

W0930-05-30 Carbopol® Polymers and Noveon® Polycarbophil Mucoadhesive Properties in Liquid and Semisolid Formulations

Liliana Miinea, Paul Basone, James Baxter, Elena Draganoiu
Lubrizol Life Science Health



Advancing Pharmaceutical Sciences,
Careers, and Community

CONTACT: Elena.Draganoiu@lubrizol.com

BACKGROUND

Mucoadhesion provides benefits in pharmaceutical and oral care applications, enhancing drug delivery and/or providing other therapeutic advantages (local protection, lubrication, etc.).

Carbopol® polymers (carbomers) and Noveon® polycarbophil are high molecular weight polymers of acrylic acid crosslinked with polyalkenyl alcohols or divinyl glycol. When placed in contact with an aqueous medium, they hydrate and swell through hydrogen bonding or electrostatic repulsion (when neutralized). These mechanisms are the basis of the excipients' functionality in mucoadhesion applications.

Earlier studies¹ showed Carbopol® polymers to have superior mucoadhesive properties when compared to other pharmaceutical excipients (Figure 1).

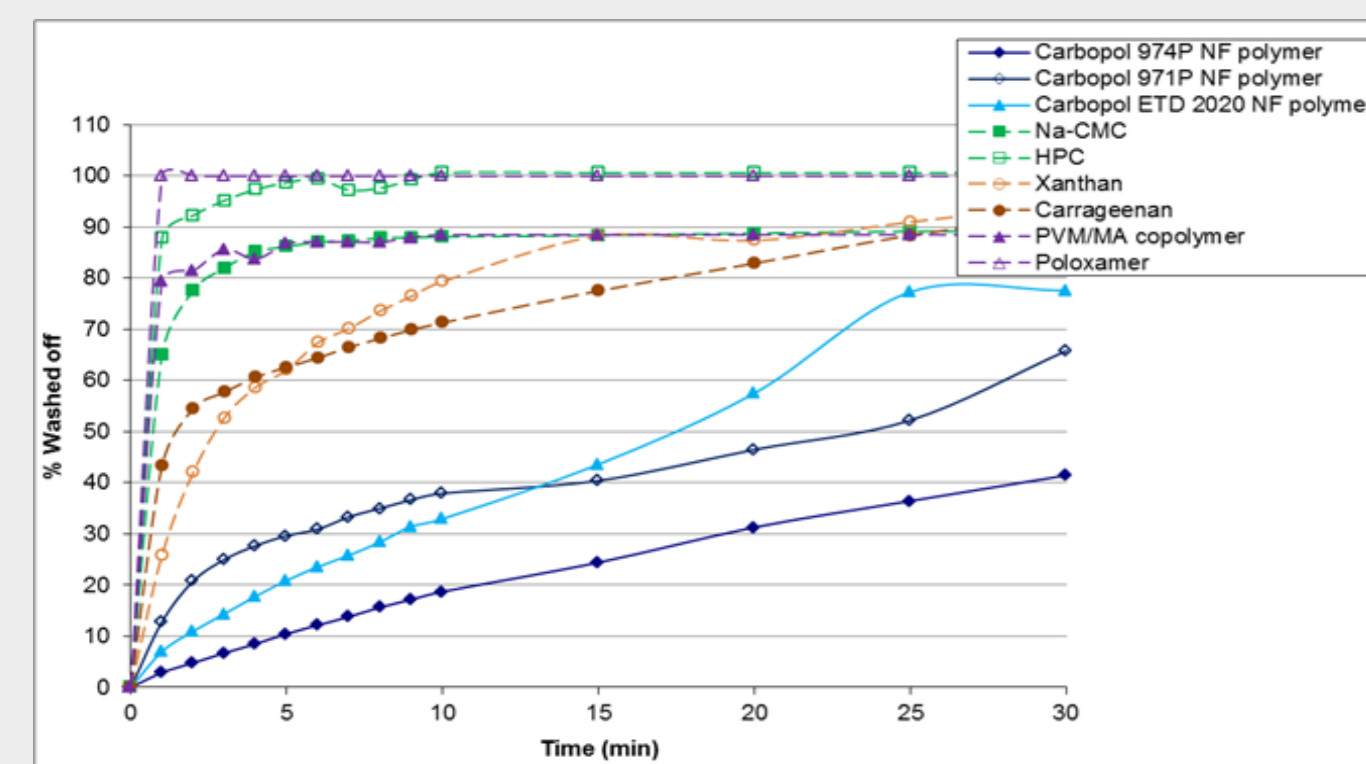


Figure 1. Elution (percent washed off) of 1% aqueous dispersions made from various pharmaceutical excipients

PURPOSE

Establish the impact of Carbopol® polymers characteristics on mucoadhesive properties in liquid and semisolid formulations (Figure 2).

