

Possible Efficacy of Aloe Vera Gel to Wound Healing and Pain Relief: Case Reports of Kampo Medicine With Aloe Vera Juice

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ABSTRACT

Aloe vera has an inhibitory system (anti-inflammatory activity) and a stimulatory system (wound-healing activity), which may act as a modulator of wound healing and inflammation. The action mechanism of aloe vera to wound healing, inflammation, and analgesic was discussed. Aloe vera reduces pain by blocking the synthesis of bradykinin, cyclooxygenase-2, and thromboxane synthase. Furthermore we presented six case reports of *Kampo* medicine with successive ingestion of aloe vera juice in which *Kampo* medicine demonstrates to be a suitable personalized medicine for wound and improves gut-microbial ecosystem in host.

Key words: Aloe vera gel; Wound healing; Pain relief; *Kampo* medicine; Six case reports

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INTRODUCTION

Aloe vera is known for its anti-inflammatory, skin protection, antibacterial, anti-viral, anti-septic, and wound healing properties. The use of aloe vera to improve wound healing is recommended as the main method. Davis RH^[1], showed how aloe vera eliminates pain, inflammation, arthritis, and wounds. His conductor-orchestra concept of aloe vera takes into account all the biologically active components working synergistically to produce the maximum desired benefits with little or no toxicity. The high molecular material; polysaccharide, pectin, glycoprotein, and protein molecule is the conductor that leads a symphony of over two hundred biologically active substances. Water plays a major role in the orchestra. Water helps to produce therapeutic activities. The interaction between the conductor and the orchestra arises from water's polarity. The orchestra molecules, as well as the conductor high molecular materials possess both polar and non-polar parts that relate with the polarity of water to form a water communication chain. The high molecular materials could be used as biodegradable safe and non-toxic adjuvants, and as an enhancer, through activation of immune systems.

Hekmatpou *et al*^[2] presented a systematic review on the effect of Aloe vera 23 clinical trials from 1990 to 2016 on prevention and healing of skin wound. Considering the availability of several clinical trials on the effect of aloe vera gel on prevention and healing of skin wounds, it can be used to retain skin moisture and integrity and to prevent ulcers. It seems that the application of aloe vera gel, as a complementary treatment along with current methods, can improve wound healing and promote the health of society.

In present review we discuss effects of aloe vera gel on pain and wound healing focusing on clinical treatment and six case reports of *Kampo* medicine with aloe vera juice.

EFFECTS OF ALOE VERA CREAM ON POST-HEMORRHOIDECTOMY, DIAPER DERMATITIS, AND PAIN IN WOUND

Eshghi *et al*^[3] assessed the effects of aloe vera cream in reducing postoperative pain, post-defecation pain, and its promotion of wound healing after open hemorrhoidectomy. A prospective, randomized, double-blind, placebo-controlled trial was conducted comparing the effects of a cream containing aloe vera versus a placebo cream on post-hemorrhoidectomy pain. Wound healing at the end of the second postoperative week was significantly greater in the aloe group compared with the placebo group. Application of aloe vera cream on the surgical site is effective in regarding postoperative pain both on resting and during defecation, healing time, and analgesic requirement in the patients compared with the placebo group.

Diaper dermatitis (DD) is a common inflammatory disorder among children and infants. Panahi *et al*^[4] presented randomized and double-blind trial comparing the therapeutic efficacies of aloe vera cream and *Calendula officinalis* ointment on the frequency and severity of DD in children. Although improvement in the severity of DD was observed in both treatment groups, patients receiving *Calendula* ointment had significantly fewer rash sites compared to Aloe group. No adverse effect was obtained from either of the medications.

Burn injuries are among the most devastating of all injuries and a major global public health crisis. Despite recent advances in antimicrobial chemotherapy and wound management, infection continues to be an important problem in the treatment of burns. One of the most effective means to achieve a microbial balance in a colonized or infected wound is the proper use of prophylactic topical agents. The introduction of topical antimicrobial agents has resulted in a significant reduction in burn mortality to date. Shahzad *et al*^[5] assessed the efficacy of aloe vera gel compared with 1% silver sulfadiazine (SSD) cream as a burn dressing for the treatment of superficial ant partial thickness burns. Thermal burns patients dressed with aloe vera gel showed advantage compared to those dressed with SSD cream regarding early wound epithelialization, earlier pain relief and cost-effectiveness.

