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Pharmaceutical Development and Physicochemical Evaluation of Polyherbal Gel for Diabetic Wounds

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ABSTRACT

Background: Diabetes is a group of metabolic disorders. Whether a patient has Type 1 or 2 Diabetes makes no difference when it comes to the factor of Diabetic wounds. More than 50% of diabetic wounds can increase the risk of amputation, if proper & fast treatment is not provided. This study is an attempt to bring ayurveda from laboratory to practice.

□ **Objectives:** Development of the standard manufacturing process of polyherbal gel with selected ingredients & analysis of the study drug physico-chemically to develop its standard.

□ **Methods:** Pharmaceutical development of polyherbal gel from *Durva* (*Cynodondactylon*), *Nimba* (*Azadirachta indica*), *Haridra* (*Curcuma longa*), *Daruharidra* (*Berberisaristata*) & *Yashtimadhu* (*Glycyrrhizaglabra*) & physico-chemical analysis was done by different parameters e.g., physical appearance, pH, skin irritation test, rancidity test, homogeneity etc.

□ **Results:** In terms of standardization pH of gel was ≤ 6 (acidic) which would be healthy for better recovery of wounds. The gel was homogenous, skin compatible & no rancidity seen.

□ **Conclusion:** Topical applications have faster & better results than oral medications. Therefore, it was necessary to develop a safe, potent, effective & easy to use on daily basis with the longer shelf life & cost effective remedy of *Ayurveda* in the form of polyherbal gel.

KEYWORDS

Diabetic Wounds, Polyherbal Gel, Analysis



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INTRODUCTION

Diabetes mellitus is a common & very prevalent group of metabolic disorders affecting the large number of population of the world due to sedentary lifestyle, improper dietary habits & daily regimen, low immunity & lack of exercises etc. As per the WHO India has the fastest growing population of Diabetic patients. Acharyas of Ayurveda have mentioned this disease in detail as “*Madhumeha*”. Some of them termed it as ‘*Kshudrameha*’ as ‘*Kshoudra*’ is the synonym of ‘*Madhu*’ i.e., honey^{1,2,3}. If we have proper control on blood sugar level then Diabetes mellitus can be nearly harmless, but the state of abnormally high blood sugar levels can lead to some serious complications like diabetic wounds, gangrene, diabetic neuropathy, diabetic nephropathy etc. If left uncontrolled for a longer time then it will be difficult to prevent these complications. One of the serious complications that diabetics may face is a Diabetic wound. Whether a patient has Type 1 or 2 Diabetes makes no difference when it comes to the factor of Diabetic wounds. More than 50% of diabetic wounds can increase the risk of amputation, if proper & fast treatment is not provided. The main factor about diabetic wounds is poor or delayed healing. Healing of wounds is the basic response to tissue

injury, takes place by a process of connective tissue repair.

Various connective tissue abnormalities are seen in Diabetes mellitus¹²³. These abnormalities contribute to the impaired wound healing observed in diabetes. Diabetic wounds may lead to the surgical amputation & prolonged hospitalization with enormous health-care expenses. Surgical treatment of diabetic wounds remains difficult & often insufficient, leading to high morbidity among those patients.

The current study is aimed to develop a safe, potent, effective, convenient & cost effective therapeutic strategy of Ayurveda for diabetic wounds to be used on daily basis with the longer shelf life in the form of this Poly herbal gel.

For this study, we have selected 5 such all well-known medicinal drugs, which are easily available & having greater potency. The reasons behind selecting these drugs are their bioavailability in abundance as fresh or dry herb, having *vranaropak*, *shothaghna*, *jantughna*, *vishaghna*, *krimighna*, *dahanashak*, *kandughna* properties & their cost effectiveness⁴.

AIMS & OBJECTIVES

Aim Pharmaceutical development & standardization of polyherbal gel for diabetic wounds.



Objectives

- I) To do collection & authentication of the selected drugs.
- II) To develop the standard manufacturing process & physico – chemical analysis of poly herbal gel for diabetic wounds with these ingredients.

