**Research Article**

# Evaluation of Crosslinking on the Water Sorption Properties of Poly(Vinyl) Alcohol

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**ABSTRACT**

Poly (vinyl) alcohol has the ability to sorb water depending on the degree of hydrolysis and its molecular weight. Thus, a low molecular weight PVA is expected to have more water solubility and more water sorbing properties. These properties could also be affected by the crosslinking conditions employed. In this study, PVA crosslinked with glutaraldehyde at the 1:10 and 1:5 PVA to GA ratios for 1 and 6h at 70 °C and a pH of 5.5 and 6.5 was conducted followed by precipitation and washing with acetone and further drying. The resulting films were exposed to water activities from 0 to 0.9 and submitted to swelling and contact angle studies. All materials exhibited a type III isotherm shape. Crosslinking induced the formation of a more porous material with a low sorption capacity as compared to the parent material. Further, the low water uptake diffused in those films explained their low water swelling capacity.

**Keywords:** PVA, Sorption, Crosslinking, Glutaraldehyde, Swelling.

## INTRODUCTION

Poly (vinyl) alcohol (PVA) is obtained from poly(vinyl) acetate (PVAc), a linear polymer consisting of vinyl acetate repeat units, by treatment with an alkaline methanol solution at boiling temperature until the degree of hydrolysis reaches more than 84%.[1] The alkaline hydrolysis of PVAc occurs on the acetate ester bonds of the chains which forms the amorphous regions. As a result, PVA grades with a high hydrolysis degree shows a high crystallinity and melting point, more flexibility, better aqueous solubility and water sorption properties than low hydrolysis degree grades.[2]

PVA has also an outstanding chemical stability and excellent film forming properties. It is also biodegradable, innocuous, non-toxic, non-carcinogenic and has good biocompatible properties.

It has also been used as a water-soluble film for packaging and controlled drug delivery systems.[3] Currently, PVA is used as a film forming material, especially for the production of coated tablets. However, compacts require the application of many coating layers to achieve the required enteric properties to protect drugs from the environmental conditions.

Nevertheless, PVA itself does not have the ideal water vapor barrier and mechanical properties due to its elevated sensibility to environmental conditions which limits its application as a desirable film coating material.[4]

In an attempt to improve the functionality of PVA-based films, several researchers have pursued physical and chemical treatments to modify the polymer network.[5] Physical treatments included UV and γ-irradiation, whereas, chemical treatments have been attempted by chemical crosslinking. In this scenario, glutaraldehyde (GA) is the preferred crosslinking agent due to its low

cost, commercial availability, good reactivity and very low toxicity. GA reacts with the hydroxyl groups of PVA chains under acidic conditions forming acetal bonds.[6]

The mechanical and water sorption properties of the film and hence, the stability of PVA and crosslinked materials depend on its interaction with water or the presence of water in its structure. At high relative humidity water acts as a plasticizer changing these properties.[7] Therefore, these properties could also depend on the crosslinking degree. The water activity reflects a combination of water-solute and water-surface interactions as well as capillary forces and it usually increases as vapor pressure increases. It also influences the chemical and microbial stability, flow properties, compaction, hardness, and dissolution rate of solid dosage forms. Therefore, the knowledge of the moisture uptake behavior of these processed materials is essential to understand and predict their stability, especially during storage alone, or combined with other materials in coated dosage forms under different ambient conditions. Studies of the sorption ability of these crosslinked materials allow for comparing and fixing the appropriate storage conditions to maintain the quality requirements of drug products.

The goal of this study is to evaluate the influence of crosslinking with glutaraldehyde on the water sorption properties of PVA by using the non-linear models of Guggenheim-Anderson-de Boer (GAB) and Hailwood and Horrowin (HH). The non-linear curve fitting and the resulting parameters were obtained from the Statgraphic® software vs. XV (Warrenton, VA).

