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Effect of nano silver on gastroprotective activity against ethanol-induced stomach ulcer in rats

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ABSTRACT

Silver nanoparticles (Ag NPs) have unique properties and display an important role in bioactivities such as antimicrobial, antiviral, antifungal, and anticancer. Stable Ag NPs were prepared by reaction of silver nitrate solution with extract of Melissa and characterized by UV-Vis spectroscopy, AFM, SEM, XRD, and Zeta potential. The resulted Ag NPs have a size range between 20 and 35 nm. The current study aims to evaluate the gastroprotective effect of Ag NPs against ethanol-induced gastric ulcers in rats. Thirty rats were randomly divided into five groups. The experimental groups were fed 175 and 350 ppm/p.o of Ag NPs orally. Ag NPs improved the adversative influence of ethanol-induced stomach damage as confirmed by declining ulcer index and raised the percentage of ulcer prevention. Significantly reduced ethanol-induced gastric lesions were evidenced by increased mucus secretion and pH of stomach content, decreased ulcer area, nonappearance of edema, and leucocyte penetration of the subcutaneous layer. In gastric homogenate, Ag NPs displayed a substantial upsurge in superoxide dismutase (SOD), catalase (CAT) activities, and significantly reduced malondialdehyde (MDA) levels., Ag NPs increased the intensity of periodic acid Schiff stained (PAS) and produced over-regulation of HSP-70 and down-regulation of Bax proteins. Ag NPs confirmed gastro-protection which might be attributed to its antioxidant effect, increased mucus secretion, increased SOD, and CAT, reduced MDA level, over-regulation of HSP-70 protein, and down-regulation of Bax protein.

1. Introduction

Stomach ulcers, a communal investigational gastro-intestinal demonstration accompanied by augmented oxidative pressure and inflammation and disruption of the mucosal fence of gastric coating. Vulnerability to ulcers is amplified by destructive issues. There are endogenic antagonistic reasons that can cause stomach lesions such as smoking, non-steroidal anti-inflammatory treatment (NSAID) medicines, ethanol, *Helicobacter pylori* contagion [1,2], excessive production of HCl and pepsin, leukotriene, refluxed bile, and stress oxygen classes [3–5].

Metal nanoparticle synthesis has established cumulative consideration owing to its extensive assortment of practice in the arenas of remedy, liveliness, and microelectronics [6]. Training has been completed to discover their application and uses in applied practice, for example, antibacterial and anticancer treatment [6–8], anti-ulcer activity [9], anti-*H. pylori* [10], wound healing [11], treatment of gastric ulcers [12], and in-vitro anti-ulcer activity of green-synthesized silver nanoparticles [13].

The self-protective endogenic mechanisms against injury of the

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stomach mucosa comprise superficial mucus, the role of stomach mucosal blood movement, bicarbonate, antioxidants, surface-active phospholipids, the hastening of epithelial renewal, and the protection of epithelial hemostasis. If not preserved adequately, stomach ulcers can cause extensive problems, such as hemorrhage and holes [14]. Various medications are utilized for the treatment of stomach sores, such as proton pump inhibitors, anticholinergic drugs, antiacids, histamine H_2-receptor antagonists, stomach mucosal guards, and antibiotics. This may lead to unwanted adverse effects and reappearance of the sores [15–17]. Consequently, there is an excessive requirement for harmless and real anti-ulcer mediators.

Absolute ethanol is a necrotizing mediator that induces oxidative stress and gastric mucosal ulcer through the generation of extremely cytotoxic free radicals [2,4,18–21]. Oxygen-derived free radical species produced via ethanol administration are among the mucosal invasive factors responsible for the occurrence of peptic ulcers by causing oxidative injury to the stomach mucosal cells [22–25]. Mucosal impairment can occur due to the production of exogenic and endogenic vigorous oxygen and free radicals. Ethanol upsurges superoxide anion and hydroxyl radical creation and lipid peroxidation in the stomach mucosa [26]. The objective of the present training is to manufacture steady silver nanoparticles and examine their gastroprotective effect in ethanol-produced stomach ulcers in rats. Aqueous leaf extract of *Melissa* is utilized as a dropping mediator.

2. Materials and methodology

UV-Vis's absorption spectra are confirmed on UV–VIS Spectroscopy (England), whereas the size and form of elements are quantified on Scanning Electron Microscope SEM (Zeiss Scanning electron microscope) and Atomic Force Microscope AFM (Phywe, Germany). Constancy elements were documented on the Zeta Analyzer (Malven zeta seizer 2000, Malvern, UK). Crystallographic construction arranged specimens utilizing high-resolution X-ray diffractometric scheme JDX-3532 applying monochromatic Cu-Kα radiation of wavelength 1.5418Å.

2.1. Chemicals and reagents

All reagents and compounds were of analytical grade. Silver nitrate crystals were obtained from Merck in Germany. *Melissa* leaves and Arabic gum were provided by the resident shop. Omeprazole was obtained from a pharmacy. The medicine liquefied in 0.5% CMC (w/v) and gavage was administered by mouth to rodents at a dose of 20 mg/kg, which was suggested by several investigators [22,27,28].

2.2. Preparation of leaf extract

Fresh leaves of *Melissa*, recognized via Herbarium of Department of Biology University of Salahaddin-Erbil (Voucher No ERB 42156), were gathered. The leaves were cleaned thoroughly with distilled water numerous times to eliminate the dirt and desiccated below shadow at 25 °C for 2 weeks [29]. The dried leaves were cut into small fragments and minced to form a fine powder using an electrical blender. The ash was saturated in distilled water (100 g/500 mL) for 3 days, mixed every 2 h, filtered through a fine gauze and filter paper (Whatman No.1), and purified with a rotatory evaporator. Lastly, the prepared excerpt solution was cooled at 4 °C. Arabic gum (0.15 g) was added to 50 mL of purified water which was warmed to 70 °C in a 100 mL Pyrex beaker. This solution was added to an excerpt of *Melissa* with rousing.

