Thermax® N990CG in Butyl Pharmaceutical Vial Stoppers

Rubber stoppers are used in the pharmaceutical industry to seal injection vials as well as other vessels such as infusion containers and blood collection tubes. Butyl and halobutyl rubbers are excellent choices for these applications due to their low permeability, polymer purity, clean cure systems, and good aging properties. Low permeability and good sealing properties reduce the risk of contamination of the drug during transit and storage. In addition, there is a risk of contamination and particulate matter from the rubber stopper itself. For this reason, it is important to have a rubber formulation with low extractables and leachables. Thermax® N990CG is a low PAH grade of thermal black that is suitable for use in rubber stopper formulations.

The benefits of N990CG found in this study include:

- Lower mixing power consumption
- Decrease in compound viscosity
- Maintained physical properties
- Excellent aged property performance
- Compound extractable substance results similar to blank and control
- Grey or black coloring of compound

The chlorobutyl formulations can be found in Table 1. Thermax® N990CG replaced silica in the formulation and was added at 1 and 5 phr loadings. Mooney, MDR, tensile, hardness, coefficient of friction, compression set, water immersion, steam exposure, permeability, and extractables substance testing was completed for all compounds. Mixing and testing were completed by Smithers in Akron, Ohio.

Table 1. Chlorobutyl formulations

Ingredient	Control	A	B
Chlorobutyl 1066 Lanxess	100	100	100
Silica: Nipsil EL	15	14	10
Coupling Agent: SI-263	0.5	0.5	0.3
Calcined Clay	20	20	20
LDPE: LD 100.BW	1	1	1
N990CG	**0**	**1**	**5**
Titanium Dioxide	3	3	3
Hydrotalcite: DHT-4A	4	4	4
Triazine Derivative: 6-dibutylamino-1,3,5-triazine-2,4-dithiol	1.5	1.5	1.5
Total	145	145	144.8

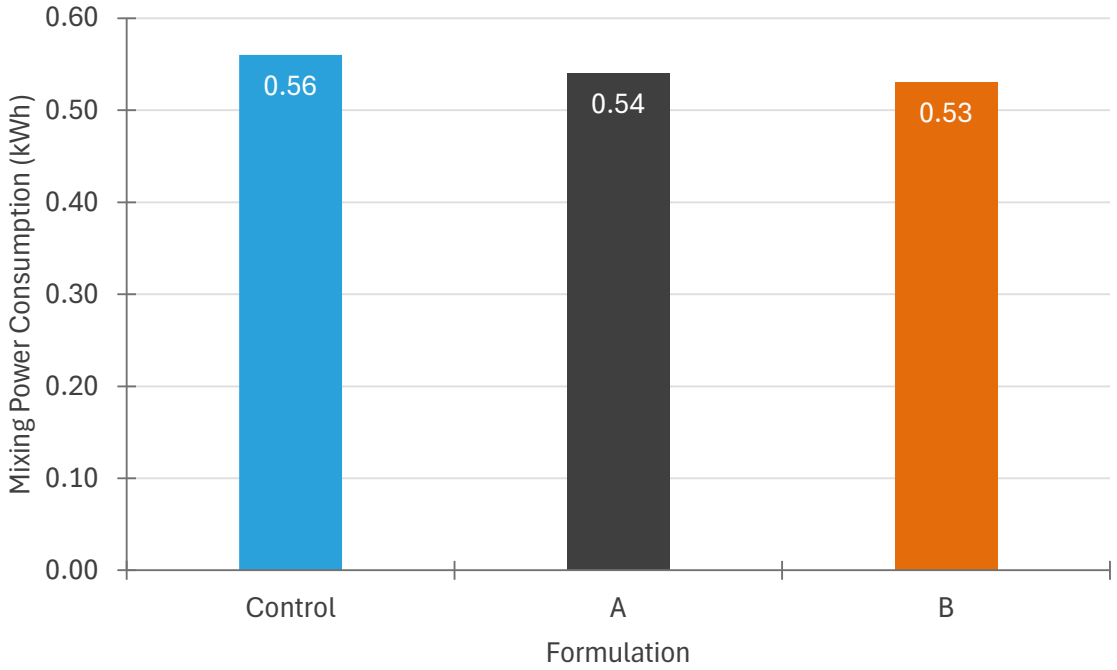

Figure 1. Mixing power consumption of the compounds. Mixing power decreased as N990CG loading increased.