## MATERIALS AND METHODS

### Materials

Poly (vinyl) alcohol (lot P04102697) with a 95.3% hydrolysis degree and 80 kDa molecular weight was

purchased from Belchem International (Longwood, FL). Glutaraldehyde (lot 2507, 50% w/v solution) was obtained from FlowChem (Medellin, Columbia). Acetone (lot K45159114) was obtained from Calbiochem (Darmstdat, Germany).

## METHODS

### Crosslinking Reactions

Approximately, 5 g of PVA was first dispersed in 100 mL of distilled water for 30 minutes and then dissolved at 90 °C with magnetic stirring (RH-KT/C, IKA, Campinas, Brazil) for 30 minutes to obtained a 5% w/v concentration. Approximately, 50 mL or 100 mL of this solution was transferred to a round bottom flask containing 50 mL of a 50% w/v glutaraldehyde solution and pH was adjusted according to the conditions listed on Table 1.

This flask was placed in a reactor composed of a heating mantle (Centricol, Medellin, Columbia) coupled with a condenser. The reaction runs were conducted at a 1:10 and 1:5 PVA:glutaraldehyde ratios at 70 °C, a pH of 5.5 and 6.5 for 1 or 6h.

**Table 1:** Reaction conditions for crosslinking of PVA with glutaraldehyde

| pH | PVA: Glutaraldehyde v/v ratio | Time (h) |
|---|---|---|
| 5.5 | 1:10 | 1 |
| 5.5 | 1:10 | 6 |
| 5.5 | 1:5 | 1 |
| 5.5 | 1:5 | 6 |
| 6.5 | 1:10 | 1 |
| 6.5 | 1:10 | 6 |
| 6.5 | 1:5 | 1 |
| 6.5 | 1:5 | 6 |

The hydrogels thus obtained were then precipitated with acetone, filtered and dried on an oven (U50, Memmert, Schwabach, Germany) at 45 °C for 48h and the resulting films were kept in a desiccator over silica gel.

### Crosslinking Degree Determination

The analysis was conducted on a Perkin-Elmer spectrophotometer (Perkin Elmer, CA, USA) equipped with the Spectra software (Spectrum BX, vs. 5.3.1, CA, USA). Spectra were recorded between 4000 and 400 cm$^{-1}$ and the resolution, interval length and number of scans employed were 16, 2.0 and 16 cm$^{-1}$, respectively.

The degree of crosslinking associated to the formation of acetal bridges was calculated as a percentage from the absorption of the CO band at 1660 cm$^{-1}$ with respect to the absorption of CO band at 1730 cm$^{-1}$.

### Porosity and Degree of Crystallinity

A PAN analytical powder X-ray diffractometer (Epirean 2012, Westborough, MA), equipped with a monochromatic CuK$_\alpha$ ($\alpha_1$=1.5460 Å, $\alpha_2$= 1.54438 Å) radiation, was employed. The degree of crystallinity (DC)

was calculated using the expression: % DC = 100*[$I_C$/($I_C$+$I_a$)], where $I_C$ is the sum of the areas of all diffracted X-rays peaks and $I_a$ is the area of the diffuse halo due to the amorphous region. Powder porosity was determined as reported previously.[8]

### Swelling Studies

Dry square films samples (5 mm thick, 10 mm in diameter) were weighed and immersed in 20 mL distilled water bath at 37 °C. At different time points, the films were taken out, the excess water was carefully removed with filter paper from the film surface, and the films were then weighed immediately. This analysis was conducted for 72h. Swelling ratios were determined from the weight change before and after swelling.

### Water Sorption Studies

They were performed on a moisture sorption analyzer (Aqualab, Decagon Devices, Pullman, WA). The sample pan assembly was cleaned with ethanol and dried before each run. Samples of ~ 3g were tested. Even though dried samples were employed, an initial drying phase at 45 °C was executed. Once a stable reading (weight change of no more than 0.01%) was obtained for 10 min, the sample was considered dry. Runs were conducted at 25 °C at relative humidity steps from 0 to 90%. Water uptake in the sample was considered at equilibrium when a stable reading (a weight change of no more than 0.01% or maximum drying time of 240 min) was reached. The fitting procedure was performed using the Statgraphic software vs XV (Warrenton, VA). A non-linear regression was then applied with the principle of least squares.

