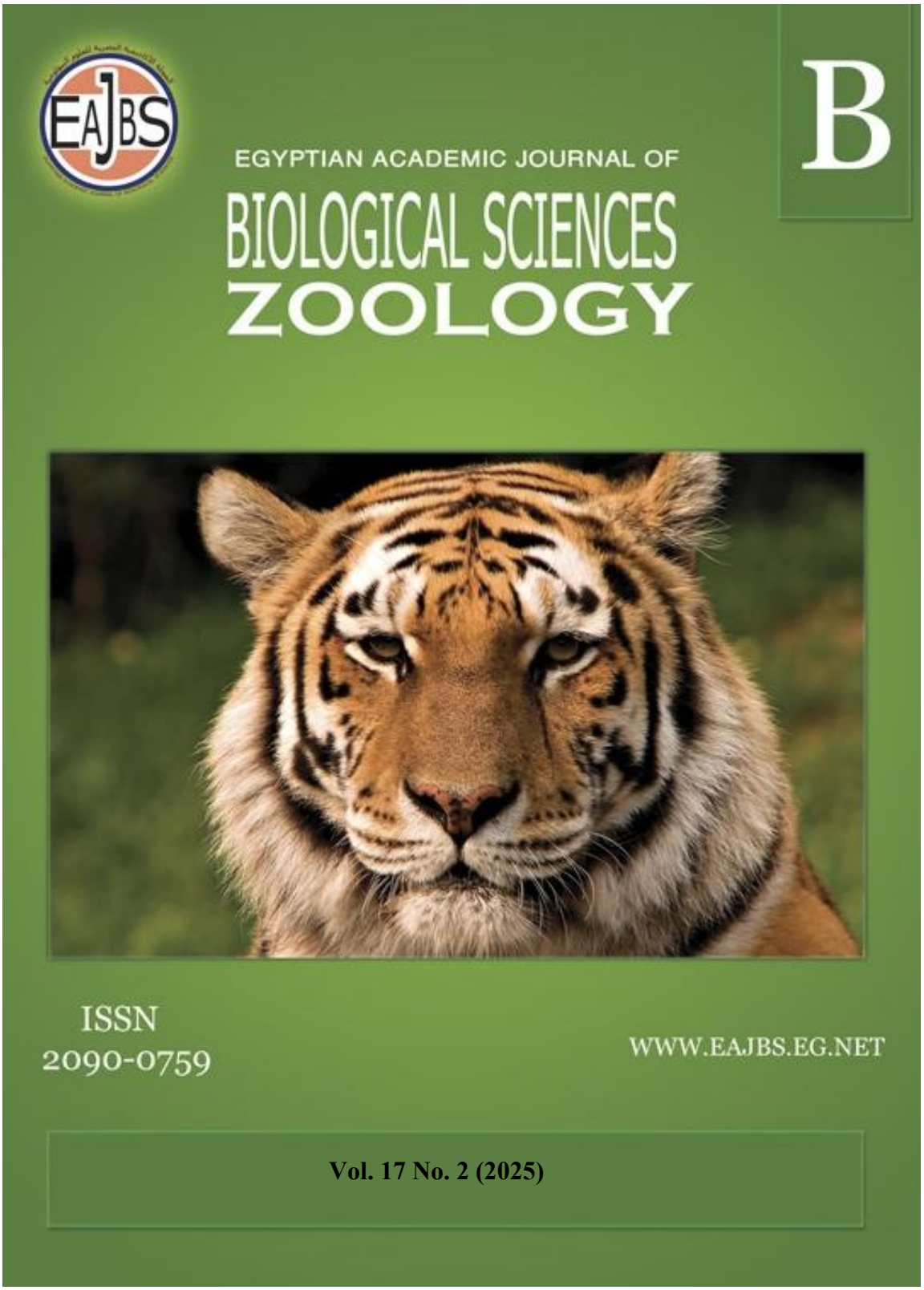


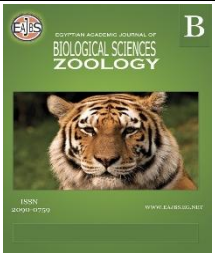
.

www.eajbs.eg.net

Citation: *Egypt. Acad. J. Biolog. Sci. (B. Zoology) Vol. 17(2) pp:55-79 (2025)*
DOI: 10.21608/EAJBSZ.2025.451531

Egypt. Acad. J. Biolog. Sci., 17(2):55-79(2025)

Egyptian Academic Journal of Biological Sciences
B. Zoology
ISSN: 2090 – 0759
Res. Ethics No.: 03-2025-0020
http://eajbsz.journals.ek b.eg/



Effect of Nanoparticles of *Moringa oleifera* Leaves Extract and\ or Low Doses of Gamma Radiation on Renal Injury Induced in Rats by Acute Pancreatitis

Safaa M. Abd El-hameed[1]*; Mona M. El-Tonsy[1]; Neamat H. Ahmed[2] and Hemmat M. Abdelhafez[1]

[1]Zoology and Entomology Department, Faculty of Science AL-Azhar University (Girls)-Naser city-Cairo, Egypt.

[2]Cell Biology& Histology National Center for Radiation Research and Technology Egyptian Atomic Energy Authority,Cairo, Egypt.

***E-mail:** safaa_magdy@outlook.com

ARTICLE INFO

Article History
Received:31/7/2025
Accepted:7/9/2025
Available:11/9/2025

Keywords:
Acute pancreatitis, nano-*Moringa oleifera*, low dose γ-irradiation, kidney, β– amyloid protein, apoptosis.

ABSTRACT

Background: One of the most prevalent conditions in gastroenterology is acute pancreatitis. Acute kidntey damage (AKI) is a significant indicator of morbidity and mortality and a frequent, major side effect of severe acute pancreatitis (SAP). Several drug classes may be transported by nanoparticles. Without any issues, the nutritional and biochemical properties of *Moringa oleifera* nanoencapsulated suggested a potential anti-hyperglycemic benefit. Low-dose gamma radiation can boost the activity of the immune system's effectors and stimulate the immune system. **Aim of the work:** This study is designed to evaluate the effect of nano-*Moringa Oleifera* leaves extract and/or low dose gamma irradiation on acute pancreatitis induced by L-arginine on the kidney tissues of rats. **Materials and Methods:** Fifty adult male rats were categorized in five separated groups. Group I: control group (C), group 2: positive control group (PC): L-arginine (250 mg/100g body weight) was administered intraperitoneally to the rats twice at 1-hour intervals, every other day for 14 days in order to cause acute pancreatitis, group 3: nano-*Moringa oleifera* treated group (NM): the positive control animals were treated with nano-*Moringa oleifera* (50 mg/kg/day) daily for 14 days, group 4: gamma irradiated group (IR): the positive control animals were exposed to 0.25 Gy x2 / week for 2weeks, group 5: nano-*Moringa oleifera* + gamma irradiated treated group (NM + IR): the positive control animals were treated with NM (50 mg/Kg/day) twice at 1-hour intervals, day by another day for 14 days and were exposed to 0.25 Gy x2/week for 2weeks. The experimental rats were sacrificed after one day of treatments; kidney functions, plasma insulin growth factor 1 (IGF1) level and C- Reactive Protein (CRP) and plasma pancreatic enzymes (lipase and amylase) , histopathological and histochemical changes in renal tissue were evaluated. **Results:** rats suffered from PC revealed a significant increase in creatinine, urea, CRP, lipase and amylase while a significant decrease in IGF1, along with severe renal tissue damage. Treatment of experimental animals suffered from PC with NM and γ-irradiation either alone or combined, a remarkable decreased creatinine, urea, CRP, lipase and amylase while remarkable increase in IGF1, resulting in notable amelioration of kidney tissues damage. **Conclusion:** To minimize the kidney damage induced by acute pancreatitis, it is recommended to use nano-*Moringa* and low γ-irradiation, either separately or in combination.

INTRODUCTION

One of the most prevalent conditions affecting the digestive system that necessitate hospitalization is acute pancreatitis (AP), which is also linked to a significant amount of morbidity. The illness starts with acute inflammation that is accompanied by severe stomach pain, nausea, and vomiting (de-Madaria and Buxbaum, 2023). Acute pancreatitis has an intolerably high death rate and can quickly progress to systemic inflammation and potentially multiple organ dysfunction syndrome (MODS) (Agarwal *et al.,* 2016). L-arginine (ARG)-induced AP was identified as a novel and distinct kind of experimental pancreatitis (Borai *et al*., 2017). Tani *et al*. (1990) described a rat model of necrotizing acute pancreatitis caused by L-arginine. In this model, 500 mg/100 g was the dosage. Death rates were relatively significant for doses beyond 500 mg/100 g of body weight. Seventy to eighty percent of the pancreatic acinar cells necrotized after a single intraperitoneal injection of 500 mg/100 g in three days.

In acute pancreatitis, retrospective investigations identified risk factors for AKI, but they did not identify the necessity of kidney replacement therapy (Li *et al*., 2010; Charilaou *et al*., 2018). Devani *et al*. (2018), found that a history of chronic kidney disease, sepsis, respiratory failure, intensive care unit admission, older age, and male gender all increased the risk of AKI. Patients with AP with AKI had a death rate that ranged from 25% to 75% (Lin *et al*., 2011). However, Devani *et al*. (2018), discovered that over the previous ten years, the death rate among individuals with AKI had decreased threefold. One significant pathophysiologic event is the early activation of pancreatic enzymes within the acinar cells. This causes the pancreas and adjacent tissues to autodigest, which sets off a series of events that culminate to AKI (Pandol *et al*., 2007). Decreased abdominal pressure, severe kidney vasoconstriction, hypercoagulability, fibrin deposition in the glomeruli, hypovolemia, hypotension, and fluid extravasation from the vascular space are all possible outcomes of endothelial damage caused by the release of activated enzymes and proteases into the systemic circulation. Additionally, autodigestive acinar damage triggers the release of cytokines and the generation of oxygen free radicals (Satake *et al*., 1991; Zhang *et al*., 2008).

Morris (2014) defines nanotechnology as the application of knowledge and influence over matter at dimensions ranging from 1 to 100 nm, where special physical characteristics enable the development of new applications. The ability of nanotechnology to alter materials at extremely small scales to get specific properties that would greatly enhance the toolbox of materials science is the basis for many of its benefits (Omietimi *et al.,* 2023).

Nanotechnology-based herbal medicines offer a lot of potential and special qualities, like the ability to turn less soluble, poorly absorbed, and unstable ingredients into viable medications. Thus, delivery systems based on nanotechnology offer a promising way to boost herbal activity and get past the problems with herbal medication (Sandhiya and Ubaidulla, 2020). Nanotechnology has enormous potential to transform how we identify, treat, and prevent diseases in the healthcare and medical fields in the future (Malik *et al*., 2023).

Due to its many medicinal and non-medical applications, *Moringa oleifera,* also known as the "tree of life" or "miracle tree," is considered an important herbal plant. For many years, the herb has been used to treat discomfort, ulcers, liver and heart illness, cancer, inflammation, and wound. The tree's vital nutrients are utilized in almost every part of it (Pareek *et al.,* 2023).

Additionally, zeatin, quercetin, and kaempferom a rich and uncommon combination found in *Moringa* leaves have demonstrated strong antifungal, anti-inflammatory, and anticancer properties (Patel *et al*., 2010). These active ingredients may help reduce hyperglycemia and hyperlipidemia by acting as antioxidants (Abdulkadir *et al*., 2015). Because of its documented antibacterial, antioxidant, antiulcer, cytoprotective, cardiovascular, antidiabetic, anticancer, and neuroprotective qualities, it can be used as a nutritional supplement or to treat a variety of clinical problems (Rao *et al*., 2001; Omotoso *et al*., 2018).

It has been demonstrated that low-dose gamma radiation can protect the kidneys; this

is referred to as radiation-induced preconditioning. Prior to exposure to low-dose radiation in mouse models, defensive mechanisms (such as angiogenesis and the oxidative stress response) were triggered, which lessened eventual damage from ischemia-reperfusion injury, which can impact urea and creatinine levels (Khbouz *et al.,* 2023).

The purpose of this investigation was to explore the potential therapeutic effects of extract from nano-*Moringa oleifera* leaves and/or low-dosage gamma irradiation to cure kidney injury in rats that was caused by acute pancreatitis triggered by L-arginine.

MATERIALS AND METHODS

Experimental Animals:

The experimental animals for the various studies conducted in this work were fifty adult male albino rats (*Rattus rattus*) weighing 180–200g, which were acquired from the Egyptian Holding Company for Biological Products and Vaccines (Cairo-Helwan, Egypt). Before the experiment began, the animals were acclimated to the lab environment. The animals were housed in specially designed cages with 10 rats each, under regulated conditions of temperature and relative humidity (continuous temperature of 25–27 °C with a 12-hour light/dark cycle) for two weeks prior to the experimental procedure. Standard rodent pellets were used to feed the animals.

