



## Review of Natural Remedies for Accelerate Diabetic Wound Healing

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### ABSTRACT

Diabetic is a metabolic disorder disease leading to hyperglycemia because of lack of insulin secretion or inadequate of insulin activity. Indonesia has 9.600 plant species that have been used for health care and treatment of various diseases. Diabetic patients can experience a problem in the form of foot blood vessels disorders and if not treated properly will become wounds that are difficult to heal and easily develop into gangrene which is high risk of amputation. Therefore, this journal will discuss natural remedies that can be used as a treatment in patients with diabetic wounds and several pharmacological testing performed for testing the diabetic wound healing activity. Various kinds of natural remedies such as *Andredera cordifolia*, *Centella asiatica*, *Curcuma longa*, *Carica papaya* and hone are proven to accelerate diabetic wound healing through various mechanisms.

**Keywords:** diabetic, diabetic wound, natural remedies

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Submitted on: 27 July 2018

Accepted on: 30 July 2018

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DOI: <https://doi.org/10.25026/jtpc.v4i3.182>

### INTRODUCTION

Diabetes mellitus is a metabolic disorder that appears in a person and characterized by elevated blood glucose level (hyperglycemia) [1] because of insulin secretion, insulin activity or both are inadequate [2].

Some Indonesian suffering from diabetes mellitus in 2000 reached 8.43 million people [3], and it will increase to 333 million people in 2025 [4]. Diabetics can experience one problem of foot blood vessel disorders and if it is not treated

properly will easily get injured and develop into gangrene which is at high risk for amputation [5]. The risk of amputation is 15-40 times more frequent in DM patients compared to non-DM, where more than 25% of DM patients given treatment is due to diabetic foot [6].

Diabetic wounds easy to cause complications such as infection due to bacterial invasion. Hyperglycemic condition is an optimal place for bacterial growth, and it inhibits wound healing process [7]. Deficiency in diabetic wound

healing process is caused by several factors such as decreased or impaired growth factor production, angiogenic response, macrophage function, collagen accumulation, epidermal barrier function, quantity of granulation tissue, keratinocytes and fibroblast migration and proliferation, number of epidermal nerves, bone healing, and balance between the accumulation of extracellular matrix components and their remodelling by matrix metalloproteinase [8].

Using plants as raw materials for treatment is still on going until now because it has relatively small side effects and is cheaper than synthetic medicine [9]. In Indonesia, there are approximately 9,600 species of plants that have been used by 400 ethnic varieties for maintenance of health and treatment of various diseases [10].

Because there are still many natural resources that can be used in Indonesia as an alternative treatment, this journal will discuss natural remedies that can be used as a treatment for diabetic wounds which have been proven its pharmacological activity in accelerating diabetic wound healing through several types of research.

## METHOD

### Excision wound model

The animals that usually used for research were Sprague-Dawley rats, Wistar rats, and mice (*Mus musculus* Albinus) and induced with streptozotocin to make them diabetes. The blood glucose level was measured, and the animals were divided into several groups. Normally, the subject groups consisted of normal control group, normal experimental group, normal positive control group, diabetic control group, diabetic experimental group, and diabetic positive control group. Then, they were anesthetized, and excision wounds

were made to take full thickness skin. The experiments were conducted by applying samples topically into the wounds for several days, and percentage wound closure was calculated. Sometimes, the regenerated tissue could be taken, and histopathology of the skin was checked using several staining methods depending on the purpose [13, 18, 23, 24, 28].

### Antimicrobial activity

*Staphylococcus aureus* and *Pseudomonas aeruginosa* were the organisms that usually appeared in diabetic wound. The bacterial colonies were grown on agar nutrient and Mac Conkey media. Then, antimicrobial activity can be assessed by determining Minimum Inhibitory Concentration (MIC), and Minimum Bactericidal Concentration (MBC) using natural remedies extract added to the media [16].

### Dead space wound models

Dead space wounds were inflicted by implanting sterile cotton pellets on the surface of each rat. The rats were divided into four groups (controls, control with sample, diabetic controls, and diabetic experimental rats). After several days, cotton pellets were carefully removed, and amount of hydroxyproline was measured, histopathology study was also conducted [28].

### Clinical tests

The severe clinical study used diabetic patients with ulcer as a subject. The endpoint of the tests could be measured in several ways, but natural remedies were added in dressing to cover the wounds. First, after wound dressing, the wounds were all reconstructed by split-thickness skin graft or primary closure and had percentage change in wound size as an endpoint [20].

Second, the experiment used Quasi-Experiment Design with one design pre-test and post-test group approach. This study compared before and after using natural remedies in modern dressing as a treatment [31, 32].

## RESULT AND DISCUSSION

### Natural Remedies that can be Used for Treatment of Diabetic Wounds

#### *Androdera cordifolia*

*Anredera cordifolia* (Ten.) Steenis or Binahong has many benefits for curing various kinds of mild or severe diseases, including as a wound medicine [11]. *A. cordifolia* grows until 4 meters, has soft cylindrical trunk and in the axillary of the leaf, there are coarsely textured tubers [12]. All parts of *A. cordifolia* can be beneficially ranging from roots, stems, leaves, tubers, and flowers [12].

