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Authenticity of Aloe vera and Acacia Honey on Wound and their Comparative Wound Healing Efficiency on Lacerated Wound in Rabbit

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ABSTRACT

Research study was conducted to analyze the effects of Acacia honey and Aloe vera gel on lacerated wound induced in rabbits. For this purpose, a total of 30 healthy male adult rabbits were selected and divided into 3 groups (A, B and C). Surgical wounds were induced in all rabbits with the help of sharp blunt scissor and each rabbit from all groups was pre-medicated by administering atropine sulphate @0.035mg/kg body weight through s/c route half an hour prior to surgical intervention. Animals were anesthetized by total parenteral (intramuscular) anesthesia using a mixture of ketamine (35mg/kg) and xylazine (5mg/kg). Rabbits of group A were treated with Acacia honey, applied twice daily, group B rabbits were treated with Aloe vera gel topically twice daily while group C served as control and treated with standard treatment pyodine. Wounds were properly covered with sterile bandages to reduced maximum infections and the efficacy of these treatments was evaluated in terms of their effects on healing time, wound contraction, period of epithelization, tensile strength, histopathology and wound index. Wound contraction rate was higher in both groups (A and B) as compared to the group C (Control group) and increased wound contraction were observed on day 10 and was completed on 20 days. In case of epithelization, decreased period of epithelization was observed in group A and B as compared to the C group (control group). Healing time was lower and statistically significant as compared to the control group (group C). Group B was significant as compared to the group C. Wound index values were reduced in both groups A and B and group C was higher wound index values on day 15 and value was 1.78 as compared to the other treatments groups. The values of group A and B was non significant at days 20 as compared to the control group. Group C was higher period of epithelization as compared to the other two groups A and B.

Key words: *Rabbit; Wounds; Aloe vera; Honey; Healing.*

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INTRODUCTION

A wound can be defined as skin mucosa stability disturbance with thermal or physical injury. In the term of surgery the wound indicates continuously aexplanation to continuity or interruption of the soft portion of body through outside trauma, but in the medicinal language it is defined as injury to any fragment of particularly body affected through a cause resulting after external trauma, however the surface of the body is injured or not damaged (Buffoni et al., 1993). Manhood are able to cover wounds through different range of resources from that time when the first written histories. From the time when 2000 BCE plasters made of mud, milk and plants were useful to cure wounds and injuries. Since 1550 to 1650 BCE papyruses of the Egyptian provide particular facts of the wound and apply honey plant fibers, and plasters of animal fat after that formerly bandage the wound area, (Majno, 1975).

The wound healing is similarly termed as a dynamically biological procedure influenced and started through several sorts of factors. The healing procedure of the wound are subdivided to the following steps: hemostasis (bloodcloting) inflammation, proliferation (involving of granulation, wound contraction and Re-epithelization) and at last remodeling of the wound (Diegelmann & Evans, 2004). After completing the stage (haemostasis) bacteria and debris are removing through the inflammatory phase. After that blood vessel invasion, re-epithelium and regeneration of the connective tissue, along with contraction wound, in phase of proliferation take place. At the final phase of the remodeling collagen is re-arranged along with rigidity lines and unnecessary materials are removed through the process of apoptosis (Stadelmann et al., 1998). Rabbits are significantly better as compared to the more commonly used animals in the laboratory e.g. rats and mice, but their handling is easy and of low cost (Ramos et al., 2008).

Rabbits are mostly used like pet animals on the other hand also for fur and meat production. Rabbit skin is extra flexible and compared with the human skin, along with an abundant area of skin tissue comparative toward body size. In rabbits, process of the wound healing includes extent contraction wound, prior to the starting of cell immigration and at last remodelling take place (Abramov et al., 2007).

The plant, officially known as Aloe vera (L.) burm,but more generally known as Aloe barbadensis Miller, belongs to the genus Aloe, which encompasses over 500 different aloe species. It also belongs to the Asphodelaceae family, which contains garlic, onion, and asparagus, and is connected to the Liliaceae family (Amar et al., 2002; & Hashemi et al., 2015).

