High-fat diet increases the level of circulating Monocyte Chemoattractant Protein-1 in Wistar rats, independent of obesity

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Submission date: 27-Oct-2021 03:25PM (UTC+0700)
Submission ID: 1685447342
File name: Effect_of_Hylocereus_polyrhizus.pdf (232.37K)
Word count: 4621
Character count: 23849

Jordan Journal of Pharmaceutical Sciences, Volume 14, No. 1, 2021

Effect of *Hylocereus polyrhizus* Extract to VEGF and TGF-β1 Level in Acute Wound Healing of Wistar Rats

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ABSTRACT

This study aims to identify the effect of *Hylocereus polyrhizus* on the level of VEGFs and TGF-β1 in acute Wistar rat wounds. Male Albino Wistar rats (n = 54) whose (250-350 g) were divided into 3 groups (negative control, positive control, and *Hylocereus polyrhizus*). The animals were wounded at right and left dorsal back with an 8 mm punch biopsy. *Hylocereus polyrhizus* 7.5% topical cream was applied on the wound surface using a cotton bud. The VEGF and TGF-β1 were evaluated with ELISA on the 3rd, 7th, and 14th days. Analyzed using independent t-test and paired t-test (SPSS 21, Chicago Ill). The *Hylocereus polyrhizus* group had higher level of VEGF and TGF-β1 compared to positive control ($p = 0.011$; $r = -0.584$) and ($p = 0.000$; $r = 0.888$), respectively, on the 14th day. It was found that there was an upward trend between the TGFβ-1 level and the tissue granulation's score (*p*: 0.051 and r: -0.466) as well as TGFβ-1 levels with epithelialization score (*p:* 0.001 and r: 0.708) in the *Hylocereus polyrhizus* topical group. This study has shown that *Hylocereus polyrhizus* can accelerate wound healing during both the inflammation and proliferation phase.

Keywords: *Hylocereus polyrhizus*, wound healing, VEGF, TGF-β1.

1. INTRODUCTION

There is an increase in the prevalence of acute wounds. The West Wound Prevalence Survey reported that the prevalence of acute wounds is 49%, pressure ulcers are 9%, abraded wounds are 17%, limb injuries are 4%, burns are 1%, malignancy is 1% and other cuts is 9%[(1,2)]. A study from the United Kingdom (UK) reported a higher prevalence of acute wounds (303 from 826 peoples) involving various forms of a traumatic wound[(2)]. In Indonesia, the prevalence of acute wounds is higher (64.3%) versus chronic wounds in the home care setting[(3)]. This burden prevalence of acute wounds is an emerging issue that requires new treatments.

Recently, there has been a renewed interest in complementary therapy. Although various approaches and attempts have been made in clinics to treat acute wounds including debridement, modern wound care dressings, and arterial reconstruction, these approaches are less effective at healing[(4)]. Meanwhile, empirical experience has proved that the traditional treatment in wound healing that is often applied includes applying a sap or herbs as an anti-bacterial and to prevent bleeding[(5,6)]. In Indonesia, putting honey on wounds accelerates acute wound healing[(7)]. Therefore,

Received on 31/3/2020 and Accepted for Publication on 20/10/2020.

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complementary therapy may have a potential role in the wound healing process.

Red dragon fruit is a common complementary therapy in Asia. Red dragon fruit (*Hylocereus polyrhizus*) contains a variety of active substances that can be used in both therapeutic approaches in cardiovascular disease and degenerative diseases[(8)]. It has many flavonoids, polyphenols, and antioxidants[(9)]. It also contains β-amyrin (23,3%), ϫ-sitosterol (19,3%), and octadecane (9,2%)[(10)]. To date, studies investigating *Hylocereus polyrhizus* in the wound care setting are rare. Thus, the purpose of this study was to investigate the potential of *Hylocereus polyrhizus* topical cream to accelerate the healing process of acute wounds in Wistar rats.

MATERIALS AND METHODS

Preparation of red dragon fruit extract

Red dragon fruit was from plantations near Samarinda, East Kalimantan, Indonesia. It is extracted using methanol, and the percentage of inhibition of free radicals (DPPH) was tested. The anti-free radical activity of the red dragon fruit and vitamin C was extracted as much as 314.69 ppm and 3.28 ppm of IC_{50} respectively. Every gram of red dragon fruit contains high levels of polyphenols 1.062 GAE and 8.3 mg of flavonoid content. A topical cream was made with 7.5% of concentration.

