D.W., cut, dried in the shadow at room temperature, then fine powdered with a mill, and stored in a dark glass container until use. The College of Agriculture's horticulture department authenticated and characterized the plant UMB. Twenty g of UMB powder was soaked overnight in 200 ml of D.W. and stirred for 24 hrs at room temperature with a constant rate of stirring. The extract was then filtered and the supernatant was concentrated by using a rotary evaporator under vacuum at 60 ℃. The obtained dry powder was stored in a dark container in freeze for subsequent experiments [12].

Biosynthesis of AgNPs of Urginea maritima follicle extracts (UMBSNPs)

UMBE was utilized as a reducing, stabilizing, and coating agent in the production of silver nanoparticles. An aqueous solution of 1 mM $AgNO_3$ and UMBE were produced separately. One mM $AgNO_3$ solution was made by dissolving 0.0421 g of $AgNO_3$ in 250 ml of DI water and storing it in an amber-colored container to prevent the auto-oxidation of Ag. To create the plant extract, 20 g of finely chopped UMBE was heated at 50-60 ℃ with 200 ml of D.I.W. for 20 minutes. The extract was then filtered using Whatman filter paper No. 1 and kept at 4 ℃ for later use [13].

Green synthesis of UMBSNPs

The $AgNO_3$ solution (1mM) section (2.5) was heated to 90-95 ℃ with the plant extract (1:10 ratio of $AgNO_3$:UMB) and stirred continuously on a hot plate stirrer for 1 hr (Fig. 1). In this phase, the color change verified the decrease of Ag^+ to Ag^0 [14]. The precipitate was collected, rinsed with D.I.W., and dried in an electric oven at 37 ℃ to produce a dry powder of UMSNPs [15].

Characterization of UMSNPs

The synthesis of UMSNP was first demonstrated by identifying the Surface Plasmon Resonance (SPR) band through the analysis of double-beam UV-Vis spectra at different wavelengths ranging from 300 to 700 nm [16]. Furthermore, FTIR spectroscopy was utilized to study the chemical external face and functional groups of exsiccated UMSNPs, using the peak location inside the wavenumber within the

spectrum extent of 4500 to 500 cm^{-1} for FTIR measurement; UMSNPs were evaluated as a powder product [17]. The XRD analysis was used to characterize metal nanoparticles using a monochromatic radiation source (Cu K α) [18].

Experimental animals

Female albino rats were bred in the Biology Department's animal facility at the University of Duhok, with the approval of the Ethical Committee under reference 767. The rats were housed in clean, well-ventilated polypropylene cages measuring 30 × 25 × 17 cm, with four rats per cage. They were provided with unrestricted access to a standard diet as per Council guidelines from [19], along with water, while being maintained by ethical and standard laboratory protocols. The rats were subjected to a 12-hour light and 12-hour dark photoperiod at a controlled temperature of 24 ± 2 ℃. Furthermore, animals were allowed to acclimate to the laboratory conditions for 10 days. Following this, they were mixed for breeding, following the method described by [20]. The bedding in the cages was changed regularly, twice a week, with particular attention given to the diabetic groups due to increased urine output (polyuria).

Induction of diabetes mellitus

Thirty female rats were subjected to an overnight fast, after which they were intraperitoneally administered a single dose of 120 mg/kg alloxan dissolved in a citrate buffer with a pH of 4.5, as per the recommendations of [21, 22]. This method was employed to induce diabetes, as the alloxan compound required immediate injection to prevent degradation. To prevent potentially fatal hypoglycemia, rats administered alloxan were orally treated with a 5% D-glucose solution 30 minutes post-injection. Symptoms of diabetes, including polyuria, polyphagia, and polydipsia, manifested within 24-72 hour. Confirmatory indicators of diabetes, as established by [23, 24], included glycosuria, ketonuria, and a fasting blood sugar exceeding 200 mg/dl.

The U. maritima follicles extract and UMSNPs toxicity

To assess the toxicity of the UMB extract and prepared UMSNPs, it is crucial to determine the median lethal dosage (LD_{50}). The LD_{50} represents the dose of a substance that, when administered to rats, causes the death of 50% of the animals. For this reason, the test substance was administered orally in graduated doses of UMBE (200, 220, 230, 240 and 250 mg/kg.bw/day) and of UMSNPs (50, 60, 70, 85 and 100 mg/kg.bw/day), to several groups contained ten rats weighing (200±20 g), one dose being used per group to calculate the LD_{50} of aqueous extract and prepared UMSNPs.

Experimental design

In this set of experiments, adult female rats of (160 - 220 g) of weight were used. Following, a total of 60 albino rats were randomly allocated into six equally sized groups, each containing 10 rats and treated with each of UMBE and UMBSNPs for two weeks and divided into the following subgroups:

Group 1: Normal rats, which were fed on a standard diet (control group).
Group 2: Normal rats treated with follicles of U. maritima extract.
Group 3: Normal rats treated with follicles of UMBSNPs.
Group 4: Diabetic rats, which were fed on a standard diet (diabetic group).
Group 5: Diabetic rats treated with follicles of U. maritima extract.
Group 6: Diabetic rats treated with follicles of UMBSNPs.

Estimation of biochemical parameters in sera of animals

Following an overnight fast with free access to water, the animals were anesthetized with $CHCl_3$ (Scharlab S.L-Spain), and blood samples were collected via cardiac puncture on the final day of the experiment. Approximately 10 ml, were collected in gel tubes (Arzer Grande-Italy), allowed to clot for 10 minutes, and then centrifuged at 4000 rpm for 15 minutes to separate the serum. The obtained serum was used immediately to measure FBS, while the remaining serum was used for other biochemical parameters such as malondialdehyde (MDA), peroxynitrite (ONOO-), xanthine oxidase (XO) activity, glutathione-s-transferases (GSTs) activity, superoxide dismutase activity (SOD), total antioxidant activity (AOA), paraoxonase activity (PON1), N-aminoacylase-1 activity (ACY-1), total lipid (TL) and total protein (TP).