### The Guggenheim-Anderson-de Boer (GAB) Model

This model has a theoretical background derived from the BET theory with a simple mathematical form with only three parameters (C, k and $m_m$). These parameters have a physical meaning in terms of the sorption process and its fitting range is from 0 to 0.95.[9] It assumes that the partition functions for the secondary and higher layers of sorbed water are energetically the same, but, different from that of liquid water, as well as different from the primary sorbed water.[7] The GAB equation is expressed as follows:

$$m = \frac{k*\frac{P}{P_0}*m_m*C_{GAB}}{\left(1-k*\frac{P}{P_0}\right)*\left(1-k*\frac{P}{P_0}+ C_{GAB}*k*\frac{P}{P_0}\right)} \tag{1}$$

$$C_{GAB} = D * e^{(H_1-H_m)/RT} \tag{2}$$

$$k = B * e^{(H_L-H_m)/RT} \tag{3}$$

Where, m is the grams of water per gram of PVA, $m_m$ is the monolayer capacity (weight of water when the surface of one gram of polymer is covered by a monolayer (g/g), $P/P_0$ is the equilibrium partial pressure. P and $P_0$ correspond to the partial vapor pressure and vapor pressure at saturation, respectively. C and k are energy constants of the monolayer and multilayer, respectively. C is the ratio of the partition function of the

primary molecules to that of the upper states,[10] whereas, k represents the partition function of the secondary sorbed molecules to that of external condensed liquid.[11] B and D are entropic accommodation factors, usually taken as 1. $H_1, H_m$ and $H_L$ correspond to the heat of water sorption in the monolayer (kJ/mol), heat of water sorption in the multilayer (kJ/mol) and the heat of condensation (J/mol), respectively. Further, R is the universal gas constant (8.3145 J/molK) and T the absolute temperature.

### Hailwood and Horrowin Model (HH)

This model was created to describe the water sorption properties of biopolymers such as cellulose. It assumes that the monolayer is evolving during the dynamic sorption process in the whole range of water activities and considers that the unhydrated polymer, monohydrated polymer and multilayer water as in equilibrium.[12] This model is expressed as:

$$m = m_h + m_s \qquad (4)$$

$$m = \frac{18}{W} * \left( \frac{\frac{P}{P_0}\alpha\beta}{1 + \frac{P}{P_0}\alpha\beta} \right) + \frac{18}{W} * \left( \frac{\frac{P}{P_0}\alpha}{1 - \frac{P}{P_0}\alpha} \right) \qquad (5)$$

Where, m is the total fractional moisture content, $m_h$ and $m_s$ are the fractional moisture content of the monolayer and multilayer, respectively. $M_h$ can also be used to determine the number of accessible OH groups in each material.[13] P and $P_0$ correspond to the partial vapor pressure and vapor pressure at saturation, respectively. W is the amount of polymer per sorption site, 18 g/mol is the molar mass of water, $\alpha$ and $\beta$ are the equilibrium constants of hydrated and non-hydrated polymer, respectively.[14]

### RESULTS AND DISCUSSION

When water molecules in the film are in contact with water vapor, these molecules exert a vapor pressure (P) which is lower than the vapor pressure of pure water ($P_0$) over a flat surface at the same temperature. An isotherm is a graphic representation of the equilibrium sorption of water as a function of the $P/P_0$ ratio. Due to the high electronegativity of oxygen compared to hydrogen in water, a strong hydrogen bonding interaction between the hydroxyl groups of PVA and incoming water molecules is expected to occur.

