JOURNAL OF INTERNATIONAL CRISIS AND RISK COMMUNICATION RESEARCH
ISSN: 2576-0017
2025, VOL 8, NO S1

Evaluation of Rosuvastatin and Selenium Effects on TNF- A and SOD Biomarkers on Indomethacin Induced Peptic Ulcer in Rat Model

M. A. Abdulhussein[1]*, H. I.Al-Qadhi[2]

1.Marwa email; Marwa.Abd2206m@comed.uobaghdad.edu.iq Pharmacology department, Baghdad University, Medicine College, Baghdad, Iraq Telephone; 07711158527
2.email; hudaibraheem@comed.uobaghdad.edu.iq Pharmacology department, Baghdad University, Medicine College, Baghdad, Iraq

Corresponding author: Marwa Abdulkareem Abdulhussien

Abstract
Peptic ulcers are lesions resulting from defects in the muscularis mucosae of the gastrointestinal mucosa. These deficiencies may result from cellular regeneration, blood circulation, acid-pepsin secretion, mucus production, mucosal barriers, and internal factors such as epidermal growth hormones and prostaglandins. Despite the availability of numerous pharmacological options for stomach ulcer management, there is an increasing interest in alternative therapies that have less adverse effects for refractory patients. Statins possess antioxidant and anti-inflammatory properties; nevertheless, their anti-ulcerative effects on gastric ulcers remain largely unexplored. Selenium, a trace mineral, is a crucial element of antioxidant enzymes such as glutathione peroxidase, which safeguard cells against oxidative damage. This research evaluated the effects of omeprazole, rosuvastatin, and selenium supplementation on indomethacin-induced gastric ulcers in male albino rats. Animals were categorized into seven groups: carboxymethylcellulose (control group), omeprazole (20 mg/kg), rosuvastatin (20 mg/kg), selenium (200 mcg/kg), a combination of rosuvastatin and omeprazole, and a combination of rosuvastatin and selenium. Thirty minutes post-administration of omeprazole and rosuvastatin, and two hours post-administration of selenium, Indomethacin (60 mg/kg) was given orally to all groups. Four hours later, the animals were euthanized, and the average ulcer indexes for each group were determined. The stomachs were examined histopathologically, and biomarkers were measured.The results indicated the ulcer index as follows: healthy 0±0, indomethacin group 3.3±0.5, omeprazole 0.8±0.4, rosuvastatin 1.3±0.5, selenium 1±0, the first combination group (rosuvastatin & omeprazole) 0.5±0.5, and the combination (rosuvastatin & selenium) 1±0. Concluded that rosuvastatin and selenium expedited ulcer healing by promoting mucosal regeneration, diminishing lipid peroxidation, enhancing antioxidant activity, and altering mucus secretion response.
***Keywords*:** Peptic ulcer; Indomethacin; SOD; TNF-a; rosuvastatin; selenium

List of Abbreviation
CMC: carboxymethyl cellulose
Se: selenium
TNF- **α**: tumor necrosis factor-alpha
SOD: superoxide dismutase
NO: nitric oxide
ROS: reactive oxygen species

Introduction
Peptic ulcers cause significant erosion of the mucosa of the stomach and/or duodenum, extending into the muscular layer due to the production of gastric acid.(Kalida, AL-Khayli and AL-Robeyii, 2010) ; (Alobaidi, 2007). A gastric ulcer, also known as an apicoectal ulcer, is a rupture in the stomach lining's mucosa that occurs in the muscular is mucosa with length more than 5 mm , the gastric mucosa changes as a consequence of modifications to the stomach defense system, leading

