



## Research Article

## A COMPARATIVE STUDY OF THERAPEUTIC EFFECT OF NEEM (*AZADIRACHTA INDICA* A.JUSS.) AND HARIDRA (*CURCUMA LONGA* LINN) IN THE MANAGEMENT OF WOUND HEALING

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**KEYWORDS:** Wound healing, *Neem*, *Azadirachta Indica* A.Juss., *Haridra (Curcuma Longa* Linn, *Vrana*, *Ropan*, *Shodhan*.

### ABSTRACT

Wound is simply a disruption of any tissues: soft tissue or bone or internal organs. Wound may be produced by physical, chemical, thermal, microbial or immunological insult to the tissue. It is common problems from ancient time. Although wound healing is a natural restorative response to any kind of tissue injury but due to bacterial contamination of an open wound delays the process of healing. In Ayurveda the term used for wound is *Vrana*. In this study *Neem* and *Haridra* was taken which has been mentioned in Ayurvedic classics for the treatment of wound. In present clinical study 54 patients with classical signs and symptoms of wound were randomly selected and divided into three groups A, B and C. The fine powder and decoction were prepared from *Neem (Azadirachta indica* A.Juss.) and *Haridra (Curcuma longa* Linn). Decoction applied externally for dressing of wound and 3gm. fine powder given orally twice a day according to their group for 30 days. The values of scores of different variables i.e. signs and symptoms recorded before and after the treatment were statistically analyzed. The result showed highly significant decline in the severity of subjective parameters like size, discharge etc. but group C showed better results in size, tenderness and discharge compare to that of group A and B. The study revealed that both drugs have excellent properties to accelerate wound healing but combined forms of two drugs are more potent than using alone.

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### INTRODUCTION

The term wound is break in the continuity of soft parts of body structures caused by violence or trauma to tissues<sup>[1]</sup> In Ayurvedic classical texts term used for wound is *Vrana*<sup>[2]</sup> and defined as "The destruction/ break/ rupture/discontinuity of body tissue /a part of body'.

### Classification of wound

In Ayurveda *Vrana* is classified as: According to aetiology *Nija* and *Agantuja vrana*<sup>[3]</sup>. Clinical classification *Suddha vrana* and *Dusta vrana*<sup>[4]</sup>. According to prognosis *Sadhya vrana*, *Krichhya sadhya vrana*, *Yapya vrana* and *Asadhya vrana*.<sup>[5-8]</sup>

According to modern classification wounds are classified as: tidy wound, untidy wound, acute, chronic, clean incised, lacerated, abrasion, crush injury, clean, contaminated, wound and clean contaminated etc.<sup>[9]</sup>

### Wound healing modern view<sup>[10]</sup>

Wound healing is a natural restorative response to any kind of tissue injury. Wound healing can be accomplished in one of the following two ways:

Healing by first intention (primary union) and healing by second intention (secondary union).

**1. Healing by first intention (primary union):** This types of healing mainly occurs in those wound which is clean and uninfected, surgically incised, without much loss of cells and tissues, and edges of wound are approximated by surgical sutures.

The sequence of events in primary union is described below:

### Initial haemorrhage

Immediately after injury, the space between the approximated surfaces of incised wound is filled with blood which then clots and seals the wound against dehydration and infection.

### Acute inflammatory response

This occurs within 24 hours with appearance of polymorphs from the margins of incision. By third day, polymorphs are replaced by macrophages.

## Epithelial changes

The basal cells of epidermis from both the cut margins start proliferation and migrating towards incisional space in the form of epithelial spurs. A well approximated wound is covered by a layer of epithelium in 48 hours. The migrated epidermal cells separate the underlying viable dermis from the overlying necrotic material and clot, forming *scab* which is cast off. By 5<sup>th</sup> day the basal cells from the margins continue to divide which forms multilayered new epidermis.

## Organisation

By 3<sup>rd</sup> day, fibroblast also invades the wound area. By 5<sup>th</sup> day, new collagen fibrils start forming which dominate till healing is completed. In 4<sup>th</sup> week, the scar tissue with scanty cellular and vascular elements, a few inflammatory cells and epithelialised surface is formed.

**Suture tracks:** Each suture track is a separate wound and incites the same phenomena as in healing of the primary wound. When sutures are removed around 7<sup>th</sup> day, much of epithelialised suture track is avulsed and remaining epithelial tissue in the track is absorbed. Thus, the scar formed in a sutured wound is neat due to close apposition of the margins of wound.

