Research Article

Impact of Serratiopeptidase vs. N-Acetyl Cysteine (NAC) on Skin Grafting Healing in Albino Male Rabbits

Hasan Ali Al-Sailawi[1], Araa Ali Hadi[1], Hussein A. Raheem[2], Mustafa Mudhafar[3,4], Sahi J Dhahi[5], Qais R. Lahhob[6*]

[1]Department of Basic Science, College of Dentistry, Karbala University, Karbala, Iraq; [2]Department of Pathology and poultry disease, Ministry of Agriculture, Iraq; [3]Department of Medical Physics, Faculty of Medical Applied Sciences, University of Kerbala, 56001, Karbala, Iraq; [4]Department of Anesthesia and Intensive Care techniques, Faculty of Al-Taff College, Karbala, 56001, Iraq; [5]Department of Biology, College of Science, Mosul University, Iraq; [6]Collage of Pharmacy, National University of Science and Technology, Dhi Qar, 64001, Iraq.

Abstract | Skin grafting is a common dermatological wound closure procedure used to heal wounds caused by removing skin damage. Although grafting is less popular than flap closures, the aesthetic outcome can still be good. The present study aimed to investigate the grafting of the skin of albino male rabbits by N-acetyl cysteine (NAC) and Serratiopeptidase and then compare their effect on the skin grafting of rabbits. Nine rabbits were divided into three groups. Each group had three animals: Group 1 (G1) was used as a control (skin grafting without any drug), and the skin was taken from the shoulder to the femoral area. In group 2 (G2), the skin graft was taken from the same area in the G1 using Serratiopeptidase, while in group 3 (G3), the skin graft was taken from the same area in G1 using NAC. The outcomes demonstrated that Serratiopeptidase and NAC both had good enhancement effects on the skin graft and demonstrated superior effects on the AST, histology, and hematology parameters. According to our findings, the skin graft can be improved by using both NAC and serratopeptidase, which will raise the AST, histology, and hematology levels.

Keywords | Skin grafting, NAC, Serrati peptidase, hematology, histology, AST

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***Correspondence** | Qais R. Lahhob, Collage of Pharmacy, National University of Science and Technology, Dhi Qar, 64001, Iraq; **Email:** qiasqiasqias@gmail.com
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INTRODUCTION

The largest organ in the human body, the skin, is vital to maintaining homeostasis and protecting internal organs from external stimuli. Cutaneous injuries, mainly burns, chronic wounds, and skin wound infections, necessitate laboriously long-term care and place a heavy financial strain on healthcare systems across the globe. Chronic wound prevalence is rising due to an aging population and rising rates of obesity and diabetes. It is estimated that between 1% and 2% of individuals in wealthy countries will experience a chronic wound at some point (Dovi et al., 2003).

Autologous skin transplants are the most widely used technique for healing chronic wounds. But in large, deep wounds or extensive, severe burns, autografts are not always an option; instead, allogeneic (produced from cadavers) or xenogeneic skin transplants are used for transplantation. However, the practical value of allogeneic/

xenogeneic tissue is limited because of the significant risk of transplant rejection associated with it (Chaudhari et al., 2019). By creating bioengineered, biomaterial-based artificial skin grafts, skin tissue engineering is one type of contemporary therapy that addresses the scarcity of donor skin graft supplies and skin allo/xenograft rejections (Khan et al., 2021). With the aid of this cutting-edge strategy for wound regeneration, it will be possible to manufacture skin substitutes that operate as bioactive wound dressings, allowing the wound to do more than need to be covered. Because bioengineered skin grafts are permeable to oxygen, their primary purposes are to provide oxygen, prevent wounds from becoming dry, promote healing, and prevent infections (Przekora, 2020). Depending on the biomaterial used, artificial skin grafts can be used as temporary wound dressings or permanent skin replacements. The biomaterials are categorized as cellular artificial skin grafts or have cells embedded in their matrix when pre-seeded. On the other hand, acellular synthetic skin grafts are biomaterials devoid of or lacking cells (Dixit et al., 2017). Similar to autologous skin transplants, artificial skin replacements can be classified as epidermal, dermal, or dermo-epidermal based on their anatomical structure.

