As shown by our previous studies, the PLGA nanoparticles (NP) coated with poloxamer 188 (P188) enable brain delivery of doxorubicin and its high anti-tumour effect against the intracranial C6 glioma in rats [1]. The objective of the present study was to evaluate the uptake of the P188-coated PLGA NP in the intracranial C6 glioma in rats. For visualization using scanning laser confocal microscopy (SLCM) and an intravital fluorescence imaging system Ivis® Spectrum CT (Perkin-Elmer), the NP were labeled with DiI (DiI-PLGA NP). The Dil-PLGA NP were administered i.v. into rats with intracranial C6 glioma on day 15 after tumour implantation. The presence of mass lesion was verified by previous MRI. Two hours after administration of the NP, the rats were perfused transcardially with paraformaldehyde, organs were recovered, and the fluorescence intensity was assessed using an Ivis® Spectrum CT system. The fluorescence intensity of the hemisphere with the implanted glioma was > 4-fold higher for the P188-coated NP (DiI-PLGA/P188 NP), as compared to the uncoated NP (45.1×10^6 vs 9.5×10^6 photons/sec/cm^2, respectively (Figure)). The quantitative fluorescence analysis on the tumor sections using SLCM also showed a significantly higher accumulation of the DiI-PLGA/P188 NP, as compared to the uncoated Dil-PLGA NP (Fig. 2). Mean fluorescence intensity values in the tumor were 1698.9±536.6 and 558.9±181.0 CU for the P188-coated and uncoated NP, respectively. The intensity values in the contralateral hemispheres for the same preparations were 293.4 ± 32.3 and 203.2 ± 22.9 CU, respectively. Thus, according to the SLCM data, the penetration of the Dil-PLGA/P188 NP into the tumor was 3 times more effective than that of the uncoated NP. The analysis of the magnified fluorescence images showed considerable accumulation of the Dil-PLGA/P188 NP both in the tumor interstitial fluid and inside the C6 glioma cells (Fig. 2B). At the same time, the Dil-PLGA-NPs were mainly localized in the epithelial cells of cerebral microvessels of the contralateral hemisphere (Fig. 2A).

In conclusion, the results of the study indicate that coating of the PLGA nanoparticles with poloxamer 188 considerably enhances their penetration into the brain tumor, which correlates with the previous results indicating the key role of this surfactant in the successful brain delivery by nanoparticles [1].

References


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