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# Adhesives: Applications and Recent Advances

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## Abstract

Adhesives can be defined as social substances capable to join permanently to surfaces, by an adhesive process. This process involves two dissimilar bodies being held in intimate contact such that mechanical force or work can be transferred across the interface. Since their early discovery by the Egyptians—3300 years ago—intensive research efforts have been made with the purpose of obtaining high-quality, biocompatible adhesives. Bitumen, tree pitches and beeswax—used in ancient and mediaeval times—were replaced by rubber cements and natural and synthetic components; nowadays, the focus is being mostly on eco-friendly adhesives. Starting with a brief history of adhesive use, this chapter then proceeds to cover the main industrial, biomedical and pharmaceutical applications of adhesives. Additionally, we focus on the new generation of adhesives, based on modern technologies such as nanotechnology, derivatised polymers, and biomimetic adhesives. The limited raw materials and the negative impact of synthetic adhesives on both human health and environment impose that further research is conducted with regard to renewable materials, in order to obtain environmentally safe bioadhesives that best fit their applicability domains.

**Keywords:** industrial adhesives, bioadhesives, mucoadhesives, sealant, tissue

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## 1. Introduction

Adhesives are social substances and can be defined as a mixture in a liquid or semi-liquid state, capable to join permanently to surfaces, by an adhesive process. The word ‘adhesive’ can be used either as a noun or as an adjective, defining substances which tend to adhere or stick to other substances. Adhesion refers to the interaction of the adhesive surface with the substrate surface, and it involves two dissimilar bodies being held in intimate contact such that mechanical force or work can be transferred across the interface. Several theories that explain the adhesion process have been postulated, the forces involved in the process being van der Waals forces, chemical bonding, or electrostatic attraction. On the other hand, the

mechanical strength of the system depends not only on the interfacial forces but also on the mechanical properties of the interfacial area, as well as the two bulk phases [1, 2].

Adhesives were first mentioned in history 3300 years ago, when Egyptian carvings depicted the glueing of a piece of veneer to what appears to be plank of sycamore. In ancient and mediæval times, bitumen, tree pitches and beeswax were used as sealants and adhesives [3]. In the nineteenth century, rubber cements were introduced, but decisive advances in adhesive technology awaited the twentieth century, when natural adhesives have been improved and many synthetic components have been developed. Adhesives are essential components of shoes, automobiles, cartons, furniture and non-woven fabrics and a host of other products. The aerospace field was the first sector that promoted the use of adhesives in the aircraft manufacturing process; hence, the growth of the aircraft and aerospace industries has influenced adhesive technology in a great extent. The requirement to get a high degree of structural strength and a high resistance to fatigue promoted the development and production of high-performance adhesive materials, which found various domestic and industrial applications [3–5].

The raw materials used as adhesives are mainly polymeric materials, both natural and synthetic. Taking into consideration the costs, natural products (such as starch, dextrin, casein, naturally gums) are still important; however, synthetic ones have largely taken over the adhesive industry, both as modifiers of natural materials and, more importantly, as high-strength, moisture-resistant additives capable of being produced in many readily usable forms.

Among the key factors influencing the evolution of adhesives are globalisation, the maturity of technological processes and governmental regulations worldwide, militating for the usage of non-volatile adhesives, including epoxies, cyanoacrylates and urethanes, to the detriment of solvent-based adhesives [6].

Adhesives are also used in the healthcare sector, thus having broad applications in dentistry, medical and pharmaceutical field. Various modern adhesives are used in medicine and dentistry, in direct physiological interactive modes or to assemble thousands of medical devices. In the pharmaceutical field, the use of adhesives aims to design modern pharmaceutical systems, in order to optimise drug release rate, as well as targeted drug delivery. This favours a more efficient use of the pharmacological potential of the active substance, leading to an increased treatment efficiency, with the reduction of overall dosages and hence of the adverse reactions [7–9].

Nowadays, the focus is not only on the production of high-quality adhesives using modern technologies such as nanotechnology but also on the production of eco-friendly adhesives, named ‘green’ adhesives, for all domains of applicability [6, 10–12].

