RESEARCH ARTICLE

Wound Healing Potential of Polyherbal Dusting Powder for the Treatment of Bedsores

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ABSTRACT

A bed sore is also known as a pressure sore and is an open ulcer on the skin. Bedsores are mostly found on the skin that covers bony areas. The primary objective of this research project was to develop and test the polyherbal dusting powder containing an aqueous extract of *Azhadirachta indica, Curcuma longa L., Aloe vera, and Tagetes erecta.* The preliminary phytochemical investigation of aqueous extract was carried out. Selected herbs have anti-inflammatory, antimicrobial and wound-healing action needed for the treatment of bedsores. The powder was then tested for physical parameters like color, texture, smell, form, and pH), and micrometric parameters like size of particles, angle of repose, Hausner's ratio, surface area, and other flow properties. The dosage form has been screened for antimicrobial activity against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus.* The formulation showed significant antimicrobial activity as compared to the standard povidone iodine drug. In the skin irritation and wound healing studies performed on albino wistar rats, significant effects were observed with 200 mg of powder. According to the *in-vivo* study, polyherbal dusting powder has been shown to be effective in the treatment of bedsores and can be further investigated.

Keywords: Bedsores, Polyherbal dusting powder, Evaluation, Antimicrobial activity, Skin irritation study, Wound healing activity.

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INTRODUCTION

If a patch of skin is exposed for a long time to continuous pressure, especially in bedridden patients, ulcers are formed which can damage that part of the skin and surrounding tissues leading to tissue necrosis and ischemia. The term "constant pressure resulting in alteration or deformation impairment" is the best way of describing a pressure ulcer. The term bedsore may also be used to include decubitus ulcers or pressure sores. The buttocks and tailbone spine, the shoulders, ankles and heels, the back of the head, and the elbows are frequent sites for bedsores. Pressure, friction, shear, and moisture all contribute to bedsores.[1]

According to the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel, bedsores are categorized into the following:

- Stage I (Non-blanchable erythema): The affected part of skin becomes discolored and appears as red in fair people while purple or blue in darker-skinned people. Stage 1 pressure ulcers never turn to white, under pressure.
- Stage II (Partial thickness): In stage II pressure ulcers, a part of the skin's innermost layer, the dermis or epidermis may be damaged, leading to loss of skin. The ulcer may appear to be blistered or sore.
- Stage III full thickness skin loss: During stage III, there is skin loss extended to the complete thickness of the skin. The muscles and bones are not injured, but the underlying tissue gets damaged. The ulcers appear as deep incisions with a hollow space in it.
- Stage IV (Full thickness tissue loss): This is the most serious and because of the severe skin damage (tissue necrosis), the cells in the vicinity start to die. In some cases, the muscles, bones and joints can be damaged very badly. Patients are having highest chances of getting an infection that can be fatal.[2]

Bedsore management is achieved by relieving the pressure, cleaning the wound, applying dressings, using topical creams, addressing incontinence, removing dead tissue, taking any required antibiotics, adjusting the diet, and discussing surgical options.[3]

Dusting Powder

Dusting powder is a powder that is applied to the skin or to wounds to reduce irritation or to absorb of moisture. A dusting

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powder is a mixture of finely powdered substances to be applied externally for the treatment of skin wounds, burns and surgical interventions. In addition to helping to relieve congestion and provide a cooling effect, the powder bases absorb the secretions and encourage a drying action.

Properties of Powder

- It should be uniform.
- It should be non-irritating.
- It should be easy to flow render it to spread evenly.
- While applying, it should stick to the skin
- It should have adsorptive and absorptive capabilities.

Types of Dusting Powder

There are two types of powders used in body cavities

Medicated powder

These are used especially for superficial skin conditions. They must be pathogen-free. As few mineral ingredients are having chance to be contaminated with spores of tetanus, gas gangrene, etc., they need to be appropriately sterilized. The label should also state that they should not be used on open wounds or regions with damaged skin.

