Comparative assessment of *in vitro* and in *vivo* biological activity of some anthracene-derived aminophosphonates, bis-aminophosphonates and poly(aminophosphonate)s

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Comparative assessment of *in vitro* and *in vivo* biological activity of anthracene-derived aminophosphonates, bis-aminophosphonates and poly(aminophosphonate)s, namely poly(oxyethylene aminophosphonate)s (**4**,**5**) and poly[oxyethylene aminophosphonate-co-H-phosphonate)]s, (**6,7**), were carried out in order to establish their value as potential drug candidates. The compounds were tested for *in vitro* cytotoxicity on a panel of seven human epithelial tumour cell lines. Safety testing was performed both *in vitro* (3T3 NRU test) and *in vivo* on ICR mice for genotoxicity and antiproliferative activity.

The structure-activity relationship analysis showed that the anthracen-based aminophosphonates demonstrate high cytotoxic activity against tumour cell lines. Compounds APhA-t and APhA-f can be successful oral drugs according the rule of Lipinski. Bis-aminophosphonates tested exerted lower cytotoxicity towards human tumour cell lines than the aminophosphonates. The copolymer **7** showed excellent antiproliferative activity against cell lines HBL-100, MDA-MB-231, MCF-7 and HepG2. However, the *in vitro* safety testing revealed significant toxicity against Balb/c 3T3 mouse embryo cells. In contrast, the copolymer **6** showed complete absence of cytotoxicity against Balb/c 3T3 cells, but it inhibited the growth of breast cancer cells, cervical carcinoma cells (HeLa) and hepatocellular carcinoma cell cultures after prolonged (72 h) exposure.

The results from the fluorescent microscopic morphological studies correlate well with the data of the *in vitro* antitumour activity of the tested polymers and revealed apoptotic and necrotic alterations in breast cancer cells and in hepatocellular carcinoma cells after prolonged exposure, which point to the mechanisms of tumour cell death. The polymers (**4**-7) exhibited low (**4**, **6** and **7)** to moderate (**5)** clastogenicity *in vivo* and slightly inhibited bone marrow cell division, compared to Mitomycin C. The tested polyphosphoesters are expected to act *in vivo* as prodrugs of aminophosphonates and could be valuable as a new class of biodegradable polymer drug carriers.