## **2. Adhesives for industrial applications**

Adhesives are designed for specific applications. Besides their role in the adhesion process, they can be used for other purposes, such as sealing agents, in order to eliminate the effect of self-loosening caused by dynamic loads, sealing of areas to prevent oxidation and corrosion, waterproofing, etc. Sealants can be used as electrical or thermal insulators, fire barriers and products for smoothing, filleting or flying. The materials that are used as sealants have lower

strength than those used as adhesives, because sealant formulations contain large amounts of inert filler material for cost reduction and gap filling purposes. Certain sealants, like adhesives, can be used to assemble parts, and many adhesives can be used to seal. The adhesives and sealants are mainly used to bond the following substrates: metals, plastics (thermosets and thermoplastics), composites, foams, elastomers, wood and wood products, glass and ceramics and sandwich and honeycomb structures [1–3, 5, 6].

The main areas using industrial adhesives are the following:

1. Construction: floor tile and continuous flooring installation, ceramic tile installation, countertop lamination, manufacture of prefabricated beams and trusses, carpet adhesives, flooring underlayment adhesives, installation of prefinished panels, joint cements, drywall lamination adhesives and covering installations.
2. Consumer adhesives: model and hobby supplies, decorative films, school and stationery products.
3. Packaging: carton-side seam and closures, composite bonding of disposable products, bags, labels, cups, cigarette and filter manufacture, speciality packages (cosmetics, toiletries), composite containers and tubes.
4. Tapes: packaging, industrial, surgical, masking, and consumer tapes.
5. Transportation: auto, truck and bus assemblies, weatherstrip and gasket bonding, aircraft and aerospace structural assemblies.
6. Other rigid bondings: shake-proof fastening; furniture manufacture; manufacture of millwork, doors, kitchen cabinets and vanitories; appliance assembly and trim attachment; TV, radio and electronics assembly and machinery manufacture and assembly.
7. Other non-rigid bondings: apparel laminates, shoe assembly, sports equipment, book binding, rug backing, flock cements, air and liquid filter manufacture, etc. [1].

The main adhesives for industrial applications are summarised in **Table 1**.

Adhesive type	Applications	Refs.
<b>Natural</b>		
Animal source: albumin, animal glue, casein, shellac, beeswax	Wood industry Food industry	[13]
Vegetable source: Natural resins: gum arabic, tragacanth, colophony	Paper, paperboard, light wood, cork	[14]
Oils and waxes: carnauba wax, different oils	Sealants in wood and metal industry	[15]
Proteins: soybean Carbohydrates: starch, dextrin	Wood industry Paper industry	[10, 15]
Mineral: Inorganic minerals: silicates, magnesia, phosphates, sulphur Mineral waxes: paraffin Mineral resins: amber	Wood industry	[1]

