4.1.2. Tensile strength

The setup for measurement consists of a sensitive balance placed on a moveable stage. A stainless-steel disk is hung by a laboratory stand with nonelastic thread over the balance. A personal computer is connected to the balance to record the change in weight on regular intervals. For measurement, the intestinal mucosa is fixed to the glass tissue mount by cyanoacrylate adhesive and a compressed tablet is attached with the stainless-steel disk by the same glue. The fixed porcine tissue is immersed in buffer and placed on the balance. The balance is raised so that the tablet comes in contact with the intestinal mucosa and is incubated for 30 min. Later the balance is lowered at a constant speed, and the total work of mucus adhesion (TWA) and maximum detachment force (MDF) are determined [10]. With a slight modification, this technique can also be used to measure the mucoadhesion of gels and other semisolid dosage forms to intestinal mucosa and skin [11].

4.1.3. Atomic force microscopy

Atomic force microscopy is used mainly for the topology study of surfaces down to nanoscale. However, it can also be used to measure the elastic nature of the sample. In this technique, the polymeric microsphere is attached to the cantilever as a colloidal tip, and this tip is used to measure force distance between the polymer tip and the mucus surface on molecular scale. This kind of technique has been used in a study of adhesion of polyether-modified polyacrylic acid to mucin where polymer coated glass beads used as cantilever tip and the bovine mucus on a planar carrier to study mucoadhesion [12]. Later, Catron et al. used a polymer functionalized tip on the cantilever for mucoadhesion study [13]. However, functionalization is more complicated and there is an issue of reproducibility [14]. This technique is suitable for dosage forms that include microspheres, microparticles, and powders. Due to its high sensitivity, this technique requires small quantities for analysis and can be used at developmental and lab scale for the analysis of mucoadhesion.

4.2. Molecular Interaction Methods

4.2.1. Rheological methods

The interaction of mucoadhesive polymers with mucus changes the rheological properties of the mixture by forming a 3D gel structure. This change in structure alters the rheological properties of the mixtures which can be measured by a rheometer. For rheological study, mucus from an animal source or artificial mucus is incubated with the mucoadhesive polymer for 4 or more hours at 37°C. Later this mixture is studied for the change in its viscosity, elastic modulus, viscous modulus, and other rheological properties within linear viscoelastic range by use of rheometer [15, 16]. This technique is quantitative and can be used for gels, solutions, and other liquid dosage forms.

4.2.2. DSC thermograms

Differential scanning calorimetry (DSC) is a qualitative technique, which is used to measure the amount of heat required to increase the temperature of a substance as a function of temperature. DSC can be used to determine the kind of interaction between polymer and mucin. For example, Yin et al. mixed the dispersion of trimethyl chitosan-cysteine (TMC-cys) nanoparticles with mucin and incubated for 8 h at 37°C. Later lyophilized products of the incubated mixture and the physical mixture of mucin and TMC-cys were tested for DSC within 30–300°C, heating at a rate of 20°C/min shows the heat flow, giving an endothermic peak at 230°C due to melting of free mucin. Such a peak is absent in incubated samples, because of the formation of complex [17]. This is a qualitative technique and can be used for liquid and particulate dosage forms (Fig. 3). A small quantity of samples is needed to evaluate the mucoadhesive strength. This technique is mainly use for research purposes [18].

4.2.3. Ellipsometry

Ellipsometry is an optical technique to determine the dielectric properties of films. Ellipsometry is a more relevant for dissolved polymers. Ivarsson et al. used this technique for mucoadhesion study. They took methylated silica surface, placed in a 5 mL cuvette and stirred with the 0.1% mucin solution at 37°C to get an adsorbed mucin layer. After rinsing with buffer, the surface was stirred with 1% polymer solution and changes in properties of the film were measured for next 1 h. They used partial specific volumes, molar weights, and molar refractivity to calculate the adsorption of polymer to mucin [19]. It is a quantitative technique and can be applied to liquid dosage forms or polymer solutions [20].

4.2.4. Quartz crystal microbalance

A quartz crystal microbalance is a scale to measure very small quantity of mass (ng) by measuring the variation of the mass per unit area of the quartz crystals due to change in frequency of resonator. In this method, first mucin solution is added to the sample chamber to form a layer on the crystal. The mucin-coated crystal is then washed with the buffer to attain a stable frequency. Afterward the solution of the mucoadhesive polymer