Combining biomaterials with regenerative medicine

Daniel Watson

Watson D. Combining biomaterials with regenerative medicine Curr. Res.: Integr. Med. 2023;8(1):01-03

ABSTRACT

This study intends to highlight recent biomaterial-based regenerative medicine. The development of regenerative medicine has sparked significant attention around the globe, with "The augmentation of cell function" serving as one of its key tenets. An important area of regenerative medicine, for instance, is drug research on drug screening, with the goal of effectively evaluating therapeutic effects. Enhancing cell activity in the body is essential for drug research since there is a gap in the evaluation of drugs due to the different cell conditions between *in vitro* and in vivo. The advancement of regenerative medicine depends on biomaterial technology because these materials effectively support cell culture or cell transplantation with high cell viability or activity.

Consequently, it has been noted that regenerative medicine can be integrated with biomaterials.

The research goal of regenerative medicine should be related to the characteristics of the biomaterial being studied in biomaterial-based regenerative medicine research. In this review, biomaterials are used to introduce regenerative medicine.

Key Words: *Regenerative medicine; Biomaterials; Cell transplantation; Tissue engineering; Drug research*

INTRODUCTION

One of the most appealing areas of current biomedical engineering is regenerative medicine. The improvement of cell activity is crucial for the development of regenerative medicine. For instance, the inherent healing potential of injured or damaged tissues is insufficient for cell migration, proliferation, and differentiation. Tissue regeneration that is "patient-friendly" could be accomplished if injured cells' inherent ability to heal itself can be increased through the use of scientific technology. Living cells with adequate capabilities and viability should be used for in *vitro* research [1].

Typically, cells are cultivated in a polystyrene-based dish; this artificial culture environment is very different from the environment of the original tissues. In contrast to in vivo, where cells interact well with one another and the Extra Cellular Matrix (ECM), the difference in the conditions of the cells results in reduced cell activity in the areas of differentiation, proliferation, metabolism, and cytokine secretion [2] Because of the differences in the condition or activity of the cells, the drug effect discovered *in vitro* drug screening circumstances is not necessarily the same as that discovered in a preclinical or clinical trial.

One of the best ways to increase cell activity is to use biomaterials. Biomaterials are defined as "any substance or combination of substances, other than drugs, synthetic or natural in origin, that can be used for any amount of time and augments or replaces any tissue, organ, or function of the body, partially or completely, in order to maintain or improve the quality of life of the individual."

One of the most important types of biomaterials is polymeric material, which may be divided into synthetic and natural types. Natural biomaterials are made of polysaccharides (such as chitosan, alginate, or hyaluronic acid) or peptides (such as collagen or gelatin), whereas well-known synthetic polymers include polyethylene glycol, poly (lactic acid), and poly (lactic-co-glycolic acid). Natural biomaterials have a significant biocompatibility advantage because endogenous enzymes can destroy them.

BIOMATERIALS COMBINED WITH REGENERATIVE MEDICINE

Collagen

The protein *collagen*, which is the most prevalent in the body, supports mechanical and structural functions. Glycine, proline, or hydroxyproline make up the majority of collagen's chemical makeup. A hydrogen bond creates the triple helix of collagen. Forms I (skin, tendon, or bone), II (cartilage), III (skin vessels), and IV (basement membrane) are the four primary types of *collagen*. *Collagen* is a necessary protein for cells to improve cell function because of the abundance of the existing ratio.

Collagen is frequently employed as a material for tissue engineering of

Editorial Office, Current Research : Integrative Medicine , UK

Correspondence: Daniel Watson, Editorial Office, Current Research : Integrative Medicine, UK, e-mail:integrativemedicine@jpeerreview.org

Received:-10 January 2023, Manuscript No. pulcrim-23-6141; Editor assigned: 13 January 2023, Pre-QC No. pulcrim-23-6141 (PQ); Reviewed:-18 January 2023, QC No. pulcrim-23-6141 (Q); Revised:-25 January 2023; Manuscript No. pulcrim-23-6141 (R); Published:-28 January 2023, DOI:10.37532. pulcrim.23.8 (1) 01-03.

skin [3], bone, cartilage , blood vessels , muscle, or cancer since, for instance, *collagen* crosslinking and stiffening accelerate the aggregation of breast cancer. For instance, the osteoblast marker, such as alkaline phosphatase activity, *collagen* production, or osteocalcin gene, is elevated when Mesenchymal Stem Cells (MSC) are cultivated on Type I *collagen* gels.