Experimental animals

This was an experimental study using a post-test design with a control group design. The samples were healthy male albino Wistar rats (250-350 gr) from the animal laboratory of the Faculty of Veterinary Medicine, Gadjah Mada University. Samples were divided into 3 groups consisting of 18 rats in each group. All groups were treated using primary topical therapy. In Group I (control), rubbing petroleum jelly was applied. Group II (established drug) used Bioplasenton®. Group III used *Hylocereus polyrhizus* as a topical therapy at 7.5% *Hylocereus polyrhizus*. Later, Fixomull® transparent film (BSN Medical) was applied s the secondary dressing. Wounds were then treated and sacrificed on the 3rd, 7th, and 14th days. This study protocol refers to The Council for International Organizations of Medical Sciences (CIOMS) consensus, and this study was approved by the ethics committee of Hasanuddin University (NO. 1684/H4.8.4.5.31/PP36-KOMETIK/2015).

Wounded procedure

Fur from the excision area was removed using cream bleach (Veet®, Reckitt Benckiser) and disinfected with 0.5% of chlorhexidine in 70% alcohol under isoflurane anesthesia (0.01 µg/kg – 0.05 µg/kg)[(11)]. A circle excision was made in the back area until the fascia profunda with an 8-mm punch biopsy[(12)]. The diameter of the wound surface area of the excision of all groups was measured using a paper ruler (Figure I).

Histological evaluation of wound healing

Skin tissues were fixed in formalin normal buffer solution 10%, dehydrated in alcohol of various concentrations (70%, 80%, 90%, and absolute alcohol I and II), cleared with xylol, and disembedded in paraffin[(13)]. The tissue was added to liquid paraffin and was allowed to harden. The tissue was cut with a microtome to five microns. The sample was rehydrated and stained with hematoxylin-eosin (HE). The thickness of the granulation tissue (proliferation) and connective tissue area was measured using a micrometer video JVC Japan with four-fold magnification[(14)]. Evaluation of wound healing was assessed by scoring the epithelialization and the thickness of granulation tissue[(15)]. The epithelialization indicator used a semi-quantitative evaluation of histological sections[(16)], where score 1 = displacement cells (<50%), 2 = transfer of cells (≥50%), 3 = closure of the entire excision, 4 = closure of the entire excision score + keratinization. Meanwhile, the thickness of granulation tissue used a histological score[(17)], where score 1 = slight, 2 = moderate, and 3 = thick.

VEGF and TGF-β1 measurement

Each group was measured with a biomarker consisting of VEGF and TGF-β1. The VEGF measurements used the ELISA techniques with serum from scar tissue excisions. The VEGF measurement used a mouse VEGF-A enzyme-linked immunosorbent assay (ELISA; p/n BMS619/2/BMS619/2 TEN). The TGF-β1 mouse ELISA TGF-Platinum kit was p/n MBS608/4/MBS608/4/4 TEN from Affymetrix eBioscience (Vienna, Austria). Examination of VEGF and TGF-β1 was conducted at the Education Laboratory, Hasanuddin University Hospital.

Statistical analysis

Data were reported as the mean and ± SD with a significant level were set up at $p < 0.05$. Spearman correlation proved the correlation between the levels of VEGF, TGF-β1, and length of treatment. Data were analyzed using SPSS software (version 21; SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

DPPH of *Hylocereus polyrhizus*

The IC_{50} of anti-free radical activity and vitamin C of the *Hylocereus polyrhizus* obtained 314.69 ppm and 3.28 ppm (Table I). The results showed that each gram of the red dragon fruit contains about 8.3 mg flavonoid levels and 10.62 mg GAE of total phenol content (Table II).

Table I

The percentage inhibition of DPPH free radical by *Hylocereus polyrhizus* and IC_{50} values.