Surgical powder

These are used in the body's deep and major wounds due to burns and umbilical cords of the infanta. These need to be sterilized before application.[4]

Herbal medicine

The earliest known type of treatment is herbal medicine, sometimes known as herbalism. All societies have utilized herbs for their medicinal or healing properties throughout history. Herbs have chemical components that have therapeutic effects on the body.[5] India is a rich source of medicinal herbs and it has been found that many essential oils and extracts are used in traditional systems of medicine such as Ayurveda, Unani, and Siddha. Plant-based natural products like flavonoids, terpenes, and alkaloids are widely studied and used for their various pharmacological applications such as anti-inflammatory, wound healing, antibacterial, antipyretic, analgesic activities, etc.[6]

Herbs Use in Dusting Powder

Turmeric

Turmeric, also called as *Curcuma*, Indian saffron, and haldi in India is a dried rhizome of *Curcuma longa*, family Zingibaraceae[7]. The main component is an oleoresin with turmerone and curcuminoids. Curcuminoids consist of curcumin, bisdemethoxycurcumin, and demethoxycurcumin. These active ingredients possess antiseptic anti-inflammatory, antimicrobial, wound healing, anti-oxidant, and anti-carcinogenic activity. Traditionally it is widely used as a spice agent in India.

Being active against gram +ve and gram -ve bacteria[8] and with significant wound-healing properties, curcumin can be the best choice of ingredient for herbal dusting powder. It improves the body's natural healing process at many stages, including the formation of granulation tissue, deposition of collagen, tissue remodeling, and wound contraction.[9]

Neem

Neem, Margosa consists of leaves of *Azadirachta indica,* family Meliaceae.[7] It contains phytoconstituents as azadirachtin, salannin, nimbolinin, nimbin, nimbidin, nimbidol, gedunin, and quercetin.[10] It is used as an anti-inflammatory, antioxidant, antibacterial, pesticide, antiviral, and produces hepatoprotective, wound healing, insecticide, and antifeedant activities.

Neem is chosen because of its antibacterial and anti-inflammatory activities, which aid in the healing process and supply nutrition that is required for the growth of new capillaries and collagen.[11]

Aloe

Aloe, musabbar, and Kumari are synonyms of *Aloe vera*. Aloes are dried juice of leaves of *Aloe vera*, belonging to the family Liliaceae[7]. The major constituents of aloe are aloin, aloe emodin, emodin, and iso barbaloin which are a composition of anthraquinones glycosides, among which barbaloin is the chief constituent. *Aloe vera* was used as a purgative, antioxidant, antibacterial, anti-inflammatory, and antiseptic agent. It accelerates wound healing and it has a moisturizing anti-aging effect.[12] *Aloe vera* is more activite against gram-positive bacteria than gram-negative ones and this is due to the presence of saponins and anthraquinone derivatives. Topical application of *Aloe vera* significantly reduces the time for wound closure.[13]

Marigold

Marigold is also known as African marigold and *Genda phul* and it contains all parts of the herbaceous plant *Tagetes erecta* belonging to the family Asteraceae. The chemical constituents of marigolds are quercetagetin, syringic acid, lutein, cis-ocimene, oscimene, I-limonene, zeaxanthin, Tagetone, β-caryophyllene, β-sitosterol, carotenoid. It exhibits antibacterial, anti-inflammatory, wound healing, antioxidant, insecticidal, antipyretic, and antifungal activities.[14,15]

Marigold is having antibacterial activity and its extract is responsible for rise in platelet count, WBC counts and decreases bleeding time and clotting time. It shows a significant reduction in the epithelization period and wound tightening.

MATERIALS AND METHODS

Aqueous extracts of neem, turmeric, and aloe are collected from Vatsal Ayurvedic Product Private Limited, Ozar, Nashik.

The marigold flowers were collected from a farm located at Adgaon, Nashik. The flowers were dried in the shade and ground in powder form. The flower powder was then extracted by using soxhlation with ethanol as solvent.

Phytochemical Analysis

Phytochemical testing of all extracts was performed for tannins, alkaloids, glycosides, steroids, saponins, carbohydrates, amino acids, and flavonoids.[16]

Thin Layer Chromatography[17]

Silica gel G is used as a stationary phase for the preparation of TLC plates and plates are activated by heating at 105ºC for 30 minutes. The extract was loaded on the plate and kept in the chromatographic chamber saturated with the respective mobile phase. The following mobile phases were used for the extracts

- Curcumin: Chloroform- methanol (98:2)
- Aloin: Ethyl acetate: Acetic acid: Methanol (100:10:13.5)
- Alkaloid: Toluene: Ethyl acetate: diethyl amine (70:20:10)
- Carotenoid: Acetone: Water (90:10)

TLC plate was allowed to develop and spot was visualized by different methods.

