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M. Yu. Dronik[1], I. Jonuškienė[2], M. V. Stasevych[1]
[1] Lviv Polytechnic National University,
Department of Technology of Biologically Active Substances, Pharmacy and Biotechnology,
[2] Kaunas University of Technology, Kaunas, Lithuania
maryna.v.stasevych@lpnu.ua

DEVELOPMENT OF THE BASICS OF SPRAY TECHNOLOGY FOR EXTERNAL APPLICATION

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The basics of the technology for the preparation of a spray formulation for external use with analgesic and anti-inflammatory effects was developed. The quantitative content of active pharmaceutical ingredients and excipients was proposed. Comparative analysis of some indicators of the obtained spray with analogues on the pharmaceutical market of Ukraine was carried out. Material calculations allowed to estimate the amount of active pharmaceutical ingredients and excipients for the preparation of the spray and its packaging in bottles with a dropper in the laboratory. Based on the material calculations, a basic technological scheme for the production of the finished product was proposed. Economic calculations have been carried out, which demonstrate a high level of economic profitability of the development of such a preparation.

Key words: joint or muscle pain; spray for external use; active pharmaceutical ingredients; excipients; principle technological scheme.

Introduction

Nowadays, the life of an ordinary person has a very fast pace: constant mechanical work, various kinds of physical activities, the desire to do as much as possible in a short period of time. And the faster the pace of a person's life, the more often he or she encounters various pain syndromes of different nature.

Pain syndrome is a pathological condition accompanied by the appearance of pain in various parts of the body. It is a psychophysiological condition that occurs as a result of various stimuli: from mechanical shocks and thermal effects to a number of diseases of the human internal organs. It is the pain that informs about the development of the disease [1, 2].

According to recent studies, almost 70 % of Ukrainian doctors see patients with complaints of pain in various parts of the body every day [3]. As already mentioned, severe pain syndrome occurs as a result of various mechanical injuries and diseases and can be triggered by various factors: unsuccessful surgery, circulatory system disorders, excessive exposure to temperature, limb fractures, sprains, pathologies of internal organs, etc. Even a person's intense emotional state can cause pain.

According to the World Health Organization, 90 % of all diseases are associated with pain. Most often, pain affects the human musculoskeletal system. According to statistics, half of all pain syndromes are related to the musculoskeletal system, and approximately 2 billion people in the world suffer from pain and diseases of the musculoskeletal system [4]. The World Pain Federation estimates that musculoskeletal pain syndromes cause 21 % of all disability worldwide. This means that billions of people around the world are limited in their physical activity because of pain. Studies in the United States show that the cost of treating musculoskeletal pain is approximately $ 600 billion dollars per year, representing a significant economic impact on society.

The most common disorders and diseases of the musculoskeletal system are characterized by pain, including constant pain, which, if treated negligently, can lead to complete disability. Therefore, in order to avoid such consequences, constant pain that haunts a person and interferes with daily activities forces

them to see a doctor. After such a visit, the patient is given an extensive list of medications to treat and relieve the pain. The complexity and multifactorial nature of modern pain syndrome explains the fact that it is not always possible to eliminate it with just one drug, so in practice, a comprehensive approach is used [5].

Therapy includes the use of various non-steroidal anti-inflammatory drugs (NSAIDs) or analgesics, as well as local anesthetics. NSAIDs are one of the most popular drugs on the Ukrainian pharmaceutical market, widely used to relieve both acute and chronic pain. Drugs from the M01A group of Nonsteroidal anti-inflammatory and anti-rheumatic drugs are the leaders in pharmacy sales in terms of sales in monetary terms [6]. Today, there are many drugs in this group on the market, and the top five brands in terms of sales of drugs in this group in monetary terms in the first five months of 2023 are Nimesil, Nurofen, Fanigan, Affida, and Dexalgin. According to recent studies, the sales share of group M01 “Anti-inflammatory and antirheumatic drugs” reaches 8 %, and the sales share of group N02 “Analgesics” reaches 7 %, which is the 1st and 2nd place in terms of sales of the entire pharmaceutical market of Ukraine [7].