The research ethics committee (REC) authorized this study process, which was created and conducted in compliance with the CIOMS and ICLAS International Guiding Standards for Biomedical Research Regarding Animals (Warnecke *et al.,*2008).

Radiation Facility:

The gamma cell-40 irradiation was carried out inside the Cairo-based Egyptian National Center for Radiation Research and Technology (NCRRT). A cesium-1 irradiation device, the gamma cell-40 is manufactured by Atomic Energy of Canada Ltd. According to Frey *et al.* (2015), the experimental animals received 0.25 Gy x2 /week for two weeks at a dosage rate of 0.423 Gy/min. At the time of the experiment, this was computed using the Dosimetry Department's guidelines from the NCRRT.

L-arginine Monohydrochloride:

The supplier of L-arginine monohydrochloride (CAS No. 53308-83-1) was Sigma Chemical Company (Sigma, USA). Reagents with a purity grade of more than 95%.

Pancreatitis Models (induction of pancreatitis):

To induce acute pancreatitis, the animals received repeated intraperitoneal injections of L-arginine at a rate of 250 mg/100g body weight twice at one-hour intervals, every day for ten days (Hegyi *et al.,* 2004; Kui *et al.,* 2015).

After diluting L-arginine-HCl in saline, its pH was brought down to 7.4 by NaOH. A fresh L-arginine solution was made before to every experiment (Kui *et al.,* 2015).

Preparation of Nano-*Moringa:*

Plant Materials:

At the National Research Center in Dokki, Giza, Egypt, the Egyptian Scientific Society of *Moringa* (ESSM) provided the aqueous extract of *Moringa oleifera* leaves (MOL)

Preparation of *Moringa* Leaves Extract-Loaded PLGA-PEG Nanoparticles:

Abd-Rabou *et al.* (2017), claim that a minor modification was made to the nanoparticle production method. To create poly D, L-lactide-co-glycolide (PLGA) nanoparticles, 100 mg of PLGA polymer was dissolved in 3 milliliters of chloroform to create an initial emulsion. An O/W emulsion was produced using a microtip probe sonicator (VC 505, Vibracell Sonics, Newton, USA) in an aqueous polyvinyl alcohol (PVA) solution (12 ml, 2% w/v).

Three separate nano-formulations of polyethylene glycol-blended PLGA (PLGA-PEG) were created using three different PLGA-PEG ratios (1:2, 2:1, and 1:1) to create PLGA-PEG nano-void. These were then added to the watery PVA solution prior to emulsification with the

PLGA polymer. To enable the organic solvent to evaporate, the emulsion was shaken for eight hours. After two washes with double-distilled water, an excess of PVA was eliminated the next day by ultracentrifugation at 50,602g for 20 minutes at 4 °C (Sorvall Ultraspeed Centrifuge, USA).

Moringa leaf extract (ML)-encapsulated PLGA-PEG nanoparticles (MLn) were similarly created for medicinal applications by adding a certain concentration before emulsification.

Analysis of Particle Size and Zeta Potential:

Using a Zeta Sizer (Nano ZS, Malvern Instruments, UK) and a red laser with a wavelength of λo=633 nm (He–Ne, 4.0 Mw), photon correlation spectroscopy (PCS) was used to quantify the particle size and zeta potential of the PLGA-PEG NPs. One milligram of the NPs was dissolved in one milliliter of water, which was then diluted ten times with water, and the readings were taken for at least 120 seconds. In the same way, materials were put in an electrophoretic cell with a potential of ±150 mV for zeta potential measurements. The nanocomposites were maintained at 25.0±0.1 °C.

Transmission Electron Microscope (TEM):

Using a transmission electron microscope (TEM, Philips CM-10, FEI Inc., Hillsboro, OR, USA), the particle morphology of the NPs was investigated. Formvar-coated copper grids were filled with 100 μg/ml of the nano-suspensions. Once the samples had completely dried, they were stained with 2% w/v uranyl acetate (Electron Microscope Services, Ft. Washington, PA). Soft Imaging Viewer software and a digital microscope were used for image capture and analysis.

Experimental Design:

The adult male albino rats in the experiment were divided into five groups (n=10) as follows:

G1: Negative control group(C): untreated normal animals.

G2: **Positive control group (PC)**: animals were administered intraperitoneal injections twice at 1h intervals with L-arginine (250mg/100g) to induce acute pancreatitis.

G3: Nano-*moringa oleifera* treated group (NM): The positive control animals were given a daily dose of nano-*moringa oleifera* leaves extract (50 mg/kg/day) for 14 days.

G4: Gamma-irradiated group (IR): for two weeks, positive control animals were exposed to 0.25 Gy x2 /week.

G5: Nano-*Moringa oleifera* + gamma irradiated treated (NM + IR): the positive control animals were treated with **NM** (50 mg/Kg/day) daily for 14 days and were exposed to 0.25 Gy x2/week/2weeks.

Rats in each group were given isoflurane anesthesia, and samples of renal tissue and blood serum were taken after a day of treatment. In order to separate the plasma for additional biochemical analysis, blood samples were drawn in sterile heparinized syringes and centrifuged for 10 minutes at 3000 rpm. As quickly as feasible, the entire kidney of each animal was removed, cleaned with isotonic ice-cold saline, fixed in 10% neutralized formalin, and embedded in paraffin for histopathological and histochemical analysis.

Biochemical Analysis:

Estimation of Kidney Functions:

1.Estimation of Creatinine:

The kinetic method of Murray (1984) was used to measure creatinine using a commercial kit from SPINREACT Company in Spain.

2.Estimation of Urea:

A commercial kit from SPINREACT Company in Spain was used to quantify urea using the kinetic approach (Kaplan, 1984).

Estimation of Insulin-Like Growth Factor 1 (IGF-1):

IGF1 levels were measured using a commercial kit that was bought from the CUSABIO

Company in the United States.

Estimation of C- Reactive Protein(CRP):

A commercial kit from My BioSource Inc. in San Diego, California, USA, was used to measure the level of C-reactive protein.

Plasma Pancreatic Enzymes Activities:

A) Lipase Activity:

A diagnostic kit from the Salucea Company was used to measure the lipase activity in plasma (Moss, 1999).

B) Amylase Activity:

A diagnostic kit from the Salucea Company was used to measure the amylase activities in plasma (Winn-Deen *et al.,* 1988).

Histological and Histochemical Analysis:

Renal samples were submerged in 10% neutralized formalin prior to being dehydrated and preserved in paraffin wax. For histological analysis, sections (5 µm) were cut using a microtome, mounted on glass slides, and stained with hematoxylin and eosin stains (H & E) (Bancroft *et al.,* 1996). Collagen fibers were stained by using Masson's Trichrome (Mao *et al.,* 2016). Amyloid-β protein was detected by Congo red technique (Bancroft and Gamble, 2008). Paraffin-positive slides were stained with 5 µg/ml propidium iodide and 50 µg/ml acridine orange in phosphate-buffered saline, and they were analyzed using fluorescence microscopy to assess apoptosis and necrosis in accordance with Bank (1988).

Statistical Analysis:

The statistics package for Windows, version 15.0, was used for all statistical analyses (SPSS Software, Chicago, IL). Results for continuous variables were presented using the average standard error. The values were compared using one-way analysis of variance (ANOVA), and p values less than 0.05 were considered statistically significant.

RESULTS

1- Characterization of Nano-*Moringa* Particles:

Moringa leaves extract nanoparticles (MLn)-based PLGA-PEG nanoparticles (poly D-L-lactide-co-glycolide-polyethylene glycol) were prepared using three different nano-formulations with three different ratios of PLGA-PEG (1:2, 2:1, and 1:1), which were then added to the aqueous PVA (Polyvinyl Alcohol) solution before the droplet size of *Moringa* leaves extract nanoemulsion was measured. Formulations No. 3 for MLn-based PLGA-PEG nanoparticles demonstrated excellent stability. Formula 3 (F3): Zeta potential (-39.60±3.52) is more stable, the nano-size (141.772±14.5) is the smallest, and the polydispersity index (0.05±0.01) is uniform in size and shape (Table 1 and Figs.1, 2&3).

As seen in Figure 4, the morphology of MLn-based PLGA-PEG nanoparticle sample F3 was examined using transmission electron microscopy (TEM). TEM revealed rounded particles with an encircling capsule and core (Figure 4A). The TEM of F3 nanoparticles in Figure 4B displays a range of diameters for a few chosen particles, from 148.42 to 152.40.

Table 1: The effect of PLGA: PEG ratios on the particle size and zeta potential of MLn-based PLGA-PEG nanoparticles.

Formulation	PLGA	PEG	Nano-Size (nm)	PDI	Zeta potential (mV)
F1	1	2	190.137± 6.5	0.5± 0.02	-13.23±3.32
F2	2	1	341.995±15.4	0.6±0.03	-5.27± 1.29
F3	1	1	141.772±14.5	0.05± 0.01	-39.60± 3.52

Notes: MLn; *Moringa* leaves extract nanoparticles, PLGA; poly D-L-lactide-co-glycolide, PEG; polyethylene glycol, F1; formula 1 (ratio 1:2), F2; formula 2 (ratio 2:1), and F3; formula 3 (ratio 1:1), PDI; polydispersity index, S.E.; standard error.

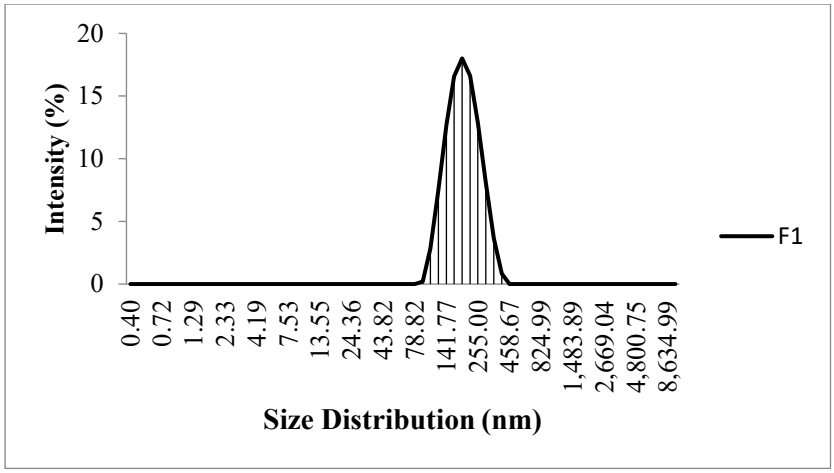


Fig. 1: Size distribution of formula 1 F1.

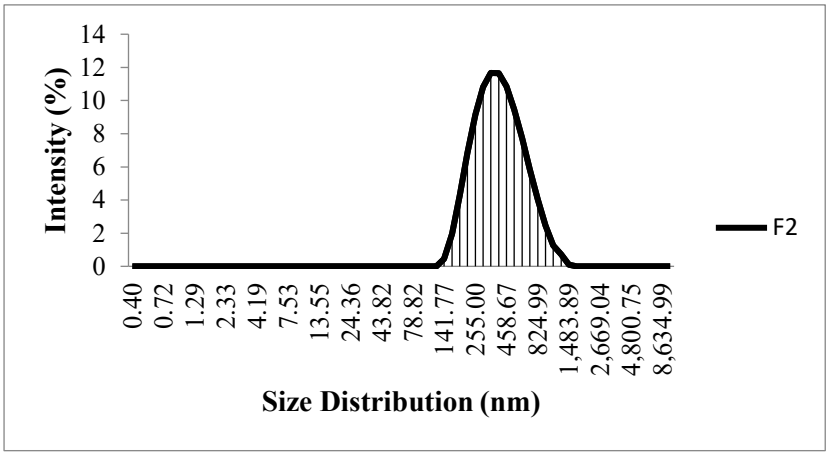


Fig. 2: Size distribution of formula 2 F2.

