

敌枯双对果蝇的致畸效应

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内容提要 本文报道了已知致畸物敌枯双能在果蝇仔代中诱发产生多种畸形及延迟效应。用果蝇作观察对象是较理想的快速致畸试验方法,并推荐0.5%吐温80作为果蝇致畸试验中非水溶性物质的溶剂。

关键词 敌枯双 果蝇 致畸效应 吐温80

敌枯双是一种强的实验动物致畸剂,在剂量低至1/2600 LD₅₀ (0.1mg/kg)时尚可引起21.05%的大鼠外观畸形,其畸形表现是多方面的,可有严重的骨骼、内脏畸形⁽¹⁾。已知其作用机理是:敌枯双是尼克酰胺的竞争剂,在细胞内与1-焦磷酸-5-磷酸核糖结合,生成一种中间产物,后者能强烈抑制IMP脱氢酶活性,使合成DNA的原料供应不足,合成量降低,细胞分裂停滞。敌枯双的这种细胞毒性作用可明显地被尼克酰胺拮抗⁽²⁾。故在给敌枯双的同时给尼克酰胺能防止敌枯双对小鼠的致畸作用⁽³⁾。为了探寻更理想的致畸试验方法,我们以已知致畸剂敌枯双对果蝇作致畸试验,现将结果报道如下:

材 料 和 方 法

敌枯双系浙江温州工科所提供的纯品

(含量为99%以上)。果蝇用野生型的Canton-S品系。试验方法按Schuler⁽⁴⁾所述进行,即敌枯双溶于吐温80,使吐温80在培养基中的最终浓度为0.5%,经数次预试,选定敌枯双在培养基中的剂量为1、4、16mg%。在制备标准培养基的即时,按剂量要求加入受试物,用电动混匀器充分混匀,分装于2.5×8cm的指管,待培养基冷却后,每一指管放入两对4天龄果蝇(其中雌蝇为处女蝇),于25℃孵育,6天后倒去亲本,待孵出仔蝇(约于交配后第11天),每天在放大20倍的解剖显微镜下观察,连续10天,记录外观形态及结构的畸形,计算致畸率,并用 χ^2 检验进行统计处理。

结 果 与 讨 论

一、实验结果见附表。

从表中可见混悬剂0.5%吐温的致畸率为

附表 敌枯双对果蝇的致畸效应

剂 量 (mg%)	观察 仔蝇 数	致 畸 表 现 (%)						致畸蝇	
		翅		色 素 带		肢 羽	其 他	数	率 (%)
		未 展	畸 形	斑 状	紊 乱	多 少	刚毛多		
1	714	4(0.56)	2(0.28)	26(3.64)	2(0.28)	13(1.82)	17(2.38)	62**	8.68*
4	513	5(0.97)	6(1.17)	19(3.70)	—	14(2.73)	16(3.12)	57***	11.11*
16	529	15(2.84)	1(0.19)	26(4.91)	—	6(1.13)	13(2.46)	58***	10.96*
0.5%吐温	938	6(0.64)	1(0.11)	1(0.11)	—	4(0.43)	10(1.07)	22	2.35

*P<0.001

** 2 只有 2 种畸形表现

*** 3 只有 2 种畸形表现

2.35%，我室长期观察空白对照组的致畸率在2~4%之间。1、4、16mg%敌枯双的致畸率分别为8.68%，11.11%，10.96%，与0.5%吐温组比较，均有极显著差异（ $P < 0.001$ ）。可以认为，敌枯双对果蝇同样有极显著的致畸效应。

二、果蝇致畸试验中，溶剂是一个值得注意的问题。目前仅知水溶性和醇溶性物质能很好地被摄入，而常用的二甲亚砜⁽⁴⁾、乙醇^(5,6)在一定浓度时均有致畸效应。我们在敌枯双大鼠致畸试验时曾以食油为溶剂，在果蝇预试时也曾以1%食油为溶剂，结果发现由于食油的粘稠性，仔蝇常被粘在培养基上而死亡，后改用吐温，但吐温的最终浓度亦不能太高，1%、2%吐温均影响仔蝇的发育，可见幼虫、蛹的死亡。0.5%吐温为理想的浓度，在该浓度下仔蝇能正常生长且不增加畸变率，可推荐作为非水溶性物质的混悬剂。