Paracetamol (acetaminophen) has gained widespread popularity. The combination of efficacy, safety and relatively low price has allowed it to gain popularity among doctors around the world. The main advantage of paracetamol is that it can be prescribed to patients with peptic ulcers, bronchial asthma, hemophilia, in the postoperative period, etc. However, compared to other NSAIDs, paracetamol has a less pronounced anti-inflammatory effect and almost no analgesic effect. At the same time, diclofenac has both a pronounced anti-inflammatory effect and good analgesic effect. Discovered in the early 70s of the XX century, diclofenac is considered the “gold standard” among NSAIDs in terms of the ratio of clinical efficacy and the frequency of adverse reactions. It still remains the most popular drug among NSAIDs and is the best-selling drug among all drugs [8].

Today, the Ukrainian pharmaceutical market offers a wide range of analgesic-antipyretics and NSAIDs, both alone and in combination with other drugs. As for combinations, adding active pharmaceutical ingredients (APIs) to each other can increase the efficacy and safety of such drugs. This idea is not new and has been used by drug manufacturers for decades. Such drugs are available in a variety of dosage forms (DF). The most common are tablets for oral use, solutions for injection, as well as topical dosage forms: ointments, liniments, gels, patches, etc. Today, there are a number of pharmaceutical aerosol compositions that are used for the topical treatment of pain syndromes and inflammatory processes by spraying them onto the surface of the human skin. This method of administering the active substances of medicinal products increases their bioavailability and accelerates the onset of the therapeutic effect. However, it should be noted that the speed of action depends on the rate of penetration of the active ingredients, i.e., when developing such medicines, it is necessary to select a range of excipients that would synergize with the API of the product.

Despite the wide range of therapeutic agents and treatments available, many patients with complex musculoskeletal pain syndromes do not receive adequate relief of their symptoms. Therefore, there is an opportunity to develop new drugs based on a combination of known compounds that could provide a rapid analgesic effect followed by an anti-inflammatory effect. Given the diversity of known drugs, the method of administering active ingredients in the form of a spray solution for external use increases the bioavailability of the active ingredients and accelerates the onset of the therapeutic effect. Ease of use for the consumer is another important factor in the selection of a spray form, and in some cases price is also a deciding factor in the selection of a drug.

According to the market research conducted in the Ukrainian pharmaceutical market, the most widely used NSAID is Diclofenac, represented by 93 trademarks in such medicinal products as gel, tablets for oral use, suppositories, solutions for injection, capsules, patches, eye drops, sprays [9]. It was also found that Diclofenac in combinations is limitedly represented on the market by 15 trade names, mostly of foreign origin [9]. Previous studies of the pharmaceutical market of topically applied medicinal products for joint and muscle pain in a previous review [10] showed that sprays as a dosage form are limited (4.26 %) on the Ukrainian market.

The aim of this study was to develop the basics of the technology for obtaining an inexpensive topical drug based on known APIs that will have anti-inflammatory and analgesic effects for use in the treatment of pain syndromes of musculoskeletal diseases.

Materials and research methods

The active pharmaceutical ingredients for the spray: procaine hydrochloride (novocaine hydrochloride), benzocaine (anesthetic), racemic menthol (purity > 99 %) were purchased from Istok-Plus, Ltd. Diclofenac sodium (purity 99.5 %) was purchased from Amoli Organics Pvt. Ltd. Ltd. in India. Anhydrous ethanol (96 %) and purified water were used as solvents. Dimethyl sulfoxide (DMSO) pharmaceutical (99.9 %), Covalent LLC, Ukraine, was used as an excipient.

The information resources of the State Register of Medicinal Products of Ukraine were used for the analysis of drugs in spray form [11]. Price information was obtained from Tabletki.ua [12]. Material calculations were performed according to the calculation methodology given in [13]. Economic calculations were performed according to [14].

Results and discussion

At the first stage of our work, we conducted a comparative characterization of sprays with anti-inflammatory and analgesic effects in terms of composition, price and volume of drugs available on the Ukrainian pharmaceutical market. At present, topical sprays with anti-inflammatory and analgesic effects are represented by three names: "Argette Spray", "Diclofenac-Zdorovye Ultra", and "Menovazan Flexspray" [11, 12].

