RESEARCH OF THE SELECTION OF A GELLING AGENT WITH FURTHER SATURATION OF WIPES WITH ACTIVE PROLONGED EFFECT

Buhai A. V., Semchenko K. V.

National University of Pharmacy, Kharkiv

Introduction

In the treatment of various types of wounds, dosage forms wipes, which are complex heterogeneous dispersed systems, the safety, quality, and effectiveness of which depends on the composition and type of the carrier base, the correct choice and expediency of the introduction of active and auxiliary substances, the effectiveness of preservatives, the dispersed state medicinal substances, storage terms and production conditions, are widely used [1]. Today, the pharmaceutical market is represented by a wide range of gelling agents of natural and synthetic origin. Each of them has its advantages and disadvantages. One of the advantages is bioavailability. When applied to the skin, they form thin films, which in some cases ensure rapid and complete absorption of the active pharmaceutical ingredient (API), on the other hand, they form protective films with a prolonged effect, have a pH close to the pH of human skin and do not have an irritating effect. A wide range of APIs can be introduced into the composition of the formed gels [1, 2]. In the development of wipes with an active prolonged effect, the gelling agent ensures the uniformity of distribution and fixation of the API on the surface of the wipe material, which affects both pharmacological and consumer qualities, which, in turn, is of great importance during the development of a medicinal product.

Aim of the study

The aim of the work is research on the choice of a gelling agent for the development of wipes with an active prolonged effect.

Materials and methods

The design of the study was to achieve several tasks (Fig. 1.).

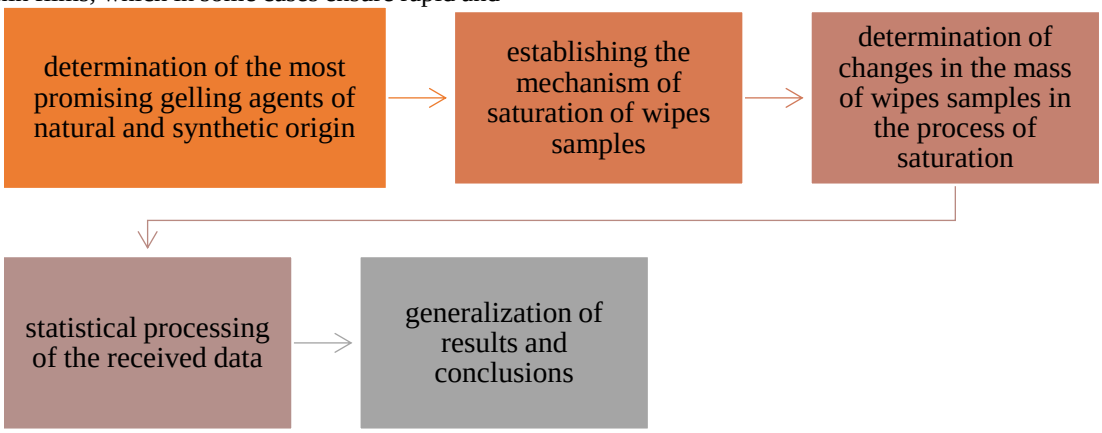

Fig. 1. The design of the study on the selection of gelling agent followed by the saturation of wipes with an active prolonged action

According to the conducted bibliosemantic analysis [3-9] several gelling agents were chosen as the most prospect for the study.

Thus, the objects of study were:

- Apple pectin: gelling agent of natural origin; beige fine powder; DSTU 29186-91 (Yerocolors, best before October 2022);
- Xanthan gum: gelling agent of natural origin; fine powder from white to beige with a characteristic odor; CAS 11138-66-2 (BASF best before March 2023);
- Aristoflex: gelling agent of synthetic origin; white fine powder; CAS 335383-60-3 (Clariant AG, best before December 2022);
- Carbopol: gelling agent of synthetic origin; white, fluffy powder (Corel Pharma Chem, best before February 2023);
- Carbomer 940: gelling agent of synthetic origin; white, fluffy powder; CAS 9003-01-4 (Synthalen M, best before January 2024);
- Non-woven fabric wipes, non-sterile, 4-layer Mesoft® (Mönlycke Health Care AB, Sweden);
- Samples of wipes of different levels of saturation.

