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THERAPEUTIC HOTLINE

Topical effectiveness of kiwifruit versus fibrinolysin ointment on removal of necrotic tissue of full-thickness burns in male rats

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ABSTRACT: Formation of necrotic tissues is a major issue affecting treatment of full-thickness burns. This study was designed to compare topical effectiveness of applying kiwifruit versus fibrinolysin on removal of necrotic tissue of burns. Ten adult male Wistar rats were randomly assigned to three groups. For group 1, the right-side wounds were treated with kiwifruit and the other side with fibrinolysin. For group 2, the wounds on the right side were treated with kiwifruit or fibrinolysin, and the left sides were kept as control group 2. All wounds in group 3 were considered as control group 1. The control wounds were left to heal naturally. In each group and for each wound, the time of debridement were noted. The results indicated that for the wounds where kiwifruit was applied, the average time for removal of dead tissue was 5.7 days, which is significantly shorter than the average 18.5 days it took for treatment with fibrinolysin ($p = 0.02$). However, there were no significant differences between control wounds 1 and 2. Findings of the present study can open new horizons and provide a new treatment modality for patients with deep burns.

KEYWORDS: fibrinolysin, full-thickness burn, kiwifruit

Introduction

Debridement is the process of removing dead tissue from wounds, which has a long history in wound care and is a vital part of it. This process helps profoundly in the faster recovery of burning wounds (1). Surgical, mechanical, autolytic, biological, and enzymatic are the most direct and rapid method for removal of necrotic tissues (2). Enzymatic debridement is the application of exogenous enzymes to the wound bed in order to degrade necrotic tissue without harming viable, granulation tissue (3).

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Table 1. Frequency distribution of samples and number of wounds according groups

Group	Number of rat	Number of wounds	Right side	Left side
1	4	8	Kiwifruit	Fibrinolysin
2	2	4	Kiwifruit	Control wounds 2
	2	4	Fibrinolysin	Control wounds 2
3	2	4	Control wounds 1	Control wounds 1

Kiwifruit contains a large amount of a protease enzyme (actinidin) that was first discovered by Arcus (4). So far, a considerable portion of structural and functional characteristics of actinidin has been revealed by researchers (5,6). The aim of the present study was to compare the topical effectiveness of kiwifruits versus fibrinolysin (Elase, Pfizer, France) ointment on removal of necrotic tissue of full-thickness burns.

Materials and methods

For the present experimental study, 10 adult male Wistar rat, with ages between 5 and 7 weeks and weights between 250 and 300 g, were selected. And after burning wounds were induced, they were randomly assigned into three groups. For ethical issues and to decrease the number of rats that were used in the current study, the present authors made two identical wounds in each rat, so 10 rats with 20 burn wounds were studied instead of 20 rats. The reason for grouping rats in this manner was to use both paired controls and unpaired controls in order to achieve highest power over the sample size that the present authors used. All ethical manners were considered and applied throughout the research while working with the animals.

Burn induction

In order to form full-thickness burn wounds, a round-edge plate with a 3-cm diameter was completely filled with 100°C water, and while in complete state of anesthesia, both sides of the rat were put in contact with water at the open top of the plate, in order, for 10 seconds. Afterward, in order to prevent hypovolemic shock, 5 mL of normal saline was injected into the peritoneum.

After 24 hours, the burn wounds were examined macroscopically by the research assistant, and with respect to clinical signs of full-thickness wounds (i.e., superficial white color, negative blanching), all subjects' burn wounds were confirmed to be full-thickness. Then each individual was kept in a separate cage and provided with equal and sufficient special food.

Method for using kiwifruit. After peeling the kiwifruits, pieces were cut from the fleshy part, each 1 cm thick and 3 cm wide to fully cover each wound.

Method for treatment of burn. After 24 hours since burning induction and formation of leather-like necrotic tissue, first, all wounds were washed with physiological solution by the attending staff responsible for wound dressing. Next, for the first group (four rats), the wounds on the each side of the same rat was symmetrically treated either with kiwi or fibrinolysin (Elase) to limit experimental variations; for the second group (four rats), the right-side wounds of two rats dressed with kiwi, and in other two rats the right-side wounds were dressed with fibrinolysin and the left-side wounds left without treatment agent (control wounds 2); and finally for the third group (two rats), all wounds (right and left) were considered as control (control wounds 1). The same kiwi and fibrinolysin treatments were applied in groups 1 and 2 (Table 1). As for the control groups, the wounds were cleansed with physiological solution similar to others; however, no other solution or substance was placed on them; they were only covered by gauze, held in place with surgical tape (Tajhizgaran Behdasht Novin, Tehran, Iran).