*A. cordifolia* leaves contain polar, semi-polar, and non-polar compounds used in wound healing processes such as tannins, saponins, alkaloids, steroids, triterpenoids, flavonoids, and essential oils [13]. *A. cordifolia* from Basellaceae family affects accelerating wound healing process from the effect to the skin proliferation. Also, its ethanolic extract could accelerate wound closing process on diabetic wounds [13]. Ascorbic acid in this plant is important to activate propyl hydroxylase enzymes that support the hydroxylation stage in the collagen formation and can accelerate wound healing process [11].

In addition, *A. cordifolia* plants also have antibacterial activity [14] which can help accelerate diabetic wound healing process and prevent subsequent infections. Activity of *A. cordifolia* leaf extracts in inhibiting bacterial growth takes place by the mechanism of inhibition of cell wall synthesis, cell

membrane function, protein synthesis, and bacterial cell growth [15]. In further research, *A. cordifolia* extracts have activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* in diabetic foot ulcer patients [16].

#### *Centella asiatica*

*Centella asiatica* or pegagan from the Umbelliferae family is often used to accelerate wound healing [17]. In some studies, topical application of *C. asiatica* herbs in diabetic wounds can increase the speed of diabetic wound healing process [18]. *C. asiatica* contains asiaticosides which can increase collagen synthesis; its water extract also can improve reepithelization from corneal epithelium during wound healing process, *C. asiatica* stimulates fibroblast proliferation, reduces metalloproteinase activity that is resulting in rapid wound contraction [19].

Other studies also explained that the cream of *C. asiatica* is safe and can be used as a wound dressing alternative in diabetic patients who are contraindicated against hydrocolloid fiber wound dressing [20]. *C. asiatica* extracts have bacteriostatic and bactericidal activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* from diabetic foot ulcer patients [16], so it can accelerate diabetic wound healing.

#### *Curcuma longa*

Turmeric (*Curcuma longa* L.) is a medicinal plant from the Zingiberaceae family which is characterized by long lifespan and tall trees [21]. Part of the plant that can be used is *rhizome* that is oval and short branched [21].

Curcumin is the most active component of turmeric and has potential as a treatment agent for diabetes and its complications suffered by diabetic patients [22] such as diabetic wounds. Curcumin can increase collagen in the

treatment of diabetic wounds and accelerate wound healing process [23]. Local application of turmeric powder can specifically heal wounds due to increasing reepithelization in diabetic patients [24]. Other studies have shown that turmeric hydrocolloids can overcome infections and shorter inflammatory phases of diabetic wounds because it accelerates reepithelization, cell proliferation, and collagen synthesis [7].

### ***Carica papaya***

Papaya (*Carica papaya* L., Caricaceae) is a tree that grows in tropical regions around the world with fruits available throughout the year [25]. Papaya tree is a tall tree and grows rapidly with a height of 7-8 m and has rod diameter of 20 cm [25]. Papaya has two bioactive components such as papain and chymopapain, as well as other components such as alkaloids, flavonoids, and phenol components where all of these are used as a treatment of various diseases [26].

Papaya latex can increase epithelization speed in wound healing process [27]. Papaya fruit extracts if applied topically can accelerate wound healing by increasing the rate of collagen growth, granulation tissue proliferation and wound contraction in diabetic wounds [28]. Papaya fruits water extracts accelerate wound closure due to rapid epithelization and increased amount of granulation tissue in the wounds [29].

### **Honey**

From ancient times, honey is a very popular food and can be used as a medicine because it contains many minerals such as sodium, calcium, magnesium, aluminum, iron, phosphorus, potassium, and various vitamins [30].

Honey has effect to help healing process of gangrene wound in diabetes

patients [31]. It is used as an alternative therapy because of hydrogen peroxide content that serves as antibacterial, anti-inflammatory, and regeneration tissue agent [30]. In addition, honey also serves as an antioxidant that produces flavonoids and can be functioned as an anti-inflammatory, oxidative reactions inhibitors, and damaged cells regeneration [30].

Modern wound dressing method using honey can accelerate diabetic wound healing process because it accelerates growth of granulation tissue, has high osmolarity level so it can inhibit bacterial growth, creates moisture environment which can be absorbed properly to the skin [32], and also stimulates angiogenesis, granulation, and epithelization [33].

## **CONCLUSION**

Diabetic patients are at high risk for foot ulcers leading to amputations. Diabetic wound healing can be accelerated using natural remedies such as *Androdera cordifolia*, *Centella asiatica*, *Curcuma longa*, *Carica papaya* and honey using various methods in rats, mice, or human.

## **ACKNOWLEDGMENT**

The author expresses gratitude to the preceptor for criticism, suggestions, and willingness in reviewing this article.

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How to cited this article :

Andranilla, R.K., Susilawati, Y., 2018. Review of Natural Remedies for Accelerate Diabetic Wound Healing. *J. Trop.Pharm. Chem.* 4(3); 147-153.