Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 142-152
Received 18April2020; accepted 23June2020

Scaffolds In Tissue Engineering

Naziya sayeed3 Revathi.K[2], Mohamed Adil A.A[1,2], Gulothungan.G[1], Srinivasan.S[1]
[1]Dept.Biomedical engg, Saveetha school of engineering (SSE), SIMATS, Thandalam, Chennai, 602105
[2]Meenakshi academy of higher education and research (MAHER), West k.K.Nagar, Chennai, India.
3 Karunya institute of technology and sciences, coimbatore, india.

Corresponding author
Mohamed Adil A.A
[2]Meenakshi academy of higher education and research (MAHER), West K.K.Nagar, Chennai, India
E-mail: Adilmdaa@gmail.com

ABSRACT
Fibrous structures are useful for tissue engineering scaffolds due to morphology similar to that of the extracellular matrix. The structural optimization and the surface modification of the scaffolds could boost the cell attachment and its proliferation. Most materials for tissue engineering applications have been developed as scaffolds. Scaffolds are created by foaming that most closely match the requirements for an ideal scaffold and most closely resemble the trabecular bone structure. These include HA foam gel-cast, bioactive glass foam, and composites of biodegradable polymer foam / bioactive glass. Nevertheless, no material or manufacturing method has met all the requirements of an ideal scaffold. Scaffolds developed by RP and SFF methods show highly ordered microstructures and can be easily manufactured to complex forms dictated directly from the patient by CT scans. To achieve the goal of an ideal scaffold, a mixture of polymers and bio-ceramics with newly generated tissue should be used.For the construction of tissue-engineering scaffolds for bone, several approaches are described. There is also a high degree of interconnected pores in the correct scaffold for soft tissues such as nerve fibers (e.g. axons transmitting nerve impulses); furthermore, the pores can require orientation and may be smaller. Homogeneous, high-water-content hydrogels are commonly used as a scaffold with mechanical properties that match the soft nerve tissue, and the methods used to make them are reviewed.

1. Introduction

Hundreds of surgical procedures are performed every day to remove or restore tissue weakened by disease or trauma. The tissue engineering (TE) technology area aims at regenerating damaged tissues by combining body cells with highly porous scaffold biomaterials that serve as models for tissue regeneration to direct the growth of new tissue.Tissue engineering is a multidisciplinary discipline that is increasingly developing as a promising new approach to damaged tissue regeneration and reconstruction. Scaffolds play a pivotal role in this approach in supporting cells to accommodate and direct their growth into a particular tissue; thus, it is of great importance to build scaffolds that promote cell growth(2). Electrospinning is a simple, cost-effective and flexible technique recently applied to the manufacture of tissue engineering nano-featured scaffolds.It offers many advantages over conventional scaffolding methodologies by imitating a natural extracellular matrix. This paper reviews the current state of the art of using the electrospinning technique to design nanostructural scaffolds. In addition, an outline of this technique and its spinning mechanism is identified, with particular attention to the readers ' areas of interest(3).Tissue engineering

tools provide scaffolds with sufficient chemistry and design to facilitate cell penetration and colonization. The scaffold is designed with biology in mind, and according to the type of tissue, the architecture and chemistry differ. In this study, we concentrate on scaffolds for two types of tissue bone and nervous tissue and identify various approaches that are used to construct them. For a hard tissue such as bone, the ideal scaffold has a high degree of interconnected macroporosity and allows in rapid cell invasion while retaining a rigid structure(1).

1.Polymeric scaffolds

In tissue engineering applications, polymeric scaffolds have been commonly used. Biodegradable polymers provide the benefits of increased inflammatory tolerance, high biocompatibility, and in vivo non-toxic enzyme degradation. Several approaches to the manufacture of these biomimetic scaffolds have been applied, including electro-spinning, phase separation, solvent casting, freezing and self-assembly(4).Electro-spun nanofibers from biomaterials form structures similar to the native fibrous ECM and have beneficial mechanical properties and increased cell infiltration(5).Pre-vascularized tissue buildings with enhanced cell proliferation have been developed by endothelial pre-seeding cells and hydrogel fibroblasts(6).

