ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES

Published by JK Welfare & Pharmascope Foundation Journal Home Page: https://ijrps.com

Comparative study of healing of Diabetic foot ulcers between conventional method and local application of probiotics

Unnikrishnan E S, Balaji D*, Velineni Bharath, Arul A

Department of General Surgery, SRM Medical College Hospital & Research Centre, SRM Institute of Science and Technology, Kattankulathur, Tamil Nadu – 603203, India

Article History:

Received on: 27 Jul 2022
Revised on: 16 Aug 2022
Accepted on: 22 Aug 2022

Keywords:

Diabetes Mellitus, Diabetic Foot Ulcers, Probiotics

ABSTRACT

Diabetes mellitus is one of the most critical health issues in the health care system. Patients with Diabetes are subject to various complications. Diabetic foot infection is one of most incapacitating kinds of human infection. Due to growing antimicrobial and antibiotic resistance, existing medications have undesirable side effects and inadequate healing mechanisms. Probiotics are either a single organism or combination of organisms capable of boosting the body's immune system, promoting anti-inflammatory action, and enhancing the wound healing process at the site of an infection. Therefore, it is a revolutionary strategy to use probiotics to eradicate harmful microorganisms and enhance wound healing. Hence the present study was performed to compare the conventional method and local application of probiotics to treat Diabetic foot ulcer. In present study average age of patients in both group were found almost similar 58.58 years in control group and 57.3 years in probiotic group. The diabetic foot wound size of all patients in both groups were evaluated and it was found that mean wound size in both group were almost same. During the study it was found that there was no significant difference in mean wound bed score between two groups on day 1(Control:8.12; Probiotic: 8.24), whereas a significant difference observed on day 7(Control: 10.36; Probiotic; 11.14) and day 14 (Control:12.78; Probiotic:13.56). An increase was seen in mean wound bed score in both groups from day 1 to day 14 but it was observed more in Probiotic group. Present study concludes that probiotics can be safely utilized in therapy of infected diabetic wounds. The probiotic when used along with conventional therapy could results in the hastening the wound healing process as evidenced by significant difference in the day 7 and 14 wound bed scores. Although more studies are needed in this field to give better evidence for support of probiotic use.

*Corresponding Author

Name: Balaji D
Phone:
Email: trace.balaji@gmail.com

ISSN: 0975-7538

DOI: https://doi.org/10.26452/ijrps.v13i3.2501

Production and Hosted by

IJRPS | https://ijrps.com

INTRODUCTION

Diabetes mellitus is one of the most critical health issues in the health care system, and its threat to global public health has expanded dramatically over the last two decades. According to studies, the number of diabetic patients increased from 30 million in 1985 to 177 million in 2000 and 285 million in 2010. It is anticipated that if the current trend continues, more than 360 million people will have diabetes mellitus by 2030.

Patients with Diabetes are subject to various com-

plications, including diabetic foot ulcers (DFU). DFU is a significant health concern as diabetes incidence rises. DFUs occur in around 15% of diabetic patients.

The management of persistent wounds, such as diabetic foot ulcers, presents clinicians and patients with a considerable problem. Significant treatment challenges linked with DFU include delayed wound healing and diabetic foot infection (DFI).

DFI is one of the most incapacitating kinds of human infection. Due to the growing antimicrobial and antibiotic resistance globally, existing medications have undesirable side effects and inadequate healing mechanisms, permitting searching for alternative therapies to accelerate the wound healing process.

The bacteriotherapy treatment is relevant and intriguing. Using non-pathogenic microorganisms in bacteriotherapy is reassuring and a different method of combating illness.

Probiotics mean "for life." It refers to the naturally occurring bacteria or yeast that has positive health benefits when provided in enough numbers. The names prebiotics and synbiotics are also related to probiotics. Prebiotics are substances that are indigestible and fermented by endogenous bacteria. This assists in altering the gut microbiome. Synbiotic are probiotic and prebiotic substances together.

