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The effect of radiation dose rate over the formation of protein-based nanoparticles for nanosized delivery of chemo and radiotherapeutics

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Recent studies demonstrated the development of papain and bovine serum albumin nanoparticles using gamma radiation (10 kGy) in presence of 20-30% (v/v) ethanol. With the purpose of producing stable and well defined nanocarriers, this work aims to determine the influence of different dose rates over protein nanoparticle formation. For this purpose, papain and BSA nanoparticles were synthetized in phosphate buffer (50 mM, pH 7.2) and ethanol (20-30%, v/v) using a radiation dose of 10 kGy and dose rate of 0.8, 2, 5 and 10 kGy.h-1. After irradiation, samples were evaluated by dynamic light scattering, fluorescence and proteolytic activity to verify the size, secondary structure and monitoring of the enzymatic activity, respectively. For papain nanoparticles it was observed that the dose rate did not influence the particle size formation, however crosslinking evidenced by bityrosine showed that samples irradiated at 0.8 and 5 kGy.h-1 presented higher bityrosine levels. On the other hand, BSA nanoparticles presented different results if compared to papain NPs. Different dose rates caused different and non-linear size increase for each condition, following the order: 5 > 10 > 0.8 > 2 kGy.h-1. However, in terms of crosslinking formation, a linear increase was registered, as at 0.8 kGy.h-1 the smallest signal was achieved, whereas at 10 kGy.h-1 the highest signal was recorded. In conclusion, BSA nanoparticles were more sensitive to different radiation dose rates than nanopapain. Optimized results in terms of size increase and higher bityrosine levels were observed for the samples irradiated at 5 kGy.h-1, in which nanoparticle formation will occur faster if compared to the synthesis carried out under distinct conditions. As final applications of the system concert their use for the delivery of chemo or radiotherapeutics, the loading of paclitaxel, a well-known chemotherapeutic agent, and radiolabeling with tecntetium-99m, a radioisotope suitable for biomedical applications, have also been performed with high efficiency, thus demonstrating a proof of concept of such systems.