THE THIRD INTERNATIONAL SCIENTIFIC CONGRESS OF SCIENTISTS OF EUROPE

as part of the III International Scientific Forum of Scientists "East - West"
(Austria - Russia - Kazakhstan - Canada - Ukraine - Czech Republic)

11th January 2019

Vienna, Austria

2019

"The Third International scientific congress of scientists of Europe". Proceedings of the III International Scientific Forum of Scientists "East–West" (January 11, 2019). Premier Publishing s.r.o. Vienna. 2019. 1253 p.

ISBN 978-3-903197-91-6

The recommended citation for this publication is:
Anohin I., Calculation of resource of cross-cutting steel girder elements with initial defects//Proceedings of the 3rd International scientific congress of scientists of Europe. Premier Publishing s.r.o. Vienna. 2019. Pp. 12 – 17.

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Typeset in Berling by Ziegler Buchdruckerei, Linz, Austria.
Printed by Premier Publishing s.r.o., in Vienna, Austria on acid-free paper.

IMPROVING THE EXTEMPORARY SUSPENSION TECHNOLOGY

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For the treatment of dermatological pathologies, physicians actively appoint drugs for both industrial and pharmaceutical production [5, 7]. Preparation of individual drugs - extemporal drugs - provides a more accurate selection of dosage, takes into account the individual characteristics of the body. After all, for each patient it is necessary to choose the dose according to age, the presence of allergies to certain components, taking into account the intake of other drugs [1].

Among extemporal drugs, ointments, powders and suspensions that contain active pharmaceutical ingredients from the group of corticosteroids, antibiotics, sulphonamides, antimicrobial drugs, and the like are most commonly prescribed[2, 3, 4]. Recently, research on the development of extemporal suspensions to expand the range of dermatological drugs is one of the leading areas of scientific research in

pharmacy [1, 8, 10].

Therefore, in our work the main goal was to conduct research on the improvement of technology and the study of the stability of the suspension of extemporal preparation [10. 11].

In pharmacies, we collected and analyzed 298 prescription prescriptions, isolated liquid dosage forms, among them were isolated suspensions for external use. For further work, 28 prescriptions of suspensions intended for the treatment of dermatological diseases were selected.

The analysis of the component composition showed that the selected dermatological supplements contain from 8 to 14 components. Most of the prescriptions require careful processing of the technology and the study of stability to determine the shelf life of drugs in order to prepare them as intra-pharmacy billets [10, 12].

Analysis of the component composition of suspensions showed that almost all prescriptions contain sulfur precipitated: it occurs in 21 of the 28 samples analyzed. 17 prescriptions contain either zinc oxide or talc or starch, or two-three of the components in various combinations and ratios. In addition, 16 prescriptions contain acid boricum, 12 - acid salicylicum in small quantities [6, 7]. The percentage of these components is shown in Fig. 1.

