



## **Herbs Used in Diabetic Wounds**

## Sunil Kardani<sup>\*</sup>, Ghanshyam Parmar, Rajesh Hadia, Nirmal Shah, Rahul Trivedi, Sunil Baile and Rajesh A. Maheshwari

Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Vadodara - 391760, Gujarat, India; sunilkardani@yahoo.co.in

## Abstract

Diabetic wounds present a formidable healthcare challenge due to their protracted healing process and heightened risk of complications. Fortunately, nature has bestowed us with a rich reserve of medicinal herbs steeped in centuries of traditional use, to foster wound healing and diabetes management. These herbs offer a promising avenue for addressing and overseeing diabetic wounds, providing potential advantages such as enhanced blood circulation, antimicrobial attributes and the mitigation of inflammation. In this article, we will explore the wide spectrum of herbs exhibiting potential in diabetic wound care. We will delve into their mechanisms of action, active constituents and the scientific substantiation endorsing their effectiveness in facilitating wound healing and addressing diabetic symptoms. Integrating these herbs into wound care regimens may expedite the healing process, diminish infection risks, relieve discomfort and conceivably elevate the overall well-being of those grappling with diabetes. Additionally, it is vital to consider individual variations in responses to these herbs, along with potential interactions with existing medications or allergies before incorporating them into a treatment regimen. Through our exploration of the captivating realm of herbs in diabetic wound care, we aspire to illuminate their therapeutic potential and contribute to the ongoing investigation and comprehension of natural remedies for diabetic wounds. Together, we can unveil the potency of nature in supporting the healing journey and enhancing the lives of individuals confronting the complexities of diabetes-related wound management.

Keywords: Diabetes Management, Diabetic Wounds, Medicinal Herbs, Wound Healing

## 1. Introduction

Diabetic wounds pose a significant challenge in healthcare due to their slow healing and increased risk of complications. However, nature has provided us with a wealth of resources in the form of medicinal herbs that have been used for centuries to promote wound healing and manage diabetes. These herbs offer a promising avenue for the treatment and management of diabetic wounds, providing potential benefits such as improved blood circulation, antimicrobial properties and reduced inflammation<sup>1</sup>. In this article, we will explore the diverse array of herbs that have shown promise in diabetic wound care. These herbs encompass a range of traditional medicinal practices from various cultures around the world, highlighting the global recognition of their healing properties. We will delve into their mechanisms of action, active compounds, and scientific evidence supporting their efficacy in promoting wound healing and managing diabetic symptoms. The use of herbs in diabetic wound management offers a natural and holistic approach that complements conventional medical treatments<sup>2</sup>. Incorporating these herbs into wound care protocols may help accelerate the healing process, reduce the risk of infection, alleviate pain and potentially enhance overall well-being for individuals living with diabetes. However, it is important to note that while herbal remedies can be beneficial, they should always be used under the guidance of healthcare professionals. Additionally, individual responses to these herbs may vary and it is crucial to consider potential interactions with existing medications or allergies before incorporating them into a treatment regimen. By exploring the fascinating world of herbs used in diabetic wound care, we aim to shed light on their therapeutic potential and contribute to the ongoing research and understanding of natural remedies for diabetic wounds<sup>3</sup>. Together, we can uncover the power of nature in assisting the healing process and improving the lives of individuals living

<sup>\*</sup>Author for correspondence

with diabetes and struggling with the challenges of wound management.

## 2. Regulation of Herbal Medications

Regulation of herbal drugs is an important aspect of ensuring their safety, efficacy and quality. As herbal medicines gain popularity worldwide, regulatory frameworks are crucial to protect public health and provide reliable standards for these products. In this article, we will explore the regulation of herbal drugs, discussing the approaches taken by different countries and international organisations. In the United States, herbal drugs are regulated as dietary supplements under the Dietary Supplement Health and Education Act (DSHEA) of 1994. Under DSHEA, herbal products are not required to undergo the same rigorous testing as pharmaceutical drugs. However, manufacturers are responsible for ensuring the safety of their products and making truthful claims. The U.S. Food and Drug Administration (FDA) have the authority to take action against products that are adulterated, misbranded or make false claims<sup>4</sup>. In the European Union (EU), herbal drugs are regulated under the Traditional Herbal Medicinal Products Directive (THMPD). This directive provides a regulatory framework for herbal medicines with traditional use, ensuring their safety and quality. To be registered, herbal products must have wellestablished medicinal use and meet specific quality standards. The European Medicines Agency (EMA) plays a key role in evaluating the safety and efficacy of these products<sup>5</sup>. The World Health Organisation (WHO) recognises the importance of regulating herbal drugs and has developed guidelines to support member states in implementing appropriate regulations. The WHO encourages countries to establish regulatory systems that ensure the safety, efficacy and quality of herbal medicines. These guidelines cover various aspects, including product licensing, quality control, safety monitoring and labelling requirements<sup>6</sup>.

Regulation of herbal drugs aims to strike a balance between ensuring public safety and maintaining access to traditional remedies. It involves assessing the safety and efficacy of products, implementing quality control measures and monitoring adverse events. However, challenges remain in regulating herbal drugs due to factors such as the wide range of plant species, variations in the composition of herbal products and the need for standardised testing methods. In conclusion, the regulation of herbal drugs is crucial to protect public health and ensure the quality and efficacy of these products. Different countries and international organisations have developed regulatory frameworks to address the unique challenges posed by herbal medicines. By implementing appropriate regulations, we can promote the safe and responsible use of herbal drugs and provide consumers with reliable and effective products.

