INVESTIGATION OF THE PHOTO-CYTOTOXICITY AND PHOTO-APOPTOTIC EFFECTS OF NALIDIXIC ACID IN MOUSE FIBROBLAST CELL LINE EXPOSED TO AMBIENT UVA RADIATION LEVEL

ALI, D.* – ALARIFI, S. – ALMUTAIRI, B. O. – ALMARZOUG, M. H. – ALKAHTANI, S.

Department of Zoology, College of Science, King Saud University, Riyadh, Saudi Arabia

**Corresponding author*
e-mail: aalidaoud@ksu.edu.sa; phone: +966-55-890-4621

(Received 12th Jul 2025; accepted 15th Oct 2025)

Abstract. In biomedical sciences, nalidixic acid has been used as a powerful antibiotic drug. In this investigation, we evaluated the photochemical characteristics of nalidixic acid as well as its potential for photocytotoxicity, apoptosis, and genotoxicity on the mouse fibroblast cell line (L929) over a 24-h period at ambient UVA (3.0 mW/cm2). The nalidixic acid produced singlet oxygen ($^1O_2$), superoxide anion radical ($O_2^{\bullet-}$) and hydroxyl radical ($^{\bullet}OH$) in a dose-dependent way. Also, nalidixic acid reduced GSH and induced LPO levels in UVA-irritated L929 cells as compared to dark control cells. In general, a significant concentration-dependent effect of nalidixic acid ($p < 0.05$) was detected in L929 cells under ambient environmental intensity of UVA (3 mW/cm^2) over 24 h. It was observed that photocytotoxicity and caspase-3 activity were induced significantly ($p < 0.05$) in L929 cells. Thus, our finding warrants that nalidixic acid can act as phototoxic and photo-apoptotic under UVA irradiation.
Keywords: *fluoroquinolone drugs, L929 cell line, ultraviolet a radiation, MTT, phototoxicity*

Introduction

UV radiation is one environmental stressor that has a significant impact on skin health. Long-term, continuous UV exposure has a number of negative effects that impair immune suppression, hasten photoaging, and raise the risk of skin cancer (Al-Sadek and Nabih, 2024). The longer wavelength UVA make up about 95% of the UV radiation that reaches the Earth's surface (WHO, 2016). The fluoroquinolone drugs are used extensively in clinical treatments and react when exposed to sunlight. Sun-sensitizing drugs that have side effects when people taking them are exposed to the sun. Some reactions are caused by exposure to the sun's UVB or "short wave", but most are caused by UVA or "long-wave" exposure (Bouchez, 2024). UVA rays can cause photosensitization reactions via penetrating the dermis or by reaching the dermal blood flow. Understanding the consequences of fluoroquinolone drugs for human safety is crucial due to their wide range of prospective and new applications (Patel and Goldman, 2016).

In this study, we investigate the photo-toxicity of nalidixic acid on UVA-exposed L929 cells. Nalidixic acid enters the environment, animals, trophic levels, and human body due to its widespread use in the treatment of urinary tract disorders. The medication nalidixic acid is used as an antibacterial agent to lower chicken illnesses (Johnson et al., 2007) and boost fish farming output (Guiberteau et al., 2012) by improving water quality and reducing infection. In order to attain the proper therapeutic concentrations, nalidixic acid in pharmaceutical goods must be closely monitored. As a result, the presence of these compounds poses a serious threat to the health of both humans and animals. According to several studies, nalidixic acid caused negative cutaneous effects when combined with UV or visible light. Simran et al. (2014) state that reactive oxygen species (ROS) produced by the mitochondria play a part in both stress signaling in healthy cells and the

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

initiation of nuclear or mitochondrial DNA changes that promote neoplastic transformation. Mitochondrial dysfunction results from excessive ROS generation (Schumacker et al., 2014). ROS generation and apoptosis are the fundamental processes of medication phototoxicity (Deavall et al., 2012). In many pathophysiological processes, oxidative stress and inflammation are linked (Biswas, 2016). This investigation looked at how nalidixic acid affected the toxicity and susceptibility of L929 cells to UVA radiation.

Materials and methods

Chemical and reagents

Sigma Aldrich USA was the supplier of nalidixic acid (N8878), chlorpromazine (C8138), RNO, NBT, TBA, trichloroacetic acid, NADPH, and L-histidine. Other chemicals were bought from the Riyadh, Saudi Arabia, local market.

Design for experiments

Nalidixic acid was dissolved in Milli-Q double distilled deionized water. Potential, conductivity, pH, and absorption spectra of chemically reactive oxygen species (ROS) were examined. The experiment uses rose bengal, a positive photosensitizer (Young, 1997). The experiments involved a 30-minute exposure to UV-A radiation.

