Lubrizol

Formulating Controlled Release Tablets and Capsules with Carbopol®* Polymers

Lubrizol recommends Carbopol® 974P NF, Carbopol® 971P NF, Carbopol® 71G NF polymers and Noveon®* AA-1 polycarbophil for oral applications. Some commercially available formulations contain Carbopol® 934P NF polymer, but this polymer is typically not used for new development due to regulatory restrictions on benzene, the solvent used in its synthesis (for more information, please refer to *Lubrizol Pharmaceutical Bulletin 1: "Polymers for Pharmaceutical Applications"*).

Carbopol® 974P NF polymer is highly crosslinked and produces highly viscous gels with short flow similar to mayonnaise. Conversely, Carbopol® 971P NF polymer is lightly crosslinked, with longer rheology, which will flow like honey in a semisolid formulation. Carbopol® 71G NF polymer is a granular form of Carbopol® 971P NF polymer. It is the same chemical with no additives and improved flow properties (Carbopol® 71G NF polymer is reviewed in detail in *Lubrizol Pharmaceutical Bulletin 32: "Carbopol® 71G NF Polymer for Controlled Release Tablets"*).

Noveon® AA-1 polycarbophil, USP has been studied primarily for use in buccal tablets for its bioadhesive properties.

Carbopol® polymers and Noveon® polycarbophil can be successfully included into a variety of different tablet forms, including swallowable (peroral), chewable, buccal and sublingual tablets; providing controlled release properties, bioadhesion and good binding characteristics.

In buccal and sublingual tablets, Carbopol® polymers and Noveon® polycarbophil can provide bioadhesive and/or controlled release properties. A significant amount of information is available regarding the use of those polymers as a bioadhesive (for information on bioadhesion, please refer to *Lubrizol Pharmaceutical Bulletin 23: "Bioadhesion"*).

Carbopol® 971P NF polymer was included in a Doxycycline sublingual tablet formulation to provide both bioadhesion and sustained drug release *(Chang, 2004)*.

Formulations of Buprenorphine sublingual tablets containing Carbopol® 974P NF polymer provided adequate mucoadhesive strength and drug release *(Das et al., 2004)*.

Carbopol® polymers and Noveon® AA-1 polycarbophil may also be suitable for chewable tablets due to their fine particle size and good compression characteristics. In addition, Carbopol® polymers can provide taste masking properties when reacted with certain amine drugs and this can be beneficial in chewable tablets.

Some of the active pharmaceutical ingredients successfully formulated in tablets or capsules using Lubrizol pharmaceutical polymers are listed in Table 1 (commercial products, patents, research papers).

Table 1

Examples of Active Pharmaceutical Ingredients
Formulated as Tablets or Capsules with
Carbopol® Polymers or Noveon® Polycarbophil

• Acetyl cysteine*	• α-Lipoic acid*
• Acetyl salicylic acid	• Loratidine*
• Amlodipine*	• Lorazepam*
• Ascorbic acid*	• Mesalamine*
• Atenolol	• Metformin*
• Buprenorphine	• Metixene*
• Bupropion	• Metoprolol*
• Carbamazepine	• Nicotine*
• Cefixime*	• Nifedipine*
• Cefprozil	• Nitrofurantoin*
• Chlorpheniramine maleate	• Pentoxifylline*
• Cloxacillin*	• Pseudoephedrine*
• Dextromethorphan*	• Propranolol
• Diclofenac	• Risperidone*
• Diethylpropion*	• Sodium fluoride
• Diphenhydramine	• Sodium valproate
• Furosemide	• Testosterone*
• Gingko biloba*	• Theophylline
• Glucosamine*	• Triamcinolone*
• Guaifenesin*	• Venlafaxine
• Isoniazid	• Verapamil*
• Lithium carbonate*	• Viloxazine

(*) denotes commercial products

Effect of Carbopol® Polymer Type on Drug Release

Drug release is affected by differences in the rates of hydration and swelling of the polymer hydrogel, which are largely defined by the crosslinker levels (please refer to Bulletin 30).

Lightly crosslinked polymers, such as Carbopol® 971P NF polymer, tend to be more efficient in controlling drug release than highly crosslinked polymers such as Carbopol® 974P NF polymer. For example, Theophylline release in pH=6.8 phosphate buffer was slower in the case of wet granulated tablets with 10% Carbopol® 971P NF polymer than with 10% Carbopol® 974P NF polymer – Figure 1.

Figure 1 – **Effect of Carbopol® polymer type on Theophylline release (USP apparatus 2, pH=6.8 buffer) from wet granulated tablets**
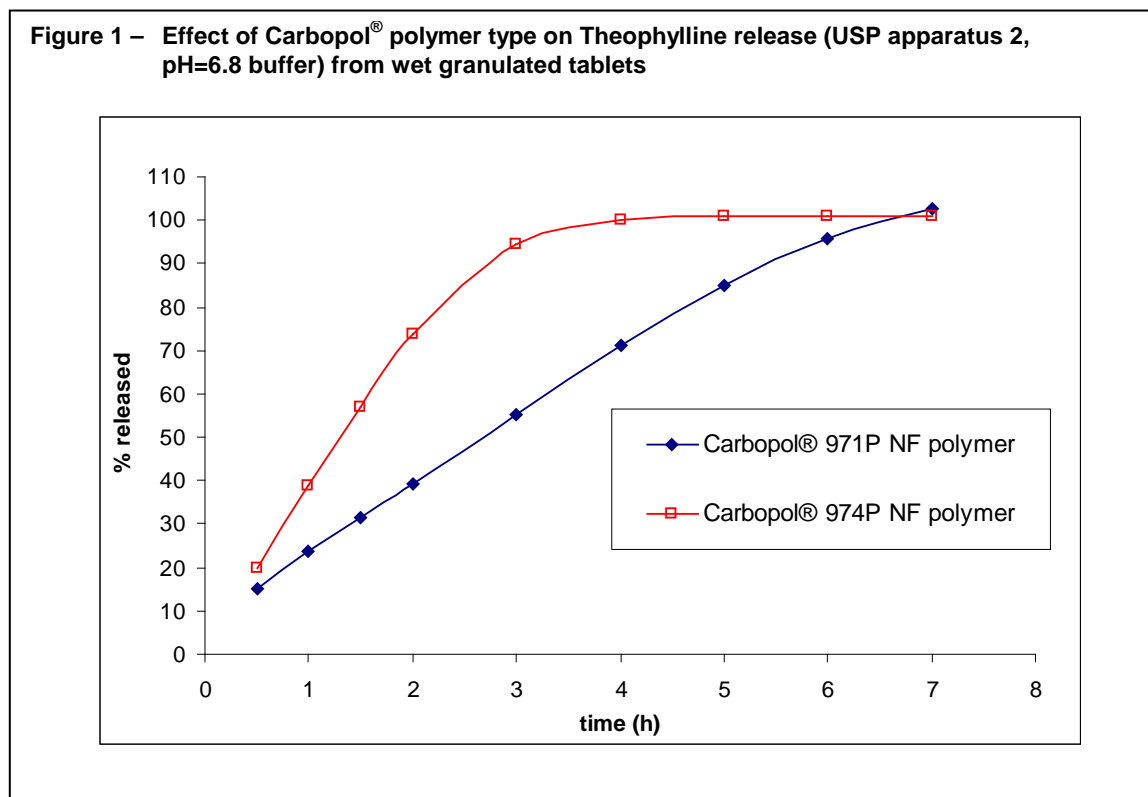
Parojcic et al. (2004b) studied Acetaminophen release in various dissolution media from tablets with Carbopol® 71G NF polymer or Carbopol® 971P NF polymer. Both polymeric excipients were added extragranularly to Acetaminophen granules. The differences in the release rate observed in 0.1N HCl medium were attributed to the difference in particle size of the two polymeric materials. In the case of granular polymer (Carbopol® 71G NF polymer), slow formation of the gel layer around the individual polymeric granules allowed penetration of the medium into the matrix, leading to the rapid and complete dissolution of Acetaminophen and matrix disintegration. In the case of matrices prepared with Carbopol® 971P NF polymer, slower formation of the gel layer resulted in an initially greater drug release rate, which tended to tail off as hydration of the matrix and gel formation occurred, sealing the pores on the tablet surface. No differences were observed in media with higher pH values, where rapid formation of the gel layer led to slower drug release for both granular and powdered polymers.

Effect of Polymer Level on Drug Release

Carbopol® polymers are highly effective at low concentrations. Typical usage levels in tablets for achieving extended release characteristics are 3 - 30%, depending on the drug properties, co-excipients and processing parameters.

At the same usage levels, Carbopol® polymers are more effective than cellulosic materials in sustaining the drug release. Unlike carbomers that are crosslinked polymers, the cellulosic materials are linear polymers. Cellulosic materials are not able to form virtual crosslinks at low concentrations, so the formed gels have low viscosity and the drug is quickly released.

Data showed that the release of Guaifenesin from wet granulated tablets (100 mg drug / tablet) with 10% polymer was slower in the case of carbomer tablets (Carbopol® 971P NF polymer) than with HPMC (Methocel® K4M) – Figure 2.

