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Diabetic Ulcer Patients : Literature Review

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ABSTRACT
Diabetic ulcer can cause infection and decrease the quality of life of sufferers. In patients with diabetic ulcers, it is not uncommon to ignore the nutrients consumed. Though nutrition is very important. If nutritional needs are not met, it can cause several conditions such as anemia (especially iron deficiency anemia), hypoalbuminemia (due to lack of protein intake), and malnutrition. In addition, the lack of nutrition intake also affects the inflammatory process in the wound healing phase of diabetic ulcer which, if it continues, can cause more severe infection to the sepsis stage. This literature review aiming to summarize the latest information related to research on nutrition in diabetes ulcer patients. The method used in this study is Literature Reviews by including research on nutrition in diabetes ulcer patients. The keywords used were " nutrition, macronutrient, micronutrient, diabetes ulcer, diabetic foot ulcers, and venous ulcers " on websites Google Scholar, Gale, and Pubmed. Results : The results of 32 journals showed inadequate intake of macronutrients (carbohydrates, proteins, and fats) and micronutrients (vitamins) and minerals) in patients with diabetic ulcer which can inhibit the diabetic wound healing process. Nutrients consumed both macronutrients and micronutrients are each needed by the body because they play an important role as a source of energy and play a role in the wound healing process

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INTRODUCTION

Ulcer Diabetic is complications chronicle from diabetes mellitus (DM) which can cause infection and decline quality life sufferer. Ulcer diabetic especially on the feet can end amputation. According to *American Diabetes Association* (ADA), it is estimated that DM sufferers around 537 million soul around the world.(McDermott et al., 2023) There is around 19% - 34% of DM sufferers have complications become ulcer diabetic or around 131 million soul.(Edmonds et al., 2021)(Basiri, Spicer, Munoz, et al., 2020; Vas et al., 2017) Sufferer ulcer diabetes in Africa is 7.2%, in Ethiopia around 12.98%. (Hirpa et al., 2023)In Indonesia, the prevalence ulcer diabetic Enough tall namely 24% in the community and 12% in hospitals.(Sari et al., 2020) Meanwhile, in South Sulawesi, according to the South Sulawesi Provincial Health Service in 2017, there were 1.6% with prevalence highest found in the

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Regency Pinrang (2.8%).(*Profil Kesehatan Provinsi Sulawesi Selatan Tahun 2017*, n.d.) According to International Diabetes Federation, male more prone to caught disease This than women.(Armstrong et al., 2017)

In patients diabetic ulcers do not rarely ignored the nutrients consumed. Even though nutrition very much important. If the need arises will nutrition No fulfilled (carbohydrates, protein, fat, vitamins and minerals) then can cause a number of condition like weakening system immunity body, anemia (especially iron deficiency anemia) substance iron), hypoalbuminemia (due to lack of protein intake), and malnutrition. In addition, the lack of intake Nutrition also affects the inflammatory process in the inflammatory phase. healing wound ulcer diabetic which if happen in a way Keep going through so can cause more infections critical until to the sepsis stage.(Mackay & Cde, n.d.; Melo et al., 2022) Description on explain importance role nutrients consumed sufferer ulcer so that objective from review literature This is to summarize the latest information related to research on nutrition in diabetic ulcer patients with approach *literature review.*

METHOD

The method used in this research is *literature review* by summarizing the latest information related to research on nutrition in diabetic ulcer patients. The data or sources come from journals, books, and other libraries. The keywords used are " *nutrition, macronutrient, micronutrient, diabetic ulcer, diabetic foot ulcer, and venous ulcer* ". The selected articles are those that meet the inclusion criteria: journal publication period up to 8 years last (2016-2024), using Indonesian and English, original articles (research articles), and articles can be accessed in full. The article search *websites* that we use are Google Scholar, Gale, and Pubmed.

RESULTS

After conducting a search for scientific articles through Google Scholar, PubMed and Gale, found 32 articles that met the inclusion criteria from a review of clinical and research articles published between 2016 and 2024, as following.

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Table 1. Results Review Article