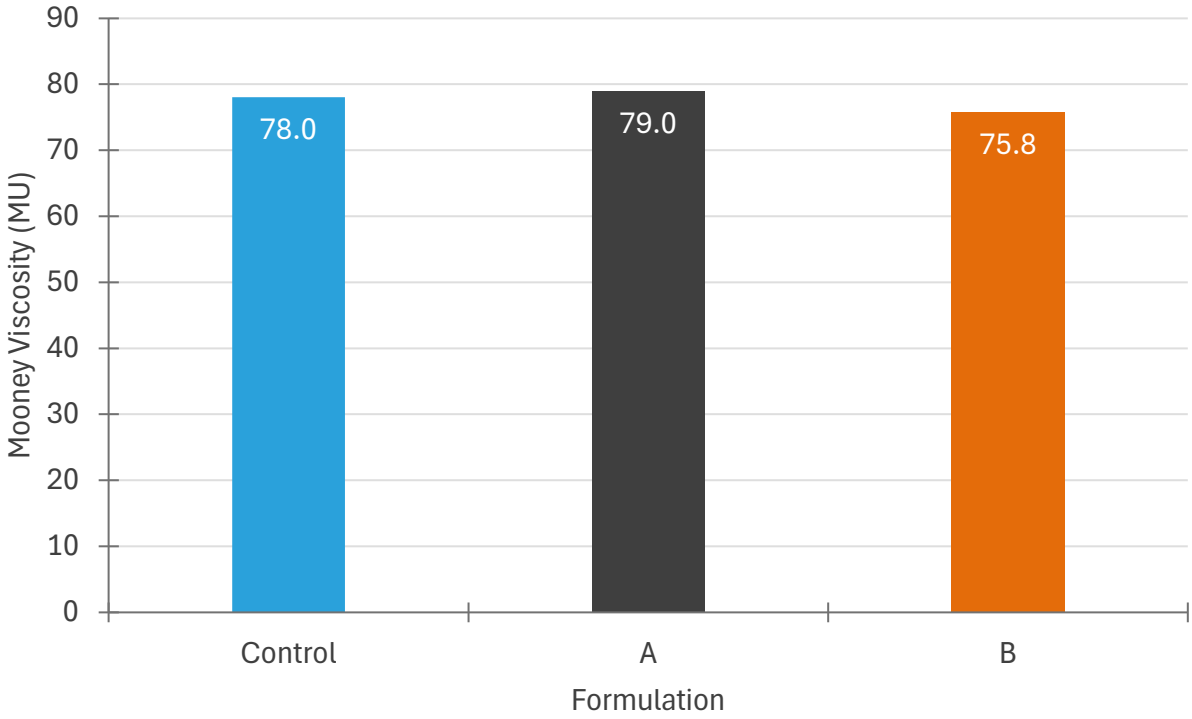

Figure 2. Mooney viscosity of the compounds measured according to ASTM D1646. A slight decrease in viscosity was observed for the compound with 5 phr N990CG.

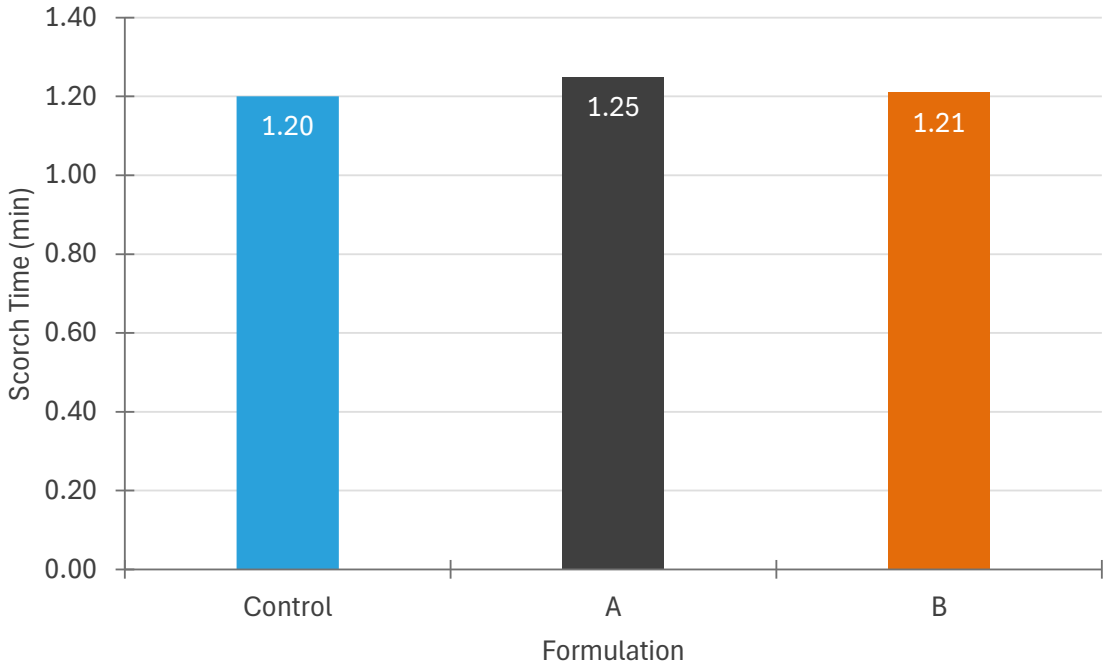

Figure 3. Scorch time, t'10, of the compounds measured according to ASTM D5289. There were no significant differences in scorch time.

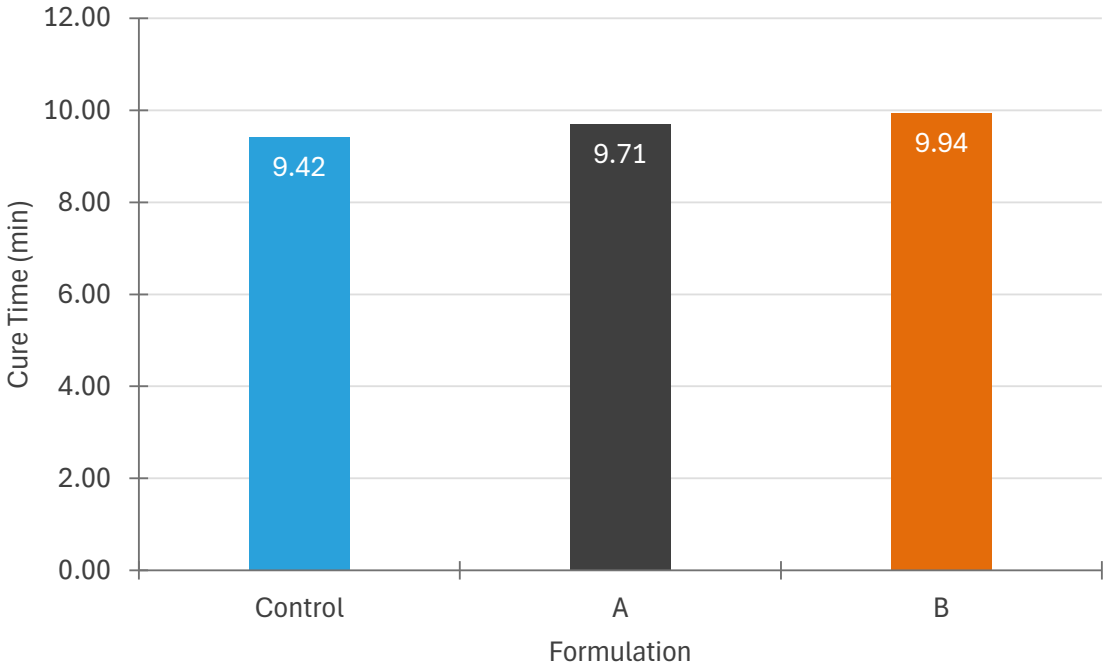

Figure 4. Cure time, t'90, of the compounds measured according to ASTM D5289. There was a slight increase in cure time as N990CG replaced silica.