Every day, after removing the wound dressing and after washing with physiological solution, all the wounds were studied for debridement process. Then, the wounds were dressed again following the same procedure previously mentioned, until debridement of all necrotic tissues was complete. After removal of necrotic tissue from each wound, treatment was continued in the same manner for both control and experimental groups, until granular tissue developed.

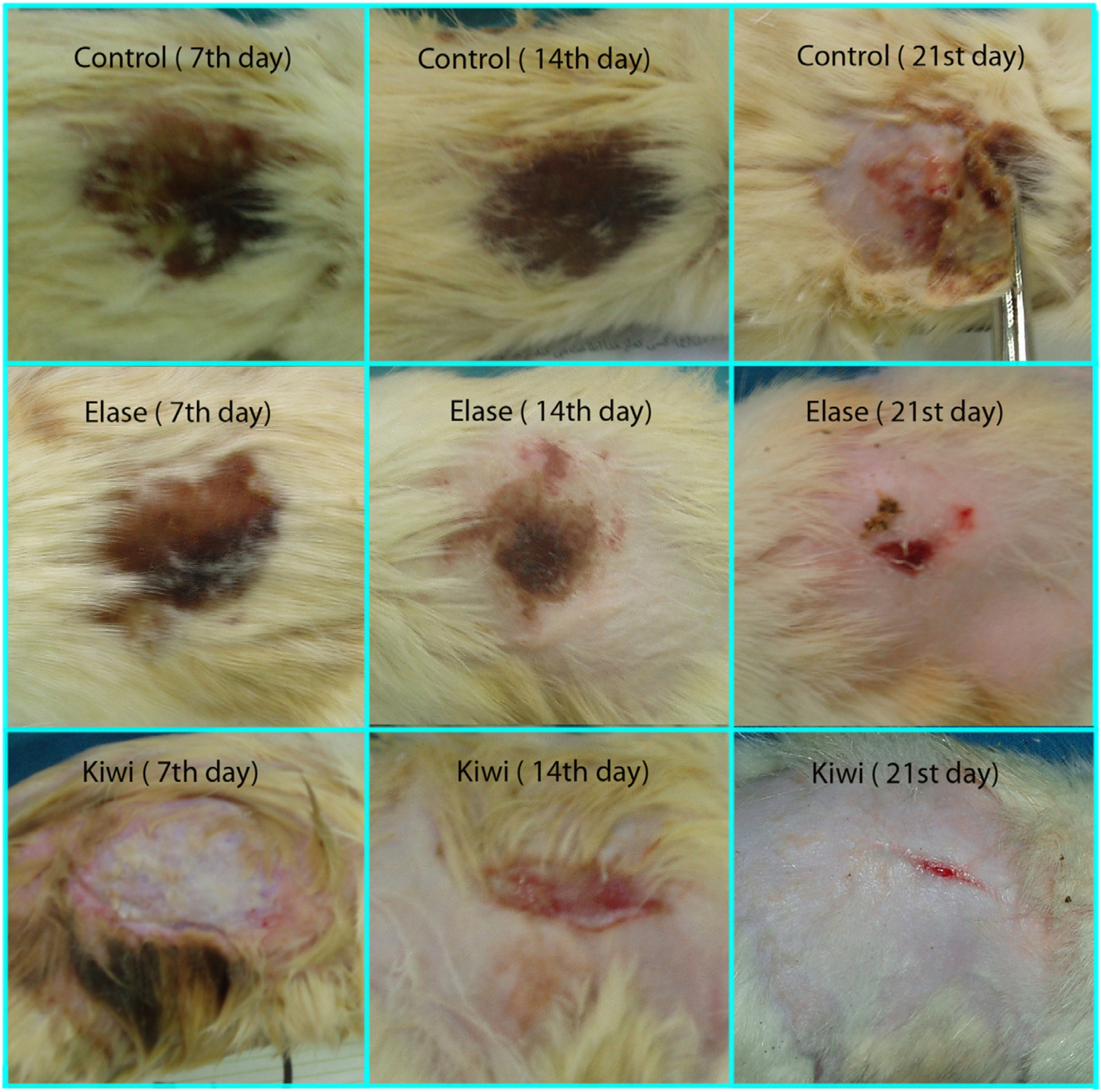

FIG. 1. Comparison wounds on Days 7, 14, and 21 in the three groups.

