Research Article

Study of Improving the Absorption and Bioavailability of the Aspirin and Promethazine on the Experimental Animals-Rabbits

Lama Habib*, A Hakim Nattouf
*Master degree in Clinical Pharmacy and Hospital Pharmacy, Damascus University, Faculty of Pharmacy, Syria.
PhD in Pharmacy, Damascus University, Faculty of Pharmacy, Syria.
***Corresponding author's E-mail:** lamahabeeb@gmail.com

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ABSTRACT

This study is aimed to improve the absorption and bioavailability of aspirin (tablets) by giving promethazine (syrup) according to the protocol of timely administration of both drugs and administration at time interval 15 minutes. Both former Protocols were applied on test animals (rabbits) and then blood samples were drawn from rabbits according to the times of sampling identified in the study and then extracting serum samples and injected into the high-liquid chromatography apparatus with UV detector. Drug interactions have been studied between aspirin and promethazine according to the previous administration protocols. Evaluation of the results of this study was performed through the calculation of the following pharmacological kinetic parameters AUC, Cmax, Tmax.

Keywords: Absorption, bioavailability, aspirin.

INTRODUCTION

Most of drugs given by oral route is absorbed generally through the gastrointestinal tract into the systemic circulation there is a great potential for drug interactions during the movement of drugs through the gastrointestinal tract.[1-5,11]

Simultaneous use of many other drugs that possess significant impacts on a number of factors affecting the absorption of the drug, Like gastrointestinal motility, the degree of the pH, and other factors (such as the formation of a physical -chemical complexes)[3] in the result can be increased or decreased drug absorption as a result of the occurrence of these drug interactions.

So the drug interaction on the level of absorption is very important to the success or failure of the therapeutic process which can be used to improve the absorption and bioavailability of some medications.[17,10,5,12]

Administration protocol

Two tablets of Aspirin 500 mg were taken, each was weight accurately, two tablets were crushed and taking the equivalent of 35 mg of aspirin suspended with 10 ml of water, and then take the equivalent of 0.35 mg of promethazin (each 1 ml of syrup promethazine used in the study contains 5.5 promethazin Hcl of equivalent to 5 mg promethazine).

The drug substances were given across the oral route, and to ensure the entry of the drug substances, we used a syringe and a flexible plastic tube such as exists in serum device enters the pharynx and injects medications through the syringe.

Studying groups

In this study, we used 44 rabbits, given the drug according to timely administration and administration at (15 minutes interval)

We used symbol (r) for rabbits group given aspirin alone In each of the timely administration and administration at (15 minutes interval).

Also we use symbol (t) for a group of rabbits that were given aspirin with promethazine at each of the timely administration and administration at 15 minutes interval.

First: the timely administration

Rabbits are divided in two groups

1. The first group (r): includes 10 rabbits each rabbit was given 35 mg of aspirin

2. The second group (t): includes 10 rabbits each rabbit was given 0.35 ml (1.75 mg) promethazine and 35 mg of aspirin.

3. Reference rabbits group: includes 2 Rabbits

Exclude rabbits that do not cover the times of puncture samples of the study.

Second: The administration at 15 minutes interval.

Rabbits are divided in administration interval into two groups

1. Third group (r): it includes 10 rabbits each rabbit was given 35 mg of aspirin.

2. Fourth group (t): includes 10 rabbits each of rabbit was given promethazine 0.35 ml (1.75 mg) and after 15 minutes of that Each rabbit was given 35 mg of aspirin.

3. Reference rabbits group: includes 2 rabbits.

Exclude rabbits that do not cover the times of puncture samples of the study.

Sampling

The blood samples were drawn to heparin pipes and that were taken from the marginal vein of rabbit ear, samples have been sediment directly (4000 rpm) for serum and retain at degree -70° C.

The Taken samples time (min): 10, 20, 30, 45, 60, 75, 90 minute.

The results

Results of timely administration

Table 1: The comparison of the average pharmacokinetics parameters of aspirin at the first and second groups.

