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LAWSONIA INERMIS LINN'S POTENTIAL FOR PROMOTING WOUND HEALING: A REVIEW

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ABSTRACT

Wound healing has become an important issue in current times as the synthetic antibiotics and antimicrobials which were used for wound healing are becoming to show adverse effects and starting to generate resistance. There is a need for an alternative course of treating the wounds to increase the wound healing rate. From the ancient period natural products are widely used for wound healing process. Among the vast pool of natural plants present on earth *Lawsonia inermis Linn.* Frequently called as henna is most widely investigated plant for wound healing. This plant catches the attention of researchers due to its various active chemical constituents present in it. It has shown an excellent healing of wound in many wound models. Although it has been studied various times still there is a need to gather all the information of henna regarding wound healing this will help the future researchers to study the full potential of this plant on wound recovery process. This study reviews the previous researches done on *Lawsonia inermis Linn.* to identify its full potential for promoting wound healing.

Keywords: Wound healing, Growth factors, *Lawsonia inermis Linn.*, Henna, Anti-bacterial activity

INTRODUCTION

Wound is defined as an accidental damage or trauma, typically describing physical harm that causes a disruption in the normal structure of the skin [1]. From the starting of the time humans are suffering from wounds.

it is not in any individuals control to be immune to accidents. Accidents occurs to any individual on any part of the body at any place or any time. It is not according to any individuals will. However the human body

has the ability to heal wounds through ongoing tissue repair and regeneration [2]. There are several overlapping stages of wound healing process namely Inflammation, proliferation, Maturation, Fibrosis [3].

The above mentioned capabilities may be delayed or decreased by the reasons like seniority, dehydration, cell death, stress at wound site, physique, ongoing disorder, infections with microbes such as bacteria [4]. Hence there is a need for proper care of wounds in the form of treatment [2]. Wounds are commonly treated with antimicrobial agents in which antiseptics like chlorohexidine, Silver nitrate, Silver nanoparticles, Povidone iodine and antibiotics like Bacitracin, Mupirocin, Neomycin, Silver sulfadiazine, Mafenide. They are applied locally on the wound site. But, these synthetic topical agents sometimes show adverse effects at the site of application [5]. The overt use of conventional antimicrobial agents can be a critical challenge in wound healing process.

To overcome the unintended consequences of these synthetic antimicrobial agents researchers have focused on the past in the folklore medicinal system application of natural products for intervention of healing of wounds. Among the vast pool of herbs present on earth there is one herb which catch the eye of researchers is *Lawsonia inermis* linn often

called Henna. *Lawsonia inermis* among the most studied plant for wound healing [5]. Henna was first used as wound healing agent by the prophet Mohammed (peace be upon him) [6]. This review is a comprehensive study of all the current and previous researches done by the researchers for wound healing potential of *Lawsonia inermis*.

Wounds

Injury that result in the loss of structural and operational stability of a tissue, leading to a disturbance in the cellular and anatomical coherence. An injury is also characterized via a disturbance in the typical organization and operational capacity of the skin, which can manifest as an opening or breakage of the dermal and a disruption or break in the continuity, with or without the degradation of the tissue that connects or supports other tissues [7, 8]. The etiology of wounds includes damage of tissue caused by surgery, a cut, a blow, chemicals, pressure, or a result of disease. Wound may occur due to microbial agents, physical trauma, chemical damage, temperature related injury or immune-mediated injury to the tissue.

Types of wounds

Wounds can span from minor to critical, and in certain situations, they can result in death.

1. Based on the site of wound

In this category the wounds are classified on the basis of their position on which site of

body do they occur, e.g., belly or armpit trauma.

2. In accordance with origin of wound development

In this category wounds are classified on the basis of causes by which the wound is inflicted on the human body. The two main types of wounds that are classified in this category are open and closed wounds [9].

i) Open wound

In this type of wounds there is a loss of blood through the body and the bleeding can be visibly seen. It is further classified into detailed categories based on the etiology of open wounds as slicing wound, laceration, puncture wound, deep wound, ballistic wound, superficial wound.

Incised wound

It is a type of injury in which there is no loss of tissue and tissue damage is also minimal. The etiology of this type of wound is due to a pointed implement like blade. The blood loss in that situation might be greater, thus there is a need for immediate action regarding this type of wounds.

Tear wound

This type of wound is nonsurgical usually occurs by accident or trauma, resulting in tissue damage.

Puncture wound

The etiology of this type of wound is sharp object piercing the skin. There are greater possibility of infection contained by this type of wounds because of the dirt and

foreign particle present on the object can penetrate and reaching the innermost part of the wound.

Permeation wound

Permeation wounds brought about by the objects which penetrate deeply into the skin and piercing the skin.

Gunfire wound

It is a result of a projectile or a analogous object penetrating or passing from one end of the body to the other.

ii) Closed wound

Closed wounds are injuries that do not break the skin. Blood does not leave the body but only escapes the circulating systems in a closed wound. Some types of the closed wounds are crush injury, bruises, hematomas etc.

3. Based on the chronicity

Acute Wounds

Acute wound typically resulting from cuts and surgical procedures and healing fully within the normal recovery period. An Acute injury is a wound that is sudden and severe, and it typically heals via punctual regenerative process that restores the tissue's normal structure and function [10].

Non-healing Wounds

Slow-healing wounds refer to wounds that don't heal within a certain period of time and result in entering the stage of inflammation that leads to disease. Wounds that are chronic require an extended healing period. Local infections, foreign bodies, trauma,

hypoxia, immune deficiency are the most frequently encountered factors of chronic wound [11, 12].

4. Based on wounds without or with tissue destruction

Wounds are usually grouped into wounds with tissue impairment (eg: burn wounds), and wounds without tissue impairment (eg: in surgery).

Avulsion

Avulsion is described as a wound in which there is a loss of tissue, preventing the closure of the wound edges. An avulsion may be caused by grooving or tearing of tissue.

