# National Journal of Physiology, Pharmacy and Pharmacology

## RESEARCH ARTICLE

# Effect of neem leaves extract irrigation on the wound healing outcome in nurse managed diabetic foot ulcers

# Muthu Srinivasan Jayalakshmi<sup>1,2</sup>

<sup>1</sup>Department of Nursing, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, Tamil Nadu, India, <sup>2</sup>Army Institute of Nursing, Guwahati, Assam, India

Correspondence to: Muthu Srinivasan Jayalakshmi, E-mail: sekarji2003@gmail.com

Received: August 20, 2020; Accepted: September 08, 2020

#### **ABSTRACT**

**Background:** Foot ulcer is a common and massive complication of Diabetes that the economic, social, and public health workers tackled throughout the world. **Aim and Objective:** This study aimed to compare and evaluate the effect of neem extract irrigation with normal saline on the wound healing outcome among diabetic foot ulcer patients. **Materials and Methods:** The present single-blind experimental design study was conducted on 160 diabetic Foot ulcer patients who attended a diabetic foot clinic center during the period February 2019–February 2020. Patients were allocated in two groups, by simple random assignment. Intervention group received Neem extract irrigation and control group received Normal saline irrigation weekly twice. In both groups, wound assessment was done using PUSH tool at baseline and then at the end of each week till 4 weeks are completed. Data were analyzed in SPSS20 software, and P < 0.05 was considered statistically significant. **Results:** The total pre intervention means and standard deviation of the Wound surface area in the intervention and control groups were respectively  $17.13 \pm 21.46$  and  $19.84 \pm 23.98$ , and the post intervention mean and standard deviation of the Wound surface area at the end of 4 weeks of study period was respectively  $6.92 \pm 16.62$  and  $14.04 \pm 21.32$ . The difference between the two groups at the end of  $3^{rd}$  and  $4^{th}$  week were statistically significant (P = 0.018 and P = 0.047). **Conclusion:** Neem leave extracts irrigation promotes wound healing activity and is preferred being natural and safe without producing any adverse effect.

KEY WORDS: Wound Management; Neem Extract; Normal Saline; Wound Healing Outcome; Nursing

### INTRODUCTION

Foot ulcer is a common complication of diabetes that has shown an increasing trend over previous decades that enhances the levels of morbidity for individuals and burdens health and social care systems with huge costs.<sup>[1]</sup> The burden of this ulcer is massive and referred to as the common problem

Access this article online					
Website: www.njppp.com	Quick Response code				
<b>DOI:</b> 10.5455/njppp.2021.10.09238202008092020					

that the economic, social, and public health workers tackled throughout the world.<sup>[2]</sup> The most feared consequences of foot ulcers are lower extremity amputations, seen more often in patients with diabetes than in general population.<sup>[3]</sup> The risk of diabetic foot ulceration increases with age, duration and increase in limb amputation as an extent. Approximately fifteen percent (15%) of patients with diabetes will suffer from foot ulcer during their lifetime.<sup>[4]</sup> Based on the complexity of ulcer the outcome of may vary.

The main principles of treatment for managing foot ulcer are local wound care, debridement to remove of necrotic tissue, reduce pressure. Wound dressings are done to provide a moist environment and to control exudate. [5] Health care professionals are showing equal interest in use of medicinal

National Journal of Physiology, Pharmacy and Pharmacology Online 2020. © 2020 Muthu Srinivasan Jayalakshmi. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creative commons.org/licenses/by/4.0/), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