Figure 2 - Effect of polymer on Guaifenesin release in 0.1N HCl from wet granulated tablets
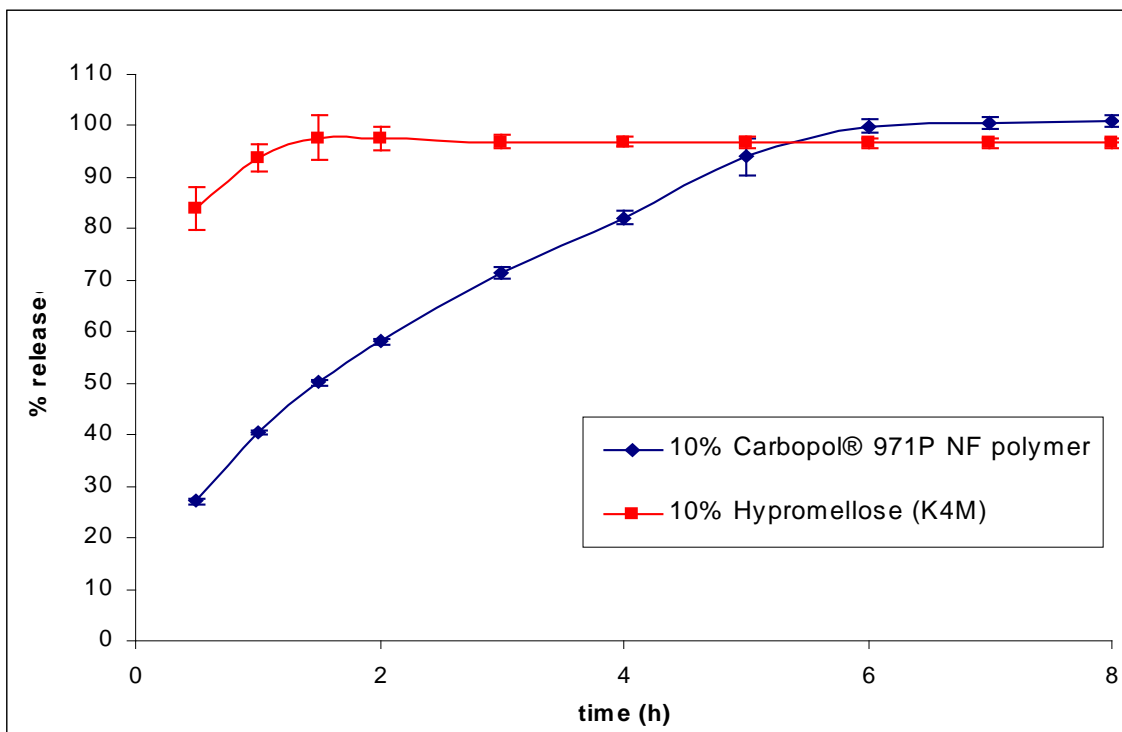
Generally, increasing the level of Carbopol® polymer in a formulation leads to slower and more linear drug release. This is because the gel layer formed around the tablet becomes stronger, with less regions of low micro viscosity in the swollen tablet (fewer interstitial spaces between the microgels).

A significant reduction in the release rate was observed in the case of direct compressible Theophylline tablets when the level of Carbopol® 71G NF polymer was increased from 15 to 30% of the tablet weight – Figure 3.

Increasing the level of Carbopol® 971P NF polymer from 2.5% to 20% in Ketoprofen tablets prepared by roller compaction led to slower and more linear release of the drug – Figure 4.

Figure 3 – Effect of Carbopol® 71G NF polymer level on Theophylline release (apparatus 2, USP method for modified release) from direct compressible tablets
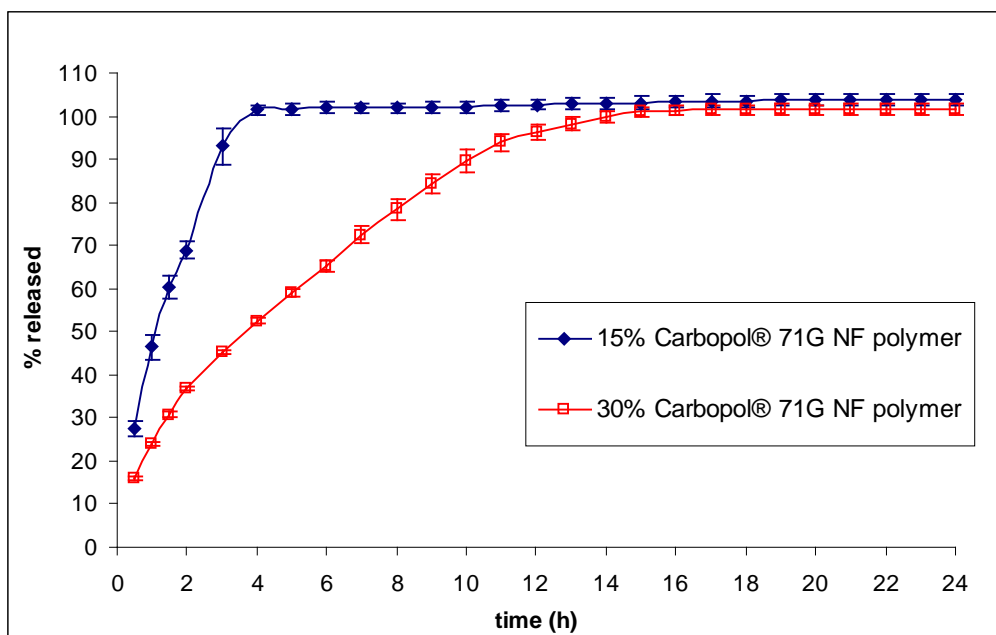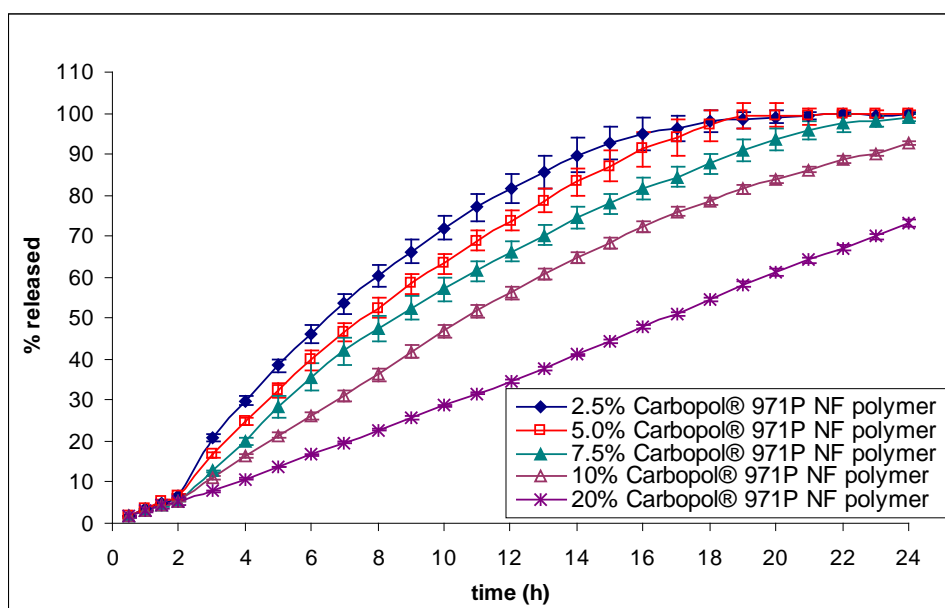

Figure 4 – Effect of Carbopol® 971P NF polymer level on Ketoprofen release (apparatus 2, USP method for modified release) from roller compacted tablets