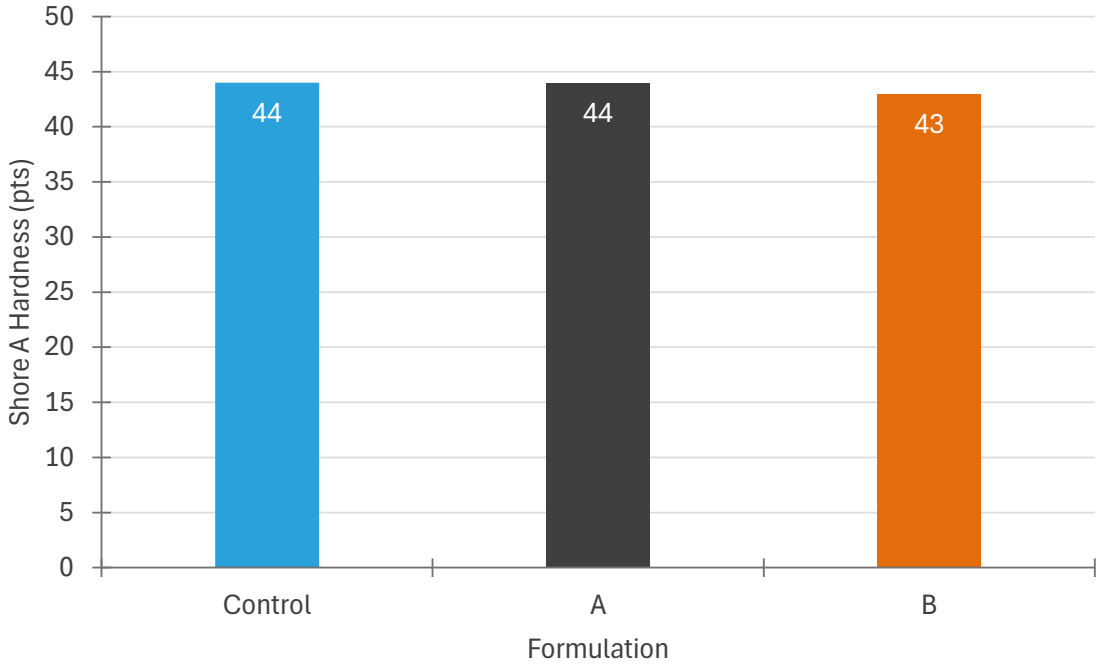

Figure 5. Shore A hardness of the compounds measured according to ASTM D2240. All compounds were at 45±3 pts.

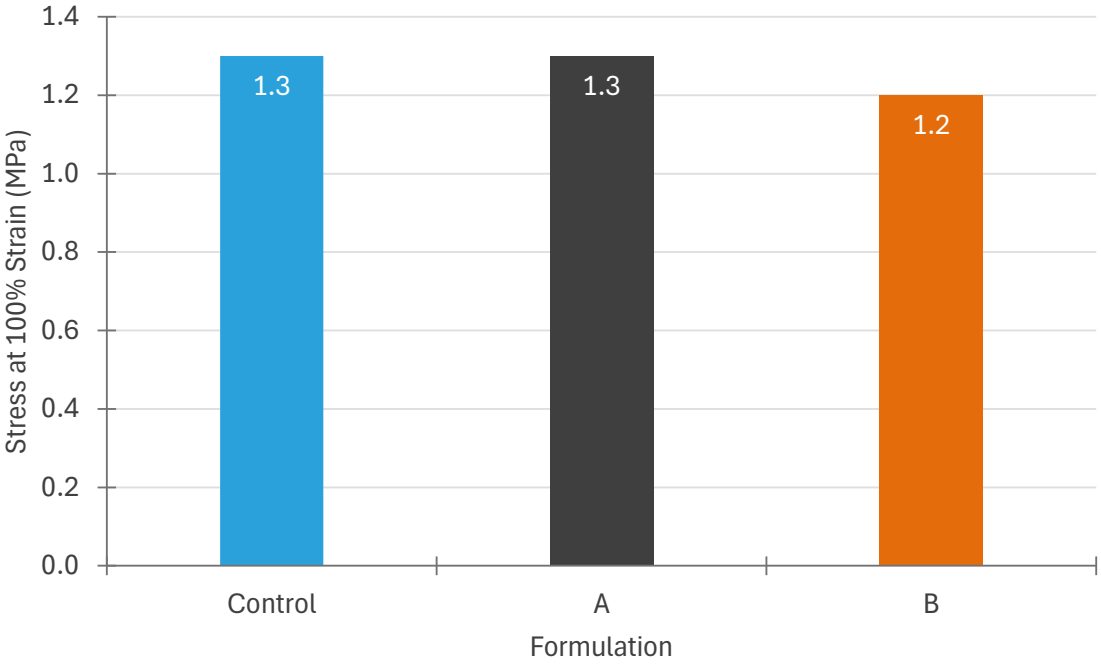

Figure 6. Stress at 100% strain of the compounds measured according to ASTM D412. There were no significant differences in 100% modulus.