plant products along with modern medical practices as they are having equal ability in healing of wounds. The use of natural products in traditional medicine is being incorporated into the primary health care systems. According to the WHO, 80% of the world's population mainly those of developing countries depend on plant derivative medicines for their healthcare. [6] All parts of the neem plant are often used in various alternative medicine such as Ayurveda, Unani and homeopathy<sup>[7]</sup> and has drawn equal attention of modern medicine.[8] Authors of a study have discussed the responsible use of natural plantbased preparations based on the literature and have concluded that complementary alternative medicine provides additional option for optimal wound bed preparation for persons with wounds. [9] As per the literature, one researcher found that Neem Leaves have medicinal compounds like nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol.[10-12] Aqueous leave extracts of Neem (Azadirachta indica) promotes wound healing activity through increased inflammatory response and neovascularization in animals, [13] has recommended further study on humans.<sup>[14]</sup> Studies have also been conducted in dentistry field which has proved effectiveness of neem extract in endodontic procedures and root canal treatment. [15,16] Researchers have found many active components such as azadirone, azadiractin, flavonoids have potential therapeutic properties.[17,18] Use of methanol extract of neem leaves could be harmful to humans by causing physiological damage when used for wound management. However, the researcher has not come across any studies using aqueous neem extract on humans for managing chronic wounds in either diabetic or non-diabetic individuals. Therefore, the main of this study was to evaluate the effectiveness of neem extract solution wound irrigation on the wound healing outcome of diabetic foot ulcer patients.

#### MATERIALS AND METHODS

#### **Study Design**

The present study was a single-blind, randomized control group experimental design.

## **Study Population**

The study population for the present study contained all patients with diabetic foot ulcer who attended the foot care clinic of Sun Valley Hospital from February 2019 to February 2020. The study included eligible diabetic foot ulcer patients who were willing to participate in the study, have confirmed diagnosis of diabetes, have minimum age of 20 years, absence of cognitive or mental illness, end stage renal disease, drug abuse, alcoholism, history of previous hospitalization for foot ulcers, have a foot ulcer of any duration with an area of at least 1 cm<sup>2</sup> (greatest length greatest width), foot ulcers of Gr

1–3 graded by Wagner Scale, uncomplicated by clinical signs of severe infection or ischemia and who have the support of caretakers to adhere to non-weight bearing practices and are hemodynamically stable. Eligible foot ulcer patients were explained about the purpose of the study. The study excluded patients who are in need of undergoing negative pressure wound therapy, having the need for urgent medical intervention due to systemic medical complications, occurrence of diabetic complications like diabetic ketoacidosis, ulcer related complication like osteomyelitis, or severe systemic infection. After explaining the purpose, procedure, risks and benefits of the study informed consent was obtained from the participants. Patients were homogenous in terms of age. gender, income, marital status, education, duration of diabetes mellitus (DM), comorbid conditions, medications for DM, Glycated hemoglobin level, loss of vibration sensation, age of the wound and wound area.

# **Study Intervention**

Foot ulcer patients were randomly assigned by simple random technique to Neem extract irrigation, weekly twice for 4 weeks (Experimental group) or the conventional normal saline irrigation group, weekly twice for 4 weeks (conventional group). On the 1st day of the enrolment for the study, pre intervention wound assessment was done using PUSH tool<sup>[19]</sup> on the wound size, type of tissue on wound bed and amount of exudate. Wound which required debridement was done by the treating surgeon according to standard procedures. The wound was irrigated with freshly prepared neem extract solution (Neem extract irrigation) using 10 ml syringe with 19 number needles in the experimental study group participants. Normal saline was used to irrigate wound (Normal Saline irrigation) with same procedure in the control study group participants. For both groups, irrigation was done following the aseptic technique. The wound was subsequently dressed by applying the topical antibiotics (Biocollaz powder, povidone -iodine and Metrogyl gel). The wound was finally dressed with any one of the dressing by (gel or foam) and covered with dressing material. A secondary dressing was allowed to add cushion for support. Offloading was done using cast walker, or diabetic shoe, or total contact cast which was required for all participants in both experimental and control groups. In both experimental and control group, Patients visited the clinic after every 3-4 days. Wound was assessed on the initial visit (base line), at the end of each week till the completion of 4 weeks assessment.

### Randomization

After screening for eligibility, participants were assigned randomly through simple random technique (lottery method) to both neem extract and normal saline irrigation group. Randomized patients received wound irrigation according to the intervention they were allocated and were blinded to treatment allocation.

#### **Study Outcomes**

The primary outcome of this study was wound percent area reduction in 4 weeks with wound tissue changes and reduction of exudate. Secondary outcomes of this study were number of adverse events.

# **Ethics Approval**

The study protocol was approved by the ethical committee of Marwari Hospital, Guwahati, registered with CDSCO, Govt of India vide Regd.No. ECR/487/Inst/AS/2013/ RR-16.