2.3. Preparation of silver nanoparticles (Ag NPs) [30]

The combination of *Melissa* extract and Arabic gum was transferred to a 250-mL pointed flask. The pH of the solution was regulated at 7.5 and the mixture was heated to 60–70 °C. Concurrently, 50 mL of 1 mM silver nitrate solution was added slowly with stirring. The color of the solution changed to yellow signifying the development of silver nanoparticles. The color of the solution showed no alteration up to six months.

2.4. Investigational animals for stomach ulcer

Sprague Dawley rats (180–210 g) were purchased from the Trial Animal House Unit, (Ethics No: BIO/13/09/2019/MAA), College of Science, Cihan University. The experimental rats obtained conferred to the standards delineated in "Director Care and usage Research test center Animals "organized via Nationwide College of Knowledges and available via Countrywide Institution Healthiness (USA).

2.5. Induction of stomach ulceration

SD rats were reserved individually in special cages with an extensive network wire base to evade coprophagia. The rodents were fed with normal pellets food and allowed free access to tap water. The experimental rats were arbitrarily divided into five clusters of six animals. The rats were kept in an animal house for one week for adaptation. The abstained animals were fed as follows:

Clusters 1 & 2 received 0.5% CMC by mouth.

Cluster 3 received 20 mg/kg of omeprazole in CMC orally as reference collection [31].

Clusters 4 & 5 were fed 175 and 350 ppm/p.o of silver nanoparticles, respectively [32].

After one hour, all clusters, except cluster 1, received absolute alcohol [5 mL/kg] by mouth. Sixty minutes later, all rats were sacrificed by overdose of ketamine & xylazine, and their stomachs were excised instantly [33,34].

2.6. Gross evaluations of the stomachs

The stomach of each investigational rat was opened along the greater curvature, and the stomachs were rinsed with ice-cold buffered saline. The stomach epithelium was inspected for any damage using a dissecting microscope. Gastric lesions on the stomach epithelium appear as extended bands of red hemorrhagic injuries. Ulcers usually appear equivalent to the long alliance of the stomach. The distance and thickness of each were quantified using a planimeter [(10 mm × 10 mm = ulcer area) under dissecting microscope (1.8 ×)]. The ulcerated part of every laceration was calculated via count number of small squares, 2 mm × 2 mm, casing measurement thickness of every hemorrhagic ulcer band [35].

Summation of parts of entire abrasions for each stomach for the practical estimation of the sore region.

Number of small squares × 4 × 1.8 = UA mm^2.

Inhibition percentage (I %) was designed via subsequent formulation.

Inhibition percentage (I %) = (UA control– UA treated/UA control) X 100 [36].

2.7. Dimension of stomach pH

The stomach contents of the specimens were collected and centrifuged to estimate the hydrogen ion concentration of the fluid content of the stomach from the supernatant via pH metric titration using 0.1 N NaOH solutions utilizing a numerical pH meter, and acidity was measured in mEq/L [29,37].

2.8. Measurement of stomach mucus content

The stomachs were cleaned using cold phosphate buffer saline [PBS]. The gastric mucosa of the stomach of each rat was mildly scrubbed off using a clean glass slide, and the mass of the secretion was quantified using accurate electronic equilibrium [33].

2.9. Formulation of stomach tissue homogenate

A small portion of the glandular stomach of each rat was washed away carefully using cold PBS. A small slice of the gastric wall homogenized (10% w/v) in cold PBS comprising mammal protease inhibitor mixture. Approximately 1000 g of the stomach homogenate was centrifugated for 10 min at 4 °C. The clear supernatant was used to quantify the amount of superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA). These evaluations were performed based on the manufacturer's instructions (Cayman, USA) [38].

2.10. Measurements of endogenous antioxidant enzymes

SOD and CAT actions of the stomach homogenate were quantified using profitable standard kits (Cayman Chemical Co., Ann Arbor, USA). The manufacturer's instructions were used to quantify their quantities in the homogenate supernatant [39].

2.11. Quantities of lipid peroxidation (MDA) amount of gastric homogenate

MDA level in the glandular gastric homogenate was measured using marketable kits conferring to the manufacturer's instructions [3].

2.12. Histological evaluation

Small slices [1–2 cm] of each stomach glandular epithelium were fixed immediately in 10% buffered formalin solution at room temperature for 24 h, followed by tissue desiccation with ethanol, clearance with xylene, and infiltration with paraffin using a tissue processing machine. Each tissue biopsy was implanted in paraffin and sliced into sections of 5 μm thickness (Leica Rotation Microtome, Germany) [40].

2.13. Hematoxylin and Eosin stain

Sectioned slides stained using routine Hematoxylin and Eosin (H&E stain) were used for histopathological investigation using light microscopy [41].

2.14. Periodic acid Schiff (PAS) stains

To assess the secretion of the glandular epithelium of the stomach, sections of 5 μm thickness stained with PAS were used to evaluate the gastric secretion variations together with acidic and basic glycoproteins after the production training technique (PAS Kit) [24].

2.15. Immunohistochemical staining

Stomach slices of 3–5 μm thickness stained via immunostaining using ARKTM (Animal Research Kit) were used to detect the immune-histochemical restrict of HSP 70 (1:100) and Bax (1:50) proteins. The proteins were obtained from Santa Cruz Biotechnology [23].

2.16. Statistical analysis of data

Data analyses are shown as mean ± SE. One-way ANOVA was performed using Tukey post-hoc assessment, SPSS software, and version 24. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Characterizations of Ag NPs

UV- Vis spectroscopy is a useful technique to confirm the formation of Ag NPs. The appearance of the yellow color of the solution was attributed to the surface Plasmon resonance (SPR) phenomena which indicate the formation of these particles. The spectra were carried out in the range of 350–600 nm. The maximum peaks were observed at 436–440 nm as shown in (Fig. 1) [42].

