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Effects of a Low-Doses Treatment With Cuprum on Neostigmine Digestive Action in Female Mice

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ABSTRACT

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A low-doses treatment with cuprum 4CH, 24 and 5 hr before neostigmine (50 μg/kg/IP) administration, has been done in the female mouse. This treatment significanlty reduces (Kruskal-Wallis—$P < 0.02$) the facilitating action of neostigmine on intestinal transit. Cuprum 4CH treatment administered alone has no significant effect on transit.

Key words: transit, intestines, cuprum 4CH

INTRODUCTION

Numerous papers on the effect of low-doses treatments are available. For example, papers have reported a highly significant increase in urinary lead excretion from lead-loaded rats treated with the homoeopathic remedy plumbum metallicum 200CH (3), enhancement of arsenic elimination in the rat with decimal and centesinal dilutions of arsenic (1), and enhancement of paf-acether synthesis by mouse peritoneal macrophages with orally administered very-high dilutions of silica (2).

Previous studies from this laboratory have demonstrated that cuprum 4CH significantly reduces the facilitating action of neostigmine on intestinal transit of male mouse (7). Male and female not necessarily have the same reaction to drugs; for example, the sleeping time induced by hexobarbitone is longer in female mice (5), and analgesics effects of morphine are increased by promethazine in male mice and inhibited in female mice (9).

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The purpose of this study was to test the incidence of cuprum 4CH on neostigmine digestive effects of female mice. (Neostigmine is an indirect parasympathomemetic drug which enhances intestinal transit.)

MATERIALS AND METHODS

Cuprum 4CH (fourth centesimal dilution) is a low-dose pharmaceutical preparation composed of a metal base of pure copper, made according to the Hahnemannian method of preparation described in the French pharmacopocia and corresponding to a molar solution of 10^{-10}.

Intestinal transit was studied in mouse by using a technique derived from Loewe (6). The transit marker used was phenolsulfone phtalein (PSP) administered in healthy mice "per os" at T = 0 in volume of 0.3 ml. At T = +10 min the mice were decapitated and the PSP migratory front was observed by applying 20% sodium hydroxide (NaOH) to the intestine (from the caecum towards the pylorus). A purplish color revealed the presence of PSP. The percentage of PSP migration was calculated for each mouse by measuring the length of small intestine and by measuring the intestinal migration of the dye from the pylorus.

The experiment was carried on 48 OF1 adult female mice,[1] fasting for 24 hr and randomly separated into four groups:

Group 1: reference group for transit which was given a placebo treatment of distilled water: 0.3 ml interperitoneally (IP) at T = −24 hr, and T = −5 hr; 0.1 ml was given at T = −10 min.

Group 2: neostigmine group, which was given 0.3 ml IP of distilled water at T = −24 hr, and T = −5 hr; and 50 μg/kg/IP of neostigmine at T = −10 min.

Group 3: neostigmine + cuprum group, which was given 0.3 ml IP of cuprum 4CH at T = −24 hr and T = −5 hr; and 50 μg/kg/IP of neostigmine at T = −10 min.

Group 4: cuprum group, which was given 0.3 ml of cuprum 4CH IP at T = −24 hr, and T = −5 hr and 0.1 ml of distilled water at T = −10 min.

Data are expressed as mean ± SEM of percent of migration. Comparison between the four groups was performed by the Kruskal-Wallis[2] nonparametric rank test.

RESULTS

The results are indicated in Table 1,which shows migration percentage (mean ± SEM) of PSP.

DISCUSSION

The comparison with group 1 shows that the acceleration of transit observed with neostigmine (+ 85.88%—group 1 vs. group 2) is reduced when cuprum 4CH is associated with neostigmine (+ 43.61%—group 1 vs. group 3). A preliminary treatment with cuprum 4CH significantly reduced ($P < 0.02$) the faciliating action of neostigmine (−49.21%).

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[2]Logiciel STATITCF (1987), 8 av. President Wilson, 75116 Paris, France.

TABLE 1. Intestinal Transit: Mean Migration Percentage (M ± SEM) of PSP in Mice for the Four Groups (Numbers of Animals Per Group Are in Parenthesis)*

Group	Mean migration percentage (M ± SEM)
1 (reference transit) (12)	46.2 ± 3.6
2 (neostigmine) (12)	85.88 ± 3.75
3 (cuprum + neostigmine) (12)	66.35 ± 7.54
4 (cuprum) (12)	44.50 ± 4.65

*Statistics on 48 values show that group 2 is different from group 1 ($P < 0.001$); group 3 is different from group 1 ($P < 0.02$); group 3 is different from group 2 ($P < 0.02$); group 4 is not different from group 1.

This study supplied us two conclusions:

1. A low-dose treatment with cuprum 4CH given alone has no significant effect on intestinal transit (group 1 no different from group 4). But a low-dose treatment can affect the response of the gastrointestinal tract to a drug, which, like neostigmine, enhances digestive transit.
2. There is no sex difference for cuprum 4CH–inhibiting effects on neostigmine.

How does cuprum 4CH antagonize neostigmine? At least 3 levels of interaction are possible: 1) at the intestine vessels: cuprum, which is an astringent substance (8), can induce a reduction of membrane vessel permeability; for this reason, neostigmine vessel penetration might be slackened, and its digestive effects reduced; 2) at the cholinesterase enzyme level, or 3) at the muscarinic (M_1 and M_2) receptors of acetylcholine: if cuprum can be fixed at these levels, it might induce copper coordination complexes formation (chelation −4), which could modify neostigmine digestive effects.

Further experiments in vivo and in vitro are needed to test these hypotheses.

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