

## New Insights to Bioadhesive-based Biomaterials for Biomedical Applications

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Biomaterials are non-viable materials which are envisioned to interrelate with the biological systems. Nowadays, biomaterials are crucial to medicine because they help to recover patients from illness or damage by restoring function and accelerating the healing process. In medical applications, biomaterials can be either natural or synthetic and are utilized to sustain, improve, or replace damaged tissue or a biological function. On a different note, bioadhesion may be defined as the binding of a natural or synthetic polymer or biological-origin adhesive to a biological substrate. Taken together, the combination of bioadhesive with biomaterials has been used in many different medical specialties. The applications of biomaterials composed of adhesive polymeric preparations have been manifested in the field of drug delivery system, cardiac tissue engineering, skin tissue engineering, corneal tissue engineering, bone tissue engineering, and cartilage tissue engineering [1]. Polymer adhesion is ubiquitous in both the natural world and human technology. For the past 30 years, bioadhesives have changed surgery with increasing significance and rapid progress. The market share for adhesives and sealants is approximately \$38 billion due to the increased interest in their production [2]. Bioadhesives have less potential to harm tissues than conventional invasive wound closure techniques like sutures, wires, and staples, and they can hasten wound healing through a variety of ways. The bioadhesives, for instance, have antioxidant, anti-inflammatory, and antibacterial effects [3,4]. The simplicity of use of bioadhesives is considerably increased by additional characteristics like biodegradable, biocompatibility, increased adherence time, self-healing and injectability [5]. Typically, tape-

like bioadhesives with high cohesion strength are utilized as surface adhesives. The mechanism of adhesion includes cross-linking, entanglement, network topology, molecular bonding, fracture or debonding with the biological surface or substrate where hydrogen bond donor and an acceptor must be in contact within 0.5 nm from each other with a specific orientation in order to establish interaction (Figure 1) [6].

**Figure 1:** Diagrammatic representation of the internal composition of an adhesive polymer film between two solid surfaces, highlighting molecular characteristics important for surface force generation. Figure reprinted with permission from [6].

The challenge of how to apply smart biomedical equipment on/in the body using non-invasive techniques without harming the tissues or the medical devices has arisen with the advent of wearable devices, implantable detectors, or sensors; to which the bioadhesive is a good answer to this problem. The recent studies have shown the application of electronics with bioadhesive

properties which have proven to monitor health with comfort and ease can also be applied on the soft, curvilinear, and dynamic human skin [7]. It is known that biological skin is soft, flexible, twistable, and stretchable with low modulus of 140-160 kPa and an elastic tensile strain of 153-% [8,9]. For soft electronics, which should have similar mechanical properties to the skin, robust and conformal contact with the skin's surface is necessary. To this end, the mountable adhesive electronics meets the similar mechanical properties to that of skin. Temperature sensors, pressure sensors, electrophysiological sensors, sweat sensors, pulse oximeters, and ultra-thin imperceptible multifunctional HMI device based adhesive devices among others has been reported [9]. Several muco-adhesive based hydrogel have been reported that binds with ease to squamous cell carcinoma tumor cells which resulted in the reduced tumor burden and enhanced survival [10]. Also, mesenchymal stem cells were loaded using alginate-based photocrosslinkable bioadhesives. It was found that the peri-implant bone loss caused by the failing dental implants was completely reversed by the cell-loaded adhesive method [11].

Millions of people worldwide suffer from inflammatory issues, bone and joint deterioration, and other related conditions. These problems frequently need surgery and replacement. Orthopedic biomaterials are substances created to replace or repair different tissues, including cartilage and bone. The two generations of biomaterials have been broadly and conspicuously categorized as bioinert materials (first generation) and bioactive or biodegradable materials (second generation) [12,13]. The first generation includes polymers such as polyethylene, polymethyl methacrylate (PMMA), polypropylene, silicone, and polyurethanes whereas second generation includes polyglycolide (PGA), polylactide (PLA), polydioxanone (PDS), polycaprolactone (PCL), polyhydroxy butyrate (PHB), polyorthoester, poly (2-hydroethylmethacrylate) (PHEMA), and hyaluronic acid among others [14]. Each generation of biomaterials has a unique functionality that is designed with applications in mind.

Over the decades, polymers like carbopol, chitosan, dopamine, gelatin or methacrylated gelatin (GelMA), carboxymethyl chitosan, alginate, polyvinyl alcohol (PVA), poly (acrylic acid) (PAA), N-hydroxy succinate (NHS) ester, Poly (lactic-co-glycolic acid) (PLGA), and xanthan gum among others with various bioadhesive

including pressure-sensitive Durotak or Bioglue® have been used in the area of mucous or transdermal applications for the targeted drug delivery and wound closure or sealing of the tissues prone to bleeding resulting from trauma and surgical process [15-20] (Figure 2).

**Figure 2.** Schematic representation of skin wound (a) and application of bioadhesive within (b) or on the surface of the skin wound (c).

Taken together, we understand the implications of bioadhesion of biomaterials for redefining healthcare management as a novel approach. The studies on bioadhesive are performed at a micro level or at nano level for the preparation of molecularly smooth patches, films, hydrogels or medical electronics and devices for healthcare benefits. However, it is necessary to continue the research in this area to obtain a better understanding about the adhesive interactions beyond hydrogen bonding, including mechanical interlocking, interpenetrating networks, and covalent linkages, on a fundamental level to improve the interfacial properties of thermoplastics, thermosets, and biopolymers. Bioadhesives are currently expanding into new ones, including tissue sealing and directed drug delivery systems. We envisage that the future direction of the bioadhesive polymeric biomaterials should pave a path towards successful clinical implications and with the availability of developed bioadhesive products in the markets.

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### Conflict of Interest

The authors declare that they have no known competing financial interests or personal interests that could have appeared to influence the work reported in this paper.

### Informed Consent

N/A.

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