Henry Tissler discovered bifidobacteria in 1899 in Paris, France. He discovered that newborns whose GI tracts were colonized with bifidobacteria had fewer digestive issues.

Metchnikoff was a Russian scientist enrolled at the Pasteur Institute in Paris. Certain natural microorganisms in the digestive system, such as clostridia, caused a kind of intestinal auto-intoxication. Metchnikoff authored a book titled "The Prolongation of Life: Optimistic Studies."

Saccharomyces, Enterococcus, Lactobacillus, Bacillus, Bifidobacterium, and streptococcus are the familiar strains investigated for probiotic function.

Probiotics enhance the function and integrity of the intestinal epithelial barrier. They promote the synthesis of mucin, antimicrobial peptides, and heat shock proteins, which all contribute to their positive impact.

Human beta-defensin-2 is an antibacterial protein that is stimulated by probiotics. It and other antimicrobial proteins inhibit harmful microorganism colonization. Probiotics emit tiny molecules that interact with TLRs and NLRs to modulate the immune system. It is helpful for infection control [1].

Probiotic therapy for chronic wounds

Researchers are investigating the impact of probiotics in chronic wounds as a result of studies highlighting the significance of skin microorganisms and biofilms [2]. There have been few animal-based trials undertaken.

According to studies, Lactobacillus acidophilus inhibits the majority of burn wounds [3].

A 2009 research by Peral et al. examined the efficacy of probiotics and silver lotions in treating burn wounds. They exhibited almost identical advantages.

Probiotics' anti-infective action is based on their ability to compete with infectious pathogens or influence the host's immunological response. Antimicrobial compounds such as organic acids, carbon peroxide, and hydrogen peroxide, as well as low molecular weight antimicrobial chemicals such as diacetyl, bacteriocins, and adhesion inhibitors, may be produced by lactic acid-generating bacteria [4, 5]. Lactobacillus acidophilus, for example, can destroy fungi such as Candida albicans.

Hence the present study was performed to compare the conventional method and local application of probiotics to treat DFU.

Aim and Objectives

To Study the comparison between the effect of local application of probiotics and conventional methods on the healing of Diabetic foot ulcers.

Objectives

1. To compare the change in wound bed scores in the test and control population
2. To compare the wound swab culture results in the test and control population.
3. Test population is one in which we are applying probiotics along with conventional methods for healing
4. Control Population is one in which we are using only conventional methods

MATERIALS AND METHODS

Study Design

A prospective Study

Place of study

SRM University, Kattankulathur, Chennai.

Period of study

18 Months

Study population and sample size

50 in each group

Inclusion Criteria

1. Age > 18 years
2. Age < 70 years
3. People with Diabetes with an average RBS < 250
4. Ulcers involving the foot
5. Wound size more than 10 $cm^2$and less than 60 cm^2

Exclusion Criteria

1. Unstable vitals
2. Peripheral Arterial Disease
3. Peripheral neuropathy
4. Diabetic Ketoacidosis
5. Osteomyelitis

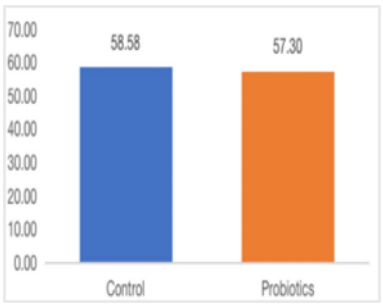

Figure 1: Observation of mean age of patients in both group

Hypothesis

Probiotic bacteria have a beneficial effect on diabetic wounds.

Tools for evaluation of wounds

1. wound bed scoring system developed by falanga
2. wound swab cultures

Collection of Data

1. Approval from Institutional Ethical Committee will be obtained
2. Informed consent will be collected from the participants who fit my inclusion criteria, and confidentiality will be assured.
3. Diabetic patients attending the General Surgery outpatient department with infected foot ulcers are included in the study.
4. 100 patients will be selected for surgical debridement on the presentation day.