to erosion and ultimately ulceration (Najm, 2011); (S Tarnawski and Ahluwalia, 2012). Relieving symptoms, healing craters, and avoiding complications are the three main objectives of medical treatment for peptic ulcer illness (Woolf, Rehman and Rose, 2019). Peptic ulcers have been treated with a number of conventional pharmaceutical medications, including proton-pump inhibitors, antacids, and histamine subtype 2-receptor antagonists, Alternative treatments are becoming more popular as a result of the many negative effects of these medications, particularly when long-term administration is recommended for instances that are resistant (Abdulwahhab, Al Hashimi and Alkhalidi, 2021); (Al-beiruty, Rasheed and Al-Zubaidy, 2008). The statins class are inhibitors of HMGCoA reductase, has been shown to be the most successful in lowering blood cholesterol levels , an entirely synthetic HMG-CoA reductase inhibitor is rosuvastatin, through its impact on inflammatory and oxaditive indicators, rosuvastatin was linked to significant anti-oxidative and anti-inflammatory gastroprotective benefits in NSAID-induced gastric mucosal injury (Murrow *et al.*, 2012) ; (zbaki -Deng z *et al.*, 2012). A vital nutrient that is important to human life is selenium (Se)(Al Doori, 2008). This has become more and clearer in recent years as fresh studies have shown this element to have a previously unknown purpose and have shown that it has a wide range of therapeutic benefits, Selenium is required for the immune system to operate properly (Broome *et al.*, 2004) ; (Baum *et al.*, 2001), for the prevention of heart disease and for the decrease in cancer mortality (Duffield-Lillico *et al.*, 2002). Selenium has been shown in earlier research to hasten wound healing in diabetic patients (Bajpai *et al.*, 2011). Additionally, it has been observed that selenium has a healing effect on gastric ulcers and is gastro protective against injury to the stomach mucosa (Sadau *et al.*, 2015).Our study's objective is to evaluate the standard therapy of omeprazole with the gastro protective effects of rosuvastatin and selenium supplements, both alone and in combination, on indomethacin-induced gastric ulcers in male albino rats.

Materials and Methods

Comparative and prospective investigation involving animals.

For the experiment, male albino Wistar rats weighing between 200 and 250 grams were utilized. They were confined in wire mesh cages, provided with commercial rat pellets, and allotted one week for acclimatization. The conditions of their habitat included a temperature of 23°C to 25°C, humidity levels above 55% to 1125%, and 12 hours of light. The study was conducted at the Iraqi Center for Cancer Research and Medical Genetics in Baghdad, Iraq.

All attempt was made to reduce the suffering of the experimental rats, including ensuring proper ventilation in the animal house, cleaning the cages every other day, handling the animals gently throughout the experiment, administering the correct anesthetic dose, and performing euthanasia away from the living animals.

.**Determine the doses of drugs:**

The dosages of omeprazole, selenium, rosuvastatin, and carboxymethylcellulose (CMC) were established based on prior research, however the indomethacin dosage was picked from a pilot study involving 30mg, 60mg, and 100mg, with 60mg being the preferred dose.

Experimental protocol

Induction of stomach ulcers in rats: Subjecting the rats to a 24-hour fasting period before to the studies. Indomethacin powder was utilized to induce ulcers, administered at a dosage of 60 mg/kg, dissolved in Carboxymethylcellulose (CMC) and delivered via a rubber stomach tube. The animals were categorized into seven groups, each comprising ten rats. Group 1 served as the control group, consisting of normal rats without gastric ulcers or medications. Group 2 was the indomethacin untreated group, where rats received 60 mg/kg of indomethacin to induce gastric ulcers without subsequent medication. Group 3 was the omeprazole treated group, in which rats were given a freshly prepared omeprazole suspension at a dosage of 20 mg/kg, followed by the induction of gastric ulcers with 60 mg/kg of indomethacin suspension one hour later; Group 4: Rosuvastatin-treated group, wherein rats were administered a rosuvastatin suspension at a dosage of 20 mg/kg

via intragastric gavage, followed by indomethacin administration for ulcer induction after one hour; Group 5: Selenium-treated group, in which rats were previously treated with selenium at 200 mcg/kg, with ulcer induction occurring two hours thereafter; Group 6: Rosuvastatin and selenium-treated group, where rats received both rosuvastatin (20 mg/kg) and selenium (200 mcg/kg), followed by indomethacin (60 mg/kg) administration after one hour and two hours, respectively, post-treatment; Group 7: Rosuvastatin and omeprazole-treated group, the final group that received rosuvastatin (20 mg/kg) and selenium (200 mcg/kg), with indomethacin suspension administered for ulcer induction after one hour.

