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Pirocarbotrat™: a new radiopharmaceutical labeled with ^{32}P for the treatment of solid tumors. Therapeutic action and radiodosimetric calculations.

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Pirocarbotrat™ is a gelatin protected charcoal suspension labeled with chromic [^{32}P] pyrophosphate. To evaluate its effectivity as a therapeutic agent for the treatment of solid tumors, studies of therapeutic action and dose calculations, were carried out after an intratumoral single dose of this radiopharmaceutical.

The preparation of the Pirocarbotrat™ (BACON Laboratories) was described elsewhere [1, 2]. We used 28 female Sprague Dawley rats in which experimental mammary adenocarcinomas were induced. The tumors were injected with a single dose of 18.5 MBq. The size of the injected and not-injected tumors (controls) was determined with a caliper along two axes as a function of time. Once the experiment was finished, animals were sacrificed to extract their organs and the injected tumors. The radioactivity of the samples as well as a ^{32}P standard (18.5 MBq) were measured in a monochannel gamma spectrometer, using the Bremsstrahlung photons of ^{32}P. Representative pieces of tissues from the treated and control tumors were selected for histopathological examination. The histological findings were evaluated according the type and degree of local response to the radiopharmaceutical, concerning the neoplasia and the nonneoplastic surrounding tissue.

The results show that after 32 days of treatment, the percentage of activity found in the tumor was 84.50 $\pm$ 2.60 %, while the percentage of activity found in the other evaluated organs was almost negligible as it can be observed in Figure 1 [1].

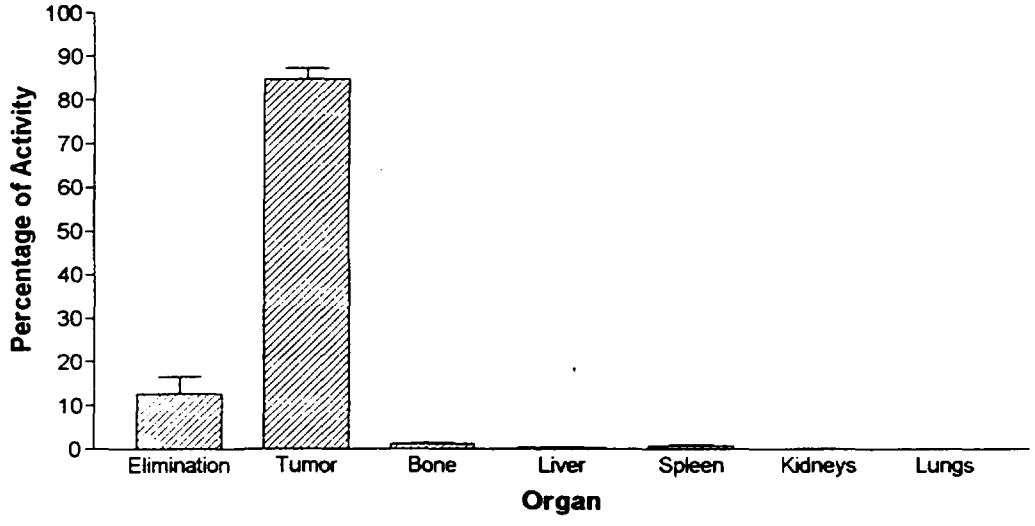

Fig. 1. Biological distribution of Pirocarbotrat™ after 32 days of treatment.

The therapeutic action was evaluated by the mean size ratios (M.S.R.) defined as the tumor size at the last day of life / tumor size at the day of the injection and the percentage of tumor regression (P.T.R.) which was 0.6 ± 0.3 and 78.3%, respectively. Our histological observations were carried out 32 days after the injection, i.e., once 80% of the ^{32}P radioactivity was delivered to and absorbed by the tumor. The treated tumors showed closely packed black charcoal particles at the injection point, which are shown always in sharply demarcated big clusters and always associated with necrotic debris from the neoplastic tissue. Nearby the border of the cluster variable tumor necrosis can be observed as well as reparative changes arising from the surrounding normal tissues that replace the necrotic areas progressively. The extension of the necrotic tissue in the tumor vicinity is variable, ranging from 1 to 4 mm. Radiodosimetric calculations demonstrate that the dose absorbed by the tumors was 6190 Gy, according to the Medical Internal Radiation Dose Committee (MIRD) of the Society of Nuclear Medicine. The dose absorbed by the rest of the organism is 0.533 Gy. The rate dose to the tumor/dose to the rest of the organism is 1.17×10^4. These results might be explained due to a low mobilization of the radiopharmaceutical from the injection point, which allows to deliver a high radiation dose to the tumor provoking a consequent tumor size reduction, confirmed by the histopathological findings, where it is clearly demonstrated that the Pirocarbotrat™ particles remain closely packed and do not move from the injection point.

The therapeutic efficiency of Pirocarbotrat™ is due to its low mobilization and its high concentration in solid tumors. This behavior allows the delivery of high doses to the tumor, with low irradiation to surrounding tissues and organs. Irradiation to the rest of the organism is insignificant. We can conclude that, Pirocarbotrat™, a non-sealed beta radiation source, behaves very closely to a sealed beta radiation source when it is intratumorally injected in solid tumors.

References

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