Utilization of chemical reagents and analytical instrumentation

A comprehensive array of chemical reagents, procured from Sigma Aldrich, were meticulously employed to facilitate the manual estimation of the relevant research parameters. These compounds included silver nitrate, phosphor vanilline, Tris-HCl, calcium chloride, phenyl acetate, (1-chloro-2,4-dinitrobenzene) CDNB, glutathione (GSH), ethylene di-aminetetraacetic acid (EDTA), Triton X-100, L-methionine, nitro blue Tetrazolium (NBT), riboflavin, sodium cyanide (NaCN), sodium benzoate, Ferrous ammonium sulfate ($Fe[(NH_4)_2(SO_4)_2]$), trichloroacetic acid (TCA), uric acid, N-acetyl methionine, thiobarbituric acid (TBA), isopropanol, phenol,

xanthine, ninhydrin, 2-methoxy ethanol, urea, as well as various buffer solutions, acids, bases, and solvents.

A Perkin Elmer Lambda 35 UV/VIS Spectrophotometer (USA) was utilized for the estimation of various biochemical parameters, including glucose, total lipids, total protein, paraoxonase, glutathione-S-transferase, superoxide dismutase, total antioxidant activity, N-aminoacylase-1, malondialdehyde, peroxynitrite, and xanthine oxidase.

Biochemical analysis

Estimation of Metabolic Markers

Serum glucose and total protein levels were estimated using commercial kits from Biolabo (France), employing enzymatic colorimetric and biuret methods, respectively. Total lipids, including cholesterols, phospholipids, and triglycerides, were determined using the phosphovanilline manual colorimetric method introduced by [25].

Estimation of antioxidant markers

Serum paraoxonase (PON1) activity was estimated using the procedure described by [26], which measures the aryl esterase enzyme's ability to break down phenylacetate into phenol and acetic acid, at the reaction's absorbance of 270 nm. Additionally, glutathione-S-transferase (GST) enzyme activity was measured according to the method of Khynriam & Prasad, (2003) [27]. This assay measures the GST-catalyzed conjugation of L-glutathione (GSH) to 1-Chloro-2,4 -dinitro-benzene (CDNB), producing a GS-DNB conjugate that exhibits absorbance at 340 nm. Furthermore, serum superoxide dismutase (SOD) enzyme activity was determined using a modified photochemical NBT technique as per the method of Brown and Goldstein, (1983) [28], which involves the use of sodium cyanide as a peroxidase inhibitor. This indirect spectrophotometric technique measures the change in optical density of the formazine product formed from the reduction of superoxide radicals ($O2^{-}$) generated through serum irradiation. Moreover, total antioxidant activity (AOA) in serum was quantified spectrophotometrically using the manual assay outlined by Koracevic *et al.*, (2001) [29]. This technique measures the inhibition of TBARS production, which results from the reaction of an Fe-EDTA complex with hydrogen peroxide to generate hydroxyl radicals. The presence of antioxidants in the serum sample reduces the formation of these TBARS, and the degree of inhibition is quantified spectrophotometrically to determine the overall AOA. Besides, N-aminoacylase-1 (ACY1) activity was measured following the technique described by Peterson, (1983) [30]. This method relies on the hydrolysis of aliphatic amino acids that contain an acetyl group, such as N-acetyl-L-methionine.

Estimation of oxidative stress markers

To evaluate the level of serum lipid peroxidation (MDA), a quantified technique was used that relies on the reaction between lipid peroxides, particularly MDA, and thiobarbituric acid (TBA), forming a colored complex, as described by Guidet & Shah, (1989) [31]. The absorbance of the MDA-TBA product was measured at 532 nm. Moreover, serum peroxynitrite ($ONOO^{-}$) levels were estimated using a modified method based on VanUffelen *et al.* (1998), which measures the nitration of phenol by the peroxynitrite radical and the subsequent spectrophotometric detection of the nitrophenol product at 412 nm [32]. Ultimately, xanthine oxidase (XO) activity was assessed using the method described by Ackermann & Brill (1974), which measures the enzymatic oxidation of xanthine to uric acid spectrophotometrically at 293 nm [33].

Statistical analysis

The data was statistically analyzed using Microsoft Excel 2021 and GraphPad Prism 5 (California-USA), employing analysis of variance (ANOVA) and Tukey's range test to compare the normal control group with other treated groups. Results are presented as mean ± standard errors, and p-values (<0.01, <0.05 and <0.001) were estimated statistically significant [34].

Results

Biosynthesis of UMBSNPs

The green synthesis of AgNPs included the bio-reduction of Ag ions from $AgNO_3$ with UMBE as the reducing agent. This fabrication of AgNPs was successful under optimal circumstances, and this approach produced UMBSNPs with a maximum yield of 4%. The color change served as an initial indication of the formation of Ag nanoparticles.

Characterization of UMSNPs

The synthesis of UMBSNPs was thoroughly characterized using UV-Vis spectrophotometry, FTIR spectroscopy, FESEM, and XRD analysis, providing comprehensive insights into their physicochemical properties and structural features.

Ultraviolet-visible (UV-Vis) spectrophotometer

UV–vis spectroscopy analysis indicated a broad band form at 416 nm, which was specific for AgNPs (Fig. 2). The absorption spectrum observed between 400 and 460 nm is attributed to the SPR phenomenon in AgNPs, as reported by numerous previous studies [35, 36].

Fourier-transform infrared spectroscopy (FTIR)

The FTIR spectrum of $AgNO_3$ with UMBE depicted in Fig. 3 demonstrates the efficiency of the biomolecules in capping, reducing, and stabilizing the AgNPs. The observed peak bands in UMBSNPs at 3406, 2936, 1637, 1412, 1132, 1059, and 1026 cm^{-1} suggest the involvement of carboxyl, alcohol, and amine groups in the reduction and stabilization processes. The unique peaks at 3406 cm^{-1} for amide and O-H of phenol, 2936 cm^{-1} and 1412 cm^{-1} for C-H in alkanes, 1636 cm^{-1} for C=O of carbonyl, 1132 cm^{-1} for C-N stretching in amide, and 1059 and 1026 cm^{-1} for major OH groups and C-C stretching provide insights into the biomolecular interactions during the synthesis of UMBSNPs.

X-Ray diffraction (XRD)

The XRD analysis provided valuable insights into the phase, structure, and dimensions of the crystalline UMBSNPs. The observed XRD peaks as shown in Fig. 4, at 2θ degrees of 37.1°, 45°, and 64.4° correspond to the (111), (200), and (220) crystalline planes of the face-centered cubic structure of metallic silver. Furthermore, the Debye-Scherrer method applied to the primary (111) diffraction peak yielded an average particle size of 107.14 ± 5 nm, which aligns with the size of the isolated nanoparticles observed in the FESEM analysis.

