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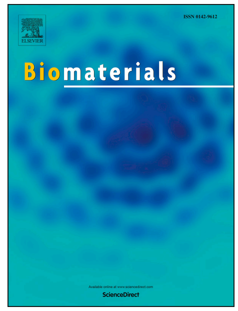

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Active Agents, Biomaterials, and Technologies to Improve Biolubrication and Strengthen Soft Tissues

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Abstract
Normal functioning of articulating tissues is required for many physiological processes occurring across length scales from the molecular to whole organism. Lubricating biopolymers are present natively on tissue surfaces at various sites of biological articulation, including eyelid, mouth, and synovial joints. The range of operating conditions at these disparate interfaces yields a variety of tribological mechanisms through which compressive and shear forces are dissipated to protect tissues from material wear and fatigue. This review focuses on recent advances in active agents and biomaterials for therapeutic augmentation of friction, lubrication, and wear in disease and injured states. Various small-molecule, biological, and gene delivery therapies are described, as are tribosupplementation with naturally-occurring and synthetic biolubricants and polymer reinforcements. While reintroduction of a diseased tissue's native lubricant received significant attention in the past, recent discoveries and pre-clinical research are capitalizing on concurrent advances in the molecular sciences and bioengineering fields, with an understanding of the underlying tissue structure and physiology, to afford a desired, and potentially patient-specific, tissue mechanical response for restoration of normal function. Small and large molecule drugs targeting recently elucidated pathways as well as synthetic and hybrid natural/synthetic biomaterials for restoring a desired tissue mechanical response are being investigated for treatment of, for example, keratoconjunctivitis sicca, xeroderma, and osteoarthritis.

Keywords: Biotribology, biolubrication, biomechanics, friction, polymers, biomaterials, osteoarthritis.

1. Introduction

The function of many mechanical, electromechanical, and biological systems depends on appropriate lubrication at the articulating interface. In general, one is most familiar with friction and wear on metal surfaces in applications such as engines, turbines, and pistons.[1,2] Our deepening understanding of frictional behavior has given rise to various strategies for modulating friction. Today, strategies exist to alter tribology,[ξ][3] including application of lubricants such as graphite, introduction of rolling rather than sliding components, e.g., ball bearings, and the use of acoustic energy to dissipate friction. Further, the articulating substrates themselves may be modified, e.g., by plasma treating, smoothing, or hardening, or by conjugating lubricious polymers to the substrate, e.g., Teflon® used to coat cookware (Figure 1).

Friction, lubrication, and wear on biological surfaces is, in our opinion, more interesting and challenging to study given that the articulating substrates are living substrates of compositionally complex mixtures that may be stiff, viscoelastic, compact, or porous and possess smooth or rough surfaces. Numerous bodily tissue interfaces require efficient biolubrication[ξ] for optimal physiological function, including diarthrodial joints[4–7] and mucosal membranes such as the eyelid, esophagus, intestine, and vagina (Figure 1). When function becomes impaired due to injury,

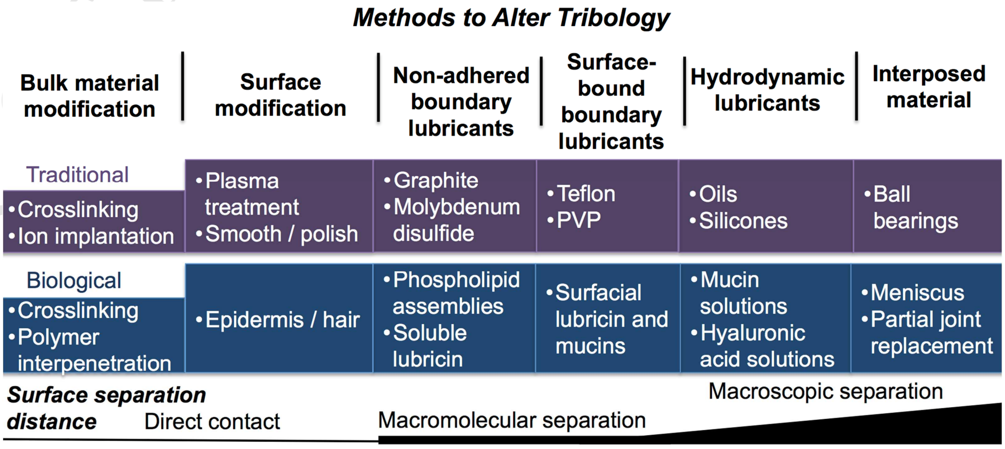

Figure 1. Methods to alter tribology at articulating surfaces and representative examples of traditional and biological approaches and materials.