## Sample Size and Statistical Analysis

The sample size was calculated as 80 participants per group based on pilot study effect size, considering the type I error value of  $\alpha = 0.05$  and with 80% power. To increase the credibility of the samples, 20% was added to the sample size, and thus 100 participants were assigned per group. Baseline characteristics of study participants in both groups were described using descriptive statistics (frequency, mean and standard deviation). Independent "t-test" was applied to

compare the means of 2 groups at each week. Chi-square test was used to evaluate the association between independent variables (patient's and clinical variables) and dependent variables (wound area reduction). F-test was used to assess the equality of means among groups. All analyses were conducted using SPSS (version 20).

#### RESULTS

A total of 246 diabetic foot ulcer patients were screened for eligibility to participate and 200 met eligibility criteria and were randomly assigned to 2 groups between February 2019 and February 2020 Out of 200 patients, 160 randomized foot ulcer patients completed the 4 weeks study period. Eighty patients randomized to the neem extract irrigation group (n = 100) received at least 2 times wound irrigation and wound care in a week for 4 weeks. Another eighty patients randomized to the Normal Saline irrigation group (n = 100) received at least 2 times wound irrigation and wound care in a week for 4 weeks is shown in Figure 1. Baseline demographic characteristics as shown in Table 1 and clinical characteristics shown in Table 2 were similar in both groups. Wound characteristics as shown in

Table 1: Demographic characteristics of participants at baseline					
Control group (n=80)		Treatment group (n=80)		Chi square	<i>P</i> -value
Frequency	Percentage	Frequency	Percentage	value	
					$0.320^{NS}$
4	5	9	11.25	2.281	
51	63.75	50	62.5	df=2	
25	31.25	21	26.25		
					$0.405^{\rm NS}$
68	85	64	80	0.693	
12	15	16	20	df=1	
					$1.000^{\mathrm{NS}}$
78	97.5	78	97.5	0.000	
2	2.5	2	2.5	df=1	
					$0.077^{\rm NS}$
5	6.25	0	0		
23	28.75	19	23.75		
6	7.5	8	10	8.430 df=4	
45	56.25	48	60		
					$0.858^{\rm NS}$
58	72.5	59	73.75	0.032	
22	27.5	21	26.25	df=1	
					$0.744^{\rm NS}$
31	38.75	29	36.25	0.107	
49	61.25	51	63.75	df=1	
					$0.77^{\rm NS}$
31	38.75	47	58.75		
33	41.25	20	25	6.831	
14	17.5	11	13.75	df=3	
2	2.5	2	2.5		
	78 2 5 23 6 45 58 22 31 49 31 33 14	Control group (n=80)   Frequency Percentage   4 5   51 63.75   25 31.25   68 85   12 15   78 97.5   2 2.5   5 6.25   23 28.75   6 7.5   45 56.25   58 72.5   22 27.5   31 38.75   49 61.25   31 38.75   33 41.25   14 17.5	Control group (n=80) Treatment   Frequency Percentage Frequency   4 5 9   51 63.75 50   25 31.25 21   68 85 64   12 15 16   78 97.5 78   2 2.5 2   5 6.25 0   23 28.75 19   6 7.5 8   45 56.25 48   58 72.5 59   22 27.5 21   31 38.75 29   49 61.25 51   31 38.75 47   33 41.25 20   14 17.5 11	Control group (n=80) Treatment group (n=80)   Frequency Percentage   4 5 9 11.25   51 63.75 50 62.5   25 31.25 21 26.25   68 85 64 80   12 15 16 20   78 97.5 78 97.5   2 2.5 2 2.5   5 6.25 0 0   23 28.75 19 23.75   6 7.5 8 10   45 56.25 48 60   58 72.5 21 26.25   31 38.75 29 36.25   49 61.25 51 63.75   31 38.75 47 58.75   33 41.25 20 25   14 17.5 11 13.75	$ \begin{array}{ c c c c c } \hline \textbf{Control group } (n=80) & \textbf{Treatment group } (n=80) & \textbf{Chi square value} \\ \hline \textbf{Frequency} & \textbf{Percentage} & \textbf{Frequency} & \textbf{Percentage} \\ \hline \hline 4 & 5 & 9 & 11.25 & 2.281 \\ 51 & 63.75 & 50 & 62.5 & df=2 \\ 25 & 31.25 & 21 & 26.25 \\ \hline 68 & 85 & 64 & 80 & 0.693 \\ 12 & 15 & 16 & 20 & df=1 \\ \hline \hline 78 & 97.5 & 78 & 97.5 & 0.000 \\ 2 & 2.5 & 2 & 2.5 & df=1 \\ \hline 5 & 6.25 & 0 & 0 & 0 \\ 23 & 28.75 & 19 & 23.75 & 6 \\ 6 & 7.5 & 8 & 10 & 8.430  df=4 \\ 45 & 56.25 & 48 & 60 \\ \hline \hline 58 & 72.5 & 59 & 73.75 & 0.032 \\ 22 & 27.5 & 21 & 26.25 & df=1 \\ \hline 31 & 38.75 & 29 & 36.25 & 0.107 \\ 49 & 61.25 & 51 & 63.75 & df=1 \\ \hline 31 & 38.75 & 47 & 58.75 \\ 33 & 41.25 & 20 & 25 & 6.831 \\ 14 & 17.5 & 11 & 13.75 & df=3 \\ \hline \end{array}$

