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CASE REPORT

Putative Roles of Aloe Vera Gel in Aging and Inflammatory Process: Case Reports of Bone Mineral Regeneration, and Regression of Mesenteric Lymphadenopathy and Microscopic Polyangiitis

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ABSTRACT

The roles of acemannan and hyaluronan for inflammatory wound healing and recovery of bone were discussed. In case reports bone mineral regeneration, regression of mesenteric lymphadenopathy and microscopic polyangiitis were described. Kampo medicine with aloe vera juice as an adjuvant to connective tissue repair was exhibited.

Key words: Aloe vera gel; Case reports; Wound healing; Bone mineral regeneration; Mesenteric lymphadenopathy regression; Microscopic polyangiitis regression

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INTRODUCTION

Aloe vera contains 99.5% water and 0.5% solids. Since aloe vera is 99.5% water, aloe vera increases the penetration of skin by water hydration and occlusion and increase of compound solubility in aloe vera. Aloe vera gel mucilage acts to keep moisture in wounds as a biological vehicle. A biological vehicle is one that acts as physical or physiological carrier for active biological agents, no matter what the pharmacological agent under consideration is. Aloe vera stimulates fibroblasts to increase in number in a dose-response fashion. A mixture of aloe polysaccharide; acemannan, acts to produce a balance in a biological system^[1].

Aloe vera has an inhibitory system (anti-inflammatory activity) and a stimulatory system (wound-healing activity), which may act as a modulatory of wound healing and inflammation. Aloe vera has been reported as a healing agent for wounds but advantages of oral administration have little reported. In recent paper we discussed the beneficial efficacy of aloe ingredients on management of gut microbiota and age-related senescent inflammation, known as senoinflammation^[2]. In present review we summarize the possible mechanism of action and the therapeutic implications of aloe vera gel in health maintenance, protection of inflammation and wound healing, and modulation of bone mineral in the elderly. Case reports exhibited the beneficial role of adjuvant of aloe vera juice to aim

at repairing injured tissues. Furthermore regression of mesenteric lymphadenopathy and microscopic polyangiitis were described.

Oral administration of aloe vera to wound healing

Advantages of oral administration and mechanism of wound healing of Aloe vera was evaluated by Ali *et al*^[3] for excisional cutaneous wound in Sprague Dawley (SD) rats. Aloe vera healed wound earlier than the untreated rats with gradual improvement in wound areas and collagen content. Aloe vera improved the expression of insulin like growth factor (IGF-1) and VEGF in skin and bone marrow indicating improvement in angiogenesis. Aloe vera increased expression of gene for chemotaxis in skin and bone marrow.

Biological behavior of fibroblasts and endothelial cells under aloe vera gel culturing

Aloe vera is used for its large variety of biological activities such as wound healing and inflammation. Although the beneficial effects of Aloe vera on wound healing have been proven, little is unknown about its effects at the cellular level. Shafaie *et al*^[4] evaluated the angiogenic and migratory effects of aloe vera gel on fibroblasts and endothelial cells. Aloe vera has a higher proliferative effect on fibroblasts in comparison with endothelial cells. Aloe vera induced angiogenesis and cell adhesion properties in fibroblasts more than endothelial cells.

The role of acemannan stimulating gingival fibroblast proliferation

Wound healing can be divided into three overlapping phases: inflammation, proliferation and extracellular matrix synthesis, and remodeling. Gingival fibroblasts (GFs) play an important role in oral wound healing. They proliferate several growth factors; keratinocyte growth factor-1 (KGF-1), vascular endothelial growth factor-1 (VEGF) and type I collagen, to generate new tissue. Aloe vera gel stimulated dermal wound healing by increasing collagen and glycosaminoglycan synthesis. The effects of acemannan, a mixture of polysaccharide, pectin, glycoprotein and protein, in aloe vera gel on GFs, KGF-1, VEGF and type I collagen, in rats were investigated by Jettanacheawchankit *et al*^[5]. Wound healing of rats receiving Carbopol[®] containing 0.5% acemannan (w/w) was better ($p < 0.05$) than that of the control. The findings suggest that acemannan plays a significant role in the oral wound healing processes via the induction of fibroblast proliferation and stimulation of KGF-1, VEGF, and type I collagen expression.

Aloe vera as a bioactive molecule inducing bone formation

Bone healing involves a complex process of many local and systemic regulatory and enhanced factors. Aloe vera has been used as herbal medicine including burns, wound healing, and dental treatment. Acemannan stimulates dental pulp cell proliferation and differentiation in children primary teeth^[6,7]. Al-Hijazi investigated the effect of topical application of aloe vera on bone healing by histological examination and immunohistochemical evaluation of bone morphogenetic proteins 7 (BMP). BMP7 is a protein that in humans is encoded by the BMP7 gene^[8]. The authors evaluated that aloe vera could function as a bioactive molecule inducing bone formation by stimulating proliferation and differentiation of osteoblasts with high expression of BMP7.