The experimental rats were anesthetized using the method of overdose of anesthetic agents. At the end of the experiment, tissue samples from rats in all groups were collected, and histopathological changes in the stomach of each rat were assessed and scored using the scoring table below. The extent of immunohistochemical reactions for proteins like MDA, IL1-B, SOD, and TNF-a was determined by the percentage of positively stained cells. Data analysis was conducted using SPSS version 26, with results presented as mean values and standard deviations. An analysis of variance (ANOVA) test was performed to compare the mean values across the study groups.

Results

Macroscopic evaluation: the effect of drugs on lesion number and ulcer severity were shown in (Table 1).

Indomethacin: it caused significant ($p<0.01$) mucosal injury represented as gastric damage score (ulcers number and severity, the severity is represented by the total linear lengths of lesions). The ulcers number score mean of indomethacin was found to be (3.3±0.5) with (100%) ulcer formation, versus (0%) for a healthy group.

Omeprazole: It caused a significant reduction ($p>0.01$) in gastric damage score mean, the ulcers number score mean of omeprazole was (0.8±0.4) with (20% ± 10%) ulcer formation versus (3.3±o.5) with (100%) ulcer formation for indomethacin.

Rosuvastatin: it caused a significant reduction ($p>0.01$) in gastric damage score mean, the ulcers number score mean of rosuvastatin was (1.3±0.5) with (32.5% ± 12.5%) ulcer formation versus (3.3±0.5) with (100%) ulcer formation for indomethacin.

Selenium: It caused a significant reduction ($p>0.01$) in gastric damage score mean, the ulcers number score mean of selenium was (1±0) with (25% ± 0%) ulcer formation versus (3.3±0.5) with (100%) ulcer formation for indomethacin.

Rosuvastatin and selenium combination: The combination caused a significant reduction ($p>0.01$) in gastric damage score mean, the ulcers number score mean of this combination was (1±0) with (25% ± 0%) ulcer formation versus (3.3±0.5) with (100%) ulcer formation.

Rosuvastatin and omeprazole: The combination of rosuvastatin and omeprazole resulted in a substantial decrease ($p>0.01$) in the mean stomach damage score, with the mean ulcer number score being (0.5±0.5) and an ulcer formation rate of (12.5% ± 12.5%), compared to (3.3±0.5) with a (100%) ulcer formation rate.

Histopathological evaluation: the effect of drugs on the damage score of the microscopic appearance of gastric mucosa in rats

Score zero (0) denotes intact mucosal epithelium, which may exhibit mild congestion and/or mild hyperkeratosis; score one (1) refers to a superficial lesion that involves only mucosal erosion; score

two (2) describes a deeper lesion that penetrates the mucosa and extends to the submucosa; whereas score three (3) indicates a deep lesion that affects the mucosa, submucosa, and extends to the tunica muscularis.

Indomethacin: Figure 1 and table 2 were illustated the microscopic examination of this group revealed congestion and extensive deep ulceration that penetrates the mucosal and sub-mucosal layers, reaching the muscularis tissue. Severe ulceration showed dense inflammatory infiltrates in the lamina propria and hemorrhagic patches after intragastric injection of indomethacin (60 mg/kg) on an empty stomach. The average microscopic damage score in the indomethacin group was (2.9±0.3), with (96.7%±10.5%) probability of ulcer formation, significantly higher than that in the healthy group and all other groups.

.**Omeprazole:** The microscopic examination of this group revealed a natural gastric cavity, normal parietal cell distribution, and a few unattached superficial epithelial cells. As illustrated in Figure 1 and Table 2, the average microscopic damage score in this group was (1±0), with a prospect of gastric ulcer formation of (33.3%±0%), which was substantially lower than that of the indomethacin group.

