A comparative study of the healing effects of sesame oil and TiO_2 nanoparticles gel on second-degree burn

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ABSTRACT

Burns, a severe form of soft tissue injury, can cause significant damage and, in extreme cases, be fatal. They also lead to considerable mental and emotional distress due to excessive scarring and skin contractures. Despite various treatment methods, burn care remains a challenging medical issue.

In this study, titanium dioxide (TiO_2) nanoparticles were synthesized and characterized using Field Emission Scanning Electron Microscopy (FE-SEM), revealing particle sizes ranging from 31.52 to 69.08 nanometers.

The impact of biosynthetic nanomaterials and sesame seed oil on burn healing in laboratory rats was investigated. The study compared the effects of a 1% TiO_2 solution and 20% sesame oil on burned skin with a control group of rats having natural skin. Fifteen rats were divided into three groups, each receiving daily treatment for 28 days. The results indicated that the TiO_2 treatment significantly accelerated healing compared to the sesame seed oil group, which had a slower healing rate of 0.12 points per day. The TiO_2 treatment demonstrated a marked improvement in healing speed and effectiveness.

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1. INTRODUCTION

Burns are a critical global health issue, with severe cases profoundly impacting patients' financial, psychological, and physical well-being. The complications from burns, such as hypermetabolism, sepsis, and increased mortality risk, underscore the urgency for effective treatment. Immediate and appropriate care is essential to accelerate wound healing, a complex process that replaces damaged tissue with healthy tissue. The wound healing process, extensively studied by researchers, primarily aims to minimize scarring and improve recovery outcomes [1]. This process is characterized by several stages: hemostasis, inflammation, proliferation, and tissue remodeling [2]. Recent advancements in nanoparticle-based medicines have significantly improved the diagnosis and treatment of various diseases. By manipulating the size, shape, and surface properties of nanoparticles[3], researchers have developed innovative systems that can encapsulate therapeutic and imaging agents with precision [4,5]. These smart nanostructures are meticulously engineered to be biocompatible, ensuring they do not trigger an immune response upon administration [3]. The potential of nanoparticles in medical applications continues to expand, offering promising avenues for more effective and targeted treatments.

Titanium dioxide (TiO_2) is particularly promising for medical applications due to its unique nanostructures and properties, such as the ability to induce favorable cellular responses and maintain compatibility with bodily fluids [6]. TiO_2 is utilized in various biomedical fields, including drug delivery, antimicrobial activity, biosensing, and implant administration [7]. Recent studies have demonstrated that TiO_2 nanoparticles can significantly enhance the healing process of skin wounds, positioning it as a valuable component in advanced wound care [8].

Sesamum indicum L., commonly known as sesame, is a nutritionally rich plant that provides substantial amounts of oil, protein, and carbohydrates alongside essential vitamins (A, B, D, and E), minerals, and amino acids. Sesame oil, a traditional oilseed used extensively in cooking and as an industrial ingredient, contains bioactive compounds such as sesamin, sesamol, sesamolin, sesaminol, and episesamin [9]. Among these, sesamin, the primary component of lignin present in sesame oil, is notably effective in enhancing liver detoxification, protecting against oxidative stress, and reducing hypertension [10]. Additionally, sesame oil's anti-inflammatory properties contribute to its potential in managing chronic conditions associated with oxidative stress. Sesame oil has also been found to be beneficial in promoting burn wound healing when applied orally or topically. Topical application is particularly effective in accelerating the healing process of second-degree burns by promoting collagen synthesis and reducing inflammation [11].

This study investigates the effects of nano-titanium dioxide (TiO_2) on burn wound healing through in vivo evaluations. Specifically, it compares the efficacy of sesame oil extract and nano-TiO_2 in promoting the healing of burn wounds.

2. METHOD

This study investigated the effects of titanium dioxide nanoparticles (TiO_2) and sesame seed oil extract on burn wound healing through a series of in vivo experiments. The methods employed in this study are detailed below.

