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EXPERIMENTAL DESIGN OF MIXTURE APPLIED TO STUDY PVP HYDROGELS PROPERTIES CROSSLINKED BY IONIZING RADIATION

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ABSTRACT

Hydrogels are three dimensional hydrophilic crosslinked polymeric networks that have capacity to swell by absorbing water or biological fluids without dissolve. Hydrogels have been widely used in different application fields from agriculture, industry and in biomedicine. The properties of a hydrogel are extremely important in selecting which materials are suitable for a specific application. So mixtures can offer hydrogels with different properties to different applications. The PVP hydrogels were prepared by gama radiation of an aqueous polymer solution and crosslinked by gamma ray, an effective and simple method for hydrogel formation that offers some advantages over the other techniques. In this work, a mixture experimental design was used to study the relationship between polymer cross-linking and swelling properties of PVP hydrogels with PEG as plasticizer and agar as gellifier. The gel fraction was measured for every mixture specified for the experiment D-optimal designs.

1. INTRODUCTION

Hydrogels have been widely used in different application fields from agriculture to controlled drug delivery systems [1]. PVP hydrogel itself is of limited applicability because of its poor mechanical properties. So, blending PVP with other polymers we have a significant role in a series of PVP hydrogels as biomedical materials [2]. Blending is a simple method to combine the advantages of different materials; the resulting polymer blends sometimes show synergistic properties [3]. The advantages of polymer blend systems include improving the material properties like hydration, cross-linking and mechanical properties.

Among various methods applied for the production of hydrogels, Rosiak et al developed the production process of these hydrogels using radiation processing [4]. Poly(*N*-vinyl-2-pyrrolidone)(PVP)-based hydrogels, produced by radiation-induced cross-linking and simultaneous sterilization, have been applied successfully and offers many advantages, as a simple, efficient, clean and environment-friendly process [5].

Benamer et al [6] observed an increase in gel fraction by increasing dose and concentration, whereas the equilibrium swelling rate decreases with PVP concentration. The lower is the concentration of the polymer in the system, the higher is the probability of mutual recombination of intermediate products of the radiolysis of water because in aqueous

solutions indirect effects prevails, the yield of cross linking decreases with the decreasing concentration of the polymer in the system [7]. In the last quarter century, many studies have been conducted on the swelling properties of various hydrogels and the fundamental properties of chemical cross-links have been elucidated [8], however, for future practice applications of hydrogels as functional materials it is also fundamental understand the relationship between the swelling and cross-linking with the variation in the proportion of mixture components.

In the general mixture experiment the response is assumed to depend only on the relative proportions of the ingredients present in the mixture and not in the amount of the mixture. Then, in a mixture experiment, if the total amount is held constant and the value of the response changes when changes are made in the relative proportions of those ingredients making up the mixture, then the behavior of the response is said to be a function of the joint blending property of the ingredients in the mixture [9].

In this study it was used the planning of mixtures, which employs pre-determined compositions of PVP, PEG and agar to study an experimental region about cross-linking and the composition of hydrogels membranes.

2. EXPERIMENTAL

2.1. Materials

The poly(vinylpyrrolidone) (PVP) used in this study is Kollidon 90F produced by Basf KGAa, PEG 300 supplied by Oxiteno and agar by Oxoid. All raw materials were medical grade.

2.2. Experimental Design

Table 1 shows the components level and hydrogels components amounts used to determine the design presented in table 2 suggested by Minitab® 15 software using D-Optimal design. To analyse the results was employing Statistic© 8 software and the figures were obtained from Design-Expert® software.

Table 1. Variables and levels selected to prepare the mixture design of the hydrogels.

Mixtures Components	Level (%)	
	Low	High
X_1 = PVP K 90	4.0	20.0
X_2 = PEG 300	0.0	5.0
X_3 = agar	0.0	1.5
X_4 = water	73.5	94.5

Table 2. D-optimal design used to prepare the mixture of hydrogels.

