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Latin Square Design For Selection of Excipients in the Development of the Composition of Medical Sponges Based on the Cryoliophylized Xenoderm

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ABSTRACT

Medical sponges are popular medical tools, which widely used in various fields of medicine to stop bleeding and for close wound surfaces. Therefore, the aim of our work was to study the selection of excipients in order to develop the composition and technology of medical sponges based on a material of biological origin - cryolyophilized xenoderm, which has wide practical application in combustiology.

The influence of three groups of factors on the technological parameters of 16 experimental series of the sponges was studied. The indicators: pH, appearance, water absorption, time of complete dissolution, In vitro degradation, thickness of sponges, and weight loss during drying.

The influence of factors and their levels on the quality indicators of the developed medical sponges is investigated. It is established that the influence of the type of polymer is decisive for all characteristics except for weight loss during drying, which is more influenced by the type of plasticizer. Using the generalized indicator - the desirability function, the optimal levels of factors within each factor are selected.

According to the results of the tests, it was found that the best values of technological indicators were medical sponges based on water extract obtained at 40° C, which included medical gelatin and propylene glycol.

1. Introduction

Medical sponges are popular medical tools, which widely used in various fields of medicine to stop bleeding and for close wound surface [1, 2]. At the technology of medical sponges, can be used different polymeric carriers, as well as, can be enter the active pharmaceutical ingredients with different pharmacological action, which will determine the scope of possible application of this tool [3, 4]. Due to the pronounced hemostatic, antiseptic and absorption properties of the medical sponges, they have a great practical importance in surgery and combustiology in particular [5, 6].

Nowadays, the problem of treatment of burns is relevant, as burn injuries are one of the most common domestic and industrial injuries in the world. Despite the introduction of new methods of treatment in medical practice, the use of new drugs, the improvement of existing drugs, the development of new tools for the local treatment of burn injuries is still promising [7].

For the treatment of burns in Ukraine, the technology of lyophilized xenodermoimplants has been developed and introduced into production, which approved for use in medical institutions. Therefore, the use of the powder of crushed xenoderm in the development of the various types of dosage forms is relevant and promising for today [8].

In the development of the composition of medical sponges used water extract from the cryolyophilized porcine powder (xenoderm) and chlorhexidine digluconate, which is an internationally recognized antiseptic that is widely used in surgery, dermatology, urology, ophthalmology, otolaryngology and dentistry [9]. Technological studies of the water extraction from the xenoderm`s powder have been previously developed and studied, as evidenced by Patent of Ukraine № 138600.

Therefore, the aim of the research was to study the effect of excipients, the conditions of preparation of water extract from the xenoderm powder on the technological parameters of medical sponges using the design of experiment.

During the analysis of literature data, it was found that the development of medical sponges is a promising area of modern pharmaceutical technology. For the design of the experiment Latin square 4x4 methodology was used, in order to theoretically and scientifically substantiate the choice of the most optimal excipients.

2.Materials and methods

Active pharmaceutical ingredients: crushed substrate of cryolyophilized xenoderm of the porcine skin (LCC Institute of Biomedical Technologies, Ukraine) and chlorhexidine digluconate solution 20 %, (Sigma-Aldrich, USA). Among the excipients were studied: medical gelatin (Sigma-Aldrich, USA), hydroxypropyl cellulose (HPC) (Nisso Chemical Europe GmbH), hydroxypropyl methylcellulose-50 (HPMC-50) (Biogrund GmbH), methylcellulose-15 (MC-15) (Biogrund GmbH), tween-80 (PJSC "Barva") polyethylene glycol-400 (PEG-400) (PJSC "Barva"), propylene glycol (BASF "Global") and glycerin (BASF VG).

2.1Methodology

To study three factors with the same number of levels, taking into account the design of the study, it is most rational to use Latin square 4x4. When performing three-factor comparative experiments, symmetrical orthogonal plans based on Latin squares are most often used. [10, 11, 12] The use of the Latin square 4x4 reduces the number of experiments by 4 times compared to the full factorial experiment, so it is possible to perform 16 series instead of 64. However, despite the reduced number of experiments, the properties and results of the fractional plan remain statistically correct [13, 14].

In our case, a linear model is adopted, Equation 1:

$$Y_{ijkm}=\mu+\alpha_i+\beta_j+\gamma_k+res+E_{ijkm} \quad (1)$$

Y_{ijkm} – denoting any observation for which,
$X_1 = i, X_2 = j, X_3 = k$. X_1 and X_2 are blocking factors, X_3 is the primary factor.

μ – denoting the general location parameter
α_i – denoting the effect for block i
β_j – denoting the effect for block j
γ_k – denoting the effect for treatment k
res – dispersion sources, that are not provided by the linear model.
E_{ijkm} – remainder (i, j, k =1,2,...,n), E_{ijkm} [N(0, σ^2].

According to the general algorithm, the analysis of experimental data was performed and the obtained

results were discussed.