The decrease in Atenolol release rate from tablets with increasing level of Carbopol® polymer was attributed to formation of thicker and stronger gel on the tablet surface that controlled the release in more efficient way *(Perez-Marcos et al., 1995)*.
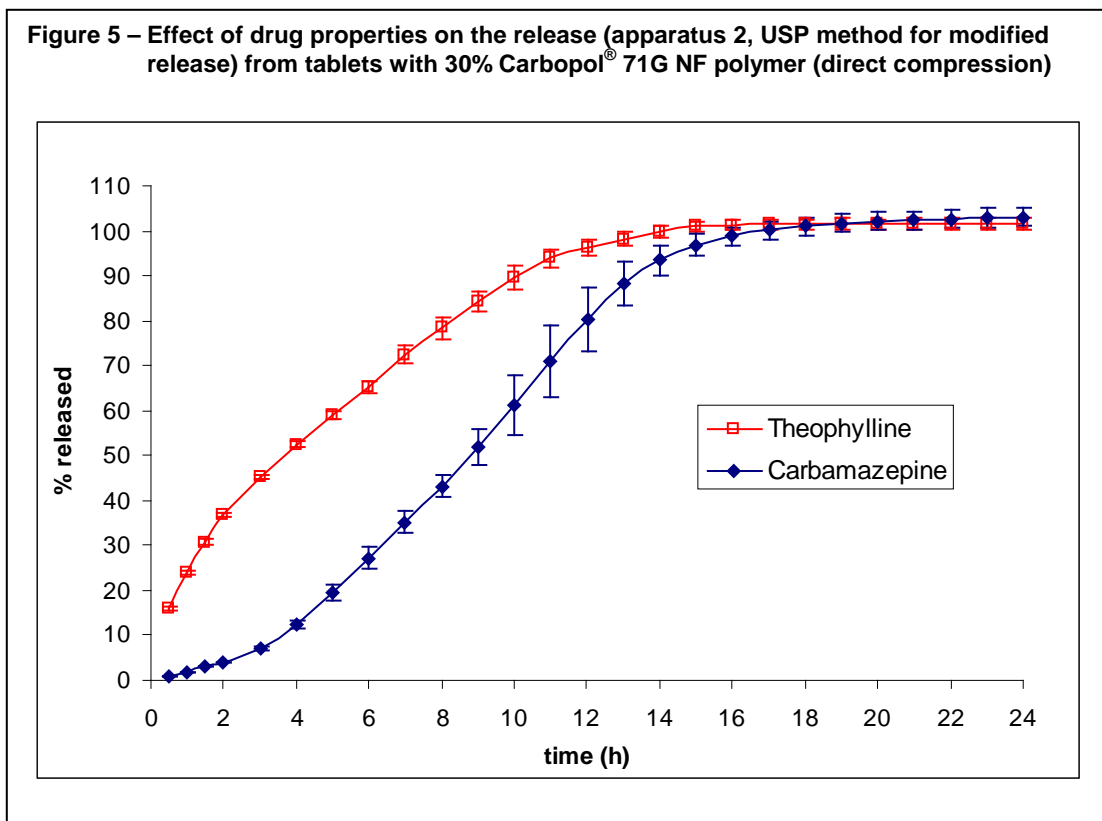
Increasing the amount of Carbopol® 974P NF polymer in Ibuprofen tablets resulted in a reduction in the drug release rate and a linearization of the drug release curve (release profiles in pH=7.2 buffer shifted from anomalous type of release towards a swelling-controlled, Case II mechanism). This phenomenon was considered to be due to a reduction in regions of low microviscosity and the closing of micropores in the swollen tablets *(Khan and Jiabi, 1998)*.

Effect of Drug Properties on the Release

Drug solubility, intrinsic dissolution rate, pKa, particle size and stability all play a major role in the release process.

The release from Carbopol® polymer tablets is generally slower for drugs with low water solubility. Drugs exhibiting poor solubility tend to partition into the more hydrophobic domains of the system (such as the acrylic backbone of the Carbopol® polymer) from where they would be released in a linear or almost linear fashion. Highly water soluble drugs are released by diffusion.

Figure 5 shows the release profiles from direct compressible formulations containing 30% Carbopol® 71G NF polymer, 50 mg drug and fillers. The release was slower and more linear in the case of Carbamazepine that is less water soluble than Theophylline.

Figure 5 – Effect of drug properties on the release (apparatus 2, USP method for modified release) from tablets with 30% Carbopol® 71G NF polymer (direct compression)

Similarly, the release from tablets with 10% Carbopol® 971P NF polymer prepared by wet granulation or roller compaction was faster for Theophylline than for the less soluble Ketoprofen – Figures 6 & 7.

Figure 6 – Effect of drug properties on the release (apparatus 2, USP method for modified release) from tablets with 10% Carbopol® 971P NF polymer (wet granulation)

Figure 7 – Effect of drug properties on the release (apparatus 2, USP method for modified release) from tablets with 10% Carbopol® 971P NF polymer (roller compaction)
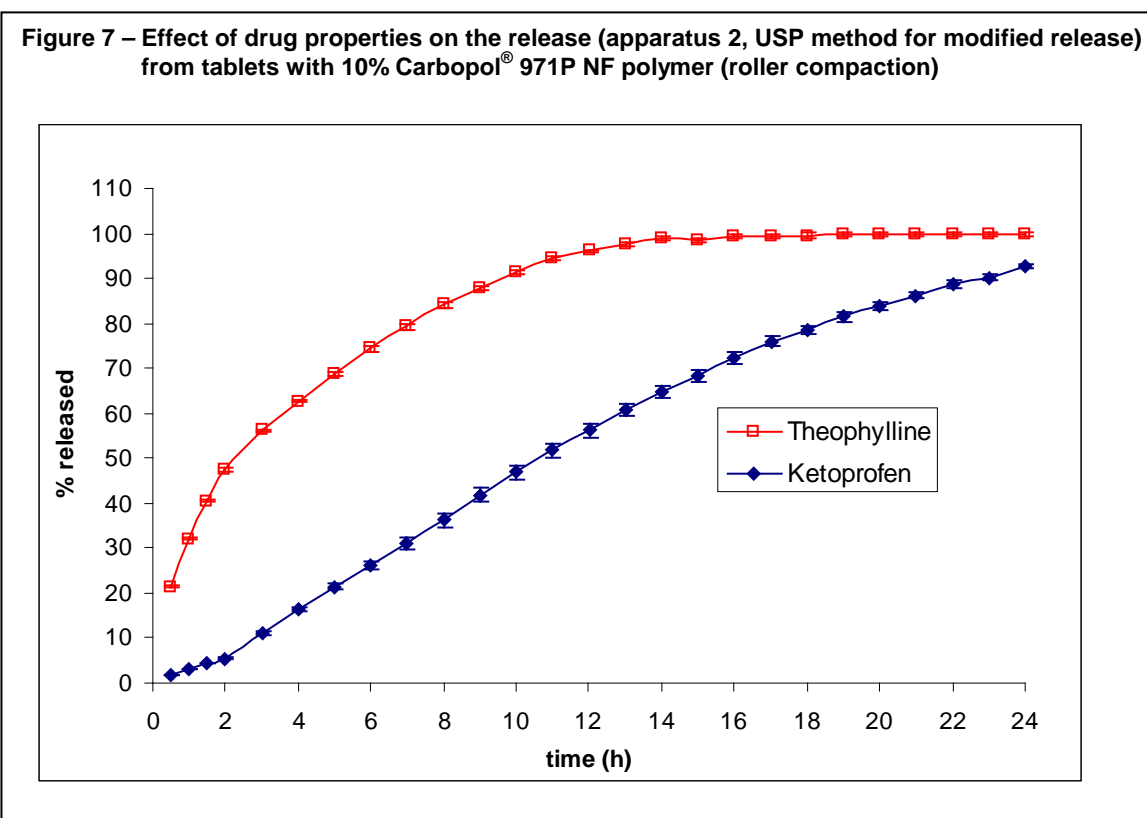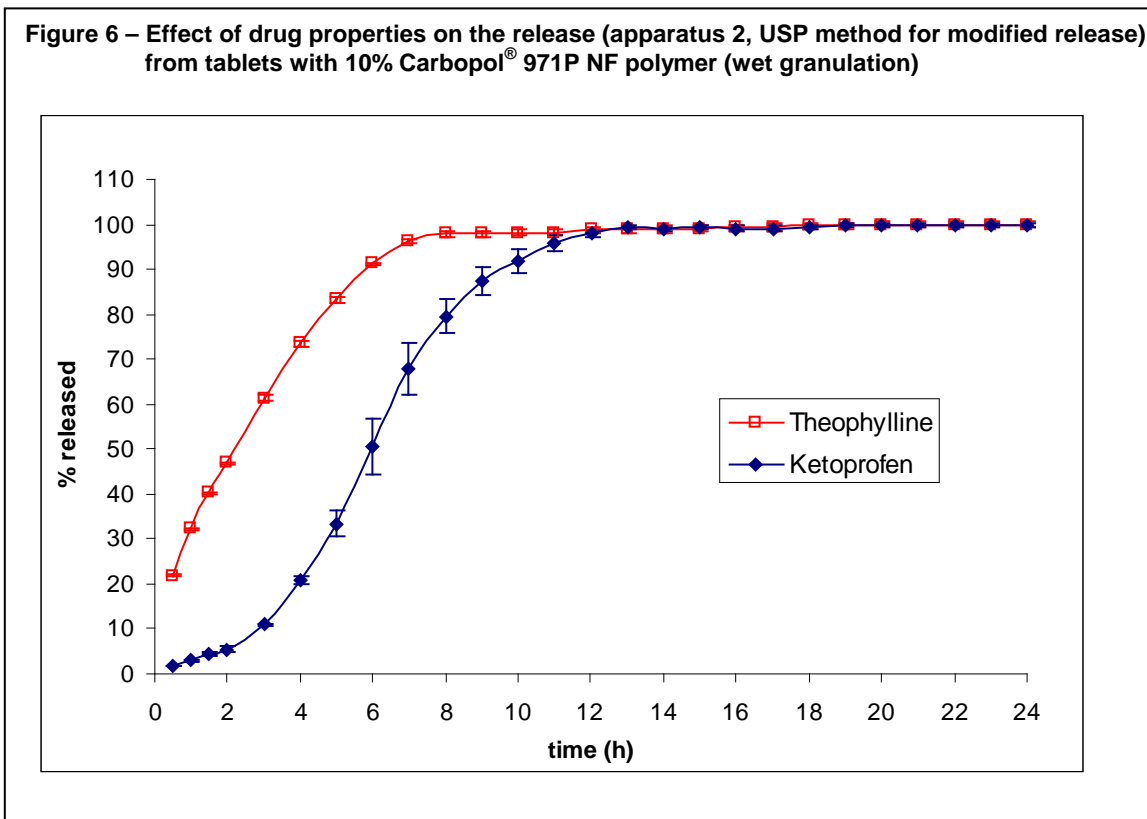
The release mechanism for water soluble drugs is mainly controlled by the diffusion process, while for the low soluble drugs polymer relaxation is the predominant mechanism.

