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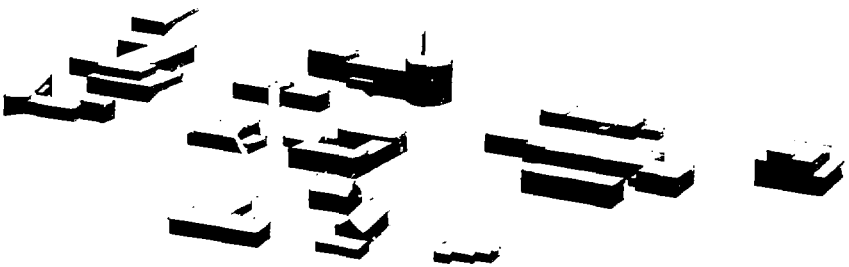

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^{131}I-3-IODOBENZYLGUANIDINE (^{131}I-3-IBG) AS A SCINTIGRAPHIC AGENT FOR THE VISUALIZATION OF ADRENAL MEDULLA TUMOURS

by

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Dag-Erik Heggli, Bjørn I. Brorson and Per O. Bremer

APPROVED

ABSTRACT

A method of labelling 3-iodobenzylguanidine with ^{131}I was developed using Cu-(II)-ions as a catalyst. ^{131}I-3-iodobenzylguanidine will be used for scintigraphic localization of pheochromocytomas, which are tumours of the adrenal medulla.

KEY WORDS
Localization of adrenal medulla tumours; ^{131}I-3-iodobenzylguanidine

CLASSIFICATION AND/OR SUBJECT GROUP
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1. INTRODUCTION

The tumours of adrenal medulla, pheochromocytomas and neuroblastomas may in some cases be small or located extra-adrenally. In those cases ^{131}I-labelled 3-iodobenzylguanidine is a valuable tool, since 3-IBG concentrates in adrenal medulla tumours because of its analogy to the catecholamines. Injecting a dose of 0.5 mCi ^{131}I-3-IBG (2.5 mCi/mg), which is an adult dose, allows the scintigraphic localization of the tumours, thus guiding the surgeon.

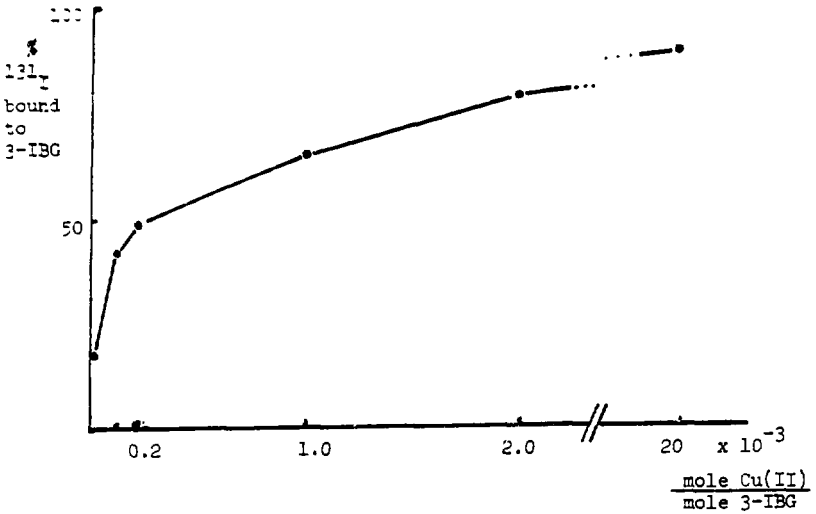
2. LABELLING OF 3-IBG WITH ^{131}I

The final step of our production of ^{131}I-3-IBG consists of an isotopic exchange of the aromatic bound iodine. That exchange was found to be catalyzed by cupric-(II)-ions. A similar effect has been reported for the labelling of iodohippuric acid and N-isopropyl-p-iodoamphetamine.

2.1. Procedure

3-IBG·$\frac{1}{2}H_2SO_4$ and Cu(II)SO_4 were dissolved in a 0.1 M $NH_4H_2PO_4$ buffer and mixed with ^{131}I-NaI. The solution was evaporated to dryness by heating. After addition of water, the solution was heated with reflux for two hours.

The figure shows the effect of the addition of Cu-(II)-ions:



The I^- ions were removed after the labelling by anionic exchange chromatography (Dowex 1). The final product was made isotonic and bacteriostatic by the addition of acetate buffer, saline and benzylalcohol. The product was filtered through a membrane filter with a pore size of 0.22 µm, and was apyrogenic tested by limulus test.

