PSORIASIS

FUNCTIONALIZED GOLD NANOPARTICLES FOR CUTANEOUS DELIVERY OF METHOTREXATE AND EFFECTS ON PSORIASIS MOUSE MODEL

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Introduction: Topical methotrexate (MTX) formulations have been used in different studies with not fully satisfactory results, mostly due to MTX insufficient percutaneous penetration.

Objective: evaluate the toxicity and effects of gold nanoparticles (AuNPs), functionalized with sodium 3-mercapto-1-propansulfonate (AuNPs-3MPS) loaded with MTX (AuNPs-3MPS-MTX) in vitro on skin model and in vivo on imiquimod-induced psoriasis like mice model.

Materials and Methods: gold-nanoparticles functionalized by sodium-3-mercapto-1-propansulfonate (Au-3MPS) were loaded with MTX. AuNPs-3MPS-MTX was tested on keratinocytes in order to assess the toxicity by Transmission electron microscopy (TEM) and 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, atetrazole test (MTT). The AuNPs-3MPS-MTX or MTX alone were topically used on mouse skin to trace absorption and drug delivery by UV-vis spectra. Subsequently, AuNPs-3MPS-MTX and AuNPs-3MPS were topically administered in vivo on imiquimod-induced psoriasis-like mice model. Clinical response (erythema and scaling), epidermal thickness, cell proliferation rate and inflammatory infiltrate were evaluated by immunohistochemistry.

Results: In vitro studies showed that AuNPs-3MPS-MTX is nontoxic. In vivo tracing of the conjugate on mouse skin showed successful delivery MTX in the epidermis and in less intensity also in the dermis, compared to MTX alone. In spite of absence of the AuNPs in the dermis and epidermis. Moreover, imiquimod-induced psoriasis-like mice model treated with AuNPs-3MPS-MTX showed a decreasing of scaling and erythema score, reduction of epidermal thickness, parakeratosis and hyperkeratosis, compared to AuNPs-3MPS treated mice. Immunohistochemistry analysis staining displayed that Ki67, K6, CD3 and CD8 staining were reduced in AuNPs-3MPS-MTX treated mice. Blood evaluation showed no

differences before and after AuNPs-3MPS or AuNPs-3MPS-MTX treatment.

Conclusions: Topical AuNPs-3MPS-MTX treatment is nontoxic carrier for the satisfactory percutaneous absorption of MTX and is able to induce a reduction of keratinocytes hyperproliferation, epidermal thickness and also inflammatory infiltrate in vivo on imiquimod-induced psoriasis-like mice model. AuNPs-MTX may represent a topical treatment of psoriasis.