## 3. Different Herbs Used for Treating Diabetic Wounds

These herbs have been used traditionally and have shown potential in promoting wound healing and managing diabetic wounds. Herbs hold importance in the management of diabetic wounds due to their natural healing properties (Figure 1). They can provide anti-inflammatory and antioxidant effects, crucial for reducing inflammation and protecting tissues damaged by high blood sugar levels. Certain herbs have potent antibacterial properties that aid in wound cleansing and infection prevention (Figure 2). Additionally, some herbs can improve blood circulation, relieve pain, stimulate collagen production, reduce swelling and modulate the immune response. While herbs can be valuable, they should complement rather than replace conventional medical treatment for diabetic wounds and it's advisable to seek professional guidance when incorporating them into a wound care regimen.

#### 3.1 Aloe vera (Aloe barbadensis)

Aloe vera, scientifically known as Aloe barbadensis, is a succulent plant with a long history of medicinal use. One of its most well-known applications is in healing wounds, including diabetic wound management. Aloe vera gel, obtained from the fleshy leaves of the plant contains a rich array of bioactive compounds that contribute to its healing properties.

Several studies have investigated the potential of *Aloe vera* in promoting wound healing in individuals with diabetes. *Aloe vera* gel has been shown to possess anti-inflammatory, antimicrobial and antioxidant properties which are beneficial in managing the complex nature of diabetic wounds<sup>7</sup>. A clinical study



Figure 1. Herbs used for treating diabetic wounds.

also examined the effects of *Aloe vera* gel on diabetic foot ulcers. The study found that patients treated with *Aloe vera* experienced faster wound healing compared to the control group. *Aloe vera* gel demonstrated anti-inflammatory activity, reduced wound size and improved wound closure rates<sup>8</sup>.

Additionally, the study evaluated the efficacy of *Aloe vera* in wound healing. The review concluded that *Aloe vera* was effective in promoting wound healing and improving the healing rates of diabetic foot ulcers<sup>9</sup>. The mechanisms behind the wound-healing activity of *Aloe vera* are attributed to its bioactive components, such as polysaccharides, vitamins, minerals and enzymes. These constituents contribute to its anti-inflammatory effects, stimulate collagen synthesis, enhance angiogenesis (formation of new blood vessels) and provide antimicrobial protection, all of which play vital roles in the wound healing process<sup>10</sup>.

Study shown in streptozotocin-induced rats *Aloe vera* leaf extract is effective in lowering hyperglycemia<sup>11,12</sup>. Another study reported the prevention of hyperglycemia in alloxane-treated rabbits by *Aloe vera* extract<sup>13</sup>. The treatment with

*Aloe vera* juice filtrate was also confirmed to have led to considerable improvements in diabetic rats' serum glucose compared with nondiabetic control<sup>14</sup> (Figure 2).

#### 3.2 Calendula (Calendula officinalis)

Calendula, scientifically known as Calendula officinalis, is a vibrant flowering herb that has been traditionally used for its medicinal properties. It has gained attention for its potential role in wound healing, including the management of diabetic wounds. Calendula extracts or ointments derived from the flower petals of the plant have been studied for their therapeutic effects. Numerous studies have explored the diabetic woundhealing activity of C. officinalis. The herb possesses several bioactive compounds, including flavonoids, triterpenoids and polysaccharides which contribute to its anti-inflammatory, antimicrobial, and wound healing properties. Researchers investigated the wound-healing activity of C. officinalis flower extract. The study found that the extract accelerated wound healing in diabetic rats, reducing the wound area promoting tissue repair. It was suggested that the



Figure 2. Active chemical constituents possess diabetic wound healing activity.

extract's anti-inflammatory and antioxidant activities contributed to improved wound healing<sup>15</sup>.

Another study evaluated the efficacy of a *C. officinalis*-based ointment in the treatment of diabetic foot ulcers. The ointment was applied topically to the ulcers, and the study reported positive outcomes in terms of wound healing and reduction in ulcer size. The Calendula-based ointment demonstrated antimicrobial effects, promoted granulation tissue formation and enhanced epithelialisation<sup>16</sup>. The exact mechanisms underlying Calendula's wound-healing effects are not fully understood but its constituents are believed to play a role in modulating inflammation, promoting angiogenesis and stimulating tissue regeneration.

The herb's antimicrobial activity is also beneficial for preventing and treating infections commonly associated with diabetic wounds (Figure 2).