Spot Visualization

Curcumin was visualized under visible light. For visualization of aloin, plates were placed in UV light at 245 nm. Alkaloids were visualized at 254 nm UV light and they showed yellow fluorescent spots and carotenoids are visualized under visible light.

Optimization of Rf Value

The Rf value was calculated by using the following formula

$$Rf = \frac{Distance\ travelled\ by\ sample\ component}{Distance\ travelled\ by\ solvent\ front}$$

Formulation of Dusting Powder[18]

The extracts and excipients as per the given formula in Table 1, were weighed and transferred to mortar and pestle. All the ingredients were powdered and mixed well. This powder was passed through sieve #120.

Evaluation of Powder

Powder was evaluated by using parameters as

Physical characteristics

Color, smell, and texture.

pH of the formulation

The pH of 1 g of powder dissolved in 100 mL of purified water was measured with the help of digital pH meter.

Particle Size:

The formulation's particle size was examined under a microscope by using a stage micrometer[4]

Abrasiveness

The abrasiveness of powder was determined by rubbing a pinch of powder between the thumb and index fingertips.

Bulk density[19]

Bulk density is the weight of the powder in grams or kg per unit volume and is expressed in per cm^3 or per m^3 or g/100 mL. The volu $Bulk\ Density(\rho_o) = M/V_o$ er, compacted by standardized tapping, was measured in a 250 mL measuring cylinder to estimate the bulk density.

The bulk density of the material is calculated using the following formula:

Where ρ_o is bulk density, M as bulk mass and V as bulk volume.

Tapped density[19]

It was obtained by tapping a graduated measuring cylinder or using a digital bulk density apparatus and the volume was recorded.

By using the formula, the tapped density was determined,

$$Tapped\ Density\ (\rho_o) = M/Vt$$

Where ρ_o is tapped density, M as the mass of powder while Vt is powder volume

Carr's index[18]

The formula was applied to determine the percent compressibility. Table 2 depicts the relation between % Compressibility and flow property.

$$C = \frac{\rho t - \rho}{\rho t} \times 100 \ldots \text{equation 6.4}$$

Here ρt is tapped density, ρ_o as bulk density and C as compressibility index.

Hausner's ratio[18]

It was calculated using tapped and Bulk density values.

$$Hausner's\ ratio = \frac{\rho t}{\rho o} \quad \ldots \text{equation 6.5}$$

Where ρt is Tapped density and ρ_o as bulk density.

Lower Hausner's ratio values indicate better flowability whereas higher values show poor flow property.

Angle of repose[18]

It is the highest value of angle that can be formed between a powder pile's surface and the flat surface. It was determined using the funnel technique. To calculate the angle of repose, the formula was employed. Table 3 shows the relation between flowability and angle of repose.

Table 1: Formula for dusting powder

S. No.	*Ingredients*	*B1 (gm)*	*B2 (gm)*	*B3 (gm)*
1	Neem extract	1	0.5	0.75
2	Turmeric extract	0.8	0.5	0.75
3	*Aloe vera* extract	0.7	0.5	0.75
4	Marigold extract	0.5	0.5	0.75
5	Zinc oxide	3.5	3.5	3
6	Boric acid	2.5	2.5	2
7	Kaolin	1	2	2

Table 2: Relationship of %compressibility and flow property

Flowing property	*%Compressibility range*	
	From	*To*
Excellent	5	15
Good	12	16
Fairly acceptable	18	21
Poor	23	35
Very poor	33	38
Very poor	More than 40	

$$\tan\theta = h/r$$

Or

$$\theta = \tan^{-1}(h/r)$$

Where θ is angle of repose, r as radius of the conical pile and h as height of the conical pile.

Antimicrobial Test[8,10]

Preparation of microbial strains

To assess the activity against bacteria like gram-positive *B. subtilis, S. aureus*, and gram-negative *E. coli* were used.

