

## EKVIVALENTI HUMANE KOŽE DOBIJENI IN VITRO KULTUROM ĆELIJA: KARAKTERISTIKE, ZAHTEVI U POGLEDU KVALITETA I MOGUĆNOSTI PRIMENE

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Rekonstruisani ekvivalenti humane kože, kao alternativa ispitivanjima na životnjama, ne samo da pružaju mogućnost istraživačima iz oblasti dermofarmaceutskih/dermokozmetičkih preparata da se izbore sa pooštrenim zahtevima zakonske regulative i jasno definisanim potrebama pacijentata/korisnika, već predstavljaju sredstvo čijim se proučavanjem proširuju saznanja o biološkim procesima koji se odigravaju u koži.

Danas se raspolaže različitim tipovima rekonstruisane kože, počev od onih koji sadrže samo epiderm (sa keratinocitima, melanocitima i Langerhansovim ćelijama), do ekvivalenata koji sadrže i dermalni sloj (sa fibroblastima i endotelnim ćelijama).

Dostignuti kvalitet omogućuje standardizovanu primenu ovih medijuma u in vitro studijama penetracije/permeacije lekova kandidata za terapiju kožnih oboljenja, ili u cilju izbora pogodnog nosača za lek ili kozmetički aktivnu supstancu. Iako su isečci humane kože, najpogodniji in vitro penetracioni medijum, korišćenjem ekvivalenata izbegava se veliki uticaj inter i intra-individualnih razlika, koje se javljaju kada se koristi koža različitih donora ili različitih delova tela istog donora.

Ekvivalenti se koriste i u ispitivanjima iritacionog, sigurnosnog profila pomoćnih i aktivnih supstanci, kao i za in vitro procenu efikasnosti lekovitih i kozmetičkih preparata. Ranije su za ova ispitivanja korišćene životinje, ali se zbog razlika u arhitekturi, metabolizmu i barijernoj funkciji humane i kože životinja, danas zahteva potpuno ukidanje testova na životnjama.

Korišćenjem ekvivalenata ostvaren je napredak u sagledavanju bazičnih bioloških mehanizama u koži (melanogeneza, proces zarastanja rana), i proučavanju prevremenog starenja kože i nekih patoloških stanja (psorijaza, kancer kože...).

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## HUMAN SKIN EQUIVALENTS PRODUCED BY IN VITRO CELLS CULTURE: CHARACTERISTICS, QUALITY REQUIREMENTS AND APPLICATION POSSIBILITIES

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The reconstructed human skin equivalents, as an alternative to animal experimentation offer to the researchers from dermopharmacy/dermocosmetology field not only a way to concede to demands of regulatory authorities and precisely defined patients/consumer's needs, but also provide a mean to improve and extend our knowledge on biological processes in the skin.

Nowadays, various skin reconstructs are available being composed either of the epidermal compartment only (with keratinocytes, melanocytes and Langerhans cells) or both the epidermal and dermal compartments (with fibroblasts and endothelial cells).

The quality of human skin equivalents has now reached the standardized criteria and suits to their use in the in vitro penetration/permeation studies for dermatological drug candidates, or aim to choosing an optimal vehicle for any drug or cosmetic active substance. Although the specimens of human skin are the most suitable in vitro penetration medium, using the equivalents the hard influence of inter and intra-individual variations could be excluded, that is normally present in the case of employing different donors' skin or skin from different body regions of the same donor.

Equivalents are used also in testing of skin irritancy and safety profiles of active substances and excipients, as well as for in vitro evaluation of drugs' and cosmetics' efficacy. In the past, animals have been often used for such testing, but due to the differences in skin architecture, metabolism and barrier function in human and animal skin, a complete repealing of animal testing presently is requested.

Using the skin constructs, the progress in understanding the basic skin biology (melanogenesis, wound repair) and researching of photoaging and some pathological skin conditions (psoriasis and skin cancer) has been made.