Field emission scanning electron microscopy (FESEM)

The FESEM analysis revealed that the green-synthesized AgNPs were well-dispersed, spherical in shape, and ranged in size from 100 to 110 nm, with the capping of nanoparticles by bioactive substances from the UMBE limiting their aggregation (Fig. 5). The morphology of metal nanoparticles significantly impacts their optical and electrical characteristics, confirming their presence and suggesting the effective reduction of Ag salts to nanoparticles by the bioactive components in the UMBE, which also served as an adequate capping agent [37, 38].

The toxicity of u. maritima plant (follicles and UMBSNPs):

The study examined the toxicity of UMBE and UMBSNPs on albino rats. Administration of higher concentrations of UMBE (250-300 mg/kg.bw/day) and UMBSNPs (100-150 mg/kg.bw/day) resulted in significant mortality rates, with 80% of the animals experiencing fatalities within 10 days. Lower concentrations of UMBE (225 mg/kg.bw/day) and UMBSNPs (75 mg/kg.bw/day) reduced the toxic effect, with 60% mortality. The best survival rates were observed at 200 mg/kg.bw/day of UMBE and 50 mg/kg.bw/day of UMBSNPs, which were used as the lethal time in the experiment.

Serum biochemical profiling

The study evaluated various metabolic and oxidative stress indicators, including oxidant and antioxidant parameters, in the serum of both normal and experimentally induced diabetic albino rats. Both groups were treated with either the UMBE or the synthesized AgNPs. The results found that oral administration of either the UMBE or the synthesized AgNPs improved the majority of assessed serum parameters in non-diabetic (normal) treated rats compared to healthy untreated controls. The blood biomarkers were presented as the mean ± SE for the following parameters.

Serum metabolic profiling

The results of Table (1) illustrate the impact of UMBE and its prepared AgNPs on fasting blood sugar (FBS), total lipid (TL) and total protein levels (TP). Generally, the results showed that diabetic groups had significantly higher glucose and TL levels compared to healthy rats with lowering in TP level. Notably, the oral administration of either UMBE or UMBSNPs to diabetic rats exhibited a beneficial effect in maintain these metabolic biomarkers.

The study revealed a significant elevation in serum glucose levels in the diabetic rats compared to the healthy control group ($p<0.001$) Table (1). Conversely, the diabetic study groups that received either UMBE or prepared AgNPs exhibited a substantial decrease in glucose levels ($p<0.001$), but there were no significant differences in this effect between the two treatment groups. Furthermore, the normal rat group treated with UMB or AgNPs did not exhibit any statistically significant changes compared to untreated normal rats.

The diabetic rats exhibited a significant increase in serum TL levels as evidenced by the data presented in Table (1), when compared to the normal group ($p<0.001$). However, both UMBE and synthesized UMBSNPs effectively lowered TL levels, with significant reductions observed in both groups ($p<0.001$). Notably, the AgNPs treatment resulted in a more distinct reduction in TL levels compared to UMBE in diabetic rats. Additionally, normal rats treated with either UMBE or AgNPs did not exhibit any statistically significant changes in TL levels.

The study highlighted the impact of UMBE and UMBSNPs on serum TP levels in diabetic and healthy rats as indicated in Table (1). Diabetic rats had significantly lower TP levels compared to normal rats ($p<0.001$). While diabetic groups treated with UMBE or UMBSNPs showed a minor increase in TP levels, this increase was not statistically significant compared to the diabetic group. Notably, UMBSNPs had a more

pronounced effect on altering serum TP levels in diabetic groups compared to UMBE.

Evaluating oxidative stress markers in rats sera

The study also evaluated the impact of UMBE and UMBSNPs on oxidant parameters, including xanthine oxidase (XO), peroxynitrite (ONOO-), and malonaldehyde (MDA) levels, in the sera of experimental animals (Table 2). The results showed that diabetic groups had significantly higher oxidant levels compared to healthy rats. Notably, the oral administration of either UMBE or UMBSNPs to diabetic rats exhibited a beneficial effect in reducing these harmful oxidants.

The MDA levels in diabetic rats exhibited a significant increase when compared to healthy rats ($P<0.001$) (Table 2). Furthermore, no significant changes were observed when comparing the normal treated group with healthy rats. However, the analysis of the data presented indicated a significant decrease ($P<0.001$) in MDA levels in both the UMBE and UMBSNPs diabetic groups compared to untreated diabetic rats. Additionally, the use of UMBSNPs was more effective than the use of UMBE alone in lowering MDA levels in the diabetic group, without any notable significant changes being observed.

According to the data presented in Table 2, the serum peroxynitrite ($ONOO^-$) levels were significantly higher in the diabetic rats compared to the healthy control group ($p<0.001$). While the diabetic group treated with UMBE showed a slight decrease in $ONOO^-$ levels, the change was not statistically significant. However, the administration of synthesized silver nanoparticles (UMBSNPs) to the diabetic group exhibited a more pronounced ability to reduce $ONOO^-$ levels compared to UMBE, with a statistically significant variation ($p<0.01$). Furthermore, the prepared UMBSNPs demonstrated superior capacity to decrease $ONOO^-$ activity compared to UMBE, with a statistically significant difference ($p<0.01$). Importantly, the $ONOO^-$ levels in normal rats treated with either UMBE or UMBSNPs were similar to those in the untreated normal group.

As illustrated in Table 2, serum XO activity was significantly elevated in diabetic rats compared to the normal group ($P<0.001$). However, in both the UMBE and UMBSNPs treated diabetic groups, XO levels were significantly reduced, reaching levels close to those of normal rats ($P<0.001$). While, no significant changes in XO activity were observed between the normal treated group and healthy rats. Additionally, the treatment with UMBSNPs was more effective than UMBE in reducing XO levels, the difference was not statistically significant.

Evaluating antioxidant markers in rats sera

The last part of this work included the influences of UMBE and UMBSNPs administration on serum levels of many vital antioxidants, including PON1 activity, GST enzyme, SOD enzyme, AOA, and ACY-1 enzyme in both normal and diabetic rats. Over all and as detailed in Table 3, the diabetic groups exhibit a significant decrease in serum antioxidant levels of diabetic rats compared to healthy rats. However, oral administration of either UMBE or UMBSNPs to diabetic rats demonstrated a beneficial effect by increasing these impaired antioxidants.

