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Traditional Chinese Medicine and Western Medicine in Promoting Diabetic Foot Ulcer Healing: Cellular and Molecular Mechanisms

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Abstract

Diabetic foot ulcer (DFU), one of the most severe complications of diabetes mellitus, presents with refractory healing mechanisms involving chronic inflammation, vascular pathology, and dysregulated cellular signaling pathways. This review systematically summarizes therapeutic strategies for promoting DFU wound healing from both Traditional Chinese Medicine (TCM) and Western medicine perspectives, as well as their related cellular and molecular mechanisms: 1) common cytokines and signaling pathways associated with DFU are outlined; 2) TCM internal therapies such as Simiao Yong'an Decoction and Huangqi Yanghe Decoction, along with external therapies including Zizhu Ointment, Xianglei Tangzu Ointment, and acupuncture, are described together with their mechanisms of action; 3) Western medical interventions such as vascular reconstruction, growth factor therapy, and physical therapies are reviewed in relation to their mechanisms. The findings indicate that both TCM and Western medicine converge on shared molecular targets, providing a scientific perspective for integrative approaches in DFU management.

Keywords

Traditional Chinese Medicine, Diabetic Foot Ulcer, Wound Healing, Cellular and Molecular Mechanisms

1. Introduction

According to the 2025 statistics released by the International Diabetes Federation,

there were 589 million adults (aged 20 - 79) worldwide with diabetes in 2024 [1]. Among these patients, an estimated 15% - 25% develop diabetic foot ulcers (DFU), and nearly 20% of DFU cases progress to amputation. DFU is regarded as one of the most severe and costly complications of diabetes, placing an enormous economic and social burden on patients' families as well as national healthcare systems. Traditional Chinese Medicine (TCM) and Western medicine, as two major medical systems, differ substantially in theoretical foundations and therapeutic philosophies. Nevertheless, both have provided a wealth of effective strategies for DFU management [2]. In recent years, advances in cellular and molecular biology have revealed that many of these therapeutic approaches converge on common molecular targets. This convergence offers a scientific perspective that supports the integration of TCM and Western medicine in DFU treatment.

2. Cellular and Molecular Mechanisms of DFU Wound Healing

Wound healing is generally divided into three overlapping phases: hemostasis, inflammation, and proliferation [3]. However, in DFU, factors such as neuropathy, vascular disease, infection, and persistent hyperglycemia result in wounds remaining in a prolonged inflammatory state. This is characterized by elevated levels of pro-inflammatory cytokines and reduced levels of growth factors, ultimately impairing tissue repair [3].

2.1. Pro-Inflammatory and Anti-Inflammatory Cytokines

Pro-inflammatory cytokines are bioactive molecules that enhance inflammatory responses, playing essential roles in infection control, tissue injury response, and immune activation by facilitating pathogen clearance and initiating repair. The major pro-inflammatory cytokines include tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6). In contrast, anti-inflammatory cytokines suppress inflammation, alleviate associated symptoms, and promote tissue repair. Key anti-inflammatory mediators include interleukin-4 (IL-4) and interleukin-10 (IL-10). In DFU wounds, pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β are persistently overexpressed, whereas anti-inflammatory cytokines such as IL-10 and transforming growth factor-β (TGF-β) are relatively deficient [4]. This imbalance maintains the wound in a chronic inflammatory state, thereby delaying tissue repair.

2.2. Macrophage Polarization

Macrophage phenotype regulation is a complex process influenced by epigenetic modifications, metabolic microenvironment, and interactions with other immune cells. Two principal phenotypes are recognized: the pro-inflammatory M1 type and the anti-inflammatory M2 type. In DFU, excessive activation of M1 macrophages coupled with impaired M2 polarization contributes to chronic inflammation, impaired angiogenesis, and delayed tissue repair [5].

2.3. Vascular Endothelial Growth Factor (VEGF)

VEGF is a highly specific mitogen for vascular endothelial cells and plays a pivotal role in angiogenesis, inflammation, and neuroprotection. VEGF expression is markedly reduced in DFU tissues compared with non-diabetic wounds, resulting in impaired neovascularization, tissue ischemia, and hypoxia, all of which hinder wound repair [6].

