Original Article

An Insight Into The Biomaterials Evolution And Its Diversity In Biomedical Dental Applications

Daya Srinivasan[1], **Shoba Narayan**[2]

[1] Chettinad Dental College and Research Institute, Chettinad Health City, Kelambakkam, Chengalpattu District, Tamilnadu, India.
Orcid id: https://orcid.org/0000-0001-5453-4380
2- Faculty of Allied Health Sciences, Chettinad Hospital and Research Institute, Chettinad Academy of Research and Education, Kelambakkam, Chengalpattu District, Chennai, Tamilnadu, India.
Orcid id: https://orcid.org/0000-0003-0019-0388.
Email: [1] dayaswathi@gmail.com, [2] shobanarayan@care.edu.in

***Corresponding Author:** Daya Srinivasan
Chettinad Dental College and Research Institute, Chettinad Health City, Kelambakkam, Chengalpattu District, Tamilnadu, India.
DOI: 10.47750/pnr.2022.13.S10.322

Abstract

A biomaterial is a substance that has been designed to take a shape that is utilized for any theranostic property by understanding in-depth interactions with elements of living bio-macromolecular systems, either alone or as part of a complex system. Nanostructured materials have been discovered to have an impact on the amount, densities, arrangement, geometry, and orientations of biomolecules adsorbed at their surfaces, as well as their involvement in cell response. Understanding chemical bonding is crucial to comprehending biomaterial characteristics. Biomaterials are classified into five categories. Polymers based, metallic or metals based, ceramics of bio origin, natural influenced materials, and composites are the materials in use. Polymeric biomaterials consist the most various types of synthetic as well as hybrid materials now used in medicine. Natural polymers are biocompatible and have a low immunogenic reaction. Synthetic polymers have poor mechanical characteristics and low repeatability. Recent developments are highlighted, particularly for biomedical applications, in the artificial development and production of substances and coatings that are inspired by nature. Biomaterials are now being used in regenerative dentistry and reconstructive therapies thanks to a better understanding of tissue material interphase. Biomaterials and technology are boosting tissue regeneration as well as restoring missing or damaged tissues.

Keywords: Biomaterials, Polymers, Natural materials, Metals, Composites.

INTRODUCTION

Biomaterials exist to interact with biological systems and are materials used to replace parts of biological systems or to build devices that operate in close proximity to living tissue [1, 2]. New technologies and inventions continue to provide a hotbed of research, as no single material is suitable for all biomaterial applications. Because of the intricacies of cell and tissue reactions to biomaterials, it has been advantageous to look to nature for guidance on biomaterial design, selection, synthesis, and production. Biomimetics is the term for this method. [3] Long before cell attachment, when a material is placed in a human environment, biomolecules compete for adsorption on its surface. As a result, the interactions of the molecules on the biomaterial's surface control its reaction. A change in surface quality influences how it interacts with molecules and, as a result, how the cells behave. Nanostructures have been found to impact biomolecules of surfaces, and their role in cell response has been demonstrated. [4] The importance of biomedical devices has gained with the advent of biomaterials. Tissue engineering along with biomaterials has helped in repairing and regenerating tissue. [5]

BONDS IN BIOMATERIALS

Understanding chemical bonds is essential for understanding the properties of biomaterials. They're non-directional, and the materials they create are uniform in all directions. The materials are normally robust but brittle due to the highly organized linkages. Metallic bonds form a cloud of valence electrons that surround atomic centers. Materials having metallic linkages are good thermal conductors. Covalent bonds are created when atoms share electrons in their outer shells. The ties are quite strong and directed. The materials are not good conductors because the electrons are trapped in place. A dipole attraction results in the formation of secondary bonds. Whenever the charge distribution is asymmetrical or unequal, dipoles form, separating the molecules' positive and negative poles. Hydrogen bonds are created when atoms like oxygen, nitrogen, or fluorine are covalently bound to hydrogen.The secondary bond that forms as a result of the secondary bond is weak. Depending on the chemical bonding, materials can be categorized into different classes.

