Chapter

Acrylic-Based Materials for Biomedical and Bioengineering Applications

Ángel Serrano-Aroca and Sanjukta Deb

Abstract

Acrylic-based polymers have been used for many years in biomedical applications because of their versatile properties. Many different polymers belong to this class of polymers, of which a significant number have been approved by the US Food and Drug Administration (FDA) and are frequently used in ophthalmologic devices, orthopaedics, tissue engineering applications and dental applications. The applications of this class of polymers have the potential to be expanded exponentially in the biomedical industry if their properties such as mechanical performance, electrical and/or thermal properties, fluid diffusion, biological behaviour, antimicrobial capacity and porosity can be tailored to specific requirements. Thus, acrylic-based materials have been produced as multicomponent polymeric platforms as interpenetrating polymer networks or in combination with other sophisticated materials such as fibres, nanofibres, carbon nanomaterials such as graphene and its derivatives and/or many other types of nanoparticles in the form of composite or nanocomposite biomaterials. Moreover, in regenerative medicine, acrylic porous supports (scaffolds) need to be structured with the necessary degree, type and morphology of pores by advanced technological fabrication techniques.

Keywords: acrylic-based materials, biomedicine, bioengineering, composites, nanocomposites, tissue engineering

1. Introduction

Acrylic-based materials have been used in medicine and dentistry over decades. Specific examples in current clinical use are corneal prosthesis, intraocular lenses and contact lenses in ophthalmology [1] and bone cements for orthopaedic applications [2], tissue engineering [3] and dental restoratives [4] because of their versatile properties [5]. A significant number of these acrylic polymers have been affirmed by the US Food and Drug Administration (FDA) for different applications. Nonetheless, a considerable number of potential clinical applications are impeded by their inadequate mechanical properties, biological behaviour, electrical and/or thermal capacity, interaction with body fluids, antimicrobial response and porosity in porous platforms (scaffolds) for tissue engineering applications. To address some of these limitations of existing acrylates, new acrylic-based materials with superior properties have been produced and are currently under being researched to resolve these problems by means of diverse fabrication strategies

such as multicomponent polymeric systems or by incorporation of other materials and/or nanomaterials such as graphene to create composites or nanocomposites with a wide range of properties and also develop extensive interconnected porous structures. Biomaterials are used to engineer functional restoration of different tissues towards the repair or restoration of damaged tissues via interacting with living systems and enabling normal function. Hence the design and development of novel biomaterials involve considering physical, mechanical and biological properties of the native tissue that is being replaced with a goal of mimicking it as closely as possible to enable repair or replace and function. One of the important aspects is designing the material with desired mechanical properties that enables survival in a complex biological milieu. Recent technological advances have seen the development of complex biomaterials, and newer manufacturing techniques allow for increased spatial control over material properties. Despite the current advances, the improvement of mechanical properties of acrylics still remains a challenge and needs further investigation [6–11].

2. Mechanical performance

The enhancement of the mechanical performance of acrylics is one of the hot themes in the area of biomedical engineering, and numerous researchers have been working on this field for many years. Acrylics can be reinforced through different methods and techniques: by incorporating ceramic additives to form composites [12]; microphase-separated morphologies such as block copolymers, in which hydrophobic and hydrophilic domains alternate [13]; increasing the cross-linking density [14]; binary systems composed of two or more mixed polymers as interpenetrating polymer networks [15, 16]; reinforced acrylic-based composites with embedded fibres [17]; plasma-induced polymerisation of an acrylic hydrogel onto a hydrophobic acrylic support [7, 18]; and nanosilica reinforcement obtained through sol-gel reactions [19]. Nevertheless, new procedures to enhance the mechanical behaviour of acrylics have been performed by incorporating advanced materials such as graphene (2010 Nobel Prize in Physics) [20] and other outstanding carbon-based materials such as carbon nanotubes (CNT) [21]. Graphene derivatives such as graphene oxide (GO) [22–24] or reduced GO (rGO) [25] have also exhibited excellent reinforcement for acrylics, especially hydrated acrylic hydrogels, and enhancement of many other properties.