For the immobilization and fixation of gels when creating a wipe, the adsorption method, which is the easiest to perform and the most economically beneficial and essentially represents the saturation of the carrier with a saturating solution, was chosen. Based on the biblio-semantic, physico-chemical and technological studies, a laboratory technology of material saturation was developed – a carrier that allows for maximum fixation of gelling agents on a wipe – the first saturation by immersion for 20 minutes, followed by wringing and drying, repeated saturation for 15 and 10 minutes with subsequent wringing and drying at temperature 75±5 ºC. 15 series of wipes samples based on selected gelling agents were investigated. The concentration of each gelling agent was established based on well-known technological recommendations and previously conducted scientific studies: apple pectin – 5.0 %, aristoflex – 0.5 %, xanthan gum – 1.0 %, carbopol – 0.5 %, carbomer 940 – 0,5 %. The mass of the wipe without saturation is 0.17 g. The saturation followed by drying was carried out in 3 stages.

Statistical studies were carried out according to such criteria as sample variance (formula 1, 2), standard deviation (formula 3) and coefficient of variation (formula 4) using a mathematical program Statistica [10].

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$$\bar{X} = \frac{\sum x_i}{n} \quad (1);$$

$$s^2 = \frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1} \quad (2);$$

$$s = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}} \quad (3);$$

$$CV = \frac{\sigma}{\mu} \quad (4);$$

where:
x – variable; n – number of observations; s^2 - sample variance; s – standard deviation; CV - coefficient of variation.

Results and discussion

The results of the study of the change in the mass of wipes during the saturation process are shown in table. 1.

The results of mathematical calculation and statistical processing of the obtained data for each type of gelling agent are given in the tables 2 and 3.

Table 1. Selection of gelling agents for saturating wipes by immersion method

Gelling agent	5 min			10 min		15 min	
	Series	Mass of the wipe after saturation I, g	Mass of the wipe after drying I, g	Mass of the wipe after saturation II, g	Mass of the wipe after drying II, g	Mass of the wipe after saturation III, g	Mass of the wipe after drying III, g
Apple pectin	P-1	2.10	0.86	2.17	1.21	2.36	1.23
	P-2	2.49	1.15	2.62	1.36	2.44	1.42
	P-3	2.51	1.25	2.63	1.32	2.71	1.43
Aristoflex	A-1	1.63	1.33	1.95	1.35	2.24	1.67
	A-2	1.94	1.45	2.05	1.45	2.82	2.09
	A-3	2.60	1.46	2.68	2.12	3.19	2.43
Xanthan gum	XG-1	1.91	1.20	2.46	1.43	1.68	1.25
	XG-2	2.25	1.52	2.55	1.80	2.03	1.26
	XG-3	2.30	1.78	2.61	1.86	2.16	1.30
Carbopol	Cl-1	1.28	1.26	2.19	2.03	3.11	2.57
	Cl-2	1.64	1.31	2.91	2.45	3.83	2.61
	Cl-3	1.67	1.33	2.53	2.02	3.91	2.79
Carbomer 940	Cr-1	1.50	0.94	1.15	1.10	1.67	1.21
	Cr-2	1.70	0.96	2.19	1.22	1.73	1.42
	Cr-3	1.92	0.98	2.38	1.26	2.29	1.57

Listed in the table. 2 and table. 3 results indicate the following:

- Apple pectin: 5 minutes after the start of the experiment, saturation of the wipe with the gel almost does not occur, since subsequent saturations with a probability of 95 % fall into the confidence interval of the five-minute experiment [2,24;2,50]. The average percentage of drying is 52.79 %, which indicates an unsatisfactory result.
- Aristoflex: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.48; 3.02], and the calculated coefficients of variation confirm the correctness of the conducted experiment. The average percentage of drying is 29.75 %, which indicates an unsatisfactory result.
- Xanthan gum: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.45; 2.63], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 35.65 %, which indicates an unsatisfactory result.

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Table 2. Statistical analysis of gelling agents research data ($p \leq 0,05$, n= 5)

