

# Improving Mucoadhesion of Oral Care Formulations with Carbopol® Polymers

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## PURPOSE

Mucoadhesive dosage forms for the oral cavity can provide enhanced therapeutic benefits through prolonged retention of actives, acting as lubricating agents, and coating and protecting damaged tissues (lesions of the oral mucosa).

The purpose of this study was to evaluate *in vitro* mucoadhesive properties of two types of dosage forms for administration in the oral cavity, formulated with different grades and concentrations of Carbopol® polymers:

- Liquid dosage form: mouthwash containing thymol, eucalyptol, methyl salicylate, and menthol, typically used for antiseptic properties, and to prevent and reduce plaque and gingivitis;
- Semisolid dosage form: oral gel containing Sanqi (Panax notoginseng extract), a Traditional Chinese Medicine (TCM) with hemostatic and anti-inflammatory properties, used in oral care products to reduce bleeding and swelling of the gums and other soft tissues.

## METHODS

The mucoadhesive properties of mouthwash and oral gel formulations were evaluated using an adapted *in vitro* esophageal retention model to simulate dynamic oral conditions (Fig. 1). The retention of the dosage form (mouthwash or oral gel) on the substrate was determined by measuring the amount eluted over time (UV-VIS or chromatographic method).

### Mouthwash formulations:

- The mouthwash formulations were based on a commercial product containing thymol, eucalyptol, methyl salicylate and menthol (reference formulation)
- Test formulations were prepared by incorporating Carbopol® 956 polymer (0.25 or 0.50% w/w) or Carbopol® 971P NF polymer (0.25, 0.50, 1.00% w/w) in the reference (commercial) formulation.
- The polymer was added directly into the mouthwash (direct method) or after pre-dispersion in water (indirect method).
- FD&C Blue No.1 was added as a marker in the mouthwash formulations and measured by UV-VIS in the eluate.

### Oral gel formulations:

- Oral semisolid formulations were prepared by dispersing Sanqi extract (1% w/w) in gels prepared with various grades of Carbopol® polymers (956, 974P NF, ETD 2020 NF) or Noveon® AA-1 polycarbophil USP (polymer inclusion level 1%).
- The mucoadhesive properties of those gels were compared to gels based on sodium carboxymethyl cellulose (Na-CMC) or xanthan (1% inclusion level).
- Rb1, a component of Sanqi extract, was measured by HPLC in the eluate.

## RESULTS

### Mouthwash formulations

- All mouthwash formulations with added Carbopol® polymer showed improved mucoadhesion vs. reference (mouthwash without carbomer). Carbopol® 956 and 971P NF polymers had comparable mucoadhesive properties when used at the same inclusion level (Fig. 2). Carbopol® 971P NF polymer imparted lower viscosity compared to Carbopol® 956 polymer due to lower crosslink density. Increasing the carbomer concentration resulted in longer retention and higher viscosity.
- No difference in elution profile was observed for direct vs. indirect addition of the carbomer in the formulation; though direct addition generally resulted in lower viscosity (Table 1; Fig. 2). The addition order may be changed to optimize for other formulation considerations (compatibility, viscosity, processing, etc), without significant impact on retention profiles.
- Carbopol® polymers imparted significant retention after 60 minutes, regardless of grade or addition method (Fig. 3).

Formulation	Carbopol® polymer level (w/w%)	Indirect addition	Direct addition
Mouthwash with Carbopol® 956	0.50	17,250	5,180
	0.25	2,145	668
Mouthwash with Carbopol® 971P NF	1.00	13,900	12,760

Table 1. Viscosity of mouthwash formulations with Carbopol® polymers by different addition method (Brookfield viscosity mPa\*s @20rpm)

### Oral gel formulations

- The elution of Sanqi from gels prepared with Carbopol® polymers or Noveon® AA-1 polycarbophil USP was prolonged, with more than 75% of the active being retained on the substrate after 35 minutes.
- The sodium carboxymethyl cellulose gel washed off very quickly (>90% at 5 min), while xanthan gel showed fast initial elution (>50% at 5 min) and less overall retention than Carbopol® polymers and Noveon® AA-1 polycarbophil USP (Fig. 4).
- After 3h elution, there was no any retention for sodium carboxymethyl cellulose gel, while Carbopol® polymers showed high retention (Fig. 5).