Rosuvastatin: Examination of this group under a microscope revealed a normal gastric cavity, The surface epithelium appeared normal, with a few superficial epithelial cells detached, some epithelial cell erosion, and areas of ulceration extending into the mucosa.Figure 1 and table 2 show that the indomethacin group had a higher probability of ulcer formation (60%±14.1%), whereas the rosuvastatin group had a considerably lower mean microscopic damage score (1.8±0.4).

Selenium: The selenium group exhibited a nearly normal microscopic appearance, with minor epithelial erosion, a typical distribution of parietal cells, a normal gastric cavity, and a surface epithelium that showed only a few detached superficial epithelial cells.. The average microscopic damage score was (1.1±0.3) with (36.7%±10.5%) prospect of ulcer formation, which was lower than the indomethacin group, as shown in (figure 1) and (table 2).

Rosuvastatin and selenium: Microscopic examination of this group revealed normal tissue, including mucosal erosions, normal submucosal layer, gastric cavity, and parietal cell distribution. The mean microscopic damage score was (1±0), with a 33.3%±0% chance of ulcer formation, significantly lower than the indomethacin group (figure 1), (table 2).

Rosuvastatin and omeprazole: Microscopic examination of this group appeared healthy, with a normal gastric cavity, surface epithelium showing only a few detached superficial epithelial cells, and a typical distribution of parietal cells. The average microscopic damage score in this group was (1±0), with (33.3%±0%) probability of ulcer formation. which was significantly lower than the indomethacin group, as shown in (figure 1), (table 2).

Biomarker evaluation:

A) Tumer necrosis factor – α

According to the pattern of TNF – an expression, the study groups could be broadly divided into three broad divisions, low, very low and very high expression, those with very low TNF-an expression is:

Healthy: TNF- **α** level of this group is within the normal range of albino rat with mean score of (86.3±8.2) and standard dev. Of (8.2), as shown in (table 3).

(Rosuvastatin & Selenium) combination: TNF- **α** level of this group seems to be like healthy group with mean score of (85.8±4.7) and standard dev. Of (4.7), as shown in (table 3).

(Rosuvastatin & Omeprazole) : this group also show normal range of TNF- **α** biomarker with mean score of (78.2±6) and standard dev. (6) , as shown in (table 3).

The second group (very high expression group) include:

Indomethacin: this group show very high TNF- **α** level with mean score of (571.6±143.1), and standard dev. Of (143.1) showing significant differences from other groups, as shown in (table 3).

Omeprazole & Rosuvastatin and Selenium, The final groups, groups with low expression of TNF – **α**, show little increase in TNF- **α** level with mean scores of (96.4±10.8), (96.7±4.7) and (91±7.4) respectively and standard dev. Of (10.8), (4.7), (7.4) respectively with significant differences from other groups, as shown in (table 3).

B) Superoxide dismutase (SOD)

SOD protein shows a different pattern from that of TNF – **α**, with the lowest expression found in **Indomethacin** medication with mean score of (2.79±0.88) and standard dev. Of (0.83) which significantly differ from another groups, as shown in (table 4).

Healthy, (rosuvastatin & selenium) combination and (rosuvastatin & omeprazole) combination shows the highest expression of this protein with mean score of (7.77±0.97), and (6.37±0.51) and (8.83+_0.44) and standard dev. Of (0.97), (0.51), (0.44) respectively showing significant differences from other groups, as shown in (table 4).

Omeprazole, Rosuvastatin and Selenium groups show expression in the middle according to the above groups, with mean scores (5.27±0.57), (4.77±0.25) and (4.69±0.32) and standard dev. Of (0.57), (0.25), (0.32) respectively showing significant differences from other groups, as shown in (table 4).