POLYMERS

Polymeric biomaterials cover the widest range of materials now employed in medicine. The general terminology for polymer classification discusses several synthetic procedures and explains the differences between different synthetic polymer repeat architectures. In various fields of medicine, polymers with various structures have been suggested or used. [(6)] They can be obtained from 2 sources- naturally (such as plant, animal, algae, or microbial sources) or synthesized in a laboratory. The polymers can be polysaccharides or polypeptides. Among polysaccharides, starch, and cellulose are examples of plant sources. Chitin, chitosan including hyaluronic acid are examples of animal origin. Alginates, carrageenan, and agar are examples of algal sources. Xanthan, dextran, and gellan gum are examples of microbial sources. Collagen, albumin, and fibrin are examples of polypeptides from animal sources. Chitosan is a natural cationic polysaccharide and inhibits the growth of S.mutans. [(7)] Granulation tissue formation and angiogenesis occur at the healing site with the placement of chitosan. [(8)] Cellulose is a high molecular weight polysaccharide found in cell walls of plants It gives structural integrity and protection to plant cells. It serves as a scaffold for wound dressings and is also used as part of a drug dose delivery. [(9)] Hyaluronic acid may improve wound healing and used for periodontitis. [(10)] Alginate is an anionic polysaccharide that has been linked to the use of mouth impressions in diagnostic and therapy planning. Poor mechanical characteristics, hydrophilicity, and microbial breakdown are all disadvantages of alginates. [(11)]Agarose acts as both a matrix for rebuilding enamel and a mineral reservoir for future remineralization by interacting with the hydroxyl group of agarose and calcium. It can be concluded that agarose hydrogel can be used in the treatment of incipient carious lesions. [(12)]

Biocompatibility and affinity for other matrix proteins are strong in protein-based materials. Collagen is the most widely distributed protein in the cell matrix. Collagen is well-known for its biocompatibility, immunogenicity, and cytotoxicity. Collagen has an osteoinductive effect that leads to the differentiation and proliferation of osteoblasts. [(13)] Platelet-rich fibrin (PRF), entrapped with cytokines, growth factors, and cells, is a promising biomaterial. [(14)] Gelatin is a hydrolyzed collagen having high hemostatic activity. They have adhesive properties with low immunogenicity. They are used as a wound dressing. [(15)] Bone morphogenic proteins belong to the members of the transforming growth factor-beta superfamily of signaling molecules derived from the non-mineralized bone matrix. [(16, 17)] Polymers has a major impact on biomedical research. Scientists must continue to collaborate with life science specialists to develop tailor-made polymers for biomedical applications and to better understand the composition of human organs. [(18)]

POLYNUCLEOTIDES

In oral squamous cell carcinoma, invasion and migration of carcinogenic cells are reduced by inhibitors of graphene oxide-polyethyleneimine. [(19)] Polymers produced by copolymerization using addition or condensation of conventional monomers are synthetic polymers. Monomers are directly added to the developing polymeric chain during addition polymerization. During condensation polymerization, some atoms are removed and a byproduct is formed, resulting in the creation of repeat units. They are cheap and reproducible polymers of synthetic origin. [(20)]Anchorage-independent cells have different morphological characteristics and cell membrane components than adherent cells. They have a small surface area and a low rate of endocytosis which make it difficult to transfer nucleic acids to them. By treating the non-adherent cells, a variety of polynucleotide base approaches and materials have been devised. [(21)] Gene therapy intends to either derive the needful proteins or minimize endogenous gene expression. Because of the limits imposed by polynucleotide pharmacokinetics, carriers play a key role in gene therapy. By shielding and/or linking numerous polynucleotide molecules, polymers and lipids protect polynucleotides from intra- and extracellular hazards while facilitating the synthesis of cell-permeable nanoparticles. The formation of nanoparticulate systems with the desired properties, as well as cellular uptake and intracellular trafficking are key processes for effective gene therapy. [(22)]

The natural polymers have a poor immunogenic response and are biocompatible. Synthetic polymers have low reproducibility and poor mechanical properties. Natural polymers are used as bioinks for 3D printing technology using extrusion, inkjet, stereolithography, and laser-assisted printing. [(23)]

METALS

Metals used as biomaterial should be biocompatible, wear-resistant, corrosion-resistant, and have good mechanical properties. Metallic plates have been used for bone fixation in the treatment of fractures for ages. During the ionization process, metal releases its valence electrons. Metals are used as biomaterials because of their splendid electric and thermal conductivity. as well as their mechanical properties. By changing position of the metal ions plastically flexible solid can be obtained. [(24)] They have excellent properties of electrical and thermal conductivity. [(25)] For dentistry, gold has been used inlay,onlay, full coronal crown, post and core, and implants. [(26)] Titanium has good corrosion resistance and has a modulus of elasticity similar to bone.