2.1 Interpenetrating polymer networks

Interpenetrating polymer networks (IPN) as reinforced polymer networks containing acrylic polymers have gained much attention in the biomedical field during the last few decades. An IPN consists of two separate but interwoven polymer networks, which can enhance and/or combine functional properties. In this advanced multicomponent polymeric system, there are not any covalent bonds between them, but at least one of them is cross-linked within the immediate presence of the other. In this field, there are six basic multicomponent polymeric structures: mechanical blends, block copolymers, graft copolymers, AB-cross-linked copolymer, semi-IPNs and full IPNs [26]. A full IPN results is produced if a cross-linker is present in the polymeric system [27]. However, a semi- or pseudo-IPN polymer network possessing linear polymers embedded within the first cross-linked network is formed in the absence of cross-linking [28, 29]. Simultaneous interpenetrating polymer networks (SINs) are produced when the precursors of

both networks are mixed and the two networks are formed at the same time or in the form of sequential IPNs, by swelling of a single-polymer network into a solution containing the mixture of monomer, initiator, activator and cross-linker. Thus, for example, urethane acrylate resin networks have been reinforced with epoxy networks in the form of SINs [30]. Full IPNs and semi-IPNs have been prepared with epoxy resin and poly(ethyl methacrylate) (PEMA) utilising the sequential mode of synthesis [31]. Both types of networks showed a gradual decrease of modulus and tensile strength performance and an increase of elongation at break and toughness with increasing PEMA content. Simultaneous semi-interpenetrating polymer networks (semi-SINs) of epoxy resin-acrylate polyurethane with high compatibility have been synthesised by simultaneous photopolymerisation [32]. More recently oxirane-acrylate IPN's were reported to enhance the hydrophobic nature of dental composites and lower degradation and shrinkage stress than commonly used bis-GMA resins; however, the mechanical properties were not adequate [16]. Pseudo-SIPNs have been prepared by melt blending of poly(methyl methacrylate) (PMMA) and double-C_{60}-end-capped poly(ethylene oxide) (FPEOF) that exhibited a storage modulus 16 times higher than PMMA, which are as similar to nanocomposites of PMMA with carbon nanotubes [29].

Acrylic-based IPN hydrogels are also produced with the goal of improving the mechanical performance and swelling-deswelling action of acrylic hydrogels [33]. In this way, for instance, hydrophilic interpenetrating polymer networks (IPN) with good mechanical properties even in the hydrated state were produced with chitosan and poly(acrylic acid) (PAA) [34].

2.2 Composite biomaterials

Most chemical modifications of acrylic hydrogels do not result in a significant change of the overall mechanical properties since the main structural skeletons of these polymers or copolymers remain weak. On the contrary, the reinforcement achieved by the incorporation of fibre into acrylic polymer matrices is different because the added fibres impart high strength to the networks with the main skeleton of the composites. Materials reinforced with fibre are composite materials consisting of a polymer phase embedded with high-strength fibres, such as glass, aramid and carbon [35]. In this type of materials, the mechanical performance is significantly enhanced, and the biocompatible properties of the acrylic polymer phase should remain unmodified. Thus, acrylic resin polymers have been reinforced with glass fibres for dental applications [36], and acrylic hydrogels such as poly(2-hydroxyethyl methacrylate), which is one of the most popular biomaterials, have been used to manufacture fibre-reinforced composites by inclusion of various kinds of woven and knitted fabrics and fibres, in order to improve overall qualities of the PHEMA-based artificial skin for wound dressing applications [37]. Nevertheless, in the last recent decades, natural fibres have attracted much attention as reinforcement agents for polymer-based composites due to their advantages over other types of conventional fibres made with glass or carbon [38]. Thus, natural fibres, such as flax, hemp, sisal, jute, kenaf, coir, kapok and banana, among many others, have shown many advantages over man-made glass and carbon fibres: lower cost, lower density, comparable specific tensile performance, less energy consumption, non-abrasive, not irritating, lower health risk, renewable, biodegradable and recyclable [39]. Thus, in the field of acrylic polymers, ultra-long chitin natural fibres obtained in a sustainable way, that is, from marine-river crab shell wastes, have been incorporated into PMMA resins to produce nanocomposites with outstanding properties for biomedical and bioengineering applications [40].

