Research Article

www.ijrap.net

PHARMACOLOGICAL EVALUATION OF *CISSUS QUADRANGULARIS* HERBAL GEL FOR WOUND HEALING ACTIVITY

Ayesha Siddiqua *[1], Sirisha Mittapally [2]
Deccan School of Pharmacy, Dar-Us-Salam, Aghapura, Hyderabad, Telangana, India

Received on: 10/09/17 Accepted on: 30/09/17

***Corresponding author**
E-mail: ayeshasiddiqua332@gmail.com

DOI: 10.7897/2277-4343.085246

ABSTRACT

The present work was to investigate the wound healing efficiency of Herbal gel containing ethanolic extract of *Cissus quadrangularis* on wound healing by using excision wound model on Wistar Albino rats by topical application of 20% and 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gels. In the excision wound model, wound contraction and period of epithelization was studied. The 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel (Group-IV), possess potential wound healing activity revealing that the extract has ability to induce cellular proliferation and re-epithelization that lead to complete healing of excision wound since it contains active constituents like β-sitosterol responsible for wound healing activity. The study had shown that it has potential wound healing activity that has shown significant value P<0.001 with ANOVA Analysis.

Keywords: Wound healing activity, *Cissus quadrangularis*, herbal gel, ethosomal gel.

INTRODUCTION

Cissus quadrangularis is commonly known as (Hadjod) is a perennial plant of the family Vitaceae. It is also known as Adamant creeper, Square stalked vine, veldt grape, devil's backbone, adamant creeper, asthisamharaka, hadjod and pirandai, Sannalam, Nalleru, Vajravelli, Mangara valli.

Cissus quadrangularis consists of chemical constituents such as β- sitosterol, β-stigmasterol, flavanoids, triterpenoids, and resveratrol, piceatannol, ketosteroid as major constituents of the plant. The presence of β-sitosterol helps to repair tissues and plays an important role in wound healing activity.

It is extensively used in Ayurveda and Unani. Powdered root is used as a specific for the fractures of the bones, with the same effects as plasters externally. Dose of the powder is 30-40 grains. "Leaves and young shoots are frequently taken with curry in Southern India. In Madras, young shoots of the plant are dried and powdered, are burnt to ashes in a closed vessel and administered in dyspepsia and indigestion" and certain bowel complaints. Leaves and young shoots are also considered as powerful alternatives. Juice of stem is dropped into the ear in otorrhoea and into the nose in epistaxis. It has also a reputation in scurvy and in irregular menstruation. Stem beaten into a paste is used to treat asthma. A preserve of stem prepared by boiling it in lime water is useful stomachic.[4]

In Medicinal Plants-Germplasm of Peninsular India the *Cissus quadrangularis* uses is mentioned as the stem and whole plant is used in asthma, bowel complaints and as epistatic, stem is useful in piles, diseases of the ear and bleeding of nose, paste of the stem is useful in muscular pains, burns, wounds, bites of poisonous insects and for saddle sores of horses and camels; root used in fractures and cuts. [1,5]

Wound Healing is a complex process that involves numerous cell types (epithelial and endothelial cells, lymphocytes, fibroblasts etc.) and an array of soluble factors (e.g. growth factors, cytokines etc.). Naturally, the investigative curiosity to promote healing continues since ages. A lot of research has been envisaged to develop better healing agents and it has been a challenging task to generate them and keep pace with the problems encountered. Several drugs of plant, mineral and animal origin are described in the Ayurveda for their wound healing properties. In spite of recent advances in the basic mechanism of wound healing, knowledge of factors involved in the treatment of wounds and their prevention remains limited. [16]

Plants and their extracts have immense potential for the management and treatment of wounds. The phytomedicines for wound healing are not only cheap and affordable but are also purportedly safe as hypersensitive reactions are rarely encountered with the use of these agents. These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms. However, there is a need for scientific validation, standardization and safety evaluation of plants of traditional medicine before these could be recommended for healing of the wounds. Plants or chemical entities derived from plants need to be identified and formulated for the treatment and management of wounds. In this direction, a number of herbal products are being investigated at present. Over the years, various herbal products have been used in the management and treatment of wounds. [3,6]

MATERIALS AND METHODS

Gel formulation

20% and 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gels were formulated.[2]

Experimental Animals

Adult Wistar Albino rats of either sex weighing 150–180 g was procured from National Institute of Nutrition, Tarnaka, Hyderabad. Animals were housed in standard laboratory

conditions at 25 °C with 12-hour light-dark cycle with free access to chow i.e, (Nutrimix Std-1020, Rat/ Mice Laboratory Animal Diet, Diet form-10-14 (Gr, Pellets), Mfg., by Nutrivet Life Sciences, Pune, India) and water *ad libitum*. Cleaning and sanitation work were done on alternate days. Paddy husk was provided as bedding material, which was changed every day. The research protocol was approved by (DSOP/CPCSEA/IAEC/ 3/16).