Antimicrobial activity

The antimicrobial activity of all extracts was evaluated using the agar as the medium by making well and allowing diffusion of extracts. Microbial cultures 1-mL was inoculated in a sterile nutrient agar medium by using the pour plate technique. The sterile cork borer was used to prepare wells in the medium. The test drugs (a polyherbal formulation) and the standard drug (10 and 20 mg of povidone-iodine) was added to the well in an aseptic condition and allowed to diffuse in media at room temperature. The inoculated plates were kept in an incubator at a controlled temperature of 37ºC for a further 24 hours. The zone of inhibition for all samples were measured in triplicate.

Skin Irritation Test[20]

The skin irritation test is a procedure used to determine whether a product has the potential to irritate customers' skin. A total five groups are prepared containing four rats in each. These twenty rats were kept 15 days under experimental conditions to adjust to their new environment. Skin irritancy testing was done in accordance with the OECD Guideline. Before the experiment, each rat had its dorsal sides marked and shaved (1 cm from the midline of the vertebral column). Group I acts as the control group, group II as the untreated, group III for the polyherbal formulation (100 mg), group IV as the polyherbal powder (200 mg), and group V for the standard (povidone-iodine). All groups were subjected for exposure to respective formulation. The area around it was covered with dressing gauze. After a 24-hour exposure period, the elastic gauze was removed, being cautious not to irritate the skin. With distilled water, the test location was cleaned and using the Draize cutaneous irritation scoring method, erythema and edema in animals were inspected. at intervals of 1, 24, 48, and 72 hours, and the degree of erythema and edema was assessed based on the scores.

Wound Healing Activity: Excision Wound Model[20-26]

For the first 14 days rats were allowed to get acquainted with laboratory conditions of controlled temperature of 22 to 24°C and humidity of 45 to 55%. Total five groups of four animals each were formed as shown in Table 4. It was a form of open wound that was used to examine the scar region. Diethyl ether was used to anesthetize animals. The anesthetized rat's dorsal thoracic region was imprinted at the point of 1-cm distance from the spinal column and 5 cm from its ear. Prior to the test, the targeted area of the skin was shaved. A cut was made on the dorsal region that had been shaved, and the wound area was marked. The marking was followed, and a full-thickness excision with a 500 mm^2 round area was made using a surgical blade, toothed forceps and sharp scissors. Hemostasis was achieved by dabbing the wound with a cotton swab dipped in normal saline. Tracing the open incision gave researchers the opportunity to examine the healing-promoting contractions. The wound was traced to determine the size on graph paper with a millimeter scale. For the final analysis of the data, the initial wound size (500 mm^2) for all rats in the group was measured. The mean value of wound size and then wound healing percentage was calculated for a number of days of the study, i.e., 0, 3, 6, 9, 12, and 14. The scar falling off and leaving no sign of a raw wound was considered the completion of epithelization, and the number of days needed to achieve this was considered the epithelization period.

Table 3: Relationship between the angle of repose and flowability

Angle of repose	*Flowability*
Less than 20˚	Excellent
20˚ to 30˚	Good
30˚ to 34˚	Acceptance
40˚	Very poor

Table 4: Grouping of animals

S. No.	*Group*	*Treatment days*
1.	Group I (Control)	14 days
2.	Group II (untreated)	14 days
3.	Group III (100 mg polyherbal powder)	14 days
4.	Group IV (200 mg Polyherbal Powder)	14 days
5.	Group V (Povidone iodine powder)	14 days

RESULTS

Phytochemical Analysis

Phytochemical screening for various plant extracts of turmeric, neem, aloe, and marigold showed the presence of phytoconstituents and results are shown in Table 5.

TLC Analysis

The result obtained from TLC of the successive extract. The Rf values for various constituents obtained are as per Table 6.