3. ADRENAL UPTAKE IN MICE

Species: BOM:NMRI, female, 26 - 34 g

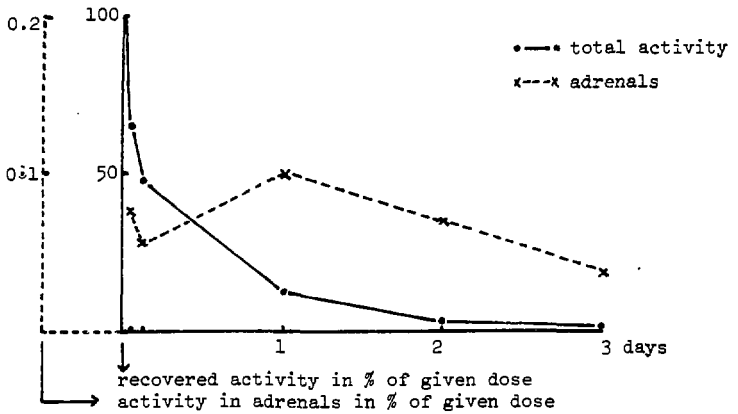
Injected dose: 10 µCi ^{131}I-3-IBG (1 mCi/mg) given by intravenous injection in the tail

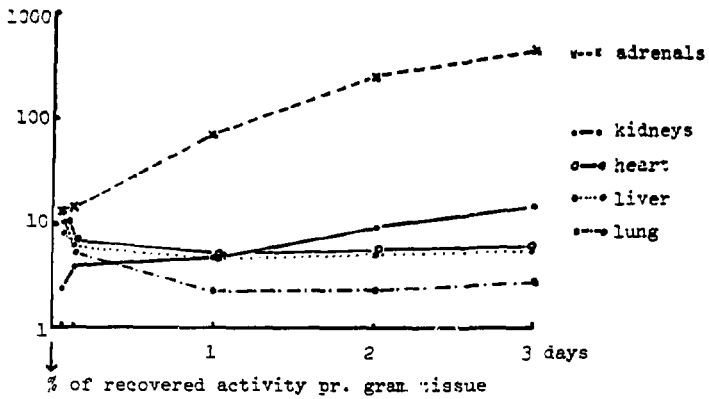
The different organs were dissected, and the activity in each organ was counted in a gamma well counter. The adrenal medulla and the cortex were counted together. The figures show the

rapid excretion of the activity from the total body and the slower elimination from the adrenals. The adrenals showed a very low uptake in per cent of the given dose, but this may be dependent on the species. In addition, hyperactive tumours will show a higher uptake than normal adrenals.

On the basis of the lower elimination rate of the adrenals, the activity concentration (per cent uptake per gram tissue) increased very much in the adrenals compared to the other organs. The adrenal activity increased from 10.4 per cent of the recovered activity per gram at one hour after the injection to 430 per cent of the recovered activity per gram at three days. All the other organs showed only minor changes, all in the range of 1 - 10 per cent of the recovered activity per gram. The blood level was between 0.5 and 1.0 per cent of the recovered activity per gram at all times (one hour - three days).

The kidney activity increased from 2.2 to 14.3 per cent of the recovered activity per gram during the test. This may reflect an urinary elimination of the productor its metabolites.





The activity in the organs that were measured, but not shown in the figures, blood, stomach, instetin, spleen and carcass, were below 10 per cent of the recovered activity per gram tissue at all times.

4. ADRENAL UPTAKE IN DOG

The test was performed on a healthy female golden retriever and showed sufficient uptake in the adrenals to allow scintigraphic imaging 90 hours after the injection.

5. RADIOCHEMICAL ANALYSIS

As a rapid method for the control of the radiochemical purity, paper electrophoresis has been used with a 0.025 M sodium acetate buffer at a pH of 4.5, Whatman paper no 1 and an electric field of 100 V per cm for ten minutes. 3-IBG migrates approximately 4 cm as a cation and iodide approximately 12 cm as an anion. The more time-consuming TLC with silica gel G plates and propan-1-ol/10% NH_3 (3:1) as an eluent has been used to verify the results which were obtained by electrophoresis.

R_f values

3-IBG: 0.5

Iodide: 0.85

6. RADIOCHEMICAL STABILITY

The radioactive concentration of the ^{131}I-3-IBG has been found to be important for the radiochemical stability of the product. In one week 10 per cent iodine is released from ^{131}I-3-IBG at an initial radioactive concentration of 1.1 mCi/ml, whereas 1.5 per cent iodine is released in one week at an initial radioactive concentration of 0.2 mCi/ml. The specific activity seems to have less influence on the stability. Increasing the specific radioactivity from 3 mCi/mg to 12 mCi/mg was not found to influence the radiochemical stability.

Presented as a poster at the "First Symposium on Radiopharmacy and Radiopharmaceuticals" 27th - 30th March 1983, Elsinore, Denmark.

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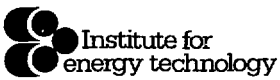

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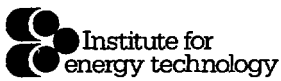

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