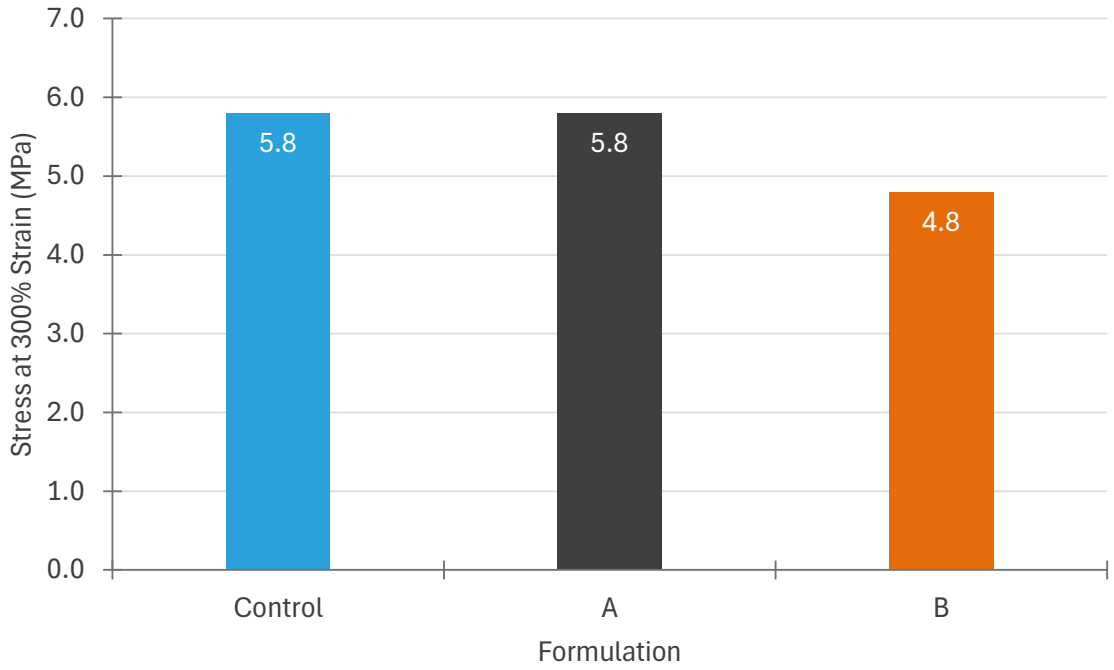

Figure 7. Stress at 300% strain of the compounds measured according to ASTM D412. The 300% modulus was lower for the compound with 5 phr N990CG.

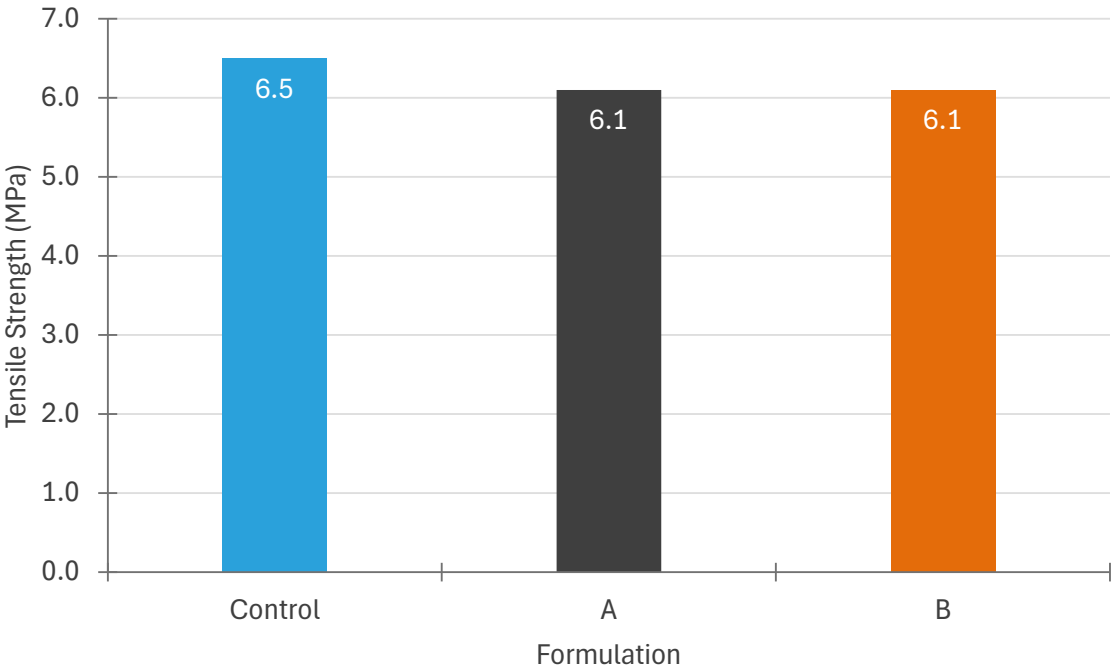

Figure 8. Tensile strength of the compounds measured according to ASTM D412. There was a small decrease in tensile strength when N990CG was added to the compound.

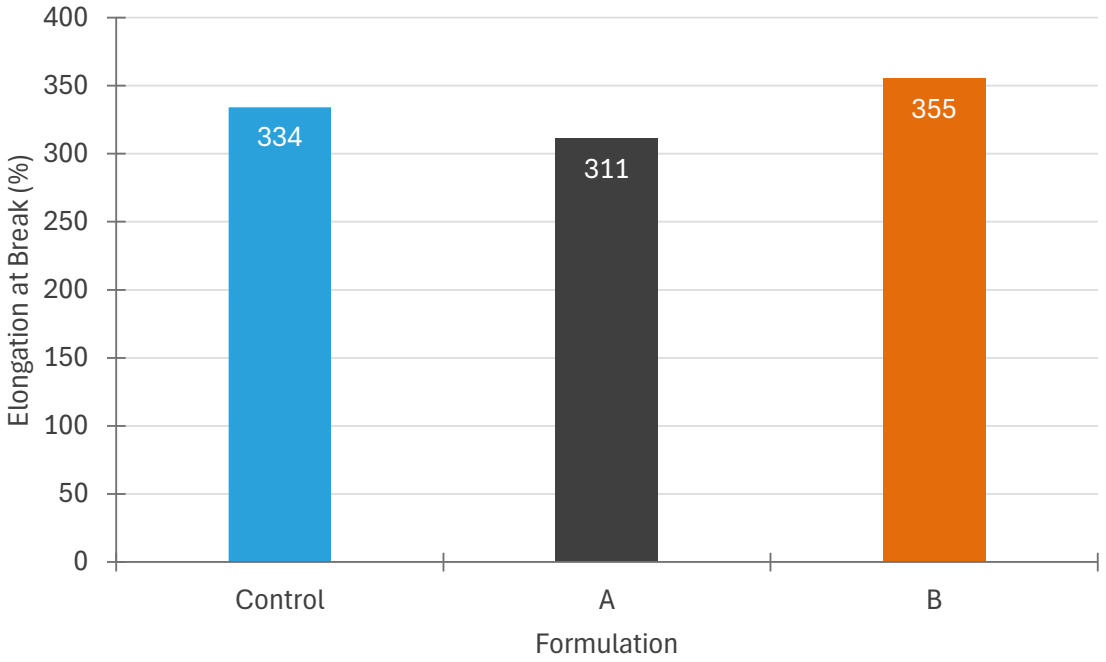

Figure 9. Elongation at break of the compounds measured according to ASTM D412. There were no significant differences in elongation.