1.1 Natural polymers

Natural polymers can be regarded as the first clinically used biodegradable biomaterials. Because of the bioactive properties, natural materials have stronger interactions with the cells, allowing them to improve the performance of the cells in the biological system. Natural polymers can be categorized as proteins (silk, collagen, gelatin, fibrinogen, elastin, keratin, actin, and myosine), polysaccharides (cellulose, amylose, dextran, chitin, and glycosaminoglycans), or polynucleotides (DNA, RNA)(7).

1.2 Synthetic polymers

Synthetic biomaterial guidance offered by biomaterials may help restore the structure and function of tissues that have been weakened or diseased. Since their properties (e.g. porosity, degradation time, and mechanical characteristics) can be tailored for specific applications, synthetic polymers are extremely useful in the biomedical field. Synthetic polymers are often cheaper than biological scaffolds; they can be produced in large standard quantities and have a long shelf life. The physicochemical and mechanical properties of many commercially available synthetic polymers are equivalent to those of biological tissues(8).The largest group of biodegradable polymers are synthetic polymers, which can be manufactured under controlled conditions. These demonstrate consistent and reproducible mechanical and physical properties in general, such as tensile strength, elastic modulus, and rate of degradation. One of the most widely used synthetic polymers in tissue engineering is PLA, PGA and PLGA copolymers. PHA is a microbial polyester form and is increasingly considered for tissue engineering applications(9).

2. Textile scaffolds

Because cells can not live on their own and are dependent on substrates, the need for tissue engineering scaffolds is unquestionable. Nevertheless, no single universal scaffold can fulfill all the requirements of different tissues and hence the choice of a tissue scaffold depends on its characteristics. The following are some considerations for the selection of textile scaffolds to be critically examined (10).

2.1 Micro structural aspects

The microstructural dimensions of scaffolds include porosity, pore size distribution, pores reproducibility and pore connectivity. These are important as they assess the successful integration of the natural tissue and the scaffold and provide the cells with optimal spatial and nutritional conditions. Scaffold reproducibility determines their dimensional stability as well as tissue shape uniformity[9].

2.2 Mechanical aspects

Scaffolding mechanical aspects include structural stability, strength, rigidity, and drapeability. We have a major influence on cellular activity. Woven scaffolds are typically inflexible and rigid due to the tight interlacing of the yarns, making them ideal for bone and ace tabular cup tissue engineering. The next rigid layer of scaffolds is the braided scaffold. Because of their looped yarn structures, knit scaffolds show significant deformability of all scaffolds, making them suitable for applications in blood vessels and bladder tissue engineering(11).

3. porous scaffold

In medicine, a paradigm shift occurs from the use of synthetic implants and tissue grafts to a tissue engineering approach using degradable porous material scaffolds integrated with biological cells or molecules to regenerate tissues(12). A new paradigm includes scaffolds to combine temporary mechanical function with mass transportation to enable biological transmission and regeneration of tissues. Since early scaffolds were not produced with precise porous architecture, little is known quantitatively about this balance(13).Recent progress in both computational topology design (CTD) and solid free-form manufacturing (SFF) has allowed regulated architecture to construct scaffolds. This paper reviews CTD's integration with SFF to construct tissue-engineering scaffolds for designers(14). It also describes the mechanical properties and tissue regeneration achieved using scaffolds from the designer. Finally, potential directions are proposed for using in vivo research designer scaffolds to refine tissue-engineering therapies, and for cell-printing coupling designer scaffolds to create model material / biofactor hybrids(15).