2.1. Preparation of titanium dioxide nanoparticles

Titanium dioxide nanoparticles (TiO_2-NPs) were synthesized using the sol-gel method. Initially, 10 mL of deionized water was mixed with 10 mL of concentrated hydrochloric acid (HCl) to create a slightly acidic solution. To this mixture, titanium (IV) isopropoxide was added dropwise under continuous stirring to form a homogenous sol. The resulting sol was transferred into a Teflon-lined stainless-steel autoclave containing a fluorine-doped tin oxide (FTO)-coated glass substrate. The autoclave was sealed and heated at 180 °C for varying durations of 1, 1.5, 2, and 3 hours to promote the formation of TiO_2-NPs. After the reaction, the autoclave was allowed to cool naturally to room temperature. The synthesized nanoparticles were then washed with deionized water and ethanol to remove impurities, followed by drying with nitrogen gas. Finally, the dried nanoparticles were annealed at 350 °C for 1 hour to enhance crystallinity and stability[12].

2.2. Preparation of sesame seed oil extract

Sesamum indicum seeds were obtained from local fields in the Diyala Governorate. The seeds were verified for species authenticity by the botanical herbarium at the College of Science, University of Baghdad. The seeds were processed using the Soxhlet extraction method with methanol as the solvent. Specifically, 100 grams of seeds were placed in a Soxhlet extractor, and 500 mL of methanol was used to extract the oil over 24 hours. The resulting extract was concentrated using a rotary evaporator to remove the solvent, yielding a thick, dark greenish-brown oil extract. This extract was stored at 4 °C until further use[13].

2.3. Characterization of extracts and nanoparticles

The chemical composition of the sesame seed oil extract was analyzed using Gas Chromatography-Mass Spectrometry (GC-MS). The analysis was conducted using an Agilent GC-MSD system with helium as the carrier gas. The system was equipped with a flame ionization detector (FID) for the separation and identification of compounds.

The morphology and size distribution of the synthesized TiO_2-NPs were characterized using Field Emission Scanning Electron Microscopy (FE-SEM). The particles were observed at a magnification of 100,000x to ensure detailed visualization of their structure and confirm their size distribution.

2.4. In Vivo burn wound model

Fifteen male Wistar rats, weighing between 195 and 230 grams, were housed in clean cages with unrestricted access to food and water. The rats were randomly divided into three groups of five animals each. All procedures involving animals were conducted in compliance with the ethical guidelines for the care and use of laboratory animals.

To induce second-degree burns, the rats were anesthetized using an intraperitoneal injection of xylazine (10%, 50 mg/kg) and ketamine (2%, 5 mg/kg). The dorsal surface of each rat was shaved, and a heated metal disc (3 cm in diameter) was applied to the skin for 10 seconds after being heated in hot water for 5 minutes. This procedure created a standardized deep second-degree burn wound on each rat[14].

2.5. Treatment and observation

The rats were treated with either a 1% TiO_2-NP gel, 20% sesame seed oil extract, or left untreated as a control group. Treatments were applied topically to the burn wounds once daily for 28 days. Wound healing progress was monitored by measuring the wound area at regular intervals using digital calipers.

2.6. Statistical analysis

Data were analyzed using SPSS version 23 and GraphPad Prism version 10. Results are presented as mean ± standard error. Group differences were assessed with a two-way ANOVA to evaluate the effects of treatment type and time on burn area reduction and to check for interaction effects. Post hoc comparisons were made using the least significant difference (LSD) test. Statistical significance was set at $p < 0.05$. A Repeated Measures ANOVA was also conducted to compare mean burn area reductions across treatments (Control, TiO_2, and Sesame Oil), accounting for within-subject correlations over time.