Method for evaluation of wounds

Clinical evaluation of complete spontaneous removal of necrotic tissue was performed by a research assistant (an experienced physician from the burn unit) in a single-blind manner (the physician had no knowledge of how the samples were divided and of the types of wound dressing).

Method for data analysis

After collection of data, analysis was performed by using the software Statistical Package for the Social Sciences (SPSS, ver. 14; SPSS Inc., Chicago, IL, USA) and nonparametric statistic test.

Results

The findings of Mann–Whitney test showed there was statistically significant differences between the kiwifruit (5.7 days) and fibrinolysin (18.5 days) groups wounds regarding spontaneous debridement time ($p = 0.02$) (FIG. 1). Comparison averages of debridement time between fibrinolysin and

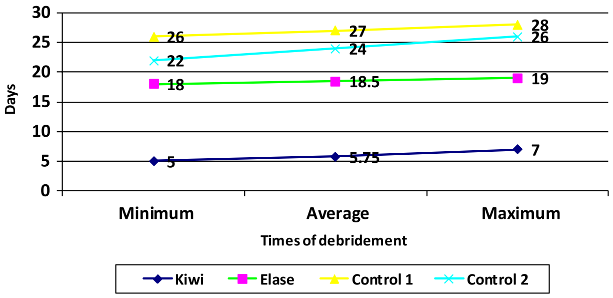

FIG. 2. Comparison of minimum, average, and maximum debridement time in study groups.

control groups wounds (p = 0.02) and kiwifruit wounds and the control groups showed meaningful difference (p = 0.02) (FIG. 2). However, there was no significant differences (p = 0.88) on debridement averages time between control groups 1 and 2.

Discussion

Clinical experience and existing research strongly support debridement as a necessary component of wound bed preparation when slough or eschar is present (3). Currently in Iran, the fibrinolysin ointment, being the most common nonsurgical way for debridement of necrotic tissues in the pharmaceutical market that is both expensive and rare, and is not produced within the country. The major goal of the present research was to study the efficacy of kiwifruit in debridement of full-thickness burn wounds and to compare this with fibrinolysin ointment. The results indicate that kiwifruit is capable of debridement in an average time significantly shorter than that of fibrinolysin.

In previous studies, some fruits and plants were used for treatment and debridement of burn wounds (2,7). A research was conducted by Hebda et al. showed that papayin/urea can be an effective wound-debriding agent, compared with fibrinolysin and collagenase, which had little effect (8). Sugiyama et al. showed that the digestive nature of protease from kiwifruit breaks cross-links between collagen domains turning them to smaller subunits, and weakens the connective tissues (9).

Nanney et al. showed that vibriolysin, extracted from the marine microorganism Vibrio proteolyticus, as a proteolytic enzyme, significantly causes more hydrolysis of eschar tissue in partial-thickness burns of porcine skin compared with the control group (10). Similar results were found in a similar study performed by Durham et al. about effects of vibriolysin on debriding and healing full-thickness burn wounds. The findings from this experimental research indicated that protease hydrolyses the protein composition of eschar (11). Rowan et al.'s findings demonstrated that compared with Travase ointment, the two cysteine protease enzymes derived from pineapple stem had better debriding effects (33 and 50% vs. 17%) (12).

A research by Mohajeri et al. has shown that second-degree burn wounds dressed with kiwifruits demonstrated significant reduction in size compared with those dressed with silver sulfadiazine cream, and all wounds were healed on the 21st day (13). In a similar study, Hafezi et al. demonstrated that eschar sloughing in kiwi and control group were 20 and 30–42 days, respectively. Subsequently, kiwifruit significantly accelerated eschar sloughing compared with control group (14).

Conclusion

According to the findings achieved from the present study, usage of kiwifruit can be an effective yet affordable and accessible agent in debridement of dead tissue in burn wounds, opening a new outlook toward enzymatic debridement and treatment of burn patients.

Because of its basic experimental nature, the findings of the present research can be used as a step toward future studies on humans, which in turn, assuming satisfactory results, can decrease number of deaths and cost of treatment, and help shorten recovery and hospitalization times. Furthermore, results from the present research can be used in pharmaceutics and many other scientific and industrial fields such as the food industry. Application of proteolytic enzymes is very diverse, and they can be used for all wounds that involve necrotic tissues and require debridement, such as pressure sores, diabetic sores, and other chronic wounds. Thus, further research in this area is highly recommended.

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