Figure 1 shows the water sorption isotherms and Table 1 lists the resulting GAB parameters. The shape of these isotherms give information about the interaction of the polymer with water vapor molecules and depend on the affinity between the surface and water molecules, interfacial binding energy, vapor pressure, temperature and RH.[15] In this case, all curves resembled a type III isotherm where weak polymer-water interactions took place showing a low water uptake at low water activity and a strong increase in sorption at higher water activity.[16] Thus, as water activity increases, water

molecules become attached at the PVA-vapor interface by weak interaction forces such as Van der Waals forces or hydrogen bonding. [17,18] This type of isotherm also indicates that most of the sorption mechanism is related to a multilayer formation. Further, PVA exhibited a significant uptake at low $P/P_0$ followed by small adsorption at intermediate water activity and a high uptake at elevated water activities indicating a rapid formation of a monolayer.[19] In terms of hygroscopicity, which is the ability of a material to interact with water vapor from the surrounding atmosphere, these polymers can be classified as moderately hygroscopic since sorbed less than 5% water when exposed to less than 0.6 $P/P_0$.[20]
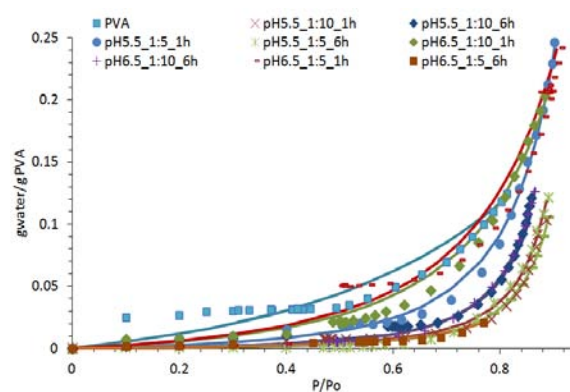


**Figure 1:** Water sorption isotherms for PVA materials fitted by the GAB model

Results suggest that glutaraldehyde suppressed the original crystal structure of PVA by inducing a glassy environment of an amorphous environment easing the formation of acetal bonds. The reduction of crystallinity by the formation of acetal bridges induced a significant reduction of the crystalline structure to less than 40% restricting the mobility of PVA chains and promoting amorphization and decreasing in the hydrogen bonding pattern. On the other hand, the induction of amorphicity in PVA led to a disordered arrangement of molecules and decreased the water sorption ability of PVA due to the formation of a tight crosslinking network. However, for PVA the absorbed water acts as a plasticizer increasing the mobility of the chains due to water penetration between the chains enhancing water sorption.

The degree of crystallinity of PVA was ~75% and that of crosslinked products ranged from ~32 to 40%. These less crystalline crosslinked materials possessed less water sorption sites available as compared to PVA. Further, the PVA powder had the lowest porosity, which did not hinder its large affinity for water. However, crosslinked materials had a larger porosity, possibly due to the remaining microbubbles formed during the drying process of hydrogels.

The GAB model explains three states of water. The first one is the tightly bound water which is non-freezing and forms a monolayer. The second is the weakly attached water, which is unbound freezing water and forms a multilayer. This water exhibits a melting/crystallization

temperature different from that of bulk water and can form clusters with other water molecules. The third type is the freezing free water, which is the portion of water that has no contact with the solid body, filling its pores in a capillary form and can be removed by centrifugation.[21]

The experimental data had a good fit to the model having $r^2$ values higher than 0.903. The monolayer value ($m_m$) expresses the amount of water that is sufficient to form a layer of water molecules of thickness of one molecule per adsorbing surface.[18] Results show that PVA had the highest affinity for water (0.91 g water/g polymer) followed by the sample having a 49% crosslinking degree. These two materials also exhibited the lowest k values which are translated in the largest $H_m$-$H_L$ values for the multilayer formation. Thus, it is probable that for these two materials the formation of secondary sites started even before the monolayer was completed. Thus, they have the largest driving force for water sorption. The energetic of multilayer sorption (k) was the lowest for the most soluble and dissolving materials identified as PVA, pH6.5_1:5_1h, pH6.5_1:10_1h, and pH5.5_1:5_1h showing dissolution times after gelling of 5h, 3h, 2h and 9h, respectively. For these highly dissolving materials it is expected that water vapor is absorbed into structure and not simply adsorbed on the surface.[15] On the other hand, $H_1$-$H_m$ was negative for all materials indicating an exothermic process for the monolayer formation.

