Polyphenol in olive oil: A promising adjuvant therapeutic agent in wound healing management and wound complication prevention

Auddrey Sindhutomo*, Gede Wara Samsarga2, Astrinita Lestari Suyata2, Shita Diwyani Sudarsa2

ABSTRACT

Wound is one of the most common findings in medical problems. Tissue repairment would return tissue integrity normally in morphology and function, but in certain cases, tissue repairment could be disrupted or uncontrolled. Disrupted tissue repair by infection agents, inadequate treatment, or other risk factors would lead to complications such as ulcers, gangrene, tissue death, or hypertrophic scar. These complications could lead to physical, mental, social, aesthetic, and financial burdens. Olive oil is a substance extracted from whole olive fruits widely used in the culinary world. Olive oil in skin treatment has been used since ancient times, and current research has developed in olive oil as an adjuvant treatment. Several researches have resulted in a positive result for olive oil as a promising agent for wound treatment to emulate tissue regeneration and prevent wound complications. According to several studies, flavonoids, oleuropein, phenolic acids, phenolic alcohols, lignans, and other compounds contribute as antioxidant and anti-inflammatory compounds. Certain substances in olive oil contribute as a cell protector, antimicrobial, and anticarcinogenic, which are important aspects of wound management, tissue recovery and complication prevention. These substances are found in eliminating oxidative species, lowering inflammatory responses, and inducing protein synthesis in tissue regeneration.

Keywords: Olive Oil, Wound, Management, Polyphenol, Therapy.


INTRODUCTION

A wound is a tissue integrity damage caused by physical, chemical, or thermal trauma toward the skin or mucosal tissue. The wound is a sign of the inflammation process and creates tissue repair. The tissue repair process will return tissue integrity normally in morphological and physiological aspects, but this process requires good condition of tissue condition, body homeostasis condition, and environment. The wound is a common founding but could cause massive complications if not treated well from infection, ulcer, necrosis, and gangrene, which could lead to amputation because of function loss of the organ damaged by the wound not treated well. The managed wounds could create complications of an uncontrolled situation like scarring or hypertrophic scar. Wound and its complication could cause a burden for patients in physiological and aesthetic aspects. Wound surface area, wound management, wound evaluation and wound complication prevention became important aspects of being evaluated in minimizing burdens that the wound could cause. Another burden that wound problems could cause is the management stage. If the management of early wounds is inadequate and prevention of complications is not done well, falling into the complication stage would cause management to be more aggressive, causing a longer process, higher funding, and a thorough and more complicated examination.

Currently, there are several methods in wound management. Wound management aims for tissue healing and regeneration, infection treatment, and preventing complications. Wound management could vary from pharmacological, physical manipulation methods (e.g., laser, radiation) or surgical methods. The pharmacological method will use various drugs such as cream, gel, or healing net, topical or oral antibiotics, and even injections. Physical manipulation is usually done as complication prevention to prevent further scarring or repair of tissue that could not be treated with the conventional pharmacological method. The surgical method is usually done for a wound situation that requires emergency, expanding wound infection, tissue loss, and wound healing complication that causes physiological and aesthetic burden such as a hypertrophic scar. As explained above, a certain management method will be implemented in the patient’s wound. A certain degree of severity will cause a
more advanced method of management, which will increase the financial burden and could cause a higher risk of further problems with the wound.\textsuperscript{4,5} Olive (\textit{Olea europaea}) oil is a fatty substance extracted from whole olive fruits. Olive oil is commonly used as a substitute for vegetable or palm oil for cooking or other uses in the culinary world.\textsuperscript{6} Besides the cuisine field, olive oil is used in health and therapy. Olive oil is believed to have a healthier content of fat to be consumed, and olive oil is also used in massage or mixed with scrub for skin treatment.\textsuperscript{7} Skin therapy using olive oil has been practiced since ancient times and is still well-developed in certain cultures. Current research has been developed for olive oil as an adjuvant therapy for skin treatment, specifically for wound management. Further research exploring constituents of olive oil such as fatty acids, polyphenols, and other constituents has demonstrated a correlation between olive oil used solely or mixed with cream, ointment, or other pharmacological methods and its effect on wound management.\textsuperscript{7} This paper will cover the pathway of olive oil and its constituents in wound management as adjuvant therapy to wound.