2.3 Nanocomposite biomaterials

Nanocomposites are of particularly interest due to the fact that they exhibit both individual properties of the polymer and properties due to the presence of nanoparticles, and this additive effect has led to several therapeutic and diagnostic applications [41]. Another reinforcing alternative for acrylic polymers consists of adding nanomaterials such as silica, carbon nanomaterials, nanofibres or other nanoparticles. Silica is biocompatible, possesses bioactive properties [42] and can improve the mechanical behaviour of acrylics through filling or by the sol–gel process [43]. Thus, for example, biphasic matrices of hybrid nanocomposite materials consisting of an organic phase of poly(2-hydroxyethyl acrylate) and an inorganic phase of silica network obtained by the sol–gel process of tetraethoxysilane (TEOS) exhibited a very significant enhancement of the mechanical properties [9]. The combination of interpenetrated polymer networks and nanosilica filling has been explored, and simultaneous polyurethane/PEMA interpenetrating polymer networks with silica filler consisting of very fine powders with an approximate diameter of 5 nm were reported to significantly improve material strength [44]. Polymer nanocomposites have significantly influenced the field of biomedicine. In this regard, graphene-based nanocomposites have been reported to enhance the physical and biological properties of a wide range of polymers of different chemical natures [24, 45–53]. Graphene (GN) is a 2D monolayer of sp^2-bonded carbon atoms [54] very promising in a wide range of industrial fields due to its outstanding electrical and thermal properties [55, 56] and high mechanical performance [57]. In addition, it has been demonstrated that graphene, in the biomedical field, promotes adherence of human osteoblasts and mesenchymal stromal cells [58]. Graphene has exhibit potential application in the development of new reinforced nanocomposites such as magnetite-GNs/poly(arylene-ether-nitrile) [59]. Furthermore, GN is able to enhance the shape memory of acrylic polymers such as poly(acrylamide-co-acrylic acid), and it possesses self-healing ability when its content is between 10 and 30% [60]. The oxidised form of GN, graphene oxide (GO), can also improve the mechanical strength and modulus of acrylic polymer networks such as poly(acrylamide) (PAM) hydrogels [61]. GO is also a two-dimensional nanomaterial usually produced from natural graphite by exfoliation into monolayer sheets. GO possesses oxygenated functional groups at the basal plane and at the edges, hydroxyl (–OH), epoxy (–C–O–C–), carboxyl (–COOH) and carbonyl (–C=O), which render its dispersion in aqueous solution easier [62]. The outstanding unique properties of GO, such as high tensile modulus (1.0 TPa), ultimate strength (130 GPa) and electrical and thermal properties [63], render this carbon nanomaterial an ideal candidate for a broad range of applications in the field of new advanced materials. Thus, for instance, when GO nanosheets are introduced into weak and brittle PAM hydrogels, their mechanical properties improve significantly [61]. The incorporation of GO nanosheets into poly (acrylic acid)/gelatin composite hydrogels increased significantly their Young's modulus and maximum stress. In this study, the hydrogel with GO (0.2% *w/w*)/PAA(20% *w/w*) exhibited the highest Young's modulus, whereas GO (0.2% *w/w*)/PAA (40% *w/w*) composites showed the highest maximum stress. These results suggest that GO nanosheets can be successfully used as reinforcing agents to enhance the mechanical performance of hydrogel materials, which is often required for certain tissue engineering applications [23]. Other graphene derivatives such as chemically modified graphene (CMG) have been proposed and compared with GO for the reinforcement of PMMA [64]. Single-wall carbon nanotubes (SWCNTs), multiwalled carbon nanotubes (MWCNTs) and carbon nanofibres (CNFs) are also very promising reinforcing nanomaterials for acrylic polymers such as poly(methyl methacrylate). For instance, nanocomposites of PMMA with small amounts of

CNFs (5% *w/w*) can enhance over 50% of the axial tensile modulus with respect to neat PMMA. PMMA/CNF nanocomposites in the form of fibres have also exhibited enhanced thermal stability, reduced shrinkage and improved modulus retention with temperature, as well as stronger compression performance [65]. The electrical and electromechanical properties of acrylic materials such as acrylic elastomers and styrene copolymers can also be enhanced to be suitable for electroactive applications such as artificial muscles and/or microelectromechanical system (MEMS) devices [66]. Natural chitosan nanofibres can act as a multifunctional cross-linker and a reinforcing agent in poly(acrylamide) (PAM) nanocomposites, which were prepared via in situ free-radical polymerisation, producing superior compression strength and storage modulus than those of pure PAM [67]. Plant fibre-based nanofibres using fibrillation of wood pulp fibres into nanofiber bundles, which are thin enough to work, as well as bacterial cellulose in maintaining the transparency of resin also enhanced the physical properties of the composites [68]. Nanoparticles such as clay can also be used to enhance the mechanical properties of acrylic polymers. Thus, for instance, reinforced PMMA/clay nanocomposites exhibit a polymer matrix reinforced by usually 10% *w/w* or less of uniformly dispersed inorganic particles with at least one dimension in the nanometre scale [69]. These nanocomposites have also shown enhanced thermal properties when compared to pure polymer or common composites. Biocomposites based on acrylated fatty acids and magnetic nanoparticles have been reported to maintain their good magnetic response and supramagnetic behaviour, and the use of acrylated fatty acids further enables chemical modification of magnetic nanoparticles extending their potential applications [70]. The modification of graphene with biomacromolecules like DNA, protein, peptide and others extends the potential applications of graphene materials. The remarkable advances in material technologies and recent developments in nanotechnology have enabled formulation of different nanocomposites with a wide range of properties, and the potential of application of these composites in healthcare is becoming more apparent. Nanocomposites are already being successfully used in drug delivery, gene therapy, tissue engineering and imaging and as biosensors [70–74].