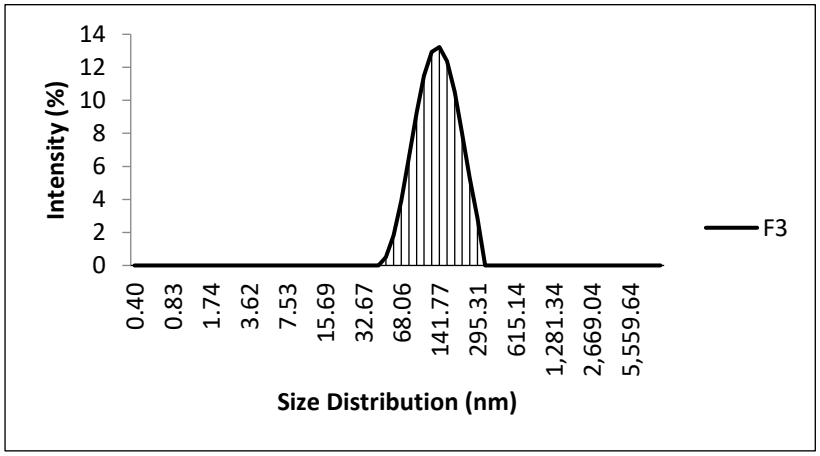


Fig. 3: Size distribution of formula 3 F3.

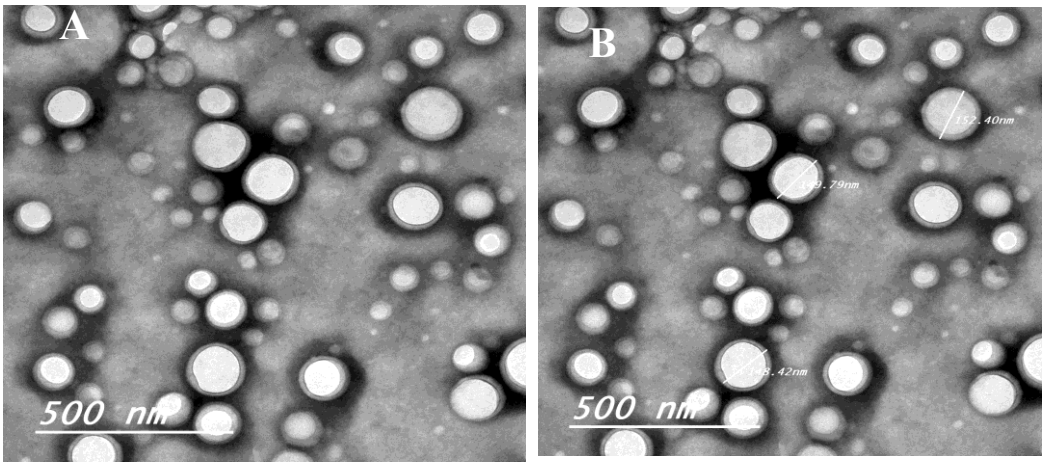


Fig. 4: Characterization of F3 nanoparticles. A) TEM of F3 nanoparticles showing rounded particles containing core and surrounded capsule. B) TEM of F3 nanoparticles showing some sizes of selected particles.

Biochemical Results:

-The kidney Functions:

A group of rats suffering from PC revealed a significant increase in creatinine (105%) and urea (32.53%) levels in comparison with the control group.

Treatment of experimental animals, suffered from PC with NM and γ-irradiation either alone or combined, a remarkable decrease in in creatinine (-30.49%, -14.63% and -32.93% respectively) and urea (-19.42%,-22.45% and -17.87% respectively) levels were observed when compared with the PC group (Table 2).

Table 2: Effect of nano-*Moringa oleifera* leaves extract and/or low doses of gamma irradiation on creatinine and urea levels in adult male albino rats suffering from pancreatitis.

Parameter	Creatinine(mg/dl)			Urea(mg/dl)		
Time / Groups	One day			One day		
	Mean± S.E	% change (C)	% change (PC)	Mean± S.E	% change (C)	% change (PC)
Control (C)	0.40±0.04	0 %	- 51.22%	8.69±1.81	0 %	- 24.55%
Positive control (PC)	0.82±0.05 a	105%	0%	64.53±1.82 a	32.53%	0 %
Nano-*Moringa* (NM)	0.57±0.02 ab	42.5%	- 30.49%	52±0.73 b	6.80%	- 19.42%
Gamma-irradiated group (IR)	0.70±0.03 a	75%	-14.63%	50.04±0.95 b	2.77%	- 22.45%
NM+IR	0.55±0.01 ab	37.5%	- 32.93%	53±1.53 b	8.85%	- 17.87%

N=10.

- Each value represents the mean ± standard error (SE).

(a) Significant from control at $P \leq 0.05$.

(b) Significant from positive control at $P \leq 0.05$.

Plasma Insulin Growth Factor 1 (IGF1) level and C- Reactive Protein CRP:

A group of rats suffering from PC revealed a significant decrease in IGF1 level (- 49.29 %) while a significant increase in CRP level (304.71%) in comparison with the control group was recorded.

Treatment of experimental animals, suffered from pancreatitis with NM and γ-

irradiation either alone or combined, a remarkable increase in IGF1 levels (32.47%, 50.75% and 41.94% respectively) was observed. In contrast a remarkable decrease in CRP level (-68.23%, -66.14% and -69.44%, respectively) were revealed when compared to the PC group (Table 3).

Table 3: Effect of nano-*Moringa oleifera* leaves extract and/or low doses of gamma irradiation on IGF1 and CRP levels in adult male albino rats suffering from pancreatitis.

Parameter	IGF1(µg/l)			CRP (mg/L)		
Time / Groups	One day			One day		
	Mean± S. E	% Change (C)	% Change (PC)	Mean± S. E	% change (C)	% change (PC
Control (C)	9.17±0.35	0.0 %	79.20%	14.45±1.32	0%	-75.29%
Positive control (PC)	4.65±0.11 [a]	- 49.29 %	0.0%	58.48±1.59 a	304.71%	0%
Nano-*Moringa* (NM)	6.16±0.07 [ab]	-32.82%	32.47%	18.58±1.55 [b]	28.58%	- 68.23%
gamma-irradiated group IR	7.01±0.06 [ab]	-23.56%	50.75%	19.80±0.50 [ab]	37.02%	-66.14%
Nano- *Moringa* (NM+IR)	6.60±0.03 [ab]	-28.03%	41.94%	17.87±0.47 [ab]	23.67%	-69.44%

Ligands as in table 2

Plasma Pancreatic Enzymes (lipase and amylase) Activities:

A group of rats of the PC revealed a significant increase in lipase (102.49%) and amylase (38.91%) activity in comparison with the control group. Treatment of experimental animals, suffered from pancreatitis with NM and γ-irradiation either alone or combined, a significant decrease in lipase (-46.02%, -46.18% and -33.26%, respectively) and amylase activity (25.87%,-23.76%, and -25.23%, respectively) were noted when compared to the PC group (Table 4).

Table 4: Effect of nano-*Moringa oleifera* leaves extract and/or low doses of gamma irradiation on lipase and amylase activity in adult male albino rats suffering from pancreatitis.

Parameter	Lipase(U/ml)			Amylase(U/ml)		
Time / Groups	One day			One day		
	Mean± S. E	% change (C)	% change (PC)	Mean± S. E	% change (C)	% change (PC)
Control (C)	38.50±1.06	0.0 %	-50.62%	2722.25±49.20	0.0 %	-28.01%
Positive control (PC)	77.96±1.0 4 [a]	102.49%	0.0 %	3781.58±36.52 [a]	38.91%	0.0%
Nano-Moringa (NM)	42.08±1.45 [b]	9.3%	-46.02%	2803.17±45.09 [b]	2.97%	-25.87%
IR	41.96±1.23 [b]	108.99%	-46.18%	2902.67±7.51 [ab]	6.63%	-23.76%
Nano-Moringa (NM+IR)	52.03±1.77 [ab]	35.14%	-33.26%	2827.50±48.04 [b]	3.87%	-25.23%

Ligands as in table 2

Histological Results of the Kidney Tissue:

The Control Group:

The renal cortex of the control adult male albino rat exhibits normal architecture. Renal tubules encircled the dense, rounded structures that were known as renal corpuscles. Each glomerulus is surrounded by narrow Bowman's space and Bowman's capsule.

The primary components of the cortical tubules are the distal and proximal convoluted tubules. The proximal tubules consist of simple cuboidal epithelium and narrow lumens with intensely stained cytoplasm. The distal convoluted tubules are differentiated from the proximal by the absence of brush borders, larger defined lumens and less affinity to stain (Fig. 5 A). Sections in the kidney cortex tissue of rats of the PC group showed congested and lobulated glomeruli. Interstitial hemorrhage and necrotic areas containing inflammatory cells were recorded (Fig. 5 B). Sections in the liver tissue of the NM treated group showed nearly normal appearance of glomeruli, proximal and distal convoluted tubules. At the same time, the hemorrhage was still detected (Fig. 5C). On the other hand, sections in kidney cortex tissue from IR treated group showed well-developed kidney architecture (Fig. 5D). At the same time, sections from the kidney tissue of the NM+IR treated group showed nearly normal appearance of most convoluted tubules but the glomeruli were still congested (Fig. 5 E).

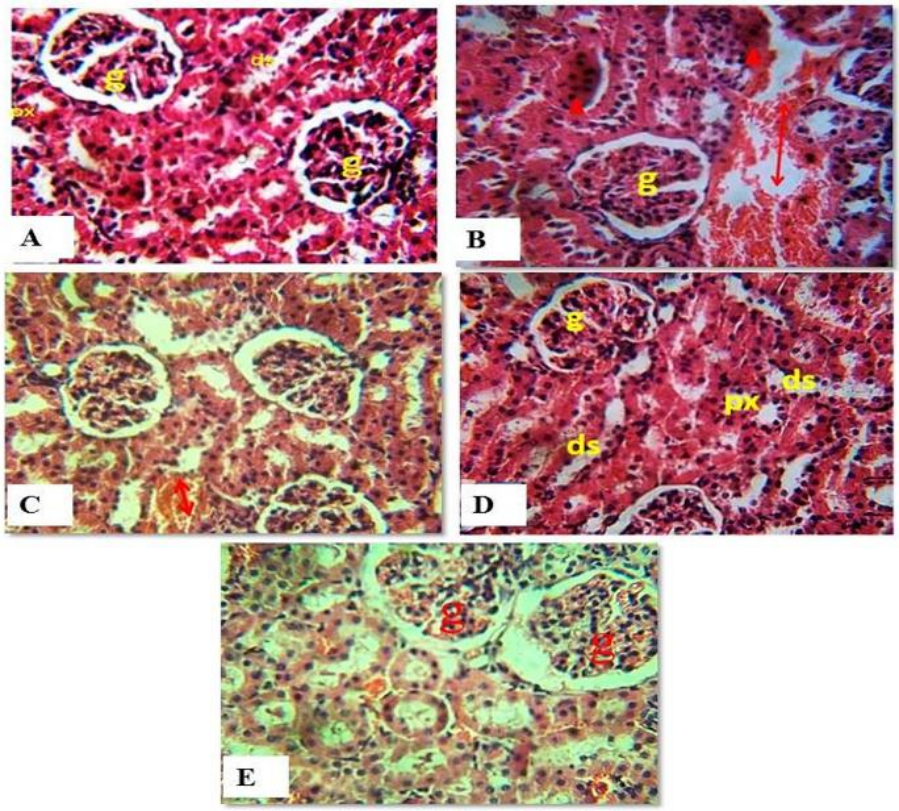


Fig. 5(A-E): photomicrographs from sections of the kidney cortex tissues of different experimental groups of adult male albino rats, stained with hematoxylin and eosin showing **A**: the control group with normal architecture of the kidney cortex consisting of **glomeruli (g)**, proximal **(px)** and distal **(ds)** convoluted tubules. **B:** the **PC** group with congested and lobulated glomeruli (**g**). Interstitial hemorrhage (↕) and necrotic (▲) areas contain inflammatory cells are recorded. **C: the** NM treated group with nearly normal appearance of glomeruli, proximal and distal convoluted tubules while the hemorrhage (↕) is still detected. **D:** the IR treated group with well-developed kidney architecture**. E:** the NM+IR treated group with nearly normal appearance of most convoluted tubules, but the glomeruli **(g)** are still congested. **(H&E stain, A, B, C and D X 400)**

Collagen Fibers:

Figure 6(A) revealed that the control group's proximal and distal convoluted tubule walls, glomeruli, and Bowman's capsules were supported by thin collagen bundles.

Meanwhile, experimental animals of the PC group demonstrated significantly higher levels of collagen fibers in the kidney cortex, particularly in the Bowman's capsules, the basement membranes of the convoluted tubules, and the brush borders. (Fig.6 B).

Furthermore, section in the renal cortex tissue of the NM treated group showed to some extent normal collagen fibres distribution with moderately staining affinity in Bowman's capsules, glomeruli and brush borders of the proximal convoluted tubules (Fig. 6 C).

On the other hand, section in the renal cortex tissue of the IR treated group showed nearly moderately stained and normal distribution of collagen fibres in the kidney cortex (Fig. 6 D).

At the same time, section in the kidney cortex tissue of the NM+IR treated group showed a collagen fiber distribution that was almost normal (Fig. 6 E).