**METHOD**

To approach a comprehensive review through studies about olive oil and wound management correlated to the topic discussed in this paper, writers have reviewed several journals systematically that follow the topic of this writing. Eight journals are used as the database within 10 years of publication and discussion of this review. A total of 53 journals were used in this writing, fulfilling the criteria that these journals are published within 10 years. These journals were acquired from Google Scholar, PubMed, and other online journal sites. Keywords that have been used in these reviews are “Olive Oil,” “Wound,” “Complication,” “Management,” and “Prevention.”

**RESULTS**

After thorough searching and reviewing journals available regarding the topic mentioned above, 8 journals were used as the main base date of this literature review. The research used in this writing ranged from animal and human clinical studies, fulfilling the criteria mentioned above. The summary result of the study used in this review can be seen in Table 1.

**DISCUSSION**

**Wound complications and burden**

The wound is a condition of damage causing a disturbance within tissue integrity, such as exposure of inner tissue to the outer environment, cell junction disturbance, bleeding, and loss of function.\textsuperscript{1} The wound is classified by the mechanism of trauma (vulnus laceratum, vulnus scissum, vulnus abrasum) or by an agent of cause (physical trauma wound, chemical wound, burn wound, infection wound, pressure wound, vascular and metabolic wound).\textsuperscript{1,2} Wound healing is a chain of mechanical processes that informs pro-inflammatory agents and cell regeneration factors to recover tissue integrity, which occurs naturally through signaling and cell communication. Several stages should be known in wound healing.\textsuperscript{16} The first stage is hemostasis, which occurs directly after the wound, where vasoconstriction occurs, and platelets undergo activation, adhesion, and aggregation at the injury site. The second stage is inflammation, characterized by redness, heat, swelling, and pain around the wound sites. Neutrophils, monocytes, and macrophages are the main cell that acts at this stage in releasing proinflammatory cytokines and growth factors.\textsuperscript{17} The next phase is the proliferative phase. Within this phase, fibroblast plays a very important role in replacing the provisional fibrin matrix with a new matrix of collagen fibers, proteoglycans, and fibronectin to restore the structure. This event also induces angiogenesis to restore circulation within the tissue and ends with granulation and reepithelization, which induce wound closure.\textsuperscript{18} The final stage of wound healing is the remodeling stage, where granulated tissue will mature as a scar with increased tissue tensile strength, which balances out of extracellular matrix condition and protease activity is regulated.\textsuperscript{19,20}

The normal wound-healing process would take less than a month to progress.\textsuperscript{19} A prolonged wound healing duration over one month would be defined as chronic wound healing. Prolonged duration in chronic wound healing causes further problems and complications of wound healing.\textsuperscript{19} A complication that could be found would be deficient healing, seen in non-healed wounds such as ulcers and inadequate healed wounds such as dehiscence or excessive healed wounds such as hypertrophic scars, strictures, adhesions, keloids, and fibrosis.\textsuperscript{21} Chronic wound healing would cause continuous and uncontrolled inflammation, proliferation, and minimal tissue recovery that could tear with minimal tension.\textsuperscript{21}

Acute untreated or chronic non-healed or inadequate healed wounds would lead to local infection, which could progress to systemic infection, usually from \textit{Staphylococcus aureus}, \textit{Enterococcus sp.}, \textit{Pseudomonas aeruginosa}, \textit{Acinetobacter sp.}, \textit{Candida sp.}, and \textit{Aspergillus sp.}\textsuperscript{22} Besides it, skin and soft tissue infection held to account for annual treatment costs of US$ 3.3 billion and increased inpatient treatment duration. Excessive wound healing would lead to functional and aesthetic concerns, such as a functional deficit, decreased quality of life, and psychosocial burdens within the patient.\textsuperscript{22} Besides, within-patient, excessively healed wounds lead to increased demand for scar treatment, which induces more effective and higher quality scar treatment and prevention, which leads to the higher market price of wound healing treatment.\textsuperscript{23} Chronic wounds impact the healthcare system due to their increasing prevalence and cost. A 2018 retrospective analysis of Medicare in the United States of America found that chronic, nonhealing wounds impact about 8.2 million Medicare beneficiaries. Medicare cost projections for all wounds ranged from US$28.1 to US$96.8 billion, including costs for infection management, among which surgical wounds and diabetic ulcers were the most expensive to treat. Furthermore, outpatient costs (US$9.9–$35.8 billion) were higher than inpatient costs (US$5.0–$24.3 billion), possibly because of increased outpatient wound treatments that are currently provided.\textsuperscript{24}

