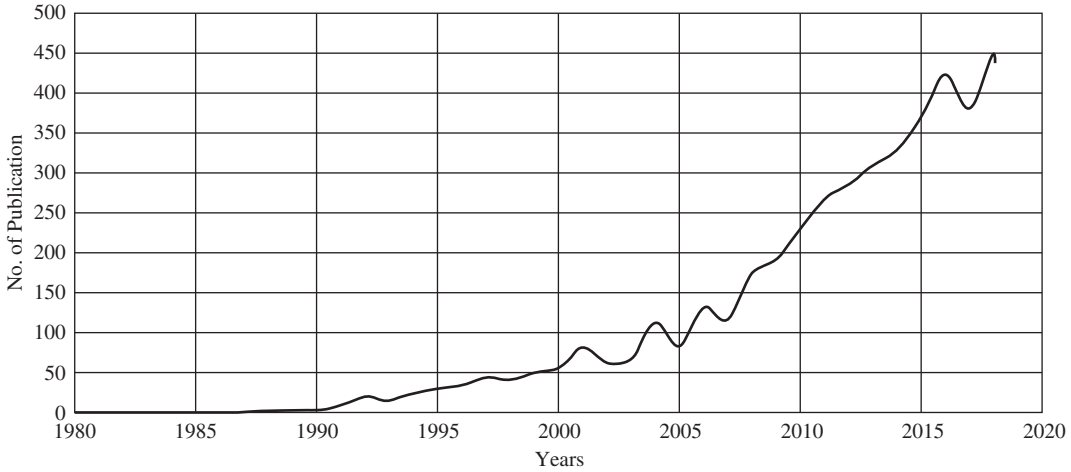

FIG. 1 Number of publications over the period of 40 years in the field of mucoadhesive drug delivery systems.

a slight positively charge and is therefore is attracted to other electronegative atoms present in the mucus.

Van der Waals bonds: These are some of the weakest forms of interaction that occurs between the mucoadhesive polymers and mucus due to dipole–dipole and dipole-induced dipole attractions between the polar molecules.

Covalent bonds: These are very strong forces formed by the polymers having functional groups that can share electrons pairs with the mucus substructures to form covalent bonds.

Moreover, to elaborate the process of adhesion of two surfaces, several theories have been proposed but none of these theories individually explains the mechanism of adhesion between polymers and mucus membrane.

3. MUCUS GEL LAYER

Mucus is a viscous gel layer produced from goblet cells, mucus secretory cells or submucosal glands found on various mucous membranes including eyes, gastrointestinal tract, urogenital tract, and respiratory tract. Beside water (95% by weight), mucus comprises lipids, fatty acids, phospholipids and cholesterol, and a glycoprotein, which is responsible for viscoelastic properties of the mucus and hence provides the mucus its unique features.

3.1. Mucins

Mucins are large, extracellular glycoproteins with molecular weights ranging from 0.5 to 20 MDa [5]. Mucin fibers are long flexible strings highly covered by glycans, possessing negative charge due to carboxyl or sulfate groups. Mucin consists of hydrophilic region which alternate with relatively hydrophobic region consisting of beads of coiled protein part rich in cysteine, stabilized by disulfide bonds [6].

At least 20 genes (MUC1, MUC2, MUC3A, MUC3B, MUC4, MUC5AC, MUC5B, MUC6, MUC7, MUC8, MUC12, MUC13, MUC15, MUC16, MUC17, MUC19, MUC20, MUC22 and MUC22) have been identified which are responsible for the production of respective types of mucins. Further, mucin is grouped as membrane bound and secreted gel forming secreted nongel forming. Their distribution in different parts of the body is listed in Table 1.

3.2. Production

The mucus glycoproteins are mainly synthesized and secreted from goblet cells present in mucosal layers. Within these goblet cells, the mucin precursors after N-glycosylation, dimerization, O-glycosylation, and sulfonation in various parts of endoplasmic reticulum and Golgi complex are stored in large secretory vesicles known as mucin granules. These mucin granules are extensively distributed in the cytoplasm of goblet cells. The constitutive mucin is secreted very slowly during the normal physiological condition however, some of physiological/pathological agents like cytokines/chemokines, bacterial exotoxins, nucleotides, neurotransmitters, and proteases can trigger Ca^{2+} regulated rapid discharge of mucin granules from goblet cells. This triggered secretion provides higher amounts of mucins