## 2. Healing by second intention (Secondary union):

This is defined as healing of a wound which has the following characteristics:

- Open with a large tissue defect, at times infected,
- Having extensive loss of cells and tissues,
- The wound is not approximated by surgical sutures but is left open.

The basic events are similar to primary union but differ in having a large tissue defect which has to be bridged. Hence healing takes place from the base upwards as well as from margins inwards. Here wound healing is slow and results in a large, at times ugly, scar as compared to rapid healing and neat scar of primary union.

## Wound contraction

Contraction of wound is an important feature of secondary healing, not seen in primary healing. Due to the action of myofibroblasts present in the granulation tissue, the wound contracts to one-third to one-fourth of its original size. The wound contraction occurs at a time when active granulation tissue is being formed.

Detail review of wound and its management are discussed by Sushruta. During this time the knowledge of wound was on its peak level. He has also elaborated clinical presentation of wound, its pathogenesis (*Shata Kriyakala*),<sup>[11]</sup> prognosis and sixty essential procedures (*Shasti Upakrama*)<sup>[12]</sup> for management. In Ayurveda the two types of measures have been advocated for good healing.

## Vrana Shodhana

It refers to the cleaning process of wound and is aimed to dissolve slough, debris and other unwanted agents from the wound in order to provide a healthy field for proper healing. It is done by medicaments, para-surgical or surgical methods.<sup>[13]</sup>

## Vrana Ropana

The drug which augment the healing process are called *Vrana Ropana* drugs.<sup>[14]</sup>

Though a variety of chemical substance and formulations have been evaluated and patented as wound healing agent but ideal wound healing agent is still awaited. Various classics of Ayurveda have described the role of the *Neem (Azadirachta indica A Juss)*<sup>[15]</sup> and *Haridra (Curcuma longa L.)*<sup>[16]</sup> in wound healing. According to Acharya Charaka and Vagbhata decoction of *Nimb patra* has *Vrana shodhan* (Purification) properties.<sup>[17,18]</sup> *Neem panchang* have *Vrana Nashak* (wound healing) properties<sup>[19]</sup>. According to *Sushruta Haridra* have *Vrana shodhak* properties which accelerate the wound healing<sup>[20,21]</sup>. The *Katu* and *Tikta rasa* and *Ruksha, Ushna* properties of *Haridra* play important role in wound healing.<sup>[22,23]</sup>

## Aims and objectives

To evaluate the therapeutic effect of *Neem (Azadirachta indica A.Juss.)* and *Haridra (Curcuma longa L)* on wound healing.

## MATERIALS AND METHODS

### Selection of Patients

For the present study, 54 patients with classical signs and symptoms of wound who were attending the OPD/IPD of *Shalya Tantra* (Surgery) department of Govt. Ayurved Hospital Patna, randomly selected for the study in three groups A, B and C. Fine powder of *Neem panchanga* and *Haridra* and decoction of *Neem patra* and *Haridra* was prepared in the pharmacy wings of Govt. Ayurved College and Hospital, Patna.

**Table 1: Treatments planned for specific groups**

Gr.	Drugs	Form	Dose	Duration
A	<i>Neem-panchang</i> (leaf, bark of stem & root, fruit and flower)	Fine powder (orally)	3 gm. twice a day	30 days
	<i>Neem Patra</i> (leaf)	Decoction (Externally on alternate day)	According to size of wound	
B	<i>Haridra</i> (dry rhizome)	Fine powder (orally)	3 gm. twice a day	

		Decoction (externally on alternate day)	According to size of wound	30 days
C	Mixture of <i>Neem-panchang</i> and <i>Haridra</i>	Fine powder (orally)	3 gm. twice a day	30 days
	Mixture <i>Neem Patra</i> and <i>Haridra</i>	Decoction (externally on alternate day)	According to size of wound	

**Inclusion criteria**

1. Patients having signs and symptoms of the wound.
2. Age between 16 – 60 year.

**Exclusion criteria**

Patient suffering from callus /tubercular / rodent ulcer, deep sinuses, diabetic, aids, cancer, leprosy etc.

**Follow Up**

Alternate day.

**Local examination of wound**

The wound was assessed by naked eye examination and size of wound was determined by manual tracing methods.<sup>[24]</sup>

**Procedure adopted for dressing of wound**

Wound was washed with decoction 4-5 times and cleaned with sterilized gauze pieces and finally wound was covered with thin gauze piece moistened with decoction of drugs. No other wound care or systemic antibiotic was provided to them.