Design Points	Mixtures Components (%)			
	X_1	X_2	X_3	X_4
1	12.00	2.50	1.50	84.00
2	20.00	5.00	1.50	73.50
3	20.00	5.00	0.00	75.00
4	12.00	5.00	0.75	82.25
5	4.00	5.00	1.50	89.50
6	20.00	2.50	0.75	76.75
7	20.00	0.00	1.50	78.50
8	4.00	0.00	1.50	94.50
9	20.00	0.00	0.00	80.00
10	4.00	2.50	0.00	93.50
11	12.00	0.00	0.00	88.00
12	8.00	3.75	0.39	87.86
13	16.00	3.75	0.75	79.50
14	12.00	1.25	0.75	86.00
15	16.00	1.25	0.39	82.36
16	20.00	0.00	1.50	78.50
17	4.00	0.00	1.50	94.50
18	20.00	5.00	0.00	75.00
19	20.00	5.00	1.50	73.50
20	12.00	2.50	1.50	84.00

2.3. Preparation of Hydrogels

The hydrogels solutions have been prepared dissolving the PVP in distilled water and then mixing with the others constituents, according to mixture design as showed in Tab. 2. Nitrogen was bubbled in the solution to remove the oxygen and the samples were irradiated with gamma rays generated from a ^{60}Co at dose of 25 kGy in sealed impermeable packaging.

3. HYDROGELS CHARACTERIZATION

3.1. Gel Content of PVP Hydrogel

The hydrogels samples were placed the Soxhlet apparatus, using water as solvent, during 40h to remove sol content and then dried at 60°C until constant weight. The gel content was

calculated as Eq. (1): Where Wf is the weight dried gel after extraction, and Wi the initial weight of the dried polymer before extraction.

$$\text{Gel}(\%) = \frac{\text{Wf}}{\text{Wi}} \text{x}100 \quad (1)$$

4. RESULTS

4.1. Gel Content of PVP Hydrogel

Table 3 presents D-optimal design and the gel fraction results of hydrogels prepared.

Table 3. Component proportions and the observed response values at the design points.

Design points	Components (%)				Gel Fraction
	PVP (X_1)	PEG (X_2)	agar (X_3)	water (X_4)	
1	12.00	2.50	1.50	84.00	82.3
2	20.00	5.00	1.50	73.50	73.2
3	20.00	5.00	0.00	75.00	80.7
4	12.00	5.00	0.75	82.25	63.0
5	4.00	5.00	1.50	89.50	56.9
6	20.00	2.50	0.75	76.75	85.3
7	20.00	0.00	1.50	78.50	87.3
8	4.00	0.00	1.50	94.50	70.0
9	20.00	0.00	0.00	80.00	97.5
10	4.00	2.50	0.00	93.50	37.1
11	12.00	0.00	0.00	88.00	97.6
12	8.00	3.75	0.39	87.86	78.4
13	16.00	3.75	0.75	79.50	73.6
14	12.00	1.25	0.75	86.00	70.9
15	16.00	1.25	0.39	82.36	91.3
16	20.00	0.00	1.50	78.50	91.6
17	4.00	0.00	1.50	94.50	68.6
18	20.00	5.00	0.00	75.00	81.6
19	20.00	5.00	1.50	73.50	73.8
20	12.00	2.50	1.50	84.00	74.5

4.2. Data Analysis

The best mathematical model was selected based on the comparisons of statistical parameters including the determination coefficient (R^2) and the adjusted determination coefficient (adj-R^2) and the F-value provied by analyses of variance (ANOVA).

The analysis of variance (Tabela 4) to adjusted equation (2) showed that the coefficient of variation (R^2) was 98,4%, the contribution of pure experimental error (R^2-adjusted) was 94,8%. The MS Residual was 10,59818. These results showed that the special cubic model adjusts to the experimental data.

The equation that express the response ($y\hat{}$ = gel fraction), as an explicit function of the proportions of PVP, PEG, agar and water in the mixture, obtained from the special cubic model is shown in Eq. 2, where X_1 is the PVP concentration, X_2 is PEG concentration, X_3 is agar concentration and X_4 is water concentration.

$$\hat{Y} = \underset{(\pm 7.8\%)}{-55.25X_1} + \underset{(\pm 757.4\%)}{2886.94X_3} - \underset{(\pm 03\%)}{0.96X_4} + \underset{(\pm 7.2\%)}{27.93X_1X_3} + \underset{(\pm 0.1\%)}{0.8X_1X_4} - \underset{(\pm 133.6\%)}{356.36X_2X_3}$$
$$- \underset{(\pm 7.6\%)}{28.03X_3X_4} + \underset{(\pm 1.5\%)}{3.28X_1X_2X_3} - \underset{(\pm 0.1\%)}{0.79X_1X_3X_4} + \underset{(\pm 1.4\%)}{3.37X_2X_3X_4} \quad (2)$$

Table 4. Analysis of variance of the special cubic model.