T	R
C max (t) =3.80 µg/ml	C max (r) =3.50 µg/ml
T max (t) =30.00 min	T max (r) =30.00 min
K (t) =0.05 min-1	K (r) =0.04 min-1
T 1/2 (t) =13.90 min	T 1/2 (r) =15.50 min
AUC (t) (0 - ∞) =116,50 µg/ min /ml	AUC (r) (0 - ∞) =113.50 µg/ min /ml
F= 102%	

Statistical study of the results of timely administration

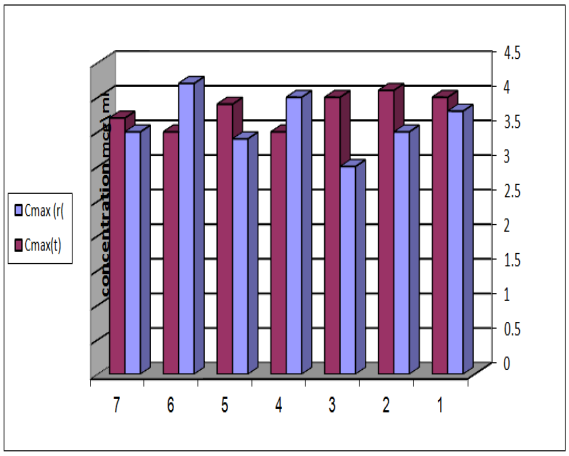

Figure 1: Differences Cmax values of aspirin when rabbits in the first and second group.

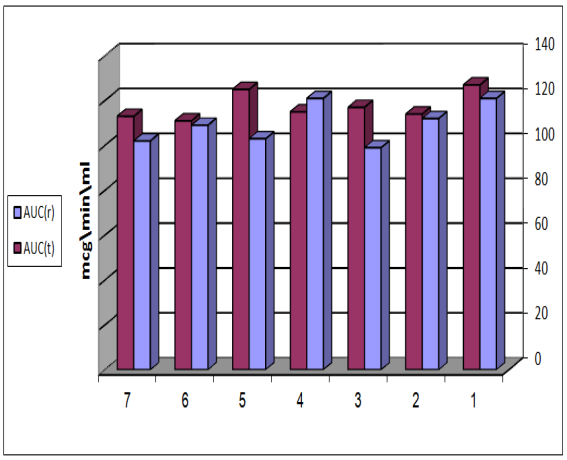

Figure 2: Differences AUC values (0 - ∞) of aspirin when rabbits in the first and second group.

Results of administration at 15 minutes interval

Table 2: Comparison of average pharmacokinetics parameters of aspirin at the third and fourth groups

T	R
C max (t) =4.00 µg/ml	C max (r) =3.50 µg/ml
T max (t) =20.00 min	T max (r) =30.00 min
K (t) =0.06 min-1	K (r) =0.04 min-1
T 1/2 (t) =11.55 min	T 1/2 (r) =17.32 min
AUC (t) (0 - ∞) =135.00 µg/min/ml	AUC (r) (0 - ∞) =110.00 µg/min/ml
F=122%	

Statistical study of the results of administration at time 15 minutes interval.

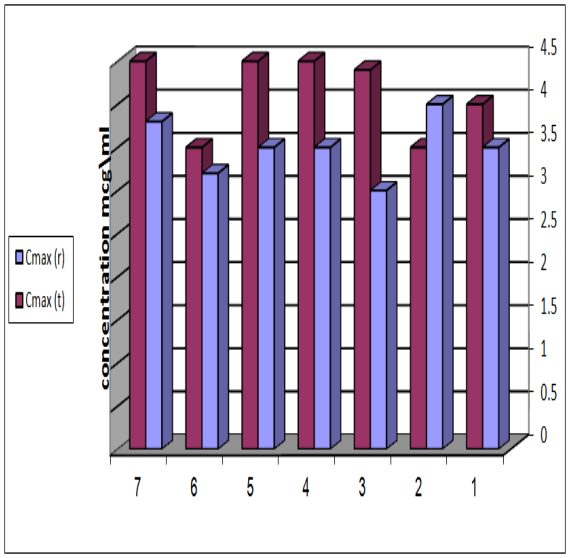

Figure 3: Differences Cmax values of aspirin with and without promethazine at the rabbits of the third and fourth group.

