Metabolic kinetics of P-aminobenzoic acid in rabbits.

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Abstract

The metabolic kinetics of p-aminobenzoic acid (PABA) in rabbits was studied. PABA is predominantly metabolized by acetylation and glycine conjugation to form p-acetamidobenzoic acid (PAABA), p-aminohippuric acid (PAHA), and p-acetamidohippuric acid (PAAHA). After PABA IV administration (20 mg/kg) to rapid (n=16) and slow (n=8) acetylation rabbits, PABA was eliminated rapidly. The half-lives of PABA were 7.01±0.32 min in rapid acetylation rabbits and 7.08±0.78 min in slow acetylation rabbits. Significant differences were obtained in formation of PAABA and PAHA formed from PABA in both acetylation phenotype rabbits. The formation fraction of PAABA, formed by acetylation of PABA, was 0.8029±0.0267 in rapid acetylators and 0.2385±0.0428 in slow acetylators ($p<0.001$). PAHA formed from PABA was 0.0462±0.0102 in rapid acetylators and 0.6652±0.0562 in slow acetylators ($p<0.001$). Only 0.0156±0.0030 of PABA could be detected as PAAHA in rapid acetylation rabbits which was obtained by acetylation of PAHA. After individual IV injection of PAHA, PAAHA, and PAABA to both phenotypes of rabbits, PAABA and PAAHA were eliminated in their unchanged forms whereas PAHA was further acetylated to form PAAHA. The formation fraction of PAAHA formed from the acetylation of PAHA was 0.4408±0.0570 in rapid acetylators and 0.0539±0.0084 in slow acetylators ($p=0.002$). From the results obtained, metabolic pathways of PABA show significant differences in both acetylation phenotypes of rabbits. Acetylation is the major metabolic route of PABA in rapid acetylation rabbits, while glycine conjugation is more predominant in slow acetylation rabbits.