Biosynthetic Sesame Oil and Nano Titanium Dioxide As a Therapy For Second Degree Burns

Osamah Riyadh Abbood[1], Mohanad W. Mahdi Alzubaidy[1], Ahmed Majeed AL-Shammari[2]

[1,2]Department of Biology, College of Education for Pure Sciences, University of Diyala, Iraq
Iraqi Center of Cancer and Medical Genetic Research – Mustansiriyah university

KEYWORDS
Sesamum Indicum Plant, Nano Titanium Dioxide, Healing Of Burn Wound, Organism

ABSTRACT
As the healing of burn wounds delay that affect the skin and lead to tearing and damage to its parts, as well as the remaining traces and scars on the skin because of exposure to heat, radiation, radioactivity, electricity, friction, or contact with chemicals, it has become necessary to investigate and discover effective medicines. Burns that affect the skin have an important purpose, Therefore, it is important to continue studying and experimenting with new and effective medicines, including effective nanomaterials, to reach efficient treatments to treat such injuries. In the current study, nanoparticles of titanium dioxide (TiO2) were prepared, and this material was examined using a device a Field Emission Electron Scanning Microscope (FE-SEM). The results obtained were on the nanoscale, with sizes ranging from (31.52-69.08) nanometers. The effectiveness and effect of biosynthetic nanomaterials and sesame seeds were investigated in vivo at a concentration of 1% TiO2 and 20% sesame oil on burns in the skin of laboratory rats and compared with a control group of natural skin of the same type of laboratory rats. They were also compared with rats treated with Mebo ointment. Randomly, 18 rats were put into three equal groups and treated once daily for 28 days. The results of the study showed effective activity and a noticeable speed in the healing of burns that affected the skin of laboratory rats using a nano-titanium dioxide preparation supported by sesame seed extract whose burn mean amounted to 0.005 compared to the control treatment, whose burn mean was 2.443. According to the current study's findings, using biosynthetic nano-titanium dioxide and sesame oil together results in better burn wound healing than using each of them separately.

1. Introduction

A burn is an injury affecting the skin or more organic tissues, usually resulting from exposure to heat or other forms of blunt trauma [1 Thermal burns result from the destruction of skin cells or other tissues due to exposure to hot liquids or hot solid substances or flame [2]. Burns may be the result of exposure to radiation, electricity, radioactivity, friction, or contact with chemicals [3]. Burn injuries typically show variation in depth, often affecting a combination of deep and superficial components [4]. Accurately determining the depth of a burn wound can be difficult in the early stages due to the dynamic nature of burn injuries. These wounds have the potential to progress and develop into deeper tissue damage over time [5]. Dividing the skin burns is according to the depth of tissue injury [6]. Healing potential and the necessity of surgical grafting are largely governed by the burn depth [7]. They are classified into first-degree burns, also known as skin burns [8]. Second degree burns wich known superficial [9]. Third ones, also known as complete burns [10]. Fourth-degree burns, deep, severe [11]. The Second are superficial, partial thickness burns affecting both the epidermis and some dermis and lead to damage to the upper layers of the papillary dermis [9]. Many experimental studies have described the beneficial effects of treating wounds, especially burn wounds, with natural materials. Medicinal plants and herbs around the world are valuable materials in the treatment of various diseases [12], due to their ease of use, effectiveness, and low cost when compared to expensive chemical treatments [13], as phytochemicals are natural compounds that have enormous antioxidant potential and are of great importance in providing health benefits against many diseases [14], and that each part of the plant has its own medicinal properties that possess different types of Secondary receptors as important in treating different types of diseases [15]. Natural products help in developing important therapeutic drugs in modern medicine and are a fruitful and logical study strategy for new analgesic and anti-inflammatory drugs [16]. Sesame (*Sesamum indicum L.*) is an oldest crop. Cultivated throughout human history, the most beneficial part of sesame is its seeds, of which approximately 75% of its mass has fat and protein [17]. It is known that sesame oil has about 5.1% lignans, including toxins and seminols. Also, its seed has vitamin B complex and eight critical amino acids, significant fo the function of liver cell as they are significant in cell oxygenation [18]. This substance controls the distinctive physiological and biochemical features of sesame oil, like its antioxidant, anti-mutagenic, and anti-inflammatory activities. Sesame oil also has an important role in treating burns and reducing resulting scars in record time because of its antioxidant and anti-inflammatory properties and effective materials in this aspect. [19]. Titanium is a chemical element with the symbol (Ti), and it is widely distributed in various living organisms, water bodies, and soil. It ranks ninth among the plentiful in the Earth's crust, making it an element of great importance [20]. Titanium is known as a metal that is widely used in the medical industry. Titanium has emerged as a vital material in the field of medicine. Its applications extend to what is Beyond surgical equipment, orthopedic rods, nails, and plates, making it an indispensable component in various medical procedures, the human body shows a remarkable ability to tolerate titanium without experiencing any adverse reactions. In fact, titanium exhibits superior biocompatibility and resistance compared to many other metals commonly used in medical applications [21]. Titanium dioxide (TiO_2) has exceptional properties that make it versatile and applicable in various industries, the most important of which are medical and therapeutic applications [20][22]. Hybrid nanomaterials regulate sensing functions in nanomedicine and the pharmaceutical industries. The mechanical strengths, chemical stabilities, durability function, and hybrid nanomaterial flexibility make them suitable for developing healthy human life. Important applications such as drug deliveries, antimicrobial impacts, nutrition's, orthopedics, dentistry, and innovating antibiotics, antifungals, antioxidants, and wound healing promotion [23]. The nanoTiO_2 use healing of wound has received great attention due to its ability to harness the catalytic effect of photosynthesis, facilitating the generation of reactive oxygen type specifically targeting bacteria in wound infections [24]. The study aimed to prepare a nanomaterial of titanium dioxide (TiO_2) onto which the plant extract of the sesame plant is loaded. Study the effect of nano-titanium dioxide (TiO_2) on not only burns wound healing but also conduct in vivo evaluations.