**Diet and Restrictions**

Patients were advised to follow the *Pathyapathya* available in Ayurvedic literature.

**Criteria of assessment****Subjective criteria**

To assess the improvement or effect on subjective parameters grade/score system was designed according to severity were given marks (0-4).

**Score system**

To assess the improvement or effect on subjective parameters grade/score system was designed as below.

**Symptoms Score/Grade****Size**

- 0 = None
- 1 =  $\leq 4$  Sq.cm
- 2 = 4.1 - 9 Sq.cm
- 3 = 9.1 - 16 Sq.cm
- 4 = 16.1 Sq.cm and above

**Pain:**

- 0 = No Pain
- 1 = Only during movement
- 2 = Localized feeling of pain even during rest but not disturbing the sleep
- 3 = Localized continuous feeling of pain and not relieved by rest

**Tenderness**

- 0 = Tolerance to Pressure
- 1 = Little response on sudden pressure

2 = Wincing of face on super slight touch

3 = Resists to touch & rigidity

**Discharge**

0 = Absent

1 = Sanguineous

2 = Serosanguineous : thin, watery, pale red/pink

3 = serous: thin watery, clear

4 = purulent: thin or thick, opaque, tan / yellow, with or without odour

**Odour (Smell)**

0 = Absent

1 = Bad

2 = Unpleasant, Tolerable

3 = Foul smell which is intolerable

**Colour(Abnormal)**

0 = Normal pigmentation of skin

1 = Slight red

2 = Reddish black

3 = Pale yellow/blackish/bluish

**Burning sensation**

0 = No burning

1 = little, localized & some time feeling of burning sensation

2 = More localized & often burning sensation which does not disturb sleep

3 = Continuous burning sensation with disturbed sleep

**Itching Sensation**

0 = No itching.

1 = Slight, localized itching sensation which is relieved by rest

2 = More localized & often itching but not disturbs sleep

3 = Continuous itching with disturbed sleep

**Swelling**

0 = Absent

1 = Slight red, tender & hot with painful movement & without indurations

2 = More red, having painful movement, with more local temperature &with indurations

3 =Angry look, hot, resist to touch & with more indurations.

**Statistical analysis**

All information which was based on various parameters was gathered and statistical analysis was carried out in terms of Mean (X), Standard deviation (S.D.), Standard error (S.E.), Paired test (t) and finally results were incorporate in term of probability "p" as

**Table 2: Criteria for assessment of result**

p > 0.05	Insignificant
p < 0.05, p < 0.01	Significant
p < 0.001	Highly Significant

**Criteria for assessment**

The assessment was done on the basis of change in signs and symptoms of wound. To assess the effect of therapy on subjective parameters, wound area, signs and symptoms level was assessed every follow up and finally after completion of treatment.

**Table 3: Criteria for assessment of overall effect**

Percentage of Relief	Overall effect
100%	Cured
More than 75% relief in signs and symptoms	Markedly improved
50-75% relief in signs and symptoms	Moderately Improved
25-50% relief in signs and symptoms	Partially Improved
Less than 25% relief in signs and symptoms	Unchanged

**OBSERVATION AND RESULTS**

**Demography of clinical profile**

**Table 4: mode of onset wise distribution of 54 patients of wound**

Mode of onset	Group A		Group B		Group C		Total	
	No.	%	No.	%	No.	%	No.	%
Sudden	16	80	12	75	15	83.33	43	79.62
Gradual	04	20	04	25	03	16.66	11	20.37

**Table 5: cause-wise distribution of 54 patients of wound**

Cause	Group A		Group B		Group C		Total	
	No.	%	No.	%	No.	%	No.	%
Endogenous	05	25	06	37.50	06	33.33	17	31.48
Exogenous	15	75	10	62.50	12	66.66	37	68.51

**Table 6: showing incidence of type of trauma of 54 patients of wound**

Trauma	Group A		Group B		Group C		Total	
	No.	%	No.	%	No.	%	No.	%
Physical	13	65	09	56.25	10	55.55	32	59.25
Chemical	00	00	00	00.00	00	00.00	00	00.00
Thermal	01	05	02	12.50	01	5.55	04	07.40
Electrical	00	00	00	00.00	00	00.00	00	00.00
None	06	30	05	31.25	07	38.88	18	33.33

