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ORIGINAL ARTICLE

Aloe Vera Gel Accelerates Wound Healing in Oral Mucosa by Promoting Epithelialization and Cell Proliferation (Fibroblasts)

MADIHA RASHID[1], NEDAL IQBAL[2], ADNAN BASHIR[3], RUHINA ALI[4], SAIMA RASHEED[5], SEHRISH NAZ[6]
[1]Associate Professor of Oral Biology & Tooth Morphology, Watim Medical & Dental College Rawat Islamabad
[2]Assistant Profess & HOD of Oral Biology, Fatima Memorial Hospital/College of Medicine & Dentistry, Lahore
[3]Associate Professor of Pharmacology, Watim Medical & Dental College Rawat Islamabad
[4]Assistant Professor of Community Medicine, Watim Medical & Dental College Rawat Islamabad
[5]Associate Professor of Biochemistry, Niazi Medical College, Sargodha
[6]Assistant Professor of General Pathology, Watim Medical & Dental College Rawat Islamabad
Correspondence: Dr. Madiha Rashid, E-mail: madiha63@gmail.com Cell: 0324-4333932

ABSTRACT

Aim: To evaluate the accelerating effects of Aloe vera gel on the healing process of tongue wounds.
Study design: Experimental animal study.
Place and duration of study: Department of Anatomy, Postgraduate Medical Institute (PGMI), Lahore Pakistan from 29th April 2021 to 29th October 2021.
Methodology: Forty two albino rats were divided into one control (group A) and two experimental groups (groups B & C) with 14 rats in each group. Each group was divided into two sub groups with 7 rats each. Surgical excisional wounds were inflicted on anterior 2/3rd of dorsal surface of the tongue of each rat on day 1 of the study. The control group animals were given distilled water while animals in the experimental groups were given two different doses of Aloe vera gel daily (300 mg/kg and 500 mg/kg).
Results Histological evaluation of the wounds revealed that epithelialization and fibroblast cell proliferation were promoted in Aloe vera groups as compared with the control groups. Healing time was significantly decreased in group B and C animals as compared with group A. Aloe vera gel accelerated healing in experimental groups.
Conclusion: Aloe vera gel accelerates healing in tongue mucosa wounds in Wistar rats and it plays its role by bringing enhanced epithelialzation and fibrosis.
Keywords: Haematoxylin & Eosin (H&E), Immune Histochemical (IHC), Effect

INTRODUCTION

Oral diseases and ulcers are the common occurrences among human ailments. Amongst the causes are nutritional (vitamins and folic acid) deficiency, stress, infections and injuries culminating in pain, inability to eat and generalized debility.[1] There is a general term used for the mouth ulcers called "aphthae".[2] Generally the smaller ones (lesser than 1 cm in size) heal within 5-7 days. Large ulcers may take more than 4 weeks to heal completely.[3]

Aloe vera, a miraculous herb has been considered a medicinal plant and a natural healer for centuries. As the experimental data already available regarding its wound healing effects is not enough, further researches are required in this context[4].

Aloe vera (Aloe Barbadensis Miller) is a succulent plant with thick leaves. The gel inside the leaf is viscous with various active ingredients like sugars, polysaccharides (acemannan and polymannans), vitamins, enzymes, anthraquinones amino acids, minerals. 99% of the gel is water that soothes the wound keeps it hydrated and flushed. The significant properties of the plant due to its active ingredients are: wound healing, anti bacterial, anti viral, anti inflammatory, anti fungal, anti neoplastic and immunomodulating.[5,6]

MATERIALS AND METHODS

An experimental animal study comprising of 42 rats was designed. Rats were divided into one control (group A) and two experimental groups (groups B and C) with 14 rats in each group. Each group was sub divided A1 &A2; B1 & B2 and C1 & C2 having 7 rats each. Surgical excisional wounds were inflicted on anterior 2/3rd of dorsal surface of the tongue of each rat on day 1 of the study. The control group animals were given distilled water while animals in the experimental group (B) were given Aloe vera gel daily with the dose of 300 mg/kg and animals in the experimental group (C) were given Aloe vera gel daily with the dose of 500 mg/kg and . The drug was administered orally with insulin syringe and gastric tube. On day5 and day7pw, animals from each of control and experimental groups were sacrificed for histological evaluation of the wound. Tongue from each rat was removed and tissue specimens were preserved, processed, stained with H&E stains and examined under light microscope to analyze their wound healing status.

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Group A: Fourteen rats as control group, received 1ml distilled water orally with the help of insulin syringe and gastric tube as a single morning dose. **Group A1:** Seven rats (sacrificed on day 5) and **Group A2:** Seven rats (sacrificed on day 7).
Group B: Fourteen rats as an experimental group, received Aloe vera gel extract (300mg/kg body weight/day) dissolved in distilled water, orally with the help of insulin syringe and gastric tube, as a single morning dose. **Group B1:** Seven rats (sacrificed on day 5) and **Group B2:** Seven rats (sacrificed on day 7).
Group C: Fourteen rats as an experimental group, received Aloe vera gel extract (500mg/kg body weight/day), dissolved in distilled water, orally with the help of insulin syringe and gastric tube, as a single morning dose. **Group C1:** Seven rats (sacrificed on day 5) and **Group C2:** Seven rats (sacrificed on day 7).

Two parameters were used to evaluate the healing status of the wounded tissue i.e. fibroblast count and degree of epithelialization. The cell counting was done at high power field (HPF) i.e. with magnification of X400. Different zones of the tissue were examined to see the cellular changes in the anatomy of wounded tongue mucosa for evaluation of healing status of the tissue in experimental as well as the control groups.[7] Mean of three most cellular areas per high power field was calculated. The Abramov's scoring system (modified Greenhalgh's scoring system) was used for scoring fibroblast count and degree of epithelialization as follows.[8]
Epithelization: None = 0, Partial = 1, Complete but immature and thin = 2 and Complete and mature = 3
Fibroblasts: None to minimal fibroblasts = 0, Few fibroblasts = 1, More fibroblasts = 2 and Predominant fibroblasts = 3
The data was entered and analyzed through SPSS-25.