In a Lubrizol study, the diffusion coefficient (n) for release from direct compressed tablets with 30% Carbopol® 71G NF polymer and various drugs (50 mg /tablet) was calculated based on the Peppas mathematical model.

The release mechanism was determined based on the values of the diffusion coefficient from the equation *(Peppas, 1985)*:

$$\frac{M_t}{M_\infty} = k \cdot t^n$$

where: M_t amount of drug released in time t
M_∞ - amount of drug released after an infinite time
k- constant related to properties of the delivery system
n- release (diffusion) exponent

- n<0.5 (0.45) - quasi-Fickian Diffusion
- n=0.5 (0.45) - Diffusion mechanism
- 0.5<n<1 - Anomalous (non-Fickian) Diffusion – both diffusion and relaxation (erosion)
- n=1 (0.89) - Case 2 transport (zero order release)
- n>1 (0.89) - Super Case 2 transport (relaxation)

The resulting values were n=0.59 for Theophylline (release - anomalous diffusion), n=1.11 for Hydrochlorothizide (relaxation), n=1.48 for Ketoprofen (relaxation).

Release of Furosemide (poorly soluble), from Carbopol® 974P NF polymer formulations in pH=5.8 buffer was attributed mainly to polymer relaxation followed by diffusion of the drug, mainly from the surface of the tablet. This was caused by the strong entanglement of polymer molecules that delayed the movement of drug molecules from the interior of the polymer mass toward the surface; the erosion of the polymer during dissolution studies was extremely limited *(Efentakis et al., 2000)*.

Perez-Marcos et al. studied the release profiles of carbomer matrix tablets. According to them, Atenolol (hydrosoluble drug) release profiles fitted Higuchi's square root diffusion kinetics, while Furosemide (insoluble) release followed zero-order profile *(Perez-Marcos et al., 1991a, 1991b)*.

Based on the values of the diffusion exponent (n>1), *(Parojcic et al., 2004a)* described the release of Acetaminophen (water soluble) from Carbopol® 71G NF and 971P NF polymer matrix tablets as super case II transport, controlled by the swelling and relaxation of the polymers.

Effect of Dissolution Medium on Drug Release

Due to the anionic nature of the polymer, drug release from Carbopol® polymer matrices may be media dependent, as the gel characteristics are pH-dependent. In general, the faster the swelling, the longer the dissolution time for a given drug.

Carbopol® polymers have a pKa of 6, so at pH 1.2 they are virtually un-ionized; they will start to ionize at pH 4.5. At lower pH values the polymer is not fully swollen, and there are larger regions of low microviscosity; the solvent can penetrate fast and deep into the glassy core and the drug is release faster, before complete formation. As the pH increases, the ionization of the carboxylic acid groups causes maximum swelling, resulting in fewer and smaller regions of microviscosity. The rapid gel formation acts as a barrier for the release of the drug, thus prolonging the release.

The release tend to be more diffusion controlled in the lower pH region (stomach), while at higher pH (intestine), the drug release mechanism is more polymer relaxation controlled.

Bulut-Oner et al. (1989) showed that the release of Isoniazid, a water soluble drug from carbomer tablets was faster in simulated gastric fluid that in distilled water or simulated intestinal fluid ($t_{50\%}$ was less than one hour, five and seven hours respectively).

Parojcic et al. (2004b) evaluated the release of Acetaminophen in different buffered and unbuffered media from Carbopol® polymer matrices. In the case of Carbopol® 971P NF polymer matrices, the most rapid drug release was observed in unbuffered 0.05 M KH_2P04 and 0.1N HCI, where, after 8 hours the majority of drug has been released. Drug release in water and phosphate buffers (pH=5.8, 6.8) was slower, leading to total amount of 60-70% of Acetaminophen dissolved after 8 h.

In the case of Carbopol® 71G NF polymer tests conducted in the 0.1N HCI and unbuffered KH_2P04 resulted in rapid drug release. In pH=4.5 acetate buffer, drug release was slow, with less than 60% of drug dissolved after 8 h. USP phosphate buffers pH=5.8 and 6.8 demonstrated the further retardation of drug release.

Carbopol® polymers being both gel forming materials as well as acidic in nature, have the advantage of acting as good matrix formers and also enhancing release of poorly soluble, weakly basic drugs in neutral or basic buffers. Generally, weakly basic drugs show a sharp drop in aqueous solubility with an increase in pH, thus resulting in high release in acidic media and low release in neutral or basic media.

Tatavarti et al. (2004) reported that incorporation of Carbopol® 71G NF polymer in matrix tablets resulted in enhanced release in buffer of both Verapamil HCl (solubility at pH=6.8 2.71 mg/ml) and Papaverine HCl (solubility at pH=6.8 0.01 mg/ml). The phenomenon was attributed to modulation of the microenvironmental pH to the acidic side and hence increased solubility of the active ingredients inside the matrix.

Due to their anionic character, Carbopol® polymers may form ionic complexes with cationic soluble drugs, and this fact is advantageous for retarding the drug release. The release of Propranolol hydrochloride, a cationic drug with acceptable solubility over the physiological range (220 mg/ml and 254 mg/ml in 0.1N HCl and pH=7.4 phosphate buffer) was extended by incorporation of Carbopol® 71G NF polymer in the matrix and the effect was attributed to the drug – polymer ionic complexation *(Draganoiu et al., 2004)*.

It is important to note that the pH effect on the polymer does not significantly impact drug release in various media (Figure 8). The most significant factor impacting drug release is API solubility and how it is affected by pH. No significant difference in release profiles due to dissolution medium was observed in the case of Guaifenesin which has a pH-independent solubility.

Figure 8 - Guaifenesin release from tablets (600 mg) with 10% Carbopol® 971P NF polymer (wet granulation)
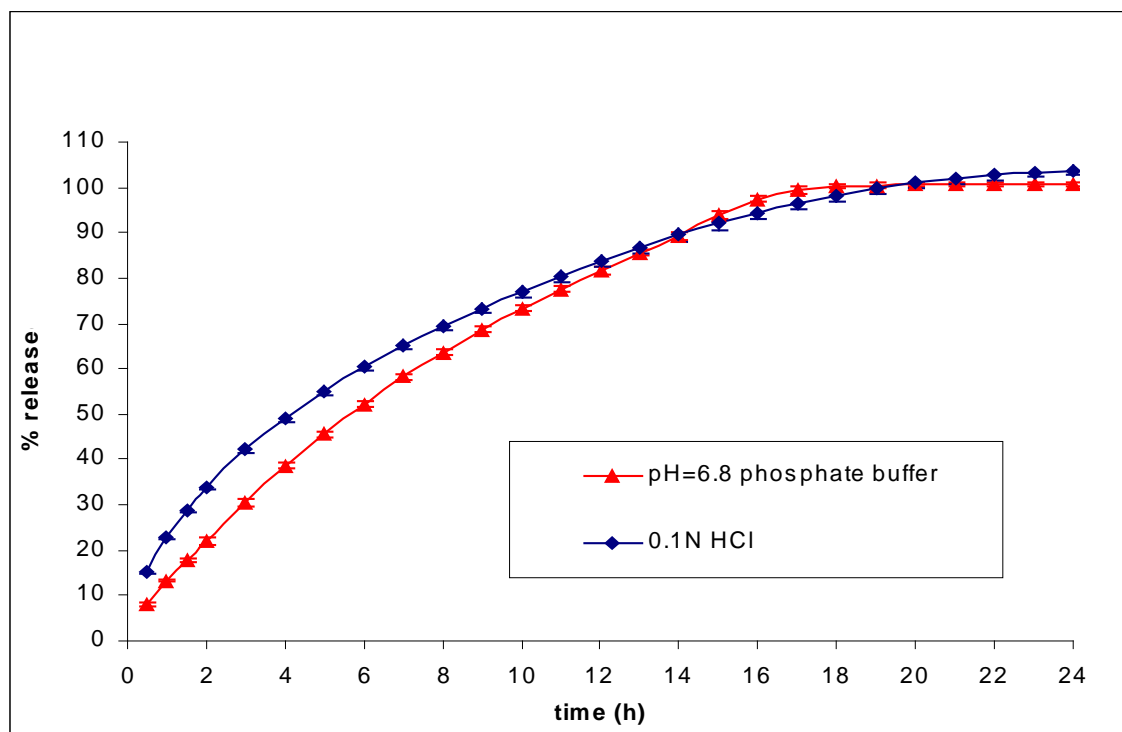

Recommended Co-Excipients

Carbopol® polymers are compatible with most of the tablet excipients and can be successfully used as controlled release agents with a variety of pharmaceutical active ingredients when processed by direct compression, roller compaction or wet granulation methods.

