7.7. Mucoadhesive Microsphere

Microspheres in spite of their small size show higher drug-carrying capacity but exhibit a smaller residence time. This problem, however, was solved by the preparation of mucoadhesive microspheres which showed an increase in efficiency and residence time, making them suitable for extended-release of drugs [173]. Adebisi et al. prepared ethyl-cellulose/chitosan microspheres containing clarithromycin and functionalized their surfaces with concanavalin A to produce a floating-mucoadhesive formulation; later, they conjugated the microspheres with lectin which showed a higher degree of mucoadhesion [174]. In a rat in vivo studies Madgulkar et al. determined 3.22-fold increase in bioavailability, 1.9-fold increase in Cmax and 1 h increase in gastric residence time of thiolated xyloglucan microspheres in mice [175]. In a human in vivo study, the nasal clearance of chitosan microspheres was found to be 84 min against 64 min for starch microspheres [176]. Tafaghodi et al. found in human in vivo study that sodium alginate microspheres have clearance half-life of >2.5 h, as compared to control lactose microspheres [177].

7.8. Polymeric Micelles

Micelles are nanometric drug delivery systems that comprise amphiphilic polymer molecules, which have prominent hydrophobic and hydrophilic parts. When such a substance reaches a certain concentration in an aqueous phase, the critical micelle concentration, it forms spherical structures with a hydrophobic core. These spheres are able to accommodate hydrophobic drugs such as BCS class II and IV in the core [178]. Pluronic F127 decorated with acrylate moieties and *N*-isopropyl acrylamide on chitosan are examples of such mucoadhesive polymeric micelles [179, 180].

7.9. Polymer-Coated Liposomes

Liposomes have many advantages including the similarity with the biological membrane, entrapping ability of structurally diverse drugs and low toxicity [181]. In previous studies it has been reported that liposomal drug delivery systems significantly improve the membrane permeability and cellular absorption of highly hydrophilic drugs such as acyclovir and cefotaxime [182]. Klemetsrud et al. coated the liposomes with chitosan, low methoxylated pectin, high methoxylated pectin, amidated pectin, Eudragit, poly (*N*-isopropylacrylamide-*co*-methacrylic acid), and hydrophobically modified hydroxyethyl cellulose. They concluded that coating of liposomes with mucoadhesive polymers can be effective way of increasing the residence time for oro-mucosal drug delivery [183]. In an in vivo study, chitosan-coated liposomes increased the absorption of drug up to 3 folds as compared to noncoated liposomes [184].

7.10. Self-Emulsifying Drug Delivery System

SEDDS formulations are the preconcentrates that comprise a hydrophobic phase, surfactant. and co-surfactant. Upon adding to the aqueous phase, they immediately form thermodynamically stable emulsion. The diameter of the globule in more stable SEDDS, falls in the range of nanometers to micrometers. They are a robust tool for the delivery of hydrophobic drugs however, in recent years with the development of hydrophobic ion pairing, can also deliver hydrophilic macromolecular drugs such as proteins, peptides, and pDNA [185]. When SEDDS are added with mucoadhesive hydrophobic thiolated polymers, it renders them mucoadhesive and enhances the residence time of the SEDDS. For example, SEDDS loaded with entirely S-protected thiolated Eudragit L100–55 exhibited 2.5 folds more mucoadhesive than its corresponding blank SEDDS [186]. Similarly SEDDS loaded with pre-activated thiolated Pemulin TR-2 and pre-activated chitosan increased the residence time by 6 and 5.2 folds, respectively [187, 188].

8. MARKETED MUCOADHESIVE PRODUCTS

A number of mucoadhesive marketed products are discussed in Table 4 in detail providing information about the manufacturer as well.

9. FUTURE PERSPECTIVES OF MUCOADHESIVE DRUG DELIVERY SYSTEMS

Mucoadhesive drug delivery systems have a high potential of being providing controlled delivering of drugs to achieve maximum therapeutics effect. Current use of mucoadhesive polymers to increase contact time for a wide variety of drugs and routes of administration has shown dramatic improvement in bioavailability of the active agent by improving the residence time. The progress and achievements made since we have entered a new era of polymer chemistry 30 years ago has reshaped the field of drug delivery. The progress in developing covalent binding polymers such as thiolated polymers improves the understanding of mucoadhesion. The greatest challenges that we encounter are certainly the