4. 2D and 3D scaffolds

In general, the types of cell culture are explained as 2D or 3D cell cultures in terms of the dimension of cell growth.2D suggests cell growth in culture flasks as a monolayer, usually involving a single type of cells growing on a planar surface. Due to factors such as simpler cell observation, direct measurement viability, inexpensive design, primary scope for drug testing, and cytocompatibility, 2D crops are commonly used in cell research(16). 2D cultures,

however, are not a perfect representation of an organism's natural cellular environment. As a consequence, in vivo testing, the 2D cultures display peculiar structural features, mechanical limitations, and often resulted in misleading tests(17). In the final analysis, a surprising disparity in findings was found in 2D and 3D cell cultures while considering pro-apoptotic factors in drug discovery and biocompatibility research. Major changes have been observed with regard to cell polarity, cell morphology, intracellular-extracellular protein production, receptor organization, gene expression, etc(18).In addition, 2D scaffold-based tissue engineering is concerned with mass transmission, whereby nutrient and oxygen availability is restricted to cells.(19)

A cellular microenvironment is produced in 3D cell culture in the interactions of cell–cell or cell–ECM, which imitates the usual real-life scenario. Accordingly, this device will promote cell growth, differentiation, and proliferation. A 3D tissue culture offers a broader forum for therapeutic and drug discovery investigations(20). It provides a physiologically relevant morphology, a normal cellular microenvironment, and the possibility of co-culturing a variety of cells. Different approaches to 3D culture preparation such as forced floating, hanging drop, agitation-based methods, microfluidic cell culture platforms, matrices, and scaffolds are available.The choice of 3D cell culture scaffolds depends on the type of feature and cell. The properties of Scaffold vary based on concentration of polymer, ligand density, pore size, shape, strength, rigidity, etc(21). Natural polymers such as collagen, gelatin, elastin, silk fibroin, chitosan (CS), chitin, fibrin, and fibrinogen are commonly used in the preparation of 3D scaffolds because of their biocompatibility. Also used in the preparation of 3D scaffolds were synthetic polymers such as polylactic acid (PLA), poly(glycolic acid), polyhydroxyalkanoate, and poly(lactic-co-glycolic acid) (PLGA) due to their porosity, degradation time, and mechanical characteristics easily adapted(22).

5. Nano in scaffolds

Scaffolds act as ECM, providing an effective medium for cellular interactions, transportation of nutrient-gas, removal of toxic metabolites, etc. The ECM follows a variety of nanotopographic patterns in normal cells to promote tissue formation, while ECM occurs in various nanostructures in bone tissues. Nanomaterials with a size range of 100 nm when introduced to 3D scaffolds can mimic the natural tissue conditions by enhancing tissue growth, differentiation, proliferation, cell signaling, etc(23).In addition, 3D scaffolds composed of nanofibers, nanotubes and nanoparticles made from polymers such as PLA, PLGA, polyvinyl alcohol (PVA) and polycaprolactone (PCL) have been found to be effective in affecting stem cell fate(24). Because of their biocompatibility and tremendous mechanical power, carbon materials offer a great choice of nanomaterials for tissue engineering as well as polymers.Carbon-based scaffolds have unique features consistent with the natural ECM and have been found to improve tissue engineering cell-cell interaction and normal cell functions. Therefore, these scaffolds with unique nanotopographic structures may affect the cells ' survival and their functions(25).

6. Graphene-based scaffolds

Annals of R.S.C.B., Vol. 24, Issue 1, 2020, pp. 142-152
Received 18April2020; accepted 23June2020

Graphene-based nanomaterials serve as excellent components for scaffolding materials because of their unique electrical / thermal conductivity, mechanical stability, chemical composition, porous structure, biocompatibility, bioadhesion property, etc. Graphene preparation uses either top-down or bottom-up approaches.For various tissue engineering investigations such as neural, bone, lung, dental, and stem cells, the new graphene derivative, RGO foams, are used(26). Generally, either liquid exfoliation, ball milling, spray coating, chemical vapor deposition (CVD), GO reduction, etc. synthesize graphene.Graphite oxidation results in GO synthesis. GO is reduced through a number of reduction processes by reducing agents to create RGO. GO has excellent aqueous processability, amphiphilicity, surface-functional ease, surface-enhanced Raman scattering properties, and fluorescence quenching capability(27). GO derives these fascinating properties from its unique chemical structures (sp2 carbon domains surrounded by sp3 carbon domains) and oxygen containing functional hydrophilic groups.The latter, RGO, which is synthesized by GO reduction, includes various methods of reduction such as hydrothermal, mechanical, photocatalytic, electrochemical, solvothermal, sonochemical, phytochemical (green chemistry) or multi-stage electrical conductivity, hydrophilicity, colour, and functional side groups. GO undergoes thermal deoxygenation, chemical deoxygenation, long-range conjugated structure reconstruction, and defect healing during the reduction process(28).