THE EFFECTIVENESS AND RATE OF HEALING OF ALOE VERA GEL IN TREATMENT OF CHRONIC WOUNDS

Chronic wounds are the defect in the skin that shows no tendency to heal after 3 months of appropriate treatment or is still not fully healed at 12 months. Ulcers can be defined as wounds with a full thickness depth and a slow healing tendency. Despite of many advances in technology and research, chronic ulcers take a lot of time to heal by the conventional methods. Athavale *et al*^[6] compared the effectiveness of aloe vera gel with conventional dressing (normal saline and povidone iodine) and assessed the percentage reduction of wound healing with aloe vera gel dressing. The study concluded that aloe vera gel is highly effective in treatment of chronic ulcers and stimulates the growth of wound healing, thus reduces the hospital stay. Apart from being efficacious in wound healing, aloe vera gel is safe product. No-allergic reaction/infections were associated with aloe vera gel. Varaei *et al*^[7] investigated that to determine local pain of the burn wound, pain intensity was assessed with 10 min before change of dressing and 24, 48, and 72 hour after dressing with 2% nitrofurazone ointment and aloe vera gel using visual analogue scale. So dressing pain intensity decreased significantly during 72-h

period in both areas, but aloe vera gel could reduce pain faster than nitrofurazone. The reason may be presence of carboxypeptidase in aloe vera gel which inter-activates bradykinin which is the powerful factor of acute inflammatory pain^[8].

Walash *et al*^[9] evaluated the efficacy of dressing by aloe vera gel versus conventional dressing on the healing process and pain among burned patients. Depending on the study results it can be concluded that aloe vera gel promoted wound healing of first and second degree of burns better than traditional dressing in management methods, it also reduces pain level so lesser length of patient hospitalization stay.

REDUCTION IN THE INCIDENCE OF ALVEOLAR OSTEITIS BY ACEMANNAN HYDROGEL

Alveolar osteitis (AO), also known as dry socket, is the most common complication occurring after the extraction of a permanent tooth. The condition has generally been characterized by degraded or delayed healing associated with clot degradation. AO can be a burden for both patients and surgeons.

A Baylor college of dentistry group in Dallas, Tx. in USA, found that acemannan hydrogel accelerated healing and reduced pain associated with aphthous ulcers. Participants received either acemannan hydrogel (AH), freeze-dried AH or active control which was OTC remedy. AH found effective in treating oral ulcers has been approved by the US Food and Drug Administration for market distribution. Poor *et al*^[10] compared the incidence of AO in patients treated with either clindamycin-soaked gel-foam or acemannan hydrogel. The study results suggest that acemannan hydrogel significantly reduces the incidence of AO compared clindamycin-soaked gel-foam. Bhalang *et al*^[11] elucidated the safety and effectiveness of acemannan in the treatment of oral aphthous ulceration. The effectiveness of acemannan in reducing ulcer size and pain was superior to that of control, but inferior to that of 0.1% triamcinolone acetonide. Acemannan can be used for the treatment of oral aphthous ulceration in patients who wish to avoid the use of steroid medication, although the effectiveness was not comparable to that of 0.1% triamcinolone acetonide. Giroh *et al*^[12] evaluated efficacy of aloe vera gel and triamcinolone acetonide (TA) 0.1% in recurrent aphthous stomatitis. TA oral paste was found to be effective than aloe vera in wound healing. In contrast, aloe vera gel had a better response in terms of pain and burning sensation. Aloe vera gel is a promising agent in treating oral lesion in the field of oral medicine. It can be used as an alternative medicine and in patients who are allergic to steroid medication. Babae *et al*^[13] evaluated topically administered aloe vera gel on oral cavity minor aphthous healing. Aloe vera gel is not effective in decreasing the recurrent aphthous stomatitis patient's pain score and wound size but also decreases the aphthous wound healing period.