Based on the data presented in Table 3, it was observed that serum PON1 activity was significantly reduced in diabetic rats compared to healthy controls ($p<0.001$). However, diabetic rats treated with either UMBE or synthesized UMBSNPs showed a substantial increase in serum PON1 activity ($p<0.05$ and $p<0.01$, respectively) compared to untreated diabetic rats. Notably, UMBSNPs exhibited a stronger influence in increasing PON1 enzyme levels compared to UMBE alone.

The study found a significant reduction in serum GST activity in diabetic rats compared to healthy controls ($p<0.001$) as documented in Table 3. However, there were no statistically significant differences in GST activity between the normal treated rats and the untreated normal group. Importantly, both UMBE and UMBSNPs led to a substantial increase in serum GST levels ($p<0.05$) in the diabetic rats receiving treatment, compared to the untreated diabetic group, with no significant differences observed between the two treatment groups.

As illustrated in Table 3, a significant decrease in serum SOD activity in diabetic rats compared to healthy controls ($p<0.001$). However, the oral administration of UMBE and UMBSNPs led to a notable enhancement in serum SOD activity in the diabetic rats, demonstrating a highly significant difference compared to the untreated diabetic group ($p<0.001$). While UMBSNPs exhibited a slightly greater increase in SOD activity compared to UMBE, there were no statistically significant differences in serum SOD levels between the normal rats treated with either UMBE or UMBSNPs and the untreated normal group.

The data presented in Table 3, indicate a significant decrease in serum AOA levels in the diabetic group compared to the healthy group ($P<0.001$). Nevertheless, there were no statistically significant distinctions observed in the antioxidant activity of normal rats treated with either UMBE or UMBSNPs in comparison to the normal group. The findings indicated that both UMBE and prepared UMBSNPs

played a role in enhancing serum AOA levels in diabetic-treated groups, with better ability of aqueous extract of UMBE to increase AOA activity than prepared UMBSNPs with a statistically significant difference ($P<0.001$ and $P<0.05$) respectively.

The data presented in Table 3, indicate that the serum ACY-1 activity in diabetic rats was significantly lower compared to healthy rats ($P<0.001$). Furthermore, the levels of ACY-1 did not show any enhancement in both normal treatment groups when compared to the control group. Interestingly, treatment with UMBE and UMBSNPs resulted in a significant increase in serum ACY-1 activity, in the diabetic groups ($P<0.01$ and $P<0.001$, respectively). Besides, prepared UMBSNPs showed a better ability to increase ACY-1 activity than UMBE with a statistically significant variation ($P<0.001$).

Discussion

The synthesis of silver nanoparticles using plant extracts is an eco-friendly, cost-effective, and safe approach. In this study, the researchers attempted to synthesize AgNPs from the extract of the *U. maritima* follicle.

The color change served as an initial indication of the formation of Ag nanoparticles. This color change confirms the reduction of Ag^+ to Ag^0. The color shift went from colorless to light brown, then brown to dark brown, providing preliminary evidence for the synthesis of AgNPs [14]. The brown color of the AgNPs is a result of the surface plasmon vibrations occurring in the aqueous solution. Furthermore, the presence of numerous compounds such as flavonoids, sugars, phenolic constituents, and alkaloids in the UMBE contributed to the formation of the AgNPs [39], as previously obtained by many investigators during the biosynthesis and functionalization of Ag nano particles using different plant extracts [40, 41].

The size evolution of the Ag nanoparticles can be monitored using the UV-vis spectrophotometer method, which detects changes in the localized surface plasmon resonance (SPR) band at 416 nm in the UV–vis spectra as shown in Fig. 2. The optical properties of the Ag nanoparticles are associated with the excitation of plasmon resonance [42]. FTIR is used to analyze the chemical composition of the AgNP surface and identify the biomolecules responsible for capping and stabilizing the metal nanoparticles (Fig. 3). The presence of various functional groups in the UMBE may have facilitated the bio-reduction of Ag^+ ions, with the phenolic compounds in UMBE potentially acting as powerful reducing agents, leading to the formation of the synthesized AgNPs [43].

XRD analysis revealed detailed information about the phase, structure, and dimensions of the crystalline UMBSNPs (Fig. 4). The morphology of AgNPs synthesized through green methods was examined using FESEM. The FESEM image, depicted in Fig. 5, revealed that the AgNPs exhibited a well-dispersed spherical shape or a spherical-like appearance, with particle sizes ranging from 100 to 110 nm. The shape of nanoparticles significantly influences their optical and electronic properties, thus confirming the presence of nanoparticles [44]. The dark shading observed on the surface of nanoparticles indicates the presence of secondary materials. This can be attributed to the bio compounds present in the UMBE. It is worth noting that these bio components can effectively reduce silver salts to nanoparticles and act as suitable capping agents, preventing aggregation [45].

It's worth noting that the best survival rates were observed at 200 mg/kg.bw/day of UMBE and 50 mg/kg.bw/day of UMBSNPs, which were used as the lethal time in the experiment. The *U. maritima* follicle is known for its toxic effects on humans and mammals, as high consumption can induce emesis, catharsis, and potentially lead to cardiac depression [46]. The high mortality observed in the study can be attributed to the presence of cardiac glycosides in the *U. maritima* follicle, which can lead to severe toxicity if consumed in excessive amounts [47].

The study assessed metabolic and oxidative stress markers, including oxidants and antioxidants, in the serum of normal and diabetic albino rats. Overall, the UMBE and the UMBSNPs confirmed antioxidant properties that favorably modulated metabolic and oxidative stress markers in the serum of diabetic rats. The natural antioxidant properties found in UMBE and the prepared AgNPs, demonstrate a diverse array of biological and antioxidant effects. This antioxidant effect may explain the significant improvement observed in the blood biomarkers of the healthy treated rats. The importance of these compounds for health and disease should be further considered.