Discussion

This study compared the gold standard therapeutic approach of oral rosuvastatin and selenium versus omeprazole before inducing gastric ulcers as a preventive measure to assess the anti-oxidative, anti-inflammatory, and anti-ulcerative effects of these medications on indomethacin-induced gastric ulcers in male albino rats (Matloub and Manna, 2010) . The present investigation shown that the indomethacin model of gastric ulceration in rats resulted in a substantial drop in SOD level and an increase in ulcer index, percentage of stomach layer damage, and TNF- **α** level , in a localised manner, elevated levels of TNF- **α** may intensify tissue inflammation, leading to mucosal ischemia and hypoxia, as well as reduced gastric mucosal blood flow (Yu *et al.*, 2020). This can be important for the occurance of successive cascades of apoptotic and inflammatory events(Mahmoud *et al.*, 2021). One effective and widely used treatment options for peptic ulcer disorders is proton pump inhibitors, This crucial class of drugs has its prototype in omeprazole, which lowers gastric acid output while having protective effects on the stomach mucosa , within this current investigation, the periodical oral omeprazole adminstration are decrese the ulcerative, inflammatory, and oxidative effects caused by indomethacin. (Kamada *et al.*, 2021) . In our study we used the most successful medication for lowering serum cholesterol, Rosuvastatin , as it has interesting side effects that are unrelated to lowering cholesterol, such as antioxidant and anti-inflammatory properties, which are being explored as potential new targets for treating diabetes, peptic ulcer, atherosclerosis, and inflammation (Ruscica *et al.*, 2022). Also we used the trace mineral , selenium supplement, each of these drugs alone and in combination to evaluate their efficacy in preventig gastric ulcer as aprophylaxis in comparision with omeprazole (Liu and Feng, 2024) . The results of this research demonstrated a strong anti-ulcerative impact on indomethacin-induced stomach ulcers in rats given oral rosuvastatin and selenium, and their combination (Ugan and Un, 2020) .The ulcer score, ulcer index, ulcer surface area, and histological alterations were all successfully decreased, They also effectively decrease the higher levels of anti inflammatory biomarker TNF- **α** while raising those of stomach SOD (Al-Qadh, 2022) . Rosuvastatin's gastroprotective effects have been linked to scavenging free radicals, increasing NO production by prostaglandin-E2 and iNOS levels, and increasing the production of gastric juice mucin while lowering gastric levels of TNF-α, according to previous studies (Lee, Kim and Kim, 2022). The investigation further shown that, in contrast to mice treated with CMC, animals treated with Selenium exhibited a considerable decrease in lipid peroxidation, This aligns with findings indicating a role in increase reactive oxygen species (ROS) for occurance of stomach ulcers(Ali *et al.*, 2024). Thus, by raising the animal's antioxidant state, selenium can decrease peroxidation of

the lipid, by boosting the activity of antioxidant enzymes, selenium has been shown in earlier studies to protect macromolecules and membrane lipid from oxidative damage caused by peroxides (Shen *et al*., 2022).

Conclusions

This study revealed that the antihyperlipidemic drug, Rosuvastatin and the trace mineralSelenium, both alone and in combination, helps heal gastric ulcers by reducing lipid peroxidation, boosting antioxidant levels, and promoting a rapid increase in mucus secretion in response to mucus damage. These effects make the drugs as effective as the standard treatment, omeprazole, in preventing and treating gastric ulcers.

Conflict of interest

The authors declare no conflict of interest.

Ethics approval

We conducted the research in accordance the Ethical Committee of Department of pharmacology, College of medicine, university of Baghdad.

References

ABDULWAHHAB, S.H., Al HASHIMI, B.A.R. AND AlKHALIDI, N.M. (2021) .Prevalence and associated factors of gastro-esophageal reflux disease among a sample of undergraduate medical students in Baghdad', *Journal of the Faculty of Medicine Baghdad*, 63(4), 163–170.

Al-BEIRUTY, O.A., RASHEED, A.M. AND Al-ZUBAIDY, H. (2008) .The Effect of Omeprazol in the Treatment of Laryngeal Manifestations of Gastro-oesophageal Reflux', *Journal of the Faculty of Medicine Baghdad*, 50(2), 154–159.

Al-QADH, H.I. (2022) .The potential protective effects of Aliskiren on diclofenac sodium induced gastric ulcer in a rat model', *HIV Nursing*, 22(2), 3428–3433.

D. ALI, R. EL - SHIEKH, M. EL SAWY *et al.* (2024) .In vivo anti-gastric ulcer activity of 7-O-methyl aromadendrin and sakuranetin via mitigating inflammatory and oxidative stress trails', *Journal of Ethnopharmacology*, 335, 118617.