Gelatin

Collagen is a key component of the ECM, making collagen material effective. Due to its limited solubility in water and biological activity, collagen has some limitations as a biomaterial. In biomedical procedures, *gelatin*, a denatured form of *collagen*, is frequently utilised as a water-soluble substance. Due to their high water content, gelatin hydrogels are permeable to oxygen and nutrients, which makes them useful in regenerative medicine [4]. For instance, the cells in the middle of spheroids or the middle layer of a multilayer cell sheet are hypoxic and dead.

To address this issue, Tabata et al. have inserted the gelatin hydrogels within the spheroids or in between each cell sheet. Spheroids or cell sheets can be cultured for a long time using this method.
In addition to allowing oxygen to get through, gelatin hydrogels also contain growth hormones. Growth factors are necessary to increase cell activity, as was already indicated.

Basic Fibroblast Growth Factors (FGF)-containing gelatin hydrogels were injected into injured tissues, and efficient vascularization was seen, leading to tissue regeneration [5]. The gelatin hydrogel microspheres have two benefits, one of which is the drug release system. By using degradation enzymes to break down the materials instead of diffusion to release the growth factors, the medicine is delivered sustainably when the gelatin materials are injected into injured tissues.

Chitosan

Additionally, negatively charged biomaterials can interact with chitosan. Chitosan is a useful biomaterial for food packaging films [6], food and drink preservation , pharmaceutical science , cosmetics , and antibacterial agents due to its affordability and adaptability. Chitosan is frequently used in regenerative medicine for the regeneration of blood vessels, cartilage [7], bone, the intervertebral disc , or skin . For instance, Glycos Amino Glycan (GAG) is required to promote cartilage production. Chitosan and the negatively charged GAG produce an electrical interaction. 14 days or 21 days after the transplant, there was a greater GAG quantity of cartilage cells on the chitosan scaffold.

Chitosan's structure is similar to that of GAG, in addition to their interaction. GAG is one of the most important components of the ECM, hence the chitosan scaffold can support cell culture [8]. Human fibroblasts, endothelial cells, or keratinocytes can multiply both *in vitro* and *in vivo* when grown on a chitosan scaffold. Heparin and chitosan scaffold have been reported in one experiment for blood vessel regeneration.

Silk *fibroin*

Fibroin makes up 75% of silk, and sericin makes up 25% [7]. Sericin is an amorphous structured polymer, whereas silk fibroin is a semicrystalline structured protein and as a result plays a role in load-bearing capacity [8]. Sericin has various undesirable qualities for tissue engineering. The first effect of sericin on silk fibroin fibre is a reduction in its mechanical strength. The mechanical strength of silk without sericin is roughly double that of silk with sericin . Second, sericin can occasionally trigger an inflammatory reaction, however this isn't necessarily a bad thing to avoid. Due to these factors, sericin is frequently eliminated using a degumming procedure in a boiling alkaline environment.

H-chains (Mw=391.6 kDa) and L-chains (Mw=25.2 kDa) make up silk *fibroin*. The disulfide connection between the two chains interacts with one another to generate the H-L complex [9].

The silk fibroin is broken down by proteolytic enzymes such chymotrypsin, actinase, and carboxylase. The degraded fraction does not also trigger an immune reaction. Silk fibroin is a helpful biomaterial for tissue engineering of bone cartilage , tendon , skin, tympanic membrane , or blood vessel due to its biocompatibility or biodegradability.

Agarose

D-galactose and 3,6-anhydro-L-galactopyranose are the two main components of agarose, which has a molecular weight of about 12 kDa Agarose has the ability to absorb water, which enables it to penetrate living cells that are enclosed in it to deliver nutrients and oxygen [10]. Additionally, agarose gels are created via electrical contact and hydrogen bonding without the use of any risky crosslinking chemicals. Additionally, agarose has been reported to not exhibit immunogenicity.

Additionally, the customizable characteristics are appropriate for tissue engineering because varying stiffnesses are needed depending on where it is employed. As a result, some researchers attempt to apply regenerative medicine using an agarose gel. For instance, the water content and cell adhesion of agarose gel are increased when polydopamine is added. Collagen deposition and angiogenesis are thereby promoted. Investigating the precipitation of proteoglycan and GAG, two components of cartilage, on agarose gels with different cell seeding densities.