Strains

Strains are injuries caused by stretching forces. It usually occurs to muscles or muscle fibers. There may occur some swelling in this type of wounds. Often patients complain about pain. Strains usually treated with rest by following mobilization.

Sprains

A sprain is an injury to the fibrous tissue surrounding a joint. Sprain injury damages the fibrous ligaments around the joint, it usually caused by excessive movements of joints. In a mild sprain there is tearing of only a few fibrous ligaments, whereas in chronic sprains tumor formation in the joints can also happen. In severe cases complete tearing of ligaments can occur. Sprains require more time to heal as compared to

strains. Some common symptoms of sprains includes pain, swelling, local heat, disability and discoloration of the affected area.

Stages of Wound Healing

The skin has the ability to repair itself by a succession of stages like hemostasis, inflammation, proliferation, maturation and fibrosis. The process of wound healing usually divided into two major categories primary healing and secondary healing. Primary healing occurs when the destruction of tissue is less and the edge of the damaged tissue is close to each other, whereas in secondary healing the tissue damage is more and the damaged edges are way too far from each other resulting in fibrosis or scar formation. The significant contrast between primary recovery and secondary recovery is that the primary healing does not have fibrosis phase.

1. Hemostasis

Immediately after the wound inflection Hemostasis takes place. The main vital cell that oversees the duty of hemostasis is platelet, who forms the clot on the wounded site preventing the loss of blood. Collagen and other extracellular matrix components interact with the blood components and platelets when the blood is spilled into the area of trauma. The blood clot also acts as a temporary support structure for cellular migration during the intermediate phase between hemostasis and inflammation [14, 15]. Platelet cytoplasm houses signaling

molecules and immune system regulators, including (PDGF), (TGF- β), (EGF) and (IGF). These compounds promotes wound restoration process by stimulating neutrophils and later immune cells, endothelium and collagen-producing cells [13].

2. Inflammatory phase

This is the repair stage. Some molecular events start in this stage by neutrophils present on the wounded site, neutrophils contains phagocytes which contains macrophages and fibroblasts [16-20]. Phagocytes remove the blood clot and destroy bacteria, cell debris and any other foreign particles and damage tissue, stimulating fibroblast activity. Fibroblasts are the molecules which secrete collagen bundles. These collagen bundles then tend to bind the damaged surface together.

3. Proliferative phase

The growth phase begins three days after the wound is inflicted and lasts for approximately two weeks. In this phase the epidermis grows upwards until full thickness is restored. After 3 to 10 days the scab present above the new tissue which was previously the clot, separates from the newly generated tissue. In this phase also there is also development of regenerative tissue, composed of fresh capillary sprouts, phagocytic cells and fibroblastic cells. Infiltrated the clot and the bloodstream is

revived on the injury site, continues to release fibrous protein, the clot and any other microbes are wiped out, these all occurs through the help of new capillary buds, fibroblasts and phagocytes respectively [21-23].

4. Maturation or Remodeling

This is the end of the healing process. This phase may go on up to 1 or 2 annum or occasionally for an extended duration. In this phase the granulation tissue is substituted with the fibrosis. The wound's potency grows as collagen fibers amass. Collagen fibers may recover about 80% of their original durability in contrast to normal tissue. As time elapses, the scar becomes less vascular over time, and after a few months, it appears as a thin line. the tissue can never fully recover its original strength. As wound heals, capillary growth ends, blood stream to the injured are decreases, and metabolic processes during wound repair lessens. ultimately there is a fully developed scar which has diminished number of blood vessels and cells and have a high tensile potency [24-26].

Different Mitogenic Factors and Their Functions in Wound Healing

There are several Mitogenic factors which are secreted from the cells at the wound site [27]. **Table 1** lists some functions of the Mitogenic factors responsible for wound healing.

Table 1: Functions and period of release of various mitogenic factors in healing of the wounds

Mitogenic Factors	Abbreviation	Period of release	Functions
Platelet Derived Growth Factor	PDGF	Hemostasis Phase Inflammatory Phase Angiogenesis Remodeling Phase	Enhances proliferation; Stimulates cells to produce Extracellular matrix; Stimulates fibroblasts to contract collagen matrices [28]
Transforming Growth Factor - α	TGF- α	Late inflammatory Phase Proliferative Phase	Mitosis of keratinocytes and fibroblasts [29, 30]
Transforming Growth Factor - β	TGF- β	Hemostasis phase Late inflammatory phase Angiogenesis Remodeling phase	Chemoattractant; Stimulates re-epithelialization and formation of granulation tissue; Stimulates angiogenesis, fibroblast proliferation, myofibroblast differentiation and matrix deposition [31, 32]
Fibroblast Growth Factor	FGF	Late inflammatory Phase Angiogenesis Remodeling Phase	Angiogenesis stimulation; Proliferation of keratinocytes and fibroblasts [33]
Vascular Endothelial Growth Factor	VEGF	Angiogenesis	Stimulates Angiogenesis [34]
Epidermal Growth Factor	EGF	Hemostasis Phase Granulation Phase Re-epithelialization	Attractant for fibroblast; Division of Epithelial cells [35]
Insulin-like Growth Factor	IGF	Hemostasis Phase	Stimulator of mitogenesis; Increase dermal and epidermal synthesis with PDGF [36]
Connective Tissue Growth Factor	CTGF	Proliferative Phase Granulation Phase	Stimulates proliferation; Induce extracellular matrix production [37]
Tumor Necrosis Factor - α	TNF- α	Angiogenesis Phase	Angiogenesis mediator; Collagen synthesis [38]
Interleukin - 1	IL-1	Inflammatory Phase Proliferative Phase Remodeling Phase	Chemotaxis of neutrophils; Proliferation of keratinocytes and fibroblasts; Angiogenesis; Matrix synthesis and collagen production [39]
Interleukin - 4	IL-4	Proliferative Phase	Fibroblast migration and proliferation; synthesis of extracellular matrix [39]
Interleukin - 6	IL-6	Proliferative Phase	Mitogenic for keratinocytes; Chemoattractive for neutrophils; stimulate fibroblast proliferation; Inhibit extracellular matrix breakdown [39]
Interleukin - 8	IL-8	Proliferative Phase	Chemoattractant for polymorphonuclear leukocytes [39]
Interleukin - 10	IL-10	End of Inflammatory Phase	Termination of inflammatory process [40]
Macrophage Chemoattractant Protein	MCP	Hemostasis Phase	Monocyte chemoattractant; lymphocyte recruitment [41]
Macrophage Inflammatory Protein - α	MIP- α	Proliferative Phase	Attract macrophages [42]
Interferon- γ -induced Protein - 10	IP-10	Hemostasis Phase Proliferative Phase	Lymphocyte infiltration; Inhibitory effect in angiogenesis [43]