Many measurements conducted to clarify the stability of the Ag NPs at different times. Atomic force microscopy (AFM) is used to obtain three-dimensional images of the surface as well as the distribution of silver nanoparticles. The 2D and 3D images of the Ag NPs show that the size of the particle ranges from 1 to 90 nm with a spherical shape as shown in (Fig. 2). The resulted theoretical average size of Ag NPs was 10 nm.

Ag NPs size were measured by SEM, which indicated that the particles are spherical with size range between 20 and 35 nm as shown in (Fig. 3).

3.2. Influence of Ag NPs on gross assessment of stomach

Rats fed with Ag NPs exhibited a significant reduction in ulceration in the stomach compared with that of the sore control clusters (Fig. 4). Flattened stomach epithelial surface reduction of mucosal damage was also detected during the gross evaluation of the experimental rat's stomach administered Ag NPs when compared with the ulcer control cluster (Fig. 4).

3.2.1. Influence of Ag NPs on gastric mucus content

The experimental animals fed Ag NPs showed a substantial increase in the mucus secretion of the stomach compared with the ulcer control cluster (Table 1).

The data are presented as mean ± SE (n = 6 per group). Significant difference from the normal control group at $^{*}p < 0.001$. Significant difference from the ulcer control group at $\#p < 0.001$.

3.2.2. Effect of Ag NPs on the pH of the stomach

Experimental rats fed with silver nanoparticle before the administration of absolute ethanol showed significantly increased gastric pH compared with the ulcer control cluster (Table 1).

3.3. The influence of Ag NPs on the histology assessment of absolute ethanol-produced stomach sore in rats

3.3.1. H & E stain

The ulcer control cluster presented with extensive injury to the gastric epithelium, and the lacerations intensely infiltrated the stomach epithelium with edema and white blood cells leucocytes permeation in the subcutaneous layer. The rats in investigational assemblies fed with

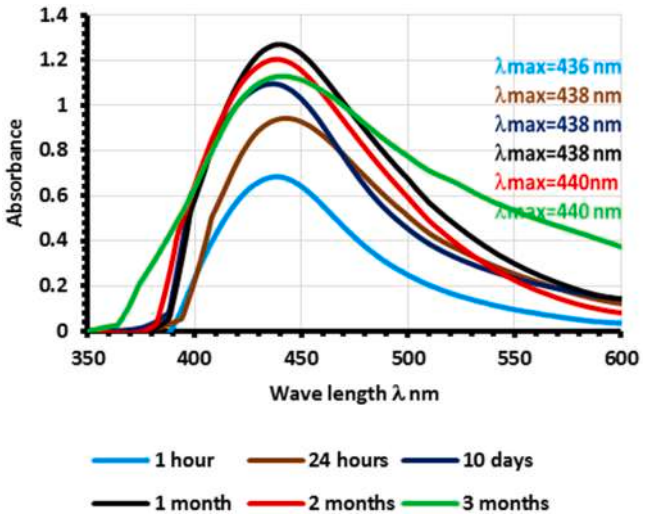

Fig. 1. UV–VIS spectra of synthesized Ag NPs at different times.