The size of their wounds is assessed by wound tracing and planimetry methods. A household plastic wrap is placed over the wound. A marking pen is used to mark wounds. A wrap is placed over graph paper, and the area is measured. The patients are screened for peripheral vascular disease using ankle-brachial pressure index ABPI > 0.9. The patients are also screened for peripheral neuropathy.

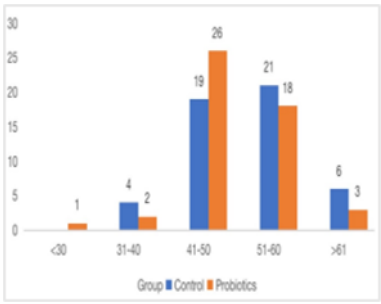

Figure 2: Age group distribution of patients in both groups

Severe ill patients and those with diabetic ketoacidosis are excluded from the study. The patients who consented to participate in the study were allocated into two groups. The current ward regimen of sharp and chemical debridement, cleansing and dressing, glycaemic management, and antibiotic medication is administered to the control group.

In the intervention group, in addition to the above, a probiotic solution is applied daily during dressing [6, 7]. The wound bed scoring system developed by Falanga was utilized to monitor the wound objectively. Wound swab cultures are taken on Day 0, Day 5, and Day 10. Both the groups will be compared concerning the wound bed score on day 1, day 7, and day 14 and the wound swab cultures and outcomes identified. The results were analysed.

Statistical analysis

A descriptive statistical analysis will be undertaken. Observations from proforma will be entered into the computer, and Data analysis will be done using the Statistical Package for social sciences version 24 software. P-values <0.05 were considered significant.

Table 1: Observation of mean age of patients in both groups

	Group	Mean	Std. Deviation	P value
Age	Control	58.58	10.78	0.538
	Probiotics	57.30	9.91	

Table 2: Age group distribution of patients in both groups

			Age group						
			<30	31-40	41-50	51-60	>61	Total	P value
Group	Control	Count	0	4	19	21	6	50	0.408
		% within Group	0.0%	8.0%	38.0%	42.0%	12.0%	100.0%	
	Probiotics	Count	1	2	26	18	3	50	
		% within Group	2.0%	4.0%	52.0%	36.0%	6.0%	100.0%	
Total		Count	1	6	45	39	9	100	
		% within Group	1.0%	6.0%	45.0%	39.0%	9.0%	100.0%	

RESULTS

In the present study average age of patients in both groups was recorded as almost similar; 58.58 in the control (CTR) group and 57.3 years in the probiotic (PRB) group (Table 1, Figure 1).

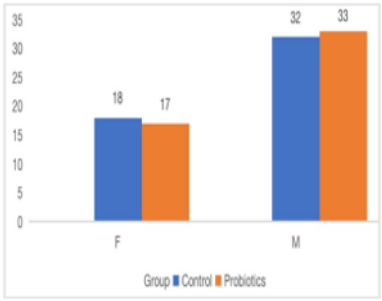

Figure 3: Gender distribution amongst patients of both groups

The age group distribution of patients in both was recorded and it was found that maximum patients were observed in the age group of 41 to 50 years in the PRB group (52%) and 51 to 60 years in the CTR group (42%). Whereas minimum patients were observed in the age group of less than 30 years (CTR: 0%; PRB: 2%) (Table 2, Figure 2).

In the present study majority of the patients were reported to be male in both groups (CTR: 64%; PRB: 66%) (Table 3, Figure 3).

The duration of diabetes illness was recorded in all patients of both groups. CTR group patients showed a maximum duration of illness of more than 16 years 21 (42%) whereas in the PRB group observed with a maximum duration of illness was observed at 11 to 15 years (38%) (Table 4, Figure 4).