The medications were widely used to speed up and improve the skin's ability to heal injuries. There were many types of drugs were mentioned in the literature studies, such as N-acetyl cysteine (NAC) (Li et al., 2019) and Serratiopeptidase (Jadhav et al., 2020), which were used to enhance the cells for growth during the injury. According to previous studies, the NAC was used widely in the medical field; for example, Researchers examined how NAC, which replenishes glutathione reserves, affected peripheral insulin resistance and insulin production in PCOS-affected individuals. Moreover, it has been found that administering NAC to hyperinsulinemic individuals modified their glucose regulation features. Their peripheral insulin sensitivity improved and their insulin levels decreased as a result. Consequently, in PCOS patients with hyperinsulinemia, NAC's antioxidant properties may be a therapeutic strategy to raise circulating insulin levels and insulin sensitivity (Mokhtari et al., 2017).

Owing to its therapeutic qualities, NAC was applied to wound healing by combining it with collagen-graphene oxide composite and evaluating its performance on rat skin. The findings demonstrated that the N-Col-GO hybrid membrane showed superior mechanical properties, a greater capacity to retain water, and a slower rate of NAC release compared to the Col-only scaffold, all likely to encourage fibroblast migration and proliferation. However, in the present study, NAC was used as a graft material for the skin against the albino male rabbits as a first report for using NAC as a grafting for the albino male rabbits by analysis of the histopathology and hematological. The present study aimed to enhance the grafting of the skin by using N-acetyl cysteine (NAC) and Serratiopeptidase in the skin of albino male rabbits to compare the best effect of these materials to be used in future studies as skin graft materials.

MATERIALS AND METHODS

Animals

Nine albino male rabbits weighing 750g^{-1}Kg were used in this study. The rabbits were fed standard rabbit chow and allowed ad libitum access to water. The study protocol forwarded to the appropriate ethics committee in the University of Karbala as well as the ethical committee at Karbala College of Veterinary Medicine. Nine rabbits were divided into three groups, each group having 3 animals as following Group 1 (G1) as a control (skin grafting without any drug), the skin was taken from shoulder to femoral area. In group 2 (G2), the skin graft was taken from the same area in G1 using Serratiopeptidase, while in group 3 (G3), the skin graft was taken from the same area in G1 using NAC.

Preparation of N-acetyl cysteine (NAC)

Each ingredient for the combination was weighed, and a 3% NAC cream was made. Next, the required amount of NAC was broken into small pieces and mixed with water to create a paste. Once the desired amount of this combination was added, cool cream was added and well blended, as mentioned in some previous studies, it was prepared and used N-acetyl cysteine (NAC) (Sarris et al., 2015; Omran et al., 2024).

Preparation of serratiopeptidase ointment

A 1% solution of serratiopeptidase ointments was made. The cream was refrigerated at 40 degrees Celsius in plastic containers until needed. The study included adult male rabbits in good health, weighing 1.25 ± 0.25 kg.

Surgical operation

Preoperative preparation

Prior to surgery, the trial's animals were fasted for twelve hours and then given food and liquids. Additionally, Figure 1A shows that the medial tibial region was clipped, shaved, and aseptically prepared. The skin was exfoliated using a 2.5% bovidine-iodine solution. The rabbits were placed in a lateral recumbency and covered with surgical drapes, which were secured to their skin with towel clips (Figure 1B).

Anesthesia

A combination intramuscular dose of Xylazine and Ketamine (3:35 mg per kg B.W.) was used for general anesthesia for all surgeries, and an additional dose of

Xylazine was administered to deepen and prolong the anesthesia.

Surgical technique

For the purpose of to prevent infection, a square piece of skin, measuring one centimeter in diameter, was transplanted from the forelimb to a hole in the hindlimb and filled with powdered NAC and serrapeptase. After that, a gauze pad was changed every two days and the graft's borders were sewn together with the native skin using simple interrupted suturing (Figure 3).