MATERIALS & METHODS

Materials

For this study, drugs were selected by the classical textual references which are having *vranaropak*, *shothaghna*, *jantughna*, *vishaghna*, *krimighna*, *dahanashak* & *kandughna* properties & they are *Durvapatra* (*Cynodondactylon*), *Nimbapatra* (*Azadirachta indica*), *Haridra* (*Curcuma longa*), *Daruharidra* (*Berberisaristata*) & *Yashtimadhu* (*Glycyrrhiza glabra*)⁷⁻⁹. These drugs were collected from the local flower market of

Dadar, Mumbai & authenticated from the Dravyaguna department of Y.M.T. Ayurvedic Medical College, Kharghar, Navi Mumbai. For gel preparation, carbopol, methyl paraben, EDTA (Ethylenediaminetetraacetic acid) & essential oil were purchased from RJK International Chemical manufacturer, Kalbadevi, Mumbai. Triethanolamine was taken from Quality control laboratory of Y.M.T.A.M.C., Kharghar, Navi Mumbai.

The drugs identified are tabulated as in following table no. 1.

Ingredients for Soxhlet Extraction are given in table no. 2)

Ingredients for Poly herbal Gel for Diabetic Wounds (Per 100 ml of extraction) are mentioned in table no. 3)

Batches of Polyherbal Gel for standardization (Per 180 ml of extraction) are discussed in table no. 4)

Table 1 The drugs identified are tabulated

Name of drugs	Botanical name and Family	Rasa	Guna	Virya	Vipaka	Karma
<i>Durvapatra</i>	<i>Cynodondactylon</i> – Poaceae	<i>Kashaya, Madhura</i>	<i>Laghu</i>	<i>Sheeta</i>	<i>Madhura</i>	<i>Kapha – Pitta hara, Dahanashak, Varnya</i>
<i>Nimbapatra</i>	<i>Azadirachta indica</i> – Meliaceae	<i>Tikta, Kashaya</i>	<i>Laghu, Ruksha</i>	<i>Sheeta</i>	<i>Katu</i>	<i>Kapha – Pitta hara, Vranaropaka, Krimighna, Kandughna</i>
<i>Haridra</i>	<i>Curcuma longa</i> – Zinzeberceae	<i>Tikta, Katu</i>	<i>Ruksha, Laghu</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kapha – Vatahara, Vranaropaka, Krimighna, Kandughna, Lekhaniya, Vishaghna</i>



<i>Daruharidra</i>	<i>Berberisaristata</i> – Berberidaceae	<i>Tikta,</i> <i>Kashaya</i>	<i>Laghu,</i> <i>Ruksha</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kapha – Pitta</i> <i>hara,</i> <i>Vranaropak</i>
<i>Yashtimadhu</i>	<i>Glycyrrhizaglabra</i> – Fabaceae	<i>Madhura</i>	<i>Guru ,</i> <i>Snigdha</i>	<i>Sheeta</i>	<i>Madhura</i>	<i>Tridosahara,</i> <i>Shothahara,</i> <i>Vranaropak</i>

Table 2 Ingredients for Soxhlet Extraction

Sr. No.	Ingredients (Name of drugs)	Quantity
1	<i>Durvapatra</i> (<i>Cynodondactylon</i>)	5 gm
2	<i>Nimbapatra</i> (<i>Azadirachtaindica</i>)	5 gm
3	<i>Haridra</i> (<i>Curcuma longa</i>)	5 gm
4	<i>Daruharidra</i> (<i>Berberisaristats</i>)	5 gm
5	<i>Yashtimadhu</i> (<i>Glycyrrhizaglabra</i>)	5 gm
6	Water	8 parts = 200 ml

Table 3 Ingredients for Poly herbal Gel for Diabetic Wounds (Per 100 ml of extraction)

Sr.No.	Ingredients	Action	Proportion
1	Herbal extraction		100 ml
2	EDTA	Chelating agent	0.1%
3	Carbopol	Gelling agent	2%
4	Methyl paraben	Preservative	0.065%
5	Triethanolamine	pH stabilizer	1.5%
6	Essential oil	Fragrance	2%

Table 4 Batches of Poly herbal Gel for standardization (Per 180 ml of extraction)

Sr. No.	Ingredients	PG – 1	PG – 2	PG – 3
1	Herbal extraction	180 ml	180 ml	180 ml
2	EDTA	0.18 ml	0.18 ml	0.18 ml
3	Carbopol	3.6 gm	3.6 gm	3.6 gm
4	Methyl paraben	117 mg	117 mg	117 mg
5	Triethanolamine	2.7 ml	2.7 ml	2.7 ml
6	Essential oil	3.6 ml	3.6 ml	3.6 ml

Instruments for Soxhlet Extraction

Khalvayantra, weighing balance, measuring cylinder, stirrer, cotton cloth/ filter paper, soxhlet apparatus, petroleum jelly, glass beads, glass beaker, glass bottle for storage.