No.	Name Writer	Year	Title Article	Objective	Results	Conclusion
1.	Haiyan M. Maier, Jasminka Ilich - Ernst, Bahram Arjmandi, et al.	2016	*Nutritional Deficiencies Intake of Patients with Diabetic Foot Ulcer*	Assessing nutritional components in patients with diabetes mellitus with or without diabetic foot ulcers	A total of 82 research subjects (male n = 27, female n = 55) In this study, most of the samples had an *overweight body mass index.* or obesity. Patients with *diabetic foot ulcers* (DFU) have inadequate intake of protein, fiber, vitamins B1, B2, B3, B6, C, D, E, calcium, magnesium, phosphorus, potassium, selenium, and zinc, while excessive intake of saturated fat, trans fat, and sodium.	Malnutrition is very common occurs in patients with DM and DFU. Administration adequate intake such as protein and vitamins maybe useful in the prevention and management of DM and DFU.
2.	Naufal Zuhdi Rabbani, Barkah Djaka Purwanto, Dyah Suryani, et al.	2022	*Relationship between the amount of protein intake of DM patients with the healing process of diabetic ulcer at the Ampel Sehat Inpatient Primary Clinic*	Know connection between amount Dietary protein intake of DM patients with the healing process ulcer diabetic	A total of 32 research subjects are known that the respondents are mostly aged 51-60 years, namely 14 people (43.8%), respondents with female gender numbered 21 people (65.6%), respondents who did not work numbered 13 people (40.5%), the weight mass index of respondents had the same number in the normal and obese categories with a total of 16 people (50%), and respondents with the longest duration of diabetic ulcers were 1-6 months with a total of 19 people (59.3%).	In this study, it can be concluded that there is a relationship between the amount of dietary protein intake of DM patients and the healing process of diabetic ulcers at the Ampel Sehat Inpatient Clinic. The need for protein in DM patients with diabetic ulcers is inadequate. DM patients with diabetic ulcers should increase their protein intake to support the formation of new tissue in the healing process of diabetic ulcers.

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No.	Name Writer	Year	Title Article	Objective	Results	Conclusion
					Most DM patients with diabetic ulcers did not meet their daily protein intake with a total of 21 respondents (65.6%), while in the healing process of diabetic ulcers, most respondents did not experience a healing process in their diabetic ulcers.	
3.	Nida Sajid, Zahid Miyan, Syed Obedience Hussain Zaidi, et al.	2018	*Protein requirements and its intake in subjects with diabetic foot ulcer at a tertiary care hospital*	Knowing the protein intake and requirements of type 2 DM patients with diabetic foot ulcer complications	A total of 542 subjects of this study, 365 (67.2%) were male and 178 (32.8%) were female. The average age of the subjects was 54.61±10.51 (years) with the duration of diabetes and the average body mass index of 14.22±7.98 (years) and 26.65±5.38 (kg/m2), respectively. Food records showed that the protein intake of diabetic foot ulcer patients was not yet appropriate when compared to daily needs. The average protein intake was 76.87 grams in men and 56.84 grams in women. On the other hand, protein requirements were much higher than intake, which was 219.5 grams in men and 130.2 grams in	Type 2 diabetic patients with foot ulcers do not consume the amount of protein needed for wound healing. Dietary counseling should be part of the treatment of subjects with diabetic foot ulcers to identify the nutritional needs.

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					women.	
4.	Raedeh Basiri, Maria T. Spicer, Cathy W. Levenson, et al	2020	*Nutritional Supplementation Concurrent with Nutrition Education Accelerate the Wound Healing Process in Patients with Diabetic Foot Ulcer*	Evaluating the impact of a nutrient-dense formula combined with nutritional education on wound healing in DFU patients.	In this study there were 29 samples (male n = 19, female n = 10) for 12 weeks (control group of 14 patients, and experimental group of 15 patients) obtained results in the experimental group (2 servings of supplements containing 500 kcal, 28 grams of protein, vitamins, and important minerals) experienced a faster wound healing rate (6.43 mm^2 / week reduction in wound area) compared to the control group. The comparison of wound area reduction in the experimental group and the control group in the first four weeks was 13: 1 (18.0 mm^2: 1.4 mm^2)	From the research results, it can be concluded that the combination of supplements and nutritional education significantly accelerates wound healing in DFU patients.
5.	Raedeh Basiri, Maria T. Spicer, Thomas Ledermann, et al	2022	*Effects of Nutrition Intervention on Blood Glucose, Body Composition, and Phase Angle in Obese and Overweight Patients with Diabetic Foot Ulcer*	To determine the impact of nutritional education and body composition supplementation on overweight and obese patients with DFU.	A total of 29 subjects (male n = 19, female n = 10) with DFU in this study were aged between 30 and 70 years. At baseline, the mean body mass index (BMI) was 33.5 kg/m2 for the treatment group and 34.1 kg/m2 for the control group. HbA1c decreased	Dietary recommendations for overweight and obese individuals with DFU should be made with prioritizing proper wound healing by encouraging patients to consume adequate energy sources and essential nutrients.

