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论著

# 苯丁酸氮芥及环磷酰胺对大鼠肝微粒体谷胱甘肽*S*-转移酶的激活

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摘要 目的 探索苯丁酸氮芥（CHB）和环磷酰胺（CP）在体外是否通过烷化激活大鼠肝微粒体谷胱甘肽*S*-转移酶（mGST）。方法 微粒体粗提物与CHB或CP体外共孵育，测定mGST催化动力学改变，结合*N*-乙基马来酰亚胺（NEM）再激活实验和结合二硫苏糖醇（DTT）逆转实验，研究酶激活机制。结果 CHB或CP浓度(0～5 mmol·$L^{-1}$)与时间（0～5 min）依赖性地激活mGTS。增强的mGST活性能被NEM进一步增强，不被二硫键断裂剂DTT逆转，NEM对CHB或CP活化后的mGST活性的增强效应与NEM单独的增强效应无差异。结论 CHB或CP体外可激活大鼠肝mGST，激活机制可能与mGST的$Cys^{49}$的巯基被CHB或CP修饰激活有关。

关键词 酶激活 微粒体 谷胱甘肽转移酶 苯丁酸氮芥 环磷酰胺 谷胱甘肽

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# Activation of rat liver microsomal glutathione *S*-transferase by chlorambucil and cyclophosphamide *in vitro*

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**Abstract**

AIM To study whether chlorambucil (CHB) and cyclophosphamide (CP) activate rat liver microsomal glutathione *S*-transferase (mGST) by alkylation. METHODS Partially purified mGST was incubated with CHB or CP *in vitro*, kinetic parameters of mGST were measured. *N*-ethyl maleimide (NEM) activation and dithiothreitol (DTT) reversibility tests were performed to demonstrate the relevant mechanism. RESULTS The activity of mGST was activated by CHB or CP in a concentration and time-dependent manner. NEM can enhance the increased activity pretreated with CHB or CP , while DTT failed to reversed the effect of CHB or CP on mGST activity. The mGST total activation on $Cy^{49}$-SH after CHB or CP pretreatment by alkylating agent NEM was similar to that of NEM alone group. CONCLUSION Rat liver mGST can be activated by CHB or CP, possibly via alkylating of the single cysteine ($Cys^{49}$) in mGST.

**Key words** enzyme activation microsomes glutathione transferases chlorambucil cyclophosphamide glutathione

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