2. Methodology

Investigating the effect of Sesamum indicum extract and titanium dioxide nanoparticle TiO2 on healing burn wounds and conducting in vivo tests.

Plant collection

Sesamum seeds were collected from the General Directorate of Agriculture in Diyala Governorate and the herbarium confirmed by its classification by in the College of Education for Pure Sciences/according to the Flora of Iraq book..

Preparation of the hot alcoholic extract

Sesamum indicum seeds extracted by using the saxolite system , using methanol as a solvent according to the method which in [25]. 100 grams of sesame seeds were placed in a funnel-shaped filter paper and tightly closed to avoid the seeds coming out. After that, they were placed in the saxolite device and placed on it 500 ml of solvent for one day, then we concentrated the solution by means of a rotary evaporator and separate the solvent, making a thick liquid of a dark greenish-brown color storing the filtered extract in the refrigerator at 4°C for later use.

Detection of plant-active compounds

The active compounds in Sesamum indicum seeds were detected using alcoholic seed extract gas chromatography-mass spectrometry (GC-MS).

GC-MASS analysis

The essential oils were evaluated in the laboratories of Basra Oil Company using gas chromatography with flame ionization detector (FID) and GC-MS using Agilent GC-mass detection (MSD) system by helium as a carrier gas and then the separation conditions in the device and the volume of the extract injected were adjusted according to the company's instructions.

Preparing TiO_2-NPs by the sol-gel method

The experiment included preparing TiO_2-NPs by the sol-gel, which was a method mentioned by [26]. TiO2-NPs were manufactured using a single-step hydrothermal technique on a transparent glass substrate coated with FTO under somewhat acidic conditions. A typical preparation involved mixing DI (10) mL (deionized water) with (10) concentrated HCl mL (hydrochloric acid) solution for making a total 20 mL, agitated for 10 minutes. To ensure a suitable supply of titanium requires adding an amount of titanium (IV) isopropoxide to the prior mixture's solution and agitated for 30 minutes. The finished solution was placed in a Teflon-lined stainless-steel autoclave with a two-thirds volume ratio. Yet, a clean FTO glass substrate piece placed at the autoclave bottom. Hydrothermal reaction was performed at 180 °C for one, 1.5, two, and three hours. The related samples are labeled TO-x, with x referring to the time of growth. Then, the reaction was finished, cooling the autoclave to room temperature. To eliminate contaminants, we rinsed samples with DI water and ethanol and dried by N_2 gas annealed at 350 °C for 60 minutes.

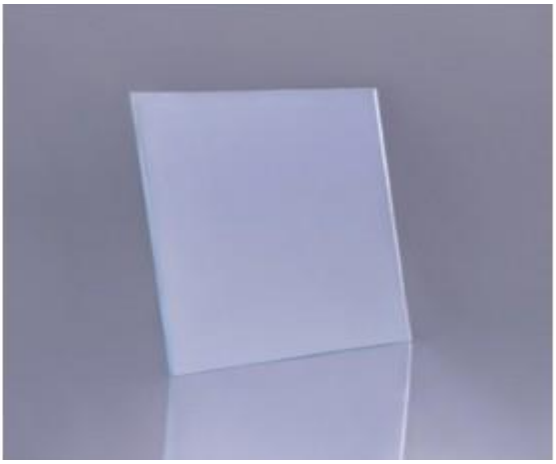


Figure1: Transparent glass substrate coated with FTO**.**

Preparation of compounds used to treat burn wounds in vivo

The compound used in in vivo experiments was prepared by mixing nanoTiO_2 and sesame seed oil at a concentration of 1% TiO_2 and 20% sesame oil.

Experimental animals:

This work uses 18 male rats, their weights ranging between 190 and 210 grams. The rats were kept in clean cages. Each group contains six rats provided with enough food and water. We observed every ethical standard regarding using laboratory animals. For second-degree burn procedures, general anesthesia was administered with xylazine 10% (50 mg/kg) and ketamine 2% (5 mg/kg) intraperitoneally. Next, the dorsal upper layer of the animal was shaved with a hair remover and made for the burn. All rats had the same burn wounding. It was formed using a hot plate in the same way and at an identical temperature. Briefly, a heated disc (diameter: 3 cm) was used to create a deep second-degree burn wounds at a similar temperature (heated by placing it for 5 minutes in hot water and holding for 10 seconds on the skin with equal pressure).[27]

Figure2: The process of causing a second-degree burn in a rat.