Based on the study's findings, the increased serum glucose levels in diabetic rats were attributed to the pathophysiological effects of alloxan, as reported in previous studies [48]. The elevated glucose levels in the diabetic group contributed to increased free radicals (FR), generating reactive oxygen species that disrupted the antioxidant defense system and impaired glucose metabolism [49]. Despite this, UMBE possesses a wide range of phytochemicals, including saponins, steroids, flavonoids (such as quercetin), dietary fiber, and vitamins C and K [50]. These components have been shown to have a positive impact on pancreatic tissues that are exposed to OS

induced by alloxan. They directly counteract lipid peroxides by quenching them and indirectly enhance the production of endogenous antioxidants, thereby promoting a healthier state for the pancreatic tissues [51]. Additionally, the inhibition of α-amylase and glucosidase enzymes plays a crucial role in managing diabetes by preventing the breakdown of carbohydrates into simple sugars, thus reducing blood glucose levels. AgNPs are referred to as α-amylase inhibitors in several studies in *vitro* and in *vivo* which may be considered as strong anti-diabetic [52, 53].

The diabetic rats group exhibited a considerable significant increase in serum TL levels when compared to the normal group. Dyslipidemia is a common complication in diabetes due to insufficient insulin levels, which deactivates lipoprotein lipase and impairs the liver's conversion of free fatty acids into phospholipids and cholesterol, leading to their accumulation in the bloodstream [54]. Furthermore, the reduction in TL of oral administration of UMBE may be due to the presence of specific compounds, such as steroidal glycosides and saponins, in *U. maritima* that could potentially account for its potential anti-hyperlipidemic effects. These compounds have been proposed to regulate lipid metabolism and decrease lipid levels in animal studies [55]. In this context, a previous study by Gupta *et al.*, 2012, reported that supplementation with *U. maritima* resulted in reduced triglyceride and total cholesterol levels, along with increased HDL levels, similar to the results observed in the current investigation [54]. Nevertheless, the findings suggest that AgNPs could be beneficial in normalizing abnormal lipid levels. This effect of AgNPs appears to be mediated by their ability to stimulate the lipolytic (fat-degrading) activity of plasma lipoprotein lipase [56]. Additionally, the decrease in lipid levels may be due to reduced fatty acid re-esterification and, subsequently, lower lipid (particularly triglyceride) secretion by the liver [57].

The study found significantly lower serum TP levels in diabetic rats compared to normal rats. This decrease in serum TP of diabetic rats can be attributed to increased catabolism, reduced synthesis, and impaired absorption due to oxidative stress, which can also lead to liver damage. Effective glycemic control in diabetes may help improve liver function and overall health [58]. In contrast, the diabetic groups treated with UMBE or UMBSNPs showed a slight increase in serum TP levels, but it was not statistically significant. The lack of significant results may be due to the short treatment duration. A longer treatment period could lead to more substantial outcomes. UMBE's bioactive compounds, with antioxidant properties, can protect the liver from oxidative stress, enhancing protein biosynthesis [59]. Additionally, UMBSNPs have more effect than UMBE to alter serum TP in diabetic groups. The UMBSNPs may enhance the liver's protein production capacity, facilitate damaged liver cell repair, and increase liver tissue protein concentrations [58]. Furthermore, the cellular uptake of AgNPs is influenced by their interactions with blood proteins like albumin, transferrin, and immunoglobulin G [60].

The MDA levels in diabetic rats exhibited a significant increase when compared to healthy rats. This significant variation can be explained by hyperglycemia, where FRs target and oxidize lipids within cells and tissues. The presence of this extremely reactive and harmful aldehyde leads to the elevation of lipid peroxidation, contributing to cell damage and is associated with various conditions like cancer, diabetes, as well as liver and cardiovascular diseases [61]. According to the current results, *U. maritima* follicle appears to effectively inhibit lipid peroxidation in biological systems. This antilipoperoxidant activity of *U. maritima* follicle is likely due to its bioactive compounds with antioxidant properties that protect against oxidative damage [62]. Previous studies have shown that UMBE reduce MDA levels in diabetic rats, suggesting its potential to mitigate oxidative stress and associated damage [63]. Additionally, the use of UMBSNPs was more effective than the use of UMBE alone in lowering MDA levels in the diabetic group. The AgNPs' impact on OS is attributed to their synthesis using UMBE, a natural antioxidant, as a reducing agent, which produced highly stable AgNPs and demonstrated UMBE's antioxidant properties by reducing MDA levels in the rats' serum [64].

According to the data presented in the current study, the concentration of $ONOO^{-}$ radicals in the diabetic rats was significantly higher compared to the healthy rats. This alteration of $ONOO^{-}$ in diabetic rats might be due to the imbalance of NO and $O2\cdot^{-}$ in the body, leading to the formation of $ONOO^{-}$ through a diffusion-limited reaction. This process can cause nitrosative and oxidative reactions in proteins, lipids, and DNA, leading to endothelial dysfunction and vascular complications [65]. However, in the diabetic group treated with UMBE, there was a slight decrease in $ONOO^{-}$ levels. This suggests that the antioxidant properties of the bioactive components present in UMBE, including flavonoids, polyphenols, minerals, and pigments, collectively contribute to the reduction of reactive species [66]. Conversely, UMBSNPs administration to diabetic group exhibited a more ability to reduce $ONOO^{-}$ levels. The synthesized AgNPs using plant extracts or secondary metabolites may lower elevated nitric oxide (NO•) levels by inhibiting the gene expression of inducible nitric oxide synthase, the enzyme responsible for NO• production.

Additionally, these AgNPs can reduce the activity of the NADPH-Oxidase enzyme, mitigating the inflammatory conditions associated with its increased activity [67].

As shown in our data, serum XO activity was significantly elevated in diabetic rats compared to the normal group. This increase is linked to hyperglycemia, indicating XO's role in generating oxidants that can cause oxidative damage to the pancreas and/or decrease insulin resistance [68]. However, in both the UMBE and UMBSNPs treated diabetic groups, XO levels were significantly reduced. This could be attributed to the antioxidant properties of the UMBE, which contains phytochemicals like tannins, flavonoids, proanthocyanidins, and phenols that can reduce inflammation, act as antioxidants, and inhibit XO activity, potentially addressing related health issues like gouty arthritis, ROS, and hyperuricemia [69]. Additionally, the treatment with UMBSNPs was more effective than UMBE in reducing XO levels. The inhibition of XO activity by AgNPs is likely due to direct interactions between the nanoparticles and the XO enzyme, where the AgNPs bind to the enzyme, altering its structure and/or function, and thereby inhibiting its catalytic activity [70]. Drawing from the preceding discourse, it can be deduced that both UMBE and UMBSNPs have the potential to inhibit the production of free radicals and counterbalance the oxidative processes linked to the over activity of XO.

