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ORIGINAL ARTICLE

Nutrition, Metabolism, and Prevention of NCDs | Human and Clinical Nutrition

The Inhibitory Effect of Selenium Supplementation on Tumor Progression in a DMBA-Induced Breast Cancer Model in Wistar Rats

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ABSTRACT

Background: Breast cancer remains a significant global public health concern, necessitating the ongoing exploration of novel preventive and therapeutic strategies. Selenium supplementation has been proposed as a potential chemopreventive agent, yet its efficacy lacks robust *in vivo* validation.

Aims: This study aimed to evaluate the chemopreventive potential of selenium supplementation and its effect on tumor progression in a 7,12-dimethylbenz[a]anthracene (DMBA)-induced breast cancer model in Wistar rats.

Methods: Twenty-four adult female Wister rat were allocated into four experimental groups (n=6): Control (vehicle only); DMBA (carcinogen control); DMBA + Se 200 µg/kg; and DMBA + Se 400 µg/kg. Mammary tumors were induced via a single intragastric administration of DMBA (80 mg/kg). Over a 23-week period, hematological, biochemical, and histopathological analyses were conducted. The volume of excised mammary tumors was measured post-sacrifice.

Results: Supplementation with selenium at a dose of 400 µg/kg resulted in a statistically significant reduction in mean tumor volume (0.13 cm^3) compared to the DMBA-only group (1.32 cm^3). Concurrently, this high-dose group exhibited significant amelioration in serum levels of specific biochemical markers including aspartate aminotransferase (AST), urea, and creatinine. Histopathological assessment further supported these findings, revealing a more preserved mammary tissue architecture in rats receiving the high-dose selenium.

Conclusions: While selenium supplementation at 400 µg/Kg demonstrated a significant inhibition effect on tumor progression and conferred hepatorenal protection, a definitive chemopreventive effect against DMBA-induced carcinogenesis was not established. These results indicate that selenium may function as a therapeutic modulator rather than a primary preventive agent in this model. Further investigation employing higher doses and alternative administration regimens is warranted to elucidate its full chemopreventive potential.

Keywords: Breast cancer; Selenium; DMBA; Chemoprevention; Tumor Progression; Wistar rats.

ARTICLE INFORMATION

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1 INTRODUCTION

Selenium (Se), first discovered and isolated in 1817 by Swedish scientist Jöns Jakob Berzelius, was initially regarded as a toxic substance during the production of sulfuric acid in the 1930s. This perception persisted until 1957, when Schwarz and Foltz demonstrated its preventive effect on hepatic necrosis in mice. Following this pivotal discovery, selenium was recognized as an essential microelement required in trace amounts for various critical bodily functions. These include the reduction of oxidative stress, regulation of immune function, support for thyroid metabolism, promotion of fertility, maintenance of endocrine function, and its role in cardiovascular health, muscle development, and antimutagenic effects. (Cardoso *et al.*, 2015; Kieliszek *et al.*, 2021; Savitha, 2014; Guido *et al.*, 2016, Szwiec *et al.*, 2021).

Selenium exerts its biological functions primarily through 30 selenoproteins (SePs), in which it is integrated as selenocysteine (SeCys) (the 21st amino acid). Prominent selenoprotein include glutathione peroxidase (GPx), a crucial intracellular antioxidant enzyme; thioredoxin reductases (TrxR), which are involved in redox regulation; and selenoprotein P (SeP), which is responsible for Se transport to tissues and for reducing lipid hydroperoxides (Toyama *et al.*,

2022). Selenium is absorbed from food in either an organic form, such as selenocysteine and selenomethionine or an inorganic form, such as selenite, selenate, and selenide, primarily sourced from plants in selenium-rich soil.

Dietary Se concentrations depend on the degree and physicochemical forms found in the soil. Both organic and inorganic forms of Se are equally efficient in the body to generate selenoprotein. (Hamdy *et al.*, 2011).