According to recent genetic studies, the plant is native to the Arabian Peninsula1, but it is commercially grown in India, South Africa, the United States, Mexico, Venezuela, and Haiti. Aloe is a succulent with the ability to store water in its leaves, allowing it to thrive in both desert and semiarid climates. Despite the fact that it is a succulent, the plant is It's not a cactus, and it needs at least 100 cm of water every year to thrive. Water availability has a considerable impact on the quality of the final extract. In its full stage, which takes 4-6 years, the plant develops to a height of 60-100 cm and can live for more than 15 years. Every 6-8 weeks, remove 3-4 leaves from each plant to collect the leaves. The active ingredients are found in the leaves, which contain three major structural components: the clear inner gel, also known as mucilage tissue or pulp, which is a soft, slippery tissue made up of 98% water; the middle latex, a bitter yellow sap; and the leaf's outside thick cuticle or rind.

Aloe Vera gel contains many vitamins, amino acids, minerals, natural

sugars, enzymes as well as substances which are anti-inflammatory and anti-microbial. More over Aloe Verais used as anti-bacterial, anti-septic and it is excellent for tissue restoration. Also normally used for burns, slight cuts, vaginal yeast infections and skin cancer management. Eyes washing with Aloe Veraoffers ultra violet rays protection. More over provided skin protection from wrinkles (kumar et al., 2010).

All health care providers, both in animals and people, are concerned about wound treatment. Antibiotics are currently being avoided by the general public due to antibiotic resistance. Many commonly available, affordable, naturally occurring compounds have been used in wound treatment during the last few decades, including aloe vera and honey. Aloe vera thrives in a wide range of climates, and the gel can be manufactured locally and used in the home to assist wound healing at a minimal cost. Honey is inexpensive, easy to use, and helpful for wound healing (Tanaka et al., 2016).

Honey had been known antimicrobial activity because of acidic pH, low water activity as well as generating hydrogen peroxide (Mundo et al., 2004; & Barrientos et al., 2008). Because of honey high osmolarity, it draws the fluids into the wound resulting in the formation of viscous solution that acts as a defensive barrier against the infections (Lusby et al., 2002; & Perkins, 2016).

Large wounds are technically challenging to treat, and various attempts have been made to improve wound healing. Aloe vera has been demonstrated to have some wound-healing benefits, but the mechanism by which it works at different phases of the healing process is unknown. In sensitive people, aloe vera can produce redness, burning, stinging, and even generalised dermatitis. Anthraquinones, such as aloin and barbaloin, are the most common cause of allergic responses. It is recommended that you test a small area first for allergic responses. It can be used if there are no allergic responses. Oral aloe is not suggested during pregnancy because it may stimulate uterine contractions, and it may induce gastrointestinal upset in the nursing infant in breastfeeding moms (Boudreau & Beland, 2006; & Syyed et al., 2015).

MATERIALS AND METHODS

Experimental animals

30 locally bred, clinically healthy male adult rabbits, weighing between 2 – 2.5 kg were purchased from local market of D.I. Khan. Animals were kept in Rabbit Research House, PARC, Arid Zone Research Centre, D.I. Khan. Animals were randomly divided into 3 groups (A, B and C).

Clinical examination

All animals were kept on uniform feeding regimen and manage mental conditions in the PARC, AZRC, Rabbit Research House, DI Khan. Clinical and laboratory examination was carried out of each animal and animals showing any signs of disease were replaced with healthy ones. An acclimatization period of at least two weeks was provided to the rabbits during which 2 doses of ivermectin (@400microgram/kg; S/C) were provided to each rabbit. Moreover, to avoid the chances of pasturellosis, amoxicillin (@15mg/kg S/C) was injected to all the rabbits for three consecutive days.

Premedication and anesthesia

Each rabbit from all groups was pre-medicated by administering atropine sulphate @0.035mg/kg body weight through s/c route half an hour prior to surgical intervention. Animals were anesthetized by total parenteral (intramuscular) anesthesia using a mixture of ketamine (35mg/kg) and xylazine (5mg/kg) (Razaini et al., 2004).