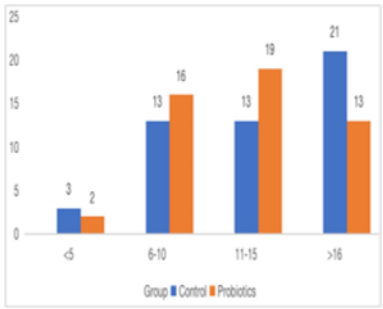

Figure 4: Observation of duration of illness amongst all patients of both group

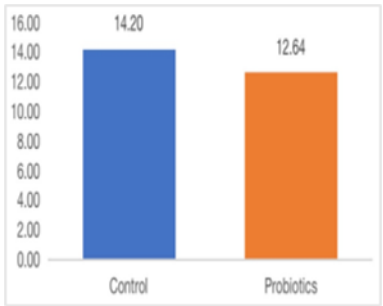

Figure 5: Mean duration of diabetes illness amongst patients of both groups

In the present CTR group, patients showed a mean duration of diabetes illness of 14.2 years whereas PRB group patients showed a mean duration of illness of 12.64 years (Table 5, Figure 5).

The diabetic foot wound size of all patients in both groups was also recorded and it was found that the mean wound size in both groups was almost the

Table 3: Gender distribution amongst patients of both groups

			Sex			
			F	M	Total	P value
Group	Control	Count	18	32	50	0.834
		% within Group	36.0%	64.0%	100.0%	
	Probiotics	Count	17	33	50	
		% within Group	34.0%	66.0%	100.0%	
Total		Count	35	65	100	
		% within Group	35.0%	65.0%	100.0%	

Table 4: Observation of duration of illness amongst all patients of both group

			Duration of diabetes					
			<5	6-10	11-15	>16	Total	P value
Group	Control	Count	3	13	13	21	50	0.318
		% within Group	6.0%	26.0%	26.0%	42.0%	100.0%	
	Probiotics	Count	2	16	19	13	50	
		% within Group	4.0%	32.0%	38.0%	26.0%	100.0%	
Total		Count	5	29	32	34	100	
		% within Group	5.0%	29.0%	32.0%	34.0%	100.0%	

Table 5: Mean duration of diabetes illness amongst patients of both groups

Group	Control	Mean	Std. Deviation	P value
Duration of diabetes		14.20	5.70	0.136
	Probiotics	12.64	4.61	

Table 6: Observation of mean wound size in both groups of patients

Group	Control	Mean	Std. Deviation	P value
Wound size (cm^2)		32.10	10.75	0.936
	Probiotics	31.92	11.51	

Table 7: Mean wound bed score amongst all patients on day 1 of both groups

Group	Control	Mean	Std. Deviation	P value
Wound bed score Day 1		8.12	0.75	0.447
	Probiotics	8.24	0.82	

same (CTR: 32.1 cm^2; PRB: 31.92 cm^2) (Table 6, Figure 6).

The mean wound bed score of all patients from both groups was recorded on days 1, 7 and day 14. During the study, it was observed that there was no significant difference in mean wound bed score between the two groups on day 1 (CTR: 8.12; PRB: 8.24), whereas a significant difference was observed on day 7 (CTR: 10.36; PRB; 11.14) and day 14 (CTR: 12.78; PRB: 13.56) (Tables 7, 8 and 9, Figures 7, 8 and 9).

Wound swab C and S analysis was carried out for both groups of patients during the study on day 0, day 5 and day 10. On day 1 all patients wound swabs were found positive for Klebsiella, proteus and Staph. aureus with maximum patients positive for staph aureus in both group (CTR:58%; PRB: 62%) (Table 10, Figure 10).

