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Pharmacological Evaluation of Wound Healing Activity of *Citrullus colocynthis* - Bitter Apple Cream on Wistar Albino Rat

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ABSTRACT

Herbal treatment has been targeted in the study, as of their greater demand in market nowadays. *Citrullus colocynthis* distributed in UAE desert and other parts of the world and formulated in the pharmacological activity wound heal activity using excision wound. The grouped animals anesthetized different concentration with natural bees wax base as a *Citrullus colocynthis* cream (CCC). Asses and an excision wound was inflicted by cutting away a 30 mm full thickness of skin from a predetermined shaved area and kept as opened and treated topical once in a day. *Citrullus colocynthis* Cream 25% group shows significant effect wound area cured within a period of 11^{th} day and wound area is (± 1.15 mm) compare to control group (25±5.90 mm). *Citrullus colocynthis* Cream showed healing of the open wound more significantly effective compare other natural creams.

INTRODUCTION

Wound healing can be divided into 3 stages, inflammation, proliferation, remodeling and maturation phases which involved the interaction of various cells, cytokines, and growth factors. Thus, the wound healing process can be accelerated by using antioxidants.

Herbal medicines have been enjoying revitalization among clients all over the world. There are hundreds of medicinal plants that have a long history of curative properties against various diseases and ailments. However, screening of herbs for their activity is very crucial and needs imperative attention in order to know the value of the herbs.[1-3]

Citrullus colocynthis (L.) Schrad is a valuable plant from Cucurbitaceae family, widely distributed in the barren region, is a non-hardy, herbaceous perennial vine, branched from the base[4]. *Citrullus colocynthis* fruits are generally documented for its broad range of pharmaceutical uses as well as medicinal and nutraceuticals potential. It a well recognized plant in traditional medicine and was used by people in rural areas as a purgative, antidiabetic, and insecticide[5]. Recently, research has focused on the use of natural antioxidants like herbal extract on wound healing. The beneficial effects of natural source on wound healing have mainly been studied using animal models. Topical application of natural source is more effective in accelerating wound healing compared to oral administration.

Honey, beeswax and olive oil are natural materials that contain flavonoids, antioxidants, antibacterial ingredients and effects cytokines production by skin cells when applied topically[6,7].

Hence, in this study, we formulate the *Citrullus colocynthis* cream (CCC) and aimed to evaluate the effect of CCC topical application in the form of cream on excision wound healing on rat.

AIMS AND OBJECTIVE

This study, we formulate the *Citrullus colocynthis* cream (CCC) and aimed to evaluate the effect of CCC topical application in the form of cream on excision wound healing on rats.

MATERIALS AND METHODS

CCC cream was prepared by thoroughly mixing of *Citrullus colocynthis* dry fruit and beeswax. Natural unprocessed beeswax was obtained from farmhouse, Dhaith, Sharjah, UAE. *Citrullus colocynthis* fruit was obtained from desert, Dhaith, Sharjah, UAE.

Formulation of DHC cream

The cream was prepared in different concentration 5%, 10% and 25% by using a natural beeswax cream base. Standard method of fusion was used, where the natural beeswax were melted and mixed by continuous trituration. The required quantity of the natural wax was weighed and melted at a temperature of about 70ºC in a hot water bath. The designated quantity of the content (s) were respectively added to the melted base at 70ºC and the mixed *Citrullus colocynthis* fruit dry according to the following concentration of different formula 5%,10% and 25%, stirred gently and continuously until a homogenous dispersion is obtained. Formulations were stored at 4, 25, and 40ºC for two weeks and then the stability was evaluated.

Evaluation of DHC

PH 1.0 g cream was weighed and dispersed in 100 ml water. Using digital pH meter, the pH of the dispersion was calculated. The pH meter was calibrated before use with standard buffer solution at 4.0, 7.0 and 9.0. The readings of pH were done in triplicate and average values were calculated.

Spreadability

One of the important criteria for a topical formulation is that it should possess good spreadability. It is the term used to denote the extent of area to which formulation readily spreads when applied to skin or affected part. The therapeutic efficacy of a formulation depends upon its spreading value. To determine the spreadability of *Citrullus colocynthis* cream (CCC) formulations, 0.5 g of DHC was placed in a circle of 1 cm diameter pre-marked on a glass plate of 20 × 20 cm, over which a second glass plate was placed. A weight of 500 g allowed resting on the upper glass plate for 5 min. The increase in the diameter due to *Citrullus colocynthis* cream (CCC) spreading was noted.

Homogeneity

The developed formulations were tested for homogeneity by visual inspection after the CCC had been filled in the container. They were tested for the appearance of CCC and presence of any aggregates in *Citrullus colocynthis* cream (CCC).