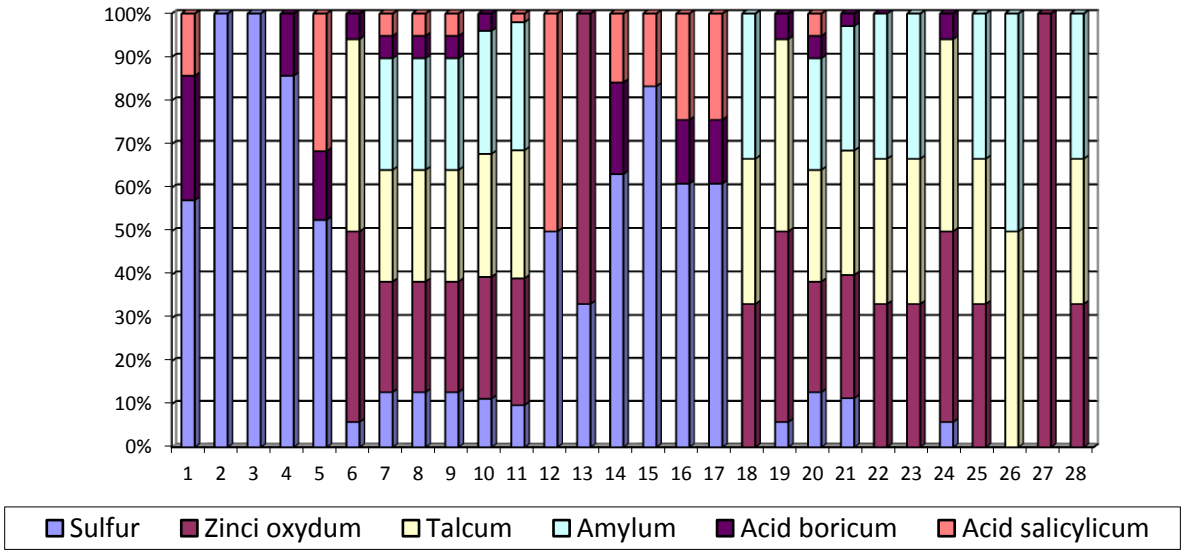


Fig. 1. The ratio of the main components in the dermatological suspensions of extemporal production

More than half of the prescriptions contain antibacterial agents of the J01 group according to ATC classification: levomitsetin - 7, erythromycin - 4, kanamycin - 1, cefazolin - 2, and also derivatives of imidazole (ornidazole, metronidazole, trichopolol), 6 prescriptions containing sulfanilamides (streptocide, biseptol, nursulfazol) One prescription contains corticosteroids (dexamethasone), 3 antihistamines (dimedrol), 3 antimicrobials (resorcinol), 7 prescriptions contained separately or in combination of menthol, thymol, 4 prescriptions containing ichthyol or tar [9].

The analyzed suspensions contain 2 to 4 solvents in various combinations. Ethyl alcohol is prescribed more often in a concentration of 70%, but there are prescriptions and 96% alcohol, or a mixture of alcohol with water in a ratio of 1: 1 or 1: 2. In addition, in the form of prescriptions often contain other solvents: glycerol, camphor alcohol, medical aether, dimethoxide, chloroform.

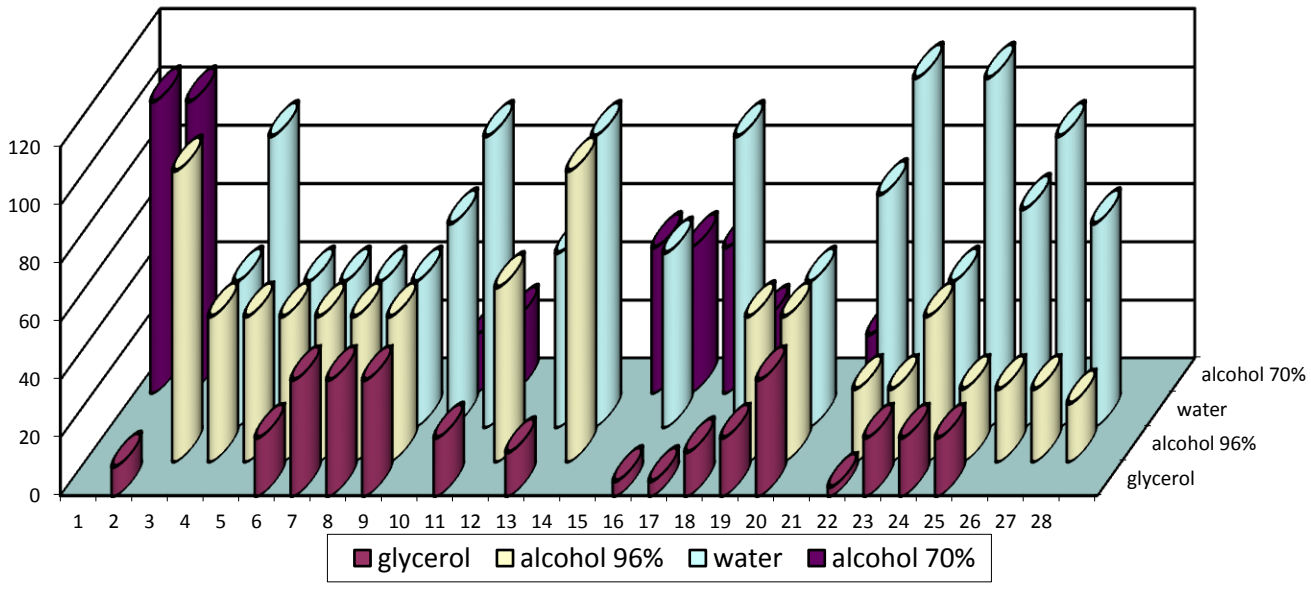


Fig. 2. The ratio of the main solvents in the composition of the extemporal suspensions

