Nanoencapsulation of a ruthenium(II) complex with triazolopyrimidine in liposomes as a tool for improving its anticancer activity against melanoma cell lines.

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Streszczenie

Two types of ruthenium(II) complexes containing 1,2,4-triazolo[1,5-*a*]pyrimidines of the general formulas $[RuCl_2(dmso)_3(L)]$ (**(1)–(3)**) and $[RuCl_2(dmso)_2(L)_2]$ (**(4)–(6)**), where L represents 1,2,4-triazolo[1,5-*a*]pyrimidine (tp for (**1**)), 5,7-dimethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (dmtp for (**2**)), 7-isobutyl-5-methyl-1,2,4-trizolo[1,5-*a*]pyrimidine (ibmtp for (**3**)), 5,7-diethyl-1,2,4-triazolo[1,5-*a*]pyrimidine (detp for (**4**)), 5,7-ditertbutyl-1,2,4-triazolo[1,5-*a*]pyrimidine (dbtp for (**5**)) and 5,7-diphenyl-1,2,4-triazolo[1,5-*a*]pyrimidine (dptp for (**6**)), have been synthesized and characterized by elemental analysis, infrared, multinuclear magnetic resonance spectroscopic techniques (^{1}H, ^{13}C, and ^{15}N), and X-ray (for (**3**), (**4**), and (**5**)). All these complexes have been thoroughly screened for their *in vitro* cytotoxicity against melanoma cell lines A375 and Hs294T, indicating *cis*,*cis*,*cis*-$[RuCl_2(dbtp)_2(dmso)_2]$ (**5**) as the most active representative, in addition to being non-toxic to normal human fibroblasts (NHDF) and not inducing hemolysis of human erythrocytes. In order to develop an intravenous formulation for (**5**), liposomes composed of soybean phosphatidylcholine (SPC), cholesterol (Chol) and 1,2-distearoyl-*sn-glycero*-3-phosphoethanolamine-*N*-[amino(polyethylene glycol)-2000] ($DSPE\text{-}PEG_{2000}$) were prepared and subsequently characterized. (**5**)-Loaded liposomes, with spherical morphology, assessed by transmission electron microscope (TEM), exhibited satisfactory encapsulation efficiency and stability. In *in vitro* experiments, PEG-modified (**5**)-loaded liposomes were more effective (10-fold) than free (**5**) for growth inhibition of both human melanoma cell lines. Furthermore, such an approach resulted in the reduction of cancer cell viability that was even 10-fold greater than that observed for free cisplatin.