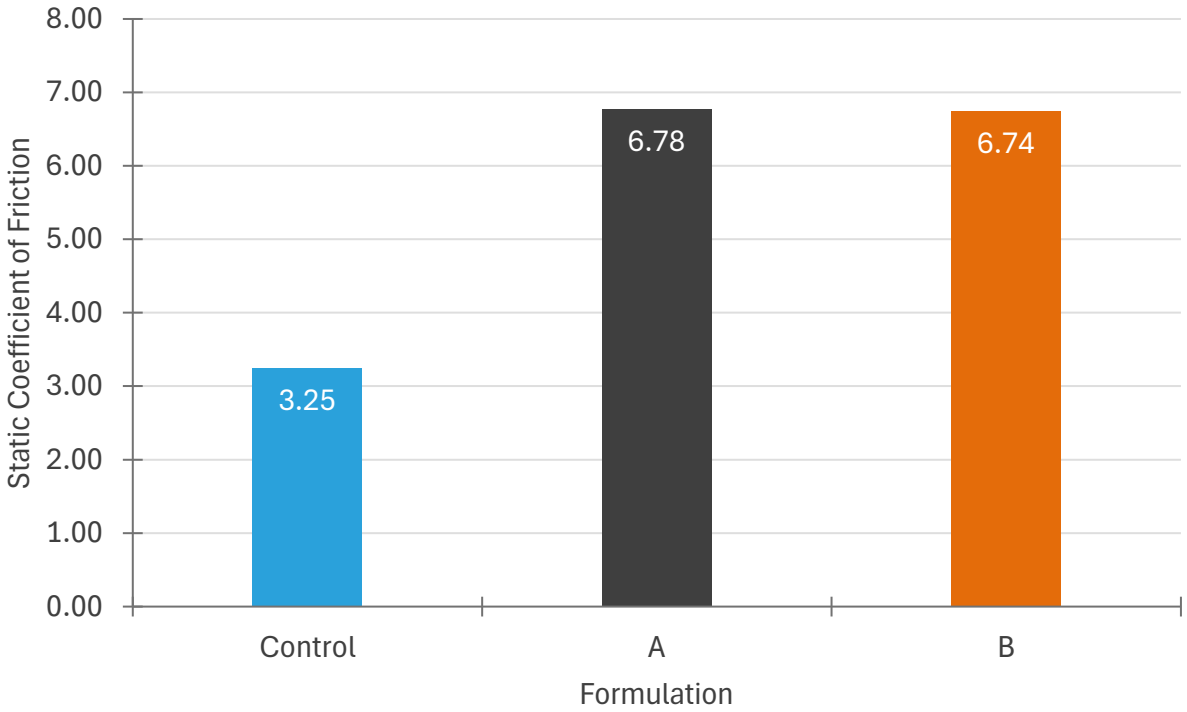

Figure 10. Static coefficient of friction of the compounds measured according to ASTM D1894. There was a significant increase in static CoF when N990CG was added to the compound.

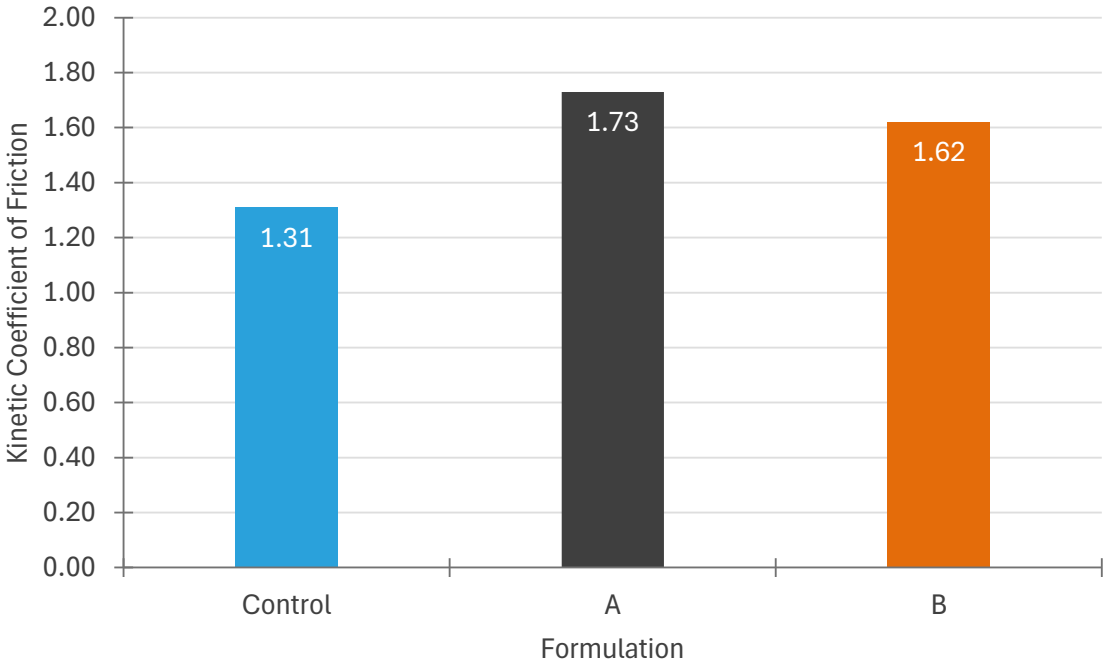

Figure 11. Kinetic coefficient of friction of the compounds measured according to ASTM D1894. There was a slight increase in kinetic CoF when N990CG was added to the compound.