**Olive oil and its properties**

Olive (\textit{Olea europaea}) oil is a fatty substance extracted from olive fruits. Olive oil is commonly used in the culinary world.
as additional food such as salad dressing, dipping, or as a substitute for healthier cooking oil.\textsuperscript{25} Besides culinary, olive oil is also widely used in physical therapy, massaging or skin treatment.\textsuperscript{25,26} Olive oil can be classified into several subtypes, and the highest and purest form of olive oil is extra virgin olive oil. Extra virgin olive oils are obtained only by pressing, which doesn't undergo additional refining, maintaining substance and compounds within olive oil.\textsuperscript{25}

Olive oil consists of 98% triacylglycerols, fatty acids, mono- and diacylglycerols, and 2% of it consists of minor compounds, mostly made up of phenolic compounds such as flavonoids, lignans, phenolic acids, phenolic alcohols and secoiridoid.\textsuperscript{27} All the phenolic compounds mentioned above could be found in numerous varieties of fruits and vegetables within plant families, except secoiridoids. Secoiridoid is a compound characterized by the presence of an elenolic acid derivative in its molecular structure, which is specifically only found in the Oleaceae family, including the olive tree.\textsuperscript{27} Several studies have researched the function of olive oil properties with the role in cardiovascular, endocrine-

Table 1. Result of Study

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>Method</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>Santorelli et al., 2021\textsuperscript{8}</td>
<td>240 women went through 1-stage augmentation-mastopexy with the inverted T incision divided into two groups (n=120) of oxygen-enriched olive oil bra group and Fitostimoline group</td>
<td>Retrospective study</td>
<td>Scars significantly improved and better scar quality between the olive oil group compared to Fitostimoline group (20 ( v ) 23, ( P&lt;0.0001 )), patients that received olive oil treatment reported significantly lower pain levels.</td>
</tr>
<tr>
<td>Biefeldt et al., 2017\textsuperscript{9}</td>
<td>80 volunteers with non-hypertrophic scar or stretch marks</td>
<td>Observer Blind Randomized Controlled Study</td>
<td>Treated areas are measured using the Observer Scar Assessment Scale, which reduced treated areas by 5% (( p=0.006 )). Overall of product effect of 14% were found to be significant (( p=0.001 ))</td>
</tr>
<tr>
<td>Bayir et al., 2018\textsuperscript{10}</td>
<td>60 male rats modeled with second-degree burn into a group of healthy (n=6), burn control (n=18), Silver Sulfadiazine (n=18), Beeswax+Olive Oil+Butter (n=18)</td>
<td>In Vivo Study (Rat Model)</td>
<td>A mixture of beeswax, olive oil, and butter significantly increased the expression of TGF-B1 and VEGF-a compared to the burn group. This mixture augmented the regeneration of the epidermis and dermis layer injured due to burning.</td>
</tr>
<tr>
<td>Donato-Trancoso et al., 2016\textsuperscript{11}</td>
<td>Forty-five mice were induced with ulcers by magnet placement. Administered olive oil and water</td>
<td>In Vivo Study (Mice Model)</td>
<td>Olive oil administration accelerates ROS and NO synthesis, which reduces oxidative damage compared to the water group. Re-epithelization and blood vessel numbers were higher to be found in the olive oil group compared to the water group</td>
</tr>
<tr>
<td>Schanuel, Saguie, and Monte-Alto-Costa, 2019\textsuperscript{12}</td>
<td>24 male Swiss mice divided into three groups (n=8) induced pressure injury</td>
<td>In Vitro Study</td>
<td>Oil-based diet promoted wound closure 7,10, and 14 days after the end ischemia-reperfusion cycle</td>
</tr>
<tr>
<td>Abdoli et al., 2022\textsuperscript{13}</td>
<td>60 patients with diabetic foot ulcer, divided into two groups (n=30) to standard wound care against standard wound care added with topical olive oil</td>
<td>Randomized Controlled Trial</td>
<td>Treatment with topical olive oil led to a significantly high score in every aspect of wound measurement. The total wound status score was significantly better than the control group (( p&lt;0.001 )). Proportions of completely healed wounds were found to be higher in the experiment group compared to the control group (76.6% vs. 0%)</td>
</tr>
<tr>
<td>Gumus and Ozlu, 2017\textsuperscript{14}</td>
<td>64 burn injury patients, divided into a group of standard wound dressing (n=33) and experimental dressing (n=31)</td>
<td>Experimental Control Study</td>
<td>Epithelisation initiation time average was found to be earlier; the mean pain score was found to be lower, hospitalization duration was found to be lower in the experimental group compared to the control group and statistically significant (( p&lt;0.05 ))</td>
</tr>
<tr>
<td>Miraj et al., 2020\textsuperscript{15}</td>
<td>Seventy-two patients with grade 1 pressure ulcers were divided randomly into two groups: standard skincare program as control and standard skin + topical olive oil in the experimental group.</td>
<td>Clinical Trial</td>
<td>The PUSH score is significantly lower in the experimental group compared to the control group (( p&lt;0.001 )). Difference improvement in the experimental group was found to be significantly improved compared to the control group (( p&lt;0.001 \ vs. 0.052 ))</td>
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</table>
### Table 2. Phenolic Compounds of Olive Oil, Role, And Wound Healing Mechanism