Due to its antioxidant activity and its capacity to enhance DNA damage repair, regulate cell proliferation, and induce apoptosis, Se has been suggested as a chemopreventive agent against breast cancer progression (Fontelles & Ong, 2017). Numerous studies have observed a correlation between low serum selenium concentration and the incidence of breast cancer, thereby underscoring its potential anticarcinogenic effect (Charalabopoulos *et al.*, 2006). Despite some findings indicating that selenium supplementation reduces tumorigenesis in rats, further studies have reported contradictory results. This inconsistency has created confusion and leaves the definitive role of selenium in cancer prevention largely undefined (Tu *et al.*, 2023). Accordingly, the present study was conducted to investigate whether selenium has a direct chemopreventive effect or simply inhibits the growth of DMBA-induced breast cancer in Wistar rats.

2 Material and Methods

2.1 Chemicals

7,12-Dimethylbenz[a]anthracene (DMBA, purity ≥ 98%), product number D3254–100mg, was purchased from Sigma-Aldrich (Algeria). Anhydrous sodium selenite (Na_2SeO_3) with 99% purity was obtained from Biochem Chemopharma, France.

2.2 Experimental Animals

Twenty-four adults female Wistar rats, aged 6–8 weeks and weighing 160 ± 20 g were obtained from Pasteur Institute of Algiers, Algeria. The animals were maintained in propylene cages (three per cage) for a two-week acclimatization period under controlled conditions (natural light cycles, ambient temperature of 22 ± 3°C, and adequate ventilation) and were provided with a standard rodent pellet diet and water *ad libitum* throughout the experiment (Karnam *et al.*, 2017).

2.3 Ethical Statement

The housing and experimental use of animals were approved by the Ethics Committee of Mustapha Stambouli University (N/Ref: 04/CSF/SNV/2016) in full compliance with the European directive concerning animal testing (Directive 2010/63/EU) (decision N°: L276/33).

2.4 Induction of Mammary Carcinogenesis

Mammary tumors were induced via a single oral administration of DMBA (80 mg/kg), which was dissolved in olive oil and thoroughly mixed using a vortex mixer. This dos of DMBA is expected to cause a 100% tumor incidence within approximately 8–10 weeks without the subsequent administration of any promoters. (Baltaci *et al.*, 2018; Hosny *et al.*, 2021; Wang & Zhang, 2017).

2.5 Study Design

Although mammary tumors typically develop within 8 to 10 weeks following a single dose of DMBA, the treatment was extended to 23 weeks to monitor and evaluate the potential long-term effects of selenium supplementation on carcinogenesis and tissue regeneration. (Gopalakrishnan *et al.*, 2019). The 24 female rats were distributed equally among four groups (n = 6/group).

- **Group 1 (Control):** orally gavaged with distilled water three times weekly throughout the experimental period and fed a standard rodent pellet diet.
- **Group 2 (DMBA-treated):** After two weeks of acclimation, this group received a single oral dose of DMBA (80 mg/kg) in olive oil to induce mammary carcinogenesis. Olive oil was used as a vehicle for DMBA administration since it is biocompatible and has the potential to enhance the solubility and oral absorption of lipophilic compounds such as DMBA (Gokul Raj *et al.*, 2015). The rats subsequently received distillate water by gavage and maintained on a standard diet.
- **Group 03 and 04 (Selenium-treated groups): These groups** were treated with Selenium at doses of 200 µg/kg and 400 µg/kg, respectively. Selenium was administered via gavage three times per week before, beginning two weeks before the DMBA administration and continuing until week 23. The prolonged post-DMBA administration was intended to assess the long-term preventives effect of selenium. All rats in these groups were maintained on a standard diet with *ad libitum* access to water and were maintained under standard laboratory conditions.

All rats, including the control group and treated groups, were weighed weekly to record any changes in body weight. They were also palpated at the thoracic and abdominal-inguinal mammary glands to detect the location, appearance, and size of any tumors.

At the end of the 23-week study period, all experimental animals were fasted overnight, anesthetized with a 3% chloral solution, and then euthanized. Blood samples were collected from the jugular veins for subsequent biochemical and hematological examinations. Additionally, breast tissues were