Replication	Concentration (ppm)	Absorbant	% Retardation	IC_{50} (ppm)
Hylocereus polyrhizus	100	0.635	28.774	314.69
	200	0.589	33.968	
	300	0.485	45.553	
	400	0.382	57.100	
	500	0.320	64.088	
Vitamin C	1.0	0.720	17.676	3.28
	1.4	0.683	21.943	
	1.8	0.565	35.352	
	2.6	0.511	41.600	
	3.4	0.429	50.933	

Table II

Average levels of polyphenols and flavonoids in *Hylocereus polyrhizus*

Sample	Repetition	Absorbant	Polyphenols Level (%)	Mean of Polyphenols Level
Hylocereus polyrhizus	1	0.24	1.090	1.062
	2	0.233	1.041	
	3	0.236	1.059	
Sample	Repetition	Absorbant	Flavonoids Level (%)	Mean of Flavonoids Level
Hylocereus polyrhizus	1	0.074	0.830	0.830
	2	0.074	0.830	
	3	0.074	0.830	

VEGF level on wound healing

The Spearman correlation test evaluated the correlation between the VEGF levels based on the length of treatment. The VEGF levels of *Hylocereus polyrhizus* group increased between day 3 to day 7 after treatment: 169.17±107.54; $p = 0.011$; r = -0.702. This declined between the 7th and 14th day (60.34±33.70), but this was not significant (p = 1.000; r = 0.000). In addition, VEGF declined from the 3rd day to the 14th day (46.47±31.26; p = 0.007; r = -0.727) indicating a correlation between VEGF levels with the duration of treatment during the first week. On the contrary, VEGF levels declined in the second week (7th to 14th day) of treatment in the Bioplasenton group and increased after treatment (98.23±66.73; $p = 0.015$; r = -0.681). Meanwhile, VEGF significantly declined between the 3rd day (107.45±55.87) to the 14th day (27.86 ± 16.49) ($p = 0.000$; r = -0.874) (Table III).

Table III

Correlation between VEGF levels based on length of Treatment

Group	3rd Day		7th Day 7		14th Day		Correlation		
	Mean	SD	Mean	SD	Mean	SD	3rd-7th day	7th-14th day	3rd-14th day
Control	107.45	55.87	80.49	55.12	27.86	16.49	-0.097	0.389	-0.874***
Drug-Established	55.19	31.61	98,.23	66.73	34.55	21.41	0.438	-0.681***	-0.267
Hylocereus polyrhizus	169.17	107.54	60.34	33.70	46.47	31.26	-0.702**	0.000	-0.727***

*Correlation between VEGF levels based on length of treatment at three different groups were analyzed using Spearman correlation (*p < 0.05, **p <0.01, and ***p <0.001).*

The VEGF levels on day 3 were higher in the *Hylocereus polyrhizus* topical group (169.17 µg/g ± 107.54 µg/g) as well as on day 14 (46.47 µg/g ± 31.26 µg/g) compared to the Bioplasenton and control groups (27.86 µg/g ± 16.49 µg/g). VEGF stimulates angiogenesis, affects epidermal wound closure and repair, and improves granulation tissue and wound repair quality[18]. VEGF effectively accelerates wound closure that is stimulated by angiogenesis, epithelialization, and collagen deposition[19].

This study shows that in macro, wound closure is better in the *Hylocereus polyrhizus* topical group than the control and Bioplasenton group (Figure II adnd Figure III) due to the high levels of VEGF at each stage of wound healing. VEGF illustrates the development of wound healing. During the proliferation phase, VEGF appears approximately 3-7 days after injury in which the capillary growth and differentiation are highest. During this period, VEGF induces the early stages of angiogenesis including dilation, permeability, migration, and proliferation[20].

The mean VEGF levels were higher in the *Hylocereus polyrhizus* topical group (108.84 µg/g) on day 3-7 versus the Bioplasenton group (-43.03 µg/g) and the control group (26.96 µg/g). Moreover, on day 3-14, the mean difference in VEGF was higher in the *Hylocereus polyrhizus* topical group (122.70 µg/g) compared to the Bioplasenton (20.64 µg/g) and control group (79.58 µg/g). This increase in VEGF can predict the occurrence of angiogenesis and better epithelialization process on the wound healing process.

This study is consistent with research concluding that the application of topical VEGF increases epithelialization and increased matrix deposition of collagen and cell proliferation[21]. VEGF also stimulates wound healing through angiogenesis, proliferation, and epithelialization[20]. VEGF is produced by many types of cells that participate in wound healing including endothelial cells, fibroblasts, soft tissue cells, platelets, neutrophils, and macrophages VEGF[22].