<table>
<thead>
<tr>
<th>Substance</th>
<th>Role</th>
<th>Mechanism</th>
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<tbody>
<tr>
<td><strong>Flavonoids</strong></td>
<td></td>
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</tr>
<tr>
<td>Rutin&lt;sup&gt;30–32&lt;/sup&gt;</td>
<td>Anti-inflammatory, Antioxidant, and Cell Protection</td>
<td>Reducing wound area by stimulating antioxidant enzymes and inhibiting expression of metalloproteinases and VEGF leads to decreased oxidative stress and inflammatory response. Promoting fibroblasts viability and increasing keratinocytes activity</td>
</tr>
<tr>
<td>Luteolin&lt;sup&gt;33,34&lt;/sup&gt;</td>
<td>Anti-inflammatory, Antioxidant, and Cell Protection</td>
<td>Raising the level of E-Cadherin to bind certain cells in creating tissue integrity. Reduces initial inflammatory process to prevent prolonged inflammatory. Reduces migration of leukocytes, loss of plasma, and reduces edema. Increase proliferation of fibroblasts and or keratinocytes</td>
</tr>
<tr>
<td>Apigenin&lt;sup&gt;35,36&lt;/sup&gt;</td>
<td>Antioxidant, Cell Proliferation, Antimicrobial</td>
<td>Neutralise ROS. Induces faster reepithelialization and higher collagen concentration. Inhibit collagenase and hyaluronidase enzymes for wound regeneration. Stimulates the growth and migration of human fibroblasts. Bacteriostatic and Bactericidal against a broad spectrum of bacteria</td>
</tr>
<tr>
<td><strong>Secoiridoids</strong></td>
<td></td>
<td></td>
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<tr>
<td>Oleuropein&lt;sup&gt;37–39&lt;/sup&gt;</td>
<td>Antioxidant, Anti-Inflammatory</td>
<td>Intervenes in dermal regenerative bioprocesses by anti-inflammatory role in reducing oxidative stress and LPS-induced cell death. Reepithelialization by increasing the number of collagen fibers and upregulation of VE</td>
</tr>
<tr>
<td><strong>Phenolic Acids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vanillyl Acid&lt;sup&gt;42&lt;/sup&gt;</td>
<td>Antioxidant, Antimicrobial, and Antibacterial</td>
<td>Protective event against ROS, specifically in chronic wounds. Improved healing of chronic wounds Bacteriostatic and bactericidal</td>
</tr>
<tr>
<td>Caffeic Acid&lt;sup&gt;36,41&lt;/sup&gt;</td>
<td>Antimicrobial, anti-inflammatory, antioxidant, anxiolytic, anti-tumor</td>
<td>Inhibiting ROS generation and releasing Arachidonic acid and Prostaglandin-2 (PGE-2). Fibroblast proliferation from upregulation of COL-I, VEGF, PDGF, FGD, and TGF beta. Stimulating wound contraction and reepithelialization</td>
</tr>
<tr>
<td>Ferulic Acid&lt;sup&gt;44&lt;/sup&gt;</td>
<td>Antioxidant, anti-inflammatory, anti-tumor, cell protection</td>
<td>Increases angiogenesis and neovascularization by stimulating VEGF- dan PDGF-mediated pathways. Reepithelialization and repair response. Reducing the time of wound closure</td>
</tr>
<tr>
<td>p-Coumaric Acid&lt;sup&gt;45&lt;/sup&gt;</td>
<td>Antioxidant, anti-inflammatory, anti-tumor, antimicrobial, cell protection, UV radiation protection</td>
<td>Regenerative effects in stimulating cell growth, differentiation, and migration of fibroblast and keratinocytes. Antioxidant activity on fibroblasts and keratinocytes</td>
</tr>
<tr>
<td><strong>Phenolic Alcohols</strong></td>
<td></td>
<td></td>
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<tr>
<td>Hydroxytyrosol&lt;sup&gt;46,47&lt;/sup&gt;</td>
<td>Antiatherogenic, cell protection, anticancer, antimicrobial, anti-inflammatory, antiplatelet, UV radiation protection</td>
<td>Modulate cell signaling in inhibiting NO, PGE-2, COX-2 expression, and metalloproteinases-9. Increasing production of TNF alpha. Promoting proliferation and migration of keratinocytes, vascular endothelial cells, which lead to angiogenesis, neovascularization, and reepithelialization. Protects DNA damage and reduces intracellular ROS. Reducing cell senescence which promotes anti-aging effect. Diminishing microbial load in wound</td>
</tr>
<tr>
<td>Tyrosol&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Antioxidant, anti-inflammatory</td>
<td>Reduces secretion of proinflammatory cytokines. Inhibited ROS production and kinase phosphorylation. Reduce NO level, TNF alpha level, PGE-2 level, and COX-2 expression. Improvement of blood pressure and circulation in the wound site. Inhibiting bacteria through inhibition of ATP synthase.</td>
</tr>
<tr>
<td><strong>Lignans</strong></td>
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<tr>
<td>Pinoresinol&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Cell proliferation</td>
<td>The current study is still limited, stimulating the proliferation of fibroblasts and keratinocytes</td>
</tr>
<tr>
<td><strong>Other Compounds</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vanillint&lt;sup&gt;55&lt;/sup&gt;</td>
<td>Antioxidant, anti-inflammatory, anti-apoptotic</td>
<td>Vascular regeneration, collagen deposition, and hair follicle reconstruction. Reducing wound size, reducing pro-inflammatory cytokines. Bactericidal and bacteriostatic</td>
</tr>
</tbody>
</table>
metabolism, and gastrointestinal systems and prevention of disease risks in systems as mentioned above from anti-inflammatory and specific cardiovascular roles. Phenolic compounds in olive oil could also give certain effects that function holistically in wound healing.\(^{28}\)