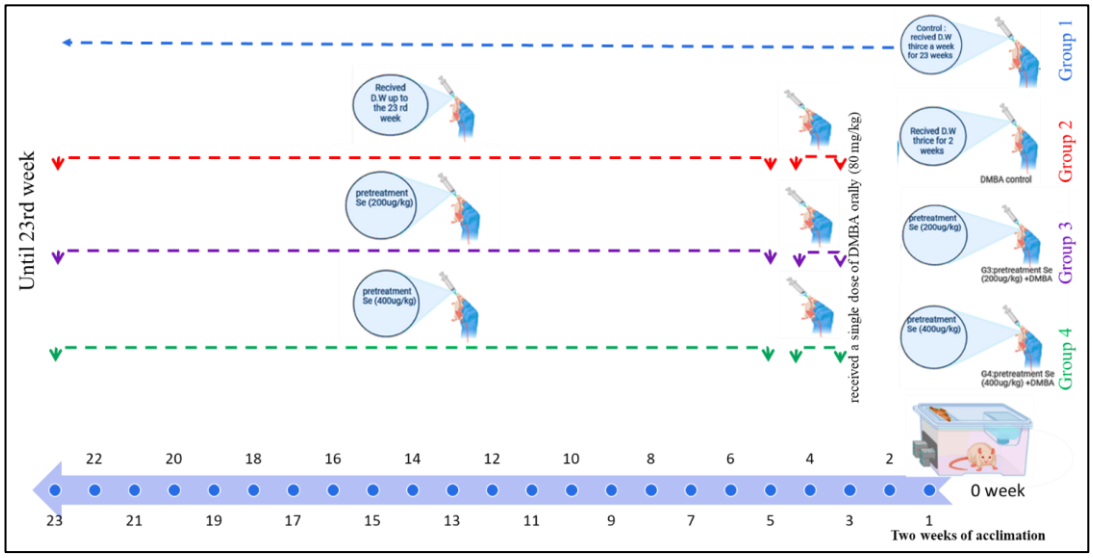

Figure 1. Experimental Design for Breast Cancer Induction using DMBA in Female Albino Rats

fixed in 10% formalin for histopathological analysis (Baltaci *et al.*, 2018; Wang & Zhang, 2017).

2.6 Hematological Analysis

The level of red blood cells (RBC), white blood cells (WBC), Hemoglobin (Hb), Hematocrit (Hct), platelet (PLT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) in the blood were measured using an auto-hematology analyzer (Nihon Kohden Mek7300, Japan).

2.7 Biochemical Analysis

The plasma levels of albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatinine, and urea were estimated in plasma using standard kits with the respons®920–DiaSys Diagnostic system.

2.8 Measurement of Mammary Tumor Volume

The isolated mammary tumors were measured using a Vernier caliper. The tumor volume (V) in cubic centimeters (cm^3) was calculated using the following formula:

$$V(cm^3) = \frac{(L \times B^2)}{2}$$

where L is the larger diameter and B is the smaller diameter, both measured in centimeters (cm) (Akhouri *et al.*, 2020).

2.9 Histology

Breast tissues from all experimental groups were first immersed in a 10% formalin solution. The tissues were then dehydrated using a series of graded alcohol concentration (100%, 96%, 95%), toluene, and acetone. Following dehydration, the tissues were embedded in liquid paraffin to create a solid block. Sections of the blocks were cut into 5 µm slices using a rotary microtome, stained with hematoxylin and eosin, and then covered with glass slips. The slides were examined under a microscope at 100x and 400x magnification to assess histological changes.

2.10 Statistical Analysis

Data are presented as mean ± standard deviation (SD). A one-way analysis of variance (ANOVA), followed by Tukey's post hoc test, was employed to adjust for multiple comparisons. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 26 for windows. A p-value of < 0.05 was considered statistically significant.

3 Results

3.1 Effect of Selenium on Body Weight

Table 1 summarizes the effects of both selenium treatment and DMBA administration on the body weight changes of all test animals. Our results showed no statistically significant variations in the body weights of the DMBA and Se (200 µg/kg and 400 µg body weight) groups compared with the control group.

3.2 Effect of Selenium on Biochemical Parameters

As displayed in Table 2, our results revealed no significant changes in the levels of AST, ALT, urea, and creatinine in the DMBA and selenium (200 µg/kg body weight) groups compared with the control group. However, the creatinine

Table 1. Effect of Selenium on Body Weight Changes in Control and Treated Animals

Experimental group	Initial weight (mg/kg) Mean ± Std. Error	Final weight (mg/kg) Mean ± Std. Error
Control	162.62 ± 4.69	232.50 ± 10.97
DMBA treated	162.33 ± 0.56	228.50 ± 7.89
DMBA + Se (200 µg)	168.00 ± 3.30	230.67 ± 4.71
DMBA + Se (400 µg)	172.50 ± 2.60	236.50 ± 7.33