Operative site preparation and Wound creation

The skin and hair follicles are the prime medium for the bacteria, which in essence cannot be sterilized completely. However, bacterial flora on the skin surface are responsible for the wound associated

infection in animals but it can be reduced transiently to a relatively safe level for surgery by removal of hair and mechanical scrubbing, using some germicidal solution. Surgical site and liberal surrounding area was meticulously period in order to remove as many bacteria as possible without harming skin which might interfere with wound healing. For removal of hairs firstly antiseptic solution was applied to the operative site and hairs were removed with the help of sharp scissor and razors. Wounds were created on thoracolumbar region in rabbits for testing the effect of Aloe vera gel and Accasia Honey on surgical wounds.

Figure A: Lacerated wounds induced by sharp blunt scissor in rabbit

Treatment protocols:

Rabbits of group A were treated topically with commercially available Acacia honey twice a day. Group B were treated topically with Aloe vera gel twice a day. After applying the treatments, the wound area was covered with sterilized cotton bandages to protect the wounds from environment contamination. Rabbits of group C served as control group and were treated with pyodine.

Evaluation criteria

Wound contraction rate %:

Wound contraction was expressed as a reduction in percentage of the original wound size. Measurement of the dimensions of wound was carried out with the help of Vernier caliper 34 on day 5, 10, 15, 20 and was compared with the area of respective wound on day zero. The percent contraction was then calculated using the following formula (Ghosh et al., 2011).

$$\text{Contraction \%} = 100 - \frac{\text{(Area of wound on that day)}}{\text{Area of wound at day 0}} \times 100$$

Tensile strength:

Tensile strength of healed wound tissue of different treatment groups were measured by using a tensiometer. After complete healing, animals were slaughtered (six rats in each group). Dorsal skin was excised at the deep fascia and put immediately in normal saline to prevent drying. Then, a narrow strip (8 cm in length and 1 cm in width) was attached to tensiometer holders. The tissue stress (maximum force tensile leading to skin rupture) was evaluated.

Healing time:

The time between wound creation and the day that each wound healed were evaluated and compared with other treatment groups.

RESULTS AND DISCUSSION

Wound contraction rate %:

In case of wound contraction an increased trend was observed in all the groups A, B and C. Group A was significant at days 5, 10 and 15 as compared to the group C. higher wound contraction rate was observed at day 10. Wound contraction rate significantly different in group B as compared to the group C at days 5, 10 and 15. Wound contraction rate was higher in both groups (A and B) as compared to the group C (Control group). Increased wound contraction was observed on day 10. Wound contraction of groups A and B was completed at day 20. Iftekhar et al. (2010) observed that the both Acacia honey and Aloe vera gel produced a significant increase in wound contraction, when compared to the control group. Ali et al. (2014) also observed that the honey promoted wound contraction. The similar findings have been observed by various early researchers in the world (Ghaderi et al., 2010).