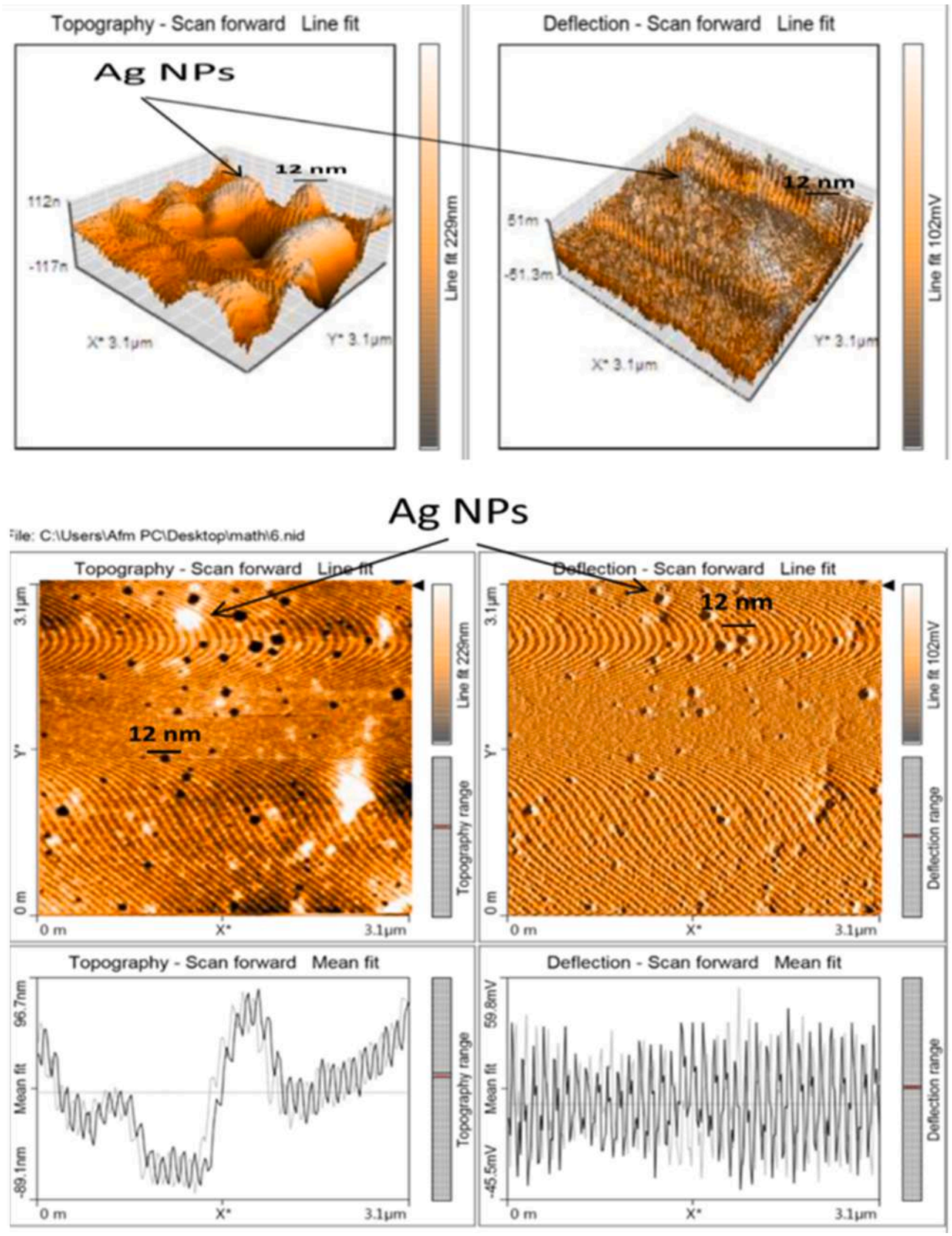

Fig. 2. AFM image (Topography) of Ag NPs.

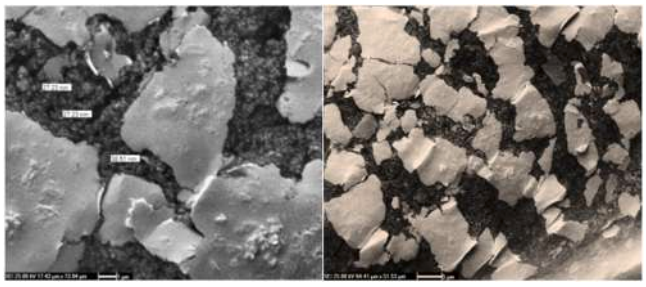

Fig. 3. SEM images for Ag NPs.

Ag NPs showed comparatively improved defense of the stomach epithelium, as shown by the decrease in the ulceration, lessening or nonappearance edema, and inflammatory cell penetration of the submucosal layer (Fig. 5).

3.3.2. PAS stain

Experimental rats fed with Ag NPs displayed comparatively augmented PAS stains strength of glycoprotein of the gastric epithelium compared to the ulcer control cluster (Fig. 6).

3.4. Immunohistochemical staining

The appearance of Bax protein in the ulcer control cluster signified over-expression. Bax protein was absent in the experimental rats fed Ag NPs (Fig. 7).

The existence of HSP-70 protein in the gastric epithelium in the experimental clusters displayed up-regulation, while in the ulcer control clusters down-regulation of HSP-70 protein was observed. The antigen location showed brown staining in the cytoplasm of the mucosal cells of the stomach (Fig. 8).

3.5. Influences of Ag NPs on the endogenous antioxidant enzymes of the gastric tissue homogenate

The rats in the ulcer control cluster exhibited meaningfully inferior SOD and CAT actions compared with the normal cluster. The rats in the trial clusters fed Ag NPs significantly restored the depletion of SOD and CAT to normal values (Fig. 9).

3.6. The effects of Ag NPs on malondialdehyde in the stomach epithelial homogenate

The rats in the ulcer control cluster exhibited a substantial upsurge in the MDA level of gastric epithelial homogenate compared with the normal cluster (Fig. 9). MDA level of the stomach homogenate expressively reduced in rats fed Ag NPs. MDA utilized a pointer designed for lipid peroxidation.

4. Discussion

Absolute alcohol as a necrotizing mediator could induce numerous adversarial properties in the stomach mucosal epithelium, such as injuries causing a reduction in the abundant protein attentiveness [4,24,25,43]. The mucus sheath was identified as the primary line of protection in the gastric tissues; accordingly, absolute ethanol abolishes mucus, leading to a mutable irreversible loss being recognized [2,26]. The gastric mucosa does not permit the entry of collapse enzymes, for example, the pepsin verbose gastric partition [5,23,40]. The mucus permits little penetrability of big particles, such as pepsin. Nevertheless, absolute ethanol increases penetrability by causing a discharge of vasoactive products and vascular injury. Destruction of the vasculature

Table 1
Influence of Ag NPs on mucus weight, pH of the stomach, ulcer area, and inhibition percentage of ulcer area in the rats' stomachs.

Animal Groups (Pre-treatment)	Mucus weight [g]	pH [acidity]	Ulcer area [mm^2]	Inhibition [%]
Normal control	1.03 ± 0.008	4.40 ± 1.33	0	–
Ulcer control	0.85 ± 0.007 *	2.82 ± 0.09 *	185 ± 0.93	–
Omeprazole	1.92 ± 0.007#	5.78 ± 0.008#	31.17 ± 1.07#	83.15
Nano silver 175 ppm	1.46 ± 0.008#	4.35 ± 0.009#	44.5 ± 1.11#	75.94
Nano silver 350 ppm	1.85 ± 0.01#	3.83 ± 0.84#	35.3 ± 0.88#	80.91