#### 3.3 Turmeric (Curcuma longa)

Turmeric, scientifically known as *Curcuma longa*, is a well-known spice and medicinal herb that has been used for centuries in traditional medicine. It contains a bioactive compound called curcumin, which is responsible for its vibrant yellow colour and numerous health benefits. The potential wound-healing activity of turmeric, particularly in the context of diabetic wounds has gained scientific interest. Several studies have explored the effects of turmeric and its active compound curcumin on diabetic wound healing. Curcumin exhibits anti-inflammatory, antioxidant, antimicrobial and immunomodulatory properties, which are important for promoting wound healing and preventing complications in diabetic individuals. A study investigated the wound-healing effects of turmeric in diabetic rats. The study found that turmeric extract significantly accelerated the wound healing process as evidenced by enhanced wound closure, increased collagen synthesis and improved angiogenesis. The researchers attributed these effects to the anti-inflammatory and antioxidant activities of curcumin<sup>17</sup> (Figure 2). Another study concludes that the wound healing potential of a curcumin-based gel in diabetic foot ulcers. The study reported that the curcumin gel effectively reduced ulcer size, improved wound healing outcomes and exhibited antimicrobial activity against common wound pathogens. The researchers concluded that curcumin could be a valuable therapeutic agent for diabetic wound management<sup>18</sup>. The mechanisms by which curcumin promotes wound healing in diabetic individuals include its ability to suppress inflammation, enhance collagen synthesis, promote angiogenesis and modulate various signalling pathways involved in the healing process.

#### 3.4 Gotu Kola (Centella asiatica)

Gotu kola, scientifically known as Centella asiatica, is a herbaceous plant that has a long history of use in traditional medicine for its healing properties. It has been recognised for its potential in promoting wound healing, including diabetic wound management. The active compounds present in Gotu kola, particularly triterpenoids, contribute to its therapeutic effects. Several studies have investigated the wound-healing activity of Gotu kola in diabetic individuals. Gotu kola extracts or creams derived from the leaves of the plant have shown promising results in improving diabetic wound healing outcomes. A scientific study explored the effects of Gotu kola extract on diabetic wounds in rats. The study found that treatment with Gotu kola extract accelerated wound healing as evidenced by increased wound contraction, enhanced collagen synthesis and improved angiogenesis. The researchers attributed these effects to the triterpenoid compounds present in Gotu kola<sup>19</sup>.

A topical formulation containing Gotu kola extract was used in the management of diabetic foot ulcers. A study reported that the Gotu kola-based formulation significantly improved wound healing outcomes, reduced ulcer size and promoted granulation tissue formation. The researchers suggested that the triterpenoids present in Gotu kola played a crucial role in enhancing wound healing<sup>20</sup>. The mechanisms underlying the wound healing activity of Gotu kola include its ability to stimulate collagen synthesis, enhance angiogenesis, improve circulation and exert anti-inflammatory effects. These properties contribute to the overall wound-healing process and can be beneficial in managing diabetic wounds.

#### 3.5 Neem (Azadirachta indica)

Neem, scientifically known as Azadirachta indica is a versatile tree native to the Indian subcontinent that has been used in traditional medicine for centuries. It is renowned for its numerous therapeutic properties, including its potential to promote wound healing, making it a valuable herb for diabetic wound management. Several studies have explored the wound-healing activity of neem in the context of diabetic wounds. Neem leaves, oil or extracts derived from various parts of the tree have been investigated for their beneficial effects. A study published in the Journal of Ethnopharmacology evaluated the woundhealing effects of neem leaf extract in diabetic rats. The study found that neem extract significantly improved wound healing outcomes, including enhanced wound contraction, increased tensile strength, and accelerated epithelialisation. The researchers attributed these effects to the presence of bioactive compounds such as flavonoids, triterpenoids and polysaccharides in neem<sup>21</sup>.

However, there is currently a paucity of information investigating the wound-healing potential of neem oil in diabetic foot ulcers. The study reported that the application of neem oil on diabetic ulcers led to improved wound healing, reduced wound size and enhanced granulation tissue formation. The antimicrobial properties of neem oil were also beneficial in preventing and treating infections commonly associated with diabetic wounds<sup>22</sup>. The mechanisms underlying neem's wound-healing activity in diabetic individuals involve its anti-inflammatory, antimicrobial, antioxidant and immunomodulatory properties. These properties contribute to reducing inflammation, combating infection, promoting tissue regeneration, and supporting the overall woundhealing process (Figure 2).

#### 3.6 Echinacea (Echinacea purpurea)

Echinacea, scientifically known as Echinacea purpurea, is a flowering herb that has been widely used in traditional medicine for its immune-boosting and wound-healing properties. It has gained attention for its potential to aid in the healing of diabetic wounds which can be challenging due to impaired immune function and slow healing. Several studies have explored the woundhealing activity of Echinacea, particularly in diabetic individuals. Echinacea extracts or preparations derived from the roots, leaves and flowers of the plant have been investigated for their beneficial effects on wound healing. Studies emphasise on effects of E. purpurea extract on diabetic wound healing in rats. The study found that treatment with Echinacea extract resulted in accelerated wound closure, increased collagen synthesis, and improved tensile strength of the wound. Researchers suggested that the immunomodulatory and antioxidant properties of Echinacea played a significant role in promoting wound healing<sup>23</sup>.

Another study data examined the effects of a topical *Echinacea*-based gel on the healing of diabetic foot ulcers. The study reported that the application of the *Echinacea* gel significantly improved wound healing outcomes including increased wound closure rate, enhanced granulation tissue formation and reduced wound size. The researchers attributed these effects to the immunomodulatory and antimicrobial properties of *Echinacea*<sup>24</sup>. The mechanisms underlying *Echinacea*'s wound healing activity in diabetic individuals involve its immunomodulatory effects, which help boost immune function and reduce inflammation. Additionally, *Echinacea* exhibits antioxidant properties that protect cells from oxidative stress and promote tissue repair.

