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DOES *LYCOPERSCON ESCULENTUM* (TOMATO) ACCELERATE OR RETARD WOUND HEALING IN WISTAR RATS?

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ABSTRACT

The study aimed at determining the effects of *Lycoperscon esculentum* on the wound healing processes of wistar rats. Excisional wounds were inflicted on the upper dorsolateral trunk of 20 adult male wistar rats. The wounds were dressed every three days (experimental with methanol extract of *Lycoperscon esculentum* and control with saline). Wound dimensions along two perpendicular axes were taken prior to dressings for the purpose of estimation of wound contraction rates. Granulation tissues were excised from five animals in each group and scar tissues obtained from the remaining animals. Fibroplasia and angiogenesis were evaluated histologically. Matched wound contraction rates were higher in the experimental group. Duration of healing was shorter in the experimental group (19.80 ± 1.64 vs 28.80 ± 4.55 days). Fibroblast counts of granulation tissue were 35.20 ± 17.53 (experimental) and 24.00 ± 8.00; with respective angiogenesis counts of 12.60 ± 8.32 and 15.60 ± 5.77. Respective values for fibroblast and angiogenesis of the scar tissues in experimental and control groups were 18.40 ± 3.7 vs 20.80 ± 5.21; and 14.20 ± 1.92 vs 13.20 ± 1.64). Histological sections of the granulation and scar tissues revealed abundance of collagen and paucity of macrophages in the experimental group. *Lycoperscon esculentum* promotes wound healing via bactericidal activity, rapid initiation and acceleration of wound contraction, increased fibroblast production and collagen synthesis.

Key words: Wound healing, Lycoperscon esculentum, Wound contraction, fibroplasia, angiogenesis.

INTRODUCTION

Natural chemicals such as butanol extract of *Argyreia speciose* and snakehead fish extract and have been used experimentally to promote wound healing (Jaiswal et al., 2011, Khan et al., 2014). Clinically, recombinant human granulocyte-macrophage colony stimulating factor (rhGM-CSF) and mixture of fibrin glue with rat bone marrow stem cells are also used to enhance healing in refractory chronic skin ulcers (Mendel, 2002; Huang et al., 2014; Yang et al., 2014).

Novel as these approaches are, they may not be affordable by and accessible to majority of Nigerians. A significant percentage of Nigerian population (60.9-69 %) is at or below the poverty line (National Bureau of Statistics, 2012). Thus it becomes pertinent to find alternatives, which are not only affordable and accessible but also efficacious.

Tomato (*Lycoperscon esculentum*) has diverse health and medicinal applications. Useful secondary metabolites of tomato include phenolic compounds, phytoalexins, lycopenes, protease inhibitors, carotinoids and glycoalkaloids (Taveirat et al., 2010). These compounds exhibit antibacterial (Mendel, 2004), antifungal and antiviral properties amongst others. We sought to investigate the role of *L. esculentum* in the management of wound.

MATERIALS AND METHOD

Twenty adult male wistar rats with a weight range of 150 to 220 g were utilized for the experiment. They were procured from the Animal House of the College of Medicine, University of Ibadan. The animals were fed with standard rat pellets and water ad libitum.

They were housed in well ventilated cages placed in well lit room with good air flow. This period of acclimatization lasted two weeks. The animals were handled in accordance with guidelines of the University of Ibadan Ethical Committee on Experimental Animals. Thereafter, they were randomly allotted into two equal groups namely, control and experimental.