2.4. Basic Fibroblast Growth Factor (bFGF)

bFGF, a member of the fibroblast growth factor family, exerts multiple biological effects, including promoting cell proliferation, differentiation, angiogenesis, and tissue repair. By binding to fibroblast growth factor receptors (FGFRs), bFGF stimulates endothelial cell proliferation and migration, accelerating neovascularization and alleviating ischemia in DFU lesions [7]. Moreover, bFGF has been shown to upregulate VEGF expression, thereby synergistically enhancing revascularization [8].

2.5. Epidermal Growth Factor (EGF)

EGF, a small polypeptide composed of 53 amino acids, binds to its receptor EGFR to activate downstream signaling pathways that stimulate proliferation and differentiation of keratinocytes and fibroblasts, thereby accelerating wound closure. In DFU tissues, EGF levels are significantly reduced, contributing to delayed wound healing [9].

2.6. Platelet-Derived Growth Factor (PDGF)

PDGF is a key peptide growth factor regulating cell proliferation, migration, angiogenesis, and tissue repair. Hyperglycemia in DFU patients suppresses PDGF secretion and signaling, resulting in impaired tissue repair and delayed wound closure [10].

2.7. Wnt/β-Catenin Signaling Pathway

The Wnt/β-catenin pathway is critical for embryonic development, tissue homeostasis, and disease progression [11]. It promotes platelet formation and maturation, thereby enhancing the secretion of PDGF, TGF-β1, and VEGF. In DFU patients, this pathway is downregulated, leading to impaired wound healing [12]. Activation of Wnt/β-catenin signaling has been shown to accelerate DFU wound repair.

2.8. Notch Signaling Pathway

The Notch signaling pathway is an evolutionarily highly conserved intercellular communication system involved in the regulation of embryonic development, tissue homeostasis, and injury repair [3]. It also plays a significant role in modulating macrophage function [13]. Studies have shown that this signaling pathway exhibits a spatiotemporally dependent dual regulatory effect during wound healing

[14]. Specifically, on one hand, inhibition of Notch signaling has been demonstrated to enhance the repair of diabetic foot ulcers [15]; on the other hand, evidence also suggests that activating Notch signaling after skin injury can accelerate the healing process by promoting angiogenesis and modulating inflammatory responses [16]. This discrepancy indicates that Notch signaling may play distinct roles in physiological and pathological healing processes, and its precise regulation requires consideration of the specific healing stage and cellular microenvironment. Therefore, therapeutic strategies targeting this pathway must fully account for its spatiotemporal specificity, implementing precisely timed or cell type-specific interventions to achieve therapeutic benefits and avoid potential adverse effects.

2.9. TGF-β/Smad Signaling Pathway

The TGF-β/Smad pathway regulates cell proliferation, differentiation, apoptosis, migration, and immune modulation. In DFU wounds, activation of this pathway promotes M2 macrophage polarization while reducing M1 macrophage activity [17]. Consequently, stimulation of TGF-β/Smad signaling facilitates wound healing in DFU.

2.10. PI3K/AKT/mTOR Signaling Pathway

The PI3K/AKT/mTOR cascade is one of the most critical intracellular signaling pathways, governing processes such as cell growth, proliferation, metabolism, survival, and migration. Its activation enhances VEGF expression and promotes angiogenesis [18]. Experimental studies confirm that PI3K/AKT/mTOR activation accelerates DFU wound healing.

2.11. NF-κB Signaling Pathway

The NF-κB pathway is a central transcriptional regulator involved in inflammation, immune responses, cell proliferation, and apoptosis. In DFU, NF-κB is abundantly expressed in perivascular macrophages and drives chronic inflammation [19]. Suppression of NF-κB signaling reduces inflammation within DFU wounds and promotes tissue repair.

3. Traditional Chinese Medicine in Promoting Diabetic Foot Ulcer Healing

From the perspective of TCM, DFU falls under the category of tuojü (gangrene). The Huangdi Neijing-Lingshu-Yongju records: "When it occurs at the toes, it is called tuojü. If its appearance is red, black, necrotic, and incurable; if not red or black, it is not fatal. If weakness persists, amputation must be performed immediately, otherwise death will ensue." In 2025, the Diabetes Committee of the World Federation of Chinese Medicine Societies (WFCMS) issued an expert consensus, emphasizing that TCM treatment should integrate both holistic pattern differentiation and local syndrome differentiation. According to this consensus, DFU syn-

dromes can be classified into several categories, including: damp-heat toxin with tendon and flesh decay; heat-toxin with yin injury and vascular stasis; qi and blood deficiency with collateral stasis; liver-kidney yin deficiency with vascular stasis; and spleen-kidney yang deficiency with phlegm-stasis obstruction [20]. Corresponding therapeutic methods are selected based on the specific syndrome pattern.