The fastest release from direct compressible Theophylline tablets with Carbopol® 71G NF polymer (52.33% filler) was observed in the case of microcrystalline cellulose, followed by lactose and dibasic calcium phosphate – Figure 9. All tablets were compressed at a target hardness of 10 kP. Microcrystalline cellulose has disintegrating properties when incorporated at high use level and this caused tablet erosion and fast drug release. The difference in the filler solubility explains the slower release observed for the tablets with dibasic calcium phosphate (insoluble) as compared to lactose (soluble). Using 1:1 filler blends resulted in release intermediate to the single filler formulations.

Figure 9 – Effect of filler on Theophylline release (apparatus 2, USP method for modified release) from tablets with Carbopol® 71G NF polymer
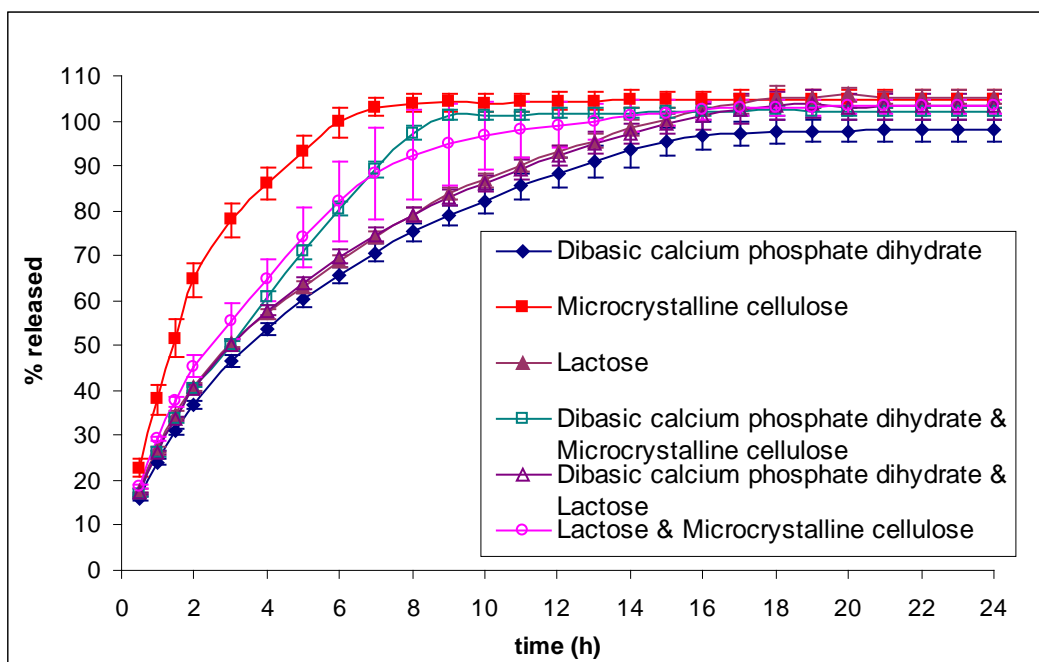
The influence of several co-excipients (lactose, microcrystalline cellulose, and starch) on the release rate of the drug from ibuprofen-carbomer controlled release matrix tablets was investigated by Khan and Jiabi *(1998),* Khan and Zhu *(1999).* The dissolution $T_{50\%}$ and $T_{90\%}$ values for the three co-excipients were in the order lactose>microcrystalline cellulose>starch, with lactose demonstrating slower and more linear release behavior as compared to microcrystalline cellulose or starch. The authors explained that the presence of carbomer and starch, both swellable, resulted in an extremely rapid swelling of the tablets and "explosion" of the gel barrier and thus dose dumping.

Capan et al. *(1991)* discussed the use of dibasic calcium phosphate dihydrate, microcrystalline cellulose, lactose, and dextranes (Emdex®) as filler for Lithium carbonate tablets containing Carbopol® polymers. No significant differences were observed between the formulations with different fillers in terms of prolongation of in vitro drug release. Bioavailability studies in humans comparing cumulative 48-h urinary excretions revealed a lower bioavailability for formulations containing water-insoluble excipients compared to conventional tablets, while those containing soluble fillers exhibited a similar bioavailability to the conventional tablets.

Combinations of Carbopol® Polymers and Other Control Release Excipients

Carbopol® polymers have been investigated in combination with other controlled release excipients (hypromellose, hydroxypropyl cellulose, sodium carboxymethyl cellulose, polyethylene oxide, sodium alginate, methacrylic polymers, etc.) for tablet formulations.

Potential benefits of those combinations are:

- Lower total controlled release agent due to synergistic interaction
- Flexibility in delivering target release profiles by varying the ratio and the total amount of the controlled release excipients
- Lower variability in the drug release profiles
- Better flow properties of the formulation blends by using Carbopol® 71G NF polymer in combination with polymers with low flowability
- Bioadhesive properties

Combinations of powder and granular Carbopol® polymers are beneficial in targeting various release profiles. The release rates can be modulated by incorporating the powder carbomer (Carbopol® 971P NF or 974P NF polymers) in the granules and then blending with granular carbomer (Carbopol® 71G NF polymer).

Khamanga and Walker *(2005)* reported that when Carbopol® 974P NF polymer was used in combination with other polymers, controlled-release performance was enhanced as a result of an interaction between the polymers and/or drug.

Various polymers were evaluated for the manufacture of sustained release Verapamil tablets by direct compression and wet granulation. Tablets with carbomer (Carbopol® 974P NF polymer) and methacrylic acid copolymers (Eudragit® RS) manufactured by direct compression exhibited a large degree of capping and lamination; the blends showed poor flow characteristics.

Tablets prepared with blends of HPMC (Methocel® K100M) and Carbopol® 974P NF polymer using Surelease® E-7-19010 or Eudragit® NE 30D as granulating agents sustained the release of Verapamil, better than when Carbopol® 974P NF polymer or Eudragit® RS were used alone (in direct compression). The authors concluded that the combination of Carbopol® 974P NF and Methocel® K100M produces a synergistic increase in viscosity due to the stronger hydrogen bonding between the carbomer and HPMC. This in turn formed a stronger cross-link between the two polymers resulting in a more rigid structure through which drug diffusion occurred.

Samani et al. *(2003)* evaluated the effect of polymer blends on the in vitro release profile of diclofenac sodium. When an appropriate blend of HPMC and carbomer was used, the drug release became more uniform, the fluctuations were diminished and the kinetics approached to zero order. They concluded that with polymer blends it was possible to reduce the total amounts of polymer in the formulation and minimize the size and weight of the tablets.

Guaifenesin extended release tablets (mono- or bi-layer) were designed to provide therapeutically effective levels for at least twelve hours post dosing. The formulations used a combination of Methocel® E10M and Carbopol® 974P NF polymer *(Davis et al., 2004).*

Propranolol hydrochloride tablets containing Carbopol® 974P NF polymer and HPMC K4M were investigated for drug release in various media: 0.1N HCl or phosphate buffer at pH 4.5 or pH 7.5. In 0.1N HCl, HPMC K4M predominantly controlled the release and as the pH increased, the carbomer became increasingly ionized and interacted with propranolol hydrochloride to form an insoluble complex which

retarded the release of the drug. At pH=7.5 a synergistic interaction of the two polymers was observed, thus both contributing to matrix integrity and to the control of drug release *(Perez-Marcos et al., 1996).*

Using a combination of Carbopol® 71G NF polymer and HPMC in the case of directly compressible Propranolol tablets allowed lower polymer level and resulted in more linear release profiles than using HPMC alone. The effect was attributed to an ionic interaction between the cationic drug and the anionic polymer. The variability was lower for the polymer combination than for the carbomer matrix. Changing the polymer ratio and percentage in the formulation were recommended as ways to achieve the target release profiles *(Draganoiu et al., 2004).*

A combination of Carbopol® 971P NF, Carbopol® 974P NF polymers and hydroxypropyl cellulose was included in the sustained-release portion of a Nitrofurantoin controlled-release dosage form, which also had an immediate release portion *(Sharma et al., 2004).*

Captopril bilayer floating tablets were formulated with the floating layer consisting of HPMC, citric acid and sodium bicarbonate and the release layer containing the drug, HPMC, carbomer and povidone. The in vitro release mechanism was Fickian diffusion. In vivo studies in human volunteers showed that the tablets remained in the stomach and upper part of intestine for ten hours *(Rahman and Ali, 2003).*

Singh and Ahuja *(2002)* optimized Diltiazem controlled-release buccoadhesive hydrophilic matrices by varying the amount of carbomer and HPMC in the formulation. Suitable combinations of the two polymers provided adequate bioadhesive strength and release for up to ten hours. Bioadhesive strength varied linearly with increasing amount of each polymer. The drug release pattern for all the combinations was found to be non-fickian, approaching zero-order kinetics. The values of permeation coefficient tended to vary non-linearly with polymer amount, depicting possible interaction between the two polymers.