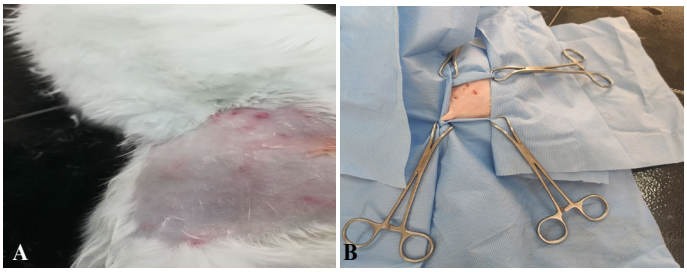

Figure 1: (A) Shaving and cleaning of skin for the surgical operation and (B) Preparation of animals for the surgical operation.

Blood sample collection

The blood samples were collected directly by syringe through heart puncture (Figure 3a) and then put in the tubes with and without anticoagulant; In order to prevent hemolysis, these tubes were cooled in ice boxes before being sent for analysis to create the hematological tests (Figure 3b).

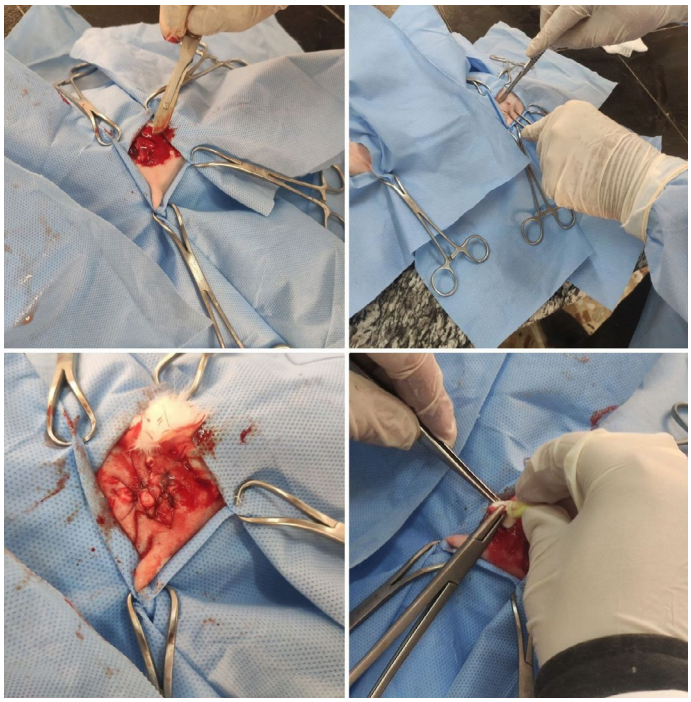

Figure 2: The surgical procedure steps which made during skin grafting.

Figure 3: The blood sample (a) collection and (b) storing.

RESULTS AND DISCUSSIONS

Determine the effect of N-acetyl cysteine (NAC) on healing of skin grafting in albino male rabbits

In this section the histological, hematological and biochemical analysis for the skin graft of the albino male rabbits after treated with N-acetyl cysteine (NAC).

Histological of G3 treated with NAC

The histological dissection showed significant enhancement of skin grafting healing, as shown in Figure 4. Based on Figure 4b routine healing with normal keratin and epidermis layer as well as hair follicle, blood vessels, and muscular layer in comparison with the control group, which shows normal epidermis and keratin with standard dermis layer.

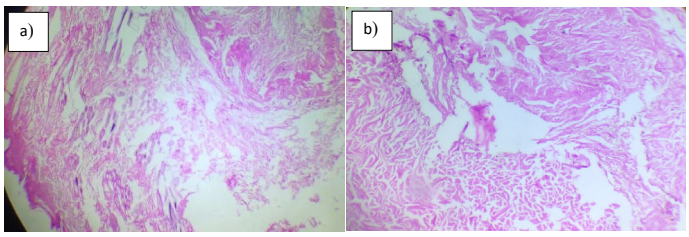

Figure 4: Histological section for skin graft of rabbit with (a) without treated and (b) treated with NAC.

