

NOVEL APPLICATIONS OF BIOADHESIVES

Over 300 million surgical procedures are estimated to be performed globally each year and over 50 million surgical procedures are performed in the US¹. Once the surgery is completed, about 5 to 30% of patients may develop a surgical site infection and the probability of developing an infection depends on the invasiveness of the surgery and the site. Traditionally, surgical wounds are closed with staples, sutures, wires and other inorganic materials which may not seal the surgical site completely resulting in leakages, infections and inflammation². Additionally, these materials can also result in tissue damage thus prolonging recovery times. Bioadhesives are a viable alternative to inorganic staples and sutures and are natural and/or synthetic macromolecules that have intrinsic sticky properties and can adhere to tissues. Currently, some surgical bioadhesives that are poly ethylene glycol or PEG based are available commercially to prevent leakage after specific surgeries. For example, FocalSeal® is used to avoid air leakage during lung surgery while Coseal® is used to prevent the leakage of blood vessels. However, these adhesives address a specific application, which is wound closure to prevent leakage².

Bioadhesives typically fall into one of 3 types – derived from natural biomaterials, synthetic or a hybrid of natural and synthetic materials. Natural bioadhesives are commonly derived from fibrin, gelatin or polysaccharides. Essentially natural molecules that can polymerize efficiently can be investigated as bioadhesives and there is active research in developing the next-generation of natural bioadhesives with desired characteristics. For example, a recent paper highlighted the development of a natural bioadhesive that combined alpha-lipoic acid and tannic acid with ferric chloride to generate a supramolecular bioadhesives that had anti-bacterial properties³. Polyethylene glycol or PEG derived bioadhesives are likely the most broadly used synthetic bioadhesives. Cyanoacrylate and polyurethane are other examples of synthetic adhesives. Synthetic adhesives have challenges in binding to cells and tissues and can potentially trigger an inflammation reaction, but also have manufacturing advantages as the process can be controlled². The third class of bioadhesives are hybrids combining natural and synthetic adhesives. Biomimetics are a fast-growing class of bioadhesives that are synthetically engineered to have the characteristics of natural bioadhesives. Therefore, the development of biomimetics requires comprehensive characterization (structure, function and composition) of natural bioadhesives⁴.

Bioadhesives can be used for multiple applications including local drug delivery and immobilization of a specific area to promote healing. Since bioadhesives are typically polymers, they have the potential to deliver drugs in a controlled fashion to manage inflammation and prevent microbial infections at the surgical sites. Additionally, bioadhesives are a viable option to deliver protein or peptide therapeutics to difficult to access sites such as the GI tract. Bioadhesives carrying therapeutics can bind the surface of intestinal epithelial cells overcoming the mucus barrier⁵. Nanoparticles are being actively investigated as drug delivery devices but the challenge is that they are rapidly cleared by the lymphatic system, reducing the therapeutic window⁶. Recent research has shown that combining drug carrying nanoparticles with bioadhesives allows for easier administration and access to the tissue or organ of interest, while increasing retention due to the bioadhesive binding to the target tissue⁷.

Another area of active development is smart bioadhesives that combine wound closure and adhesion with sensors and real-time feedback. It is important to monitor the healing process in the wound area and typically wounds have to be monitored in a clinical setting that is done intermittently. Due to occasional monitoring, complications associated with healing may not be detected in time. However, the development of bioadhesives that cover the wound site and can monitor physiological and biochemical conditions such as moisture, pH, cytokine expressions will allow early detection of infection or complications⁸. The additional component of wireless transmission of data from the sensors makes it very convenient for patients, caregivers and clinicians to monitor wound healing in real time, potentially reducing healing time and improving the patient's quality of life⁸.

It is clear that bioadhesives have come a long way from traditional fibrin and gelatin materials and there is significant interest in leveraging bioadhesives for multiple applications, such as drug delivery and real-time monitoring.

References:

- ¹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7388795>
- ² <https://www.frontiersin.org/articles/10.3389/fbioe.2021.716035/full>
- ³ <https://pubs.acs.org/doi/10.1021/acscami.2c17415>
- ⁴ <https://www.sciencedirect.com/science/article/abs/pii/S0001868621001627>
- ⁵ <https://pubmed.ncbi.nlm.nih.gov/7600586>
- ⁶ <https://www.pnas.org/doi/10.1073/pnas.1523141113>
- ⁷ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8874699>
- ⁸ <https://www.sciencedirect.com/science/article/pii/S2452199X22001906>