Also, when planning the study, it was decided to choose the most optimal pharmaco-technological indicators of the quality of medical sponges and determine their value in accordance with the recommendations of the world literature [15, 16], because the developed form is not pharmacopoeial, according to SPU.

When planning a comprehensive study, it was necessary to determine the sequence of stages of the experiment and select the appropriate research methods:

- to propose methods for determining pharmaco-technological indicators for medical sponges in accordance with the literature data and the requirements for this form;
- select excipients in order to study their effect on the technological properties of sponges on the basis of literature sources;
- develop the composition of experimental samples of sponges and then examine them for certain quality indicators.

The design scheme of the experiment is shown in Figure 1.

All studied excipients and the temperature regimes for preparation of water extract from crushed xenoderm powder were grouped into three main groups (factors): polymers (factor A), plasticizers (factor B), and temperature of preparation of water extract from crushed xenoderm (factor C). The corresponding list of factors and their levels are presented in Table 1.

2.2.Procedure

On the pharmaceutical market, medical gelatin, collagen, chitosan, and cellulose derivatives are most often used to obtain medical sponges [9]. In this experiment, we selected medical gelatin and cellulose derivatives (HPC, HPMC, MC) for study, because sponges based on them are cost-effective, efficient, and technologically simple. To date, there are no sponges of domestic production, obtained on the basis of selected polymers (factor A). Selected plasticizers (factor B) were introduced to provide plasticity and reduce the brittleness temperature, which improves frost resistance and is necessary at the stage of freezing the viscous mass to obtain sponges in liquid nitrogen before lyophilization. An important feature of this experiment is the study of the influence of the temperature of preparation of water extract from crushed xenoderm powder (factor C) on the technological parameters of the obtained sponges. Previous studies have determined that the temperature of preparation of water extract from crushed xenoderm powder significantly affects the pharmaco-technological properties of the obtained water extract, which at different production temperatures characterized by different dynamic viscosity[17]. Under the conditions of obtaining water extract from crushed xenoderm powder at 20 °C, it was characterized by a dynamic viscosity of 6.99±0.20 mPa*s and a density of 1.031±0.030 g/cm^3; at 40 °C the dynamic viscosity was 4.24±0.11 mPa*s, density 1.045±0.03 g/cm^3.

Therefore, the temperature of preparation of water extract from crushed xenoderm powder affects its density, dynamic viscosity, the consistency of the mass for the production of sponges, and in general the porosity of the obtained sponges after lyophilization. Moreover, on the basis of previously conducted pharmacological studies, it was found that the water extract prepared at different temperatures affects the regeneration process on the model of aseptic burns in animals [18, 18.] Thus, the temperature of the preparation of water extract from crushed xenoderm powder is an important condition in the development of medical sponges based on it and therefore selected as a factor C for research.

*2.*3.Preparation of medical sponge

Pre-prepared water extract from the xenoderm at different temperatures (Levels of factor C) according to the patent of Ukraine № 138600. In the xenoderm water extract (Levels of factor C), the polymers (Levels of factor A) was left at 37 °C for swelling and dissolution. Then the remainder of the xenoderm water extract was added to the polymers solution by parts, with constant stirring until foam formation. To

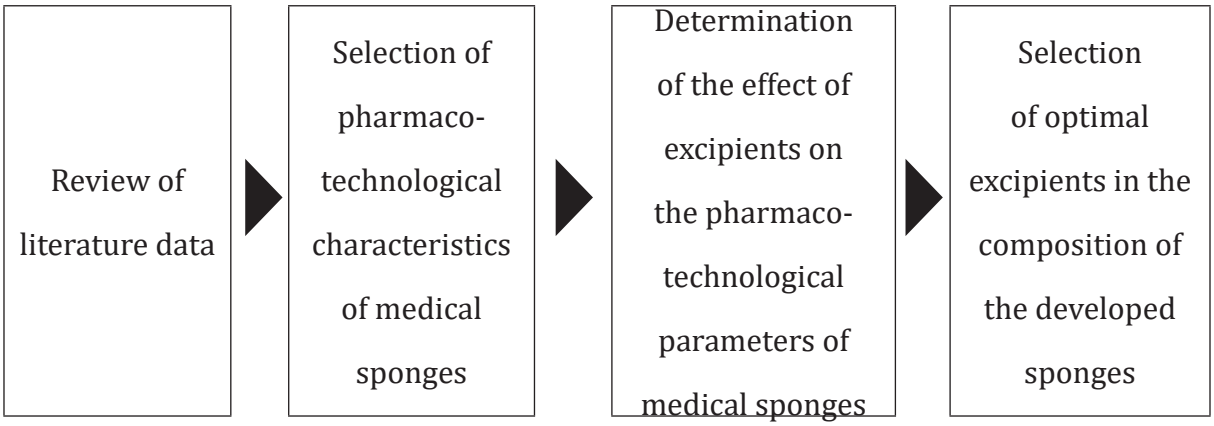

Figure 1. *Experimental design scheme*

Table 1. Factors and their levels studied using the Latin square 4x4.

