



# Mucoadhesion Guide:

## Mucoadhesion 101

Why mucoadhesion matters and how it can add value to your pharma product.

# The ability for a pharmaceutical formulation to adhere to mucous membranes within the body – known as “mucoadhesion” – can have a significant impact on a drug’s performance.

By ensuring the active ingredient remains at the target site for longer, mucoadhesion can bring benefits to formulators and help improve the patient experience. To achieve the appropriate mucoadhesive performance, the choice of polymer excipient for a formulation is key.

In this guide, we will explore what mucoadhesion is, the benefits it can bring to formulators and patients, and the role of polymers in achieving mucoadhesive properties.

- **Section 1: What is mucoadhesion?**
- **Section 2: The benefits for your formulation**
- **Section 3: How to achieve mucoadhesion & initial formulation considerations**
- **Conclusion**

## Section 1: What is mucoadhesion?

Mucoadhesion is a specific type of bioadhesion in which two materials are held together for extended periods by interfacial forces. In the case of mucoadhesion, at least one of the materials in question is mucus or a mucous membrane.

A mucous membrane is an epithelial tissue which secretes mucus, and lines many body cavities and organs. Examples include the gastrointestinal tract (GI tract), vagina, and rectum.

Mucous membranes serve protective and lubricating roles, keeping underlying tissues moist. They are hydrophilic and contain glycoproteins, both of which make mucoadhesion possible.

Multiple factors influence the extent, strength, and duration of mucoadhesion for a drug product:

- **Mucus properties** – these can affect the strength of the adhesion
- **Dosage form characteristics** – every dosage form has different considerations, e.g. vaginal cream vs an oral film
- **Displacement** – the forces acting on the mucous membrane, such as the activity and movement of the surrounding tissue, as well as the rate of mucus turnover, can impact the strength and duration of mucoadhesion
- **Other substances present** – other substances, such as food, liquids, or air can influence the duration of adhesion

Mucoadhesion is becoming increasingly valuable in the pharmaceutical industry, as even small changes to the mucoadhesive profile of new and existing products can deliver countless benefits for formulators and patients.



## Section 2: The benefits of mucoadhesion for a drug formulation

### a) Holds drug at the site of action for longer

By enabling a pharmaceutical product to be applied directly to a target site and remain for longer, mucoadhesion ensures that an active pharmaceutical ingredient (API) has more time to achieve the desired therapeutic effect. This maximizes the effective duration of the drug, resulting in a longer therapeutic effect and subsequent improvements to the patient experience.

For example:

- **Eye drops** – by improving the formulation’s ability to adhere to the surface of the eye, mucoadhesion can prevent eye drops from running off the eye after application. This not only enhances the drop’s therapeutic effect but improves convenience by potentially reducing the number of daily applications needed.

In addition, by allowing API to stay at the site of application, the amount of drug needed in a final formulation can be reduced. This can help minimize any potential negative side effects for patients that may result from exposure to high amounts of drug and could provide cost savings for the manufacturer.

See an example below of the benefits mucoadhesion can bring to a liquid cough & cold formulation.

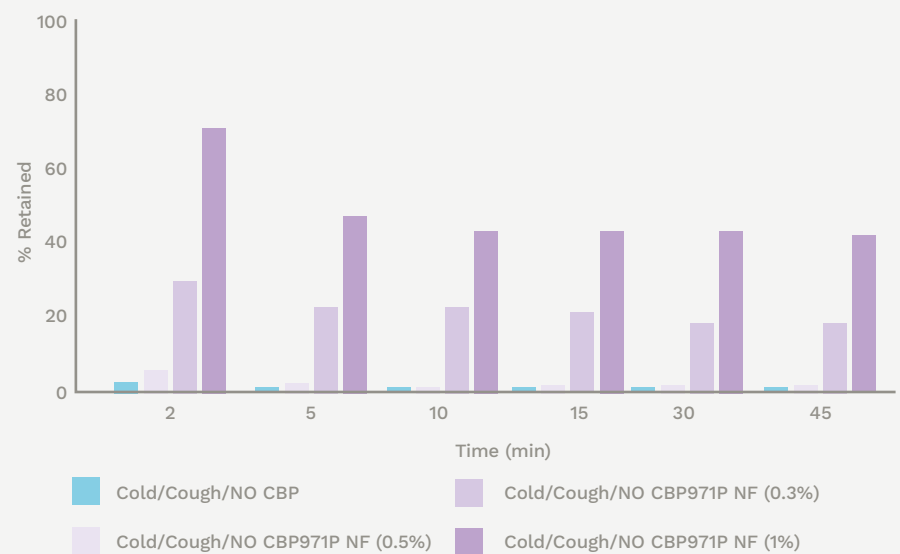
### Mucoadhesion effectively achieved with carbomers

A recent Lubrizol Life Science Health (LLS Health) study compared the mucoadhesive properties of a commercial liquid cough & cold formulation, both with and without Carbopol® polymers (carbomers).