Formulation Evaluation

The color of the powder was peach color with a mild aromatic odor and smooth and fine appearance. The pH of formulations was found to be around 5.6. The particles of powder were ranged from 0.125 to 0.127 microns in size. The grittiness was absent in all three poder batches. The bulk density was found to be o.66, 0.68 and 0.71 g/cm^3 and tap density was 0.90 and 1.0 g/cm^3. The angle of repose of the powder was found as

Table 5: Preliminary phyto-chemical analysis

S. No	*Chemical constituents*	*Turmeric*	*Neem*	*Aloe vera*	*Mari gold*
1.	Carbohydrates	+	+	+	+
2.	Protein	+	+	+	+
3.	Amino acid	-	-	-	-
4.	Steroids	-	-	-	+
5.	Anthraquinone Glycosides	+	-	+	-
6.	Saponin glycosides	-	+	+	-
7.	Flavonoids	-	+	-	+
8.	Alkaloids	-	+	-	+
9.	Tannin	-	+	+	+

Table 6: Rf value of extracts

S. No.	*1*	*2*	*3*	*4*
Sample	curcumin	aloin	Carotenoid (Marigold)	Alkaloid (Neem)
Rf value	0.75	0.43	0.58	0.57

Table 7: Evaluation parameters for polyherbal dusting powder

S. No.	*Parameters*	*Batch B1*	*Batch B2*	*Batch B3*
1	Color	Peach color	Peach color	Light peach color
2	Odor	Mild aromatic	Mild aromatic	Mild aromatic
3	Appearance	Smooth and fine	Smooth and fine	Smooth and fine
4	pH	5.5	5.6	5.6
5	Particle size (mm)	0.125	0.127	0.126
6	Abrasiveness	No grittiness	No grittiness	No grittiness
7	Bulk density (g/cm^3)	0.66	0.68	0.71
8	Tap density (g/cm^3	0.90	1	0.90
9	Angle of repose (^{0})	23	21	21
10	Carr's index (%)	26	32	21
11	Hausner ratio	1.36	1.47	1.26

21˚ and 23˚, Carr's index 21, 26 and 32% and Hausner ratio as 1.26, 1.36 and 1.47. All the parameters for three trial batches were noted in Table 7.

Antimicrobial Study

The formulations and extracts have shown comparable antimicrobial activity when zone of inhibitions as shown in Table 8 was compared with the standard.

Skin Irritation Test

According to Draize cutaneous irritation scoring method, the degree of erythema and edema were evaluated. The 100 mg polyherbal formulation and povidone-iodine powder showed no noticeable inflammation but slight redness so the score was found to be 0.5 and for 200 mg polyherbal powder showed redness and the score was 1. All results are noted in Table 9.

Table 8: Zone of inhibition of different concentration

Zone of inhibition (mm)						
Microbial strain	*S. aureus*		*B. subtilis*		*E. coli*	
Amount of sample	*10 mg*	*20 mg*	*10 mg*	*20 mg*	*10 mg*	*20 mg*
Batch 1	19	20	21	20	19	18
Batch 2	19	20	11	19	18	21
Batch 3	18	21	17	19	18	22
Standard	20	22	20	21	24	20
Turmeric extract	19	21	18	17	17	18
Neem extract	13	18	19	20	17	17
Aloe extract	17	20	19	20	16	17

Table 9: Effect of polyherbal dusting powder on behavioral parameters on albino wister rat

Group	*Sign*	*Score*
Group I (Control)	-	0
Group II (untreated)	-	0
Group III (100 mg polyherbal powder)	Not visible inflammation but slight redness	0.5
Group IV (200 mg Polyherbal Powder)	Redness	1
Group V (Povidone iodine powder)	Not visible inflammation but slight redness	0.5

Table 10: Effect of %wound contraction area in excision

Treatment group	*Number of days*						
	Day 2	*Day 4*	*Day 6*	*Day 8*	*Day 10*	*Day 12*	*Day 14*
Group II (Untreated)	15.91 ± 1.31	22.72 ± 1.85	30.96 ± 1.25	36.87 ± 1.92	48.52 ± 3.58	66.33 ± 3.14	81.81 ± 2.45
Group III (100 mg polyherbal Dusting Powder)	21.59 ± 2.17	32.10 ± 1.87	40.28 ± 1.95	52.72 ± 3.03	65.25 ± 2.46	77.27 ± 1.60	90.34 ± 1.94
Group IV (200 mg Polyherbal Dusting Powder)	22.72 ± 1.85	34.37 ± 1.17	41.41 ± 1.46	58.96 ± 3.50	74.43 ± 2.51	84.09 ± 2.07	93.1 8 ± 2.93
Group V (Standard)	22.84 ± 1.94	31.07 ± 1.14	38.01 ± 1.07	48.52 ± 3.58	65.50 ± 2.63	77.84 ± 1.94	88.0 6 ± 1.08