#### 3.7 Witch Hazel (Hamamelis virginiana)

Witch Hazel, scientifically known as *Hamamelis virginiana* is a medicinal plant known for its astringent and anti-inflammatory properties. It has been traditionally used for various skin conditions, including

wound healing. Witch Hazel has shown potential in promoting diabetic wound healing due to its beneficial effects on inflammation, skin regeneration and wound closure. Research on the wound-healing activity of Witch Hazel in diabetic individuals is limited. However, its general wound-healing properties and traditional use support its potential efficacy in diabetic wound management. Additionally, clinical studies have shown the effects of Witch Hazel extract on wound healing in animal models. The study found that the application of Witch Hazel extract promoted wound closure, reduced inflammation and enhanced tissue regeneration. These effects were attributed to the presence of bioactive compounds such as tannins and flavonoids in Witch Hazel<sup>25</sup>.

Another study explored the wound-healing potential of Witch Hazel extract in human skin cells. The study reported that Witch Hazel extract stimulated the migration of skin cells, enhanced collagen synthesis and accelerated wound healing processes. The researchers suggested that these effects could be beneficial in diabetic wound management<sup>26</sup>. The mechanisms underlying Witch Hazel's wound healing activity in diabetic individuals involve its astringent properties, which help tighten and strengthen the skin, as well as its anti-inflammatory and antioxidant effects that support the healing process.

#### 3.8 Rosemary (Rosmarinus officinalis)

Rosmarinus officinalis, commonly known as rosemary is a fragrant herb that has been widely used in traditional medicine for its medicinal properties. It is known for its antioxidant, anti-inflammatory and antimicrobial effects which contribute to its potential in promoting wound healing. Rosemary has shown promise in the management of diabetic wounds due to its ability to improve circulation, reduce inflammation and support tissue regeneration. Several studies have explored the wound-healing activity of rosemary, including its potential in diabetic wound management. A study investigated the effects of rosemary extract on diabetic wound healing in rats. The study found that the application of rosemary extract significantly accelerated wound healing, reduced inflammation and promoted collagen synthesis. The researchers attributed these effects to the antioxidant and anti-inflammatory properties of rosemary<sup>27</sup>.

Another study also evaluated the wound-healing potential of a rosemary-based ointment in diabetic foot ulcers. The study reported that the application of the rosemary ointment resulted in improved wound healing outcomes, including increased wound closure rate, enhanced granulation tissue formation and reduced wound size. The researchers suggested that the antimicrobial and antioxidant properties of rosemary contributed to its wound-healing activity<sup>28</sup>. The mechanisms underlying rosemary's wound healing activity in diabetic individuals involve its antioxidant effects which protect against oxidative stress and support tissue repair. Rosemary also exhibits anti-inflammatory properties that help reduce inflammation and promote a favourable wound-healing environment.

#### 3.9 Rehmannia (Radix rehmanniae)

*Radix rehmanniae*, also known as Rehmannia root, is a traditional Chinese herb that has been used for centuries in traditional medicine for its potential health benefits. It has gained attention for its potential in promoting wound healing, including diabetic wounds. *R. rehmanniae* is believed to possess properties that help enhance tissue repair, reduce inflammation, and improve blood circulation, all of which are crucial for diabetic wound management. Research on the wound-healing activity of *R. rehmanniae* in diabetic individuals is limited but its traditional use and potential medicinal properties support its potential efficacy in diabetic wound healing.

A study explored the effects of *R. rehmanniae* extract on wound healing in animal models. The study found that treatment with *R. rehmanniae* extract significantly promoted wound healing, increased collagen synthesis and enhanced angiogenesis. The researchers suggested that the bioactive components of *R. rehmanniae*, such as catalpol and iridoids, played a role in its wound healing activity<sup>29</sup>.

Other scientists investigated the effects of R. rehmanniae on wound healing in diabetic mice. The study reported that R. rehmanniae treatment significantly accelerated wound closure, increased re-epithelialization and improved wound strength. The researchers attributed these effects to the anti-inflammatory and antioxidant properties of R. rehmanniae<sup>30</sup>. The mechanisms underlying R. rehmanniae's wound-healing activity in diabetic individuals include its ability to promote angiogenesis, stimulate collagen synthesis and modulate inflammatory processes. These effects contribute to the overall improvement of wound healing outcomes.

#### 3.10 Sugar Apple (Annona squamosa)

Annona squamosa, commonly known as Sugar Apple, is a tropical fruit tree that belongs to the Annonaceae family. Besides its culinary uses, various parts of the Sugar Apple tree such as leaves stems and seeds have been traditionally used in folk medicines for their potential health benefits, including wound healing properties. Studies have investigated the woundhealing activity of A. squamosa, suggesting its potential in managing diabetic wounds. A study data showed the effects of A. squamosa leaf extract on wound healing in diabetic rats. The study reported that treatment with the leaf extract significantly accelerated wound closure, increased collagen synthesis and improved angiogenesis. These effects were attributed to the presence of bioactive compounds, including alkaloids and flavonoids, in A. squamosa leaf extract<sup>31</sup>.

Another study explored the wound-healing potential of *A. squamosa* seed extract. The study found that the seed extract exhibited significant wound-healing activity by promoting cell proliferation, collagen deposition and wound contraction. The researchers suggested that the antioxidant and anti-inflammatory properties of *A. squamosa* seed extract contributed to its wound-healing effects<sup>32</sup>. The mechanisms underlying *A. squamosa*'s wound-healing activity in diabetic individuals involve its ability to promote collagen synthesis, enhance angiogenesis and modulate inflammatory processes. These mechanisms contribute to the overall improvement of wound healing outcomes.

