

# A Novel Method to Study the Effect of pH and Excipients on Water Uptake and Swelling Behaviour of Carbopol Polymers

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## Abstract

Conventional hydrophilic excipients used in controlled drug delivery release drugs mainly by diffusion and erosion. Therefore, perfect zero order release rate cannot be achieved. Carbopol polymers can be used to solve this problem. These polymers do not dissolve but swell in water. Depending on the gel characteristics, zero order or anomalous release is obtained. The present study is intended to evaluate the swelling as well as water uptake properties of these polymers. Pure polymeric tablets of 200mg using three different grades of Carbopol polymers (934P NF, 974P NF and 971P NF) were prepared by direct compression in a hydraulic press at 5ton pressure for 1min. Effect of pH, acidic and basic ingredients and ionic strength on water uptake and swelling of the tablets were observed. Carbopol 971P showed maximum water uptake (3g) and swelling (10.13mm) in distilled water. On the other hand, water uptake was maximum(4.993g) when tablets were prepared with Carbopol 971P and Na<sub>3</sub>PO<sub>4</sub>. It was also observed that, water uptake decreases as the ionic strength of NaCl solution increases. Water uptake was minimum (0.26gm) in 5% NaCl solution.

**Keywords:** Carbopol polymer, cross linking, water uptake, swelling, ionic strength.

## Introduction

In the recent decades, there has been considerable interest in using Carbopol as an excipient in a diverse range of pharmaceutical applications (Avinash, 2006). These are readily water-swella-ble and are used in controlled release of tablets, as bioadhesive i.e. site specific agent, as thickening, suspending and emulsifying agent. Carbopol polymers were first described in scientific literature in 1955. Carbopol polymers are high molecular weight, crosslinked, acrylic, acid-based polymers. Carbopol homopolymers are polymers of acrylic acid crosslinked with allyl sucrose or allylpentaerythritol. These polymers are offered as fluffy, white, dry powders. The carboxyl groups provided by the acrylic acid backbone of the polymer are responsible for many of the product benefits (Bulletin 1, 2002). All of the carbopol polymers have the same acrylic acid backbone. The main differences are related to the presence of a comonomer and the crosslink density (Bulletin 2, 2002). Carbopol 934 P is cross-linked with allyl sucrose. Carbopol 971 P and 974 P are cross-

linked with allyl penta erythritol. Though Carbopol 971 P and Carbopol 974 P are manufactured by same process under similar conditions, the difference in them is that Carbopol 971 P has slightly lower level of cross-linking agent than Carbopol 974 P (Avinash, 2006).

Drugs can be released in the body following Fickian, zero order, non-Fickian or First order mechanism. Among these, zero order mechanism is ideal for drug release. Carbopol polymers can enable near zero order release rates. These polymers are effective at low concentrations even in less than 10% and feature extremely rapid and efficient gelation characteristics under both simulated gastric fluid (SGF) and simulated intestinal fluid (SIF) test conditions. They also produce tablets of excellent hardness and low friability over a range of compression forces. In the dry state, the drug is trapped in a glassy core. As the external surface of the tablet is hydrated, it also forms a gelatinous layer upon hydration. This gel layer is different structurally from the traditional matrix tablet. The hydrogels are not

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entangled chains of polymer, but discrete microgels made up of many polymer particles, in which the drug is dispersed. The crosslink network enables the entrapment of drugs in the hydrogel domains. Since these hydrogels are not water soluble, they do not dissolve, and erosion in the manner of linear polymers does not occur. Rather, when the hydrogel is fully hydrated, osmotic pressure from within works to break up the structure, essentially by sloughing off discrete pieces of the hydrogel. Because of this structure, drug dissolution rates are affected by subtle differences in rates of hydration and swelling of the individual polymer hydrogels, which are dependent on the molecular structure of the polymers, including crosslink density, chain entanglement, and crystallinity of the polymer matrix. The magnitude and rate of swelling is also dependent on the pH of the dissolution medium (Bulletin 17, 2002). Therefore, tablet hydration capacity and swelling at different pH are very important to be considered because water penetration is responsible for drug release (Luana *et al*, 2007). In addition to this, polymer swelling is a property related to mucoadhesion of the system (Juan *et al.*, 2002).