Complications in Healing Process

The above mentioned healing cascade can be delayed by a variety of factors which are liable for compromised or improper wound

healing. The most common factor which leads to impaired wound healing or delayed wound healing is microbial infection. Most common microbes or bacteria involved in

the complication of wound are *S. aureus*, *E. coli*, and *S. typhi* among these microbial agents, *E. coli* and *S. aureus* are known to main reason for impaired wound healing [44].

Wound Healing Treatment by Synthetic Antimicrobial Agents

The growth of microbial agents on the wound site is the primary reason for impaired process of healing a wound. The best strategic approach to get faster wound healing would be the use of antimicrobial agents [45]. Most of the times the wounds

are inflicted on the outside of the body therefore, majorly topical antimicrobial agents are used for the normal wound healing process [46]. There are various antimicrobial agents synthesized by the researchers which are categorized as antiseptics and antibiotics. These topical antimicrobial agents are widely used in the whole world as they can be applied on the wounded site topically to the greater extent. Some of the synthetic antiseptics and antibiotics used for wound healing are given in **Table 2**.

Table 2: Synthetic anti-microbial agents used for wound healing

Sr. No.	Antimicrobial agents	
	Antiseptics	Antibiotics
1	Chlorohexidine	Bacitrain
2	Silver nitrate	Silver sulfadiazine
3	Silver nanoparticles	Neomycin
4	Povidone iodine	Mafenide

But, the use of these synthetic antimicrobial agents are often not as useful as it seems. There is an increased changes that the prolonged use of these antimicrobial agents can lead to generate resistance [47]. There is reported evidence of the local and systemic side effects or adverse effects shown by these antimicrobial agents. These side effects includes pain on the wound site, rashes, toxic impact on the cells that aid in wound healing, formation of *boils* and *abscesses*. These effects occurs on the site of application [48].

Wound Healing Strategies by Herbal Alternatives

The most frequent way to overcome the resistance occur by the use of synthetic antimicrobial agents is the employment of natural remedies such as herbal medicines [49]. Form the ancient times mankind constantly uses the herbal ingredients to cure various types of diseases by using the phytoconstituents present in the plants. Traditionally, the treatment of wounds are also done by these natural alternatives [50]. The healing process is improved by isolating phytoconstituents form these plants. These phytoconstituents shows improved or faster wound healing by various mechanisms by giving synergistic effect [51]. The

phytochemicals that present in the plants shows improved wound healing activity because they possess antibacterial activity, reduction of oxidative damage, free radical scavenging activity, stimulated cell growth, augmented collagen manufacturing, enhanced angiogenesis, boosted DNA synthesis [52]. The natural plants improve

the process of healing a wound by helping in coagulative process, defense against bacterial infections associated in wounds, and therefore, there is an increase in wound healing rate. Some reported studies of plants that shows wound healing activity are mentioned in Table 3 [53-61].

Table 3: Investigated plants used for wound repair process

Sr. No.	Botanical name	Therapeutic component	Reference
1	<i>Lawsonia inermis</i>	Leaves	[53]
2	<i>Annona squamosa</i>	Leaves	[54]
3	<i>Aloe vera</i>	Leaves	[55]
4	<i>Embelia ribes</i>	Leaves	[56]
5	<i>Morinda citrifolia</i>	Fruit	[57]
6	<i>Aegle marmelos</i>	Whole plant	[58]
7	<i>Glycine max</i>	Seeds	[59]
8	<i>Allamanda cathartica</i>	Leaves	[60]
9	<i>Laurus nobilis</i>	Leaves	[60]
10	<i>Nelumbo nucifera</i>	Rhizomes	[61]

Wound Repair Properties of Henna Leaves

From the vast pool of natural ingredients used for wound healing the most used plant is *Lawsonia inermis* frequently referred to as mehendi or henna. *Lythraceae* family member and the species belongs to the genus *Lawsonia*, [62]. Traditionally, *Lawsonia inermis* leaves are used as a coloring agent, also *Lawsonia inermis* leaves is used as an antibacterial, Hepatoprotective, immunomodulatory [63]. *Lawsonia inermis* leaves was first used as wound healing agent by the holy prophet Muhammad (peace be upon him) [6]. *Lawsonia inermis* is extensively researched plant for wound healing. The main ingredient present in *Lawsonia inermis* is 2-

dihydroxynaphthoquinone (lawsone) which is present in abundant amount in the leaves of *Lawsonia inermis*. Lawsone's hydroxyl groups may bind with bacterial cell wall components, leading to antimicrobial activity [64].

Bouhlali *et al.*, studied that *Lawsonia inermis* shows both outside and inside the body anti-inflammatory activity [65]. Henna contain flavonoid content which shows anti-oxidant activity and the regulation of cytokine and adhesion molecule gene expression [66]. Chaibi *et al* states that the methanolic preparation obtained from *Lawsonia inermis* leaves suppresses the biosynthesis of prostaglandins while decreasing nitric oxide and pro-inflammatory cell production [67].

Nayak *et al.* studied that *Lawsonia inermis* leaves extract shows high healing rate because of the existence of secondary metabolites it in [68]. elebeedy *et al.* studied that *L. plantarum* and henna plant work together against *S. aureus* in a synergistic way in which he state that *Lawsonia inermis* alone shows the most effective antibacterial inhibition zone [49].