7. Scaffold requirements

Various platforms created from an assortment of biomaterials and made utilizing a plenty of manufacture methods have been utilized in the field in endeavours to recover various tissues and organs in the body. Despite the tissue type, various key contemplations are significant when planning or deciding the reasonableness of a platform for use in tissue designing:

Biocompatibility

The absolute first basis of any framework for tissue building is that it must be biocompatible; cells must follow, work typically, and relocate onto the surface and in the end through the platform and start to multiply before setting down new lattice. After implantation, the framework or tissue designed develop must evoke an immaterial resistant response so as to forestall it causing such a serious incendiary reaction, that it may diminish recuperating or cause dismissal by the body.

Biodegradability

The target of tissue building is to permit the body's very own cells, after some time, to in the end supplant the embedded framework or tissue built develop. Platforms and develops, are not proposed as perpetual inserts. The framework should in this way be biodegradable in order to enable cells to deliver their very own extracellular matrix5. The side-effects of this corruption ought to likewise be non-harmful and ready to leave the body without impedance with different organs. So as to enable corruption to happen couple with tissue development, a fiery reaction joined with controlled implantation of cells, for example, macrophages is

required. Since tissue building systems are entering clinical practice all the more routinely, the field of immunology is an assuming a job of expanding noticeable quality in the examination area.

Mechanical properties

In a perfect world, the platform ought to have mechanical properties predictable with the anatomical site into which it is to be embedded and, from a reasonable point of view, it must be sufficiently able to permit careful taking care of during implantation. While this is significant in all tissues, it gives a few difficulties to cardiovascular and orthopaedic applications explicitly. Creating frameworks with sufficient mechanical properties is one of the extraordinary difficulties in endeavouring to build bone or ligament. For these tissues, the embedded platform must have adequate mechanical uprightness to work from the hour of implantation to the finish of the rebuilding process. A further test is that recuperating rates fluctuate with age; for instance, in youthful people, cracks ordinarily mend to the point of weight-bearing in around about a month and a half, with complete mechanical respectability holding off on returning until roughly one year after break, yet in the older the pace of fix backs off. This too should be considered when planning platforms for orthopaedic applications. In any case, as the field has advanced, it could be contended that an excess of spotlight has been set on attempting to create platforms with mechanical properties like bone and ligament. Numerous materials have been delivered with acceptable mechanical properties yet to the inconvenience of holding a high porosity and numerous materials, which have exhibited potential in vitro have bombed when embedded in vivo because of lacking limit with regards to vascularization. Obviously a harmony between mechanical properties and permeable engineering adequate to permit cell invasion and vascularization is vital to the accomplishment of any framework.

Scaffold architecture

The design of frameworks utilized for tissue building is of basic significance. Frameworks ought to have an interconnected pore structure and high porosity to guarantee cell entrance and sufficient dispersion of supplements to cells inside the build and to the extra-cell lattice shaped by these cells. Moreover, a permeable interconnected structure is required to permit dissemination of waste items out of the framework, and the results of platform corruption ought to have the option to leave the body without impedance with different organs and encompassing tissues. The issue of centre debasement, emerging from absence of vascularization and waste expulsion from the focal point of tissue designed develops, is of significant worry in the field of tissue engineering. Another key segment is the mean pore size of the framework. Cells basically cooperate with frameworks by means of compound gatherings (ligands) on the material surface. Frameworks orchestrated from regular extracellular materials (for example collagen) normally have these ligands as Arg-Gly-Asp (RGD) restricting successions , while frameworks produced using engineered materials may require intentional consolidation of these ligands through, for instance, protein adsorption. The ligand thickness is impacted by the particular surface zone, for example the accessible surface inside a pore to which cells can follow. This relies upon the mean pore size in the