Table 1

Comparative characteristics of sprays with anti-inflammatory and analgesic effects in the pharmaceutical market of Ukraine

Drug (manufacturer)	API	Excipients	Price per package, UAH	Volume of primary packaging, ml
Argette Spray (Pharbil Waltrop GmbH, Germany) [12, 15]	diclofenac sodium	isopropyl alcohol, ascorbyl palmitate, propylene glycol, purified water, peppermint oil, sodium dihydrogen phosphate, sodium dihydrate, sodium hydrogen phosphate, sodium dodecahydrate, trilon B, lecithin, anhydrous ethanol	164.8 - 250.99	25
Diclofenac-Zdorovye Ultra (Pharmaceutical Company "Zdorovye" LLC) [12, 15]	diclofenac sodium	96 % ethyl alcohol, propylene glycol, glycerin, methylparaben, propylparaben, methylpyrrolidinone, castor oil, peppermint oil, disodium edetate, sodium hydrogen phosphate, sodium dihydrogen phosphate, purified water	88.42 - 100.1	50
Menovazan Flexspray (DKP Pharmaceutical Factory, LLC) [12, 15]	benzocaine (anesthetic), procaine hydrochloride (novocaine), menthol	70 % ethyl alcohol	87.50 - 159.70	50

Table 1 shows that the cost of domestically produced topical sprays is half that of a foreign representative with a smaller package volume. It is also worth noting that the package inserts for "Argette Spray" and "Diclofenac-Zdorovye Ultra" indicate that the approximate time for drying and the onset of the drug's effect is 3–5 minutes. However, several experimental tests carried out by us showed that the time indicated by the manufacturer was not experimentally confirmed, but was much longer (more than 10–15 minutes), which is a limiting factor for the consumer when it comes to quick use.

In addition, the stickiness and slow absorption of the solution at the site of application of these topical sprays remained. In contrast, the drying time of "Menovazan Flexspray" was on average up to 2 minutes and the local anesthetic effect was rapid.

At the second stage of our work, we proposed the optimal composition of a spray for topical use with anti-inflammatory and analgesic effects.

The active substances for the development of the spray can be different in chemical nature and properties of APIs that have the necessary therapeutic effect when applied to the skin, mucous membrane or other parts of the human body. Preference is given to APIs that do not lose their therapeutic effect when applied topically. The final product should be a spray comprising APIs selected from the list of non-steroidal anti-inflammatory drugs (NSAIDs) or local anesthetics, a solvent and excipients. In this case, the composition should contain at least one excipient that improves the penetration of the active pharmaceutical ingredient and accelerates the absorption of the API.

In the vast majority of cases, the active ingredient of our spray analogs is a non-steroidal anti-inflammatory drug selected from the group that includes diclofenac, ibuprofen, nimesulide, indomethacin, ketoprofen, methyl salicylate, piroxicam, naproxen, phenylbutazone, etc. Among these APIs, we chose diclofenac, which has a number of advantages. It has anti-inflammatory, analgesic and antipyretic effects due to inhibition of prostaglandin synthesis and thus reduces all manifestations of inflammation (pain, edema, local hyperthermia). Prostaglandins play an important role in the genesis of inflammation, pain and fever. In rheumatic diseases, anti-inflammatory and analgesic properties of diclofenac provide a therapeutic effect characterized by a significant reduction in the severity of such manifestations of the disease as pain at rest and during movement, as well as improvement of the functional state. In post-traumatic and postoperative inflammatory reactions, diclofenac quickly and effectively relieves pain, reduces inflammatory edema and swelling of the postoperative wound [16, 17]. According to the ATC classification, it is included in the drugs affecting the musculoskeletal system, namely under the code M01A B05. Diclofenac is a NSAID chosen by doctors of various specialties for short-term use. Today, it is used in surgery, traumatology, sports medicine, neurology, gynecology, urology, oncology, ophthalmology, etc. Diclofenac or its salt in the amount of 1–10 % (by weight) is mainly used in liquid dosage forms. The preferred salt of diclofenac is its sodium salt.

To enhance the local anesthetic and analgesic effect, it was decided to add other active ingredients to the spray. Since "Menovazine", a well-known, effective and inexpensive topical anesthetic, is widely used among local anesthetics, its APIs are a good complement to diclofenac. The solvents used for the components of the medicinal product are 96 % anhydrous ethanol and purified water with a final concentration of 70 % ethyl alcohol. As an excipient that improves the penetration of APIs through the skin, we choose a substance from the group including dimethyl sulfoxide, *N*-methylpyrrolidone, 1-methylpyrrolidone, 2-methylpyrrolidone, etc. We chose dimethyl sulfoxide, which has a wide range of pharmacological activities, including membrane penetration, anti-inflammatory effects, local analgesia, and is used as a carrier for active substances [15].

