properties, alginates are used in limited preparations due to the risk of dose dumping that this polymer poses. Alginate matrix is prone to cracking at lower pH (stomach), which may lead to burst release of the drug [41]. At lower pH, the predominant mechanism of drug release is through diffusion, given that the drug has high solubility at a given pH [31,42].

4.1.4. Carbomers

Carbomers are synthetic high molecular weight acrylic acid polymers. Acrylic acid monomers are crosslinked with allyl sucrose or allyl ethers of pentaerythritol depending upon the grade of carbomer [32]. Grade-934 is crosslinked with allyl sucrose, and Grade-71, 971, and 974 are crosslinked with allyl pentaerythritol [27]. Carbomers differ from all other hydrophilic polymers we have studied so far in almost all properties. Unlike other polymers, the gel formation is due to the formation of discrete macro gels and not due to polymer chain entanglement [43]. Furthermore, unlike other linear polymers, carbomers do not show erosion. Instead, the discrete macro gel particles remain intact, and the drug continuously diffuses out. The anomaly does not end there. Carbomers, with an increase in viscosity, do not show a decrease in release rate, whereas the ones with low viscosity (lightly crossed linked polymers) show more efficient release control. Carbomers are also pH dependent in terms of swelling. Carbomers can swell up to 1000 folds their original volume and 10 folds in diameter in pH range of 4–6, due to the repulsion between the carboxylate anions on the polymer [27].

4.2. Hydrophobic Polymers

Hydrophobic polymers are in use for controlled-release systems since 1959, when for the first time, a hydrophobic polymer was used for the preparation of controlled-release Premarin tablets [44]. For the preparation of controlled-release systems, the drugs can either be dispersed into inert matrices or be coated in an inert shell as a reservoir. In the case of matrix tablets, the release is retarded due to the fact that the dissolved drug has to diffuse through the narrow channels formed in the matrix. The release of the drug from these systems can follow several mechanisms such as permeation of bodily fluids into the matrix, diffusion of the drug through the matrix as stated earlier, and matrix erosion. The rate-controlling step in all these mechanisms is the permeation of fluids into the system. Because of the insolubility of certain polymers of this class, the delivery systems retain their dimensions and the diffusion path length [45].

The FDA has a long list of approved water-insoluble polymers in their database. Some of them are ethylcellulose (EC), cellulose acetate, cellulose acetate phthalate, polyvinyl acetate (PVA), zein, shellac, etc. A number of natural fats and waxes are also used, namely, beeswax, Carnauba wax, stearyl alcohol, hydrogenated oils, etc. A few of the most widely used hydrophobic polymers are discussed herewith.

4.2.1. Ethyl cellulose

EC is a nonswellable water-insoluble cellulose ether prepared by the reaction of ethyl chloride with alkali cellulose. EC is available in different grades based on the degree of ethoxy substitution ranging from 44% to 52.5%. With an increase in substitution, the hydrophobicity increases. The most remarkable property of this polymer is its flexibility over a temperature range of −70°C to its softening point (156°C). EC is employed in both matrix and reservoir systems. Drug release from EC nondisintegrating prolonged-release matrix tablets is either through pores formed due to dissolution of drug or by diffusion through the membrane, depending on the extent of dispersion of the drug in the matrix [27].

4.2.2. Cellulose acetate

Cellulose acetate is a biodegradable polymer known to be nonirritant, heat resistant, nontoxic, and relatively less hygroscopic in nature. Both partial and complete acetylated derivatives are available,that is all or only a portion of hydroxyl groups may be substituted with an acetyl group [46]. This results in mono-, di-, or tri-substituted cellulose derivatives with different solubility characteristics. The extent of acetyl substitution ranges from 29.0% to 44.8%. Cellulose acetate is mainly employed in osmotic pump-type systems because of its ability to form semipermeable membranes [47,48]; hence, it does not require drilling of a mechanical orifice. Another derivative of cellulose acetate called cellulose acetate butyrate (CAB) is also widely used in the preparation of matrix tablets. Drug release profiles from CAB matrices were reported to be slower than those from cellulose acetate matrices [32].

4.2.3. Polymethacrylates

Polymethacrylates are anionic or cationic esters of acrylic resins with varying functional properties based on the substituents [49]. More commonly known by one of their trade name, they are called Eudragits. Various types of polymethacrylates polymers with their structural difference and functional characteristics are commercially available for solid oral dosage forms. These polymers because of the ionic nature show pH-dependent release: hence, different parts of the GIT can be targeted. Also, they form complexes with some drugs due to the ionic nature of the polymer [50].