

WANIDA MARAYOUNGK : COMPARATIVE STUDIES OF BIOAVAILABILITY OF METHYLDOPA TABLETS COMMERCIALY AVAILABLE IN THAILAND. THESIS
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This investigation was to assess the bioequivalence of the local manufactured brands of 250 milligrams methyldopa film coated tablets relative to the original brand, Aldomet^R. These tablets were evaluated both in vitro and in vivo.

The in vitro studies were conducted to determine both the disintegration time and dissolution rate of the tablets. Of the nine brands studied, tablets of eight brands were able to be disintegrated within one hour. Only three brands met the USP XXI specification for dissolution test in which the methyldopa tablet can be dissolved within 20 minutes.

Four brands of methyldopa tablets with difference in their dissolution rate constants were selected for bioavailability study which was conducted in the twelve healthy Thai male volunteers, ages ranged from 19 to 27 years. The 250 milligrams single dose of methyldopa from four different brands was administered to the volunteer according to a complete crossover design. Blood sample of every subject were collected before the administration of the drug and within the 24 hours there after. The plasma was immediately separated and kept frozen for subsequent analysis using reversed-phase high-performance liquid chromatographic technique with an electrochemical detector. Analysis of the plasma profiles indicated that the absorption rate were statistically significant difference among the four brands ($P < 0.05$). Correlation between the in vitro and in vivo parameters implied that the disintegration time was the rate limiting step of the absorption rate. The extent of absorption, on the other hand, did not show statistically significant difference among brands ($P > 0.05$). In addition, the significant differences in the correlation between the extent of absorption and the height and weight of individual volunteer were observed.

The average of time to peak plasma concentration was 2.73 hours and the average half-life was 2.19 hours in Thai male which were shown to be similar to those previously reported while the average peak plasma concentration was 1.65 microgram/millilitre that was higher.