Pharmaceutical Bulletin 32
Edition: October 29, 2008
Previous Edition: October 28, 2004 / April 28, 2006

Application of Carbopol®* 71G NF Polymer in Controlled Release Tablets

Carbopol® 71G NF Polymer – Development and Properties

Carbopol® polymers have demonstrated good performance in tablet applications. When used at low levels (0.5 - 3%) as binders, they improve the hardness and friability of the tablets and enable target properties to be achieved at low compression forces. At higher levels (3 - 30%), they provide controlled release of the drugs.

Powder Carbopol® polymers (971P NF, 974P NF) have very fine particle size and static charge, thus they do not flow freely and at high inclusion levels, are not ideal candidates for direct compression.

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 process. It is chemically the same polymer, with no additives.

Carbopol® 71G NF Polymer (Granular Form)

Carbopol® 971P NF Polymer (Powder Form)

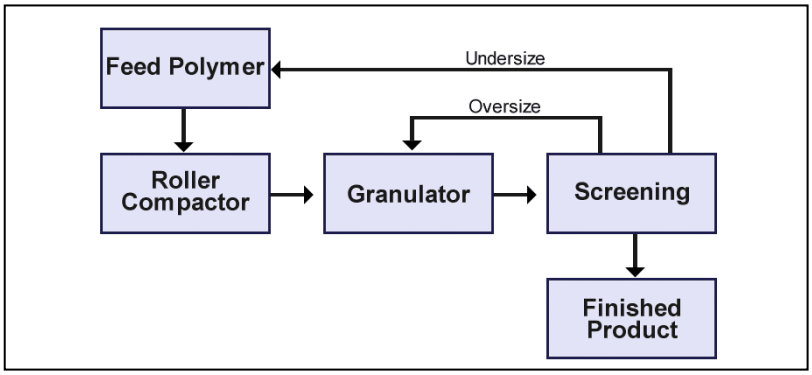
Lubrizol Advanced Materials, Inc. / 9911 Brecksville Road, Cleveland, Ohio 44141-3247 / TEL: 800.379.5389 or 216.447.5000

For further information, please visit www.pharma.lubrizol.com

Carbopol® 71G NF polymer is manufactured by roller compaction of Carbopol® 971P NF polymer. The process consists of the following steps and it is schematically presented in Figure 1:

- delivering a fine polymer powder to the compaction device;
- compacting into larger agglomerates and/or aggregates;
- fracturing of agglomerates and/or aggregates into smaller granules (grinding);
- screening the granules to obtain the desired particle size range and recycling the oversized and/or undersized granules.

Figure 1 – Schematic representation of the manufacture of Carbopol® 71G NF Polymer



Process variables such as the compaction pressure, roll speeds, attrition device, operation speed, and screening parameters are used to control the densification and particle size distribution.

The resulting granules are free flowable, have increased bulk density, and contain minimal amounts of very small particles that can cause dusting and/or static adherence compared to the powder polymer.

Roller compaction has been used to granulate Carbopol® polymers as it avoids processing with water or flammable solvents. The polymers swell rapidly in water, thus the wet granulation process might be difficult.

The particle size distribution of Carbopol® 971P NF and 71G NF polymers (Micron AirJet Sieve) are shown in Figures 2 and 3. Carbopol® 971P NF polymer has very fine particles, while the granular grade has most of the particles in the 40-100 mesh range.