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					in both groups, with no significant differences between groups. On average, patients in the treatment group lost less lean body mass and gained less fat than the control group ((3.8 kg vs. 4.9 kg) and (0.9 kg vs. 3.6 kg), respectively). Mean dietary intake of essential micronutrients for wound healing was also significantly lower than the DRI in this population. Energy intake from food did not change significantly over the course of the study for either the treatment or control groups, and the interaction between time and group was not statistically significant. Compared with the NPUAP recommendations, energy intake increased from 52.0% to 68.0% in the treatment group and from 43.7% to 57.8% in the control group. The increase in protein intake in the treatment group was higher (from 54.5% to 84.9%) than in the control group (from 43.1% to 54.7%) when	

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					compared with the NPUAP recommendations. The interaction between group and time was not statistically significant; however, the changes in protein intake in the treatment group diet were clinically relevant. Although the treatment group was given an additional 500 kcal of energy and an additional 28 g of protein, they still did not meet their requirements. NPUAP recommendations for energy and protein intake. Intakes of foods containing copper, zinc, vitamin A, vitamin C, and vitamin E increased significantly in the treatment group.	
6.	Hailey R. Donnelly, Erin D. Clarke, Clare E. Collins	2024	*Most individual with diabetes -related foot ulceration do not meet dietary consensus guidelines for wound healing*	Determine how the macronutrient status and micronutrient status of individuals with DFU compare with the *American Limb intervention. Preservation Society Nutririon*	A total of 115 subjects with DFU complications, the results obtained sample population has a high level of saturated fat intake (14% of total energy intake), total omega-3 intake is 89mg, with 77% of subjects meeting the recommendation of this intake.	Food intake of a sample population of individuals living with DFU with guidelines derived from international nutrition consensus. The majority of participants did not meet guideline recommendations,

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				In adults with consensus and guidance from DFU experts.	The average intake of individuals with DFU compared with the consensus guidelines on average was not met. The average intake of vitamin E did not meet the recommendation of the guidelines (86%), intake of vitamin A (45%), vitamin C (26%), and zinc (37%).	particularly for nutrients such as protein, fiber, zinc, vitamins E and A, all of which have an impact wound healing capacity.
7.	Zahra Soleiman, Fatemeh Hashemdokht, Fereshteh Bahmani, et al.	2017	*Clinical and metabolic response to flaxseed omega-3 fatty oil acids* supplementation *in patients with diabetic foot ulcers : a randomized, doubleblind, placebo-controlled trial*	Evaluating the effects of flaxseed oil omega-3 fat supplementation on wound healing and metabolic status in subjects with DFU.	There were 60 subjects in this study (46 male subjects, 14 female subjects). After 12 weeks of intervention, compared with placebo, omega-3 fatty acid supplementation resulted in a significant decrease in ulcer length (-2.0±2.3 vs. -1.0±1.1 cm, P=0.03), width (-1.8±1.7 vs. -1.0±1.0 cm, P=0.02) and depth (-0.8±0.6 vs. -0.5±0.5 cm, P = 0.01). In addition, significant decreases in serum insulin concentrations (-4.4±5.5 vs. +1.4±8.3 μIU/ mL, P=0.002), homeostasis model estimated insulin resistance (-2.1±3.0 vs. +1.0±5.0, P=0.005) and HbA1c (-0.9±1.5 vs. -0.1±0.4%, P=0.01),	Omega-3 fatty acid supplementation for 12 weeks among subjects with DFU had beneficial effects on ulcer size parameters, insulin metabolism markers, serum hs - CRP, plasma TAC and GSH levels. In addition, flaxseed oil omega-3 fatty acids play an indirect role in wound healing due to their effect on improving metabolism.

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					and significant increases in quantitative insulin sensitivity test index (+0.01±0.01 vs. -0.005±0.02, P=0.002) were seen after supplementation with omega-3 fatty acids compared with placebo. In addition, omega-3 fatty acid supplementation significantly decreased serum high-sensitivity C-reactive protein (hs -CRP) (-25.5±31.5 vs. -8.2±18.9 µg/ mL, P=0.01), and significantly increased plasma total antioxidant capacity (TAC) (+83.5±111.7 vs. -73.4±195.5 mmol /L, P<0.001) and glutathione (GSH) concentrations (+60.7±140.2 vs. -15.5±129.7 µmol/L, P=0.03) compared with placebo.	
8.	Murillo Gstinelli Barbosa, Viviane Fernandes Carvalho, Andre Oliveira The.	2022	*Hydrogel Enriched With Sodium Alginate and Vitamins A and E for Diabetic Foot Ulcer : A Randomized Controlled Trial*	To evaluate the effectiveness of using amorphous hydrogels rich in butyric acid, vitamin A, and vitamin E in the treatment of DFU.	A total of 35 research subjects (26 subjects as the control group, and 19 subjects as the experimental group) obtained the average results of patient age, duration of open wounds, and duration of diabetes similar	Use hydrogel rich in sour butyrate, vitamin A, and vitamin E were found No give significant benefits touched DFU treatment.

