

# Evidence Summary: Wound Management Low Resource Communities - Aloe vera for wound healing

February 2017, Author – Wound Healing and Management Node Group – E.Haesler

## QUESTION

What is the best available evidence regarding aloe vera for promoting wound healing?

## SUMMARY

Aloe vera is a succulent plant that has traditionally been used for natural wound healing.<sup>1-3</sup> The leaves contain a gel substance that is harvested, then stabilised and sterilised with heat, before application to a wound (generally a burn) (Level 5.b evidence).<sup>1</sup> Despite its wide spread use as a cost effective agent for wound management, there is minimal evidence on the efficacy of aloe vera in wound healing. The evidence identified for this summary included efficacy of aloe vera for healing partial thickness burns,<sup>4-8</sup> diabetic ulcers,<sup>4</sup> leg ulcers,<sup>4, 9</sup> surgical wounds,<sup>7, 10</sup> biopsy sites<sup>7</sup> and stage  $\geq 2$  pressure injuries (Level 1.b to 4.c evidence).<sup>7</sup> The findings were contradictory; however, aloe vera was not inferior to contemporary wound care products, particularly for burn management. The different aloe vera products used, or the high risk of bias observed in most trials, may account for inconsistent findings. Safety reviews indicate that risks of using aloe vera products in wound management are low (Level 5.b evidence).<sup>1, 11</sup>

## BACKGROUND

Aloe vera (*Liliaceae* family) is a tropical plant that has been used in traditional healing for centuries, particularly in Asian and African regions.<sup>1-3</sup> The active component of the plant is a gel substance that is cultivated from the inside the leaves. The gel contains vitamins, enzymes, amino acids, sugars, minerals, anthraquinones and polysaccharides (including acemannan).<sup>1, 3, 11</sup> It has water content of approximately 99%,<sup>1, 12</sup> which contributes to its attributed effect in preventing wound desiccation, and its soothing characteristics.<sup>13, 14</sup> The pH of aloe vera gel is 4.5.<sup>1, 12</sup>

Laboratory evidence from animal studies suggests that aloe vera stimulates fibroblast cell proliferation, promotes collagen synthesis and stimulates angiogenesis.<sup>11, 12, 14, 15</sup> Aloe vera also is claimed to improve microcirculation, which in turn increases wound bed oxygenation.<sup>6, 14</sup> Aloe vera is also claimed to have antibacterial, antifungal and antiviral qualities<sup>9, 11, 14</sup> that are attributed to the acemannan content.<sup>11, 14</sup>

Aloe vera gel is produced from the leaves of the aloe vera plant. The outer layer of the washed leaf is peeled and the inner gel is pulverised. In commercial production, this gel is filtered, sterilised and pasteurised.<sup>11</sup> Heating reduces the slimy consistency and stabilises the gel material.<sup>9, 11</sup> More traditional preparation of aloe vera involves carefully washing the leaves, removing the outer leaf rind with a sterilised knife, grounding the inner flesh to a pulp with a mill or blender and storing it in an air tight container in a dry, cool place.<sup>16</sup> This method produces a non-sterile product that is not recommended in contemporary wound care.