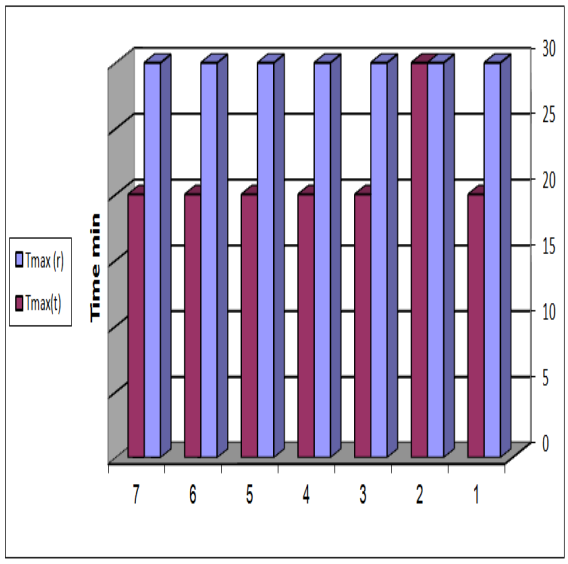

Figure 4: Differences Tmax values of aspirin with and without promethazine at the rabbits of the third and fourth group.

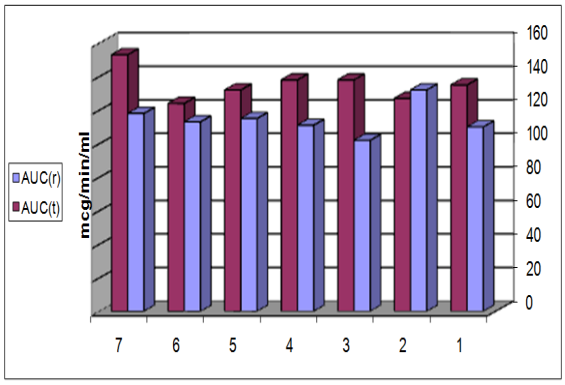

Figure 5: Differences AUC values (0 - ∞) of aspirin with and without promethazine at the rabbits of the third and fourth group.

DISCUSSION AND CONCLUSION

Both Cmax, Tmax and AUC (0 - ∞) are important parameters in the absorption and bioavailability assessment.[5,6,10,1]

Cmax: is the maximum noticeable concentration of the drug in serum after a dose of the drug.

Tmax: is the time required to reach the Cmax and therefore the drug absorption rate (Rate of absorption) reflected by the Cmax and Tmax, as an increase in the rate of absorption leads to an increase in Cmax and a decrease in Tmax [1][3][4] .

The AUC (0 - ∞) (area under the curve) shall be considered as representative of the full amount of the drug absorbed into the circulation after giving a single dose of the drug and is considered a common measure of bioavailability of the drug.[11,4,1]

Statistical study of the results of giving promethazine with aspirin at 15 minutes time interval (the results of third and fourth group) showed an increase in Cmax and AUC values (0 - ∞) of aspirin this increases were with statistical significance (figure 3,figure 5, table 2), there was also a decrease in the values of Tmax of aspirin (figure 4) and these decreases were with statistical significance and this mean an increase in aspirin absorption rate and aspirin bioavailability when you give promethazine with aspirin at 15 minutes interval due to the increase in Cmax and lower Tmax, as well as the increase in AUC (0 - ∞) means increasing amount of drug absorbed into the blood which mean an increase in bioavailability.[1,3,12]

While the results of timely administration for aspirin and promethazine (the results of first and second group) showed that increases in Cmax and AUC values (0 - ∞) of aspirin were not with statistical significance (table 1, figure 1, figure 2), this mean no increase to absorption rate and bioavailability of aspirin in case of timely administration with promethazine.

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