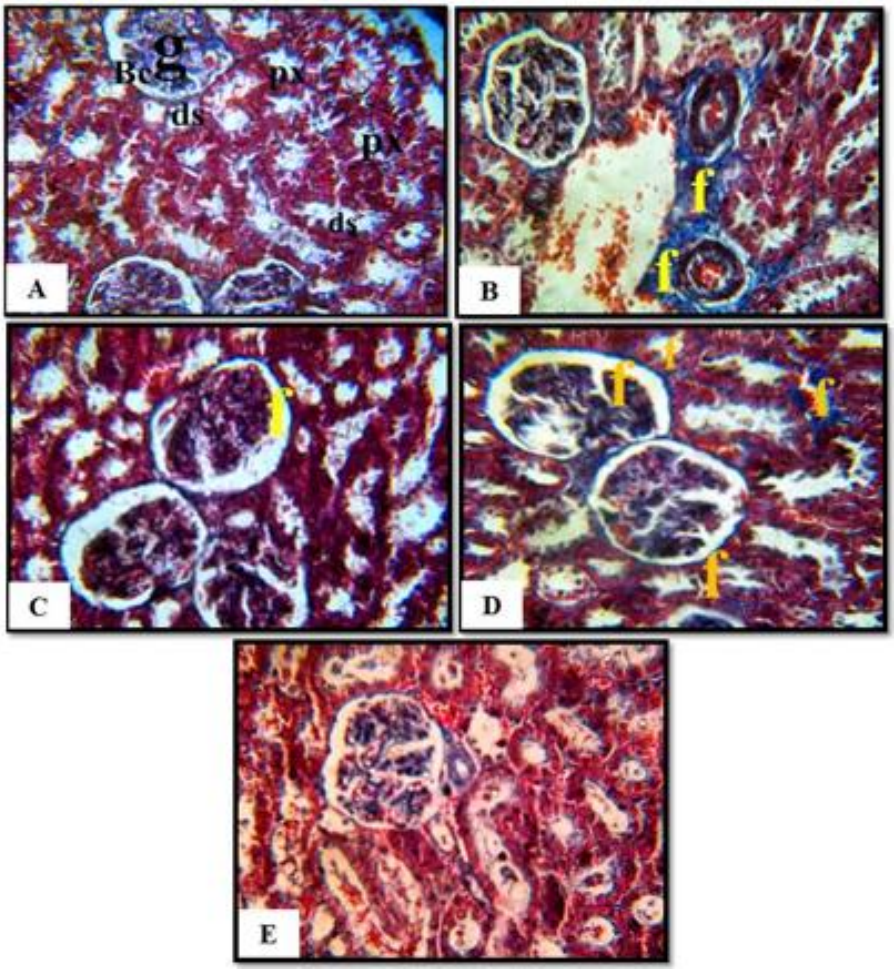


Fig. 6(A-E): photomicrographs from sections of the kidney cortex tissues of different experimental groups of adult male albino rats, stained with masson trichrome showing **A**: the control group with normal distribution of collagen fibers. Notice: thin collagen bundles supporting the Bowman's capsules **(Bc)**, glomeruli **(g)** and walls of the proximal **(px)** and distal convoluted tubules**(ds)**. **B:** the PC group with highly increased collagen fibers **(f)** deposition in the kidney cortex**. C:** the NM treated group with some extent normal collagen fibres (**f**) distribution. **D:** the IR treated group with nearly moderately stained and normal distribution of collagen fibers **(f)** in the kidney cortex. **E:** the NM+IR treated group with thin scattered collagen fibres which support the glomeruli and convoluted tubules.

(Masson trichrome (MT)stain, A, B, C and D X 400)

Histochemical Results of The Kidney Tissue:

Amyloid β – Protein:

Figure 7 (A) represents faintly stained deposition of β– amyloid in the kidney cortex tissue of albino rats of the control group.

Meanwhile, section in the kidney cortex tissue of the PC group showed densely stained β- amyloid (Aβ) proteins in most convoluted tubules (Fig. 7B).

Furthermore, section in the renal cortex tissue of the NM treated group showed comparatively to some extent faintly stained β- amyloid (Aβ) deposition in convoluted tubules and glomeruli (Fig. 7 C).

While sections in the kidney cortex tissue of the IR treated group showed mild to moderate deposition of β- amyloid (Aβ) protein in convoluted tubules and glomeruli (Fig. 7 D)

At the same time, section in the kidney tissue of the NM+IR treated group showed faintly stained β – amyloid deposition in the convoluted tubules and glomeruli (Fig. 7 E).

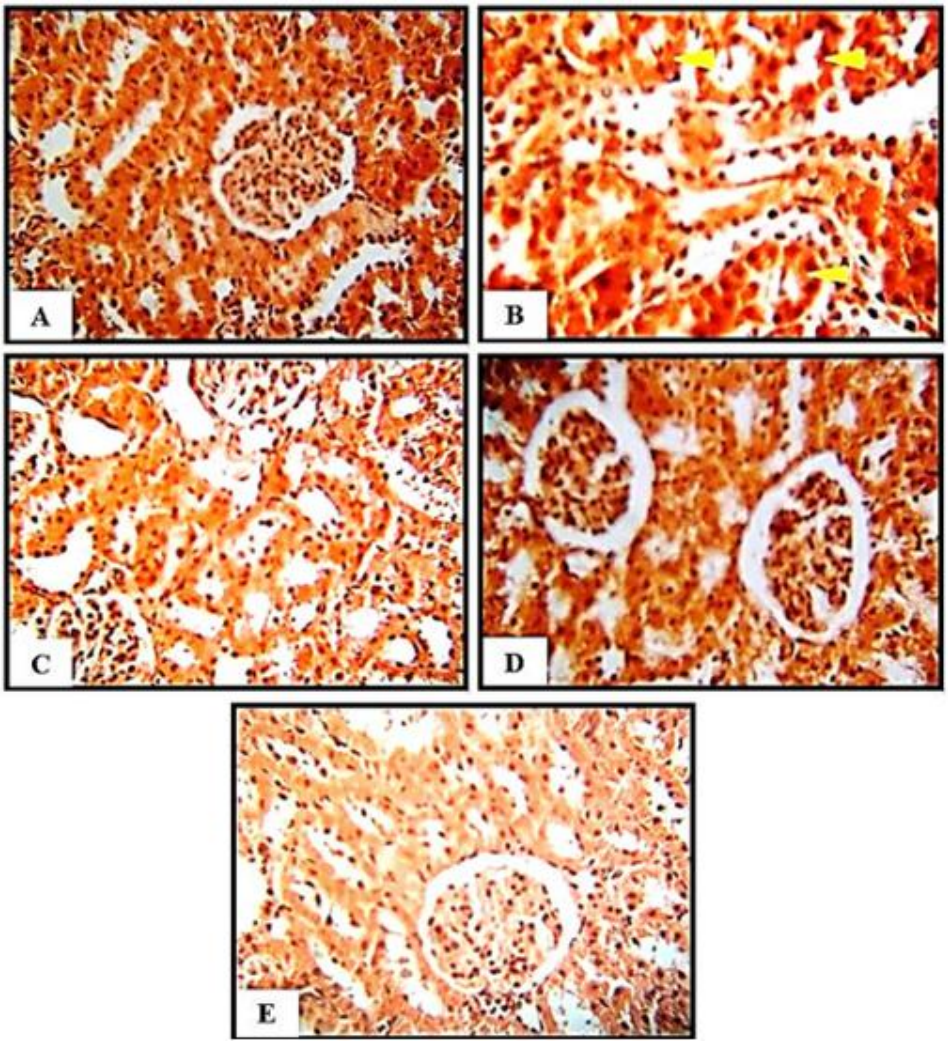


Fig. 7(A-E): photomicrographs from sections of the kidney cortex tissues of different experimental groups of adult male albino rats, stained with congo red n **showing A**: the control group with faintly stained β- amyloid protein in the convoluted tubules and glomeruli. **B**: the PC group with densely stained β- amyloid (Aβ) proteins (▲) in most convoluted tubules. **C**: the NM treated group with comparatively to some extent faintly stained β- amyloid (Aβ) plaque and its deposition in convoluted tubules and glomeruli. **D**: the IR treated group with mild to moderate staining of β- amyloid (Aβ) plaque deposition in convoluted tubules and glomeruli. **E**: the NM+ IR treated group with faintly stained β–amyloid deposition in the convoluted tubules and glomeruli. **(Congo red stain, A, B, C and D X 400)**

Apoptosis:

Section in the kidney cortex tissue of albino rat of the control group showed green viable cells in glomeruli and convoluted tubules (Fig. 8 A). While section in the kidney tissue of the BC group showed increased apoptotic cells in glomeruli and convoluted tubules (Fig. 8 B).

Moreover, section in the kidney tissue of the NM treated group showed aggregation of apoptotic cells especially in convoluted tubules (Fig. 8 C).

Furthermore, section in the kidney tissue of the IR treated group showed somewhat apoptotic cells were observed either in glomeruli or in convoluted tubules (Fig. 8 D).

Meanwhile, section in the kidney tissue of the NM+IR treated group showed few apoptotic cells in glomeruli and convoluted tubules (Fig. 8 E).

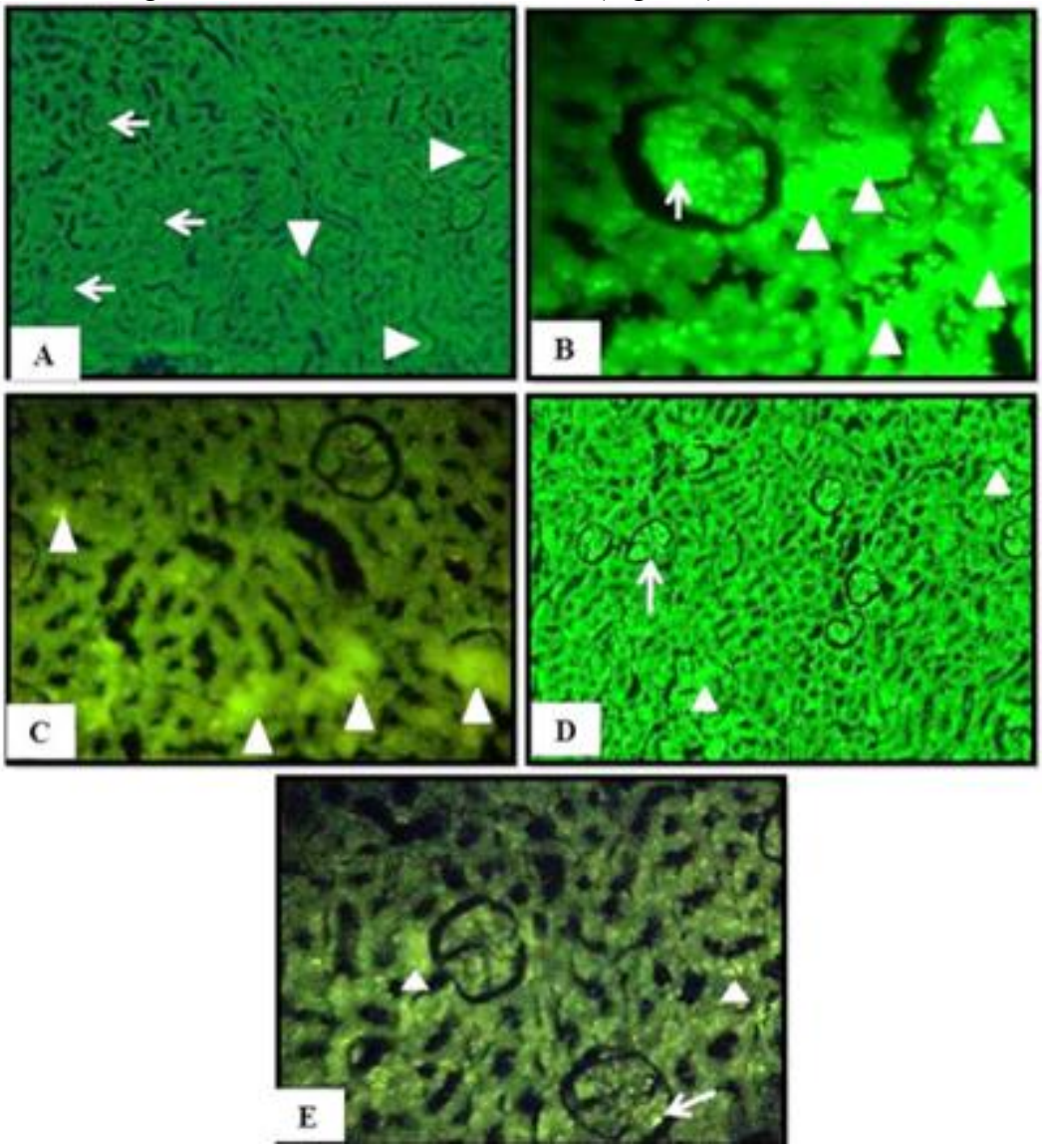


Fig. 8(A-E): photomicrographs from sections of the kidney cortex tissues of different experimental groups of adult male albino rats stained with Propidium iodide and acridine orange showing **A**: the control group with green viable cells in glomeruli **(g)** and convoluted tubules **(↓)**.**B:** the PC group with increased apoptotic cells in glomeruli (↑) and in convoluted tubules (▲). **C:** the NM treated group with aggregation of apoptotic cells, especially in convoluted tubules. **D:** the IR treated group with apparently somewhat apoptotic cells are observed either in glomeruli (↑) or in convoluted tubules (▲). **E:** the NM+ IR treated group with few apoptotic cells in glomeruli (↑) and convoluted tubules (▲).