Each value represents the Mean ±SE (n=6). One-way ANOVA followed by Tukey post hoc test. Values are statistically significant at p<0.05.

and lymphocytes (L) compared with the DMBA group. In contrast, oral administration of Se (200 µg/kg) led to a marked increase ($p < 0.05$) in the number of monocytes compared with both the Se (400 µg /kg) and DMBA groups. Likewise, rats treated with Se (200 µg/kg) had a significantly higher number of polymorphonuclear neutrophils (PNN). The mean corpuscular hemoglobin (MCH) level recorded a significant increase ($p < 0.05$) in the Se (200 ug/kg and 400µg/kg) groups compared to the control and DMBA groups. Conversely, a significant decrease was observed in the MCHC in these same groups compared to the control and DMBA groups.

Table 2. Effect of Selenium on Biochemical Parameters in the Experimental Groups

Parameter	Control	DMBA	DMBA + Se 200 µg	DMBA + Se 400 µg
AST(U/mL)	70.33 ± 7.27	88.00 ± 5.29	79.67 ± 5.67	75.00 ± 1.00
ALT(U/mL)	143.67 ± 7.33	138.67 ± 25.18	163.00 ± 34.12	154.67 ± 17.30
UREA (mmol/L)	7.65 ± 0.04	8.47 ± 0.16	7.99 ± 0.84	7.12 ± 0.74
Creatinine (µmol/L)	38.00 ± 2.08*	33.00 ± 0.57	33.67 ± 1.86	26.00 ± 2.52*

(*) Each value represents the Mean ± SE (n=6). One-way ANOVA followed by Tukey post hoc test. Values are statistically significant at p < 0.05.

level in selenium (400 µg/kg body weight) exhibited a significant decrease ($p < 0.05$) compared to control group.

3.3 Effect of Selenium on Hematological Parameters

A significant elevation ($p < 0.05$) in both monocytes (M) and white blood cells (WBCs) was observed in the DMBA group compared with the control (Table 3). Oral administration of Se at a dose of 400 µg /kg body weight, however, resulted in a significant decrease ($p < 0.05$) in WBCs

3.4 Effects of Selenium on Tumor Volume

Despite the administration of DMBA, no visible tumor was distinctly detected in this group. Unlikely, the DMBA + Se 200 µg/kg demonstrated a noticeable tumor development, with a measured volume of 1.32 cm^3. However, the tumor volume in group 4 was significantly reduced. In fact, this treated group with selenium 400 µg/kg exhibited a tumor volume of 0.13 cm^3. These findings suggest a dose-dependent inhibitory effect of selenium on tumor growth (Figure 2).

Table 3. Effect of selenium on hematological parameters

Parameter	Control	DMBA	DMBA + Se 200 µg	DMBA + Se 400 µg
PLt (10^3)/m	483.3 ± 88.70	637.00 ± 236.18	636.33 ± 261.48	601.00 ± 67.54
L (10^3)/mm^3	1.80 ± 0.76	5.87 ± 1.80*	1.87 ± 0.29	1.30 ± 0.10*
M (10^3)/mm^3	0.13 ± 0.03*	0.50 ± 0.12*	0.63 ± 0.09*	0.20 ± 0.00*
PNN (10^3)/mm^3	0.57 ± 0.15	1.83 ± 0.52*	1.10 ± 0.15*	0.53 ± 0.03
WBCs (×10^3)/mm^3	2.50 ± 0.91*	8.20 ± 2.25*	3.60 ± 0.51	2.03 ± 0.12*
RBCs (×10^6)/mm^3	6.38 ± 0.63	9.59 ± 1.14	6.34 ± 1.83	5.91 ± 0.43
Hb (g/dL)	12.10 ± 1.16	19.50 ± 2.60	11.63 ± 3.77	12.43 ± 0.74
Hct t%	33.3 ± 3.21	50.33 ± 7.18	32.73 ± 9.23	33.33 ± 1.94
MCV (fl)	52.33 ± 0.26	52.23 ± 1.19	51.83 ± 1.39*	56.50 ± 0.78*
MCH (pg)	18.97 ± 0.07*	19.63 ± 0.59*	38.87 ± 2.08*	37.33 ± 0.12*
MCHC (g/dL)	36.23 ± 0.29*	38.27 ± 1.24*	20.20 ± 1.31*	21.47 ± 0.07*
RDI %	11.90 ± 0.21	12.60 ± 0.21	12.93 ± 0.68	12.27 ± 0.35
MPV (fl)	6.60 ± 0.25	6.53 ± 0.30	5.93 ± 0.09	6.97 ± 0.15

(*) Each value represents the Mean ±SE (n=6). One-way ANOVA followed by Tukey post hoc test. Values are statistically significant at p<0.05.