The results of the present study showed that the enhancement effects of NAC on skin grafting and healing have been observed clearly. According to previous studies, NAC enhances skin grafting due to the NAC's antioxidant effects in the present study, which are in line with the results obtained from the studies reported previously. This study, which is thought to be a novel investigation into rabbit varieties, was conducted on male albino rabbits.

Hematological G3 treated with NAC

The hematological analyzed include to check the White Blood Cell (WBC), Red Blood Cell (RBC) and platelets while (PLT) of the albino male rabbits in G1 and G3. As shown in the Table 1 the WBC, RBC and PLT of the treated rabbits with the NAC were 10.3 x $10x^3$ µl, 3.15 x $10x^6$ µl and 387 x $10x^3$ µl, respectively, compare with the

control animals groups were 6.5 x $10x^3$ µl , 5.21 x $10x^6$ µl and 315 x$10x^3$ µl. The hematological results showed increase in the WBC and platelets while the RBC and other hematological parameters were normal in the rabbit which treated by NAC topically, the increase in the WBC and platelets occur due to inflammatory reaction of skin graft.

Table 1: The comparison of blood parameters between NAC group and control group.

Parameters	WBC x $10x^3$ µl	RBC x $10x^6$ µl	PLT $10x^3$ µl
Control	6.5	5.21	315
NAC group	10.3	3.15	387

The hematological study's results showed that the G3's PLT and WBC leaves were higher than those of the G1, and prior research suggested that this increase in WBC might be the result of the body's reaction to an injury or an inflammatory response. The G3 animals in our study were injured prior to receiving NAC treatment, which explained the elevated WBC and PLT.

Biochemical analysis of G3 treated with NAC

The biochemical analysis for the G3 was done using aspartate aminotransferase (AST). Table 2 shows the AST analysis of G1 and G3, which were 0.4 mg/ dl and 0.6 mg/ dl, respectively. The results that were obtained from this analysis showed a mild increase in this enzyme in comparison with the control group; this increase in the level of the enzyme may have occurred due to an inflammatory reaction of the skin grafting in the NAC-treated rabbit, the result of chemical analysis in this group showed the better enhancement than the serattopeptide treated rabbit in comparison with the control group, the enhancement effects of NAC due to antioxidant properties of it (DW, 1988; Pietruski et al., 2021).

Table 2: The comparison of AST between NAC and control group.

Parameters	AST mg/ dl
Control	0.4
NAC group	0.6

Determine the effect of serratiopeptidase on healing of skin grafting in albino male rabbits

This section describes the histological, hematological, and biochemical analyses that were performed after the animals in group 2 (male albino rabbits) received a serratiopeptidase treatment.

Histological of G2 treated with serratiopeptidase

The histological study of this part measured the G2 of the animals after they were treated with Serratiopeptidase. The histological dissection showed moderate enhancement of skin grafting healing, as shown in Figure 5, which shows healing with an increase in the collagen fiber and epidermis layer formation. In contrast, the dermis layer is regular, compared with a non-treatment group of rabbits, which show normal epidermis and keratin with a standard dermis layer. The enhancement effects of serratiopeptidase can be seen in this section due to the antibacterial effects (DW, 1988) and antioxidant properties (Tsai et al., 2014).

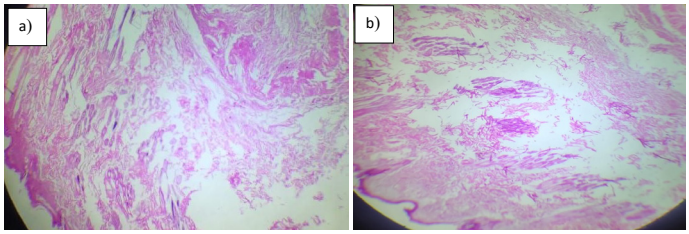

Figure 5: Histological section for skin graft of rabbit (a) control group and (b) treated group with using serattopeptidease.

Previous studies were reported to study the histology of the skin of the animals after being treated with serratiopeptidase for grafting purposes. Rath et al. (2011), reported the enhancement of wound healing by using serratiopeptidase. Their results showed that the wounds had partial epithelization, inflammatory cell predominance with few fibroblasts, and sparse collagen deposition was noticeable, especially at the wound centers. In the present study, similar results were obtained.

