中国药理学与毒理学杂志 2004 18 (2): 127-133 ISSN: 1000-3002 CN: 11-1115/R

论著

马兜铃酸对培养的叙利亚仓鼠胚胎细胞形态学转化的影响

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收稿日期 2003-11-3 修回日期 网络版发布日期 2008-8-21 接受日期 2004-1-8

摘要 目的 大量的研究证据表明，叙利亚仓鼠胚胎(SHE)细胞转化试验可能是目前用于检测致癌物和研究化学致癌机制的试验中生物相关性最强短期试验。本研究旨在检测来源于马兜铃鼠属类草药中的主要活性成分马兜铃酸(AA)引起SHE细胞形态学转化的可能性和抗氧化剂α-生育酚对AA所诱导的SHE细胞形态学转化的影响，并以此为例来说明SHE细胞转化试验可以用于检测营养保健品和中草药中可能存在的致癌或抗癌成分。方法 在进行正式的细胞形态学转化试验之前，先进行了初步的剂量范围选择试验，以确定用于形态学转化试验的AA的浓度。剂量范围选择试验是在24 h染毒或7 d连续性染毒的两种条件下进行的。根据剂量范围选择试验的结果，那些引起0%～50%细胞毒性的剂量被用于24 h染毒或7 d连续性染毒的细胞形态学转化试验来检测AA引起SHE细胞形态学转化的可能性。至于α-生育酚对AA所诱导的SHE细胞形态学转化的影响，则使用了用可引起SHE细胞形态学转化浓度的AA和100 μmol•L^{-1} α-生育酚同时处理SHE细胞的方法进行了观察。结果 在7 d连续性染毒的条件下，0.4, 0.8以及1.6 mg•L^{-1}的AA引起了SHE细胞形态学转化率的显著性升高；在24 h染毒的条件下，1.0, 1.5, 2.5, 4.5和5.0 mg•L^{-1}等5个剂量组的形态学转化率明显地高于阴性对照组。当在培养液中加入100 μmol•L^{-1} α-生育酚后，AA诱导的SHE细胞形态学转化则被抑制了16%～76%。结论 本研究的结果表明，无论在24 h染毒还是7 d连续性染毒的条件下，AA都可以引起培养的SHE细胞的形态学转化。抗氧化剂α-生育酚可以抑制这种由AA引起的形态学转化。此结果提示，氧化损伤可能是AA引起细胞转化和致癌作用的机制之一。本研究的结果也表明，SHE细胞形态学转化试验对于研究开发营养保健品和中草药的机构来说是一个非常有用的工具。它可以用来检测这些产品中可能存在的致癌成分，也可以用来筛选产品中可能存在的抗癌成分。

关键词 马兜铃酸 细胞转化,肿瘤 胚胎,金仓鼠 维生素E

分类号 R965.1

Effects of aristolochic acid on morphological transformation of cultured Syrian hamster embryo cells

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Abstract

AIM A large body of evidence has shown that transformation of Syrian hamster embryo(SHE) cell cultures is perhaps the most biologically relevant short-term system for identifying carcinogens and studying the mechanisms of chemical carcinogenesis. The purpose of the present study is to examine the ability of aristolochic acid(AA), the active component of many herbal medicines derived from Aristolochia to induce morphological transformation(MT) in cultured SHE cells. In addition, the effect of α-tocopherol on AA-induced MT was studied. **METHODS** Prior to the transformation assay, a dose range-finding study was conducted employing a wide range of concentrations of AA following either a 24 h or a 7 d treatment to establish an appropriate range of concentrations for the cell transformation assay. AA concentrations causing approximately 0%－50% cytotoxicity were chosen for testing in the cell transformation assay. The effect of α-tocopherol on AA-induced MT was investigated by co-treatment of the cultured SHE cells with transforming concentrations of AA and 100 μmol•L^{-1} α-tocopherol. **RESULTS** Following a 7 d continuous treatment, AA induced significant increases in MT at concentrations of 0.4, 0.8 and 1.6 mg•L^{-1} (maximum sub-toxic concentration tested). Significant increases in MT were also observed in SHE cells treated with AA at concentrations of 1.0, 1.5, 2.5, 4.5 and 5.0 mg•L^{-1} (maximum subtoxic concentration tested) for 24 h. Transformation induced by AA was inhibited (16%－76%) by co-treatment with the antioxidant, α-tocopherol (100 μmol•L^{-1}). **CONCLUSION** The results of the present study show that AA can induce MT in cultured SHE cells following either a 24 h treatment or a 7 d continuous treatment. MT induced by AA can be inhibited by antioxidant, α-tocopherol, suggesting that oxidative stress be involved in AA-induced transformation and carcinogenesis. The present study also shows that the SHE cell transformation assay can be a useful tool for the nutraceutical and herbal medicine industry to detect potential carcinogenic ingredients as well as to screen potential anticarcinogenic ingredients in their products.

Key words aristolochic acid cell transformation neoplastic embryo mesocricetus vitamin E

DOI:

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