Letter to Editor

Topical Vinpocetine as a Potential Adjuvant Therapy for Chronic Anal Fissure: A Drug Repurposing Hypothesis

Dear Editor

Chronic anal fissure remains a distressing anorectal disorder that significantly reduces patients' quality of life. Conventional topical therapies, including nitrates, calcium channel blockers, and botulinum toxin, primarily target internal sphincter relaxation and local perfusion. However, relapse rates remain high, and complete healing is often delayed or incomplete.[1] Glyceryl trinitrate (GTN) is frequently associated with dose-limiting headaches, whereas calcium channel blockers such as diltiazem and nifedipine, despite better tolerability, do not directly address chronic inflammation or impaired wound repair, which are key contributors to fissure persistence.[1, 2] Botulinum toxin injection is generally reserved for refractory cases. Its clinical utility is constrained by the need for injection, variability in dosing, cost, and the risk of transient fecal incontinence.[1, 3] These limitations highlighted the need for alternative or adjunctive topical therapies with broader mechanistic coverage.

Given the multifactorial pathophysiology of chronic fissure, involving ischemia, oxidative stress, and local inflammation, agents with vasodilatory, antioxidant, and anti-inflammatory actions may offer additional benefit.[1, 2] Vinpocetine, a semisynthetic derivative of vincamine and a selective phosphodiesterase-1 (PDE1) inhibitor currently used to increase blood flow in cerebrovascular disorders, exhibits precisely these multiple properties. It enhances cyclic nucleotide–mediated smooth muscle relaxation, improves microvascular blood flow, attenuates inflammatory signaling through inhibition of nuclear factor-kappa B (NF-κB) and downregulation of cyclooxygenase-2 (COX-2) and pro-inflammatory cytokines, and promotes wound healing. Unlike conventional topical therapies, vinpocetine might simultaneously target vascular dysfunction, inflammation, and oxidative injury, key drivers of fissure chronicity.[4-7] Experimental studies further demonstrated that vinpocetine accelerated epithelialization, enhanced collagen deposition, and promoted angiogenesis.[5] Beyond its neurovascular indications, topical vinpocetine formulations indicated promising outcomes in experimental models of chronic inflammatory dermatoses such as psoriasis and atopic dermatitis, with excellent tolerability and negligible systemic absorption.[8, 9] Additionally noteworthy in this regard is a recent study that confirmed the safety of a mucoadhesive *in situ* gel formulation for intranasal delivery of vinpocetine.[10] Although direct data on rectal mucosal application are lacking, these findings support the formulation's potential safety and pharmacologic plausibility for mucocutaneous use.

Although no clinical studies have yet evaluated vinpocetine in anal fissure, its mechanisms align well with the key pathophysiologic drivers of fissure persistence, namely, sphincter hypertonia, reduced mucosal perfusion, and local inflammation. Repurposing vinpocetine as an adjuvant topical agent could therefore represent a rational, low-risk strategy deserving of pilot clinical evaluation. It is suggested that future studies examine topical vinpocetine's efficacy, optimal concentration, and safety in chronic anal fissure, especially in patients unresponsive to standard medical therapies. By integrating vasodilatory, anti-inflammatory, and pro-healing effects, vinpocetine might help bridge the therapeutic gap between conservative and surgical management.

Authors' Contribution

Z.N.T: Conception, writing, and reviewing. The author has read and approved the final manuscript and agrees to be accountable for all aspects of the work, in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

AI Declaration

The authors declare that no artificial intelligence (AI) tools or generative AI technologies were used in the preparation, writing, analysis, or editing of this manuscript.

Conflict of Interest: None declared.