Figure 2 – Typical particle size distribution of Carbopol® 971P NF polymer

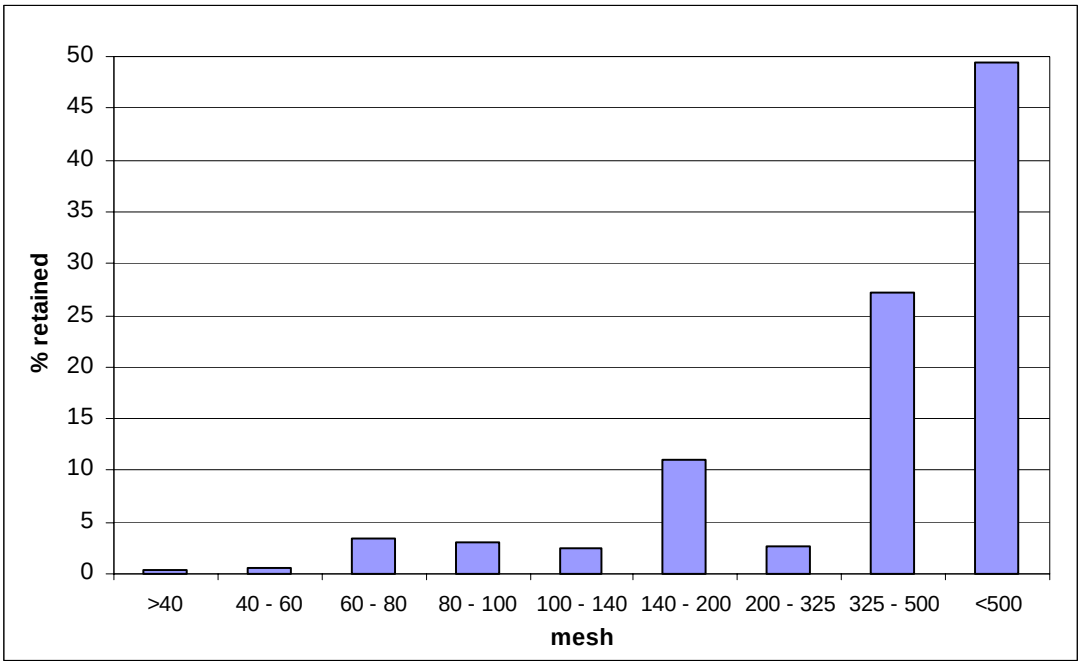
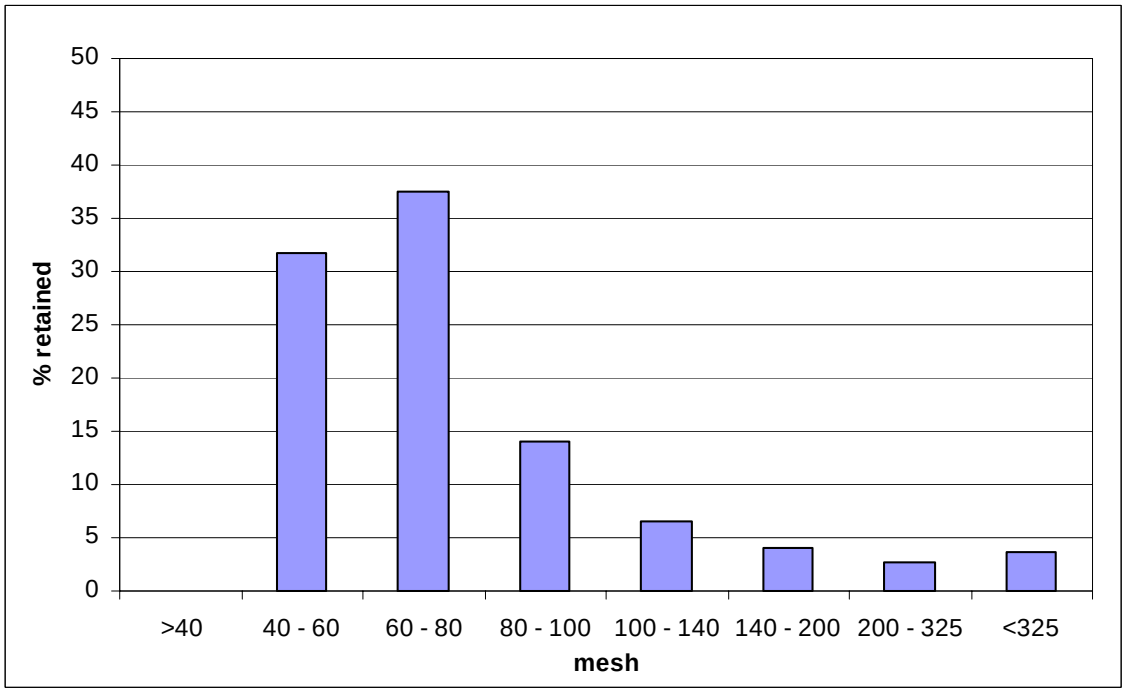


Figure 3 – Typical particle size distribution of Carbopol® 71G NF polymer



Figures 4 & 5 show the scanning electron micrographs of Carbopol® 971P NF and 71G NF polymers.

