JPPIPA 9(Special Issue) (2023)
Jurnal Penelitian Pendidikan IPA
Journal of Research in Science Education
http://jppipa.unram.ac.id/index.php/jppipa/index

Effect of Foot SPA in Improving Touch Perception in Patients with Type 2 Diabetes

Ruslan Hasani[1*], Gede Wiadnyana[1], Bahtiar[1], Junaidi[1], Rahman[1], Sri Angriani[1], Sukriyadi[1], Ningsih Jaya[1], Simunati[1], Hamsina[2]

[1]Department of Nursing, Politeknik Kementerian Kesehatan, Makassar, Indonesia
[2]Department of Chemical Engineering, Universitas Bosowa, Makassar, Indonesia

Received: October 15, 2023
Revised: November 21, 2023
Accepted: December 25, 2023
Published: December 31, 2023

Corresponding Author:
Ruslan Hasani
hasani.ruslan@gmail.com

DOI: 10.29303/jppipa.v9iSpecialIssue.6840

Abstract: Amputation of lower limbs and the development of foot ulcers are primarily associated with Diabetes Mellitus (DM) and its associated sensory peripheral neuropathy (SPN). A diminished perception of touch perception leads to decreased responsiveness to pressure and is recognized as a risk factor for diabetic foot ulcers. Increasing SPN patients' sense of touch perception in their feet may help prevent foot ulcers. This study aimed to prove the effects of foot SPA in improving touch perception in patients with type 2 Diabetes. This research method is quasi-experimental with one group pre and post-test design without a control group. Sampling was done by purposive sampling with 22 research subjects. The research instrument used a 10-g monofilament test. Foot SPA is carried out 6 days for week. Data analysis used the Paired sample t-test. Statistical test results obtain a p-value <0.05. The results of a week-long study found that foot SPA significantly affects touch perception in type 2 diabetes patients.

Keywords: Foot SPA; Sensory Peripheral Neuropathy; Touch Perception; Type 2 Diabetes

Introduction

Diabetes mellitus (DM) is a medical condition characterized by the dysfunction of pancreatic endocrine hormones, specifically insulin, and glucagon Galicia-Garcia et al. (2020); Lassie et al. (2023); Wardani (2023), and is a chronic metabolic disease that makes it difficult for the body to regulate blood sugar levels. Type 2 diabetes (T2DM), a serious health risk associated with DM, is becoming more common and has been connected to lifestyle factors. The significant morbidity and mortality of the condition are caused by long-term microvascular and macrovascular consequences, which highly stress individuals and healthcare systems (Dixon et al., 2017).

Among complications, diabetic polyneuropathy (DPN) is the most prevalent. It is linked to long-term diabetes and poor glycemic control, both of which are extremely painful and distressing (Aljohani et al., 2020). Indonesia is the 5th country with the highest prevalence of diabetes in the world in 2021, namely 19.50 million people. Based on IDF research, the world population aged 20-79 years in 2021 is estimated to reach 5.10 billion people. It is regarded as one of the twenty-first century's biggest risks to emerging health. It is projected that 380 million people will be affected by DM by 2025 (Maiorino et al., 2017); (Atkins & Zimmet, 2010), in addition to the classic complications of this disease, DM has been associated with impaired T-cell response, impaired neutrophil function, and impaired humoral immunity (Ayelign et al., 2019).

DPN, which causes loss of protective feeling, failure of the intrinsic muscles of the foot, and anhidrosis of the foot, is a progressive degeneration of the peripheral nerves that affect the sensory, motor, and autonomic components of nerves (Mustapa et al., 2016). If not treated appropriately, this raises the costs of public health and significantly lowers the quality of life for

How to Cite:
Hasani, R., Wiadnyana, G., Bahtiar, B., Junaidi, J., Rahman, R., Angriani, S., … Hamsina, H. (2023). Effect of Foot SPA in Improving Touch Perception in Patients with Type 2 Diabetes. *Jurnal Penelitian Pendidikan IPA*, *9*(SpecialIssue), 1334–1339. https://doi.org/10.29303/jppipa.v9iSpecialIssue.6840

patients. Even so, with the right precautions taken, the deadliest outcomes of this illness-plantar ulceration and amputation-can be prevented. 40–59% of people with diabetes develop diabetic peripheral neuropathy (DPN) (Deli et al., 2013), (Ziegler et al., 2014), and numerous studies have shown that age is a significant risk factor for DPN (Bansal et al., 2014; Lu et al., 2010; Sharma et al., 2010).