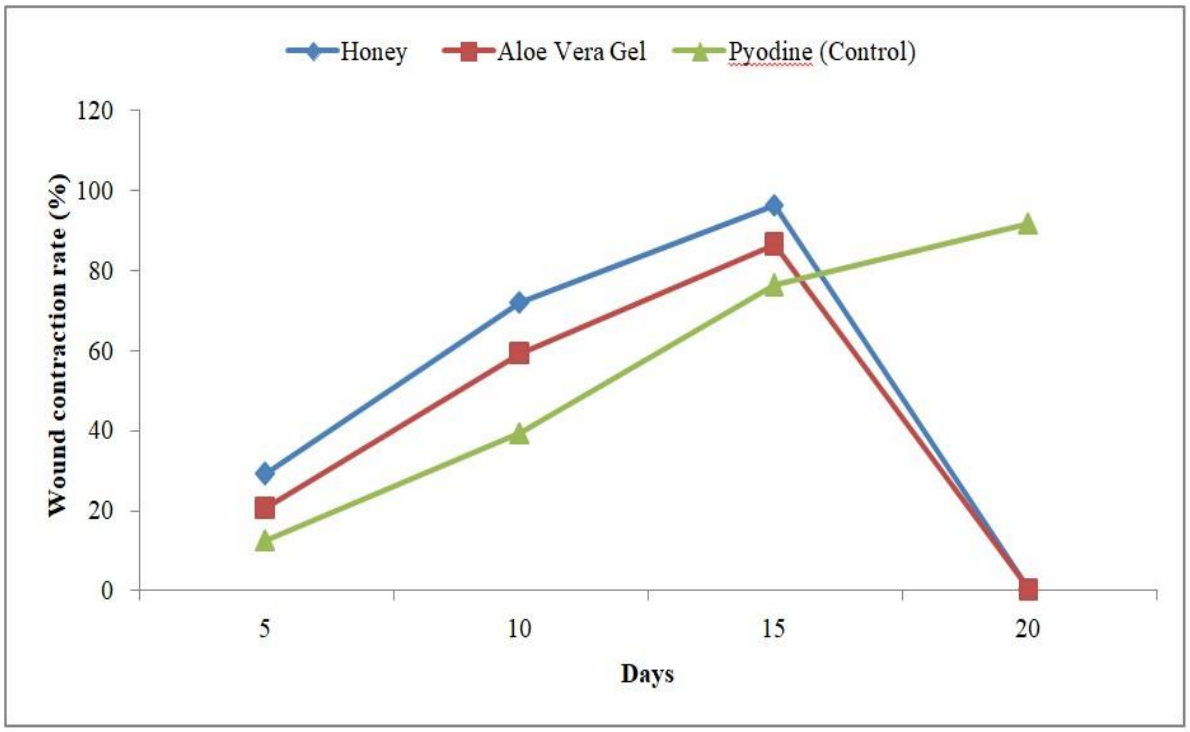

Fig: 1 Graphical comparison of Acacia honey, *Aloe vera* gel and pyodine on wound contraction rate (%)

Tensile Strength:

Group A was significant and higher tensile strength as compared to the group C (Control group). Group B was also significant and higher value of tensile strength as compared to group C. An increased tensile strength was observed in the honey treated group (group A) and significant as compared to the control group. Group B was higher value of tensile strength and significant than the control group. Kundu et al. (2005) reported that honey treated group had significantly higher mean tensile strength than the other groups. Ali et al. (2011) demonstrated thathoney accelerate the wound healing as well as tensile strength.

Healing time:

In case of healing time, group A was lower and statistically significant as compared to the group C. An increased healing time was observed in group C

(Control Group). Healing time of group B was lower and significantly different as compared to the group C.

Healing time was lower and statistically significant as compared to the control group (group C). Group B was significant as compared to the group C. Group A healed faster as compared to the other groups. Nisbet et al. (2010) reported that the honey treated groups healed much faster than the control group. Iftekhar et al. (2010) observed that the wounds treated with acacia honey healed faster than the Aloe vera gel and control group. Okeniyi et al. (2005) demonstrated that honey treated wounds healed quicker.

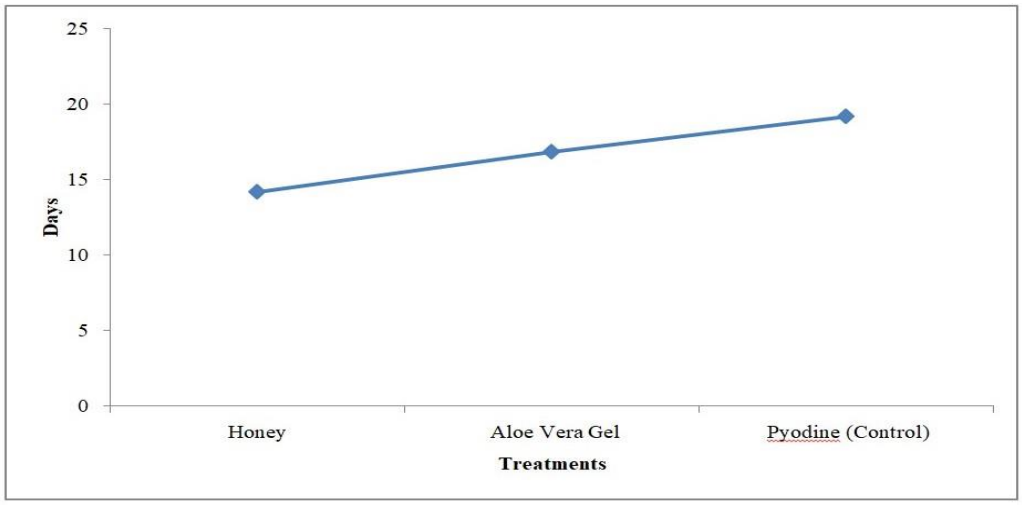

Fig: 2 Graphical comparison of Acacia honey and *Aloe vera* gel and pyodine on healing time

