

Lubrizol

Controlled Release Ingredients

For Nutraceutical Applications



Lubrizol LifeScience Polymers

Links Science to Life™

Introduction

Lubrizol LifeScience Polymers combines an in-depth understanding of functional polymer systems with a portfolio of specialty materials to deliver application-specific solutions to the medical device, pharmaceutical and healthcare industries.

Lubrizol Advanced Materials, Inc., is a global producer of high-performance pharmaceutical ingredients that have been used in a wide range of applications for over 50 years. All Lubrizol pharmaceutical polymers are manufactured according to current good manufacturing practice (cGMP) standards in ISO:9001-certified facilities. The polymers are supported by substantial toxicological data, which demonstrates the safety of the products for their intended applications.

Lubrizol polymers have a proven track record of use in a variety of different commercial tablet forms for the nutritional and pharmaceutical industries.

The Lubrizol Advantage

Lubrizol LifeScience Polymers' customers not only receive high-performance polymer products, but the support of one of the leading global organizations in the polymer industry, as well—that is The Lubrizol Advantage.

- The Lubrizol Corporation offers superior science and support to LifeScience Polymers on a global level.



- LifeScience Polymers' innovative research and development and technological advancements are powered by Lubrizol technology.
- The Lubrizol Corporation is a Berkshire Hathaway company—providing financial stability, a strong international presence and a keen understanding of industry standards and regulations.

A History of Quality Products

Carbopol® polymers are recognized by manufacturers around the world for their quality and performance. The products are high-molecular-weight crosslinked polymers of acrylic acid. Carbopol polymers provide highly effective controlled release properties at low concentrations. Typical usage levels in extended-release nutritional tablets are 5%–30%.

Key Benefits

Key Benefits of Carbopol Polymers in Controlled Release Nutritional Tablets:


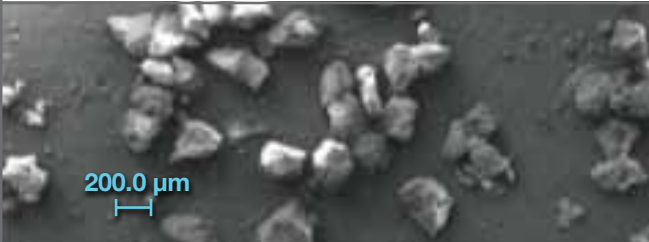
- Highly efficient matrix formers for controlling active release in nutritional tablets
- Controlled-release technology can minimize the dosing frequency, making the product more convenient and easy to use for consumers
- Offer formulation flexibility
 - Nutritional actives with different properties can be formulated to achieve various extended-release profiles
 - Can be used alone or in synergy with other polymers
 - Widely compatible with commonly used tablet ingredients
- Provide controlled release at lower use levels than other polymers, allowing for smaller tablet size and/or higher potency
- Provide consistent release of actives (low standard deviation)
- Available in both powder (Carbopol 971P NF polymer) and granular (Carbopol 71G NF polymer) forms
- Can be used in all types of tablet-manufacturing processes
- Manufactured according to cGMP standards in ISO:9001-certified facilities
- Transmissible Spongiform Encephalopathy (TSE)/Bovine Spongiform Encephalopathy (BSE) and Genetically Modified Organism (GMO) free
- Kosher-certified (Carbopol 971P NF polymer)



Recommended Polymers for Nutritional Tablets

Lubrizol recommends use of particular Carbopol polymers for controlled-release nutritional tablets as highlighted in Table 1. These polymers are also promoted for use in controlled-release oral solid dosage forms in the pharmaceutical industry.

Table 1. Recommended Polymers for Nutritional Tablets

Carbopol® 971P NF polymer	Carbopol® 71G NF polymer
Powder	Granular
Lightly crosslinked polymer	Chemically the same as Carbopol 971P NF polymer with no additives. Ideal for use in direct-compression processes, due to its improved flow properties.
Carbopol 971P NF polymer has very fine particle size in the 2 to 7 micron range. It also has a static charge, so it does not flow freely. Therefore, wet granulation may be necessary when considering Carbopol 971P NF polymer at levels greater than 5% in a formulation. At lower levels, it can often be incorporated in direct-compression formulations to provide extended-release and binding characteristics	Carbopol 71G NF polymer is a granular form of Carbopol 971P NF polymer, designed to have improved flow properties and be suitable for direct-compression processes. Most of the polymer particles are in the 40–100 mesh range. Due to the reduced surface area of Carbopol 71G NF polymer, higher usage levels (20%–30%) are needed for equivalent sustained release when compared to Carbopol 971P NF polymer.
	