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					between groups. However, the initial wound area was larger in the experimental group than in the control group. There was no significant comparison regarding the severity of wounds between groups. Histological analysis showed a decrease in inflammatory infiltration in the experimental group, but no increase in collagen production.	
9.	Guilherme Pena, Beatrice Kuang, Prue Cowled, et al.	2020	*Micronutrient Status in Diabetes Patients with Foot Ulcer*	micronutrient deficiencies in patients with diabetic foot ulcers and relate them to the severity of foot disease and other clinical factors.	There were 133 subjects in this study (104 male subjects, 27 female subjects). vThe most common nutritional deficiency found was vitamin D affecting 55.7% of patients. Suboptimal vitamin C levels affected 73% of patient cases, consisting of marginal levels of 22.2% and deficiency levels of 50.8%. Zinc deficiency, vitamin A deficiency, and low ferritin levels also occurred in 26.9%, 10.9%, and 5.9% of patients, respectively. There was no correlation between BMI, grip strength, duration of diabetes, HbA1c, or	micronutrient deficiencies is high in diabetic patients with foot ulcers. Of particular concern is the high prevalence of vitamin C and zinc deficiencies, given their role in foot ulcers. healing.

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					smoking status with micronutrient deficiencies. The increasing severity of diabetic foot disease was associated with lower vitamin C levels (p = 0.02)	
10.	Adriano A Mehl, Adérson OMC Damião, Sâmela DDO Viana, et al	2021	*Hard- to - Heal Wounds : A Randomised Trial of an Oral Proline-Containing Supplement to Aid Repair*	Evaluating the nutritional effects of special oral supplements / *Oral Nutrition Supplement* (ONS) which contains arginine and proline, high levels of vitamins A, C, and E, zinc and selenium levels in healing diabetic wounds that are difficult to heal	A total of 30 patients participated in this study. The average age was 65 years and 50% of patients had diabetes. Of the total evaluated wound surface area, 78% had a wound surface area of <50cm², 14% had a wound surface area of 50-150cm² and 8% were >250cm². In 96% of cases, the wound was on the lower leg. statistically significant decrease in wound area (p = 0.004) due to ONS.	ONS appears as a new, easy-to-use protein source, enriched with elements such as proline and arginine, vitamins A, E and C, zinc and selenium, which are directly related to the wound healing process. Therefore, ONS can be used as a therapeutic option for healing difficult-to-heal wounds.
11.	Triantafyllos Didangelos, Eleni Karlafti, Evangelia Kotzakioulafi, et al	2021	*Vitamin B12 Supplementation in Diabetes Neuropathy : A 1-Year, Randomized, Double-Blind, Placebo-Controlled Trial*	Investigating the effects of normalizing vitamin B12 levels with oral B12. (methylcobalamin) 1000 µg/day for one year in patients with neuropathy diabetic (DN).	There were 90 subjects in this study (48 males, 42 females). B12 levels increased from 232.0 ± 71.8 at baseline to 776.7 ± 242.3 pmol /L at follow-up, p < 0.0001, in the active group but not in the control group. VPT, MNSIQ, QoL, pain score, SNCV,	Treatment of patients with DN with 1 mg Twelve months of oral methylcobalamin increased plasma B12 levels and improved all neurophysiological parameters, sudomotor function, pain scores, and QoL, but did not improve CARTS and

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					SNAP, and ESCF increased significantly in the active group ($p < 0.001$, $p = 0.002$, $p < 0.0001$, $p < 0.000$, $p < 0.0001$, $p < 0.0001$, and $p < 0.014$, respectively), whereas CARTS and MNSIE increased but not significantly. MCR, MNSIQ, SNCV, SNAP, and pain scores significantly worsened in the control group ($p = 0.025$, $p = 0.017$, $p = 0.045$, $p < 0.0001$, and $p < 0.0001$, respectively)	MNSIE.
12.	Mohammed Badedi, Hussain Darraj, Abdulrahman Hummadi, et al	2019	*Vitamin B12 Deficiency and Foot* Ulcers *in Type 2 Diabetes Mellitus : A Case – Control Study*	To assess the relationship between vitamin B12 deficiency and the development of diabetic foot ulcers (DFU) in type 2 diabetes mellitus.	In this study there were 323 samples (192 men, 131 women). The highest DFU rate was found in men and over 45 years of age. Neuropathy, vasculopathy, vitamin B12 deficiency, poor glycemic control, poor foot care, *Charcot foot,* physical inactivity, and spending long periods of standing at work were significantly associated with DFU, and all but physical inactivity were independent predictors of DFU. After adjusting for covariates, vitamin B12	Vitamin B12 deficiency has a significant association with DFU among the Saudi population with T2DM.