3. RESULTS AND DISCUSSION

a. GC-Mass analysis of essential oils

The individual components of the seed extract were identified through computer matching with commercial mass spectral libraries, including the Wiley GC/MS Library, 3 Mass Finder Library, and Baser Library, which are specifically tailored for endogenous essential oil components. These libraries contain data on over 3,200 authentic compounds, providing mass spectra and retention times for pure substances.

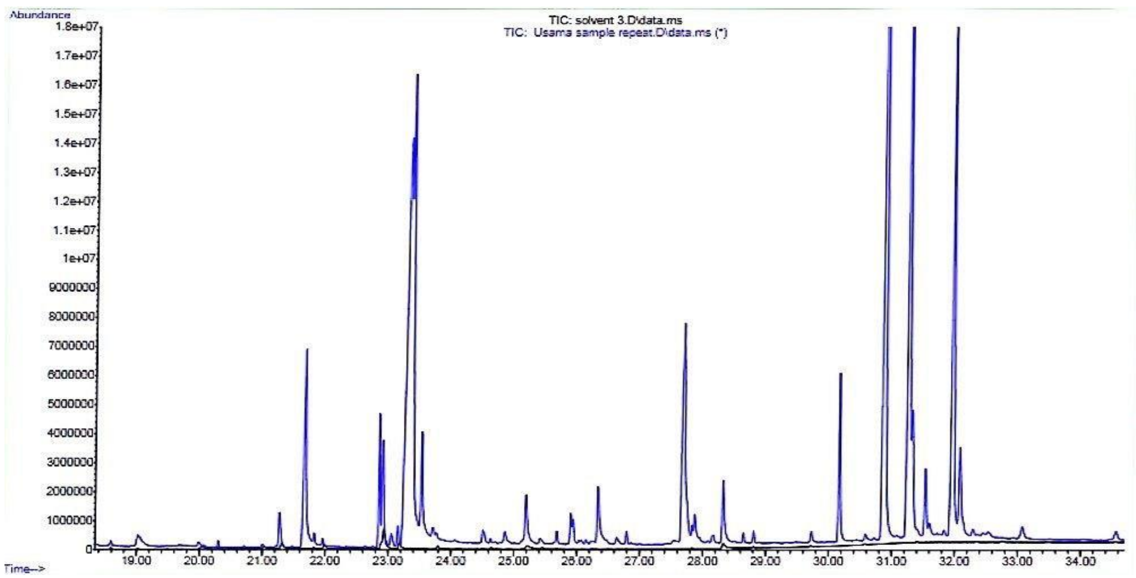
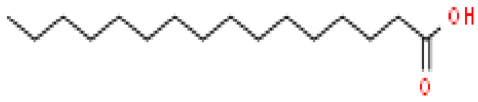
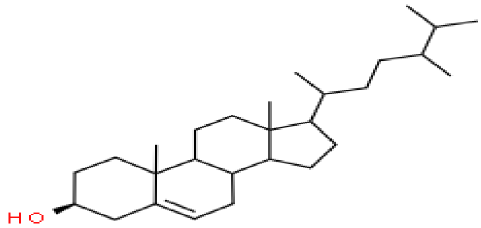
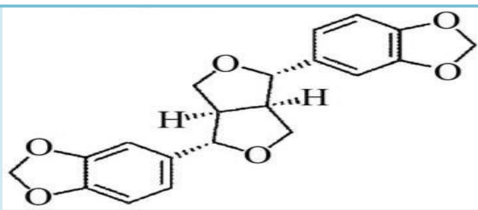
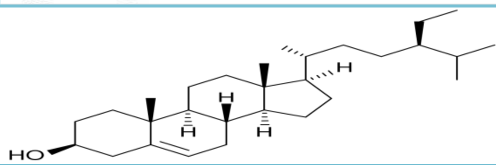
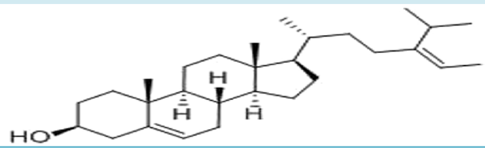
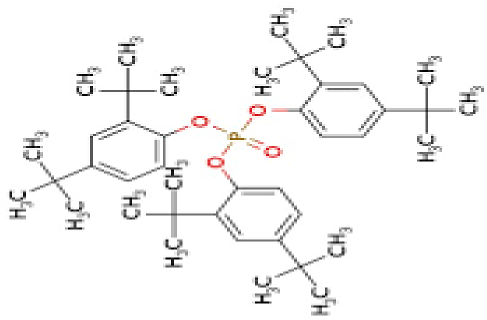
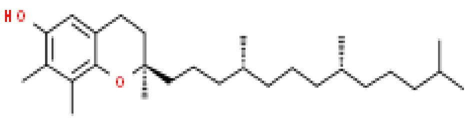


