

双酚胺酸在小鼠整体放射自显影中的定位分布¹

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Whole-body autoradiographic localization of catecholamic acid in mice¹

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ABSTRACT Catecholamic acid [catechol-3,6-bis-(methyleneimino diacetic acid)] is a chelating agent synthesized in our institute. Whole-body autoradiographic study was carried out to determine the distribution of [¹⁴C]catecholamic acid in 5 adult ♂ mice. Each mouse was injected iv 370 kBq. After various times the mice, under ether anesthesia, were immersed in a mixture of dry ice and hexane. Whole-body sections were made at -20 °C, 20 μm in thickness. Results showed: (1) At 5 min, higher radioactivities appeared in blood, kidneys, gastrointestinal mucosa, bone, skin, and hair; moderate concentrations in liver, lungs, spleen, and salivary glands. (2) During 20 min and 3 h, the radioactivities decreased (gradually) in all tissues except the bone. (3) Intense radioactivity persisted in the bone, while only traces remained in the kidneys and intestinal mucosa throughout the 24 h period of observation.

KEY WORDS catecholamic acid; tissue distribution; autoradiography

摘要 小鼠 iv [¹⁴C]双酚胺酸370 kBq/鼠。不同时间后乙醚麻醉浸入干冰己烷混合液冻死,用整体放射自显影观察¹⁴C的分布。5 min,血、肾、胃肠道粘膜、骨、皮毛的放射性最高;肝、肺、脾和唾液腺次之。除骨外20 min至3 h其它组织均降低。24 h,肾和肠还残留少量放射性,但骨中还保持高的放射性。

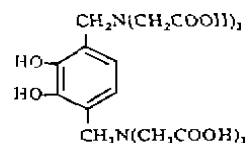
关键词 双酚胺酸; 组织分布; 放射自显影术

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铀中毒可引起严重的肾、肺、骨等脏器和组织的损害并能诱发肿瘤^[1,2]。目前对铀的解毒和促排尚无满意药物。在研究铀的解毒和促排过程中,我所首先发现儿茶酚-3,6-双(甲叉亚氨基二乙酸),定名为双酚胺酸(catecholamic acid),一种邻苯二酚结构氮羧型螯合剂,结构式如下:



Catecholamic acid

双酚胺酸对铀有明显解毒和促排效果^[3],并对其他金属也有一定的解毒和促排作用^[4]。本文用整体放射自显影术和微光密度法对双酚胺酸进行了定位、定量和分布的观察。

MATERIALS AND METHODS

[¹⁴C]双酚胺酸由本所合成室合成,放射性活度为45.62 MBq·g⁻¹,用前加蒸馏水配制成4%浓度,用NaHCO₃调至pH 7供小鼠iv用。♂小鼠5只,体重27.6±1.8 g。切片采用LKB-2250型整体冰冻切片机。F₅型X片,上海感光胶片厂产品。

小鼠iv [¹⁴C]双酚胺酸370 kBq/鼠。分别在注射后5, 20 min, 1, 3和24 h用乙醚深度麻醉,浸入己烷和干冰混合液(<-70 °C)中速冻15 min取出,剪去四肢和尾巴,用1.5% CMC在金属盒内冰冻包埋。在-20 °C整体切片机中制成20 μm厚的整体切片,冰冻干燥5 d,取出在暗室中和X片对贴^[5]。在4 °C冰箱中曝光6 wk后,显影5 min,定影20 min,水洗30 min,晾干,制成像片。像片的白色部分表示放射性。微光密度计测定每鼠相邻3张X光片上的血、肾、肝、骨等组织。

RESULTS

小鼠 iv [^{14}C]双酚胺酸, 5 min, 肾、骨、血、胃肠道粘膜、皮和毛放射性最高; 肺、肝、脾和唾液腺的放射性次之 (Fig 1, 5 min, Plate 3). 20 min, 1, 3 h 骨、肾和尿的放射性最高, 其次血、肝、胃肠道粘膜等组织 (Fig 1, 20 min, 1, 3 h, Plate 3). 24 h 时骨还留有较高放射性, 肾、肝、胃肠道粘膜、脾、皮和毛放射性低, 肺和血的放射性已基本消失 (Fig 1, 24 h, Plate 3).

微光密度计测定, 5, 20 min, 1, 3, 24 h 血、肝、肾和骨其结果和上述像片结果相似。

Tab 1. Comparative densitives of radioactivities in tissues on X-films after iv [^{14}C]catecholamic acid 370 kBq/mouse. $n=3$, $\bar{x}\pm s$.

	Blood	Bone	Kideny	Liver
5 min	8.1 \pm 0.5	8.2 \pm 0.8	9.8 \pm 1.2	6.2 \pm 0.2
20 min	6.5 \pm 0.4	8.2 \pm 0.8	7.5 \pm 1.1	5.5 \pm 0.3
1 h	3.2 \pm 0.2	7.9 \pm 1.4	6.5 \pm 0.5	4.5 \pm 0.1
3 h	1.6 \pm 0.1	7.9 \pm 1.2	5.2 \pm 0.4	3.9 \pm 0.5
24 h	0.9 \pm 0.12	7.8 \pm 1.3	4.1 \pm 0.5	2.5 \pm 0.2

DISCUSSION

本实验采用的整体放射自显影术和微光密度法, 能准确地显示出双酚胺酸在小鼠体内各脏器组织中的定位、分布和含量。这种实验均在低温条件下操作, 排除了药物在体内的扩

散、移位等人工假象。

在给 [^{14}C]双酚胺酸后5个不同时间中, 各组织的放射性强度依次为肾、尿、血、胃肠道粘膜、皮、毛、肺、肝、脾和唾液腺并随时间延迟有规律地下降, 在24 h 时小鼠体内还残留少量的放射性, 但骨是例外, 骨在各个时间均很高。

小鼠 iv [^{14}C]双酚胺酸对骨有较强的亲和性, 而骨又是铀中毒的靶器官之一, 所以双酚胺酸易进入骨中, 对清除骨中积蓄的铀或许是有利因素。另外此药和短半衰期放射性核素螯合还有可能成为核医学中的骨显像剂, 这对诊断骨质病变是很值得试探的。

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