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					deficiency was significantly associated with DFU (odds ratio 3.1), indicating that patients with T2DM and vitamin B12 deficiency have a threefold higher risk of developing DFU than those with normal vitamin B12 levels.	
13.	Anil Yadav, Sabita Jyoti, Ram Kumar Mehta, et al	2023	*Vitamin B12 Deficiency among Metformin Treated Type 2 Diabetic Mellitus Patients Visiting the Department of Medicine of a Tertiary Care Center*	To determine the prevalence of vitamin B12 deficiency among type 2 DM patients treated with metformin. who visited the Department of Medicine at a tertiary care center.	Among 330 patients, vitamin B12 deficiency was seen in 33 (10%) (6.76-13.24, 95% *Confidence Interval*). Among them, 27 (81.82%) were male and 6 (18.18%) were female.	The prevalence of vitamin B12 deficiency was found to be higher than in other studies conducted in similar conditions.
14.	Joseph V. Boykin, Glenn D. Hoke, Cassandra R. Driscoll, et al	2020	*High Dose Folic AC ID and Its Effect on Early Stage Diabetic Foot Ulcer Wound Healing*	Investigating the relationship between *High Dose Folic Acid* (HDFA) with *Early Stage-Diabetic Wound Healing Foot Ulcer* (ES-DFU)	During the study period, 29 subjects with ES-DFU wounds who received HDFA treatment were identified. This group of ES-DFU patients who received HDFA reported 90% (26/29) experienced complete DFU wound closure during the study period. There was evidence of a significant increase in wound closure before and after HDFA treatment (P <.05).	Observations from this study on the effects of HDFA on ES-DFU wound healing, have provided evidence of the recovery pattern of chronic ES-DFU wounds which showed a significant increase in wound closure (area reduction) and wound healing after HDFA treatment.

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Discussion

In patients ulcer diabetic, one of the things that must be be noticed is incoming nutrients into the body. Often matter This neglected, especially in fulfillment calories daily. The principle is pattern Eat balanced Good macronutrients and micronutrients for blood sugar can controlled.(American Diabetes Association, 2019)

Macronutrients In Patients Ulcer Diabetic

Carbohydrates, fats and proteins are macronutrients needed body For fulfil calories daily. In patients ulcer diabetic at least needed around 30-35 kcal / KgBW or even up to 40 kcal / KgBW If patient lack underweight. Fulfillment calories daily This as source energy for body and also helps in the healing process wounds on patients ulcer diabetic.(Khardori & Quain, 2015)

Carbohydrates

Carbohydrate is source energy main for body. Therefore that, the need will carbohydrate more big compared to with other macronutrients namely around 50-60% of total needs energy. However, in DM sufferers, especially those who have complications like ulcer diabetic, pattern Eat especially portion carbohydrate must more be noted. This is can trigger No under control blood sugar levels that lead to stages hyperglycemia. Generally need calories patient will fulfilled with Eat three times in a day. So that arrangement Eat regular carbohydrates can help control glycemic. Generally patient requires 1500-2000 kcal / day with 12-15 grams carbohydrates per serving eat (36-45 grams/ day).(Luis et al., 2023) According to *The American Diabetes Association* (ADA) highly recommends source carbohydrate originate from food with index glycemic low for example whole grains, fruit, low- fat milk, and vegetables.(Food for Thought Key Takeaways from ADA's Nutrition Consensus Report, 2019)

Protein

Protein plays a very important role important towards the healing process wound. This is because protein (amino acids) has material formation macrophages, and antibodies as system immunity body. If the protein requirement is not met Enough so will extend the healing period wound (inflammatory process) elongated) which will cause wound become chronic. Needed around 1.25-1.5 grams/ kgBW of protein for support the healing process wounds. (Mackay & Cde, n.d.)In a study conducted by Haiyan et al in 2016 with title *Nutritional Deficiencies Intake of Patients with Diabetic Foot Ulcer* Results obtained from patients with *diabetes foot ulcers* (DFU) have inadequate protein intake, while excessive saturated fat and trans fat intake. (Maier et al., 2016)The results of this study are in line with research conducted by Naufal Zuhdi, et al., which found that most DM patients with diabetic ulcers did not have sufficient daily protein intake with 21 respondents (65.6%), while in the healing process of diabetic ulcers Most respondents did not have a healing process for their diabetic ulcers.(Rabbani et al., n.d.) Research conducted by Nida Sajid, et al in *Baqai Institute of Diabetology & Endocrinology* (BIDE) which is a diabetes care center in Karachi, Pakistan also supports the results of previous studies, it was found that the protein intake of diabetic foot ulcer patients was not appropriate when compared to daily needs. The average protein intake was 76.87 grams in men and 56.84 grams in women. On the other hand, protein needs are much higher than intake, which is 219.5 grams in men and 130.2 grams in women.(Sajid et

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al., 2018)