Based on the data presented in the current study, it was observed that serum PON1 activity was significantly reduced in diabetic rats compared to healthy rats. PON1 is an antioxidant enzyme associated with HDL that helps prevent lipoprotein oxidation. Decreased serum PON1 activity may be linked to increased lipid peroxides and/or glycation of HDL [71]. The increased serum lipid peroxidation products in diabetic rats are due to the heightened susceptibility of serum lipoproteins to oxidation and a decline in the serum's antioxidant defenses [72]. A study conducted by Ferretti *et al.*(2004) revealed a notable decrease in PON1 activity among individuals with type 1 diabetes in comparison to healthy rats [73]. The findings also demonstrated a substantial increase in serum PON1 activity among diabetic rats treated with either UMBE or prepared UMBSNPs. The increase in PON1 activity can be attributed to the ability of UMBE and AgNPs to enhance the antioxidant defense system by facilitating ROS removal, likely due to the antioxidative phytochemicals like alkaloid, flavonoids, triterpenes, and phenolic compounds present in UMBE [74]. Moreover, UMBSNPs exhibited a stronger influence in increasing the levels of the PON1 enzyme compared to the UMBE alone. The increased PON1 activity and concentration may result from higher HDL levels and interactions between the enzyme's sulfhydryl groups and oxidized lipids formed during LDL oxidation, suggesting AgNPs' potential to induce atherosclerosis by increasing PON1 [75].

A noteworthy reduction in GST activity was noted in the serum of diabetic rats when compared to healthy rats. Hyperglycemia in diabetes leads to increased ROS and byproducts, depleting the antioxidant GST and disrupting the balance between FRs and antioxidant defenses, contributing to cellular, organ, and enzyme damage, as well as lipid peroxidation and diabetic complications [76]. Likewise, Boussekine *et al*. (2021) demonstrated that elevated blood sugar levels induced oxidative stress and led to a decrease in GST levels in vascular smooth muscles [77]. Both UMBE and UMBSNPs significantly increased serum GST levels in diabetic rats compared to the untreated diabetic group, with no significant difference between the two treatments. This may be the responses of various extracts derived from *U. maritima* have been assessed for their antioxidant activities, revealing a notable antioxidant capacity in this plant species, particularly in its follicles and leaves [78]. With the trend towards using extract's phenolic compounds and flavonoids that are present in UMB to synthesize AgNPs enhances their antioxidant properties and increases enzymatic and non-enzymatic antioxidants like GST, strengthening the antioxidant defense system [79].

As illustrated in the present study, a significant reduction in serum SOD activity was observed in diabetic rats compared to healthy rats. The decline in SOD activity in diabetic rats may be associated with either the inactivation induced by hydrogen peroxide or the glycosylation of the enzyme, as documented in cases of diabetes [80]. The present results were in agreement with the findings of researcher Hartnett *et al.*, who investigated the reduction in SOD activity in diabetic mice retinopathy [81]. The oral intake of both UMBE and prepared UMBSNPs led to a notable enhancement in SOD serum activity when compared to diabetic rats. These findings suggest that *U. maritima* exhibits significant antioxidant properties due to its contents of Proscillaridin A, a cardiac glycoside component of *U. maritima*, and chrysin, a natural flavone, that may impact the activity of SOD enzyme, highlighting its potential role in combating OS and to enhance ROS generation [82]. Concerning the effect of UMBE and UMBSNPs, there is a little enhancement in SOD activity in UMBSNPs than UMBE, this is could be due to that the AgNPs have an overall protective effect against OS, both by directly scavenging and neutralizing ROS as

antioxidants, and by improving the plant's ability to mitigate OS and ROS generation [83].

A significant reduction in serum AOA levels was confirmed in the diabetic group compared to the healthy group. The observed decline may be attributed to an imbalance between the production of FR and the body's antioxidant defense system. This disproportion may be caused by the increased demand for internal antioxidants to counteract the higher levels of FRs, leading to their depletion and a reduced ability to neutralize OS [84]. The improvement of AOA activity in diabetic treated groups with either UMBE and UMBSNPs (with better ability of UMBE than prepared UMBSNPs). This better displayed of plant extract antioxidant activity compared to AgNPs may be due to that plant extracts are generally biocompatible and non-toxic, making them suitable for *in vivo* applications. AgNPs, while showing promise in certain contexts, can also exhibit toxicity and adverse effects [85].

Serum ACY-1 activity in diabetic rats was significantly lower compared to healthy rats. The decrease in ACY-1 activity observed in diabetic rats may be linked to the accumulation of ROS and oxidative stress associated with diabetes mellitus. Consequently, the enzyme serves as a robust intracellular defense mechanism against oxidative stress in animals, leading to a reduction in its activity [86]. Interestingly, treatment with UMBE and UMBSNPs resulted in a significant increase in serum ACY-1 activity, in the diabetic groups. This may be due to UMB higher contents of amino acids specially methionine [87]. Amino acids are crucial for protein synthesis, with methionine being essential for transmethylation and cysteine being the key substrate for the antioxidant glutathione, which also requires glutamate and glycine [88]. Besides, prepared UMBSNPs showed a better ability to increase ACY-1 activity than UMBE. The enhanced ACY-1 activity in the presence of AgNPs can be attributed to their ability to stabilize the enzyme, increase enzyme loading on the surface, and facilitate electron transfer between the enzyme and substrate, preventing denaturation and aggregation while enhancing reaction rates. [89,90].

Conclusion

This study presents a simple and environmentally friendly method for the synthesis of AgNPs using UMBE. The UMBE contains various phenolic compounds that are likely responsible for the bio-reduction, capping, and stabilization of the synthesized AgNPs, as confirmed by FTIR analysis. Additionally, this study concludes that the UMBE and UMBSNPs can be considered to be safe within a range of accepted doses. Based on the latest findings, it is evident that UMBE and UMBSNPs have the potential to enhance the antioxidant status and decrease the oxidative impact on DM linked to metabolic indicators as a substitute treatment. Furthermore, the study illuminates the use of both UMBE and its synthesized nanoparticle UMBSNPs as rich sources of naturally occurring antioxidants, highlighting that the oral administration of both UMBE and UMBSNPs plays a crucial role in improving the antioxidant defense system and modulating metabolic and oxidative stress biomarkers *in vivo*.