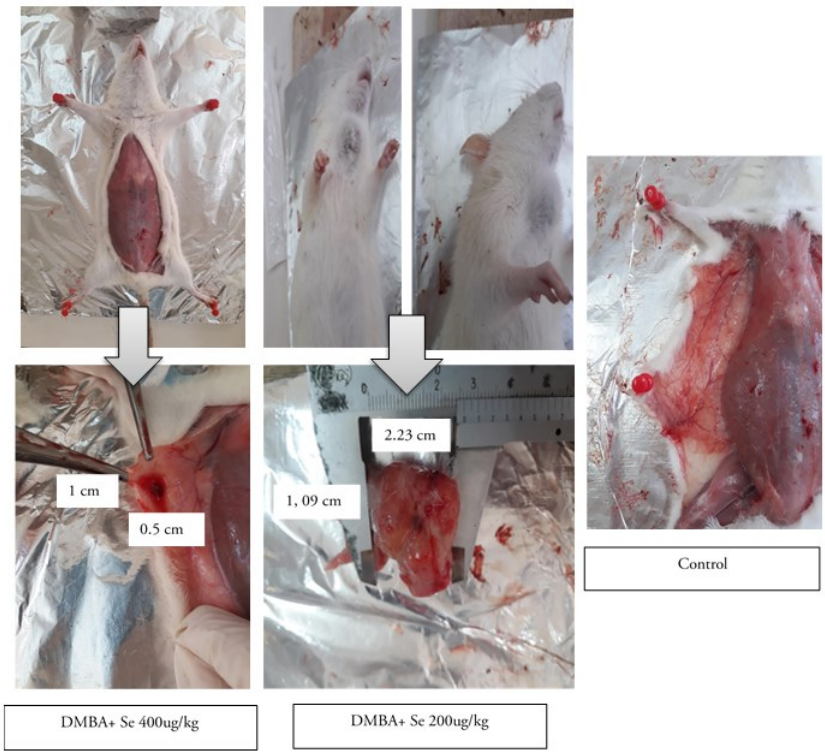

Figure 2. Rat Mammary Tumor in Selenium Treated Groups Compared to Control

A tumor in the neck region of one rat in the group treated with DMBA + Se (200ug/kg) was observed, as displayed in Figure 3. The development of this tumor may be attributed to the migration of breast cancer cells to the lymph nodes in the chest, under the arm, or near the collarbone, which are connected to the lymphatic vessels to the breast.

3.5 Histological findings

Figure 4 illustrates the histopathological examinations of the mammary glands from the control and experimental groups. The mammary glands of the control group exhibited a normal histological structure, with a typical ductular and alveolar architecture lined with one to two epithelial layers surrounded with connective and fatty tissue. However, the DMBA-induced breast tumor group exhibited mammary glandular modification characterized by high proliferation of glandular and ductal epithelium with more than two epithelial layers, forming a significant papillary pattern (1). This proliferation infiltrated the duct wall and extended into the canal lumens with the presence of cell clusters (2). The glandular cells also displayed hyperchromasia, anisokaryosis, and anisonucleosis along with a loss of fatty tissue. These glandular changes indicative of a well-differentiated invasive adenocarcinoma, predominantly adenocarcinoma *in situ*, with a highly inflammatory stroma. Histopathological examination of breast tissue of female rats treated with selenium (200 µg/kg and 400 µg/kg) revealed an architecture nearly identical to that of the DMBA-treated group, nonetheless with more glandular tissue and ductal branching and less voluminous adipocytes separated by an inflammatory infiltrate.