The Ibadan Forest Herbarium did identification and authentication of the Lycoperscon esculentum plant as L. esculentum of the Solanaceae family. The leaves were subsequently dried and used to prepare the methanolic extract. Using the excisional wound model, a 2cm by 2cm wound was created on the dorsolateral aspect of the thoracic wall under aseptic condition; achieving prior sedation with parenteral diazepam (2mg/kg) and ketamine hydrochloride at a dose of 120mg/Kg body weight. The hair over the wound site was initially removed with an electric shaver. The animals in the control group had their wounds dressed with saline soaked gauze while those of the experimental group were dressed with gauze impregnated with the methanolic extract of *l. esculentum.* Both groups had four cycles of wound dressing at an interval of three days. Prior to change of dressing in each group, the dimensions of the wounds were measured along two perpendicular plane for the purpose of calculating the degrees of wound contraction in percentages. At the last wound dressing (D_9), granulation tissues from five randomly selected rats of each group were excised. Light microscopy slides using Hematoxyline and Eosine dye were prepared from the harvested granulation tissue for the purpose of fibroplasia and angiogenesis estimation. Fibroplasia was estimated by fibroblast count and the number of blood vessels was used to determine the degree of angiogenesis. The wounds of the remaining ten rats were allowed to heal. Thereafter, the scars were excised for histological examinations (fibroplasia and angiogenesis). The last scar was excised on Day 37. The numerical aspects of the results were analyzed with Statistical Package for the Social Sciences (SPSS) version 20 and expressed as percentages, means plus standard deviation of means (SD). The student t- test was used for inter group comparison and level of significance was set at $p<0.05$.

RESULTS

Although square shaped wounds were inflicted in all the animals, subsequent observed wound shapes varied from oval to round. The gradual reduction in wound size in both groups did not follow any specific order. The wounds of the experimental group were dark brown while those of the control were varied degree of redness. The resultant scars in both groups were observed to be fine and linear. At each change of wound dressings, the animals in the experimental group exhibited greater wound contraction rates than the control animals (Figure 1). The mean group interval values of wound contraction rate were lower in the control group (Table 1). A plot of the degree of wound contraction against duration of healing revealed a more linear with higher gradient graph in the experimental group than that of the control group (Figure 1). Eighty percent wound contraction rate was achieved on Day 9 in the experimental group as opposed to its being achieved on Day12 in the control group. The wound contraction rate peaked 3 days earlier in the experimental group (D15 vs D24) (Figure1). The parameters that were used to assess healing include the degrees of fibroplasia and angiogenesis; and durations of healing (Table 2). The mean duration of healing was significantly lower in the experimental group (19.80 ±1.64 vs 28.80 ± 4.55) [p= 0.003]. The levels of abundance of fibroblasts, collagen bundles and macrophages are depicted in the histological sections of granulation and scar tissues of both groups (Figures 2).

Table 1: Comparison of mean wound contraction between the two groups (%)

Group	D_0	D_3	D_6	D_9	D_{12}	D_{15}	D_{18}	D_{21}	D_{24}
Control	0	1.97	25.72	65.86	83.76	86.98	91.66	93.90	95.20
Experimental	0	23.02	48.59	81.86	91.12	95.93			

Table 2: Indices of healing

Parameter	Control (N=5)	Experimental (N=5)	p-value (0.05)
Duration of Healing (days)	28.80 ± 4.55	19.80 ± 1.64	0.003
Granulation tissue for: (a) Fibroblast count	24.00 ± 8.00	35.20 ± 17.53	0.23
(b) Angiogenesis	15.60 ± 5.77	12.60 ± 8.32	0.52
Healed scar for:			
(a) Fibroblast	20.80 ± 5.21	18.40 ± 3.57	0.42
(b) Angiogenesis	13.20 ± 1.64	14.20 ± 1.92	0.40