3.1. Internal Therapies

In TCM, internal therapy refers to the administration of herbal prescriptions or dietary adjustments aimed at regulating qi and blood, harmonizing yin and yang, and restoring the functional balance of the internal organs. It represents a fundamental approach to the systemic treatment of disease.

3.1.1. Application of Single Herbs

Curcuma longa (turmeric) is a traditional Chinese medicinal herb with functions of invigorating blood circulation, promoting qi flow, unblocking meridians, and alleviating pain. Its primary bioactive component, curcumin, has been extensively studied [21]. In an animal study, Yunjingmo *et al.* [22] reported that curcumin, the active component of Curcuma longa, promotes wound healing by activating the TGF-β/Smad signaling pathway, thereby suppressing inflammatory responses and inducing angiogenesis.

3.1.2. Application of Classical Formulas

Simiao Yong'an Decoction (composed of *Lonicera japonica* [honeysuckle], *Scrophularia ningpoensis*, *Angelica sinensis*, and licorice) was first proposed by the Qing dynasty physician Bao Xiang'ao. It is a representative prescription for heat-toxin type gangrene and continues to be widely applied in modern clinical practice. Modern pharmacological studies have shown that key components of the formula, such as chlorogenic acid from *Lonicera japonica* [23], harpagoside from *Scrophularia ningpoensis* [24], and ferulic acid from *Angelica sinensis* [25], possess anti-inflammatory, antioxidant, and angiogenesis-promoting activities. Chen Xiao [26] reported that Simiao Yong'an Decoction promotes wound healing by elevating the expression of bFGF, EGF, and VEGF. Yanghe Decoction was first recorded by the Qing dynasty physician Wang Hongxu in Waike Zhengzhi Quansheng Ji (Complete Collection of External Medicine). Its original composition includes *Rehmannia glutinosa*, deer horn gelatin, cinnamon, ephedra, white mustard seed, prepared ginger charcoal, and licorice. With a therapeutic focus on warming yang, nourishing blood, dispersing cold, and unblocking stagnation, it is primarily used for the treatment of yin gangrene. Huangqi Yanghe Decoction is a clinical modification of Yanghe Decoction, in which Astragalus membranaceus (Huangqi) is added to strengthen qi and tonify the spleen. This modification is particularly indicated for patients with marked qi and blood deficiency or pronounced yang deficiency, enhancing circulation and reinforcing the original warming and tonifying effects. Research indicates that components such as astragaloside IV from

Astragalus membranaceus [27] and cinnamaldehyde from cinnamon [28] may exert their effects by modulating immune and inflammatory signaling pathways. In animal studies, Bao Yaling *et al.* [29] found that Huangqi Yanghe Decoction activates the PI3K/AKT signaling pathway while inhibiting NF-κB activation, thereby reducing inflammation and promoting angiogenesis.

3.2. External Therapies

In TCM, external therapy refers to the use of surface stimulation, topical herbal applications, or physical interventions applied to meridians, acupoints, or affected areas. The goal is to regulate qi and blood, harmonize yin and yang, and thereby achieve therapeutic effects.

3.2.1. Topical Herbal Applications

Zizhu Ointment (composed of cinnabar, *Lithospermum erythrorhizon* [gromwell root], *Daemonorops draco* [dragon's blood], donkey-hide gelatin, borneol, and astragalus) possesses the functions of clearing heat and detoxifying, removing necrotic tissue and promoting granulation, as well as tonifying qi and nourishing blood. In an animal study, Han Qiang *et al.* [30] demonstrated that Zizhu Ointment accelerates DFU wound healing by downregulating inflammatory mediators such as IL-1, IL-6, and TNF-α, and by suppressing NF-κB and PI3K signaling pathways. Xianglei Tangzu Ointment (primarily derived from *Plectranthus amboinicus* extract and total saponins of *Centella asiatica*) is a domestically developed, nature-inspired formulation. It promotes DFU wound healing by inhibiting polarization toward the M1 macrophage phenotype and enriching M2 macrophages, thereby shifting the inflammatory microenvironment toward repair [31].

