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基础研究

3种新型核苷类似物抗鸭乙型肝炎病毒活性及其对肝脏组织形态学的影响

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摘要：

目的：研究3种具有新型结构的核苷类似物在体内的抗鸭乙型肝炎病毒的活性及其对鸭肝脏组织形态学的影响，探寻新型高效核苷类抗乙型肝炎病毒药物。方法：实验组鸭分为2、10和50 mg • kg^{-1} 3个剂量组，分别给予核苷类似物030703、030605和030705，对照组鸭给予阿德福韦10 mg • kg^{-1}，每日1次，经口服连续给药30 d。分别在给药前、给药第15天、第30天和停药后第2周时静脉采血，采用荧光定量PCR方法进行血清鸭乙肝病毒脱氧核糖核酸（DHBV DNA）检测，同时设DHBV DNA阳性和阴性对照组。实验结束后处死鸭，取肝脏，进行光镜下的病理组织形态学检查。 结果：受试药物030703的高、中、低剂量组在给药后分别有3只（60%）、2只（40%）、1只（20%）鸭的DHBV DNA含量下降至原含量1/3，与阿德福韦对照组比较，高剂量组DHBV DNA含量差异有统计学意义（P<0.01），而中、低剂量组差异无统计学意义（P>0.05）。受试药物030605的高、中、低剂量组在给药后分别有4只（80%）、3只（60%）、1只（20%）鸭的DHBV DNA含量下降至原含量1/3，与阿德福韦对照组比较，高、中剂量组DHBV DNA含量差异均有统计学意义（P<0.01），而低剂量组差异无统计学意义（P>0.05）。受试化合物030705药物的高、中、低剂量组在给药后分别有3只（60%）、2只（40%）、0只（0%）鸭的DHBV DNA含量下降至原含量1/3，与阿德福韦对照组比较，高剂量组DHBV DNA含量差异有统计学意义（P<0.01），而中、低剂量组差异则无统计学意义（P>0.05）。所有测试药物高、中、低剂量各组干预后的鸭肝脏组织形态分别与病毒阳性对照组比较，炎症均有不同程度的减轻，与阿德福韦对照组的表现相似。结论：3种新型核苷类似物030703、030605及030705具有体内抗鸭乙型肝炎病毒的活性，并且能够不同程度地缓解鸭肝脏组织炎症，是一类高效的新型核苷类抗乙型肝炎病毒药物。

关键词：

Activities of anti-duck hepatitis B virus of three novel nucleoside analogues and their effects on histomorphology of duck liver

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Abstract:

Abstract:Objective To study the activities of anti-duck hepatitis B virus (anti-DHBV) of three novel nucleoside analogues and their effects on histomorphology of duck liver,and to explore novel potential anti-HBV agents.Methods The anti-DHBV activities were analyzed by fluorescent quantitative PCR in experimental groups with various doses of 030703,030605,030705 (2,10 and 50 mg • kg^{-1}) and adefovir dipioxil control group (10 mg • kg^{-1}).Compounds were taken by oral administration per day and last 30 d.The serum specimens were obtained at the time of before adminstration,15 d and 30 d after administration and 2 weeks after withdraw.The serum DHBV DNA was detected with fluorescence quantitative PCR.At the same time,DHBV DNA positive and negative groups were set up.The duck liver specimens were obtained after experiment.The histomorphological changes of duck liver caused by three tested compounds were observed under optic microscope.Results After administration with compound 030703,there were 3 ducks (60%) in high dose group,2 ducks (40%) in middle dose group,1 duck (20%) in low dose group,in which the DHBV DNA contents were decreased to 1/3 of primary contents;compared with adefovir dipioxil control group,the inhibitory effects in high dose group had significant difference (P<0.01),whereas the inhibitory effects in middle and low dose groups had no significant difference (P>0.05).After administration with compound 030605,there were 4 ducks (80%) in high dose group,3 ducks (60%) in middle dose group,1 duck (20%) in low dose group,in which the DHBV DNA contents were decreased to 1/3 of primary contents;compared with adefovir dipioxil control groups,the inhibitory effects in high dose group and middle group had significant difference

(P<0.01),whereas the inhibitory effect in low dose group had no significant difference (P>0.05).After administration with compound 030705,there were 3 ducks(60%) in high dose group,2 ducks (40%) in middle dose group,0 duck (0%) in low dose group,in which the DHBV DNA contents were decreased to 1/3 of primary contents;compared with adefovir dipioxil control groups,the inhibitory effects in high dose group had significant difference (P<0.01),whereas the inhibitory effects in middle and low groups had no significant difference (P>0.05).Compared with adefovir dipioxil control group,the effects of all three test compounds(high,middle and low dose groups) on duck liver inflammation were similar to that in adefovir dipioxil control group.Conclusion Three novel test compounds 030703,030605 and 030705 have obvious anti-DHBV activities and might improve duck liver inflammation to some extent.It has been suggested that all of these novel compounds be potential anti-HBV agents.

Keywords: ucleoside analogues;hepatitis B,chronic/ drug therapy

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