Factors	Levels of factor
A – Polymers	a_1 – medical gelatin a_2 – hydroxypropyl cellulose (HPC) a_3 – hydroxypropyl methylcellulose-50 (HPMC-50) a_4 – methylcellulose-15 (MC-15)
B – Plasticizers	b_1 – tween-80 b_2 – polyethylene glycol-400 (PEG-400) b_3 – glycerin b_4 – propylene glycol
C – The temperature of preparation of water extract from crushed xenoderm powder (°C)	c_1 – 20 °C c_2 – 30 °C c_3 – 40 °C c_4 – 50 °C

prepared solutions of xenoderm water extract with polymers, the plasticizers (Levels of factor B) were added. To the resulting mixtures was added a 1 % chlorhexidine digluconate solution. The mixtures were foamed to form a stable foam that increased 2-3 times in volume. The resulting solution was poured out into the cooled aluminum moulds and left at temperature 20-22°C for 2-3 hours. Thereafter, the solutions were frozen in liquid nitrogen and lyophilized during 18-20 h.

Developed experimental series of medical sponges in two replicates were evaluated on the following indicators:

pH of water solutions of sponges. The pH values of the test samples were determined using a pH meter pH 150-MI. All tests were performed at room temperature. The pH meter was calibrated using standard buffer solutions (Table 2).

Appearance of sponges. Medical sponges were characterized by appearance, organoleptic properties (color, odor, consistency), as well as signs of physical instability (delamination, fragility, density, surface homogeneity). Appearance was assessed on a five-point scale, proposing appropriate criteria for each score (Table 2).

Determination of water absorption. To the

Table 2. Experimental planning matrix and results of medical sponges' research

Series number	Factor			pH		Appearance, mark		Water absorption, %	
	A	B	C	y_1	y_1'	y_2	y_2'	y_3	y_3'
	a_1	b_1	c_1	6.5	6.8	5	5	962	950
	a_1	b_2	c_2	6.8	6.5	5	4	1179	1170
	a_1	b_3	c_4	6.3	6.5	5	4	671	665
	a_1	b_4	c_3	6.5	6.9	5	5	1344	1350
	a_2	b_1	c_2	7.6	7.4	4	3	401	405
	a_2	b_2	c_1	7.1	6.9	3	3	222	220
	a_2	b_3	c_3	6.4	6.5	5	4	526	521
	a_2	b_4	c_4	7.2	7.1	3	3	270	272
	a_3	b_1	c_3	7.5	7.2	5	4	785	790
	a_3	b_2	c_4	6.9	6.8	5	5	248	245
	a_3	b_3	c_1	7.1	7.5	5	5	328	325
	a_3	b_4	c_2	7.0	7.1	5	4	183	188
	a_4	b_1	c_4	6.5	7.0	4	4	177	175
	a_4	b_2	c_3	7.3	7.1	4	4	135	132
	a_4	b_3	c_2	6.6	6.7	1	1	83	85
	a_4	b_4	c_1	6.9	7.2	3	2	15	18

Table 3 .Experimental planning matrix and results of medical sponges' research

Series number	Time of complete dissolution, min		Thickness, cm		Weight loss during drying, %		Desirability function	
	y_4	y_4'	y_5	y_5'	y_6	y_6'	D	D'
	4320	4380	0.5	0.6	0.12	0.18	0.147	0.189
	4200	4380	0.6	0.6	0.30	0.40	0.205	0.193
	3600	3720	0.6	0.7	2.0	2.50	0.12	0.121
	4380	4400	0.7	0.6	0.40	0.44	0.229	0.214
	60	90	0.4	0.4	2.53	3.02	0.0001	0.0001
	180	190	0.4	0.4	1.25	1.45	0.00002	0.00003
	600	720	0.4	0.4	0.42	0.48	0.0008	0.0009
	180	210	0.3	0.3	4.80	4.90	0.00004	0.00006
	540	600	0.7	0.7	6.53	6.55	0.007	0.007
	30	30	0.6	0.6	0	0.05	0	0
	30	45	0.6	0.6	1.01	1.07	0	0
	55	55	0.7	0.7	0.14	0.16	0.0002	0.0002
	3	5	0.6	0.6	2.45	2.55	0	0
	10	10	0.6	0.6	2.0	2.10	0	0
	10	10	0.3	0.3	1.75	1.95	0	0
	10	10	0.5	0.6	8.52	8.67	0	0

Note. y^1 , $y^{1'}$: pH of the sponges of the first and second series of experiments, respectively. y^2 , $y^{2'}$: the appearance of the sponges of the first and second series of experiments, respectively, ball. y^3 , $y^{3'}$: water absorption of sponges of the first and second series of experiments, respectively, %. y^4 , $y^{4'}$: time of complete dissolution of the sponges of the first and second series of experiments, respectively, min. y^5 , $y^{5'}$: the thickness of the sponges of the first and second series of experiments, respectively, cm. y^6 , $y^{6'}$: weight loss during drying of the first and second series of experiments, respectively, %. D , D' : the desirability function of the first and second series, respectively.

flat-bottomed cup (preheated to 37±1 °C) added a simulation solution containing 8.398 g/l sodium chloride and 0.278 g/l anhydrous calcium chloride (the given proportion of ion content equal to the amount in human serum). A piece of dry sponge 1×1 cm^2 (X_0), pre-weighed, and immersed in a simulation solution for 10 minutes. Then the sponge removing and, after removing the surface moisture with filter paper, weighed (X_1)[17].

