

# **Blueberry Extract Can Improve Wound Healing**

Analysis by Dr. Joseph Mercola



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#### STORY AT-A-GLANCE

- > Research presented at Experimental Biology 2022 showed how wounds treated with a phenolic extract from wild blueberries had a 12% increase in wound closure by enhancing cell migration and the formation of new blood vessels
- > There are four distinct stages of wound healing that begin within seconds of the wound occurring and may last for up to one year or more after the skin closes; blueberry extract works during the proliferative stage when new blood vessels are constructed
- > Wound care begins with cleaning the area. Do not use hydrogen peroxide or antibacterial soap; instead, use mild soap and water and rinse the area for five to 10 minutes before bandaging it
- > Aloe vera and virgin coconut oil both accelerate healing time. Your body also uses specific nutrients to heal a wound, including vitamins A, C and B complex, as well as zinc, L-arginine and bromelain

Chronic wounds are a pervasive problem. Data presented at Experimental Biology 2022 from the University of Maine showed wound treatments with wild blueberry extract may help improve vascularization and cell migration, leading to better wound healing.<sup>1</sup>

According to data from the Agency for Healthcare Research and Quality,<sup>2</sup> 1% of the patients now account for about 22% of health care expenses and the top 5% spend 40% of inpatient health care dollars.

One of the more complex segments within this patient population is people with chronic wounds. According to data published in Value in Health,<sup>3</sup> nearly 15%, or 8.2 million people, who were enrolled in Medicare in 2014 had at least one type of wound or infection. The total Medicare costs range from \$28.1 billion to \$96.8 billion, with the highest estimates for surgical wounds and diabetic foot ulcers.

A 2019 review of 11 studies estimates that the prevalence of chronic wounds was 2.21 per 1,000 and chronic leg ulcers accounted for 1.51 per 1,000.<sup>4</sup> When you extrapolate this number for New York City, assuming a population of 20.106 million in 2019,<sup>5</sup> 44,434 people had chronic wounds.

Chronic wounds are sometimes disguised under the diagnosis of a comorbid condition, and they represent a silent epidemic that may affect up to 2% of the total population during their lifetime.<sup>6</sup>

# **Blueberry Extract Improves Wound Healing**

In studying the possibility of using blueberry extract for wound healing, the researchers were seeking an intervention that might improve vascularization of chronic wounds, often characterized as non-healing wounds. These include pressure ulcers and diabetic sores.

One issue is these wounds are often poorly vascularized, which has a significant impact on the development of new tissue and wound closure. The team's past research<sup>7</sup> had shown that a phenolic extract from wild blueberries increased vascularization and cell migration. In the current study, researchers looked at the effect the same extract would have on live wounds in an animal model.

The animals were either not treated, treated with a gel without phenolic extract or treated with a phenolic extract topical gel. The team compared wound healing across the three groups and found the animals that were treated with the phenolic extract had a 12% increase in wound closure. One of the scientists commented in a press release:8

"Wild blueberries have the potential to enhance cell migration, new blood vessel formation (angiogenesis) and vascularization and to speed up wound closure. This is especially important in conditions that require enhanced wound closure in patients with chronic wounds such as diabetic wounds, burns and pressure ulcers."

Polyphenols found in plants are potent antioxidants and have a marked effect on oxidative stress.<sup>9</sup> Over the past two decades, plant phenolic extracts have become an area of study, including in wound healing. In 2009,<sup>10</sup> researchers found extracts with total phenolic content of 11% and 17% "exhibited good wound healing activity probably due to phenols constituents."

In 2015,<sup>11</sup> researchers studied a polyherbal extract with a history of use in traditional medicine for wound healing. Using lab analysis, they found the extract had phenolic constituents with pharmacological properties, including apigenin, chlorogenic acid, caffeic acid and luteolin. The data showed that the multiple herbal formula had high antioxidant activity and induced collagen synthesis that may contribute to stronger wound healing.