Instruments & equipments for Poly herbal Gel for Diabetic Wounds.

Planetary mixer, weighing balance, measuring cylinder, conical flask, spatula, dropper, filter paper, container for filling gel.

Methods

Pharmaceutical method: Schematic presentation of Soxhlet extraction (Figure 1, Figure 2, Figure 3)

1. *Durvapatra* + *Nimbapatra* + *Haridra* + *DaruHaridra* + *Yashtimadhu* (each 5 gm) were taken in a cotton cloth & tied it in a pottali.
2. Extraction was done by continuous hot extraction (Soxhlet) method using 200 ml distilled water.

Schematic presentation of Poly Herbal Gel for Diabetic Wounds (Figure 4, Figure 5)



Fig 1 SE



Fig 2 SE



Fig 3 SE (Soxhlet Extraction)

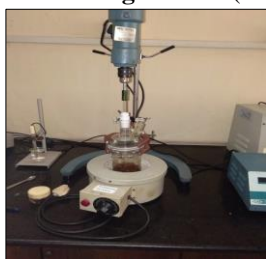


Fig 4 & 5 Pharmaceutical preparation of Poly herbal gel for diabetic wounds

1. 180 ml of Soxhlet extract was taken into the planetary mixer.
2. To the above extract 0.018 ml of EDTA was added & mixture was stirred for 2 mins.
3. Then 3.6 gm carbopol was added & the mixture was stirred at 300 rpm for initial 15 mins.
4. The rpm of the mixer was gradually increased for every 5 mins and continued till 30 mins.
5. Then Tri-ethanolamine (2.7 ml) was added & the mixture was stirred at 3000 rpm for 5 min.

6. Methyl paraben (117mg) was added & the mixture was stirred at 3000 rpm for 5 mins.

7. Essential oil (3.6 ml) was added & the mixture was stirred at 3000 rpm for 5 mins.

8. After sufficient stirring a homogenous mixture of gel was prepared, it was stored in an appropriate container & labeled. The process was repeated for 3 times to prepare 3 batches for the purpose of standardization.

For the purpose of standardization 3 batches were prepared of this poly herbal gel. They were named as PG-1, PG-2 & PG-3 respectively. (PG-Polyherbal gel).

OBSERVATION

Physico-chemical analysis of Poly Herbal Gel

a. *PanchabhautikaParikshana* (*Shabda, Sparsha, Roop, Rasa, Gandha*)

b. Modern Parameters

❖ **Physical appearance** - The gel formulation was evaluated in terms of physical character like change in colour, odour & rheological parameters.

❖ **pH value** - The pH of the gel formulation was determined by using digital pH meter i.e., electrode method and pH strip method. 500 mg of gel was taken & dissolved in 50mL distilled water.



Measurement of pH was done in triplicate & average value was calculated.

❖ **Homogeneity** - Developed gel was tested for homogeneity by visual inspection after the gel was set in the container. It was tested for appearance & presence of any aggregates.

❖ **Skin irritation test** - Test for irritation was performed on human volunteers with their consent. Five volunteers were selected & 1.0 g of formulated gel was applied on an area of 2 square inch to the back of hand. The volunteers were observed for lesions or irritation.

❖ **Rancidity test (Kreis test)** – The test depends upon the formation of a red colour when oxidized fat is treated with conc. HCl & a solution of phloroglucinol in ether. The compound in rancid fats

responsible for the colour reaction is epihydrin aldehyde. All oxidized fats respond to the Kreis test & the intensity of the colour produced is roughly proportional to the degree of oxidative rancidity. Mix 1 ml of melted fat & 1 ml of conc. HCl in a test tube. Add 1 ml of a 1 % solution of phloroglucinol in diethyl ether & mix thoroughly with the fat-acid mixture. A pink colour formation indicates that the fat is slightly oxidized while a red colour indicates that the fat is definitely oxidized (Figure 9, Figure 10, Figure 11).

The study was repeated three times for standardization purpose.