ALOBAIDI, M.A.A. (2007) .Management of Gastrointestinal Cutaneous Fistulae.', *Journal of the Faculty of Medicine Baghdad*, 49(3), 286–291.

S. BAJPAI, M. MISHRA, H. KUMAR *et al.* (2011) .Effect of selenium on connexin expression, angiogenesis, and antioxidant status in diabetic wound healing', *Biological trace element research*, 144, 327–338.

M. BAUM, A. CAMPA, M. MIGUEZ - BURBANO *et al.* (2001) .Role of selenium in HIV/AIDS', *Selenium: its molecular biology and role in human health*, 247–255.

C. BROOME, F. MC ARDLE, J. KYLE *et al.* (2004) .An increase in selenium intake improves immune function and poliovirus handling in adults with marginal selenium status', *The American journal of clinical nutrition*, 80(1), 154–162.

Al DOORI, K.M. (2008) .Serum status of selenium and chromium in patients with cardiovascular diseases and controls in Iraq.', *Journal of the Faculty of Medicine Baghdad*, 50(4), 428–430.

A. DUFFIELD - LILLICO, M. REID, B. TURNBULL *et al.* (2002) .Baseline characteristics and the effect of selenium supplementation on cancer incidence in a randomized clinical trial: a summary report of the Nutritional Prevention of Cancer Trial', *Cancer Epidemiology Biomarkers & Prevention*, 11(7), 630–639.

KALIDA, A.-M., AL-KHAYLI, N.G. AND AL-ROBEYII, M.R. (2010) .The role of pepsinogen test among the patients with gastric cancer', *Journal of the Faculty of Medicine Baghdad*, 52(2).

T. KAMADA, K. SATOH, T. ITOH *et al.* (2021) .Evidence-based clinical practice guidelines for peptic ulcer disease 2020', *Journal of gastroenterology*, 56, 303–322.

LEE, J., KIM, M.-H. AND KIM, H. (2022) .Anti-oxidant and anti-inflammatory effects of astaxanthin on gastrointestinal diseases', *International journal of molecular sciences*, 23(24), 15471.

LIU, J. AND FENG, G. (2024) .The causal relationship between trace element status and upper gastrointestinal ulcers: a Mendelian randomization study', *Frontiers in Nutrition*, 11, 1443090.
M. MAHMOUD, M. NABIL, W. ABDO *et al.* (2021) .Syzygium samarangense leaf extract mitigates indomethacin-induced gastropathy via the NF- B signaling pathway in rats', *Biomedicine & Pharmacotherapy*, 139, 111675.
MATLOUB, S.Y.N AND MANNA, M.J. (2010) .The cytoprotective effect of different doses of Sildenafil on indomethacin-induced gastric mucosal damage in rats', *Journal of the Faculty of Medicine Baghdad*, 52(4), 426–431.
MURROW, S. SHER, S. ALI *et al.* (2012) .The differential effect of statins on oxidative stress and endothelial function: atorvastatin versus pravastatin', *Journal of clinical lipidology*, 6(1), 42–49.
NAJM, W.I. (2011) .Peptic ulcer disease', *Primary Care: Clinics in Office Practice*, 38(3), 383–394.
M. RUSCIA, N. FERRI, M. BANACH *et al.* (2022) .Side effects of statins: from pathophysiology and epidemiology to diagnostic and therapeutic implications', *Cardiovascular Research*, 118(17), 3288–3304.
S TARNAWSKI, A. AND AHLUWALIA , A. (2012) .Molecular mechanisms of epithelial regeneration and neovascularization during healing of gastric and esophageal ulcers', *Current medicinal chemistry*, 19(1), 16–27.
Y. SADAU, A. ADELAIYE, R. MAGAJI *et al.* (2015) .Role of selenium and vitamin E on gastric mucosal damage induced by water-immersion restraint stress in wistar rats', *IOSR J. Pharm. Biol. Sci*, 10(1), 34–39.
Y. SHEN, H. HUANG, Y. WANG *et al.* (2022) .Antioxidant effects of Se-glutathione peroxidase in alcoholic liver disease', *Journal of Trace Elements in Medicine and Biology*, 74, 127048.
UGAN, RUSTEM ANIL; UN, HARUN (2020) .The protective roles of butein on indomethacin induced gastric ulcer in mice', *The Eurasian Journal of Medicine*, 52(3), 265.
WOOLF, A., REHMAN, R.B. AND ROSE, R. (2019) .Gastric ulcer'.
L. YU, R. LI, W. LIU *et al.* (2020) .Protective effects of wheat peptides against ethanol-induced gastric mucosal lesions in rats: vasodilation and anti-inflammation', *Nutrients*, 12(8), 2355.
G.ZBAKI -DENG Z, A. HEK MO LU, N. KANDEM R *et al.* (2012) .Effects of statins in an indomethacin-induced gastric injury model in rats.', *The Turkish journal of gastroenterology: the official journal of Turkish Society of Gastroenterology*, 23(5), 456–462.

