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Therapeutic effect of Nano Phytosome Pumpkin Loaded Lidocaine on Induced Burned Wound in Rabbits

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ABSTRACT

The primary objective of this study was to enhance the therapeutic potential of conventional Lidocaine by encapsulating it within a phytosome derived from ordinary pumpkin seed oil. This modification was pursued with dual aims: to enhance the physical stability of the oil and to improve the therapeutic efficacy while minimizing the adverse effects typically associated with Lidocaine. To evaluate the therapeutic impact of Nano-phytosome pumpkin-lidocaine gel (referred to as Nano-Lidocaine) on the healing of third-degree burn wounds. A cohort of thirty adult rabbits, comprising both male and female individuals aged between 10 and 18 weeks, characterized by white fur and weighing between 2.5 to 3 kg, was utilized. These rabbits were stratified into five groups, each consisting of five subjects: Negative Control Group: This group received no treatment and served as the baseline control for comparison. Positive Control Group: In this group, rabbits were administered empty liposomes, serving as a control for the liposomal carrier without active ingredients. Ordinary Pumpkin Seed Oil Group: Rabbits in this group received treatment with ordinary pumpkin seed oil, serving as a reference for evaluating the therapeutic effects of the base oil. Nano-Lidocaine 100% Gel Group: Rabbits in this group were treated with Nano-Lidocaine gel at a concentration of 100%, containing both Lidocaine and pumpkin phytosomes. Nano-Phytosome Pumpkin 100% Gel Group: Rabbits in this group were treated with Nano-Phytosome pumpkin gel at a concentration of 100%, serving as a control for the carrier without Lidocaine.

After a 30-day treatment period, it was observed that both Nano-Lidocaine gel (100%) and Nano-Phytosome pumpkin gel (100%) demonstrated significant wound contraction, with measurements of 0.235 cm and 0.274 cm, respectively. These results were in stark contrast to the ordinary pumpkin seed oil-treated group, as well as both the negative and positive control groups, which exhibited measurements of 0.313 cm, 0.313 cm, and 0.274 cm, respectively.

In conclusion, the study successfully developed a Nano-Lidocaine formulation encapsulated within pumpkin phytosomes, which

exhibited enhanced therapeutic effects in terms of wound healing. These findings suggest the potential utility of this novel formulation in clinical applications, particularly for the treatment of third-degree burn wounds.

1. Introduction

Pumpkin seeds are a by-product obtained from pumpkins, it is a rich source of edible oil, and it is becoming increasingly popular to incorporate pumpkin seeds in the medicine field, the food industry, and agriculture because of their health benefits and nutraceutical properties 1]. Furthermore, pumpkin seed oil (PSO) considerable one of the commonly used and versatile edible oils that can meet the high demand for oil in the food industry [2]. PSO possesses potent nutraceutical and antioxidant effects because of its high content of various phytoconstituents ingredients. The PSO exerts different pharmacological effects including antibacterial, anti-inflammation, antioxidant, and wound healing effects [3]. In addition, it has many health advantages against diseases like diabetes, hypertension, and cancer, and the leading advantage of the PSO is inhibiting prostate development and reducing its size [4].

wounds are one of the leading causes of skin injury. In general burn wounds face several obstacles in treatment with problems of fluctuated effectiveness [5]. In severe burn wounds, the cells and blood vessels are frequently damaged, and the blood flow to the site is disrupted. Many variables, including oxygenation, infection, age, hormones, and diet, can impact burn development and disturb healing through the uneven release of different growth factors and cytokines [6)] Nanopharmacology is an emerging field at the intersection of nanotechnology and pharmacology, which focuses on the structure, development, and implementation of Nanomaterials and Nanodevices for therapeutic purposes. It seeks to utilize the unique properties and functionalities exhibited by nanoscale materials to enhance drug delivery, improve drug efficacy, and enable targeted treatment approaches [7)] Phytosomes are a specialized form of herbal extracts that are designed to enhance the bioavailability and absorption of plant-based compounds. The term "phytosome" originates from the Greek words "phyto" which refers to plants, and "soma" which refers to the body [8]. They are created by combining standardized plant extracts with phospholipids, typically derived from soybeans or lecithin [9].

The aim is to confront the difficulties associated with treating severe burn wounds by gaining a comprehensive understanding of the factors that influence burn progression and the healing process. Additionally, the objective involves delving into the emerging domain of Nano pharmacology, which focuses on the creation and application of Nanomaterials as phaytosomal pumpkin for therapeutic purposes of burning wounds. Finally, the goal is to augment the bioavailability and assimilation of plant-based compounds by employing phytosomes, specialized herbal extracts combined with phospholipids, with the intention of enhancing overall health and promoting well-being.

2. Materials and Methods

Pumpkin seed extraction

The pumpkin seeds were obtained from a local herbalist, 500 g were oven-dried for 2 minutes 40°C, then grinded for paste forming by electric grinder, subsequently extracted with 700 mL (70%) methanol for 15 g of pumpkin seed paste using Soxhlet at 40 °C for 35 h until extract cleared colored. The extract yield was condensed via rotary evaporator 40°C[10]. The extract was stored at -18°C until used.

Experimental Animals

Male and female adult rabbits, aged between 10 and 18 weeks, with a white fur coat and weighing between 2.5 to 3 kg, were allowed a two-week period to acclimate. During this time, they were freely provided with food and water.