The HH model assumes the formation of three species in equilibrium such as unhydrated polymer, polymer with a monolayer and polymer with a multilayer of water molecules. The HH isotherms and the parameters derived from this model are shown in Figure 2 and Table 3, respectively, and all the data had a good fit to this model ($r^2$ >0.9516). Figure 3 shows the deconvoluted sorption curves. The deconvoluted monolayer and multilayer curves exhibited a Brunauer type I and type III isotherms, respectively. The rate of water uptake increased with higher P/P$_0$, especially for PVA which showed the largest monolayer sorption at low P/P$_0$. It is expected that the first water molecule binds to the most exposed hydroxyl group located on the PVA surface forming a monolayer. Conversely, crosslinked products showed a reduced number of exposed hydroxyl groups and thus, the formation of a monolayer was more prevalent at low P/P0.

This model shows that the monolayer formation of most materials starts as early as 0.01 P/P$_0$. Further, PVA was the only material that exhibited the largest monolayer formation at P/P$_0$<0.5. Further, at a water activity of ~0.5, most materials were already covered by a monolayer. Results also indicate that the formation of a complete monolayer was not required for the development of a multilayer. Thus, secondary sorption centers emerged before the monolayer was complete. This means that a single water molecule had the same probability of binding to a monomolecular occupied or an empty sorption site. The rapid and massive formation of a monolayer curve in

PVA indicates the substantial presence of hydroxyl groups holding large amounts of water at low water activity. The limiting uptake may be ruled by the accessible micropore volume and capillary effects.[16,18] Most crosslinked materials reached a monolayer plateau curve at a water activity of 0.4-0.5 and then remained constant. This indicates a low affinity for water since the formation of hydrogen bonds occurred only through the few remaining hydroxyl groups. Thus, all the hydroxyl groups available for binding are occupied rapidly at a water activity of ~0.5.

On the other hand, the multilayer isotherm shape exhibited an exponential increase with P/P$_0$ where crosslinked materials showed the lowest increasing tendency. In this case, there was a steady increase of sorbed water up to a relative pressure of 0.5. It is also observed that, initially at a low relative pressure, water molecules prefer binding to an empty site rather than to an already monomolecular occupied site. Nevertheless, at ~0.5 relative pressure an incoming water molecule has the same probability of binding a monomolecular occupied or an empty site. Further, at relative pressure higher than 0.55 in crosslinked materials, incoming water molecules are more likely to be attracted to already occupied sites than to the few remaining empty centers. Further, the formation of a second layer probably starts at lower water levels than those corresponding to the complete monolayer formation.
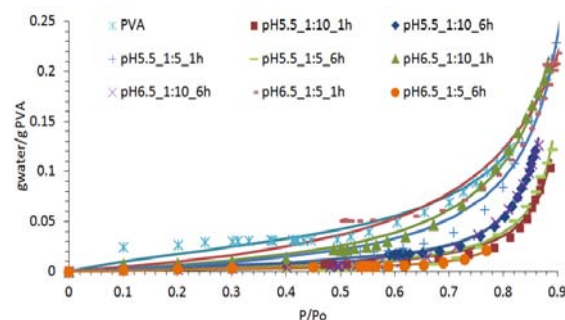


**Figure 2:** Water sorption isotherms according to the HH model

**Table 3:** Hailwood-Horrowin parameters obtained from the water sorption isotherms

| Summary | w | α | β | $r^2$ |
|---|---|---|---|---|
| pH6.5_1:10_1h | 0.45 | 1.01 | 0.00 | 0.9933 |
| pH6.5_1:10_6h | 0.14 | 1.09 | 0.00 | 0.9860 |
| PVA | 0.48 | 0.97 | 3.66 | 0.9600 |
| pH6.5_1:5_6h | 0.03 | 1.19 | 5.00 | 0.9670 |
| pH5.5_1:10_1h | 0.11 | 1.07 | 0.00 | 0.9830 |
| pH6.5_1:5_1h | 0.73 | 0.94 | 0.04 | 0.9873 |
| pH5.5_1:5_6h | 0.12 | 1.07 | 0.00 | 0.9753 |
| pH 5.5_1:10_6h | 0.12 | 1.10 | 2.73 | 0.9975 |
| pH5.5_1:5_1h | 0.37 | 1.02 | 0.00 | 0.9516 |