This work aims at evaluating the characteristics of Carbopol polymers to be used as an excipient in site specific and controlled drug delivery systems.

For this purpose, effect of pH, excipients and ionic strength on water uptake and swelling of Carbopol polymers were evaluated.

## Materials and Methods

### Materials

Carbopol 934P, 974P and Carbopol 971P were obtained from Noveon Pharmaceuticals (USA). Citric acid, Sodium chloride, Sodium dihydrogen phosphate, tri-sodium hydrogen phosphate were obtained from Merck limited, India. Disodium hydrogen phosphate was obtained from Thomas Baker (chemicals), India. All other materials were of reagent grade.

### Methods

#### Water uptake studies of Carbopol polymers

**Preparation of pure Polymeric Tablets:** Two types of tablets were prepared, one containing pure polymers and others in combination with excipients. To prepare pure polymeric tablets, 200mg of each of the Carbopol® 934P NF, Carbopol® 974P NF and Carbopol® 971P NF were taken. Flat faced tablets of 13mm diameter, 0.48mm thick were prepared by directly compressing the polymer, using an IR hydraulic press at 5ton pressure for 1min. Table 1 contains the formulations of the second type of tablets and the method of preparation is same to first one.

**Table 1: Formulation of tablets containing Carbopol polymers different excipients**

Carbopol 934P (mg)	Carbopol 974P (mg)	Carbopol 971P (mg)	Citric acid (mg)	Sodium dihydrogen phosphate (mg)	Di-sodium hydrogen phosphate (mg)	Trisodium phosphate (mg)
200	-	-	20	-	-	-
200	-	-	-	20	-	-
200	-	-	-	-	20	-
200	-	-	-	-	-	20
-	200	-	20	-	-	-
-	200	-	-	20	-	-
-	200	-	-	-	20	-
-	200	-	-	-	-	20
-	-	200	20	-	-	-
-	-	200	-	20	-	-
-	-	200	-	-	20	-
-	-	200	-	-	-	20

**Preparation of the Device:** 3.5 inch diameter of PVC pipe was cut into small pieces of about ¼ inch height. Stainless steel meshes were cut according to the diameter of the pipe. The pieces were attached with one end of the pipe by glue.



**Figure 1: Device used to measure water uptake and swelling of Carbopol polymers**

**Preparation of Phosphate Buffer Solution (pH 6.8):** pH 6.8 Phosphate buffer was prepared with Di-sodium hydrogen orthophosphate and Citric acid. 7.15% w/v solution of Di-sodium hydrogen orthophosphate was mixed properly with 2.1% w/v solution of Citric acid. The pH of the solution was confirmed with the help of a pH meter.

**Preparation of NaCl solution of different Ionic Strength (0.01M, 0.1M, 0.5M, 1M, 3M, 5M)**

NaCl solution of different ionic strength (0.01M, 0.1M, 0.5M, 1M, 3M, 5M) were prepared by using NaCl according Table 2.

**Table 2: Formulation for preparation of NaCl solution of different ionic strength**

Ionic strength of NaCl solution (%)	gm of NaCl in 100ml solution
0.01	0.058
0.1	0.58
0.5	2.9
1	5.8
3	17.4
5	29

**Effect of pH on water uptake and swelling of Carbopol polymers:** Pure polymeric tablets were weighed ( $W_1$ ). Tablets were kept upon the device and reweighed ( $W_2$ ). Three pure polymeric tablets from each grade were taken and along with the devices were immersed in petridishes containing distilled water, 0.1N HCl (pH 1) and pH 6.8 Phosphate buffer. At one hour interval, the

assemblies were raised out of the petridish and were reweighed ( $W_3$ ) after wiping off the water droplets that adhered to the surface of the assembly. At the same time, images of the tablets were taken every hour. The amount of water absorbed by the tablets were calculated using the following formula:

$$\text{Increase in weight of tablets or Water uptake by the tablets} = W_3 - W_2$$

The method was done in duplicate.