三、从附表可见敌枯双对果蝇致畸表现是多方面的，主要为翅未展及翅的畸形，可有翅切迹，翅呈扇形，两翅大小、形态不等、翅残缺，个别有翅脉缘中断等表现，这种翅畸形，可能是在发育时翅芽的大量细胞死亡之故⁽⁷⁾。最多的是雄蝇腹背片靠近尾部的二条宽色素带呈斑状，此外，尚有肱羽增加到三条，其他还可见沟前羽，小盾鬃等增多。当然，这些畸变表现与其他实验动物完全不同，但为了筛选目的，这种不同并不重要，重要的是在化学物处理后，果蝇形态发育反应的明显性和重现性⁽⁸⁾。

四、按常规观察仔蝇，应在仔蝇开始孵出后连续观察十天，但考虑到在化学物影响下，仔蝇的生长可能延缓，使发育周期延长，故在常规观察十天后，又继续观察十天。在第二个十天观察中，发现一只出现严重胸及小盾片歪曲，左翅残缺（图1），另一只在腹部生长出似翅质的额外组织（图2），这两只畸蝇经继续饲养均存活数天。在重复实验时也见到一只胸及翅严重畸形的果蝇。

在16mg%剂量组的第二个十天观察时，496只仔蝇中有19只呈各种翅畸形，占3.83%，比第一个十天中的翅畸形率0.19%高得多，因此我们认为，对某些能影响生长发育的化学物的致畸作用观察，延长观察天数是必要的，这也是用果蝇作为观察对象优于其他实验动物的一个优点。

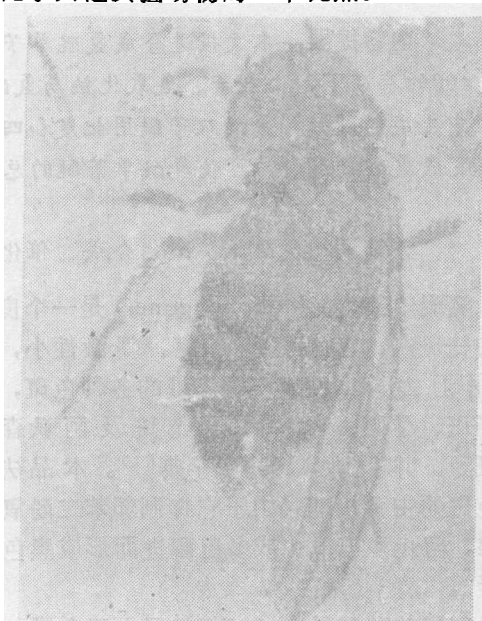


图1 胸及小盾片弯曲、左翅残缺



图2 腹部生长出似翅质的额外组织

氢醌单苄醚合成方法的改进

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内容提要 本文报道合成氢醌单苄醚的一种改良方法。在相转移催化剂PEG 400的存在下,由氯苄、氢氧化钠与氢醌反应得氢醌单、双苄醚的混合物。若将反应中生成的副产物氢醌双苄醚用钨炭和四氢苯进行催化转移氢化,并脱去一个苄基转变成氢醌单苄醚,可使氢醌单苄醚的总收率达93%。

关键词 氢醌单苄醚 合成 催化转移氢化

氢醌单苄醚(Monobengone)是一个良好的祛斑药。它比氢醌稳定、刺激性小,常用于去除面部、皮肤等处的各种色斑,如雀斑、孕斑、肝色斑、日光斑及阿狄森氏斑等,并已收入美国药典⁽¹⁾。本品法除色斑的主要机理是由于它抑制邻苯二酚氧化酶,阻止多巴氧化成多巴醌进而形成黑色素⁽²⁾。

氢醌单苄醚早在1883年就已人工合成。由于氢醌对位的二个酚性羟基都可以被苄醚化,因此一直存在着单苄醚收率低和纯度差等问题。1974年Newman等研究了氢醌的单苄醚化⁽³⁾,据报道,氢醌二钠盐在50%二氧六环的水溶液中与氯苄反应可得氢醌单苄

醚,其收率为70%。但我们重复该方法的结果,不仅单苄醚的总收率低,且量也很少。曾有专利报道^(4,5),用季铵型相转移催化剂使氢醌醚化可得单、双醚的混合物。我们发现,用TEBA作相转移催化使氢醌苄醚化的效果不如PEG400,后者催化生成的氢醌单、双苄醚的比例,因所用的碱不同而波动于1:0.24~1.3之间。

由于氢醌苄醚化时总有氢醌双苄醚生成,有时甚至是主要产物。因此,如何使氢醌双苄醚转化成氢醌单苄醚,就成为提高氢醌单苄醚收率的关键。据文献报道^(6,7),苄基的氢解可经催化转移氢化(Catalytic transfer hydrogenation)实现,以钨炭为

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本实验的结果表明,敌枯双同样能对果蝇产生严重致畸效应,用果蝇作致畸试验是一个较理想的快速初筛的方法。(本文图片承陈平同志拍摄,特此致谢。)

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HBV INTRAUTERINE INFECTION

Zhou Chaocong, et al. Study on the Mother-Infant Transmission Route of HBV Infection. *J Zhejiang Med Univ* 1987; 16(4): 149.