Statistical analysis:

The data in this work was statistically analyzed by the statistical programs SPSS version 23 and GraphPad Prism version 10. Quantitative data were in Mean±St.error format. ANOVA analysis compared more than two of the studied groups. The Least Significant Difference (LSD) test compared the burned areas' arithmetic means at a significance level of P≤0.05.

3. Results and Discussion

GC-Mass analysis of essential oils:

Computer matching for commercial mass spectral libraries (Wiley GC/MS Library, 3 Mass Finder Library, and Baser Library) was used to obtain individual seed extracts for endogenous vital oil of over 3,200 authentic compounds with mass spectra and retention data from the pure so revealing an active compound in the extract: beta-tocopherol, sesame, gamma-sitosterol, fucosterol, methyl 12-hydroxy-9-octadecenoate, and tris(2,4-di-tert-butylphenyl) phosphate. As shown in Figure 3. The results were consistent with the findings of [28].

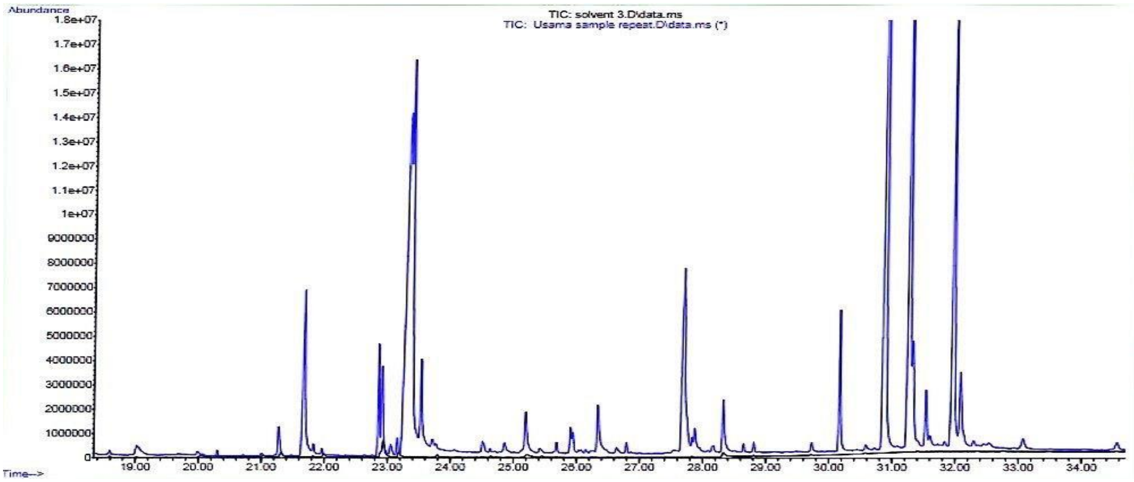
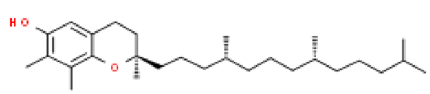
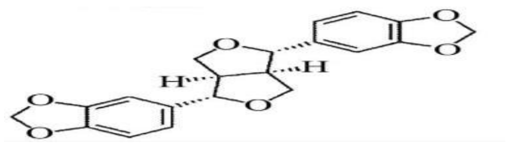
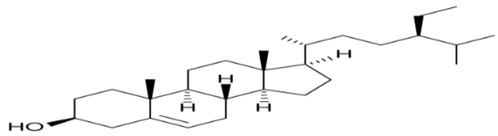
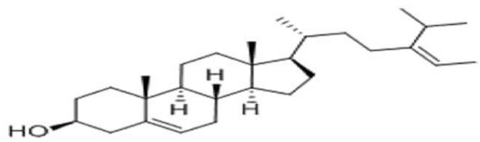
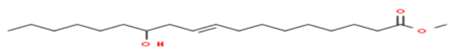
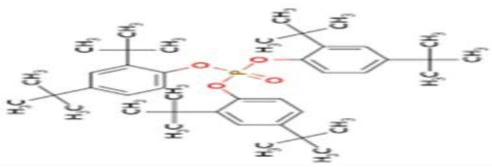


Figure3: Shows the results of the GC-Mass analysis of sesame seed extract.

Table1. Shows the active components of sesame seed extract.

No.	compound	formula	Concentration %	Structure
1.	beta-Tocopherol	C28H48O2	2.087987639	
2.	(+) - Sesamin	C20 H18 O6	18.06672224	
3.	gamma-Sitosterol	C29H50O	10.34978171	
4.	Fucosterol	C29H48O	1.9308161	
5.	Methyl 12-hydroxy-9-octadecenoate	C19H36O3	0.186714276	
6.	Tris(2,4-di-tert-butylphenyl) phosphate	$C_{42}H_{63}O_4P$	0.205425051	

Field Emission Scanning Electron Microscopy (FE-SEM) tests:

The TiO_2 nanobodies were characterized by a FE-SEM, as Figure 4 shows. The image had a 100,000X magnification, and most of the TiO_2 particles are dense and shaped like irregular spheroids with sizes ranging between 31.52 and 69.08 nanometers, as these results were like what was achieved by [29].