Figure 1. Gas Chromatography-Mass Spectrometry (GC-MS) analysis of *Sesamum indicum* seed extract

The analysis revealed that the extract contains several active compounds, including n-Hexadecanoic acid, Ergost-5-en-3-ol (3β), (+)-Sesame, gamma-Sitosterol, Fucosterol, Methyl 12-hydroxy-9-octadecenoate, Tris(2,4-di-tert-butylphenyl) phosphate, and beta-Tocopherol, as illustrated in Figure 1 and detailed in Table 1.

Table 1. Active compounds identified in *Sesamum indicum* seed extract

No.	Compound	Formula	Concentration (%)	Structure
1	n-Hexadecanoic acid	C16H32O2	3.817	
2	Ergost-5-en-3-ol, (3beta.)-	C28H48O	2.116	
3	(+) - Sesamin	C20H18O6	18.067	
4	gamma-Sitosterol	C29H50O	10.35	
5	Fucosterol	C29H48O	1.931	
6	Methyl 12-hydroxy-9-octadecenoate	C19H36O3	0.187	
7	Tris(2,4-di-tert-butylphenyl) phosphate	C42H63O4 P	0.205	
8	beta-Tocopherol	C28H48O2	2.088	

b. Morphological characterization of TiO_2 nanoparticles

Figure 2 presents a high-resolution field emission scanning electron microscopy (FE-SEM) image, magnified 100,000 times, illustrating the morphology of TiO_2 nanoparticles. The image reveals that the nanoparticles predominantly exhibit dense, irregular spheroidal shapes, with sizes ranging from approximately 31.52 to 69.08 nanometers. The nanoparticles are closely packed and display a rough surface texture, indicative of their aggregated form. This morphological description aligns with previous research, such as that conducted by Shi et al. (2018), which also observed similar irregular spheroidal structures in TiO_2 nanoparticles [15]. The detailed visualization provided by FE-SEM underscores the successful synthesis of TiO_2 nanoparticles, highlighting their potential applications in various fields, including photocatalysis and biomedical technologies.