NS=Not significant

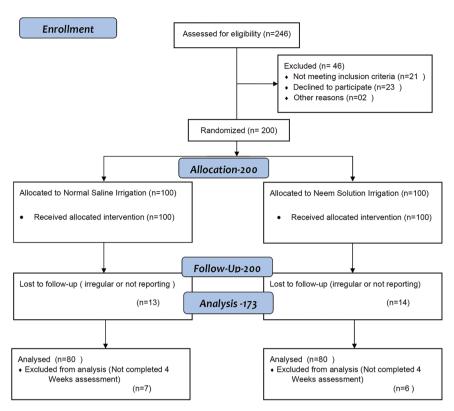


Figure 1: The research process

Table 2: Clinical variables of foot ulcer patients at baseline						
Clinical variables	Control group (n=80)			Treatment group (n=80)		<i>P</i> -value
	F	0/0	$\overline{\mathbf{F}}$	%	_	
Duration of DM					4.564	0.335 <sup>NS</sup>
<5 years	23	28.75	29	36.25	Df=4	
5–15 years	26	32.5	28	35		
15–25 years	20	25	18	22.5		
>25 years	11	13.75	5	6.25		
Comorbid conditions					10.140	$0.119^{NS}$
Nil	33	41.25	47	58.75	Df=6	
HTN	27	33.75	21	26.25		
HTN+other	3	3.75	2	2.5		
Hypothyroidism	9	11.25	2	2.5		
PAD	2	2.5	4	5		
Cardiac disease	5	6.25	2	2.5		
Others	1	1.25	2	2.5		
Medications taken for DM						
Nil	1	1.25	0	0		
Insulin	60	75	48	60	7.181	
OHA	9	11.25	21	26.25	Df=3	$0.66^{\mathrm{NS}}$
Insulin + OHA	10	12.5	11	13.75		
HbA1C level						
<7	6	7.5	8	8.8	0.08	
>7	74	92.5	73	91.3	Df=1	$0.772^{NS}$
Vibration sensation						
Present	34	42.5	36	45	0.626	$0.429^{NS}$
Absent	46	57.5	44	55	Df=1	

NS=Not significant, DM: Diabetes mellitus, HbA1C: Glycated hemoglobin

Table 3 were similar in both groups in terms age of wound, size of the wound with the exception of ulcer grade, tissue condition and exudate level. The mean wound area of patients in neem extract irrigation group was 17.13 (SD 21.46) compared to 19.84 (SD 20.96) in the normal saline irrigation group. Week wise analysis of the results was done in both groups is shown in Table 4. Analysis of the primary outcome of >50% reduction of wound area in the post intervention period identified significant difference between groups in  $3^{rd}$  and  $4^{th}$  weeks, P < 0.05.