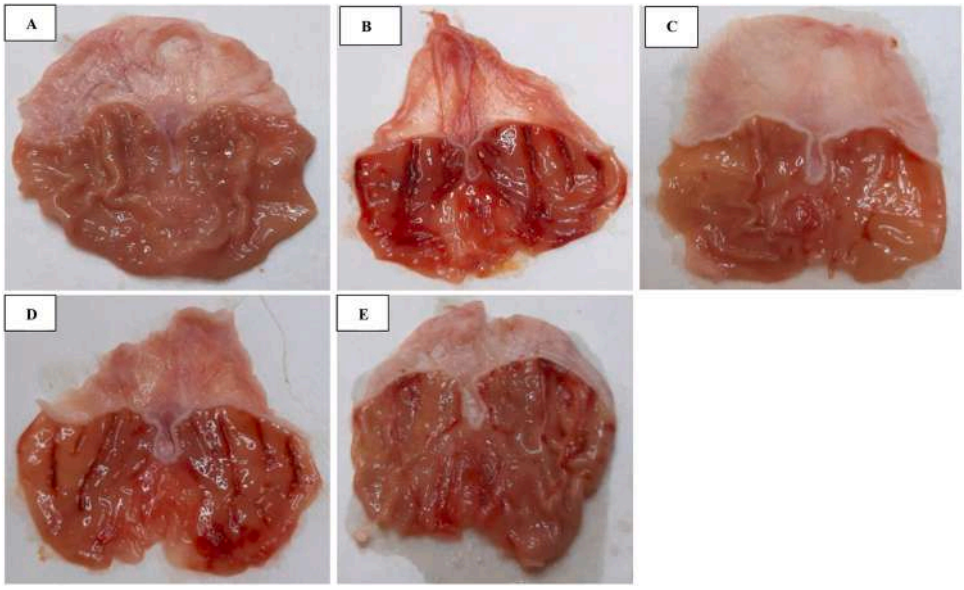

Fig. 4. Influence of Ag NPs shown in macroscopic images of absolute alcohol-induced stomach injury in rats. A. Normal cluster showing intact stomach epithelium. B. The ulcer control cluster displays widespread hemorrhagic lesions on the stomach mucosa. C. The Omeprazole cluster shows minor injuries to the gastric mucosal surface. D. & E. The experimental clusters showed a visible reduction in gastric mucosal ulceration.

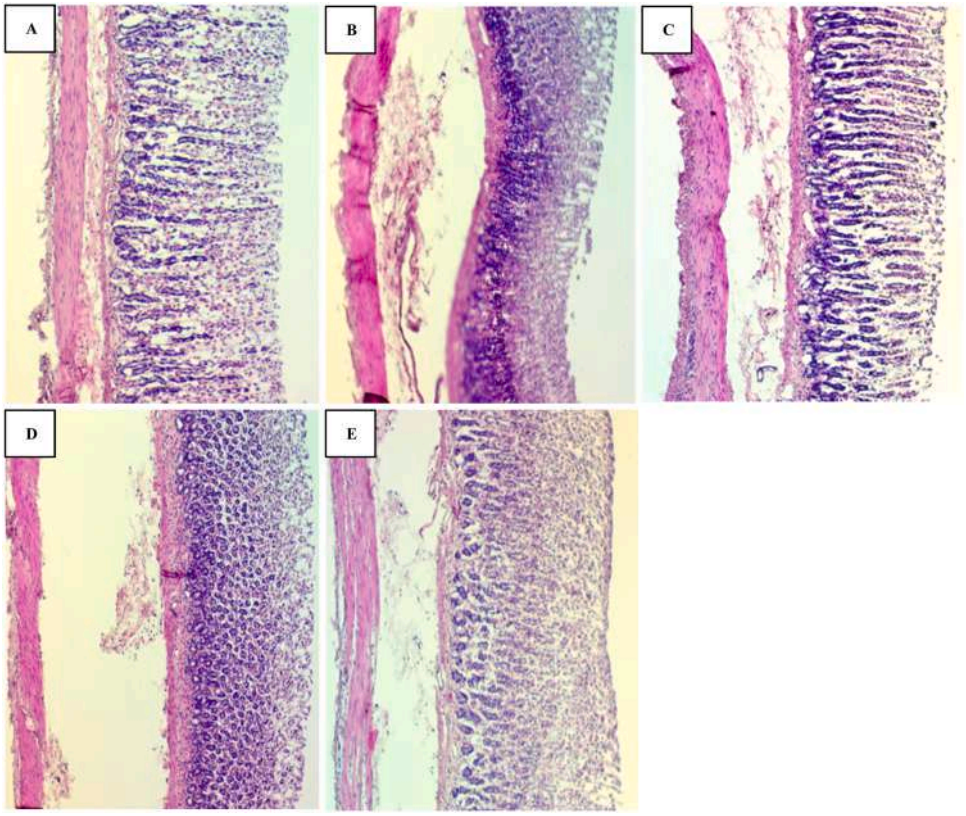

Fig. 5. Effect of Ag NPs the histological structures of gastric mucosa against ethanol-induced mucosal damages in Sprague Dawley rats. A. The normal control cluster exhibits undamaged gastric mucosa. B. Ulcer control cluster exhibiting severe mucosal injury together with necrosis, edema, and neutrophils infiltrating the submucosal layer. C. The omeprazole cluster exhibited slight mucosal damage. D & E. The experimental clusters exhibited reduced mucosal impairment.