Flavonoids are among the primary components of henna. Flavonoids are reputed for their part in the healing of wounds. The bacteria responsible for common skin infections are susceptible to henna leaf extract's antimicrobial activity [69]. Barkat Ali Khan [70] suggests that using *Lawsonia inermis* leaves may be a safe way to hasten wound healing.

A pilot study was done on *Lawsonia inermis* leaves extracted oil for wound healing by saliha AM *et al* on Sprague-dawley rats which shows full re-epithelialization and collagen fibers that are neatly arranged and devoid of any inflammatory cell growth. resulting in improved wound healing [71].

Another study was performed on oryctolagus cuniculus rabbits by Djerrou Z *et al* in which he stated that extract of henna leaves has remarkable effects on wound healing. Also Histological study done on henna leaves revealed that henna given at low dose and high dose in comparison to

control positive and control negative has better wound healing [72].

Henna powder when applied topically in combination with honey it shows an improved burn wound healing and also there is an improvement in hair growth at the location of the wound [72].

Ethanol henna leaf extract exhibit better wound healing properties when applied locally as compared to the same given through oral administration. It's activity of healing a wound was studied on wound models in rats using incision and excision techniques [73]. Hamdi YP *et al* also studied that henna leaf extract in ethanol when given in dose of 200 mg/kg it shows increased in wound contraction, decreased in the rate of epithelial cell migration, high skin durability, and a notable increase in hydroxyproline content and density of granulation tissue when applied topically on burn wounds [74].

Muhammad HS *et al* studied the utilization of isolates of *Lawsonia inermis linn.* (Henna) for burn wound care. In which they established that the organic solvent and water-based extract of the henna leaves shows anti-microbial activity on the wounded site which results in improved burn wound healing [75].

An evidence based research conducted by Nayak BS *et al* for the ability of *Lawsonia inermis linn* to promote wound healing. The microscopic examination of

tissue indicated an amplified number of structured collagen fibers with limited inflammatory cells and also an elevation in the amount of fibroblasts [76].

Another study for the healing benefits of *Lawsonia inermis* Linn for wounds. On Arabian horses by towfik AL *et al* shows that the wounds treated with 20% concentration of the extracts of henna leaves shows no swelling, increased growth of epithelial tissue, dryness of wound, absence of bleeding, abscess-free wound and scar tissue formation from the very early stage of medication. Also by contrast with the standard group the Histopathological examination shows hyperproliferation of epidermal layer and clear growth of new blood vessels [77].

An ointment made from the hydro-ethanolic isolate of henna leaf was evaluated to achieve wound healing activity on wister rats. The early inflammatory stage of healing a wound was shortened by the topical use of the ointment. Enhanced wound contraction and an increased in cellular proliferation can also be seen in the rat models treated with the *Lawsonia inermis* ointment. Also there was an improved re-epithelialization rate and an increase in the collagen deposition rate [78].

Saeed naseri *et al* studied the outcome of using natural henna and flaxseed organic cream for the regenerative healing purpose for partial thickness burns. The

prepared ointment shows reduced inflammation and an elevation in the healing rate when compared to other control groups. Also there is an increased in the epithelialization process and speeded the collagen synthesis rate [79].

A wound healing study was done by kalbaza ahmed yassine by formulating a topical ointment from the powder of *Lawsonia inermis* leaves. The topical application of the ointment on excision rat model shows an excellent wound contraction as compared to the group receiving no intervention. Microscopic tissue examination of treated tissue shows increased epithelialization, increased blood vessel formation and good angiogenesis [80].

Analyzing various *Lawsonia inermis* leaf extract and lawsone in various rat models. Ethanolic extract administered orally and applied topically shows notable increase in wound healing. The topical use was more beneficial and advantageous in contrast to administered orally [81].

The treatment of *Lawsonia inermis* extracted oil for wound healing shows better wound healing than commercial wound healing cream cicaflora. This was because of various phytochemicals present in the extract of *Lawsonia inermis* Linn [82].

Simultaneous use of henna powder and honey expedite the burn wound recovery procedure in rabbit test subject.

The hair growth promoting activity of henna was also noted on the wounded area [72].

Anti-Microbial Potential of Henna Leaves for Wound Healing

The alcohol-based isolate of hennaleaves has more potent anti-microbial activity in contrast to the aqueous isolate of the same. The inhibition zone of the ethanol-derived extract of henna leaves was greater than the synthetic gentamycin antibiotic. It was found that this anti-bacterial activity of henna leaves extract was due to the occurrence of 2-hydroxynaphthoquinone (lawsone) which is the main component of *Lawsonia inermis* [83].

Lawsonia inermis leaves extract possess anti-bacterial activity due to the presence of some pharmacological ingredients present in it which results in better wound healing process. The responsible chemical constituent for anti-bacterial activity of *Lawsonia inermis* includes lawsone (2-hydroxynaphthoquinone) [84].

Lawsonia inermis decreases the extent of (TNF- α) individually when anti-bacterial property of henna was studied against *staphylococcus aureus*. Anti-microbial activity of extraction of henna leaf might be the cause of accelerated phytotherapeutic wound healing [85].

The main chemical constituent found in *Lawsonia inermis* leaves which is present in abundant quantity in it is 2-

hydroxynaphthoquinone (lawsone). It is assumed that the presence of many reactive oxygen species present in henna leaf may indicate anti-microbial behavior by the mechanism of deactivating the components present within the bacterial cytoplasmic membrane [86].

The aqueous extract of *Lawsonia inermis* leaves shows better anti-bacterial than the methanolic and chloroform extract. The inhibition zone of aqueous extract was more as compared to methanolic and chloroform extract [87]. Whereas in some studies methanolic extract of *Lawsonia inermis* leaves has shown anti-microbial properties against *E. coli*, *K. pneumonia*, *S. aureus* by agar well diffusion method [88].