Panchabhautika Parikshana (Shabda, Sparsha, Roop, Rasa, Gandha) are given in table no. 5)

Modern Parameters are given in table no. 6 & figure 6 to 8)

Table 5 *Panchabhautika Parikshana (Shabda, Sparsha, Roop, Rasa, Gandha)*

Pariksha	Batch – 1 (PG-1)	Batch – 2 (PG-2)	Batch – 3 (PG-3)
Shabda	No specific sound	No specific sound	No specific sound
Sparsha	Slakshan-mrudu	Slakshan-mrudu	Slakshan-mrudu
Roop	Yellow coloured homogenous mixture	Yellowish brown coloured homogenous mixture	Dark yellow coloured homogenous mixture
Rasa	Not applicable	Not applicable	Not applicable
Gandha	Characteristic smell	Characteristic smell	Characteristic smell

Table 6 Modern Parameters

Modern parameters	PG – 1	PG – 2	PG – 3
Physical appearance	Yellow coloured homogenous mixture	Yellowish brown coloured homogenous mixture	Yellow coloured homogenous mixture
pH	5.58 (By strip – 6)	5.59 (By strip – 6)	5.68 (By strip – 6)
Homogeneity	Homogeneous, smooth and, consistent gel. No aggregates found.	Homogeneous, smooth and consistent gel. No aggregates found.	Homogeneous, smooth and consistent gel. No aggregates found.
Skin irritation test	Skin compatible. No irritation found	Skin compatible. No irritation found	Skin compatible. No irritation found
Rancidity test	No colour change. No Rancidity seen.	No colour change. No Rancidity seen.	No colour change. No Rancidity seen.



Fig 6, 7, 8 Batch 1, Batch 2 and Batch 3 of Poly herbal gel

RESULTS & DISCUSSION

Reports of physical appearance, pH, homogeneity, skin irritation test & rancidity test are given in above table. It can be found from literature survey that pH mean value of human skin is about 5-5.5, which is acidic. Applying acidic remedies to the wound surface lowers the pH of the infected surfaces & makes an environment unsuitable for the growth & multiplication of the bacteria. This has been proved by microbiological studies & the rapid clearing up of infected surfaces. The pH of the formulated gel was found to be 5.61 which is close to the aforesaid values as well as skin pH. Thus, application of acidic remedy is effective in clearing bacterial pathogens from contaminated or infected wound beds by creating an acidic environment⁵ unfavorable for the growth of bacterial pathogens present on the wound surface. A good viscosity is required to have an acceptable formulation, too viscous gel may cause pourability problem whereas too low viscosity may cause settling of dispersed contents while storage. The gels

were appeared to be moderate viscous in appearances or application. Application of a gel is comfortable if the base spreads easily, exhibiting maximum slip & drag. The prepared gel produces good spreadability. The physical appearance of the gel in batches– 1& 3 were yellow coloured homogenous mixtures & batch – 2 was yellowish brown coloured homogenous mixture. All the 3 batches were homogenous, smooth & consistent with no aggregates or sediments with skin compatible & no irritation found on application & no colour change & no rancidity was seen.

CONCLUSION

In the present study, the gel was formulated successfully. The topical application of this gel may have minimum side effects as compared to allopathic drugs which is needed to

be established by preclinical & clinical studies. From the above study it is observed that most of these drugs are having *Tikta, Kashaya, Katu & Madhur rasa, Laghu, Ruksha, Guru, Snigdha guna, Ushna Virya, Madhu & Katu vipaka & Kapha – Pittashamaka* properties. As *Durvapatra* are having *Dahashamak & vranaropak* properties, *Nimbapatra, Haridra & Daruharidra* are having *shothaghna,*



krimighna, *lekhaniya*, *kandughna* & *vranaropak* properties & *Yashtimadhu* is having *tridosahara* & *shothahara*⁶⁻⁸ properties, hence these drugs are collectively helpful in treating Diabetic wounds.

So these drugs are converted into new dosage form i.e. gel form for better application providing more stability & easily applied therapeutic strategy with longer shelf life. However an elaborate protocol for the pre-clinical & clinical trials is needed to be designed & implemented to check the anti-microbial, anti-bacterial & wound healing activity on human volunteers & in-vitro study.

By this present study, related to Diabetic wounds, it can be concluded that these types of wound need special care to patient with proper attention & ayurvedic management gives satisfactory results to them through new dosage forms⁹. If proper care is not taken then it will increase the risk of hospitalization or amputation. Hence, this new dosage form of ayurvedic therapeutic strategy may provide better recovery option to such patient which reduces their chances of amputation.

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Conflict of interest: None



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