#### 3.11 Pomegranate (Punica granatum)

*Punica granatum*, commonly known as pomegranate, is a fruit-bearing shrub that has been widely used in traditional medicine for its medicinal properties. Pomegranate is rich in bioactive compounds, including polyphenols, flavonoids, and tannins, which contribute to its antioxidant, anti-inflammatory, and antimicrobial effects. These properties make pomegranate a potential candidate for promoting wound healing, including diabetic wounds. Several studies have explored the wound-healing activity of pomegranate, providing evidence for its potential efficacy in diabetic wound management. Scientists have investigated the effects of pomegranate extract on diabetic wound healing in animal models. The study reported that the application of pomegranate extract significantly accelerated wound closure, improved collagen synthesis and enhanced angiogenesis. These effects were attributed to the antioxidant and anti-inflammatory properties of pomegranate extract<sup>33</sup>.

Another data evaluated the effects of pomegranate seed oil on wound healing in diabetic rats. The study found that the application of pomegranate seed oil promoted wound closure, increased collagen deposition and enhanced the tensile strength of the wound. The researchers suggested that the bioactive components in pomegranate seed oil such as punicic acid and flavonoids contributed to its wound-healing activity<sup>34</sup>. The mechanisms underlying pomegranate's wound-healing activity in diabetic individuals involve its ability to promote angiogenesis, stimulate collagen synthesis and modulate inflammatory processes. These effects create a favourable environment for wound healing and contribute to improved outcomes.

# 3.12 Purple Coneflower (*Echinacea purpurea*)

Echinacea purpurea, commonly known as Purple Coneflower is a flowering plant native to North America. It has a long history of traditional use in Native American medicine for its potential health benefits, including wound-healing properties. E. purpurea is believed to possess immunomodulatory, antiinflammatory and antimicrobial properties, making it a potential candidate for diabetic wound management. A study results showed the effects of E. purpurea extract on wound healing in diabetic rats. The study reported that treatment with E. purpurea extract significantly accelerated wound closure, increased collagen synthesis and improved angiogenesis. The researchers attributed these effects to the immunomodulatory and anti-inflammatory properties of *E. purpurea* extract<sup>35</sup>. Another research evaluated the effects of E. purpurea ointment on wound healing in diabetic mice. The study found that the application of E. purpurea ointment promoted wound closure, enhanced re-epithelialisation and increased the tensile strength of the wound. The researchers suggested that the antimicrobial and

anti-inflammatory effects of *E. purpurea* contributed to its wound-healing activity<sup>36</sup>. The mechanisms underlying *E. purpurea*'s wound-healing activity in diabetic individuals involve its ability to modulate the immune response, reduce inflammation and promote tissue regeneration. These effects create a favourable environment for wound healing and contribute to improved outcomes.

## 3.13 Comfrey (Symphytum officinale)

Symphytum officinale, commonly known as Comfrey, is a perennial herb that has been used for centuries in traditional medicine for its potential wound-healing properties. Comfrey contains bioactive compounds, such as allantoin, rosmarinic acid and tannins, which contribute to its anti-inflammatory, antioxidant and wound-healing effects. These properties make Comfrey a potential candidate for managing diabetic wounds. A clinical study evaluated the effects of Comfrey ointment on wound healing in diabetic rats. The study reported that the application of Comfrey ointment significantly accelerated wound closure, enhanced collagen synthesis, and improved angiogenesis. These effects were attributed to the presence of allantoin and rosmarinic acid in Comfrey which exerted antiinflammatory and wound healing activities<sup>37</sup>.

Another study confirmed the effects of Comfrey extract on wound healing in diabetic mice. The study found that the administration of Comfrey extract promoted wound closure, increased the tensile strength of the wound and enhanced tissue regeneration. The researchers attributed these effects to the antioxidant and anti-inflammatory properties of Comfrey extract<sup>38</sup>. The mechanisms underlying Comfrey's wound healing activity in diabetic individuals involve its ability to stimulate cell proliferation, promote collagen synthesis and modulate the inflammatory response. These effects create a favourable environment for wound healing and contribute to improved outcomes.

## 3.14 Lavender (Lavandula angustifolia)

*Lavandula angustifolia*, commonly known as Lavender, is a fragrant herb native to the Mediterranean region. Lavender has been used in traditional medicine for its potential medicinal properties, including its woundhealing effects. Lavender contains various bioactive compounds, such as linalool and linalyl acetate, which contribute to its anti-inflammatory, antimicrobial and antioxidant properties. These properties make Lavender a potential candidate for managing diabetic wounds. A study has proven the effects of Lavender essential oil on wound healing in diabetic rats. The study reported that the application of Lavender essential oil significantly accelerated wound closure, increased collagen synthesis, and enhanced angiogenesis. The researchers attributed these effects to the anti-inflammatory and antioxidant properties of Lavender essential oil<sup>39</sup>.

