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原著

DNAコンフォメーション変化を介した遺伝子発現に対する有機および無機水銀（II）の影響 Vol.1、No.2、p.73-79

上田浩二、牧野玲奈、戸部隆夫、岡本美登、児島中尾
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概要 全文PDF [593K]

遺伝子発現に対する有機および無機水銀イオンの影響は、転写および翻訳のためのインビトロ無細胞アッセイによって研究された。有機水銀（塩化メチル水銀、MeHgCl）は効果を示さなかったが、テンプレートDNAを無機水銀（$HgCl_2$）で処理した。）バクテリオファージT7RNAポリメラーゼ転写システムにおけるmRNA合成を阻害した。阻害された転写は、Sf21昆虫細胞溶解物からなる翻訳システムへの転写物のその後の適用後にタンパク質合成の低下をもたらしました。mRNAを無機水銀で処理すると、翻訳も減少しましたが、この抑制効果はDNA曝露によって生じる効果よりも弱かったです。DNAとRNAを水銀で処理しても、鎖の切断や塩基の酸化などの酸化的損傷は増加しませんでした。代わりに、円二色性分光分析は、メチル水銀ではなく水銀イオンがDNAとRNAの鎖コンフォメーションを劇的に変化させたことを示しました。したがって、この研究で観察された遺伝子発現阻害は、DNA塩基と水銀イオンとのクロスブリッジによって引き起こされたと考えられました。転写機構をブロックしました。動物における有機水銀の無機形態への生物学的変換に関する報告と合わせて、我々の結果は、DNAのコンフォメーション変化を介した転写阻害が水銀中毒に関与する毒性メカニズムである可能性があることを示しています。

ページトップ

原著

回復期間が2週間のラットにおけるL-アラニンの4週間経口毒性試験 Vol.1、No.2、p.63-72

青木真美、望月正博、岡村敏也、秦山和久、中村敦、森下浩二
リリース：2014年10月23日

概要 全文PDF [206K]

L-アラニンの安全性を調査するために、オスとメスのSprague-Dawley系統SPFラット[Crj：CD（SD）IGS]にL-アラニンを2,000 mg / kg /日で4週間強制経口投与しました。投与期間の終了後、2週間の回復期間の後に可逆性を評価した。結果では、全身状態、体重、食物消費、眼科、血液学、血液化学、臓器重量、または剖検時に、L-アラニンによって引き起こされる毒物学的に有意な変化はありませんでした。尿検査では、男性と女性で尿タンパク陽性またはリン酸塩を示す動物の数の増加が観察されました。さらに、尿量は男性で有意に増加しました。組織病理学的検査では、胃の限定隆起における扁平上皮過形成が男性と女性で観察された。これらの変化は、2週間の回復期間後に減少するか、観察されなくなったため、可逆的な変化でした。これらの結果は、L-アラニンを2,000mg / kg /日で4週間繰り返し経口投与することは、雄および雌のラットで十分に許容されることを示唆している。

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Original Article

A 13-week feeding toxicity study of L-threonine in rats with a recovery period of 5 Vol.1, No.2, p.49-62

weeks

Mami Aoki , Shigeru Ishida , Hideki Fukuzumi , Koji Morishita
Released: October 23, 2014

Abstract Full Text PDF[104K]

Rats were administered L-threonine in the diet at concentrations of 0 (basal diet control), 1.25%, 2.5%, or 5.0% for 13 weeks. Animals were sacrificed following the treatment period or after a 5-week recovery period (for animals receiving the control or 5.0% L-threonine diet). The mean achieved doses of L-threonine during the treatment period were 0, 811.5, 1615.3, and 3266.9 mg/kg body weight/ day in males, and 0, 909.9, 1850.0, and 3673.3 mg/kg body weight/day in females. No toxicologically significant changes in general condition, body weight, food consumption, feed efficiency, water intake, ophthalmoscopy, urinalysis, hematology, blood chemistry or pathology were observed. Based on the results of the study, no-observed-adverse effect levels (NOAEL) of 3266.9 and 3673.3 mg/kg body weight/day can be established for male and female rats, respectively, under the present experimental conditions.

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Original Article

Safety evaluation of morphological changes in corneal endothelial cells induced by K-115 in cynomolgus monkeys — Vol.1, No.2, p.39-47

Eiji Wato , Kozo Omichi , Shigeki Yoneyama , Mamoru Tanaka , Masataka Kagawa , Yukinori Amano
Released: October 15, 2014

Abstract Full Text PDF[416K]

The present study was designed to evaluate the morphological changes in corneal endothelial cells (CECs), induced by K-115 ophthalmic solution in the ophthalmology, using a specular microscope. Unclear borders between CECs and slightly decreasing trends in corneal thicknesses were noted following ocular instillation of the K-115 ophthalmic solutions into cynomolgus monkeys. These changes were transient and disappeared within 24 hr after instillation. In addition, no significant differences were noted in the degrees or frequencies of these lesions, between the single and 10-day repeated instillations, and no appreciable changes were noted in the number of CECs at 24 hr after instillation. No significant structural changes were noted by histopathological examinations using light, transmission electron, and scanning electron microscopy. Similar changes were also noted following ocular instillation of Y-39983 ophthalmic solution at 0.25%, with Rho-Associated, Coiled-Coil Containing Protein Kinase (ROCK) inhibitory effects, similar to the K-115 ophthalmic solution 2.0%. Therefore, the changes were due to pharmacological effects of the K-115 ophthalmic solution. In conclusion, some morphological changes in CECs, following instillation with K-115, were considered to be of minimal toxicological significance because, 1) they were noted transiently after instillation, and CECs recovered by 24 hr after instillation, 2) no enhancement by repeated instillation was noted, 3) no appreciable changes were noted in the corneal thickness or the number of CECs at 24 hr after instillation, and 4) no significant structural changes were noted.

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Original Article

28-Day dietary toxicity study of L-phenylalanine in rats — Vol.1, No.2, p.29-38

Yusuke Shibui , Tadashi Miwa , Terutaka Kodama , Akinori Gonsho
Released: September 27, 2014

Abstract Full Text PDF[100K]

The purpose of this study was to evaluate the toxicity of L-phenylalanine when administered daily in the diet to rats for at least 28 days. Male and female Crl:CD®(SD)IGS BR rats were assigned to four groups. Each group received diets containing basal diet or 0.5, 1.5, or 5.0% (w/w) L-phenylalanine. There were no clinical

or ophthalmic observations that were considered to be related to L-phenylalanine. Effects of L-phenylalanine administration were noted in mean body weights and mean body weight gains in females fed 0.5% and in males and females fed 5.0% (w/w) L-phenylalanine diets. Effects were also noted in mean food consumption in males and females fed the 5.0% (w/w) L-phenylalanine diet. The lower food consumption and body weights of the males and females fed the 5.0% L-phenylalanine diet were considered to be signs of mild toxicity. Administration of L-phenylalanine at a dose of 5.0% of the diet was associated with mildly increased red blood cell count and mildly decreased mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and glucose in females. There were no L-phenylalanine-related toxic changes for organ weight, or macroscopic or microscopic findings. In conclusion, the no-observed-effect level (NOEL) of dietary exposure of male rats to L-phenylalanine is 1.5% (w/w) L-phenylalanine. The NOEL of dietary exposure of female rats to L-phenylalanine is less than 0.5% (w/w) L-phenylalanine. However, the no-observed-adverse-effect level (NOAEL) for males and females is 1.5% (w/w) L-phenylalanine.

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