#### DISCUSSION

A total of 80 (50%) foot ulcer patients met primary outcome of achieving ≥50% wound area reduction. Among foot ulcer patients in the Neem extract irrigation group, 51 (63.75%) met achieved primary outcome compared to 29 (36.25%) in the normal saline irrigation group. At the end of 4 weeks, it was observed slow healing in 33 (20.62%), 12 (7.5%) underwent toe amputation. Only in 4 (2.5%) patients, complete healing of wound was observed in both groups. Persistent no change in wound area was observed in 5 (3.12%) patients. No adverse events like skin allergy, itching was observed in either group.

Different types of extracts from different part of neem plant were used for different activities. [20] Iabichella et al., noted in a clinical case of foot ulcer, that the fusion of two plant extracts, Hypercom (Hypercom perforatum) and neem oil helped to decrease the dimension of the ulcer, thereby increasing the granulated tissue and remodeling the skin tissue. In a different study, the same researchers have found improvement of peripheral micro vascular circulation in neuropathic patients with advanced DFU using the same extract. [21,22] Jaya Mary in her study compared the effectiveness of conventional and herbal treatment in diabetic foot ulcer patients and results showed a highly significant change in the third visit after 30 days of posttest (P < 0.001). In the aforementioned study, dressing was done with mixture of herbal oil prepared with fresh dark green neem (A. indica) leaves, coconut oil (cocos nucifera) along with turmeric powder.<sup>[23]</sup>

It is assumed that ingredients from medicinal plants are lesser toxic in nature and have fewer side effects. Leaf extract of neem has antimicrobial activity against human pathogenic bacteria.<sup>[24]</sup> An author has reported that in one particular case, application of medicinal plant-based ointment has prevented 85% of

Table 3: Wound characteristics of foot ulcer patients at baseline							
Wound variables	Experimental group (n=80) (%)	Control group (n=80) (%)	Chi-square	<i>P</i> -value			
Age of wound (days)							
<100	74 (92.5)	74 (92.5)	0.533	$0.911^{\rm NS}$			
101-200	2 (2.5)	3 (3.75)	Df=3				
201–300	2 (2.5)	1 (1.25)					
>300	2 (2.5)	2 (2.5)					
Ulcer site							
Dorsum	29 (36.25)	18 (22.5)	0.030	$0.011^*$			
Dorso Plantar	19 (23.75)	39 (48.75)	Df=3				
Plantar	5 (6.25)	9 (11.25)					
Heel	23(28.75)	17 (21.25)					
	9 (11.25)	6 (7.5)					
Ulcer grade			27.321	0.001***			
Grade I	19 (23.75)	3 (3.75)	Df=2				
Grade II	49 (61.25)	38(47.5)					
Grade III	12 (15)	39 (48.75)					
Wound area (Sq cm)			3.520	$0.318^{\rm NS}$			
<10	36 (45)	30 (37.5)	Df=3				
10-50	40 (50)	43 (53.75)					
51–90	1 (1.25)	5 (6.25)					
>90	3 (3.75)	2 (2.5 )					
Tissue type			6.131	0.013*			
Granulation	21 (26.25)	36 (45)	Df=1				
Slough	59 (73.75)	44 (55)					
Exudate level			20.62	0.0001***			
Moderate	20 (25)	0	Df=1				
High	60 (75)	80 (100)					

NS=Not significant, \*=Significant, p<0.05\*\*\*=Highly significant <0.001

**Table 4:** Comparison of wound surface area among diabetic foot ulcer participants in both groups at different times during the study (n=80 in each group)

Stage	Group (n)	Mean±SE	MeanD±SED	Cohen D	t	df	<i>P</i> -value		
Pre intervention	Control (80)	19.84±2.68	2.71±3.60	0.119	0.75	158	0.452 <sup>NS</sup>		
	Treatment (80)	17.13±2.4							
Week-1	Control (80)	18.41±2.34	3.73±1.13	0.178	1.13	158	$0.261{}^{\rm NS}$		
	Treatment (80)	14.68±2.33							
Week-2	Control (80)	16.87±2.29	5.58±1.78	0.279	1.78	158	$0.077^{\mathrm{NS}}$		
	Treatment (80)	11.29±2.15							
Week-3 Con	Control (59)	17.23±2.82	8.19±2.39	0.407	2.39	133	0.018*		
	Treatment (76)	$9.04\pm2.08$							
Week-4	Control (53)	$14.04\pm2.93$	$7.12\pm2.01$	0.371	2.01	113	0.047*		
	Treatment (62)	$6.92\pm2.11$							
	Statistical test result								
	Group factor F=119	Group factor <i>F</i> =119.16 <i>P</i> ≤0.001** df=1							
	Time factor $F=75.93$	Time factor $F=75.93 P \le 0.001** df=1$							
	Interaction of group	and time F=2.50 <i>P</i> =0.	042* df=1						