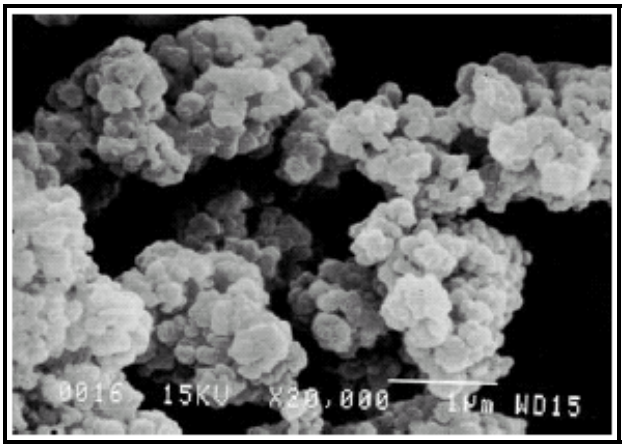


Figure 4 – SEM of Carbopol® 971P NF polymer

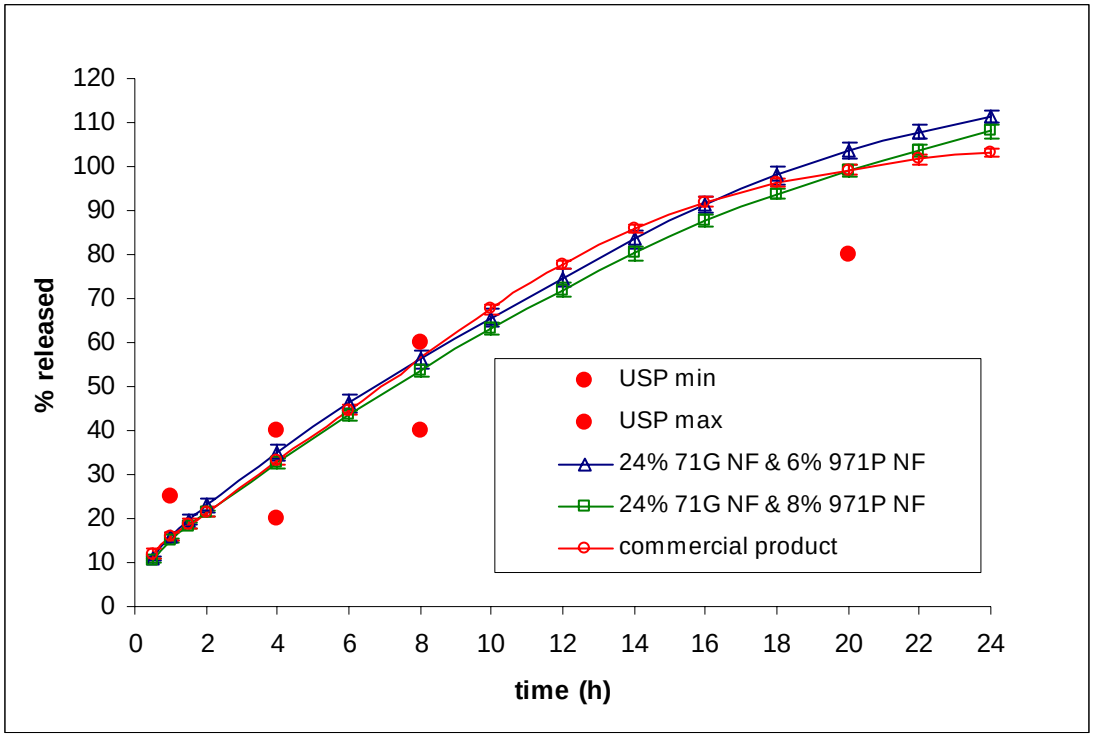
Figure 5 – SEM of Carbopol™ 71G NF polymer

Carbopol® 71G NF polymer has the following typical properties (not specifications):

Property	Value Range
Bulk density (kg/m^3)	325 - 400
Tap density (kg/m^3)	400 - 465
BET surface area (m^2/g)	10 - 12

Recommended usage levels for Carbopol® 71G NF polymer are 10 - 30% of the tablet weight. Granular and powder Carbopol® polymer grades can be combined in direct compression and wet granulation formulations to reduce the total polymer level and drug release variability. Carbopol® 71G NF polymer is added extragranularly to the formulation while the powder grades can be added either intra or extragranuarly. For example, Metoprolol tablets were formulated with Carbopol® 71G NF polymer (24%) and Carbopol® 971P NF polymer (6 or 8%) and had release profiles that met U.S. Pharmacopeial requirements – Figure 6.

