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DEVELOPMENT OF THE GEL TECHNOLOGY FOR TREATING INFLAMMATORY DISEASES OF THE ORAL MUCOSA

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With the help of pharmacotechnological, structural and mechanical, physical and chemical, as well as microbiological studies we have developed the gel's composition (carbomer, trometamol, sorbitol, triclosan, «Rotokan», a preservative and purified water). The technology of a new medicine, a dental gel «Rotrin Denta» for treating inflammatory diseases of the oral mucosa has been theoretically and experimentally proven. Currently the stability studies have been conducted in order to choose the duration and conditions for storage of the gel developed.

The prevalence of dental diseases, the growth of the incidence of disease of the oral mucosa causes the search for new more effective medicines for treating the given pathologies. According to statistics in individuals from 15 to 19 years old the disease incidence is 30.5%, at the age of 25-29 – 88.4%, and at the age of 45-49 – 98.7%. Among them 92-95% are periodontal inflammations such as gingivitis, paradentitis, paradontosis [6, 10, 11].

The choice of the medicinal form and the way of drug introduction into the body have a great importance for successful treatment. The wrongly selected medicinal form can cause increase or decrease of the therapeutic effect of the active substance or its absence. The optimal dispersion system must provide a sufficient release and resorption of the active substances by creating a high therapeutic concentration at the sites of drug application without influencing on the system circulation [1, 2, 3, 9].

In that respect, in our opinion, the gel is the most balanced medicinal form for the local therapy of periodontal diseases, which well distributes and absorbs on the mucosa and it stipulates the high bioavailabilitv of active substances [7, 8].

With the help of complex research the optimal composition of a new medicine – «Rotrin Denta» gel with triclosan and original combined phytogenous medicine «Rotokan» manufactured by «LubnyPharm» JSC, Ukraine, has been developed. Triclosan is antibacterial agent with a wide spectrum of action, which has anti-inflammatory properties and influences on the gram-positive and gram-negative flora, as well as the fungal organisms. «Rotokan» is chosen due to its marked anti-inflammatory, regenerating and haemostatic action [4, 5].

Considering the above mentioned facts we had a task to develop such technology of the gel production, which would allow us to obtain an effective, stable medicine with the physical and chemical, as well as consumer characteristics required.

Experimental Part

The aim of this phase was to develop the rational gel technology, as well as the step-by-step substantiation of the dental gel components introduction.

When developing the technology the samples of the gel with triclosan and «Rotokon» were chosen as research objects. To determine the optimal technological parameters the laboratory equipment (minireactor with mixers, homogenizer, etc.) was used. The study of rheological indicators (structural viscosity ŋ (mPa·s), shear stress τ_r (Pa), shear rate Dr or γ (s^{-1}) was carried out on the BROOKFIELD DV-II + PRO viscosity analizer (USA). The indicators of pH value for the gel samples were determined by the potentiometric method with the help of the pH Meter Metrogm 744 device (Germany).

Results and Discussion

The technological process of production should consist of the rationally planed system of interrelated processes with the optimally coordinated inputs and outputs of each them.

According to the SPhU the technology of the soft medical forms should consist of preparation of the base and introduction of active substances to it.

Thus, the technological process starts with preparing carbopol gel of Ultrez-10NF grade, which basic advantage is the fact that it does not require a special temperature mode.

However, during the preparation of carbopol aqueous solution the powder should be arranged in layers on the water surface through the sieve in order to avoid clustering. After neutralization of carbopol solution with trometamol solution the gel obtained is vacuumed in the reactor to eliminate air bubbles.

The optimal quantities of the solvents required for each technological stage taking into account the solubility of the components of the gel, sequence and stepping of mixing the components, temperature and other parameters and their impact on the quality of the medicine have been calculated.

The technological process of obtaining the gel consists of such stages as auxiliary works, the basic technological process, packing, labeling and shipment of finished products to the warehouse.

The technological process of the gel production is carried out keeping to sanitary rules and requirements stated in the standards of the enterprise «The sanitary preparation for the gel production».