3.2.2. Acupuncture

Acupuncture, an essential component of traditional Chinese therapy, integrates needling and moxibustion techniques to stimulate meridians and acupoints. Its therapeutic effects are achieved by regulating qi and blood, harmonizing yin and yang, thereby treating disease and promoting health. In a clinical study conducted at Shenyang Seventh People's Hospital, Wang Zengmin and colleagues [32] demonstrated that acupuncture combined with conventional pharmacotherapy enhanced the clinical efficacy in DFU patients. This combined approach improved serum levels of bFGF and VEGF, thereby accelerating wound healing and shortening ulcer closure time.

4. Western Medicine in Promoting Diabetic Foot Ulcer Healing

From the perspective of Western medicine, DFU is a common and severe complication of diabetes, arising from the interplay of multiple pathophysiological factors. The development of DFU is closely associated with neuropathy, vascular disease, infection, and a persistent hyperglycemic environment. Accordingly, different therapeutic strategies are employed to address these contributing factors.

4.1. Conventional Therapy

Standard treatment for DFU includes glycemic control, local debridement, and antibiotic therapy. Glycated hemoglobin (HbA1c) levels should be maintained below 7% [33]. Glycemic control can be achieved through oral hypoglycemic agents or insulin therapy. Local management involves removal of necrotic tissue, purulent exudates, and infectious foci. Based on bacterial culture and drug susceptibility testing, appropriate antibiotics are selected to reduce microbial proliferation.

4.2. Vascular Reconstruction and Regenerative Techniques

4.2.1. Endovascular Intervention of Lower Limb Arteries

This technique involves balloon angioplasty or stent implantation of stenotic or occluded arteries under the guidance of X-ray or other imaging modalities, with the goal of restoring blood flow to the affected limb. In a meta-analysis, Yi Tingwan *et al.* [34] concluded that peripheral endovascular intervention significantly improves the ankle-brachial index in DFU patients, enhances ulcer healing efficiency, shortens healing and hospitalization time, and reduces the risk of amputation.

4.2.2. Free Flap Transplantation for Repair

This technique involves harvesting skin and subcutaneous tissue with an intact vascular system from a donor site in the patient and transplanting it to the defect site. Blood vessels are anastomosed under a microscope to reconstruct circulation, thereby restoring both the function and appearance of the wound. Liu Xin *et al.* [35] conducted a systematic review of numerous domestic and international clinical cases of DFU treated with this technique, demonstrating that free flap transplantation significantly improves limb salvage rates and five-year survival. However, the procedure is associated with a relatively high incidence of postoperative complications, and perioperative management remains complex and challenging [36]. Therefore, clinicians must carefully weigh the risks and benefits when considering free flap transplantation for DFU repair.

4.2.3. Tibial Transverse Transport (TTT)

This technique originates from the "Law of Tension-Stress" proposed by Russian orthopedic surgeon Ilizarov in the 1950s. By applying controlled mechanical tension to the tibia, TTT improves local microcirculation, thereby enhancing foot perfusion and promoting healing of leg and foot ulcers. In a clinical study, Wei Jihua *et al.* [37] reported that TTT significantly increased serum VEGF and bFGF levels in DFU patients and activated the Notch signaling pathway. Computed tomography angiography (CTA) of the lower limbs performed eight weeks postoperatively revealed abundant new arterioles in the calf muscles and subcutaneous tissue of the treatment group, whereas no obvious neovascularization was observed in the control group. Ultimately, in the treatment group, nine patients achieved complete ulcer healing, with minimal scar formation and wound appearance resembling normal tissue.

4.3. Growth Factor Therapy

Platelet concentrates (PC) are prepared by centrifugation of whole blood to yield a concentrate rich in platelets. The main components include high concentrations of platelets, leukocytes, fibrin, and multiple growth factors such as PDGF, VEGF, and TGF-β. Depending on preparation methods, PC can be classified as platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factors (CGF) [38]. The therapeutic effect of PC is mediated through the release of growth factors and other bioactive molecules from platelets, thereby promoting tissue repair and exerting anti-inflammatory effects.

In a clinical study, Chen Xiaoyan [39] demonstrated that PRF therapy in DFU patients enhanced VEGF expression and stimulated angiogenesis. Moreover, PRF modulated macrophage polarization, shifting M1-type macrophages toward the M2 phenotype, thereby augmenting anti-inflammatory activity at the wound site and accelerating healing.