A study was done by Awadh ANA *et al* on the anti-bacterial and cytotoxic activity of 20 different medicinal plants. Among them the ethanol-based isolate of henna leaf has shown the maximum anti-bacterial property in opposition to all the bacterial species in the test system [89].

The anti-bacterial effect of Yemeni henna leaves was studied contrary to *S. aureus*, *E. coli*, *P. aeruginosa* by Kirby-Bauer test along with minimal inhibitory concentration was calculated. The methanol extract showed evidence of high anti-microbial property in opposition to broad spectrum of bacteria when juxtaposed with aqueous extract. The aqueous isolate showed minimum anti-bacterial effect

against *Escherichia coli* while the methanolic extract showed maximum inhibition against *Staphylococcus aureus*.

Lawsonia inermis inhibits the growth of Amp C β -lactamases producing *Proteus mirabilis*, this *Proteus mirabilis* shows resistance to commonly used

antibiotics. But, *Lawsonia inermis* shows inhibition to *Proteus mirabilis* [90].

There are number of bacteria present in the world which are susceptible to various extracts of *Lawsonia inermis* leaves. some of the extracts which shows anti-bacterial activity are given in **Table 4**.

Table 4: extracts of *Lawsonia inermis* that shows anti-bacterial activity

Types of Extract	Types of Bacteria which are susceptible	Reference
Aqueous Extract	<i>Bacillus cereus</i> , <i>B. anthracis</i> , <i>S. aureus</i> , <i>E.coli</i> , <i>Proteus vulgaris</i> , <i>Erwinia carotovora</i> , <i>X. canpestris</i> , <i>A. tumefaciens</i> .	[91]
Ethanollic Extract	<i>Bacillus megaterium</i> , <i>bacillus subtilis</i> , <i>bacillus fusiformis</i> , <i>streptococcus pyogenes</i> , <i>streptococcus faecalis</i> , <i>staphylococcus aureus</i> , <i>streptococcus pneumonia</i> , <i>salmonella typhi</i> , <i>E.coli</i> , <i>Pseudomonas aerogenosa</i> , <i>shigella flexneri</i> , <i>enterobacter aerogenes</i> , <i>vibrio cholera</i> , <i>klebsiclia neumonia</i> .	[92]
Methanolic Extract	<i>B.subtilius</i> , <i>S.aureus</i> , <i>S. epidermidis</i> , <i>E. coli</i> , <i>S. flexneri</i> , <i>P. aereginosa</i> , <i>K. pneumonia</i> .	[93]
Chloroform Extract	<i>P. aeruginosa</i> , <i>S. aureus</i> , <i>Fusarium oxysporum</i> , <i>Candida albicans</i> , <i>Aspergillus niger</i>	[75]
Hydro-Alcoholic Extract	<i>A. actinomycetemcomitans</i>	[94]

CONCLUSIONS

The present antibiotics used for the wound healing process shows adverse effects and generate resistance. The need for an alternative method to prevent these side effects is necessary. *Lawsonia inermis* has been studied a lot for it's wound healing activity from the starting of the time. This review conclude all the studies done on *Lawsonia inermis* giving the best outcome for the potential use of this plant in the field of wound care. More future study are expected on this plant to formulate a conventional dosage form for wound healing. Which would be easily applicable, economic, shows minimal or no side effects.

REFERENCES

- [1] Dorland WAN, Dorland. Dorland's pocket medical dictionary. 25th ed. London, England: W B Saunders; 1995. P. 925.
- [2] Kumar A, Fausto M. Robbins' Basic Pathology. 8th Edition. - Philadelphia: Elsevier Inc. (2007).
- [3] Waugh A, Grant A. Ross & Wilson anatomy and physiology in health and illness E-book. 11th ed. Churchill Livingstone Title; 2010. P. 367-368.
- [4] Thomas HC. Checklist for Factors Affecting Wound Healing: Advances in Skin and Wound Care Journal. - Harrisburg, Pennsylvania: Lippincott Williams and Wilkins 24 (2011): 192.
- [5] Punjataewakupt A, Napavichayanun S, Aramwit P. The downside of

- antimicrobial agents for wound healing. *Eur J Clin Microbiol Infect Dis* 2019;38(1):39-54.
- [6] Tirmizi: 2192; Book. 28, English vol. 4; Book. 2, Hadees. 2054
- [7] Ramzi SC, Vinay K, Stanley R. *Pathologic Basis of Diseases*. 5th ed. WB Saunders Company, Philadelphia; 1994. 86.
- [8] Strodtbeck F. Physiology of wound healing. *Newborn & Infant Nursing Reviews* 2001; 1(1): 43–45.
- [9] Schultz GS. Molecular Regulation of Wound Healing. In: Bryant RA, editor. *Acute and Chronic Wounds: Nursing management*. 2nd ed. WB Saunders Publisher, USA; 1999. 413- 429.
- [10] Lazarus GS, Cooper DM, Knighton DR, Margolis DJ, Pecoraro RE, Rodeheaver G, Robson MC. Definition and guidelines for assessment of wounds and evaluation of healing. *Archives of Dermatology* 1998; 130(4): 489-493.
- [11] Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF. Impaired wound healing. *Clinics in Dermatology* 2007; 25: 19- 25.
- [12] Krishnan P. The scientific study of herbal wound healing therapies: Current state of play. *Current Anaesthesia & Critical Care* 2006; 17: 21-27.
- [13] Broughton G, Janis JE, Attinger CE. The basic science of wound healing. *Plastic and Reconstructive Surgery* 2006; 117(7 suppl): 12S – 34S.
- [14] Jespersen J. Pathophysiology and clinical aspects of fibrinolysis and inhibition of coagulation. Experimental and clinical studies with special reference to women on oral contraceptives and selected groups of thrombosis prone patients. *Danish Medical Bulletin* 1988; 35: 1 – 33.
- [15] Pool JG. Normal haemostatic mechanisms: A review. *American Journal of Medical Technology* 1977; 43: 776 – 780.
- [16] Hunt TK. The physiology of wound healing. *Annals of Emergency Medicine* 1998; 17: 1265 – 1273.
- [17] Sieggreen MY. Healing of physical wounds. *Nursing Clinics of North America* 1987; 22: 439 – 447.
- [18] Ennis WJ, Meneses P. Wound healing at the local level: The stunned wound. *Ostomy Wound Management* 2000; 46(1A suppl): 39S – 48S.
- [19] Hess CT. Skin care basics. *Advances in Skin & Wound Care*. 2000; 13 (3 pt 1): 127 – 128.
- [20] Witte MB, Barbul A. General principles of wound healing. *Surgical Clinics of North America* 1997; 77: 509 – 528.
- [21] Servold SA. Growth factor impact on wound healing. *Clinics in Podiatric Medicine and Surgery* 1991; 8: 937 – 953.
- [22] Baum CL, Arpey CJ. Normal cutaneous wound healing: Clinical correlation with cellular and molecular