Amount of water uptake was plotted against the corresponding time. Diameters of the tablets for each hour were obtained using Microsoft Visio software 2000. From these values increase in the diameter of the tablets were calculated and plotted against time.

**Effect of Excipients on the Water uptake and swelling of Carbopol® Polymers:** Three tablets from each formulation (F1, F2, F3, F4, F5, F6, F7, F8, F9) were taken and immersed in three different media (Distilled water, 0.1N HCl and pH 6.8 Phosphate buffer). Increases in weight of the tablets were obtained following the above method for six hours. Amount of water uptake was plotted against time. The experiment was done in duplicate. Similarly, increases in diameter of the tablets were obtained using previous method and the values were plotted against time.

**Effect of Ionic Strength on the Water uptake of The Carbopol® Polymers**

Six of the pure polymeric tablets (wt 200mg) of each grade of Carbopol polymers were taken and immersed in six petridishes containing 0.01M, 0.1M, 0.5M, 1M, 3M and 5M of NaCl solution. Increases in the weight of the tablets were recorded for six hours using the previous method and the values were plotted against time.

## Results and Discussion

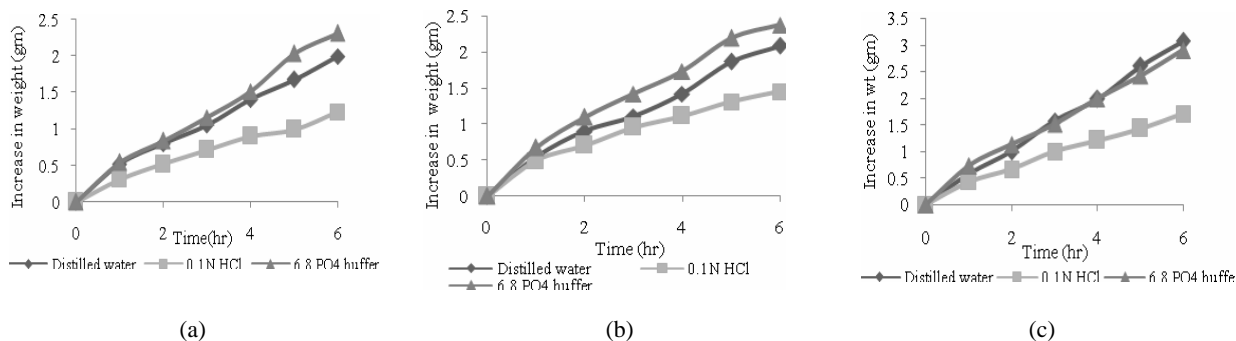
**Effect of pH on water uptake and swelling of Carbopol polymers**

Initial weight of the pure polymeric tablets was 200mg. It can be seen from Figure 1 and 2 that, after 6 hours, weight of the tablets in distilled water, 0.1N HCl and pH 6.8 phosphate buffer were 2.154gm, 1.235gm and 2.316gm respectively for Carbopol 934P. For Carbopol 974P and Carbopol 971P the weights of the tablets in