The UV-A radiation levels in sunlight were measured using the UV340B UV light meter (China). Mean UVA (3 ± 1 mW/cm2) was used in the experiment. The temperature and relative humidity throughout the exposure times ranged from 27 to 36°C and 30 to 46%, respectively.

Corning glass petri plates (15 × 60 mm) were used to produce three duplicates of each of the three sets of reaction mixtures. One set was exposed to nalidixic acid under UVA light for half an hour while the other was kept in the dark as a control. Petri dishes were set on a platform with ice packs to prevent thermal change during UVA exposure (Polar Tech Industries, USA). The experiment was carried out in triplicate.

Photochemical assays

Measurement of singlet oxygen ($^1O_2$) generation

Reaction mixture having N, N-dimethyl-p-nitrosoaniline (RNO, 3.5×10^{-5} M), histidine (10^{-2} M) and nalidixic acid, chlorpromazine and nalidixic acid (8 µg/µl) in 0.01 M phosphate buffer (pH 7.4) was exposed under UVA for 30 min. The bleaching of RNO was recorded spectrophotometrically at 440 nm against the control (Ali et al., 2010).

Measurement of superoxide (O_2^-) generation

Reaction mixture having nitro blue tetrazolium (NBT, 1.67×10^{-4} M) and nalidixic acid, chlorpromazine and nalidixic acid (8 µg/µl) in 0.01 M carbonate buffer (pH 10.0) was exposed under UVA for 30 min. Reduction of NBT to nitro blue formazan was observed at 560 nm (Ali et al., 2010).

Measurement of ·OH radicals

The generation of hydroxyl (·OH) radicals was determined according Cohen method (Cohen and Heikkila, 1974). Then, using the technique suggested by Nash (1953), the

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

samples were examined for the production of formaldehyde. At 412 nm, the formaldehyde production was seen. Mannitol (0.5 M) and sodium benzoate (0.5 M) were used as specialized quenchers to further quench the ·OH.

Cell culture

The mouse fibroblast cell line L929 was grown in DMEM culture medium with 10% FBS and antibiotic-antimycotic solution (1%) at CO_2 (5%) and RH (95%) at 37°C in CO_2 incubator.

Photo toxicity assay

MTT assay

The MTT assay is based on the protocol described by Ali et al. (2011) with minor modifications. Briefly, chlorpromazine (5.0 µg/ml) and l-histidine (100 µg/ml) were used as positive and negative controls, respectively.

Neutral red uptake test

The NRU assay is based on the initial protocol described by Borenfreund and Puerner (1985) and determines the accumulation of the neutral red dye in the live lysosomes. The absorbance was recorded at 540 nm by using multi-well micro plate reader (BioTek Synergy H1, St. Louis, USA).

Determination of intracellular ROS generation

According to the procedures outlined by Ali et al. (2011), the production of ROS in L929 cells as a result of drug exposure to nalidixic acid (8 µg/mL) under UVA irradiation was carried out using H2DCFDA. Following incubation, the culture plate was rinsed with cold PBS, and a plate reader (Spectra MAX Gemini EM, Molecular Devices) was used to measure the fluorescence of dichlorofluorescein at 480 nm excitation and 530 nm emissions.

We also set up another experiment in a 6-well transparent plate (1×10^3 cells/well) to qualitatively analyze the generation of ROS in cells caused by the drug nalidixic acid (8 µg/ml) under UVA irradiation. Intracellular ROS generation was observed using a fluorescent microscope (Olympus CKX41; Olympus: Center Valley, Pennsylvania), with images taken at ×10 magnification.

Oxidative stress

Cell lysate

After 20 min of exposure to UVA (3.0 mW/cm^2) irradiation, L929 cells were treated to the antibiotic medication nalidixic acid (8 µg/ml) and incubated in a CO_2 incubator for the night in order to observe oxidative parameters. Following exposure, cells were scraped into an Eppendorf tube and washed with PBS. Scraped cells were combined with lysis buffer, centrifuged for 15 min at 4°C at 13000 rpm, and the cell lysate (supernatant) was placed on ice for additional tests for lipid peroxide (LPO) and reduced glutathione (GSH). Using BSA as the standard, the Bradford method (1976) was used to determine the amount of total protein in the cell lysate.

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

GSH test

The GSH content was evaluated according to Ellman's method (1959).

LPO test

LPO was measured according to the Alarifi et al. method (2017).