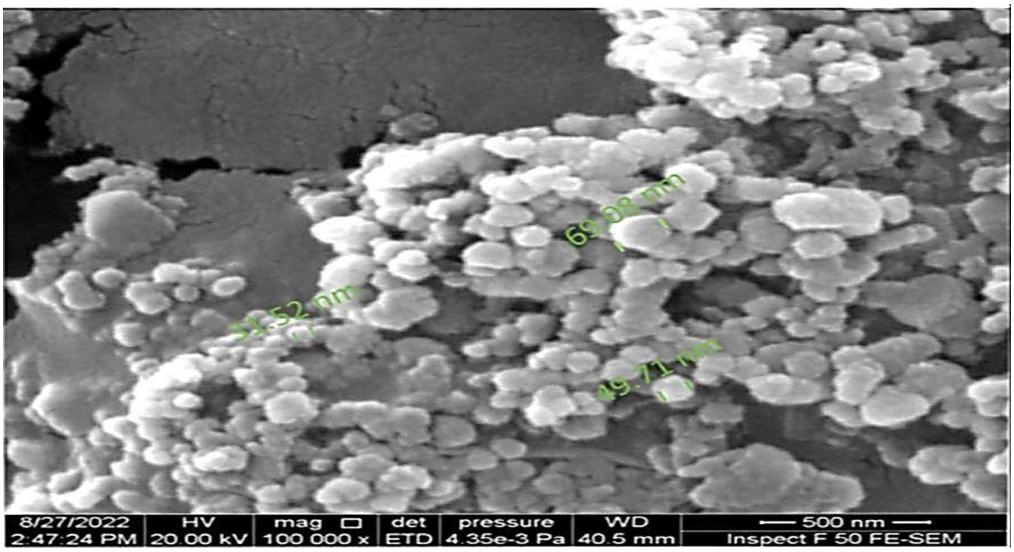


Figure 2. Field Emission Scanning Electron Microscopy (FE-SEM) Image Depicting the Morphology of TiO_2 Nanoparticles

c. Effect of TiO_2-NPs and *Sesamum indicum* seed extract on burn wound healing

This study aimed to evaluate the effects of titanium dioxide nanoparticles (TiO_2-NPs) and sesame oil (*Sesamum indicum*) on the healing of burn wounds in a rat model over four weeks. The results demonstrate differential therapeutic efficacies between these treatments over time (Figure 3).

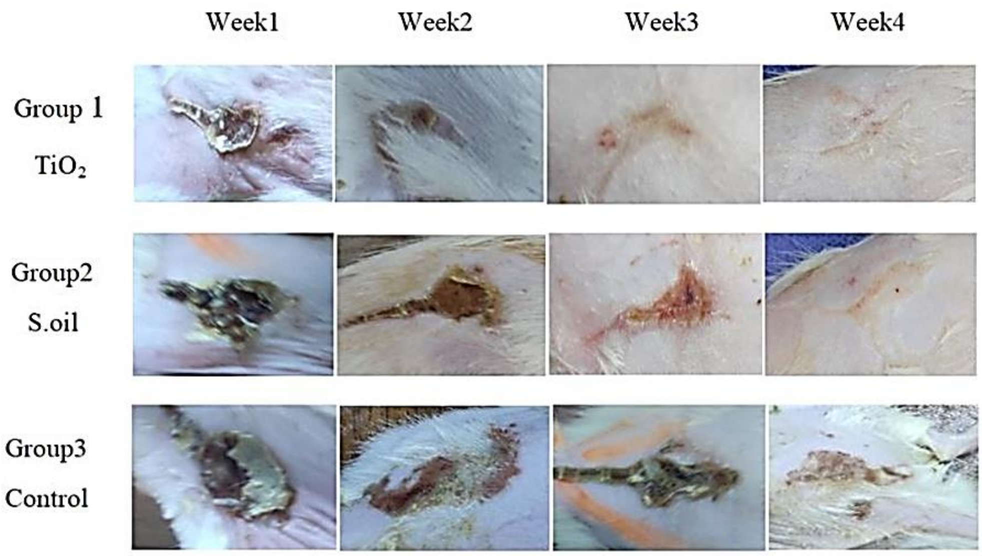


Figure 3. Healing stages of burn wounds in rats treated with TiO_2 nanoparticles and sesame oil

During the first week, there were no statistically significant differences in burn area reduction between the groups treated with TiO_2-NPs, sesame oil, and the control ($p > 0.05$). However, in subsequent weeks, TiO_2-NPs showed a significantly higher reduction in burn area, suggesting superior efficacy in enhancing wound healing. Specifically, TiO_2-treated rats demonstrated a significant decrease in burn area, with mean values dropping to 1.56 ± 0.67 in the second week, 0.23 ± 0.08 in the third week, and 0.013 ± 0.025 in the fourth week ($p < 0.05$) (Figure 4).

