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# EVALUATION OF THE WOUND HEALING ACTIVITY OF *HYOSCYAMUS NIGAR* SEED POWDER ON THE WISTAR ALBINO RATS

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## ABSTRACT

Wounds remain a huge public health issue, at least in terms of morbidity and long term disability, throughout the world, especially in the developing countries. Plant-derived natural products are significant as sources of medicinal agents and models for the design of new remedies. This study was done to prove the effectiveness of *Hyoscyamus niger* on the management of wounds through evaluating the wound healing activity of *Hyoscyamus niger* seed powder on wistar albino rats. Along with that compare the effectiveness of *Hyoscyamus niger* seed powder between male and female rates based on Unit Healing Time and wound closure rate. Wister albino rats weighing 200-250g used for experimental study. Animals were divided into three groups of each with 6 animals. Each group consists of 3 male and 3 female rats. The animals of group A was left untreated and considered as control. Group B was served as standard and it received cicatrin powder. Group C was considered as test and treated with prepared test drug. The independent t-Test analysis of the wound circumferences of standard and the test drug initially showed a significant value of 0.374 and 0.305 which is much higher than the p-value of 0.05. Whereas the final readings of the wound circumference between the test drug and the standard drug showed a significant value of 0.001 and 0.004. In other words, which indicates that the test drug is much more effective in the treatment of wound healing than that of the standard drug. The present study revealed *Hyoscyamus niger*

seed powder has the significant accelerating wound healing activity in excised wound model in wistar albino rats also readings shows the female rats have higher healing rate than the male rats. The readings of drug effectiveness and Unit Healing Time leads to the conclusion of that, the test drug is more effective for wound healing than stranded .It confirms the potential value of *Hyoscyamus niger* seed powder to be considered as a natural product for wound healing.

**KEYWORDS:** *Hyoscyamus niger*, Wound Healing, Wistar albino rats.

## 1. INTRODUCTION

Siddha system of medicine is most ancient spiritually enriched one. Traditionally it is taught that the siddhas laid the foundation for this siddha system of medicine. Traditional Siddha medicine uses the knowledge, skills and practices based on theories, beliefs and experiences indigenous to its people and culture, for maintenance of health (Subramanian et al., 2018). Wounds have affected humans since prehistoric times and the treatment and healing of wounds is an art as old as humanity (Robson et al., 2001). Wounds remain a huge public health issue, at least in terms of morbidity and long term disability, throughout the world, especially in the developing countries (Mantle et al., 2001).

Wound care has returned to the roots of medicine and is embracing some of the remedies used millennia ago. Plant-derived natural products are significant as sources of medicinal agents and models for the design of new remedies (Fan et al., 2006). Nowadays plant-derived compounds play an important role in drug development (Balandrin et al., 1993). As plants are a source of many bioactive compounds and many plant ingredients are traditionally used to accelerate healing, scientists go back to traditional folk medicines as they are generally characterized by high acceptability and good toleration (Jagetia et al., 2004).

The wound may be defined as a loss or breaking of cellular and anatomical or functional continuity of living tissues (Suruse, 2011). A wound is characterized by the loss of epithelial integrity, disruption of normal structure and function of the skin and its underlying tissues (Senthil et al., 2006). It may be produced by physical, chemical, thermal, microbial, or immunological insult to the tissue.

*Hyoscyamus nigar* commonly known as Black henbane, is a member of the Solanaceae or nightshade family. Black henbane is an annual or biennial plant. Previous phytochemical

studies on *Hyoscyamus nigar* included characterization of hyoscyamine, apohyoscine, apohyoscine, scopolamine, skimmianine, apoatropine, a-belladonnine, b-belladonnine, tropine (Hashimoto et al., 1989). The action of seeds of the plant include hypnotic, sedative, anodyne, antispasmodic, astringent and mild diuretic (Murugesamudaliyar, 2008).

*Hyoscyamus nigar* is widely used by the traditional medical practitioners for curing various diseases in their day to day practice. commonly in bleeding gums, dental caries, rheumatoid arthritis, worm infection, dyspepsia, flatulence, cardiac debility, epistaxis, hematemesis, haemoptysis, asthma, conjunctivitis, anxiety, insomnia, scabies, spermatorrhoea, leucorrhoea, amenorrhoea, and neuralgia (Aparna et al., 2015).

Murugesamudaliyar, 2008 stated that the *Hyoscyamus nigar* is used to treat polyuria, spermatorrhoea, wound, diarrhoea, eczema, *vatha* and *kapha* disorders.