Regulatory Information

GRAS Status

Lubrizol has made a self determination that Carbopol 971P NF and Carbopol 71G NF polymers may be used in nutritional tablet applications and are Generally Recognized As Safe (GRAS) within the meaning of such terms under the Food, Drug and Cosmetic (FD&C) Act.

Labeling of Carbopol Polymers in Nutritional Tablets

Carbopol polymers can be listed as “carbomer” in nutritional product ingredient listings. “Carbomer” is one of several descriptions that complies with the Dietary Supplement and Health Education Act (DSHEA) and U.S. FDA guidelines [21 CFR 101.4(a) (1)] for naming ingredients in dietary supplements.

Case Study 1 – Ascorbic Acid 500 mg Extended-Release Tablets

Ascorbic acid 500 mg extended-release tablets were manufactured by direct compression using Carbopol polymers as matrix-forming excipients.

Carbopol 971P NF polymer was included at a 5% level alone or in combination with Carbopol 71G NF polymer. At this level, 971P NF was able to provide extended-release properties without compromising the flowability of the blends.

Table 2: Composition of Ascorbic Acid

Ingredients (%) / Formulation	No Polymer	5% 971P NF	20% 71G NF & 5% 971P NF
Ascorbic Acid C-97DC-A (BASF Corporation)	94.00	89.00	69.00
Carbopol® 971P NF Polymer (Lubrizol)	0.00	5.00	5.00
Carbopol® 71G NF Polymer (Lubrizol)	0.00	0.00	20.00
Starch 1500® Pregelatinized Starch NF (Colorcon, Inc.)	5.00	5.00	5.00
Cab-O-Sil® M5 Fumed Silica (Cabot Corporation)	0.50	0.50	0.50
Synpro® Magnesium Stearate NF (Ferro Corporation)	0.50	0.50	0.50
Total:	200.00	100.00	100.00
Tablet Weight (mg)	548.37	579.17	747.05

In the presence of the polymer(s), it was possible to obtain tablets with acceptable hardness and friability at lower compression forces compared to the formulation without polymers. Tablets had uniform properties and showed low variability during dissolution. Carbopol polymers efficiently extended the release of ascorbic acid in various media for 8–12 hours.



Figure 1. Vitamin C 500 mg – Release in pH=6.8 Buffer

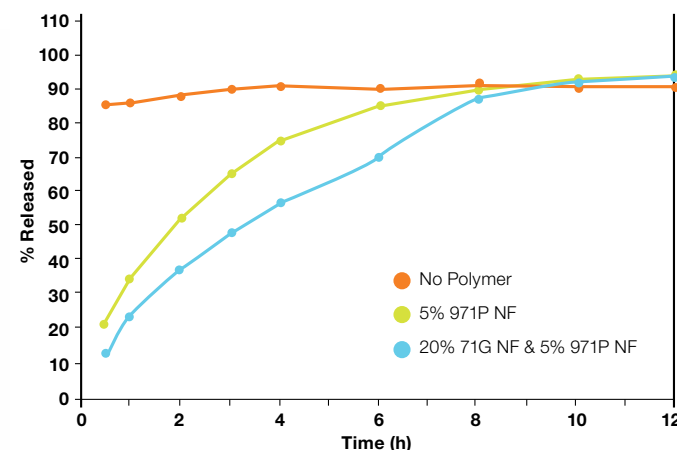


Figure 2. Vitamin C 500 mg – Release in Deionized Water

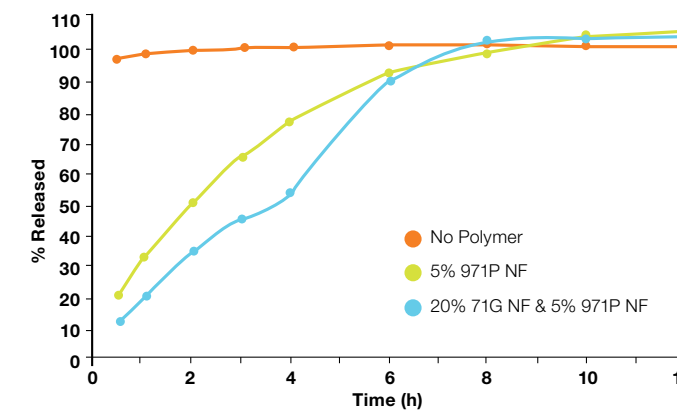
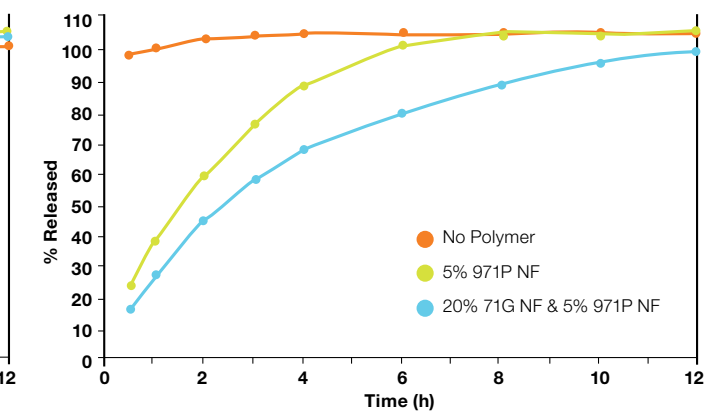