[27] Iron- alloys with 18% chromium form stainless steel. Chromium oxide (Cr_2O_3) layer provides corrosion resistance to the alloys. 316LStainless steel having lesser carbon content has been used in implants in dentistry. The nickel in stainless steel enhances corrosion resistance. 316L can also corrode an oxygen-depleted environment. Thus its used as fracture plates and screws for temporary fixation. [28] Nitinol, tantalum, magnesium are also metals used in dentistry. Nitinol, a nickel-titanium alloy, is a shape memory material. These alloys can be distorted plastically at low temperatures and then returned to their original shape by raising the temperature. Because of its persistent surface oxide layer, tantalum has good corrosion resistance and biocompatibility. Cardiovascular and orthopaedic applications have been using magnesium alloys with improved mechanical properties. It is new or modified materials that can address the issues currently faced by existing implants, and offer biomaterials that not only reduce the risk of medical consequences but may also provide patients with more realistic, aesthetically acceptable outcomes. Materials engineering can bring substantial value to future biomaterials, and next-generation implants can be made with nanoparticles that have various functions. [29] Metal biomaterials are required not only for implantable medical devices, but also for bio-related devices such as nano-needles, nanoparticles, and nanowires. Metal biomaterials are distinguished by their key mechanical qualities and processability. Their surface biocompatibility, on the other hand, is insufficient and should be increased. Other materials, such as surface coatings with bioceramics and biocompatible polymers, are used in traditional modification. [30].

BIOCERAMICS

Inorganic biomaterials such as crystalline ceramics, amorphous glasses, and glass-ceramics are known as bioceramics. Repair, restoration, and regeneration of bone and teeth are familiar applications, but they are expanding. [31] Although bioceramics are biocompatible, they don't have much mechanical strength, so a polymer phase must be added.. [32] They are ceramics used in the diseased and damaged areas that are rebuilt and repaired. They typically have ionic and covalent bonds. They have high compressive strength but low tensile strength, making them brittle. They are generally effective heat and electricity insulators. They can be bioinert, bioactive, or bioresorbable. Stainless steel, titanium, alumina, and zirconia are examples of bioinert materials that have little interaction with their surroundings. The bioactive substance interacts with the bone and soft tissue in the area which causes kinetic alteration of the surface in time dependent manner .Synthetic hydroxyapatite, glass-ceramic, and bioglass are some example of bioactive materials. Third-generation bioceramics are ceramics utilised in regenerative medicine as temporary constructs or scaffolds. They can promote tissue regeneration and induce tissue integration, and they are often non-toxic and non-carcinogenic.

Nanophase calcium phosphate is used as an osseo-conductive used in orthopedic applications. Inertness of biomaterial is required to counter the allergic reactions . Biomaterials have a wider range of applications, in restorative dentistry, valve replacements in cardiac patients , orthopedic implants. Modern society has access to intelligent biomaterials that can mimic structure and reactivity of natural elements. The three major categories of conventional biomaterials are polymers, metals, and ceramics. [33]

NANOCERAMICS

The conception of prospective artificial body parts and post surgical care would occur with better understanding of the interactions between bioceramics tissues in the human body at the nanoscale. The new-generation implants combine nanosensors with electronics in improving tissue compatibility, patient well-being, and implant longevity. [34] The transition from micro-sized to nano-sized particles results in increased surface area and reactivity, increased hydrophilicity, and grain boundaries. Nanoparticles can be formed either by a top-down or bottom-up approach. The bottom-up method can be the condensation process which produces nanoporous ceramic particles. [28] The qualities that directly affect interactions with biological organisms are discussed, along with the processing procedures for creating ceramics. The literature examined shows that the nanostructure of ceramic surfaces has a direct impact on these interactions. One of the most important aspects of nanomedicine development is to regulate and analyze the interactions between nanoceramics and biological entities. [35]

NATURAL MATERIALS

They are biocompatible, biodegradable, and can be remodeled. They work at the molecular level. Limitations are, that they can elicit an antigenic response and are difficult to maneuver. Collagen is got from porcine, bovine, or equine sources. Human-derived collagen is got from cadavers, the placenta. Type-I collagen is commonly used collagen ,it's also found in scar tissue that forms while the body heals. The majority of type-II collagen in articular cartilage is made up of muco and glycoprotein. The primary purpose of type-II collagen in cartilaginous tissues is to maintain the tissue's tensile integrity. Disulfide linkages in type III collagen contribute to elasticity. Type IIII collagen can be found in blood vessels, ligaments, and internal organs. Noncollagenous components interact with type-IV collagen to form a filtration mechanism for cells, molecules, and light. It can be detected in the lens of the eye, the kidneys, and blood vessels. [28] Elastin produced as an extracellular matrix provides elasticity and resiliency to tissues and organs. properties to internal organs.