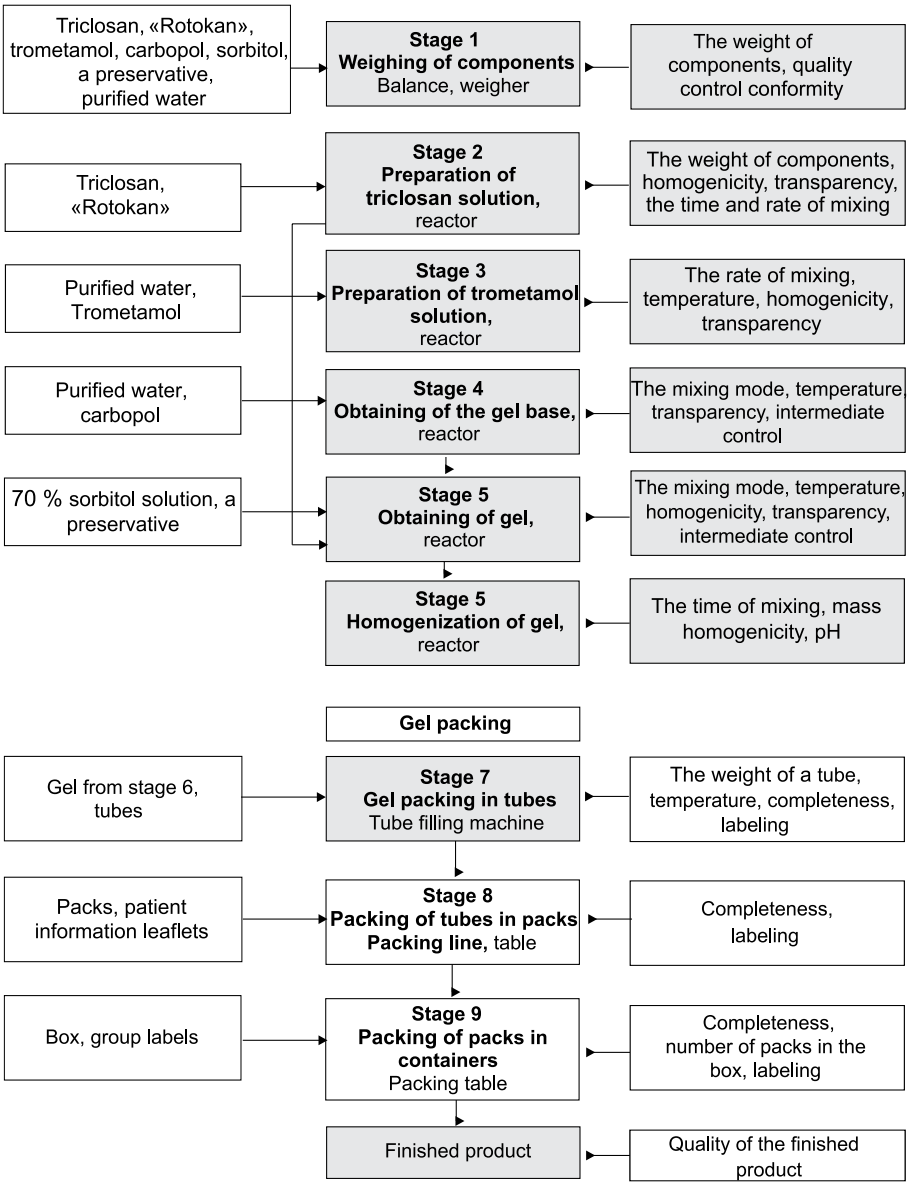

Fig. The flowchart of «Rotrin-Denta» gel.

Stage 1. Weighing of components

The raw material for the gel preparation after the input control are delivered to the site with the help of a cart.

Stage 2. Preparation of the solution of triclosan and «Rotokan»

The necessary amount of triclosan and «Rotokan» alcohol solution is weighted to the reactor and mixed with the help of mixers till the full dissolution of triclosan. Transparency is controlled visually.

Stage 3. Preparation of trometamol solution

In the collector the necessary amount of trometamol is weighted and from the weigher the neccesary amount of purified water is poured. The solution of trometamol is mixed till its complete dissolution. The transparency is controlled visually. The solution is supposed to be transparent without any visual particulate matter.