F=Repeated measure analysis of variances (ANOVA)

infected diabetic wound from the amputation. [25] In the present study too, patients who underwent neem extract irrigation did not experience any kind of reactions or adverse events. The researcher felt neem extract might actually added synergistic antimicrobial effect without causing adverse drug interaction. Ineffectiveness of neem extract on all patients in achieving ≥50% WAR might be due to the higher grade of ulcers, age of wound and could be due to other confounding factors like nutritional factors. It is crucial to find an enhanced treatment option for wound healing dressings to assist patients and physicians. [26] There is a good scope of wound healing process using neem and curcumin extract.<sup>[27]</sup> The present study indicates the demand for developing alternative methods for managing diabetic foot ulcers using plant extracts that have significant wound healing properties to establish a holistic approach in the evidence based wound management by the nurse practitioners.

## **Strength and Limitation**

This is the first study done using neem extract for wound irrigation to manage diabetic foot ulcer. Hence the present study is a novel attempt in managing chronic wounds. The limitations of this study were, only those diabetic foot ulcer patients having Grade 1–3 ulcers were included, followed only for 4 weeks in the post intervention period and were not followed till the closure of wounds. Confounding factors that could not be managed by the researcher in this study are nutritional intake, dietary restriction, antibiotics prescribed by the treating physician and number of wound debridement performed by the surgeon.

## **CONCLUSION**

Among the diabetic foot ulcers who have completed in the study, the mean decrease in ulcer size at the end of 4 weeks was

higher in neem extract irrigation compared to normal saline irrigation practice. Findings of the present study indicate that, neem leave extracts irrigation promotes wound healing activity and is an appropriate option, preferred being natural, ease of access and safe without producing any adverse effect. Results of this study suggest that neem irrigation could be adopted by home visit nurses or at Primary health care centers to manage foot ulcers wounds at an early stage without being hospitalized.

# ACKNOWLEDGMENTS

The author would like to thank Dr. Sudhir K. Jain, MBBS, MS, PhD, Department of Limb Complications and Foot Care, Sun Valley hospital and foot ulcer patients who cooperated to participate in the study.

## REFERENCES

- 1. Crawford F, Nicolson DJ, Amanna AE, Martin A, Gupta S, Leese GP, *et al.* Preventing foot ulceration in diabetes: Systematic review and meta-analyses of RCT data. Diabetologia 2019;63:49-64.
- 2. Naves CC. The diabetic foot: A historical overview and gaps in current treatment. Adv Wound Care 2016;5:191-7.
- 3. Narres M, Kvitkina T, Claessen H, Droste S, Schuster B, Morbach S, *et al.* Incidence of lower extremity amputations in the diabetic compared with the non-diabetic population: A systematic review. PLoS One 2017;12:e0182081.
- Beyaz S, Güler ÜÖ, Bağır GŞ. Factors affecting lifespan following below-knee amputation in diabetic patients. Acta Orthop Traumatol Turcica 2017;51:393-7.
- 5. McIntosh C, Ivory JD, Gethin G. Managing wound exudate in diabetic foot ulcers. Diabetic Foot J 2019;22:46-53.
- 6. Dar RA, Nawaz MS, Qazi PH. Natural product medicines: A