Figure 3. DMBA-Induced Breast Cancer at the Neck Region in Rats Treated with DMBA + Se (200ug/kg). The circle marks the location of DMBA-induced papilloma

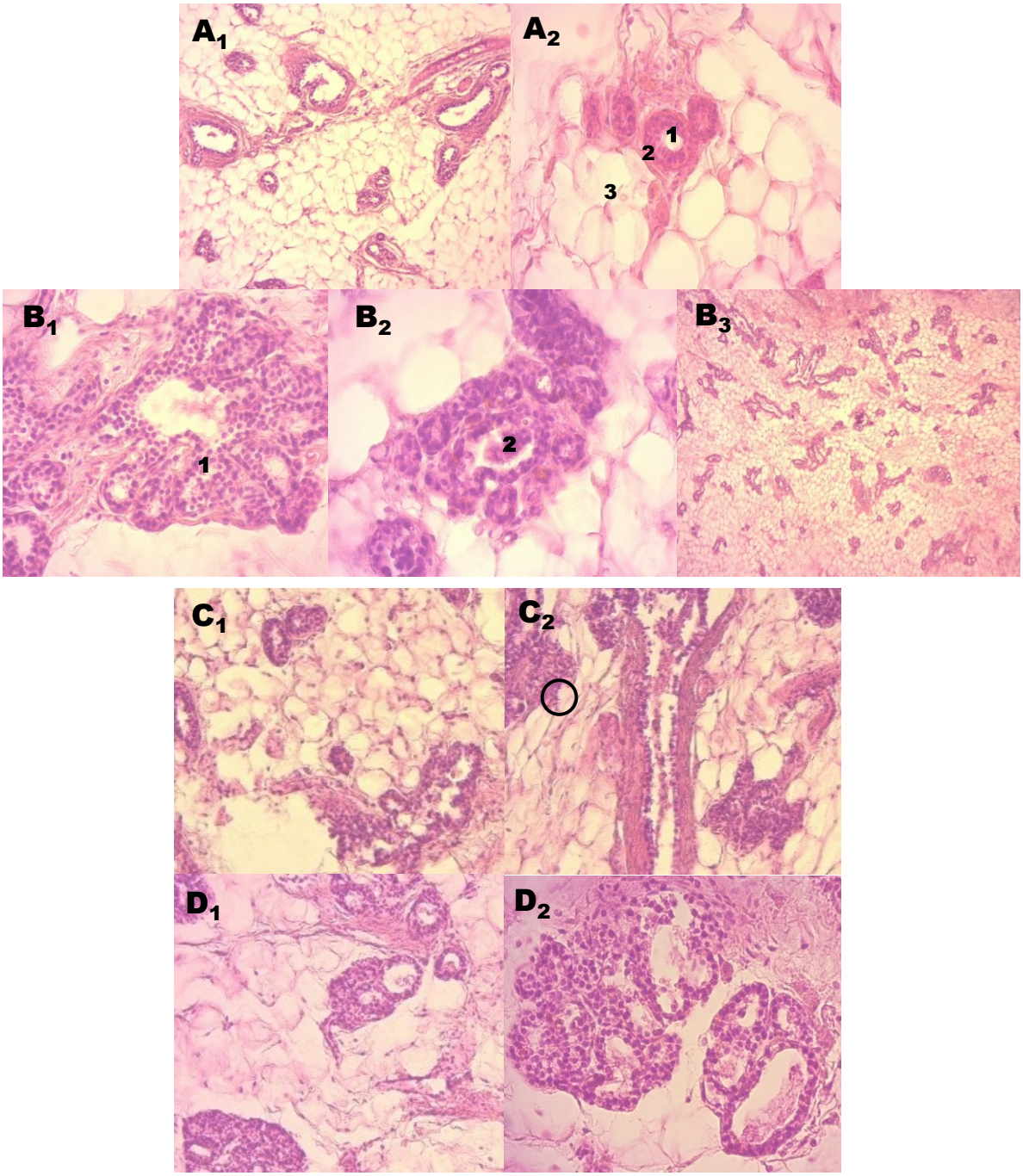

Figure 4. Representative Histological Image (Hematoxylin and eosin, x 100 and x 400 magnification) of Control and Treated Groups (**A**: control group; **1**: excretory ducts; **2**: glandular alveoli; **3**: adipose tissue; **B**: DMBA control; **C**: DMBA + Se (200 µg/kg); **D**: DMBA + Se (400 µg/kg)