There are many researches were conducted on *Hyoscyamus nigar* such as anti-inflammatory, analgesic, antipyretic effects, antimicrobial effect, antioxidant effect, insecticidal effect, anti-asthmatic, anti-allergic effects, hepatoprotective effect, anti hyperuricemic, and xanthine oxidase inhibitory effects. However none of the researches were conducted on wound healing activity.

There are several medications available for wound healing such as silver sulfadiazine, framycetin sulphate, povidone-iodine, chlorhexidine gluconate, betamethasone valerate, clobetasol propionate, mometasone furoate etc (Davidson, 2010). but these substance have several adverse effects such as causing anaphylaxis, deposited in various organ like brain, liver, kidney then produce toxicity to cells, hyper or hypothyroidism and cytotoxicity(Apirujee punjataewakupt et al., 2019). There is a need to discover high effectiveness, less side effect and cost effective medicine. Since *Hyoscyamus niger* used to treat ulcers by the siddha traditional physicians for more than 1000 years, it has selected to evaluate its effectiveness through animal study.

The study was conducted to prove the effectiveness of *Hyoscyamus niger* on the management of wounds. The objective of the study is to evaluate the wound healing activity of *Hyoscyamus niger* seed powder on wistar albino rats. We measure the Wound Healing Rate in control, standard and test groups of wistar albino rats and compare the Wound Healing Rate among these groups of wistar albino rats through the following criteria; Assessment of

wound size, Assessment of wound edges, Assessment of necrotic tissue type, Assessment of necrotic tissue amount, Assessment of exudate type, Assessment of exudate amount and Assessment of skin colour surrounding wound along with that we compare the effectiveness of *Hyoscyamus niger* between male and female rates based on Unit Healing Time and wound closure rate.

## 2. METHODOLOGY

It is a Randomized Controlled Comparative Animal Experimental Trial. Seeds of *Hyoscyamus niger* was selected according to the literature citation. Murugesamuthaliyar, 2008 stated that the *Hyoscyamus niger* could be used to treat wound. Seeds of *Hyoscyamus niger* was collected from the medical shop, which is situated in Trincomalee. Seeds of *Hyoscyamus niger* was authenticated by the Kunapadam Division, Unit of Siddha Medicine, Trincomalee Campus. Seeds of *Hyoscyamus niger* was collected and removed the dirt and dust from it. Seeds were thoroughly washed under running tap water. After that it was dried under sun shade. Dried seeds of *Hyoscyamus niger* was made as powder by using mechanical grinder. The powder was stored air tightly and labelled.

Wister albino rats weighing 200-250g were obtained from Medical Research Institute of Sri Lanka for experimental study. Wister albino rats were habitat in well ventilated room and feed with pellets twice a day and watered per hour. The cages of every group was cleaned once in three days. Wister albino rats weighing 200-250g used for experimental study. Animals were divided into three groups of each with 6 animals. Each group consists of 3 male and 3 female rats. Group A was consider as control, group B was consider as standard and group C was *Hyoscyamus niger* powder treated group in excision wound model. Each group consists of 3 male and 3 female rats (Ehab et al, 2018).

The surgical interventions were carried out under the sterile conditions using ketamine anaesthesia (30 mg/kg, IP). Hairs were removed from the dorsal thoracic region of the rats. A circular wound of approximately 120 $mm^2$ was marked on the back of the rat by a standard ring. Full thickness of the marked skin was cut carefully. Then Animals were kept in separate cages (Agarwal et al., 2009).

The animals were divided into 3 groups of 6 each. The animals of group A was left untreated and considered as control. Group B was served as standard and it received cicatrin powder. Group C was considered as test and treated with prepared test drug. Powder of test drug and

standard drug was topically applied every day on respective groups and bandaged starting from the day of operation, till complete wound healing enclosure occurs (Susman, 1967).

The parameters assessed to check the wounds healing activity include Bates-Jensen wound assessment tool (BJWAT), wound contraction rate and unit healing time. The data was entered, coded, and analysed using statistical package for the social sciences (SPSS). Statistical analysis was done by Levene's test, Independent sample T-test and one-way analysis of variance (ANOVA) by using IBM, SPSS Version 23 for the circumference of wound and p value < 0.05 was considered statistically significant (Masuram et al., 2014).