Table 8: Mean wound bed score amongst all patients on day 7 of both groups

Group	Control	Mean	Std. Deviation	P value
Wound bed score Day 7		10.36	0.90	<0.0001
	Probiotics	11.12	0.94	

Table 9: Mean wound bed score amongst all patients on day 14 of both groups

Group	Control	Mean	Std. Deviation	P value
Wound bed score Day 14		12.78	1.28	0.002
	Probiotics	13.56	1.20	

Table 10: Wound swab C&S observation of both groups of patients on day 0

			Wound swab C&S Day 0					
			Klebsiella	Proteus	Pseudomonas	Staph aureus	Total	P value
Group	Control	Count	9	3	9	29	50	0.393
		% within Group	18.0%	6.0%	18.0%	58.0%	100.0%	
	Probiotics	Count	9	6	4	31	50	
		% within Group	18.0%	12.0%	8.0%	62.0%	100.0%	
Total		Count	18	9	13	60	100	
		% within Group	18.0%	9.0%	13.0%	60.0%	100.0%	

Table 11: Wound swab C&S observation of both groups of patients on day 5

			Wound swab C&S Day 5						
			Klebsiella	No Growth	Proteus	Pseudomonas	Staph aureus	Total	P value
Group	Control	Count	9	18	0	7	16	50	0.013
		% within Group	18.0%	36.0%	0.0%	14.0%	32.0%	100.0%	
	Probiotics	Count	9	24	6	1	10	50	
		% within Group	18.0%	48.0%	12.0%	2.0%	20.0%	100.0%	
Total		Count	18	42	6	8	26	100	
		% within Group	18.0%	42.0%	6.0%	8.0%	26.0%	100.0%	

DISCUSSION

Diabetic foot is a leading cause of death and disability. It varies from an untreated persistent ulcer to full-blown limb gangrene. It causes severe physical and psychological impairment. Also substantial are the patient's economic expenses, which include health care expenditures, lost work days, and indirect costs. In addition, antibiotic resistance is a fast-growing issue as a result of the indiscriminate use of antibiotics. Therefore, innovative medicines and interventions are required to minimise cost, time, and the issue of antibiotic resistance [8–10].

In the present study average age of patients in both group were found almost similar 58.58 years in the control (CTR) group and 57.3 years in the probiotic (PRB) group. The age group distribution of patients showed that the maximum number of patients were observed in the age group of 41 to 50 years in the PRB group (52%) and 51 to 60 years in the CTR group (42%).

Table 12: Wound swab C&S observation of both groups of patients on day 10

			Wound swab C&S Day 10						
			Klebsiella	No Growth	Proteus	Pseudomonas	Staph aureus	Total	P value
Group	Control	Count	3	30	0	7	10	50	0.010
		% within Group	6.0%	60.0%	0.0%	14.0%	20.0%	100.0%	
	Probiotics	Count	9	33	3	1	4	50	
		% within Group	18.0%	66.0%	6.0%	2.0%	8.0%	100.0%	
Total		Count	12	63	3	8	14	100	
		% within Group	12.0%	63.0%	3.0%	8.0%	14.0%	100.0%	