4 Discussion

Mammary cancer, more commonly known as breast cancer, is characterized by the uncontrolled proliferation of cells within the mammary gland, including the ducts, lobules, and surrounding connective tissues. It typically originates in the milk ducts or lobules and can metastasize through the bloodstream or lymphatic system (Pratama *et al.*, 2024). In 2020, breast cancer surpassed lung cancer to become the most frequently diagnosed cancer globally, accounting for 11.7% of all new cancer cases. The global incidence of breast cancer has risen significantly, from 1.38 million new cases in 2008 to 2.3 million in 2020 (Lakkis *et al.*, 2024). The etiology of breast cancer is multifactorial, with contributing elements including age, genetics predispositions such as BRCA1 and BRCA2 mutations, prolonged estrogen exposure, and environmental factors including lifestyle, smoking, and exposure to pollutants such as polycyclic aromatic hydrocarbons (PAHs), exemplified by DMBA (Zingué *et al.*, 2024).

Animal models are frequently employed to replicate the carcinogenic process. 7,12-dimethylbenz[a]anthracene (DMBA), is a well-established compound known to specifically induce mammary tumors. DMBA-induced carcinogenesis leads to oxidative stress, which causes cellular damage through lipid peroxidation (Cinato *et al.*, 2024; El makawy *et al.*, 2022; Gamal *et al.*, 2025). Furthermore, DMBA causes DNA damage by disrupting gene expression and signaling pathways, which promotes tumor progression (Tran & Tran, 2024). This model is highly effective for evaluating the chemopreventive potential of compounds including selenium.

In the current research, we induced mammary carcinoma in female Wistar rats using DMBA and conducted biochemical and histological analyses. Our data indicated that DMBA administration led to elevated levels of the liver enzyme and increased renal markers (urea), consistent with hepatotoxicity and renal toxicity. These findings are consistent with previous reports that have demonstrated the detrimental effects of DMBA on liver and kidney function, largely as a result of oxidative stress (El makawy *et al.*, 2022; Zeweil *et al.*, 2023). Identical results were observed in Group 3. However, selenium supplementation at 400 µg/kg in Group 4 significantly reduced creatinine levels and moderately improved AST and urea levels, suggesting a dose-dependent protective effect.

Furthermore, we observed a significant increase in WBC counts in the DMBA group compared with the control and treated groups. This elevation is likely associated with the inflammatory response to the presence of cancer cells. White blood cells (WBCs), or leucocytes, are a critical component of the immune system produced in the bone marrow (Glenn & Armstrong, 2019). An imbalance in WBCs count is frequently a marker of disease. While a low WBC count may increase infection risk, an elevated WBC count typically indicates an inflammatory response or is associated with tumor progression, as observed in invasive breast cancer (Glenn & Armstrong, 2019; Shankar *et al.*, 2006). Tumor stromal tissues frequently contain large numbers of WBCs, and the levels of these cells and their cytokine production are associated with cancer severity. Hence, the increased WBC count in our study may reflect an inflammatory response or immune activation resulting from DMBA-induced carcinogenesis. Cytokines released by inflammatory cells can promote tumor growth and inhibit cell death through key signaling pathways, such as nuclear factor-kappa B (NF-κB), thereby contributing to tumor progression (Elen & Turan, 2019).

In addition, a significant elevation ($p < 0.05$) in lymphocytes, monocytes, and neutrophils was observed in the DMBA group. While lymphocytes play a crucial role in cancer immune surveillance, inhibiting tumor cell proliferation and metastasis. the increased count in our study may represent an early immune response to carcinogenic stress rather than an indication of tumor progression, especially since this group did not have a detectable tumor. The differentiation of monocytes into tumor-associated macrophages (TAMs) within the tumor is well-documented. TAMs contribute to tumor progression by secreting a range of cytokines and growth factors that promote angiogenesis and suppress immune responses. Selenium supplementation normalized the levels of WBCs, lymphocytes, monocytes, and neutrophils and reduced the risk of inflammation. These results are consistent with those of Selamoglu *et al.*, (2015), who studied the effects of novel synthetic organoselenium compounds on hematological parameters in DMBA-induced rats and found that selenium administration reduced the elevated count of leukocytes, eosinophils, neutrophils, and monocytes. The levels decreased with the administration of novel synthetic organoselenium compounds (Soukupová & Rudolf, 2018).