α: hydrated equilibrium constant, β: non-hydrated equilibrium constant, w: g polymer/ mole or unit of sorption site (number of sorption sites per gram polymer)

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Most materials swelled, but did not dissolve after 72h of testing. The w value indicates the amount of water bound per mole of sorption site and appeared reduced for some crosslinked materials. As a result, only few remaining hydroxyl groups of most crosslinked materials will be available to bind water molecules. Further, the rapid dissolving materials also had a w values between 0.45 to 0.73 g polymer/sorption site. Conversely, all other

materials had w values between 0.03-0.14 g/sorption site.

Therefore, it is expected that in highly dissolving materials a large number of hydroxyl groups of the polymer form hydrogen bonds with incoming water molecules not only at the surface and thus, it is also expected that absorbed water has diffused through pores into the core of the films.

**Table 2:** GAB parameters obtained from the water sorption isotherms

| Sample ID | Crosslinking degree (%) | K | $m_m$ | c | $H_m-H_L$ (kJ/mol) | $H_1-H_m$ (kJ/mol) | $r^2$ | Porosity (%) | DC (%) |
|---|---|---|---|---|---|---|---|---|---|
| pH6.5_1:10_1h | 93.1 | 0.83 | 0.29 | 0.08 | 0.46 | -6.3 | 0.989 | 31.3 ± 0.2 | 32.7 |
| pH6.5_1:10_6h | 84.3 | 0.99 | 0.35 | 0.01 | 0.02 | -11.7 | 0.999 | 40.5 ± 0.1 | 39.6 |
| PVA | 0 | 0.57 | 0.91 | 0.09 | 1.39 | -6.0 | 0.903 | 22.2 ± 0.7 | 74.5 |
| pH6.5_1:5_6h | 70.6 | 1.00 | 0.01 | 0.27 | 0.00 | -3.2 | 0.984 | 68.3 ± 0.2 | 39.0 |
| pH5.5_1:10_1h | 98.6 | 1.00 | 0.07 | 0.03 | 0.00 | -8.7 | 0.981 | 51.5 ± 0.5 | 34.3 |
| pH6.5_1:5_1h | 49 | 0.81 | 0.53 | 0.05 | 0.52 | -7.4 | 0.987 | 53.3 ± 0.1 | 34.0 |
| pH5.5_1:5_6h | 96.1 | 0.99 | 0.18 | 0.01 | 0.023 | -11.4 | 0.992 | 49.2 ± 0.1 | 37.2 |
| pH 5.5_1:10_6h | 93.2 | 0.99 | 0.16 | 0.02 | 0.025 | -9.7 | 0.996 | 26.8 ± 0.1 | 39.9 |
| pH5.5_1:5_1h | 98.9 | 0.93 | 0.25 | 0.04 | 0.181 | -8.2 | 0.980 | 58.7 ± 0.3 | 39.1 |

