

论文

口服二巯基丁二酸的毒性和对铅、铜、锑、镉、铊、钷的促排作用

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摘要:

小鼠一次灌胃二巯基丁二酸(DMSA)混悬剂的LD₅₀为6g/kg,大白鼠为4g/kg。正常狗每天灌DMSA0.5g/kg共6周(5天/周)给药后食量减少,呕吐,体重减轻。血象、血糖、心电图、肝功能和肾功能均无显著变化。解剖一狗见十二指肠有少量充血。灌服0.2g/kg组无明显症状。兔一次灌服DMSA后半小时,血中SH含量达高峰,5小时内血中SH浓度已明显下降。小鼠皮下注射²¹⁰Pb-醋酸铅后以骨和肾²¹⁰Pb含量最高。静注二巯基丁二酸钠(Na-DMS)或灌服DMSA可排除体内吸收²¹⁰Pb,二者均非常显著降低骨和肾中²¹⁰Pb。兔皮下注射硫酸铜后,DMSA可明显促进尿铜的排泄。加服NaHCO₃或枸橼酸钠可加强DMSA的排铜作用。小鼠分别肌注¹²⁵Sb-吐酒石、⁹⁰Sr-硝酸锶、²⁰⁴Tl-硫酸亚铊和¹⁴⁷Pm-硝酸钷后立即灌胃DMSA和NaHCO₃,DMSA明显增加放射性金属在尿中排泄。促使¹²⁵Sb排泄增加6倍、⁹⁰Sr 2倍、²⁰⁴Tl 11倍和可提高¹⁴⁷Pm 12倍。血和大多组织中放射性都有降低。上述结果提示口服DMSA可用于金属中毒治疗。DMSA比Na-DMS稳定低毒,值得继续研究。

关键词:

DIMERCAPTOSUCCINIC ACID PER OS PROMOTED THE EXCRETIONS OF Pb,Cu,Sb,Sr,TI AND Pm

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Abstract:

After a single intragastric gavage to mice and rats, the LD₅₀ of 2,3-dimercaptosuccinic acid (DMSA) were found to be 6 and 4g/kg, respectively. Dogs were given intragastrically DMSA 0.5 g/kg daily (5 days/week) for 6 weeks. Vomiting occurred and food intake decreased, thus causing a loss of body weight. However, no remarkable changes were found in blood picture, blood glucose, electrocardiogram, liver function tests (BSP, serum alkaline phosphatase, thymol turbidity and SGPT) and renal function tests (NPN and creatinine). Autopsy revealed a slight congestion in the duodenum. A daily dose of 0.2 g/kg caused no pathological signs. In rabbits given an intragastric gavage of DMSA, the blood SH content rose to a peak at 1/2 hour, and then declined in 5 hours. In mice given a subcutaneous injection of lead acetate (²¹⁰PbAc₂) the bone and kidney contained more ²¹⁰pb than other organs. Both DMSA and sodium dimercaptosuccinate (Na-DMS) could diminish the ²¹⁰pb contents in tissues and promote the urinary excretion of ²¹⁰pb. In rabbits given a subcutaneous injection of CuSO₄ an intragastric garage of DMSA hastened the urinary excretion of copper markedly. Both sodium bicarbonate and sodium citrate enhanced the effect of DMSA. Mice were given an intramuscular injection of K-¹²⁵Sb-tartrate, ⁹⁰Sr (NO₃)₂, ²⁰⁴Tl SO₄ or ¹⁴⁷Pm(NO₃)₃, followed immediately by an intragastric gavage of DMSA and NaHCO₃. There appeared a striking increase of metal excretion into the urine, amounted to about 6 times for ¹²⁵Sb, 2 times for ⁹⁰Sr, 11 times for ²⁰⁴Tl and 12 times for ¹⁴⁷pm as compared to the control mice. The radioactivities in blood and tissues decreased. These results indicate the benefits of DMSA per os in the treatment of intoxications by certain metallic compounds. DMSA is very stable and may be administered orally with little toxicity. Further studies on DMSA is warranted.

Keywords:

收稿日期 1979-04-17 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

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