Adhesive type	Applications	Refs.
Bitumen: asphalt	Binder in roads, roofing and flooring, installation of asphalt tile, sealant	[16]
<b>Synthetic</b>		
<b>Elastomers:</b> Natural rubber and derivatives	Bonding paper, plastic, leather, shoe industry	[1]
Synthetic rubber: butyl, polyisobutylene, polybutadiene blends, polyisoprenes, polychloroprene, polyurethane, silicone, polysulfide, polyolefins	Bonding rubber to itself and plastic materials or metals; forms good bonding with most plastic films, glass, wood Some of them are sealants	[17, 18]
Reclaimed rubber	Bonding paper, rubber, plastic and ceramic tile, adhesive for electrical installations	[1]
Neoprene rubber	Bonding weather stripping and fibrous soundproofing materials to metal Sealant	[1]
Nitrile rubber	Bonding plastic films to metals and fibrous materials and nylon to nylon and other materials Sealant	[19]
<b>Thermoplastics:</b>		
Cellulose derivatives: acetate, acetate-butyrate, caprate, nitrate, methyl cellulose, hydroxyl ethyl cellulose, ethyl cellulose, carboxymethyl cellulose	Bonding non-metallic material: wood, leather, plastic, paper Used in packaging	[10, 20]
Polyacrylates: methacrylate and acrylate polymers, cyanoacrylates	Generally, adhesives for metals, some of them for plastic; thread lockers, thread sealants, retaining compounds, gasket Electronics, toys, cosmetic packaging, automotive sealants Bonds only to non-porous materials Glass industry	[16, 21]
Anaerobic: based on synthetic resins (acrylates)	Secure, seal and retain machined, threaded or similarly close-fitting parts	[22–24]
Polyesters (saturated): polystyrene, polyamides	Sealants for potting, moulding and encapsulating	[1]
Vinyl polymers and copolymers: polyvinyl acetate, polyvinyl alcohol, polyvinyl chloride, polyvinylidene chloride	Bond porous materials Paper, wood and general packaging applications	[1]
<b>Thermosettings</b>		
Amino plastics: urea and melamine formaldehydes	Wood industry	[15]
Epoxies: epoxy polyamide, epoxy bitumen, epoxy polysulfide, epoxy nylon	Ability to bond many substrates Sealants in constructions, electricity	[25]
Phenolic resins and derivatives: phenol and resorcinol, formaldehydes, phenolic nitrile, phenolic neoprene, phenolic epoxy	Wood industry Metal industry	[26, 27]

**Table 1.** Industrial applications of the main adhesives (adapted from ref. [1]).

### 3. Adhesives for biomedical and pharmaceutical applications

The use of adhesives in the medical field has been restricted for a certain while, to the production of self-adhesive strips or plasters. The first reported pressure-sensitive adhesive used in the composition of bandage materials was natural rubber, followed by synthetic rubber, and, lastly, polyacrylic acid ester-based adhesives gained significance nowadays. Various medical adhesive tapes/dressings/devices are used to cover and protect wounds, to seal the skin edges of a wound or to support an injured part of the body [28, 29]. Advanced adhesives have a wide range of biomedical and pharmaceutical applications and are currently used in various medical procedures, as medical devices: restorative dental fillings, blood transfusions, anaesthetic administration, intravenous drug delivery, heart bypass surgery, urological surgery and plastic surgery (Table 2) [7, 30–33].

Adhesive type	Applications	Refs.
<b>Natural or biological</b>		
Albumin	Haemostat in vascular and cardiac surgeries	[64, 76]
Alginate	Binds the tissue, even after exposure to an aqueous environment Adhesive, pharmaceutical excipient: stabilising agent, tablet and capsule disintegrant, tablet binder	[76, 77]
Chitosan-based adhesives	Bioadhesives, antibacterial, haemostatics, wound-closing agents Pharmaceutical excipient: bioadhesives coating agents, disintegrants, film-forming agents, tablet binders	[64, 76, 78]
Collagen-based adhesives	Haemostatics for general and vascular surgeries, retroperitoneal injuries, sealants (clot formation), wound dressing	[64]
Chondroitin sulphate glue	Bonds the native cartilage tissue, wound-closing agent Bonds implants, seals corneal incisions	[67, 79]
Fibrin-based adhesives	Haemostatics, sealants (clot formation), wound-closing agents	[32, 80]
Gelatine and gelatine-based products	Haemostatics in various surgical procedures and anatomical sites (clot formation), sealants, adhesives	[64, 65]
Hyaluronate sodium	Bioadhesive, sealant Plastical surgery Pharmaceutical excipient: humectant, lubricant, matrix for sustained release	[81–83]
<b>Synthetic and semisynthetic</b>		
Cyanoacrylates	Tissue adhesives in surgical procedures: vascular surgery, urology, cosmetic surgery, skin graft fixation Fistula repair, closure of hernia incisions Endoscopic, laparoscopic and interventional radiology procedures Sealants in dentistry Disposable plastic medical devices Transdermal patches	[33, 69, 71, 84]