**Table 7: showing incidence of type of wounds of 54 patients**

Type of wounds	Group A		Group B		Group C		Total	
	No.	%	No.	%	No.	%	No.	%
Incised	05	25	03	18.75	04	22.22	12	22.22
Lacerated	05	25	04	25.00	06	33.33	15	27.77
Penetrating	02	10	01	06.25	00	00.00	03	05.55
Contused	03	15	00	00.00	01	05.55	04	07.40
Burn	01	05	02	12.50	01	05.55	04	07.40
Other	04	20	06	37.50	06	33.33	16	29.62

**Table 8: showing the effect of drugs (Planned) in Group A on various signs & symptoms of wound**

Signs & Symptoms	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Size	1.70	0.15	91.17	0.60	0.13	11.46	p < 0.001
Pain	2.45	0.30	87.75	0.93	0.20	10.30	p < 0.001
Tenderness	2.10	0.65	69.04	0.51	0.11	12.70	p < 0.001
Smell	1.71	0.14	91.66	0.53	0.20	07.77	p < 0.001
Swelling	1.56	0.12	88.00	0.61	0.15	08.88	p < 0.001
Discharge	2.00	0.14	86.66	0.70	0.18	09.53	p < 0.001
Burning sensation	2.00	0.22	88.88	0.44	0.14	12.09	p < 0.001
Itching sensation	1.87	0.12	93.33	0.46	0.16	10.69	p < 0.001
Colour(Abnormal)	2.50	1.50	40.00	0.91	0.20	04.87	p < 0.001

**Table 9: Showing the effect of drugs (Planned) in Group B on various signs & symptoms of wound**

Signs & Symptoms	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Size	1.43	0.18	86.95	0.68	0.17	07.31	p < 0.001
Pain	2.50	0.18	92.50	0.87	0.21	10.59	p < 0.001
Tenderness	2.50	0.62	75.00	0.71	0.17	10.43	p < 0.001
Smell	1.83	0.16	90.90	0.81	0.33	05.00	p < 0.01
Swelling	2.27	0.18	92.00	0.53	0.16	12.85	p < 0.001
Discharge	1.91	0.33	82.60	0.51	0.14	10.65	p < 0.001
Burning sensation	1.85	0.42	76.92	0.53	0.20	07.07	p < 0.001
Itching sensation	2.40	0.20	83.33	0.70	0.31	06.32	p < 0.01
Colour(Abnormal)	2.50	1.18	52.50	0.70	0.17	07.45	p < 0.001

**Table 10: Showing the effect of drugs (Planned) in Group C on various signs & symptoms of wound**

Signs & Symptoms	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Size	1.94	0.11	94.28	0.61	0.14	12.57	p < 0.001
Pain	2.83	0.27	90.19	0.92	0.21	11.76	p < 0.001
Tenderness	1.88	0.38	79.41	0.51	0.12	12.36	p < 0.001
Smell	2.83	0.16	94.11	0.81	0.33	08.00	p < 0.001
Swelling	1.71	0.07	91.66	0.85	0.22	06.90	p < 0.001
Discharge	2.18	0.09	95.83	0.94	0.28	07.34	p < 0.001
Burning sensation	1.57	0.28	81.81	0.48	0.18	06.97	p < 0.001
Itching sensation	2.60	0.20	92.30	0.54	0.24	09.79	p < 0.001
Colour(Abnormal)	2.60	1.38	46.80	0.94	0.22	05.50	p < 0.001

**Table 11: Showing effect of Group A drugs on Haematological value of 20 patients of Wound**

Haematological value	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Hb%	12.64	12.89	02.01	1.08	0.24	1.05	p > 0.05
ESR	14.15	11.80	16.60	4.22	0.94	2.48	p < 0.05
TLC	8340	7452.6	10.64	1764.9	394.64	2.24	p < 0.05
Polymorph	61.90	60.65	02.01	2.22	0.49	2.51	p < 0.05
Lymphocyte	30.5	30.90	02.82	2.64	0.59	1.43	p > 0.05
Eosinophil	04.70	04.10	12.76	2.03	0.45	1.31	p > 0.05
Monocyte	03.45	03.60	04.34	1.08	0.24	0.61	p > 0.05

**Table 12: Showing effect of Group B drugs on Haematological value of 16 patients of Wound**

Haematological value	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Hb%	12.88	13.44	04.36	1.25	0.31	1.79	p > 0.05
ESR	10.50	09.12	13.09	2.52	0.63	2.17	p < 0.05
TLC	8156.25	7387.5	09.42	1443.01	360.75	2.13	p < 0.05
Polymorph	61.43	59.06	03.86	4.44	1.11	2.13	p < 0.05
Lymphocyte	31.06	31.18	00.40	1.78	0.44	0.28	p > 0.05
Eosinophil	05.12	03.93	23.17	1.93	0.48	2.44	p < 0.05
Monocyte	03.43	03.93	14.54	2.50	0.62	0.79	p > 0.05