k: energy constant of multilayer sorption; c: energy constant of monolayer sorption; $H_m-H_L$: enthalphy of multilayer sorption; $H_1-H_m$: enthalpy of monolayer sorption; $m_m$: monolayer capacity ($g_{water}/g_{polymer}$); $r^2$: determination coefficient.
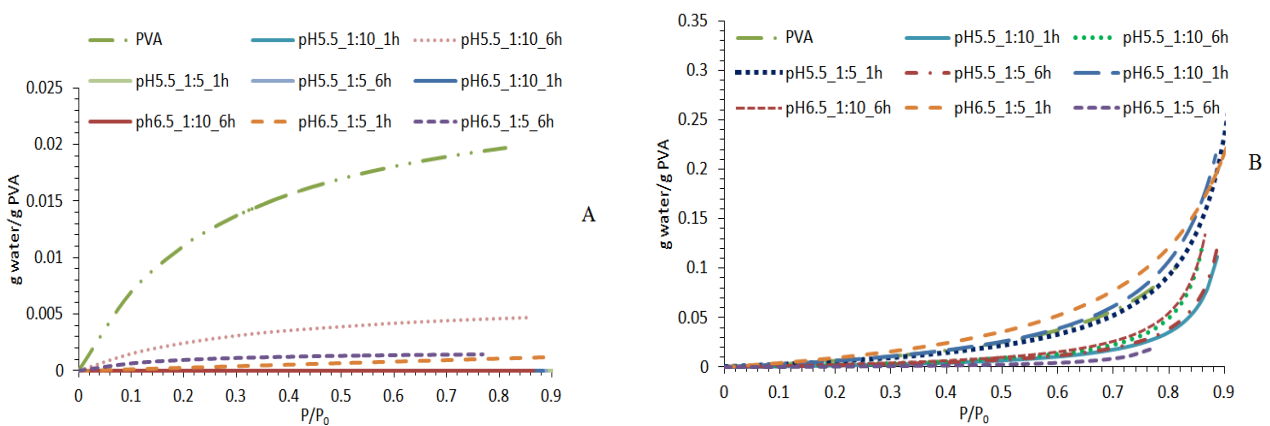


**Figure 3:** Deconvoluted water sorption curves for the monolayer (a) and multilayer formation (b) according to the HH model.
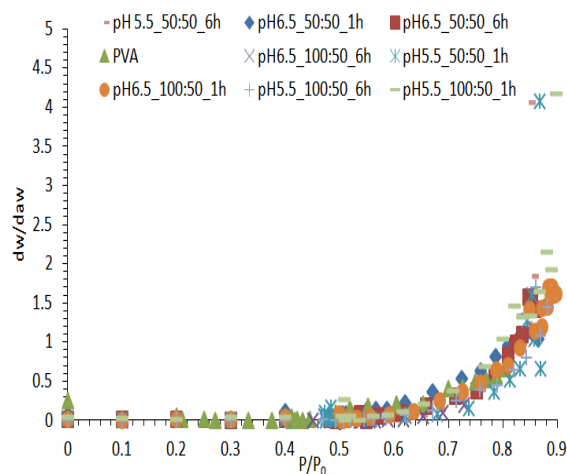


**Figure 4:** Rate of water uptake as a function of water activity

The first derivative of the moisture content as a function of relative pressure is shown in Figure 4. All the curves presented an exponential shape in which two regions are identified. Region 1 (P/P_0 from 0.1 to 0.5). In this region, no major changes in the rate of water uptake occurred and it is expected that all water molecules have the same energy, so all binding sites have the same probability to bind water. At the end of this region (RH of ~0.6) it is possible that water molecules start forming clusters and possibly jump from one adsorption site to another.[11] Thus, clustering is expected to occur if the amount of water molecules in the polymer is higher than the quantity that is expected for bonding. Therefore, water molecules entered and opened the PVA chains allowing for a cluster formation. At ~0.6 relative pressure is expected that a complete monolayer adsorption takes place for most materials except for PVA. Beyond this

point divergence occurred possibly due to the gain of rotational freedom, since the chains expands and occupy more space. Thus, incoming water molecules are able to fill the voids between the polymer chains and diffuse into denser regions forcing additional chains apart. A significant upswing at a water activity beyond 0.65 might result from the water liquefaction on the surface due to capillary condensation into pores.

## CONCLUSION

The water sorption properties of PVA were modified by crosslinking with glutaraldehyde. Crosslinking reduced the degree of crystallinity, but increased the porosity of PVA. Hydrophilicity was larger in PVA than crosslinked materials. The highly hydrophilic properties of PVA were attributed to not only to adsorption, but also absorption of water into the core of the films which induced swelling and in some cases, dissolution of the structure. On the contrary, this hydrophilicity was reduced by crosslinking due to the partial replacement of hydroxyl groups by acetal bonds. These results can be useful during the drug development stage to predict the desired ambient storage conditions for coated solid dosage forms.

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