Adhesive type	Applications	Refs.
Dendrimers	Studied as sealant agents in corneal incisions	[28, 67]
<b>Polymers and their hydrogels</b>		
PEG-based adhesives	Sealants in gynaecologic and colorectal procedures Sealing of fluid leaks, acute aortic dissection, haemostasis in anastomotic bleeding wound closure Bone fixation, sealant for vascular graft, haemostatic, wound-closing agent	[67, 75, 79]
Carbomer	Bioadhesive Pharmaceutical excipient: release-modifying agent, tablet binder, viscosity-increasing agent, suspending agent, tablet binder	[37, 58]
Polycarbophil	Bioadhesive Pharmaceutical excipient: absorbent, controlled-release tablet binder, emulsifying agent, thickening agent, suspending agent	[58, 85]
Polyethylene oxides and derivatives	Bioadhesive, surgical tissue adhesive Pharmaceutical excipient: tablet binder, thickening agent	[58, 86]
Poly(methyl vinyl ether/maleic anhydride)	Bioadhesive Pharmaceutical excipient: colour dispersant, complexing agent, film former, emulsion stabiliser, viscosity-increasing agent	[58]
Povidone	Bioadhesive Pharmaceutical excipient: disintegrant, tablet binder	[58]
Urethane-based	Sealant, tissue adhesive Fixation of vascular graft and bone Cosmetic surgery Preventing seroma formation in abdominoplasty	[67, 87]
<b>Nano-enabled adhesive materials</b>		
Polar lipids: glyceryl monooleate	Bioadhesive, pharmaceutical excipient Nano-vehicle for many active substances	[60–62]
Nanoparticles (based on different components)	Bioadhesives Antibacterial properties Wound-closing agents	[64, 87, 88]
<b>Biomimetic adhesives</b>		
Marine mussel extract adhesives	Bioadhesives, repairing gestational fatal membrane ruptures Islet transplantation at extrahepatic sites Prosthetic mesh fixation Some derivatives: haemostatic and wound-closing agents	[31, 33, 89]
Gecko-inspired adhesives	Wound sealing, suture and staple replacement Suture/staple replacement/supplements Waterproof sealant for hollow organ anastomoses and for prevention of air leaks in lung resection Haemostatic, wound dressing, mesh grafts (ulcers, hernias, burns)	[33, 64]

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Adapted from [28, 58, 64, 67, 76]

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**Table 2.** Summary of the representative adhesives with biomedical and pharmaceutical applications.

When an adhesive comes in contact with a biological tissue, it is named 'bioadhesive'. Bioadhesion is the capacity of a compound to adhere to the biologic substrate for a long time. When the biologic substrate is represented by a mucosa, the phenomenon is called mucoadhesion. The mucoadhesive materials interact with the glycoproteins in the mucus covering the epithelia of the mucosae. The generally accepted idea is that the mucoadhesion process involves several stages: wetting and swelling of the hydrophilic polymer which allows its contact with the biologic tissue and the interpenetration of the polymer chain with the molecules in the mucin, which leads to an adequate interpenetration of the substrate and creates a semi-permanent adhesive bonding. Other theories explain the forces that underpin bioadhesion: van der Waals forces, hydrogen bondings, disulphide bridges, hydration forces, hydrophobic interactions, steric forces, covalent bonds, etc. [34, 35].

Bioadhesive drug delivery systems are promising systems for delivery of numerous and various active substances, from common ones to prebiotics [36], herbal products [37] and proteins [38]. They present themselves as solids, semisolids and liquids (gels, films, tablets, etc.) in conventional formulations or as nanoparticulated systems, designed for various routes like oral route [39, 40], skin route [41, 42] or mucosal route (buccal [43], ocular [44], vaginal [45], nasal [46], oesophageal [47]). The use of nanoparticulate bioadhesive systems can substantially improve the absorption of the active substances while offering protection against certain factors. Moreover, nanoparticulate bioadhesive systems represent potential targeted protein delivery systems [48].

Testing of the mucoadhesion represents a very important objective during the development of bioadhesive systems for drug release, as it can reveal the compatibility with the other components of the system, their stability and the strength of the adhesion capacity. Most methods used for the control of the mucoadhesive capacity of drug systems cited in the literature are based on the measurement of the force required to the disruption of the adhesive bond between the model membrane and the adhesive material [49].