## CLINICAL BOTTOM LINE

### Effectiveness in promoting healing

- Outcomes for healing of **deep partial thickness burns** are reported in a moderate quality systematic review (SR) that included four low quality trials, two of which were randomised. Participants had burns to 2-40% of total body surface area that were classified as second or third degree. In two studies, aloe vera soaked gauze was applied. An aloe cream was used in one trial and the fourth trial used 1% aloe powder with white petroleum jelly gauze. Pooled results showed significant benefits from using aloe vera compared to control treatments of petroleum jelly gauze or framycetin sulphate cream for time to complete healing (weighted mean difference 8.79 days, 95% confidence interval [CI] 2.51 to 15.07,  $p=0.006$ ). One trial reported improved healing compared to 1% silver sulfadiazine (95% versus 83% participants' wounds classified as successful healing). The last trial reported improved rate of epithelisation on the eighth day following skin grafting ( $5.84\pm 0.27$ mm versus  $3.95\pm 0.33$  mm) (Level 1.b evidence).<sup>5</sup>
- In a randomised controlled trial (RCT)<sup>17</sup> reported in narrative form in a SR,<sup>7</sup> 0.5% aloe vera powder was compared to 1% silver sulfadiazine (SSD) for promoting healing of **deep partial thickness burns**. In this study 100% of the aloe vera treated burns healed by 19 days, compared with 80% of those treated with silver. This was not a significant difference (Risk ratio [RR] 1.41, 95% CI 0.70 to 2.85,  $p>0.05$ ) (Level 1.c evidence).<sup>7, 17</sup>
- In the same SR,<sup>7</sup> no significant effect was found for aloe vera for healing **haemorrhoidectomy** (1 RCT, comparison was placebo), **shave biopsy** (1 RCT, comparison was hydrogel dressing) or **chronic pressure injures** (1 RCT, comparison was saline gauze) (Level 1.c evidence).<sup>7</sup>
- Aloe vera applied to surgical wounds was reported in a double-blind RCT involving 90 women in Iran who had a caesarean section. The aloe vera gel was harvested from the leaf in the operating theatre by the surgeon and applied immediately to the **surgical wound** without any additional preparation. The gel was covered with gauze. The control group received a simple gauze dressing. Wound healing was assessed using the previously validated REEDA scale. After eight days, there was no significant difference in wound healing ( $p=0.283$ ) (Level 1.c evidence).<sup>10</sup>
- Efficacy of aloe vera gel for **deep partial thickness burns** was demonstrated in an RCT conducted in individuals with second degree burns covering less than 25% total body surface area. Patients were randomised to receive either gauze soaked in aloe vera gel ( $n=25$ ) or 1% SSD ( $n=25$ ). Mean healing time was significantly faster in the aloe vera group (mean  $11\pm 4.18$  days versus mean  $24.24\pm 11.16$  days,  $p<0.00001$ ) (Level 1.c evidence).<sup>6</sup>

- In a very low quality case series, 30 individuals with **diabetic ulcers, post-traumatic wounds and burns of unspecified severity** were treated with an aloe vera gel from the species *Aloe barbadensis*. After two weeks, 87% of the wounds were completely healed. Although there was a control group (treatment not specified), the outcomes for that group were not reported (Level 4.c evidence).<sup>4</sup>

#### Effectiveness in managing infection

- Laboratory studies have reported aloe vera gel has an antibacterial effect against *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida albicans* and other organisms commonly seen in wounds. One study that explored antibacterial effect of aloe vera gel on organisms harvested from burns established sensitivity of *P. aeruginosa* at a minimum inhibitory concentration (MIC) of less than 400 µg/mL (Level 5.c evidence).<sup>18</sup>
- In a quasi-experiment, infected leg ulcers (n=30) were treated with topical aloe vera gel from the species *Aloe barbadensis*. A control group was treated with topical antibiotics. Cultures were taken from the ulcers on alternate days. At baseline, ulcers were colonised with *S.aureus* (46%), *P.aeruginosa* (27%), *Citrobacter koserii* (13%), as well as other organisms. One third of the ulcers were colonised with methicillin resistant *S. aureus* (MRSA). Growth of bacteria in ulcers treated with aloe vera significantly decreased (: 100% growth of bacteria on day 1 of 100% versus day growth of bacteria on day 11 of 6.7%, p<0.001). In comparison, 100% of the control ulcers remained colonised by day 11 (Level 2.c evidence).<sup>9</sup>