Although (27–57) % of all DPN residents are between the ages of 50 and 60, this percentage jumps to 50%–100% when an individual reaches the age of 70 or older DPN. Middle-aged adults (40–60 years) and older persons (60+ years) have the highest prevalence of DPN, which reduces control over balance and gait coordination due to sensory loss in areas such as vibration perception, pressure, pain, and joint position (Ahmad et al., 2019). Diabetes mellitus (DM) frequently results in sensory peripheral neuropathy (SPN) (Kärvestedt et al., 2011). One of the main risk factors for developing foot ulcers is the lack of vibration sensation (Ko & Cha, 2012). According to Lipsky et al. (2011), the greatest risk factor for lower limb amputation in patients with diabetes mellitus is foot ulcers.

Since vibration is essentially pressure applied to the skin, the same mechanoreceptor in the skin that detects pressure—the Pacinian corpuscle—is also responsible for detecting vibration. If a therapy intervention aiming at enhancing the vibration perception of a patient with SPN proves effective, ulcer formation may be prevented. Diabetic foot ulcers lead to pain, which impairs a patient's ability to move around and balance. Reduced mobility can further exacerbate circulation problems already present in diabetics and lengthen the time it takes for ulcers to heal, raising the risk of infection and amputation of lower limbs.

Mobility issues can restrict the person's ability to engage in social and economic activities of daily living. Losing movement independence can therefore result in psychological issues including anxiety and despair, a decline in social interaction, and eventually social marginalization. Preventing diabetic foot ulcers from developing could potentially avert disability. Massage can play a role in improving local microcirculation, increasing blood flow rate, and correcting metabolic disorders (Needs et al., 2023). In recent years, studies have found that the application of massage in DPN can improve the blood circulation of local tissues, improve the body's local pain threshold, enhance the range of motion of joints, and improve the blood supply and nutrition metabolism of peripheral nerves (Chatchawan et al., 2015).

Method

This type of research is quasi-experimental research. This study used a one-group pretest-posttest design without a control group. Before doing leg exercises, a pretest touch perception examination was performed using a 10-g monofilament test. After that, treatment is given in the form of foot exercises. Finally, a touch perception post-test was conducted using a 10-g monofilament test. The 10-g monofilament test is used to assess Perception of touch at 8 points on the soles of the feet. A score of 2 is given if the patient feels 8 touch points, a score of 1 is given if the patient feels 1 to 7 touch points, and a score of 0 is given if the patient does not feel any touch sensation. The research flow diagram is summarized in Figure 1.

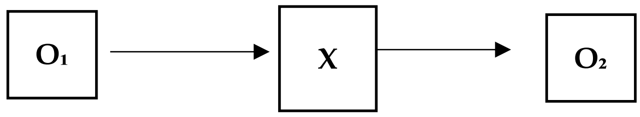

Figure 1. Research flow chart

Information:

O_1 = A pretest peripheral neuropathy sensitivity examination was carried out

× = Diabetic foot exercise intervention was provided

O_2 = A posttest peripheral neuropathy sensitivity examination was carried out

O_1-O_2 = Comparison of pretest and posttest peripheral neuropathy sensitivity results

Result and Discussion

Characteristics of study participants

General characteristics of the study, there were more than half of the participants aged between 51 and 60 years (68.18%). More women, namely 63.64%, more than half of the respondents (59.09%) were self-employed and more than half had a high school education (68.18%) as seen in Table 1.

Table 1. General characteristics of study participants (n=22)

Characteristics of study participants	Frequency	Percentage (%)
Age (years)		
51 – 60	15	68.18
61 – 70	7	31.82
Gender		
Man	8	36.36
Woman	14	63.64
Employment		
Self-employed		
Employee	13	59.09
	9	40.91
Education background		
High school	15	68.18
College	7	31.82
Total	22	100

Table 2. Results of examination of touch perception of type 2 diabetes patients before and after administering foot SPA on the second, fourth, and sixth days

a 10-g Monofilament test	Value of touch perception	Pre-test		Post-test	
		f	%	f	%
	2	0	0	0	0
second day of intervention	1	15	68.18	19	86.36
	0	7	31.82	3	13.64
	2	0	0	5	22.73
fourth day of intervention	1	17	77.27	17	77.27
	0	5	22.73	0	0
	2	7	31.82	17	77.27
sixth day of intervention	1	15	68.18	5	22.73
	0	0	0	0	0
Total		22	100	22	100

Regarding exploration with a 10-g monofilament test after being given foot SPA for 6 days, it was found that on the second day, there was an increase in the touch perception score of 18.18%. On the fourth day after being given foot SPA there was an increase in touch perception scores of 22.73%. On the sixth day after the foot SPA was carried out, there was an increase in the touch perception score by 45.45% (Table 2).