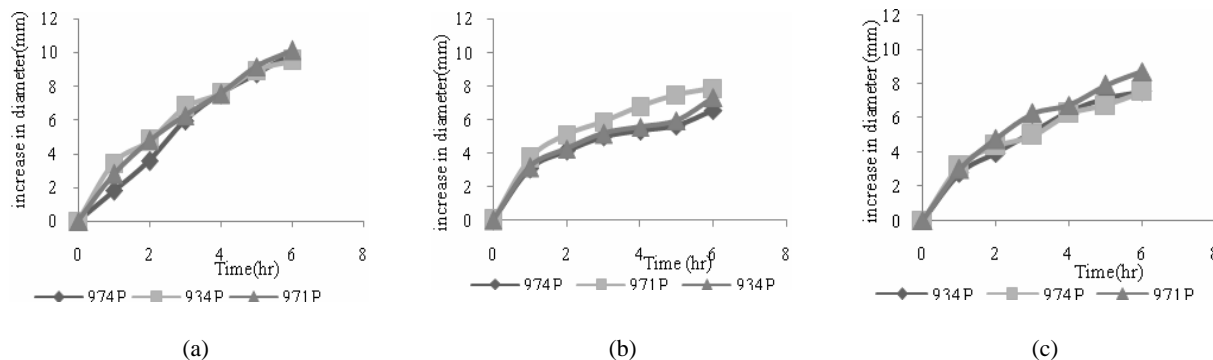
distilled water, 0.1N HCl and pH 6.8 phosphate buffer were 2.209gm, 1.655gm, 2.579gm and 3.272gm, 1.903gm and 3.101gm respectively. On the other hand, the initial radial diameters of the tablets were 13mm. For Carbopol 934P, the diameter in distilled water, 0.1N HCl and pH 6.8 phosphate buffer were 22.52mm, 19.56mm and 21.73mm respectively. Whereas for Carbopol 974P they were 22.92mm, 20.86mm and 20.55mm respectively and for Carbopol 971P they were 23.13mm, 20.34mm and 20.54mm respectively. Weight and volume of the tablets increased in greater amount in distilled water and phosphate buffer than in 0.1N HCl. When the polymers come into contact with water, plasticization of the Carbopol® polymers by water causes the polymer chains to start gyrating. As the radius of gyration becomes bigger and bigger, and the end-to-end distances increase and the polymers swell. In phosphate buffer (pH 6.8), the carboxylate groups of the polymers are ionized greatly due to repulsion of similar charges which results in greater swelling (Bulletin 17, 2002). Compared to these, water uptake was minimum for 0.1N HCl.

Because, negative charges of the polymers cause repulsion of chloride ions and prevents entrance of water.

Carbopol 971P showed largest amount of water absorption and swelling either in pH 1 or pH 6.8 environment than other two. This is because, the water uptake and swelling tendency of the Carbopol polymers are largely dependent on the crosslinking density. Carbopol 971P is the most lightly crosslinked of the three. Since it has few crosslink sites to constrain the polymer, it opens up easily resulting in greater water uptake and greater swelling. But Carbopol 934P and Carbopol 974P are more highly crosslinked, the crosslinking sites constrain the polymer to open up easily. So, extent of swelling is less (Bulletin 17, 2002). Results obtained from these studies support data published in Noveon Company Literature (Bulletin 16, 2002). In vitro water uptake studies have been reported for several drugs using Carbopol polymers (Boaz Mizrahi *et al*, 2004; Ramana *et al*, 2007; Kamel *et al*, 2002; Michael *et al*, 2003) and other polymers also (Parakh *et al*, 2003).



**Figure 1: Effect of pH on water uptake of Carbopol polymers a) for Carbopol 934P, b) for Carbopol 974P, c) for Carbopol 971P**

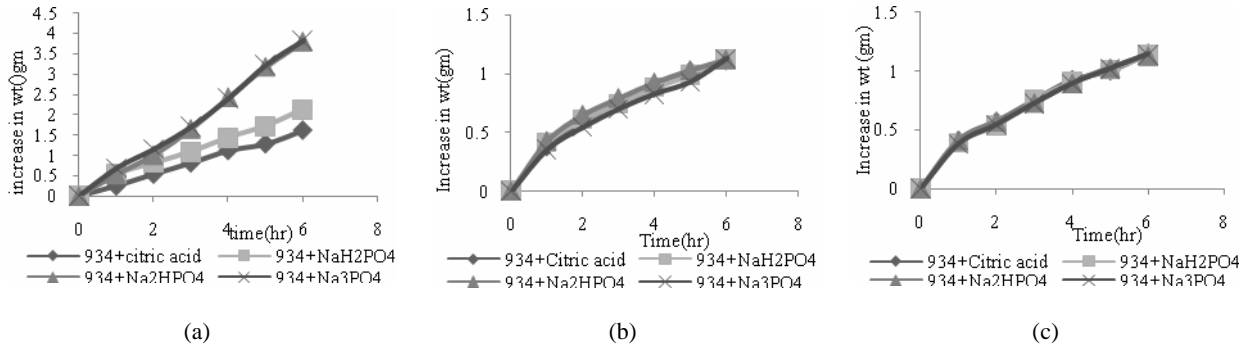


**Figure 2: Effect of pH on swelling of Carbopol polymers a) for distilled water, b) for 0.1N HCl and c) for pH 6.8 phosphate buffer**

