IOCB 2024 Conference
The 1st International Online Conference on Biomimetics
15–17 May 2024 | Online

The regenerative potential of biomimetic construct based on hydrogel loaded with biological agents and hypoxic-MSCs

Maryam Ghahremani-Nasab[1]*, Azizeh Rahmani Del Bakhshayesh[1], Soraya Babaie[2], Ahmad Mehdipour[1]*

1. Department of Tissue Engineering, Faculty of Advanced Medical Sciences, Tabriz University of Medical Sciences, Tabriz, Iran
2. Physical Medicine and Rehabilitation Research Center, Aging Research Institute, Tabriz University of Medical Sciences, Tabriz, Iran

INTRODUCTION & AIM

Skin tissue engineering is a novel approach to treating skin damage that has gained popularity in recent times. Hydrogel scaffolds are commonly used to promote wound healing. Studies have shown that chitosan, alginate, and ascorbic acid are highly effective in this regard [1, 2, 3, 4]. Ascorbic acid as a biological agent, plays a significant role in wound healing by increasing repair intermediaries and decreasing inflammation at the wound site [5]. Applying hypoxia has been shown to enhance therapeutic performance of mesenchymal stem cells [6]. Moreover, Hypoxia-inducible factor-1 (HIF-1) plays a crucial role in wound healing and remodeling [7]. The aim of our study is to investigate the role of biological agents and MSCs loaded onto biomimetic constructs based on chitosan-alginate hydrogel and determine their performance under hypoxic conditions [8].

KEYWORDS: Skin Wound Healing, Ascorbic Acid, Hypoxia-Induced Factor.

METHOD

Biomimetic constructs based on chitosan/alginate hydrogel were mixed with ascorbic acid and cross-linked with CaCl2 [8]. The scaffold's physicochemical properties, including swelling and biodegradation rate, wettability, and FTIR analysis, were assessed. Further analysis was conducted using MTT, DAPI, and H&E staining [8]. The study investigated the expression of key genes (HIF-1α, VEGF-A, and TGF-β1) involved in the healing of skin wounds under hypoxic and normoxic conditions using real-time PCR [8].

RESULTS & DISCUSSION

The study revealed that the biomimetic construct based on chitosan-alginate hydrogel (Fig.1) was highly porous (Fig.2), biodegradable (Fig. 3), and had a high swelling capacity (Fig. 4) [8]. The hydrogel was not only hydrophilic (Fig. 5), but also compatible with blood. The hydrogel provided a suitable substrate for cell growth and proliferation as indicated by MTT (Fig. 6), DAPI, and H&E staining tests. Under hypoxic conditions, MSCs showed increased expression of VEGF and TGF-β1 genes (Fig. 7) according to the RT-PCR analysis [8].

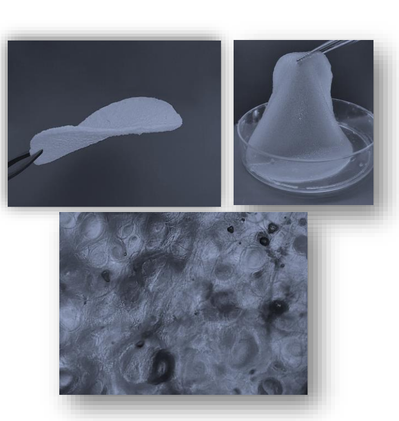

Fig.1: Appearance of the hydrogels [8]

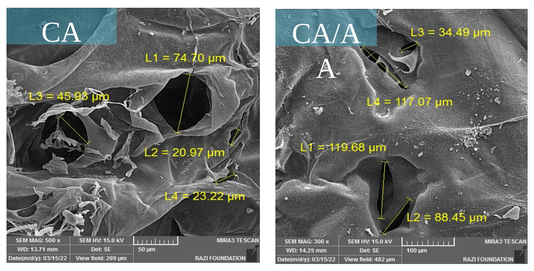

Fig.2: SEM images of hydrogels [8]

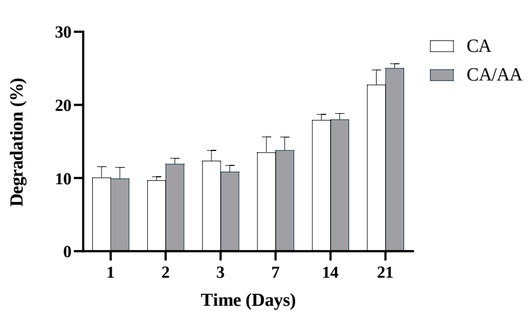

Fig. 3: Weight loss assay over 21 days [8]

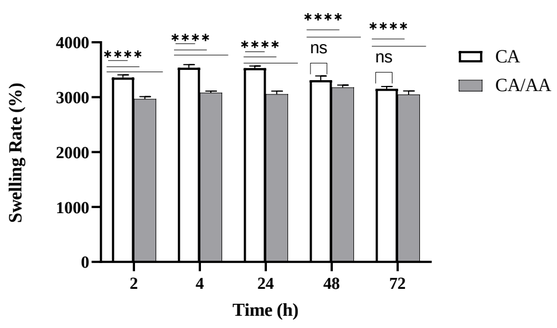

Fig. 4: Swelling rate of lyophilized composite hydrogels [8]

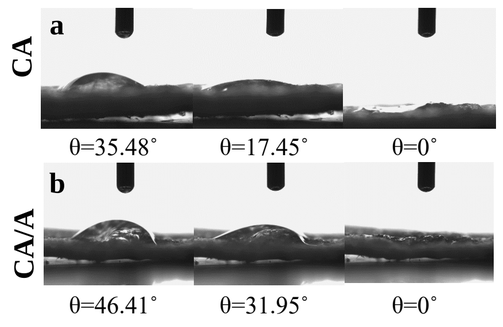

Fig. 5: The pictures of the dynamic contact angle [8].

