

EMULSIONS WITH NATURAL ALKYL POLYGLUCOSIDES AS CARRIERS FOR TOPICAL SPIRONOLACTONE – *IN VIVO* SKIN PENETRATION STUDY

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Acne vulgaris is a chronic disease that affects sebaceous glands. Two key factors in the pathogenesis of acne are controlled by androgens. As an antiandrogen drug, spironolactone (SP) has the ability to block androgen receptors, so it is being used in dermatology as off-label topical acne therapy (1). Alkyl polyglucosides (APGs) are class of “green” surfactants produced from renewable resources. Glycolic acid (GA) is often used as an adjuvant treatment of acne, but at the same time it is presumed that GA could act as a penetration enhancer.

In our previous research APG-based emulsions with 5% SP have shown satisfactory physical stability and safety profile (2). The next step is to examine the penetration of SP through *stratum corneum* (SC) using tape stripping technique (3).

Table I Composition of the test samples

Ingredient	F1 (%m/m)	F2 (%m/m)	F3 (%m/m)
Cetearyl-glucoside & cetearyl-alcohol	7	7	
Cetostearyl-alcohol	2	2	
Caprylic/Capric Triglycerides	10	10	
Isopropyl-myristate	10	10	
Glycerol	2	2	
Spironolactone	5	5	5
Glycolic acid		2	
Ethanol 96%	5	5	
Preservative	0.5	0.5	0.5
Carbomer mucilago (MF2008)			ad 100
Purified water	ad 100	ad 100	

To that aim, we prepared three different samples. We planned to compare SP penetration from different vehicles, with or without GA. Five volunteers participated in the study. Each sample was applied on the appropriate place on the inner side of the forearm. After a defined period of time, residues were removed. Removing of SC was performed using 10 self-adhesive tapes. After application to the skin, each strip was exposed to constant

pressure, then it was removed. All strips from one test site were stored overnight in a solvent mixture of phosphate buffered saline pH 7.4:acetonitrile 1:2 (V/V). The resulting solutions were centrifuged and analyzed by HPLC to determine SP content (3).

The obtained results show statistically significant difference in SP content after the application of samples F1 and F3, indicating that SP penetrates into skin more quickly and to a greater extent from the gel vehicle. The cumulative amount permeated from F3 was almost 2-fold higher than that observed for F1, which indicates that applied SP remains on the skin to a greater extent when incorporated into emulsion vehicle, or that SP release was slower from the F1 sample. Also, no difference in SP penetration was observed from the samples F1 and F2, presuming that GA does not affect SP penetration through SC. Additional *in vitro* release and percutaneous absorption studies are needed.

References

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3. Salama A, Badran M, Elmowafy M, Soliman G.M. Spironolactone-Loaded LeciPlexes as Potential Topical Delivery Systems for Female Acne: In Vitro Appraisal and Ex Vivo Skin Permeability Studies. *Pharmaceutics* 2020; 12, 25; doi:10.3390/pharmaceutics12010025

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EMULZIJE SA PRIRODNIM ALKIL-POLIGLUKOZIDNIM EMULGATORIMA KAO NOSAČI ZA SPIRONOLAKTON – *IN VIVO* STUDIJA PENETRACIJE KROZ KOŽU

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Akne predstavljaju hroničnu bolest koja pogađa sebacealne žlezde. Dva ključna faktora u patogenezi akni su pod uticajem androgena. Kao antiandrogeni lek, spironolakton (SP) ima sposobnost da blokira androgene receptore. SP se u dermatologiji koristi u „*off-label*” lokalnoj terapiji akni (1). Alkil-poliglukozidi (APG) su klasa „zelenih” surfaktanata proizvedeni iz obnovljivih izvora. Glikolna kiselina (GK) se koristi u lokalnom tretmanu akni, a u isto vreme pretpostavlja se da bi mogla da deluje i kao penetracioni enhenser. U našem prethodnom istraživanju, emulzije na bazi APG emulgatora sa 5% SP su pokazale zadovoljavajuću fizičku stabilnost i bezbednosni profil (2). Sledeći korak je ispitivanje penetracije SP kroz stratum corneum (SC) tzv. „*tape-stripping*” tehnikom sa samolepljivim trakama (3).

Tabela I Sastav ispitivanih uzoraka

Sastojak	F1 (%m/m)	F2 (%m/m)	F3 (%m/m)
Cetearil-glukozid & cetearil-alkohol	7	7	
Cetostearil-alkohol	2	2	
Kaprilni/Kaprilni trigliceridi	10	10	
Izopropil-miristat	10	10	
Glicerol	2	2	
Spironolakton	5	5	5
Glikolna kiselina		2	
Etanol 96%	5	5	
Konzervans	0,5	0,5	0,5
Carbomeri mucilago (MF2008)			ad 100
Prečišćena voda	ad 100	ad 100	

S tim u vezi, pripremili smo tri različita uzorka. Namera nam je bila da uporedimo penetraciju SP iz različitih podloga, sa i bez dodatka GK. U istraživanju je učestvovalo pet dobrovoljaca. Tačna količina svakog uzorka je naneta na odgovarajuće mesto na unutrašnjoj strani podlaktice. Nakon određenog vremenskog perioda, ostaci uzoraka su uklonjeni. Uklanjanje SC je izvedeno pomoću deset samolepljivih traka. Nakon lepljenja na kožu, svaka traka je bila izložena konstantnom pritisku, nakon čega bi bila odlepljena sa kože. Sve trake sa jednog ispitivanog mesta na koži su ostavljane da prenoće u mešavini fosfatnog pufera

pH 7,4 i acetonitrila u zapreminskom odnosu 1:2. Dobijeni rastvori su centrifugirani i analizirani pomoću HPLC-a u cilju određivanja sadržaja SP (3).

Dobijeni rezultati ukazuju na postojanje statistički značajne razlike u sadržaju SP nakon nanošenja uzoraka F1 i F3, što ukazuje na to da SP brže i u većoj meri prodire u kožu iz gela. Kumulativna količina SP koja je penetrirala nakon aplikacije uzorka F3 je bila skoro duplo veća od one iz uzorka F1, što ukazuje na to da se SP iz emulzionog uzorka zadržava na koži u većoj meri, ili da je njegovo oslobađanje bilo sporije iz emulzije sa APG. Takođe, nije primećena razlika u penetraciji SP između uzoraka F1 i F2, što stvara pretpostavku da GK ne utiče na penetraciju kroz SC. Potrebno je uraditi dodatne studije in vitro otpuštanja leka i perkutane resorpcije.

Literatura

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