Water absorption (%) is calculated according to Equation 2:

$$\text{Water absorption (\%)} = (X_1\text{-}X_0) / X_0 \times 100\% \quad (2)$$

X_0 - the mass of the sponge before absorption;

X_1 - the mass of the sponge after absorption.

The results of the study are shown in table 2.

In vitro degradation of sponges. Degradation can be determined by immersing a piece of sponge (1×1 cm^2) in phosphate buffer solution (PBS) with pH 7.4 for 24 h. The tests carried out incubation chamber (37 ºC). After 24 hours, the sponge is re-dried and the change in sponge mass is calculated. In vitro degradation of sponges calculated by Equation 3:

$$\text{In vitro degradation (\%)} = (X_f - X_s) / X_s \times 100\% \quad (3)$$

X_f – the final mass of the sponge after drying;

X_s – the initial mass of the sponge before immersion.

After determining the percentage of In vitro degradation of the sponges, the obtained percentages for 1 day of the experiment were re-calculated into hours and determined the time of complete dissolution at temperature 37 ºC [18]. The results of the study shown in table 3.

The thickness of the sponges. It is known that the greater the thickness of the sponge, the greater the number of pores it holds. Thus, the thickness of the sponge is directly proportional to the percentage of moisture absorption and dissolution time. The thickness of the sponges was measured using a thickness gauge with an accuracy of 10 μm (Table 3).

Weight loss during drying. This indicator allows assessing the condition of the sponges after lyophilization, namely the presence or absence of residual moisture after lyophilization, as well as during storage. The results of the study shown in Table 3.

Desirability function. In the presence of a large number of indicators and the absence of clearly defined priority levels of factors influencing the feedback, a generalized indicator (desirability function) is used[12], and all indicators are summarized into a single quantitative feature. Desirability for one response - d, and for many - D. The desirability scale has an interval from 0 to 1, with zero desirability values corresponding to the worst value of this indicator, and the value of D=1 - the best value (Table 3).

Results and Discussion

The results of the research were subject to analysis of variance according to the scheme of the Latin square 4x4. Medical sponges were obtained by lyophilization according to the experimental plan shown in table 2. The obtained sponges were examined according to the following indicators: pH (y_1, y_1'), appearance (y_2, y_2'), water absorption (y_3, y_3'), time of complete dissolution (y_4, y_4'), thickness of sponges (y_5, y_5'), weight loss during drying (y_6, y_6'). The results of the study of these indicators are shown in tables 2, 3.

The obtained research results were subjected to analysis of variance, the influence of factors was investigated by F-test. In cases where the experimental value of the F-criterion was greater than the tabular ($F_{0.05}$), it was concluded that the statistical significance of the studied factor. To reflect the influence of factors and their levels on the studied indicators, ranked series of advantages were built. Qualitative factors were arranged in the sequence of their influence on the studied indicator.

Analysis of variance of the obtained results showed that polymers and plasticizers significantly affected the pH (y1, y1') of medical sponges, namely, the influence of factors illustrate the following advantages: A > B > res (Table 4). The type of polymer (factor A) shows the most significant effect on pH, a number of advantages have the following form: HPMC-50 > HPC > MC-15 > medical gelatin (Fig. 2).

The effect of factor B (type of plasticizer) on the pH of medical sponges can be represented as follows:

Table 4. Analysis of the results of the study of indicators of medical sponges' research