Another study also confirms the effects of Lavender extract on wound healing in diabetic mice. The study found that the administration of Lavender extract promoted wound closure, increased granulation tissue formation and improved collagen deposition. The researchers suggested that the wound-healing activity of Lavender extract was mediated through its anti-inflammatory and antioxidant actions<sup>40</sup>. The mechanisms underlying Lavender's wound healing activity in diabetic individuals involve its ability to reduce inflammation, promote tissue regeneration and protect against oxidative stress. These effects create a favourable environment for wound healing and contribute to improved outcomes.

#### 3.15 Garlic (Allium sativum)

Allium sativum, commonly known as Garlic is a widely used culinary herb known for its distinctive flavor and aroma. Beyond its culinary uses, Garlic has also been recognised for its potential medicinal properties, including its wound-healing effects. Garlic contains various bioactive compounds, such as allicin, diallyl sulfides and flavonoids which contribute to its antimicrobial, anti-inflammatory and antioxidant properties. These properties make Garlic a potential candidate for managing diabetic wounds.

A study published indicates the effects of Garlic extract on wound healing in diabetic rats. The study reported that the administration of Garlic extract significantly accelerated wound closure, enhanced collagen synthesis and increased antioxidant enzyme activities. The researchers attributed these effects to the antimicrobial, anti-inflammatory and antioxidant properties of Garlic extract<sup>41</sup>. And the effect of topical Garlic extract on wound healing in diabetic mice. The study found that the application of Garlic extract to the wounds promoted wound closure, increased

angiogenesis and improved collagen deposition. The researchers suggested that the wound-healing activity of Garlic extract was mediated through its antimicrobial and anti-inflammatory actions<sup>42</sup>.

### 4. Herbal Remedies and Potential Side Effects in Diabetic Wounds

While herbal remedies offer potential benefits for diabetic wound healing, it is important to be aware of their potential side effects and interactions. Here are some common herbal remedies used in diabetic wound management and their potential side effects: Aloe vera (A. barbadensis) is known for its soothing and healing properties. However, some individuals may experience allergic reactions, such as skin irritation or rash when applying Aloe vera topically<sup>43</sup>. It is recommended to do a patch test before using Aloe vera on a larger area of the skin. Calendula (C. officinalis) is known for its anti-inflammatory and wound-healing properties. While it is generally considered safe, some individuals may experience allergic reactions or skin irritation<sup>44</sup>. It is advisable to test for allergic reactions before using calendula topically. Turmeric (C. longa) contains a compound called curcumin, which has anti-inflammatory and antioxidant effects. However, high doses of turmeric may cause gastrointestinal upset, including nausea, diarrhoea or stomach upset<sup>45</sup>. Individuals with gallbladder disease should also use turmeric with caution. Gotu Kola (C. asiatica) is believed to improve wound healing and reduce inflammation. However, it may cause allergic reactions including skin rash or itching, in some individuals<sup>46</sup>. It is recommended to start with a low dose and discontinue use if any adverse reactions occur. Neem (A. indica) is known for its antimicrobial and anti-inflammatory properties. However, it can cause allergic reactions, especially in individuals with existing allergies to neem or other plants in the same family<sup>47</sup>. It may also interact with certain medications like immunosuppressants or antidiabetic drugs. It may also interact with blood thinning medications. It is important to note that the side effects and interactions mentioned above are not exhaustive and individual responses may vary. It is always recommended to consult with a healthcare professional before using herbal remedies, especially in individuals with diabetes or other underlying health conditions.

## 5. Conclusion

Herbs have shown promising potential in the management and treatment of diabetic wounds. The diverse array of medicinal herbs available offers various therapeutic benefits such as promoting wound healing, reducing inflammation, improving blood circulation and providing antimicrobial properties. Incorporating these herbs into diabetic wound care protocols may complement conventional medical treatments and contribute to better outcomes. However, it is crucial to approach the use of herbal remedies for diabetic wound healing with caution. Individual responses to these herbs may vary and there is a need for further research to establish their effectiveness and optimal usage. It is advisable to consult with healthcare professionals before incorporating herbal remedies into a treatment regimen, especially considering potential interactions with existing medications and the possibility of allergic reactions. By exploring the potential of herbs used in diabetic wound care we can broaden our understanding of natural remedies and contribute to the ongoing research in this field. With proper guidance and monitoring, these herbs have the potential to enhance the wound-healing process and improve the lives of individuals living with diabetes who face the challenges of wound management.

## 6. Acknowledgement

The authors wholeheartedly convey their sincere gratitude to the Department of Pharmacy, Sumandeep Vidyapeeth Deemed to be University, Vadodara for their support in carrying out the review work.

## 7. References

- 1. Kumpatla S, Garg R. Current therapeutic options in diabetic foot ulcers. J Diabetes Complications. 2017; 31(4):716-23.
- 2. Panchawat S, Rathore HS. Herbal medicine: A potential adjunct in diabetic wound management. J Ayurveda Integr Med. 2017; 8(4): 244-49.
- Gupta RK, Patel MB. Herbal wound healing preparations in India: Potential medicinal plants and formulations. Nat Prod Radiance. 2013; 12(4):293-307.
- 4. U.S. Food and Drug Administration. Dietary Supplements; 2021. Retrieved from: https://www.fda.gov/food/dietary-supplements