4.4. Physical and Adjunctive Therapies

4.4.1. Vacuum Sealing Drainage (VSD)

VSD is a wound management technique that promotes healing by applying continuous negative pressure while sealing the wound surface. The sustained negative pressure removes exudates, necrotic tissue, and bacteria, while simultaneously stimulating granulation tissue formation. In a clinical study, Jiao Jiao [40] reported that VSD increased VEGF levels in DFU wound tissue, thereby accelerating ulcer healing.

4.4.2. Hyperbaric Oxygen Therapy (HBO)

HBO involves placing the patient in a pressurized chamber above one atmosphere and administering high-concentration oxygen. The therapeutic principle is to increase environmental pressure and oxygen intake, thereby raising the level of physically dissolved oxygen in the blood. This process improves tissue oxygenation, promotes repair, and suppresses infection. In a systematic review, Wang Zhi [41] found that HBO facilitated ulcer healing in DFU patients and significantly reduced the incidence of major amputations.

5. Limitations and Future Perspectives

While the mechanistic findings discussed herein are promising, it is crucial to acknowledge the limitations of the current evidence base. For many TCM interventions, such as specific herbal formulas and acupuncture protocols, the supporting clinical data often come from small-scale studies or single-center trials. Larger, multi-center, randomized controlled trials (RCTs) with standardized protocols and rigorous blinding are needed to robustly validate the efficacy of these interventions and confirm their molecular mechanisms of action in human patients. Additionally, the multi-component nature of TCM formulas presents a challenge in pinpointing exact active constituents and their interactions. Future research should integrate systems biology and network pharmacology approaches

to better understand the synergistic effects of TCM. For Western medical interventions, future work should focus on optimizing patient selection for advanced therapies like free flap transplantation and TTT, and on standardizing protocols for emerging treatments like platelet concentrates.

6. Conclusions

In summary, TCM approaches for DFU include internal therapies such as curcumin, Simiao Yong'an Decoction, and Huangqi Yanghe Decoction; external applications such as Zizhu Ointment and Xianglei Tangzu Ointment; and acupuncture. Western medical strategies, in addition to conventional measures such as glycemic control, debridement, and infection management, encompass vascular reconstruction and regenerative techniques (e.g., endovascular intervention, free flap transplantation, tibial transverse transport), growth factor therapy with platelet concentrates, and adjunctive modalities such as vacuum sealing drainage and hyperbaric oxygen therapy.

Remarkably, both TCM and Western medicine demonstrate convergent mechanisms at the cellular and molecular levels, targeting common biological pathways involved in inflammation, angiogenesis, and tissue repair, as summarized in Table 1.

Table 1. Interventions of traditional Chinese and western medicine in targeting diabetic foot ulcers.

Therapeutic Target/Pathway	TCM Interventions	Western Medicine Interventions
VEGF/Angiogenesis	Simiao Yong'an Decoction, Acupuncture, Huangqi Yanghe Decoction.	Tibial Transverse Transport (TTT), Platelet Concentrates (PRP/PRF), Vacuum Sealing Drainage (VSD).
NF-κB/Inflammation	Zizhu Ointment (inhibits NF-κB), Huangqi Yanghe Decoction (inhibits NF-κB), Curcumin.	Hyperbaric Oxygen Therapy (HBO), targeted anti-inflammatory drugs.
Macrophage Polarization (M1/M2)	Xianglei Tangzu Ointment (promotes M2).	Platelet-Rich Fibrin (PRF).
PI3K/AKT Pathway	Huangqi Yanghe Decoction (activates).	Growth Factor Therapies.
TGF-β/Smad Pathway	Curcumin (activates).	Platelet Concentrates (source of TGF-β).

As shown in Table 1, interventions from both medical systems can influence key targets like VEGF for angiogenesis, NF-κB for inflammation, and specific pathways like PI3K/AKT and TGF-β/Smad. This convergence suggests that regardless of theoretical framework, in-depth investigation ultimately reveals the fundamental principles of disease and therapy. Looking ahead, the development of integrative medicine for DFU will be advanced through the shared language of cellular and molecular biology, fostering dialogue and collaboration between the two medical systems. Such integration will not only strengthen the healthcare enterprise but also benefit patients worldwide.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Duncan, B.B., Magliano, D.J. and Boyko, E.J. (2025) IDF Diabetes atlas 11th Edition 2025: Global Prevalence and Projections for 2050. Nephrology, Dialysis, Transplantation: Official Publication of the European Dialysis and Transplant Association. European Renal Association.