Evaluation of caspase-3 activity

In order to determine the caspase-3 activity in L929 cells, the cells were cultured in a CO_2 incubator for the entire night after being co-exposed to the medicines nalidixic acid (8 µg/mL) and UVA (3.0 mW/cm^2) for 20 min. Following the manufacturer's instructions, a colorimetric kit (Cayman Chemical) was used to measure the amount of caspase-3 activity in L929 cells.

Phosphatidylserine expression in L929 cells

After 20 min of co-exposure to nalidixic acid (8 µg/mL) and UVA (3.0 mW/cm^2) irradiation, L929 cells were cultured in a CO_2 incubator for the entire night in order to monitor the translocation of PS (an indicator of early apoptosis). Following the guidelines provided by the kit's manufacturer (Santa Cruz Biotechnology, Santa Cruz, CA, USA), staining was carried out. To put it briefly, cells were suspended in 200 µl of binding buffer and allowed to sit at room temperature for 30 min while being treated with 5 µl of Annexin V-FITC. Following the addition of 10 µl of propidium iodide, stained cells were seen under a confocal microscope.

Statistical analysis

Each experiment was conducted in duplicate in at least three separate experiments. The data were evaluated using one-way analysis of variance (ANOVA) and presented as mean (±S.E.). Statistical significance was defined as a p-value greater than 0.05.

Results

Photochemically, UVA-photosensitized nalidixic acid generates $^1O_2$, $O_2^{\bullet-}$, and $^{\bullet}OH$

In a concentration-dependent style, photosensitized nalidixic acid produced $^1O_2$, $O_2^{\bullet-}$, and $^{\bullet}OH$ (*Figs. 1, 2,* and *3*). ROS formation was not significant at lower concentrations, but it was substantial at higher doses. Under UVA exposure, $^1O_2$ generation increased linearly from the lowest to the highest values (*Fig. 1A, B*). Under both UVA irradiation, a significant amount of $O_2^{\bullet-}$ was generated in all nalidixic acid concentrations (*Fig. 2A, B*). UVA-exposed samples showed the lowest and highest concentrations of $^{\bullet}OH$ radical production. (*Fig. 3A, B*).

Viability of cells

Nalidixic acid exposure (0, 1, 8, 20, 40, 80, and 120 µg/mL) over 24 h was found to affect the cell viability of L929 cells. The cytotoxicity data were displayed in *Figure 4*. Cells were made cytotoxic by nalidixic acid in a concentration-dependent manner. Nalidixic acid had the maximum toxicity in cells at 120 µg/mL (*Fig. 4*).

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

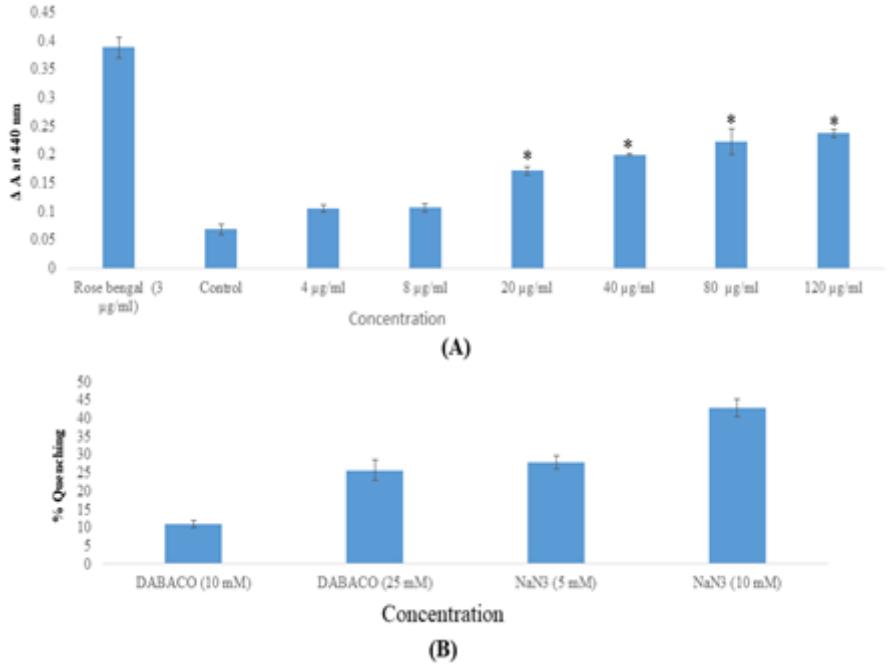

Figure 1. *(A) Photochemical generation of $^1O_2$ under UVA (3.0 mW/cm^2) by nalidixic acid at various concentrations. Rose Bengal used as positive control. (B) Percent photochemical quenching of $^1O_2$ under UVA (3 mW/cm^2) at nalidixic acid (80 µg/mL). Each value represents the mean ± SE of three experiments. *p < 0.05 vs. control*