(Propidium iodide and acridine orange stain A, D X 100- B, C& E X 250).

DISCUSSION

Acute pancreatitis can result in a systemic illness that can cause death or malfunction of several organs (Rehman *et al.*, 2021). Acute kidney damage is a systemic consequence of acute pancreatitis (AP) (AKI). In patients with AP, the development of acute renal injury raises treatment costs, morbidity, and mortality (Uğurlu and Tercan, 2023).

Sahoo *et al*. (2007) stated that tools and materials with a high level of specificity for interactions with the body that are subcellular (i.e., molecular) are used in medicine and physiology when using nanotechnology. Nanotechnology in healthcare and medicine has enormous potential to transform how we identify, treat, and prevent illnesses. Future medical and healthcare applications of nanotechnology have enormous promise to transform how we identify, treat, and prevent illnesses. (Malik *et al.,* 2023).

Extracts from *Moringa oleifera* effectively lower the synthesis of inflammatory mediators (Fard *et al.*,2015; Arulselvan *et al.*, 2016).

According to Lau *et al.* (2021), A small amount of infrared radiation is required for life, acknowledging that the natural production of reactive oxygen species (ROS) is adequate to power defense mechanisms and produce radiation hormesis, a beneficial effect on health.

This study used biochemical parameters, histopathological, and histochemical studies to demonstrate the potential therapeutic role of nano-*Moringa oleifera* leaf extract and/or low dose gamma irradiation against kidney injury caused by acute pancreatitis induced by L-arginine.

The Biochemical Measurements:

The kidney Functions:

In the current investigation, a group of rats with pancreatitis showed significantly higher levels of urea and creatinine after just one day of treatment compared to the control group. The current results are consistent with those of Disoukey *et al.* (2023), who found that acute pancreatitis caused by L-arginine significantly increased creatinine and urea levels when compared to the control group. Hypoxemia, the release of pancreatic amylase from the injured pancreas, and disruption of renal microcirculation may all be contributing factors to acute kidney injury linked to AP. These results agree with the results of Mayumi *et al*. (2002) and Amy *et al*. (2014). According to Pando *et al.* (2021), variations in blood urea have been suggested as a risk factor for AP problems.

In this investigation, as compared to the PC group, rats with pancreatitis treated with nano-*Moringa* and γ-radiation, either separately or in combination, showed a significant decrease in creatinine and urea levels after one day of treatment. According to Onah *et al.* (2016), *M. oleifera* was shown to significantly prevent lead-induced kidney damage, as evidenced by a decrease in kidney lipid peroxidation, an increase in kidney antioxidant enzymes (CAT, SOD, and GST), and a decrease in kidney damage markers (creatinine, urea, and uric acid). The stabilizing function of the cell membrane, which stops enzyme leakage and restores the integrity of the cells, may be the reason for MO's decrease in the indicators of kidney injury (Pari and Karthikesan, 2007). Quercetin and kaempferol may be the cause of MO's protective effects (Selvakumar and Natarajan, 2008), vitamin A, and ascorbic acid (Toppo *et al*., 2015).

By lowering inflammation and oxidative stress, low doses of gamma radiation (e.g., ≤ 0.5 Gy) may trigger protective kidney mechanisms that subsequently normalize creatinine and urea levels**(** Khbouz *et al*., 2023).

IGF1and CRP:

In this study a group of rats suffering from PC revealed a significant decrease in IGF1 level while a significant increase in CRP level in comparison with the control group.

The protein known as insulin-like growth factor 1 (IGF-1) is a member of the IGF axis. Insulin secretion and sensitivity are regulated by IGF-1, which also affects β-cell mass.

Numerous studies demonstrate the intimate connections between glucose metabolism, including pancreatic disorders, and the IGF axis. IL-6 and TNF-α are two examples of pro-inflammatory cytokines that hinder the IGF-1 axis's function (Osman *et al.*, 2025).

Abdelzaher *et al.* (2021) revealed that rats given L-arginine injections had lower insulin levels, a sign of Langerhans islet degeneration. Additionally, AP puts islets at risk for an excessive release of cytokines, which contribute to the development of hyperglycemia and may worsen the inflammatory response. Insulin resistance and increased hepatic gluconeogenesis are caused by the intricate interactions between hormones and cytokines under stress (Dungan *et al.*, 2009). Acute glucotoxicity and intracellular glucose overload can be caused by stress hyperglycemia, according to experimental and clinical data (Yang *et al.*, 2022a). In chronic pancreatitis, elevated oxidative stress may be the cause of the concurrent rise in insulin and blood glucose levels. This supported the findings of Rains and Jain (2011)*;* Zardooz *et al.* (2012)*;* Ayuob and ElBeshbeishy (2016) and Zheng *et al.* (2018) who reported that Insulin resistance resulted from oxidative stress raising serum glucose and insulin levels.

It is commonly recognized that C-reactive protein (CRP) levels react to inflammation, infection, and damage in any part of the body. C-reactive protein, or CRP, is primarily categorized as an acute phase reactant, or marker of inflammation. However, studies are beginning to show that CRP plays a significant role in inflammation. CRP is mostly produced by IL-6-dependent hepatic biosynthesis and is the main downstream mediator of the acute-phase response (APR) after an inflammatory event (Pradhan *et al.,* 2001).

Zhao *et al.* (2020) reported that acute pancreatitis (AP) frequently results in an increase in the level of blood C-reactive protein. Al-Hashem (2021) found that toxic dosages of L-arginine promoted pancreatic tissue damage and raised pro-inflammatory mediators like TNF- while decreasing the anti-inflammatory cytokine IL-10.

Treatment of experimental animals, suffered from pancreatitis with NM and γ-irradiation either alone or combined, a remarkable increase in IGF1 levels was observed while a remarkable decrease in CRP level were revealed when compared to the PC group.

The ability of *Moringa oleifera* to reduce inflammation has been proven. The anti-inflammatory qualities of several bioactive components found in *M. oleifera* extrac (Kooltheat *et al.,* 2014; Arulselvan *et al.,* 2016). Experiments have demonstrated that *Moringa oleifera* extracts decrease the generation of proinflammatory mediators and NO in LPS-stimulated macrophages (Kou *et al.,* 2018).

Osman *et al.* (2025) discovered that LDR was associated with reduced levels of various circulating markers of inflammation, including CRP concentrations, and increased levels of the anti-inflammatory cytokine IL-10. Intriguingly, LDR (0.5–1.5 Gy) exhibits anti-inflammatory properties and promotes the production of cytokines (IL-10) by endothelial cells, polymorphonuclear leukocytes, and macrophages all of which are involved in the inflammatory response. LDR administered to both lungs is thought to be helpful at this phase because it functions as a potent anti-inflammatory drug that inhibits the production of proinflammatory cytokines (Conti *et al.*, 2020).

Plasma Pancreatic Enzymes (lipase and amylase) Activities:

In the present study, a group of rats suffered from pancreatitis revealed a significant increase in lipase and amylase activity after one day of treatment in comparison with the control group. These results are consistent with those of Disoukey *et al*. (2023) who demonstrated how serum biochemical markers were impacted 24 hours and 7 days following an injection of L-arginine-induced pancreatitis. When compared to the control group, they discovered that serum lipase and amylase levels had dramatically increased. The imbalance between the oxidant and antioxidant systems with damage in the experimental model of acute pancreatitis (AP) may be the cause of the increase in lipase and amylase levels. Oxygen free radicals (OFR) damage proteins and lipids in biofilms and induce lipid oxidation in cell membranes, protein cell solutes, DNA, and macromolecules in the nucleus when activated

leucocytes increase the production of ROS in AP. Additionally, the inherent defense system causes cell membrane damage when the production of ROS increases in acute pancreatitis (Ozgul *et al*., 2019; Disoukey *et al*., 2023). Yang *et al.* (2022 b) showed that adipose lipolysis and elevated levels of unsaturated fatty acids were caused by pancreatic lipase interstitial leakage. These harmful fatty acids can accelerate the development of the disease and ultimately lead to multi-organ failure by inducing an inflammatory storm and the excessive release of inflammatory markers. Acute pancreatitis is a pancreatic inflammatory disease that affects both nearby tissues and distant organs (Mallick *et al.*, 2019).

In this study NM+IR treated group showed a significant decrease in lipase, amylase activity after one day of treatment when compared to the PC group.

Devy *et al.* (2024) revealed that administering *Moringa oleifera* flower extract to obese Wistar white rats lowers their serum lipase and amylase levels, improving pancreatic function. It was shown unequivocally that *Moringa oleifera* leaves had strong antioxidant properties and that they significantly inhibit pancreatic lipase and α-amylase. They also reported that, out of all the solvent extracts, the *M. oleifera* leaf hydroalcoholic extract had a high concentration of flavonoids and polyphenols (Swamy and Meriga, 2020).

Kilicheva (2023) verified that gamma radiation decreases the production of the pancreatic enzymes lipases and amylases as well as their release into the blood, depending on the dosage.

Histopathological Changes in the Kidney Tissue:

In the current study sections of the PC group's kidney tissue examined under a microscope revealed lobulated and congested glomeruli. While the other proximal convoluted tubules reflected necrotic cells, some of the distal convoluted tubules represented apoptotic nuclei. Necrotic regions with inflammatory cells and interstitial hemorrhage were seen. Elevated creatinine and urea are indicators of these alterations. The damage seen in the renal tissue was indicated by these biochemical markers.

Stojanovi´c *et al*. (2024) discovered that the kidneys of rats fed L-arginine had tubular deposits, inflammatory infiltration, vascular congestion, tubular degeneration, and sporadic cell necrosis. Following L-arginine-induced AP, the peritoneal cavity undergoes a multitude of processes, such as fluid and cell extravasation, enzyme leakage, and inflammatory activation. The observed acute kidney injury was most likely caused by this type of fluid extravasation to the peritoneal cavity (also known as third spacing), which decreased the glomerular filtration rate. Kudari *et al*. (2007) stated that histopathological analysis of the kidneys in the AP group revealed patchy areas of interstitial hemorrhage and vacuolization of the tubular lining epithelium, primarily in the subcapsular region. A few tubules pointing toward the medullary area displayed tubular lining epithelial necrosis, which is indicative of early acute tubular necrosis.

Sections of the kidney tissue of albino rats with pancreatitis treated with nano-*Moringa* after a day of treatment in the current study revealed proximal and distal convoluted tubules and glomeruli that appeared almost normal, although the hemorrhage was still visible. In this investigation, reduced levels of urea and creatinine in the group supplemented with nano-*Moringa* after pancreatitis induction demonstrated the anti-inflammatory and antioxidant properties of nano-*Moringa*.

Wijayanti *et al*. (2023) showed that MO leaf extract can lessen gentamicin-induced nephrotoxicity. The low levels of necrosis and degeneration in the renal tubular cells suggest that co-administration with MO leaf extract and gentamicin has a nephroprotective effect. It has been demonstrated that the antioxidant chemicals lower the risk of kidney damage brought on by gentamicin use (Mahmood *et al.,* 2014; Tavafi, 2013). The anti-inflammatory and anti-oxidative qualities of *M. oleifera* help to explain this observation. High concentrations of carotene, ascorbic acid, iron, methionine, and cysteine are seen in *M. oleifera* (Jiwuba *et al*., 2016). *M. oleifera* contains terpenoids, glycosides, flavonoids, tannins, and saponins, all of

which have antibacterial, anti-carcinogenic, and antioxidant qualities. Additionally, these components enhance the immunological response (Davinelli *et al*., 2015).

In this study, sections in the kidney tissue of the IR group showed well developed kidney architecture but some tubules were dilated and some of the glomeruli were still lobulated.