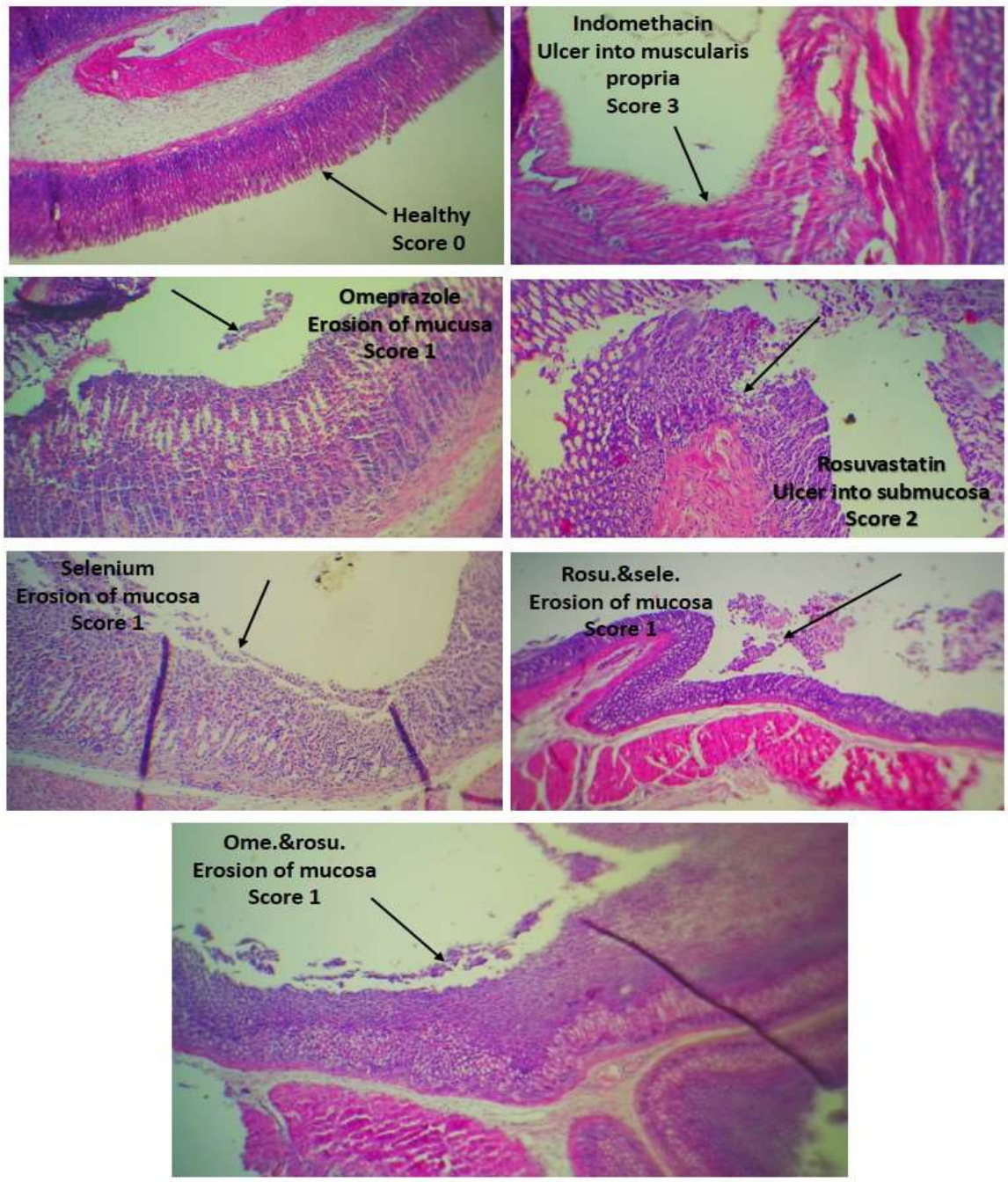

Figure 1: photograph shows the effect of different drugs on histopathological examination of gastric mucosal tissue section in indomethacin induced gastric ulceration in rat model, and represents by different scores.

Table 1: mean score of a number of lesions and damage percentage comparison, according to study groups, by using ANOVA test and values are expressed as mean ±SD different.

Groups	Number of lesions	percentage
	Mean ± Standard dev.	Mean ± Standard dev.
Healthy	0 ± 0	0% ± 0%
Induction	3.3 ± 0.5	82.5% ± 12.5%
Omeprazole + indomethacin	0.8 ± 0.4	20% ± 10%
Rosuvastatin + indomethacin	1.3 ± 0.5	32.5% ± 12.5%
Selenium + indomethacin	1 ± 0	25% ± 0%
Rosuvastatin & selenium + indomethacin	1 ± 0	25% ± 0%
Rosuvastatin & Omeprazole + indomethacin	0.5 ± 0.5	12.5% ± 12.5%
P-Value	<0.001**	<0.001**

**Significant at 0.01 level by ANOVA test

Table 2: mean histological score comparison, according to study groups, by using ANOVA test and values are expressed as mean ± SD different.

Groups	Damage	
	Mean scores ± Standard dev.	Mean percent ± Standard dev.
Healthy	0 ± 0	0% ± 0%
Induction	2.9 ± 0.3	96.7% ± 10.5%
Omeprazole + indomethacin	1 ± 0	33.3% ± 0%