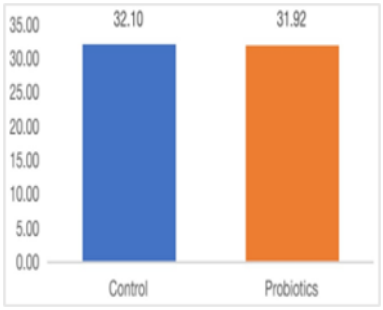

Figure 6: Observation of mean wound size in both group of patients

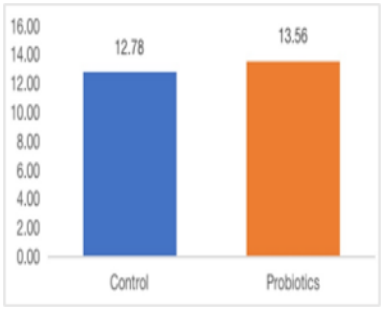

Figure 9: Mean wound bed score amongst all patients on day 14 of both groups

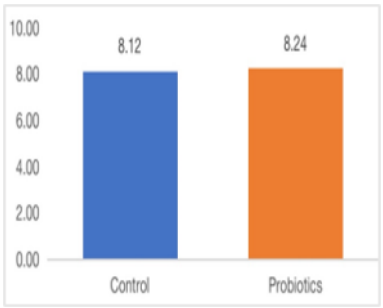

Figure 7: Mean wound bed score amongst all patients of both groups on day 1

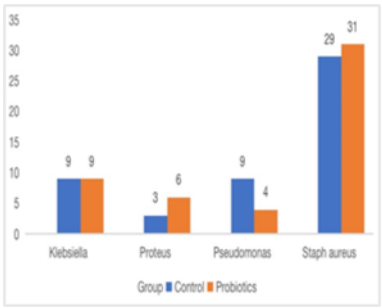

Figure 10: Wound swab C&S observation of both groups of patients on day 0

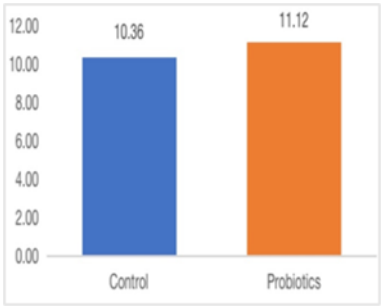

Figure 8: Mean wound bed score amongst all patients on day 7 of both groups

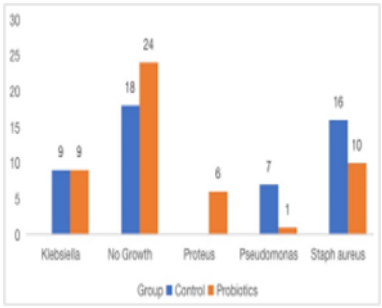

Figure 11: Wound swab C&S observation of both groups of patients on day 5

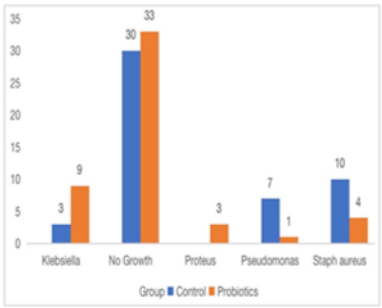

Figure 12: Wound swab C&S observation of both groups of patients on day 10

These findings in the present studies are in accordance with the earlier reported studies [11].

In the present study majority of the patients were reported to be male in both groups (CTR: 64%; PRB: 66%). [5] in their study also reported male predominance (67%) in their study.

The CTR group patients showed a maximum duration of illness of more than 16 days 21 (42%) with a mean duration of diabetes illness of 14.2 days whereas in PRB group observed a maximum duration of illness of 11 to 15 days (38%) and mean duration of illness of 12.64 years. These findings in the present studies were in agreement with the results of [7] investigations.

The diabetic foot wound size of all patients in both groups was evaluated and it was found that mean wound sizes in both groups were almost the same (CTR: 32.1 cm^2; PRB: 31.92 cm^2) with no significant difference (p=0.936). The findings in the present study are in accordance with earlier reported studies [12].

The mean wound bed score of all patients from both groups was studied on days 1, 7 and 14. It was found that there was no significant difference in mean wound bed score between the two groups on day 1 (CTR: 8.12; PRB: 8.24; p=0.447), but there was a significant difference on day 7 (CTR: 10.36; PRB; 11.14, p=0.0001) and on day 14 (CTR: 12.78; PRB: 13.56, p=0.002) between both groups. The mean wound bed score in the CTR group was increased from 8.12 on day 1 to 12.78 on day 14 confirming an improvement in DFU condition by the treatment. Similarly in the PRB group mean wound score increased from 8.24 on day 1 to 13.56 on day 14, showing better improvement in DFU condition than in CTR group patients. [13] also reported similar findings in their study.