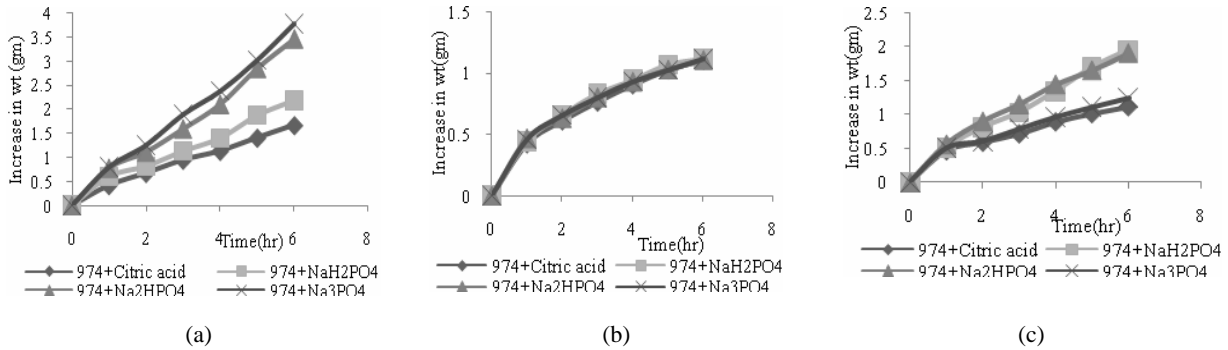
**Effect of excipients on water uptake and swelling of Carbopol polymers**

Figure 3-5 show that all tablets containing Carbopol polymers and  $\text{Na}_3\text{PO}_4$  in combination absorb greatest amount of water and also swell most [Figure 6-8]. Since Carbopol polymers are anionic in nature, in aqueous system they were neutralized by basic excipients. Thus generate negative charges along their backbone. Repulsion

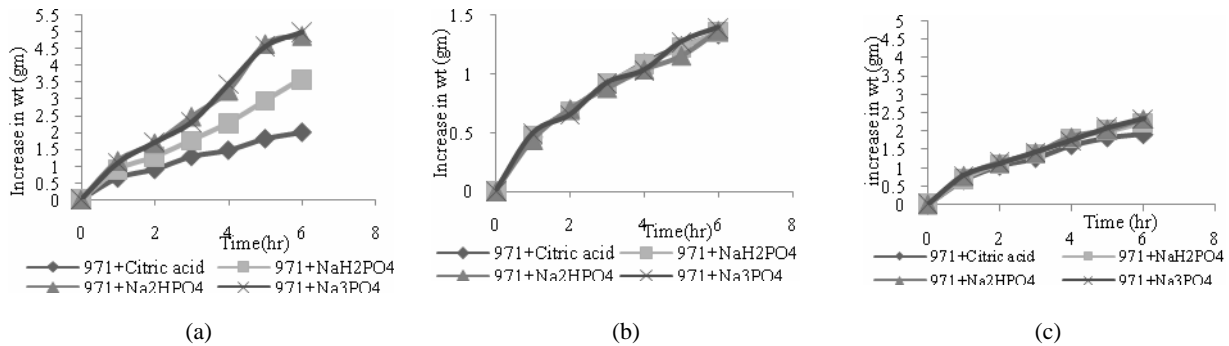
of like charges causes uncoiling of the polymer and an extended structure (Bulletin 10, 2002).  $\text{Na}_3\text{PO}_4$  being the most basic excipient of the other three, neutralization was maximum for it. Carbopol 971P is lightly crosslinked, so uncoiling and water uptake was greatest for it. For Citric acid, it lowered the pH of the environment, so water uptake and swelling was much less for tablets containing citric acid.