Table 3. The effect of foot SPA on touch perception in type 2 diabetes patients

a 10-g Monofila ment test	Pretest	Post-test Touch perception (mean±SD)	Change (mean ±SD)	p-value
	Pretest	Post-test		
First test	1.32±0.48	1.14±0.35	0.18±0.13	0.042*
Second test	1.23±0.43	0.77±0.43	0.46±0.00	0.001*
Third test	0.68±0.48	0.23±0.43	0.45±0.05	0.001*

*Paired -sample t-test

In Table 3, you can see the average difference before and after the intervention The first posttest had a mean difference of 0.18, the second posttest was 0.46 and the third posttest was 0.45 with p values of 0.042, 0.001, and 0.001 α < 0.005, meaning there was a significant influence-Foot SPA intervention to improve tactile perception in type 2 diabetes patients.

Diabetic Macrovascular Complications

Vascular problems can result from hyperglycemia via several potential pathways. A critical mediator that controls several pro-inflammatory and pro-atherosclerotic target genes in endothelial cells (EC), vascular smooth muscle cells (VSMC), and macrophages, core factor-κB (Piga et al., 2007), can be activated by elevated glucose concentrations. Increased blood sugar levels have the potential to accelerate protein glycation, leading to the production of AGEs, protein cross-linking, and reactive oxygen species. Oxidative stress, which has been closely linked to atherosclerosis, can be triggered by hyperglycemia itself (Aronson & Rayfield, 2002; Yuan et al., 2019; Schleicher & Friess, 2007).

Unsurprisingly, vascular cells that directly experience hyperglycemia exhibit a large number of the earliest pathogenic responses to glucose. The first stage of atherogenicity is the loss of the endothelium's non-adhesive characteristics, which occurs when monocytes adhere to ECs. The adherence of monocytes to cultured ECs is enhanced by hyperglycemia (Otsuka et al., 2005). Hyperglycemia and AGEs can increase the generation of EC (Quagliaro et al., 2005), superoxide, suggesting a connection between AGEs, hyperglycemia, and oxidative stress. Similar reactions in VSMCs can also be brought on by glucose-activating matrix-degrading metalloproteinases, which are enzymes involved in plaque rupture and arterial remodeling. Additionally, glucose can alter vascular smooth muscle cells (VSMC) responsiveness and promote migration, proliferation, and renin-angiotensin activation, among other effects.

Type 2 diabetes mellitus (T2DM) and atherosclerosis have both been closely linked to inflammation Biddinger & Kahn (2006); Shoelson (2006), this, there is currently no one mechanism that explains why patients with diabetes exhibit this pattern. High glucose concentration-grown monocytes or those isolated from diabetics with poorly managed diabetes look active Negrato & Tarzia (2010); Alam et al. (2021); Tamarai et al. (2019), exhibiting the activation of several inflammatory mediators, including nuclear factor-κB and protein kinase C. These and other targets have the potential to encourage oxidative stress (S Valvassori et al., 2020; Silnitsky et al., 2023.; Xiao et al., 2023)

Diabetic Microvascular Complications

Pathological alterations in the diabetic microvasculature can impact the microvasculature supply to the organs, especially the kidneys, retina, and peripheral nervous system, which are strongly dependent on it for organ perfusion. Retinopathy, nephropathy, and neuropathy are the three clinical issues linked to these alterations that account for a significant portion of T2DM morbidity. Reduced myocardial vascularization, inadequate wound healing, and peripheral vascular disease are further consequences of microvascular illness (Li et al., 2023; Del Buono et al., 2021; Mauricio et al., 2023; Patel et al., 2019; Orasanu & Plutzky, 2009). Diabetic microvascular illness has received relatively little attention in terms of research and clinical implications (Gottwald-Hostalek & Gwilt, 2022). An evaluation of the anatomic makeup of the microvasculature should be the first step in any further analysis of microvascular illness.

