Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 411 - 412 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.198
Short communication

Multicomponent herbal mixtures: target approach for chronic wound management

Iskra Davkova*, Ana Trajkovska Matevska, Veronika Stoilkovska Gjorgievska, Filip Todorov, Ivana Cvetkovikj Karanfilova, Gjoshe Stefkov, Marija Karapandzova

Institute of Pharmacognosy, Faculty of Pharmacy, Ss. Cyril and Methodius University in Skopje, Majka Tereza 47, 1000 Skopje, Republic of North Macedonia

Introduction

The treatment of chronic wounds remains a complex and challenging process that requires a multidimensional and multifunctional therapeutic approach (Martinengo et al., 2019). Considering that chronic wounds are often associated with underlying comorbidities, therapeutic strategies must be not only effective but also safe, non-toxic, and well tolerated.

Conventional therapies are frequently limited by single-target mechanisms and may be associated with adverse effects, potentially impairing the healing process (Han et al., 2017). In this context, herbal therapies have emerged as promising alternatives or complementary approaches, primarily due to their multicomponent nature and their ability to simultaneously target multiple biological pathways.

Role of multicomponent herbal mixtures (MHMs)

The effectiveness of multicomponent herbal mixtures (MHMs) in chronic wound management is largely based on the presence of bioactive compounds capable of targeting several pathological processes at once. Among these, polyphenols and alkaloids represent two of the most important classes due to their complementary and synergistic biological activities (Alipieva et al., 2014; Zhou et al., 2021).

Polyphenols in wound healing

Polyphenols, particularly flavonoids and phenylethanoid glycosides, are well recognized for their strong antioxidant, anti-inflammatory, and antimicrobial properties. Their functional role is especially relevant in wound healing, where they reduce oxidative stress by neutralizing free radicals and enhancing endogenous antioxidant defense systems, thereby protecting cellular components and promoting tissue regeneration (Subramanian et al., 2023). In addition, they modulate inflammatory pathways through inhibition of key mediators and transcription factors such as cyclooxygenase (COX), nuclear factor kappa B (NF-κB) and nuclear factor erythroid 2-related factor 2 (Nrf-2), contributing to the resolution of prolonged inflammation (Rahman et al., 2022; Saha et al., 2024).

Polyphenols also exhibit significant antimicrobial activity through multiple mechanisms, including disruption of bacterial membrane integrity, interference with enzyme activity, and inhibition of virulence factors and biofilm formation (Alipieva et al., 2014; Lobiuc et al., 2023). Furthermore, they promote fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization, all of which are essential for effective wound closure (Mittal et al., 2013).

*iskra.davkova@gmail.com

Alkaloids in wound healing

Alkaloids complement the effects of polyphenols by contributing additional biological activities relevant to wound healing. Compounds such as berberine have demonstrated the ability to modulate oxidative stress, regulate inflammation in a phase-dependent manner, and stimulate cell proliferation and extracellular matrix formation, thereby accelerating tissue repair (Zhou et al., 2021). Their antimicrobial activity, including inhibition of bacterial virulence factors and key enzymes, further supports their role in preventing infection and improving healing outcomes (Oh et al., 2006).

Synergistic action in MHMs

The inclusion of both polyphenols and alkaloids in MHMs is functionally justified. Chronic wounds are characterized by oxidative stress, persistent inflammation, microbial colonization, and impaired tissue regeneration, making it unlikely that a single compound can effectively target all underlying pathological processes (Martinengo et al., 2019). MHMs enable simultaneous targeting of these mechanisms through synergistic interactions between different classes of bioactive compounds (Wagner et al., 2009; Yang et al., 2014).

Such combinations provide a balanced and efficient therapeutic effect, where antioxidant protection, anti-inflammatory regulation, antimicrobial defense, and stimulation of tissue repair occur concurrently. This multitarget approach enhances overall efficacy and may reduce the required doses of individual components, improving safety and minimizing potential side effects (Wagner et al., 2009; Yang et al., 2014).

Conclusion

Rational design of MHMs should include complementary classes of bioactive compounds, such as polyphenols and alkaloids, in order to achieve a comprehensive and optimized therapeutic response in chronic wound management.

References

Martinengo, L. et al., 2019. Prevalence of chronic wounds in the general population: systematic review and meta-analysis of observational studies. Ann. Epidemiol. 29, 8–15. https://doi.org/10.1016/j.annepidem.2018.10.005

Han, G. et al., 2017. Chronic wound healing: a review of current management and treatments. Adv. Ther. 34(3), 599–610. https://doi.org/10.1007/s12325-017-0478-y

Alipieva, K. et al., 2014. Verbascoside – a review of its occurrence, (bio)synthesis and pharmacological significance. Biotechnol. Adv. 32(6), 1065–1076. https://doi.org/10.1016/j.biotechadv.2014.07.001

Zhou, R. et al., 2021. Berberine accelerated wound healing by restoring TrxR1/JNK in diabetes. Clin. Sci. 135(4), 613–627. https://doi.org/10.1042/CS20201145

Subramanian, S. et al., 2023. Wound healing properties of a newly formulated flavonoid-rich fraction from *Dodonaea viscosa* Jacq. leaves extract. Front. Pharmacol. 14, 1096905.
https://doi.org/10.3389/fphar.2023.1096905

Rahman, M.M. et al., 2022. Role of phenolic compounds in human disease: current knowledge and future prospects. Molecules. 27(1), 233. https://doi.org/10.3390/molecules27010233

Saha, R. et al., 2024. Verbascoside: a comprehensive review of its pharmacological properties and therapeutic potential. Inflammopharmacology. 32(1), 1–20. https://doi.org/10.1007/s10787-023-01186-3

Lobiuc, A. et al., 2023. Future antimicrobials: natural and functionalized phenolics. Molecules. 28(3), 1114.

Mittal, A. et al., 2013. Herbal boon for wounds. Int. J. Pharm. Pharm. Sci. 5(2), 1–12.

Oh, K. et al., 2006. Inhibition of sortase-mediated *Staphylococcus aureus* adhesion to fibronectin via fibronectin-binding protein by sortase inhibitors. Appl. Microbiol. Biotechnol. 70, 102–106. https://doi.org/10.1007/s00253-005-0040-8

Wagner, H., Ulrich-Merzenich, G., 2009. Synergistic therapeutic actions of herbal ingredients and their mechanisms from molecular interaction and network perspectives. Drug Discov. Today 14(11–12), 579–588. https://doi.org/10.1016/j.drudis.2009.03.012

Yang, Y., Zhang, Z., Li, S., Ye, X., Li, X., He, K., 2014. Synergy effects of herb extracts: Pharmacokinetics and pharmacodynamic basis. Fitoterapia 92, 133–147. https://doi.org/10.1016/j.fitote.2013.10.010