Mucoadhesion for Enhanced Drug Delivery

Pawel Balcerzak¹ | Liliana Miinea² | Elena Draganoiu³

¹ Lubrizol Advanced Materials, Inc.; Chaussee De Wavre 1945 B-1160 Brussels, Belgium; email: pawel.balcerzak@lubrizol.com
² Lubrizol Advanced Materials, Inc.; 9911 Brecksville Road, Cleveland, OH 44141 USA; email: liliana.miinea@lubrizol.com
³ Lubrizol Canada Limited; 3700 Stelies Ave W, Vaughan Ontario, Canada L4L 8H8; email: elena.draganoiu@lubrizol.com

BACKGROUND

Mucoadhesion is a state where two materials (at least one of which is a mucous membrane) are held together for extended periods of time by interfacial forces (Figure 1).

Mucoadhesive dosage forms can be designed to ensure prolonged contact with mucosal membranes present in the human body (buccal, nasal, ophthalmic, intestinal, rectal, vaginal) providing increased efficacy, patient compliance and product differentiation (Figure 2).

The design of such formulations requires the use of an excipient that imparts mucoadhesive properties and ensures prolonged contact between the drug product and the mucosa. Polymers with mucoadhesive properties are hydrophilic molecules containing functional groups that can interact with the mucin glycoproteins via non-covalent bonds such as hydrogen bonds, van der Waals forces and ionic interactions. Examples include carbomers (e.g., Carbopol® polymers), xanthan gum, sodium carboxymethylcellulose (NaCMC), polyvinyl alcohol (PVA), and carrageenan.

OBJECTIVE

Compare the in-vitro mucoadhesive properties of various polymers in pharmaceutical formulations and their application in designing patient compliant dosage forms.

METHODS

In-vitro oesophageal retention model

Lubrizol Life Science Health has developed a method based on the in-vitro oesophageal retention (IVOR) model that allows for mucoadhesion evaluation in a dynamic environment. The dosage form is subjected to a continuous fluid flow during testing. The device is depicted in Figure 3.

RESULTS and DISCUSSIONS

Mucoadhesive properties of polymer semisolid formulations

The mucoadhesive properties of Carbopol® polymers were compared in viva with other materials, including xanthan gum, carrageenan, sodium carboxymethylcellulose (NaCMC), polyvinyl alcohol, and xanthan gum polyvinyl alcohol (XG/PVA). The mucoadhesive properties of the Carbopol® polymer solution were evaluated in the IVOR model to create a more in vivo-like environment. Compared to other materials, Carbopol® polymers provided the longest retention over time, with more than 20% retention on this substrate even after 240 minutes (Figure 5).

Preparation of cold/cough formulations containing Carbopol® polymers

Cold/cough liquid formulations were prepared by dissolving the acetaminophen, dextromethorphan and seabream, followed by mixing with dispersion of Carbopol® polymer. The inclusion levels of the mucoadhesive polymer in the formulations were 0.3, 0.5 and 1.0%.

Preparation of films containing Carbopol® polymers

Films formulations containing Carbopol® polymer and PVA 1/2 were prepared by solvent casting from aqueous/ethanolic gels. Typically, the Carbopol® polymer was dispersed at the desired concentration in an aqueous PVA solution and plasticizer mixture. The resulted dispersion was followed by neutralization to pH of ~7.0 according to recommended procedure.

CONCLUSION

The benefits of mucosal drug delivery over other routes are the following:

• Reduced drug side-effects
• Convenient (administration/removal)
• Localized – dosage form at site of action
• Improved drug efficacy, patient compliance and product differentiation

Mucoadhesion enhancement of films containing Carbopol® polymers

Polyvinyl alcohol is known in pharmaceutical formulations as a binder and film former. Numerous low molecular weight polymers have demonstrated mucoadhesive properties. The mucoadhesiveness of a film was influenced by Carbopol® polymer degree of neutralization, longer retention being observed in films containing Carbopol® 971P NF polymers with the lower degree of neutralization as expected. Lower films showed better retention. At neutralization, PVA/PVA containing Carbopol® 971P NF polymer showed longer retention when compared to carbopol/PVA films (Figure 6). After 120 minutes, the PVA 1/2 was almost entirely washed off, whereas the Carbopol polymer remained almost intact to a wash at 240 minutes (Figure 7).

The presence of Carbopol® polymers enhanced mucoadhesive properties of the films, offering flexibility of formulation.

REFERENCES


2 Lubrizol Advanced Materials, Inc.; Chaussee De Wavre 1945, B-1160 Brussels, Belgium; email: pawel.balcerzak@lubrizol.com

3 Lubrizol Advanced Materials, Inc., 9911 Brecksville Road, Cleveland, OH 44141 USA; email: liliana.miinea@lubrizol.com