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In-vitro and in-vivo comparisons of two different propranolol tablets

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Some patients had claimd that propranolol generic tablets (Tolidarou, Iran) are more effective than Inderal (propranolol made by I.C.I England). Thus dissolution tests and bioavailability of two preparations were compared in 10 healthy male volunteers (aged 20-25 years). Two 40 mg tablets of each preparations was administered to fasting volunteers in a cross-over manner and blood samples were collected at 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 7, 8, 10, 12 hours after drug administration in heparinized test tubes. plasma was separated and kept at $-20°C$ prior to assay. The blood pressure and pulse rate were recorded at half an hour intervals. The propranolol plasma concentration was determined using a HPLC method and results were compared using t-student test.

It has been found that propranolol generic tablets took 3.2 ± 1.2 min. and Inderal tablets 2.35 ± 6.1 min. to disintegrate and PH of dissolved solutions are 6.13 ± 0.4 and 6.55 ± 0.3 respectively.

The pulse rate and blood pressure decreased by a value of 9.5 ± 3.5b/min. and 15 ± 5.3 mmHg, 2-4 hours after administration of propranolol generic tablets and by a value of 8.5 ± 2.7 b/min 15 ± 7.5 mmHg after Inderal. propranolol peak level is obtained at 2.6 ± 0.25 hours after generic tablets and 2.2 ± 0.25 hours after Inderal tablets. The AUC of propranolol concentration vs time curves were found to be 632.3 ± 142.8 and 676.5 ± 146.7 for generic and Inderal tablets respectively.

These results showed that these two preparations are statistically comparable.

It is also noted that in 4 individual the pulse rate and blood pressure decrease up to 9.12 ± 1.8 b/min and 16.2 ± 6.4 mmHg respectively during 8-12 hours after generic tablets administration and 8.57 ± 4.8 b/min and 19.4 ± 6.7 mmHg respectively after Inderal. A corresponding increase in propranolol plasma levels were also observed. This unexpected observation had been in re-calculation of other investigator's data findings and need further works to clarify.

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Bioavailability of two formulations of carbocysteine in healthy volunteers

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Carbocysteine is a derivative of acetylcysteine, which is used routinely as an expectorant. The drug is well absorbed after peroral administration and partially metabolized in the liver, while the larger part is eliminated unchanged through the kidney. There are considerable interindividual differences in the metabolism of carbocysteine, which depend on the rate of sulfoxidation of carbocysteine. Bioavailability of carbocysteine after peroral administration of two tablet and syrup formulations were examined.

Nine volunteers, nonsmokers, both sexes, aged between 20 and 45 years took part in this study. They gave their written consent after a full explanation of the nature of the study. Subjects were examined by physical, hematological and biochemical examination and they were deemed healthy. They did not take drugs and alcohol two weeks before the study. 18 hours prior to administration of the drug, they were on standardized diet with limited daily intake of proteins.

The study was a randomized, single-blind cross-over trial, with at least one week difference between series. Volunteers received two 375 mg tablets (750 mg) of carbocysteine or 750 mg in syrup, with 150 ml of matter. Blood samples were taken through intravenous cannula, before and 0.5, 1, 1.5, 2, 3, 4, 6, 8, and 12 h after administration of the drug. The blood was anticoagulated with heparin (10 units/ml of blood).

Plasma carbocysteine concentrations were determined by a spectrophotometric method, using ninhydrin.

Carbocysteine was separated from plasma proteins and other amino acids using a Sephadex 10 column (28 × 10 mm).

There were marked interindividual differences in concentrations, ranging from 3-11 mcg/ml and in pharmacokinetic parameters as well. There were no differences in bioavailability between the two different formulations of tablet and syrup.

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Pharmacokinetics of ketorolac tromethamine following oral and rectal administration

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Ketorolac tromethamine (kt), a potent analgesic with cyclooxygenase inhibitory activity, was administered in an open, randomized, single dose study of Latin-square design to 12 healthy male volunteers. Doses of 10 mg oral tablets and 10 and 30 mg rectal suppositories were administered. Plasma samples, obtained at various time intervals up to 24 hrs after administrations were analyzed for ketorolac (k) by reversed-phase high-performance liquid chromatography. Kt was absorbed at a slower rate from the 10 mg suppositories than from the tablets (mean observed Tmax resp. 1.10 and 0.75 hrs). The mean Tmax was not statistically different for the tablets (0.75 hrs) and for the 30 mg suppositories (0.97 hrs). The mean total AUC for 10 mg suppositories was statistically significantly lower than that for tablets: the AUC ratio (relative bioavailability) was 0.82. The ratio of mean total AUC and mean Cmax between 30 mg and 10 mg suppositories were respectively 318.3% and 306.7%, indicating an absorption from the suppositories proportional to the dose. The mean plasma half-life of k was remarkably consistent between oral and rectal administration and was independent of dose, ranging from 5.18 to 5.81 hrs. The time covered by a k plasma concentration of 0.25 μg/ml, suggested as still therapeutically effective, was similar for the 10 mg suppositories and the 10 mg oral tablets (about 6 hrs) and was about 18-20 hrs for the 30 mg suppositories. No complaints of local irritation or clinically significant side effects were reported.

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Bioavailability of frusemide from lasix plain and sustained release preparation-kinetic and dynamic study

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Single dose bioavailability of frusemide was compared from 40 mg Lasix Plain and 30 mg Lasix Sustained-Release preparation in 9 healthy subjects using cross-over design. The blood levels of frusemide were studied up to 24 hours and urinary excretion Na, K, and Cl were measured up to 24 hours. The standard restricted breakfast, lunch and dinner were served at 6, 8 and 14 hours respectively with a controlled water intake after drug administration.