## 3. RESULTS AND DISCUSSION

The data were obtained from the day of wounded and once in every two days. Wounds have measured once in two days. The direct observation of wound circumferences, edges, exudate type, exudate amount, skin colouration around wound and necrotic tissue were recorded.

| Day | Control | Standard | Test |
|---|---|---|---|
| **Day 0** |  |  |  |
| **Day 2** |  |  |  |
| **Day 4** |  |  |  |
| **Day 6** |  |  |  |
| **Day 8** |  |  |  |

| | | | |
|---|---|---|---|
| **Day 10** |  |  |  |
| **Day 12** |  |  |  |
| **Day 14** |  |  |  |

**Figure No 01: Wound contraction of the all groups of rats**

Medicinal plants are used directly or indirectly for the treatment of many diseases. Especially, in most developing countries, the use of medicinal plants in traditional medicine has been observed for maintaining good health. Around the world, scientists are trying to investigate the benefits of medicinal plants to assist the sufferings of humanity. Plants are used in more than 30% of the world's pharmaceutical preparations (Shinwari et al., 1998). The stanza about general character of *Hyoscyamus niger* plant mentioned in the ancient siddha text book of *Kunapadam* was indicated that, *Hyoscyamus niger* plant can cure the wound, based on that I selected the seed powder of this plant for the study hence the study focus to evaluate the wound healing activity of seed powder of *Hyoscyamus niger* on wistar albino rats. In this study healing activity was studied for 14 days in 3 groups. The animals were divided into 3 groups of 6 each. The animals of group A was left untreated and considered as control. Group B was served as standard and it received cicatrin powder. Group C was considered as test and treated with prepared test drug.

Data was collected once in 2 days from each three groups and recorded clearly. The parameters assessed to check the wounds healing activity will be Bates-Jensen wound assessment tool (BJWAT), wound contraction rate and unit healing time. Each group was observed that changes of healing activity wound size, Exudates type, exudates amount, edges, necrotic tissue type and skin colour surrounding the wound that compare with other group and also recorded. Wound contraction rate was measured by planimetric measurement of wound area on alternate days of post wounding. This was done by tracing the wound on a

transparent butter paper and then transferred to 1mm2 graph sheets. Reduction in the wound area was expressed as percentage of the original wound size.

The data was entered, coded, and analysed using statistical package for the social sciences (SPSS). Statistical analysis was done by Levene's test, Independent sample T-test and one-way analysis of variance (ANOVA) by using IBM, SPSS Version 23 for the circumference of wound and p value < 0.05 was considered statistically significant.

**Table 3.1: Reduction of circumference of wound before and after treatment in standard and test groups.**

| | **Levene's Test for Equality of Variances** | | **t-test for Equality of Means** | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **F** | **Sig.** | **t** | **df** | **Sig. (2-tailed)** | **Mean Difference** | **Std. Error Difference** | **95% Confidence Interval of the Difference** | |
| | | | | | | | | **Lower** | **Upper** |
| 1st Day<br>Equal variances assumed | 1.750 | .215 | -.931 | 10 | .374 | -3.50000 | 3.76017 | -11.87818 | 4.87818 |
| standard<br>Equal variances assumed test | | | -.931 | 9.669 | .305 | -3.50000 | 3.76017 | -11.91724 | 4.91724 |
| 8th Day<br>Equal variances assumed | 21.575 | .001 | 4.025 | 10 | .042 | 17.33333 | 4.30633 | 7.73824 | 26.92843 |
| standard<br>Equal variances assumed test | | | 4.025 | 5.388 | .030 | 17.33333 | 4.30633 | 6.49934 | 28.16732 |
| 14th Day<br>Equal variances assumed | 6.250 | .031 | 5.000 | 10 | .004 | .83333 | .16667 | .46198 | 1.20469 |
| standard<br>Equal variances assumed test | | | 5.000 | 5.000 | .001 | .83333 | .16667 | .40490 | 1.26176 |

According to the table 5.1, the independent t-Test analysis of the wound circumferences of standard and the test drug initially showed a significant value of 0.374 and 0.305 which is much higher than the p-value of 0.05. On 8th day the values are 0.042 and 0.030. Whereas the final readings of the wound circumference between the test drug and the standard drug showed a significant value of 0.001 and 0.004. In other words, which indicates that the test drug is much more effective in the treatment of wound healing than that of the standard drug.

