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Македонско фармацевтско друштво, ул. Маршал Тито 13б/8, Скопје, Македонија
Macedonian Pharmaceutical Association, Marshal Tito 13b/8, Skopje Macedonia

Dear colleagues

The 14th CESPT in 2023 offers a platform to discuss new ideas in formulation design, drug delivery research, as well as share ideas about technological advances for high-quality drug production. The current and future aspects of pharmaceutical development, innovative product technologies, manufacturing processes, pharmaceutical quality and regulatory challenges will be addressed by scientists and engineers from academia, industry, regulatory bodies and students. Also, the symposium aims to tackle, from a multi-disciplinary perspective, the challenges and future outlook of the rapidly developing class of chemically engineered pharmaceutical products so called nanopaharmaceuticals and their application in biomedical field. Presentations from multidisciplinary researches and international expert speakers as well as fruitful discussions on the topics of the symposium will take us beyond the limits of current knowledge in the development and manufacture of safe, reliable and effective medicines.

The programme contains 10 invited lectures, 35 oral presentations and 114 poster presentations from more than 20 countries. Considering the number and quality of contributions we believe that the 14th CESPT will offer a good opportunity to promote scientific achievements in the field of pharmaceutical development and nanopaharmaceuticals.

Besides sharing knowledge and experience we believe that future collaborations and research projects will be born on site during both, the working sessions of the meeting and the social events.

Looking forward to having a productive Symposium in Ohrid, 28-30 September 2023!

Prof. Katerina Goracinova

President of the 14th Central European Symposium on Pharmaceutical Technology

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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.



**. Pharmaceutical
development and
manufacturing**

***In vitro* spironolactone permeation study: role of different alkyl polyglucoside emulsifiers and glycolic acid**

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Introduction

The skin is the largest human organ covering the entire body. It is composed of layers of cells that act like a barrier and keep substances from permeating and entering the systemic circulation. The release of the active substance from vehicle is the first important step in achieving an adequate effect of the drug. In case of topical application, it should permeate through the skin in order to achieve a local effect, avoiding systemic absorption (Hadgraft et al., 2005). Franz diffusion cells are a widely used methodology to evaluate *in vitro* drug permeation (Bielfeldt et al., 2022). Recently, spironolactone (SP) was introduced as off-label topical acne therapy, in order to reduce side effects when administered orally (Salama et al., 2020). Alkyl polyglucoside (APG)-based emulsions with 5% of SP showed acceptable skin irritation profiles, which indicate that these emulsions could be used as prospective carriers for off-label topical SP (Ilic et al., 2021). This work's main objective was to examine the SP permeation through skin from different APG-based topical emulsions with or without glycolic acid (GA) as excipient, using Franz diffusion cells.

Materials and methods

We prepared four different emulsion vehicles based on APG emulsifiers Cetearyl glucoside and cetearyl alcohol and Arachidyl glucoside and arachidyl behenyl alcohol (Tables 1 and 2). GA in samples F2 and F4 was tested as a potential penetration enhancer. *In vitro* release study was performed using Franz diffusion cells (chamber volume 12 ml, effective diffusion area 2.01 cm²). Ethanol 70%,

previously preheated to 32°C, was used as an acceptor medium. Polycarbonate membranes, activated in the same ethanol solution during the 12-hours period, were used in the experiment. The donor chamber was filled with 1 g of the investigated samples and afterwards covered with silicone film. Cells were placed in the water bath where the temperature of 32°C was maintained through the whole experiment. Acceptor phase was under continuous magnetic stirring at 500 rpm. Aliquots of 0.6 µl of the acceptor phase were withdrawn at 5 time points (0.5 h, 1 h, 2 h, 4 h and 6 h). HPLC technique was used for determination of SP content.

Table 1. Ingredients of tested samples

Ingredient	F1 (m/m%)	F2 (m/m%)
Arachidyl glucoside & arachidyl behenyl alcohol	10	10
Cetostearyl alcohol	2	2
Caprylic/Capric Triglycerides	10	10
Cyclomethicone	10	10
Glycerol	2	2
Spironolactone	5	5
Ethanol 96%	5	5
Glycolic acid		4
Preservative	0.5	0.5
Purified water	ad 100	ad 100

Results and discussion

Cumulative SP amount permeated through the polycarbonate membranes as a function of time is shown in Fig. 1. APG-based emulsions with 5% of SP have already proved both acceptable skin irritation profile and high potential for skin hydration (Ilic et al., 2021). The similarity of these emulsion structures with the organization of intercellular lipids of the stratum corneum (SC) gives them an advantage compared to traditional emulsion systems, especially due to their effect of increasing penetration through SC, as the main barrier of the skin (Savic et al., 2011). All tested samples showed satisfactory SP permeation profiles: SP permeation profile was almost linear, which indicates its uniform release from both emulsions. Percentage of SP permeated through the membrane ranged from 2.4 after 0.5 h to 11.49 after 6 h for sample F1 and from 3.11 after 0.5 h to 12.55 after 6 h for sample F2. On the other hand, percentage of SP permeated through the membrane ranged from 2.79 after 0.5h to 14.72 after 6 h and from 4.38 after 0.5 h to 23.82 after 6 h for samples F3 and F4, respectively. The difference between samples F1 and F3 is probably due to the fact that sample F3 has a more liquid consistency. On the other hand, both samples with GA showed better SP permeation compared to samples without GA. This indicates that GA can enhance SP permeation from APG-based emulsions.

Table 2. Ingredients of tested samples

Ingredient	F3 (m/m%)	F4 (m/m%)
Cetearyl glucoside & cetearyl alcohol	7	7
Cetostearyl alcohol	2	2
Caprylic/Capric Triglycerides	10	10
Isopropyl myristate	10	10
Glycerol	2	2
Spirinolactone	5	5
Ethanol 96%	5	5
Glycolic acid		4
Preservative	0.5	0.5
Purified water	ad 100	ad 100

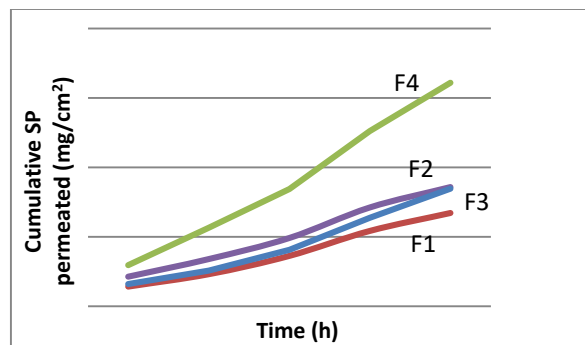


Figure 1. In vitro permeation of SP from investigated samples as a function of time

Conclusion

SP showed satisfactory permeation profile from emulsions with both types of emulsifiers using Franz diffusion cells. GA proved to be an acceptable penetration enhancer. Further investigations of potential synergistic action of SP and GA on skin with acne should be done, alongside additional in vivo studies on human.

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