#### Effectiveness in managing wound pain

- In an RCT comparing aloe vera with 1% SSD for treating second degree burns, aloe vera gel was superior in managing pain. Pain was reported as days taken for complete pain relief, and was measured on a visual analogue scale. The aloe vera group achieved a pain free state significantly faster than the control group (1% SSD) (mean 21 days versus mean 26 days, p=0.01) (Level 1.c evidence).<sup>6</sup>
- A double blind RCT included 120 individuals with second and third degree burns covering less than 5% of total body surface area. Half the participants were treated with 1% SSD cream and the second half received a herbal cream that contained aloe vera gel and essential oils. There was no difference in pain scores at day two. Aloe vera herbal cream was more effective in reducing pain by days seven (p=0.014) and fourteen (p=0.05) (Level 1.c evidence).<sup>8</sup>

#### CONTRAINDICATIONS AND SIDE EFFECTS

- Aloe vera is contraindicated in individuals with allergy to plants in the *Liliaceae* family, for example onions and garlic (Levels 5.b and 5.c evidence).<sup>1, 19</sup>
- Urticaria and contact dermatitis are reported adverse events (Levels 1.b and 5.b evidence).<sup>1, 5</sup> It is proposed that these effects may be greater when gel is harvested from the centre part of the leaf, because the active ingredients are more condensed in this part of the plant. In one SR that included individuals with burns,

approximately 40% of participants reported irritation or itching, but this was not different from individuals treated with SSD (Level 1.b evidence).<sup>5</sup> Applying the gel to a small area of skin as a test prior to application to a wound is recommended (Level 5.c evidence).<sup>19</sup>

#### OTHER FACTORS FOR CONSIDERATION

In the cost analysis conducted for an Indian RCT the cost of one aloe vera gel dressing (5ml) was 2.40 Indian rupee. This compared to 4.92 Indian rupee for one SSD wound dressing (2 grams) (Level 4.c evidence).<sup>6</sup>

#### CHARACTERISTICS OF THE EVIDENCE

This evidence summary is based on a systematic literature search conducted in Medline, EMBASE, the Cochrane Library, AMED and the WHO Afro library, combining search terms that describe management of skin wounds and aloe vera. Retrieved papers were appraised for relevance and rigour using JBI appraisal tools. The evidence in this summary comes from:

- Experimental designs<sup>5-8, 10, 17</sup> (Level 1 evidence)
- Quasi-experimental design<sup>9</sup> (Level 2 evidence)
- Case series<sup>4</sup> (Level 4 evidence)
- Expert opinion and bench research<sup>1-3, 11-16, 18</sup> (Level 5 evidence)

#### BEST PRACTICE RECOMMENDATIONS

- The current evidence provides moderate support for the use of aloe vera to promote healing of partial thickness burns. Natural Aloe vera gel was not inferior to contemporary products such as 1% SSD cream for managing burns. (Grade B).
- Apply aloe gel to a small area of skin to test for allergies prior to application to a wound (Grade B)
- Aloe vera can be considered for pain relief in burns, post-acute stage. (Grade B)

#### KEY WORDS

Wound care; aloe vera; traditional wound care; natural wound healing; acemannan

#### REFERENCES

1. Ulbricht C, Armstrong J, Basch E, Basch S, Bent S, Dacey C, Dalton S, Foppa I, Giese N, Hammerness P, Kirkwood C, Sollars D, Tanguay-Colucci S, Weissner W. An evidence-based systematic review of aloe vera by the natural standard research collaboration. *J Herb Pharmacother*, 2007;7(3-4):279-323. (Level 5.b evidence).
2. Manvitha K, Bidya B. Aloe vera: A wonder plant its history, cultivation and medicinal uses. *J Pharmacogn Phytochem*, 2014;2(5):85-8. (Level 5.c evidence).
3. Pazyar N, Yaghoobi R, Rafiee E, Mehrabian A, Feily A. Skin wound healing and phytomedicine: A review. *Skin Pharmacol Physiol*, 2014;27(6):303-10. (Level 5.b evidence).
4. Nagar P, Magesh Kumar J, Vardharajan P. Efficacy of aloe vera gel dressing in chronic leg ulcer of diabetic, traumatic and burns origin. *Res J Pharm Biol Chem Sci*, 2015;6(6):482-4. (Level 4.c evidence).
5. 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):713-8. (Level 1.b evidence).
6. Shahzad MN, Ahmed N. Effectiveness of aloe vera gel compared with 1% silver sulphadiazine cream as burn wound dressing in second degree burns. *J Pak Med Assoc*, 2013;63(2):225-30. (Level 1.c evidence).