VEGF levels on day 3 were higher in the *Hylocereus polyrhizus* topical group (169.17 µg/g ± 107.54 µg/g) as well as on day 14 (46.47 µg/g ± 31.26 µg/g) compared to the Bioplasenton and control group (27.86 µg/g ± 16.49 µg/g). High levels of VEGF are produced during normal wound healing. This produces a strong angiogenic response. VEGF protein levels tend to be low in individuals who have chronic wounds such as patients with diabetes.

TGF-β1 levels of each group

Levels of TGF-β1 on the 3rd day after treatment were relatively similar across all groups (control group = 143.11±12.80; Bioplasenton group = 143.43±17.69; *Hylocereus polyrhizus* group = 141.98±5.16). There was an increase ($p = 0.003$; r = 0.775) of TGF-β1 levels on the 7th day after treatment (control group = 167.57±23.37; Bioplasenton group = 148.62±5.93; *Hylocereus polyrhizus* group = 149.59±3.98). While on the day 14th after the treatment, the TGF-β1 level was lower in the control group (153.80±6.55; p = 0.158; r = 0.435), whereas both *Hylocereus polyrhizus* and Bioplasenton group continued to increase, and the trend was nearly identical (178.59±36.62 and 157.53± 11.46 µg/g).

The Spearman correlation test from the control group showed that there was no correlation of time of the treatment (day 3, day 14) with high levels of TGF-β1 (p = 0.158, r = 0.435). The same thing also happened in the Bioplasenton group (p = 0.215, r = 0.386). Otherwise, the result in the *Hylocereus polyrhizus* group (p = 0.000. r = 0.872) implies a correlation of treatment time (day 3 or day 14) with high levels of TGF-β1. This indicated the tendency of TGF-β1 to increase over time during *Hylocereus polyrhizus*-enhanced wound healing (Table IV).

Table IV

Correlation between TGFβ-1 levels based on Length of Treatment

Group	3rd Day		7th Day		14th Day		Correlation		
	Mean	SD	Mean	SD	Mean	SD	3rd-7th day	7th-14th day	3rd-14th day
Control	143.11	12.80	167.57	23.37	153.80	6.55	0.676**	-0.314	0.435
Drug-Established	143.43	17.69	148.62	5.93	157.53	11.46	0.048	0.459	0.386
Hylocereus polyrhizus	141.98	5.16	149.59	3.98	178.59	36.62	0.755**	0.775**	0.872***

*Correlation between TGFβ-1 levels based on length of treatment at three different groups were analyzed using Spearman correlation (*p < 0.05, **p <0.01, and ***p <0.001).*

Correlation of TGF β-1, granulation score, and epithelialization score

Spearman correlation testing between the TGFβ-1 level with the tissue granulation score showed a correlation in the *Hylocereus polyrhizus* topical group that there is a tendency to improves tissue granulation (*p*: 0.051 and r: -0.466); the control group and the Bioplasenton group showed no correlation between the TGFβ-1 level with tissue granulation's score (*p*: 0.498 and r: 0.171) and (p: 0.890 and r: 0.035), respectively.

Another research related use of topical concentration red dragon fruit extract 7.5% proved better in repairing the granulation tissue and epithelialization tissue in the Wistar Non-DM group compared with the DM Wistar, so red dragon fruit extract potential to be used as a therapy in wound healing[23].

In the epithelialization score, the Spearman correlation testing between the TGFβ-1 level with epithelialization shows that there is a correlation with *Hylocereus polyrhizus* topical group (*p:* 0.001 and r: 0.708), while in the control group and Bioplasenton group, we found no correlation between the TGFβ-1 level with the epithelialization score (*p*: 0.075 and r: 0.429; and *p*: 0.651 r: 0.127), respectively (Table V).

Table V
The correlation between TGF β-1 and granulation, TGF β-1 and epithelialization based on different groups.

Group	TGF β-1 and Granulation		TGF β-1 and Epithelialization	
	r*	*p*	r*	*p*
Control	0.171	0.498	0.127	0.615
Bioplasenton	0.035	0.890	0.429	0.075
Hylocereus polyrhizus	-0.466	0.051	0.708	0.001

All of data were analyzed using Spearman correlation.