Keywords ● Vinpocetine ● Anal canal ● Vasodilation ● Wound healing ● Inflammation

Zahra Nazari Taloki[1,2], PharmD, PhD

[1]Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran; [2]Department of Clinical Pharmacy, School of Pharmacy, Babol University of Medical Sciences, Babol, Iran

Correspondence:
Zahra Nazari Taloki, PharmD, PhD;
Department of Clinical Pharmacy, School of Pharmacy, Babol University of Medical Sciences, Ganj Afroz St., Postal code:4717647745, Babol, Iran
Tel: +98 11 32207924
Email: zahra_nazari_taloki@yahoo.com
Received: 15 November 2025
Accepted: 14 March 2026
Accepted: 28 March 2026

Please cite this article as: Nazari Taloki Z. Topical Vinpocetine as a Potential Adjuvant Therapy for Chronic Anal Fissure: A Drug Repurposing Hypothesis. Iran J Med Sci. doi: 10.30476/ijms.2026.109670.4502.

References

1 Lyle V, Young CJ. Anal fissures: An update on treatment options. Aust J Gen Pract. 2024;53:33-5. doi: 10.31128/AJGP/05-23-6843. PubMed PMID: 38316476.
2 Fagan C, Kolber MR, Lindblad AJ. Topical treatments for anal fissure. Can Fam Physician. 2023;69:33. doi: 10.46747/cfp.690133. PubMed PMID: 36693740; PubMed Central PMCID: PMC9873286.
3 Chen X. Advancements in the application of botulinum toxin type a in the treatment of anorectal disorders. Toxi-con. 2025;260:108346. doi: 10.1016/j.toxicon.2025.108346. PubMed PMID: 40246206.
4 Alshehri AA, Al-Kuraishy HM, Al-Gareeb AI, Jawad SF, Khawagi WY, Alexiou A, et al. The anti-inflammatory prop-erties of vinpocetine mediates its therapeutic potential in management of atherosclerosis. J Inflamm (Lond). 2024;21:19. doi: 10.1186/s12950-024-00394-x. PubMed PMID: 38858751; PubMed Central PMCID: PMC11165849.
5 Barakat W, Anwar H, Mahmoud M. Sildenafil and vinpocetine promote wound healing in diabetic rats. J. Adv. Pharm. Res. 2021;5(1):211-21. doi: 10.21608/aprh.2020.34224.1113.
6 Al-Kuraishy HM, Al-Gareeb AI, Naji MT, Al-Mamorry F. Role of vinpocetine in ischemic stroke and poststroke out-comes: A critical review. Brain Circ. 2020;6:1-10. doi: 10.4103/bc.bc_46_19. PubMed PMID: 32166194; PubMed Central PMCID: PMC7045535.
7 Abu-Alghayth MH, Al-Kuraishy HM, Al-Gareeb AI, Alexiou A, Papadakis M, Bahaa MM, et al. Atheroprotective role of vinpocetine: an old drug with new indication. Inflammopharmacology. 2024;32:3669-78. doi: 10.1007/s10787-024-01529-5. PubMed PMID: 39141151; PubMed Central PMCID: PMC11550280.
8 Salman HR, Alzubaidy AA, Abbas AH, Mohammad HA. Attenuated effects of topical vinpocetine in an imiquimod-induced mouse model of psoriasis. J Taibah Univ Med Sci. 2024;19:35-53. doi: 10.1016/j.jtumed.2023.09.002. PubMed PMID: 37868105; PubMed Central PMCID: PMC10585306.
9 Lee YJ, Song JY, Lee SH, Lee Y, Hwang KT, Lee JY. Vinpocetine, a phosphodiesterase 1 inhibitor, mitigates atopic dermatitis-like skin inflammation. Korean J Physiol Pharmacol. 2024;28:303-12. doi: 10.4196/kjpp.2024.28.4.303. PubMed PMID: 38926838; PubMed Central PMCID: PMC11211756.

10 Hard S, Shivakumar HN, Bafail DA, Moqbel Redhwan MA. Development of in vitro and in vivo evaluation of mucoad-hesive in-situ gel for intranasal delivery of vinpocetine. J Drug Target. 2025;33:528-45. doi: 10.1080/1061186X.2024.2433557. PubMed PMID: 39601452.