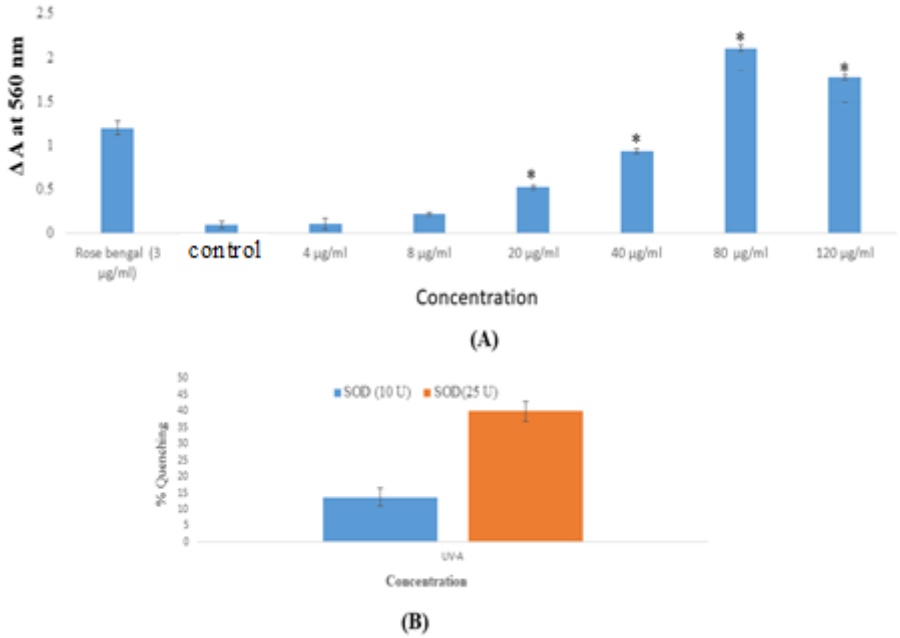

Figure 2. *(A) Photochemical generation of $^1O_2$ under UVA (3 mW/cm^2) by nalidixic acid at various concentrations. Rose Bengal used as positive control. (B) Percent photochemical quenching of $^1O_2$ under UVA (3 mW/cm^2) at nalidixic acid (80 µg/mL). Each value represents the mean ± SE of three experiments. *p < 0.05 vs.* control

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

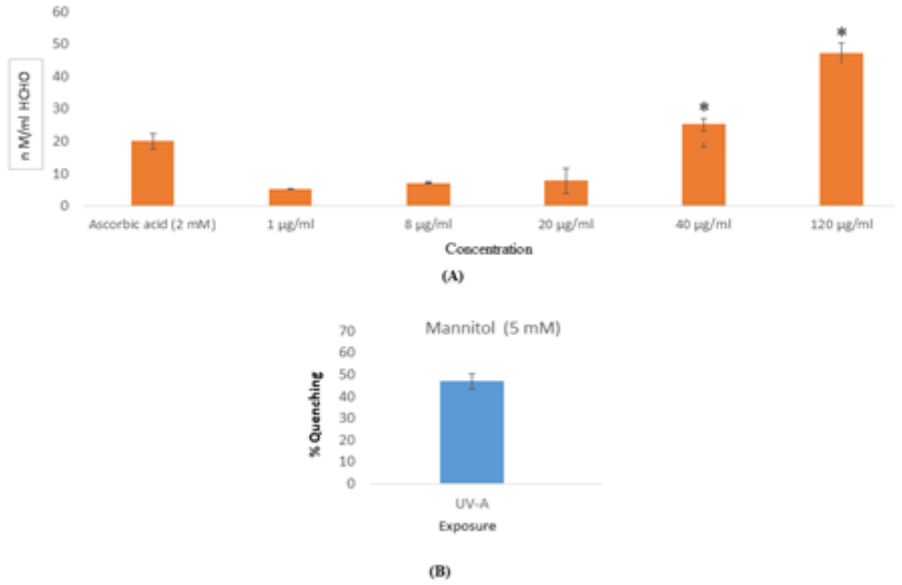

Figure 3. *(A) Photochemical generation of ˙OH under UVA (3 mW/cm^2) by nalidixic acid at various concentrations. Ascorbic acid used as positive control. (B) Percent photochemical quenching of ˙OH under UVA (3 mW/cm^2) at nalidixic acid (8 µg/mL). Each value represents the mean ± SE of three experiments. *p < 0.05 vs. control*