3. Electrical properties

The electrical properties of acrylics are important in some biomedical and bioengineering fields because various types of electrical stimulation can regulate cell physiological activities such as division [75], migration [76], differentiation and cell death [77]. Promotion of spinal cord repair and successful cancer therapy has been also achieved by a combination of electrical stimulation and the non-invasive nature of these polymers [78–80]. For that reason, the development of new conductive acrylic-based materials for biomedical applications is gaining much attention during the last decades. Graphene, a nanocarbon material, has been recently very effective as an electrode material with very high conductivity [41]. Although graphene exhibits high transmittance and excellent conductivity [55], its fabrication is still expensive. However, GO, which is more cost-effective, possesses low conductivity due to its oxygen-containing functional groups, and it must be modified to obtain reduced graphene oxide (rGO) in order to develop electrically conductive acrylic-based resins. Thus, for instance, single-step procedures can be performed starting from a homogeneous water dispersion of GO in order to effect a reduction induced by the UV radiation during the photopolymerisation of an acrylic resin [81]. Transparent conductive films can be also fabricated by grafting of poly(acryl amide)/poly(acrylic acid) onto the GO surface followed by a reduction

to rGO nanosheets by a two-step chemical reduction [82]. Flexible and conductive double networks (DN) of rGO and poly(acrylic acid) hydrogels have also been synthesised by a two-step preparation with a reduction-induced in situ self-assembly [83]. Nacre-inspired acrylic-based nanocomposites of rGO and PAA have also been prepared via a vacuum-assisted filtration self-assembly process. Higher strength and toughness (2 and 3.3 times higher) were achieved with these bioinspired nanocomposites in comparison with those of the pure reduced GO film due to the high amount of hydrogen bonds between the GO nanosheets and PAA polymer chains. Furthermore, this nanocomposite also displayed high electrical conductivity (108.9 $S{\cdot}cm^{-1}$), which renders it a promising biomaterial for many advanced applications in biomedicine and bioengineering, such as flexible electrodes and artificial muscles. The one-dimensional carbon nanomaterials discovered by Iijima [84], named as carbon nanotubes (CNTs), have caused increasing interest due to their excellent electrical conductivity and remarkable mechanical properties with numerous potential nanotechnological applications [85]. Ultrasensitive electrochemical biosensors can be developed with CNTs due to their unique electrical properties. Thus, glucose biosensor for diabetics has been developed with nanofibrous membranes of poly(acrylonitrile-co-acrylic acid) (PANCAA) filled with multiwalled carbon nanotubes (MWCNT) [86]. Other acrylic polymers such as poly(methyl methacrylate) have been developed as nanocomposites containing various multiwalled carbon nanotube (MWCNT) contents by melt mixing to achieve high conductivity levels [87].