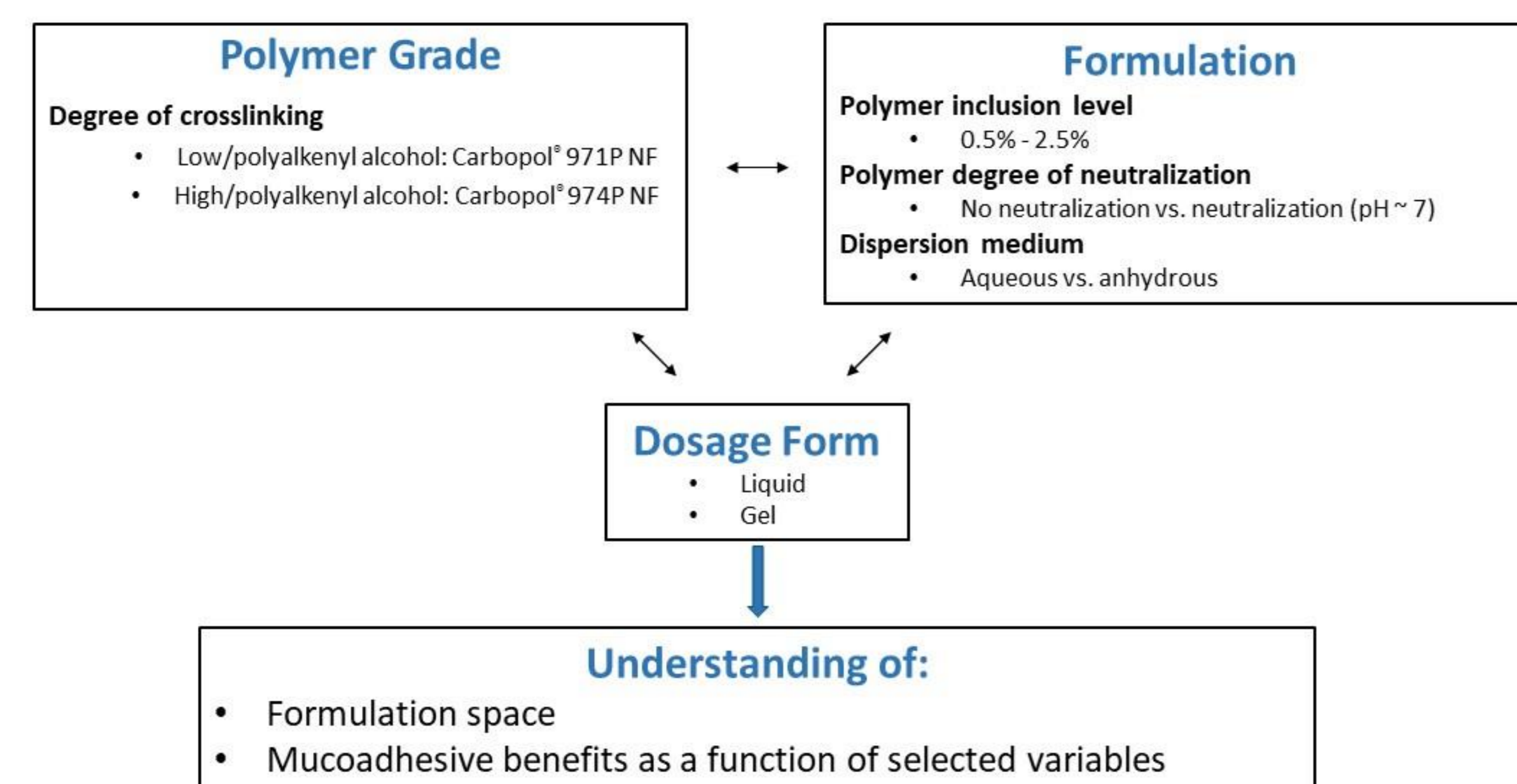


Figure 2. Design space for the study of mucoadhesive liquid and semisolid formulations containing Carbopol® polymers

METHODS

Carbopol® 971P NF and 974P NF polymers were dispersed at desired concentration in deionized water or anhydrous medium (glycerin/propylene glycol/PEG 400 mixture), followed by neutralization (when required). Mucoadhesive properties were evaluated using an in-house adapted in-vitro esophageal retention (IVOR) model to simulate oral/peroral conditions (Figure 3) and UV-Vis quantification.

