IAEA-SR-209/43

Re-186 Bleomycine : Radiopharmaceutic for diagnosis and therapy ?

S.SZOSTAK, S. TUSTANOWSKI, B. BIRKENFELD, R. ALMAKIEWICZ
Department of Nuclear Medicine, Pomeranian Medical Academy, Szczecin, POLAND

There is tremendous interest in developing of new radiopharmaceuticals for diagnosis and treatment of malignant diseases. Last decade development of beta emitting radiopharmaceuticals for palliative treatment of bone metastases is a good example of that [1] . Among other chemical compounds usefulness of bleomycine was investigated for diagnosis of malignant tumours. Cold bleomycine is a chemiotherapeutic agent used for therapy of malignant tumours. While labelled with Co57 [2], Tc99m [3] or In111 [4] and was used for scintigraphic diagnosis of different kind of tumors. There was different biodistribution and stability of radiolabelled bleomycine according to which radinuclide it was labelled. Though it was not widely used very promising results were obtained with Tc99m labelled bleomycine (BLM). It was rapidly cleared from the blood pool and taken up by neoplastic tumors. There were reports showing its usefulness for diagnosis of eye ball neoplastic diseases, breast cancer , neck tumours [5].

In this work we undertook the effort to label BLM with Re186. Re186 and Tc99m belong to the same group in periodic table. Re186 has a relatively short physical half -life of 90.64 h. It has both beta emission suitable for therapy (Emax = 1.07 MeV) and gamma emission suitable for external imaging (Eg = 137 KeV). Chemical properties of Tc99m and Re186 are similar so one can assume that probably methods of labelling and biodistribution of BLM-Re186 and BLM-Tc99m could be comparable as well. Labelling BLM with Re186 allow for obtaining the radiopharmaceutical suitable for radioisotope therapy of neoplastic tumours.

The aim of this work was to develop methods of BLM labelling with Re186.

There were the following methods used for labelling :

- conventional one with SnCl 2,
- electrolitic,
- with the use cationit -Sn complex ,

Natriumperr(Re186) Mallincrodt Medical , $SnCl_2$ (Fluka) , Dowex1x8, Dowex 50x8, Dowex 50Wx4 in sodium or hydrogen form ,100-200 mesh Serva were used for labelling . The methods were the same as for BLM-Tc99m [5]. The products were analysed by thin layer chromatography on Silica Gel developed in a mixture of 10% CH_3COONH_4 : CH_3OH (1:1 V/V). The yield of labelling by these three methods was very unsatisfactory.

Methods of HEDP-Re186 labelling were taken into consideration [6,7]. Gentisic acid (2,5-Dihydroxybenzoic acid) was used during the labelling and the reaction mixture was incubated at 100°C for 10 min.

In spite of changes in labelling procedure the yield of labelling by conventional method was still very poore. But by cationit-Sn complex method yield of labelling was 95%, by electrolitic method was 98%.

Authors showed that it is possible to label BLM with Re186. BLM-Re186 can be pottentially a new agent for diagnosis and treatment of malignant tumours. Further investigations are carried out.

References

1. JMH De Klerk, A van Dijk, AD van het Schip, BA Zonnenberg, PP van Rijk Pharmacokinetics of rhenium-186 after administration of rhenium-186-HEDP to patients with bone metastases. *J Nucl Med* 1992;33:646-651.
2. Maeda T, Kono A, Kojima M. Tumor scanning with 57Co - Bleomycin. *Radioisotopes* 1972;21:436-438.
3. Yokoyama A, Terauchi Y, Horiuchi K et al. The importance of the chemical state of 99mTc radiopharmaceuticals : an effective tumor imaging form of 99mTc -Bleomycin. *Inter J Appl Radiat Isotop* 1978;29:549-555.
4. Renault H, Rapin J, Rudler M, Robert J, Nouel JP, Silvestre M. Labelling method using the chelation of various radioactive cations by some polypeptides application to bleomycin. *Chim Ther* 1972;7:232-235.
5. Szostak S. Doctorate thesis: Pomeranian Medical Academy, 1993, Szczecin, Poland: Methods of bleomycin labelling with different radionuclides suitable for scintigraphy.
6. A van Aswegen, A Roodt, J Marais et al. Radiation dose estimates of 186Re-hydroxyethylidene diphosphonate for palliation of metastatic osseous lesions : An animal model study. *Nuc Med Comm* 1997;18:582-588.
7. Owunwanne A, Patel M, Sadek S. The handbook of radiopharmaceuticals. Chapman & Hall Medical, 1995, 185-186.