Hematological of G2 treated with serratiopeptidase

In this part the hematological analysis was done for the G2 of the rabbits after treated with the serratopeptidase enzyme. The blood samples taken from the rabbits at different times of experiment and compare with other groups. Table 3 shows the levels of WBC, RBC, and PLT for the G1 and G2 of the rabbits. The results of the G2 showed 11.5 x $10x^3$ µl, 5.07 x $10x^6$ µl and 405 $10x^3$ µl for WBC, RBC, and PLT, respectively, while the control group showed 6.5 x $10x^3$, 5.21 x $10x^6$ µl and 315 x $10x^3$ µl , for WBC, RBC, and PLT, respectively. The hematological analysis for the serratopeptidase treated rabbits showed mild increase in the WBC countt due to inflammatory reactions of skin graft while the other hematological parameters were normal in comparison with control group, the enhancement effects of serattopeptide on these parameters due to anti-inflammatory effects of serattopeptide (Nejatifar et al., 2022). the results showed significant increase in the WBC, RBC and PLT due to inflammatory reaction of the skin graft (El-Abd and Ibrahim, 2020).

Table 3: The comparison of blood parameters between the serratopeptidase and control group.

Parameters	WBC x $10x^3$µl	RBC x $10x^6$µl	PLT $10x^3$µl
Control	6.5	5.21	315
Serratopeptidase	11.5	5.07	405

Based on the results that have been obtained from the hematological study, the leave of the WBC and PLT of the G2 was increased compared with the G1; according to the previous studies, the enhancement of the WBC may be due to the effect of the body by injury or get inflammatory. However, our study included injuring the animals of the G2 before being treated with the NAC, which was the reason for the WBC and PLT increase.

Biochemical analysis of G2 treated with Serratiopeptidase Table 4 shows the biochemical analysis for the aspartate aminotransferase (AST) for the animals treated with serratopeptidase, which showed a moderate increase in this enzyme in comparison with the control group; this increase in this enzyme occurred due to an inflammatory reaction of the skin grafting in the treated rabbit, the result of chemical analysis in this group showed the enhancement lower than the NAC treated rabbit in comparison with the control group, the enhancement effects of serratiopeptidase due to antioxidant properties of it (Rath et al., 2011; Tiwari, 2017).

Table 4: The comparison of AST enzyme between serratopeptidase and control groups.

Parameters	AST mg/ dl
Control	0.4
Serratopeptidase	0.9

Compare the effects of NAC and Serratiopeptidase on the healing of skin grafting in albino male rabbits

This objective included to compare the G2 and G3 of the rabbits after treated by Serratiopeptidase and NAC, respectively, via a histological, Hematological and Chemical analysis.

Comparison of histological between serratiopeptidase and NAC

Histological study of the G2 of the rabbits, as shown in Figure 2b, showed moderate enhancement of skin grafting healing after being treated with serratiopeptidase. At the same time, Figure 1b shows the G3 of the rabbits after being treated with NAC. The results obtained form that figure show routine healing with normal keratin and epidermis layer as well as hair follicle, blood vessels, and muscular layer, which indicates the use of NAC in skin grafting is better than serratiopeptidase based on the results that were obtained in the present study.

Comparison of histological between serratiopeptidase and NAC

The hematological study of the G1, G2 and G3 were determine according to three parameters as mentioned in previously parts which included WBC, RBC and PLT as it shows clearly in Table 5. WBC of the G1 was 6.5 x $10x^3$ µl which normal level, WBC were increased in the G2 and G3 (11.5 and 10.3), the levels of WBC in the rabbits that were treated with serratiopeptidase is more than the NAC treated group, and since this increase was due to inflammation, we conclude that the G3 was better than G2 in the progress of the grafting, which gave indicated to that the use of the NAC can be more effective that serratiopeptidase in the Hematological. Moreover, the level of PLT in G2 was more that G3 which also gave another indicted to be G2 more inflammation than G3 (Dixit et al., 2017), due to same reason that were mentioned above.