ALOE VERA GEL IN TREATMENT FOR ORAL MUCOSA, TONGUE PROTECTOR, AND ACUTE RADIATION-INDUCED PROCTITIS

Oral sub-mucous fibrosis (OSMF) is a potentially malignant disorder of the oral mucosa, mainly associated with the practice of chewing gutka and betel quid. The pathogenesis is obscure, and till date, no definitive therapy is available for the management of OSMF. Sudarshan *et al*^[14] compared the efficacy of aloe vera with antioxidants in the treatment of OSMF. Overall assessment of the

parameters depicted that aloe vera group showed a better treatment response compared to the antioxidants group. It proves to be a relatively safe, can be applied topically, easily available, economical, noninvasive, and efficacious in the treatment for OSMF.

Lopez-Jornet *et al*^[15] evaluated the efficacy of aloe vera applied in combination with a tongue protector, comparing this with a placebo. A total 75 patients with burning mouth syndrome (BMS) were divided into three groups randomly. Group 1 (tongue protector three times a day), Group 2 (tongue protector and 0.5ml aloe vera at 70% three times a day) and Group 3 (tongue protector and 0.5 ml placebo three time a day). Regarding quality of life, no significant differences were found. The overall clinical improvement was greater for Group 2. The concomitant prescription of tongue protector and aloe vera is effective for treating patients with BMS.

Acute radiation-induced proctitis (ARP) is the most common side effect following radiotherapy for malignant pelvic disease. Sahebnaasagh *et al*^[16] evaluated the efficacy of aloe vera ointment in prevention of ARP. Forty-two patients receiving external-beam radiotherapy (RT) for pelvic malignancies were randomized to receive either aloe vera 3% or placebo topical ointment during radiotherapy for 6 weeks. The study showed that aloe vera topical ointment was effective in prevention of symptoms of ARP in patients undergoing RT for pelvic cancers. Although the mechanism of action which aloe vera might facilitate healing is not clearly delineated, one hypothesis is that it exerts its effects as a result of antioxidant and immune-modulatory properties, and cyclo-oxygenase-2 suppression^[8].

ASSESSMENT OF ANTI-HERPES SIMPLEX VIRUS 1 AND 2, HERPES ZOSTER, AND POSTHERPETIC NEURALGIA BY ALOE VERA GEL

Herpes simplex virus (HSV) is a DNA virus, belonging to the family *Herpesviridae*. Sequence homology between HSV type 1 and 2 is about 50%. Serological assays of antibody can differentiate between the two by using type specific antigens, such as the gG1 and gG2 proteins. Upon primary infection, the virus establishes latency in neuronal cells of ganglia. Varicella zoster virus (VZV) is also herpesvirus. As such it shares structural characteristics with HSV. Furthermore the virus causes similar histopathologic features, e.g. intra-nuclear inclusions and multinucleated giant cell. VZV causes two major syndromes: varicella (chickenpox) and zoster (shingles). HSV infection is one of the most common and debilitating oral diseases, yet, there is no standard topical treatment to control it. The extract of aloe vera leaves has been reported to have anti-inflammatory, ant-bacterial, and antiviral effects. The finding on anti-HSV type 1 activity of aloe vera gel was shown in Vero cell line, suggesting that the gel could be a useful topical treatment for oral HSV-1 infections without any significant toxicity^[17]. Herpes simplex virus type 2 (HSV-2) is an enveloped virus which causes genital herpes and some other important complications such as encephalitis, meningitis, eye infections and cold sore. The virus can produce latent infection in the host for life and is reactivated by stimulus to cause recurrent infections and lesions. Zandi *et al*^[18] tested the anti-viral activity of a crude hot glycerin extract of aloe vera gel against HSV-2 replication in Vero cell line. The extract showed antiviral activity against HSV-2 not only before attachment and entry of virus to the Vero cells but also on post attachment stages of virus replication. Roxas ^[19] reviewed herpes zoster and postherpetic neuralgia and