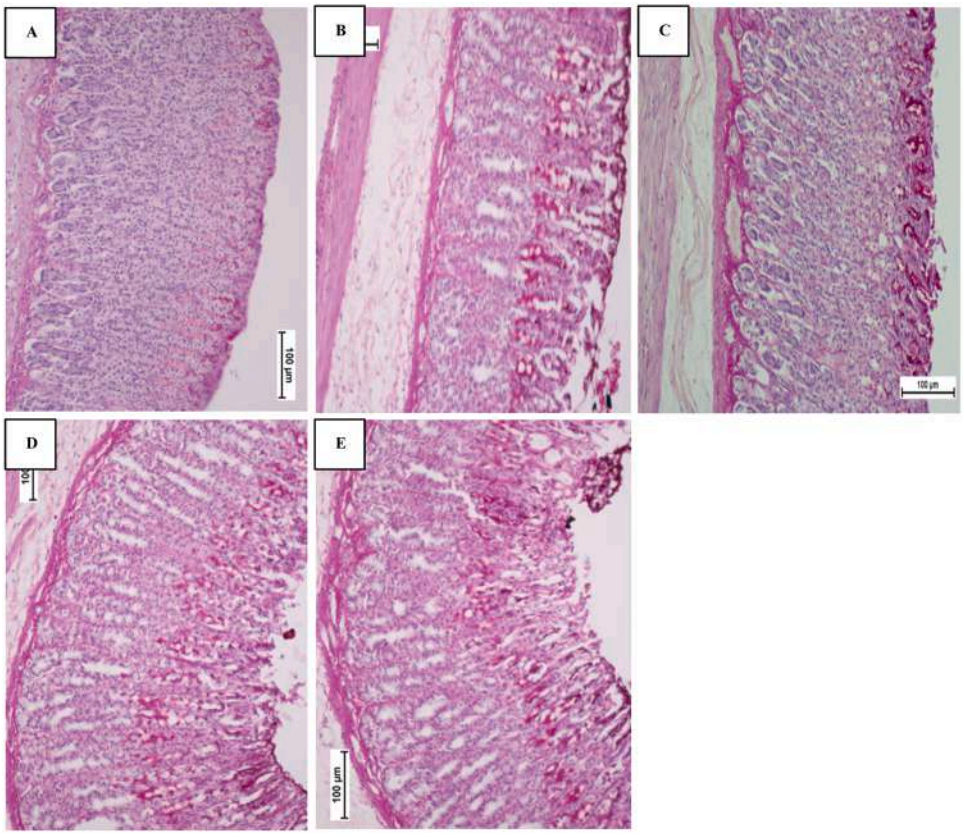

Fig. 6. Influence of Ag NPs on Periodic Acid Schiff (PAS) staining of stomach glycoproteins excretion on ethanol-induced gastric damage in rodents. A. The normal control cluster exhibited normal magenta color of the stomach mucosa. B. The ulcer control cluster exhibits a reduction or absence of PAS staining of the stomach epithelial tissues with widespread mucosal injuries. C. The omeprazole cluster exhibited powerful PAS staining. D & E. The experimental clusters exhibited a strong uptake of PAS stain.

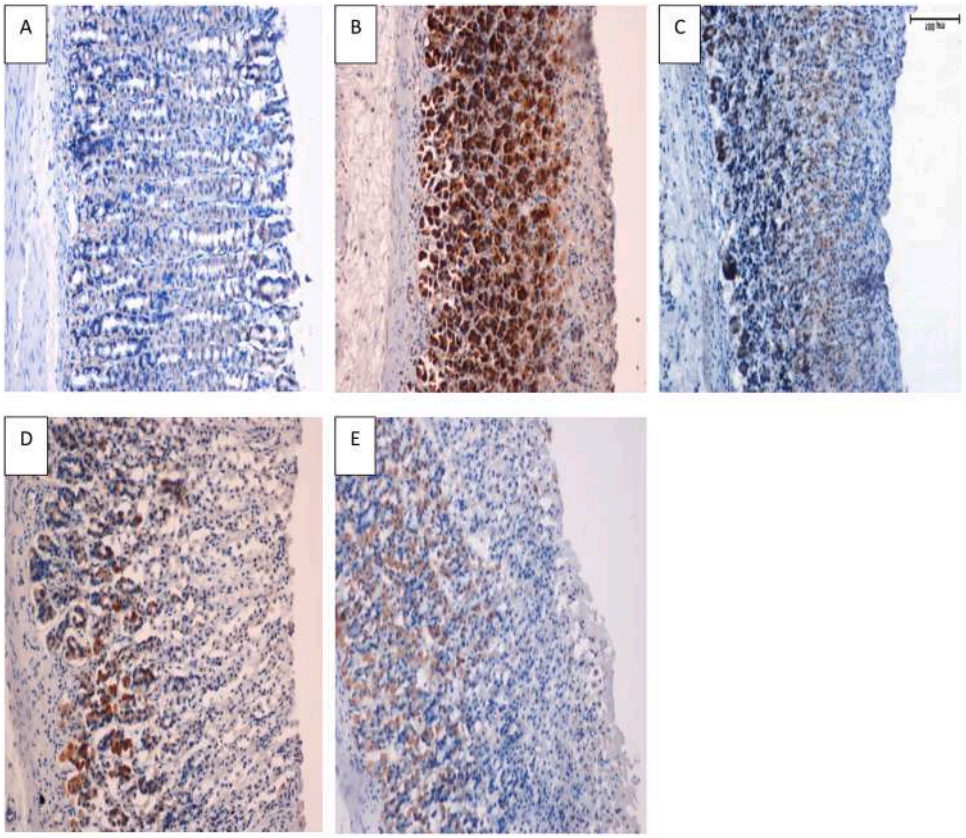

Fig. 7. Effects of Ag NPs on the expression of Bax protein of the stomach epithelium on ethanol-induced gastric damage in rats. A. The normal control cluster exhibits the absence of expression. Bax. The ulcer control cluster exhibited up-regulation of Bax protein in the gastric mucosa. C. The omeprazole cluster exhibiting down-regulation of Bax protein in the stomach epithelium. D. & E. The experimental clusters exhibited down-regulation of Bax protein in the gastric mucosa.

increases the necrotizing achievement of the stomach cells, and the inequality in the evacuation of bicarbonate and the mucus [3,44,45]. In addition, the hypothetical production of reactive oxygen species (ROS) through the action of absolute ethanol plays an important role in ulcer progression [2,4,46,47]. Earlier investigations suggested adjacent the reduction of stomach juice acid efficacy. A decline in the ability to release stomach acid provides a means of action for the stomach ulcer [12,48–50]. It is well documented that omeprazole reduces the supplementary bulk acid in the stomach. Omeprazole plays a role in self-governing acid reproduction and employs mucosal defense in non-antisecretory dosages [49,51]. Correspondingly, the anticipated antioxidants confer the anti-gastric ulcer effect [20,23,26,46].

In the present study, rats pre-fed Ag NPs improved the gastric mucosal epithelium upsurge leading to an extensive upsurge in protein attentiveness in the stomach excretions of pre-fed clusters [52,53]. The results of the study were in agreement with previous studies that measured the gastroprotective and antiulcer action conferred by diverse Ag NPs and herbal compounds [54–56]. Pre-treatment with Ag NPs proactively blocks the stomach acid and protects against the damage in the gastric wall mucosa of the rodents caused by ethanol, representing the gastroprotective influence of Ag NPs on the defense of stomach barrier mucus. Equilibrium trepidation among the gastroprotective devices and gastro poisonousness of the diverse mediator's base of acute inflammation could lead to the emission of numerous inflammatory cytokines [57,58]. It is suggested that acute inflammation induced via the action of ethanol leads to neutrophils permeating the stomach partition mucus [9,59].