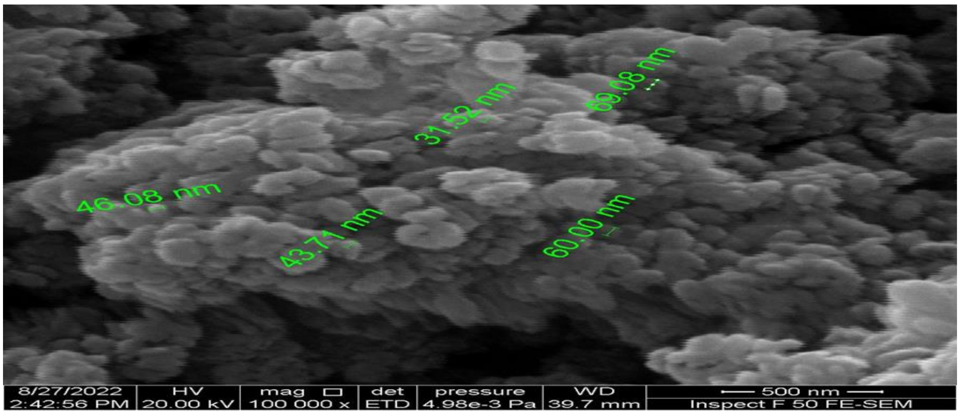


Figure4: FE-SEM image which shows the morphology TiO_2 nanoparticles**.**

Results of the effect of titanium dioxide nanoparticles (TiO_2-NPs) mixed with Sesamum indicum seed extract on in vivo burns:

This work shows that there are no statistical differences (P > 0.05) between the average burn areas of rats exposed to different treatments (MEBO, TiO2, mixture, and S.oil) in the first week of exposure. In contrast, TiO_2 and Mixture recorded the highest therapeutic effectiveness in the second week (1.110±0.071 and 0.096±1.314), the third (0.033±0.398 and 0.066±0.398), and the fourth week (0.086±0.021 and 0.003±0.005), with statistical differences ($p<0.05$). (Table 1 and Figure 2). This gives a clear indication that, firstly, there is a noticeable effect of nano-TiO_2 on burns wounds healing in a shorter time than Mebo, and nano-TiO_2 controls the progress of the healing process by improving the moisture content and anti-bacterial properties of the skin confirming [30], where the recovery rate was (99.85%) for one group. The use of nanosized TiO_2 in wound healing has received important attention because it can harness the photocatalytic effect, facilitating the generation of reactive oxygen specifically targeting bacteria in wound infections [31]. Advances in the use of metal oxide nanoparticles in uses of the environment have increased the necessity for synthesizing them. The use of green chemical approaches on ecologically sensitive biological systems [32]. Sesame oil has an important role in treating burn wounds and reducing the resulting scars in record time because of its antioxidant and anti-inflammatory properties and effective materials in this aspect [33]. NPs have been studied for their ability of reducing skin infections and burn wounds. The goal of wound healing is an instantaneous recovery with maximum function and minimal scarring [34]. The effective materials for healing burns found in sesame oil were loaded onto TiO_2 nanoparticles. Which is known as the biosynthesis process, gives much better results in burn wound healing and removing resulting scars than if each of them were used separately.