TGF-β1 level on wound healing

The results showed that TGF-β1 undergoes variations in the increased value in each group, but it increases the TGF-β1 on day 3 (inflammatory phase). This does not show a significant difference. The average levels of TGF-β1 increased in the Bioplasenton group (143.43 µg/g). This was slightly lower than the *Hylocereus polyrhizus* topical group (141.98 µg/g) compared to the control group (143.11 µg/g). On the 14th day, the average levels of TGF-β1 decreased significantly in the control group (6.55 µg/g) and the Bioplasenton group (11.46 µg/g) versus the *Hylocereus polyrhizus* topical group (36.62 µg/g).

The presence of TGF-β in the granulation tissues is important for efficient wound healing because TGF-β1 stimulates angiogenesis, fibroblast proliferation, differentiation of myofibroblasts, and matrix deposition. Moreover, TGF-β1 also plays an essential role in the three phases of wound healing: inflammation, proliferation, and maturation. Besides, hemostasis can be defined as a blockage of bleeding after injury, and it is involved in vasoconstriction, platelet collection, and blood coagulation[(24)].

The TGF-β1 increases the angiogenic properties of the endothelial source cells to facilitate blood supply to the injured area and stimulate fibroblast contraction for wound closure[(25)]. *Hylocereus polyrhizus* can increase the formation of fibroblast tissue. TheTGF-β1 is higher in *Hylocereus polyrhizus* than the Bioplasenton group and the control group. The results show that the *Hylocereus polyrhizus* topical group has a *p*-value = 0.000 implying that there is a correlation to treatment time (day 3, day 14) with high levels of TGF-β1 (r = 0.872).

Hylocereus polyrhizus also has a good effect on wound healing during the granulation phase. The results indicate that the granulation score of the *Hylocereus polyrhizus* topical group categories of thickness was 50% on day 3, 33.3% on day 7, and 0% on day 14. A Kruskal-Wallis statistical test indicated that *p* = 0.026 which means that there are differences in the granulation score of the *Hylocereus polyrhizus* topical group based on time (day 3, day 7, day 14).

In the maturation phase of wound healing, *Hylocereus polyrhizus* can nicely epithelialize. The wound closure on day 14 in the *Hylocereus polyrhizus* group was keratinized in one of the rats. The Kruskal-Wallis statistical test showed *p* = 0.002, which means that there is a difference in the epithelialization score of *the Hylocereus polyrhizus* topical group as a function of time (day 3, day 7, day 14).

Several studies have been conducted using similar active substances (polyphenolics) with the same content as dragon fruit in the treatment of wound healing in rats with induced allowance[(26)]. Similar observations have also been done on the effect of dragon fruit extract as a topical cream for granulation tissue. This supports collagen growth because it contains hexosamine that can accelerate the wound healing process[27].

CONCLUSION

Hylocereus polyrhizus topical (7.5%) increases VEGF levels in the inflammatory phase and increases the levels of TGF-β1 in the proliferative phase. The level of TGF-β1 have a tendency improves tissue granulation and epithelialization. Topical *Hylocereus polyrhizus* 7.5% has the same potential as Bioplasenton during wound healing.