Sourse	Degrees of freedom	Sum of squares	Mean squares	F_{test}	$F_{0,05}$
pH (y_1, y_1')					
Factor A	3	1.308359	0.43612	12.54457	4.76
Factor B	3	0.600859	0.200286	5.761049	4.76
Factor C	3	0.207109	0.069036	1.985768	4.76
Residual	6	1.186719	0.197786	5.689139	4.76
Total	31	3.859297	-	-	-
Appearance (y_2, y_2')					
Factor A	3	19.625	6.541667	34.88889	4.76
Factor B	3	2.125	0.708333	3.777778	4.76
Factor C	3	5.125	1.708333	9.111111	4.76
Residual	6	10	1.666667	8.888889	4.76
Total	31	39.875	-	-	-
Water absorption (y_3, y_3')					
Factor A	3	3808964	1269655	92338.53	4.76
Factor B	3	143805.3	47935.08	3486.188	4.76
Factor C	3	615181.8	205060.6	14913.5	4.76
Residual	6	344888.8	57481.46	4180.47	4.76
Total	31	4913060	-	-	-
Time of complete dissolution (y_4, y_4')					
Factor A	3	97212957	32404319	14619.38	4.76
Factor B	3	109329.6	36443.2	16.44154	4.76
Factor C	3	795652.1	265217.4	119.6542	4.76
Residual	6	631644.2	105274	47.49495	4.76
Total	31	98785047	-	-	-
Thickness (y_5, y_5')					
Factor A	3	0.34965	0.11655	93.24	4.76
Factor B	3	0.02865	0.00955	7.64	4.76
Factor C	3	0.03265	0.010883	8.706667	4.76
Residual	6	0.1058	0.017633	14.10667	4.76
Total	31	0.53675	-	-	-
Weight loss during drying (y_6, y_6')					
Factor A	3	35.77616	11.92539	588.6355	4.76
Factor B	3	36.38146	12.12715	598.5946	4.76
Factor C	3	10.03441	3.344803	165.099	4.76
Residual	6	102.1641	17.02735	840.4676	4.76
Total	31	184.6803	-	-	-
Desirability function (D, D')					
Factor A	3	0.187065	0.062355	935.0306	4.76
Factor B	3	0.002783	0.000928	13.91288	4.76
Factor C	3	0.003242	0.001081	16.20408	4.76
Residual	6	0.005522	0.00092	13.80137	4.76
Total	31	0.19968	-	-	-

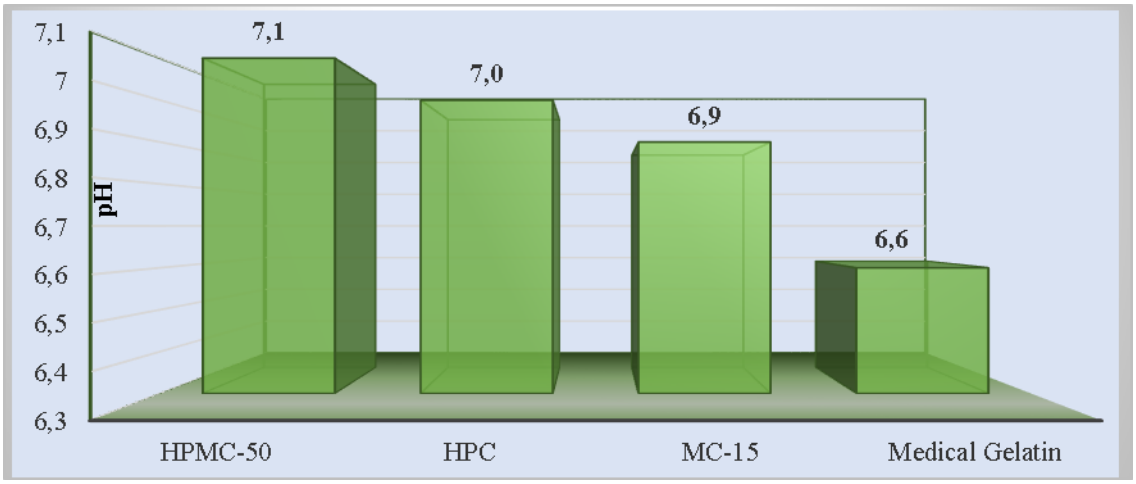

Figure 2.*The effect of polymers on the pH of solutions of medical sponges*

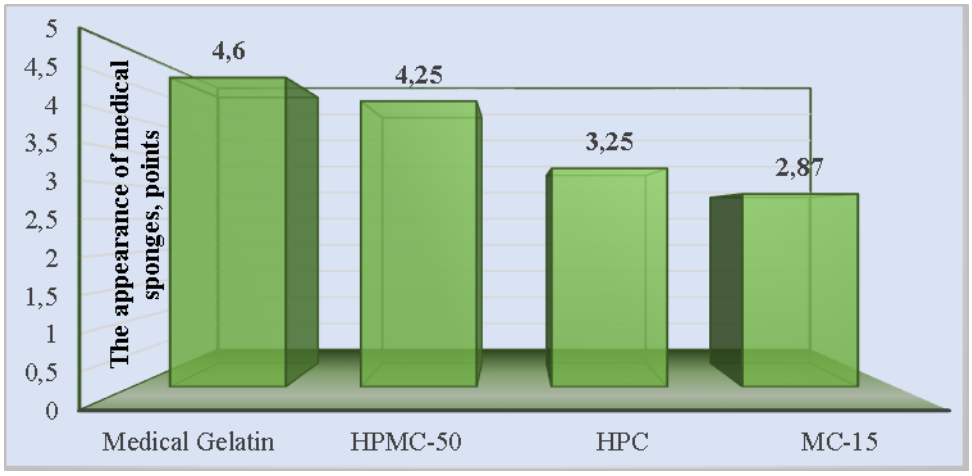

Figure 3.*The effect of polymers on the appearance of medical sponges*

tween-80 > propylene glycol > PEG-400 > glycerin. Factor C, in this case, is statistically insignificant; the change in the temperature of preparation of the water extract from xenoderm powder does not affect the pH value of the obtained medical sponges. The value of res indicates that there is an interaction between the levels of the studied factors.