4. Thermal properties

The enhancement of the thermal properties of acrylics can increase its long-term operation at the human body temperature. Thus, for instance, semi-IPNs based on polyurethane and poly(acrylamide) exhibited enhanced thermal properties due to higher cross-link density produced by the hard segment content [28]. Differential scanning calorimetry PHEMA/SiO_2 hybrids are complicated showing complex results with two glass transition temperatures (*Tg*). In addition, the SiO_2 content showed to be an important factor in influencing the *Tg* shift of the thermal transition [88]. Nevertheless, polymer nanocomposites with functionalized graphene sheets (FGNS) exhibited an unprecedented shift in *Tg* of up to 40°C and 30°C in poly(acrylonitrile) with 1% *w/w* of FGNS and in PMMA with only 0.05% *w/w*, respectively [89]. Furthermore, the thermal stability of magnetite-graphene/poly(arylene-ether-nitrile) nanocomposites was significantly improved by the addition of magnetite-graphene hybrids [59]. PMMA-based nanocomposites produced with CMG and GO by in situ polymerisation also exhibited large shifts in the *Tg* with loadings as low as 0.05% *w/w* [64]. Another approach to enhance the thermal behaviour of acrylic polymers is by incorporating nanoparticulate fillers. Thus, the thermal performance of common acrylic polymers such as PMMA has been significantly enhanced by filling with several percentages (5%, 10%, 15% and 20%) of nanometric particles of titanium oxide (TiO_2) and ferric oxide (Fe_2O_3) by the solvent casting method [90, 91]. Thermal degradation can also be enhanced in acrylic polymers by the addition of nanoparticulate fillers. Thus, the thermogravimetric analysis (TGA) of PMMA-TiO_2 and PMMA-Fe_2O_3 composites showed that these nanoparticles can improve the thermal stability of neat PMMA by about 50°C with just a low filling of 5% *w/w* [91]. TGA has also shown that the presence of very low amounts of Pd nanoparticles (0.0005–0.005 vol%) in PMMA can significantly enhance its thermal stability, as shown by a 75°C degradation initiation retardation and a 32°C gain at the maximum decomposition rate [92]. Acrylic hydrogels

as hydrophilic polymers are able to absorb large amounts of water in biomedicine due to their contact with fluids in cells or tissue in the human body. Therefore, the thermal analysis of water and its influence on the hydrated hydrogel performance becomes essential. Thus, many studies have been reported in this way with acrylic hydrogels such as PHEMA [93], bulk and plasma-poly(2-hydroxyethyl acrylate) (PHEA) [6] and poly(ethyl acrylate) [94].

5. Water sorption and diffusion

Water sorption and diffusion are also very important in biomedicine because these properties play a very important role in cell survival, dimensional changes and release of small molecules which are all factors that need to be considered especially in tissue engineering applications [3]. Thus, acrylic hydrogels such as poly(2-hydroxyethyl methacrylate) or poly(2-hydroxyethyl acrylate) are important due to their hydrophilicity, swelling and deswelling capacity [95–97]. Their outstanding water sorption properties have made this kind of hydrophilic materials very promising for a broad range of biomedical and bioengineering applications such as wound healing, controlled drug delivery, tissue engineering, etc. [5, 98]. The hydrophilic functional groups attached to the polymeric backbone of these polymers provide the ability to absorb water, whilst their resistance to dissolution arises from cross-linking of polymer chains [99]. Nevertheless, these single-network hydrogels possess very weak mechanical performance and slow swelling response. Therefore, reinforcement strategies, such as the combination of hydrophilic and hydrophobic functional groups as multicomponent polymeric systems, are usually required for these types of polymer, which can also decrease their water sorption. The reinforcement of acrylics through the incorporation of GO nanosheets can also modify their water sorption behaviour. Thus, for example, the swelling rates of GO/poly(acrylic acid-co-acrylamide) nanocomposite hydrogels increased with increasing GO content to about 0.30% *w/w* and then decreased with further increase in amounts of GO. It is worth noting that the hydrogel with only 0.10% *w/w* GO exhibited significant improvement in swelling capacity in a neutral medium and could retain relatively higher swelling rates in acidic and basic solutions. Therefore, these GO-based superabsorbent acrylic hydrogels have potential applications in biomedical engineering and hygiene products [62]. The mechanism of water diffusion [100] can also be altered by reinforcement of acrylics through any of the methods discussed in Section 1. Thus, poly(acrylic acid)-GO nanocomposite hydrogels, which are potential carriers for drug release, can be manipulated by changing the concentration of GO and tend to exhibit non-Fickian anomalous diffusion with decrease in deswelling ratio with increasing GO content [63]. There are many acrylic hydrogels, which exhibit non-Fickian diffusion behaviour such as poly(2-hydroxyethyl acrylate) [97, 101]. Important water-swellable biomedical polymer such as PHEMA has shown to be governed by Fickian diffusion, even though water sorption is not classically Fickian [102]. Thus, advanced hydrogels based on 2-hydroxyethyl methacrylate (HEMA) and epoxy methacrylate (EMA) produced via bulk polymerisation exhibited also a Fickian swelling process, and the equilibrium water content (EWC) decreased with increasing the hydrophobic EMA content [103]. The pH has a substantial influence in swelling properties and diffusion mechanism of acrylic-based materials. Hence, the swelling properties of semi-interpenetrating polymer networks of acrylamide-based polyurethanes decrease in acidic pH, whilst a reverse trend is observed in alkaline medium. However, these semi-IPNs are hydrolytically stable in phosphate buffer solution, which renders them a potential material in biomedicine and bioengineering [28]. Acrylic polymers which are pH-sensitive