framework. The pores along these lines should be sufficiently enormous to enable cells to move into the structure, where they in the long run become bound to the ligands inside the platform, yet little enough to set up an adequately high explicit surface, prompting an insignificant ligand thickness to permit productive authoritative of a basic number of cells to the scaffold. Subsequently, for any platform, a basic scope of pore sizes exists, which may differ contingent upon the cell type utilized and tissue being designed.

8. Conclusion

There is a socio-economic need to completely treat and replace damaged or non-functional tissues with innovative methods, designs and innovations that focus on the reconstitution of functional tissue. TERM has emerged as a research field based on materials engineering, biology, and medical knowledge seeking to create alternative methods for tissue regeneration and repair. Innovative strategies, such as those mentioned in this study, present out - of-the-box solutions to some of the current TERM challenges, and may be key breakthroughs in the future. Such approaches will provide specific porosity and structure for the production of bulk bioactive temporary implants to help build new tissues to complete the medical tasks. The 3D scaffolds and hydrogel-based matrices are able to meet the challenges of personalized medicine, delivering effective treatments for a wide range of pathologies. There is no overarching scaffold that can fulfill all the needs of the human body's different tissues. That's why in tissue engineering scaffolds play a vital role. Textiles are used mainly in the field of tissue engineering since they can alter a wide range of scaffolds with a wide range of properties. While tissue engineering is in its relative infancy, considerable progress is being made through partnerships between stem cell biologists and chemists of materials. Problems surrounding the origins of cells and structure of scaffolds, however, control research into engineered tissues. This cycle will be improved by discovering novel stem cell populations such as UC-MSCs and scaffolds with unique properties.

References

1. Karp JM, Dalton PD, Shoichet MS. Scaffolds for Tissue Engineering. MRS Bulletin. 2003;28(4):301-6.
2. Saha K, Keung AJ, Irwin EF, Li Y, Little L, Schaffer DV, et al. Substrate Modulus Directs Neural Stem Cell Behavior. Biophysical Journal. 2008;95(9):4426-38.
3. Nano-Featured Scaffolds for Tissue Engineering: A Review of Spinning Methodologies. Tissue Engineering. 2006;12(3):435-47.
4. Lu T, Li Y, Chen T. Techniques for fabrication and construction of three-dimensional scaffolds for tissue engineering. Int J Nanomedicine. 2013;8:337-50.
5. Liu W, Thomopoulos S, Xia Y. Electrospun Nanofibers for Regenerative Medicine. Advanced Healthcare Materials. 2012;1(1):10-25.
6. Sengupta D, Waldman SD, Li S. From In Vitro to In Situ Tissue Engineering. Annals of Biomedical Engineering. 2014;42(7):1537-45.
7. Jalili RB, Moeen Rezakhanlou A, Hosseini-Tabatabaei A, Ao Z, Warnock GL, Ghahary A. Fibroblast populated collagen matrix promotes islet survival and reduces the