Period of Epithelization:

In group a minimum period of epithelization was observed and it was significant against group C (Control group). Period of epithelization in group B was also significantly different as compared to the group C. Group C was higher period of epithelization as compared to the other two groups A and B. In case of epithelization, decreased period of epithelization was observed in group A as compared to the control group (group C). Group B was also lower epithelization as compared to the control group. Iftekhar et al. (2010) reported that topical treatments of honey and Aloe vera gel produced a significant reduction in the period of epithelization.

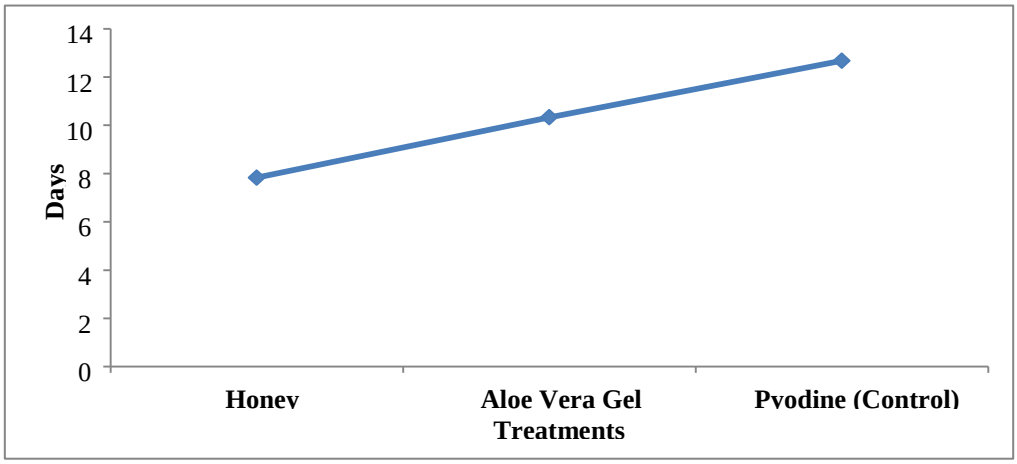

Fig: 3 Graphical comparison of Acacia honey, *Aloe vera* gel and pyodine on period of epithelization

Wound index:

In case of wound index, group A (Honey) was significant at days 5, 10 and 15 as compared to the group C (Control Group). While at day 20 the group A was non significant as compared to the group C (Control Group). Group B (gel) was also significant at days 5, 10 and 15 as compared to the group C (Control Group). The mean values of group C were higher at days 5, 10 and 15 as compared to the groups A and B. Wound index of all three groups (Honey, gel & control group) showed a decreasing trend throughout the study period. While at day 20 Group A & B were non significant. Wound index values were reduced in both groups A and B and group C was higher wound index values on day 15 and value was 1.78 as compared to the other treatments groups. The values of group A and B was non significant at days 20 as compared to the control group.

The results of present study are in line with Kundu et al. (2005) who observed thatgroup I (control) had significantly higher mean values 2.33 on day 14, respectively. Reductions in wound index values were also recorded in both treatment groups compared to the control group. Wound index values for (treatment) groups II and III were not statistically significant on day 14.