Effect of bone generation and balance between tooth size and tooth number controlled by hyaluronan

Hyaluronan (HA, moisturizer) is able to absorb large amount of

water (HA 1g to water 6L) and can signal by binding to cell-surface receptors. During organ development and regeneration, HA has been shown to regulate cell proliferation, cell shape, and migration. Sanchez *et al*^[9] highlighted a novel role of HA in controlling proliferation, cell orientation, and migration in the developing tooth, impacting cellular decision regarding tooth size and number. HA was found by Putri *et al*^[10] on the surface of aloe vera, just below the waxy cuticle of rind, there is an area where aloe correlated bacteria live. Endophytic bacteria, Gram-positive *Streptococci* which are able to produce HA through bacterial pathway were found on the surface of *Aloe vera*, whereas *Coccobacilli*; *Streptococcus morbillorium*, Gram-negative rods are observed only in gel part. The absorption of HA in the intestine was investigated by Kimura *et al*^[11]. HA excretion into the feces, degradation in the intestine tract, absorption through the large intestine, and translocation to the blood and skin were examined. The results of the study suggested that orally administered HA is degraded to oligosaccharides by intestinal bacteria, and oligosaccharide HA is absorbed in the large intestine and is subsequently distributed throughout the tissues, including the skin.

Hyaluronan has been used in bone regeneration and is currently a popular topic, particularly in the craniofacial and dental fields. From maxilla augmentation to craniofacial bone trauma, there is a large demand for bone regenerative therapy. Serving as a cell-seeding scaffold or a carrier for bioactive components, hyaluronan-incorporated scaffolds and carriers in bone regeneration can be fabricated into either rigid or colloidal forms. Zhai *et al*^[12] reviewed the application of hyaluronan in bone regeneration. Wolf and Kumar^[13] summarize how HA-based signaling regulates cell behavior and discussed how these signals can be leveraged to create cell-instructive biomaterials. In our previous paper we discussed prophylactic role of aloe components specially, butyrogenic microbiome and bone regeneration^[14]. Gonzalez *et al*^[15] reviewed the efficacy and safety of dermal fillers, such hyaluronan and poly-L-lactic acid, used to treat cutaneous defects such as lipoatrophy. The authors discussed that despite limited available evidence, dermal fillers seem to be safe as an adjunctive treatment for cutaneous defects in patients with connective tissue disease.

CASE REPORTS: RECOVERING TO BONE MINERAL DENSITY AND REGRESSION OF MICROSCOPIC POLYANGIITIS AND LYMPHOID POLYP

Case Report 1 Regeneration of bone mineral density

A 59-years-female started to take aloe vera juice (AVJ) to health maintenance for climacteric disturbance in April, 2003. The bone mineral density (BMD) was quantitatively evaluated by digital image processing method and the BMD data (0.590 g/cm², 108%) showed that she was as well as the same year female. On continuous taking AVJ to 72-years old, the BMD data (0.570g/cm². 117%) showed the property of being younger than that the same years-female.

Case report 2: Regeneration of bone mineral density

An 83-years-male started to take AVJ after treatment of prostatic hypertrophy to health maintenance in April, 2016. His BND in femoral length was quantified by dual X-ray absorptiometry (DXA) and the DXA data (80%, 0.6689g/cm²) showed the property of being as well as the same year male. On continuous taking AVJ to 86-years old, the BMD data in femoral length (92%, 0.673g/cm²) showed the

property of younger than that the same years-male.

Case report 3: Regeneration of dermatologic microscopic polyangiitis

A ~50-years-old female being hard and strong fatigue after her job change, had heavy pain and swollen around both ankles in 2010, and coloration of the ankles changed to purple. Skin biopsy did not show exact illness. She retired from the job on 2013, and was hospitalized and diagnosed to be dermatologic microscopic polyangiitis (DMP). She took prednisolone (5mg/day) and azathiopurine (50mg/day) for 50 days on May, 2018. She started to ingest aloe vera juice (AVJ, 660ml/day) with prednisolone (4mg/day) on July, 2020, and then AVJ (1000ml/day) with Kampo medicine (Rokumigan) and prednisolone (1mg/day) on Oct, 2020. Finally she only ingested AVJ (660ml/day). Since then she had well regression for DMP.

Case report 4: Regression of mesenteric lymphadenopathy

A ~40-years-old female had loose passage and diarrhea during several months. She took the colonoscopy and lymphoid polyp was found around the large intestine on March 27, 2007 (Figure 1). She was diagnosed mesenteric lymphadenopathy (ML) and this diagnosis was supported by second opinion. The doctor told her the colectomy after three weeks. Then she took AVJ (660ml/day) with the supplement of bee pollen and bee propolis for 3 months. ML almost disappeared (Figure 2) on April 15, 2007. And the colectomy was suspended. The AVJ supplement ingestion was continued during half year, and finally she recovered from ML.

DISCUSSION IN CASE REPORTS

The long-term ingestion of aloe vera juice (AVJ) provided the properties being young and a well QOL after some health troubles. AVJ could play a role as a beneficial herbal adjuvant for a promising bone generation. Furthermore Kampo medicine with AVJ in successive ingestion may support wound healing in connective tissue disease. Supplementation of AVJ having hyaluronan and acemannan would enhance connective tissue repair via angiogenesis. Regression of mesenteric lymphadenopathy achieved with AVJ ingestion without colectomy.

