In vitro evaluation of the genotoxicity of polymeric nanoparticles as carriers for oral drug administration

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In the last years, there has been an increased interest in the development of biocompatible and biodegradable compounds that can be used as drug delivery nanosystems for oral administration. To this aim, nanoparticles (NPs) synthesized with compounds which are commonly recognized to be safe, are used.

The aim of this study was to evaluate the genotoxicity of two polymeric (anhydride) NPs, Gantrez^{TM} (NPA) and Gantrez^{TM}–covered with mannosamine (NPA-M). The comet assay in combination with the enzyme formamidopypiridine DNA-glycosylase (FPG) and the mouse lymphoma assay (MLA) were used for this purpose. In addition, cell viability after NPs treatment was evaluated by a proliferation assay.

To study their genotoxicity potential, the comet assay was performed in L5178 TK$^{+/-}$ cells treated with the two NPs at five different concentrations (0.074-0.6 mg/mL) for 24h. Negative and positive controls were included in each experiment and three independent experiments were carried out. Furthermore, a cell proliferation assay was performed in parallel with the comet assay where cells were counted at 48 h after their incubation with the NPs at 37°C.

The MLA was conducted in L5178 TK$^{+/-}$ cells using the microwell version, according to the procedure described by the Organization for Economic Co-operation and Development guideline 490. A negative control, a positive control (MMS, 100 µM) and 10 concentrations of each NP were included in each experiment. The highest concentration tested in this test was 0.6 mg/mL; the rest of the concentrations were calculated by a decreasing factor of 3. The treatment was carried out with gentle shaking at 37°C during 24 h in a humidified CO_2 incubator. Two independent experiments were performed.

As a result, both NPs did not show any increase in the frequency of strand breaks, alkali-labile or FPG-sensitive sites in L5178 TK$^{+/-}$ cells treated at tested concentrations. Furthermore, treated cells did not indicate changes in the proliferation rate. However, NPA and NPA-M-SD did induce a statistically significant increase in the mutation frequency in this cell line at all tested concentrations after 24 h of treatment.