Chitosan is a naturally occurring polysaccharide with antibacterial properties that is non-toxic, non - immunogenic, and bioresorbable. [36] The most significant impact is on gram-positive microbes like Streptococcus sanguis, S. mutans, S. mitus, and S. salivarius. It aids in preventing enamel demineralization. It encourages bone regeneration and impedes plaque and biofilm formation. [37]

Some bacteria and prokaryotes, secrete cellulose and for fast medication release, cellulose is used as a medication binder.For longer release formulations, highly viscous cellulose are used. Alginate is used for making an impression. The biomaterial chosen in any implant has a huge impact on its success. When compared to synthetic biomaterials, naturally generated biomaterials have been shown to offer various advantages. Biocompatibility, biodegradability, and remodelling are three of them. Biomaterials are quite often used to rebuild or substitute compromised human tissue This chapter's goal is to provide a basic understanding of naturally produced biomaterials, as well as their production and application methods. Nature's more significant structural and mechanical features are presented as a foundation, inspiring scientists and engineers to develop biomimetic methodologies that could be valuable in fields like materials research, biomaterials development, and nanotechnology. The current breakthroughs in the synthetic design and fabrication of nature-inspired materials and coatings, particularly for use in biomedical applications, are heavily emphasized. [38]

COMPOSITES

Fiberglass and other reinforced polymers, as well as bone, are composite materials, but alloys like brass, bronze are not. [39] Composites are made up of organic, inorganic phases, to join the organic and inorganic phases, silane is utilized as a coupling agent. [40] The silanization of fillers improves the properties of composite resins. [41] Composites contain two or more integral materials. Dental composites are examples of synthetic composites. Bone is an example of a natural composite. They are easily manipulated. Initially, quartz was added to the composite, but they had difficulty polishing. [42] The dental composite is categorized based on the size of the filler particles. [43] Colloidal silica gel particles with a diameter of about 25 nm are often used to make nanofillers.. [44] Flowable composites are associated with increased polymerization shrinkage. [45] They are to be used only in small restorations where less wear is expected. Understanding of tissue material interphase has made biomaterials to be used in regenerative dentistry and reconstructive therapies. Biomaterials and technology are boosting tissue regeneration as well as restoring missing or damaged tissues.

CONCLUSION

Recent developments in the creation and use of smart biomaterials have the potential to hasten the development of promising new medications and enhance the treatment of chronic illnesses. Smart multifunctional stimuli-responsive materials have been studied to some extent and have garnered a lot of interest in the fields of antibiotic therapy, tumour therapy, inflammation prevention, and tissue repair stimulation. Although there are still some obstacles to overcome and a long way to go in terms of clinical translation, smart stimuli-responsive materials are predicted to have significant biomedical uses in the future.

ACKNOWLEDGMENT

The authors thank Chettinad Dental College and Research Institute and Chettinad Academy of Research and Education for infrastructure support

REFERENCES:

1. Williams DF, Williams DF. The Williams dictionary of biomaterials: Liverpool University Press; 1999.
2. Wong, J.Y., Bronzino, J.D., & Peterson, D.R. (Eds.). (2013). Biomaterials: Principles and Practices (1st ed.). CRC Press. https://doi.org/10.1201/b13687.
3. Kuhn LT. 6 - BIOMATERIALS. In: Enderle JD, Blanchard SM, Bronzino JD, editors. Introduction to Biomedical Engineering (Second Edition). Boston: Academic Press; 2005. p. 255-312.
4. Mouthuy PA, Ye H. 5.04 - Biomaterials: Electrospinning. In: Moo-Young M, editor. Comprehensive Biotechnology (Second Edition). Burlington: Academic Press; 2011. p. 23-36.
5. Chen FM, Liu X. Advancing biomaterials of human origin for tissue engineering. Progress in polymer science. 2016;53:86-168.
6. Love B. Chapter 9 - Polymeric Biomaterials. In: Love B, editor. Biomaterials: Academic Press; 2017. p. 205-38.
7. Battistella E, Varoni E, Cochis A, Palazzo B, Rimondini L. Degradable polymers may improve dental practice. Journal of applied biomaterials & biomechanics: JABB. 2011;9(3):223-31.
8. Aguilar A, Zein N, Harmouch E, Hafdi B, Bornert F, Offner D, et al. Application of Chitosan in Bone and Dental Engineering. Molecules (Basel, Switzerland). 2019;24(16).
9. Sun B, Zhang M, Shen J, He Z, Fatehi P, Ni Y. Applications of Cellulose-based Materials in Sustained Drug Delivery Systems. Current medicinal chemistry. 2019;26(14):2485-501.
10. Casale M, Moffa A, Vella P, Sabatino L, Capuano F, Salvinelli B, et al. Hyaluronic acid: Perspectives in dentistry. A systematic review. International journal of immunopathology and pharmacology. 2016;29(4):572-82.
11. Ahmad A, Mubarak NM, Jannat FT, Ashfaq T, Santulli C, Rizwan M, et al. A Critical Review on the Synthesis of Natural Sodium Alginate Based Composite Materials: An Innovative Biological Polymer for Biomedical Delivery Applications. Processes. 2021;9(1):137.
12. El Moshy S, Abbass MMS, El-Motayam AM. Biomimetic remineralization of acid-etched enamel using agarose hydrogel model. F1000Research. 2018;7:1476.
13. Conte R, Di Salle A, Riccitiello F, Petillo O, Peluso G, Calarco A. Biodegradable polymers in dental tissue engineering and regeneration. AIMS Materials Science. 2018;5(6):1073-101.

