

Lubrizol



**LUBRIZOL POLYMERS FOR CONTROLLED RELEASE
NUTRITIONAL TABLETS**





Introduction

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 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.

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 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 forms (Carbopol® 71G NF polymer)
- Can be used in all types of tablet manufacturing processes
- Manufactured according to cGMP standards in ISO 9001 certified facilities
- TSE/BSE and 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

| Product Trade Name | Physical Form | Comments |
|---------------------------|---------------|--|
| Carbopol® 971P NF Polymer | Powder | Lightly crosslinked polymer |
| Carbopol® 71G NF Polymer | Granular | 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 (Figure 1). 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.

Figure 1: Scanning Electron Micrograph (SEM) of Carbopol® 971P NF polymer

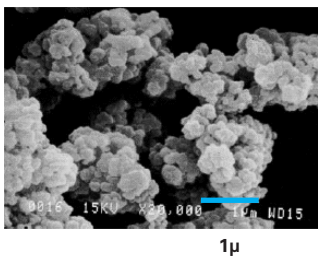
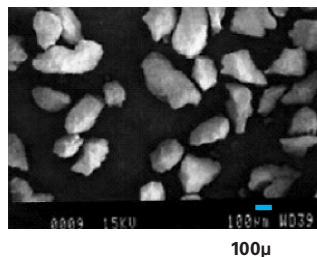


Figure 2: Scanning Electron Micrograph (SEM) of Carbopol® 71G NF polymer



Carbopol® 71G NF polymer is a granular form of Carbopol® 971P NF polymer (Figure 2), 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 term 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.



Formulation Data with Vitamin C (Ascorbic Acid)

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: Test Formulation

| Ingredients (%) / Formulation | No Polymer | 5% 971P NF | 20% 71G NF & 5% 971P NF |
|--|-------------------|-------------------|------------------------------------|
| Ascorbic acid C-97 DC-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 | 100.00 | 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 3: Vitamin C 500 mg – Release in pH = 6.8 Buffer

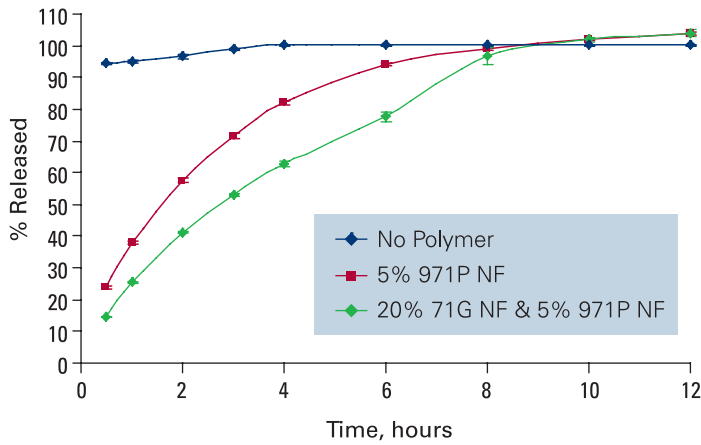


Figure 4: Vitamin C 500 mg – Release in Deionized Water

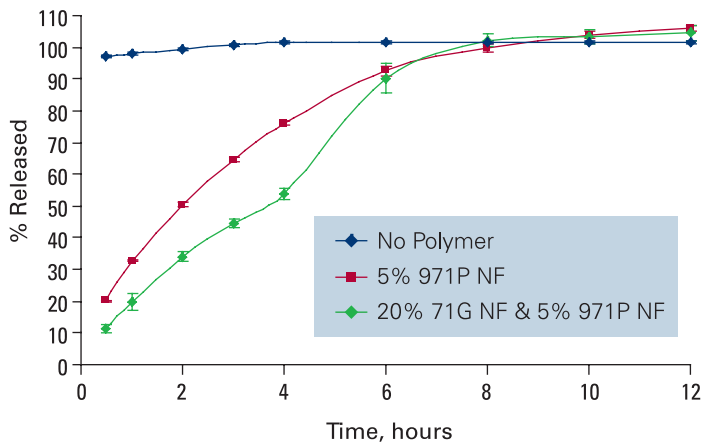
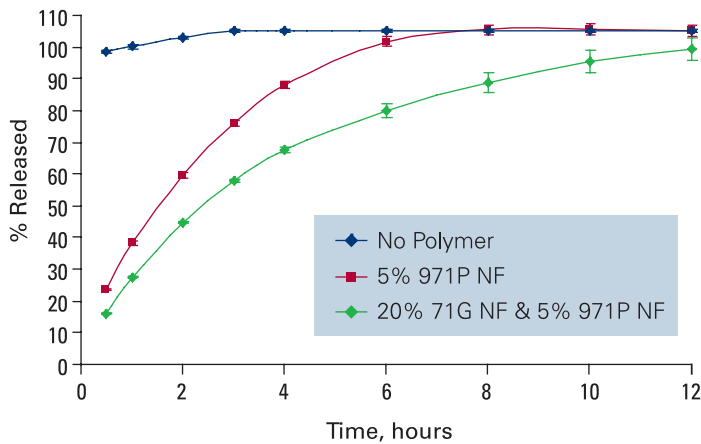


Figure 5: Vitamin C 500 mg – Release in 0.1N HCl



Conclusions

- 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 formulation with 5% Carbopol® 971P NF polymer extended the release of ascorbic acid for approximately 8 hours in buffer or water.
- The formulation with 5% Carbopol® 971P NF polymer and 20% Carbopol® 71G NF polymer released slightly slower than the formulation with 5% polymer alone; active release was extended for 8 - 10 hours in all media.





Detailed product information and samples of Lubrizol's high performance specialty chemicals for the pharmaceutical industry can be obtained through our web site at www.pharma.lubrizol.com or contact your sales representative or nearest Lubrizol office.

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