The main excipients of a bioadhesive system are represented by bioadhesive polymers and their structural and functional characteristics having a decisive influence on the bioadhesion. These polymers are hydrophilic matrices consisting of a reticular network that swell in contact with water without being dissolved. The polymeric materials are available in a wide variety of molecular weights and compositions which adsorb the water, swell and generate a gel structure (hydrogel). These swollen gels act as a reservoir and ensure a prolonged release of the active substances dispersed in the meshes of the polymeric network. After swelling, a relaxation of the network chains takes place, and the incorporated drug substances are released through the spaces inside the network. The property to control the release rate of the biologically active substance, the bioadhesive performance and the nontoxic profile of the polymer are primordial criteria for the selection of a bioadhesive agent used in the designing of controlled drug release systems. The hydrogel-forming polymers used for the preparation of mucoadhesive systems are represented mainly by polyacrylates (Carbopol and polycarbo-phil), polyethylene oxide, polyvinyl alcohol, poly(*N*-acryloylpyrrolidine), reticulated gelatin, sodium alginate, natural gums (guar, xanthan, karaya), cellulose ethers, etc. [34, 35]. The polymer only plays the role of a vector or a host matrix, and it should have as neutral behaviour as

possible towards the active drug substance. The polymer-drug system must be chosen in such a way as to avoid chemical reactions between components, which may lead to the degradation of the active substance. The existence of possible interactions between the host polymer matrix and the drug can be tested at an atomic and molecular scale through well-known techniques such as differential scanning calorimetry (DSC) and spectroscopic methods such as Fourier transform infrared spectroscopy (FTIR), X-ray diffraction, electron spin resonance (ESR) spectroscopy, nuclear magnetic resonance (NMR) spectroscopy, Raman spectroscopy and others [50–52].

Different hydrogels can be combined together or with other components, obtaining derivatised polymers, with the purpose of improving their jellifying and adhesion properties [42, 53–55]. An innovative approach in the synthesis of hydrogels aims at the improvement of their mechanic properties. This can be achieved by grafting various functional groupings that allow self-assembling in aggregates or triblocks polymers (Ploxamers) that can change their consistency in the presence of certain stimuli (pH, temperature, etc.). Heat-sensitive polymers are of particular interest as drug vehicles, as they allow the preparation of formulations with a lower consistency and are easy to apply and develop a good contact in the presence of physiological medium, by forming *in situ* gels [47, 56, 57].

Besides their role as adhesives, bioadhesive polymers can also fulfil other functions in a pharmaceutical system: diluent, disintegrant, viscosity enhancer, etc. Their nature, quantity and association with other excipients highly influence the final drug product quality [58].

Bioadhesive polymers are used in many medical devices and drug delivery systems, including transdermal patches. Transdermal patch technology is another application of biomedical adhesives, ensuring drug delivery to the bloodstream through the skin; this is a highly effective method of drug administration, as the drug is incorporated into a membrane (made of adhesive) that sticks the patch to the skin and controls the rate at which the drug is absorbed. These systems ensure that the drug is continuously administered throughout the day, avoiding the fluctuations of the plasmatic concentration, usually associated with orally administered drugs. The applications of patches include hormone replacement therapy, pain cessation, smoke cessation and treatment of various cardiovascular pathologies [30, 59].

An alternative for polymeric materials with bioadhesive properties is polar lipids (e.g. glyceryl monooleate). Polar lipids are water-insoluble amphiphilic molecules that swell when in contact with water, associate and form various types of aggregates (spheric, hexagonal micelle, lamellar phase, cubic phase). The cubic crystalline phase has the aspect of a transparent, rigid, viscous gel with good mucoadhesive characteristics and can incorporate hydrophilic, amphiphilic as well as lipophilic drug substances. These bioadhesive properties make it an *in situ* forming biodegradable matrix, thus a potential nanostructured vehicle for prolonged drug release. Cubosomes represent a dispersion of the cubic crystalline phase (similar to liposomes which represent the dispersed lamellar crystalline phase). They are submicronic particles and present unique properties as they can incorporate drug substances with various polarities and molecular masses (rifampicin, carbamazepine, griseofulvin, coenzyme Q10, lycopene, phytosterols, sodium diclofenac, etc.). Some studies revealed that cubic-phase dispersions can maintain high plasma oligopeptide levels for several hours and favour insulin absorption through the nasal mucosa in rats. Moreover, cubosomes lower the rate of enzymatic degradation of the oligopeptides (insulin,