Animals

Healthy male rats (weighing 250–300 g) bred in Laboratory Animal Resource Unit, were used throughout the experimental period. They were housed under controlled environmental conditions with free access to rat pellets and clean water, caged individually. Prior ethical approval was obtained from the Animal Ethics Committees.

Grouping of animals

Groups of animals containing three per model (n=6) in each were used for excision and incision wound models. The animals of groups were considered as the control, CCM cream 5%, 10% and 25% cream respectively.

***In vivo* studies**

Excision wound model[8-10]

The animals were divided into 4 groups with six in each were anaesthetized by open mask method with anesthetic ether before wound creation. The particular skin area was shaved 1 day prior to the experiment. An excision wound was inflicted by cutting away a 30 mm full thickness of skin from a predetermined shaved area. The wounds were left undressed to the open environment. The *Citrullus colocynthis* cream (CCC) was applied topically to the 3 groups and control without treatment. In this model, wound area was monitored. Wound area was measured using vernier caliper scale as in 1, 3, 7, 11days treatment period.

Statistical Analysis: All results were expressed as mean ± standard error (SEM). Data was analyzed by using One way ANOVA followed by Tukey's multiple comparison tests using Graph Pad InStat. $P<0.05$ was considered as statistically significant.

Observation:

Table 1: Effect of *Citrullus colocynthis* cream on diabetic rat Incision wound heal

Group	3rd day	7th day	11th day
Control cream	17.66±4.50	12.33±4.04	7±2.64
Citrullus colocynthis dry fruit cream 5%	14±2.64	9.66±0.57	6.66±1.52
Citrullus colocynthis dry fruit cream 10%	13±0	10±1	7±2
Citrullus colocynthis dry fruit cream 25%	14.33±1.52	7.33±0.57	2.33±1.52*

*Values are mean ± SEM (n = 6) * p < 0.05 statically significant value. CCC (Citrullus colocynthis cream).*

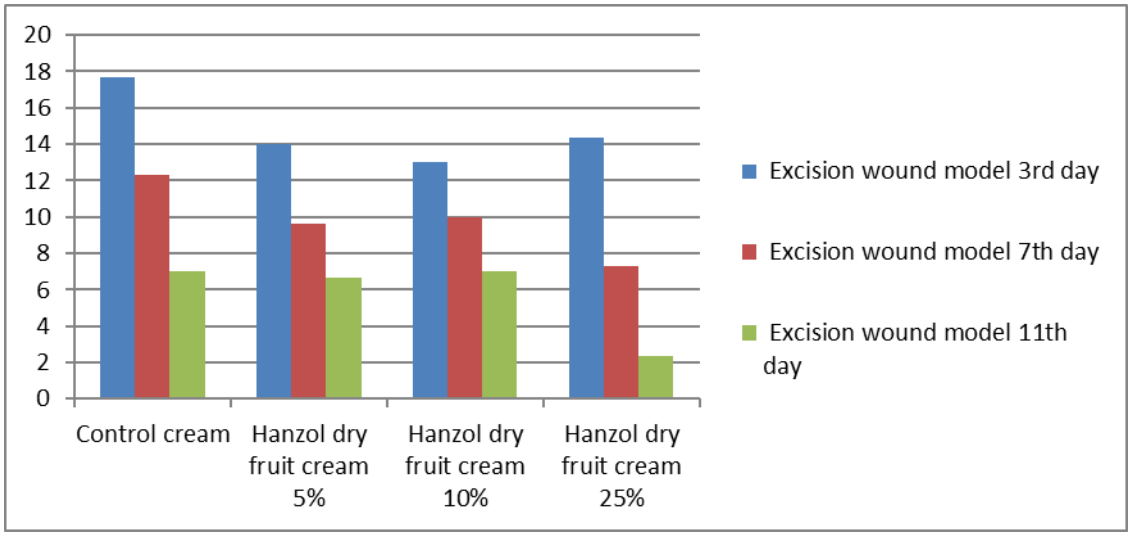

Fig. 1. Excision wound heal activity of experimental rats (values are expressed as mean of respective group of rats (n=6). Citrullus colocynthis* cream (CCC). *All values are expressed as mean±SEM (n=6); * represents significance (p<0.05) as compared to control