This study recommends the detection of HBV markers through the HBV-DNA spot test, SPRIA and ELISA in the peripheral blood of neonates within 48 hours after birth. Of 60 neonates born to HBsAg positive mothers were vaccinated with hepatitis B vaccine soon after birth to find 5 (10%) positive for HBsAg, and 48 (96%) positive for anti-HBc, but all were negative for anti-HBs and anti-HBe IgM.

During 1, 3, 6, 12 months follow-up for infants, HBV markers, 7 infants became chronic HBsAg carriers whose mothers were all HBeAg positive, of whom 4 were infected by HBV at delivery, and the remaining 3 infants (0.62%) probably caught their infection in utero. According to this study, SPRIA seems to be a more sensitive method for detecting HBsAg in the diagnosis of HBV infection in neonates. The characteristics of HBV intrauterine infection are: ① infants born to HBsAg and HBeAg positive mothers, ② positive HBsAg in their peripheral serum soon after delivery with gradual increase in HBsAg titers at 1 or 3 months of age and a ratio of S/N ≥ 10 , ③ unable to immunoprecipitate with hepatitis B vaccine for infants, ④ development into chronic HBsAg carrier.

HYDROQUINONE MONOBENZYL ETHER SYNTHESIS CATALYTIC TRANSFER HYDROGENATION

Li Guanghua, et al. Improvement in Synthesis of Hydroquinone Monobenzyl Ether. *J Zhejiang Med Univ* 1987; 16(4): 166.

This paper describes an improved method for the synthesis of hydroquinone monobenzyl ether.

The mixture compounds of hydroquinone monobenzyl and dibenzyl ether were synthesized through the reaction of hydroquinone with benzyl chloride and sodium hydroxide in the presence of phase-transfer catalyst PEG 400. When by-product of dibenzyl ether from reaction to a benzyl group was converted to monobenzyl ether through catalytic transfer hydrogenation with Pd-C and tetraline, the total yield of monobenzyl ether was as high as 93%.

PAPILLARY MUSCLE PHASE O DEPOLARIZATION TRANSMEMBRANE IONIC CURRENT PHASE-PLANE TRAJECTORY

Li Zhenyuan and Chu Pingchang. Analysis of Phase Plane Trajectory of Transmembrane Ionic Current at Depolarized Phase O of Action Potential in Single Cell of Papillary Muscle of Guinea Pig. *J Zhejiang Med Univ* 1987; 16(4): 146.

On the principle of phase-plane trajectory, the ionic current density of action potential depolarization of the single myocardium cell was first calculated and analysed with microcomputers. The results obtained were similar to those of the atrium muscle cell measured by the complex electronic circuit and voltage clamp method. The maximum ionic current density was $0.65 \pm 0.12 \text{ mA/cm}^2$ ($n=9$). The verapamil, a blockage of calcium channel, not only inhibited the V_{max} but also decreased the transmembrane ionic current density from $0.65 \pm 0.12 \text{ mA/cm}^2$ (control) to $0.46 \pm 0.13 \text{ mA/cm}^2$ (Ver. 30min, $p < 0.01$).

Therefore, it is an available technique based on the conventional microelectrode method for measuring the transmembrane ionic current besides the voltage clamp.

MAT DROSOPHILA TERATOGENIC EFFECTS

Zhu Weijun, et al. Teratogenic Effects of N', N'-methylenebis-(2-amino-1,3,4-thiadiazole) (MAT) in *Drosophila melanogaster*. *J Zhejiang Med Univ* 1987; 16(4): 152.

MAT has been identified to be able to exert teratogenic effects on mice. This paper reports its effect on the external morphology of *Drosophila melanogaster*. Different abnormalities in D. melanogaster caused by MAT has been discovered in this study, such as uninflated wings, wing notches, dark spots instead of banding on the abdominal tergites, irregular dark banding on the abdominal tergites and extra bristles. When the delayed effect of MAT on D. melanogaster was examined, one fly was found to have severe twisted thorax and truncated wings and the other to have extra winglike tissue on the abdominal sternite. The problem about solvent has been discussed in the paper and 0.5% polysorbate 80 is recommended as a desirable concentration for non-water-soluble chemical in the teratogenic test of D. melanogaster.