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Labelled esters of cytotoxic triterpenes

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Natural triterpenoids together with their semisynthetic derivatives form basis for extensive medicinal research, because they have shown various biological activities [1], e.g.: antineoplastic, antiviral, anti-inflammatory, antimicrobial activities, hepato- and cardioprotective effects; and reveal a great potential for pharmaceutical applications when their cytotoxic and anti-HIV activities were described [1,2,3]. Betulinines, as we named the group of semisynthetic derivatives, have proved multispectral cytotoxic activity on the panel of several cell tumor lines of different histogenetical origin, including multidrug resistance [1,2,3]. One of our leading compoud 3β,28-diacetoxy-18-oxo-19,20,21,29,30-pentanorlupan-22-oic acid fast and selective apoptosis of tumor cells [3], comparable to conventional anticancer drugs – paclitaxel.

Synthesis of various esters of active triterpenic acids has been described previously to improve cytotoxicity and PK parametres. Group of methyl, ethyl, acetoxymethyl, pivaloyloxymethyl and benzyl esters were described and their cytotoxicity has been studied in vitro. Selectively labelled analogues of the most cytotoxic active compounds are used for the investigation of mechanism of action and binding interactions. As a standard for mass spectroscopy together 33 deuterated and C-13 labelled methyl esters were synthesized and fully characterized by spectral data.

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