Conclusion

This study shows that foot SPA improves tactile perception in type 2 diabetes patients. Therefore, foot SPA makes it a suitable alternative for preventing diabetic foot ulcers.

Acknowledgments
Thanks to all parties who have supported the implementation of this research. I hope this research can be useful.

Author Contributions
Conceptualized the research idea, R. H, G. W., B, J, designed methodology, R, S. A.; conducted literature review, N. J., S, and S, provided critical feedback on the manuscript, H.

Funding
Researchers independently funded this research.

Conflicts of Interests
No Conflicts of Interests

References

Ahmad, I., Noohu, M. M., Verma, S., Singla, D., & Hussain, M. E. (2019). Effect of sensorimotor training on balance measures and proprioception among middle and older age adults with diabetic peripheral neuropathy. *Gait & Posture*, *74*, 114–120. https://doi.org/10.1016/j.gaitpost.2019.08.018

Alam, S., Hasan, Md. K., Neaz, S., Hussain, N., Hossain, Md. F., & Rahman, T. (2021). Diabetes Mellitus: Insights from Epidemiology, Biochemistry, Risk Factors, Diagnosis, Complications and Comprehensive Management. *Diabetology*, *2*(2), 36–50. https://doi.org/10.3390/diabetology2020004

Aljohani, M., Karam, A., Alamri, A., Manfaloti, M., Alnakhli, H., & Shaqroon, H. (2020). Diabetic neuropathy in Saudi Arabia: A comprehensive review for further actions. *International Journal of Medicine in Developing Countries*, 2008–2013. https://doi.org/10.24911/IJMDC.51-1601343665

Aronson, D., & Rayfield, E. J. (2002). How hyperglycemia promotes atherosclerosis: molecular mechanisms. *Cardiovascular Diabetology*, *1*(1), 1. https://doi.org/10.1186/1475-2840-1-1

Atkins, R. C., & Zimmet, P. (2010). Diabetic kidney disease: Act now or pay later. *Acta Diabetologica*, *47*(1), 1–4. https://doi.org/10.1007/s00592-010-0175-7

Ayelign, B., Negash, M., Genetu, M., Wondmagegn, T., & Shibabaw, T. (2019). Immunological Impacts of Diabetes on the Susceptibility of Mycobacterium tuberculosis. *Journal of Immunology Research*, *2019*, 1–8. https://doi.org/10.1155/2019/6196532

Bansal, D., Gudala, K., Muthyala, H., Esam, H. P., Nayakallu, R., & Bhansali, A. (2014). Prevalence and risk factors of development of peripheral diabetic neuropathy in type 2 diabetes mellitus in a tertiary care setting. *Journal of Diabetes Investigation*, *5*(6), 714–721. https://doi.org/10.1111/jdi.12223

Biddinger, S. B., & Kahn, C. R. (2006). FROM MICE TO MEN: Insights into the Insulin Resistance Syndromes. *Annual Review of Physiology*, *68*(1), 123–158. https://doi.org/10.1146/annurev.physiol.68.040104.124723

Chatchawan, U., Eungpinichpong, W., Plandee, P., & Yamauchi, J. (2015). Effects of Thai Foot Massage on Balance Performance in Diabetic Patients with Peripheral Neuropathy: A Randomized Parallel-Controlled Trial. *Medical Science Monitor Basic Research*, *21*, 68–75. https://doi.org/10.12659/MSMBR.894163

Del Buono, M. G., Montone, R. A., Camilli, M., Carbone, S., Narula, J., Lavie, C. J., Niccoli, G., & Crea, F. (2021). Coronary Microvascular Dysfunction Across the Spectrum of Cardiovascular Diseases. *Journal of the American College of Cardiology*, *78*(13), 1352–1371. https://doi.org/10.1016/j.jacc.2021.07.042

Deli, G., Bosnyak, E., Pusch, G., Komoly, S., & Feher, G. (2013). Diabetic Neuropathies: Diagnosis and Management. *Neuroendocrinology*, *98*(4), 267–280. https://doi.org/10.1159/000358728

Dixon, C. J., Knight, T., Binns, E., Ihaka, B., & O'Brien, D. (2017). Clinical measures of balance in people with type two diabetes: A systematic literature review. *Gait & Posture*, *58*, 325–332. https://doi.org/10.1016/j.gaitpost.2017.08.022