Screening model for Wound healing activity of *Cissus quadrangularis* herbal gel
Excision Wound Creation

The animals were anesthetized with slight vapour inhalation of anesthesia ether. The particular skin area was located and the skin was pulled upwards with the help of forecep and carefully the hair's on the dorsal thoracic side were cut-off with the help of sterilized scissors. The skin of impressed area was excised to the full thickness to obtain a wound area of about 500 mm^2 on dorsal thoracic region was made. Animals were closely observed for any infection and those which showed signs of infection were separated and excluded from the study and replaced. The animals were observed for wound closure at 0, 1, 4, 8 and 12^{th} day using a transparency sheet and a permanent marker and for period of epithelialisation.[17,18]

Percent wound contraction = healed area / total wound area × 100

Significance in wound healing of the test groups are derived by comparing healed wound area on respective days with healed wound area of control group.

The period of epithelization that is, day of fall of eschar and scar area were also noted down.[14,15]

Where, Healed area = Original wound area − Present wound area.

Figure 1: Excision wound model in Albino rats

The albino rats were divided into 4 groups containing 6 animals each (n=6) as follows;
The Group –I animals are Control group that involves no application of any medication.
The Group-II animals are Standard group that were applied standard/marketed ointment i.e., mebo ointment.
The Group-III animals were applied topically herbal formulation of 20% Ethanolic extract of *Cissus quadrangularis* ethosomal gel.
The Group-IV animals were applied topically herbal formulation of 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel.[9,11,12]

Group I: (control group): No application of any medication.
Group II: **(standard group):** Animals of this group were applied topically Mebo ointment (consisting 0.25 %w/v of β-sitosterol).
Group III: (test group): Animals of this group were applied topically herbal formulation of 20% Ethanolic extract of *Cissus quadrangularis* ethosomal gel.
Group IV: (test group): Animals of this group were applied topically herbal formulation of 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel.[8,13]

Statistical Analysis

Analysis of data was performed using statistical package for social version 11.0 (SPSS) computer software. Descriptive statistics were adopted to display data in mean of ± SEM ANOVA was used to compare the mean value obtained between the different groups. Differences were considered significant whenever the P value are reported as mean ± SEM. ***P<0.001, **P<0.01 and *P<0.05.

RESULTS

A significant decrease in period of epithelization was observed after 20% and 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel application. Treatment with Mebo ointment (standard) also significantly reduced period of epithelization as compared with control group. At the same time 20% and 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel decreased the wound contraction (50%) as compared with control.

Comparative analysis revealed that 20% and 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gels possess potential wound healing activity when compared to that of standard (mebo ointment) in 12-14 days.

The 40% Ethanolic extract of *Cissus quadrangularis* ethosomal gel possess potential wound healing activity (E6) that lead to complete healing of excision wound in 12 days.

Figure 2: Re-epithelization of wound

Table 1: Effect of topical application of ethosomal gels containing 20% and 40% ethanolic extract of *Cissus quadrangularis* on wound contraction of Excision wound

Group	2nd day	4th day	8th day	12th day	Period of epithelization (day)
Control	10.4±0.10	23.6±0.83	42.8±0.04	73.5±0.91	20
Standard	13.9±0.71	32.6±0.71	65.9±0.06	90.3±1.46**	16
20% ethanolic extract of *Cissus quadrangularis* ethosomal gel	14.7±0.10	39.8±0.10	79.1±1.87*	94.5±0.65***	14
40% ethanolic extract of *Cissus quadrangularis* ethosomal gel	15.8±0.96	43.1±0.92	92.3±0.65**	100***	12

Mean % wound contraction ± SEM, 20% and 40% ethanolic extract of *Cissus quadrangularis* ethosomal gels, n=6 animals in each group. The treated groups are compared by student t-test with the control group.***P<0.001, **P<0.01, *P<0.05.

CONCLUSION

The basic principle of optimal wound healing is to minimize tissue damage and provide an adequate tissue perfusion and oxygenation, proper nutrition and moist wound healing environment to restore the anatomical continuity and function of the affected part.

The results of excision wound model indicate that in the first 4 days there is no significant increase in the wound contraction in all the groups as compared to the control group. The results of the 12th day indicate that there is significant increase ($P < 0.001$) in the percentage in wound contraction in the group treated with 40% ethanolic extract of *Cissus quadrangularis* ethosomal gel (Group-IV), revealing that the extract has ability to induce cellular proliferation and re-epithelization that lead to complete healing of excision wound since it contains active constituents like β-sitosterol responsible for wound healing activity.

From the above observations it was concluded that ethosomal gel formulation containing 40% ethanolic extract of *Cissus quadrangularis* was found to be the best gel for wound healing activity.