Factor	Coefficient	Standart Error	t	probability	-95 % Cnf. Limt	+95 % Cnf. Limt
X_1 [PVP]	-55.250	7.8504	-7.03786	0.000411	-74.459	-36.041
X_2 [PEG]	-74.237	109.8888	-0.67556	0.524487	-343.125	194.652
X_3 [agar]	2886.936	757.3882	3.81170	0.008846	1033.674	4740.199
X_4 [water]	-0.955	0.2665	-3.58216	0.011613	-1.607	-0.303
X_1X_2	2.991	2.6226	1.14032	0.297619	-3.427	9.408
X_1X_3	27.928	7.1812	3.88899	0.008086	10.356	45.500
X_1X_4	0.800	0.1102	7.25737	0.000348	0.530	1.069
X_2X_3	-356.357	133.5996	-2.66735	0.037158	-683.264	-29.451
X_2X_4	1.004	1.1244	0.89318	0.406160	-1.747	3.755
X_3X_4	-28.032	7.6223	-3.67760	0.010360	-46.683	-9.381
$X_1X_2X_3$	3.278	1.5067	2.17581	0.072479	-0.408	6.965
$X_1X_2X_4$	-0.033	0.0446	-0.73580	0.489605	-0.142	0.076
$X_1X_3X_4$	-0.787	0.1062	-7.41444	0.000309	-1.047	-0.527
$X_2X_3X_4$	3.367	1.4341	2.34794	0.057219	-0.142	6.876

The model indicates a strong contribution of the PVP and agar, alone in the reticulation of the membranes; unlike the PEG not appear in the equation. The model suggests that the PEG shows a strong interaction synergic with the agar favouring the cross-linking, which can be easily seen in Fig. 1, 2 and 3.

This synergy also occurs in the interaction of PVP with the agar, but with less intensity, especially for concentrations around 8% of PVP, but in this case the synergy promotes cross-ling, as can be seen clearly in Fig. 1, 2 and 3.

The Fig. 1 and 2 show the contour diagram of gel fraction to PVP concentration with 4, 8, 12 and 16% and Fig. 3 shows the triangular-dimensional surface to membrane with 20% of PVP.

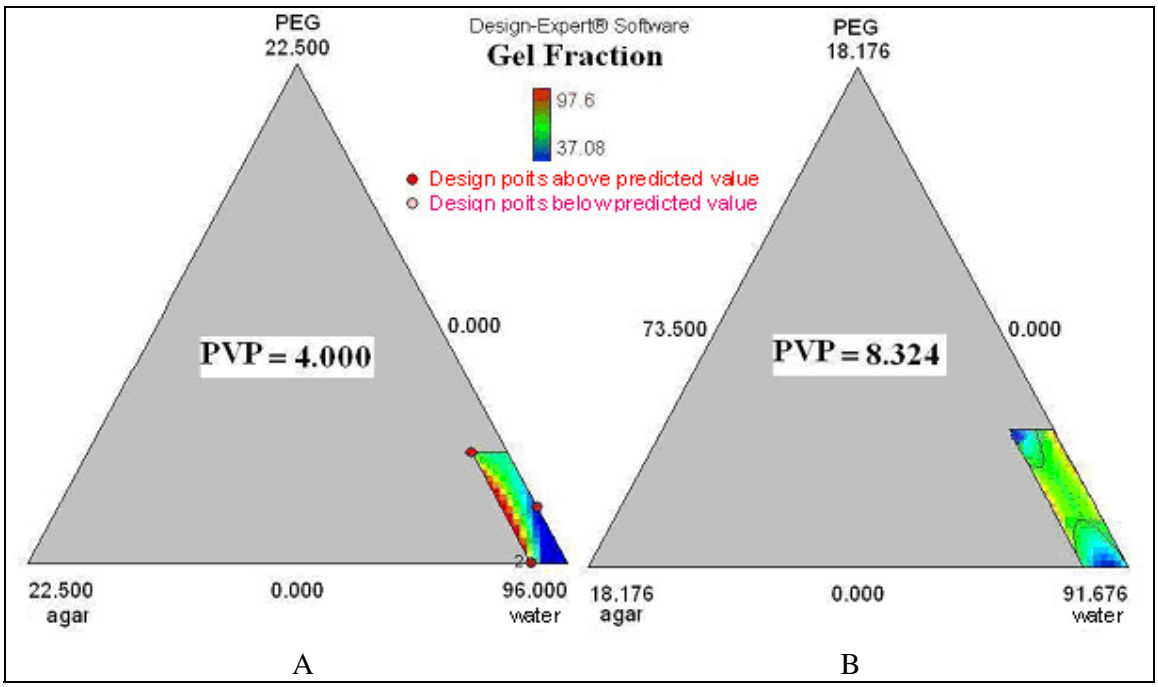

Figure 1. Contour diagram of gel fraction to membranes with 4% (A) and approx. 8% (B) of PVP.