[2] Chinese Association of Integrative Medicine Endocrinologist Branch, Endocrinology and Metabolic Disease Professional Committee, Beijing-Tianjin-Hebei Integrative Medicine Endocrinology Specialist Alliance, *et al.* (2025) Guidelines for the Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Diabetic Foot Related to Diabetic Peripheral Vascular Disease. *Chinese Journal of Clinical Healthcare*, **28**, 145-156.

[3] Zhou, B.H., Lin, W.L., Long, Y.L., Yang, Y.K., *et al.* (2022) Notch Signaling Pathway: Architecture, Disease, and Therapeutics. *Signal Transduction and Targeted Therapy*, **7**, Article No. 95. https://doi.org/10.1038/s41392-022-00934-y

[4] Fang, J.L. and Zhou, D.J. (2024) Correlation between Inflammatory Factors and Serum Intercellular Adhesion Molecule-1 Expression in Patients with Diabetic Foot Ulcers. *Chinese Journal of Diabetes*, **32**, 113-116.

[5] Ren, Q., Zhang, L., Zhang, B., Guo, Q.Q. and Zhao, Y.B. (2025) Research Progress on the Mechanism of Targeting Macrophage Phenotypes in the Treatment of Diabetic Foot Ulcers. *Chinese Journal of Diabetes*, **17**, 650-654.

[6] Wang, K.J., Luo, X.H., Xu, R.Y. and Du, J. (2015) Expression of Vascular Endothelial Growth Factor in the Dorsal Pedis Artery Ulcer Tissue of Lower Limbs in Limb Amputated Patients with Diabetic Foot. *Journal of Ningxia Medical University*, **37**, 1318–1320+1373.

[7] Chen, X.L., Cao, X.M., Zhang, J. and Jiang, C. (2025) Research Progress on the Role of Cytokines and Related Signaling Pathways in the Pathogenesis of Diabetic Foot. *Chinese Journal of Cell Biology*, **47**, 975-980.

[8] Uchida, K., Inoue, G., Matsushita, O., Horikawa, K., Sekiguchi, H., Saito, W., *et al.* (2017) Basic Fibroblast Growth Factor-Anchored Multilayered Mesenchymal Cell Sheets Accelerate Periosteal Bone Formation. *BioMed Research International*, **2017**, 1-8. https://doi.org/10.1155/2017/4371460

[9] Wang, W.X. and Lu, A.J. (2025) Roles of Different Growth Factor Families in Diabetic Wound Healing. *Advances in Clinical Medicine*, **15**, 1526-1532.

[10] Tabanjeh, S.F., Hyassat, D., Jaddou, H., Younes, N.A., Robert, A.A. and Ajlouni, K. (2020) The Frequency and Risk Factors of Diabetic Foot Ulcer Recurrence among Jordanian Patients with Diabetes. *Current Diabetes Reviews*, **16**, 910-915. https://doi.org/10.2174/1573399816666200109094329

[11] Nusse, R. and Clevers, H. (2017) Wnt/β-Catenin Signaling, Disease, and Emerging Therapeutic Modalities. *Cell*, **169**, 985-999. https://doi.org/10.1016/j.cell.2017.05.016

[12] Gumede, D.B., Abrahamse, H. and Houreld, N.N. (2024) Targeting Wnt/β-Catenin Signaling and Its Interplay with TGF-β and Notch Signaling Pathways for the Treatment of Chronic Wounds. *Cell Communication and Signaling*, **22**, Article No. 244.

https://doi.org/10.1186/s12964-024-01623-9

[13] Outtz, H.H., Wu, J.K., Wang, X. and Kitajewski, J. (2010) Notch1 Deficiency Results in Decreased Inflammation during Wound Healing and Regulates Vascular Endothelial Growth Factor Receptor-1 and Inflammatory Cytokine Expression in Macrophages. *The Journal of Immunology*, **185**, 4363-4373. https://doi.org/10.4049/jimmunol.1000720

[14] Chen, F.J., Ding, J. and Zhou, H. (2021) Interaction between Notch and Related Regulatory Signals in Promoting Wound Healing. *Chinese Journal of Biochemistry and Molecular Biology*, **37**, 733-742.