RESULTS

On 5th day post wounding, fibroblast count was highest in control group (A1) falling in grade 3 mostly, it was lower in experimental group B1 receiving Aloe gel with the dose of 300 mg/kg with the count falling in grade 2 and 3. On the other hand the experimental

group C1 receiving gel dose 500 mg/kg had very low fibroblast count i.e. grade 1 mostly. On 7th day post wounding, fibroblast count was highest in group A2 (grade 2 &3) and lower in group B2 (grade 1 & 2) and very significantly low (grade 1 and 0) in group C2. The difference among the groups was statistically significant. In case of fibroblast count, data analysis among sub groups (observations on day 5 compared with day 7 post wounding) showed significant difference in sub groups A1 & A2, B1 & B2 and difference was insignificant in sub groups C1 & C2 (Tables 1-2).

On 5th day post wounding, there was in complete epithelium formation in control group A1 falling in grade 1 mostly with partial and immature epithelium. It was better in experimental group B2 receiving Aloe gel with the dose of 300 mg/kg with grade 2 epithelium formation i.e., complete but thin. On the other hand the experimental group C1 receiving gel dose 500 mg/kg had very good epithelization falling in grade 3 i.e. complete and mature. On 7th day post wounding, control group A2 had incomplete and immature epithelium (grade 1 & 2) while experimental groups B2 and C2 had complete and mature epithelium. The difference among the groups was statistically significant.In case of epithelization, data analysis among sub groups (observations on day 5 compared with day7 post wounding) showed significant difference in sub groups B1 & B2. In sub groups A1 & A1 and C1 & C2 the difference was insignificant (Tables 3-4)

Table 1: Comparison of fibroblast counts in control and experimental groups on 5th day post wounding

Group	Few	More	Predominant	χ^2	P value
A1	-	1(14.3%)	6 (85.7%)	14.61	0.005
B1	-	3(42.9%)	4 (57.1%)		
C1	5(71.4)	1(14.3%)	1 (14.3%)		

Table 2: Comparison of fibroblast counts in control and experimental groups on 7th day post wounding

Group	None	Few	More	Predominant
A2	-	-	5 (71.4%)	2 (28.6%)
B2	1(14.3%)	3 (42.9%)	3 (42.9%)	-
C2	2(28.6%)	5 (71.4%)	-	-

$\chi^2$15.50, P value 0.01

Table 3: Comparison of epithelialization in control and experimental groups on 5th day post wounding

Group	Partial	Complete but immature	Complete but mature
A2	4 (57.1%)	2 (28.6%)	1 (14.3%)
B2	2 (28.6%)	5 (71.4%)	-
C2	-	1 (14.3%)	6 (85.7%)

$\chi^2$16.11, P value 0.003

Table 4: Comparison of Epithelialization in control and experimental groups on 7th day post wounding

Group	Partial	Complete but immature	Complete but mature
A2		4 (57.1%)	-
B2	-	1 (14.3%)	6 (85.7%)
C2	-	-	7 (100%)

$\chi^2$17.82, P value 0.001

DISCUSSION

Healing effects of Aloe vera gel relate to the essential components of the miraculous herb having various polysaccharides, vitamins and polypeptides etc[9]. The herb promotes the wound healing by various mechanisms likereducing the period of inflammation, enhancing cell migration for rapid epithelization, adequate moisture at the wound site and enhancing collagen synthesis. A study conducted in 1996 concludes that polypeptides found in Aloe vera gel play a major role in enhancing healing of the wounds (excisional). Glucomannan, are essential polysaccharides which activate the fibroblasts by interacting with receptors on them. The gel has a growth hormone namedgibberellin that plays a significant role in enhancing collagen synthesis by promoting fibroblast activity.[10]Other Studies show that anthraquinones in aloe vera reduce the inflammation at the wound site rustling in enhanced healing and improved reepithelization. Moreover, there is increased fibroblast count at the healing site resulting in rapid collagen synthesis and abundant ground substance.[8,9]Another study in 2018 showed that Aloe vera promotes proliferation of fibroblasts and keratinocytes and enhances cell migration resulting in rapid healing of the wounds.[11]Past studies have shown that glycoproteins from aloe vera gel promote keratinocyte proliferation and migration and hence promote re-epithlialization of the wounds.Acemannanand polysaccharides in Aloe vera gel play an important role in wound healing[12,13].

Detailed study of the previous researches helps to understand the mechanism of wound healing relating to the Aloe gel and also the role of the essential constituents (polysaccharides, acemannans and glycoproteins) of gel in enhanced epithelialization and fibrosis in experimental groups by proliferation of keratinocytes and fibroblasts at the healing cascade. Hence there was increased formation of collagen and matrix proteins by fibroblasts in experimental groups. All these events lead to rapid healing of oral mucosa. In the present study, on post wounding 7th day tissues from group B and C animals receiving two different doses of the Aloe vera gel showed a rapid fibrosis and re epithelialization which was slower in control group A. Difference among the doses was significant.

CONCLUSION

Aloe vera gel accelerates healing in tongue mucosa wounds in Wistar rats. It plays its role by bringing enhanced epithelialization, and fibrosis. Among the two remedial doses of the gel used in the experiment, the higher dose (500mg/kg) has proved to be more effective. Aloe vera gel can be used as a remedy to treat oral ulcers.

Conflict of interest: Nil

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