ACKNOWLEDGEMENT

The Successful accomplishment of this Article would not have been possible but by the timely help and guidance rendered by many people. My first salutation goes to Almighty Allah and my Parents for being ever so kind and courteous. It gives me an immense pleasure to acknowledge a debt of gratitude to Dr. Roshan. S M.Pharm, Ph.D Professor and Head of the Department of Pharmacognosy, Deccan School of Pharmacy for his strong support, guidance and co-operation.. I would like to express profound gratitude to Dr. Syed Abdul Azeez Basha, honourable Principal of Deccan School of Pharmacy, Hyderabad, for guiding me as well.

REFERENCES

1. Ayesha Siddiqua, Sirisha Mittapally, A Review article on *Cissus quadrangularis*, AkiNik Publications The Pharma Innovation Journal, 2017; 6 (7);329-334.
2. Ayesha Siddiqua, Sirisha Mittapally, A Research article on Formulation and Evaluation of ethanolic extract of *Cissus quadrangularis* herbal gel, International Research Journal of Pharmaceutical and Biosciences, 2017, 4 (4); 9-29.
3. Shah U. *Cissus quadrangularis* L: Phytochemicals, Traditional uses and Pharmacological Activities - A review, International Journal of Pharmacy and Pharmaceutical Sciences 2011; 3 (4): 41-44.
4. Dr. Mohd. Ataullah Shareef, Kitabul Advia Mufarradaath. Best Printers and Publishers- Hyderabad, First edition. 2012, 511-512.
5. Varaprasad KS, Abraham Z, Pandravada SR, Latha M, Divya S Raman, Lakshminarayan S *et al*. Medical Plants Germplasm of Peninsular India, Published by National Bureau of Plant Genetic Resources, New-Delhi-110 012, India, 2006, 50.
6. Mishra G, Srivastava S, .Nagori BP. Pharmacological and Therapeutic Activity of *Cissus quadrangularis*: An Overview. International Journal of PharmTech Research 2010; 2(2):1298-1310.
7. Srivastava AK, Srivastava P, Behera BR. Pharmacognostical & Phyto-chemical Investigation of *Cissus quadrangularis linn*. Stem. Ijprd 2011; 3(1):207-15.
8. Jain NK. Advances in controlled and novel drug delivery. 1st Edition, New Delhi, CBS publication, 2001; 428-451.
9. Jain S, Bhandra D, Jain S and Jain NK. Transfersomes- A novel carrier for effective transdermal drug delivery. Controlled and novel drug delivery 1st Edition. CBS publishers and distributors New Delhi, 1997; 426-451.
10. Vyas SP, Khar RK. Controlled drug delivery concepts and advances. Vallabh prakashan New Delhi. First Edition, 2002; 173-243.
11. Tauitou E, Dayan N, Bergelson L, Godin B and Eliaz M. Ethosomes – novel vesicular carrier for enhanced delivery: characterization and skin penetration properties. J Con Release, 2000; 65: 403 - 418.
12. Jain S, Umamaheshwari RB, Bhadra D and Jain NK. Ethosomes: A novel vesicular carrier for enhances transdermal delivery of a Anti HIV agent. Indian J Pharm Sci., 2004; 66(1): 72-81.
13. Barry BW. Novel mechanism and devices to enable successful transdermal drug delivery. European J Pharm Sci., 2004; 14: 101-114.
14. Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A and Levi-Schaffer f. Intracellular delivery mediated by and ethosomal carrier. Biomaterials, 2001; 22: 3053-3059.
15. Lodzki M, Godin B, Rakou L, Mechoulan R, Gallily R and Touitou E. Cannabidiol - transdermal delivery and anti-inflammatory effect in a murine model. J Control Rel., 2003; 93: 377-387.
16. Nitin gupta, Ankit R. Patel and Ravindra R. P. Design of Akkalkara (Spilanthes acmella) Formulations for antimicrobial and topical anti-inflammatory activities, International Journal of Pharma and Bio Sciences 2012 Oct; 3(4): (P) 161 – 170.
17. Suguna, L., Singh, S., Sivakumar, P., Sampath, P., Chandrakasan, G., Influence of Terminalia chebula on dermal wound healing in rats. Phytother. Res. (2002); 16: 223–227.
18. McFarlin, K., Gao, X., Liu, Y.B., Dulchavsky, D.S., Kwon, D., Arbab, A.S., Bansal, M., Li, Y., Chopp, M., Dulchavsky, S.A., Gautam, S.C., Bone marrow-derived mesenchymal stromal cells accelerate wound healing in the rat. Wound Repair Regen. (2006); 14: 471–478.

Cite this article as:

Ayesha Siddiqua and Sirisha Mittapally. Pharmacological evaluation of *Cissus quadrangularis* herbal gel for wound healing activity. Int. J. Res. Ayurveda Pharm. 2017;8(5):65-68 http://dx.doi.org/10.7897/2277-4343.085246

Source of support: Nil, Conflict of interest: None Declared