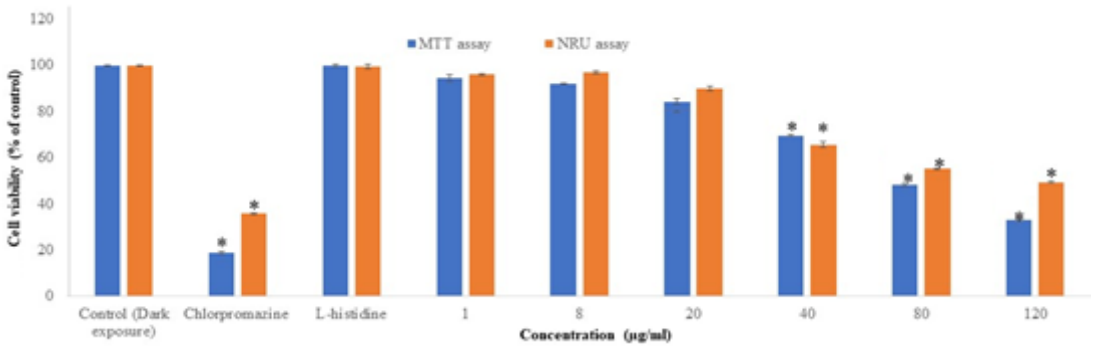

Figure 4. *Cytotoxicity of nalidixic acid on L929 cells under UVA (3.0 ± 1 m/cm^2) using MTT and NRU assays. Chlorpromazine (5 µg/mL) and L-histidine (20 µg/mL) were used positive and negative control, respectively. Each value represents the mean ± SE of three experiments. *p > 0.5 vs. control*

Nalidixic acid triggered by UVA increases the formation of ROS inside cells

Intracellular ROS were produced by photoexcited nalidixic acid in a concentration-dependent manner (*Fig. 5 A, B*). Percent DCF fluorescence was determined under UVA irradiations and it was induced as per concentration dependent manner (*Fig. 5A, B*). While experimental sets demonstrated a notable increase in fluorescence as a result of increased oxidative stress and intracellular ROS production, dark control samples did not exhibit DCF fluorescence (*Fig. 5A, B*). The ROS generation was concentration as well as exposure dependent. Maximum ROS were observed under UVA at 8 µg/mL (*Fig. 5A, B*). Cells photograph under UVA radiation had increased green fluorescence in comparison to the dark control (*Fig. 5B*).

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

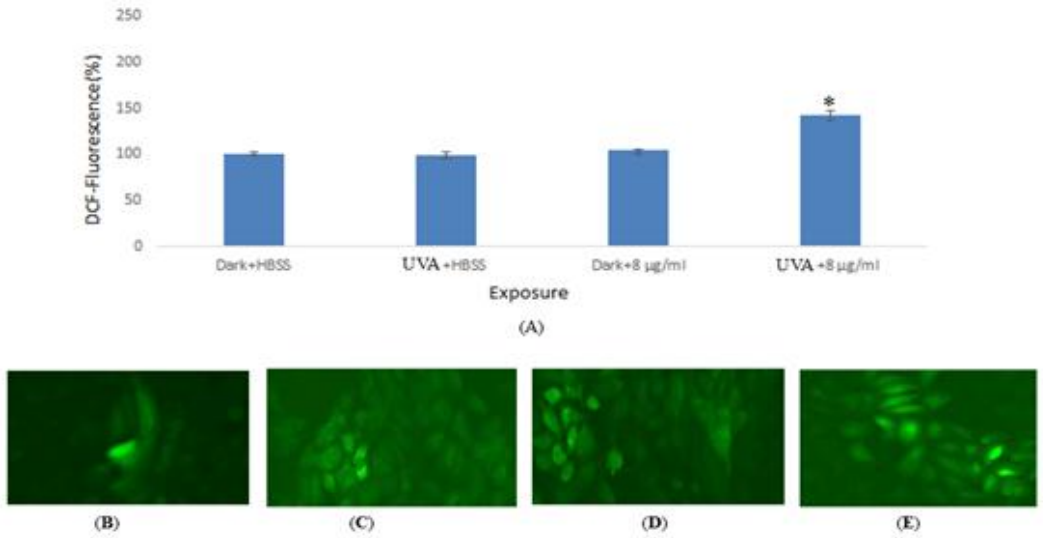

Figure 5. *Intracellular ROS generation in L929 cells as a result of nalidixic acid exposure to UVA (3 mW/cm^2) using (A). Percent of DCF fluorescence intensity and generation of green fluorescence in L929 cells for 24 h (B). L929 cells under dark (C). L929 cells at UVB + HBSS (D). L929 cells at dark + 8 ug/mL (E). L929 cells at 80 ug/mL + UVA. Each value represents the mean ± SE of three experiments. *p < 0.05 vs. control*