Non-polar solvents allow the introduction of a hydrophobic substance into a suspension in a dissolved form, so when developing the optimum suspension

technology, we can test the technology with replacing part of the water with ethyl alcohol.

To conduct research, we selected a suspension containing me-nitol, anestezin, talc, zinc oxide, starch. As water soluble solvents and glycerin. In one of the production pharmacies, the slurry is planned to be prepared as an intra-pharmacy blank.

This record contains substances with different physico-chemical properties: they have different solubility and different surface properties. Therefore, the preparation of this suspension causes some difficulties [11, 12, 13]. To overcome them, we conducted a series of technological studies to optimize technology.

Before starting work it is necessary to theoretically substantiate the optimum technology of medicine [10]. In the composition of this suspension two substances with a sharply hydrophobic surface of particles - menthol and anes-tezin - are added. These components are dispensed in small quantities - 1 g and 2 g are answered. Analyzing their properties, it should be pointed out that menthol is a heavy detergent, so it needs to be crushed with the addition of 10 drops of alcohol per 1 gram of powder to achieve a proper degree of grinding. After all, in suspensions, the degree of grinding is one of the important indicators of the quality of the prepared preparation.

At the first stage of our technological research, we prepared a suspension according to the general rules without a stabilizer.

Technology 1. In a mortar, 1 g of menthol was ground with 10 drops of alcohol (as hardly crushed with a sharply expressed hydrophobic properties of the substance), triturated until the alcohol evaporated and the powder dried. To menthol, anesthetic 2 g was added, carefully ground and mixed with menthol. Then 10 g of zinc, 10 g of starch and 10 g of starch were added alternately. 15 g of glycerin was added to the powder mixture according to the rule of Deryagin (its amount is just half the mass of dry matter) and carefully dispersed for better degradation of the substances, and then gradually began add water The mixture was homogeneous in a mortar and the prepared suspension was transferred to a

vial for clear glass. Clogged with a polymer stopper and a screw cap.

Observations recorded by us in the process of this technology showed the following: the distribution of hydrophobic substances occurred unevenly. Therefore, we have analyzed the literature data on the possibility of using in the second variant of technology such technological reception as the previous formation of eutectic alloy between hydrophobic substances. For a more rapid eutectic formation, we used a pre-heated mortar to prepare a suspension, since it is known that the temperature, time and intensity of the mixing of components are significantly influenced by the rate of formation of eutectics.

Technology 2. In a heated mat, the menthol 1 g was rinsed and anesthezin 2 g rubbed, while eutectic was formed. To it gradually added zinc oxide, starch and talc 10 g. Then, according to the rule of Deryagin, the mixture was triturated with glycerol, after which the water was added gradually, mixed. The finished slurry was transferred to the vial for delivery.

In this variant of the technology, it was difficult to achieve the uniform distribution of the ecthetic mixture of powders - the receipt of the loose powder was quite long. In addition, when adding glycerin, a brewed mixture was obtained, which can be explained by the hydrophobicity of the eutectic and, as a result, the poor wettability of the mixture of powders with hydrophilic solvents (glycerol and water).

At the second stage of technological studies, we were proposed to hydrolyze hydrophobic substances with surface-active stabilizers. As such, pharmacies usually use tween-80 or 5% aqueous solution of methylsululose. We have prepared a suspension on the following technology.