Bioadhesive tablets were developed for delivery of nicotine into the oral cavity by using Carbopol® 974P NF polymer in combination with HPMC. Magnesium carbonate was incorporated into the formulations as a pH increasing agent, to improve the absorption of nicotine from the buccal mucosa on pH-partition considerations *(Ikinci et al., 2004).*

A combination of 20% w/w carbomer and 20% w/w hydroxypropyl cellulose was included in Nicotine buccal tablets to provide adhesion and controlled drug release. The bilayer tablet consisted of a fast releasing layer which provided an initial burst release and an adhesive, controlled release layer which extended the release for a period of up to four hours. The same type of release was identified in human volunteers and it was considered that the biphasic profile could represent an improvement over other current methods of nicotine replacement therapies *(Park and Munday, 2002).*

Carbopol® Polymers as Tablet Binders

Carbopol® polymers at lower levels (0.5 - 3% w/w) can be used as binders. These polymers improve the physical characteristics of the tablets, allowing increased hardness and low friability under low compression forces.

Carbopol® polymers can be added in the formulation in the dry state and activated with water. The advantage consists in eliminating the step of preparing the binder dispersion. Alternatively, part of the polymer can be added in the dry state and part dispersed in water (to avoid viscous dispersions, concentration of the dispersion should be below 1%).

Carbopol polymers may be beneficial as binders for direct compression formulations; if the powder grades are used, the level in the formulation should be limited to maximum 2 - 3% to avoid effects on drug dissolution.

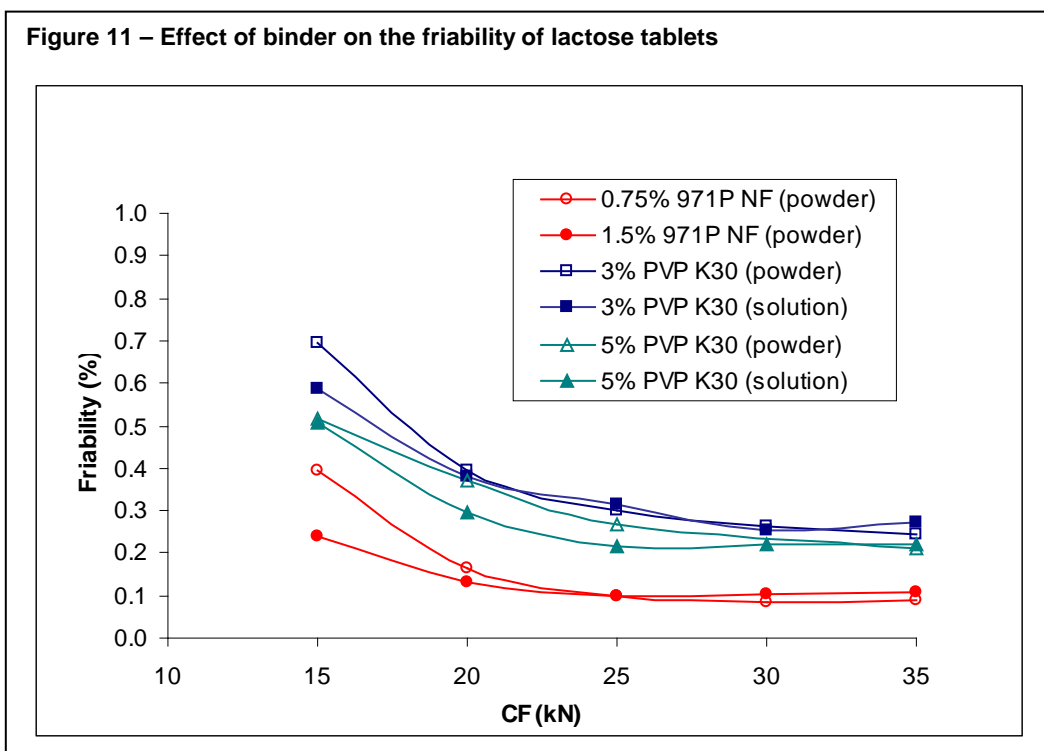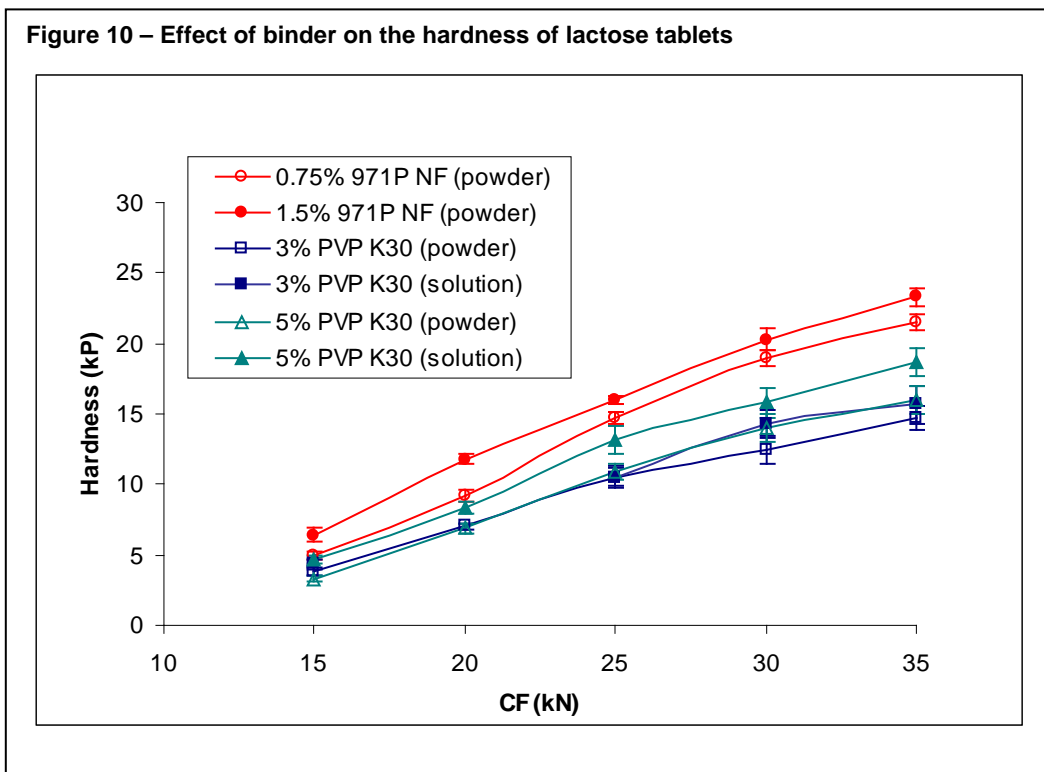### Carbopol® 971P NF polymer - binder for placebo tablets

The binding properties of Carbopol® 971P NF polymer were tested in the case of placebo tablets of lactose or dibasic calcium phosphate and compared to povidone (PVP K30) – Table 2. Carbomer was added in dry state and activated with water, while PVP was incorporated either in the dry state (powder) or as a solution in water.
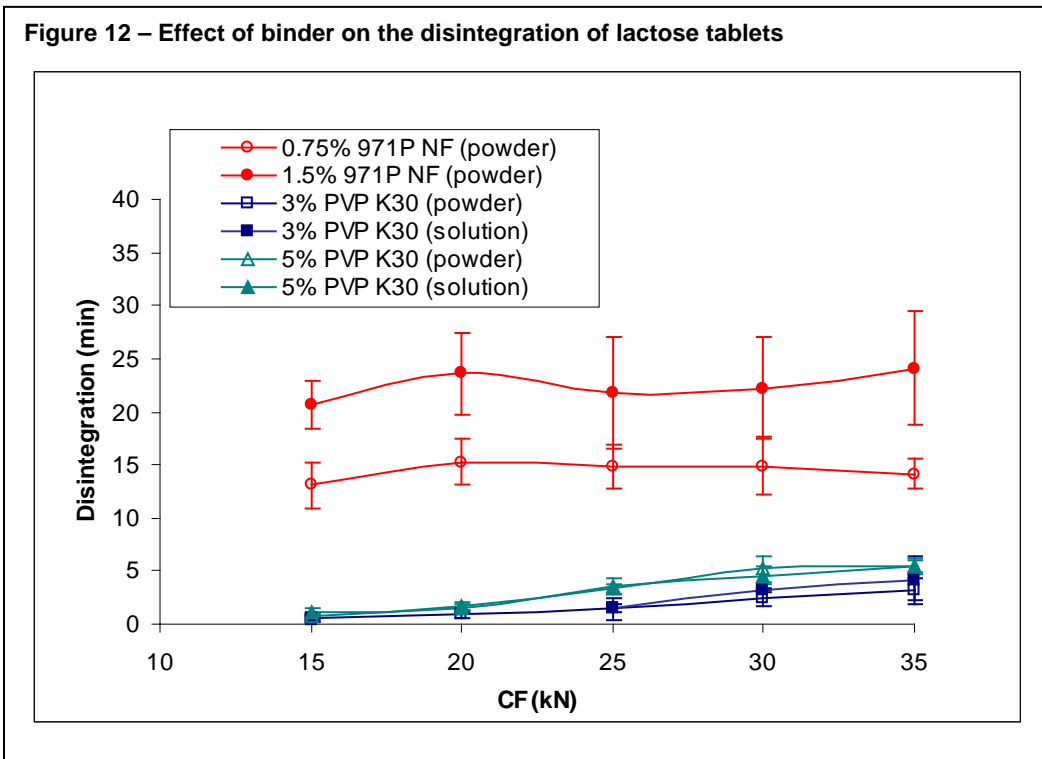
Table 2
Composition of Placebo Tablets

