Enhanced Healing Potential of Stem Cells and α-Terpineol Loaded Hydrogel in Full Thickness Acid Burn Wounds: A Step Toward Advanced Wound Care Solutions

Fatima Jameel[1], Maria Khalid[2], Asmat Salim[1], Irfan Khan[1,3], Muhammad Raza Shah[2]

[1]Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi, 75270, Pakistan,

[2]HEJ Research Institute of Chemistry, International Center for Chemical and Biological Sciences, University of Karachi, Karachi, 75270, Pakistan,

[3]Center for Regenerative Medicine and Stem Cell Research, The Aga Khan University, Stadium Road, P. O. Box 3500, Karachi 74800, Pakistan,

*E-mails: fatimajameel43@gmail.com

ABSTRACT

Background: Clinical management of burn wounds typically involves autologous skin grafting (Khalid *et al*., 2024) (Jameel *et al*., 2024). However, this approach is limited in full-thickness burns due to insufficient donor skin availability (Jameel *et al*., 2024) (Zaidi *et al*., 2024). Synthetic skin substitutes offer a promising alternative approach for restoring tissue integrity.

Objective/aim: This study aimed to develop an advanced wound care product (a hybrid polyvinyl alcohol (PVA)/tapioca starch-based hydrogel loaded with the cytoprotective compound α-terpineol (AT) for full-thickness burn wounds.

Methods: The structural and functional properties of the hydrogel were characterized post-fabrication. *In vitro*, biocompatibility assays using skin fibroblasts demonstrated 90% cell viability with the AT-loaded hydrogel, and *in vivo*, skin sensitivity tests on normal rat skin confirmed its non-inflammatory nature. After confirmation of its biocompatibility, the hydrogel was evaluated in combination with mesenchymal stem cells (MSCs) in a third-degree acid burn wound model. Hydrogel was applied topically for one week (5 h/day), followed by MSC transplantation after 48 h. Experimental groups included: (Khalid *et al*., 2024) control (untreated wound), (Jameel *et al*., 2024) blank hydrogel, (Jameel *et al*., 2024) AT-loaded hydrogel, (Zaidi *et al*., 2024) blank hydrogel + MSCs, and (Irfan *et al*., 2022) AT-loaded hydrogel + MSCs (Irfan *et al*., 2022).

Result: Macroscopic wound evaluation over one month indicated significant tissue destruction and incomplete regeneration in the control group compared to all hydrogel-treated groups. The AT-loaded hydrogel + MSC group showed markedly enhanced wound closure compared to the blank hydrogel + MSC group ($p \leq 0.05$). These findings were consistent with the histological, gene expression, and immunohisstochemical analyses. The AT-loaded hydrogel maintained a moist wound environment, facilitating hydration, while AT further promoted healing by reducing inflammation and oxidative stress. The direct transplantation of MSCs synergistically enhanced tissue regeneration, as evidenced by extracellular matrix deposition and re-epithelialization.

Conclusion: This study concluded that the combination of AT-loaded hydrogel and MSCs represents a synergistic strategy for improving burn wound healing. This approach holds significant potential for the clinical management of extensive burn injuries, providing a scaffold for regeneration and a platform for cellular therapies.

Keywords: Mesenchymal Stem Cells (MSCs), Full Thickness Acid Burns, Alpha Terpineol, Hydrogels, Wound Healing.

ACKNOWLEDGMENT

This study is financially supported by the National Research Program for Universities (NRPU-HEC) project under grant number 20-17590. Human umbilical cord samples were provided by the Zainab Panjwani Memorial Hospital after getting consent from donors.

REFERENCES

1. Khalid, M., Jameel, F., Jabri, T., Jabbar, A., Salim, A., Khan, I., & Shah, M. R. (2024). α-Terpineol loaded, electron beam crosslinked polyvinyl alcohol/tapioca starch hydrogel sheets; fabrication, characterization and evaluation of wound healing potential on a full thickness acid burn wound. RSC advances, 14(38), 28058-28076.
2. Jameel, F., Irfan, F., Salim, A., Khan, I., & Khalil, E. A. (2024). Alpha terpineol preconditioning enhances regenerative potential of mesenchymal stem cells in full thickness acid burn wounds. *Regenerative Therapy*, *26*, 188-202.
3. Jameel, F., Khan, I., Malick, T. S., Qazi, R. E. M., Zaidi, M. B., Salim, A., & Khalil, E. A. (2024). Single dose human perinatal stem cells accelerate healing of cold-induced rat burn wound. *Cell Biochemistry and Function*, *42*(3), e4008.
4. Zaidi, M. B., Khan, F., Jameel, F., Khan, I., Musharraf, S. G., & Salim, A. (2024). Temporal and differential proteomic profile of molecular mediators associated with chronic and acute wound healing. *Cell Biochemistry and Function*, *42*(2), e3946.
5. Irfan, F., Jameel, F., Khan, I., Aslam, R., Faizi, S., & Salim, A. (2022). Role of quercetin and rutin in enhancing the therapeutic potential of mesenchymal stem cells for cold induced burn wound. *Regenerative Therapy*, *21*, 225-238.