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The Induction of Apoptosis by Labd-14-ene-8,13-diol (Sclareol) and the Suppression of Tumour Growth of Human Colon Cancer Cells is p53-Independent

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SUMMARY. The labdane diterpene sclareol has demonstrated significant cytotoxicity against human tumor cell lines and colon cancer xenografts. However, there is further need to study the mode of action of this compound as very little information is known for the anticancer activity of sclareol and other labdane diterpenes, in general. Scla-reol-induced cell cycle arrest and apoptosis were assessed by flow cytometry and Western blot analyses. Finally, the anticancer ability of sclareol *in vivo* was assessed by using human colon cancer xenograft/mouse models. Sclareol arrested further *in vitro* the growth of human colon cancer and induced apoptosis by activating both caspases-8 and -9 in p53-deficient ($HCT116^{p53-/-}$) colon cancer cells. Intraperitoneal administration of liposome-encapsulated sclareol at the maximum tolerated dose induced a marked growth suppression of $HCT116^{p53-/-}$ tumors established as xenografts in NOD/SCID mice. Concluding sclareol kills human tumor cells by inducing arrest at the G_1-phase of the cell cycle and apoptosis via a novel, as yet unknown, mechanism that involves activation of caspases-8, -9 and -3, and it is p53-independent. These findings further suggest that liposomes-encapsulated sclareol may possess chemotherapeutic potential for the treatment of colorectal and other types of human cancer regardless of the p53-status.