Experimental Desingh

Thirty rabbits divided into 5 groups (n=5); each group received different treatments as follows: 1st group: negative control, rabbits received no treatment. 2nd group : positive control, rabbits recived empty liposome. 3rd group: rabbits received treatment with ordinary pumpkin seed extract (oil). 4th group: rabbits received treatment with Nano phytosome pumpkin-lidocaine 100% gel. 5th group: rabbits received treatment with Nano phytosome pumpkin 100% gel.

Preparation of Nano Phytosome Pumpkin-Lidocaine

To create the phytosome, 0.5 grams of cholesterol and 0.5 grams of phosphatide choline were dissolved in a mixed organic solvent consisting of 15 ml of chloroform and methanol. The mixture was agitated using a vortex and

subjected to vacuum conditions for 15 minutes. Subsequently, it was incubated in a water bath at 40°C, followed by another round of vortexing and vacuuming for 20 minutes [11]. In parallel, a blank liposome was generated and also incubated in a water bath at 40°C for 5 minutes. Afterward, 1 ml of pumpkin seed oil was added to the blank liposome, thoroughly mixed using a vortex for 2 hours. The supernatant was then removed, resulting in the formation of the phytosome[12]. The Nano phytosome pumpkin was subjected to incubation in a 40°C water bath for 15 minutes. Subsequently, 0.5ml of Lidocaine (0.2%) was introduced to 1 gram of pumpkin Nano phytosome, followed by vortexing for a duration of 1 hour. Afterward, the supernatant was carefully removed, resulting in the formation of pumpkin Nano phytosomes encapsulating Lidocaine [13, 14].

Nano Phytosome $_{\text{Pumpkin-Lidocaine}}$ Loaded in Gel

The gel was made by dissolving 0.125 g of Carbopol in 3 ml of pure distilled water for prepared the gel phase. The acidic component of the gel was then buffered by 1 ml of NaOH 0.1N, which was thoroughly manually blended until being appeared thick and clear. Lastly, the gel was heated for 15 minutes to remove air bubbles [15].The prepared phytosome was mixed with gel, 100 mg of Nano phytosome pumpkin-lidocaine mixed with 100 mg gel, to achieve the concentratio 100%.

Institutional Animal Care and Use Committee (IACUC)

Before commencing any experiments, the methodology and procedures employed in this research were scrutinized and approved in adherence to animal welfare ethical standards by both the Scientific Committee of the Department of Physiology, Biochemistry, Pharmacology, and Toxicology at the College of Veterinary Medicine, University of Tikrit, and the Ethics Committee of the College of Veterinary Medicine, University of Tikrit, Salah Aldin, Iraq (IACUC#: 1285-18-7).

Burn Wound Induction

"Initially, according to the ethical guidelines, the rabbits underwent euthanasia through the administration of general anesthesia by infiltration. Next, we used an electric shaver machine to clip the dorsal region of the rabbits and subsequently disinfected the prepared area with 70% alcohol. Following this, we marked a section of the skin measuring 0.8 cm and carefully removed the layers of skin at that location. To create consistent burn wounds, we employed an electric soldering tool fitted with a copper tip heated to 95°C, which was applied to the designated skin area for one minute. This technique was employed to ensure that the burn wounds were uniform and did not penetrate beyond the skin layers, thus preventing damage to the underlying muscle layer [16] .

Histological analysis of burn wound healing

After the treatment time was over, a histological study was performed on the skin wound healing, lay the harvested healed tissue in between two layer of filter paper to avoid the folding of tissue during fixation process and fix it in a histology cassette for 24 hours in 10% formalin solution, then follows the process of paraffin embedding [17], hematoxylin and eosin (H &E) stain was used to stain sectional slice. In stained tissues, a wound histological qualitative study was done, it performed by using a certain score at certain timeline, as follows [18].

1. Extracellular matrix deposition

Assessment of the amount of extracellular matrix deposition and assessment of the thickness of collagen fibers.

Table 1: The morphological scores descriptive of extracellular matrix deposition

Score	Parameter of extracellular matrix deposition
0	Whole skin: all extracellular matrix
1	Discrete: the incomplete Prescence of extracellular matrix, with thin collagen fibrils filaments, and many fibroblasts
2	Moderate: the presence of extracellular matrix throughout the whole wound area, with thin collagen fibrils filaments, and high number of fibroblasts
3	high: the existence of extracellular matrix throughout the whole wound area, with thick collagen fibril filaments and a small number of fibroblasts

2. **Epithelization:** Estimating the newly formed epithelial layer in the hematoxylin and eosin-stained section.

Table 2: Epithelization score of newly formed epithelial layer in an excisional burn wound in the H&E-stained section

Score	The parameters of the new tissue generated
0	Whole skin: whole skin epithelium
1	Discrete: incomplete epithelization with a little new layer of epithelium (the majority of the wound gap was occupied by 1/3 epithelial tongue).
2	Moderate: incomplete epithelization with a longer new layer of epithelium (the majority of the wound gap was occupied by more than 1/3 epithelial tongue).
3	Complete epithelization

Statistical analysiss: Data analysis statistically was performed using Graph Pad Prism 8.lnk, two-way analysis of variance ANOVA, and values of $p < 0.05$ were considered significant, whereas values of $p > 0.05$ were not considered significant.