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REFERENCES

1. McCosker, L., Tulleners, R., Cheng, Q., Rohmer, S., Pacella, T., Graves, N., & Pacella, R. Chronic wounds in Australia: a systematic review of key epidemiological and clinical parameters. *International Wound Journal*. 2018; 16:84–95.
2. Guest, J. F., Ayoub, N., McIlwraith, T., Uchegbu, I., Gerrish, A., Weidlich, D., Vowden, K., & Vowden, P. Health economic burden that different wound types impose on the UK's National Health Service. *International Wound Journal*. 2017; 14:322-330.
3. Yusuf, S., Kasim, S., Okuwa, M. & Sugama, J. Development of an enterostomal therapy nurse outpatient wound clinic in Indonesia : a retrospective descriptive study. *Wound Pract. Res.* 2013; 21:41–47.
4. Lobmann, R., Schultz, G. & Lehnert, H. Proteases, and diabetic foot syndrome: mechanisms and therapeutic implications. *Diabetes Care*. 2015; 28:461–71.
5. Sharad, S., Thangapazham, R. L. & Maheshwari, R. K. Phytochemicals in wound healing. *Adv. Wound Care*. 2016; 5:230–24.
6. Ruben F. Pereira, P. J. B. Traditional Therapies for Skin Wound Healing. *Adv. Wound care*. 2016; 5:208–229.
7. Haryanto *et al.* Effectiveness of Indonesian honey on the acceleration of cutaneous wound healing: an Experimental study in mice. *Wounds*. 2012; 24:110–119.
8. Abduelkarem, A., Dada, M. & Sharif., S. The provision of wound management service by community pharmacists in Dubai, Unated Arab Emirate. *Jordan Journal of Pharmaceutical Science*. 2012; 5:194-202.
9. Ramli, N. S., Brown, L., Ismail, P. & Rahmat, A. Effects of red pitaya juice supplementation on cardiovascular and hepatic changes in high-carbohydrate, high-fat diet-induced metabolic syndrome rats. *BMC Complement. Altern. Med.* 2014; 14, 189.
10. Sim Choo, W., & Khing Yong, W. Antioxidant properties of two species of Hylocereus fruits. *Advances in Applied Science Research*. 2011; 2:418–425.
11. Luo, H., Cai, Y., Peng, Z., Liu, T. & Yang, S. Chemical composition and in vitro evaluation of the cytotoxic and antioxidant activities of supercritical carbon dioxide extracts of pitaya (dragon fruit) peel. *Chem. Cent. J.* 2018; 8.
12. Masoko, P., Picard, J. & Eloff, J. N. The Use of a Rat Model to Evaluate the in Vivo Toxicity and Wound Healing Activity of Selected Combretum and Terminalia (Combretaceae) Species Extracts. *Onderstepoort J. Veterinary*. 2010; 77:1–7.
13. Prestes, Manoel Alberto, C. *et al.* Wound healing using ionic silver dressing and nonocrystalline silver dressing in rats 1 Cicatrização de feridas em ratos utilizando curativos com prata iônica e nanocristalina 1. *Acta Cir. Bras.* 2012; 27:761–767.
14. Wu, G., Ma, X., Fan, L., Gao, Y., Deng, H., & Wang, Y. Accelerating dermal wound healing and mitigating excessive scar formation using LBL modified nanofibrous mats. *Materials and Design*. 2020; *185*.
15. Abdullah, B. J., Atasoy, N., & Omer, A. K. Evaluate the effects of platelet rich plasma (PRP) and zinc oxide ointment on skin wound healing. *Annals of Medicine and Surgery*. 2019; 37:30–37.
16. Piskin, A., Altunkaynak, B. Z., Tümentemur, G., Kaplan, S., Yazici, Ö. B., & Hokelek, M. The beneficial effects of Momordica charantia (bitter gourd) on wound healing of

rabbit skin. *Journal of Dermatological Treatment*. 2014; *25*:350–357.

17. Sami, D. G., Heiba, H. H., & Abdellatif, A. Wound healing models: A systematic review of animal and non-animal models. *Wound Medicine*. 2019; 24:8–17.
18. Perini, J. A., Angeli-Gamba, T., Alessandra-Perini, J., Ferreira, L. C., Nasciutti, L. E., & Machado, D. E. Topical application of Acheflan on rat skin injury accelerates wound healing: A histopathological, immunohistochemical and biochemical study. *BMC Complementary and Alternative Medicine*. 2015; 15:1–8.
19. Johnson, K. E. & Wilgus, T. A. Vascular Endothelial Growth Factor and Angiogenesis in the Regulation of Cutaneous Wound Repair. 2014; 3:647–661.
20. Semadi, N. I. The role of VEGF and TNF-alpha on epithelialization of diabetic foot ulcers after hyperbaric oxygen therapy. *Open Access Macedonian Journal of Medical Sciences*. 2019; *7*:3177–3183.
21. Johnson, K. E., & Wilgus, T. A. Vascular Endothelial Growth Factor and Angiogenesis in the Regulation of Cutaneous Wound Repair. *Advances in Wound Care*. 2014; 3:647–661.
22. Muguregowda, H. T., Pramod, K., Padmanabha, U. E. G., Udesh, K., Udaya, K., & Pragna, R. Role of angiogenesis and angiogenic factors in acute and chronic wound healing. *Plastic and Aesthetic Research (PAR)*. 2015; 2:243–249.
23. Zarei, F., & Soleimaninejad, M. Role of growth factors and biomaterials in wound healing. *Artificial Cells, Nanomedicine and Biotechnology*. 2018 46:906–911.
24. Tahir, T., Syakib, B., Patelongi, I., Aman, M., Miskad, U. A., Maryunis, M., Yusuf, S., Rahayu, A. I., Syam, A. D., & Hasriyani. *Evaluation of Topical Red Dragon Fruit Extract Effect (Hylocereus Polyrhizus) on Tissue Granulation and Epithelialization in Diabetes Mellitus (DM). International Journal of Sciences.* 2017; 2:309–320.
25. Finnson, K. W., Mclean, S., Guglielmo, G. M. Di & Philip, A. Dynamics of Transforming Growth Factor Beta Signaling in Wound Healing and Scarring. *Wound Heal. Soc.* 2013; 2:195–214.
26. Pakyari, M., Farrokhi, A., Maharlooei, M. K. & Ghahary, A. Critical Role of Transforming Growth Factor Beta in Different Phases of Wound Healing. *Adv. wound care*. 2013; 2:215–224.
27. Feng-mei, D., Peng, Z., Jia-gui, J. I. N. & Xin-chun, W. Effect of pomegranate peel polyphenol gel on cutaneous wound. 2013; 126:1700–1706.
28. Eldeen, I., Foong, S., Ismail, N., & Wong, K. Regulation of Pro-Inflammatory Enzymes by the Dragon Fruits from Hylocereus undatus (Haworth) and Squalene - its Major Volatile Constituents. *Pharmacognosy Magazine*. 2019; 15:38.46.