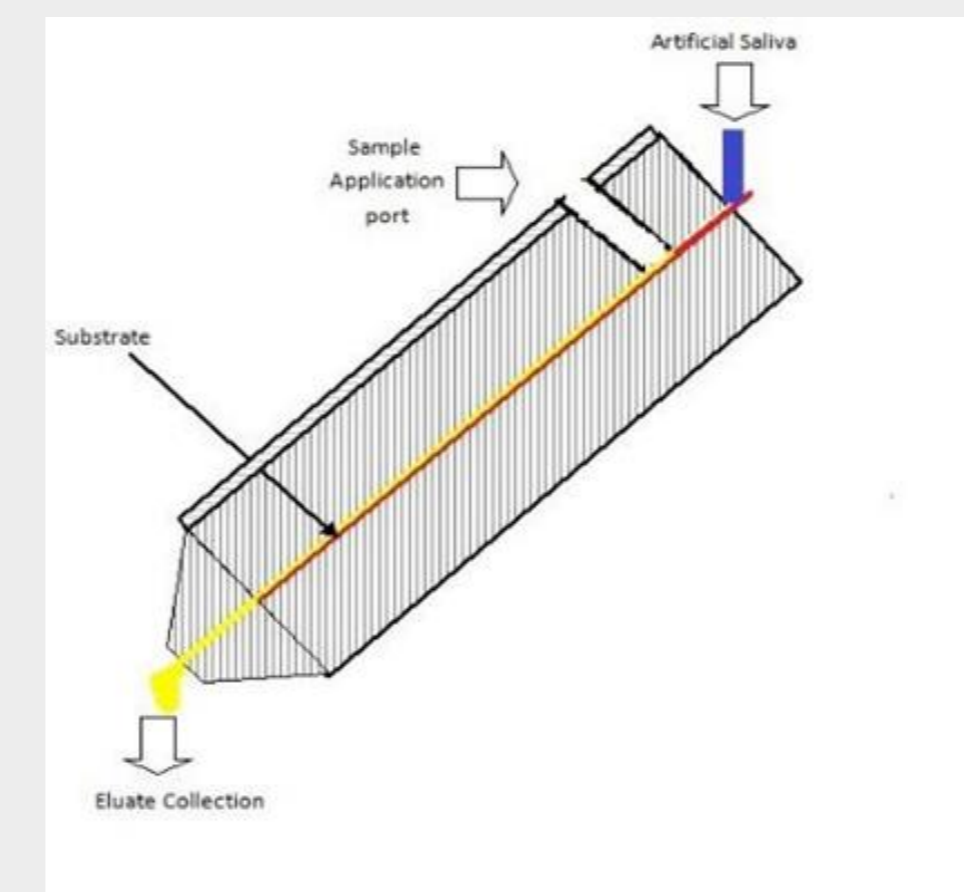


Figure 3. Schematics of IVOR set-up for evaluation of mucoadhesive properties

RESULTS

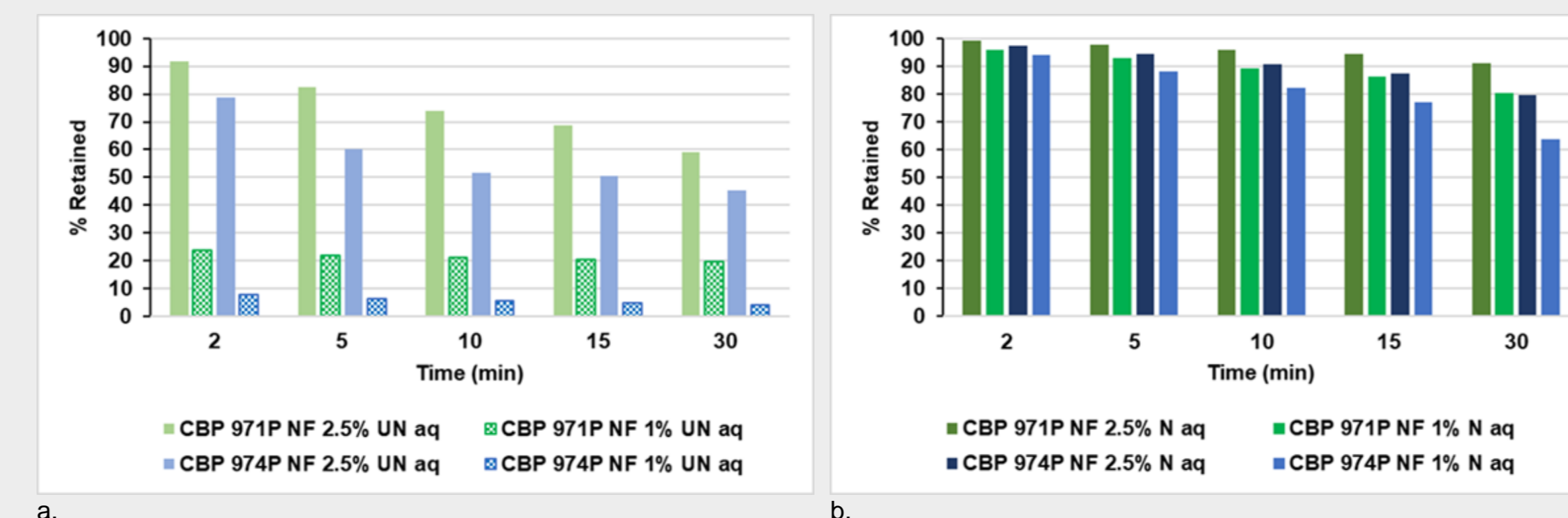


Figure 4. In vitro evaluation of mucoadhesion of Carbopol® 971P NF and 974P NF polymers in aqueous gels a. un-neutralized b. neutralized