The present study established that submucosal permeation was efficiently blocked-in rats pre-fed rats with Ag NPs. A widespread liberation of ROS and free radicals leads to metabolic diminishing and permanent cell impairment in the human body [32]. Stomach mucosal defense, decrease or nonappearance of edema besides inflammatory reactions of submucosal coat in rats pre-fed Ag NPs in comparison with the ulcer control cluster was confirmed by assessment of the stomach tissue's histology [60–62].

Pre-treatment with Ag NPs meaningfully augmented the stomach mucus production and reduced the acidity of the gastric content. The PAS stain outcomes exhibited an upsurge in mucus production in the stomach walls of rats pre-fed Ag NPs, suggesting the gastroprotective action of Ag NPs on the strength potency of mucus discharge. These results support the findings of other studies that presented an increase in the stomach mucus intensity (PAS) staining in rodents pre-fed numerous artificial composites against necrotizing mediators to encourage stomach mucosal injuries [63–65]. PAS stains decreased by ethanol were augmented by Ag NPs pre-treatment, which also increased the glycoprotein content [17,63]. ROS, such as superoxide radical anion, is produced via polymorph nuclear neutrophils resulting in a response from the cellular lipids and the creation of lipid peroxides. The primary pointer of oxidative pressure causing mucosal damage might be MDA, which is a chief metabolite of fat peroxidation [9,66].

According to the results of the present study, oral administration of Ag NPs might defend against stomach ulcers by increasing the action of SOD and CAT and reducing the amount of MDA. The results of our study are consistent with the outcomes stated by numerous studies concerning SOD and CAT actions being improved in Ag NPs-fed clusters compared to rodents administered ethanol [58,67]. Moreover, a decrease in the amount of MDA was observed in rats administered numerous herbal and synthetic compounds plants [65,68]. ROS, such as hydroxyl radicals, superoxide anions, and lipid peroxides, are destructive classes that aggravate stomach ulcer expansion [69]. Free radicals eventually induce damage to the gastric tissue causing lipid peroxidation. Antioxidants scavenge free radicals, playing a chief role in preventing cellular injury.

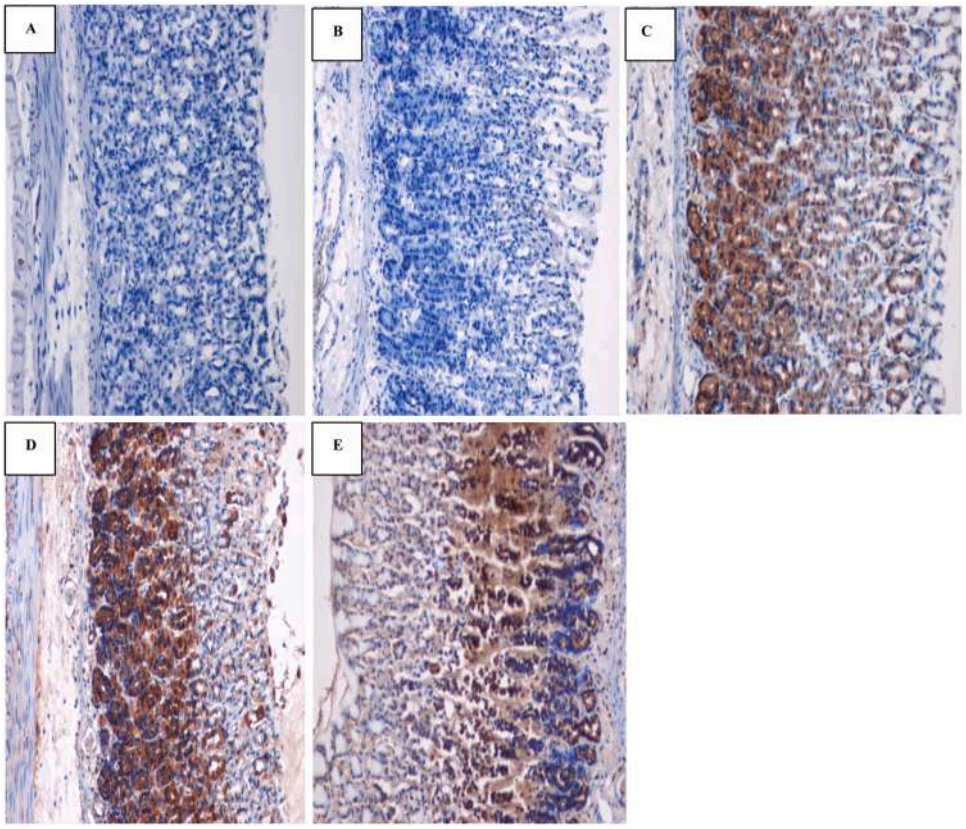

Fig. 8. Effects of Ag NPs on the expression of HSP-70 protein of stomach epithelium on ethanol-induced gastric damage in rats. A. The normal control cluster exhibits non-appearance of expression. B. The ulcer control cluster exhibited down-regulation of HSP-70 protein in the gastric mucosa. C. The omeprazole cluster exhibiting up-regulation of HSP-70 protein in the stomach epithelium. D. & E. The experimental clusters exhibited up-regulation of HSP-70 protein in the gastric mucosa.