Table 5: The comparison of blood parameters of serratopeptidase, NAC and control group.

Parameters	WBCx $10x^3$µl	RBCx $10x^6$µl	PLT $10x^3$µl
Control	6.5	5.21	315
Serratopeptidase	11.5	5.07	405
NAC	10.3	3.15	387

Comparison of chemical analysis of AST between serratiopeptidase and NAC

This part compares the AST of G1, G2, and G3. Table 6 shows the AST level of all groups. AST level was increased from 0.4 mg/ dl in the group without treated and reached 0.9 mg/ dl in the treated group with serratiopeptidase. In comparison, the treated group with NAC was 0.6 mg/ dl, the increase in the AST level due to inflammatory reaction and the greater the inflammation, the higher the level. That indicates the use of NAC was a better enhancement than the Serratiopeptidase (Tamimi et al., 2021; Olariu et al., 2017).

Table 6: The comparison of AST enzyme between serratopeptidase, NAC and control groups.

Parameters	AST mg/ dl
Control	0.4
Serratopeptidase	0.9
NAC	0.6

CONCLUSIONS AND RECOMMENDATIONS

The present study has been conducted to determine the effect of NAC and serratopeptidase on the skin grafting of albino male rabbits. The results were divided into

Histological, hematological, and Chemical analysis. The conclusions from these results show that the NAC showed sound enhancement effects on the skin graft and better enhancement effects on the hematology, histology, and AST parameters. In contrast, the serratopeptidase showed sound enhancement effects on the hematology, histology, and AST parameters but less than NAC. Our results showed that both NAC and serratopeptidase can be used to enhance the skin graft, which will cause an increase in the hematology, histology, and AST levels.

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NOVELTY STATEMENT

The novelty statement are (our findings), the skin graft can be improved by using both NAC and serratopeptidase, which will raise the AST, histology, and hematology levels.

AUTHOR'S CONTRIBUTION

Hasan Ali Al-Sailawi and Mustafa Mudhafar: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, writing – original draft, Writing – review & editing

Araa Ali Hadi and Hussein A. Raheem: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources.

Sahi J Dhahi: Conceptualization, Data curation, Formal Analysis, Methodology

Conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Chaudhari AA, Joshi S, Vig K, Sahu R, Dixit S, Baganizi R, Pillai S (2019). A three-dimensional human skin model to evaluate the inhibition of Staphylococcus aureus by antimicrobial peptide-functionalized silver carbon nanotubes. J. Biomater. Appl., 33(7): 924-934. https://doi.org/10.1177/0885328218814984

Dixit S, Baganizi DR, Sahu R, Dosunmu E, Chaudhari A, Vig K, Dennis VA (2017). Immunological challenges associated with artificial skin grafts: available solutions and stem cells in future design of synthetic skin. J. Biol. Eng., 11: 1-23. https://doi.org/10.1186/s13036-017-0089-9

Dovi JV, He LK, DiPietro LA (2003). Accelerated wound closure in neutrophil-depleted mice. J. Leucocyte Biol., 73(4): 448-455. https://doi.org/10.1189/jlb.0802406

DW H (1988). A rat model of resorption of bone at the cement-bone interface in the presence of polyethylene particles. J. Bone Joint Surg., 70: 257-263. https://doi.org/10.2106/00004623-198870020-00015

El-Abd MA, Ibrahim EA (2020). Production and one-step purification of Serratiopeptidase enzyme from Serratia marcescens with potent anti-inflammatory and antioxidant power. Egypt. Pharma. J., 19(3): 238-243. https://doi.org/10.4103/epj.epj_65_19

Jadhav SB, Shah N, Rathi A, Rathi V, Rathi A (2020). Serratiopeptidase: Insights into the therapeutic applications. Biotechnol. Rep., 28: e00544. https://doi.org/10.1016/j.btre.2020.e00544