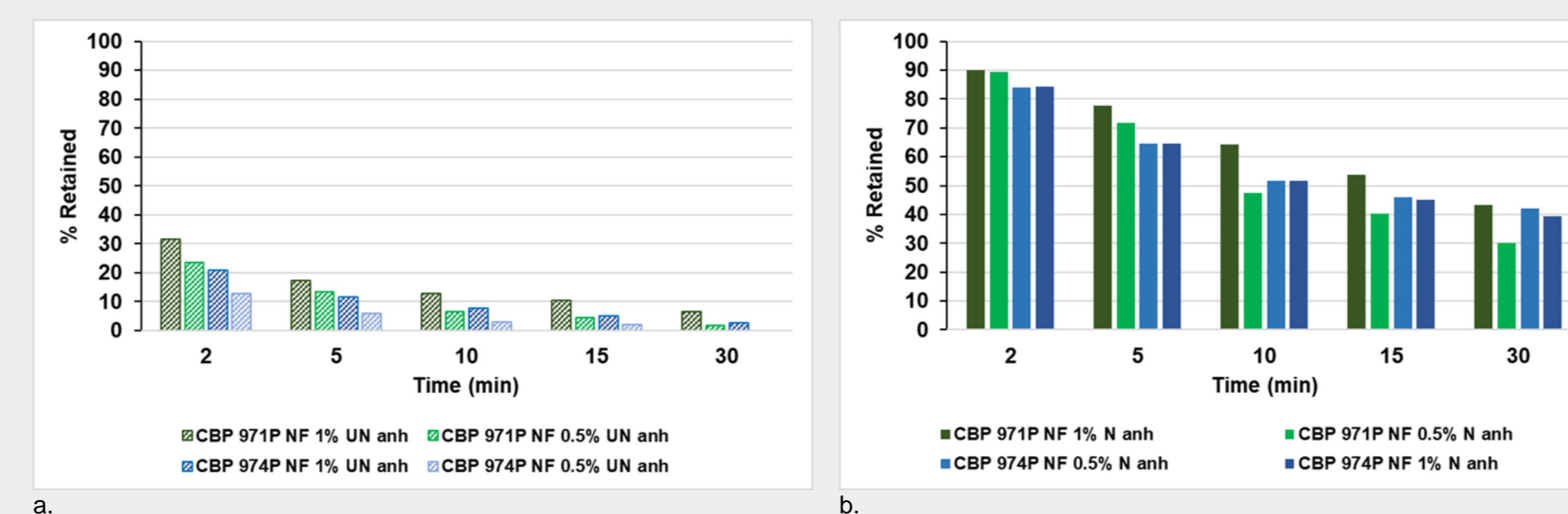


Figure 5. In vitro evaluation of mucoadhesion of Carbopol® 971P NF and 974P NF polymers in anhydrous gels a. un-neutralized b. neutralized



Figure 6. Impact of gel viscosity on in vitro mucoadhesion of Carbopol® 971P NF and 974P NF polymers

RESULTS

Mucoadhesion strength in liquid/semisolid formulations of Carbopol® polymers was dictated by:

- **Polymer inclusion level**
Longer retention of formulations was achieved with higher polymer inclusion levels. The impact was more pronounced in the un-neutralized form (Figure 4 and 5).
- **Degree of neutralization**
Carbopol® polymers had better mucoadhesion in neutralized vs. un-neutralized form for same dispersion medium and concentration (Figure 4 and 5).

- **Dispersion medium**
Anhydrous neutralized formulations tend to have similar retention as the aqueous formulations for the initial time points (2 – 5 min), however they eluted much faster as time progressed (Figure 4 and 5).

- **Degree of crosslinking**
Carbopol® 971P NF polymer in aqueous systems, despite lower viscosity, showed better retention when compared to Carbopol® 974P NF polymer (Figure 6).

These results support the mechanism of adhesion for Carbopol® polymers:

- Initial contact with the mucus (wetting):** The hydration potential of Carbopol® polymers allows to quickly establish contact with mucus upon application of dosage form;
- Consolidation of adhesion:** Hydrogen bonding and/or macromolecular interchain penetration between Carbopol® polymers and components of mucin.

The Carbopol® polymer in its neutralized form is swollen at its largest extent and macromolecular interpenetration with the mucus glycoprotein chains provides strong mucoadhesion. In anhydrous media and in un-neutralized form the predominant mechanism is the hydrogen bonding between the carboxylic groups and the mucus components, which leads to less retention of formulation on the membrane.

CONCLUSIONS

Carbopol® polymers mucoadhesive properties in liquid and semisolid formulations were demonstrated by in-vitro IVOR studies. Longer retention of formulations was achieved with higher polymer inclusion levels and for higher degree of neutralization, irrespective of the dispersion medium.

Carbopol® polymers offer pharmaceutical scientists the flexibility to tailor properties of mucoadhesive liquid and semisolid formulations.

REFERENCE

1. "Properties of mucoadhesive polymers and their use in tablets and other dosage forms" Tablets and Capsules 2016, vol. 14 (5) 17-23 <http://www.e-digitaleditions.com/i/701238-tc0716/18>

Carbopol® and Noveon® are registered trademarks of The Lubrizol Corporation USA