**Table 3.2: ANOVA analysis of the circumference of the wound for test, standard and control group with days.**

| | | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|---|
| FirstDay | Between Groups | 40.333 | 1 | 40.333 | .917 | .361 |
| | Within Groups | 439.667 | 10 | 43.967 | | |
| | Total | 480.000 | 11 | | | |
| SecondDay | Between Groups | .083 | 1 | .083 | .003 | .958 |
| | Within Groups | 282.833 | 10 | 28.283 | | |
| | Total | 282.917 | 11 | | | |
| FourthDay | Between Groups | 147.000 | 1 | 147.000 | 5.140 | .087 |
| | Within Groups | 286.000 | 10 | 28.600 | | |
| | Total | 433.000 | 11 | | | |
| SixthDay | Between Groups | 385.333 | 1 | 385.333 | 3.833 | .079 |
| | Within Groups | 1005.333 | 10 | 100.533 | | |
| | Total | 1390.667 | 11 | | | |
| EighthDay | Between Groups | 901.333 | 1 | 901.333 | 16.201 | .059 |
| | Within Groups | 556.333 | 10 | 55.633 | | |
| | Total | 1457.667 | 11 | | | |
| TenthDay | Between Groups | 80.083 | 1 | 80.083 | 2.735 | .049 |
| | Within Groups | 292.833 | 10 | 29.283 | | |
| | Total | 372.917 | 11 | | | |
| TwelethDay | Between Groups | 14.083 | 1 | 14.083 | 1.988 | 025 |
| | Within Groups | 70.833 | 10 | 7.083 | | |
| | Total | 84.917 | 11 | | | |
| FouteenthDay | Between Groups | 1.333 | 1 | 1.333 | 1.081 | .003 |
| | Within Groups | 12.333 | 10 | 1.233 | | |
| | Total | 13.667 | 11 | | | |

One-way ANOVA analysis of the circumference of the wound for test, standard and control groups on 1$^{st}$, 2$^{nd}$,4$^{th}$, 6$^{th}$, 8$^{th}$, 10$^{th}$, 12$^{th}$ and 14$^{th}$ dy. Initial circumference of the wound of the three different groups is 0.396 which is much higher than the p value of 0.05. However, the significant value of the final circumference of the wound of the three different groups is 0.003 which is lesser than the p value of 0.05. Which means the final circumferences of the wound showed that the significant differences statistically between the three groups.

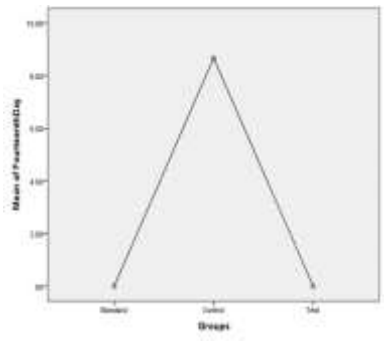

**Figure 02: Mean value of the three different groups Test, Standard and Control.**

These graphs elicits the mean value of the three different groups Test, Standard and Control. Whereas on the 14th day of the research process wound circumference between the test drug and the standard drug showed a significant value of 0.001 and 0.004. test groups showed less mean values than standard in the reduction of the circumferences of the wound created, whereas the control doesn't heal that much this also is a good evident that the test drug test drug is much more effective in the treatment of wound healing than that of the standard drug.