Rosuvastatin + indomethacin	1.8 ± 0.4	60% ± 14.1%
Selenium + indomethacin	1.1 ± 0.3	36.7% ± 10.5%
Rosuvastatin & selenium + indomethacin	1 ± 0	33.3% ± 0%
Rosuvastatin & Omeprazole + indomethacin	1 ± 0	33.3% ± 0%
P-Value	<0.001**	<0.001**

**Significant at 0.01 level by ANOVA test

Table 3: mean TNF- **α** scores comparison, according to study groups, by using ANOVA test and values are expressed as mean ± SD different.

Groups	TNF-alpha	
	Mean	Standard dev.
Healthy	86.3	8.2
Induction	571.6	143.1
Omeprazole + indomethacin	96.4	10.8
Rosuvastatin + indomethacin	96.7	4.7
Selenium + indomethacin	91	7.4
Rosuvastatin & selenium + indomethacin	85.8	4.7
Rosuvastatin & Omeprazole + indomethacin	78.2	6
P-Value	<0.001**	

**Significant at 0.01 level by ANOVA test

Table (4): mean SOD scores comparison, according to study groups, by using ANOVA test and values are expressed as mean ± SD different.

Groups	superoxide dismutase	
	Mean	**Standard dev.**
Healthy	7.77	0.97
Induction	2.79	0.83
Omeprazole + indomethacin	5.27	0.57
Rosuvastatin + indomethacin	4.77	0.25
Selenium + indomethacin	4.69	0.32
Rosuvastatin & selenium + indomethacin	6.37	0.51
Rosuvastatin & Omeprazole + indomethacin	8.83	0.44
P-Value	<0.001**	

**Significant at 0.01 level by ANOVA test