In addition, research conducted by Raedeh Basiri, et al. in 2020 with serving 2 portions supplement nutrition containing 500 kcal and 28 grams of protein in the group intervention proven experience level healing more wounds fast compared to with group control with ratio 13 : 1 on four Sunday First study.(Basiri, Spicer, Levenson, et al., 2020) Another study conducted by Raedeh Basiri, et al. in 2022 found that results although group intervention given addition intake of 500 kcal of energy and an additional 28 grams of protein, the need will protein remain Not yet fulfilled.(Basiri et al., 2022) In addition, protein can slow down emptying stomach so that No easy hungry (so that blood sugar levels can more easy controlled). Foods that are rich in protein such as meat, fish, poultry, dairy products, eggs, and nuts.(Basiri, Spicer, Levenson, et al., 2020; Mackay & Cde, n.d.) If carbohydrates are consumed No reach need nutrition daily so body will using protein as source energy and things This can cause the disturbance healing wounds on patients ulcer, decrease mass muscles, and can happen malnutrition.(Mackay & Cde, n.d.)

Fat (Omega-3)

Fat is one of the macronutrients source energy for body. Fat can classified into saturated fat and non-saturated fat saturated. Fat is not fed up classified become fat no fed up single (omega-9) and fat is not fed up double (omega-3 & omega-6). (Rohr et al., 2020)In DM patients, especially those accompanied by with ulcer diabetic must notice intake of fat consumed. Recommendations from The Indonesian Ministry of Health said that the maximum limit fat consumption is about 67 grams/ day.(*Permenkes Nomor 30 Tahun 2013 Tentang Pencantuman Gula, Garam, Dan Lemak*, 2013) Fatty acids consumed will changed become triglycerides are stored and become material burn mitochondria to produce energy. If someone consuming excessive fat so cell will overwhelmed in convert fat into triglycerides so that can formed *diacylglycerides* and *ceramides* (toxic lipids / dyslipidemia). This accumulation of lipids (dyslipidemia) can contribute to *reactive oxygen species* (ROS), stress reticulum endoplasmic reticulum (ER), and dysfunction mitochondria, can also cause inflammation, insulin resistance, disorders vessels blood (atherosclerosis), and apoptosis (skeletal muscle cells, cells - β, and cells adipocytes). But a number of fatty acids no fed up like fatty acids no fed up double (*Polyunsaturated Fatty Acid* / PUFA) such as omega-3, it turns out can against toxic lipids (lipotoxicity). (Da Porto et al., 2022) In a study conducted by Hailey R, et al in 2024, it was found that results as many as 115 subjects waiting own level high saturated fat intake (14% of total intake) energy), with recommendation omega-3 intake was 89 grams and only 77% of subjects met it recommendation the.(Donnelly et al., 2024) Study done by Zahra Soleiman with objective evaluate omega-3 oil fat supplementation flax seeds in healing wounds and metabolic statistics in patients ulcer diabetic obtained results in groups intervention experience healing significant injury in comparison with group control.(Soleimani et al., 2017) In patients wound chronicle have more PMN (*polymorphonuclear*) derived proteases Lots compared to with wound in phase healing. If PMN -derived proteases are abundant, then will inhibit the healing process. Omega-3 fatty acids have been shown to can lower PMN activity. Resolvin D3 from omega-3 functions slow down migration PMN cells to area inflammation. In addition, prostaglandin E3 which is chemoattractant weak for PMN is results metamolism from omega-3.(McDaniel et al., 2020)

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Micronutrients In Patients Ulcer Diabetic

Micronutrients are nutrients that are needed by the body even in small amounts. Although this substance is only needed a little, micronutrients cannot be ignored because they have many benefits including in the wound healing process in ulcer patients. diabetic. Vitamins and minerals are part of micronutrients.(Kumar et al., 2023)

Vitamin A

In a study conducted by Murilo et al., in 2022, it was found that with giving hydrogel rich in vitamin A is proven to show decline infiltration inflammation in the group experiment.(Gustinelli et al., 2022) Another study conducted by Guilherme on " *Micronutrient Status in Diabetic Patients with Foot Ulcers* " found that results happen vitamin A deficiency in subjects study by 10.9%.(Pena et al., 2020) Whereas research conducted in 2021 regarding *" Hard - to-Heal Wounds : A Randomised Trial of an Oral Proline-Containing Supplement to Aid Repair "* Where giving oral supplements rich in vitamin A in 30 subjects study in a way significant experience healing wounds (p = 0.004).(A et al., 2021) Recommended daily vitamin A supplementation around 25,000 IU mainly For healing wounds. Vitamin A has role important For differentiation cell, formation bones, and as system defense body. Vitamin A can increase monocytes and macrophages which will oppose object foreign to the wound area. In addition, vitamin A has been shown to can increase synthesis collagen. Vitamin A helps increase proliferation fibroblasts, synthesis hyaluronate, and bonding cross collagen. Vitamin A also participates share in growth and differentiation cell epithelium in the epidermis of the skin.(Kulprachakarn et al., 2017)