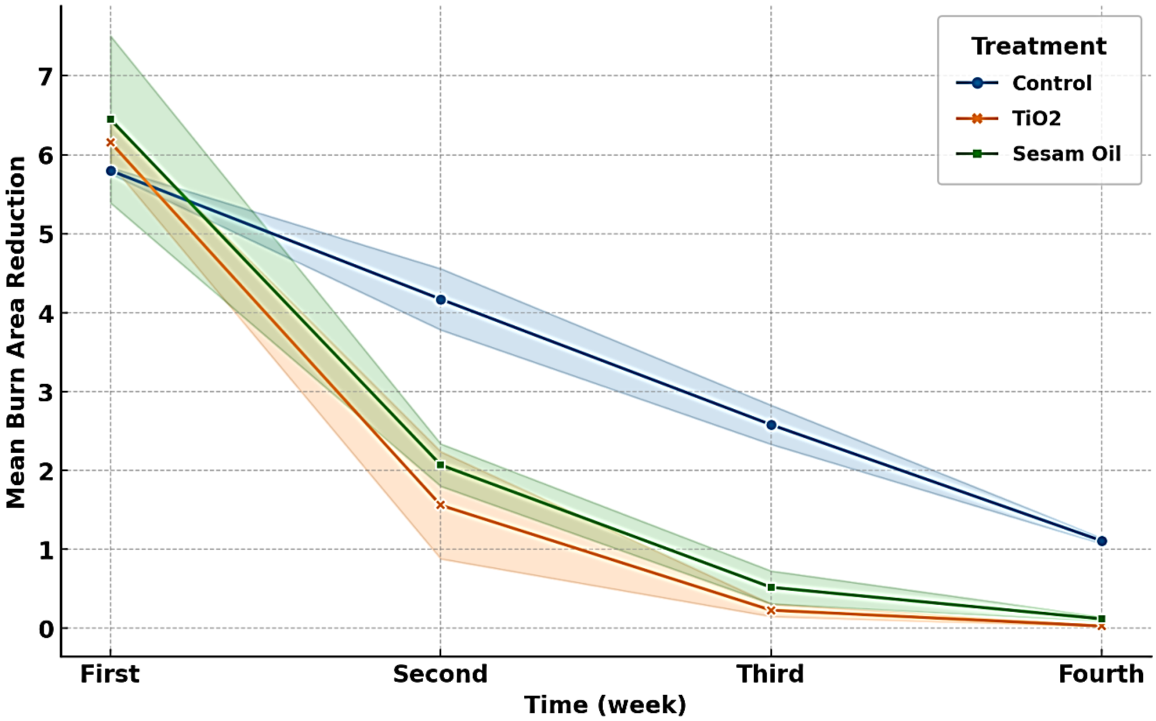


Figure 4. Comparative analysis of mean burn area reduction in rats treated with TiO_2 nanoparticles and sesame oil over four weeks

These findings align with those of Jafari et al. (2020), who reported that TiO_2-NPs exhibit potent bactericidal activity, inhibit bacterial growth, and reduce biofilm formation, thereby functioning as an effective broad-spectrum disinfectant that promotes wound healing [16].

The high biocompatibility of titanium dioxide also supports its effectiveness in wound healing. Upon application, TiO_2 forms a uniform, protective nano-film on the wound surface, which enhances tissue regeneration and minimizes scar formation. Nogueira et al. (2021) found that this effect could be attributed to TiO_2's photocatalytic properties, which facilitate cellular repair mechanisms and accelerate wound healing [17]. Furthermore, Seisenbaeva et al. (2018) demonstrated that TiO_2-NPs minimize scar formation on burn wounds, evidenced by a significant reduction in scar size in rats treated with nano-TiO_2 [18].