Technology 3. In a mortar, 1.0 g of menthol was ground with 10 drops of alcohol, triturated and left to dry, anesthetic 2.5 g was added, triturated and 11 drops of tween-80 added. Then zinc oxide was added 10.0 g, starch 10.0 g, thalium 10.0. At the same time a lumpy mass was formed. Then, according to the rule, Deryagin was triturated with 15.0 g of glycerin, then gradually added water, dispersed. The finished slurry was transferred to the vial for delivery.

The prepared slurry was evaluated for organoleptic parameters and sedimentation stability. The appearance of the resulting suspension had a non-transparent superimposed layer, therefore, it was impossible to estimate the precipitation rate of the dispersed phase in the first 15 minutes. Measuring the height of the siege after 15 minutes showed less sedimentation stability of the suspension than the first sample.

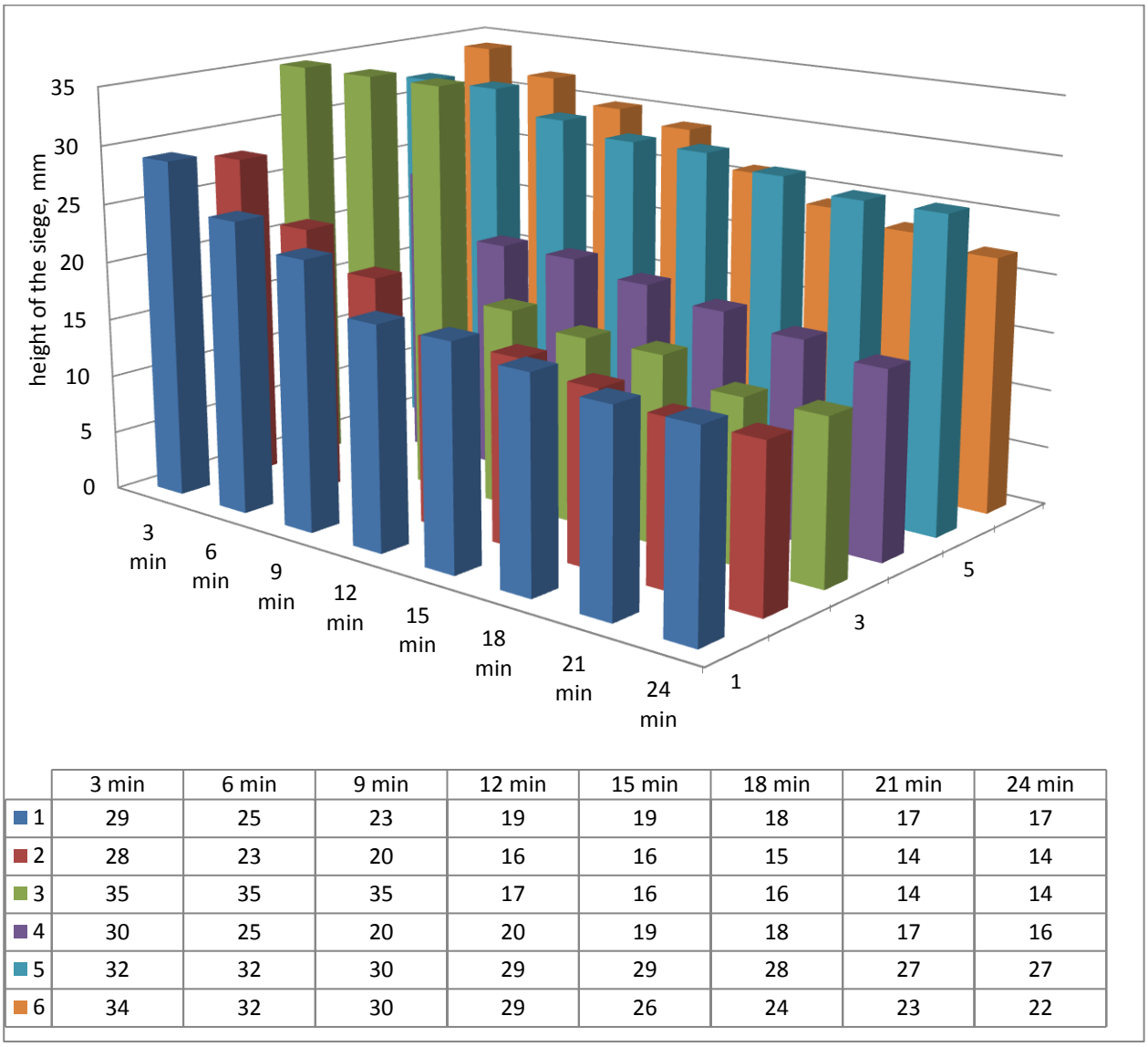
Next, we were asked to replace half the water with 70% ethyl alcohol. Given the presence of a nonpolar solvent in propylene, the technology of suspension is changing: menthol and anestezin can be dissolved in 70% of alcohol.