The choice of the concentration of active ingredients for the spray was based on the following. In finished medicinal products, the concentration of diclofenac sodium salt is in the range of 1–10 % (by weight), depending on the dosage form. For example, in gels and other soft dosage forms, the concentration of diclofenac sodium salt is 5 % by weight, and in solutions for injection – 2.5 %. In foreign patents for medicinal products in the form of a spray containing diclofenac, the recommended content of diclofenac sodium salt is 4 % [18, 19]. As for menthol, novocaine and benzocaine, their quantitative composition corresponds to the drug "Menovazine", i.e., 2.5 % of menthol, as well as 1 % of novocaine and benzocaine.

The optimal concentration of DMSO has been determined as follows. Patents for finished drugs containing DMSO recommend a concentration of 0.5 to 12 % (w/w) [15]. To determine the DMSO content required for the preparation of the spray, four 10 ml solutions of DMSO in 70 % ethanol were prepared with corresponding concentrations of 10, 9, 8 and 5 %. The main selection indicator was the drying time after application of the solution of the corresponding concentration to the skin (Table 2).

Table 2

Comparative analysis of the concentration of DMSO alcohol solution by drying time

No. of the sample of the test solution	DMSO solution concentration / drying time			
	10 %	9 %	8 %	5 %
Sample No. 1	5 min 34 sec	4 min 7 sec	3 min 37 sec	1 min 29 sec
Sample No. 2	5 min 49 sec	4 min 38 sec	3 min 42 sec	1 min 44 sec
Sample No. 3	4 min 37 sec	4 min 52 sec	3 min 55 sec	1 min 37 sec
Average value	5 min 20 sec	4 min 32 sec	3 min 45 sec	1 min 37 sec

It is noteworthy that no film remained on the skin after application of a 5 % solution, whereas other concentrations did not give such results. The 10 % DMSO solution left the most noticeable film, which dried completely after some time. As a result, we have chosen to use a 10 % concentration of DMSO for the preparation of the spray.

In the third stage of the work, the spray was produced on the basis of the experimental data of the previous stage and based on the literature [15, 18, 19]. The following three stages were chosen for its production: preparation of the solution, $\eta_1 = 1$; filtering the solution, $\eta_2 = 0.99$; packaging, and labeling packaging, $\eta_3 = 1$. The total yield is $\eta_{total} = 0.99$. For each stage, material calculations of raw material consumption were performed in the laboratory to obtain 50 40 ml spray bottles. As a result, a solution for external use in the form of a spray in vials was obtained from the last stage "Packing, labeling and packaging" (Table 3). The drying time of the resulting spray was on average 5 min 35 s, which is significantly less compared to "Argette Spray" and "Diclofenac-Zdorovye Ultra".

Table 3

Consumption of raw and auxiliary materials and supplies for the production of the final spray

Spent:			Received:		
Name of raw materials and intermediate products	Amount		Name of the final product and waste	Amount	
	kg	pcs.		kg	pcs.
Raw materials			Product in its original packaging		
Solution of active substances (diclofenac sodium – 4 %, menthol - 2.5 %, novocaine – 1 %, benzocaine – 1 %, dimethyl sulfoxide – 11 %, anhydrous ethanol – 53.5 %, purified water – 27 %)	1.9912		Final spray	1.9514	49
Plastic bottle 40 ml		50	Waste:	–	–
Spray nozzle		50	Losses:	0.0398	1
Self-adhesive label		50			
Carton box		50			
Total:	1.9912		Total:	1.9912	50

Therefore, the principal technological scheme for the production of a spray for external use is presented in Fig. 1. It includes the implementation of the following three technological stages: solution production, solution filtration and packaging, labeling and packaging (Fig. 1).

Anhydrous ethanol is fed from the storage tank ST-1 through the measuring tank MT-1 with

compressed nitrogen to the reactor R-1, which is equipped with an anchor stirrer. Then purified water is fed into the reactor through a flow meter. The sodium salt of diclofenac, menthol, novocaine, and benzocaine are manually added through a manhole and mixed until a homogeneous, clear solution is formed. Dimethyl sulfoxide is then added from storage tank ST-2 through the measuring tank M-2 and stirred until the solution is homogeneous. The ready reaction mass from the reactor R-1 is pressed by compressed nitrogen onto the print filter F-1. The filter precipitate is transferred for recycling, and the filtrate is collected into the collector Col-1 and transferred for packing in bottles.

The production of a spray for external use with anti-inflammatory and analgesic effect includes three stages, as well as auxiliary works: sanitary preparation of production (AW1) and preparation of raw materials and materials (AW2) (Fig. 2).