Sesame oil also positively influenced burn wound healing, particularly in the second and third weeks of treatment. The mean burn area reduction was 2.07 ± 0.265 in the second week and 0.52 ± 0.205 in the third week, with a further decrease to 0.12 ± 0.025 by the fourth week. Although its effects were less pronounced than those of TiO_2, sesame oil significantly enhanced epithelialization and neovascularization, contributing to faster wound contraction and reduced healing time. Cakmak Kafadar et al. (2022) found that sesame oil's beneficial effects are likely due to its antioxidant, anti-inflammatory, and antimicrobial properties, which promote tissue repair by enhancing fibroblast proliferation and angiogenesis [19].

Jangholi et al. (2016) corroborated these findings, noting that sesame oil-treated wounds showed more substantial reductions in wound area, collagen bundle volume density, hair follicle number, fibroblast population, and vessel length density compared to the control group, indicating enhanced wound healing ($p < 0.05$) [20]. Vaghardoost et al. (2018) further supported these results, emphasizing that sesame oil's effects on epithelialization and neovascularization contribute significantly to wound healing and contraction [14].

The Repeated Measures ANOVA confirmed significant main effects of both treatment type and time on burn area reduction ($p < 0.001$). There was also a significant interaction between treatment and time ($p < 0.001$), indicating that the efficacy of the treatments varied over the weeks. Notably, TiO_2 consistently showed the greatest improvement in burn reduction, reinforcing its potential as a powerful agent for burn treatment.

4. CONCLUSION

In conclusion, this study provides compelling evidence of the superior efficacy of nano-TiO_2 nanoparticles in promoting burn wound healing, showcasing a remarkable reduction in burn area over time. With nanoparticles ranging from 31.52 to 69.08 nanometers, effectively characterized through FE-SEM, nano-TiO_2 demonstrated a significantly faster healing rate in vivo compared to sesame seed oil, which also showed beneficial effects but to a lesser extent. These findings underscore the potential of nano-TiO_2 as a promising therapeutic agent for burn wound management, while sesame seed oil may serve as a valuable complementary treatment. Future research should delve deeper into the mechanisms by which these treatments enhance healing and further evaluate their applicability and effectiveness in clinical settings.

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REFERENCES

[1] Al-Dhuayan, I., Kotb, E., Alqosaibi, A., & Mahmoud, A. (2021). Histological studies on a newly isolated Bacillus subtilis D10 protease in the debridement of burn wound eschars using mouse model. Pharmaceutics, 13(7), 923.

[2] Apsari, R., Nahdliyatun, E., & Winarni, D. (2017, September). The regeneration of thermal wound on mice skin (Mus Musculus) after Q-Switch Nd: YAG laser irradiation for cancer therapy candidate. In AIP Conference Proceedings (Vol. 1888, No. 1). AIP Publishing.

[3] Khan, A. U., Khan, M., Cho, M. H., & Khan, M. M. (2020). Selected nanotechnologies and nanostructures for drug delivery, nanomedicine, and cure. Bioprocess and biosystems engineering, 43(8), 1339-1357.

[4] Heba.Y. Jassim1, Mustafa Hammadi. (2024) .Synthesis,Green Chemistry Method Characterization of CuFe5O8 Nanocomposite and Assessment of Its Prostate Cancer-Preventive Effects", IJApSc, (Vol. 1, No. 1, 81–87).

[5] Abdul Latif, B. M., & Mahdi Alzubaidy, M. W. (2023, May). Effect of zinc oxide nanoparticles on activity of skin cancer cell line (A-375). In AIP Conference Proceedings (Vol. 2593, No. 1). AIP Publishing.

[6] Hovazi, E., & Rostami, E. (2023). Fabrication, characterization, and biological applications of TiO2 nanoparticles coated by chitosan. Nanomedicine Research Journal, 8(1), 50-60.

[7] Baranowska-Wójcik, E. (2021). Factors conditioning the potential effects TiO2 NPs exposure on human microbiota: a mini review. Biological Trace Element Research, 199(12), 4458-4465.