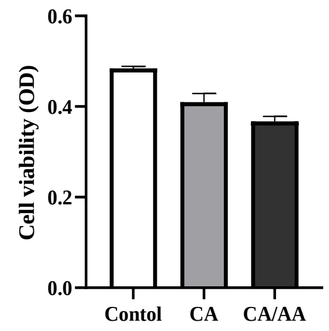

Fig. 6: Histogram of the MTT assay after 72 hours of cell seeding [8].

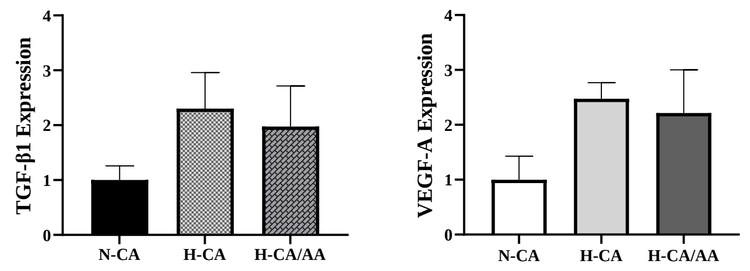

Fig. 7: Real-time PCR analysis of HIF-1α, VEGF-A, and TGF-β1 [8].

CONCLUSION

The findings of the study suggest that the developed biomimetic construct, comprising a hydrogel loaded with AA and hypoxic-MSCs, serves as a viable alternative due to its notable characteristics. This construct exhibits high blood compatibility and non-toxicity, along with significant porosity and hydrophilicity, so fibroblasts and keratinocytes could migrate into this structure and grow and proliferate [8]. Also, due to the high swelling rate, it can absorb exudates, so by absorbing the secretions of the wound area, it prevents infection and also keeps the wound moist. Also, chitosan has anti-pain properties and therefore this construct reduces pain in the wound area [8]. One of the goals of the study was to compare the effects of normal oxygen levels and low oxygen levels (hypoxia) on the expression and secretion of growth factors that help with healing skin wounds. Studies have shown that hypoxia can increase the production of certain growth factors that promote angiogenesis and speed up the healing process [8]. It can also improve the migration and proliferation of skin fibroblasts, leading to faster wound closure. Based on the research findings, a hydrogel made of chitosan-alginate-AA that is seeded by MSCs under hypoxic conditions may be effective in reducing inflammation and oxidative stress at the wound site [8]. It can also help in increasing wound closure and modulating scar formation, making it a promising approach to improving wound healing [8]. In the end, it can be said that this construct could represent a significant advancement towards personalized medicine by using patient autologous cells and seeding them onto the hydrogel, and then grafting the construct on the wound [8].

FUTURE WORK / REFERENCES

1. Metcalfe, A.D. and M.W.J.J.o.t.R.S.I. Ferguson, *Tissue engineering of replacement skin: the crossroads of biomaterials, wound healing, embryonic development, stem cells and regeneration.* 2007. **4**(14): p. 413-437.
2. Vacanti, J.P. and R.J.T.I. Langer, *Tissue engineering: the design and fabrication of living replacement devices for surgical reconstruction and transplantation.* 1999. **354**: p. S32-S34.
3. Hoffman, A.S.J.A.d.d.r., *Hydrogels for biomedical applications.* 2012. **64**: p. 18-23.
4. Caló, E. and V.V.J.E.P.J. Khutoryanskiy, *Biomedical applications of hydrogels: A review of patents and commercial products.* 2015. **65**: p. 252-267.
5. Mohammed, B.M., et al., *Vitamin C promotes wound healing through novel pleiotropic mechanisms.* 2016. **13**(4): p. 572-584.
6. Elabd, C., et al., *Comparing atmospheric and hypoxic cultured mesenchymal stem cell transcriptome: implication for stem cell therapies targeting intervertebral discs.* 2018. **16**(1): p. 222.
7. Ruthenborg, R.J., et al., *Regulation of wound healing and fibrosis by hypoxia and hypoxia-inducible* factor-1. 2014. 37(9): p. 637.
8. Ghahremani-Nasab, Maryam, et al. *"Synergistic effect of chitosan-alginate composite hydrogel enriched with ascorbic acid and alpha-tocopherol under hypoxic conditions on the behavior of mesenchymal stem cells for wound healing." Stem Cell Research & Therapy* 14.1 (2023): 326.

****Please note that the results presented in this poster have been previously published in the following article: Maryam Ghahremani-Nasab, Naeimeh Akbari-Gharalari, Azizeh Rahmani Del Bakhshayesh, Armita Ghotaslou, Abbas Ebrahimi-Kalan, Mahdi Mahdipour, Ahmad Mehdipour "Synergistic effect of chitosan-alginate composite hydrogel enriched with ascorbic acid and alpha-tocopherol under hypoxic conditions on the behavior of mesenchymal stem cells for wound healing" Stem Cell Research & Therapy. 2023; 14: 326, (DOI: 10.1186/s13287-023-03567-2).**