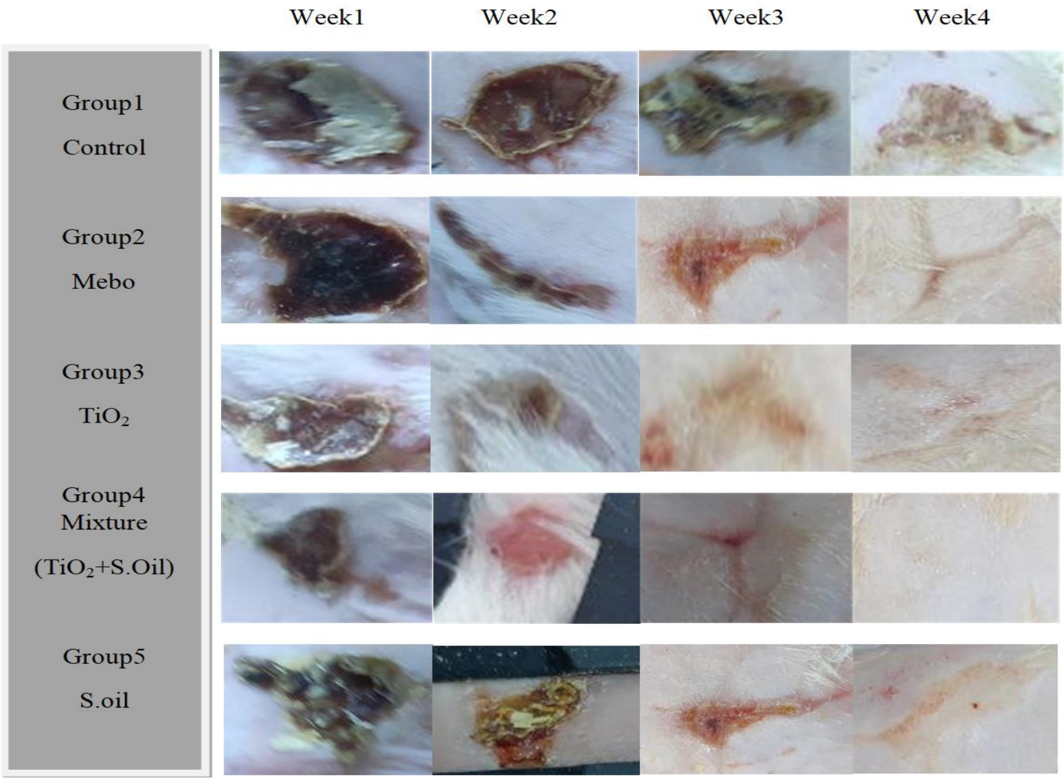


Figure 5: shows healing stages of rats from burn wounds for each treatment group.

Table2: comparative means of burned area of rats treated with different drugs at four weeks.

Times	Control		MEBO		TiO_2		Mixture (TiO_2+S.oil)		S.oil		Statistics
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
First	2.426	0.045	2.607	0.095	2.428	0.117	2.443	0.086	2.521	0.107	Non-significant
Second	2.007 d	0.037	1.600 c	0.093	1.110 a	0.071	1.314 b	0.096	1.381 b	0.095	LSD=0.19 *P<0.01***
Third	1.561 c	0.053	0.758 b	0.053	0.398 a	0.033	0.398 a	0.066	0.677 b	0.049	LSD=0.24 *P<0.001****
Fourth	0.971 e	0.054	0.175 c	0.03	0.086 b	0.021	0.005 a	0.003	0.271 d	0.047	LSD=0.070 *P<0.001****

P>0.05 Not significant difference, P<0.05* significant difference, P<0.01 Highly significant difference, P<0.001*** Very high significant difference, and different lowercase letters indicate significant differences.**

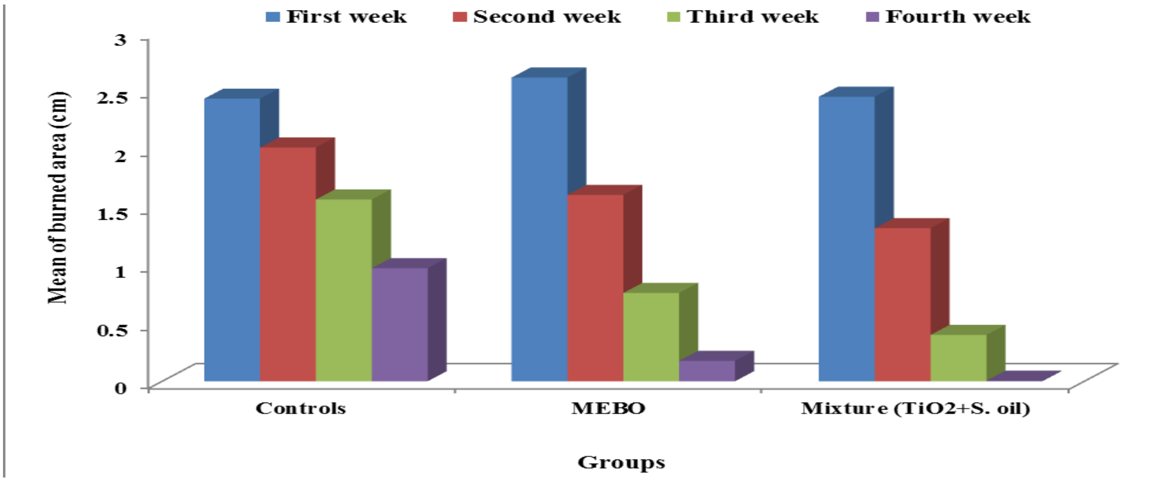


Figure6: comparative means of burned area of rats treated with different drugs at four weeks.

Histological Examination

Hematoxylin and eosin staining revealed that normal rat skin has two thin layers: epidermis and dermis. The epidermis' keratinized is a stratified squamous epithelial tissue of two to three layers t linking to the basement membranes. The dermis has dense connective tissues and hair follicles. The hypodermis, or subcutaneous tissue, is under the dermal layer with loose connective tissue and white fatty tissue arranged in lobules which are divided by many connective tissue septa. Rat skin is distinguished from human skin by the panniculus carnosus, a layer of skeletal muscle beneath the dermal fatty tissue. (Figure 7).