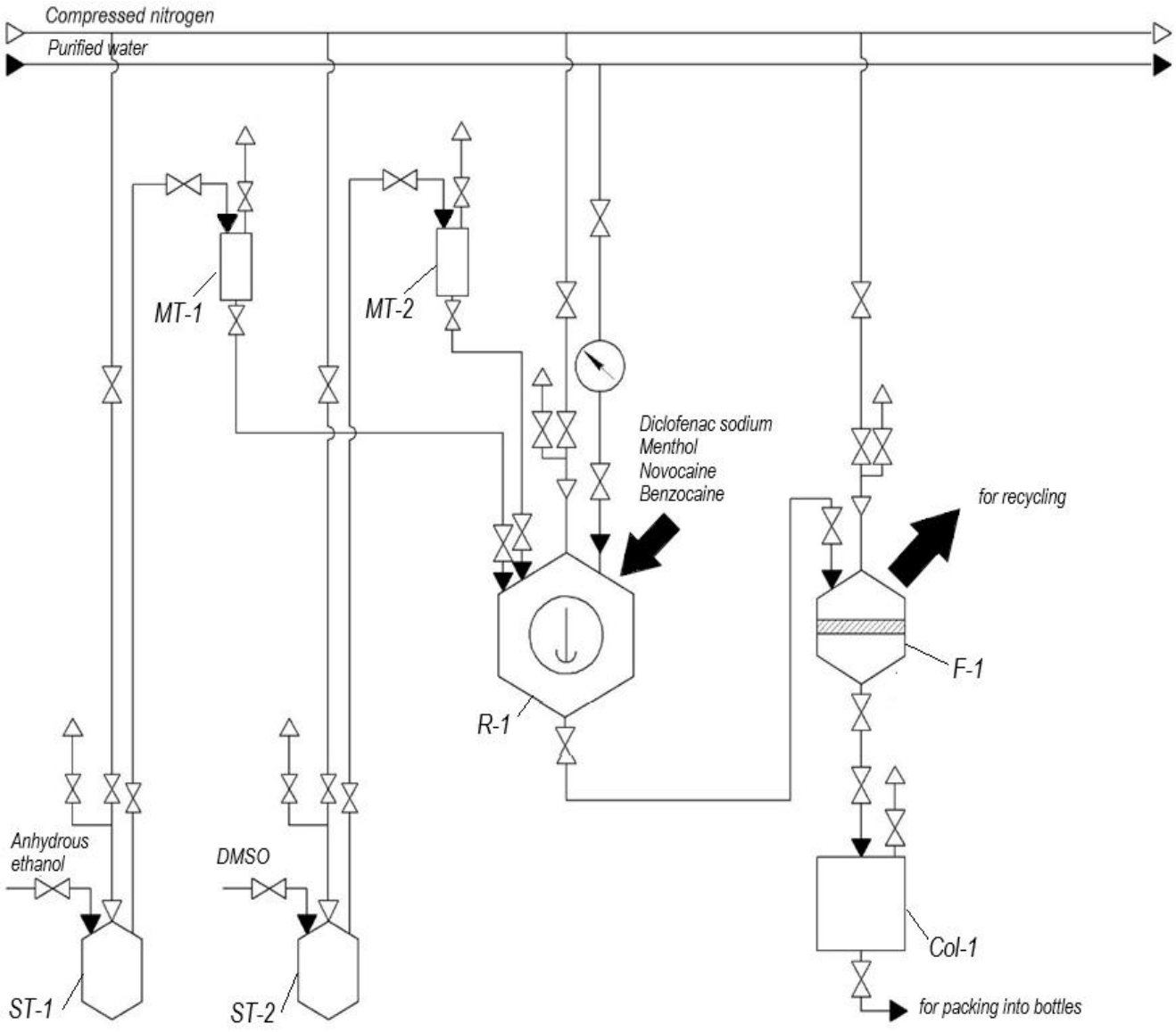

Fig. 1. A principal technological scheme for the production of a solution for spray packaging