Results and Discussion

Pumpkin seed oil extraction and yield

Table 3 showed the yield percentage of pumpkin seed oil, the siphons cycle number, as well as the total time taken to complete extraction process. The extraction was manifested by dark grayish brown color oil the floated upper layer and light pale greenish color **(fig. 1)** stored until phytosome creation at 4 C°.

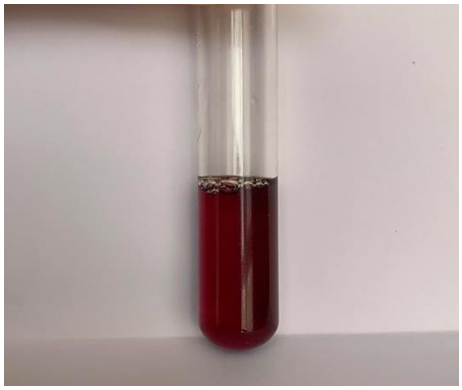

Figure1: Pumpkin seed extract (oil)

Table 3: Pumpkin seed extract yield indices-yield

Raw pumpkin seed weight	Yielding extract %	Siphons number	Time
15 g	58.2 ± 3.2	10±0.4	3.5±0.2 hour

The yield percentage of pumpkin seed oil extraction was 58± 3.2% after ten siphonation of 5 patches (each 15 g of raw pumpkin seed), this result was almost matched and agreed with the results of [19]. The differences between extraction yield percentages of pumpkin results maybe presumably attributed to the difference in many factors influencing the extraction process, including extraction time, gridding time (particle size), heat or cold extraction, genetic diversity, climate conditions, and differ organic solvents in extraction [20, 21].

The effect of pumpkin seed oil and Nano phytosome pumpkin-lidocaine on burn wound healing

The morphometrical appearance calculation of the wound shows the changes in wound diameter between all experimental groups on days 0, 10, 20, 30, and 40. On day 0, all the burn wounds had the same radicals 0.8 cm **(fig. 2)**. On day 10, both Nano phytosome pumpkin-lidocaine gel 100% and Nano phytosome pumpkin gel 100% treated wounds show a significant ($p \leq 0.005$) wound contraction represented as healing distance diameters 0.26 and 0.2 cm respectively compared with ordinary pumpkin seed oil, and both -ve and +ve control groups were 0.435, 0.619, and 0.62 cm respectively. While on day 20 the Nano phytosome pumpkin-lidocaine gel 100% and Nano phytosome pumpkin gel 100% showed entirely and sifgnificant($p \leq 0.005$) wound contraction as compared with both -ve &+ve control and ordinary pumpkin seed oil (PSO). At day 30 Nano phytosome pumpkin gel and Nano phytosome pumpkin-lidocaine ge100% treated wounds showed completely wound contraction as compared with ordinary PSO and both -ve &+ve control group 0.235, 0.313, and 0.274 cm respectively. At the end of the experiment, on day 40 the ordinary pumpkin seed oil had almost complete wound contraction of 0.05 cm as compared with both -ve and +ve control groups 0.2 and 0.14cm respectively.

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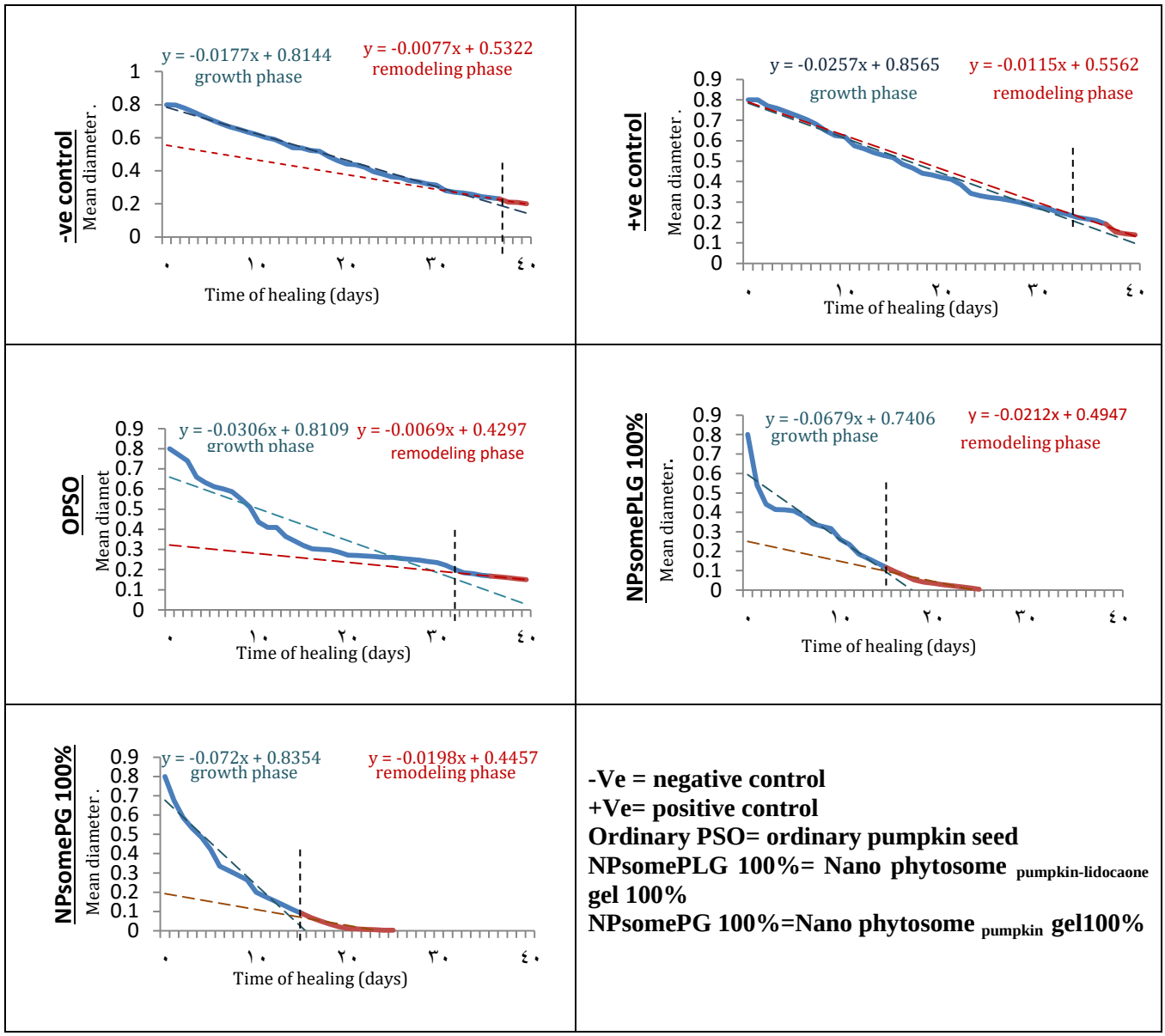