[8] Nandhini, S. N., Sisubalan, N., Vijayan, A., Karthikeyan, C., Gnanaraj, M., Gideon, D. A. M., ... & Sadiku, R. (2023). Recent advances in green synthesized nanoparticles for bactericidal and wound healing applications. Heliyon, 9(2).

[9] Wei, P., Zhao, F., Wang, Z., Wang, Q., Chai, X., Hou, G., & Meng, Q. (2022). Sesame (Sesamum indicum L.): A comprehensive review of nutritional value, phytochemical composition, health benefits, development of food, and industrial applications. Nutrients, 14(19), 4079.

[10] Alborzi, Z., Izadi-Vasafi, H., & Ghayoumi, F. (2021). Wound dressings based on chitosan and gelatin containing starch, sesame oil and banana peel powder for the treatment of skin burn wounds. Journal of Polymer Research, 28, 1-16.

[11] Valizadeh, A., Shirzad, M., Pourmand, M. R., Farahmandfar, M., Sereshti, H., & Amani, A. (2020). Preparation and comparison of effects of different herbal oil ointments as wound-healing agents. Cells Tissues Organs, 207(3-4), 177-186.

[12] Mezzourh, H., Moumen, S. B., Amjoud, M., Mezzane, D., El Amraoui, Y., Marbati, B., ... & El Marssi, M. (2022). Effect of growth time on structural and surface properties of TiO2 nanostructures deposited by single-step hydrothermal method. Materials Today: Proceedings, 51, 2053-2058.

[13] Hassan, H. E., & Ahmed, S. H. (2023). Synergistic effect of Moringa Leaves and Antifungal on Candida albicans. Research Journal of Pharmacy and Technology, 16(3), 1369-1374.

[14] Vaghardoost, R., Majd, S. G. M., Tebyanian, H., Babavalian, H., Malaei, L., Niazi, M., & Javdani, A. (2018). The healing effect of sesame oil, camphor, and honey on second degree burn wounds in rat. World journal of plastic surgery, 7(1), 67.

[15] Shi, J., Chen, G., Zeng, G., Chen, A., He, K., Huang, Z., ... & Liu, W. (2018). Hydrothermal synthesis of graphene wrapped Fe-doped TiO2 nanospheres with high photocatalysis performance. Ceramics International, 44(7), 7473-7480.

[16] Jafari, S., Mahyad, B., Hashemzadeh, H., Janfaza, S., Gholikhani, T., & Tayebi, L. (2020). Biomedical applications of TiO2 nanostructures: recent advances. International journal of nanomedicine, 3447-3470.

[17] Nogueira, R. P., Deuzimar Uchoa, J., Hilario, F., Santana-Melo, G. D. F., De Vasconcellos, L. M. R., Marciano, F. R., ... & Lobo, A. O. (2021). Characterization of optimized TiO2 nanotubes morphology for medical implants: biological activity and corrosion resistance. International journal of nanomedicine, 667-682.

[18] Seisenbaeva, G. A., Fromell, K., Vinogradov, V. V., Terekhov, A. N., Pakhomov, A. V., Nilsson, B., ... & Kessler, V. G. (2017). Dispersion of TiO2 nanoparticles improves burn wound healing and tissue regeneration through specific interaction with blood serum proteins. Scientific reports, 7(1), 15448.

[19] Cakmak Kafadar, G., Büyükuslu, N., KOLBAŞI, B., Keskin, İ., & Mercan, Y. (2022). Effect of oral use of various edible oils on wound healing in rats: randomized controlled experimental study. Acta Pharmaceutica Sciencia, 60(2).

[20] Jangholi, E., Tehrani, S., Lotfi, P., Tehrani, S., Aryan, H., & Aidun, A. (2016). Healing effect of sesame ointment on second-degree burn wound in rats. Galen Medical Journal, 5(2), e658-e658.

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