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³¹P NMR Determination of the Urinary Excretion of the Antitumor Drug Cyclophosphamide in Humans

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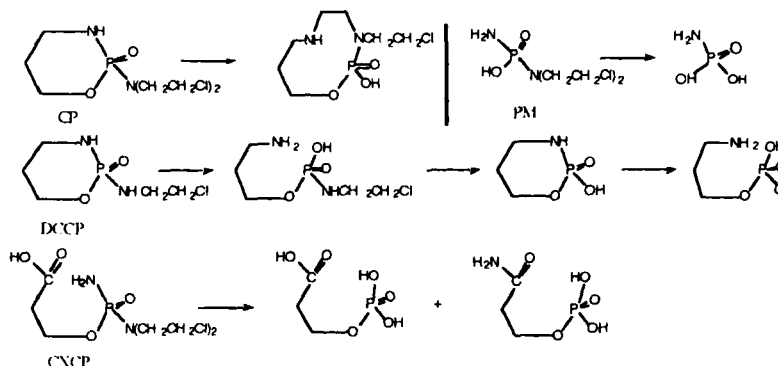
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³¹P NMR Determination of the Urinary Excretion of the Antitumor Drug Cyclophosphamide in Humans

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³¹P NMR was used to analyze urine from 4 patients treated with cyclophosphamide (CP) over 2 days. CP and most of its phosphorylated metabolites (carboxyCP (CXCP), dechloroethylCP (DCCP), alcoCP, ketoCP and phosphoramidate mustard (PM)) were assayed. Several other signals (10-15) corresponding to unknown compounds were observed. Seven new compounds were identified: all were hydrolysis products of CP or its metabolites CXCP, DCCP and PM as reported below.



CP urinary recovery was not significantly different on the second day (16% of injected dose) than on the first day of treatment (17%). On the other hand, the amount of phosphorylated metabolites excreted in urine was much higher after the second dose (37%) than after the first (20%), suggesting auto-induction of CP metabolism. CXCP and its two degradation compounds were by far the major metabolites (11.5% and 23% after first and second dose respectively). Levels of PM, the active metabolite, and its degradation compounds were extremely low. (Supported by ARC, grant 6635).