Stage 4. Obtaining of the gel base

The necessary amount of purified water is measured into the reactor and the powder of carbopol is weighted gradually by small portions and allowed to stand for an hour (for the full powder swelling of gel-forming carbopol). After swelling of carbopol the dispersed water solution is mixed with the help of switched-on reactor mixers till the formation of a homogenous water dispersion. Homogenicity of dispersion is controlled visually. It should be homogenous, without any lumps. Then at the mixer's rotation (not more than 700 rps) the solution of trometamol prepared is loaded to the reactor. With the help of vacuum after the full loading of the neutralizer solution the mass is mixed for 20 min till the formation of homogenous gel base under the following conditions: the rotation speed of the spade mixer is 42 rpm, speed of the anchored mixer is 20 rpm, the vacuum depth is (0.6-0.7 bar). The turbomixer is switched off. The gel mass obtained is checked for homogenicity and pH value of the gel.

Stage 5. Obtaining of the gel

In the reactor with the gel base preliminary prepared the solution of triclosan, 70% solution of sorbitol and a preservative are consistently added. Then the frame mixer is switched on and the substance is mixed till for-

mation of a homogenous mass. The gel is checked for homogenicity and pH value.

Stage 6. Homogenization of the gel

Homogenization is carried out inside the reactor with the frame mixer for 20 min along with vacuumization to prevent the process of aeration.

After homogenization the control samples from the different zones of the reactor are taken and the analysis of the intermediate product – the finished gel is carried out. This gel should be a homogeneous and opaque mass of the light brown colour with the specific herbal odour and must meet the requirements of the normative documentation. The gel is checked for homogenicity and pH value.

Stage 7. Packing of the gel in tubes

The gel obtained is pumped into the bunker of the tube filling machine, with its help the gel is packed in 30.0 g aluminum tubes with a membrane and boushons with the inner lake coatings of the type Paclac 11-15-000. The precise dosing and the machine productivity and accuracy of the tube packing (batch number and shelf life) are controlled.

Stage 8. Packing of tubes in packs

Tubes with the patient information leaflet are packed into packs. The completeness of packing is controlled (tube, patient information leaflet, bouchon).

Stage 9. Packing of packs in containers

On the packing table the packs are packed manually into boxes.

The flowchart for manufacturing «Rotrin-Denta» medicine under conditions of the commercial production is given in Fig.

CONCLUSIONS

1. The rational technology of a dental gel «Rotrin-Denta» of the local action has been experimentally grounded; it has been proven commercially.

2. The technological aspects of introduction of active substances (triclosan, the original medicine «Rotokan») and excipients to the gel composition have been studied.

3. The flowchart for manufacturing a new medicine – a dental gel «Rotrin-Denta» for treatment of inflammatory diseases of the oral mucosa has been developed.

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РАЗРАБОТКА ТЕХНОЛОГИИ ГЕЛЯ ДЛЯ ЛЕЧЕНИЯ ВОСПАЛИТЕЛЬНЫХ ЗАБОЛЕВАНИЙ СЛИЗИСТОЙ ОБОЛОЧКИ ПОЛОСТИ РТА

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С помощью фармакотехнологических, структурно-механических, физико-химических и микробиологических исследований нами был разработан состав геля (карбомер, трометамол, сорбитол, триклозан, «Ротокан», консервант и вода очищенная). Теоретически и экспериментально обоснована технология нового лекарственного средства стоматологического геля «Ротрин-Дента» для лечения воспалительных заболеваний слизистой оболочки полости рта. На данный момент проводится исследование стабильности с целью выбора срока и условий хранения разработанного геля.

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РОЗРОБКА ТЕХНОЛОГІЇ ГЕЛЮ ДЛЯ ЛІКУВАННЯ ЗАПАЛЬНИХ ЗАХВОРЮВАНЬ СЛИЗОВОЇ ОБОЛОНКИ ПОРОЖНИНИ РОТА

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За допомогою фармакотехнологічних, структурно-механічних, фізико-хімічних та мікробіологічних досліджень нами було розроблено склад гелю (карбомер, трометамол, сорбітол, триклозан, «Ротокан», консервант та вода очищена). Теоретично та експериментально обґрунтовано технологію нового лікарського засобу стоматологічного гелю «Ротрин-Дента» для лікування запальних захворювань слизової оболонки порожнини рота. На даний час проводиться дослідження стабільності з метою вибору терміну та умов зберігання розробленого гелю.