Moreover, section in the kidney tissue of albino rat suffering from pancreatitis treated with nano-*Moringa* and irradiation after one day of treatment showed nearly normal appearance of most convoluted tubules but the glomeruli were still congested.

Abbas *et al*. (2022), revealed that, in addition to its hypolipidemic effect and enhancement of oxidant-antioxidant status, the combination of *Moringa leaf* extract and γ-radiation exposure produced super-additive cytotoxic effects on cancer cells and super-relieving effects on hematological and renal testing parameters. Soliman *et al*. (2020), revealed that mice fed methotrexate and protected by *Moringa* had kidneys with tubules and glomeruli that were essentially normal.

In the current study, experimental animals of positive control rats suffering from pancreatitis after one day of treatment revealed highly increased collagen fibers in the kidney cortex, particularly in the Bowman's capsules, the basement membranes of the convoluted tubules, and the brush borders.Michałek *et al.* (2023) found that increased collagen accumulation following cerulein injection in pig kidneys stained with Masson's trichrome indicated interstitial fibrosis. In response to an increase in reactive oxygen species, collagen fibers can be seen or absent using Masson's trichrome staining. This is significant because it has the potential to boost extracellular matrix synthesis (Mondal, 2017).

In the current study, sections in the kidney tissue of rats treated with nano- *Moringa* showed to some extent normal collagen fibres distribution with moderately staining affinity in Bowman's capsules, glomeruli and brush borders of the proximal convoluted tubules after one day of treatment.

These results are in accordance with those of Kamel *et al.* (2023) who discovered that the fibrotic region in the Masson trichrome-stained section was used to measure the tubulointerstitial fibrosis score in renal tissues. The decrease in the fibrotic score demonstrated that there was no sign of fibrosis in the renal tissues of the MOE-treated group.

In this study, sections in the kidney tissue of IR group showed nearly normal distribution of collagen fibres in the kidney cortex after one day of treatment. These results are in accordance with those of Nakatsukasa *et al*. (2008) who discovered that oxidative stress and pro-inflammatory cytokines, two major causes of fibrosis in AP-associated kidney injury, are suppressed by low dose gamma irradiation.

Exposure to LDR for four weeks considerably improved renal dysfunction and decreased pathological alterations, including fibrosis, in a study involving type 2 diabetic mice. The antioxidant transcription factor Nrf2, which lowers oxidative stress and inhibits collagen formation, was upregulated in the protective effects (Shao *et al*., 2014).

Because low doses of radiation suppress inflammation and oxidative stress, they can lessen glomerular and tubulointerstitial fibrosis (Klaus *et al*., 2021).

In this study, sections of rats suffering from pancreatitis and treated with nano- *Moringa* and irradiation showed nearly normal distribution of collagen fibers after one day of treatment.

Furthermore, Abd-Elhakim *et al*. (2021) found that MOE's antioxidant and anti-inflammatory qualities are thought to be the source of the anti-fibrosis mechanism. The ethanol extract of MO leaves inhibited fibrogenesis by decreasing the expression of a tissue inhibitor of metalloproteinases called "TIMP1." Flavonoids and phenolic acids, two kind of polyphenols, are abundant in the dried leaves of Mo.

Gamma irradiation at low levels can reduce lipid peroxidation and improve antioxidant defences, thereby mitigating radiation-induced oxidative stress in the kidneys and pancreas (Nakatsukasa *et al*., 2008).

The Histochemical Changes in the Kidney Tissue:

In the present study, experimental animals treated with L- arginine and suffering from pancreatitis, the kidney tissue sections showed densely stained β-amyloid (Aβ) proteins in most convoluted tubules after one day of treatment.

These results agree with those of Iglesias-Fortes *et al*. (2024), He stated that β-cell damage brought on by acute pancreatitis results in abnormal human amylin (amyloidogenic) production. Amylin aggregates in the pancreatic islets and travels to the kidneys through extracellular vesicles or circulation. According to *in vivo* research, mice that overexpress human amylin form amylin aggregates in their renal tubules and glomeruli, which are linked to characteristics of diabetic nephropathy such as inflammation and glomerulosclerosis.

In the current work, sections in the kidney cortex tissue of NM group showed comparatively to some extent faintly stained β-amyloid plaque and its deposition in convoluted tubules and glomeruli after one day of treatment.

The most polyphenol-rich part of *Moringa oleifera* is its leaves, which are mostly composed of quercetin, kaempferol, and chlorogenic acid (Vergara-Jimenez *et al*., 2017). Polyphenols prevent several amyloidogenic proteins linked to kidney disease from fibrillating (Ruan *et al*., 2022).

In the current study, sections in the kidney tissue of the IR group showed mild to moderate deposition of β-amyloid (Aβ) plaque in convoluted tubules and glomeruli after one day of treatment .One well-known treatment for localized amyloid deposits in organs such as the kidney is radiotherapy. Radiotherapy is already used to stabilize amyloid deposits in systemic amyloidosis. Fractionated low-dose radiation slows the formation of amyloid in organs such as the kidneys and heart (Coelho *et al*., 2022).

In the present study, sections in the kidney tissue of the NM+IR treated group showed nearly normal deposition of β–amyloid in the convoluted tubules and glomeruli after one day of treatment.Whole-body irradiation showed positive effects in rodent models of diabetic kidney disease, including decreased amyloid precursor protein (APP) expression, enhanced glucose metabolism, and decreased renal inflammation (Paithankar *et al*., 2023).

In the present study, sections in the kidney tissue of rats suffered from pancreatitis after one day of treatment showed increased apoptotic cells in glomeruli and convoluted tubules.

These results are aligned with those of Li *et al*. (2023) who showed that systemic inflammatory response syndrome (SIRS), which is brought on by severe acute pancreatitis, releases reactive oxygen species and pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β, which encourage renal tubular cell death. This inflammatory reaction exacerbates endoplasmic reticulum stress and mitochondrial malfunction in kidney cells, which results in programmed cell death (Liu *et al*., 2025).

In the current work, sections in the kidney tissue of the NM treated group showed aggregation of apoptotic cells especially in convoluted tubules after one day of treatments.

These findings were supported by the study which conducted by Akter *et al*. (2021) who stated that *Moringa* leaf methanol extract also demonstrated protective effects against nephrotoxicity caused by nickel and gentamicin, most likely by lowering oxidative stress and apoptosis.

In the present work, sections in the kidney tissue of the IR treated group showed somewhat apoptotic cells were observed either in glomeruli or in convoluted tubules.

These results are supported by the study of Chen *et al*. (2025) They reported that LDR was found to lower oxidative stress markers like MDA and activate antioxidant defenses (e.g., SOD, GSH, and CAT) to lower apoptosis in kidney cells. This protective effect was also noted in doxorubicin-induced nephrotoxicity, where LDR pretreatment markedly reduced the expression of important pro-apoptotic markers, Bax and caspase-9.

In this study, sections in the kidney tissue of the NM+IR showed few apoptotic cells in glomeruli and convoluted tubules after one day of treatment.

These results agree with those of Meles *et al*. (2025) who demonstrated that *Moringa* leaf extract inhibited interstitial inflammation and tubular epithelial cell necrosis, as seen by histological slides that displayed intact renal tubules and fewer apoptotic bodies.

In cisplatin-induced nephrotoxicity, rutin, a flavonoid, and LDR (0.03 Gy) dramatically decreased urea and creatinine levels, suggesting better kidney function and less apoptotic damage (Radwan and Abdel Fattah, 2017).

CONCLUSION

Overall, the current investigation discovered that *nano- Moringa,*low dose γ-irradiation either alone or combined ameliorated physiological, histopathological and histochemicals alterations, improved kidney functions, and decreased creatinine, urea, CRP, lipase and amylase while remarkable increase in IGF1, to counteract the kidney impairment brought on by AP.

Declarations:

Ethical Approval: This study does not contain any studies with human participants or animals performed by any of the authors.

Competing interests: The authors declare that there is no conflict of interest.

Author's Contributions: Safaa M. Abd El-hameed, carried out field execution to all experiment stages, collect blood samples and field data and contributed in wrote this article. Mona M. El-Tonsy & Hemmat M. Abdelhafez helped in wrote this article and contributed in drafting the manuscript and revision and performed the histological and histochemicals parameters. Neamat Hanafi Ahmed wrote this article and performed the biochemical analysis, the statistical analysis of the results, contributed in drafting the manuscript and revision. All authors approved the final manuscript.

Funding: This study didn't receive any funding support.

Availability of Data and Materials: All data sets are available in the manuscript and supplementary file.

Acknowledgments: Not applicable.

REFERENCES

Abbas, M. M., Mahmoud, A. H., & Alhadary, A. A. (2022). Evaluation of antioxidant & antitumor activities of *Moringa* extract in mice. *Egyptian Journal of Radiation Sciences and Applications*, 35 (1-2), 29–37. https://doi.org/10.21608/EJRSA.2022. 165298. 1139.

Abd-Elhakim, Y. M., Mohamed, W. A. M. & El Bohi, K. M. (2021). Prevention of melamine-induced hepatorenal impairment by an ethanolic extract of *Moringa oleifera*: Changes in KIM-1, TIMP-1, oxidative stress, apoptosis, and inflammation-related genes. *Gene, 764*, 145083. https://doi.org/10.1016/j.gene.2020.145083.

Abdelzaher, W. Y., Ahmed, S. M., Welson, N. N., Marraiki, N., Batiha, G. E.-S., & Kamel, M. Y. (2021). Vinpocetine ameliorates L-arginine induced acute pancreatitis via Sirt1/Nrf2/TNF pathway and inhibition of oxidative stress, inflammation, and apoptosis. *Biomedicine & Pharmacotherapy, 133*, 110976. https://doi.org/10. 1016/j. biopha.2020.110976

Abd-Rabou1. A., Aboelfetoh, M. Abdalla2, Naglaa, A. Ali1, & Khairy, M.A. Zoheir3. (2017). *Moringa oleifera* root induces cancer apoptosis more effectively than leave nanocomposites and its free counterpart. *Asian Pacific Journal of Cancer Prevention*, 18 (8), 2141-2149. DOI: 10.22034/APJCP.2017.18.8.2141

Abdulkadir, A. R., Jahan, M. S., & Zawawi, D. D. (2015). Effect of chlorophyll content and maturity on total phenolic, total flavonoid contents and antioxidant activity of *Moringa oleifera* leaf (Miracle tree). *Journal of Chemical and Pharmaceutical Research,* 7 (5),

1147–1152.

Agarwal, S., George, J., Padhan, R. K., Vadiraja, P. K., Behera, S.,Hasan, A., & Garg, P. K. (2016). Reduction in mortality in severe acute pancreatitis: A time trend analysis over 16 years. *Pancreatology, 16*(2), 194–199.

Akter, T., Rahman, M. A., Moni, A., Apu, M. A. I., Fariha, A., Hannan, M. A., & Uddin, M. J. (2021). Prospects for protective potential of *Moringa oleifera* against kidney diseases. *Plants, 10*(12), 2818. https://doi.org/10.3390/plants10122818.

Al-Hashem, F. (2021): Suppression of L-arginine-induced acute necrotizing pancreatitis in rats by metformin associated with the inhibition of myeloperoxidase and activation of interleukin-10. *International Journal of Morphology,* 39 (1): 102-108.

Amy, S. S., Paul, R. T., & Joseph, L. W. (2014). Acute kidney injury in acute pancreatitis: Incidence and outcome. Pancreatology, 14(3), S39-S40. https://doi.org/10.1016/j. pan. 2014.05.292.

Arulselvan, P., Tan W. S., Gothai, S., Muniandy, K., Fakurazi, S., Mohd Esa, N., Alarfaj, A. A., & Kumar, S. S. (2016.(Anti-Inflammatory potential of ethyl acetate fraction of *Moringa oleifera* in downregulating the NF-κB signaling pathway in lipopolysaccharide-stimulated macrophages. *Molecules,* 21(11), 1452; https://doi. org/10.3390/molecules21111452.

Ayuob, N., & ElBeshbeishy, R. (2016). Impact of an energy drink on the structure of stomach and pancreas of albino rat: Can omega-3 provide a protection? *PLOS ONE, 11*(2), e0149191. https://doi.org/10.1371/journal.pone.0149191

Bancroft, J. D., & Gamble, M. (2008). *Theory and Practice of Histological Techniques*. 6th Edition, Churchill Livingstone, Elsevier, China.

Bancroft, J., Stevens, A., & Turner, D. (1996). Theory and Practice of Histological Techniques 4th Ed. Churchill Living Stone, New York Edinburgh. *Madrid, Sanfrancisco*,p. *20*.

Bank, H. L. (1988). Rapid assessment of islet viability with acridine orange and propidium iodide. *In Vitro Cellular & Developmental Biology*. 24(4):266-273.