number of islets required for diabetes reversal. Journal of Cellular Physiology. 2011;226(7):1813-9.
8. Gunatillake P, Mayadunne R, Adhikari R. Recent developments in biodegradable synthetic polymers. In: El-Gewely MR, editor. Biotechnology Annual Review. 12: Elsevier; 2006. p. 301-47.
9. Chen LJ, Wang M. Production and evaluation of biodegradable composites based on PHB–PHV copolymer. Biomaterials. 2002;23(13):2631-9.
10. Engler AJ, Sen S, Sweeney HL, Discher DE. Matrix Elasticity Directs Stem Cell Lineage Specification. Cell. 2006;126(4):677-89.
11. Fuchs S, Jiang X, Schmidt H, Dohle E, Ghanaati S, Orth C, et al. Dynamic processes involved in the pre-vascularization of silk fibroin constructs for bone regeneration using outgrowth endothelial cells. Biomaterials. 2009;30(7):1329-38.
12. Hollister SJ. Porous scaffold design for tissue engineering. Nature Materials. 2005;4(7):518-24.
13. Haynesworth SE, Reuben D, Caplan AI. Cell-based tissue engineering therapies: the influence of whole body physiology. Advanced Drug Delivery Reviews. 1998;33(1):3-14.
14. Cutroneo KR. Gene therapy for tissue regeneration. Journal of Cellular Biochemistry. 2003;88(2):418-25.
15. Hollister SJ, Levy RA, Chu T-M, Halloran JW, Feinberg SE. An image-based approach for designing and manufacturing craniofacial scaffolds. International Journal of Oral & Maxillofacial Surgery. 2000;29(1):67-71.
16. Geetha Bai R, Muthoosamy K, Manickam S, Hilal-Alnaqbi A. Graphene-based 3D scaffolds in tissue engineering: fabrication, applications, and future scope in liver tissue engineering. Int J Nanomedicine. 2019;14:5753-83.
17. Lavik E, Langer R. Tissue engineering: current state and perspectives. Applied Microbiology and Biotechnology. 2004;65(1):1-8.
18. Tissue Engineering: From Biology to Biological Substitutes. Tissue Engineering. 1995;1(1):3-13.
19. Marx V. Organs from the lab. Nature. 2015;522(7556):373-7.
20. Adachi T, Osako Y, Tanaka M, Hojo M, Hollister SJ. Framework for optimal design of porous scaffold microstructure by computational simulation of bone regeneration. Biomaterials $V 27. 2006(21):3964-72.
21. Hollister SJ, Maddox RD, Taboas JM. Optimal design and fabrication of scaffolds to mimic tissue properties and satisfy biological constraints. Biomaterials. 2002;23(20):4095-103.
22. Pampaloni F, Reynaud E, Stelzer E. Pampaloni F, Reynaud EG, Stelzer EH.. The third dimension bridges the gap between cell culture and live tissue. Nat Rev Mol Cell Biol 8: 839-845. Nature reviews Molecular cell biology. 2007;8:839-45.
23. Kim JB, Stein R, O'Hare MJ. Three-dimensional in vitro tissue culture models of breast cancer — a review. Breast Cancer Research and Treatment. 2004;85(3):281-91.
24. Li L, Fukunaga-Kalabis M, Herlyn M. The three-dimensional human skin reconstruct model: a tool to study normal skin and melanoma progression. J Vis Exp. 2011(54):2937.