Carbopol® polymer inclusion levels were varied to determine their effect on retention of the formulation over the study time.

It was found that formulations containing Carbopol® polymers had significantly longer retention than formulations that did not contain Carbopol® polymers; the formulation not containing Carbopol® polymers was almost entirely washed off the test substrate after only two minutes (Figure 1).

Figure 15: Impact of Carbopol® 971P NF polymer (CBP971P NF) on mucoadhesion in oral liquids



### b) Lubricates the target tissue

Mucoadhesion enables a formulation to coat a mucous membrane, providing a soothing and lubricating cover for the tissue. This can be beneficial for a variety of dosage forms products, such as lozenges to ease a sore throat or mouthwash for xerostomia (dry mouth).

### c) Provides a protective covering over damaged tissue

Similar to covering tissue for lubrication, mucoadhesive coatings can also provide a shield for damaged or sensitive tissue. This keeps the tissue isolated from irritants that can cause pain or delay healing.

For example, mucoadhesion can optimize a cover for a canker sore, allowing the product to adhere to the lesion and protecting it from bacterial infection or contact with saliva or acidic foods. In doing so, it can increase comfort for patients and promote faster healing.

### d) Enables more convenient, non-invasive products

Mucoadhesion can allow formulators to utilize topical mucosal dosage forms, where otherwise these might be unfeasible with a particular API. Topical formulations are often preferred by patients because they are more convenient, painless, and can sometimes have less severe potential side effects compared with other dosage forms such as injectable or oral.

Oral solid dose (OSD) products can be unpleasant for patients due to difficulty swallowing, or the inconvenience of often needing multiple daily doses. A recent study by Drumond et al. concluded that swallowing difficulties with OSD products are predicted to affect one in 25 adults.

Injectables are also traditionally not patient-preferred due to the discomfort caused by needle penetration or the hassle of needing to visit a medical facility for administration.

## Section 3: How to achieve mucoadhesion & initial formulation considerations

Mucoadhesion offers real-world benefits in terms of product performance that a growing number of pharmaceutical companies are already taking advantage of. But, how can enhanced mucoadhesion in a formulation be achieved?

The key to achieving the right mucoadhesive profile for the unique needs of your pharmaceutical product lies in the choice of excipient. See below for more information on mucoadhesive excipients, as well as other initial formulation considerations when designing a mucoadhesive drug product.



## Initial formulation considerations:

### 1) Inactive ingredients

The design of a mucoadhesive formulation requires the presence of an excipient that imparts mucoadhesive properties and ensures prolonged contact between the drug product and the mucosa. In addition, the selection of the other inactive ingredients is extremely important given that they may alter the API release rate, mucosal permeation and stability, among other properties.

A number of polymers are widely used across the pharmaceutical and healthcare industries to create and enhance mucoadhesion in product formulations.

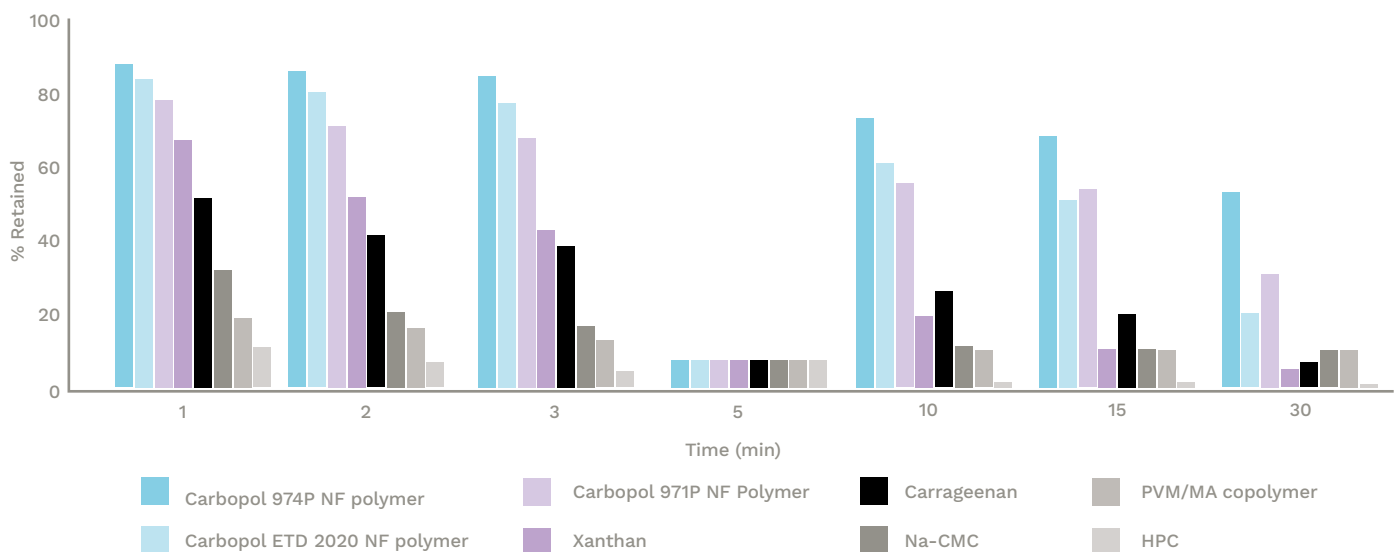
Some of the most common include:

- Carbomers (such as Carbopol® polymers)
- Xanthan gum
- Sodium carboxymethylcellulose (Na-CMC)
- Carrageenan
- Copolymer of methyl vinyl ether and maleic anhydride (PVM/MA)
- Hydroxypropyl cellulose (HPC)

Each polymer type has its own unique features that can impact the mucoadhesive profile of the finished product. However, formulations containing Carbopol® polymers, manufactured by LLS Health, have been shown to provide significantly improved dosage form retention at the target site compared with those containing alternative polymers.

Carbopol® polymers have been shown to offer significantly longer retention than other mucoadhesive excipients, even after 30 minutes

Figure 9: Retention of aqueous dispersion made from various materials (1.0 weight percent)





## 2) Active Pharmaceutical Ingredients (API)

API considerations will provide the basis for dosage form and excipient selection in the formulation process. The physicochemical properties of the API (e.g., solubility, permeability, and stability) together with its dose strength requirements will play a key role in the formulation of mucoadhesive drug products.

A formulator needs to consider whether an API is suitable for mucosal drug delivery, i.e. is it permeable. In general, smaller molecules are most likely to be readily absorbed through mucous membranes. Models have been developed to predict permeability of the API as a function of its physicochemical characteristics. A multi-API product will also have unique formulation requirements to ensure proper release at the intended site of action.

## 3) Dosage form

It is possible to develop a range of mucoadhesive formulation types, from solid, to semi-solid, to liquid. The choice of formulation base will depend on the requirements of the intended dosage form and the end goal of the product set out in the Target Product Profile (TPP).

The selection of ideal dosage form for the TPP encompasses an appropriate route of administration that ensures sufficient exposure to allow the drug to have its intended therapeutic effect. This is determined by a number of factors, ranging from API stability and compatibility, to the type of disease your product is intended to treat and the part of the body it affects.

Patient convenience and adherence is also an important consideration when selecting the ideal dosage form. Limited side effects, as well as ease of handling and administration at the required frequency even by patients with dexterity issues or visual impairments, can ensure patients adhere to their treatment, maximizing its effectiveness.

Once the dosage form has been selected, then it is possible to consider the specific mucoadhesive properties required for the formulation to maximize its effectiveness and achieve the TPP.

The dosage forms the performance of which can be enhanced by mucoadhesion include:

- Topical gels and emulsions
- Patches and films
- Oral solutions and suspensions
- Eye drops
- Nasal sprays
- Lozenges and buccal tablets
- Toothpastes and mouth washes



#### 4) Site of delivery

The ultimate goal of any mucoadhesive formulation is to allow active pharmaceutical ingredients to be delivered and achieve desired therapeutic effect. It is therefore necessary to understand the target tissue, i.e the site of drug delivery.

When designing a mucosal formulation, tissue penetration has to be considered, as not all surfaces are the same. For example, drug uptake for the rectum is different from the inside of the nose.

Additionally, not only must a formulation be designed for the specific target mucosa, but it must also be optimized either for localized or systemic delivery as mucosal drug delivery can accommodate either.

The sites of delivery for which mucoadhesive drug delivery can be considered include:

- Buccal
- Ocular
- Nasal
- Esophageal
- Vaginal
- Rectal

### Conclusion: Mucoadhesion offers significant product performance benefits for formulators and patients

The global pharmaceutical market is becoming increasingly crowded. Pharma companies need to find new ways to deliver improved product performance and ensure their products are differentiated in the market.

Developing formulations with an appropriate mucoadhesive profile has a key role in achieving this goal, but not all polymers are alike. With the use of Carbopol® polymers formulators can achieve an ideal mucoadhesive profile for any of the listed dosage forms (Section 3). As a result, they can create more effective, differentiated products that offer an improved patient experience.



For more information on the benefits of mucoadhesion [read our technical brief](#) or [contact us today](#).



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