[15] Zheng, X.W., Narayanan, S., Sunkari, V.G., Eliasson, S., *et al.* (2019) Triggering of a Dll4-Notch1 Loop Impairs Wound Healing in Diabetes. *Proceedings of the National Academy of Sciences*, **116**, 6985-6994. https://doi.org/10.1073/pnas.1900351116

[16] Wang, Y.X., Chen, J.J., Cen, Y., Li, Z.Y. and Zhang, Z.Y. (2022) Research Advances on Exosomes Derived from Adipose-Derived Mesenchymal Stem Cells in Promoting Diabetic Wound Healing. *Chinese Journal of Burns and Wounds*, **38**, 491-495.

[17] Geng, K., Ma, X., Jiang, Z., Gu, J., Huang, W., Wang, W., *et al.* (2023) WDR74 Facilitates TGF-β/Smad Pathway Activation to Promote M2 Macrophage Polarization and Diabetic Foot Ulcer Wound Healing in Mice. *Cell Biology and Toxicology*, **39**, 1577-1591. https://doi.org/10.1007/s10565-022-09748-8

[18] Karar, J. and Maity, A. (2011) PI3K/AKT/mTOR Pathway in Angiogenesis. *Frontiers in Molecular Neuroscience*, **4**, Article 51. https://doi.org/10.3389/fnmol.2011.00051

[19] Atic, R. and Deveci, E. (2019) Endothelin 1, NF-κB, and ADAM-15 Expression in Diabetic Foot Wounds. *Bratislava Medical Journal*, **120**, 58-64. https://doi.org/10.4149/bll_2019_009

[20] World Federation of Chinese Medicine Societies Diabetes Professional Committee Diabetic Foot Group, Liu, G.B. and Gao, H.L. (2025) Expert Consensus on Traditional Chinese Medicine External Therapy for Diabetic Foot Ulcers. *World Chinese Medicine*, **20**, 1442-1449.

[21] You, L. (2025) Investigating the Effects of Curcumin on Organism Metabolism through Integrated Metabolomics and Pharmacokinetics. Master's Thesis, Gannan Medical University.

[22] Run, J.M., Run, X.D., Gao, Z.S. and Li, S.L. (2024) Effect of Curcumin on Wound Healing of Diabetic Foot Ulcer Based on TGF-β1/Smad3 Signaling Pathway. *Hebei Medical Journal*, **30**, 1978-1982.

[23] Miao, M. and Xiang, L. (2020) Pharmacological Action and Potential Targets of Chlorogenic Acid. *Advances in Pharmacology*, **87**, 71-88.

[24] Xu, C., Tang, Y., Yang, H., Jiang, S., Peng, W. and Xie, R. (2024) Harpagide Inhibits the TNF-α-Induced Inflammatory Response in Rat Articular Chondrocytes by the Glycolytic Pathways for Alleviating Osteoarthritis. *International Immunopharmacology*, **127**, Article 111406. https://doi.org/10.1016/j.intimp.2023.111406

[25] Zduńska, K., Dana, A., Kolodziejczak, A. and Rotsztejn, H. (2018) Antioxidant Properties of Ferulic Acid and Its Possible Application. *Skin Pharmacology and Physiology*, **31**, 332-336. https://doi.org/10.1159/000491755

[26] Chen, X., Li, M., Wang, Z.W., Zhu, M.D., Zhang, Z.W., Wei, Z.Q. and Li, Q. (2022) Analysis of the Application of Simiao Yong'an Decoction in Promoting Angiogenesis in Diabetic Foot Ulcer Wounds. *Chinese Journal of Traditional Chinese Medicine*, **40**, 62-64.

[27] Zhang, W.J. and Frei, B. (2015) Astragaloside IV Inhibits NF-κB Activation and Inflammatory Gene Expression in LPS-Treated Mice. *Mediators of Inflammation*, **2015**,

Article 274314. https://doi.org/10.1155/2015/274314

[28] Xu, X.Q., Zhu, H., Deng, T.Y., Yang, L., Meng, Z.R., Xie, F.F. and Zhang, M. (2025) Research Progress on the Pharmacological Effects of Cinnamaldehyde. Zhuang and Yao Medicine Research, No. 1, 37-39.