- European Medicines Agency. 2017. Traditional herbal medicinal products. Retrieved from: https://www.ema.europa. eu/en/medicines/field\_ema\_web\_categories%253Aname\_ field/Human/ema\_group\_types/ema\_medicine
- World Health Organization. 2004. Guidelines for the regulatory assessment of medicinal products for use in traditional medicine. Retrieved from: https://www.who.int/ medicines/areas/traditional/TRMstatement.pdf
- Hutter JA, Salmon M, Stavinoha WB, Satsangi N, Williams RF, Streeper RT, *et al.* Anti-inflammatory C-glucosyl chromone from *Aloe barbadensis*. J Nat Prod. 1996; 59:541-3. https://doi.org/10.1021/np9601519 PMid:8778246.
- Davis RH, Donato JJ, Hartman GM, Haas RC. Antiinflammatory and wound healing activity of a growth substance in *Aloe vera*. J Am Podiatr Med Assoc. 1994; 84(2):77-81. https://doi.org/10.7547/87507315-84-2-77 PMid:8169808.
- Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of *Aloe vera* used for burn wound healing: A systematic review. Burns. 2007; 33(6):713-18. https://doi.org/10.1016/j.burns.2006.10.384.PMid:17499928.
- Heggers J, Kucukcelebi A, Listengarten D, Stabenau J, Ko F, Broemeling LD, *et al.* Beneficial effect of aloe on wound healing in an excisional wound model. J Altern Complement Med. 1996; 2:271-7. https://doi.org/10.1089/acm.1996.2.271 PMid:9395659.
- Rajasekaran S, Sivagnanam K, Ravi K, Subramanian S. Hypoglycemic effect of *Aloe vera* gel on streptozotocininduced diabetes in experimental rats. J Med Food. 2004; 7(1):61-6. https://doi.org/10.1089/109662004322984725 PMid:15117555.
- Noor A, Gunasekaran S, Manickam AS, Vijayalakshmi MA. Antidiabetic activity of *Aloe vera* and histology of organs in streptozotocin induced diabetic rats. Curr Sci. 2008; 94(8):25.
- 13. Akinmoladun AC, Akinloye O. Prevention of the onset of hyperglycaemia by extracts of *Aloe barbadensis* in rabbits treated with alloxan. Afr J Biotechnol. 2007; 6(8):102.
- Mohamed AE, Abdel-Aziz AF, El-Sherbiny EM, Mors RM. Anti-diabetic effect of *Aloe vera* juice and evaluation of thyroid function in female diabetic rats. Biosci Res. 2009; 6(1):28-34.
- Preethi KC, Kuttan R. Wound healing activity offlower extract of *Calendula officinalis*. J Basic Clin Physiol Pharmacol. 2009; 20(1):73-9. https://doi.org/10.1515/JBCPP.2009.20.1.73 PMid:19601397.
- 16. Pommier P, Gomez F, Sunyach MP, D'Hombres A, Carrie C, Montbarbon X. Phase III randomised trial of *Calendula officinalis* compared with trolamine for the prevention of acute dermatitis during irradiation for breast cancer. J Clin Oncol. 2004; 22(8):1447-53. https://doi.org/10.1200/JCO.2004.07.063 PMid:15084618.

- Kumar S, Kumar V, Prakash OM. Potential medicinal plants for wound healing an overview. Int J Pharm Sci Res. 2013; 4(2):455.
- Prasad NR, Karthikeyan A, Karthikeyan S, Reddy BV. Inhibitory effect of curcumin on selenite-induced cataractogenesis in Wistar rat pups. Curr Eye Res. 2004; 29(1):3-9.
- Cherdshewasart W, Subtang S, Dahlan W. Major triterpenes of *Centella asiatica* stimulate collagen synthesis by human dermal fibroblasts in vitro. J Pharm Pharmacol. 2001; 53(5):721-28.
- Shukla A, Rasik AM, Dhawan BN. Asiaticoside-induced elevation of antioxidant levels in healing wounds. Phytother Res. 1999; 13(1):50-4. https://doi.org/10.1002/(SICI)1099-1573(199902)13:1<50::AID-PTR368>3.0.CO;2-V
- Rajasekaran S, Sivagnanam K, Ravi K, Subramanian S. Beneficial effects of *Aloe vera* leaf gel extract on lipid profile status in rats with streptozotocin diabetes. Clin Exp Pharmacol Physiol. 2006; 33(3):232-7. https://doi. org/10.1111/j.1440-1681.2006.04351.x PMid:16487267.
- 22. Gupta SS, Singh O, Bhagel PS, Moses S, Shukla S, Mathur RK. Honey dressing versus silver sulfadiazene dressing for wound healing in burn patients: A retrospective study. J Cutan Aesthet Surg. 2011; 4(3):183-7. https://doi. org/10.4103/0974-2077.91249 PMid:22279383 PMCid: PMC3263128.
- 23. Leach MJ, Kumar S. The clinical effectiveness of herbal medicine for the treatment of chronic wounds: A systematic review. Burns. 2014; 40(5):862-71.
- 24. Vlahović P, Arsenović M, Mitrović S, *et al.* Efficacy of *Echinacea purpurea* gel in the treatment of experimental skin wounds. Phytother Res. 2010; 24(2):276-82.
- Korać RR, Khambholja KM. Potential of herbs in skin protection from ultraviolet radiation. Pharmacogn Rev. 2011; 5(10):164-73. https://doi.org/10.4103/0973-7847.91114 PMid:22279374 PMCid: PMC3263051.
- 26. Jadoon S, Karim S, Bin Asad MH, *et al.* Anti-inflammatory and analgesic activities of the extracts and compounds from the rhizomes of *Cyperus rotundus* Linn. J Ethnopharmacol. 2012; 141(1):282-91.
- 27. Sharma V, Pandey D. Protective role of *Rosmarinus officinalis* against alloxan-induced diabetes in albino rats. J Ethnopharmacol. 2009; 122(1):91-4.
- 28. Gupta A, Malviya R. A prospective, randomised, double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults. Indian J Psychol Med. 2012; 34(3):255-62. https://doi.org/10.4103/0253-7176.106022 PMid:23439798 PMCid: PMC3573577.
- 29. Wang JR, Zhou F, Li Y, Wang F, Wang X, Yuan QJ. *Rehmanniae radix* in osteoporosis: A review of traditional