Figure 2: The burn wound closure curves in treated groups as –ve &+ve control groups, ordinary pumpkin seed oil, Nano phytosome $_{\text{Pumpkin-lidocaine}}$ gel 100%, and Nano $_{\text{phytosome Pumpkin}}$ gel 100%.

The effect of pumpkin seed oil (PSO) on wound healing had been documented by [22], the seed oil was positively implicated with wound healing and acceleration of closure rate due to different mechanisms. The anti-inflammatory properties of PSO have an optimistic effect on wound healing and the regeneration of healthy cells, this could be attributed to its ability to promote hemostasis and restrict blood flow in the initial phase of healing [23]. The flavonoid compounds and fatty acids; such as oleic acid and linoleic acid of PSO presumably had anti-inflammatory effects due to their ability to either inhibit the expression or prevent an exodus of inflammatory chemical mediators from macrophage and mass cells promotion anti-inflammatory and allergic responses inhibitor, because of this, the behavioral active components own the pumpkin seed oil the inflammatory activity [24]. As well as, the pumpkin seed oil's flavonoid and phenolic compounds presumably promote closure and wound healing by antibacterial activity, this might have sped up the healing timeline, resulting in facilitated healing [19]. The antioxidant activity of pumpkin seed oil may be presumably could accelerate wound healing in a variety of ways, including demined promoting DNA synthesis, preventing cell damage, increasing vascularity, as well as increasing the strength of collagen fibers, and improving the viability of collagen fibrils [25, 26]. The

pumpkin seed oil may be attributed the liberate their activity on wound via have an antimicrobial activity associated with the combined or individual antioxidant effect of its phytoconstituents [27]. Accordingly, pumpkin seed oil contains many compounds that exert antioxidant activity via several mechanisms, such as scavenging free radicals, where pumpkin seed oil has been found to contain high levels of tocopherols, which were effective scavengers of free radicals and super oxidase, and hydroxyl furthermore, pumpkin seed oil presumably donate electrons to lipid peroxyl radicals, effectively neutralizing them and preventing lipid peroxidation [28]. As well as Phenolic compounds and lignans containing pumpkin seed oil may be attributed to upregulate the expression of genes that encode antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). Besides, carotenoids can quench lipid peroxyl radicals and prevent the propagation of lipid peroxidation [29].

Histopathological evaluation and scores

On day 40, the burned wound tissues stained with H&E were examined and histopathological assessed.

Extracellular matrix deposition

The second phase of wound healing is indicated by the distribution of tissue fibers as an indication of wound closure and by the fibroblast and collagen fibers' extracellular matrix deposition score. Nano phyrosome pumpkin-lidocaine gel 100% and Nano phytosome pumpkin gel treated groups revealed significant ($p \leq 0.05$) dense and well-organized collagen type I and II as compared with the ordinary pumpkin seed oil group and other treated groups, these collagen bundles spread regularly in the dermis with the diffusion of fibroblasts within the collage fibers **(fig. 3,4)** and **(fig. 8)** for supportive information. these observations can potentially be clarified the rapid initiation of the healing process and the prolonged beneficial impacts of Nano Phytosome pumpkin-lidocaine gel and Nano Phytosome pumkin gel on the burn wound. In contrast, ordinary pumpkin seed oil treated groups show irregular diffuse of collagen type II with loose and irregular diffuse of collagen type I as well as showed many fibroblasts diffused within the dermis. A large inflammatory mass was observed within the reticular dermis and congestion of blood vessels **(fig. 5)**. Furthermore, -ve control groups revealed loose irregular collagen fibers type II as compared with treated groups. As well as congestion of blood vessels besides diffusion of WBCs within the dermis as compared with +ve control **(fig. 6)**.While the +ve control showed significant ($p<0.05$) loose collagen fibers type I as compared -ve control group, as well as there was obvious congestion of blood vessels within the dermis **(fig. 7)**.