The burn depth reached the deep dermis layer of treated rats, corresponding to the second to third degree of burns. In the case of untreated rats, they showed severe necrosis and loss in the epidermal layer on day 7 after burning, reaching none and mild on day 28. There was also disorder and disorganization in the dermis with diffuse infiltration around the blood vessels, which began to be severe until they became mild to nonexistent on day 28. Collagen appeared in the papillary dermis layer, it was moderate to mild, while the regeneration of the epidermal layers and blood vessels was slow in this group. These results are similar to what was found [35]. The group treated with MEBO showed results similar to those seen in the first group, with a slight advantage in renewing the skin and its layers. The third group treated with nano-TiO_2 showed a relative advantage over the previous two groups in that the dermis returned to order and blood vessels appeared in it on day 28. These results for the nanomaterial appear to be very similar to [35]. While the best results appeared in the fourth group treated with a biosynthetic mixture of nano-TiO_2 and sesame oil, necrosis, loss of the epidermis layer, and disruption of the dermis appeared moderate, and slight regeneration of the epidermis layers began on the seventh day after the burn. Epidermal necrosis, disruption of the dermis, collagen, and perivascular infiltration disappeared as well. The layers of the skin were completely regenerated, with the scars disappearing on day 28. As for the fifth group treated with sesame oil, its readings were remarkably similar to the readings of the third group treated with nano-TiO_2, (Table 1 and Figure 8).

Table 3: Descriptive qualitative and semi-quantitative evaluations for healing process in positive control-, Mebo, nano-TiO_2, and mixture of nano-TiO_2 and sesame oil-treated groups over 28 days (4 animals per group on 7, 14, 21, and 28 days post experiment).

Items	G1				G2				G3				G4				G5			
Time lesion	D7	D14	D21	D28	D7	D14	D21	D28	D7	D14	D21	D28	D7	D14	D21	D28	D7	D14	D21	D28
Epidermal necrosis .	+++	-	-	-	+++	+	-	-	+++	+	-	-	++	-	-	-	++	-	-	-
Epidermal losses.	+++	+++	++	+	+++	+++	+++	-	+++	+++	++	+	++	+	-	-	+++	++	-	-
Disorganization of the dermis.	+++	+++	+	+	+++	++	++	+	+++	+++	+	-	++	++	-	-	+++	+++	+	-
Diffuse perivascular infiltration.	+++	++	+	-	++	++	+	-	+++	+	-	-	+++	++	+	-	+++	+	+	-
Collagen degeneration at level of papillary dermis.	+++	++	+	+	+++	+	+	-	+++	+++	+	-	+++	+++	+	-	+++	+++	++	-
Epidermal regeneration.	-	-	+	+	-	-	+	+++	-	-	+	++	+	++	+	+++	-	+	++	+++
Basal, granular, spinous, and cornified cell layers.	-	-	++	++	-	-	+	+++	-	-	+	+++	+	++	+++	+++	-	+	+++	+++
Vascularization at the dermal subcutaneous interface.	-	+	+	+	+	+	+	+	+	+	++	++	++	++	+++	+++	+	++	++	++

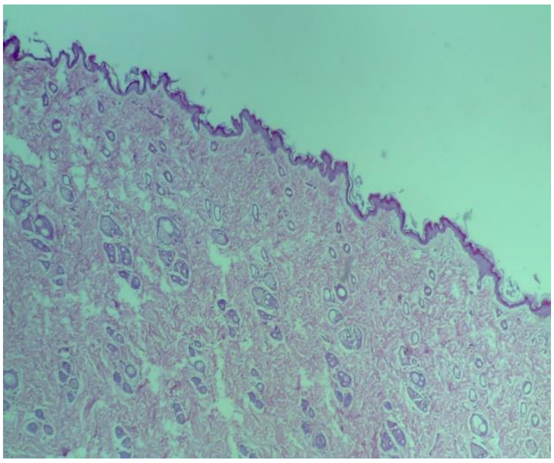


Figure7;Histological analysis of Rat, normal (unburned) skin(×4 magnification H&E stain).