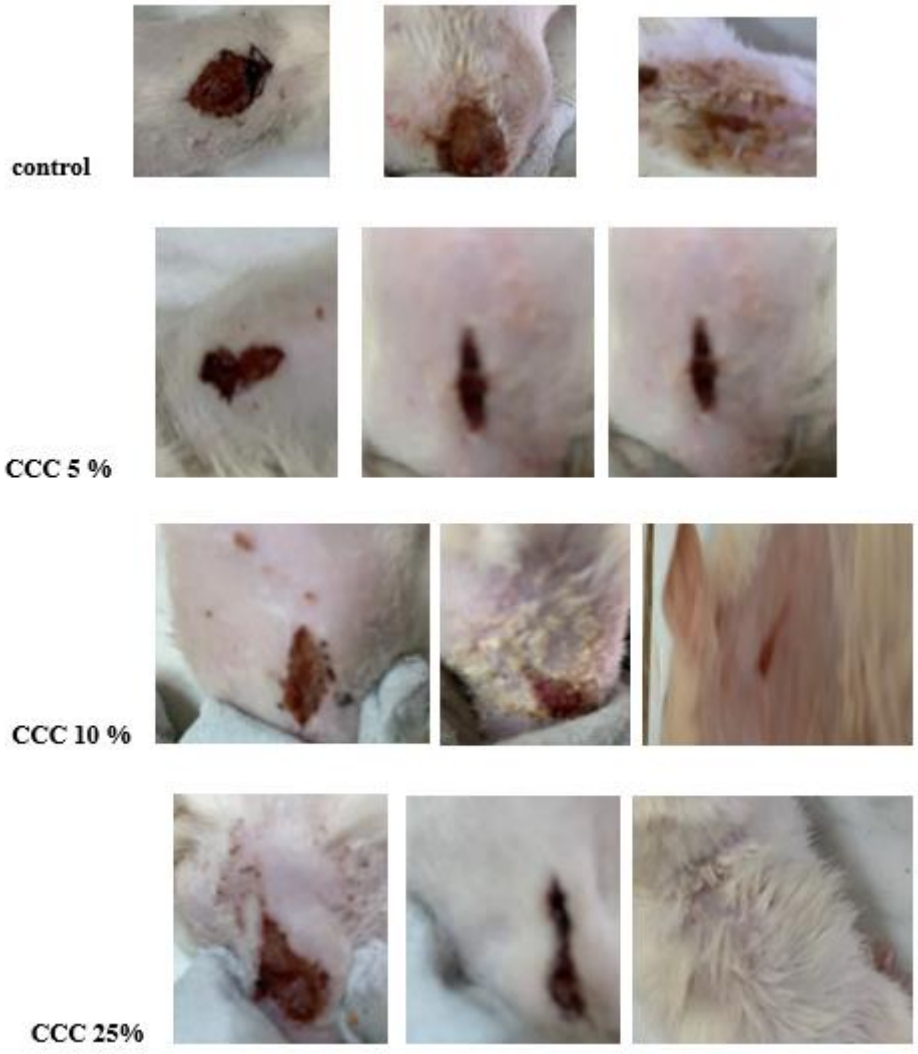

Fig 2: Photographic representation of contraction rate showing percent wound concentration area on different excision days on control Citrullus colocynthis cream (CCC) 5%, 10% and 25%

RESULTS

Evaluation of *Citrullus colocynthis* cream

The pH was found to be neutral pH, thus the formulations can be used without the risk of skin irritancy. By this we can infer that the selected ingredients for cream formulation did not alter the pH of the formulation. The values of spreadability for *Citrullus colocynthis* cream (CCC) was found out to be 5.4, 6.5, 8.6 cm indicating that the cream is easily spreadable by small amount of shear. The results concluded that the formulation can be applied easily without being runoff. This assures that the formulation maintains a good wet contact time when

applied to the targeted site. *Citrullus colocynthis* cream (CCC) formulations were good in appearance and homogeneity.

Excision wound model

In this excision wound model, the wound was measured. The mean area of wound heal on 1st day in normal group was 17.66 ± 4.93mm and in *Citrullus colocynthis* cream (CCC) group 25% it was 14.33± 1.52 mm. After 11th day the mean area of *Citrullus colocynthis* cream (CCC) treated groups was 2.33± 1.52 mm, it was highly significant effect when comparable to control group 7 ± 2.64 mm. The diabetic animals groups mean area of treated of 5± 1.15 mm when compared with the control group animals 25±5.90 mm. This has significant difference with a *p*-value <0.05 compared to control and CCC treated group (Figure1, 2 &Table 1).

DISCUSSION

Wound healing is a complex and natural response of the body that results in the achievement of the restoration of the normal physiological function and integrity of the injured/damaged tissues and also produces several extracellular matrix proteins and growth factors. The use of natural products such as bitter apple, beeswax and olive oil to treat wounds and burns has great appeal especially in developed countries. A verity of natural products has been reported for the treatments. These results indicate that *Citrullus colocynthis* cream is able to accelerate the rate of wound healing. The present study shows decrease the wound healing faster as comparable to other natural products.

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