Borai, I. H., Hanafi, N., Elgawish, M. A., Kandili, E., & Arafa, M. I. K. (2017). Role of chitosan nanoparticles in reducing pancreatitis in rats treated with L-arginine. *International Journal of Advanced Scientific and Technical Research*, 7 (3), 44-58.

Charilaou, P., Radadiya, D., Brahmbhatt, B., Young, M., & Reddy, C. (2018). Acute pancreatitis: Trends in outcomes and the role of acute kidney injury in mortality - A propensity-matched analysis. *Pancreatology, 18*(8), 870–877. https://doi.org/10. 1016/ j.pan.2018.09.011.

Chen, M., He, K., Wang, K., Cai, Y., Ying, Z., Li, X., Liu, Y., Xiang, L., Yang, P., Wu, H., & Jiang, J. (2025). Low-dose radiation ameliorates doxorubicin-induced renal injury via reducing oxidative stress and protecting mitochondrial function. *PLOS ONE, 20*(2), e0313649. https://doi.org/10.1371/journal.pone.0313649.

Coelho, C. M., Pereira, L., Teubig, P., Santos, P., Mendes, F., Viñals, S., Galaviz, D., & Herrera, F. (2022). Radiation as a tool against neurodegeneration—a potential treatment for amyloidosis in the central nervous system. *International Journal of Molecular Sciences, 23*(20), 12265. https://doi.org/10.3390/ijms232012265.

Conti, P.; Ronconi, G.; Caraffa, A.; Gallenga, C.; Ross, R.; Frydas, I. & Kritas, S. (2020): Induction of pro-inflammatory cytokines (IL-1 and IL-6) and lung inflammation by Coronavirus-19 (COVI-19 or SARS-CoV-2): anti-inflammatory strategies. *Journal of Biological Regulators and Homeostatic Agents,* 34 (2): 327-331.

Davinelli, S., Bertoglio, J. C., Zarrelli, A., Pina, R., & Scapagnini, G. (2015). A randomized clinical trial evaluating the efficacy of an anthocyanin–maqui berry extract (Delphinol®) on oxidative stress biomarkers. *Journal of the American College of Nutrition, 34*(Suppl. 1), 28–33. https://doi.org/10.1080/07315724.2015.1080108.

de-Madaria, E., & Buxbaum, J. L. (2023). Advances in the management of acute pancreatitis. *Nature Reviews Gastroenterology & Hepatology, 20*, 691–692.

Devani, K., Charilaou, P., Radadiya, D., Brahmbhatt, B., Young, M., & Reddy, C. (2018). Acute pancreatitis: Trends in outcomes and the role of acute kidney injury in mortality - A propensity-matched analysis. *Pancreatology, 18*(8), 870-877. https://doi.org/10.1016/j.pan.2018.09.011.

Devy, Jansen, & Yani,H. ((2024). Obesity Model in white male Wistar rats: the impact of *Moring*a (*Moringa oleifera*) flower extract on pancreatic function as deduced from serum amylase and lipase levels and the histopathological image of the pancreas. *International Journal of Public Health Excellence (IJPHE,)* 3(2),559-569. DOI: 10.55299/ijphe. v3i2.752.

Disoukey, M. A., Fararh, K. M., Farid, A. S., & Gad, F. A. (2023). Biochemical and histopathological changes of L-arginine experimentally induced acute pancreatitis in rats. *Benha Veterinary Medical Journal*, 45 (2), 77-81.

Dungan, K. M., Braithwaite, S. S., & Preiser, J.-C. (2009). Stress hyperglycaemia. *The Lancet, 373*(9677), 1798–1807. https://doi.org/10.1016/S0140-6736(09)60553-5

Fard, M. T., Arulselvan, P., Karthivashan, G., Adam, S. K., & Fakurazi, S. (2015). Bioactive extract from *Moringa oleifera* inhibits the pro-inflammatory mediators in lipopolysaccharide stimulated macrophages. *Pharmacognosy Magazine*, 11(Suppl. 4), S556-S563. https://doi.org/10.4103/0973-1296.172961.

Frey, B., Hehlgans, S., Rödel, F., & Gaipl, U. S. (2015). Modulation of inflammation by low and high doses of ionizing radiation: Implications for benign and malign diseases. *Cancer letters,* 368(2), 230-237.

Hegyi, P., Rakonczay Jr, Z., Sári, R., Góg, C., Lonovics, J., Takács, T., & Czakó, L. (2004). L-arginine-induced experimental pancreatitis. World Journal of Gastroenterology, *10*(14), 2003-2009.

Iglesias-Fortes, S., González-Blanco, C., García-Carrasco, A. (2024). The overexpression of human amylin in pancreatic β cells facilitates the appearance of amylin aggregates in the kidney contributing to diabetic nephropathy. *Scientific Reports, 14*, 24729. https://doi.org/10.1038/s41598-024-77063-9.

Jiwuba, P. C., Ikwunze, K., Ume, S. I., & Nsidinanya, N. O. (2016). Performance, apparent nutrient digestibility and cost benefit of West African Dwarf goats fed dietary levels of *Moringa oleifera* leaf meal. *Journal of Advances in Biology & Biotechnology, 8*(3), 1–9. https://doi.org/10.9734/JABB/2016/27390.

Kamel, A. H., Fouad, M. A., & Mohamed, H. A. (2023). Protective effect of aqueous extract of *Moringa oleifera* leaves against potassium bromate-induced renal toxicity in rats. *Egyptian Journal of Zoology*,79, 29–47. https://doi.org/10. 21608/ejz. 2022. 135884.1081.

Kaplan, A. (1984): Urea. *Clinical Chemistry;The CV Mosby Co. St Louis. Toronto. Princeton*: 1257–1260.

Khbouz, B., Gu, S., Pinto Coelho, T., Lallemand, F., & Jouret, F. (2023). Radiotherapy advances in renal disease focus on renal ischemic preconditioning. *Bioengineering, 10*(1), 68. https://doi.org/10.3390/bioengineering10010068.

Kilicheva, I. B. (2023). Activity of pancreatic tissue's enzymes in different doses of gamma-radiation. *Academicia Globe: Inderscience Research*,4 (3), 197–200.

Klaus, R., Niyazi, M., & Lange-Sperandio, B. (2021). Radiation-induced kidney toxicity: molecular and cellular pathogenesis. *Radiation Oncology*, 16 (1), 43. https://doi.org/10.1186/s13014-021-01764-y.

Kooltheat, N., Sranujit, R.P., Chumark, P., Potup, P., Laytragoon-Lewin, N., & Usuwanthim, K. (2014). An ethyl acetatefraction of *Moringa oleifera Lam*. Inhibits human macrophage cytokine production induced by cigarettesmoke. Nutrients, 6, 697–710.

Kou, X., Li, B., Olayanju, J. B., Drake, J. M., &Chen, N. (2018). Nutraceutical or pharmacological potential of *Moringa oleifera* Lam. Nutrients. 10(3) (2018) 343. https://doi.org/10.3390/nu10030343.

Kudari1, A., Wig, J. D., Vaiphei, K., Kochhar, R., Majumdar, S., Gupta, R. Yadav, T. D.,& Doley, R. P.(2007). Histopathological sequential changes in sodium taurocholate-induced acute pancreatitis. *Journal of the Pancreas*, 8(5) , 564-572.

Kui, B., Balla, Z., Vasas, B., Végh, E. T Pallagi, P. Kormányos, E. S. Venglovecz, V. Iványi, B. Takács, T. Hegyi, P., & Rakonczay, Jr. Z. (2015). New insights into the methodology of L-arginine-induced acute pancreatitis. *Plos One.* 10(2), e0117588. https://doi.org/10.1371/journal.pone.0117588.

Lau, Y. S., Chew, M. T., Alqahtani, A., Jones, B., Hill, M. A., & Nisbet, A. (2021). Low dose ionising radiation-induced hormesis: Therapeutic implications to human health. *Applied Sciences*, 11 (19), 8909.

Li, H., Qian, Z., Liu, Z., Liu, X., Han, X., & Kang, H. (2010). Risk factors and outcome of acute renal failure in patients with severe acute pancreatitis. *Journal of Critical Care, 25*(2), 225–229. https://doi.org/10.1016/j.jcrc.2009.10.010.

Li, H., Wu, D., Zhang, H., & Li, P. (2023). New insights into regulatory cell death and acute pancreatitis. *Heliyon, 9*, e18036. https://doi.org/10.1016/j.heliyon.2023.e18036.

Lin, H. Y., Lai, J. I., Lai, Y. C., Lin, P. C., Chang, S. C., & Tang, G. J. (2011). Acute renal failure in severe pancreatitis: A population-based study. *Upsala Journal of Medical Sciences, 116*(2), 155–159. https://doi.org/10.3109/03009734.2010.544397

Liu, X., Dou, B., Zhu, Q., & Liu, C. (2025). Targeting the programmed cell death signaling mechanism with natural products for the treatment of acute pancreatitis: A review. *Frontiers in Pharmacology, 16*, 1567552. https://doi.org/10. 3389/fphar. 2025. 1567552.

Mahmood, N., Haleh, M., & Mohammad, P. (2014). Pathological changes of gentamicin in liver tissue and antioxidant property of cinnamon extract on Wistar rats. *Biomedical Pharmacology Journal, 7*(1), 341–347. https://doi.org/10.13005/bpj/496.

Malik, S., Muhammad, K., & Waheed, Y. (2023). Nanotechnology: A revolution in modern industry. *Molecules*, 28, 661. https://doi.org/10.3390/molecules28020661.

Mallick, B.; Tomer, S.; Arora, S.K.; Lal, A.; Dhaka, N.; Samanta, J.; Sinha, S.K.; Gupta, V.; Yadav, T.D. & Kochhar, R. (2019): Change in serum levels of inflammatory markers reflects response of percutaneous catheter drainage in symptomatic fluid collections in patients with acute pancreatitis. *Gastroenterology & Hepatology Journal Open,* 3 (4): 295-301.

Mao, H., Su, P., Qiu, W., Huang, L., Yu, H., & Wang, Y. (2016). The use of Masson's trichrome staining, second harmonic imaging and two-photon excited fluorescence of collagen in distinguishing intestinal tuberculosis from Crohn's disease. *Colorectal Disease*, *18*(12), 1172-1178.

Mayumi, T., Ura, H., Arata, S., Kitamura, N., Kiriyama, I., Shibuya, K., Sekimoto, M., & Takada, T. (2002). Evidence-based clinical practice guidelines for acute pancreatitis: Proposals. *Journal of Hepato-Biliary-Pancreatic Surge*ry, 9 (3), 413-422. https://doi.org/10.1007/s005340200051.

Meles, D. K., Mustofa, I., Wurlina, W., Rosyada, Z. N. A., Khairullah, A. R., Rachmawati, K., Hidayah, A. N., Suwasanti, N., Mustofa, R. I., Akintunde, A. O., Ahmad, R. Z., Ekawasti, F., Riwu, K. H. P., & Riwu, A. G. (2025). Impact of *Moringa oleifera* leaf extract on renal histopathology, malondialdehyde, superoxide dismutase, and calcium oxalate crystals in rats (*Rattus norvegicus*) exposed to ethylene glycol. *Open Veterinary Journal, 15*(4), 1734–1746. https://doi.org/10.5455/OVJ.2025.v15.i4.25

Michalek, K., Oberska, P., Murawski, M., Schwarz, T., Tomaszewska, E., Muszynski, S., Świątkiewicz, M., Korytkowski, Ł., Bonior, J., Zelent, M., Ayomide, D. S.-A., &

Grabowska, M. (2023). Kidney morphology and renal expression of aquaporins 2, 3 and 4 during cerulein-induced chronic pancreatitis in pigs. *Advances in Medical Sciences, 68*, 306–313. https://doi.org/10.1016/j.advms.2023.09.002

Mondal, S. (2017). The role of reactive oxygen species in extracellular matrix synthesis and collagen fiber formation: Implications for tissue regeneration. Journal of Cellular Biochemistry, 118(6), 1234-1245.

Morris, V. J. (2014). Foods, materials, technologies and risks. In : *Encyclopedia of food safety* (). Academic Press,Vol. 1, pp. 1-10. https://doi.org/10.1016/B978-0-12-378612-8.00001-2

Moss, D. W. &Henderson, A. R. (1999). Digestive enzymes of pancreatic origin.In: Tietz Textbook of Clinical Chemistery.3rd ed. Burtis, C. A., Ashwood, E. R., editors.Philadelphia: W. B Saunders Company; 1999. p: 689-708.

