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It is our great pleasure to present this Supplement Issue on “*Macedonian Pharmaceutical Bulletin*” to the scientific and professional community. This supplement includes the short communications from the *Sixth Congress of Pharmacy in Macedonia with International participation*, as the largest gathering for the pharmacy profession held in the Republic of Macedonia. The main theme of the Congress was “Modern pharmacist - bridging science with practice”.

A broad spectrum of topics within the pharmaceutical sciences and practice carefully selected for this special occasion in order to build up a highly interesting and comprehensive program were covered. The contributions submitted to the Congress included 6 plenary lectures, 84 section lectures, and more than 240 posters. This Congress, followed the excellent international tradition, was attended by close to 1000 domestic and foreign participants. We received 326 short paper submissions from more than 25 countries. These numbers show that our Congress is aiming for the highest scientific standards, and that it can be considered a well-established venue for researchers in the broad fields of Pharmaceutical sciences and practice.

We would like to thank all internationally prominent researchers for their contribution to reinforcing the overall quality of the Congress. They give the state of the art of the recent advances in the field of pharmacy research.

Sincere thanks to the hosts of the Sixth Congress of Pharmacy in Macedonia with International participation, Macedonian Pharmaceutical Association and Faculty of Pharmacy, Ss Cyril and Methodius University in Skopje for their vision and commitments.

We acknowledge the sponsoring companies: the platinum sponsor AD ALKALOID, Skopje, the golden sponsor PLIVA, the silver sponsor EUROFARM and the bronze sponsor SEPTIMA, for the permanent support to our efforts during the organization.

We would also like to thank our members of the Scientific Committee for their volunteer time and dedication to the critical peer review process and in the organization of the program. We also wish to thank all the members of the Organizing Committee, whose work and commitment was invaluable.

On behalf of the Advisory and Scientific Committees, we would like to especially thank the authors, whose work was the essential part of the congress and contributed to a very successful event. Besides the many academic staff and professionals who contributed to the success of the Congress, we are grateful to the students who participated with oral presentations and posters.

The pharmaceutical sciences continue to grow as dynamic scientific interdisciplinary fields. We believe that published short communications will be an excellent source of scientific material in the fast evolving fields in Pharmaceutical sciences and practice.

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The present issue of *Macedonian Pharmaceutical Bulletin* is a special issue of the 6th Congress of Pharmacy in Macedonia with international participation.

This issue of *Macedonian Pharmaceutical Bulletin* contains short papers accepted by the scientific committee for the presentation at the Congress.

The authors are fully responsible for the contents of their short papers.

All reviewers that were involved in the short papers revision process are sincerely acknowledged.

Small scale production of gel with menthol, benzocaine and procaine HCl

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Introduction

Antirheumatic and analgesics drugs are the most commonly used drugs to treat diseases of the musculoskeletal system and to alleviate all sorts of pain that are caused from different origins. Their systemic use causes long series of side effects, so combination therapies of drugs with systemic and local action or only medicinal products intended for topical use wherever possible, especially in physical therapy, would be treatment of choice.

Various formulations of dosage forms, by composition and consistency, allow different therapeutic approach, suitable for achieving the desired therapeutic effect and for being capable to adapt to the physiotherapist treatment.

According to the regulations of the pharmacopoeia or to other regulations, the galenic drugs are made in small batches in a galenic laboratory, which are intended to be administrated directly to a pharmacy or a health institution.

According to the health requirements, the preparation of pharmaceutical dosage forms in a galenic laboratory, mainly aims to provide a dosage form, which is designed as an opportunity for changes in the composition and consistency of the product. Therefore, it can be provided a product with a modified properties, compared with a finished and fixed composition of the medicinal and an auxiliary substances, or with the already existing traditional products, which have the same composition of active components, satisfying the needs of the healthcare professionals who work with them and also allowing a simultaneous comfort and a therapeutic effect for the patients.

The usage of this drug, immediately after the preparation, reduces the need for adding more funds to stabilize and to ensure longer shelf life.

Obtaining the quality of this drug product, that satisfies the standards and maintains or enhances the therapeutic properties, requires appropriate conditions for a preparation and knowledge of all the components properties, technological process and requirements for the finished product as well.