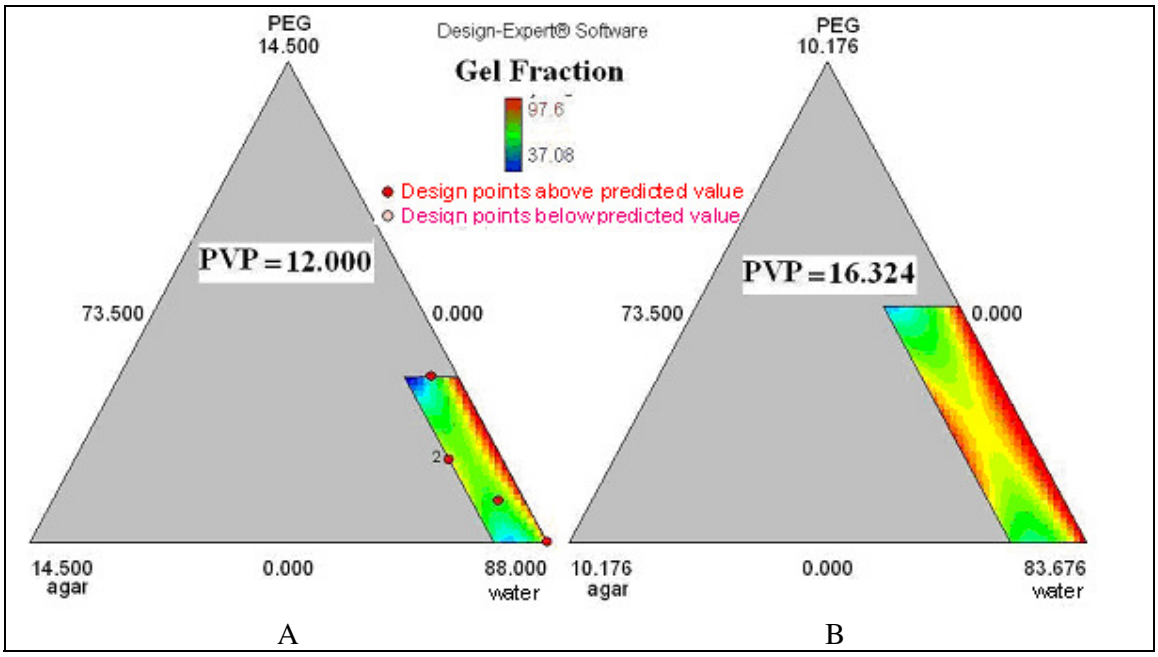

Figure. 2. Contour diagram of gel fraction to membranes with 12% (A) and approx. 16% (B) of PVP.

