Proceedings of the 7th World Congress on Recent Advances in Nanotechnology (RAN'22)
~~Lisbon, Portugal~~ Virtual Conference – April 04 – 06, 2022
Paper No. ICNNFC 135
DOI: 10.11159/icnnfc22.135

Responsive Nanoparticles for Triggered Delivery of Anti-scar Drug to the Burn Wound

Farinaz Jonidi Shariatzadeh[1], Sarvesh Logsetty[2] and Song Liu[3*]
[1]Biomedical Engineering, Faculty of Engineering, University of Manitoba, Winnipeg, Manitoba, Canada, Jonidisf@myumanitoba.ca
[2]Departments of Surgery and Psychiatry, Rady Faculty of Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada, sarvesh.logsetty@umanitoba.ca
[3]Department of Biosystems Engineering, Faculty of Agricultural and Food Sciences, University of Manitoba, Winnipeg, Manitoba, Canada, song.liu@umanitoba.ca

Extended Abstract

The importance of developing anti-scar wound dressing comes from the fact that scar as an abnormal tissue affects aesthetics and changes the functionality of tissue strength and pliability[1]. The main group of patients who are at risk of scar formation is burn survivors. The World Health Organization (WHO) reports that annually 11 million people suffer from severe burn wounds that need medical care [2]–[6]. Burn scar has devastating effects, including pain, intolerance of heat, severe itching, limitations in movement, and dyspigmentation; these factors lead to problems with social integration [7] and discrimination in the community [8] which can reduce the burn survivors' quality of life.

Commonly available treatments for scar prevention or reduction, such as stem cell therapy or surgical approaches, are limited in reaching a satisfying result. These limits drive the need for advanced progress in the field of drug delivery. Numerous studies have been published on developing anti-scar wound dressings; nevertheless, a clinical product has not been produced yet.

Our goal is to incorporate biomolecules with the ability to bind to cell receptors that can affect scar formation and wound healing rate [9]. Although growth factors and cytokines are choices as anti-scar agents, the challenges related to sterility, short half-life, short shelf life, and regulatory hurdles limit their application [10]. But, anti-scar small molecules such as kynurenine (Kyn) do not have those drawbacks associated with growth factors. Human trials as cream-based treatments have shown promising results concerning scar reduction [11]. The main problem of cream-based treatments is related to the unprotected route of administration. Also, another problematic fact is associated with the daily usage of these anti-scar drugs as topical creams during wound healing [13]. This treatment necessitates frequent removal of the wound dressing while the wound is in the healing stages. The unnecessarily frequent wound dressing changes elevate complications for patients and increase the risk of infection for open wounds.

To overcome the mentioned drawbacks of developed anti-scar remedies, we propose incorporating smart nanoparticles (NP) into wound dressings as carriers for on-demand delivery of anti-scar agents. The smart NPs can target the scar formation stage and release the drugs in the desired stage. The smart NPs are responsive to reactive oxygen species (ROS), which increase inside the cells in the scar formation stages.

We synthesized the PEG-co-PPS polymer that undergoes an oxidative transition in ROS presence. NPs based on PEG-co-PPS were fabricated through the double emulsion technique. It is hypothesized that the NP enters the cell through the lipid diffusion pathway and forms pores in the endosome membrane and in the cytosol, where ROS concentration is high and releases the payload. The fabricated NPs (200 ±5 nm) showed a promising responsive delivery *in vitro* in the presence and absence of H_2O_2, 92% and less than 6% within three days.

The fabricated responsive nanoparticles showed excellent results regarding having on-demand delivery. Thus, the next step would be cellular assessments of the particles to identify the endocytosis route and evaluate gene expression to demonstrate anti-scar activities.

References

[1] Z. Meng, D. Zhou, Y. Gao, M. Zeng, and W. Wang, "miRNA delivery for skin wound healing," *Adv. Drug Deliv. Rev.*, vol. 129, pp. 308–318, 2018.

[2] B. N. Blackstone, J. Y. Kim, K. L McFarland, C. K. Sen, D. M. Supp, J. K. Bailey, H. M. Powell, "Scar formation following excisional and burn injuries in a red Duroc pig model," *Wound Repair Regen.*, vol. 25, no. 4, pp. 618–631, Aug. 2017.

[3] B. S. Atiyeh, A. M. El Khatib, and S. A. Dibo, "Pressure garment therapy (PGT) of burn scars: Evidence-based efficacy," *Ann. Burns Fire Disasters*, vol. 26, no. 4, pp. 205–212, 2013.

[4] A. Goel and P. Shrivastava, "Post-burn scars and scar contractures," *Indian J. Plast. Surg.*, vol. 43, no. 3, p. 63, 2010.

[5] WHO, "No Title." [Online]. Available: https://www.who.int/violence_injury_prevention/other_injury/burns/en/#:~:text=Globally%2C burns are a serious,-and middle-income countries.

[6] B. C. Brown, S. P. McKenna, K. Siddhi, D. A. McGrouther, and A. Bayat, "The hidden cost of skin scars: quality of life after skin scarring," *J. Plast. Reconstr. Aesthetic Surg.*, vol. 61, no. 9, pp. 1049–1058, Sep. 2008.

[7] L. H. Engrav, M. H. Covey, K. D. Dutcher, D. M. Heimbach, M. D. Walkinshaw, and J. A. Marvin, "Impairment, Time Out of School, and Time Off from Work after Burns," *Plast. Reconstr. Surg.*, vol. 79, no. 6, pp. 927–932, Jun. 1987.

[8] S. McGarry, C. Elliott, A. McDonald, J. Valentine, F. Wood, and S. Girdler, "Paediatric burns: From the voice of the child," *Burns*, vol. 40, no. 4, pp. 606–615, Jun. 2014.

[9] M. Leena, A. Barade, D. Rana, C. Dhand, S. Ramakrishna, and M. Ramalingam, *Nanofiber composites in biomolecular delivery*. Elsevier Ltd, 2017.

[10] A. J. Whittam, Z. N. Maan, D. Duscher, V. W. Wong, J. A. Barrera, M. Januszyk, G. C. Gurtner, "Challenges and Opportunities in Drug Delivery for Wound Healing," *Adv. Wound Care*, vol. 5, no. 2, pp. 79–88, 2016.

[11] A. Papp, R. Hartwell, M. Evans, and A. Ghahary, "The Safety and Tolerability of Topically Delivered Kynurenic Acid in Humans. A Phase 1 Randomized Double-Blind Clinical Trial," *J. Pharm. Sci.*, vol. 107, no. 6, pp. 1572–1576, 2018.

[12] K. N. Dolynchuk and E. E. Tredget, "A Preliminary Report of the Biochemical and Clinical Effects of 1,4-Diaminobutane on Prevention of Human Hypertrophic Scars," *Plast. Reconstr. Surg.*, vol. 145, no. 1, pp. 76e-84e, 2020.

[13] M. S. Poormasjedi-Meibod, S. Salimi Elizei, V. Leung, R. Baradar Jalili, F. Ko, and A. Ghahary, "Kynurenine Modulates MMP-1 and Type-I Collagen Expression Via Aryl Hydrocarbon Receptor Activation in Dermal Fibroblasts," *J. Cell. Physiol.*, vol. 231, no. 12, pp. 2749–2760, 2016.