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Funding statement

This study didn't receive any funding support.

Conflicts of interest

The authors declare that there are no difficulties linked with this study project.

Ethical of approval

This study was conducted in accordance with the ethics guidelines approved by the Animal Ethics Committee (code: AEC-023) of the College of Science, University of Duhok, Duhok, Kurdistan, Iraq.

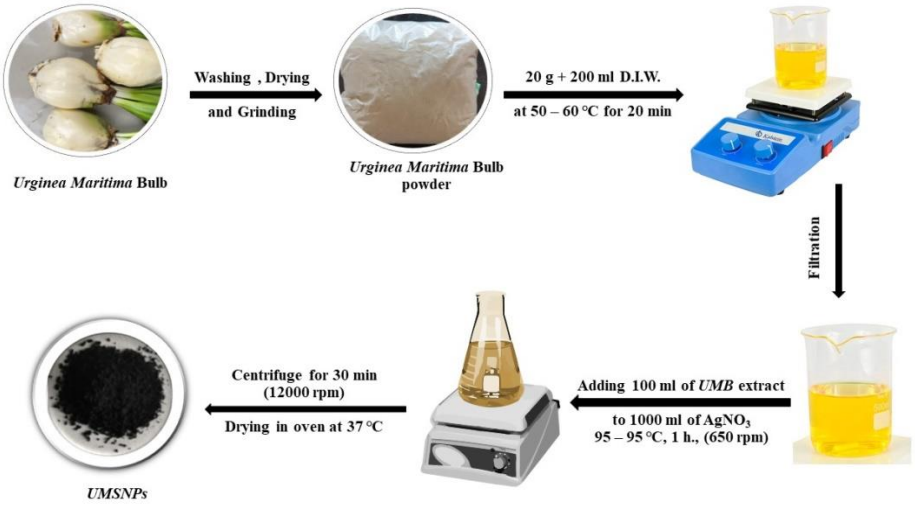

Fig. 1. Schematic representation of the synthesis of AgNPs from UMBE.

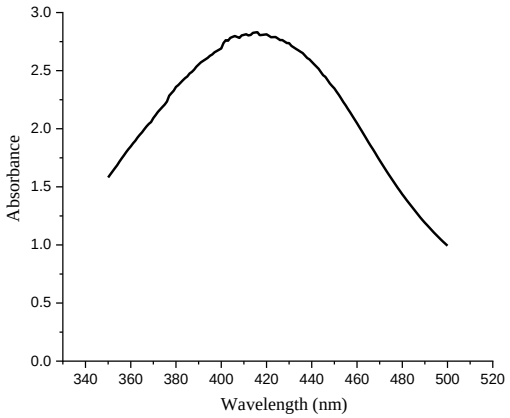

Fig. 2. UV–vis spectra of of the synthesis of AgNPs from UMBE.

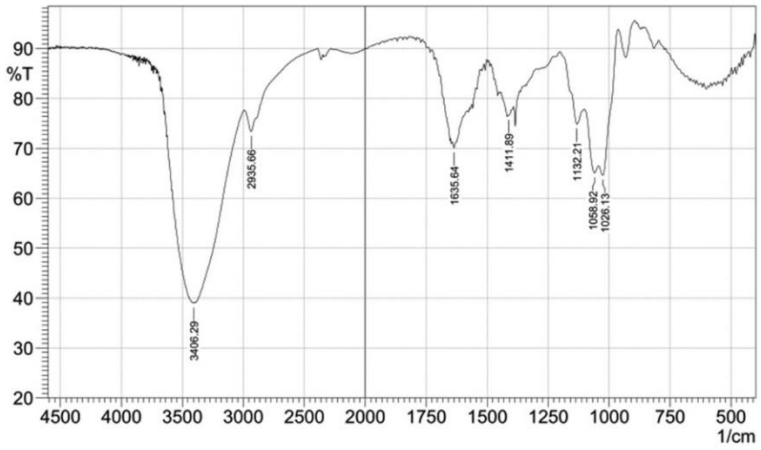

Fig. 3. FTIR analysis of UMBSNPs.

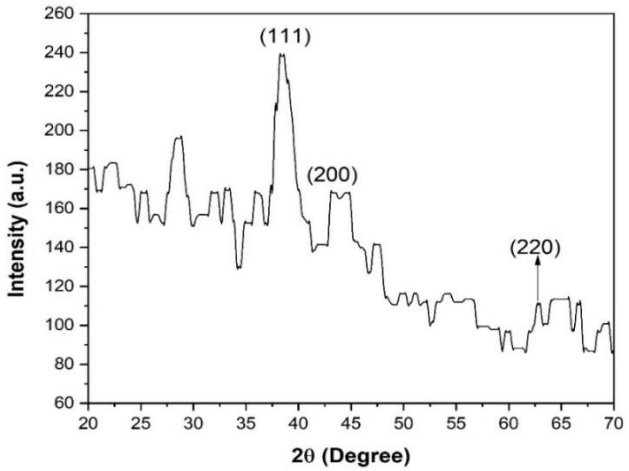

Fig. 4. XRD spectra of synthesized UMBSNPs.

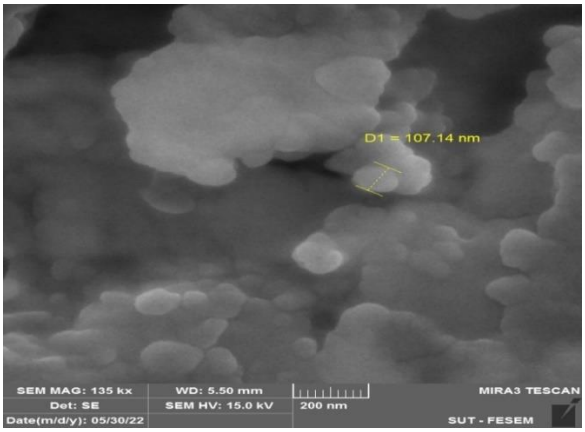

Fig. 5. FESEM pattern of UMBSNPs.