- events. *Dermatologic Surgery* 2005; 31: 674–686.
- [23] Greenhalgh DG. The role of apoptosis in wound healing. *International Journal of Biochemistry & Cell Biology* 1998; 30: 1019–1030.
- [24] Mulder GD, Vande Berg JS. Cellular senescence and matrix metalloproteinase activity in chronic wounds. Relevance to debridement and new technologies. *Journal of the American Podiatric Medical Association* 2002; 92: 34–37.
- [25] Falanga V. Wound healing and chronic wounds. *Journal of Cutaneous Medicine and Surgery* 1998; 3(suppl 1): 1S–5S.
- [26] O’Kane S. Wound remodelling and scarring. *Journal of Wound Care* 2002; 11: 296–299.
- [27] Edwards J. Growth factors - the healing messengers. *Journal of Community Nursing* 2001; 15(7): 14–21.
- [28] Heldin C, Westermark B. Mechanism of action and in vivo role of platelet derived growth factor. *Physiological Reviews* 1999; 79(4): 1283–1316.
- [29] Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. *Physiological Reviews* 2003; 83(3): 835–870.
- [30] Kim I, Mogford JE, Chao JD, Mustoe TA. Wound epithelialization deficits in the transforming growth factor- α knockout mouse. *Wound Repair and Regeneration* 2001; 9(5): 386–390.
- [31] Bennet NT, Schultz GS. Growth factors and wound healing: Biochemical properties of growth factors and their receptors. *American Journal of Surgery* 1993; 165(6): 728–737.
- [32] Roberts AB, Sporn MB, Assoian RK, Smith JM, Roche NS, Wakefield LM. Transforming growth factor type β : rapid induction of fibrosis and angiogenesis 36 in vivo and stimulation of collagen formation in vitro. *Proceedings of the National Academy of Sciences of the United States of America* 1986; 83(12): 4167–4171.
- [33] Werner S. Keratinocyte growth factor: a unique player in epithelial repair processes. *Cytokine & Growth Factor Reviews* 1998; 9(2): 153–165.
- [34] Brown LF, Yeo K, Berse B, Yeo T, Senger DR, Dvorak HF. Expression of vascular permeability factor (vascular endothelial growth factor) by epidermal keratinocytes during wound healing. *Journal of Experimental Medicine* 1992; 176(5): 1375–1379.
- [35] Franklin JD, Lynch JB. Effects of topical applications of epidermal growth factor on wound healing. Experimental study on rabbit ears. *Plastic and Reconstructive Surgery* 1979; 64(6): 766–770.
- [36] Lynch SE, Colvin RB, Antoniades HN. Growth factors in wound healing. Single and synergistic effects on partial thickness porcine skin wounds.

- Biochemical and Biophysical Research Communications 1989; 84(2): 640–646.
- [37] Frazier K, Williams S, Kothapalli D, Klapper H, Grotendorst GR. Stimulation of fibroblast cell growth, matrix production and granulation tissue formation by connective tissue growth factor. *Journal of Investigative Dermatology* 1996; 107(3): 404–411.
- [38] Mast BA, Schultz GS. Interactions of cytokines, growth factors and proteases in acute and chronic wounds. *Wound Repair and Regeneration* 1996; 4(4): 411 - 420.
- [39] Gillitzer R, Goebeler M. Chemokines in cutaneous wound healing. *Journal of Leukocyte Biology* 2001; 69(4): 513–521.
- [40] Moore KW, de Waal Malefyt R, Coffman RL, O’Garra A. Interleukin-10 and the interleukin-10 receptor. *Annual Review of Immunology* 2001; 19: 683–765.
- [41] Damme Van J, Proost P, Put W, Arens S, Lenaerts JP, Conings R, *et al*. Induction of monocyte chemotactic proteins MCP-1 and MCP-2 in human fibroblasts and leukocytes by cytokines and cytokine inducers. Chemical synthesis of MCP-2 and development of a specific RIA. *Journal of Immunology* 1994; 152(11): 5495–5502.
- [42] Jackman SH, Yoak MB, Keerthy S, Beaver BL. Differential expression of chemokines in a mouse model of wound healing. *Annals of Clinical & Laboratory Science* 2000; 30(2): 201–207.
- [43] Engelhardt E, Toksoy A, Goebeler M, Debus S, Brocker E, Gillitzer R. Chemokines IL-8, GRO α , MCP-1, IP-10, and Mig are sequentially and differentially expressed during phase-specific infiltration of leukocyte subsets in human wound healing. *The American Journal of Pathology* 1998; 153(6): 1849–1860.
- [44] Adamu BF, Gao J, Tan S, Gebeyehu EK. Comparison of antibacterial property of herbal plant-based bio-active extract loaded polymer electrospun nanofibrous mat wound dressings. *J Ind Text.* 2022;51(2_suppl):1793S-1814S.
- [45] Lipsky BA, Hoey C. Topical antimicrobial therapy for treating chronic wounds. *Clin Infect Dis* 2009;49(10):1541-9.
- [46] Kaye ET. Topical antibacterial agents. *Infect Dis Clin North Am* 2000;14(2):321-39.
- [47] Thomas GW, Rael LT, Bar-Or R, Shimonkevitz R, Mains CW, Slone DS, *et al*. Mechanisms of delayed wound healing by commonly used antiseptics. *J Trauma* 2009;66(1):82-91.
- [48] Punjataewakupt A, Napavichayanun S, Aramwit P. The downside of antimicrobial agents for wound healing. *Eur J Clin Microbiol Infect Dis* 2019;38(1):39-54.