The daily intake of 200 g of selenium among patients with cancer has been associated with decreased mortality and lower incidence of liver, lung, colorectal, and prostate cancers (Selamoglu *et al.*, 2015). A negative correlation was observed between serum selenium levels and breast cancer risk (Cai *et al.*, 2016). Experimental evidence further suggests that selenium supplementation inhibits breast tumorigenesis (Lippman *et al.*,2009). However, the absence of a selenium-only group in this study limits the interpretation of results, as it is known that selenium itself possesses biological effects on hematological and biochemical parameters. For instance, Çay and Naziroğlu (1999) reported that intraperitoneal selenium treatment significantly increased WBC counts in rats without affecting RBC, PCV, MCV, MCH, MCHC, ALT, or LDH. Thus, we cannot definitively rule out the possibility that some

of the observed effects in our study are attributable to selenium.

It is noteworthy that Se (400 µg/kg body weight) resulted in a significant regression of tumor mass (0.13 cm^3) compared with the Se (200 µg/kg body weight) group (1.25 cm^3), confirming selenium's tumor-reducing potential. This effect may be associated to selenium's redox activity, where it acts as an antioxidant at adequate nutritional levels via selenoprotein and as a pro-oxidant at supranutritional levels (Kieliszek *et al.*, 2017). Redox-active selenium compounds that produce reactive oxygen species (ROS) are being explored as a new type of therapy targeting the imbalanced redox state in cancer cells. While high levels of ROS may promote cancer development, low levels maintain normal homoeostasis. (Soukupová & Rudolf, 2018). High-dose sodium selenite has demonstrated promising anti-cancer effects in preclinical studies (Soukupová & Rudolf, 2018; Nilsonne *et al.*, 2009), with greater cytotoxicity against cancer cells compared to normal cells at similar doses. The effects of selenite are primarily due to increased ROS levels from its intracellular metabolism; it targets multiple intracellular processes in cancer cells and can induce various cell death pathways. Given that numerous cancers develop resistance to apoptosis, selenite may overcome this resistance through alternative mechanisms (Rataan *et al.*, 2022). Furthermore, the observation of a tumor in the neck region of one rat in the DMBA + Se (200 µg/kg) group, while not histologically confirmed as metastasis, may represent secondary tumor spread. The longer duration of the experiment (23 weeks) compared to shorter studies (8–10 weeks) likely allowed for tumor progression and advanced manifestations such as metastasis (Russo and Russo, 1996), highlighting the importance of employing long-term experimental models to understand the later stages of carcinogenesis.

Histopathological analysis of the mammary glands in the DMBA-induced tumor group revealed marked architectural alterations. These included extensive proliferation of glandular and ductal epithelium, forming a prominent papillary pattern that infiltrated the duct wall and extended into the canal lumens. These features are indicative of a well-differentiated invasive adenocarcinoma, predominantly adenocarcinoma *in situ*, within a stroma rich in inflammatory infiltrates (Russo and Russo, 1996). Although the mammary tissues of rats treated with selenium at doses of 200 µg/kg and 400 µg/kg exhibited an architecture identical to that of the DMBA-treated group, the adipocyte volume was reduced, and the epithelial arrangement was closer to that of normal tissue, particularly in the high-dose selenium group. These findings suggest that selenium may exert partial protective effects on mammary tissue integrity during DMBA-induced carcinogenesis (El-Bayoumy *et al.*, 2001).

Our findings suggest that selenium, particularly at higher doses, may prevent DMBA-induced tumor growth and systemic toxicity through antioxidant and potential pro-oxidant actions. However, these findings do not provide strong evidence of a chemoprevention effect in this context.

5 Conclusions

Despite the absence of a significant inhibitory effect against the initial induction of DMBA-induced breast cancer, this study demonstrates that selenium supplementation (400 µg/kg body weight) significantly reduced the mass of established tumors. This effect may be attributed to the pro-oxidant role of selenium at higher concentrations. The redox potential of selenium is dependent on dosage, cell type, and genotype. Therefore, further investigation into the effects of even higher selenium doses (> 400 µg/kg body weight) is warranted to fully explore these findings.

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Conflicts of Interest: The authors declare no conflict of interest.

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