Excipient	0.75% 971P NF	1.5% 971P NF	3% 971P NF	3% PVP K30	5% PVP K30
Lactose monohydrate or Dibasic calcium phosphate	96.75	96.0	94.5	94.5	92.5
Carbopol® 971P NF polymer	**0.75**	**1.5**	**3.0**	-	-
PVP K30	-	-	-	**3.0**	**5.0**
Crosspovidone	2.0	2.0	2.0	2.0	2.0
Magnesium stearate	0.5	0.5	0.5	0.5	0.5

All the components except for the lubricant were blended in a low shear mixer and granulated with deionized water. PVP K30 was also incorporated as a solution: the filler and disintegrant were blended, then granulated with PVP dispersion in water. The resulting granules were dried, sized, blended with the lubricant and compressed on an instrumented rotary press, while recording the compression and ejection forces.

Figures 10 - 12 show the effect of binder type and concentration on the properties of the lactose tablets compressed at different compression forces. At all compression forces (15-35 kN) and use levels (0.75 and 1.5%), Carbopol® 971P NF polymer formed tablets with higher hardness and lower friability than 3 or 5% PVP K30. The disintegration time was higher for the carbomer tablets, but higher disintegrant level or lower binder level may correct this aspect.

Figure 10 – Effect of binder on the hardness of lactose tablets

Figure 11 – Effect of binder on the friability of lactose tablets

Figure 12 – Effect of binder on the disintegration of lactose tablets

The properties of dibasic calcium phosphate tablets are presented in Figure 13 - 15. The hardness achieved with 0.75 or 1.5% carbomer, was comparable to 3 or 5% PVP K30. Friability was lower for all the carbomer tablets as compared to PVP tablets. The disintegration time was similar for 0.75% carbomer and 3% PVP K30, and shorter for 1.5% carbomer than for 5% PVP K30.

For the carbomer tablets, the disintegration time was shorter for the insoluble filler (dibasic calcium phosphate) than for the soluble lactose.
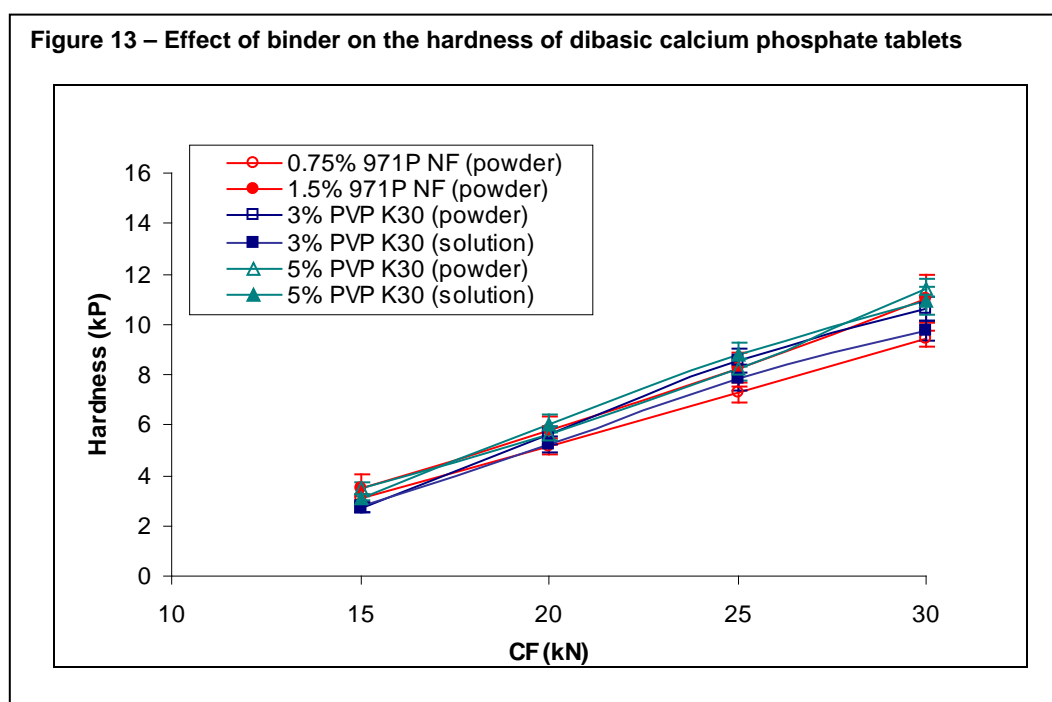
Figure 13 – Effect of binder on the hardness of dibasic calcium phosphate tablets

Figure 14 – Effect of binder on the friability of dibasic calcium phosphate tablets
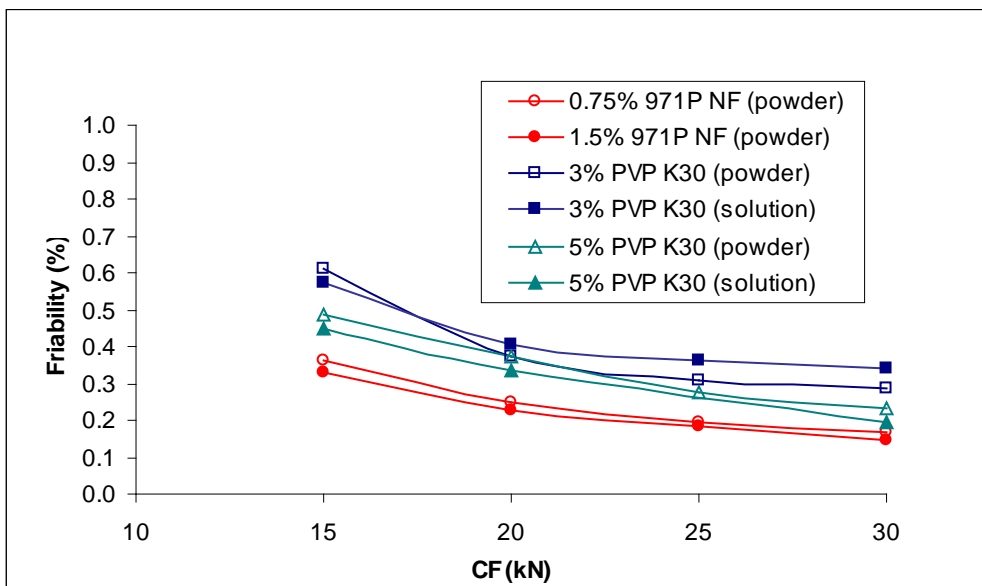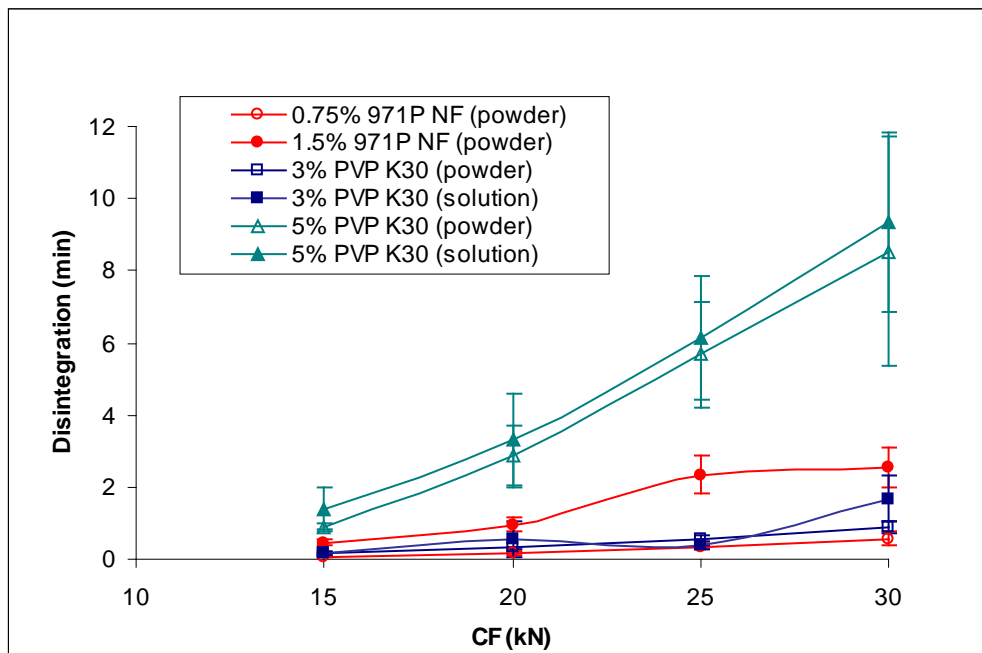

Figure 15 – Effect of binder on the disintegration of dibasic calcium phosphate tablets

Carbopol® 971P NF polymer - binder for Theophylline tablets

Theophylline 125 mg tablets were manufactured by wet granulation using Carbopol® 971P NF polymer or povidone (PVP K30) as binders – Table 3.