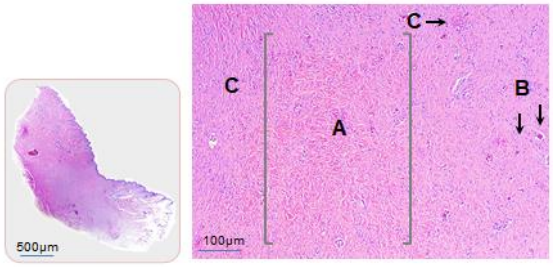

Figure 3: The histological profile of burned wound of skin dressed Nano phytosome pumpkin-lidocaine 100% gel at day 40. A: Dense collagen (type 1), B:loose collagen (type 2), C: fibroblasts

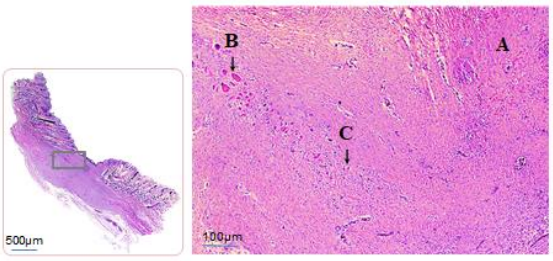

Figure 4: The histological profile of burned wound of skin dressed Nano phytosome Pumpkin gel at day 40. A: Dense collagen (type 1), B:loose collagen (type 2), C: fibroblasts.

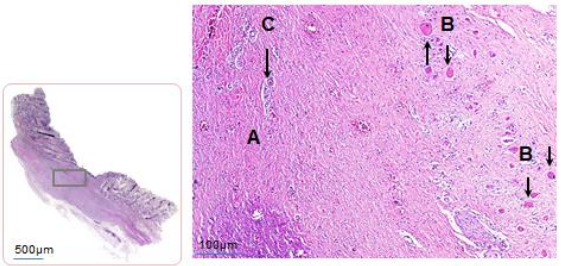

Figure 5: The histological profile of burned wound of skin dressed ordinary pumpkin seed oil at day 40. A: Dense collagen (type 1), B:loose collagen (type 2), C: fibroblasts.

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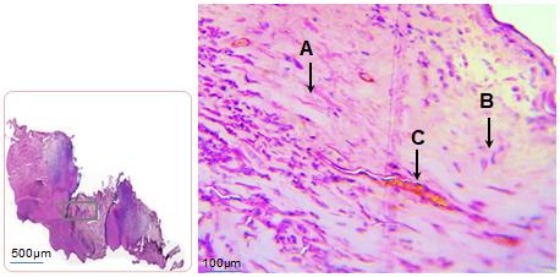

Figure 6: The histological profile of -ve burned wound of skin at day 40. A: loose collagen (type 1), B: fibroblasts, C: congestion blood vessels.

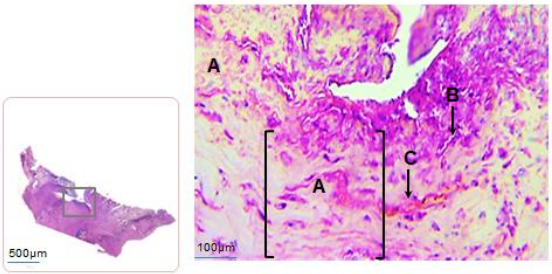

Figure 7: The histological profile of +ve burned wound of skin at day 40. A: collagen (type 1), B: fibroblasts, C: congestion blood vessels

Extracellular matrix score

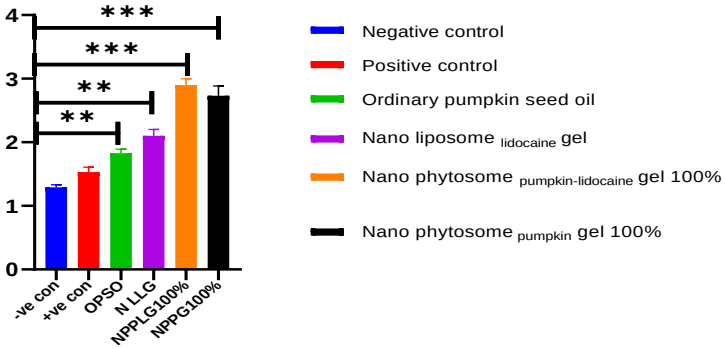

Figure 8: The extracellular matrix score of burn wound healing in the control and treated groups

