Controlled Gamma Irradiation Approach as a Tool for Production of Uncommon Bradykinin Analogues.

Nardi, D. T.[1]; Rosa, J. C.[2]; Jubilut, G. N.[1]; Silva, M. C.[3]; Nascimento, N.[3]; Nakaie, C. R.[1*]

[1]Departamento de Biofísica – UNIFESP. dtnardi@biofis.epm.br;
[2]Faculdade de Medicina de Ribeirão Preto – USP
[3]Instituto Nacional de Pesquisas Energética (IPEN)-USP, SP., Brazil.

The reaction products and mechanisms involved in the radiolysis of macromolecules of biological relevance are object of several studies. These factors (mainly the oxidation induced by free radicals) are known to be involved in many pathological disorders such as diabetes, cancer, Alzheimer's and Parkinson's diseases. In order to unravel the potential of gamma radiation approach for focusing this field throughout the investigation of peptide structure modifications and characterization of generated analogues, the present report selected the vasoactive bradykinin (RPPGFSPFR, BK). This work is indeed a continuation of our recent work [Nardi et al., *Int. J. Radiat. Biol*. (2008) 84: 937-944], where modifications of angiotensin II structure were focused. Purified BK was submitted to 1 to 15 kGy gamma radiation doses and a progressive decrease in the amount of native BK in solution was observed as the radiation dose increases. The irradiated BK solutions were purified and two prominent analogues were isolated - Tyr^{8}-BK and m-Tyr^{8}-BK. Pharmacological assays in muscle preparation (rat uterus) indicated that these analogues retained 51% and 13% of the native BK activity, respectively. Surprisingly, these findings allowed concluding that the gamma irradiation affects only the Phe residue at position 8 and not 5, thus stressing an interesting residue and sequence dependent effect in the peptide gamma irradiation strategy. An expanded investigation is underway involving other physiologically relevant peptides aiming at elucidating the potential of this innovative irradiation approach for producing unusual peptides not easily achieved through the conventional peptide synthesis methodology. Supported by Fapesp and CNPq.