This table shows the parameters that were used to access wound healing

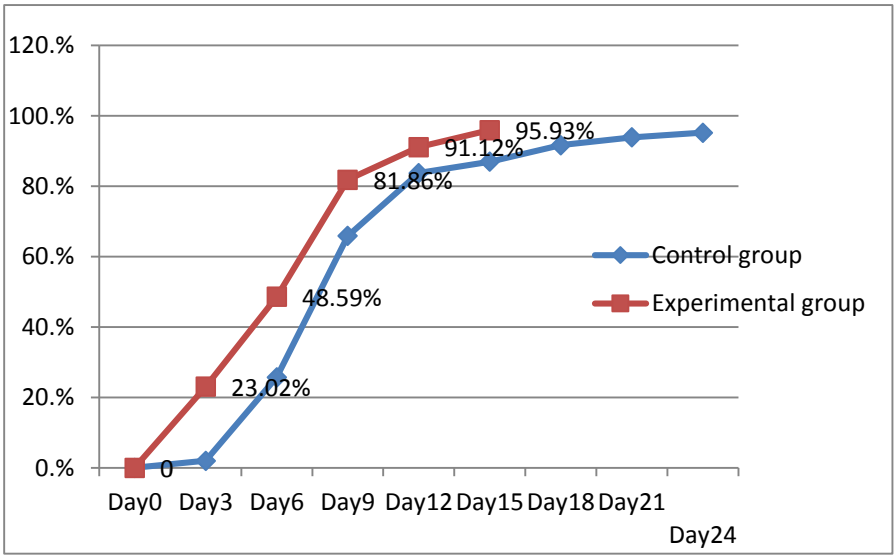

Figure 1: **Graphic representations of wound contraction rates in the two groups**: There was a lag period of about three days in the contraction rate of the control group, while the experimental group exhibited a linear take off. The percentages on the graphs indicate the contraction rates at specific comparable period.