Figure 3. Vitamin C 500 mg – Release in 0.1N HCl



Conclusion

- Tablet formulations containing 5% Carbopol 971P NF polymer with and without Carbopol 71G NF polymer showed significantly slower release of ascorbic acid compared to the formulation with no polymer.
- The formulations with 5% Carbopol 971P NF polymer extended the release of ascorbic acid for approximately 8 hours in buffer or water.
- The formulations with 5% Carbopol 971P NF polymer and 20% Carbopol 71G NF polymer released slightly slower than the formulations with 5% polymer alone; active release was extended for 8–10 hours in all media.

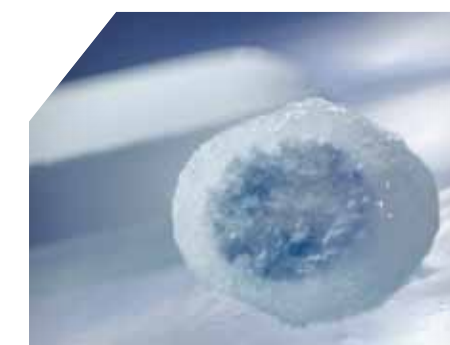
Case Study 2 – Caffeine 100 mg and 200 mg Extended-Release Tablets

Caffeine 100 mg and 200 mg extended-release tablets were manufactured by direct compression using 0%–7% w/w Carbopol 971P NF polymer as the matrix-forming ingredient.

Table 3. Composition of Caffeine Tablets

Formulation (% w/w)	A	B	C	D
Caffeine anhydrous granular	82.0	82.0	82.0	82.0
Carbopol® 971P NF polymer	0.0	3.0	5.0	7.0
Prosolv® SMCC 90 silicified microcrystalline cellulose	17.0	14.0	12.0	10.0
Aerosil® R972 pharma fumed silica	0.50	0.50	0.50	0.50
Magnesium stearate	0.50	0.50	0.50	0.50
Total:	100	100	100	100

- Target tablet weight: 122 mg for 100 mg dose or 244 mg for 200 mg dose.
- Caffeine anhydrous granular 0.07/0.5 (BASF Corporation).



Cross-section of tablet containing Carbopol polymer during dissolution.



Figure 4. Caffeine Release from 100 mg and 200 mg Dose Tablets in pH=6.8 Phosphate Buffer

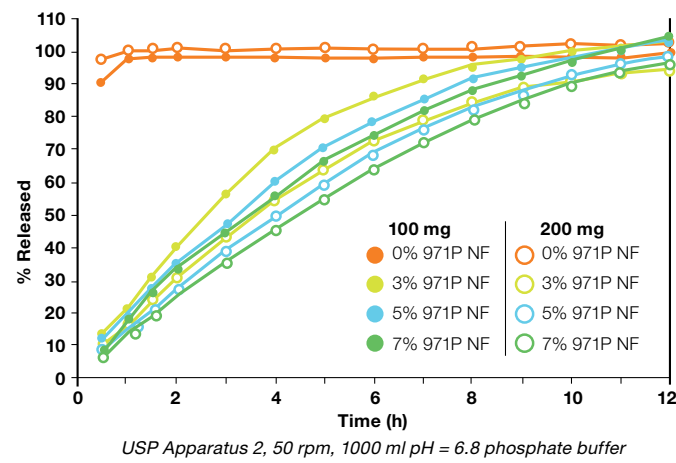
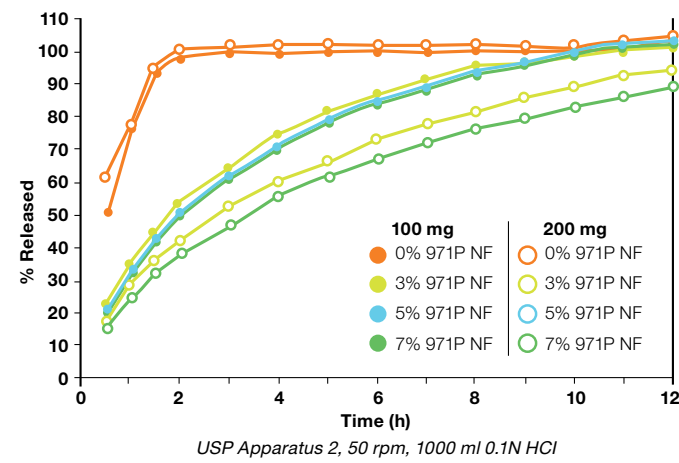