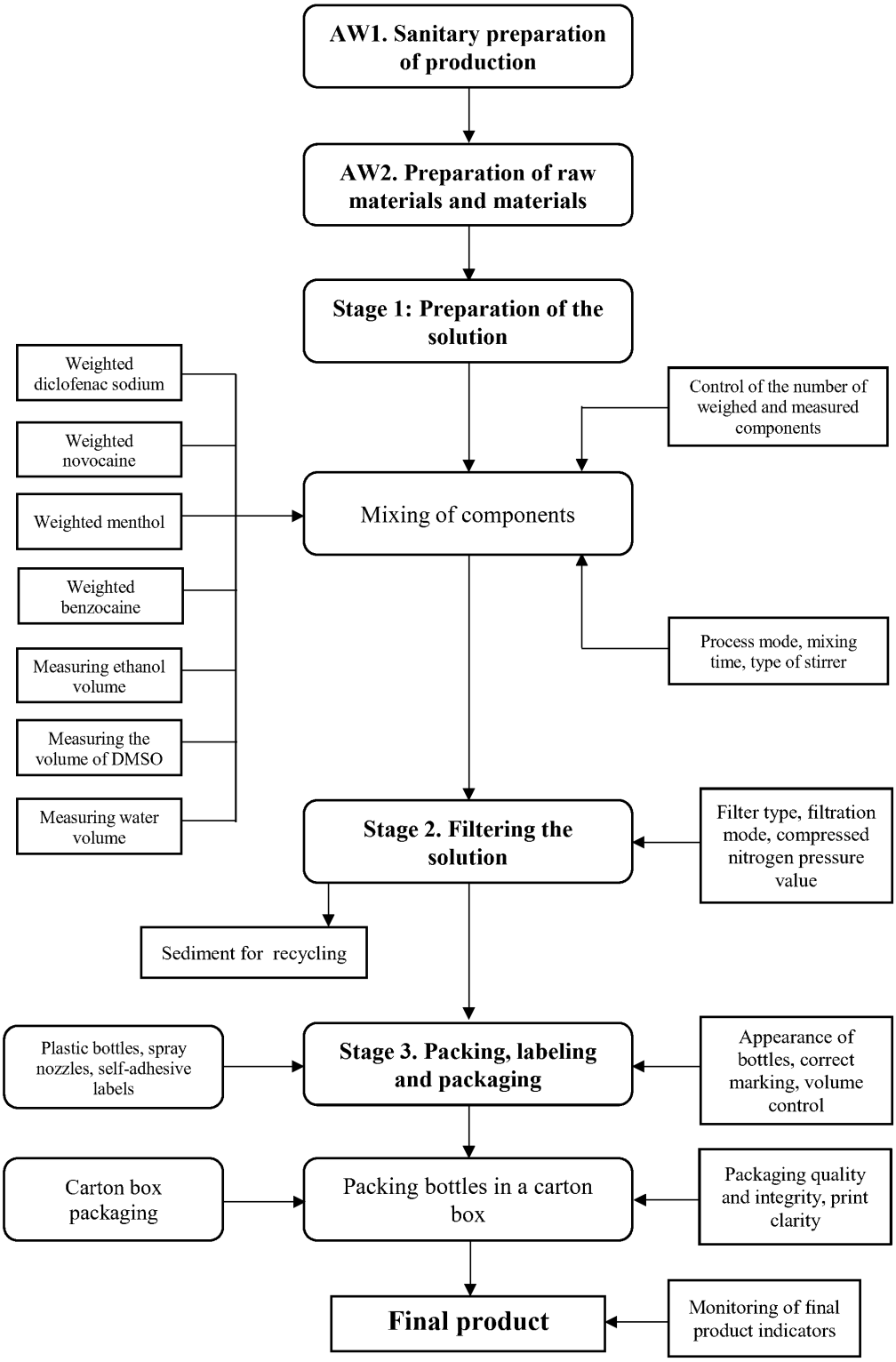

Fig. 2. Technological stages of the spray production process

In Stage 1, “Preparation of the solution” ethyl alcohol and purified water are added into the reactor, and the sodium salt of diclofenac, menthol, novocaine, and benzocaine are added to form a solution. Dimethyl sulfoxide is then added. The process is stirred by controlling the process mode, stirrer speed and stirring time.

Stage 2 of the production, “Filtering solution”, begins with the selection of the filter brand and filtration mode, and the value of the compressed

nitrogen pressure is controlled. The sediment remaining on the filter is removed, and the filtrate is fed to the next Stage 3, "Packaging, labeling and packaging". The final solution is packaged in 40 ml plastic bottles equipped with spray nozzles and labeled with self-adhesive labels. The appearance of the bottles, the accuracy of the packaging and the correctness of the labeling are monitored. The bottles are packaged in cartons that are inspected for quality and integrity, as well as the clarity of the label printing. The finished product is checked according to the final product indicators.