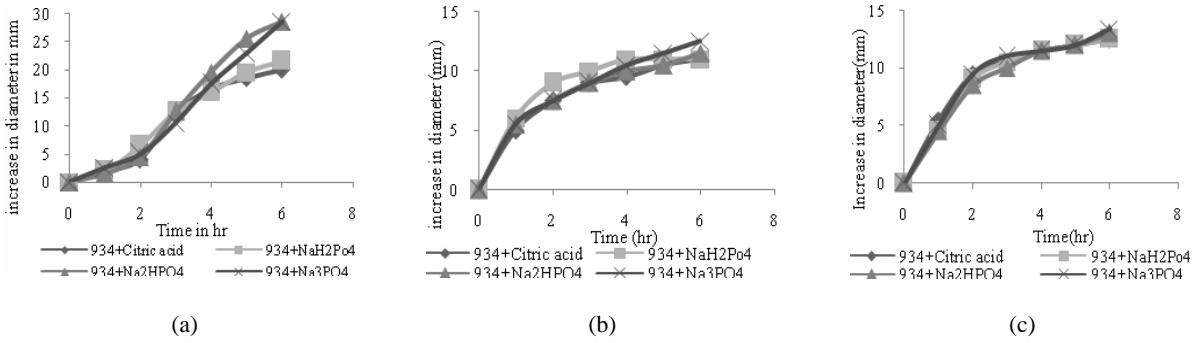
**Figure 3: Effect of excipients on water uptake of Carbopol 934P polymers a) in distilled water, b) in 0.1N HCl; c) in pH 6.8 phosphate buffer**



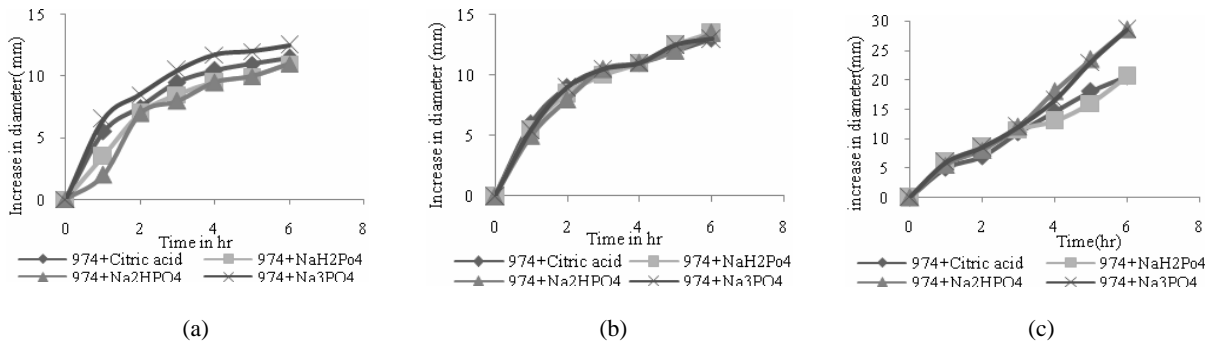
**Figure 4: Effect of excipients on water uptake of Carbopol 974P polymers a) in distilled water, b) in 0.1N HCl; c) in pH 6.8 phosphate buffer**



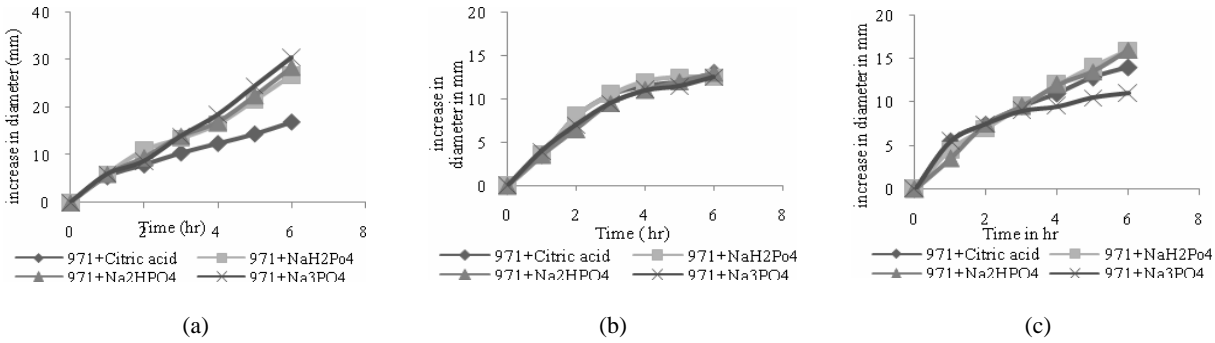
**Figure 5: Effect of excipients on water uptake of Carbopol 971P polymers a) in distilled water, b) in 0.1N HCl; c) in pH 6.8 phosphate buffer**