تأثيرات مستخلصات فاكهة التنين الحمراء (Hylocerus polyrhizus) على مستوى العامل النموي لبطانة الأوعية الدموية (VEGF) وتحويل العامل النموي بيتا 1 (TGF-β1) في علاج الجروح الحادة لجرذان ويستار

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ملخص

هذه الدراسة تهدف إلى تحديد تأثيرات مستخلصات فاكهة التنين الحمراء (Hylocerus polyrhizus) على مستوى العامل النموي لبطانة الأوعية الدموية (VEGF) وتحويل العامل النموي بيتا 1 (TGF-β1) في علاج الجروح الحادة لجرذان ويستار . وكانت مادة ألبينو لجرذان ويستار الذكور (n = 54) تنقسم إلى ثلاثة مجموعات، وهي التحكم السلبي والتحكم الإيجابي و فاكهة التنين الحمراء. أصيبت هذا الجرذان–في هذه التجربة–على الظهر الأيمن والأيسر مع خزعة 8 ملم لكمة. وثم وضع كريم مستخلصات فاكهة التنين الحمراء بقدر 7.5 بالمائة على سطح الجرح باستخدام قطعة قطن. واستخدم الباحث المقايسات المناعية المرتبطة بالإنزيم (ELISA) في اليوم الثالث والسابع والرابع عشر من أجل تقييم العامل النموي لبطانة الأوعية الدموية و تحويل العامل النموي بيتا 1. تم تحليل هذه التجربة باستخدام اختبار t المستقل واختبار t المزدوج (SPSS 21, Chicago Inc.). وكان لمجموعة مستخلصات فاكهة التنين الحمراء أعلى المستوى من العامل النموي لبطانة الأوعية الدموية وتحويل العامل النموي بيتا 1 بمقارنة بالتحكم الإيجابي بقدر (p = 0.011; r = -0.584) و (p = 0.000; r = 0.888) على التوالي في اليوم الرابع عشر. لقد وجدنا ارتباطًا بين مستوى تحويل العامل النموي بيتا 1 ودرجة تحبيب الأنسجة بقدر p (0.051) وr (-0.466) بالإضافة إلى مستويات تحويل العامل النموي بيتا 1 مع درجة الاندمال الظهاري بقدر p (0.001) وr (0.708) في المجموعة الموضعية لفاكهة التنين الحمراء. واستنتج هذا البحث إلى أن مستخلصات فاكهة التنين الحمراء يمكن أن يؤدي إلى سرعة علاج الجروح أثناء مرحلة الالتهاب والانتشار.

الكلمات الدالة: فاكهة التنين الحمراء (Hylocerus polyrhizus) ، العامل النموي لبطانة الأوعية الدموية (VEGF)، تحويل العامل النموي بيتا 1 (TGF-β1) ، علاج الجروح.

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