**Figure 03: Relations between the Benson score for wound edges related with number of days.**

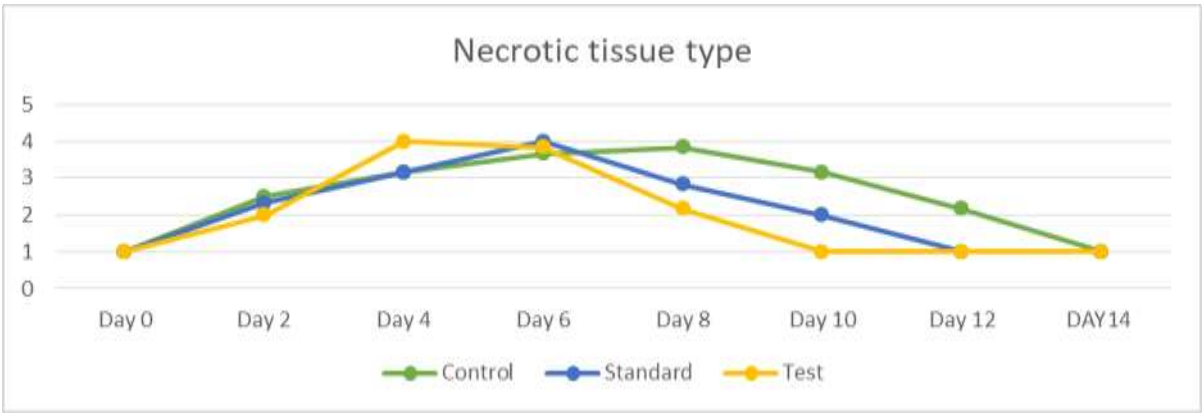


**Figure No 04: Relations between the Benson score for necrotic tissue type and number of days.**

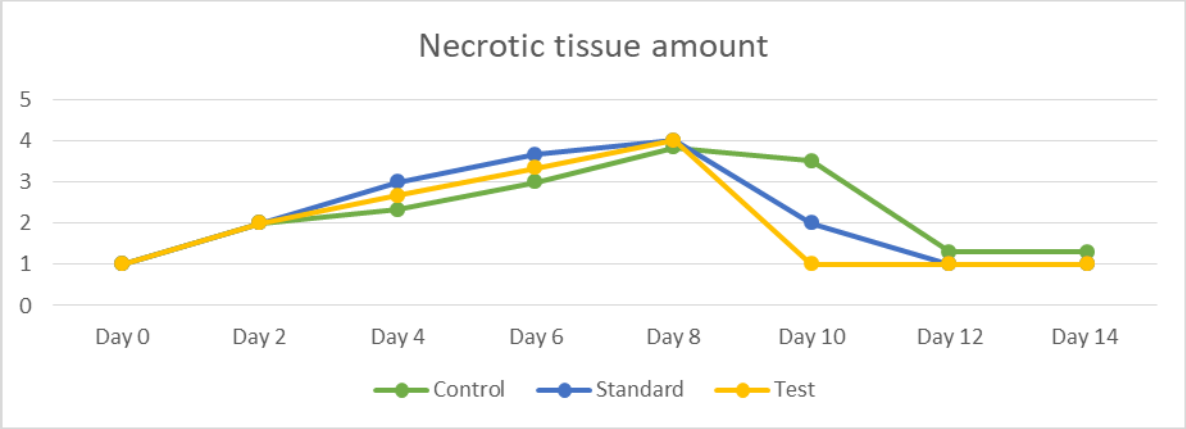


**Figure No 05: Relations between the Benson score for necrotic tissue amount and number of days.**

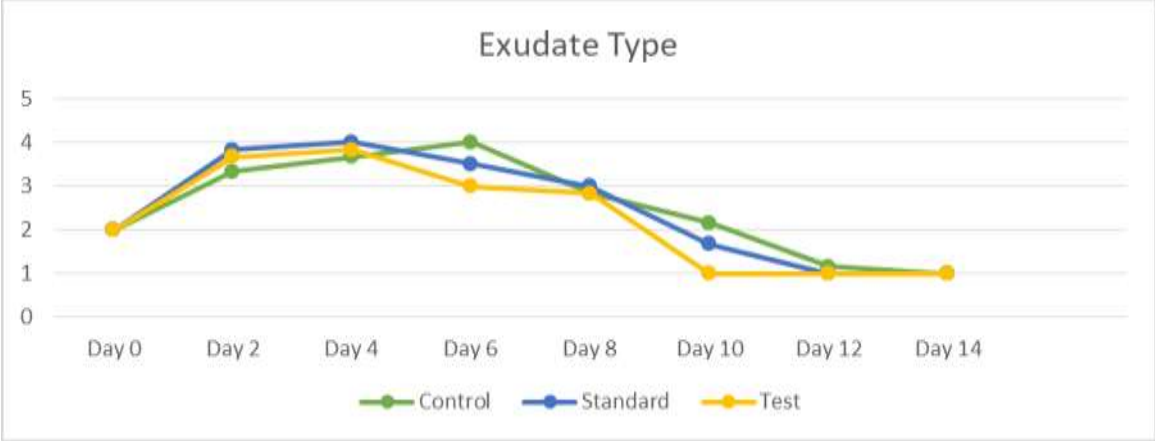


**Figure No 06: Relations between the Benson score for necrotic tissue type and number of days.**

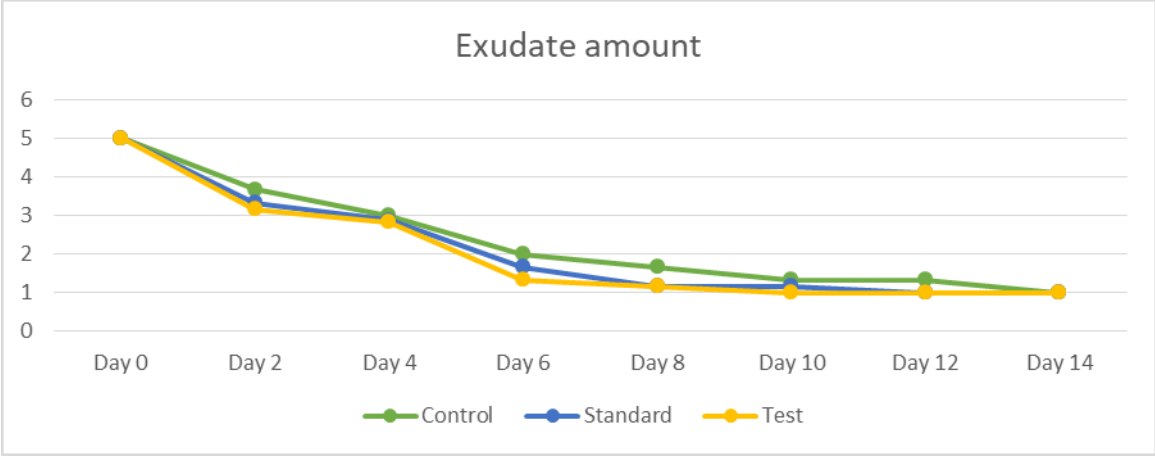


**Figure No 07: Relations between the Benson score for exudate amount and number of days.**

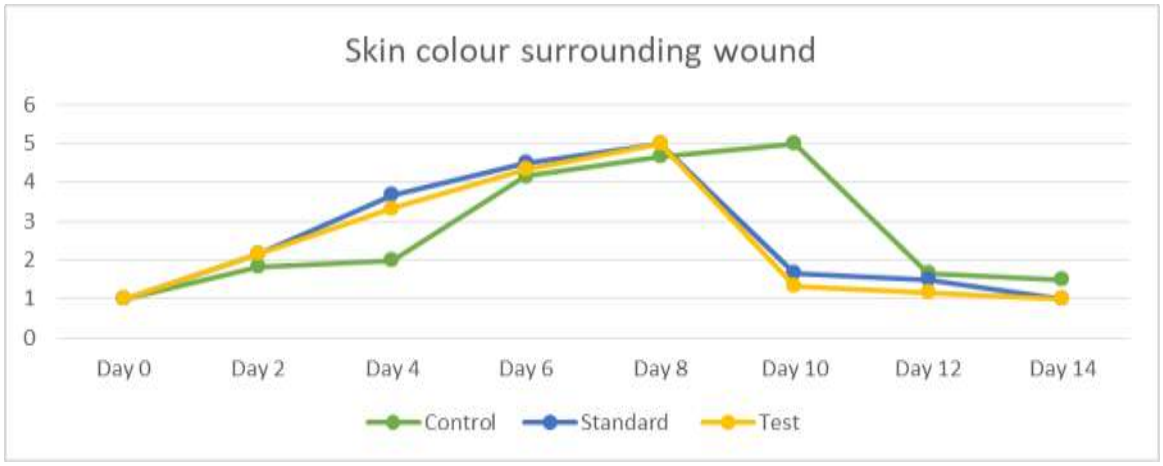


**Figure No 08: Relations between the Benson score for skin colour of wound surrounding and number of days.**

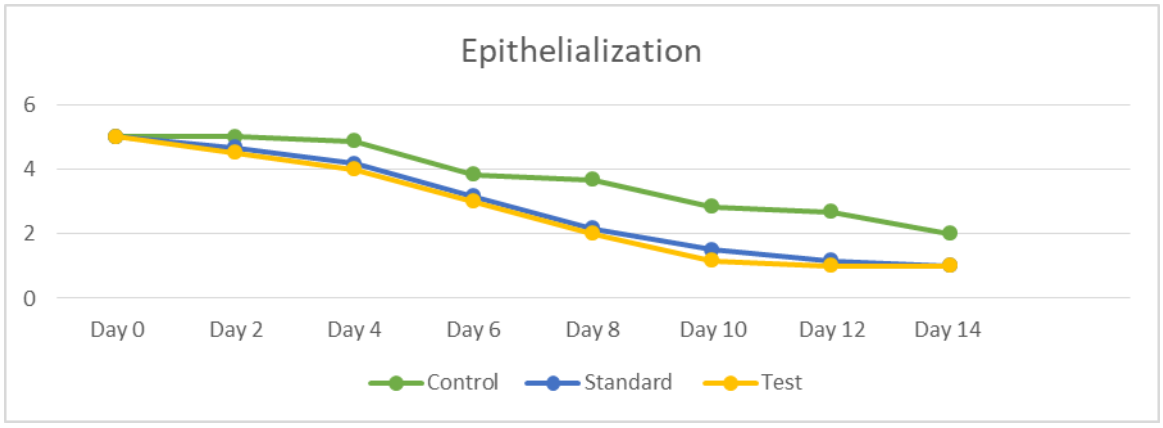


**Figure No 09: Relations between the Benson score for epithelialization and number of days.**

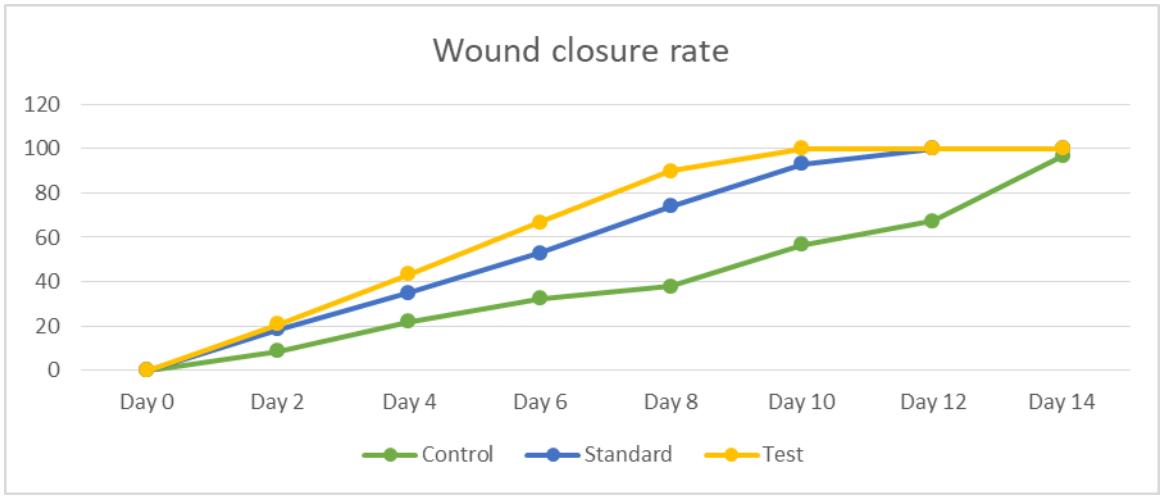


**Figure No 10: Relations between the Benson score for wound closure rate and number of days.**

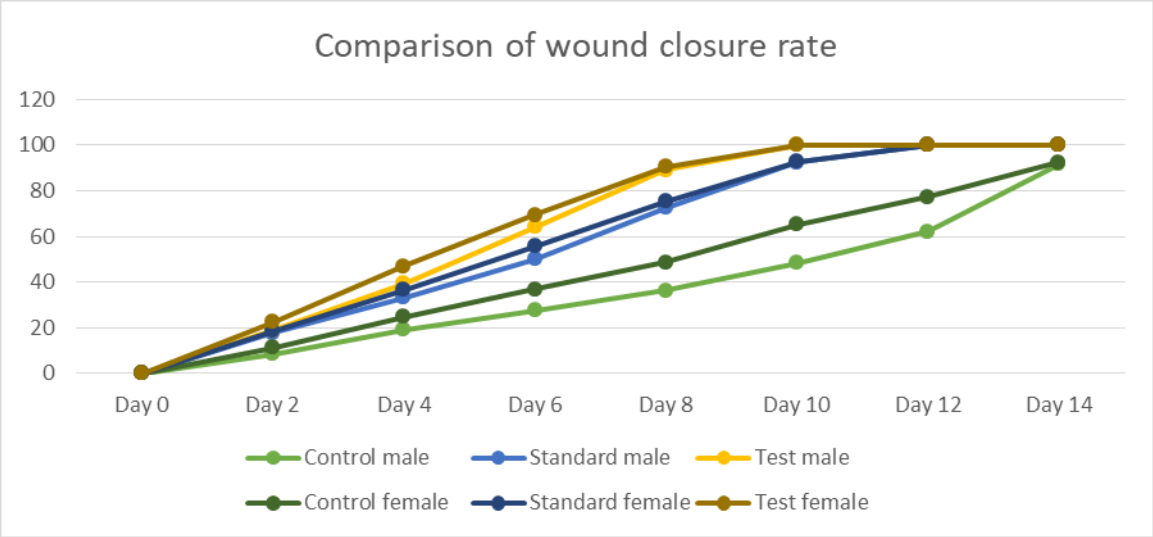


**Figure No 11: Comparison of wound closure rate among the groups.**

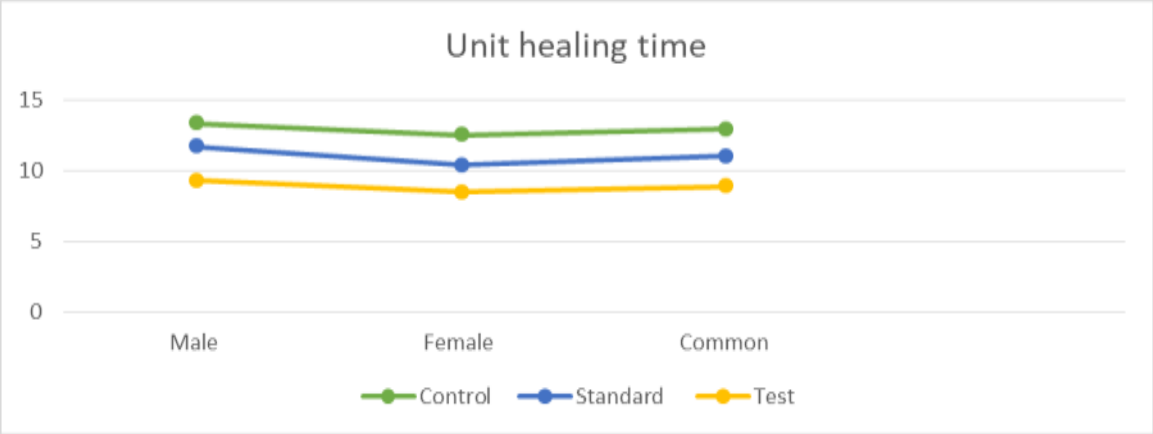