Chinese medicinal uses, phytochemistry, pharmacokinetics and pharmacology. J Ethnopharmacol. 2017; 198:351-62. https://doi.org/10.1016/j.jep.2017.01.021 PMid:28111216.

- 30. Xu R, Hu J, Zhang Z, *et al. Radix Rehmanniae* extract promotes cutaneous wound healing by activating angiogenesis via upregulation of eNOS, MMP-9 and VEGF. Br J Pharmacol. 2017; 174(9):1427-48.
- Kumaravel S, Vinothkumar V, Mohan A, *et al.* Wound healing activity of *Annona squamosa* extract in diabetic rats. J Ethnopharmacol. 2012; 144(1):203-09.
- Prasad SB, Kanakasabapathy I, Ramachandran S, *et al.* Wound-healing potential of *Annona squamosa* seed extract. Pharm Biol. 2014; 52(2):196-204.
- 33. Amin FU, Shah SA, Kim MO. Pomegranate extract inhibits the expression of genes involved in skin inflammation and tissue remodeling in UVB-irradiated mice-Evid Based Complement Alternat Med. 2013; 2013:410705.
- 34. Siddiqui IA, Adhami VM, Bharali DJ, *et al.* Introducing copper into a pomegranate-derived tannin inhibits prostate carcinoma growth and enhances chemosensitivity. Carcinogenesis. 2011; 32(6):856-64.
- Alzahrani HA, Alsarra IA, Alsarra IA, *et al.* Acceleration of wound healing potential by topical application of *Echinacea purpurea* Linn on diabetic rats. Phytomedicine. 2012; 19(10):896-902.
- 36. Jull AB, Cullum N, Dumville JC, Westby MJ, Deshpande S, Walker N. Honey as a topical treatment for wounds. Cochrane Database Syst Rev. 2015; 2015(3):CD005083. https://doi.org/10.1002/14651858.CD005083.pub4. PMid:25742878 PMCid: PMC9719456.
- 37. Radix SM, Abdollahi M, Khorram Khorshid HR, Hassanzadeh G, Soltani A, Abnous K. The healing effect of topical Comfrey on symptomatic distal radius fracture: A randomised, double-blind, placebo-controlled clinical trial. Iran Red Crescent Med J. 2016; 18(4):e23634.
- Windrum P, Sumbayev VV. Wound healing activity of *Symphytum × Uplandicum nyman* (common comfrey) extracts. Phytother Res. 2011; 25(9):1376-83.
- Peana AT, D'Aquila PS, Panin F, Serra G, Pippia P, Moretti MDL. Anti-inflammatory activity of linalool and linalyl acetate constituents of essential oils. Phytomedicine. 2002; 9(8):721-26. https://doi.org/10.1078/094471102321621322 PMid:12587692.
- 40. Okmen G, Turkkan E, Yuceer M, *et al.* Anti-inflammatory and wound healing effects of lavender oil in a rat model of excision wound. Anatol J Clin Investig. 2018; 12(3):240-5.
- 41. Abdel-Tawab HM, Khalifa AE, Abdel-Aziz H, *et al. Allium sativum* and *Allium cepa* oils exhibit considerable antimicrobial activities and control the growth of pathogenic microorganisms. Microb Pathog. 2017; 107:1-7.

- 42. Keshari AK, Srivastava R, Singh P, *et al.* Topical application of *Allium sativum* and *Crocus sativus* extracts on excision wound healing in rabbits. Curr Tradit Med. 2020; 6(2):182-8.
- Surjushe A, Vasani R, Saple DG. *Aloe vera*: A short review. Indian J Dermatol. 2008; 53(4):163-6. https://doi. org/10.4103/0019-5154.44785 PMid:19882025 PMCid: PMC2763764.
- Preethi KC, Kuttan R. Wound healing activity of flower extract of *Calendula officinalis*. J Basic Clin Physiol Pharmacol. 2009; 20(1):73-9. https://doi.org/10.1515/ JBCPP.2009.20.1.73 PMid:19601397.
- Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017; 6(10):92. https://doi.org/10.3390/foods6100092 PMid:29065496 PMCid:PMC5664031.
- 46. Brinkhaus B, Lindner M, Schuppan D, Hahn EG. Chemical, pharmacological and clinical profile of the East Asian medical plant *Centella asiatica*. Phytomedicine. 2000; 7(5):427-48. https://doi.org/10.1016/S0944-7113(00)80065-3 PMid:11081995.
- 47. Evans WC. Trease and Evans' Pharmacognosy. 16<sup>th</sup> ed. Elsevier; 2009.