Figure 6 - Metoprolol tablets formulated with Carbopol® 71G NF and Carbopol® 971P NF polymers



Performance of Carbopol® 71G Polymer in Tablets

Intra-Lot Reproducibility

Theophylline tablets manufactured with Carbopol® 71G NF polymer (Table 1) were very uniform and no segregation was observed during the compression run.

Table 1
Theophylline Tablets with Carbopol 71G NF Polymer

Formulation		Process Flow	Blend Properties	
Ingredient	**%**			
Theophylline	32.9	• Blend all ingredients except the lubricant for 25 min. in V-blender • Add the lubricant and mix for additional 2 min. • Compress on Korsch PH101 tablet press (target weight 303 mg, hardness 10 kP) • Batch size: 1.5 kg	Flow rate (g/sec)	3.67
Carbopol® 71G NF polymer	25.0		Bulk density (g/cc)	0.533
Anhydrous lactose	20.8		Tap density (g/cc)	0.673
Dibasic calcium phosphate	20.8		Hausner ratio	1.263
Magnesium stearate	0.5			

Tablets collected at the beginning and end of the compression run had similar physical properties and drug release – Table 2, Figures 7 & 8.

Table 2

Properties of Theophylline Tablets with Carbopol® 71G NF Polymer - Intra-Lot Variability

Tablet property	First 20%	Last 20%
Weight (mg)	302 ± 0.6	303 ± 0.6
Hardness (kP)	10.6 ± 0.5	10.4 ± 0.5
Friability (%)	0.14	0.10

Figure 7 – Intra-lot variability of Theophylline release (USP apparatus 2, simulated gastric fluid) from tablets with Carbopol® 71G NF polymer

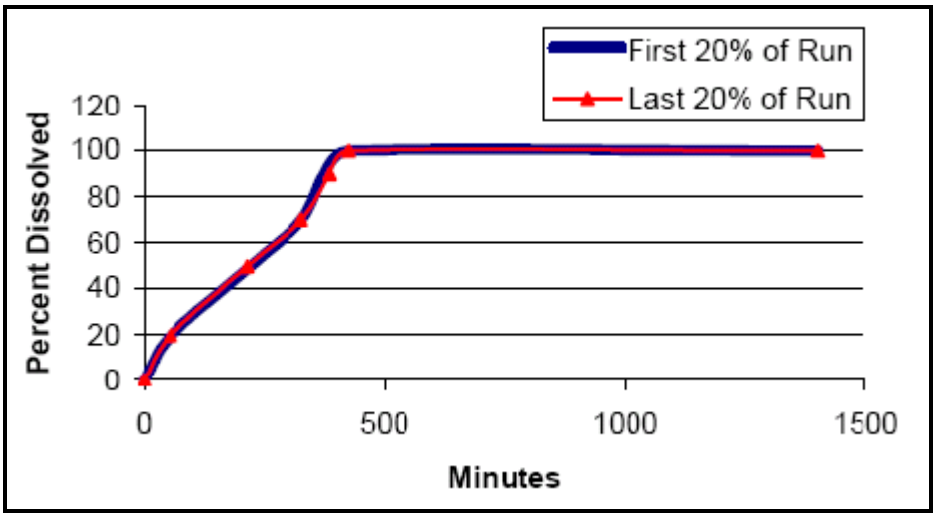
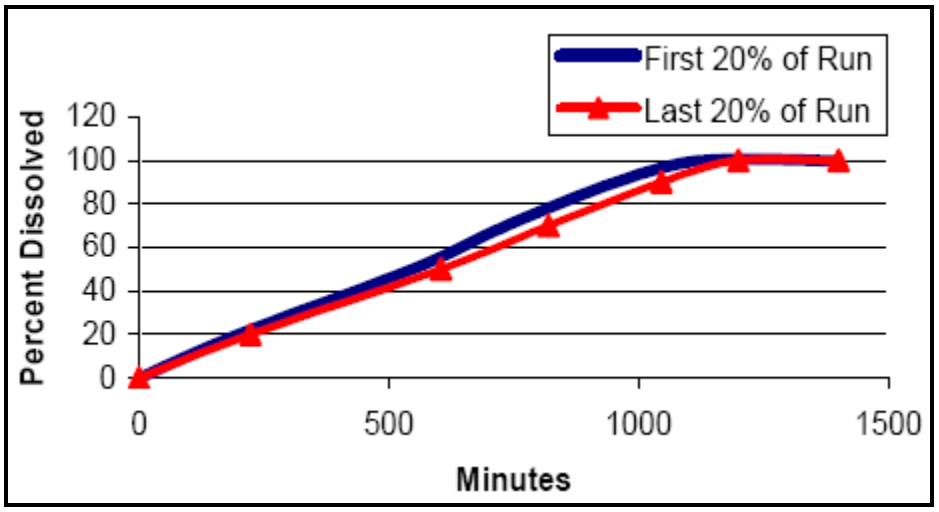


