# In vitro human plasma leucine5-enkephalin degradation is inhibited by a select number of drugs with the phenothiazine molecule in their chemical structure

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A number of drugs with the phenothiazine molecule in their chemical structure inhibit in a dose-dependent manner human plasmatic aminopeptidase leucine5-enkephalin (LEU) metabolism. Half-life peptide degradation was significantly increased by thioridazine > fluphenazine > As-1397 [10-(?-diethylaminopropionyl)phenothiazine] ? promethazine ? chlorpromazine (final drug conc. 10-4 M); t1/2 (± SD) 21.2 ± 1.1, 19.6 ± 1.0, 17.2 ± 0.9, 17.1 ± 1.0, and 17.1 ± 1.1 min, respectively. Control and bacitracin (known aminopeptidase inhibitor) values were 11.8 ± 1.0 and 31.3 ± 1.7 min, respectively. These drugs significantly decreased (listed in the same order) LEU degradation initial velocity; Iv (± SD) 0.77 ± 0.2, 0.82 ± 0.2, 0.92 ± 0.3, 0.93 ± 0.2, 0.94 ± 0.3 pg LEU/min, respectively. Control and bacitracin 1.10 ± 0.3 and 0.20 ± 0.1 pg LEU/min, respectively. Values represent results from 5 samples, each obtained by pooling 6 individual plasmas (4 male and 2 female; n =30 healthy, drug-free voluntee