At the last stage of our work, we carried out economic calculations of the cost and value of the proposed spray. The calculated price of 100 ml of the product is 288.54 UAH, so the price of the final spray in a 40 ml bottle is 115.41 UAH. The price of "Diclofenac-Zdorovye Ultra" ranges from 88.42 UAH to 100.1 UAH (Table 1). The slight increase in price relative to "Diclofenac-Zdorovye Ultra" is due to the addition of novocaine, benzocaine and menthol as active ingredients to the spray. If we compare the price with foreign analogues, the proposed product has a price that is half the average retail price of the drug "Argette Spray" (Table 1). Thus, the total cost of developing this drug is optimal, given the fact that the manufacture of such a drug on an industrial scale is quite affordable and simple. Comparison of the price of the drug developed by us with analogs shows that this development has a high level of profitability and indicates the prospect of introduction into the pharmaceutical industry.

Conclusions

As a result of the research, the basics of the technology for obtaining an analgesic and anti-inflammatory agent for external use based on known APIs and excipients in the form of a spray were proposed. The quantitative content of active pharmaceutical ingredients and excipients for the preparation of the spray was proposed and substantiated. Material calculations allowed to estimate the amount of active pharmaceutical ingredients and excipients for the preparation of the spray in the laboratory and its packaging in 40 ml vials. A basic technological scheme and a flow chart for the preparation of the spray were developed and presented. It was found that the drying time of the resulting spray is on average 5 min 35 s, which is significantly lower in comparison with the drugs "Argett Spray" and "Diclofenac-Zdorovye Ultra". Comparison of the proposed spray with the closest analogues in the pharmaceutical market of Ukraine in terms of price showed that the cost of a bottle of the proposed spray slightly exceeds the price of domestic analogues and is half the price of foreign analogues. The results of the work demonstrate a high level of economic profitability of the development of such a product for use in the treatment of pain syndromes of diseases of the musculoskeletal system and indicate the prospect of introducing this development into the pharmaceutical production.

References

1. Harden, R. N., McCabe, C. S., Goebel, A., Massey, M., Suvar, T., Grieve, S., & Bruehl, S. (2022). Complex regional pain syndrome: practical diagnostic and treatment guidelines, 5th Edition. *Pain medicine* (Malden, Mass.), 23(Suppl 1), S1–S53. https://doi.org/10.1093/pm/pnac046

2. Arévalo-Martínez, A., Moreno-Manso, J. M., García-Baamonde, M. E., Blázquez-Alonso, M., & Cantillo-Cordero, P. (2022). Psychopathological and neuropsychological disorders associated with chronic primary visceral pain: Systematic review. *Frontiers in psychology*, 13, 1031923. https://doi.org/10.3389/fpsyg.2022.1031923

3. Pohovorymo pro bil′: kreatyvno, tsikavo ta z posmishkoyu! *Shchotyzhnevyk "Apteka"* № 1266. 2020. Retrieved from URL: https://www.apteka.ua/article/573161

4. Sobeeh, M. G., Hassan, K. A., da Silva, A. G., Youssef, E. F., Fayaz, N. A., & Mohammed, M. M. (2023). Pain mechanisms in complex regional pain syndrome: a systematic review and meta-analysis of quantitative sensory testing outcomes. *Journal of orthopaedic surgery and research*, 18(1), 2. https://doi.org/10.1186/s13018-022-03461-2

5. Melf-Marzi, A., Böhringer, B., Wiehle, M., & Hausteiner-Wiehle, C. (2022). Modern principles of diagnosis and treatment in complex regional pain syndrome. *Deutsches Arzteblatt international*, 119(51–52), 879–886. https://doi.org/10.3238/arztebl.m2022.0358

6. NPZP ye odnymy z naybil′sh zatrebuvanykh v Ukrayini. *Shchotyzhnevyk "Apteka"*, 2023. Retrieved from URL: https://www.apteka.ua/article/669686

7. Aptechnyy prodazh likiv na foni viyny. *Shchotyzhnevyk "Apteka"*, No. 1345/1346, 2022. Retrieved from URL: https://www.apteka.ua/article/644822