somatostatin) and enzymes. Multiple possibilities of using cubosomes as drug vehicles for various routes of administration (oral, parenteral, cutaneous or mucosae: nasal, ophthalmic, vaginal, buccal, periodontal pocket) have been reported so far in literature [60–63].

Wound closure is a key step in the success of surgical procedures. Surgical adhesives represent a convenient method for wound closing, having several advantages: less pain, no suture removal, excellent cosmetic result, and localized drug release [64]. A tissue adhesive can be defined as any substance with characteristics that allow in situ polymerisation to cause adherence of tissue to tissue or tissue to non-tissue surfaces. Their applications include prostheses, bleeding control (haemostats) and serving as a barrier to gas and liquids (sealants) [65]. Many tissue adhesives and haemostats have been developed over the past 30 years, based on various materials. The existing models are not sufficient for an in-depth study of the attachment of adhesives to living tissues; therefore, the strength of the adhesive joint is determined experimentally, according to standard tests and under conditions that are close to a real surgical situation. A bioadhesive must exhibit distinct characteristics, depending on the targeted tissue [66]. The successful usage of a tissue adhesive depends on its specific indications/limitations, which need to be thoroughly analysed by surgeons in order to choose the best product [67].

There are different commercially available tissue adhesives: natural or biological, synthetic, semisynthetic and biomimetic. The biomimetic action of adhesives is based on algae's abilities to wet a surface and the gecko's ability to 'adhere' on to surfaces. Surgical adhesives and sealants based on natural polymers offer a more biocompatible alternative to synthetic glues. The composition of a new bioadhesive material from fish parasite *Neobenedenia girellae* was recently reported, proteomic analysis revealing that the adhesive is mainly composed of cytoskeletal proteins such as actin, keratin and tubulin [28, 68].

Dental adhesives are intended to provide retention to composite fillings or composite cements. They can be defined as solutions of resin monomers (with both hydrophilic and hydrophobic groups) that make the resin-dental substrate interaction possible. Some of them are also used for their protective effect against enamel erosion. The failure of restorations occurs more often due to the inadequate sealing, with subsequent discoloration of the cavity margins, rather than loss of retention. Recent development of dental adhesives has greatly simplified the application procedure, as opposed to classical bonding agents (multistep systems), with the purpose of reducing technique sensitivity and manipulation time [69–74].

While older generation of mucoadhesive polymers lacks specificity and targeting capability, newer polymers—falling into the second generation of mucoadhesives—can form covalent bonds with the mucus and the underlying cell layers, thus exhibiting improved chemical interactions and offering new possibilities for more specific drug-receptor interactions. Examples of such new-generation adhesives are thiolated and lectin-mediated mucoadhesive polymers [75].

#### 4. Conclusions and perspectives

Adhesives have been used in industry for decades; however, the environmental influence of adhesives has not been investigated up until recently. Therefore, one must emphasise on the

necessity to develop steps that will allow obtaining environmentally safe and high-quality adhesives that best fit their applicability domains. Due to the limited raw materials (reserve of oil) and the negative impact of synthetic compounds on both human health and environment, natural and renewable resources represent an attractive alternative for the production of adhesives. One innovative alternative for synthetic reactive glues like cyanoacrylates is represented by gecko-inspired and marine-inspired bioadhesives (mussel proteins) or their combination; however, further research needs to be conducted in this direction. Taking into consideration the rapid development of bioadhesive market, more work needs to be done in both environmental and economic aspect.

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