and biocompatible, such as poly(acrylic acid), are being used in many biomedical sectors [104]. Thus, they have attracted considerable interest mainly due to its therapeutic applications, because they possess great ability to swell reversibly with changes in pH. Functionalization of GO with PAA (GO-PAA) by in situ atom transfer radical polymerisation (ATRP) has shown great potential as intracellular protein carriers [105]. Poly(acryl amide-co-2-acrylamido-2-methyl-1-propanesulfonic acid-co-acrylamido glycolic acid) is a pH-sensitive terpolymer hydrogel suitable for drug release, which has shown a quasi-Fickian diffusion behaviour. These hydrogels demonstrate a sharp change in its water sorption and molecular weight between cross-links of the network with a change in pH of the swelling media [106]. The effect of temperature on swelling properties of acrylic hydrogels such as the thermosensitive poly(N-isopropyl acrylamide-co-acrylic acid) hydrogels is also very important [103], and they can be modified to exhibit fast temperature sensitivity and enhanced oscillating swelling-deswelling properties [107].

6. Antimicrobial capacity

Microbial infections are of serious concern and often lead to implant failure, which may cause major economic losses and suffering among patients despite the use of antibiotics and the aseptic processing conditions. Therefore, novel antimicrobial materials and strategies are urgently needed in biomedicine and bioengineering [108]. Nevertheless, acrylics itself do not possess antimicrobial activity intrinsically, and therefore some fillers and antimicrobial agents need to be incorporated usually by physical blending in order to produce an acrylic-based material able to treat and/or impede microbial infections [109]. Thus, graphene has emerged as a novel green broad-spectrum antimicrobial material with tolerable cytotoxicity in mammalian cells. Its antimicrobial action has been reported to be produced via physical damages through direct contact of its sharp edges with microbial membranes and destructive extraction of lipid molecules. Thus, graphene-based nanocomposites can be used in a broad range of biomedical applications due to its superior antimicrobial properties and good biocompatibility [110]. Methyl methacrylate was firstly used in tooth restoration in 1937, thereby indicating methacrylate monomers on polymerisation were biocompatible and have been extensively used as dental materials such as denture bases, adhesives, tissue conditioners, etc. [109]. The most popular methacrylate monomers employed in commercial dental resin-based materials are methyl methacrylate (MMA), 2,2-bis[4-(2-hydroxy-3-methacryloyloxypropyl)-phenyl]propane (Bis-GMA), 1,6-bis-[2-methacryloyloxyethoxycarbonylamino]-2,4,4-trimethylhexane (UDMA) and tri-ethylene glycol dimethacrylate (TEGDMA) [111]. Nevertheless, these polymers are not inherently antimicrobial in nature; thus, the strategy of designing acrylic hydrogels with desired antimicrobial performance is important. Silver nanoparticles (Ag NPs) exhibit strong antibacterial activity against *Escherichia coli*, and thus composites with AgNPs have been synthesised to not only confer antimicrobial properties but also improve the mechanical performance of acrylic resins for dental applications. The release of silver ions upon immersion of the dental composite in water produces antimicrobial effect with negligible toxicity to humans [112]. Antimicrobial PMMA nanofibres with incorporated silver nanoparticles have been prepared by radical-mediated dispersion polymerisation and showed superior antimicrobial activity than silver sulfadiazine and silver nitrate at the same silver concentration [113]. Unfortunately, highly undesired infections are also frequent after orthopaedic procedures. In addition, the growing increase of antibiotic resistance is progressively decreasing the efficacy of such medical treatment. Thus, in this regard, the integration of powerful

antimicrobial silver nanoparticles in polymeric acrylic-based nanocomposites is also an alternative antimicrobial approach [114]. The combination of previous strategies (graphene and Ag NPs) to develop antimicrobial hydrogels with good water maintaining ability is of particular significance for wound healing applications. Thus, a series of hydrogels have been prepared by cross-linking of Ag/graphene composites with acrylic acid and N,N′-methylene bisacrylamide at different compositions. In that study, hydrogels with an optimal Ag to graphene mass ratio of 5:1 were prepared and exhibited simultaneously excellent biocompatibility, much better antimicrobial properties than other hydrogels, high swelling ratio and good extensibility. Furthermore, in vivo experiments demonstrated that this nanocomposite hydrogel could significantly accelerate the healing rate of artificial wounds in rats, and it helped to successfully reconstruct an intact and thickened epidermis during 15 days of healing of impaired wounds [115]. In the same way, grafting of acrylic acid (AA) onto poly(ethylene terephthalate) (PET) films by gamma ray-induced graft copolymerization with silver nanoparticles showed strong and stable antimicrobial activity [116].