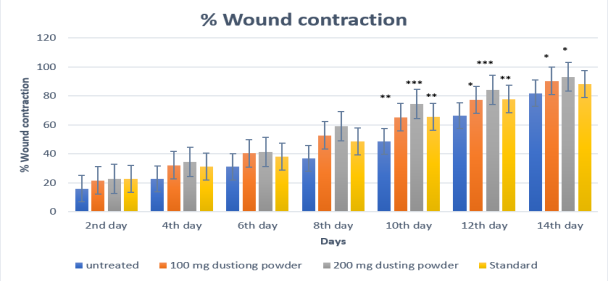

Figure 1: % Wound contraction *vs* days in (Values are expressed as mean ± SEM, N = 4 animals/group) ***p < 0.001, **p < 0.01, *p < 0.05 vs Control group data. Analysis by ANOVA and Dunnett's test

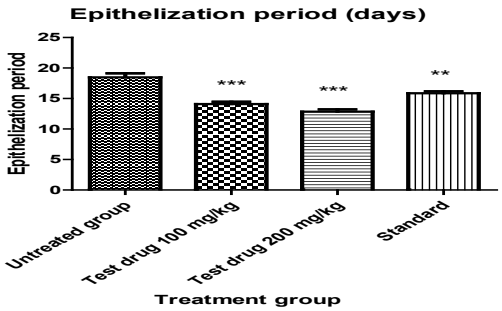

Figure 2: Effect of untreated,100 mg,200mg polyherbal dusting powder and standard on Epithelization period