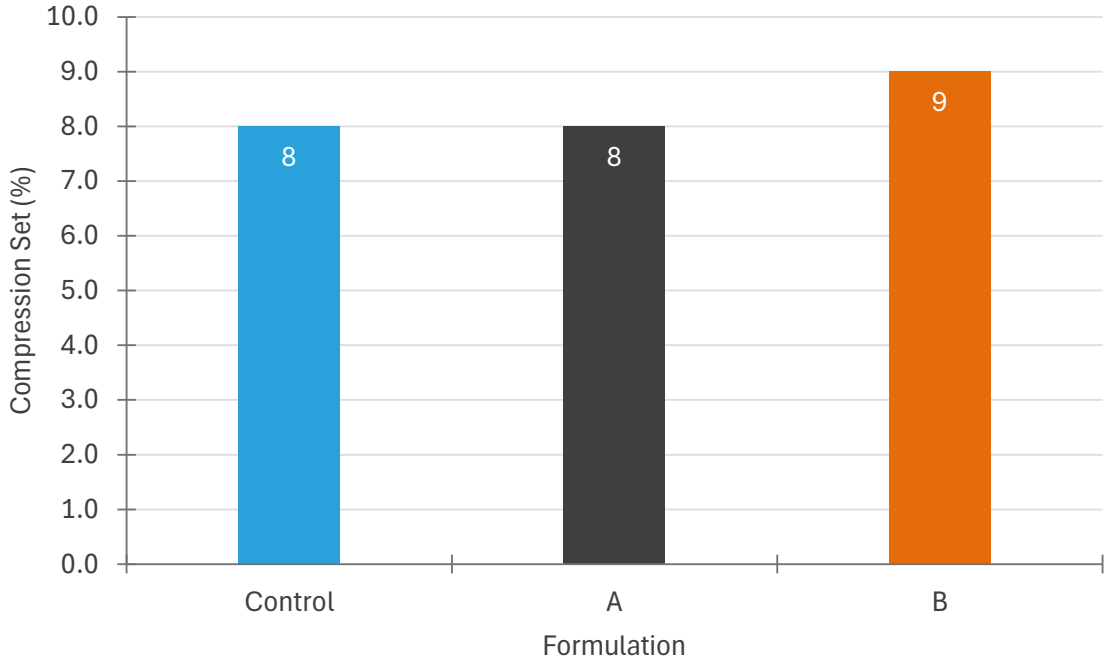

Figure 12. Compression set of the compounds measured after 22 hours at 70°C according to ASTM D395. There were no significant differences in compression set.

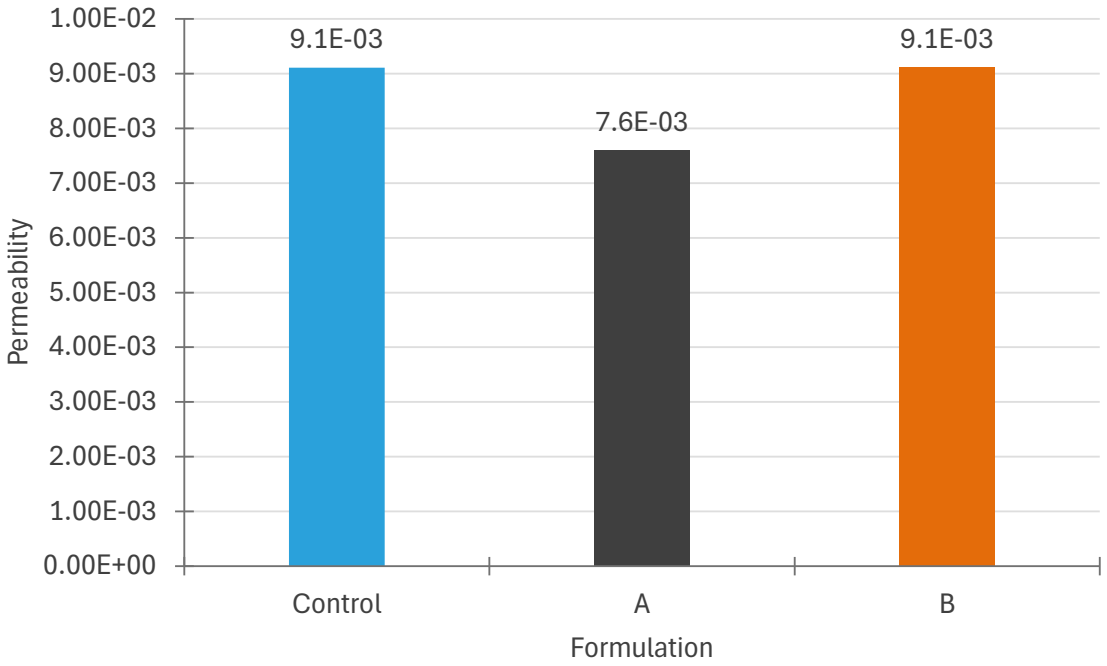

Figure 13. Permeability of the compounds measured according to ASTM E96. All compounds had similar permeability.