7. Acrylic-based scaffolds for tissue engineering

In regenerative medicine, regeneration and repair of diseased tissues can be addressed by tissue engineering approaches. A significant amount of research has focussed on the development of porous scaffolds that can interact directly with the seeded or laden cells. The porous 3D scaffolds provide the pathway for cell growth, proliferation and differentiation. The properties of the scaffolds are not only dependent on the base composition, but the structural and morphological features influence cell-material interaction. Hydrogels have emerged as leading candidates for engineered tissue scaffolds due to their biocompatibility and similarities to the native extracellular matrix. However, precise control of hydrogel properties, such as high porosity and tuning of mechanical properties, remains a challenge. Bulk porosities in polymers have been created by traditional techniques and have demonstrated success in hydrogels for tissue engineering applications. However, some problems related to direct cell encapsulation often occur. Nonetheless, a broad range of emerging technologies have demonstrated the ability to control porosity and its morphology in hydrogels, producing engineered tissues with structure and function similar to native tissues [117]. Ideal scaffolds should mimic the natural extracellular matrix (ECM), and a balance between temporary mechanical function with mass transport to aid biological delivery and tissue regeneration is of paramount importance. The interconnection and geometry of pores depend primarily on the tissue to be regenerated which then provide information on the desired physicochemical properties and mechanical resistance of the material. Several methods and techniques have been reported to produce *scaffolds*: gas foaming [118], fibre meshes sintering [119], solvent casting [120], polymerisation in solution [101, 121, 122], porogen leaching method [123, 124], freeze-drying methods [125, 126], electrospinning [127], 3D printing [128], 3D bioplotting of scaffold and cells [129], etc. For instance, acrylic scaffolds with interconnected spherical pores and controlled hydrophilicity were synthesised using a template of sintered PMMA microspheres of controlled size. In these scaffolds, their pore size, their connectivity, their porosity and their physicochemical properties could be tailored in an independent way by copolymerization of hydrophobic ethyl acrylate and hydrophilic hydroxyethyl methacrylate comonomers [124]. Four types of novel porous scaffolds of gelatin-PHEMA scaffolds were prepared with modulated architecture by freeze-drying technique and assessed by SEM and μ-CT. In this

study, it is of note that the covalently bound gelatin sequences significantly enhanced the biocompatibility of the PHEMA-based hydrogels, which is very desirable for tissue engineering applications. Superporous acrylic scaffolds can be also prepared by the salt-leaching method using NaCl or $(NH4)_2SO_4$ as a porogen agent [130] or with many other porogenic compounds such as ammonium oxalate crystals [131]. Carbon dioxide (CO_2) subjected to supercritical conditions (P = 160–260 bar, T = 60°C) with rapid depressurization methods have also yielded porous architectures that are related to the supercritical parameters and polymer blend composition [132]. Scaffolds fabricated with CO_2 to create such porosity have received much attention in the past. Thus, highly porous (porosity greater than 85%) and well-interconnected scaffolds were reported in blends of poly(ethyl methacrylate) and tetrahydrofurfuryl methacrylate (PEMA/THFMA) showing promise for bioengineering applications in cartilage repair [133]. However, CO_2 processing of polymers can lead to porous scaffolds with limited interconnectivity between the pores. Other sophisticated techniques to produce highly porous supports are electrospinning, 3D printing and bioprinting. Thus, the electrospinning set-up consists of a high-voltage DC power supply, an infusion pumps and a syringe with a needle tip of usually 0.5 mm diameter. Thus, for example, biodegradable nanofibrous poly(L-lactic acid) (PLLA) scaffolds were fabricated in this method for tissue regeneration application [134]. 3D printing promises to produce reproducible complex biomedical devices with the help of computer design using patient-specific anatomical information. 3D printing has slowly evolved to produce one-of-a-kind devices, implants, scaffolds for tissue engineering and drug delivery systems among many other important uses. Nevertheless, 3D printing has still to overcome technical printing aspects such as the type of commercially printable materials available and the current slow speed of printing. The most common 3D printing technologies includes 3D printing, fused deposition modelling, selective laser sintering, stereolithography, and 3D plotting/direct-write/bioprinting and are still under research for their progress in tissue engineering. Bioprinting is currently considered the most advanced 3D printing technology because cells combined with custom 3D scaffolds are 3D printed for personalised regenerative medicine [128, 135, 136]. Mechanical resistance of scaffolds for tissue engineering applications depends on the material properties and on the interconnected pore morphology of the scaffold. This problem is more relevant in the case of porous acrylic hydrogels, which exhibit very weak mechanical performance in hydrated state [101]. Therefore, these porous structures often need to be reinforced. For example, hydrophilic scaffolds poly(2-hydroxyethyl acrylate) were reinforced in the form of nanocomposites with silica [9]. In addition, the silica phase of the scaffold was effectively interconnected and continuous, able to withstand pyrolysis without losing the pore architecture of the scaffold. Superporous scaffolds of PHEMA with cholesterol methacrylate (CHLMA) and laminin were developed in the presence of ammonium oxalate crystals to introduce interconnected superpores in the matrix that promoted cell-surface interaction [137]. PHEMA scaffolds have also been functionalized with laminin-derived Ac-CGGASIKVAVS-OH peptide sequences to promote cell adhesion and neural differentiation. With the same aim, nanofiber scaffolds produced by electrospinning were treated with oxygen plasma and then simultaneously in situ grafted with hydrophilic acrylic acid to obtain PLLA-g-PAA with a modified surface, which significantly enhanced cell adhesion and proliferation [134]. 3D microenvironment comprising fibronectin-coated PMMA/PC-based multicomponent polymeric systems has recently promoted the differentiation of primary human osteoblasts, which hereby renders a promising tool for tissue specific in vitro preconditioning of osteoblasts designated for clinically oriented bone augmentation or regeneration. In addition, morphogenesis