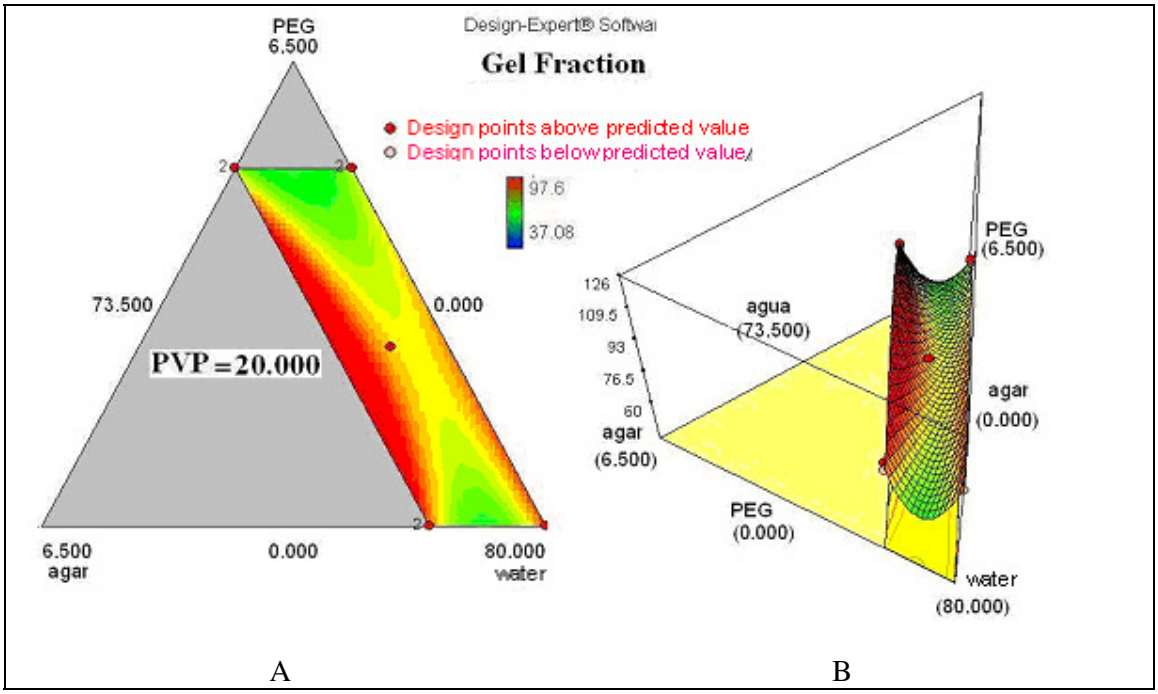

Figure. 3. Contour diagram (A) and triangular-dimensional surface (B) of gel fraction to membranes with 20% of PVP.

Swelling tests are being performed to an adjustment of the model for the analysis of results can be related to those presented in this study. Also new testes are being evaluated for assessment of other properties.

5. CONCLUSIONS

- This study shows the interaction between the components of the mixture indicating the importance of a systematic study for the system.
- The concentration of PVP / PEG / agar affects the efficiency of cross link and present synergistic and antagonistic interactions.
- It is possible to obtain high values of gel fraction for both high and low concentration of PVP
- High concentration of PVP is not essential to obtain higher cross ling in membranes.
- The results showed that the methodology allows the synthesis of membranes according to the technological interest.

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REFERENCES

1. H. Kaplan; A.G. Ner, "Characterization and Determination of Swelling and Diffusion Characteristics of Poly(N-vinyl-2-pyrrolidone) Hydrogels in Water". *Journal of Applied Polymer Science*, **Vol. 78**, pp.994–1000 (2000).
2. M. Sen, E. N. Avcı, "Radiation synthesis of poly(*N*-vinyl-2-pyrrolidone)-K-carrageenan hydrogels and their use in wound dressing applications. I. Preliminary laboratory tests." in http://www.interscience.wiley.com (2005).
3. Y. H. Bae, S. W. Kim, "Hydrogel delivery systems based on polymer blends, blockco-polymers or interpenetrating networks". *Advanced Drug Delivery Reviews,* **V. 11**, pp.109-135 (1993).
4. J. M. Rosiak, A. Rucinska-Rybus, W. Pekala, "Method of manufacturing of hydrogel dressings". US Patent 4,871,490; Polish Patent 151,581; Hungarian Patent 204,866; UK Patent 2,200,643; Germany Patent 3,744,289 (1989).
5. A. B. Lugao, S. M. Malmonge, "Use of radiation in the production of hydrogels", *Nuclear Instruments and Methods in Physics Research,* **B 185**, pp. 37-42 (2001).
6. S. Benamer, M. Mahlous, A. Boukrif, B. Mansouri, S. L. Youcef, "Synthesis and characterisation of hydrogels based on poly(vinyl pyrrolidone)". *Nuclear Instruments and Methods in Physics Research*, **B 248,** pp.284–290 (2006).

7. R. L. Clough, S.W. R. Shalaby, *Radiation effects on polymers.* Oxford University Press (1991).
8 T. Harada, Y. Hirashima, A. Suzuki, M. Goto, N. Kawamura, M. Tokita, "Synthesis, swelling behavior and surface microstructure of poly(sodium acrylate) gels cross-linked by aluminum ions". *European Polymer Journal*, **V. 41**, pp. 2189–2198 (2005).
9. J. A. Cornell, *Experiments with Mixtures: Designs, Models and the Analysis of Mixtures Data*", Wiley: New York, 3rd ed. (2002).