Wound swab C & S analysis was performed for both groups of patients during the study on day 0, day 5 and day 10. On day 0 all patients wound swabs were found positive for Klebsiella, proteus and Staph. aureus with maximum patients positive for staph aureus in both group (CTR:58%; PRB: 62%). On day 5 both groups of patients showed that 36 % of patient's wounds in the CTR group did have any growth whereas in the PRB group 48% of patient's wounds were observed without any microbial growth. On Day 10, it was found that 60 % of patient wounds in the CTR group did have any growth whereas in the PRB group 66% of patient's wounds were observed with no microbial growth. The number of wounds with a positive status came down as the course progressed in either group. Hence in our study use of probiotics with conventional therapy showed better results in the management of DFU. [5, 13] also reported similar findings in their studies where the use of probiotics significantly improved the treatment of DFU.

CONCLUSION

The present study concludes that probiotics can be safely utilized in the therapy of infected diabetic wounds. The probiotic when used along with conventional therapy could result in hastening the wound healing process as evidenced by the significant difference in the day 7 and 14 wound bed scores. Although more studies are needed in this field to give better evidence for the support of probiotic use.

Funding Support

The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest.

REFERENCES

[1] T A Oelschlaeger. Mechanisms of probiotic actions - A review. *International Journal of Medical Microbiology*, 300(1):57–62, 2010.

[2] F L Game, R J Hinchliffe, J Apelqvist, D G Armstrong, K Bakker, A Hartemann, M Löndahl, P E Price, and W J Jeffcoate. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes/Metabolism Research and Reviews*, 28:119–141, 2012.

[3] M C Peral, M A Huaman Martinez, and J C Valdez. Bacteriotherapy with Lactobacillus plantarum in burns. *International Wound Journal*, 6(1):73–81, 2009.

[4] S Fijan, A Frauwallner, T Langerholc, B Krebs, J A Ter Haar, A Heschl, D Mičetić Turk,

and I Rogelj. Efficacy of Using Probiotics with Antagonistic Activity against Pathogens of Wound Infections: An Integrative Review of Literature. *BioMed Research International*, pages 1–21, 2019.

[5] S Mohseni, M Bayani, and F Bahmani. The effects of probiotic administration on wound healing and metabolic status in patients with diabetic foot ulcer: a randomized, double-blind, placebo-controlled trial. *Diabetes Metab Res Rev*, 34(3):207–222, 2018.

[6] S S Patil, S A Katii, K A More, and S Mahajan. Topical Application of Probiotics and Novel Approach For Treatment of Diabetic Foot Ulcer. *Int J Recent Sci Res*, 13(4):1038–1081, 2022.

[7] M Sonal Sekhar, M K Unnikrishnan, K Vijayanarayana, G S Rodrigues, and C Mukhopadhyay. Topical application/formulation of probiotics: Will it be a novel treatment approach for diabetic foot ulcers? Medical Hypotheses. *Medical Hypotheses*, 82(1):86–88, 2014.

[8] L Yazdanpanah. Literature review on the management of diabetic foot ulcer. *World Journal of Diabetes*, 6(1), 2015.

[9] D R Whiting, L Guariguata, C Weil, and J Shaw. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*, 94(3):311–321, 2011.

[10] M Aalaa, O T Malazy, M Sanjari, M Peimani, and M Mohajeri-Tehrani. Nurses' role in diabetic foot prevention and care; a review. *Journal of Diabetes & Metabolic Disorders*, 11(1):24–28, 2012.

[11] C Vuotto, F Longo, and G Donelli. Probiotics to counteract biofilm-associated infections: promising and conflicting data. *International Journal of Oral Science*, 6(4):189–194, 2014.

[12] R G Frykberg, V R Driver, D Carman, B Lucero, C Borris-Hale, C P Fylling, L M Rappl, and P A Clausen. Chronic wounds treated with a physiologically relevant concentration of platelet-rich plasma gel: a prospective case series. *Ostomy/Wound Management*, 56(6):36–44, 2010.

[13] N Subramani and C Madhavan. Probiotics in Diabetic Wound Care. *IOSR Journal of Dental and Medical Sciences*, 16(7):65–71, 2017.