Oxidative stress assay

Lipid peroxidation, is a complex chemical process that leads to oxidative degradation of lipids, resulting in the formation of peroxide and hydroperoxide derivatives. It occurs when free radicals, specifically ROS, interact with lipids within cell membranes. This reaction leads to the formation of lipid radicals, referred to as lipid peroxides or lipid oxidation products, which in turn react with other oxidizing agents, leading to a chain reaction that results in oxidative stress and cell damage. The results showed that activity of lipid peroxidation increased in of L929 cells each in a dose dependent manner as shown in *Figure 6*. The results showed that glutathione after treatment with different concentrations of nalidixic acid under UVA exposure in L929 cell line were significantly increased compared to the control *Figure 6*.

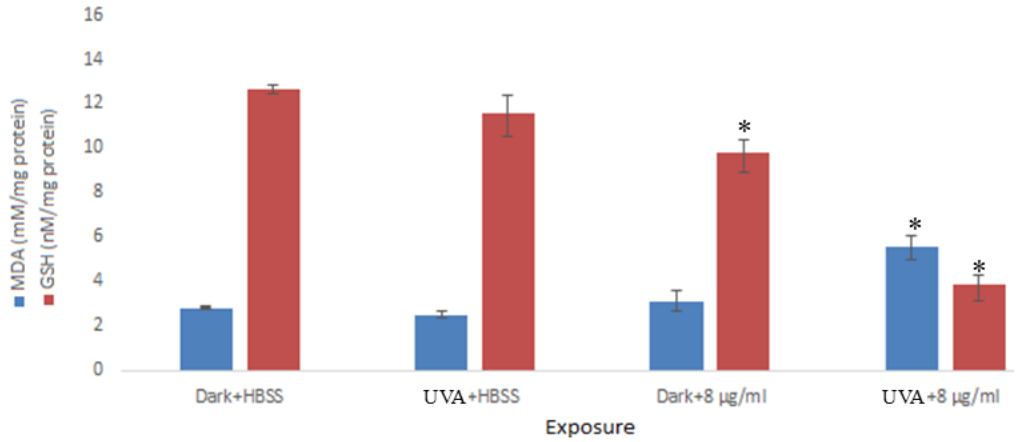

Figure 6. *Nalidixic acid under UVA (3 mW/cm^2) induced LPO and glutathione in L929 cells for 24 h. Each value represents the mean ± SE of three experiments. *p < 0.05 vs. control*

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

Caspase-3 activity

The L929 cells showed a substantial increase in caspase-3 activity (*Fig. 7*). The findings indicated that the caspase-3 enzyme levels for dark, UA alone, nalidixic acid alone, and nalidixic acid + UVA exposures were 0.090, 0.21, 0.14, and 1.23 a.u, respectively. When the experimental and control sets for caspase-3 activity were compared, the former demonstrated a notable rise in enzyme activity (*Fig. 7*).

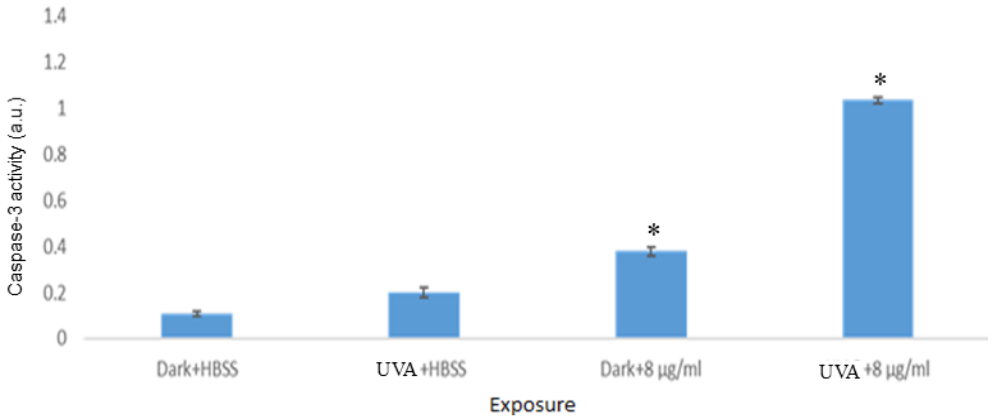

Figure 7. *Nalidixic acid under UVA (3 mW/cm^2) induced caspase-3 in L929 cells for 24 h. Each value represents the mean ± SE of three experiments. *p < 0.05 vs. control*

Phosphatidylserine translocation

Cells showed increased early apoptosis under nalidixic acid with UVA exposure (*Fig. 8*). Control L929 cells displayed no green fluorescence and UVA-exposed cells showed apoptotic cells which appeared orange-green due to merging of both red and green dye (*Fig. 8*). UVA-exposed cells also showed some bright red necrotic cells (*Fig. 8*).

