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Curcumin based possibilities for targeting protein kinase B and nuclear factor kapa B In cutaneous T-cell lymphoma

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Cutaneous T-cell lymphoma (CTCL) is an orphan disease which primarily affects the skin by clonal accumulation of neoplastic T-lymphocytes and is characterized by a 5-year overall survival of 32% of the patients, if the skin is involved and only 7% for extracutaneous involvement. CTCL therapy is challenging, often empiric because of the limited insight into the genetic basis and single drug therapy is usually not applicable. Curcumin is one well-known ethnopharmacological non-toxic drug with limited bioavailability. The objective of our study was to investigate new treatment modalities for targeting CTCL by combining nanoencapsulated curcumin with alkylphosphocholines thus affecting malignant cell proliferation, skin inflammation and related infections. The nanoparticle size and zeta-potential of Nano-systems containing curcumin were determined by photon correlation spectroscopy and electrophoretic laser Doppler velocimetry. Curcumin concentration was measured by HPLC. MTT- (ISO 10993-5) and CFU-assays were performed on CTCL cell lines for evaluation of cell viability and clonogenicity. Cell death ELISA, microscopy, Hoechst staining and Western blotting were used to monitor hallmarks of apoptosis. Antimicrobial activity was evaluated by ISO 20776-1:2006 (E). Chou & Thalalai software and response surface analysis of combination effects were used to design the experiments and to estimate drug-drug interactions. The nano-sized curcumin delivery systems were prepared using two copolymeric carriers with diameter less than 200 nm and negative surface charge. Encapsulated curcumin penetrated through the cell membranes of CTCL cells faster than curcumin solubilized in ethanol. Combination effects were evaluated as additive to slight synergistic. We have observed in treated samples induction of apoptosis and modulation of PKB/Akt and related signal proteins. Erufosine has exhibited bacteriostatic activity against Gram-positive bacteria in concentrations ranging from 32 up to 100 μM. Combination of erufosine with nano-sized curcumin has led to bactericidal effect. Taken together, our experimental findings clearly indicated that properly designed combinations of curcumin with alkylphosphocholines may show higher antineoplastic potential than single compounds and could be beneficial for the treatment of CTCL as orphan disease.

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