The Epithelialization

All the epithelialization indicated wound closure and migration of the wound edge to the center wounds. Both Nano phytosome pumpkin-lidocaine gel 100% and Nano phytosome $_{pumpkin}$ gel treated groups showed well-developed epithelialization with the formation of granulation tissue. On Nano phytosome pumpkin-lidocaine gel 100% treated groups demonstrated significant ($p \leq 0.05$) re-epithelization and differentiated to a normal structure, as well as the epidermis was full and well developed with clear stratum carenum developed. The non-remodeling burn wound area was limited as compared to ordinary pumpkin seed oil group and both -ve and +ve control groups **(fig. 9)**. As in the Nano phytosome pumpkin-lidocaine 100% gel treated group, the Nano phytosome pumpkin gel biopsies demonstrated significant ($p \leq 0.05$) and well-developed re-epithelization and the epidermis was almost completely developed, as well as developed of stratum corneum, the remodeling of burn wound area was noticed which indicated complete wound healing (**fig. 10)** and (**fig. 14)** for supportive information. while on ordinary pumpkin seed oil treated group revealed limited differentiation as well as incomplete and non-significant ($p > 0.05$) re-epithelization as compared with Nano phytosome pumpkin-lidocaine 100% and Nano phytosome pumpkin gel (**fig. 11)**. Thin keratins strands were observed. Additionally, the non-remodeling burn wound area was still wide as compared with Nano phytosome pumpkin-lidocaine 100% gel. There was no significant difference between negative and positive groups, the epithelium exhibited abnormal hypertrophied and undifferentiated layers. Moreover, there was still a significant gap at the edge of the damaged epithelium. thin scabbing was seen at the gap, particularly in the negative control (**fig. 12 and 13)**.

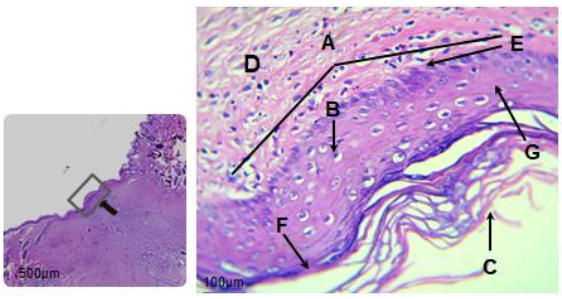

Figure 9 The histological profile of burned wound of skin dressed Nano phytosome pumpkin-lidocaine 100% gel at day 40. A:epihelia , B: basal keratinocytes, C: keratin, D: dermis, E:basal layer, F:Stratum granulosum, G:Stratum spinosum (squamas cells) (H&E x40)

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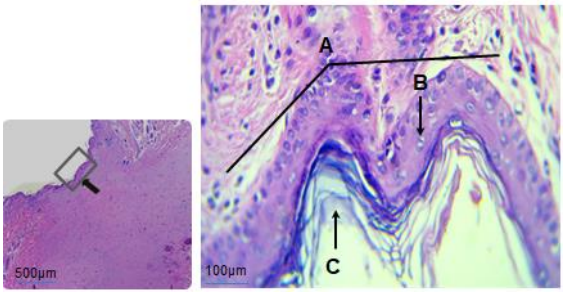

Figure 10: The histological profile of burned wound of skin dressed Nano phytosome $_{pumpkin}$ gel at day 40. A:epihelia , B: basal keratinocytes, C: keratin (H&E x40)

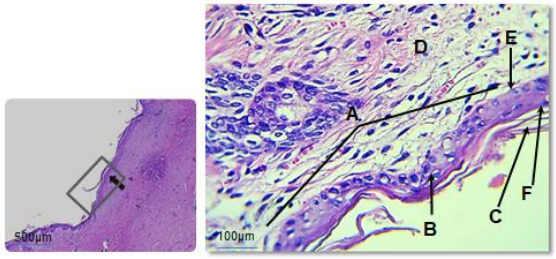

Figure 11: The histological profile of burned wound of skin dressed ordinary pumpkin seed oil at day 40. A:epihelia , B: basal keratinocytes, C: keratin, F:Stratnum spinosum (H&E X40).

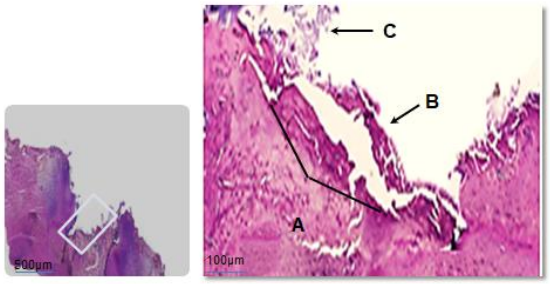

Figure 12: The histological profile of -ve burned wound of skin at day 40. A: Disorganized epithelia, B: desqumated epithelia and epidermal cells, C: plaque of scab(H&E X40).

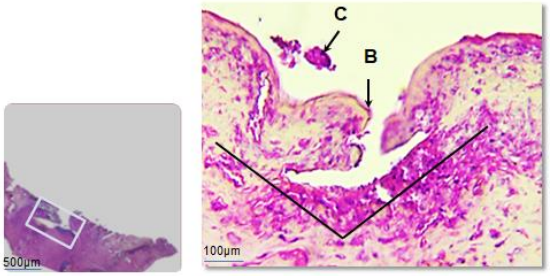

Figure 13: The histological profile of +ve burned wound of skin at day 40. A: epithelial hyperplasia, B: A gap at the edges of epidermis, C: plaque of scab.