**Figure 6: Effect of excipients on swelling of Carbopol 934P polymers a) in distilled water, b) in 0.1N HCl ; c) in pH 6.8 phosphate buffer**



**Figure 7: Effect of excipients on swelling of Carbopol 974P polymers a) in distilled water, b) in 0.1N HCl; c) in pH 6.8 phosphate buffer**



**Figure 8: Effect of excipients on swelling of Carbopol 971P polymers a) in distilled water, b) in 0.1N HCl; c) in pH 6.8 phosphate buffer**

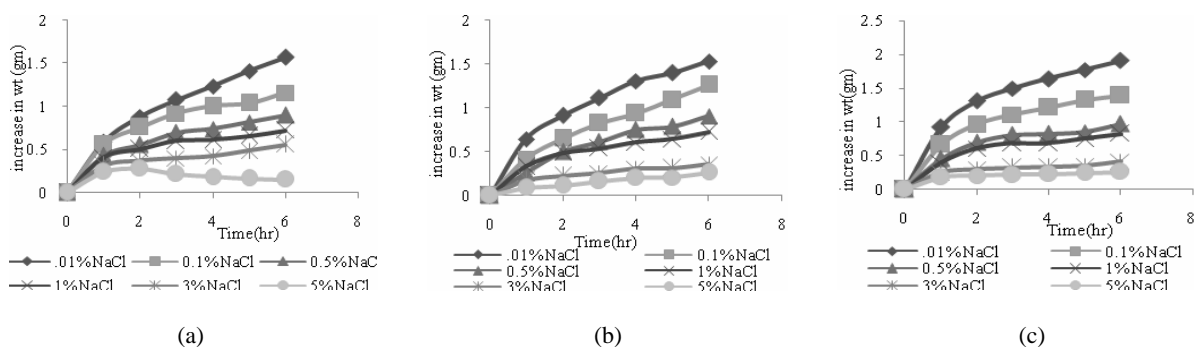
### Effect of ionic strength on water uptake of Carbopol polymers

Figure 9 shows that, water uptake by the Carbopol polymers decreases with an increase in ionic strength. Thus water uptake is maximum for 0.01M NaCl and minimum for 5M NaCl. The water uptakes of ionic hydrogels are mainly related to the ionic strength and charge number of the external solution. It is seen that when the ionic strength is no less than 1M, the swelling ratio of the polymer increased as the ionic strength

decreased. When the ionic strength was no more than 0.01M, it did not affect the swelling behavior of Carbopol polymers (Cui Tang *et al*, 2007). As the concentration of cations in swelling medium enhanced, a charge screening effect of the additional cations resulted in a nonperfect anion-anion electrostatic repulsion. Therefore, the osmotic pressure resulting from the mobile ion concentration difference between the gel and aqueous phase decreased, and consequently, the swelling ratio decreased. A similar study was

performed by Cui Tang *et al.* in “Swelling behaviour and biocompatibility of Carbopol-

containing superporous hydrogel composites” (Cui Tang *et al.*, 2007).



**Figure 9: Effect of ionic strength on water uptake of Carbopol polymers a) for Carbopol 934P, b) for Carbopol 974P; c) for Carbopol 971P**

## Conclusion

Carbopol polymers gave excellent water uptake and swelling properties in distilled water, 0.1N HCl and pH 6.8 phosphate buffer. Drug release characteristics depend on swelling and gel property of the polymers. Since, these polymers do not dissolve in water, erosion in the manner of linear polymers does not occur. Therefore, these polymers can be offered as promising candidates for controlled drug release.

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