Matrigel

Type IV *collagen*, *laminin*, heparan sulphate, growth factors, cytokines, or chemokines are components of the basement membrane. As an alternative to epithelial cells, cancer cells adhere to the basement membrane. The ability to distinguish between epithelial and stromal locations is made possible by the integrity of the basement membrane. A number of released factors, such as matrix metalloproteinase, break down cancer cells as they begin to invade through the basement barrier. In order to improve their biological processes, cancer cells need the basement membrane.

Matrigel is helpful for assessing the morphology of cancer cells as well. The profile of gene expression and the morphology of cancer cells have been shown to be highly correlated. There has already been research on the combination with different biomaterials. For instance, 3D alginate and Matrigel hydrogel preserve human breast cancer cells with high levels of malignancy, motility, invasion, or spreading in a manner comparable to that seen *in vivo*. Furthermore, fibre diameter or pore number may be altered when the hydrogels are made by varying the collagen and Matrigel mixing ratio.

Poly lactic acid

Poly Lactic Acid (PLA) has a strong thermal processability and an elastic modulus that is comparable to that of bone . PLA is therefore employed in the engineering of bone tissue. Significantly, Hydroxy Apatite (HA) plays a crucial function in the remodelling and homeostasis of the Extra Cellular Matrix (ECM). Scaffolds made of PLA-HA with a porosity of more than 85% have been created.

Due to the good HA dispersion on the surface, the scaffolds have been successfully employed for the efficient growth of mouse embryonic osteoblast cells. According to Zimina et al., the HA may increase the wettability of the polymeric biomaterial, which accounts for the adherence of MSC being about three times higher than that of the pure PLA sample.

CONCLUSIONS

Gene therapy, tissue engineering, pharmacological research, and cell transplantation are the four subfields that make up regenerative medicine. "Utilization of cells with high activity" is crucial in each area. Consequently, scientific methods to increase cell activity support regenerative medicine. While the interaction between biomaterials and targeted cells is the main focus of this review, the interaction between biomaterials and immune cells that are close to the targeted cells (such as neutrophils or macrophages) is also crucial since it triggers an immune response.

REFERENCES

1. Nii T, Makino K, Tabata Y, et al. Three-dimensional culture system of cancer cells combined with biomaterials for drug screening. Cancers. 2020;12(10):275.
2. Rodríguez-Enríquez S, Gallardo-Pérez JC, Avilés-Salas A, et al. Energy metabolism transition in multi-cellular human tumor spheroids. J cell physiol. 2008;216(1):189-97.
3. Breslin S, O'Driscoll L. Three-dimensional cell culture: the missing link in drug discovery. Drug discov today. 2013;18(5-6):240-9.
4. Bakshi PS, Selvakumar D, Kadirvelu K, et al. Chitosan as an environment friendly biomaterial–a review on recent modifications and applications. Int j biol. macromol. 2020;150:1072-83.
5. Lee YB, Kim EM, Byun H, et al. Engineering spheroids potentiating cell-cell and cell-ECM interactions by self-assembly of stem cell microlayer. Biomaterials. 2018;165:105-20.
6. Heo DN, Hospodiuk M, Ozbolat IT, et al. Synergistic interplay between human MSCs and HUVECs in 3D spheroids laden in collagen/fibrin hydrogels for bone tissue engineering. Acta biomater. 2019;95:348-56.
7. Campbell JJ, Husmann A, Hume RD, et al. Development of three-dimensional collagen scaffolds with controlled architecture for cell migration studies using breast cancer cell lines. Biomaterials. 2017;114:34-43..
8. Miyazaki K, Oyanagi J, Hoshino D, et al. Cancer cell migration on elongate protrusions of fibroblasts in collagen matrix. Sci rep. 2019;9(1):292.
9. Matsuo T, Masumoto H, Tajima S, et al. Efficient long-term survival of cell grafts after myocardial infarction with thick viable cardiac tissue entirely from pluripotent stem cells. Sci rep. 2015;5(1):1-4.
10. Inoo K, Bando H, Tabata Y, et al. Enhanced survival and insulin secretion of insulinoma cell aggregates by incorporating gelatin hydrogel microspheres. Regen Ther. 2018;8:29-37.