Technology 4. In a vial, 2 g of anesthetic and 1 g of menthol were weighed, 75 ml of 70% ethyl alcohol were weighed, closed and shaken to dissolve. 10 g zinc oxide was ground in the mortar, 10 g of starch, 10 g of talcum and mixed to homogeneity. Under the rule of Deryagin, glycerol was added, dispersed and added 77 ml of water. Lastly, in the mortar, alcohol was added to the 70% ethyl alcohol of 75 ml, mixed. The finished slurry was transferred to the vial for delivery.

During the dispersion of drugs with glycerin, the formation of a thick, loose mass, which did not provide qualitative finely divided substances according to the Deryagin rule, was observed. In order to ensure qualitative sub-milling, we propose to pre-mix the viscous glycerin with purified water to produce a more fluid liquid, which will be used to disperse under the rule of Deryagin (technology 5).

Technology 5. In a vial, 2 g of anesthetic and 1 g of menthol were weighed, 75 ml of 70% ethyl alcohol was weighed, closed and shaken to dissolution of the regrowne. 10 g zinc oxide was ground in the mortar, 10 g of starch, 10 g of talc were added and mixed to homogeneity. 15 g of glycerin was weighed into the stand and 77 ml of water was measured. The obtained mixture, according to the rule of Deryagin, was added to a mortar (15 ml), dispersed. Lastly, alcohol was added to the mortar. The finished slurry was transferred to the vial for delivery.

For prepared samples No. 4 and No. 5, studies of sedimentation stability were also conducted. The conducted studies showed greater stability of sample number 5.



	3 min	6 min	9 min	12 min	15 min	18 min	21 min	24 min
1	29	25	23	19	19	18	17	17
2	28	23	20	16	16	15	14	14
3	35	35	35	17	16	16	14	14
4	30	25	20	20	19	18	17	16
5	32	32	30	29	29	28	27	27
6	34	32	30	29	26	24	23	22

Fig. 3. Results of study of sedimentation stability of suspensions prepared by different technologies

To investigate the stability of the suspension, we have investigated the sedimentation stability of the model samples immediately after preparation and in the process of storage. The studies were carried out one day, 5 days and 30 days.

In the process of storage for the second day in the sample number 2 crystalline droplets appeared on the surface of the siege. This can be explained by the

crystallization of menthol from eutectic in an aqueous medium. Therefore, further studies of this sample were discontinued.

The obtained data on the sedimentation stability of the prepared model samples of the extemporal suspension showed that the most stable in the first minutes (up to 9 minutes) is a suspension prepared using the emulator. But after 12 minutes the deposition is intense. This can be explained by the impossibility of visual fixation of deposition in the first minutes due to the fact that the hydrophilized particles of anesthesin and menthol longer hold in curvature compared to unstable in specimens Nos. 1 and 2.

The obtained data showed that during storage, the sedimentation stability of the suspensions is reduced. Mostly it decreases in specimens Nos. 1 and 2. This is explained by various technological techniques that were used in the preparation of suspensions and the introduction of auxiliary substances - a stabilizer (sample 3) and nonpolar liquid - ethyl alcohol (samples 4 and 5).

Conclusions. To systematize and analyze the modern extemporal formulation of suspensions. The research on the improvement of the technology of extemporal suspension has been carried out. The optimum technology, which provides the stability of the preparation during the month of storage, is developed.

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