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *International Journal of Molecular Sciences*, *21*(17), 6275. https://doi.org/10.3390/ijms21176275

Gottwald-Hostalek, U., & Gwilt, M. (2022). Vascular complications in prediabetes and type 2 diabetes: A continuous process arising from a common pathology. *Current Medical Research and Opinion*, *38*(11), 1841–1851. https://doi.org/10.1080/03007995.2022.2101805

Kärvestedt, L., Mårtensson, E., Grill, V., Elofsson, S., Von Wendt, G., Hamsten, A., & Brismar, K. (2011). The prevalence of peripheral neuropathy in a population-based study of patients with type 2 diabetes in Sweden. *Journal of Diabetes and Its Complications*, *25*(2), 97–106. https://doi.org/10.1016/j.jdiacomp.2010.04.001

Ko, S.-H., & Cha, B.-Y. (2012). Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus in Korea. *Diabetes & Metabolism Journal*, *36*(1), 6. https://doi.org/10.4093/dmj.2012.36.1.6

Lassie, N., Ashan, H., Triola, S., & Widiastuti, W. (2023). Risk Factors of Opthalmoplegia in Diabetes Mellitus. *Jurnal Penelitian Pendidikan IPA*, *9*(10), 868–875. https://doi.org/10.29303/jppipa.v9i10.4676

Li, Y., Liu, Y., Liu, S., Gao, M., Wang, W., Chen, K., Huang, L., & Liu, Y. (2023). Diabetic vascular diseases: Molecular mechanisms and therapeutic strategies. *Signal Transduction and Targeted Therapy*, *8*(1), 152. https://doi.org/10.1038/s41392-023-01400-z

Lipsky, B. A., Weigelt, J. A., Sun, X., Johannes, R. S., Derby, K. G., & Tabak, Y. P. (2011). Developing and Validating a Risk Score for Lower-Extremity Amputation in Patients Hospitalized for a Diabetic Foot Infection. *Diabetes Care*, *34*(8), 1695–1700. https://doi.org/10.2337/dc11-0331

Lu, B., Yang, Z., Wang, M., Yang, Z., Gong, W., Yang, Y., Wen, J., Zhang, Z., Zhao, N., Zhu, X., & Hu, R. (2010). High prevalence of diabetic neuropathy in population-based patients diagnosed with type 2 diabetes in the Shanghai downtown. *Diabetes Research and Clinical Practice*, *88*(3), 289–294. https://doi.org/10.1016/j.diabres.2010.02.002

Maiorino, M. I., Bellastella, G., Giugliano, D., & Esposito, K. (2017). Can diet prevent diabetes? *Journal of Diabetes and Its Complications*, *31*(1), 288–290. https://doi.org/10.1016/j.jdiacomp.2016.10.009

Mauricio, D., Gratacòs, M., & Franch-Nadal, J. (2023). Diabetic microvascular disease in non-classical beds: The hidden impact beyond the retina, the kidney, and the peripheral nerves. *Cardiovascular Diabetology*, *22*(1), 314. https://doi.org/10.1186/s12933-023-02056-3

Mustapa, A., Justine, M., Mohd Mustafah, N., Jamil, N., & Manaf, H. (2016). Postural Control and Gait Performance in the Diabetic Peripheral Neuropathy: A Systematic Review. *BioMed Research International*, *2016*, 1–14. https://doi.org/10.1155/2016/9305025

Needs, D., Blotter, J., Cowan, M., Fellingham, G., Johnson, A. W., & Feland, J. B. (2023). Effect of Localized Vibration Massage on Popliteal Blood Flow. *Journal of Clinical Medicine*, *12*(5), 2047. https://doi.org/10.3390/jcm12052047

Negrato, C. A., & Tarzia, O. (2010). Buccal alterations in diabetes mellitus. *Diabetology & Metabolic Syndrome*, *2*(1), 3. https://doi.org/10.1186/1758-5996-2-3

Orasanu, G., & Plutzky, J. (2009). The Pathologic Continuum of Diabetic Vascular Disease. *Journal of the American College of Cardiology*, *53*(5), S35–S42. https://doi.org/10.1016/j.jacc.2008.09.055

Otsuka, A., Azuma, K., Iesaki, T., Sato, F., Hirose, T., Shimizu, T., Tanaka, Y., Daida, H., Kawamori, R., & Watada, H. (2005). Temporary hyperglycaemia provokes monocyte adhesion to endothelial cells in rat thoracic aorta. *Diabetologia*, *48*(12), 2667–2674. https://doi.org/10.1007/s00125-005-0005-6