Table 3
Composition of Theophylline Tablets

Ingredient	1.0% 971P NF	1.5% 971P NF	3% PVP K30
Theophylline anhydrous	40.0	40.0	40.0
Dibasic calcium phosphate	56.5	56.0	54.5
Crosspovidone	2.0	2.0	2.0
PVP K30	-	-	3.0
Carbopol® 971P NF polymer	1.0	1.5	-
Magnesium stearate	0.5	0.5	0.5

The components (drug, filler, binder and half of the disintegrant) were blended in a low shear mixer and granulated with deionized water. The resulting granules were dried, sized, blended with the remaining disintegrant and then the lubricant and compressed on an instrumented rotary press, while recording the compression and ejection forces.

At each compression force, the hardness of carbomer tablets was slightly higher than for the PVP tablets and the friability was similar or slightly lower (Figures 16 & 17). Dissolution was slower for carbomer than PVP (Figure 18).

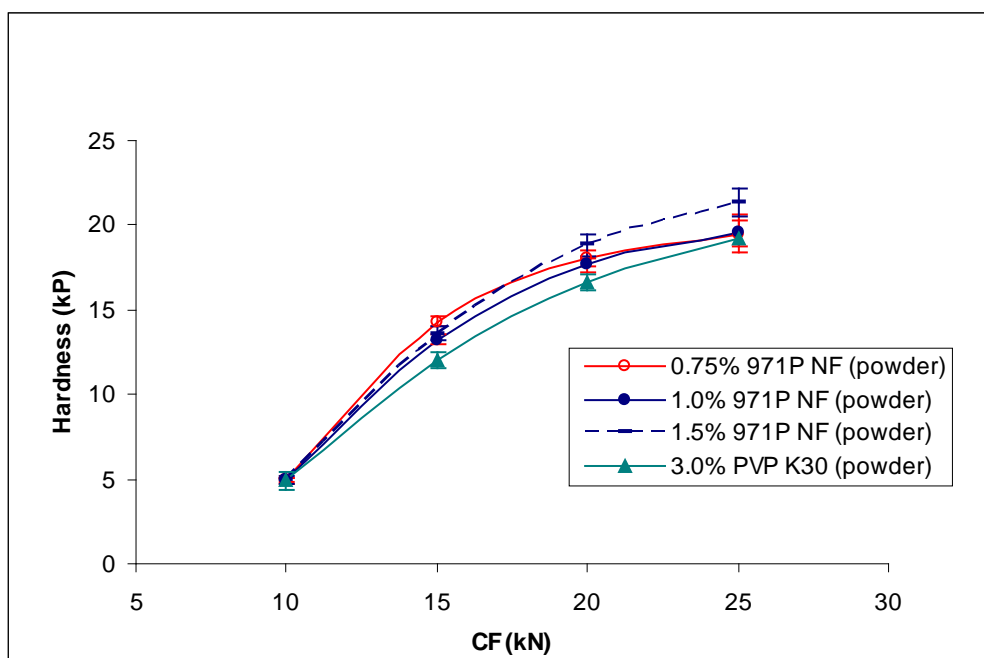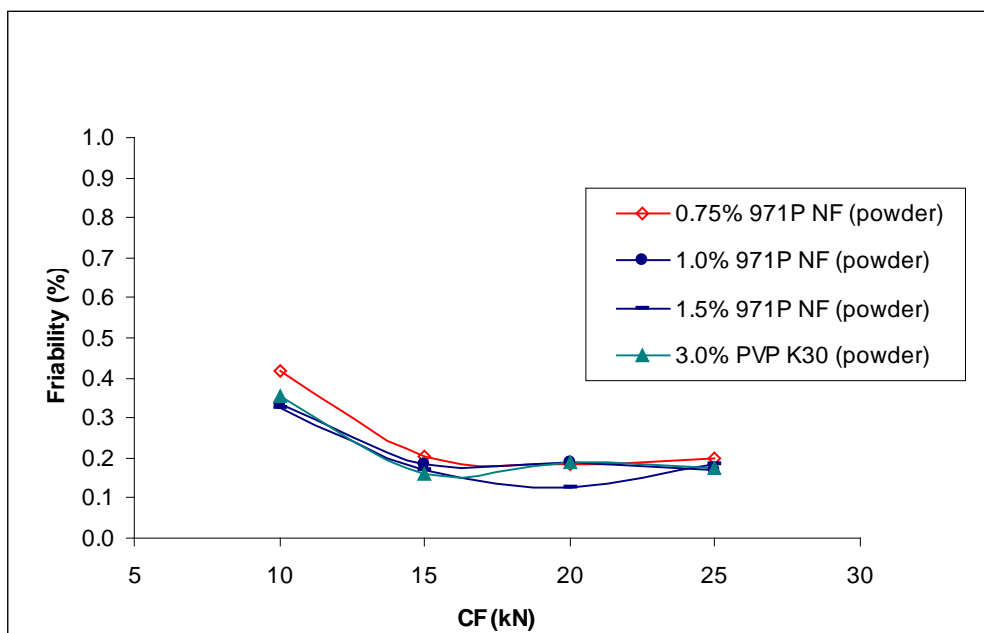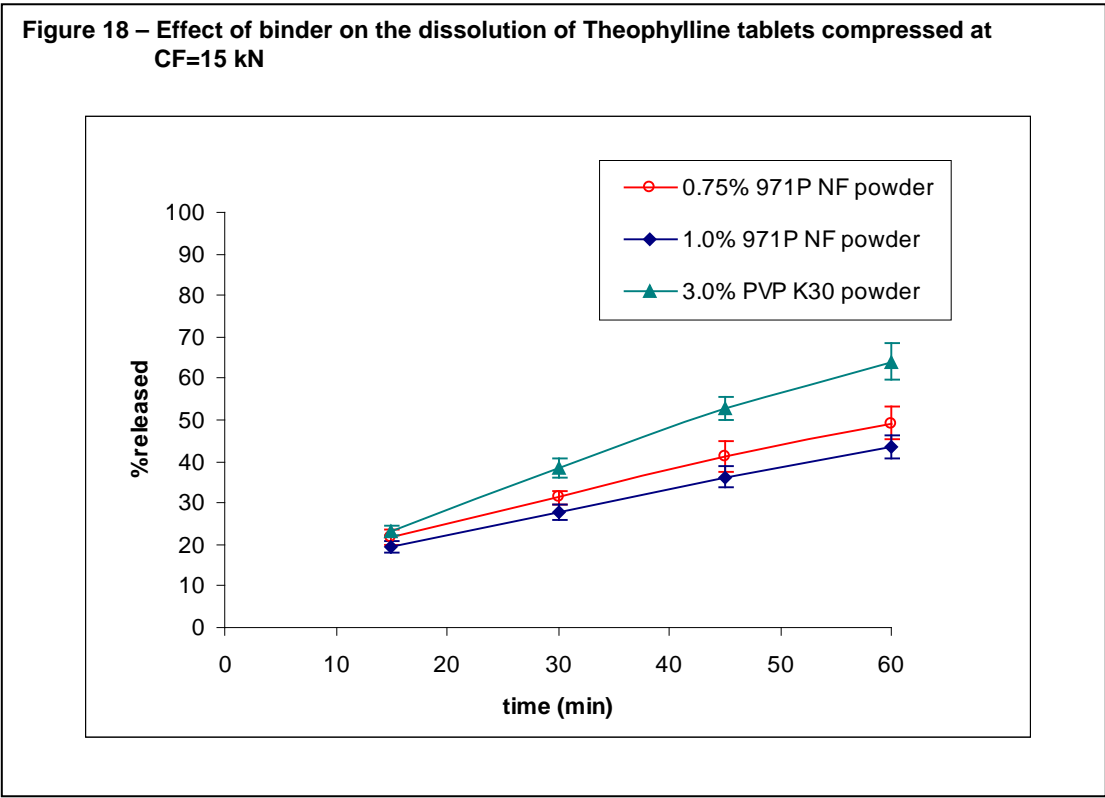**Figure 16 – Effect of binder on the hardness of Theophylline tablets**

Figure 17 – Effect of binder on the friability of Theophylline tablets

Figure 18 – Effect of binder on the dissolution of Theophylline tablets compressed at CF=15 kN

Carbopol® polymers added in the dry state in lower concentrations provided similar or better binding properties compared to PVP K30 added either in the dry state or as a dispersion.

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