Khan, AMU, Abd-Razak SI, Al-Arjan WS, Nazir S, Anand STJ, Mehboob H, Amin R (2021). Recent advances in biopolymeric composite materials for tissue engineering and regenerative medicines: A review. Molecules, 26(3): 619. https://doi.org/10.3390/molecules26030619

Li J, Zhou C, Luo C, Qian B, Liu S, Zeng Y, Wang Z (2019). N-acetyl cysteine-loaded graphene oxide-collagen hybrid membrane for scarless wound healing. Theranostics, 9(20): 5839. https://doi.org/10.7150/thno.34480

Mecikoglu M, Saygi B, Yildirim Y, Karadag-Saygi E, Ramadan SS, Esemenli T (2006). The effect of proteolytic enzyme serratiopeptidase in the treatment of experimental implant-related infection. J. Bone Joint Surg., 88(6): 1208-1214. https://doi.org/10.2106/JBJS.E.00007

Mokhtari V, Afsharian P, Shahhoseini M, Kalantar SM, Moini A (2017). A review on various uses of N-acetyl cysteine. Cell J. (Yakhteh), 19(1): 11.

Nejatifar F, Abdollahi M, Attarchi M, Roushan ZA, Deilami AE, Joshan M, Kojidi HM (2022). Evaluation of hematological indices among insecticides factory workers. Heliyon, 8(3). https://doi.org/10.1016/j.heliyon.2022.e09040

Olariu R, Denoyelle J, Leclère FM, Dzhonova DV, Gajanayake T, Banz Y, Taddeo A (2017). Intra-graft injection of tacrolimus promotes survival of vascularized composite allotransplantation. J. Surg. Res., 218: 49-57. https://doi.org/10.1016/j.jss.2017.05.046

Omran ZS, Abbas HA, Albaidhani FA, Almusawi HM, Mudhafar M, Karhib MM, Alsailawi HA (2024). Phytochemical screening of leaves of *Polyalthia sclerophylla* using classical methods and GC-mass spectroscopy: Cytotoxicity and antibacterial activities. Adv. Life Sci., 11(1): 212-219.

Pietruski P, Paskal W, Paluch Ł, Paskal AM, Nitek Ż, Włodarski P, Noszczyk B (2021). The impact of N-acetylcysteine on autologous fat graft: first-in-human pilot study. Aesthet. Plastic Surg., 45: 2397-2405. https://doi.org/10.1007/s00266-020-01633-1

Przekora A (2020). A concise review on tissue engineered artificial skin grafts for chronic wound treatment: Can we reconstruct functional skin tissue *in vitro*? Cells, 9(7): 1622. https://doi.org/10.3390/cells9071622

Rath G, Johal ES, Goyal AK (2011). Development of serratiopeptidase and metronidazole based alginate microspheres for wound healing. Artif. Cells Blood Subst. Biotechnol., 39(1): 44-50. https://doi.org/10.3109/10731199.2010.494580

Sarris J, Oliver G, Camfield DA, Dean OM, Dowling N, Smith DJ, Ng CH (2015). N-acetyl cysteine (NAC) in the treatment of obsessive-compulsive disorder: A 16-week, double-blind, randomised, placebo-controlled study. CNS Drugs, 29: 801-809. https://doi.org/10.1007/s40263-015-0272-9

Tamimi Z, Al-Habashneh R, Hamad I, Al-Ghazawi M, Roqa'a AA, Kharashgeh H (2021). Efficacy of serratiopeptidase after impacted third molar surgery: A randomized controlled clinical trial. BMC Oral Health, 21: 1-9. https://doi.org/10.1186/s12903-021-01451-0

Tiwari M (2017). The role of serratiopeptidase in the resolution of inflammation. Asian J. Pharma. Sci., 12(3): 209-215. https://doi.org/10.1016/j.ajps.2017.01.003

Tsai ML, Huang HP, Hsu JD, Lai YR, Hsiao YP, Lu FJ, Chang HR (2014). Topical N-acetylcysteine accelerates wound healing *in vitro* and *in vivo* via the PKC/Stat3 pathway. Int. J. Mol. Sci., 15(5): 7563-7578. https://doi.org/10.3390/ijms15057563