**Mechanism of olive oil in wound healing**

Olive oil has various phenolic compounds that function well as an anti-inflammatory to minimize cellular damage. This is also added with antioxidant, antimicrobial, cellular protection, and tissue recovery properties. Certain agents' mechanisms accelerate or assist the process within the normal wound healing process to prevent infection, minimize inflammation, increase reepithelization and cell proliferation, and control the risk of excessive healing.\(^{28}\) The whole mechanism of olive oil properties can be found in Table 2.

**Clinical implication of olive oil in wound healing**

Current studies and researches on olive oil as an adjuvant agent in wound healing in human subjects are still limited. But the trend of olive oil applied in wound healing is increased and take an interesting outcome. Several studies have applied olive oil as a topical agent, film, or wound dressing. A randomized controlled trial study conducted by Abdoli et al. towards 60 patients with diabetic foot ulcers divided into ulcers wound care group, which consisted of wound irrigation and oral antibiotics and standard wound care plus a topical olive oil group. Both groups were evaluated within 6 months of research in wound healing to examine degree, color, drainage, and surrounding tissue healing. The study has found that treatment with topical olive oil led to significantly better healing in all aspects of the assessment scale starting in week one until week four compared to the control group (p<0.001). And in proportion, the olive oil group has 76.6% of completely healed status, 23.3% of partially healed status, and 0% of unhealed status. While in the control group, the proportion was 0% of completely healed status, 93.3% of partially healed status, and 6.7% of unhealed status.\(^{13}\)

Another study conducted by Gumus and Ozlu among 64 patients with ba urn injury compared a mixture of beeswax, olive oil, and *Alkanna tinctoria* as wound dressing compared to standard clinical dressing within 1 year of study to compare healing process through epithelisation, pain, and hospitalization duration. Results of this study have explained that the experimental group proved earlier starting time of epithelization compared to the control group (in days, 3.00 vs 6.79, p<0.001.). Besides epithelization, experimental group patients report lower scores and shorter hospitalization duration than control group patients' findings (pain score=8.12 vs. 9.39; hospitalization duration=8.22 vs 14.42 p<0.001), which could imply a better quality of life and lower disease burden.\(^{14}\)