**Figure No 12: Relations between the unit healing time and groups.**

According to Rono, 2013 Ovariectomized mice healed dermal wounds slower than controls, Estrogens have also been shown to have beneficial effects on wound healing. In castrated male rats, estradiol, administered via a subcutaneous pellet (3.2 µg/kg/day), increased re-epithelialization rates in dermal wounds (Rono, 2013). Here also the female rats have higher healing rate than the male rats which match with the above statement.

*Hyoscyamus niger* contains chemical compositions like hyoscyamine, scopolamine grossamide, hyoscyamoside, rutin, balanophonin, vanillin, hyosgerin and saponins (Lijun, et al.,2011). Grossamide possesses potential anti-inflammatory effects, Balanophonin shows potent antioxidant, and anti-cancer activities and significant antibacterial activity. Rutin can also be used as an anti-inflammatory agent because of the binding of free radicals that

prevents the induction of inflammatory cytokine transcription factors. Vanillin has antimicrobial action and scopolamine has antioxidant activities (Kihyun, 2010).

Anti-microbial activity destroys microbes, inhibit their growth, or prevents or counteracts their pathogenic action. These actions help to stop the spreading of microorganisms as well as to destroy the microorganisms. Anti-inflammatory action helps to counter act the inflammation. The anti-inflammatory drugs all work by blocking