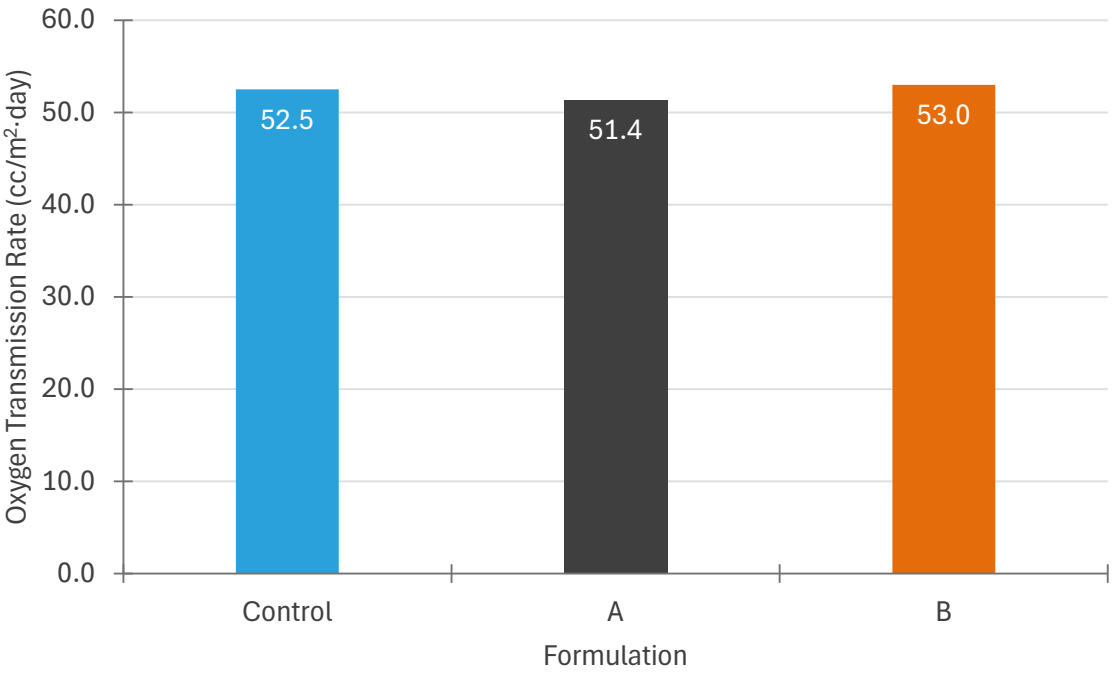

Figure 14. Oxygen transmission rate of the compounds measured according to ASTM D3985. There were no significant differences in OTR.

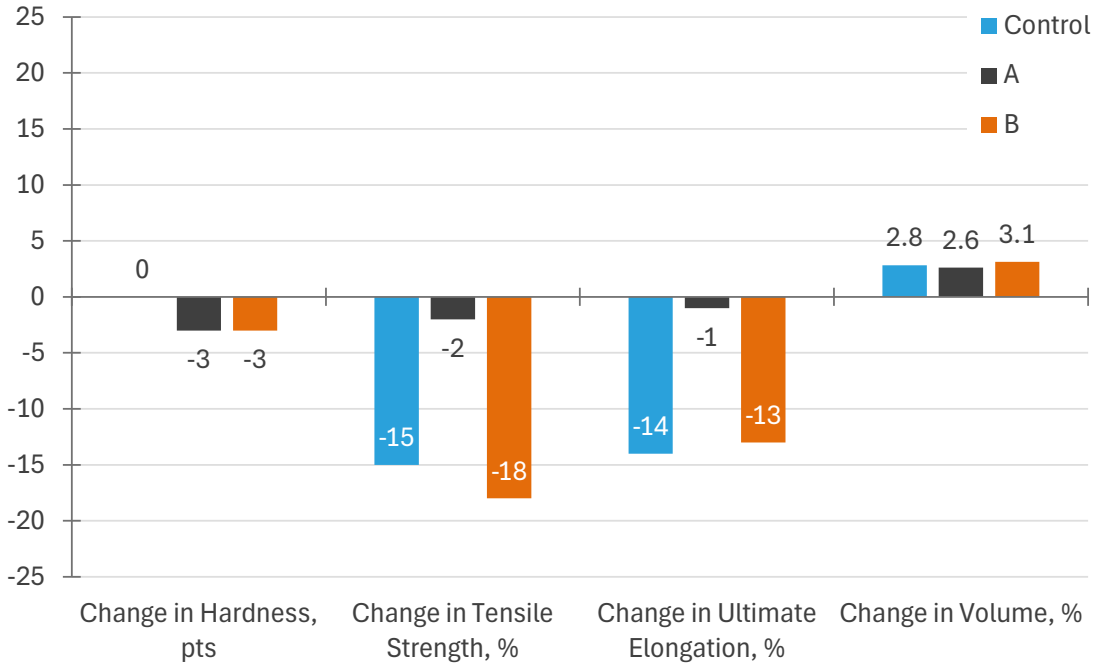

Figure 15. Change in properties after water immersion for 70 hours at 100C measured according to ASTM D471. The compound with 1 phr N990CG had the best performance.

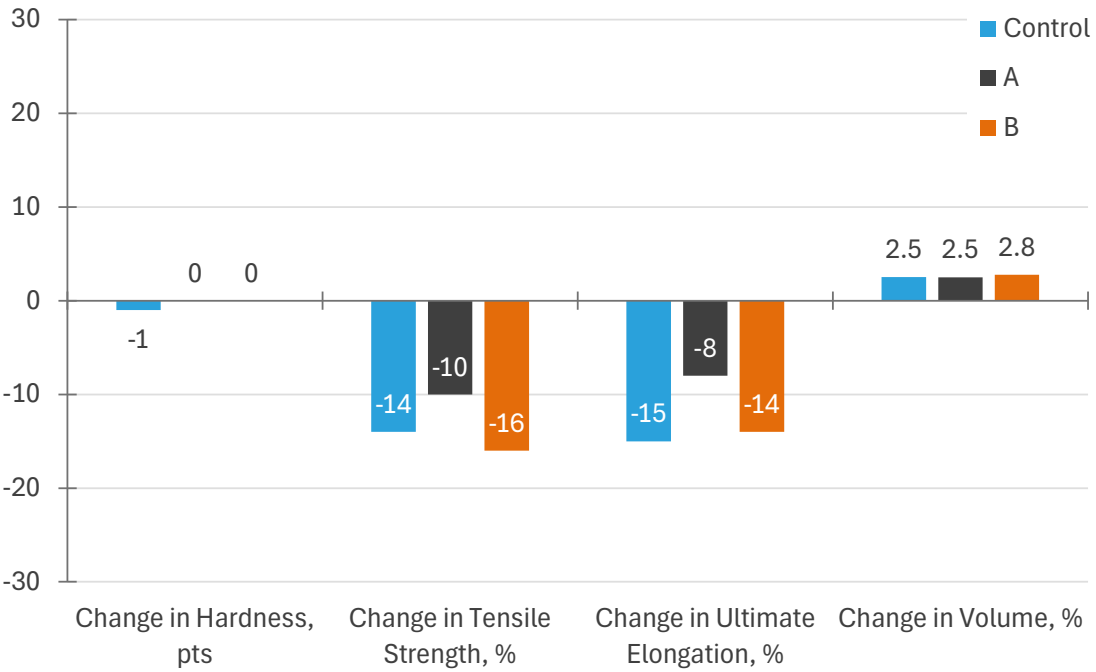

Figure 16. Change in properties after steam exposure for 24 hours at 121°C measured according to ASTM D471. All compounds had similar performance.