TABLE 1. The impact of administering UMBE and UMBSNPs orally on metabolic parameter levels:

Parameter Groups	Glucose (mg/dL)	Total lipid (mg/dL)	Total protein (g/dL)
Control group	90.00 ± 4.89	89.47 ± 2.71	7.76 ± 0.18
UMBE group	82.33 ± 4.22	86.97 ± 3.03	7.65 ± 0.21
UMBNPs group	87.17 ± 2.90	97.20 ± 3.12	7.18 ± 0.20
Diabetic group	333.2 ± 11.17***a	122.79 ± 3.93***a	5.75 ± 0.11***a
Diabetic + UMB	221.7 ± 5.94***d	100.58 ± 2.10d	5.96 ± 0.16***a
Diabetic + UMBNPs	204.0 ± 3.33***d	91.84 ± 4.03d	6.14 ± 0.15***a

Values are mean ± SE, *= (P< 0.05), **= (P< 0.01), ***= (P< 0.001) compared with control group. Capital letters represent a comparison of UMB and UMBSNPs treated groups with diabetic groups. Numbers with different letters were statistically significant at the level of significant (a= diabetic group, b= (P< 0.05), c= (P< 0.01), d= (P< 0.001).

TABLE 2. Estimation of Oxidant Biomarkers in Serum of Laboratory Animals.

Parameter Groups	MDA (µmol/L)	Peroxynitrite (µmol/L)	XO (U/L)
Control group	2.44 ± 0.11	72.56 ± 2.15	65.92 ± 2.69
UMBE group	2.70 ± 0.17	67.70 ± 2.92	64.89 ± 2.42
UMBNPs group	2.60 ± 0.12	61.61 ± 2.51	63.81 ± 2.49
Diabetic group	4.76 ± 0.17***a	153.07 ± 5.64***a	100.23 ± 1.12***a
Diabetic + UMB	3.11 ± 0.12**d	134.92 ± 6.68***a	79.02 ± 2.88**d
Diabetic + UMBNPs	2.13 ± 0.10d	126.18 ± 6.34***c	74.40 ± 2.59d

Values are mean ± SE, *= (P< 0.05), **= (P< 0.01), ***= (P< 0.001) compared with control group. Capital letters represent a comparison of UMB and UMBSNPs treated groups with diabetic groups. Numbers with different letters were statistically significant at the level of significant (a= diabetic group, b= (P< 0.05), c= (P< 0.01), d= (P< 0.001).

TABLE 3. Estimation of Antioxidant Biomarkers in Serum of Laboratory Animals:

Parameter Groups	PON1 (µmol/L)	GST (µmol/L)	SOD	AOA (mmol/l)	ACY-1 (U/l)
Control group	81.27 ± 2.29	152.99 ± 4.92	0.19 ± 0.35	8.97 ± 0.27	35.65 ± 1.74
UMBE group	78.25 ± 2.20	144.63 ± 5.53	0.18 ± 0.31	8.17 ± 0.22	33.35 ± 1.58
UMBNPs group	79.73 ± 2.00	141.94 ± 4.60	0.16 ± 0.60	8.53 ± 0.19	34.26 ± 1.65
Diabetic group	62.56 ± 1.99 ^{***a}	123.01 ± 1.55 ^{***a}	0.28 ± 0.55^{***a}	6.17 ± 0.16 ^{***a}	18.46 ± 0.72 ^{***a}
Diabetic + *UMB*	72.89 ± 2.45^{b}	141.9 ± 2.60^{b}	0.24 ±0.51^{***d}	7.80 ± 0.28 ^{**d}	25.26 ± 0.70 ^{***c}
Diabetic + *UMBNPs*	76.00 ± 2.50^{c}	139.4 ± 1.25^{b}	0.23 ± 0.62 ***d	7.15 ± 0.20 ^{***b}	28.67 ± 0.48 ^{**d}

Values are mean ± SE, *= (P< 0.05), **= (P< 0.01), ***= (P< 0.001) compared with control group. Capital letters represent a comparison of UMB and UMBSNPs treated groups with diabetic groups. Numbers with different letters were statistically significant at the level of significant (a= diabetic group, b= (P< 0.05), c= (P< 0.01), d= (P< 0.001).

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التخليق الأخضر لجسيمات الفضة النانوية ونشاطها المضاد للأكسدة/الأكسدة في المختبر وفي الجسم الحي باستخدام المستخلص المائي لجذور نبات البصل الفرعوني

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الملخص

تناولت هذه الدراسة تحفيز تصنيع جسيمات الفضة النانوية باستخدام مستخلص نبات البصل الفرعوني كعامل مختزل، بهدف تطوير تطبيق علاجي. علاوة على ذلك، مثلت الدراسة الحالية التطبيق السريري لمستخلص البصل وجسيماته النانوية المحضرة، وتقييم تأثير كلا العاملين على مستويات مختلف المؤشرات البيولوجية (الأيضية، المضادة للأكسدة والأكسدة) في مصل إناث الجرذان البيضاء المصابة بالسكري المستحث. أظهرت النتائج أن مستويات المؤشرات البيولوجية الأيضية (الجلوكوز والدهون الكلية) قد ارتفعت بشكل ملحوظ في مجموعات السكري بينما انخفض مستوى البروتين الكلي مقارنة بالمجموعة الصحية. في حين أن المؤشرات المضادة للأكسدة، أظهرت انخفاضًا ملحوظًا في تركيزها في مصل الجرذان المصابة بالسكري مقارنة بالمجموعة الصحية. وبشكل ملحوظ، أظهر كل من جسيمات الفضة النانوية المحضرة من مستخلص البصل وكذلك المستخلص نفسه القدرة على تعزيز نشاط إنزيمات مضادة للأكسدة في مجموعة السكري مقارنة بالمجموعة الصحية. وبالمثل، ارتفعت مؤشرات الأكسدة في الجرذان المصابة بالسكري مقارنة بالمجموعة الصحية بتغيير ملحوظ. استنادًا إلى أحدث النتائج، من الواضح أن مستخلص البصل وجسيماته النانوية لديهما القدرة على تعزيز الحالة المضادة للأكسدة والتخفيف من التأثير الأكسدي المرتبط بمرض السكري، مما يشير إلى إمكانياتهما الواعدة كعلاج بديل.

الكلمات المفتاحية: AgNPs، مضادات الأكسدة، داء السكري، الإجهاد التأكسدي، Urginea maritima.