**Table 13: Showing effect of Group C drugs on Haematological value of 18 patients of Wound**

Haematological value	Mean		% relief	± S.D.	± S.E.	't' Value	'p' Value
	B.T.	A.T.					
Hb%	12.45	12.65	01.56	0.52	0.12	1.58	p > 0.05
ESR	12.5	10.22	18.22	3.83	0.90	2.52	p < 0.05
TLC	8161.11	7688.88	05.78	762.97	179.83	2.62	p < 0.05
Polymorph	62.50	60.72	02.84	3.00	0.70	2.51	p < 0.05
Lymphocyte	30.83	30.33	01.62	5.00	1.18	0.42	p > 0.05
Eosinophils	05.50	04.38	20.20	2.29	0.54	2.05	p > 0.05
Monocytes	04.61	04.33	06.02	0.66	0.15	1.76	p > 0.05

**Overall effect of trial drugs****Table 14: Table showing the overall effect in all three groups**

Results	Gr. A		Gr. B		Gr. C		Total	
	N	%	N	%	N	%	N	%
Cured	00	00	00	00.00	00	00.00	00	00.00
Markedly Improved	10	50	09	56.25	12	66.66	31	57.40
Moderately Improved	10	50	07	43.75	06	33.33	23	42.59
Partially Improved	00	00	00	00.00	00	00.00	00	00.00
Unchanged	00	00	00	00.00	00	00.00	00	00.00

**DISCUSSION****Discussion on subjective parameters**

As per table no. 8, 9, and 10 the effect of therapeutics on clinical features of wound is discussed below:

In Group C the size decreased by 94.28% with statistically highly significant ( $t = 12.57$ ) value and the tenderness was decreased by 79.41% which was statistically highly significant ( $t = 12.36$ ) as well as the discharge was decreased 95.83% with statistically highly significant ( $t = 7.34$ ) value which is better than group A and B. In Group B the colour was changed by 52.5% with statistically highly significant ( $t = 7.45$ ) value and the pain was decreased 92.5% with statistically highly significant ( $t = 10.59$ ) value which is better than group A and C

**Discussion on objective parameters**

As per table no. 11, 12 and 13, the mean value of objective parameters such as Hb%, T.L.C., D.L.C. etc. was slightly changed during the course of study.

**The overall effect**

In all three groups total 57.40% patients got markedly improved and 42.59% patients got moderately improvement. There was no any wounds which partially improved or unchanged.

**Probable mode of action of group A drugs**

The *Tikta Rasa* of *Neem* having *Shodhana*, *Lekhana* (Scraping), *Kleda-puyashoshana* (Absorption of liquid & pus) and *Krimighna* (Anti-microbial) action that's why it reduces pus formation. It protect wound from contamination. *Sheeta Virya*<sup>[25]</sup> (Potency) of drug pacifies *Pitta* and *Rakta*. Both *Pitta* and *Rakta* play an important role in inflammation. *Neem-patra* (Leaf) have *Vrana Shodhana* (Purification) action so that it help in debridement of wound and also prevent as well as remove infection and accelerate wound healing.

**Probable mode of action of group B drugs**

The *Katu-Tikta Rasa* and *Ushna Virya* properties of it digests the *Ama* which is a causative factor of *Vrana*. The drug relieves in Pain and swelling by *Vranapachana* action. *Laghu-Ruksha Guna* of the drugs having *Kapha* pacifying action and act as a good absorber of liquid like pus so, it reduces secretion from wound.

**Probable mode of action of group C drugs**

The combination of above two group's drugs have also *Vrana Shodhana* and *Vrana Ropana* action.

In the present study it was observed that group C drugs have more potent action on wound healing than group A and B. It may be due to compound effect of the ingredients present in these drugs. The action of drugs may be synergetic.

**CONCLUSION**

At the end of the study, following conclusion can be drawn on the basis of observations made, results achieved It can be summarized as follows:

Though wound healing is self controlled physiological process which normally does not requires much help, but its proneness to infections which may be external or internal is of great thought. Decoction of *Neem-patra* and *Haridra* act as good dressing medicine and able to check the infections. *Neem* (*Azadiracta indica* A.Juss.) and *Haridra* (*Curcuma longa* Linn) having excellent properties to accelerate the wound healing safely. The combined forms of two drugs have more potent action than using alone.

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