[29] Bao, Y.L., Lei, H., Ma, J. and Zhao, X.M. (2024) Huangqi Yanghe Decoction Promotes Wound Healing in Diabetic Foot Ulcer Rats by Regulating the PI3K/AKT/NF-κB Signaling Pathway. *Tianjin Medical Journal*, **52**, 266-272.

[30] Han, Q., Liu, G.B., Qin, L., Yan, S.M., Huang, R.Y., Xu, F., Shi, C.Y. and Chen, J.H. (2021) Effect of Zizhu Ointment on Inflammatory Response and NF-κB/JNK/PI3K Signaling Expression in Diabetic Foot Ulcers Infected with *Staphylococcus aureus*. *Journal of Tianjin University of Traditional Chinese Medicine*, **40**, 226-234.

[31] Bai, J. and Wang, J.W. (2025) Diabetic Foot Ulcer Therapeutic Drug—Xiang Lei Tang Zu Gao. *Clinical Medication Journal*, **23**, 14-16.

[32] Wang, Z.M. and Zhou, Z.Y. (2020) Clinical Efficacy of Acupuncture-Moxibustion Combined with Conventional Medications in Treatment of Diabetic Foot and Its Effects on Serum Cytokine Levels. *Shanghai Journal of Acupuncture and Moxibustion*, **39**, 401-405.

[33] Chinese International Exchange and Promotive Association for Medical and Health Care, Peripheral Vascular Medicine Branch, Capital Medical University Clinical Diagnosis and Treatment and Research Center for Lower Extremity Arteriosclerosis Obliterans, *et al.* (2024) Chinese Guidelines for the Diagnosis and Treatment of Diabetic Foot. *Chinese Journal of Clinical Physicians*, **52**, 1287-1296.

[34] Yi, W.T., Long, L.Y., Deng, X.H. and Zhang, Y.L. (2025) A Meta-Analysis of the Clinical Efficacy of Peripheral Vascular Intervention in the Treatment of Diabetic Foot Caused by Peripheral Arterial Disease. *Chinese Journal of Burns and Wounds*, **37**, 91-95+100.

[35] Liu, X., Huang, G.T. and Wu, J. (2024) Research Progress on the Application of Free Flaps in Limb Salvage Treatment for Patients with Diabetic Foot Ulcers. *Chinese Journal of Burns and Wounds*, **40**, 985-990.

[36] Jian, Y., Wei, Z.R., Chen, W., Zhang, Y.J., Tang, M.Y., Zhong, Y.X. and Liu, C.X.X. (2023) Research Progress on the Application of Free Flaps in the Repair of Diabetic Foot Ulcers. *Chinese Journal of Burns and Wounds*, **39**, 376-380.

[37] Wei, J.H., Tang, Q.L., Luo, Q.Q., Tang, Y.J., Mo, X.G., *et al.* (2019) Clinical Observation of the Efficacy of Ilizarov Microcirculation Reconstruction Technique in Diabetic Foot Ulcer. *Journal of Youjiang Medical University for Nationalities*, **41**, 239-245.

[38] Dohan Ehrenfest, D.M., Rasmusson, L. and Albrektsson, T. (2009) Classification of Platelet Concentrates: From Pure Platelet-Rich Plasma (P-PRP) to Leucocyte- and Platelet-Rich Fibrin (L-PRF). *Trends in Biotechnology*, **27**, 158-167. https://doi.org/10.1016/j.tibtech.2008.11.009

[39] Chen, X.Y. (2024) Effect of Modified Platelet-Rich Fibrin on Diabetic Foot Healing. Master's Thesis, Chengde Medical University.

[40] Jiao, J., Wang, P.H., Chu, Y.J., Zheng, C.C. and Li, X.W. (2014) Mechanism of Vacuum Sealing Drainage in Promoting the Healing of Diabetic Foot Ulcers. *International Journal of Endocrinology and Metabolism*, **34**, 10-14.

[41] Wang, Z., Wang, F., Fan, B.X., Hu, F.F., Wang, Y.N., Ming, Y. and Huang, S.N. (2025) Evidence Summary for Hyperbaric Oxygen Therapy and Management in Patients with Diabetic Foot. *Evidence-Based Nursing*, **11**, 2634-2641.