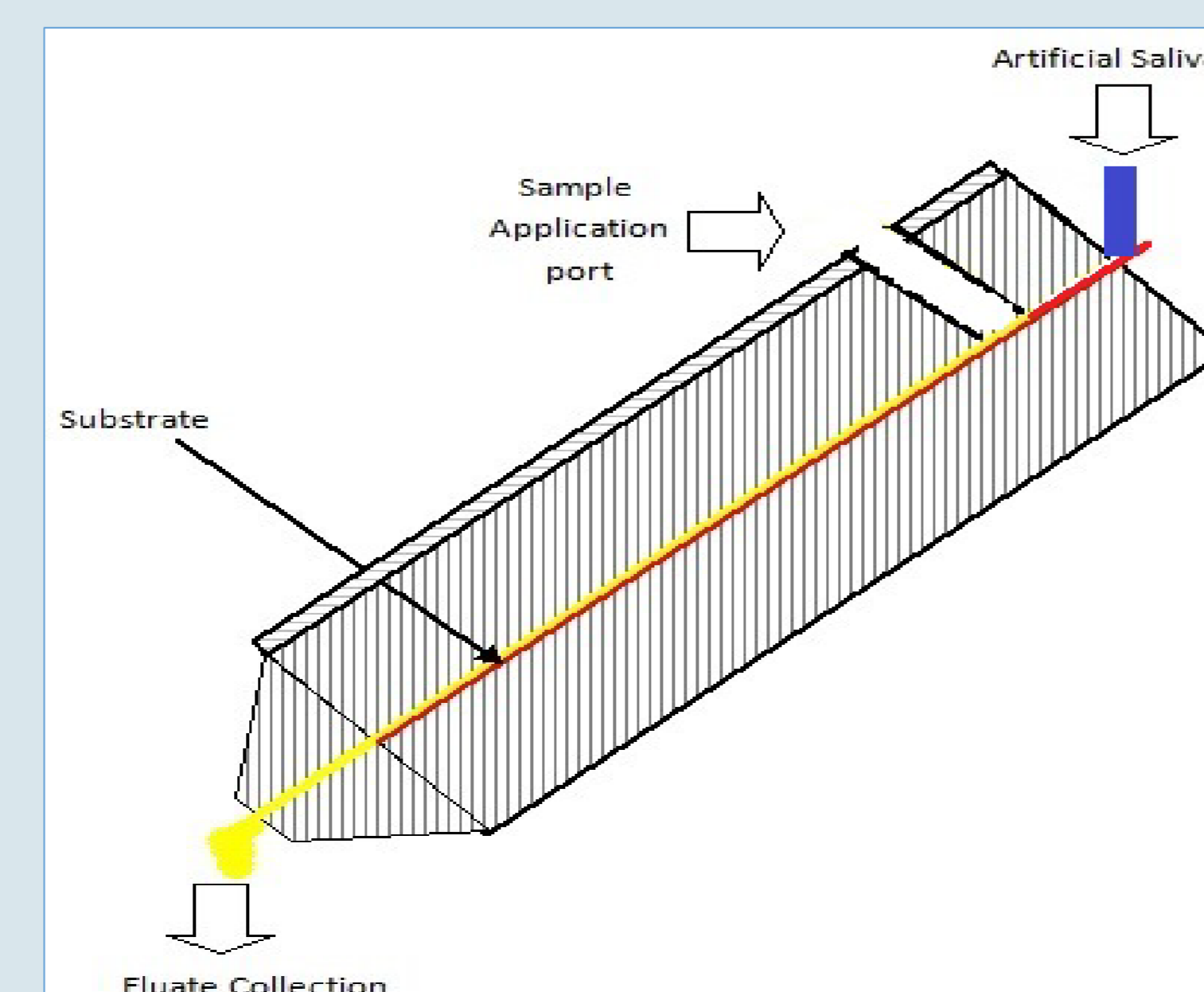


Fig. 1. In Vitro Esophageal Retention Model (IVOR), adapted from Young and Smart, J Pharm Pharmacol. (1998), 50, 167