Figure 8 – Intra-lot variability of Theophylline release (USP apparatus 2, pH=7.5 simulated intestinal fluid) from tablets with Carbopol® 71G NF polymer



Inter-Lot Reproducibility in Direct Compression Process

Theophylline tablets were manufactured by direct compression using five consecutive lots of Carbopol® 71G NF polymer (Table 3).

Table 3
Theophylline Tablets with Carbopol® 71G NF Polymer – Direct Compression

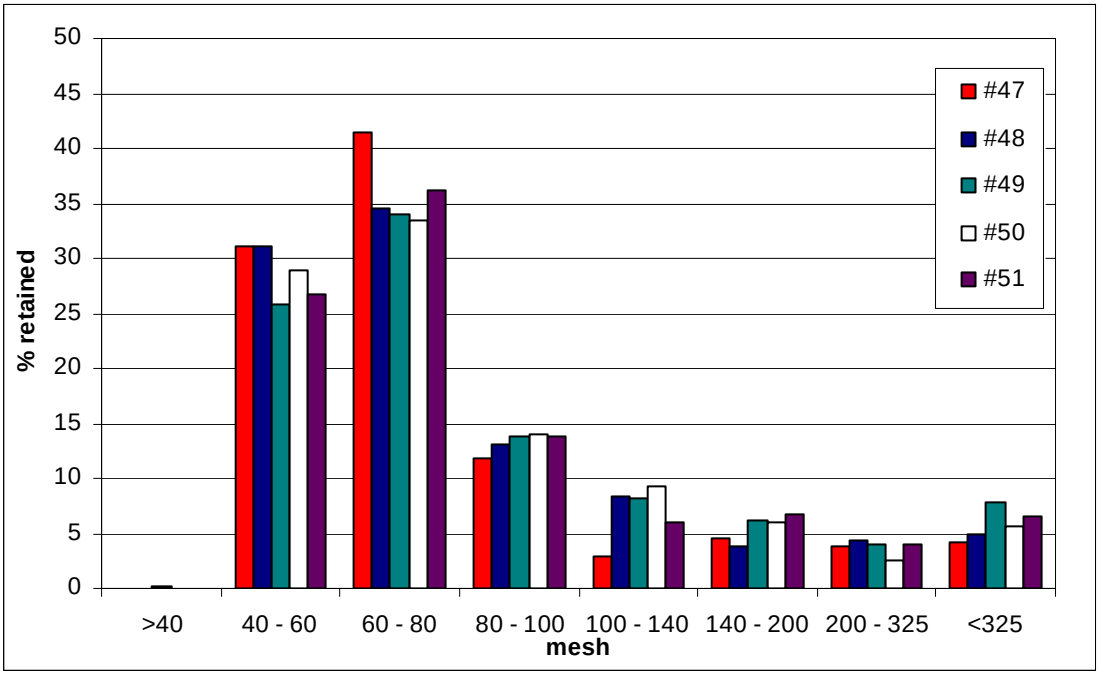
Formulation		Process Flow
Ingredient	**%**	
Theophylline	32.9	• Blend all ingredients except the lubricant for 25 min. in V-blender • Add the lubricant and mix for additional 2 min. • Compress on Korsch PH101 tablet press (target weight 303 mg, hardness 10 kP)
Carbopol® 71G NF polymer	25.0	
Anhydrous lactose	20.8	
Dibasic calcium phosphate	20.8	
Magnesium stearate	0.5	

The properties of the polymer and tablets were very similar among the five lots (Table 4, Figure 9).