25. O'Brien FJ, Harley BA, Yannas IV, Gibson L. Influence of freezing rate on pore structure in freeze-dried collagen-GAG scaffolds. Biomaterials. 2004;25(6):1077-86.
26. Itaka K, Osada K, Morii K, Kim P, Yun S-H, Kataoka K. Polyplex nanomicelle promotes hydrodynamic gene introduction to skeletal muscle. Journal of Controlled Release. 2010;143(1):112-9.
27. Jang J-H, Rives CB, Shea LD. Plasmid Delivery in Vivo from Porous Tissue-Engineering Scaffolds: Transgene Expression and Cellular Transfection. Molecular Therapy. 2005;12(3):475-83.
28. Young JL, Engler AJ. Hydrogels with time-dependent material properties enhance cardiomyocyte differentiation in vitro. Biomaterials. 2011;32(4):1002-9.
29. Kumar T.S., Chakrapani V.Y. Cutting-Edge Enabling Technologies for Regenerative Medicine. Springer; Berlin, Germany: 2018. Electrospun 3D Scaffolds for Tissue Regeneration; pp. 29–47. [PubMed] [Google Scholar]
30. Gay S., Lefebvre G., Bonnin M., Nottelet B., Boury F., Gibaud A., Calvignac B. PLA scaffolds production from Thermally Induced Phase Separation: Effect of process parameters and development of an environmentally improved route assisted by supercritical carbon dioxide. J. Supercrit. Fluids. 2018;136:123–135. doi: 10.1016/j.supflu.2018.02.015. [CrossRef] [Google Scholar]
31. Lee J.M., Yeong W.Y. Design and printing strategies in 3D bioprinting of cell-hydrogels: A review. Adv. Healthc. Mater. 2016;5:2856–2865. doi: 10.1002/adhm.201600435. [PubMed] [CrossRef] [Google Scholar]
32. Xu Y., Wang X. Application of 3D biomimetic models in drug delivery and regenerative medicine. Curr. Pharm. Des. 2015;21:1618–1626. doi: 10.2174/1381612821666150115154059. [PubMed] [CrossRef] [Google Scholar]
33. Ozbolat I.T., Moncal K.K., Gudapati H. Evaluation of bioprinter technologies. Addit. Manuf. 2017;13:179–200. doi: 10.1016/j.addma.2016.10.003. [CrossRef] [Google Scholar]
34. Neves L.S., Rodrigues M.T., Reis R.L., Gomes M.E. Current approaches and future perspectives on strategies for the development of personalized tissue engineering therapies. Expert Rev. Precis. Med. Drug Dev. 2016;1:93–108. doi: 10.1080/23808993.2016.1140004. [CrossRef] [Google Scholar]
35. Khademhosseini A., Langer R. A decade of progress in tissue engineering. Nat. Protoc. 2016;11:1775. doi: 10.1038/nprot.2016.123. [PubMed] [CrossRef] [Google Scholar]
36. Kwakwa K.A., Vanderburgh J.P., Guelcher S.A., Sterling J.A. Engineering 3D models of tumors and bone to understand tumor-induced bone disease and improve treatments. Curr. Osteoporos. Rep. 2017;15:247–254. doi: 10.1007/s11914-017-0385-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
37. Shelke N.B., James R., Laurencin C.T., Kumbar S.G. Polysaccharide biomaterials for drug delivery and regenerative engineering. Polym. Adv. Technol. 2014;25:448–460. doi: 10.1002/pat.3266. [CrossRef] [Google Scholar]
38. Sahana T.G., Rekha P.D. Biopolymers: Applications in wound healing and skin tissue engineering. Mol. Biol. Rep. 2018;45:2857–2867. doi: 10.1007/s11033-018-4296-3. [PubMed] [CrossRef] [Google Scholar]