Gelling agent	Saturation interval	Mathem. expectation, g	Coef. saturation	Dispersion	Standard deviation	Coef. variation
Apple pectin	Without saturation	0.17	-	-	-	-
	5 min	2.37 ± 0.13	12.92	0.05	0.23	0.10
	10 min	2.47 ± 0.15	13.55	0.07	0.26	0.11
	15 min	2.50 ± 0.11	13.73	0.03	0.18	0.07
Aristoflex	Without saturation	0.17	-	-	-	-
	5 min	2.06 ± 0.28	11.10	0.25	0.50	0.24
	10 min	2.23 ± 0.23	12.10	0.16	0.40	0.18
	15 min	2.75 ± 0.27	15.18	0.23	0.48	0.17
Xanthan gum	Without saturation	0.17	-	-	-	-
	5 min	1.96 ± 0.14	10.51	0.06	0.25	0.13
	10 min	2.15 ± 0.12	11.67	0.05	0.21	0.10
	15 min	2.54 ± 0.05	13.94	0.01	0.08	0.03
Carbopol	Without saturation	0.17	-	-	-	-
	5 min	1.53 ± 0.13	8.00	0.05	0.22	0.14
	10 min	2.54 ± 0.21	13.96	0.13	0.36	0.14
	15 min	3.62 ± 0.25	20.27	0.19	0.44	0.12
Carbomer 940	Without saturation	0.17				
	5 min	1.71 ± 0.12	9.04	0.04	0.21	0.12
	10 min	1.91 ± 0.38	10.22	0.44	0.66	0.35
	15 min	1.90 ± 0.19	10.16	0.12	0.34	0.18

Table 3. Statistical analysis of gelling agents research data after drying ($p \leq 0,05$, n= 5)

Gelling agent	Saturation interval	Mathem. expectation, g	Coef. saturation	Dispersion	Standard deviation	Coef. variation	% Drying up
Apple pectin	Without saturation	0.17	-	-	-	-	-
	5 min	1.09 ± 0.12	5.39	0.04	0.20	0.19	58.27
	10 min	1.30 ± 0.05	6.63	0.01	0.08	0.06	51.09
	15 min	1.36 ± 0.07	7.00	0.01	0.11	0.08	49.00
Aristoflex	Without saturation	0.17	-	-	-	-	-
	5 min	1.41 ± 0.04	7.31	0.01	0.07	0.05	34.10
	10 min	1.64 ± 0.24	8.65	0.18	0.42	0.26	28.53
	15 min	2.06 ± 0.22	11.14	0.14	0.38	0.18	26.61
Xanthan gum	Without saturation	0.17	-	-	-	-	-
	5 min	1.27 ± 0.02	6.47	0.00	0.03	0.02	38.43
	10 min	1.50 ± 0.17	7.82	0.08	0.29	0.19	32.94
	15 min	1.70 ± 0.13	8.98	0.05	0.23	0.14	35.58
Carbopol	Without saturation	0.17	-	-	-	-	-
	5 min	1.30 ± 0.02	6.65	0.00	0.04	0.03	16.91
	10 min	2.17 ± 0.14	11.75	0.06	0.25	0.11	15.87
	15 min	2.66 ± 0.07	14.63	0.01	0.12	0.04	27.85
Carbomer 940	Without saturation	0.17	-	-	-	-	-
	5 min	0.96 ± 0.01	4.65	0.00	0.02	0.02	48.59
	10 min	1.19 ± 0.05	6.02	0.01	0.08	0.07	41.07
	15 min	1.40 ± 0.10	7.24	0.03	0.18	0.13	28.76

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Table 4. Drying of the studied gelling agents, %

Gelling agents	Drying, %			
	5 min	10 min	15 min	Average % of drying
Apple pectin	58.27	51.09	49.00	52.79
Aristoflex	34.10	28.53	26.61	29.75
Xanthan gum	38.43	32.94	35.58	35.65
Carbopol	16.91	15.87	27.85	20.21
Carbomer 940	48.59	41.07	28.76	39.48

Table 5. Coefficient of saturation of gelling agents

Gelling agents	Coefficient of saturation			
	5 min	10 min	15 min	Average coefficient of saturation
Apple pectin	12,92	13,55	13,73	13,40
Aristoflex	11,10	12,10	15,18	12,79
Xanthan gum	10,51	11,67	13,94	12,04
Carbopol	8,00	13,96	20,27	14,08
Carbomer 940	9,04	10,22	10,16	9,80

- Carbopol: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.45; 2.63], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 20.21 %, which indicates a satisfactory result and the advisability of using carbopol to saturate wipes.
- Carbomer 940: the maximum saturation of the wipe material with gel occurs after 10 min, which with a probability of 95 % falls into the confidence interval [1.54; 2.29], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 39.48 %, which indicates an unsatisfactory result.