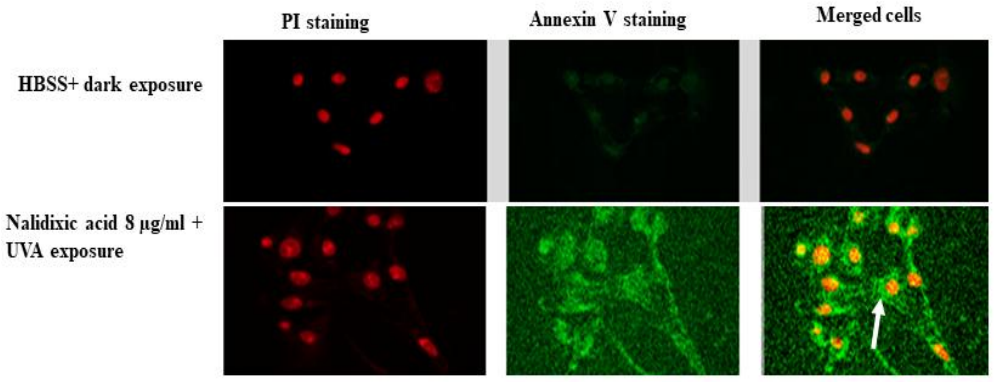

Figure 8. *Phosphatidylserine translocation in L929 cells after treatment of nalidixic acid for 24 h. Arrow is showing early and late apoptotic L929 cells. Arrow indicate phosphatidylserine translocation*

Discussion

The current study investigates a novel understanding of how photosensitized nalidixic aid generates intracellular ROS, which causes cell toxicity and damage to cell organelles

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

like mitochondria and lysosomes. Additionally, it produced glutathione and LPO, two photo-biomarkers of oxidative stress. The L929 could eventually develop apoptosis and cytotoxicity as a result of all these incidents. Nalidixic acid was photosensitized by UVA irradiation, which led to the production of ROS. Normal cell functions include the generation of ROS and their concomitant quenching by the cellular defense system. However, excessive intracellular ROS generation can interact with the nucleus, membrane-bound organelles, and other macromolecules, ultimately having a damaging effect on the cell. Photosensitized drugs may not always cause apoptosis in response to non-phototoxic UV light doses. However, higher levels of UV rays may trigger the fatal process that may end up with apoptosis (Valencia and Kochevar, 2008). When a photolabile drugs interacts with UVA radiation at a suitable dose, adverse phototoxic responses are anticipated. The structure of nalidixic acid was altered by UVA exposures, resulting in photodegradation and the potential production of photoproducts. Under non-lethal UVA levels, nalidixic acid produced $^1O_2$ and $O^{\bullet -2}$, demonstrating the involvement of both type I and type II photodynamic processes. This could be the reason why L929 cells have higher intracellular ROS levels. According to Tsubone et al. (2017), compounds specific to mitochondria and lysosomes also encourage photoinduced apoptosis. When hydroxychloroquine triggers lysosome-initiated apoptosis, a crucial step is mitochondrial membrane permeabilization (Boya et al., 2003). Released caspase enzymes assist in the apoptotic pathway's start. Apoptotic induction depends strongly on the subcellular location and the entire dosage of photosensitizer. Furthermore, there was a notable rise in LPO and a decline in glutathione. Additionally, a notable rise in apoptosis and intracellular ROS production were examined. The generation of intracellular reactive oxygen species was investigated in this experiment, and it increased in a dose-dependent manner. As a result, the production of ROS was higher in cells at higher concentrations. Using Annexin-V-FITC staining, we found that nalidixic acid exhibits an apoptotic response when exposed to UVA. Under UVA irradiation, larger concentrations of nalidixic acid caused the induction of necrotic and apoptotic cells. Based on the aforementioned results, we validated that nalidixic acid caused toxicity when exposed to UVA light. Based on our research, we found that L929 cells are susceptible to nalidixic acid when exposed to UVA light. In the future, we will investigate the toxicity of nalidixic acid in an in vivo model exposed to UVA.

Acknowledgments. This project was funded by the National Plan for Science, Technology and Innovation (MAARIFAH), King Abdul-Aziz City for Science and Technology, Kingdom of Saudi Arabia, Award Number (2-17-01-001-0031).

Conflict of interests. The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

[1] Alarifi, S., Ali, D., Alkahtani, S. (2017): Oxidative stress-induced DNA damage by manganese dioxide nanoparticles in human neuronal cells. – Biomed Res Int. 5478790.