The study by Santorelli et al., conducted among 240 patients following 1-stage augmentation-mastopexy, was divided into two equal groups: the Fitostimoline treatment bra group and an oxygen-enriched olive oil bra group. Both groups are evaluated in postoperative pain intensity within 10 days and Patient and Observer Scar Assessment Scale (POSAS) until 12 months post-procedure. Within one month of postoperation, complications arise higher in the fitostimoline group than in the olive oil group (wound dehiscence=10 vs. 2; scar diastasis 6 vs. 1). Patients with olive oil bra have reported similar postoperative pain surgery compared to fitostimoline group on day 2. But by day three, patients with olive oil bra reported significantly less pain than the fitostimoline group (median pain intensity=3.5 vs. 5, a median reduction of pain -41.7% vs. -9.1%). On day ten, patients with olive oil bra reported better and significantly lower pain scores than the fitostimoline group, and where 79% of patients with olive oil bra reported no pain, while the fitostimoline group only 5% of patients reporting of no pain. In scar quality, the olive oil bra group showed a better scar score than the fitostimoline group in six months and twelve months post-surgery (mean scar score, 6 months=25 vs. 38; 12 months=6 vs. 9.5, p<0.0001).\(^{8}\)

Following that, Biefeldt et al., in an observer-blind randomized controlled study among 80 human volunteers with non-hyperpertensive scars and keloid that less than 3 years period applied a cosmetic blend of safflower oil, olive oil, grapefruit oil, and tocopherol for 8 weeks and compared to untreated control and observed using POSAS after the intervention. Looking upon the OSAS scale, the mean score of scars found on the treated area compared to the untreated area is significantly reduced by approximately 5% (p=0.006). On the PSAS scale, the approximate reduction of the mean score of the scar on the treated area compared to the untreated area was found in 6%, with the overall effect of a product found at 14% and found to be significant (p=0.001). Patients also reported satisfaction, positive experience, and agreement toward the product in treating their scars.\(^{9}\)

In a study of chronic wounds or complicated wounds conducted by Miraj et al., 72 ICU patients were found with pressure ulcer grade one divided into two groups the control group using the pressure ulcer care method and the experimental group using 15ml olive oil rubbing in the wounded area. Healing status was assessed using a pressure ulcer scale for healing (PUSH) that examines wound surface area, exudate rate, and tissue type. This study has resulted in patients in the experimental group has shown better closure area starting on the fourth day of application compared to the control group (wound area, control vs. experimental; First day=43.22 vs. 28.75 p=0.093; Fourth day=44.75 vs. 16.70 p<0.001; Seventh day=46.76 vs. 11.72 p<0.001). Evaluation of mean PUSH score was found to be significantly lower in the experimental group compared to the control group and found starting on the fourth day of the experiment (Mean PUSH score, control vs. experimental; First day=9.08 vs. 9.00 p=0.533; Fourth day=9.50 vs. 7.50 p<0.001; Seventh day=8.83 vs. 5.44 p<0.001).\(^{15}\)

Besides human clinical trials, in vivo studies have been conducted widely to examine the properties of olive oil examined in various types of wounds modeled on animal subjects, which can be seen in Table 1. Several olive oil agent types, such as topical ointment, film, wound dressing, and mixed bandage, has been evaluated and predicted as a possible route of olive oil usage as treatment. These animal studies also have shown similar findings histologically in better progress.
of wound healing.\textsuperscript{11,12,13} These studies of animal students altogether with human clinical trials could be concluded that olive oil properties, either as the sole main active therapy or part of mixed therapy, have a crucial role in wound healing as it acts for minimizing inflammation, reducing wound area, accelerating wound healing and closure, preventing infection and complication of the wound. Olive oil has shown benefits for patients with acute or chronic wounds that need proper treatment, where olive oil could be treated as sola e therapy agent or as an adjuvant therapy agent of wound healing.

**CONCLUSION**

Wound is one of the most common findings in hospital situations that could lead to burden due to inadequate or excessive healing progress. Current therapy is developing to wound can heal faster with a better quality of outcome and prevent possible complications as much as possible. Olive oil has been studied as a strong candidate for adjuvant therapy due to its richness in phenolic compounds that could provide therapy properties holistically in wound healing mechanisms to control inflammation, minimize infection, control cell growth, reduce treatment duration, and prevent complications. Olive oil has been studied with human and animal subjects, and such positive outcomes could lead to huge possibilities as a potential therapy in wound treatment. Even though current studies on human subjects are still limited, this review could lead to better research on human subjects and the development of new substitutes or adjuvant agents in wound healing that could increase the quality of life and decrease the burden situation of wounds.

**CONFLICT OF INTEREST**

We declare that there were no conflicts of interest in this study.

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**AUTHOR CONTRIBUTION**

All of the authors equally contributed to the study.

**REFERENCES**