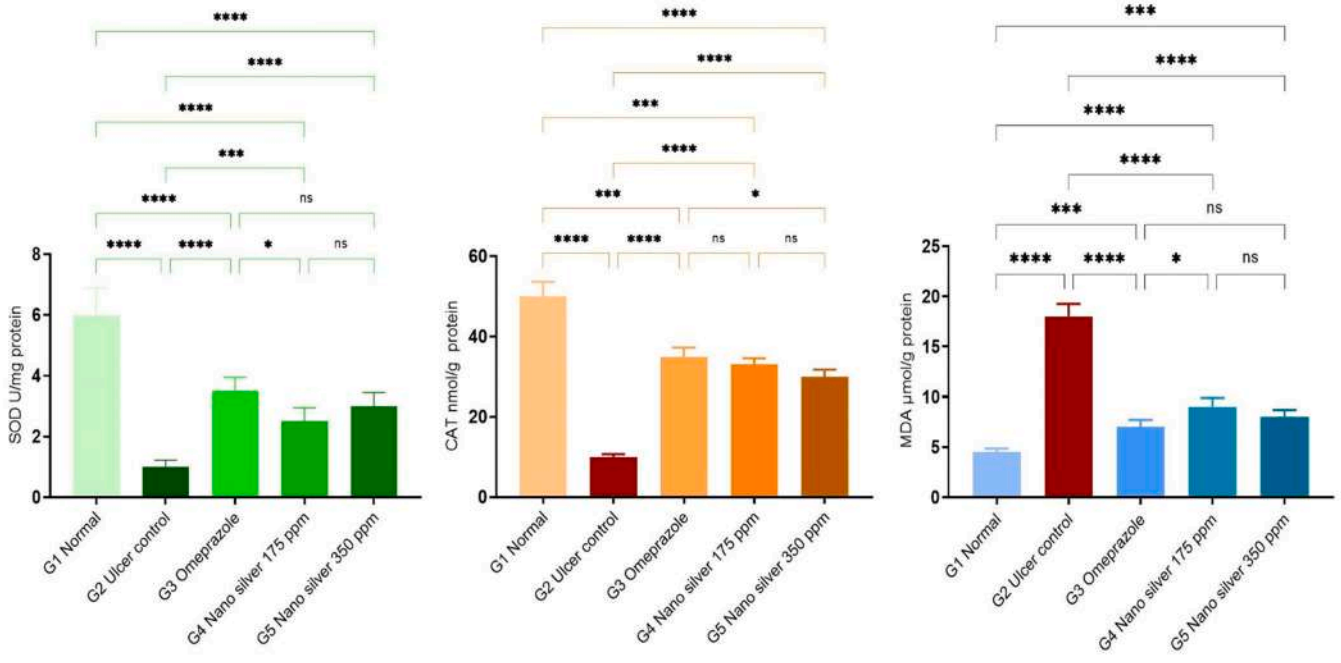

Fig. 9. Effects of Ag NPs on the antioxidant enzyme activities (SOD and CAT) and MDA level in the liver. Statistically significant differences were examined using one-way ANOVA and Tukey's post-hoc multiple comparisons test. * ** *P < 0.0001, * **P < 0.001, * *P < 0.005, *P < 0.05 above columns specify significant differences from the normal control clusters and above lines for the differences between treated clusters. ns P > 0.05 denotes to non-significant differences.

Administration of Ag NPs improved the action of antioxidant enzymes compared with the ulcer clusters by avoiding free radical production that might occur through ulcer progression. Similar results have been reported by several investigators [2,52].

HSP-70 is a 70 kDa protein belonging to the heat shock protein family, which is plentifully formed in response to numerous types of stress, such as poisonous mediators, oxidative tension, infection, and heat shock [32,70]. In addition, HSP-70 accounts for defending cellular homeostatic progressions from ecological and physiologic damages through the preservative construction of usual proteins [71]. Ethanol-activated ROS might inhibit HSP-70 appearance and strengthen oxidative impairment [32]. Numerous studies presented up-regulation of HSP-70 protein in rodents administered numerous active artificial or ordinary composites designed to defend the stomach mucosa against damage caused by ethanol [70,71]. Similarly, our results exhibited that administration of Ag NPs leads to important up-regulation of HSP-70 protein in the reference and experimental clusters. Consequently, the up-regulation of HSP-70 detected in the present study proposed that Ag NPs defend the gastric tissues by upregulation of HSP-70. Furthermore, HSP-70 is recommended due to its cytoprotective action via defensive mitochondria intrusion with stress-produced apoptosis. The gastroprotective action of Ag NPs occurs via increased SOD and CAT actions, blocked gastric acidity, and banned obliteration of stomach mucus wall. Likewise, a prominent decrease is observed in the MDA level upon consumption of Ag NPs [17,65]. In histology, a reduction in the hemorrhagic epithelial area in the gastric wall or absence of edema and white blood cells infiltration of sub-mucosal coats was correspondingly detected.

5. Conclusion

The present study showed that Ag NPs have gastroprotective outcomes against gastric damage caused by ethanol in rats supported by the macroscopic appearance, histology, immunohistochemistry, endogenous enzymes, and MDA peroxidation. Ag NPs strongly increase the action of CAT & SOD, whereas it reduces the level of MDA. Silver nanoparticle efficiently prevents ethanol-produced gastric damage by causing marked up-regulation of HSP-70 protein and downregulation of Bax protein. The protective action of Ag NPs in ethanol-produced gastric ulcers could be due to its capacity to reduce oxidative stress, lipid peroxidation, and its antioxidant and free radical scavenging properties.

CRediT authorship contribution statement

Conceptualization, A.T.M., M.A.A., and S.H.S.; Data curation, M.A.A., A.T.M., and S.H.S.; formal analysis, S.H.S.; investigation, M.A.A., A.I.H., M.S.M., A.T.M., and S.H.S.; methodology, A.T.M., and M.A.A.; Software, S.H.S., and M.H.A.; supervision, M.A.A., and A.T.M.; visualization, A.T.M., and S.H.S.; writing original draft, M.A.A., and A.T.M.; writing review and editing, M.A.A., A.T.M., S.H.S., P.Y.A., and N.F.S.; funding acquisition, I.A.A.I. All authors have read and agreed to the published version of the manuscript.

Declaration of Interest

The authors declare no conflict of interest.

Data availability

Data will be made available on request.

Acknowledgment

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