[2] Ali, D., Ray, R. S., Hans, R. K. (2010): UVA-induced cyototoxicity and DNA damaging potential of Benz (e) acephenanthrylene in human skin cell line. – Toxicology Letters 199(2): 193-200.

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420

[3] Ali, D., Verma, A., Mujtaba, S. F., Dwivedi A., Hans, R. K., Ray, R. S. (2011): UVB-induced apoptosis and DNA damaging potential of chrysene via reactive oxygen species in human keratinocytes. – Toxicology Letters 204: 199-207.
[4] Al-Sadek, T., Nabih, Y. (2024): Ultraviolet radiation biological and medical implications. – Curr Issues Mol Biol. 46(3): 1924-1942.
[5] Biswas, S. K. (2016): Does the interdependence between oxidative stress and inflammation explain the antioxidant paradox? – Oxid Med Cell Longev 5698931.
[6] Borenfreund, E., Puerner, J. A. (1985): Toxicity determined in vitro by morphological alterations and neutral red absorption. – Toxicol Lett. 24(2-3): 119-24.
[7] Bouchez, C. (2024): Sun-sensitizing drugs. – https://www.webmd.com/skin-problems-and-treatments/sun-sensitizing-drugs.
[8] Boya, P., Gonzalez-Polo, R. A., Poncet, D. et al. (2003): Mitochondrial membrane permeabilization is a critical step of lysosome-initiated apoptosis induced by hydroxychloroquine. – Oncogene 22: 3927-3936.
[9] Bradford, M. M. (1976): A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein dye binding. – Anal. Biochem. 72: 248-254.
[10] Cohen, G., Heikkila, R. E. (1974): The generation of hydrogen peroxide, superoxide radical, and hydroxyl radical by 6-hydroxydopamine, dialuric acid, and related cytotoxic agents. – J Biol Chem. 249(8): 2447-52.
[11] Deavall, D. G., Martin, E. A., Horner, J. M., Roberts, R. (2012): Drug-induced oxidative stress and toxicity. – Journal of Toxicology 645460.
[12] Ellman, G. L. (1959): Tissue sulfhydryl groups. – Arch Biochem Biophys 82: 70-7.
[13] Guiberteau, C. A., Rodríguez Cáceres, M. I., Martínez Cañas, M. A., Ortiz Burguillos, J. M., Galeano Díaz, T. (2007): Square wave adsorptive stripping voltametric determination of the mixture of nalidixic acid and its main metabolite (7-hydroxymethylnalidixic acid) by multivariate methods and artificial neural network. – Talanta 72(3): 932-940.
[14] Johnson, J. R., Murray, A. C., Gajewski, A., Sullivan, M., Snippes, P., Kuskowski, M. A., Smith, K. E. (2003): Isolation and molecular characterization of nalidixic acid-resistant extraintestinal pathogenic Escherichia coli from retail chicken products. – Antimicrob Agents Chemother. 47(7): 2161-8.
[15] Nash, T. (1953): The colorimetric estimation of formaldehyde by means of the Hantzsch reaction. – Biochem, J. 55: 416-421.
[16] Patel, K., Goldman, J. L. (2016): Safety concerns surrounding quinolone use in children. – J Clin Pharmacol. 56(9): 1060-1075.
[17] Schumacker, P.T, Gillespie, M. N., Nakahira, K., Choi, A. M. K., Crouser, E. D., Piantadosi, C. A., et al. (2014): Mitochondria in lung biology and pathology: more than just a powerhouse. – Am J Physiol Lung Cell Mol Physiol 306(11): L962-L74.
[18] Tsubone, T. M., Martins, W. K., Pavani, C., Junqueira, H. C., Itri, R., Baptista, M. S. (2017): Enhanced efficiency of cell death by lysosome-specific photodamage. – Sci Rep. 7(1): 6734.
[19] Valencia, A., Kochevar, I. E. (2008): Nox1-based NADPH oxidase is the major source of UVA-induced reactive oxygen species in human keratinocytes. – Journal of Investigative Dermatology 128(1) 214-222.
[20] WHO (2016). Radiation: Ultraviolet (UV) radiation 2016. https://www.who.int/news-room/questions-and-answers/item/radiation-ultraviolet-(uv).
[21] Young, D. S. (1997): Effects of drugs on clinical laboratory tests. – Ann Clin Biochem. 34(Pt 6): 579-81.

http://www.aloki.hu ● ISSN 1589 1623 (Print) ● ISSN 1785 0037 (Online)
DOI: http://dx.doi.org/10.15666/aeer/2306_1141111420