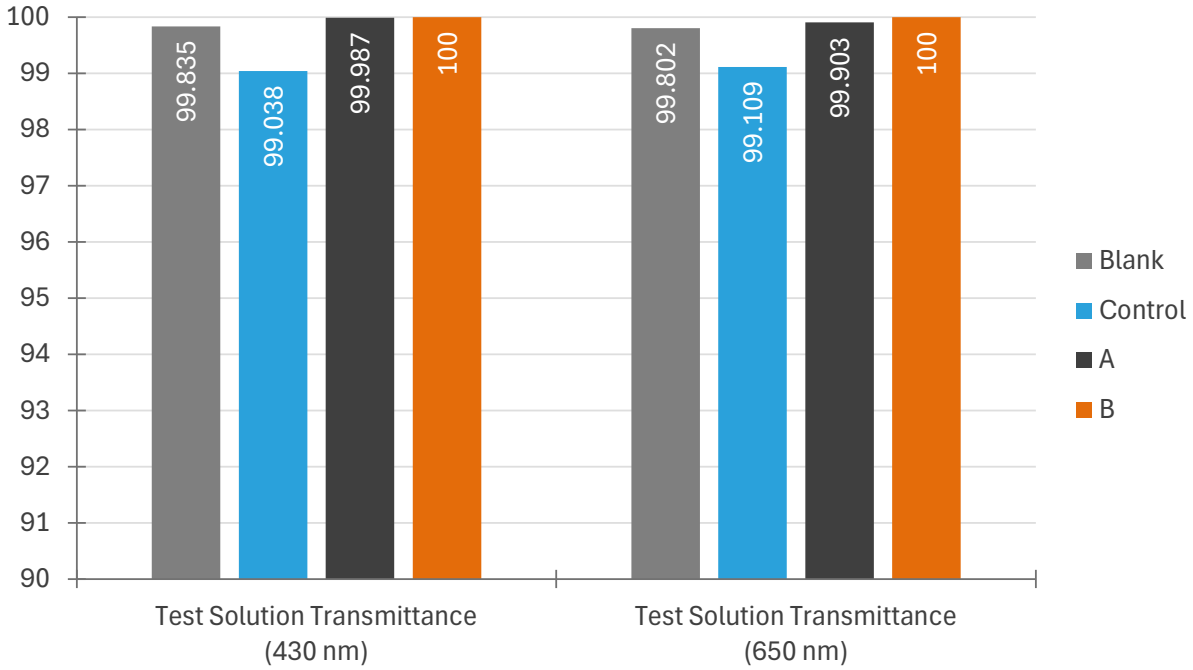

Figure 17. Test solution transmittance as measured according to *7.03 Test for Rubber Closure for Aqueous Infusions* Part 3 Extractable Substances of the Japanese Pharmacopoeia.

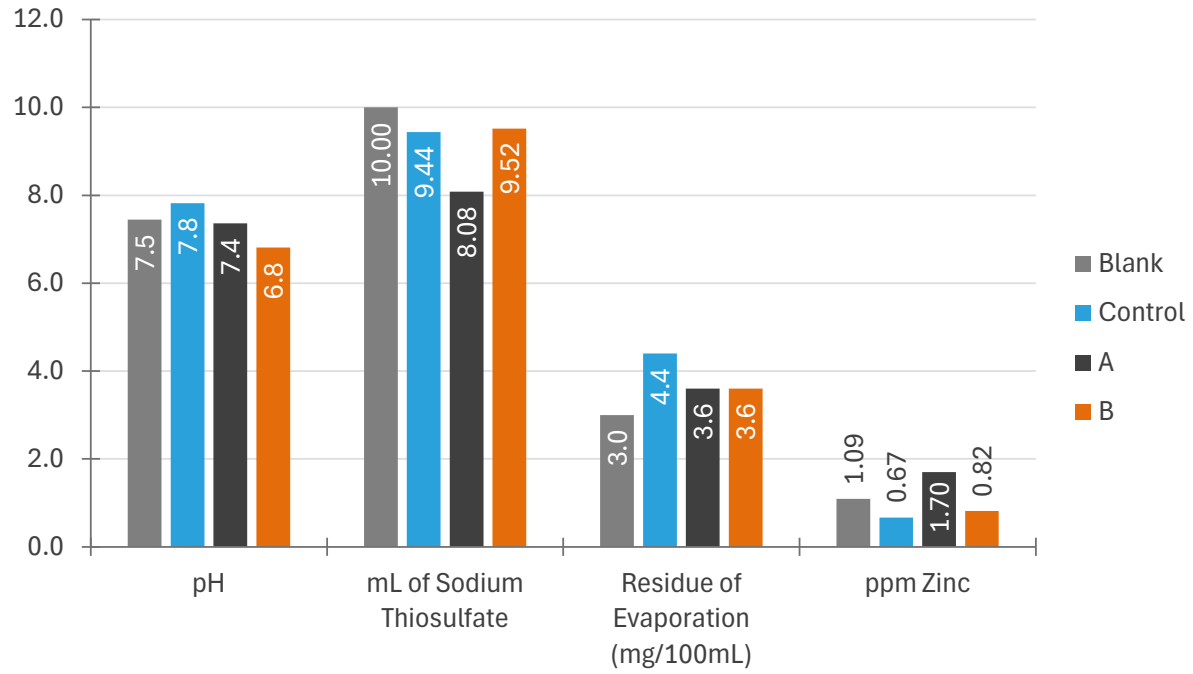

Figure 18. The pH, mL of sodium thiosulfate, residue on evaporation, and ppm Zinc measured according to *7.03 Test for Rubber Closure for Aqueous Infusions* Part 3 Extractable Substances of the Japanese Pharmacopoeia. Compounds with N990CG had similar results to blank and control.