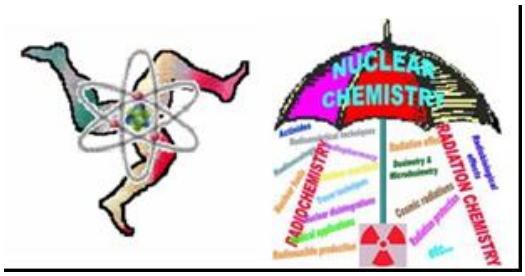


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# In vivo biodistribution of I-131 labeled bleomycin (BLM) and isomers (A2 and B2) on experimental animal models

*Tuesday 20 September 2011 12:00 (15 minutes)*

BLM isolated from the fermentation products of Streptomyces verticillus in 1966 by Umezawa in Japan belongs to a family of structurally related small glycopeptides (1 kDa) that give rise to single-stranded DNA breaks and DNA double-strand breaks (DSBs) in a metal- and oxygen dependent manner1. The BLM used clinically is a mixture of three distinct isomers, A2 (the most abundant, 65 %), B2 (30 %), and DM, which is a deme thylated form of A2 (5 %). BLM is known to form complexes with a range of metals, some of which have been shown to exhibit tumor-localizing properties as demonstrated by radiotracer experiments, and subsequently by clinical imaging studies2. Furthermore, it has been proposed that BLM complexes may be useful for targeted radiotherapy using isotopes of indium or ruthenium 3. Although BLM catalyzes DNA cleavage with some degree of sequence specificity, it differs from conventional endonucleases by generating 3-phosphoglycolate blocked DNA ends. BLM is a potent cancer chemotherapeutic , but its clinical use is hampered by DNA damage-independent side effects including life-threatening pulmonary fibrosis. As these side effects are dose-dependent, rational combination of BLM with appropriate DNA repair inhibitors could conceivably be highly beneficial in the clinic1. Of the range of DNA lesions caused by BLM, DSBs are believed to be the most cytotoxic1, 4. In yeast, where even a single unrepaired DSB is eventually lethal. Telomeres consist of tandem hexanucleotide (TTAGGG)n repeats that cap the termini of eukaryotic chromosomes and play essential roles in maintenance of chromosomal stability and cell viability. The complex that is responsible for telomerase activity includes a reverse transcriptase that adds on telomeric repeats at the end of chromosomes using an RNA template. This enzyme is not active in most somatic cells but is active in most human tumors, and is, therefore, considered as being of high potential as a selective target for different anti-tumor strategies. One approach in the search for tumor-localizing radiopharmaceuticals of greater specificity and diagnostic accuracy is to investigate available chemotherapeutic drugs.

This paper deals with BLM compounds, BLMs, and the attempts to radiolabel these compounds with an appropriate nuclide (such as 131I) and evaluate the usefulness of the resultant radiopharmaceutical for the diagnosis and management of malignant tumors using nuclear methods . In case of combination of the cytotoxicity of BLMs with high radiotoxicity of an appropriate radionuclide such as 125I or another Auger and/or a -emitting radionuclide, it is expected that very effective radiolabeled anti cancer drugs will be designed, which will have large potential applications in cancer therapy.

Bleomycins (BLMs; BLM, A2, and B2) were labeled with 131I and radiopharmaceutical potentials were investigated using animal models in this study . Quality control procedures were carried out using thin layer radiochromatography (TLRC), high performance liquid chromatography (HPLC), and liquid chromatography (LC/MS/MS). Labeling yields of radiolabeled BLMs were found to be 90, 68, and 71 %, respectively. HPLC chromatograms were taken for BLM and cold iodinated BLM (127I-BLM). Five peaks were detected for BLM and three peaks for 127I-BLM in the HPLC studies. Two peaks belong to isomers of BLM. The isomers of BLM were purified with using HPLC. Biological activity of BLM was determined on male Albino Wistar rats by biodistribution and scintigraphic studies were performed for BLMs by using New Zelland rabbits. The biodistribution results of 131I-BLM showed high uptake in the stomach, the bladder, the prostate, the testicle, and the spinal cord in rats. Scintigraphic results on rabbits agrees with that of biodistributional studies on rats The scintigraphy of radiolabeled isomers (131I-A2 and 131I-B2) are similiarly found with that of 131I-BLM.

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