### **Stages of Wound Healing**

Phenolic extract of wild blueberries interacts with wound healing at a specific stage in recovery. Although healing is a natural reaction to tissue injury, it is a complex system that classically is described in four stages. Each stage is coordinated by cellular events. Hemostasis is the first stage of wound healing that starts as soon as the wound occurs.<sup>12</sup>

Blood vessels begin to constrict to restrict flow as platelets begin to seal the break. Coagulation reinforces what the platelets started with threads of fibrin. This happens quickly, often within seconds. The next stage is inflammation, which begins when the injured vessels leak clear fluid which causes localized swelling. This helps to control bleeding and prevent infection.<sup>13</sup>

During the proliferative phase, the body begins to rebuild new tissue with collagen and extracellular matrix. During this stage, new blood vessels are constructed to feed granulation tissue oxygen and nutrients. The proliferative phase begins with new tissue being built and ends when epithelial cells have covered the injury. Phenolic extract impacts this stage of wound healing.

After epithelial cells have covered the injury, the body begins the remodeling stage, also called the maturation phase. Collagen is remodeled and cells that are no longer being used are removed through apoptosis.

In healthy wound healing, maturation begins 21 days after the injury and may continue for more than a year, depending on the depth and severity of the wound. Interestingly, the injured area will never be as strong as unwounded skin, generally having just 80% of the previous strength.

## **Hydrogen Peroxide Is Not Ideal to Clean Wounds**

Getting cuts and scrapes is not uncommon, and they go through the same healing process as diabetic foot ulcers or surgical incisions. Initially cleaning your wound can help flush out unwanted pathogens and create a positive environment for the area to heal, depending on what you use to clean it.

People have been using hydrogen peroxide for decades as an antiseptic because it is effective at killing bacteria and viruses. In fact, nebulized food-grade hydrogen peroxide is one of my favorite ways of reducing the impact of upper respiratory viruses. <sup>14</sup> The problem with wound care is that hydrogen peroxide is indiscriminate and will also kill other living tissue, including your healthy cells.

You might think that antibacterial soap would be a good choice, but this may include triclosan, which may interfere with hormone levels and increase the growth of drugresistant bacteria. According to the FDA:15

"Consumers may think antibacterial washes are more effective at preventing the spread of germs, but we have no scientific evidence that they are any better than plain soap and water. In fact, some data suggests that antibacterial ingredients may do more harm than good over the long-term."

The best way to clean your cut, scrape or wound is with mild soap and plenty of water. Choose one without fragrance, triclosan or triclocarban. Wash your hands before washing your cut to reduce the potential for transferring bacteria to the wound.

Rinse the area with water for five to 10 minutes to remove dirt and debris with either cool or warm water, whichever feels better to you. After cleaning, there are several steps you can take that may help speed and strengthen wound healing.

# Aloe Vera, Honey and Coconut Oil — Options for Wound and Skin

Scientists have also found other topical applications that help accelerate wound healing. Aloe vera is one that has been used in the treatment of burns for many years. The plant is easy to grow and care for at home. It has 75 potentially active ingredients, including amino acids, vitamins, lignan and saponin. Vitamins include vitamin A, C and E, as well as vitamin B12, choline and folic acid.

Aloe vera has a long traditional medicine history for the treatment of burns and wounds. A systematic review of the literature in 2007 revealed wounds treated with aloe vera healed 8.79 days more quickly than those in the control group. The Another review of the literature in 2019 found aloe vera was successful in preventing skin ulcers and treating burns, postoperative wounds, genital herpes, psoriasis and chronic wounds. The system of the literature in 2019 found aloe vera was successful in preventing skin ulcers and treating burns, postoperative wounds, genital herpes, psoriasis and chronic wounds.

Aloe vera has been so successful that wound dressings impregnated with aloe vera have been developed.<sup>19</sup> Research has also shown that topical use of aloe vera gel in the treatment of split-thickness skin graft donor sites could significantly accelerate healing.<sup>20</sup>

A study in 2018 looked at the cellular effects that aloe vera may have on wound healing and found it "promotes proliferation and migration of fibroblasts and keratinocytes" and protects "keratinocytes from preservative-induced death."<sup>21</sup> Fresh aloe vera should not be used internally, or externally if you have an allergy to the plant. If you're unsure,

perform a patch test on a small area and wait to be sure that no signs of an allergic reaction occur.