- [49] Elebeedy D, Ghanem A, El-Sayed M, Fayad E, Ali OAA, Alyamani A, et al. Synergistic Antimicrobial Effect of *Lactiplantibacillus plantarum* and *Lawsonia inermis* Against *Staphylococcus aureus*. *Infect Drug Resist*. 2022;15.
- [50] Santos-Buelga C, Mateus N, De Freitas V. Anthocyanins. Plant pigments and beyond. *J Agric Food Chem* 2014;62(29):6879-84.
- [51] Maver T, Maver U, Stana Kleinschek K, Smrke DM, Kreft S. A review of herbal medicines in wound healing. *Int J Dermatol* 2015;54(7):740-51.
- [52] Ghosh PK, Gaba A. Phyto-extracts in wound healing. *J Pharm Pharm Sci* 2013;16(5):760-820.
- [53] Nithya V, Baskar A. A preclinical study on wound healing activity of *Lawsonia ulba* Linn. *Res J Phyto Chem* 2011;5:123-9.
- [54] Ponrasu T, Suguna L. Efficacy of *Annona squamosa* on wound healing in streptozotocin-induced diabetic rats. *Int Wound J* 2012;9(6):613-23.
- [55] Daburkar M, Lohar V, Rathore AS, Bhutada P, Tangadpaliwar S. An in vivo and in vitro investigation of the effect of Aloe vera gel ethanolic extract using animal model with diabetic foot ulcer. *J Pharm Bioallied Sci* 2014;6(3):205.
- [56] Swamy HK, Krishna V, Shankarmurthy K, Rahiman BA, Mankani KL, Mahadevan KM, et al. Wound healing activity of embelin isolated from the ethanol extract of leaves of *Embelia ribes* Burm. *J Ethnopharmacol* 2007;109(3):529-34.
- [57] Nayak BS, Isitor GN, Maxwell A, Bhogadi V, Ramdath DD. Wound-healing activity of *Morinda citrifolia* fruit juice on diabetes-induced rats. *J Wound Care* 2007;16(2):83-6.
- [58] Jaswanth A, Loganathan V, Manimaran S. Wound healing activity of *Aegle marmelos*. *Indian J Pharm Sci* 2001;63(1):41-4.
- [59] Xu L, Choi TH, Kim S, Kim SH, Chang HW, Choe M, et al. Anthocyanins from black soybean seed coat enhance wound healing. *Ann Plast Surg* 2013;71(4):415-20.
- [60] Nayak S, Nalabothu P, Sandiford S, Bhogadi V, Adogwa A. Evaluation of wound healing activity of *Allamanda cathartica* L. and *Laurus nobilis* L. extracts on rats. *BMC Complement Alternat Med* 2006;6(1):1-6.
- [61] Mukherjee PK, Mukherjee K, Pal M, Saha BP. Wound healing potential of *Nelumbo nucifera* (Nymphaeaceae) rhizome extract. *Phytomedicine* 2000;7(2):66-74.
- [62] G. Chaudhary, S. Goyal, P. Poonia, *Lawsonia inermis* Linnaeus: a phytopharmacological review, *Int. J. Pharmaceut. Sci. Drug Res.* 2 (2) (2012) 91–98.
- [63] Yusuf M. Phytochemical analysis and antibacterial studies of *Lawsonia inermis* leaves extract. *J Chem Pharm Res* 2016;8:571-5.

- [64] Nigussie D, Makonnen E, Tufa TB, et al. Systematic review of Ethiopian medicinal plants used for their anti-inflammatory and wound healing activities. J Ethnopharmacol. 2021;276:114179. doi:10.1016/j.jep.2021.114179
- [65] Bouhlali, E. dine T., Sellam, K., Bammou, M., Alem, C., Filali-Zehzouti, Y., 2016. In vitro antioxidant and anti-inflammatory properties of selected moroccan medicinal plants. J. Appl. Pharmaceut. Sci. 6, 156–162.
- [66] Castell, M., 2016. Flavonoids, inflammation and immune system. Nutrients 8, 8–11.
- [67] Chaibi, R., Drine, S., Ferchichi, A., 2017. Chemical study and biological activities of various extracts from *Lawsonia inermis* (henna) seeds. Acta Med. Mediterr. 33, 195–201.
- [68] Nayak, B.S., Isito, G., Davis, E.M., Pillai, G.K., 2008. The evidence based wound healing activity of *Lawsonia inermis* linn. Phyther. Res. 22, 544–549.
- [69] F. El Bergadi, M. Laachari, A. Sadiki, et al., Antifungal effect of Moroccan *Lawsonia inermis* leaf extracts on the growth of filamentous fungi isolated from historical wood, Int. J. Curr. Res. 7 (2015) 14237–14240.
- [70] Khan BA, Khan A, Khan MK, Braga VA. Preparation and properties of High sheared Poly(Vinyl Alcohol)/Chitosan blended Hydrogels films with *Lawsonia inermis* extract as wound dressing. J Drug Deliv Sci Technol [Internet]. 2021;61(October):102227. Available from: <https://doi.org/10.1016/j.jddst.2020.102227>
- [71] Saliha AM, Kakamad FH, Salih RQ, Hussein DA, Hassan HA, Mekail TM, Abdul-Aziz JM, Aube H. Effect of *Lawsonia inermis* L. (Henna) on wound healing in Sprague-Dawley rats: A pilot study, Wound Medicine. 2017;18:41-42.
- [72] Djerrou Z, Mokhbi I, Hadeif KS, Boutobza N, Bouzeguine S, Brighet I, Khelfa B. Burn wound healing effect and hair growth promoting activity of *Lawsonia inermis* L. and Honey in *Oryctolagus cuniculus* Rabbits, OnLine Journal of Biological Sciences. 2016;16(2):82-89.
- [73] Sakarkar DM, Sakarkar UM, Shrikhande NV, Vyas JV, Mandavgade S, Jaiswal SB, Purohit RN. Wound healing Properties of Henna Leaves. 2004;3(6):406-412.
- [74] Hamdi YP, Benazzouz M, Belkhir H, Chari Z, Serakta M, Bensgni L. Healing effect of *Lawsonia inermis* L. (henna) as exemplified by the third degree burns. Revue de Medecines et Pharmacopees Africaines. 1997;11-12:151-156.
- [75] Muhammad HS, Muhammad S. The use of *Lawsonia inermis* Linn. (Henna) in the management of burn