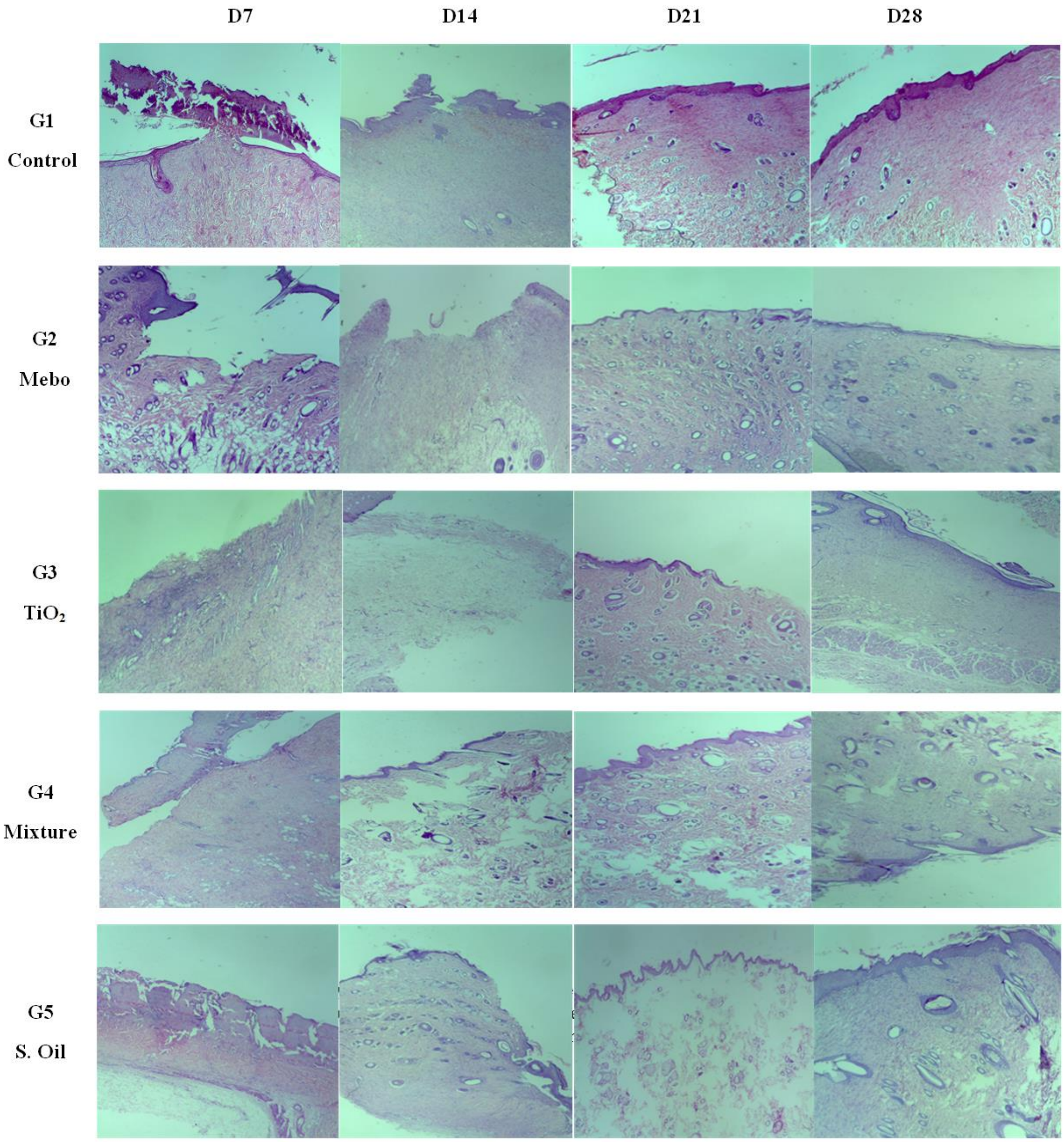


Figure8;Histological analysis of Rats evaluations for healing process in positive control-, Mebo, nano-TiO_2, and mixture of nano-TiO_2 and sesame oil-treated groups over 28 days (4 animals in each group on 7, 14, 21, and 28 days posy experiment) (× 4 magnification H&E stain).

Conclusion

The preparation of nanoparticles TiO_2 produced a nanomaterial having high features and unique sizes (31.52 to 69.08) nanometers. Which was loaded with the active ingredient of the sesame plant, Sesamum indicum L., as a compound whose effectiveness and effect on burn wounds affecting the skin were proven when used in in vivo experiments, where the speed of healing of burn wounds and the effectiveness of the prepared substance were proven.

Thanks, and appreciation

We extend special thanks to all the workers at Mustansiriyah University-the Iraqi Center for Cancer Research and Medical Genetics for helping in the data collection.

Reference

[1] Rossella, E., Giulio, M., & Michele, M. (2022). Burns: classification and treatment. Textbook of Plastic and Reconstructive Surgery: Basic Principles and New Perspectives, 285-301.

[2] Jeschke, M. G., van Baar, M. E., Choudhry, M. A., Chung, K. K., Gibran, N. S., & Logsetty, S. (2020). Burn injury. Nature reviews. Disease primers, 6(1), 11. https://doi.org/10.1038/s41572-020-0145-5.

[3] Rice, P. L., & Orgill, D. (2021). Assessment and classification of burn injury. UpToDate, [Internet], 8.

[4] Burgess, M., Valdera, F., Varon, D., Kankuri, E., & Nuutila, K. (2022). The immune and regenerative response to burn injury. Cells, 11(19), 3073.

[5] Żwierełło, W., Piorun, K., Skórka-Majewicz, M., Maruszewska, A., Antoniewski, J., & Gutowska, I. (2023). Burns: Classification, pathophysiology, and treatment: A review. International journal of molecular sciences, 24(4), 3749.

[6] Abazari, M., Ghaffari, A., Rashidzadeh, H., Badeleh, S. M., & Maleki, Y. (2022). A systematic review on classification, identification, and healing process of burn wound healing. The International Journal of Lower Extremity Wounds, 21(1), 18-30.

[7] Stone II, R., Natesan, S., Kowalczewski, C. J., Mangum, L. H., Clay, N. E., Clohessy, R. M., & Christy, R. J. " Advancements in regenerative strategies through the continuum of burn care. Frontiers in pharmacology", (2018). 9, 672.

[8] McAuley, J. (2023). Burns: An Introduction to Burns and Basic Wound Care. Physician Assistant Clinics, 8(1), 67-77.

[9] Warby, R., & Maani, C. V. (2019). Burn classification.