Coconut oil also has a long history of use in skin care and the treatment of wounds. One animal study<sup>22</sup> in 2010 showed wounds heal much faster with the application of virgin coconut oil, which the researchers attributed to the biologically active components. A cell analysis showed an increase in fibroblast proliferation and new blood vessels in treated wounds.

A second study<sup>23</sup> confirmed an increase in blood vessel proliferation and wound healing that researchers thought might be mediated by regulating vascular endothelial growth factor signing pathway. An animal model<sup>24</sup> showed burns treated with 70% hydrolyzed virgin coconut oil healed far more quickly than those that were untreated.

Virgin coconut oil has also been tested on diabetic ulcers,<sup>25</sup> which become chronic and are a major complication of diabetes. Diabetic animals were either treated with topical application of virgin coconut oil, silver sulfadiazine cream or not treated at all for 14 days. Throughout the study, they found the wound closure rate was highest in animals who were treated with virgin coconut oil.

The animals also demonstrated re-epithelialization and increased collagen in the wound tissue. In summary, they found the coconut oil worked better than silver sulfadiazine cream, which is a topical antimicrobial typically used in the prevention and treatment of wound infections in patients with second- and third-degree burns.<sup>26</sup>

Honey is another natural product that is used in wound and burn care. In hospitals, Manuka honey<sup>27</sup> in hydrogel form is often implemented in treating burns and diabetic ulcers. A 2021 journal article reported:<sup>28</sup>

"Thanks to the anti-inflammatory capability of honey, its incorporation into hydrogels reduced the expression of the proinflammatory cytokines, attributing beneficial healing. Besides, in-vitro and in-vivo studies revealed that their administration significantly improved angiogenesis, reepithelialization, and granulation tissue formation."

Other studies show that medical-grade honey can be used as an alternative to antibiotics in non-healing wounds,<sup>29</sup> and that it even can be successful in reducing wound size, pain, odor and exudate (fluids leaking from the wounded tissue).<sup>30</sup>

# **Nutrients Required for Wound Healing**

Your body also requires specific nutrients to improve wound healing at different stages. Your food and supplement choices can affect wound healing and lower the potential a wound may become chronic. These nutrients can include:

**Beta-carotene or vitamin A** — During wound healing, vitamin A regulates growth and differentiation, stimulates epidermal turnover, increases re-epithelialization and restores structure.<sup>31</sup>

Vitamin A deficiency is common during infection and topical application may improve collagen formation.<sup>32</sup> Foods high in vitamin A<sup>33</sup> or beta-carotene<sup>34</sup> include fruits and vegetables. Do not take a vitamin A supplement if you are pregnant, nursing or trying to get pregnant.

**Vitamin C** — Your body uses water-soluble vitamin C to make collagen and form new tissue. Vitamin C interacts with some medications including chemotherapy, estrogen, warfarin and others.<sup>35</sup> Check with your pharmacist for known interactions if you are taking any medication. Foods rich in vitamin C include red bell peppers, dark leafy greens, broccoli and berries.<sup>36</sup>

**Zinc** — This micronutrient stimulates wound healing through cell proliferation and growth and deficiency can impair wound healing.<sup>37,38</sup> It can be used as an oral supplement or applied directly to the wound in cream form. Do not apply to open wounds and do not take it as a supplement long-term as it creates a copper imbalance.<sup>39</sup> Foods high in zinc include pumpkin seeds, oysters, beef, oatmeal and mushrooms.<sup>40</sup>

**B-Complex vitamins** — Multiple B vitamins have been shown to speed wound healing and improve skin health<sup>41</sup> and may help improve wound healing in diabetics.<sup>42</sup> Foods high in many of the B vitamins include avocado, wild-caught salmon, pastured eggs, sunflower seeds and spinach.<sup>43</sup>

**Bromelain** — This enzyme that is found in pineapple may help improve healing time and reduce pain without increasing bleeding.<sup>44,45</sup>

**L-arginine** — This has been used post-surgically to improve healing by enhancing wound strength and collagen deposition.<sup>46,47</sup> Protein-rich foods are also high in arginine, such as organic, pasture-raised meat and dairy products, nuts, seeds and fish.<sup>48</sup>

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