8. Ziesenitz, V. C., Welzel, T., van Dyk, M., Saur, P., Gorenflo, M., & van den Anker, J. N. (2022). Efficacy and safety of NSAIDs in infants: a comprehensive review of the literature of the past 20 years. *Paediatric*

drugs, 24(6), 603–655. https://doi.org/10.1007/s40272-022-00514-1

9. Dronik, M. & Stasevych, M. (2022). Analysis of the pharmaceutical market of diclofenac preparations. *Scientific Foundations in Medicine and Pharmacy*, 104–123. https://doi.org/10.46299/isg.2022.mono.med.2.4.1

10. Stasevych, M. & Viktor Zvarych (2022). Medicines of the M02AX group on the Ukrainian market: analysis of the range and search for possible market niches. The role of medical science in implementing innovative medical technologies in the EU countries and Ukraine, 292–306. https://doi.org/10.30525/978-9934-26-199-2-15

11. Derzhavnyy reyestr likarsʹkykh zasobiv Ukrayiny. URL: http://www.drlz.com.ua (Retrieved: 15.05.2023).

12. Tabletki.ua. URL: https://tabletki.ua (дата звернення: 15.05.2023).

13. Sydorov, Yu. I., Chuyeshov, V. I., & Novikov, V. P. (2009). *Protsesy i aparaty khimiko-farmatsevtychnoyi promyslovosti*. Vinnytsya: Nova Knyha.

14. Ekonomika khimiko-farmatsevtychnykh pidpryyemstv: Metodychni vkazivky do vykonannya rozrakhunkiv ekonomichnoyi chastyny naukovo-doslidnoyi mahistersʹkoyi kvalifikatsiynoyi roboty dlya studentiv spetsialʹnosti 226 *"Farmatsiya, promyslova farmatsiya"* / Komar V. S., Baranovych D. B., Krychkovsʹka, A. M., Zhurakhivsʹka L. R., Lubenetsʹ V. I., Novikov V. P. Vydavnytstvo kafedry TBSFB NULP, 2020. 22 c.

15. Kompendium – likarsʹki preparaty. URL: https://compendium.com.ua (дата звернення: 20.05.2023).

16. Skoutakis, V. A., Carter, C. A., Mickle, T. R., Smith, V. H., Arkin, C. R., Alissandratos, J., & Petty, D. E. (1988). Review of Diclofenac and evaluation of its place in therapy as a nonsteroidal antiinflammatory agent. *Drug Intelligence Clinical Pharmacy*, 22(11), 850–859. https://doi.org/10.1177/106002808802201102

17. Diclofenac uses, dosage and side effects. Drugs.com. (n.d.). Retrieved February 13, 2023, from https://www.drugs.com/diclofenac.html

18. *Novyy bezvodnyy rozchyn dyklofenaku mistsevoho zastosuvannya ta protses yoho pryhotuvannya*: pat. 97529 Ukrayina. No. a201000120. zayavl. 09.06.2008; opubl. 27.02.2012, Byul. No. 4.

19. *Farmatsevtychna aerozol'na kompozytsiya u formi spreyu*: pat. 81238 Ukrayina. No. u2012 14971; zayavl. 26.12.2012; opubl. 25.06.2013, Byul. No. 12.

М. Ю. Дронік[1], Ілона Йонускене[2], М. В. Стасевич[1]
[1] Національний університет "Львівська політехніка",
кафедра технології біологічно активних сполук, фармації та біотехнології
[2] Каунаський технологічний університет, Каунас, Литва

РОЗРОБЛЕННЯ ОСНОВ ТЕХНОЛОГІЇ ОДЕРЖАННЯ СПРЕЯ ДЛЯ ЗОВНІШНЬОГО ЗАСТОСУВАННЯ

Розроблено основи технології одержання засобу для місцевого застосування зі знеболювальною та протизапальною дією у формі спрея. Запропоновано кількісний вміст активних фармацевтичних інгредієнтів та допоміжних речовин. Виконано порівняльний аналіз деяких показників одержаного спрея з аналогами на фармацевтичному ринку України. Матеріальні розрахунки дали змогу оцінити кількості активних фармацевтичних інгредієнтів та допоміжних речовин для одержання спрея та фасування його у флакони у лабораторних умовах. На основі матеріальних розрахунків запропоновано принципову технологічну схему виробництва готового лікарського засобу. Виконано економічні розрахунки, що демонструють високий рівень економічної вигідності розроблення такого лікарського засобу.

Ключові слова: біль у суглобах або м'язах; спрей для зовнішнього застосування; активні фармацевтичні інгредієнти; допоміжні речовини; принципова технологічна схема.