The interval of saturation of the wipe material with gel based on the studied gelling agents is shown in Fig. 2 a-d. Summarizing the above results of the conducted research, the following results, shown in the table 4, were obtained. In order to establish the permissible deviations of some critical parameters, for which going beyond the established limits can lead to a failure in the technological process or to obtaining products that do not meet the established quality criteria, there was developed a criterion by which the quality of prepared samples of wipes was evaluated – the saturation coefficient. The saturation coefficient (K) per unit mass of the material was calculated using the formula (5):

$$K = \frac{(m_1 - m)}{m}, \qquad (5)$$

where m_1- mass of saturated material samples, g,
m – mass of material samples to saturation, g.

The results of the calculations are given in the table

Conclusions

Gelling agents of natural and synthetic origin were studied and analyzed for the purpose of the further saturating of wipes with API of prolonged action. The data of the experimental study were processed statistically.

The obtained results showed that carbopol has the best technological and organoleptic indicators among the other gelling agents as an effective gelling agent with a low percentage of drying (24.37 %) and a high saturation coefficient (15.81 %). The results of the studies on the average saturation of each of the selected gelling agents are shown in fig. 4.

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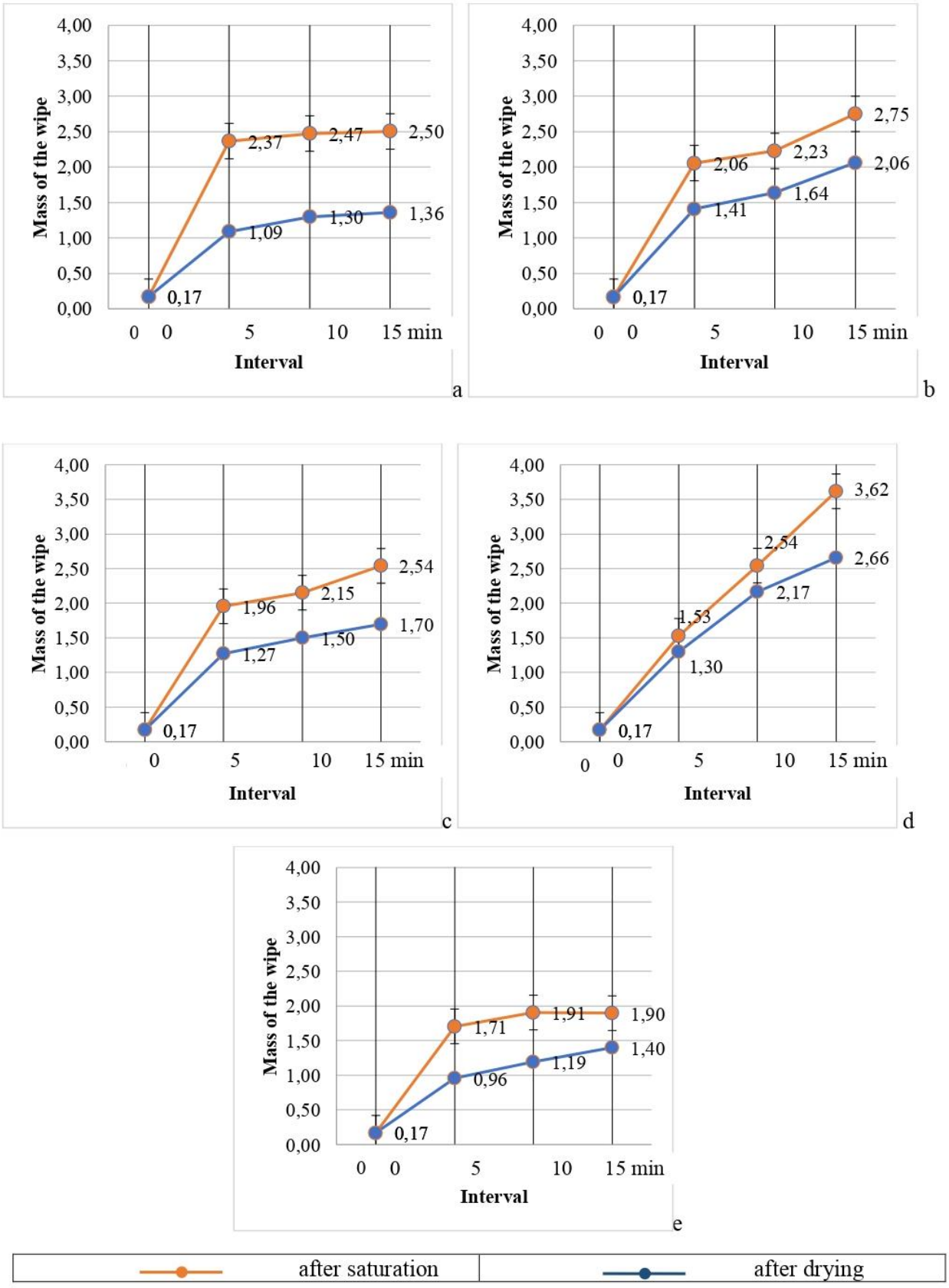