Epithelization score

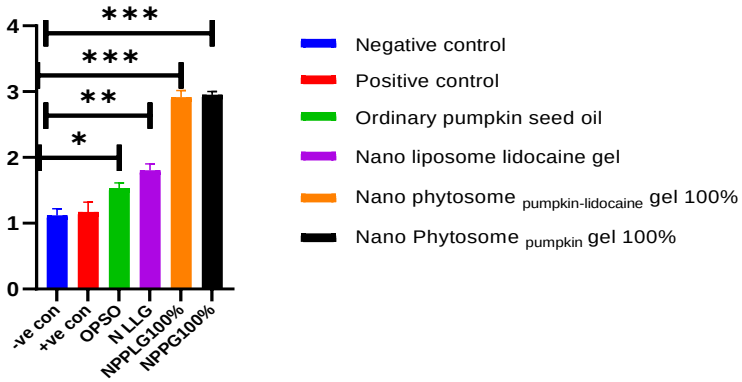

Figure 14: The epithelization score of burn wound healing in the control and treated groups

The pumpkin seed oil (PSO) has the ability to stimulating the fibroblast formation and migration to the wound area during the proliferation phase. The PSO containing fatty acids metabolism may be upregulation of epidermal growth factor especially TGF-β, that presumably led to increased fibroblasts mitogenesis [30], as a result inducing an early development of granulation tissue [31]. These findings consequently impact in wound healing process such as diminish open wound area, speed up liner wound healing rate, closure velocity, and decrease the closure half-life this coincided with our morphometric indices. PSO increased collagen deposition in dermis by increasing fibroblast filtration, especially collagen type I and II [32] this coincided with our histopathological result, showed that the treated group with ordinary pumpkin seed oil showed increase in the infiltration of fibroblast and increase in the collagen deposition as compared with both -ve and +ve control groups. As well as the PSO well-known convert collagen type III to more regular and organized collagen types I and II, as the TGF-β level increased [33]. Furthermore, according to [34] Pumpkin seed oil may be enhance the extracellular matrix via the linoleic acid of pumpkin seed oil which induce increase the transforming growth factor (TGF), Keratinocyte growth factor (KGF), and

cytokines especially interleukin 6 are among cytokines that play stimulate and promote the proliferation and differentiation of keratinocytes, accordingly speeding up the re-epithelization of wound, contraction of wound, and increase the closure velocity. Finally, this is in agreement and matched with the our histological and closure curve findings the healed biopsies from the group treated with Nano phytosome pumpkin-lidocaine gel 100%, Nano phytosome pumpkin gel 100% , and ordinary pumpkin seed oil exhibited re-epithelialization in contrast to the untreated control groups demonstrated a uncompleted and damaged unorganized epithelium.

The results of burn wound healing in the terms of healing curve and histological profile demonstrated superior results that the Nano Phytosome pumpkin gel 100% and Nano Phytosome pumpkin-lidocaine gel 100% dressed wound exhibited considerable healing outcomes than the PSO, and both -ve and positive treated groups. the increased effectiveness of pumpkin seed oil and lidocaine was probably achieved as a result of their behavior of Nano phytosome physical properties such as, tiny Nano size with large surface area to volume ratio, high drug capacity integration into nanoparticles, higher potency, and a promising novel formula created for wound healing using a bio-pharmaceutics of pumpkin seed oil and lidocaine phytosome [35, 36]. The Nano phytosome formula of pumpkin seed oil and lidocaine affected burn wound healing presumably as a result of increased loading, which caused increased entrapment as a result of reduced or disrupted ordered crystalline arrangement, which prevented pumpkin seed oil (PSO) or lidocaine leakage and increased effective amount of drug in phytosome in certain dose, this viability of drug delivery in certain nanoscale size enables it to penetrate the stratum corneum layer of rabbit skin with a significant amount of viable drug load during horizontal diffusion, the physical and chemical properties of phytosome formulas containing PSO and lidocaine may improve the fluidity and organization of the lipid matrix in the stratum corneum, potentially increasing the permeability of PSO and lidocaine and trapping water-based moisture to prevent dehydration of the affected skin, this can ultimately result in continuous rehydration of the affected skin, leading to increased bioavailability of the drugs [37]. Another suggested mechanism might be attributed to the slow sustained release of Nano phytosome pumpkin-lidocaine, the high capacitation of the drug, targeted the active site, high stability, as well as target the active site that may be reduced the harmful and allergic effect by reduced concentration used, eventually increase the closure rate [38], this coincided with results , showed augment in the closure rate curve. Several studies have proposed that using a Nano formulated phytosome for wound treatment could potentially prevent the promotion of the inflammatory phase, phytosome and their phospholipids encouraging the macrophage to migrate and inhibition the production of inflammatory cytokines in the initial phases of a wound [39,40]. As well as, may be prevent an acute wound from turning into a chronic one duo to the scavenging activity of lecithin phytosome which inhibiting the oxidative stress induction, promoting the growth of new blood vessels and [41], these factors can be collectively referred to as the Nano liposome, which involves increasing the half-life of loaded phytoconstituent and improving skin viability, all while minimizing toxicity [42, 43]. Moreover, the surfactant like phosphatidylcholine was presumably plays a crucial rule in wound healing via decreased immunological interaction pathways and decreased of their mediators, in addition to achieving intermolecular interactive bonding between liposome and pumpkin seed oil at the amide group [41, 44]. The lidocaine encapsulated by the Nano phytosome pumpkin provides a sedative effect as well as short-term relief of itch along the treatment period which subsequently enhancement wound healing and reduces the number of dressing changes [13]. Furthermore, the Nano phytosome Pumpkin-lidocaine formulated with gel carpool presumably provided the suitable condition of speeding up the burn wound duo to lipid-gel carpobol formula form occlusive properties which act on the occlusive properties of the lipid and gel formulations may act on the wound by reducing skin moisture loss, furthermore increasing moisturization levels at wound site, in turn facilitating the acceleration of cellular regeneration in the wound healing process [45]. Carpobol gel characterized as non-firm, non-toxic, non-allergenic, non-adherent like jelly texture giving full edges and compartment shapes to wounds and skin loss that rebound in regular cell healing [46]. In the term of histological profile, Moreover, alongside using the gel, moisture retentive occlusive dressings