Table 4
Properties of Carbopol® 71G NF Polymer and Resulting Theophylline Tablets – Inter-Lot Variability

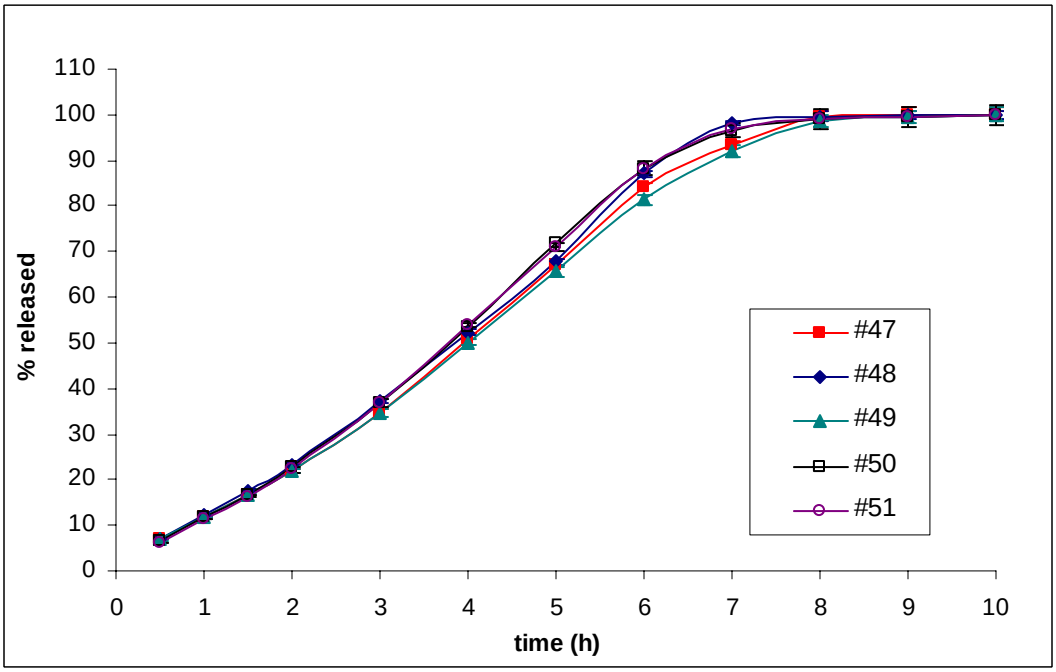
Properties / lot	#47	#48	#49	#50	#51
Polymer					
Bulk density(g/cc)	0.362	0.366	0.363	0.368	0.373
Tap density(g/cc)	0.426	0.428	0.428	0.433	0.437
Hausner ratio	1.175	1.169	1.178	1.178	1.172
Compressibility index	14.91	14.43	15.14	15.08	14.66
Tablets					
Weight (mg)	303.00 ± 2.71	303.13 ± 2.04	303.98 ± 2.08	303.26 ± 2.43	304.37 ± 1.91
Thickness (mm)	4.27 ± 0.02	4.25 ± 0.02	4.25 ± 0.02	4.25 ± 0.01	4.24 ± 0.01
Hardness (kP)	10.31 ± 0.62	10.24 ± 0.90	10.93 ± 0.57	10.42 ± 0.68	10.80 ± 0.3
Friability (%)	0.08	0.07	0.10	0.07	0.12

Figure 9 – Particle size distribution of Carbopol® 71G NF polymer – inter-lot variability



Drug release profiles demonstrated good inter-lot reproducibility (Figure 10).

Figure 10 – Theophylline release (USP apparatus 2, pH=7.5 buffer) from tablets with Carbopol® 71G NF polymer - inter-lot reproducibility



Effect of Compression Force on Tablet Properties and Drug Release

Increasing the compression force in the case of Theophylline tablets (100 mg with 25% 71G NF) led to an increase in the hardness (Figure 11). However, the release profiles were similar (Figure 12).