Fig.2. The interval of saturation of the wipe material with a gel based on: a – apple pectin; b - aristoflex; c – xanthan gum; d – carbopol; e - carbomer 940

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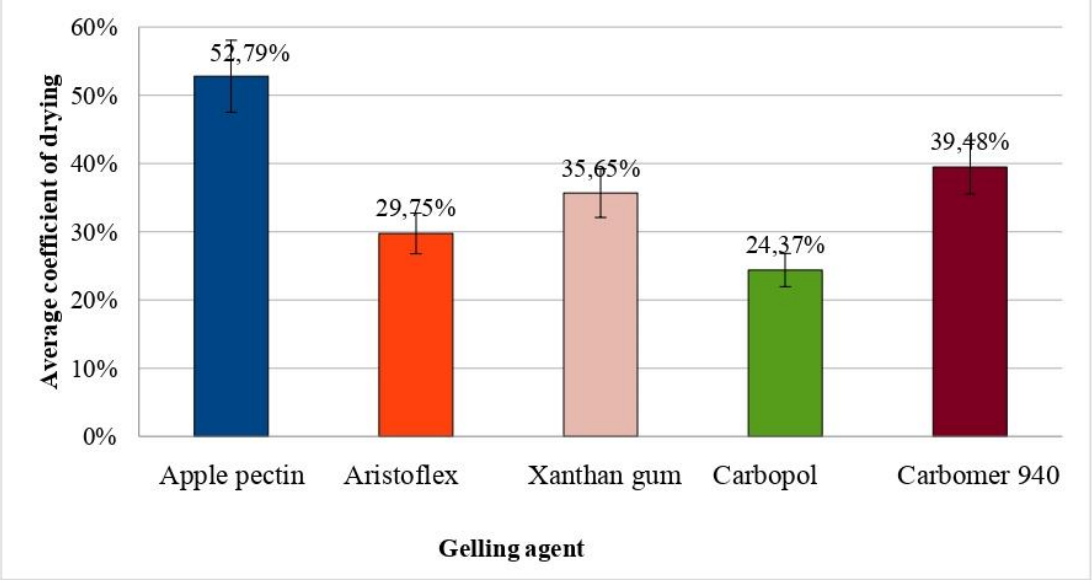

Fig. 3. Drying of the studied gelling agents, %

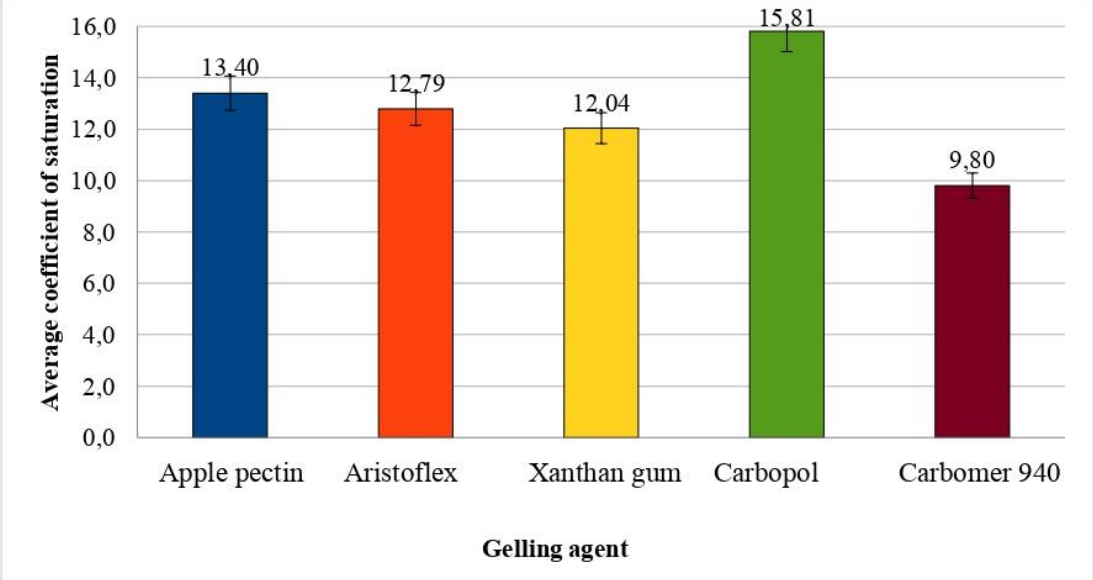

Fig. 4. The average saturation coefficient of the studied gelling agents

Research of the selection of a gelling agent with further saturation of wipes with active prolonged effect

Buhai A. V., Semchenko K. V.

