THE INFLUENCE OF STORAGE CONDITIONS ON THE ANTI-CANCER EFFICACY OF PLASMA-TREATED SOLUTIONS

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Over the last decade, plasma pharmacy has been an emerging research field within plasma medicine [1]. It mainly consists in the plasma activation of solutions that can then be used in contact with cells and tissues for therapeutic purposes. The anti-cancer properties of plasma-treated solutions are mainly due to the delivery of reactive oxygen and nitrogen species (RONS) [2,3]. To be considered as efficient anti-cancer drugs, plasma-treated solutions should be easily produced and stored. It is also essential that they maintain their anti-cancer properties over time and, if possible, that they can be stored at conditions accessible to most of the people. Given that among the variety of plasma-generated RONS, H_2O_2 and NO_2^- have been established as the main anti-cancer drivers of plasma-treated solutions [3], the cytotoxic activity of these liquids is highly dependent on the stability over time of these two reactive species. The purpose of this work was to assess the chemical stability of plasma-treated PBS(Ca^{2+}/Mg^{2+}), in terms of H_2O_2, NO_2^- and NO_3^- degradation, as a function of storage time and temperature. An atmospheric pressure plasma jet of coaxial electrode configuration driven by high voltage pulses in the kHz range was used to produce the plasma [4]. PBS(Ca^{2+}/Mg^{2+}) solutions were treated by the plasma, and then stored at 4 different temperatures: ~+20°C, +4°C, –20°C and –80°C. Alongside, untreated PBS(Ca^{2+}/Mg^{2+}) containing concentrations of H_2O_2, NO_2^- and NO_3^- (i.e., mimicking solutions) were stored at the same temperatures. The absolute concentrations of H_2O_2, NO_2^- and NO_3^- were measured in these stored solutions after 1, 7, 14, 21 and 75 days. Thus, the percentage of the degradation of those reactive species, in respect to their initial concentration, was determined. In parallel, the anti-cancer capacity of plasma-treated PBS stored at 4 or –20°C after 1, 7, 14 and 21 days was assessed on different cancer cell lines, in terms of cells viability and permeability. Our results show that for both plasma-treated and mimicking solutions of PBS, these long-lived reactive species remain stable for 21 days at room temperature or at +4°C and are slightly degraded after 75 days. On the contrary, significant degradation of the chemical reactivity of both plasma-treated and mimicking solutions is observed at –20 and –80°C, even after the first days of storage. This degradation is more significant for a storage temperature of –20°C, and especially for NO_2^-, whose concentration is reduced over 90% after 21 days of storage. These results were strongly supported by our findings on the cancer cells, as we show that the plasma-treated solutions stored at 4°C retain their anti-cancer effects over 21 days but not when stored at –20°C. We conclude that both plasma-treated and mimicking solutions of PBS(Ca^{2+}/Mg^{2+}) can preserve their cytotoxic activity, at least for 21 days, if stored at +20°C or +4°C, providing a basis for practical application of plasma-treated PBS or even mimicking solutions in cancer therapy. In the future, other storage conditions such as light and packaging should be appraised.

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Références

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