14. Naik B, Karunakar P, Jayadev M, Marshal VR. Role of Platelet rich fibrin in wound healing: A critical review. Journal of conservative dentistry: JCD. 2013;16(4):284-93.
15. Ndlovu SP, Ngece K, Alven S, Aderibigbe BA. Gelatin-Based Hybrid Scaffolds: Promising Wound Dressings. Polymers. 2021;13(17):2959.
16. Wang RN, Green J, Wang Z, Deng Y, Qiao M, Peabody M, et al. Bone Morphogenetic Protein (BMP) signaling in development and human diseases. Genes & diseases. 2014;1(1):87-105.
17. Díaz-Sánchez R-M, Yáñez-Vico R-M, Fernández-Olavarría A, Mosquera-Pérez R, Iglesias-Linares A, Torres-Lagares D. Current approaches of bone morphogenetic proteins in dentistry. Journal of Oral Implantology. 2015;41(3):337-42.
18. He W, Benson R. 4 - Polymeric Biomaterials. In: Modjarrad K, Ebnesajjad S, editors. Handbook of Polymer Applications in Medicine and Medical Devices. Oxford: William Andrew Publishing; 2014. p. 55-76.
19. Ou L, Sun T, Liu M, Zhang Y, Zhou Z, Zhan X, et al. Efficient miRNA Inhibitor Delivery with Graphene Oxide-Polyethylenimine to Inhibit Oral Squamous Cell Carcinoma. 2020;15:1569-83.
20. Moussa DG, Aparicio C. Present and future of tissue engineering scaffolds for dentin-pulp complex regeneration. Journal of tissue engineering and regenerative medicine. 2019;13(1):58-75.
21. Ansari AS, Santerre PJ, Uludağ H. Biomaterials for polynucleotide delivery to anchorage-independent cells. Journal of Materials Chemistry B. 2017;5(35):7238-61.
22. Meneksedag-Erol D, Tang T, Uludağ H. Molecular modeling of polynucleotide complexes. Biomaterials. 2014;35(25):7068-76.
23. Khoeini R, Nosrati H, Akbarzadeh A, Eftekhari A, Kavetskyy T, Khalilov R, et al. Natural and Synthetic Bioinks for 3D Bioprinting. Advanced NanoBiomed Research. 2021;1(8):2000097.
24. Park JB, Kim YK. Metallic biomaterials. Biomaterials: CRC press; 2007. p. 1---22.
25. Schmalz G, Garhammer P. Biological interactions of dental cast alloys with oral tissues. Dental materials: official publication of the Academy of Dental Materials. 2002;18(5):396-406.
26. Fonseca RG, de Almeida JG, Haneda IG, Adabo GL. Effect of metal primers on bond strength of resin cements to base metals. The Journal of prosthetic dentistry. 2009;101(4):262-8.
27. Freese H, Volas M, Wood J, Textor M. Titanium and its alloys in biomedical engineering. Encyclopedia of Materials: Science and Technology. 2011:9374-80.
28. Ong J, Appleford MR, Mani G. Introduction to biomaterials: basic theory with engineering applications: Cambridge University Press; 2014.
29. Prasad K, Bazaka O, Chua M, Rochford M, Fedrick L, Spoor J, et al. Metallic Biomaterials: Current Challenges and Opportunities. Materials. 2017;10(8):884.
30. Ishihara K, Choi J. 12 - Biocompatible polymer assembly on metal surfaces. In: Niinomi M, editor. Metals for Biomedical Devices: Woodhead Publishing; 2010. p. 283-302.
31. Jones JR, Gibson IR. 1.3.4 - Ceramics, Glasses, and Glass-Ceramics: Basic Principles. In: Wagner WR, Sakiyama-Elbert SE, Zhang G, Yaszemski MJ, editors. Biomaterials Science (Fourth Edition): Academic Press; 2020. p. 289-305.
32. George AM, Reddy Peddireddy SP, Thakur G, Rodrigues FC. Chapter 29 - Biopolymer-based scaffolds: Development and biomedical applications. In: Pal K, Banerjee I, Sarkar P, Kim D, Deng W-P, Dubey NK, et al., editors. Biopolymer-Based Formulations: Elsevier; 2020. p. 717-49.
33. Balakrishnan P, Thomas S. 5 - Inert ceramics. In: Thomas S, Balakrishnan P, Sreekala MS, editors. Fundamental Biomaterials: Ceramics: Woodhead Publishing; 2018. p. 117-27.
34. Ben-Nissan B. Nanoceramics in biomedical applications. MRS bulletin. 2004;29(1):28-32.
35. Traykova T, Aparicio C, Ginebra MP, Planell JA. Bioceramics as nanomaterials. Nanomedicine (London, England). 2006;1(1):91-106.
36. Qasim SB, Zafar MS, Najeeb S, Khurshid Z, Shah AH, Husain S, et al. Electrospinning of Chitosan-Based Solutions for Tissue Engineering and Regenerative Medicine. International journal of molecular sciences. 2018;19(2):407.
37. Cervino G, Cicciù M, Biondi A, Bocchieri S, Herford AS, Laino L, et al. Antibiotic Prophylaxis on Third Molar Extraction: Systematic Review of Recent Data. Antibiotics. 2019;8(2):53.
38. Luz GM, Mano JF. Biomimetic design of materials and biomaterials inspired by the structure of nacre. Philosophical transactions Series A, Mathematical, physical, and engineering sciences. 2009;367(1893):1587-605.
39. Park JB, Lakes RS. Composites as biomaterials. Biomaterials. 2007:207-24.
40. Geurtsen W. Substances released from dental resin composites and glass ionomer cements. European journal of oral sciences. 1998;106(2 Pt 2):687-95.
41. Pourhashem S, Rashidi A, Vaezi MR, Bagherzadeh MR. Excellent corrosion protection performance of epoxy composite coatings filled with amino-silane functionalized graphene oxide. Surface and Coatings Technology. 2017;317:1-9.
42. Fortin D, Swift EJ, Jr., Denehy GE, Reinhardt JW. Bond strength and microleakage of current dentin adhesives. Dental materials: official publication of the Academy of Dental Materials. 1994;10(4):253-8.
43. Lutz F, Setcos JC, Phillips RW. New finishing instruments for composite resins. Journal of the American Dental Association (1939). 1983;107(4):575-80.
44. Mitra SB, Wu D, Holmes BN. An application of nanotechnology in advanced dental materials. Journal of the American Dental Association (1939). 2003;134(10):1382-90.
45. Sabbagh J, Ryelandt L, Bachérius L, Biebuyck JJ, Vreven J, Lambrechts P, et al. Characterization of the inorganic fraction of resin composites. Journal of oral rehabilitation. 2004;31(11):1090-101.