Patel, S., Srivastava, S., Singh, M. R., & Singh, D. (2019). Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing. *Biomedicine & Pharmacotherapy*, *112*, 108615. https://doi.org/10.1016/j.biopha.2019.108615

Piga, R., Naito, Y., Kokura, S., Handa, O., & Yoshikawa, T. (2007). Short-term high glucose exposure induces monocyte-endothelial cells adhesion and transmigration by increasing VCAM-1 and MCP-1 expression in human aortic endothelial cells. *Atherosclerosis*, *193*(2), 328–334. https://doi.org/10.1016/j.atherosclerosis.2006.09.016

Quagliaro, L., Piconi, L., Assaloni, R., Daros, R., Maier, A., Zuodar, G., & Ceriello, A. (2005). Intermittent high glucose enhances ICAM-1, VCAM-1 and E-selectin expression in human umbilical vein endothelial cells in culture: The distinct role of protein kinase C and mitochondrial superoxide production. *Atherosclerosis*, *183*(2), 259–267. https://doi.org/10.1016/j.atherosclerosis.2005.03.015

S Valvassori, S., H Cararo, J., Peper-Nascimento, J., L Ferreira, C., F Gava, F., C Dal-Pont, G., L Andersen, M., & Quevedo, J. (2020). Protein kinase C isoforms as a target for manic-like behaviors and oxidative stress in a dopaminergic animal model of mania. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *101*, 109940. https://doi.org/10.1016/j.pnpbp.2020.109940

Schleicher, E., & Friess, U. (2007). Oxidative stress, AGE, and atherosclerosis. *Kidney International*, *72*, S17–S26. https://doi.org/10.1038/sj.ki.5002382

Sharma, T., Raman, R., Pal, S., Rani, P., Rachapalli, S., & Kulothungan, V. (2010). Prevalence and risk factors for severity of diabetic neuropathy in type 2 diabetes mellitus. *Indian Journal of Medical Sciences*, *64*(2), 51. https://doi.org/10.4103/0019-5359.94400

Shoelson, S. E. (2006). Inflammation and insulin resistance. *Journal of Clinical Investigation*, *116*(7), 1793–1801. https://doi.org/10.1172/JCI29069

Silnitsky, S., Rubin, S. J. S., Zerihun, M., & Qvit, N. (2023). An Update on Protein Kinases as Therapeutic Targets—Part I: Protein Kinase C Activation and Its Role in Cancer and Cardiovascular Diseases. *International Journal of Molecular Sciences*, *24*(24), 17600. https://doi.org/10.3390/ijms242417600

Tamarai, K., Bhatti, J. S., & Reddy, P. H. (2019). Molecular and cellular bases of diabetes: Focus on type 2 diabetes mouse model-TallyHo. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, *1865*(9), 2276–2284. https://doi.org/10.1016/j.bbadis.2019.05.004

Wardani, I. S. (2023). Hidroksi Metil Glutaril Coenzyme-A (HMG CoA) Reduktase Inhibitor and New Onset Diabetes Mellitus: A Review of Correlation and Clinical Implication. *Jurnal Penelitian Pendidikan IPA*, *9*(9), 580–585. https://doi.org/10.29303/jppipa.v9i9.5274

Xiao, Q., Wang, D., Li, D., Huang, J., Ma, F., Zhang, H., Sheng, Y., Zhang, C., & Ha, X. (2023). Protein kinase C: A potential therapeutic target for endothelial dysfunction in diabetes. *Journal of Diabetes and Its Complications*, *37*(9), 108565. https://doi.org/10.1016/j.jdiacomp.2023.108565

Yuan, T., Yang, T., Chen, H., Fu, D., Hu, Y., Wang, J., Yuan, Q., Yu, H., Xu, W., & Xie, X. (2019). New insights into oxidative stress and inflammation during diabetes mellitus-accelerated atherosclerosis. *Redox Biology*, *20*, 247–260. https://doi.org/10.1016/j.redox.2018.09.025

Ziegler, D., Papanas, N., Vinik, A. I., & Shaw, J. E. (2014). Epidemiology of polyneuropathy in diabetes and prediabetes. In *Handbook of Clinical Neurology*, *126*, 3–22. https://doi.org/10.1016/B978-0-444-53480-4.00001-1