The study of the influence of the studied factors showed, that two of the three studied factors influence the appearance (y2, y2') of medical sponges: A > C > res (Table 4). The ranked number of advantages of the effect of polymer on the appearance of medical sponges is as follows: medical gelatin > HPMC-50 > HPC > MC-15 (Fig. 3).

The influence of the temperature of preparation of water extract from crushed xenoderm powder (factor C) on the appearance of the obtained sponges can be depicted as follows: 40 °C = 50 °C > 20 °C > 30 °C. That is, the sponges, which used the temperature of water extract from crushed xenoderm powder pre-

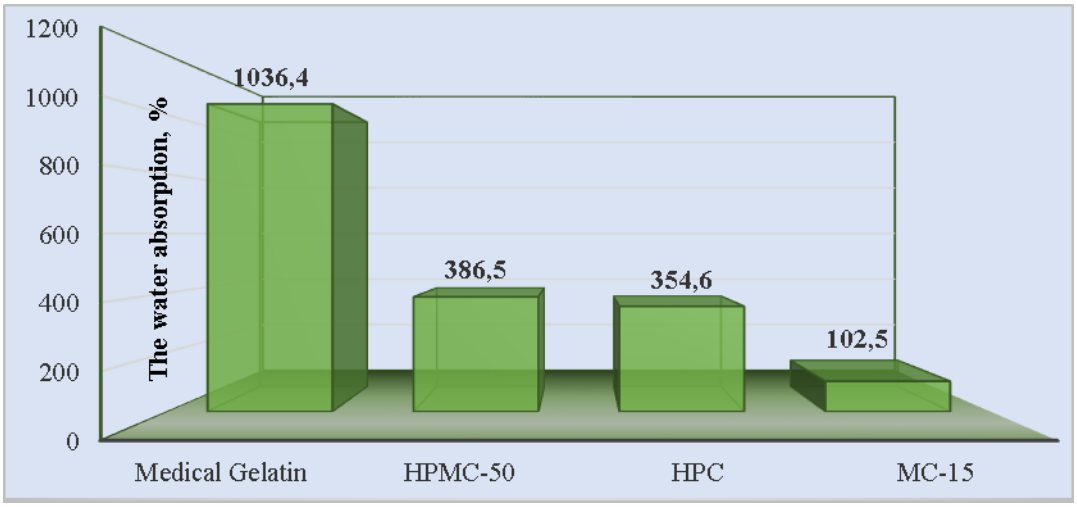

Figure 4. *The effect of polymers on the water absorption of medical sponges*

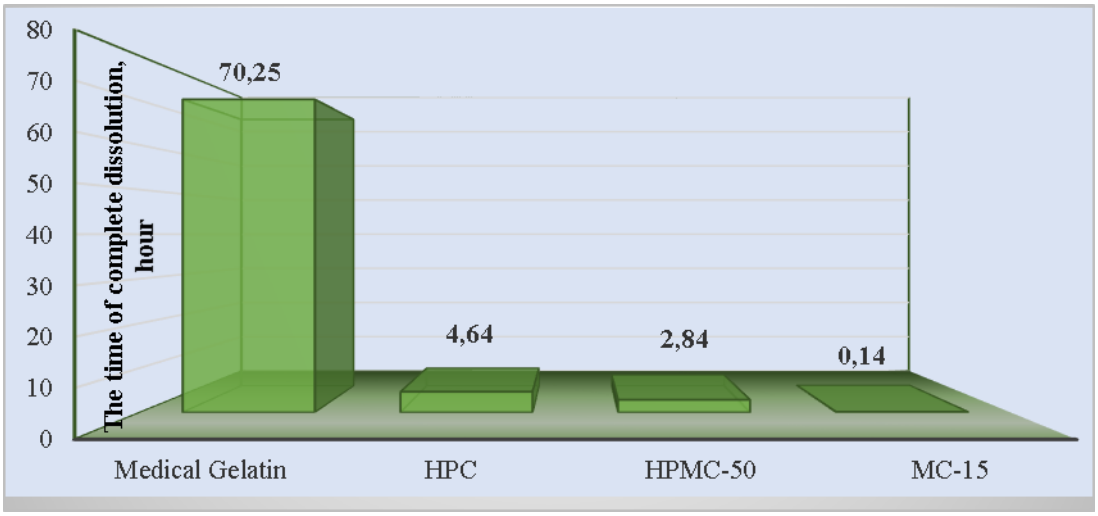

Figure 5. *The effect of polymers on the time of complete dissolution of medical sponges*

pared at 40 °C, were the best in appearance – porous, quite loose, soft and pliable.

The effects of the studied factors on the percentage of water absorption (y3, y3') are as follows: A > C > res > B (Table 4). The highest percentage of water absorption was observed when using medical gelatin (1036.4 %), which is almost three times higher than this value for sponges based on HPMC-50 (386.5 %) and HPC (354.6 %), and 10 times more, than in sponges based on MC-15 (102.5 %) (Fig. 4).