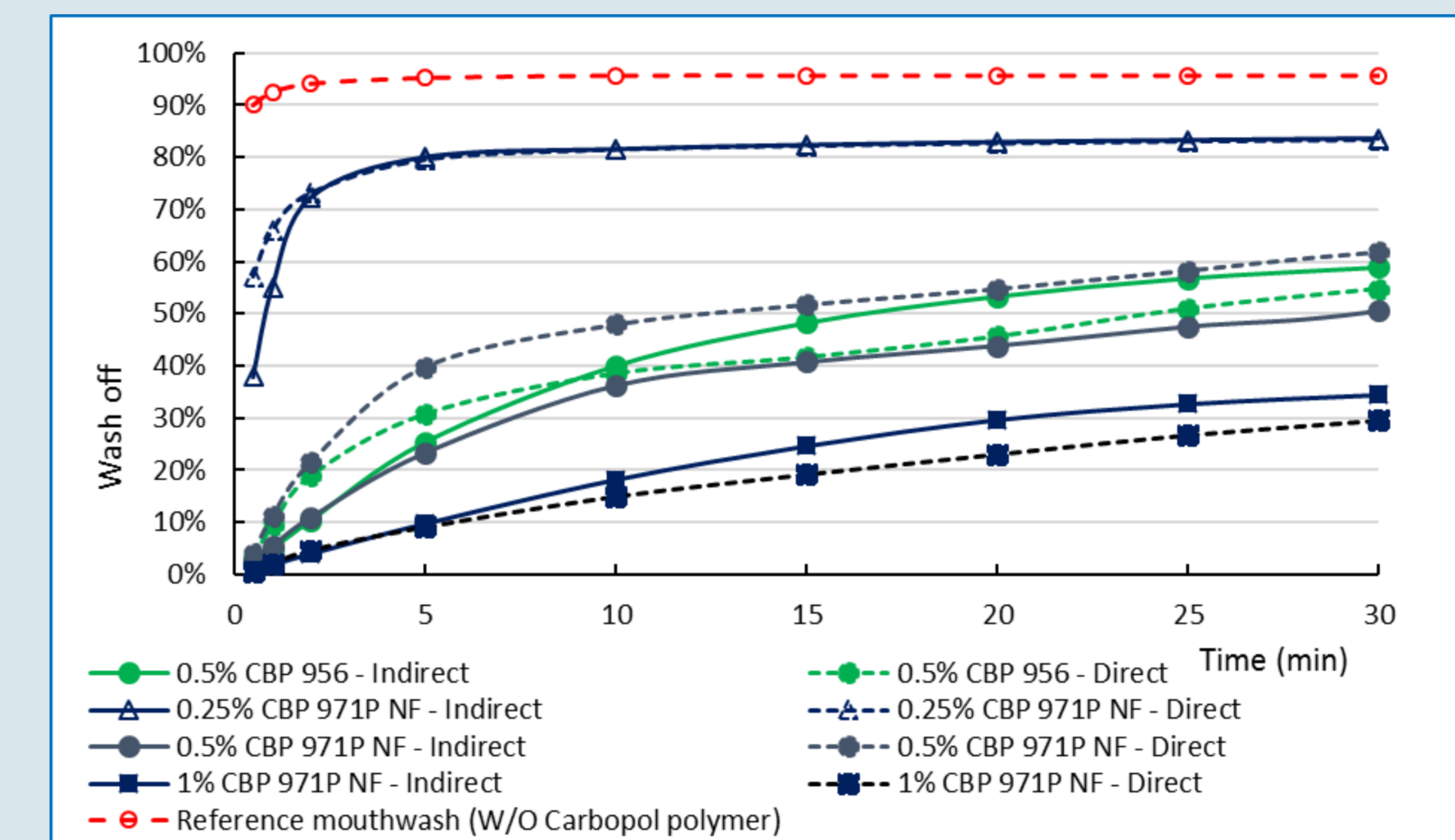


Fig. 2. Elution profiles of mouthwash formulations with/without Carbopol® polymers (added by different methods)