SUMMARY

Angiogenesis in wound was described as an essential part of proliferation phase of the wound healing process. Acemannan, a mixture of bioactive high molecular substance, showed the activity to bone mineral regeneration and wound healing. Hyaluronan (hyaluronic acids having several molecular weight levels) was reviewed as one of dermal fillers in patients with a connective tissue disease. In case reports the successive aloe vera juice (AVJ) ingestion provided well remission to connective tissue, angiogenetic disease and bone mineral regeneration. Supplementation of AVJ suggested the enhancement of connective tissue repairmen via angiogenesis.

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REFERENCE

- Davis RH, DiDonato JJ, Hartman GM, Haas RC. Anti-inflammatory and wound healing activity of growth substance in Aloe vera *J. of the American Podiatric Medical Association* 1994; **84**: 77-81 [PMID: 8169808]
- Yagi A, Ataka S, Yu BP. Putative roles of Aloe ingredients in aging and age-related diseases: management of microbiota senoinflammatory process *J. of GHR* 2021; **10(2)**: 3460-3465 [DOI: 10.17554/j.issn.2224-3992.2021.10.1003]
- Ali E, Wajid N, Sarwar MG, Qazi AM. Oral administration of Aloe vera ameliorates wound healing through improved angiogenesis and chemotaxis in Sprague Dawley rats *Curr Pharm Biotechnol.* 2020; Oct 1 [DOI: 10.2174/1389201021999201001204345]
- Shafaie S, Andalib S, Shafaie H, Montaseri A, Tavakolizadeh M. Differential biological behavior of fibroblasts and endothelial cells under Aloe vera gel culturing *Int J Mol Cell Med.* 2020; **9(3)**: 234-245 [DOI: 10.22088/IJMCM.BUMS.9.3.234]
- Jettanacheawchankit S, Sasithanasate S, Sangvanich P, Banlunara W. Acemannan stimulates gingival fibroblast proliferation; Expressions of keratinocyte growth factor-1, vascular endothelial growth factor, and type I collagen; and wound healing *J. of Pharmacological Science* 2009; **109**: 525-531 [DOI: 10.1254/jphs.08204FP]
- Gonna S, Deraz E, Ghoname N, Kabbash A, Yagi A. Acemannan and formocresol pulpotomies in primary teeth: a comparative histopathological study *J. of GHR* 2017; **6(4)**: 2386-2391 [DOI: 10.17554/j.issn.2224-3992.2017.06.711]
- Gonna S, Ghoname N, Kabbash A, Yagi A. Efficacy of aloe vera as a pulpotomy agent in children primary teeth: clinical and radiographic studies *J. of GHR* 2019; **8(5)**: 2946-2951 [DOI: 10.17554/j.issn.2224-3992.2019.08.842]
- Al-Hijazi AY, Al-Mahammadawy AKA, Altememe E. Expression of BMP7 in bone tissue treated with aloe vera *Int Res J. of Natural Sci.* 2015; **3(2)**: 39-48
- Sanchez N, Gonzalez-Ramirez MC, Contreras EG, Ubilla A, Li J, Valencia A, Wilson A, Green JBA, Tucker AS, Gaete M. Balance between tooth size and tooth number is controlled by hyaluronan *Front. Physiol.* 2020; 24 August [DOI: 10.3389/fphys.2020.00996]
- Putri RR, Nugrahe T, Chreisty S. Extraction of hyaluronic acid from *Aloe barbadensis* (Aloe vera) *J. of Fun. Food and Nutr.* 2020; **11(2)**: 95-102 [DOI: 10.33555/jffn.v1i2.33]
- M Kimura, T Maeshima, T Kubota, H Kurihara, Y Masuda, Y Nomura Absorption of orally administered hyaluronan *J. Med Food* 2016; **19(12)**: 1172-1179 [PMID: 27982756]; [DOI: 10.1089/jmf.2016.3725]
- Zhai P, Peng X, Li B, Liu Y, Sun H, Li X. The application of hyaluronic acid in bone regeneration *Int J. of Biological Macromolecules* 2020; **151**: 1224-1239 [DOI: 10.1016/j.jbiomac.2019.10.169]
- Wolf KJ, Kumar S. Hyaluronic acid: Incorporating the bio into the material *ACS Biomater. Sci Eng.* 2019; **5(8)**: 3753-3765 [DOI: 10.1021/acsbmaterials.8101268]
- Yagi A, Hasegawa M, Ataka S. Prophylactic role of aloe components, butyrate fermented, micrnas, and hyaluronan on Alzheimer's disease, Parkinson's disease, and osteoarthritis in knee joints: case reports of aloe vera juice ingestion producing intestinal butyrogenic microbiome and bone regeneration *J. of GHR* 2021; **10(1)**: 3398-3406 [DOI: 10.17554/j.2224-3992.2020.10.983]
- Gonzalez CD, Pamatmat JJ, Heather G. Safety and efficacy of dermal fillers in patients with connective tissue disease: Review *Dermatologic Surgery* 2021; **47(3)**: 360-364 [DOI: 10.1097/DSS.0000000000002870]