39. Bressan E., Favero V., Gardin C., Ferroni L., Iacobellis L., Favero L., Vindigni V., Berengo M., Sivolella S., Zavan B. Biopolymers for Hard and Soft Engineered Tissues: Application in Odontoiatric and Plastic Surgery Field. Polymers. 2011;3:509–526. doi: 10.3390/polym3010509. [CrossRef] [Google Scholar]
40. Mano J., Silva G., Azevedo H., Malafaya P., Sousa R., Silva S., Reis R. Natural origin biodegradable systems in tissue engineering and regenerative medicine: Present status and some moving trends. J. R. Soc. Interface. 2007;4:999–1030. doi: 10.1098/rsif.2007.0220. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
41. Nair L.S., Laurencin C.T. Biodegradable polymers as biomaterials. Prog. Polym. Sci. 2007;32:762–798. doi: 10.1016/j.progpolymsci.2007.05.017. [CrossRef] [Google Scholar]
42. Malafaya P.B., Silva G.A., Reis R.L. Natural—Origin polymers as carriers and scaffolds for biomolecules and cell delivery in tissue engineering applications. Adv. Drug Deliv. Rev. 2007;59:207–233. doi: 10.1016/j.addr.2007.03.012. [PubMed] [CrossRef] [Google Scholar]
43. Pina S., Ferreira J. Bioresorbable Plates and Screws for Clinical Applications: A Review. J. Healthc. Eng. 2012;3:243–260. doi: 10.1260/2040-2295.3.2.243. [CrossRef] [Google Scholar]
44. Katti D.S., Lakshmi S., Langer R., Laurencin C.T. Toxicity, biodegradation and elimination of polyanhydrides. Adv. Drug Deliv. Rev. 2002;54:933–961. doi: 10.1016/S0169-409X(02)00052-2. [PubMed] [CrossRef] [Google Scholar]
45. Pereira D., Canadas R., Silva-Correia J., Marques A., Reis R., Oliveira J. Gellan gum-based Hydrogel Bilayered Scaffolds for Osteochondral Tissue Engineering. Key Eng. Mater. 2014;587:255–260. doi: 10.4028/www.scientific.net/KEM.587.255. [CrossRef] [Google Scholar]
46. Gunja N.J., Athanasiou K.A. Biodegradable materials in arthroscopy. Sports Med. Arthrosc. 2006;14:112–119. doi: 10.1097/00132585-200609000-00002. [PubMed] [CrossRef] [Google Scholar]
47. Salinas A.J., Vallet-Regi M. Bioactive ceramics: From bone grafts to tissue engineering. RSC Adv. 2013;3:11116
48. Daculsi G., Laboux O., Malard O., Weiss P. Current state of the art of biphasic calcium phosphate bioceramics. J. Mater. Sci.-Mater. Med. 2003;14:195–200. doi: 10.1023/A:1022842404495. [PubMed] [CrossRef] [Google Scholar]
49. Bohner M. Calcium orthophosphates in medicine: From ceramics to calcium phosphate cements. Inj.-Int. J. Care Inj. 2000;31:37–47. doi: 10.1016/S0020-1383(00)80022-4. [PubMed] [CrossRef] [Google Scholar]
50. Silva T.H., Alves A., Ferreira B.M., Oliveira J.M., Reys L.L., Ferreira R.J.F., Sousa R.A., Silva S.S., Mano J.F., Reis R.L. Materials of marine origin: A review on polymers and ceramics of biomedical interest. Int. Mater. Rev. 2012;57:276–306. doi: 10.1179/1743280412Y.0000000002. [CrossRef] [Google Scholar]
51. Oliveira J.M., Grech J.M.R., Leonor I.B., Mano J.F., Reis R.L. Calcium-phosphate derived from mineralized algae for bone tissue engineering applications. Mater. Lett. 2007;61:3495–3499. doi: 10.1016/j.matlet.2006.11.099. [CrossRef] [Google Scholar]

52. Differential expression of Helios, Neuropilin-1 and FoxP3 in head and neck squamous cell carcinoma (HNSCC) patients A.A.Mohamed Adil, Anil Kumar Bommanabonia, AnandrajVaithy, Sateesh Kumar 3biotech 9 (178)
53. Protagonist of Immuno-Profiling, Immuno-Scoring, and Immunotherapy Towards Colitis-Associated Cancer: Systematic Review, Mohamed Adil a.a, AK Pandurangan, M Waseem, N Ahmed Diagnostic and Treatment Methods for Ulcerative Colitis and Colitis 2020
54. Emerging Role of Mitophagy in Inflammatory Diseases: Cellular and Molecular Episodes, Mohamed Adil AA, S Ameenudeen, A Kumar, S Hemalatha, N Ahmed, N Ali 2020 Curr Pharm Des. 2020;26(4):485-491. doi: 10.2174/1381612826666200107144810
55. Increased Expression of TGF-β and IFN-γ in Peripheral Blood Mononuclear Cells (PBMCs) Cultured in Conditioned Medium (CM) of K562 Cell Culture AAM Adil, L Vallinayagam, K Chitra, S Jamal, AK Pandurangan, N Ahmed Journal of Environmental Pathology, Toxicology and Oncology 38 (2)
56. Cancer immunotherapy: Targeting immunosuppressive tumor microenvironment NA A.A Mohamed Adil Oncobiology and Targets 2014