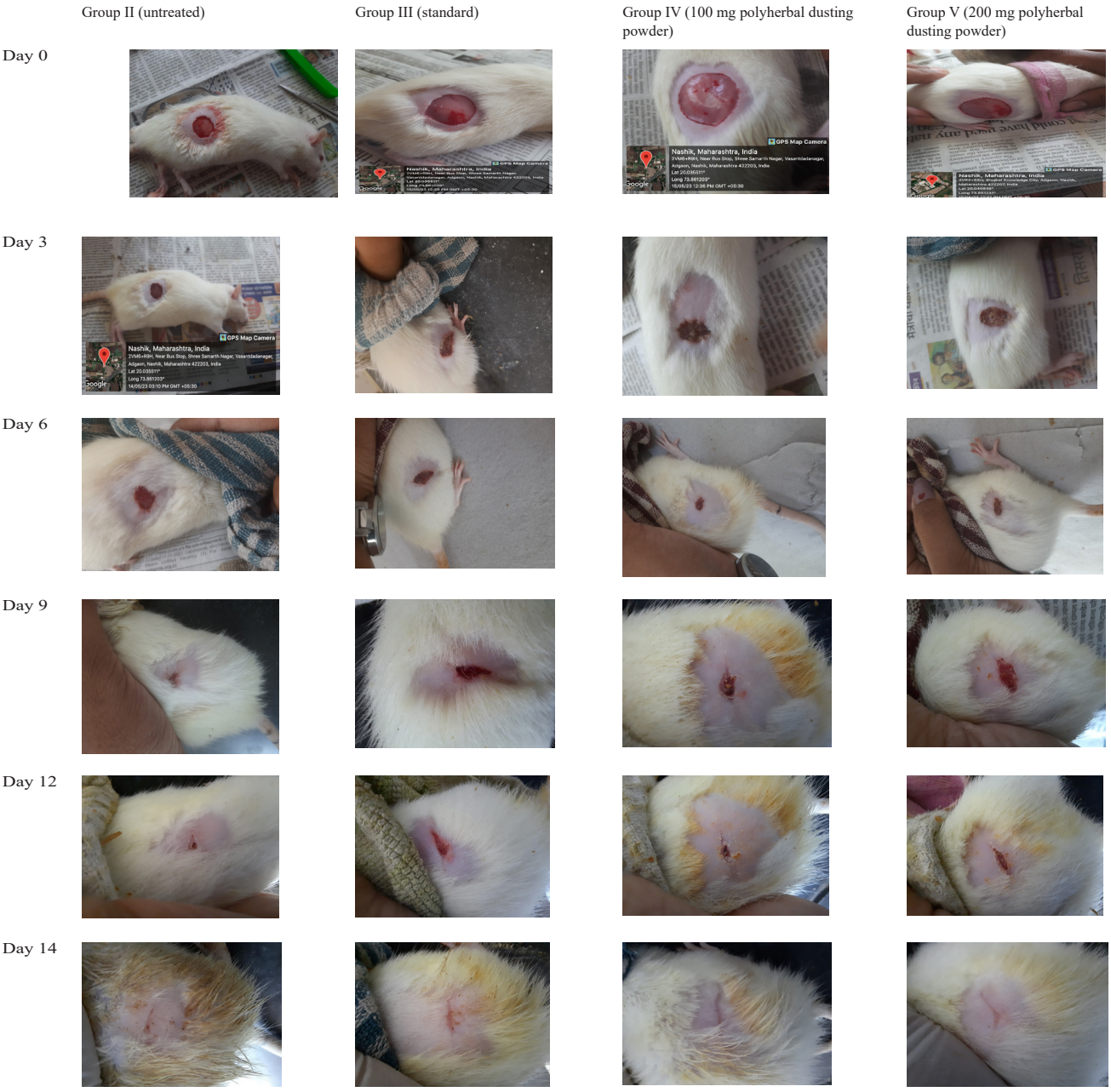

Figure 3: Wound repair at different time intervals in albino wistar rat

Table 11: Epithelization period

Treatment group	*Epithelization period (day)*
Untreated	18.47 ± 0.65
100 mg polyherbal dusting powder	14.09 ± 0.38***
200 mg polyherbal dusting powder	12.84 ± 0.38***
Standard	15.86 ± 0.31**

Each value is the mean of ± SEM for N = 4 rat, ***p < 0.001, **p < 0.01, *p < 0.05 related to untreated. Table 11 shows results which were evaluated by using One-way ANOVA and then Dunnett's test.

Wound Healing Activity: Excision Wound Model

The effect of wound contraction area in the excision wound model in albino wistar rat was monitored in all five groups by measuring the wound contraction area (Table 10). A significant difference was noted in the reduction of area of wound contraction in standard (povidone-iodine powder) and test (100 mg and 200 mg polyherbal powder) groups when compared with control groups after fourteen days of treatment. Effect of topical application of Polyherbal dusting powder (100 and 200 mg) on albino wistar rat expressed as percentage wound contraction (Figure 1). Each value is the mean ± SEM for N = 6.

Epithelization Period

The result of topical application of polyherbal dusting powder (100 and 200 mg) on excision wound expressed as %wound epithelization period (Figure 2).

Table 11 shows results which were evaluated by using One-way ANOVA and then Dunnett's test. With the help of Figure 3, it was observed the development of wound healing for various group of animals over the period of number of days.

DISCUSSION

In this study, polyherbal formulations of turmeric, neem, aloe, and marigold showed synergistic effects for the treatment of bedsores. The phytochemical investigation indicated the presence of carbohydrates, alkaloids, phenols, flavonoids, saponins, terpenoids and glycosides in the extracts. A total of three batches were prepared by using different concentrations of the drug. All the batches were tested for color, odor, and appearance. abrasiveness. pH, particle size, flow properties, and antimicrobial study. Batch B2 was shown all the parameters in the desired range and hence selected for animal studies like skin irritation tests and in-vivo wound healing activity. Polyherbal formulations also show significant antimicrobial activity in comparison to the standard one against both gram +ve and gram -ve bacteria. Batch B2 formulation also showed no skin irritation during the animal study. The wound healing activity of polyherbal dusting powder was carried out which indicated good wound healing potential when compared with povidone-iodine as standard.

CONCLUSION

The polyherbal dusting powder showed encouraging antibacterial properties on both gram +ve and gram -ve pathogens. In comparison to the 100 mg polyherbal dusting powder, the 200 mg polyherbal dusting powder contains an appropriate combination of phytoconstituents that support a natural healing process and can be used more effectively as a wound healing agent. Using 200 mg of polyherbal dusting powder, the wound area's strength is effectively stimulated, and the process of epithelization is accelerated. The 200 mg polyherbal dusting powder showed faster and better wound closure and contraction compared to the standard marketed formulation (Povidone Iodine powder). Formulated polyherbal dusting powder can be used for the treatment of bedsores.

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