The effect of the temperature of preparation of water extract from crushed xenoderm powder (factor C) on water absorption (%) can be represented by the following ranked number of advantages: 40 °C (697.80 %) > 30 °C (461.75 %) > 20 °C (380.01 %) > 50 °C (340.37 %). The leader among plasticizers in terms of impact on the rate of water absorption is

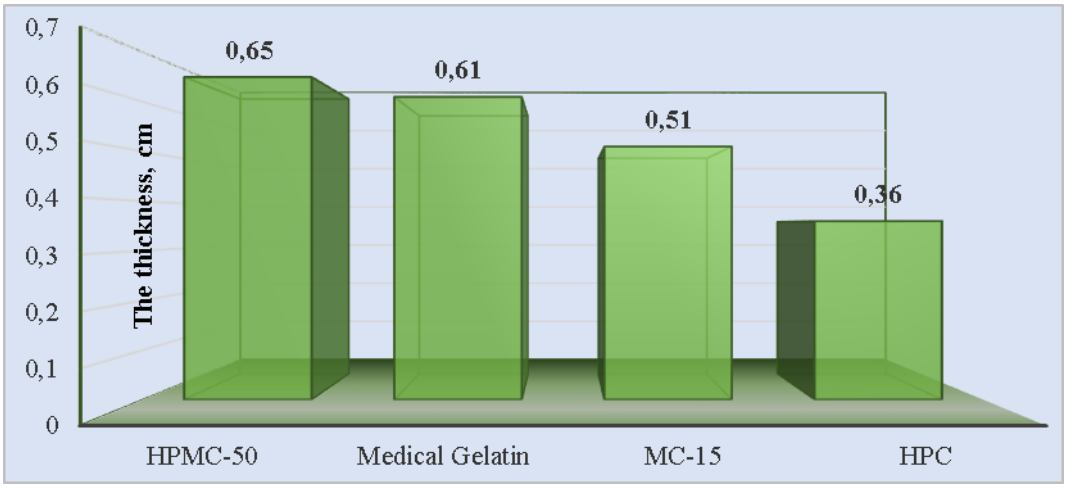

Figure 6.*The effect of polymers on the thickness of medical sponges*

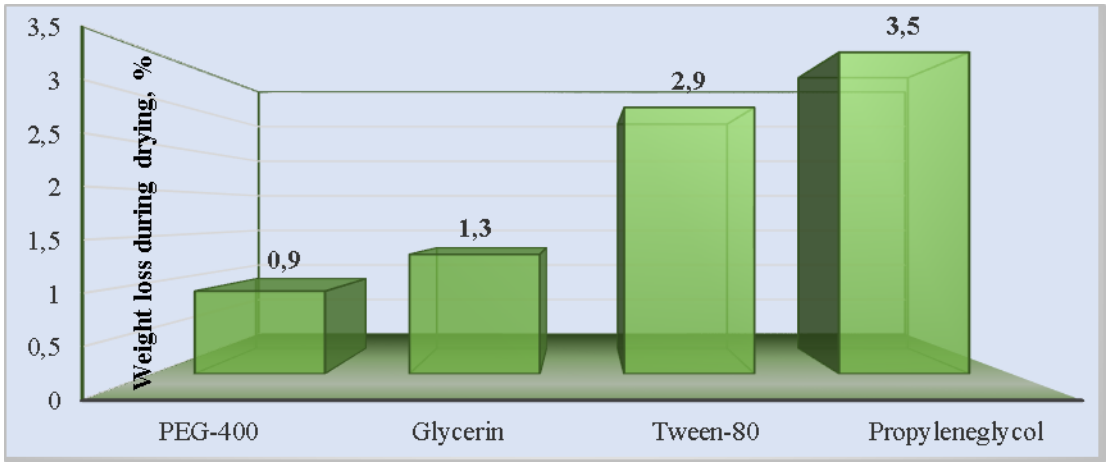

Figure 7. *The effect of plasticizers on weight loss during drying*

tween-80, and the ranked number of advantages is as follows: tween-80 > propylene glycol > PEG- 400 > glycerin.

The influence of factors on the time of complete dissolution (y_4, y_4') of medical sponges illustrated as follows: A > C > res >B (Table 4) (Fig. 5).

A number of advantages of factor A levels are as follows: medical gelatin > HPC > HPMC-50 > MC-15, sponges developed on the basis of medical gelatin retain their framework and do not dissolve within 24 hours, the time of complete dissolution in the simulation solution - 70 hours (approximately 3 days), which is an advantage over other studied polymers.

The ranked series of the influence of the temperature of the water extract from the xenoderm powder (factor C) on the time of dissolution of the sponges is as follows: 40 °C > 20 °C > 30 °C > 50 °C. Among the studied plasticizers (factor B) the ranked number of advantages has the following look: tween-80 > propylene glycol > PEG-400 > glycerin.