Introduction. During our research of the selection of gelling agents followed by saturation of wipes with an active prolonged effect, many factors should be considered. This fact may influence further drug development. The most important characteristics include the physical and chemical properties of studied gelling agents, the technological characteristics of these gelling agents, the quality of gels they form, their stability and safety, the possibility of choosing a gelling agent with an active pharmaceutical ingredient without any incompatibility. Also, one of the most important characteristics of studied gelling agents is their ability to form stable and homogeneous disperse systems, that should be easy to dissolve and make it possible to create series of gels with various viscosities. **The aim of our work** is to substantiate the selection of gelling agent for further saturation of wipes with an active prolonged effect. **Materials and methods.** As the objects of research were gelling agents, as well as the resulting samples of wipes that were based on them. For a more objective analysis, gelling agents were chosen by natural and synthetic origin. There were researched such gelling agents as apple pectin (natural origin), aristoflex (synthetic origin), xanthan gum (natural origin), carbopol (synthetic origin) and carbomer 940 (synthetic origin). **Results and discussion.** For the immobilization and fixation of gels when creating a wipe, the adsorption method, which is the easiest to perform and the most economically beneficial and essentially represents the saturation of the carrier with a saturating solution, was chosen. Based on the biblio-semantic, physico-chemical

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and technological studies, a laboratory technology of material saturation was developed – a carrier that allows for maximum fixation of gelling agents on a wipe – the first saturation by immersion for 20 minutes, followed by wringing and drying, repeated saturation for 15 and 10 minutes with subsequent wringing and drying at temperature 75±5 ºC. 15 series of wipes samples based on selected gelling agents were investigated. The concentration of each gelling agent was established based on well-known technological recommendations and previously conducted scientific studies: apple pectin – 5.0 %, aristoflex – 0.5 %, xanthan gum – 1.0 %, carbopol – 0.5 %, carbomer 940 – 0,5 %. The mass of the wipe without saturation is 0.17 g. The saturation followed by drying was carried out in 3 stages. The obtained results indicate the following: Apple pectin: 5 minutes after the start of the experiment, saturation of the wipe with the gel almost does not occur, since subsequent saturations with a probability of 95 % fall into the confidence interval of the five-minute experiment [2,24;2,50]. The average percentage of drying is 52.79 %, which indicates an unsatisfactory result. Aristoflex: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.48; 3.02], and the calculated coefficients of variation confirm the correctness of the conducted experiment. The average percentage of drying is 29.75 %, which indicates an unsatisfactory result. Xanthan gum: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.45; 2.63], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 35.65 %, which indicates an unsatisfactory result. Carbopol: the maximum saturation of the wipe material with the gel occurs after 15 minutes, which with a probability of 95 % falls into the confidence interval [2.45; 2.63], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 20.21 %, which indicates a satisfactory result and the advisability of using carbopol to saturate wipes. Carbomer 940: the maximum saturation of the wipe material with gel occurs after 10 min, which with a probability of 95 % falls into the confidence interval [1.54; 2.29], and the calculated coefficients of variation also confirm the correctness of the conducted experiment. The average percentage of drying is 39.48 %, which indicates an unsatisfactory result. , it was found that the best organoleptic and technological characteristics among the presented samples were given by gelling agent of synthetic origin carbopol. It was experimentally found that this gelling agent has a low percentage of drying, as well as a high saturation coefficient compared to other gelling agents, presented in the samples. The additional statistical analysis showed that carbopol had many advantages in comparison with the other gelling agents. **Conclusions.** Based on the results obtained, carbopol is substantiated as the most prospect gelling agent for the further saturation of the wipes with an active prolonged effect. It has been experimentally proven that this gelling agent has all the necessary technological characteristics for the further development of a new drug based on carbopol.

Keywords: apple pectin, aristoflex, xanthan gum, carbopol, carbomer 940, gelling agent, wipe, technology.

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