presented the most effective currently available option. Herpes zoster (HZ), also known as shingles, is a painful vesicular rash, resulting from reactivation of the virus that also causes chickenpox-Varicella zoster virus. Typically, the rash runs its course in a matter of 4-5 weeks. The pain, however, may persist months, even years, after the skin heals. This phenomenon is known as postherpetic neuralgia. Often described as an intense burning, itching sensation, this pain can be significant to the point of being debilitating, and as such can greatly affect quality of life. Conventional therapies include prescription antivirals, corticosteroids, and analgesics, both oral and topical. Others considerations include use of over-the-counter anti-inflammatory agents, physiotherapy, and nerve block injections. The most effective conventional treatment options currently available is selected botanical and nutritional as following: vitamin A, enzyme therapy (acyclovir or trypsin+chymotrypsin+papain), capsaicin, honey/propolis, and aloe vera. Syed *et al*^[20] determined the clinical efficacy and tolerability of aloe vera extract 0.5% in a hydrophilic cream to cure patients afflicted with first episodes of genital herpes. The clinical results suggest that aloe vera extract 0.5% in a hydrophilic cream is more efficacious than placebo, thus supporting the benefits of aloe vera therapy as an alternative, reliable and effective treatment to cure the first episodes of genital herpes in men.

CASE REPORTS

Case 1: Eight-year school girl got a scald on her foot and suffered from skin injury on Nov. 2010. She was immediately treated with aloe vera cream on her foot, and diagnosed to be at stage 3 in burn. She took aloe vera cream and aloe vera juice (AVJ) without administration of antibiotics and steroid treatment for 6-months. On one month after ingestion of AVJ and treatment with aloe vera cream the pain completely ceased and the skin fully generated without any trace of scald.

Case 2: Fifty-year female had a heavy pain around her back due to Chinese cupping therapy (Cupping therapy draws toxins from the body and relieves muscle pain and has a type of deep-tissue massage-like effect) on April 2020. She was diagnosed to use steroid cream and suggested to trace scars. She took AVJ 330ml/d and spread over aloe vera cream for 9 days. After treatment of AVJ and cream she recovered without any scar after 14 days treatments showed by two photographs.

Case 3: Sixty year male had an unknown origin pain and swell on March 2018. He had an original varicose vein and expansion of it after insect bite and sting. He could not sleep and took AVJ 330ml/d with *Keisibukuryogan*-drink. After taking them for two days, the decreasing in swell and pain were clearly healed. On four days after he had fully recovered without itching showed by three photographs.

Sixty years male had varicosa with pain and swell. After two and four days of the treatment AVJ and cream with *Kampo* medicine, the foot was recovered (Photos).

Case 4: Seventy year male with foot swelling and pain for several years was difficult in walking on 2015. He was diagnosed as spinal canal stenosis and recommended to have a spine distraction implant. And he was told to have rehabilitation after surgery. He took AVJ 200ml/d with painkiller medicines for one month, and he recovered of foot swelling and pain.

Case 5: Eighty year female had pains and neuralgia around her abdomen and was diagnosed as herpes zoster on 2013. She had a poor appetite and took *Shakuyakukanzoto* with AVJ 200ml/d for ten days. She recovered after ten days and had no a piercing pain from herpes zoster.

Casa 6: Sixty eight year female had piercing pains and neuralgia around her abdomen and was diagnosed herpes zoster on Dec 2019. She does not want to have injection and took AVJ 500ml/d with propolis for three months. She recovered without a piercing pain from herpes zoster.



Capping therapy



After 14 days treatment



DISCUSSION AND CASE REPORTS

We reviewed evident effects of aloe vera gel on wound healing and pain relief. Furthermore we presented six case reports: scald, heavy pain due to Chinese cupping therapy, an unknown origin pain and swell, spinal canal stenosis, and herpes zoster. *Kampo* medicine with successive ingestion of AVJ demonstrates to be suitably personalized medicine for pain healing, and herpes zoster, and improves gut-microbial ecosystem in host. In six case reports it is suggested that AVJ ingestion and cream with *Kampo* medicine strongly alleviates the wound and pain without any scar, and accelerates the efficacy of *Kampo* medicine than that of *Kampo* medicine alone. *Kampo* medicine demonstrates to be suitable personalized medicine for wound and improves gut-microbial ecosystem in host. Prophylactic AVJ as an adjuvant is fully expected in wound healing and pain relief.

SUMMARY

The action mechanism of aloe vera gel to wound healing, inflammation, and analgesic was discussed. Furthermore we presented six case reports of *Kampo* medicine with aloe vera juice successive ingestion. It was suggested that aloe vera gel reduces pain and inflammatory properties by inhibiting the bradykinin effect^[21] and cyclooxygenase-2 synthesis^[8].

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