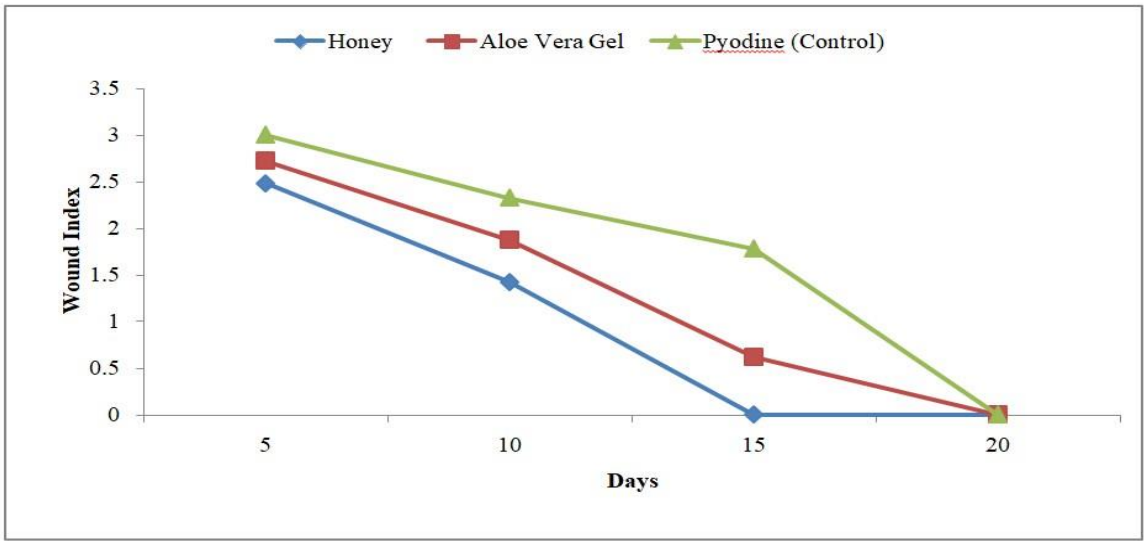

Fig: 4 Graphical comparison of Acacia honey, *Aloe vera* gel and pyodine on wound index

Histopathology:

Honey treated group showed third level of epithelization. Epithelization was seen in honey treated group. Wounds of all treatments were fully epithelized at day 20. Abundant macrophage infiltration was also seen in honey treated animals. Low macrophagic infiltration was seen in control group. Dermis of honey treated animals showed abundant collagen level and mild fibrosis. While dermis of pyodine treated animals showed mild collagen level and abundant fibrosis.

Figure B: Lacerated wound after Acacia honey and *Aloe vera* application at day 10

Figure C: Lacerated wound after Acacia honey and *Aloe vera* application at day 20

Aloe vera gel has been shown to protect the skin from radiation damage. The exact role is unknown, however after applying aloe vera gel to the skin, an antioxidant protein called metallothionein is produced in the skin, which scavenges hydroxyl radicals and prevents the skin's superoxide dismutase and glutathione peroxidase from being suppressed. It inhibits UV-induced suppression of delayed type hypersensitivity by reducing the generation and release of immunosuppressive cytokines produced from skin keratinocytes, such as interleukin-10 (IL-10). Our findings are in line with the previous researchers who had reported the similar conclusion about wound healing (Roberts & Travis, 1995; Sato et al., 1990; & Byeon et al., 1988). Our findings show that aloe vera products are safe to use on the skin. In the studies that were included, no withdrawal or significant adverse reactions were documented. Irritation, itching, discomfort, and little brief pain were the only symptoms described. These events, on the other hand, were common indications and symptoms of burns, and they occurred in both the aloe and control groups. Contamination with anthraquinone was an important consideration for the safety of topical fresh aloe vera. As documented in prior investigations, it was a possible source of irritation (WHO, 1999; Hunter, Frumkin, 1991; & Bradshaw, 1996).

CONCLUSION

The present study revealed that wounds treated with honey healed quickly as compared to the other treatments. The acidic pH of honey and its hyper tonicity are considered to be the main factors in accelerating the wound healing. Honey may enhance wound healing by accelerating glycolytic enzyme activity and supplying sufficient energy for cellular repair. It also stimulates the growth of granulation tissue and epithelial tissue so that healing is hastened. Wound contraction rate, tensile strength was higher in higher in honey treated group. Increased period of epithelization and wound index values was observed in Aloe vera gel treated and control group. Moreover, it creates a non adherent interface between the wound and the dressing so that dressings may be easily removed without pain or damage to newly re grown tissue. Honey can be considered as a low cost, easily available and potent topical agent in treatment of wounds.

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