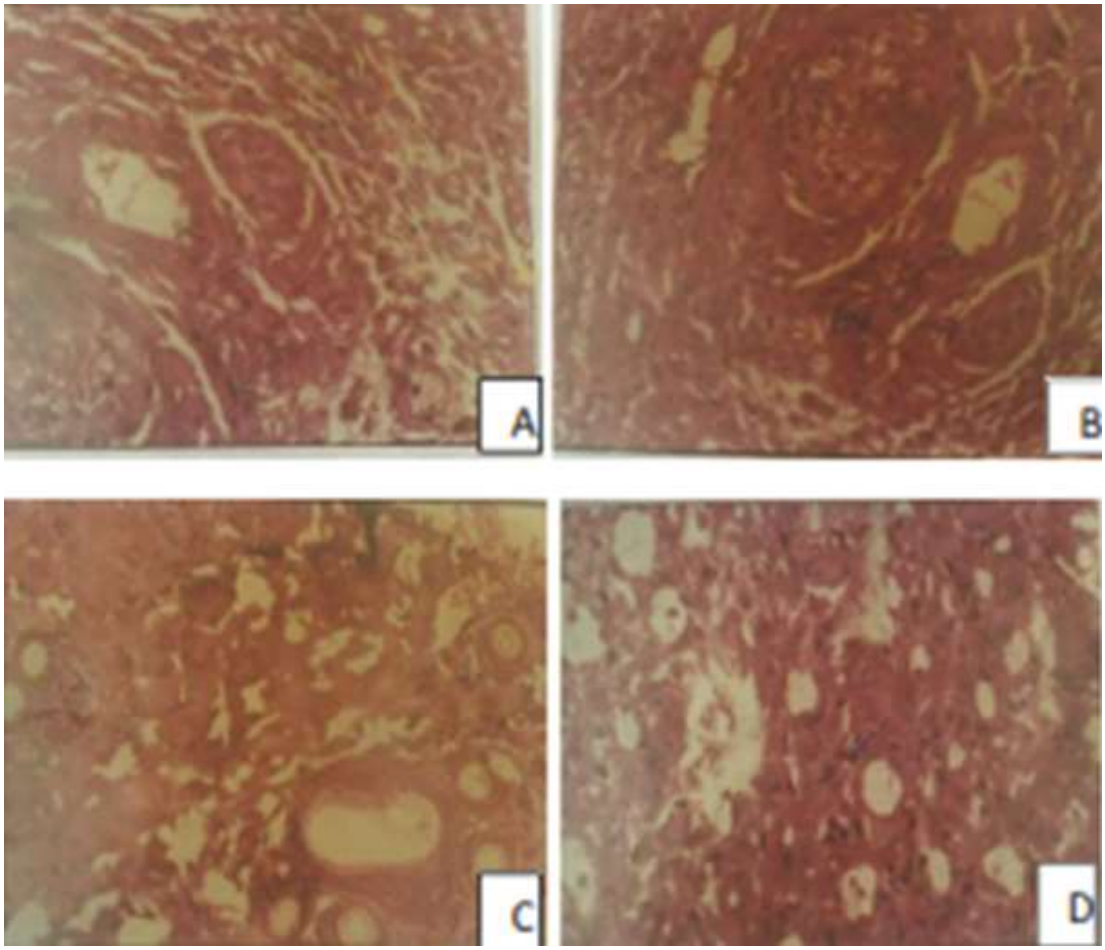

Figure 2**: (A).** Granulation tissue obtained from the control group on day 9(H &E) x 400. Fibroblast (F). Blood vessel (BV). **(B):** Granulation tissue obtained from the experimental control group on day 9(H &E) x 400. Fibroblast (F). Blood vessel (BV). Note more collagen fibres and less macrophages when compared with that of control group (A). **(C):** Scar tissue obtained from the control group.(H&E) x 400. Fibroblast (F),Blood vessel (BV). Collagen bundle (C). The macrophages are more abundant than those of the experimental group. Although collagen fibres are abundant but not as much as in the experimental group (D). **(D)**: Scar tissue obtained from the experimental group (H&E) x 400. Fibroblast (F), Blood vessel (BV). Collagen bundle (C). Note the paucity of macrophages and abundance of collagen

DISCUSSION

Results of this study clearly demonstrated greater wound contraction rates in the experimental group over the control. The negative values in Table 1 indicated expansion rather than reduction in wound size. Four of the control animals had such negative values as opposed to just one animal in the experimental group. These values were recorded at the first change of wound dressing. This expansion in wound size could be indicative of sepsis (infection). Since this was observed more in the control group, it may be reasonably concluded that L*. esculentum* possesses bactericidal property.

The interval differences in the mean percentage wound contraction were more pronounced between Day 3 and Day 9. Although Day 9 has demonstrated wound contraction to reach its peak, these wide margin differences within the stated period, imply the ability of L*. esculentum* to accelerate wound healing. This assertion was also reinforced by the shorter but statistically significant mean healing period observed in the experimental group (19.80 ± 1.64 vs.28.80 ± 4.55 days). Observations made from the graphic representations of wound contraction rates could be suggestive of the ability of L. *esculentum* to rapidly initiate and accelerate fibroblast synthesis.

The greater number of myofibroblasts in the experimental group may have accounted for the earlier wound contraction (Junqueira et al., 2005). It is plausible that *L. esculentum* increases myofibroblast proliferation.

In wound healing, as maturity advances, the granulation tissue becomes progressively pale due to reduction in neovascularization and formation of immature vessels that characterize the healed scar. In this study, the granulation tissue of the control animals exhibited greater angiogenesis than those of the experimental group (15.60 ± 5.77 vs 12.60 ± 8.32). However, angiogenesis in the healed scars of the experimental group was slightly higher than that of the control group (14.20 ± 1.92 vs 13.20 ± 1.64). When these observations are considered in the context of healing rate a reasonable deduction that could be made is that the wounds of the experimental group healed faster than those of the control group. Thus this study has been able to demonstrate the ability of L. esculentum to promote the changes in angiogenesis that occur during wound healing.

This study also demonstrated significant difference in the mean duration of healing (p=0.003), with the experimental group having shorter duration (19.80± 1.64 vs 28.80 ±4.55). The import of this observation is the wound healing enhancing ability of *L. esculentum*. Lycopene, an important abundant, active ingredient of *L. esculentum* is a more effective low-density lipoprotein antioxidant (Tsuchiya et al., 1996) than β-carotene. It has been demonstrated that any agent or compound that is capable of reducing lipid peroxidation will increase the strength of collagen fibres and improve blood circulation (Manjunatha et al., 2005). These two physiological phenomena will enhance wound healing. This explains the ability of *L esculentum* as a potent wound healing agent. Bioflavonoids are present in *L. esculentum.* Flavonoids, via their antimicrobial and astringent properties (Douglas et al., 2003) enhance wound healing.

In conclusion, this study has been able to demonstrate that the methanol extract of *L. esculentum* promotes wound healing by its bactericidal properties and rapid initiation of wound contraction.

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