Figure 5. Caffeine Release from 100 mg and 200 mg Dose Tablets in 0.1N HCl



Results

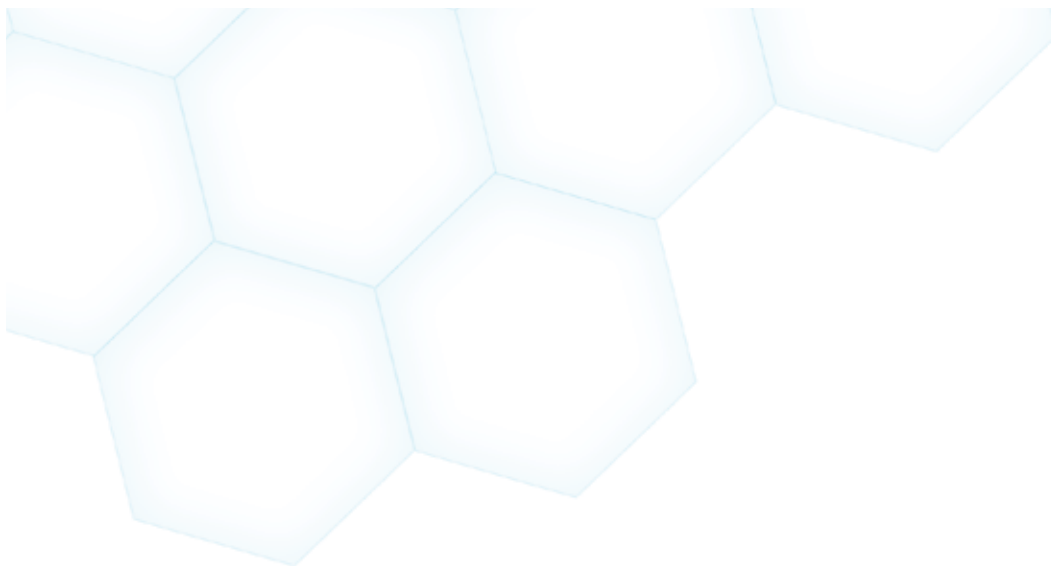
- The formulation without Carbopol 971P NF polymer resulted in immediate release of the active.
- Formulations with 3%–7% w/w Carbopol 971P NF polymer imparted extended-release properties for up to 12 hours. The ability of the polymer to extend the release at these low levels can be explained by its chemically crosslinked nature and fine particle size (median diameter 2–7 microns).
- Increasing the polymer level from 3% to 7% w/w led to a slight decrease in the dissolution in pH=6.8 buffer (Figure 1). Increasing the polymer level did not affect the release in acid except in 200 mg tablets, where a polymer increase from 5% to 7% w/w led to slightly slower dissolution (Figure 2).
- A polymer level of 7% w/w did not provide significant dissolution benefits compared to lower inclusion levels (3% or 5% w/w).

- For all extended-release formulations, the higher dose (200 mg) was characterized by slower release compared to the lower dose (100 mg). This is due to the difference in the ratio of tablet surface area to volume.

Conclusions

Cost-effective extended-release tablets with a 6- to 12-hour release target can be developed by direct compression using Carbopol 971P NF polymer as a matrix-forming excipient at a 3%–5% w/w inclusion level.

In summary, Carbopol polymers provide highly effective extended release properties at low concentrations. This is particularly beneficial when a high level of active is desired in the tablet. Carbopol polymers can be used in a variety of manufacturing methods such as direct compression, dry granulation (roller compaction, slugging) or wet granulation, and it is compatible with a wide variety of ingredients. Visit our website at www.lubrizol.com/lifescience/polymers for more case studies and information on Carbopol polymers.



LifeScience Polymers | Medical Solutions | Pharmaceutical Solutions | Oral Care and Dental Solutions



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