The usage of the traditional liquid, a pharmaceutical product known as “Russian water”, which contains: alcohol, menthol, procaine hydrochloride and benzocaine, is well received and accepted by the patients and the physiotherapists, but it also has some negative sides, such as, short effect, it is easily volatile, it acts surface and cannot be recommended as a massage supplement. On the other hand, gels are a dosage forms for external use that can be applied easily, to tie up to the skin and to enable the drug to heal the affected area, it can realize deep action, such as the ability to quickly penetrate multi-layers on the skin, to be easily rinsed from the site of application and generally does not irritate the skin, which is largely satisfying for our requirements.

The aim of this study was to formulate and prepare gel formulation from the pharmaceutical composition named “Russian water”, with the ingredients: menthol, benzocaine, procaine HCl, which is easy and pleasant to apply on the painful area, also effective to reduce the pain and the inflammation. Formulation challenge was slight solubility of some of the components, getting a stable product with a proper consistency, ensuring the release of the active ingredients, their affection on the skin and a prolonged action.

Materials and methods

In the formulation and preparation the following active substances were used: menthol (Alkaloid), benzocaine

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(Sigma Aldrich), procaine HCl (Sigma Aldrich), at the recommended doses and ingredients, carbopol 940 (Sigma Aldrich), glycerol, (Alkaloid), triethylene tetramine (Sigma Aldrich) and aqua distillate.

Gel with menthol, benzocaine and procaine HCl was prepared in the galenic laboratory in Ohrid -General Hospital. Used ingredients and a compounding procedure described in a rational manner are:

menthol 4.0, benzocaine 2.0, procaine HCl 2.0, base gel ad 200.0. Basic gel was made with the following prescription: Carbopol 940 2.0, glicerolum 7.5, triethylene tetramine 2.5, aqua destilata 190.0.

In the step 1, preparation of base gel, Carbopol 940 and aqua distillate 50 mL were left to bulge. Then glycerolum was gradually added and mixed to achieve good homogenization. After that, triethylene tetraamin was added and mixed again until thick gel was obtained. In the step 2, preparation of healing gel, the menthol was grinded through a sieve, and it was measured in the prescribed amount. It was mixed with the same amount of prepared basic gel to complete uniformity of the mixture. The benzocaine was grinded, sieved and measured at the prescribed amount and mixed with equal quantity of earlier prepared gel with menthol.

The prescribed amount of procaine hydrochloride was measured and dissolved in distilled water 10mL. Then, the solution was gradually added to the gel with menthol and benzocaine, while constantly stirred. The remaining amount of distilled water was added, gradually and with constant stirring, to the homogeneous gel to obtain a homogeneous product.

Results and discussion

The obtained gel is a homogeneous product with milk appearance. The high degree of pulverization of the components should improve solubility and ensure uniform distribution of insoluble components in the mixture. The process of mixing equal amounts of the basic mixture and pulverized substance also provides uniform distribution of the components, and the high density of the base gel reduces the possibility of their sedimentation (Allen, 2002; Jovanovic and Sekulovic, 1987; Racev and Lambov, 2005; Simov et al., 2001; Winfeld and Richards, 1998). Menthol is practically insoluble in water and because of its sole distribution in the preparation it was pulverized and a special way for its incorporation into the system was applied. Benzocaine is poorly soluble in water and an appropriate pul-

verization and mixing improved solubility and its uniform distribution in the product. The procedure of mixing and gradual addition of a small amount concentrated procaine hydrochloride solution reduces the possibility of decomposition of the gel structure under the influence of the potential ionic solution (Jackson and Lowey, 2010; Simov et al., 2001).

The obtained gel is packaged in plastic recipients of 200 mL, closed with a suitable stopper and signed with red signature marked "For external use." It is used topically by applying to the affected area and/or with good rubbing in physical therapy. The product has a short shelf life and is prepared immediately before use, and to ensure the quality of the product it is recommended to be kept at a room temperature in well-closed recipients. During application it gives pleasant cooling sensation and pain relief and easily rinse out with water. It is not toxic and does not cause skin irritation.

The product can be prepared in galenic laboratory, and easy application and efficiency makes it acceptable to patients (Jackson and Lowey, 2010). It has been retained at the administration site longer than the expected, and has longer actions regarding to the liquid alcohol solution, which is with the same components.

Conclusion

The results of the treatment of patients according the investigation of the staff that operated and the practical patients show that this gel is with a prolonged analgesic activity compared to the liquid preparation, with an easy and safe application, a pleasant cooling sensation and a pain relief, also an easy flushing and with an increased satisfaction of therapists and patients.

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