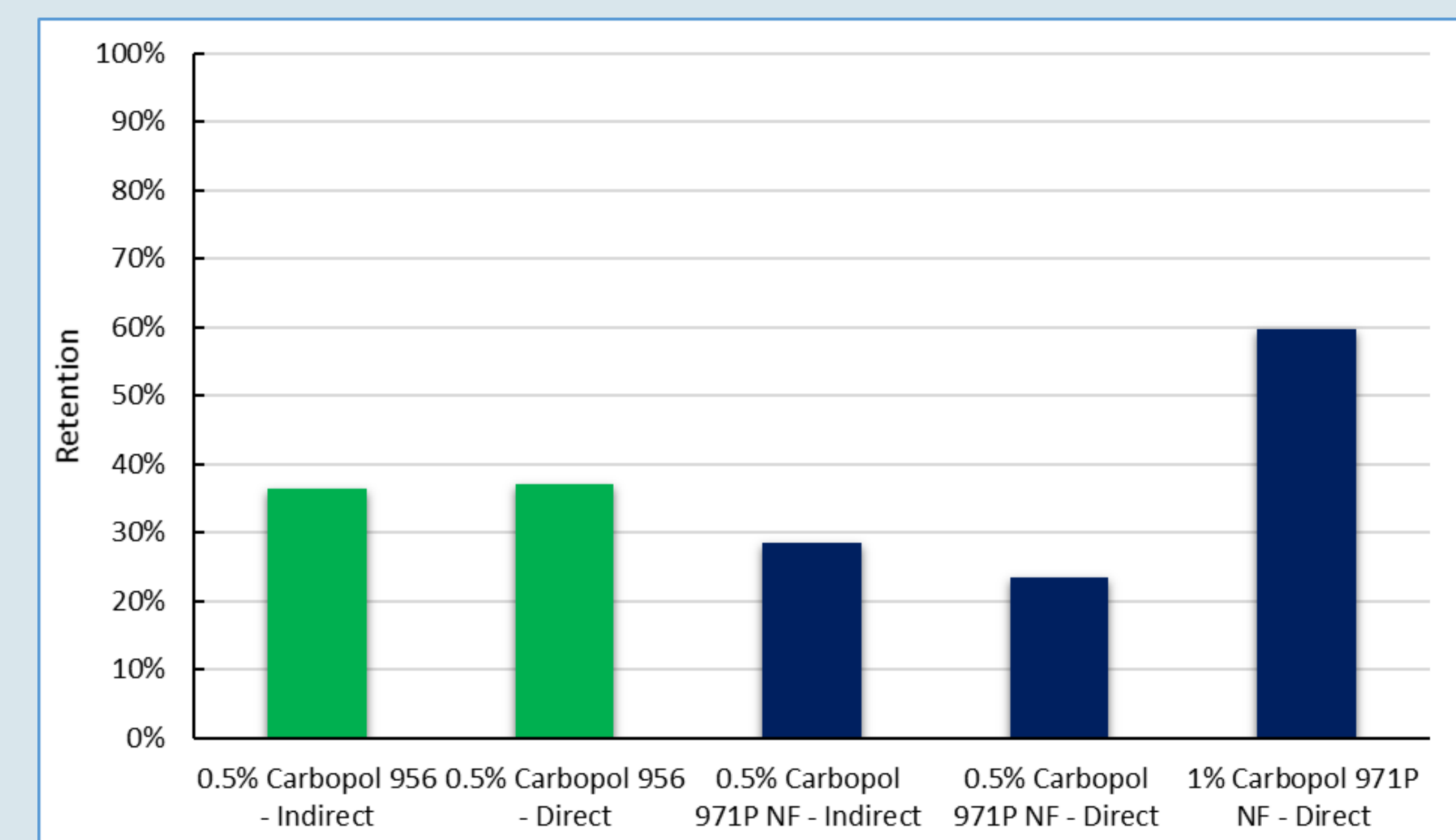


Fig. 3. Retention of mouthwash formulations with Carbopol® polymers after 60 min

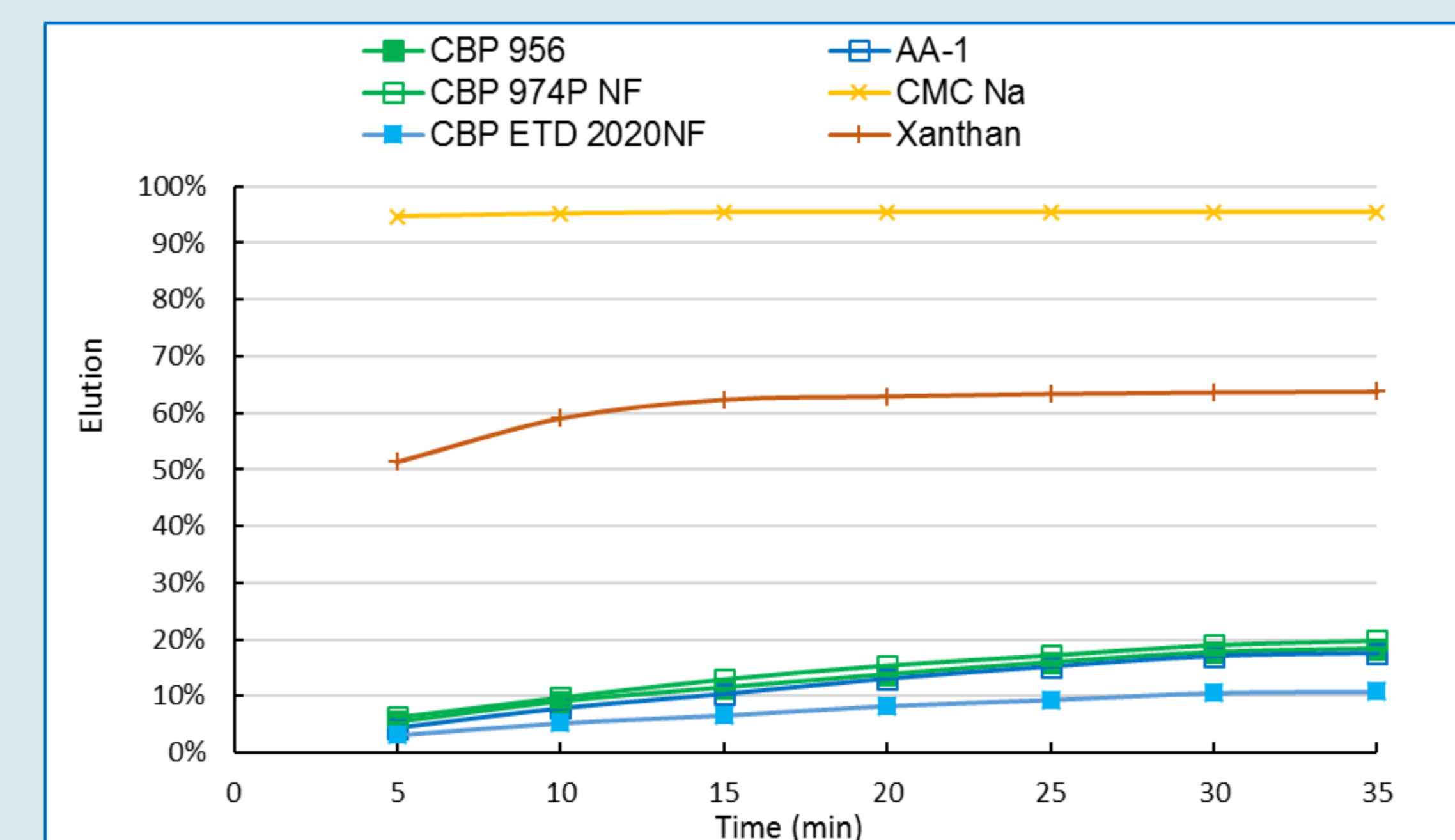


Fig. 4. Elution profiles of oral gel formulations for Sanqi extract

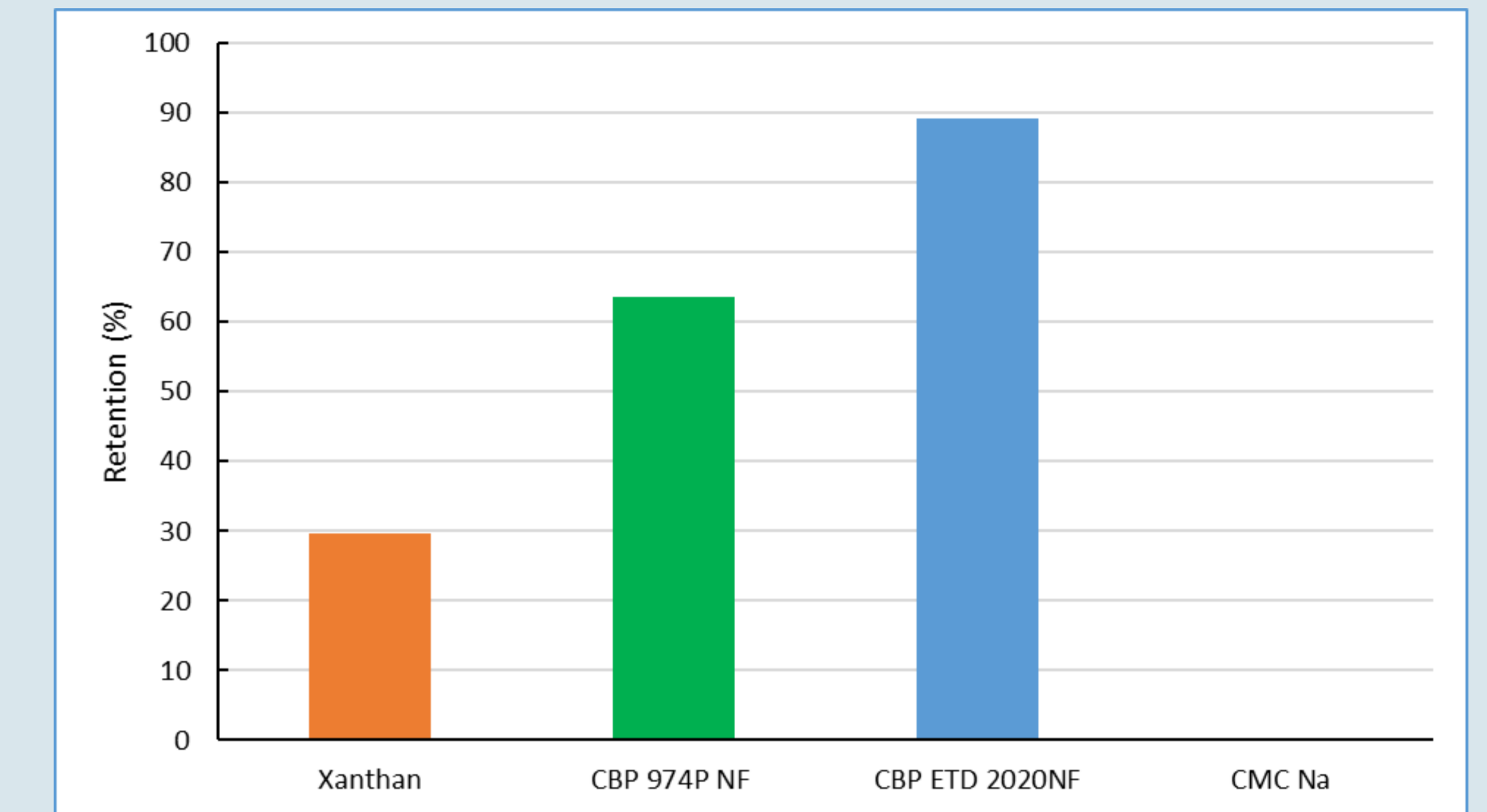


Fig. 5. Retention of oral gel formulations for Sanqi extract after 3 hours

## CONCLUSIONS

- Carbopol® polymers imparted mucoadhesive properties for oral care liquid and semisolid formulations as indicated by improved *in vitro* retention.
- The properties of the mouthwash formulations (mucoadhesion, viscosity) could be tailored by varying the carbomer type, concentration and the addition method.
- Improved retention was achieved for oral gels with Sanqi extract containing Carbopol® polymers or Noveon® AA-1 polycarbophil USP vs. sodium carboxymethyl cellulose or xanthan.
- Mouthwashes and oral gels with improved mucoadhesion can provide enhanced therapeutic benefits through prolonged retention of actives (Sanqi extract, thymol, eucalyptol, methyl salicylate, menthol), coating and protecting damaged tissues (lesions of the oral mucosa) and acting as lubricating agents.