Vitamin B

Vitamin B complex includes thiamine and its derivatives benfotiamine (vitamin B1), riboflavin (vitamin B2), nicotinic acid (vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7), folic acid (vitamin B9), cobalamin and its derivatives cyanocobalamin, hydrocyanocobalamin (vitamin B12) which have an important role in energy metabolism and are involved in increasing nerve regeneration and maintaining its function.(Farah & Yammine, 2022) Research conducted by Anil Yadav et al. found that results among 330 subjects study There were 33 (10%) patients who experienced vitamin B12 deficiency. (Yadav et al., 2023)In the study 2019 conducted by Mohammed Badedi, et al. concluded that vitamin B12 deficiency has risk three times more tall hit by DFU.(Badedi et al., 2019) Whereas study about " *Vitamin B12 Supplementation in Diabetes Neuropathy : A 1-Year, Randomized, Double-Blind, Placebo-Controlled Trials "* Where Oral administration of vitamin B12 (methylcobalamin) 1000 µg/day for one year can increase plasma B12 levels, neurophysiological parameters.(Didangelos et al., 2021) Research was also conducted by Joseph et al, by administering *High-Dose Folic AC ID* in diabetic foot patients has been shown to reduce the area of the wound by 90% of the total research subjects (26/29). (Boykin et al., 2020)Vitamin B12 deficiency can increase pro-oxidants and decrease antioxidants which can worsen DFU. These pro-oxidants can damage tissue by modifying carbohydrates, proteins, lipids, and DNA.(Farah & Yammine, 2022) In addition to Vitamin D, other vitamins such as folic acid also play an important role in reducing inulin resistance, and improving glucose homeostasis, as well as reducing endothelial dysfunction in diabetics.(Wakeman & Archer, 2020)

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Vitamin C

In research conducted by Elizabeth Bosede et al, regarding " *Relationship between selected micronutrient deficiencies and oxidative stress biomarkers in diabetes mellitus patients with foot ulcers in Ibadan, Nigeria"* found that vitamin C had a significant positive correlation with glutathione. peroxidase (GPx) which functions as an antioxidant.(Bolajoko et al., 2017)

Then research conducted by John Deakin et al., found as much as 58.7% of the total subjects study experience vitamin C deficiency, including 30.4% with level severe deficiency so that leading to amputation.(Brookes et al., 2020) Whereas research regarding " *Vitamin C Improves Healing of Foot Ulcers : A Randomized, Double-Blind, Placebo-Controlled Trial "* where 500mg of vitamin C was given to the experimental group of 7 people for 8 weeks, the results showed that all groups with vitamin C administration significantly experienced healing and without amputation. While in the control group, 44% did not experience healing.(Gunton et al., 2021) Vitamin C (recommended) For healing wound around 500 – 1000mg/ day, whereas If wounded critical like wound wide burn recommended 1-2g/ day) also plays a very important role important in the process of immunomodulation, antioxidants, and synthesis collagen. (Pullar & Vissers, 2021)Therefore that vitamin C can help phase inflammation, proliferation, remodeling phase of healing wound.(Jaffe & Wu, 2017; Shields, 2021)

Vitamin D

There are two forms of vitamin D, namely ergocarciferol (vitamin D2) and calciferol (vitamin D3). Vitamin D2 can be synthesized from plants/food (milk, supplements, fish, etc.), while vitamin D3 can be synthesized when the skin is exposed to sunlight (UV-B). When the skin is exposed to *UV radiation 7-dehydrocholesterol* then it will be converted into previtamin D, and then it will be converted into vitamin D3. (Md Isa et al., 2023)Vitamin D works by reducing the formation of cytokines by inhibiting transcription *nuclear* thus stimulating insulin secretion by pancreatic (Basiri et al., 2023)β cells. Vitamin D as an immune immunomodulator plays an important role in the activation of T and B cells by macrophages. In addition, vitamin D can also reduce levels of *Tumor Necrosis – Alpha* (TNF- *Alpha*) and *C- Reactive Protein* (CRP) as inflammatory parameters. Many studies have reported that vitamin D deficiency (<10ng/ mL) can increase the release of inflammatory cytokines such as TNF- *Alpha,* Interleukin – 6 (IL-6), and Interleukin-1 beta (IL-1Beta) in subjects with DFU and infection.(Amini et al., 2021) Research conducted by Mutasem Ababneh, et al. with title *Micronutrient status in patients with diabetic foot ulcers : A cross -sectional study in Saudi Arabia* Results Among the identified nutritional deficiencies, the most common was vitamin D, observed in 43.2% of the patient population.(Ababneh et al., 2024)