[10] Markiewicz-Gospodarek, A., Kozioł, M., Tobiasz, M., Baj, J., Radzikowska-Büchner, E., & Przekora, A. (2022). Burn wound healing: clinical complications, medical care, treatment, and dressing types: the current state of knowledge for clinical practice. International journal of environmental research and public health, 19(3), 1338.

[11] Radzikowska-Büchner, E., Łopuszyńska, I., Flieger, W., Tobiasz, M., Maciejewski, R., & Flieger, J. (2023). An Overview of Recent Developments in the Management of Burn Injuries. International Journal of Molecular Sciences, 24(22), 16357.

[12] Rasool, A., Bhat, K. M., Sheikh, A. A., Jan, A., & Hassan, S. (2020). Medicinal plants: Role, distribution, and future. Journal of pharmacognosy and phytochemistry, 9(2), 2111-2114.

[13] Adeyemi, J. O., Oriola, A. O., Onwudiwe, D. C., & Oyedeji, A. O. (2022). Plant extracts mediated metal-based nanoparticles: Synthesis and biological applications. Biomolecules, 12(5), 627.

[14] Makhaik, M. S., Shakya, A. K., & Kale, R. (2021). Dietary phytochemicals: As a natural source of antioxidants. Antioxidants-benefits, sources, mechanisms of action.

[15] Liya, F. I., Yasmin, M. F., Chowdhury, N. S., Charu, T. K., & Fatema, I. B. (2021). Mirabilis jalapa: A review of ethno and pharmacological activities. Advancement in Medicinal Plant Research, 9(1), 1-10

[16] Zang, X., Cheng, M., Zhang, X., & Chen, X. (2021). Quercetin nanoformulations: a promising strategy for tumor therapy. Food & function, 12(15), 6664-6681.

[17] Sharma, L., Saini, C. S., Punia, S., Nain, V., & Sandhu, K. S. (2021). Sesame (Sesamum indicum) seed. Oilseeds: Health Attributes and Food Applications, 305-330.

[18] Anwar, M., Bibi, T., Mustafa, H. S. B., Mahmood, T., & Ali, M. (2013). TH-6: a high yielding cultivar of sesame released for general cultivation in Punjab. Advancements in Life Sciences, 1(1).

[19] Tabatabaei, S. M., Far, A. M., Saremi, Z., Zandi, M., Aghaei, S., Gohari, M., & Asadollahi, H. (2017). The effect of sesame oil and cucurbita on healing wounds caused by third-degree burn. Journal of Skin and Stem Cell, 4(3-4).

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

[21] Akın, N., & Mutlu Danacı, H. (2021). An investigation into the architectural use of nanotechnology in the context of the titanium dioxide. Environmental Science and Pollution Research, 28, 64130-64136.

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

[23] Shehabeldine, A. M., Salem, S. S., Ali, O. M., Abd-Elsalam, K. A., Elkady, F. M., & Hashem, A. H. (2022). Multifunctional silver nanoparticles based on chitosan: Antibacterial, antibiofilm, antifungal, antioxidant, and wound-healing activities. Journal of Fungi, 8(6), 612.

[24] 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.

[25] 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.

[26] 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.

[27] 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.

[28] Tajabadi, F., Ghorbani-Nohooji, M., Gholami, A., Ghiasi Yekta, M., Ghasemi, S. V., Nabati, F., & Sadri, S. H. (2023). Gas chromatography/mass spectrometry with chemometric methods for the determination of fatty acid profiles in herbal oils. Biomedical Chromatography, 37(3), e5566.

[29] 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.

[30] Albukhaty, S., Al-Bayati, L., Al-Karagoly, H., & Al-Musawi, S. (2022). Preparation and characterization of titanium dioxide nanoparticles and in vitro investigation of their cytotoxicity and antibacterial activity against Staphylococcus aureus and Escherichia coli. Animal Biotechnology, 33(5), 864-870.

[31] Eldebany, N., Abd Elkodous, M., Tohamy, H., Abdelwahed, R., El-Kammar, M., Abou-Ahmed, H., & Elkhenany, H. (2021). Gelatin loaded titanium dioxide and silver oxide nanoparticles: implication for skin tissue regeneration. Biological Trace Element Research, 199, 3688-3699.

[32] Alzubaidy, M. W. M., & Hussain, M. N. (2022). Biosynthetic of Green Zinc Oxide Nanoparticles with Effect on Cancer Cell Line Hela. Revis Bionatura 2023; 8 (2) 22.

[33] Yin, W. T., Ma, X. T., Li, S. J., Liu, H. M., & Shi, R. (2021). Comparison of key aroma-active compounds between roasted and cold-pressed sesame oils. Food Research International, 150, 110794.

[34] Wang, P., Jiang, L., & Han, R. (2020). Biosynthesis of zinc oxide nanoparticles and their application for antimicrobial treatment of burn wound infections. Materials Research Express, 7(9), 095010.

[35] Wasef, L. G., Shaheen, H. M., El-Sayed, Y. S., Shalaby, T. I., Samak, D. H., Abd El-Hack, M. E., ... & Swelum, A. A. (2020). Effects of silver nanoparticles on burn wound healing in a mouse model. Biological trace element research, 193, 456-465.