- 
7. Dat AD, Poon F, Pham KB, Doust J. Aloe vera for treating acute and chronic wounds. *Cochrane Database Syst Rev*, 2012;2:CD008762. Doi: 10.1002/14651858.CD008762.pub2. (Level 1.c evidence).
  8. Panahi Y, Beiraghdar F, Akbari H, Bekhradi H, Taghizadeh M, Sahebkar A. A herbal cream consisting of Aloe vera, Lavandulastoechas, and Pelargonium roseum as an alternative for silver sulfadiazine in burn management. *Asian Biomedicine*, 2012;6(2):273-8. (Level 1.c evidence).
  9. Banu A, Sathyanarayana BC, Chattannavar G. Efficacy of fresh aloe vera gel against multi-drug resistant bacteria in infected leg ulcers. *Australas Med J*, 2012;5(6):305-9. (Level 2.c evidence).
  10. Molazem Z, Mohseni F, Younesi M, Keshavarzi S. Aloe vera gel and cesarean wound healing; a randomized controlled clinical trial. *Glob J Health Sci*, 2015. 01 Jan;7(1):203-9. (Level 1.c evidence).
  11. Andersen FA. Final report on the safety assessment of aloe andongensis extract, aloe andongensis leaf juice, aloe arborescens leaf extract, aloe arborescens leaf juice, aloe arborescens leaf protoplasts, aloe barbadensis flower extract, aloe barbadensis leaf, aloe barbadensis leaf extract, aloe barbadensis leaf juice, aloe barbadensis leaf polysaccharides, aloe barbadensis leaf water, ferox leaf extract. *Int J Toxicol*, 2007;26(Suppl. 2):1-50. (Level 5.b evidence).
  12. Haesler E, Watts R, Rice J, Carville K. Local resource botanicals used in wound care. *Wound Practice and Research*, 2016;84-90. (Level 5.b evidence).
  13. Lloyd ECO, Rodgers BC, Michener M, Williams MS. Outpatient burns: Prevention and care. *Am Fam Physician*, 2012;85(1):25-32. (Level 5.c evidence).
  14. Nandal U, Bhardwaj RL. Aloe vera: A valuable wonder plant for food, medicine and cosmetic use - a review. *Int J Pharm Sci Rev Res*, 2012;13(1):59-67. (Level 5.b evidence).
  15. Pereira RF, Bartolo PJ. Traditional therapies for skin wound healing. *Adv Wound Care*, 2016. 01 May;5(5):208-29. (Level 5.c evidence).
  16. Purohit SK, Solanki R, Soni M. Experimental evaluation of Aloe vera leaves pulp as topical medicament on wound. *International Journal of Pharmacological Research*, 2012;2(3):110-2. (Level 5.c evidence).
  17. Khorasani G, Hosseinimehr SJ, Azadbakht M, Zamani A, Mahdavi MR. Aloe versus silver sulfadiazine creams for second-degree burns: A randomized controlled study. *Surg Today*, 2009. July;39(7):587-91. (Level 1.c evidence).
  18. Goudarzi M, Fazeli M, Azad M, Seyedjavadi SS, Mousavi R. Aloe vera gel: Effective therapeutic agent against multidrug-resistant pseudomonas aeruginosa isolates recovered from burn wound infections. *Chemother Res Pract*, 2015;2015 (639806):(no pagination). (Level 5.c evidence).
  19. Rajeswari R, Umadevi M, Sharmila Rahale C, Pushpa R, Selvavenkadesh S, Sampath Kumar K, Bhowmik D. Aloe vera: The miracle plant its medicinal and traditional uses in India. *J Pharmacogn Phytochem*, 2012;1(4):118-24. (Level 5.c evidence).
-