Vitamin E

Vitamin E is micronutrients soluble organic in fat. Source main vitamin E for body is oil vegetable, such as flower sun, radish, seeds corn, soybeans, and seeds wheat. Vitamin E is also found in a number of nuts, fruits, and vegetables, such as avocado, spinach, almonds and kale. In addition to the function the classic as antioxidant, vitamin E also plays a role in cascade signaling and modulation activity enzymes, as well as gene and protein expression. Many responses cell including death cell programmed, response inflammation, proliferation cells, and lipid homeostasis have proven influenced by vitamin E. (Liao et al., 2022)In vitamin E (

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recommended 15-20 mg/ day) For women, and 15 mg/ day For male) which is antioxidants that can hinder aging cell skin.(Basiri, Spicer, Levenson, et al., 2020) Research conducted by Amir Yarahmadi et al, regarding effect from platelet-rich platelets together with oral vitamin E on wound healing in patients with non-healing diabetic foot ulcers, the results showed a significantly greater reduction in wound size in the intervention group compared to the control group (p = 0.019).(Yarahmadi et al., 2021) Vitamin E reacts with peroxyl radicals and prevents the oxidation of polyunsaturated fatty acids present in immune cell membranes and further damage to the cells, thus Vitamin E is a nutrient that plays an important role in immune function.(Thompson et al., 2022)

Magnesium

Magnesium is an intracellular cation in the body. Recommended daily magnesium *intake Daily Allowances* (RDA) are around 320mg for adult women and 420mg for adult men. Food sources such as nuts, seeds, and dark green vegetables are rich sources of magnesium. (Piuri et al., 2021)In a study conducted by Hasan Afzali et al., found that giving 250mg magnesium supplements to the intervention group was proven to reduce the area of ulcer wounds, reduce fasting glucose levels, increase insulin sensitivity, and reduce triglyceride levels. (Afzali et al., 2019)Similar results were also obtained in a study conducted by Reza Razzaghi et al., where in 35 intervention groups significantly experienced wound healing compared to the control group. (Razzaghi et al., 2018)Magnesium plays a role in energy and carbohydrate metabolism. In addition, magnesium plays a role in normal neurological function, neurotransmitter release, muscle contraction and relaxation. (Piuri et al., 2021)Magnesium also affects the migration and adhesion of human skin fibroblasts.(Piuri et al., 2021)

Zinc

Zinc is essential micronutrients for body. While For mineral needs such as *zinc* in patients ulcer diabetic recommended as much as 220mg/ day. Zinc has role important in activation platelets with increase activity and aggregation platelets. Another study said that *zinc* deficiency can result in improvement cytokines proinflammatory.(Lebedeva et al., 2023) Case report by Reza Dadfar et al., namely the provision of ozone therapy and *zinc supplements* 50mg for 2 months, the results showed that the patient's wounds improved and there was a significant decrease in CRP levels. (Dadfar et al., 2023)Similar results were also obtained by Mansooreh Momen Heravi et al., where the group given supplements *Zinc* significantly improved ulcer healing and decreased CRP levels compared to the control group.(Momen-Heravi et al., 2017) Lack zinc caused by impaired ion transport by the ZnT7 protein inhibits CD145- stimulated phosphorylation of p38 MAPK, which ultimately leading to T- cell - mediated inhibition of activation B lymphocytes. Lymphocytes B cells themselves has proven play a role in clean wound and produce antibodies that detect damaged network.(Lebedeva et al., 2023) *Zinc* also plays a role important For growth and replication cell as well as protein synthesis. In addition *Zinc* is also a functional antioxidant mineral as an anti -radical free (Rabess, 2015; Saghaleini et al., 2018; Viswanathan Dharini et al., 2019).

Probiotics

Probiotics are non-pathogenic microorganisms that are naturally extracted from various food sources, for example from dairy products. The purpose of consuming probiotics is to replace microbes in the body that have been damaged and to fight pathogens in the body

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(Bekiaridou et al., 2021). Research conducted by Sima Mohseni et al., where the group given probiotic supplements experienced significant wound healing compared to the control group (Mohseni et al., 2018). Probiotics play a role in activating *Natural Killer cells* (NK cells) through the induction of IL-12 which increases the secretion of *Interferon* - γ (IFN - γ). However, this this is also stimulating IL-10- induced increase production antibodies and reduce regulation response inflammation, as well as happen balancing to healing wound (Togo et al., 2022).

CONCLUSION

Based on results from 32 journals show that No adequate intake nutrition (macronutrients and micronutrients) in patients ulcer diabetic so that the need giving nutrition in accordance need DFU sufferers. Fulfillment of nutritional needs is very important especially in healing DFU wounds. *Macronutrients* such as Carbohydrates, proteins, and fats contained in omega 3 in the right amount greatly affect collagen production, growth and maintenance of muscles and body tissues, and play a role in the removal of bacteria and necrotic cells. *Micronutrients* such as vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, magnesium, zinc, and probiotics in the right amount can maximize the wound healing process starting from modulating cell proliferation, collagen metabolism, to overcoming inflammation, and strengthening the body's immune system.

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