and fluorescence dye-based live/dead staining revealed homogenous cell coverage of the microcavities. Nevertheless, azur II staining demonstrated formation of uniform sized multilayered aggregates, which exhibited progressive intracellular deposition of extracellular bone matrix constituents (fibronectin, osteocalcin and osteonectin) from day 7 on, and cells showed high viability up to 14 days [138]. Polymers based on an acrylate derivative of poly(ethylene glycol) (PEG) are currently being explored for applications in regenerative medicine. PEG is a hydrophilic, biocompatible and inert polymer that can be modified easily to alter the properties and manipulate both physical and biological properties. Acrylate derivatives such as poly(ethylene glycol) diacrylate and others are being explored to mimic native tissue environments [139]. Polysaccharide-based hydrogels have become increasingly studied as matrices in soft tissue engineering due to their known cytocompatibility [140]. Thus, for instance, cross-linkable dextran methacrylates and hyaluronan methacrylate hydrogel matrices have been proposed as excellent candidates for soft tissue reconstruction and have shown that their in vitro degradation behaviour can be controlled by the polysaccharide structure and the cross-linking density. In addition, under in vitro conditions, these biomaterials had no cytotoxic effects against fibroblasts, and the use of composite gels enhanced the adherence of cells [141]. Even though great advances are achieved in scaffold design of acrylic-based biomaterials, more research need to be carried out still in order to find new successful strategies capable of providing suitable advanced porous supports for tissue engineering applications.

8. Conclusions

Acrylic-based polymers possess versatile properties suitable for biomedical and bioengineering applications such as ophthalmology, orthopaedics, dentistry and tissue engineering. Nevertheless, the potential applications of this kind of polymers could be expanded exponentially if their chemical, physical and biological properties could be enhanced. In this regard, in the last few decades, acrylic-based materials have been produced in the form of interpenetrating polymer networks, composites with added particles such as fibres and nanocomposites with incorporated nanomaterials such as graphenes, in order to improve their mechanical, electrical, thermal, water sorption/diffusion, biological, antimicrobial and porosity properties, required for certain advanced applications. In addition, acrylic scaffolds have been fabricated with the suitable morphology for tissue regeneration by advanced fabrication methods. Nevertheless, in spite of the fabulous advancements presented in this chapter, many challenges still remain to tailor the properties of acrylate polymers for specific applications in the fields of biomedicine and bioengineering.

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Author details

Ángel Serrano-Aroca[1*] and Sanjukta Deb[2]

1 Biomaterials and Bioengineering Lab, Centro de Investigación Traslacional San Alberto Magno, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain

2 Faculty of Dentistry, Oral and Craniofacial Sciences, King's College London, Guy's Hospital, London, UK

*Address all correspondence to: angel.serrano@ucv.es

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