Murray, R. (1984): Creatinine *Clinical Chemistry; Theory, Analysis and Correlation. Kaplan, LA and Pesce, A.J. (Eds.), C.V. Mosby Company, St Louis*.

Nakatsukasa, H., Tsukimoto, M., Ohshima, Y., Tago, F., Masada, A., & Kojima, S. (2008). Suppressing effect of low-dose gamma-ray irradiation on collagen-induced arthritis. *Journal of Radiation Research*, 49 (4), 381-389. https://doi. org/10. 1269/ jrr.08002.

Omietimi, H. B., Afolalu, S. A., Kayode, J. F., Monye, S. I., Lawal, S. L., & Emetere, M. E. (2023). An overview of nanotechnology and its application. *E3S Web of Conferences, 391*, 01079. https://doi.org/10.1051/e3sconf/202339101079

Omotoso, G. O., Gbadamosi, I. T., Olajide, O. J., Dada-Habeeb, S. O., Arogundade, T. T., & Yawson, E. O. (2018). *Moringa oleifera* phytochemicals protect the brain against experimental nicotine-induced neurobehavioural disturbances and cerebellar degeneration. *Pathophysiology*, 25, 57-62.

Onah, C. E., Meludu, S. C., Dioka, C. E., Onuegbu, A. J., Onah, C. F., Ajaghaku, D. L., Nnodim, J. K., & Ejeatuluchukwu, O. (2016). Amelioratory effect of methanolic leaf extract of *Moringa oleifera* on some liver and kidney function and oxidative stress markers in lead-intoxicated rats. *European Journal of Medicinal Plants*, 12 (4), 1–12. https://doi.org/10.9734/EJMP/2016/23763.

Osman, N. A., Mosleh, M., & Zahran, F. (2025). Anti-inflammatory response of Metformin nanoparticles and/or low doses γ-irradiation on acute pancreatitis in rats via regulation of inflammatory cytokine. *Research Square*. https://doi.org/10.21203/rs.3.rs-5805377/v1

Özgül, H., Tatar, C., Özer, B., Aydın, H., Sarı, S., & Peltek Özer, S. (2019). Effects of alpha-tocopherol on acute pancreatitis in rats. *Ulusal Travma ve Acil Cerrahi Dergisi (Turkish Journal of Trauma & Emergency Surgery), 25*(1), 1-6. https://doi. org/10.5505/ijtes.2018.30413

Paithankar, J. G., Gupta, S. C., & Sharma, A. (2023). Therapeutic potential of low dose ionizing radiation against cancer, dementia, and diabetes: Evidences from epidemiological, clinical, and preclinical studies. *Molecular Biology Reports, 50*, 2823–2834. https://doi.org/10.1007/s11033-022-08211-5.

Pando, E., Alberti, P., Mata, R., Gomez, M. J., Vidal, L., Cirera, A., Dopazo, C., Blanco, L., Gomez, C., Caralt, M., Balsells, J., & Charco, R. (2021). Early changes in blood urea nitrogen (BUN) can predict mortality in acute pancreatitis: Comparative study between BISAP score, APACHE-II, and other laboratory markers A prospective observational study. *Canadian Journal of Gastroenterology and Hepatology*, 2021, Article ID 6643595. https://doi.org/10.1155/2021/6643595

Pandol, S. J., Saluja, A. K., Imrie, C. W., & Banks, P. A. (2007). Acute pancreatitis: Bench to the bedside. *Gastroenterology, 132*(3), 1127–1151. https://doi.org/10. 1053/j. gastro. 2007.01.055

Pareek, M., Pant, M. M., & Gupta, M. (2023). *Moringa oleifera*: An updated comprehensive review of its pharmacological activities, ethnomedicinal, phytopharmaceutical formulation, clinical, phytochemical, and toxicological aspects. *International Journal of Molecular Sciences, 24*(3), 2098.

Pari, L.,& Karthikesan, K. (2007). Protective role of caffeic acid against alcohol – induced biochemical changes in rats. *Fundamental & Clinical Pharmacology journal*, 21(4):355-361.

Patel, S., Thakur, A. S., Chandy, A., & Manigauha, A. (2010). *Moringa oleifera:* A review of the medicinal and economic importance to the health and nation. Drug Invention Today, 2, 339–342.

Pradhan, A. D., Manson, J. E., Rifai, N., Buring, J. E., & Ridker, P. M. (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *Journal of the American Medical Association*, 286 (3), 327-334.

Radwan, R. R., & Abdel Fattah, S. M. (2017). Mechanisms involved in the possible nephroprotective effect of rutin and low-dose γ irradiation against cisplatin-induced nephropathy in rats. *Journal of Photochemistry and Photobiology B: Biology, 169*, 56–62. https://doi.org/10.1016/j.jphotobiol.2017.02.022

Rains, J. L., & Jain, S. K. (2011). Oxidative stress, insulin signaling, and diabetes. *Free Radical Biology and Medicine,* 50(5), 567-575. https://doi.org/10.1016/j. freeradbiomed. 2010.12.006

Rao, A. V., Devi, P. U., & Kamath, R. (2001). *In vivo* radioprotective effect of *Moringa oleifera* leaves. *Indian Journal of Experimental Biology*, 39, 858-863.

Rehman, K.; Rashid, U.; Jabeen, K. & Akash, M.S.H. (2021): Morin attenuates L-arginine induced acute pancreatitis in rats by downregulating myeloperoxidase and lipid peroxidation. *Asian Pacific Journal of Tropical Biomedicine,* 11 (4): 148.

Ruan, C., Kong, J., He, X., Hu, B., & Zeng, X. (2022). Interaction between polyphenols and amyloids: From the view of prevention of protein misfolding disorders related diseases. *Food Materials Research, 2*(2), 1–15. https://doi.org/10.48130/FMR-2022-0002.

Sahoo, S. K., Parveen, S., & Panda, J. J. (2007). The present and future of nanotechnology in human health care. *Nanomedicine: Nanotechnology, Biology, and Medicine*, 3 (1), 20–31.

Sandhiya, V., & Ubaidulla, U. (2020). A review on herbal drug loaded into pharmaceutical carrier techniques and its evaluation process. *Future Journal of Pharmaceutical Sciences, 6*(1), 1-16.

Satake, K., Kanazawa, G., Hiura, A., Nishiwaki, H., Ha, S. S., Chung, Y. S., Umeyama, K., & Yukimura, T. (1991). Renal function in experimentally induced acute pancreatitis in dogs: How it is affected by the nephrotoxic substance in pancreatic exudate from ascitic fluid. *Japanese Journal of Surgery, 21*(1), 88–95. https://doi.org/10.1007/BF02470876

Selvakumar, & Natarajan, P. (2008). Hepatoprotective activity of Moringa oleifera Lam. leaves in carbon tetrachloride induced hepatotoxicity in albino rats. *Pharmacognosy Magazine*, 4: 97-98.

Shao, M., Lu, X., Cong, W., Xing, X., Tan, Y., Li, Y., Li, X., Jin, L., Wang, X., Dong, J., Jin, S., Zhang, C., & Cai, L. (2014). Multiple low-dose radiation prevents type 2 diabetes-induced renal damage through attenuation of dyslipidemia and insulin resistance and subsequent renal inflammation and oxidative stress. *PLOS ONE*, 9 (3), e92574. https://doi.org/10.1371/journal.pone.0092574.

Soliman, M. M., Al-Osaimi, S. H., Hassan Mohamed, E., Aldhahrani, A., Alkhedaide, A., Althobaiti, F., & Mohamed, W. A. (2020). Protective impacts of *Moringa oleifera* leaf extract against methotrexate-induced oxidative stress and apoptosis on mouse spleen. Evidence-Based Complementary and Alternative Medicine, 2020,

6738474. https://doi.org/10.1155/2020/6738474.

Stojanović, N. M., Mitić, K. V., Nešić, M., Stanković, M., Petrović, V., Baralić, M., Randjelović, P. J., Sokolović, D., & Radulović, N. (2024). Oregano (*Origanum vulgare*) essential oil and Its constituents prevent rat kidney tissue injury and inflammation induced by a high dose of L-arginine. *International Journal of Molecular Sciences*, *25*(2), 941. https://doi.org/10.3390/ijms25020941.

Swamy, G. M., & Meriga, B. (2020). Therapeutic effect of *Moringa oleifera* leaf extracts on oxidative stress and key metabolic enzymes related to obesity. *International Journal of Pharmaceutical Sciences and Research*, 11 (4), 1949–1957. https://doi.org/10. 13040/ IJPSR.0975-8232.11(4).1949-57.

Tani, S., Itoh, H., Okabayashi, Y., Nakamura, T., Fujii, M., Fujisawa, T., Koide, M., & Otsuki, M. (1990). New model of acute necrotizing pancreatitis induced by excessive doses of arginine in rats. *Digestive Diseases and Sciences, 35*(3), 367–374. https://doi. org/ 10. 1007/BF01537414

Tavafi, M. (2013). Protection of renal tubules against gentamicin induced nephrotoxicity. *Journal of Renal Injury Prevention, 2*(1), 5-6. https://doi.org/ 10. 12861/jrip.2013.03.

Toppo R., Roy, B. K., Gora, R. H., Baxla, S. L., & Kumar, P. (2015). Hepatoprotective activity of *Moringa oleifera* against cadmium toxicity in rats. Veterinary World.8(4): 537-540.

Uğurlu, E. T., & Tercan, M. (2023). The role of biomarkers in the early diagnosis of acute kidney injury associated with acute pancreatitis: Evidence from 582 cases. *Ulusal Travma ve Acil Cerrahi Dergisi (Turkish Journal of Trauma & Emergency Surgery)*, 29 (1), 81–93. https://doi.org/10.14744/tjtes.2022.60879

Vergara-Jimenez, M., Almatrafi, M. M., & Fernandez, M. L. (2017). Bioactive components in *Moringa oleifera* leaves protect against chronic disease. *Antioxidants, 6*(4), 91. https://doi.org/10.3390/antiox6040091.

Warnecke, R. B., Oh, A., Breen, N., Gehlert, S., Paskett, E., Tucker, K. L., Lurie, N., Rebbeck, T., Goodwin, J., Flack, J., & Srinivasan, S. (2008). Approaching health disparities from a population perspective: The National Institutes of Health Centers for Population Health and Health Disparities. *American Journal of Public Health*, *98*(9), 1608-1615.

Wijayanti, H. N., Fadhilah, Y. N., Yuniarti, W. M., Lukiswanto, B. S., Arimbi, A., Suprihati, E., & Kurnijasanti, R. (2023). Protective effect of *Moringa oleifera* leaves extract against gentamicin induced hepatic and nephrotoxicity in rats. *Iraqi Journal of Veterinary Sciences*, 37 (1), 129-135. https://doi.org/10.33899/ijvs. 2022. 133276. 2197.

Winn-Deen, E. S., David, H., Sigler, G. & Chavez, R. (1988). Development of a direct assay for alpha-amylase. *Clinical chemistry*, *34*(10), 2005-2008.

Yang, J.; Tang, X.; Wu, Q.; Ren, P. & Yan, Y. (2022b): A Severe acute pancreatitis mouse model transited from mild symptoms induced by a "Two-Hit" strategy with L-arginine. *Life,* 12 (1): 126.

Yang, X.; Zhang, R.; Jin, T.; Zhu, P.; Yao, L.; Li, L.; Cai, W.; Mukherjee, R.; Du, D. & Fu, X. (2022a): Stress hyperglycemia is independently associated with persistent organ failure in acute pancreatitis. *Digestive Diseases and Sciences,* 67 (5): 1879-1889.

Zardooz, H., Zahediasl, S., Rostamkhani, F., Farrokh, B., Nasiraei, S., Kazeminezhad, B., & Gholampour, R. (2012). Effects of acute and chronic psychological stress on isolated islets' insulin release. *EXCLI Journal, 11*, 163-175.

Zhang, X. P., Wang, L., & Zhou, Y. F. (2008). The pathogenic mechanism of severe acute pancreatitis complicated with renal injury: A review of current knowledge. *Digestive Diseases and Sciences, 53*(2), 297–306. https://doi.org/10.1007/s10620-007-9856-7

Zhao, Z., Yu, Y., Xie, R., Yang, K., Xu, D., Li, L., Lin, J., Zheng, L., Zhang, C., Xu, X., Chen, Y., Xu, Z., Chen, E., Luo, M., & Fei, J. (2020). Prognostic value of the creatinine-

albumin ratio in acute pancreatitis debridement. *BMC Surgery, 20*(1), 322. https:// doi. org/10.1186/s12893-020-00991-6.

Zheng, Y., Ley, S. H., & Hu, F. B. (2018). Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. *Nature Reviews Endocrinology, 14*, 88-98. https://doi.org/10.1038/nrendo.2017.151.