- wound infection. African Journal of Biotechnology. 2005;4: 934-937.
- [76] Nayak BS, Isitor G, Davis EM, Pillai GK, The evidence based wound healing activity of *Lawsonia inermis* Linn. Phytotherapy Research. 2007;21:827-831.
- [77] Towfik AI, Hamza AS, Munshi AK, The effect of Henna (*Lawsonia inermis* L.) on the wound healing of Local Arabian Horses, Journal of Kerbala University, 2015;13(1):78-91.
- [78] Daemi A, Farahpour MR, Oryan A, Karimzadeh S, Tajer E. Topical administration of hydroethanolic extract of *Lawsonia inermis* L. (Henna) accelerates excisional wound healing process by reducing tissue inflammation and amplifying glucose uptake. Kaohsiung Journal of Medical Sciences. 2019;35(1): 24-32.
- [79] Naseri S, Golpich M, Roshancheshm T, Joobeni MG, Khodayari M, Noori S, et al. The effect of henna and linseed herbal ointment blend on wound healing in rats with second-degree burns. Burns [Internet]. 2021;47(6):1442–50. Available from: <https://doi.org/10.1016/j.burns.2020.12.009>
- [80] Yassine KA, Houari H, Mokhtar B, Karim A, Hadjer S, Imane B. A topical ointment formulation containing leaves' powder of *Lawsonia inermis* accelerate excision wound healing in Wistar rats. Vet World. 2020;13(7).
- [81] Sakarkar DM, Sakarkar UM, Shrikhande NV, Vyas JV, Mandavgade S, Jaiswal SB, Purohit RN. Wound healing Properties of Henna Leaves. 2004;3(6):406-412.
- [82] Rekik DM, Ben Khedir S, Daoud A, Ksouda Moalla K, Rebai T, Sahnoun Z. Wound Healing Effect of *Lawsonia inermis* . Skin Pharmacol Physiol. 2019;32(6):295–306.
- [83] E. A. H. Kadhum BMMA-MA. Effect of *Lawsonia inermis* extract on the pathological changes of skin infection by *Streptococcus pyogenes* in lab. Mice. Al-Qadisiyah J Vet Med Sci. 2011;10(1):45.
- [84] Adamu BF, Gao J, Tan S, Gebeyehu EK. Comparison of antibacterial property of herbal plant-based bio-active extract loaded polymer electrospun nanofibrous mat wound dressings. J Ind Text. 2022;51(2_suppl):1793S-1814S.
- [85] Elebeedy D, Ghanem A, El-Sayed M, Fayad E, Ali OAA, Alyamani A, et al. Synergistic Antimicrobial Effect of *Lactiplantibacillus plantarum* and *Lawsonia inermis* Against *Staphylococcus aureus*. Infect Drug Resist. 2022;15.
- [86] S. Negahdari, H. Galehdari, M. Kesmati, A. Rezaie, Wound healing activity of extracts and formulations of Aloe vera, henna, adiantum capillus-veneris, and myrrh on mouse dermal fibroblast cells, Int. J. Med. 8 (1) (2017) 18.

- [87] Saadabi MAA, Evaluation of *Lawsonia inermis* L. (Sudanese Henna) Leaf Extracts as an Antimicrobial Agent, Research Journal of Biological Sciences. 2007;2: 419-423.
- [88] Omar A. Habhal, Ali A Al-Jabri, Abdulghaffar H. El-Hag, Zahra H. AlMahrooqi, Nassser A. Al-Hashmi: In vitro antimicrobial activity of *Lawsonia inermis* L. A pilot study on the omani henna, Saudi Medical Journal. 2005;26(1):447-450.
- [89] Awadh ANA, Julich WD, Kusnick C and Lindequist U: Screening of Yemeni medicinal plants for antibacterial and cytotoxic activities. Journal of Ethnopharmacology. 2002;74:173-179.
- [90] Jothiprakasham V, Ramesh S, Rajasekharan SK. Preliminary phytochemical screening and antibacterial activity of *Lawsonia inermis* Linn. (henna) leaf extracts against reference bacterial strains and clinically important ampicillin beta-lactamases producing proteus mirabilis, International Journal of Pharmacy and Pharmaceutical Sciences. 2013;5(1):219- 222.
- [91] Malekzadeh F, Antimicrobial activity of *Lawsonia inermis* L., Applied Microbiology. 1968,16(4):663-664.
- [92] Dahake R, Kamble I, Study on antimicrobial potential and preliminary phytochemical screening of *Lawsonia inermis* Linn., International Journal of Pharmaceutical Sciences and Research. 2015; 6(8): 3344-3350.
- [93] Raja W, Ovais M, Dubey A, Phytochemical screening and antibacterial activity of *Lawsonia inermis* L. leaf extract. International Journal of Microbiological Research. 2013;4 (1):33-36.
- [94] Vahabi S, Vala M, Gholami S, in vitro antibacterial effect of hydroalcoholic extract of *Lawsonia inermis* L., *Malva sylvestris*, and *Boswellia serrata* on *Aggregatibacter actinomycetemcomitans*, Adv Biomed Res. 2019;8:22.