Analysis of variance showed that the thickness of the sponges (y_5, y_5') is influenced by all the studied factors: A> res> C> B (Table 4). However, the influ-

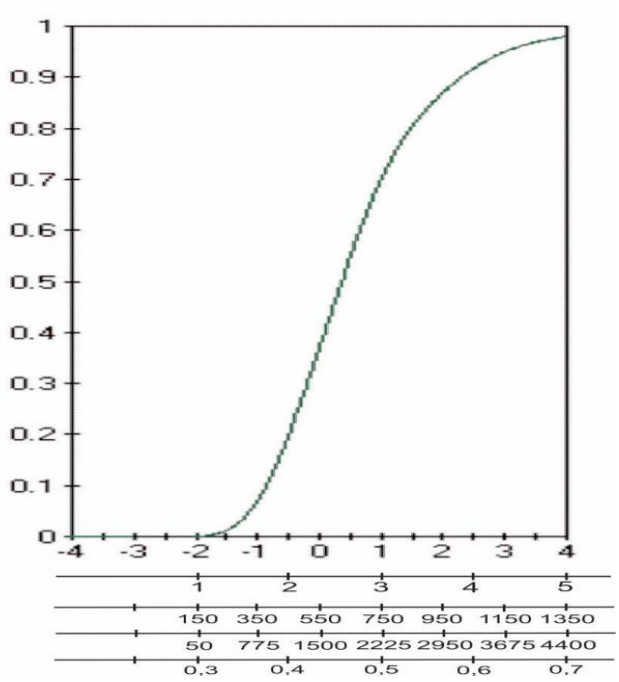

Figure 8. *Desirability function (appearance of sponges (y2), water absorption of sponges (y3), time of complete dissolution of sponges (y4), thickness of sponges (y5))*

ence of factor A (the type of polymer) on the thickness of the sponges is the most significant, the best value of this indicator is provided by HPMC-50 and medical gelatin, when using them the thickness of the sponges is 0.65 and 0.61 cm, respectively. When using MC-15 and HPC, the thickness is 0.51 and 0.36 cm, respectively (Fig. 6).

The effect of the temperature of the water extract from the xenoderm powder (factor C) on the thickness of the sponges can be represented by the following advantages: 40 °C (0.58 cm) > 50 °C (0.52 cm) = 20 °C (0.52 cm) > 30 °C (0.50 cm). The ranked range of effects of plasticizers is as follows: tween-80 (0.56 cm) > propylene glycol (0.54 cm) > PEG-400 (0.53 cm) > glycerin (0.48 cm), and therefore can conclude that the change in temperature and the type of plasticizer have little effect on the thickness of the sponges.

The influence of factors on the percentage of weight loss during drying (y_6, y_6') can be illustrated by the following ranked number of advantages: B > A > res > C (Table 4). Among the studied plasticizers, the lowest values of the studied factor are provided by PEG-400 (0.9 %), which has an advantage over glycerin (1.3 %), tween-80 (2.9 %) and propylene glycol (3.5 %) (Fig. 7).

For polymers, the ranked range is as follows: medical gelatin (0.79 %) > HPMC-50 (1.90 %) > HPC (2.30 %) > MC-15 (3.70 %). The effect of factor C can be illustrated as follows: $c_2 > c_3 > c_4 > c_1$.

The results of the conducted research made it possible to evaluate the influence of auxiliary substances and the temperature at which the aqueous extract of xenoderm is prepared on the pharmaco-technological indicators of the quality of medical sponges. Research data demonstrate a few advantages, which makes it somewhat difficult to choose the optimal excipients for the next stage of research. Therefore, we decided to use a generalized indicator - the desirability function (table 3). At the same time, the primary results of the selected indicators were converted into dimensionless values using the function and the

generalized indicator D was calculated. The results obtained using the desirability function are shown in Table 3 (columns D and D'), the results of variance analysis are shown in Table 4.

Analysis of variance showed that the influence of factors on this indicator is as follows: A > C > B > res. Comparison of the levels of factors A, C and B showed that the best result of the desirability function was obtained when using gelatin as a polymer ($a_1 > a_3 > a_2 > a_4$), propylene glycol as a plasticizer ($b_4 > b_2 > b_1 > b_3$) and 40 °C as the most optimal temperature of the water extract from the xenoderm powder ($c_3 > c_2 > c_1 > c_4$).

Conclusion

Previously developed technology for obtaining water extract from the xenoderm at different temperature regimes and studied its rheological properties and physicochemical composition. Based on the results of the research were selected the optimal excipients and the temperature regime of preparation of water extract for obtaining medical sponges. The selection of optimal pharmaco-technological characteristics for quality control of medical sponges is experimentally confirmed, which is covered in the relevant patent of Ukraine № 139854.

According to the results of conducted studies using the Latin square 4x4 and the generalized indicator of the desirability function (D), the best values of technological indicators were medical sponges based on water extract prepared at 40 °C, medical gelatin and propylene glycol. Accordingly, it is advisable to investigate in more detail the effect of changes in the amounts of excipients on the pharmaco-technological parameters of the developed medical sponges to develop their optimal composition. □

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