

## 研究报告

# 新型乏氧显像剂<sup>99</sup>Tc<sup>m</sup>-N4IPA的制备及小鼠体内外乏氧选择性研究

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**摘要** 目的 探求结构简单、易于标记、性能优良的新型乏氧显像剂。方法 用标记新型乏氧配体N4IPA (1-(4-硝基咪唑-1-基)丙醛羟氨基化合物), 用TLC及HPLC法对标记物进行质控, 并检测标记物的体外稳定性、脂水分配系数、血液清除情况, 最后通过体外细胞摄取实验及荷瘤动物体内分布研究了解标记物在乏氧细胞和肿瘤组织中的聚集情况。结果 标记物的放化纯度>90%, 脂水分配系数 $2.71 \pm 0.05$  (n=3), 为亲脂性; 在室温、37°C及37°C+人血白蛋白3种情况下均较稳定。体外细胞摄取实验表明: 加入标记物后1-4h, 乏氧体系中CHO细胞对标记物的摄取百分数均高于相应的非乏氧体系 ( $p < 0.05$ ), 且乏氧体系中CHO的摄取百分数随时间延长而逐渐增高。血液清除实验表明: <sup>99</sup>Tcm-N4IPA在正常小鼠体内的血液清除符合二室代谢模型, 其分布相半衰期为15 min, 消除相半衰期为10.2 h。荷脑胶质瘤U87裸鼠显像及体内分布数据表明: 标记物主要经肾脏排泄, 还有部分经肝肠途径排泄。标记物在肿瘤内有一定聚集, 其2 h及4 h的瘤/血分别为 $1.57 \pm 0.31$ 和 $1.98 \pm 0.25$ , 而瘤/肌肉分别为 $11.89 \pm 1.64$ 和 $13.11 \pm 1.47$ 。结论 <sup>99</sup>Tcm-N4IPA具有乏氧选择性, 可使肿瘤清晰显影, 有望成为一种新的肿瘤乏氧显像剂, 但尚有待于进一步研究。

关键词 [<sup>99</sup>Tcm](#) [乏氧](#) [硝基咪唑类化合物](#)

分类号

## Preparation and Preliminary Evaluation of the in vivo and in vitro hypoxic selectivity of a novel hypoxic agent <sup>99</sup>Tc<sup>m</sup>-N4IPA

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**Abstract** Objective To develop a novel hypoxic agent with simple structure、excellent performance and easily labeled technique. Method A new hypoxic ligand 1-(4-Nitroimidazole-1-yl)-propanhydroxyiminoamide (N4IPA) was labeled with <sup>99</sup>Tcm, then the products were analyzed by TLC and HPLC and were detected the in vitro stability、the octanol-water partition coefficient and the pattern of blood clearance. Finally, the in vivo and in vitro hypoxic selectivity of the products were researched by cell up-take test in vitro and biodistribution and imaging in vivo with nude mice bearing U87 glioma. Results The labeling yield was >90% and the octanol-water partition coefficient was  $2.71 \pm 0.05$  (n=3), and the products kept pretty good stability in room temperature、37 °C and in 37 °C with human serum albumin. The cell up-take test showed that the Chinese hamster ovary (CHO) cell took more products in hypoxic system than that in normal oxygen system ( $p < 0.05$ ), and the up-take percent in hypoxic system increased with time. Pattern of blood clearance of <sup>99</sup>mTc-N4IPA was defined as two-compartment model ( $T_{1/2\alpha} = 15$  min,  $T_{1/2\beta} = 10.2$  h). Imaging and distribution in nude mice bearing U87 glioma revealed that the products were excreted mainly by kidneys and partly by liver and intestines. <sup>99</sup>mTc-N4IPA could be accumulated in tumor, and the tumor-blood ratio in 2 hours and 4hours was  $1.57 \pm 0.31$  and  $1.98 \pm 0.25$ , respectively, and the tumor-muscle ratio in 2 hours and 4hours was  $11.89 \pm 1.64$  and  $13.11 \pm 1.47$ . Conclusion <sup>99</sup>Tcm-N4IPA possessed hypoxic selectivity with clear tumor imaging, so it would be a potential hypoxic-agent, but it would need more research work.

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