cyclooxygenase (cox) enzymes. There are two main types of cox enzymes. Cox-1, cox-2. Pain relieving and anti-inflammatory effects of anti-inflammatory drugs are mainly due to inhibition of cox-2 (Gao et al., 2010). Anti-oxidant action is play important role in treatment of wounds. Wound healing may be affected or delayed by the production of free radicals at or around the wound site. The free radicals are produced by activated platelets, neutrophils, and macrophages during the inflammatory phase. The body immune system produces this free radical to destroy any invading microorganisms at the wound site however overproduction these free radicals may cause damage to the tissue by lipid peroxidation, breakage of DNA and enzyme inactivation. Thus, agents that display significant antioxidant activities may be used to protect the cells from being damaged by the excess of free radicals there by stimulating wound healing process. (Mccarthy et al., 1992).

Anti-inflammatory, antimicrobial (antiviral, antibacterial, antifungal), styptic, counter irritant, astringent, anti-oxidant these are the main pharmacological action involving in treatment of skin diseases. Chemical constituents and their pharmacological actions suggest that *Hyoscyamus niger* have anti-inflammatory, antimicrobial, astringent and antioxidant action that helps to cure the wounds.

According to siddha philosophy wound arises due to imbalance of *vatha dosha*. This will affect the *charam* and *ceneer*. Then it will affect other t*hathukal* and produce the wound. First *vatha dosha* affected followed by *pitha dosha* and *kapha dosha*. It increases the severity of the disease. So the drug that used to treat wound should balance *vatha, pitha* and *kapha dosha*. (Sanmugavelu, 2010). *Hyoscyamus niger* have hot potency. It pacifies *vatham* and *kabham* and aggravates *pitham*. It has pungent taste. It pacify *kapham* and aggravates *vatham* and *pitham* (Ganapathy, 2007). According to Siddha aspect to treat wound the drug should balance the *tridoshas*. This drug have hot potency and pungent taste. Combination of can balance the *vatha, pitha* and *kabha doshas* and maintain the equilibrium of *tridosha.* So it is clearly denotes the *Hyoscyamus niger* seed powder is effective on wound healing.

## 4. CONCLUSION

The present study revealed *Hyoscyamus niger* seed powder has the significant wound healing activity in excised wound model in wistar albino rats. The test drug is more effective for wound healing than stranded. It confirms the potential value of Hyoscyamus *niger* seed powder to be considered as a natural product for wound healing.

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