- literature update. J Phytopharmacol 2017;6:349-51.
- 7. Singh H, Kaur M, Dhillon JS, Batra M, Khurana J. Neem: A magical herb in endodontics. Stomatol Dis Sci 2017;1:50-4.
- 8. Barman P, Ahmed N, Chakraborty D. Neem-a cynosure of modern medicine: A review. Int J Livest Res 2019;9:1-7.
- 9. Laforet K, Woodbury GM, Sibbald RG. Wound bed preparation and complementary and alternative medicine. Adv Skin Wound Care 2011;24:226-36.
- 10. Rahmani AH, Almatroudi A, Alrumaihi F, Khan AA. Pharmacological and therapeutic potential of neem (*Azadirachta indica*). Phcog Rev 2018;12:250-5.
- 11. Alzohairy MA. Therapeutics role of *Azadirachta indica* (neem) and their active constituents in diseases prevention and treatment. Evid Based Complement Alternat Med 2016;2016:1-11.
- 12. Adithya TN, Basha SJ, Koshma MM, Khalandar SD, Rani YS, Reddy VJ. A current review on *Azadirachta indica* (neem). World J Pharm Pharm Sci 2017;6:249-69.
- 13. Emeka AO, Emamoke JO, Theodore AA, Julius CO. The wound healing effects of aqueous leave extracts of *Azadirachta indica* on Wistar rats. J Natl Sci Res 2013;3:181-6.
- 14. Chundran NK, Husen IR, Rubianti I. Effect of neem leaves extract (*Azadirachta indica*) on wound healing. Althea Med J 2015;2:199-203.
- Mistry KS, Sanghvi Z, Parmar G, Shah S. The antimicrobial activity of *Azadirachta indica*, *Mimusops elengi*, *Tinospora* cordifolia, *Ocimum sanctum* and 2% chlorhexidine gluconate on common endodontic pathogens: An in vitro study. Eur J Dent 2014;8:172-7.
- 16. Kaushik A, Tanwar R, Kaushik M. Ethnomedicine: Applications of neem (*Azadirachta indica*) in dentistry. Dent Hypotheses 2012;3:112.
- 17. Uzzaman S. Pharmacological activities of neem (*Azadirachta indica*): A review. Int J Pharmacogn Life Sci 2020;1:38-41.
- 18. Trivedi A, Fatima N, Husain I, Misra A. An update on the therapeutic potential of neem and its active constituents: A panacea for all diseases. Eras J Med Res 2019;6:110-7.

- Gardner SE, Hillis SL, Frantz RA. A prospective study of the push tool in diabetic foot ulcers. J Wound Ostomy Continence Nurs 2011;38:385-93.
- 20. Patil PR, Patil SP, Mane A, Verma S. Antidiabetic activity of alcoholic extract of neem (*Azadirachta indica*) root bark. Natl J Physiol Pharm Pharmacol 2013;3:142-6.
- 21. Iabichella ML. The use of an extract of *Hypericum perforatum* and *Azadirachta indica* in advanced diabetic foot: An unexpected outcome. BMJ Case Rep 2013:2012007299.
- 22. Iabichella ML, Caruso C, Lugli M. The use of an extract of *Hypericum perforatum* and *Azadirachta indica* in a neuropathic patient with advanced diabetic foot. BMJ Case Rep 2014;2014:205706.
- 23. Fsj AJ, Vaithiyanathan R, Vijayaragavan R. Effectiveness of conventional and herbal treatment on diabetic foot ulcer using Texas and Wagner wound scales. Int J Nurs Educ 2017;9:1.
- 24. Maragathavalli S, Brindha S, Kaviyarasi NS, Annadurai B, Gangwar SK. Antimicrobial activity in leaf extract of neem (*Azadirachta indica* Linn.). IJSN 2012;3:110-3.
- 25. Oguntibeju OO. Medicinal plants and their effects on diabetic wound healing. Vet World 2019;12:653-63.
- Ghomi ER, Khalili S, Khorasani SN, Neisiany RE, Ramakrishna S. Wound dressings: Current advances and future directions. J Appl Polym Sci 2019;136:47738.
- 27. Dhinakaran M, Sundarasen S, Arumugam A. Detailed study on the synergistic effect of neem extract loaded with curcumin in wound healing using textile substrate. Int Res J Pharm 2017;8:104-9.

**How to cite this article:** Jayalakshmi M. Effect of neem leaves extract irrigation on the wound healing outcome in nurse managed diabetic foot ulcers. Natl J Physiol Pharm Pharmacol 2020;10(10):915-921.

Source of Support: Nil, Conflicts of Interest: None declared.