could enhance wound healing via improving epidermal cell migration particularly in re-epithelialization, In contrast to the dry condition, where cells tend to lose moisture and perish, leading to the formation of scabs or crusts over the wound and hindering re-epithelialization [47], this coincided and agreed with our histological profile of negative control group.

Conclusions

In conclusion, the experimental groups treated with Nano phytosome pumpkin-lidocaine gel 100% and Nano phytosome pumpkin gel 100% displayed noteworthy improvements in wound contraction and extracellular collagen deposition when compared to both the negative and positive control groups, as well as rabbits treated with regular pumpkin seed oil. Furthermore, the Nano phytosome-treated groups exhibited significant reepithelization and the development of a well-structured epidermis, in stark contrast to the limited differentiation and incomplete re-epithelization observed in the ordinary pumpkin seed oil-treated groups. As well as the Nano phytosome-treated groups exhibited significant and well organized collagen fibers, while the ordinary pumpkin seed oil treated groups demonstrated a large inflammatory mass was observed within the reticular dermis and congestion of blood vessels. These findings highlight the potential therapeutic benefits of Nano phytosome formulations in wound healing and tissue regeneration.

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التأثير العلاجي لليدوكائين المحمل بالنانو فايتوسوم اليقطين على الجروح المحروقة في الأرانب

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كان الهدف الأساسي من هذه الدراسة هو تعزيز الإمكانات العلاجية لليدوكائين التقليدي عن طريق تغليفه داخل جسيم نباتي مشتق من زيت بذور اليقطين العادي.
تمت متابعة هذا التعديل لأهداف مزدوجة: تعزيز الثبات الفيزيائي للزيت وتحسين الفعالية العلاجية له مع تقليل الآثار الضارة المرتبطة عادةً بالليدوكائين. لاجل تقييم التأثير العلاجي لجل نانو فايتوسوم اليقطين ليدوكائين (المشار إليه باسم نانو ليدوكائين) على شفاء جروح الحروق من الدرجة الثالثة.
تم استخدام مجموعة مكونة من ثلاثين أرنبًا أبيضا بالغًا، تضم ذكور واناث تتراوح أعمارهم بين 10 و 18 أسبوعًا. ، ويتراوحأ وزانها ما بين 2.5 إلى 3 كغم. تم تقسيم هذه الأرانب إلى خمس مجموعات، تتكون كل منها من خمسة أرانب: مجموعة السيطرة السلبية: لم تتلق هذه المجموعة أي علاج وكانت بمثابة مجموعة التحكم الأساسية للمقارنة. مجموعة السيطرة الإيجابية: في هذه المجموعة، تم إعطاء الأرانب الجسيمات الشحمية الفارغة، لتكون بمثابة عنصر تحكم للحاملة الدهنية دون المكونات النشطة. مجموعة زيت بذور اليقطين العادية: تلقت الأرانب في هذه المجموعة العلاج بزيت بذور اليقطين العادي، ليكون بمثابة مجموعة سيطرة لتقييم التأثيرات العلاجية للزيت الأساسي. مجموعة جل نانو ليدوكائين 100%: عولجت الأرانب في هذه المجموعة بجل نانو ليدوكائين بتركيز 100%، والذي يحتوي على فيتوسومات الليدوكائين واليقطين معا.مجموعة ارانب معالجة بجل نانوفيتوسومات الليدوكائين بتركيز100% ومجموعة ارانب تعامل بجل اليقطين لتكون سيطرة للحامل بدون ليدوكائين.
بعد فترة علاج مدتها 30 يومًا، لوحظ أن كلا من هلام النانو ليدوكائين (100٪) وهلام اليقطين النانوي (100٪) أظهرا تقلصًا كبيرًا في الجرح، بقياسات 0.235 سم و 0.274 سم على التوالي. وكانت هذه النتائج في تناقض قوي مع المجموعة العادية المعالجة بزيت بذور اليقطين، وكذلك كل من مجموعات السيطرة السلبية والإيجابية، التي أظهرت قياسات 0.313 سم، 0.313 سم، و 0.274 سم، على التوالي.
الاستنتاج، نجحت الدراسة في تطوير تركيبة نانو ليدوكائين مغلفة داخل اليقطين والتي اظهرت تأثيرات علاجية معززة لالتئام الجروح، وتشير هذه النتائج إلى الفائدة المحتملة لهذه التركيبة الجديدة في التطبيقات السريرية، وخاصة لعلاج الجروح للحروق من الدرجة الثالثة.

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