Figure 11 – Hardness of Theophylline direct compressible tablets with Carbopol® 71G NF polymer

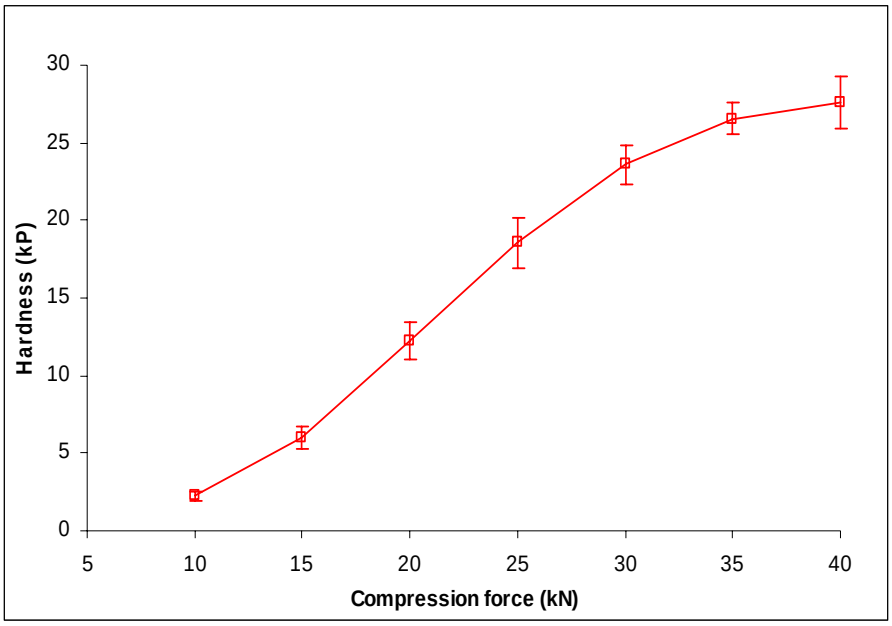
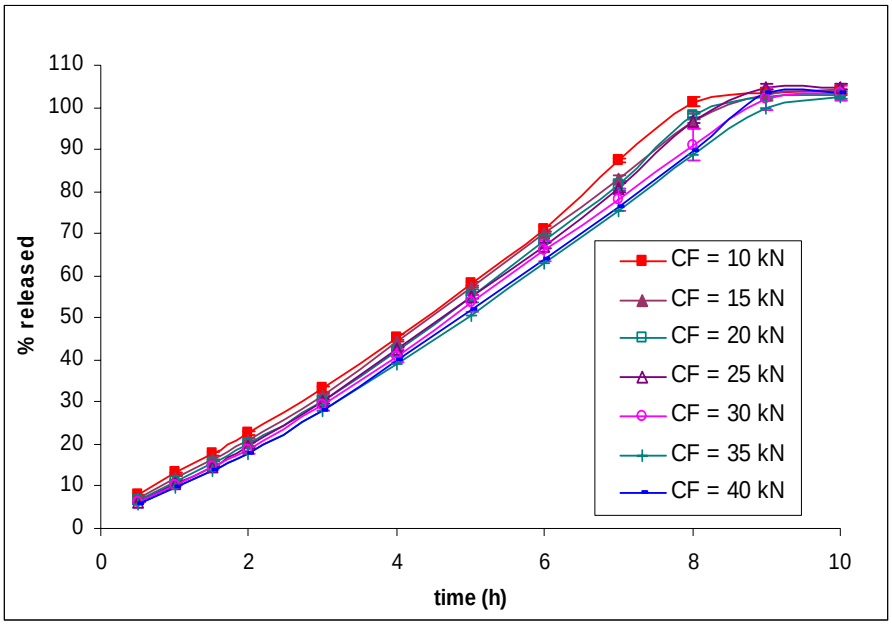


Figure 12 – Theophylline release (USP apparatus 2, pH=7.5 buffer) from tablets with Carbopol® 71G NF polymer



Benefits of Carbopol® 71G NF Polymer in Controlled Release Tablet Formulations

- Good flow in high-speed equipment
- Good compressibility
- Direct compressible excipient
- Minimal dust and static adherence
- Controlled release performance in tablet
- Can be combined with powder grade Carbopol® polymers or other controlled release excipients to improve the flowability of the formulation and achieve flexibility in drug release performance
- Reproducibility (intra- and inter-lot)
- Global pharmacopeial status and U.S. and European Drug Master Files (DMFs)