



EXPERIMENTAL STUDY ON THE ANALGESIC EFFECT OF DIMETHYLSULFOXIDE IN MICE USING THE WRITHING TEST

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Abstract. Introduction. DMSO (dimethylsulfoxide) is frequently used in fundamental pharmacology as solvent for different organic compounds, due to its amphipathic molecule, which is soluble in both aqueous and nonpolar, organic media.

Aim. In the present experiment we tried to explore if DMSO has an analgesic effect per se in the writhing test, pure or diluted 1:1 in saline. If so, the question remains if it can be used without any problem as vehicle for nonpolar substances with a possible visceral analgesic effect.

Materials and methods. Five groups of albino mice were tested with DMSO, pure or diluted in saline 1:1 vol/vol, metamizole sodium+saline and metamizole sodium+DMSO diluted in saline 1:1 vol/vol.

The writhing test was performed 120 min after substances administration and the observation of writhes lasted for 5 minutes. Statistic analysis of data was made with the programs Excel and SPSS 15.

Results and discussions. A statistically significant difference between the tested groups was obtained using a nonparametric statistic test (Kruskal Wallis). DMSO pure had a significant analgesic effect, while DMSO diluted 1:1 in saline did not. DMSO associated to metamizole sodium had a nonsignificant tendency to increase the analgesic effect of metamizole sodium in the writhing test.

Conclusions. These results raise the question of a possible interference of DMSO, used as vehicle, on the analgesic effects of other substances assayed in the writhing test.

Keywords: dimethylsulfoxide, analgesia, writhing test

Introduction.

DMSO (dimethylsulfoxide) is an amphipathic molecule with a highly polar domain and two apolar methyl groups, making it soluble in both aqueous and nonpolar, organic media.[1]

In fundamental pharmacological researches DMSO is used to solubilize different organic compounds.[1]

DMSO is not used as a drug despite the fact

that it was tried in various pathological conditions such as: interstitial cystitis by intravesical instillation (indication approved by FDA), amyloidosis, gastrointestinal disorders (anti-inflammatory effect in ulcerative colitis, for healing acute duodenal ulceration and alleviation of abdominal pain caused by alcohol-induced chronic pancreatitis), brain edema, the treatment of rheumatoid arthritis, chronic prostatitis. It also had an antipsychotic action in schizophrenia, improved the antiproliferative effect of interferon-alpha on human lung adenocarcinoma cells, had a beneficial effect in the topical treatment of herpes zoster, enhanced the efficacy of fungicides in the treatment of dermatologic mycosis, it can be used after the extravasation of certain drugs used in

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chemotherapy given intravenously, preventing the necrosis of tissues and ulceration. In experimental animal model DMSO prevented the development of liver cirrhosis induced by thioacetamide in mice. [1] Except for the indication in interstitial cystitis, the others didn't obtain an experts' consent.

Several systemic side-effects from the use of DMSO have been reported, namely nausea, vomiting, diarrhea, hemolysis, rashes, renal failure, hypertension, bradycardia, heart block, pulmonary edema, cardiac arrest, and bronchospasm.[1]

In experimental pharmacology literature there are some data about the analgesic effect of DMSO but only in two analgesia tests- tail flick and hot plate, using morphine as positive control [2].

Aim.

The question is if DMSO might have an analgesic effect *per se* in the writhing test, pure or diluted 1:1 vol/vol in saline. If it proves to have this effect, the consequent problem is if DMSO could be used, as before, as vehicle for nonpolar substances with a possible visceral analgesic effect.

Materials and methods.

Thirty male albino mice weighting between 20 and 35 g were used. DMSO (producer Merck Chemicals), metamizole sodium (positive control, producer Zentiva Romania) and saline (negative control) were intraperitoneally (i.p.) administered. Five groups were tested:

- Group I: negative control (saline),
- Group II: pure DMSO, 11g/kg body weight (bw)

- Group III: DMSO:saline 1:1 vol/vol (5g/kg bw DMSO)
- Group IV: metamizole sodium 500 mg/kg bw + saline,
- Group V: metamizole sodium 500 mg/kg bw+ DMSO:saline 1:1 vol/vol bw (2.5 g/kg bw DMSO).

When 2 substances were used each was administered in a different side of the mouse's abdomen, e.g. for group IV in the left side metamizole solution and in the right side the saline solution. Each animal received an amount of 0.1 ml fluid/10 g body weight divided into two equal doses.

The writhing test was performed 120 minutes after the substances' administration. Five minutes before the tests an irritating substance was administered (acetic acid 0.75% vol/vol). The observation of the animals lasted for 5 minutes. The counting of the writhes (a contraction of abdominal muscles accompanied by an elongation of the body and extension of the hind limbs) was performed by a single person and was "blind". Statistic analysis of data was made using the programs Excel and SPSS 15.

Results.

The mean number of writhes was (as showed in table 1 and figure 1): 17.67 for negative control (saline, group I), 0.33 for pure DMSO (group II), 8.33 for DMSO:saline 1:1 vol/vol (group III), 3 for metamizole sodium 500 mg/kg bw + saline (group IV), and 0.67 for metamizole sodium 500 mg/kg bw + DMSO:saline 1:1 vol/vol (group V). Statistic analysis of data showed that one-way ANOVA could not be performed because of inhomogeneity of vari-

	Group I	Group II	Group III	Group IV	Group V
	Control	Pure DMSO	DMSO:SF 1:1 vol/vol	Metamizole sodium 500mg/kg+saline	Metamizole sodium 500mg/kg+DMSO:SF 1:1 vol/vol
1	20	2	5	9	1
2	11	0	2	0	1
3	19	0	22	0	0
4	17	0	1	4	1
5	25	0	0	5	1
6	14	0	20	0	0
Mean	17.67	0.33	8.33	3.00	0.67
SDEV	4.89	0.82	9.97	3.69	0.52
SEM	1.99	0.33	4.07	1.51	0.21
P (Dunnett T3 test)		0.002	0.436	0.002	0.002

Table 1 Number of writhes (each animal and each group), mean number of writhes, standard deviations, standard errors, and p value relative to the control group

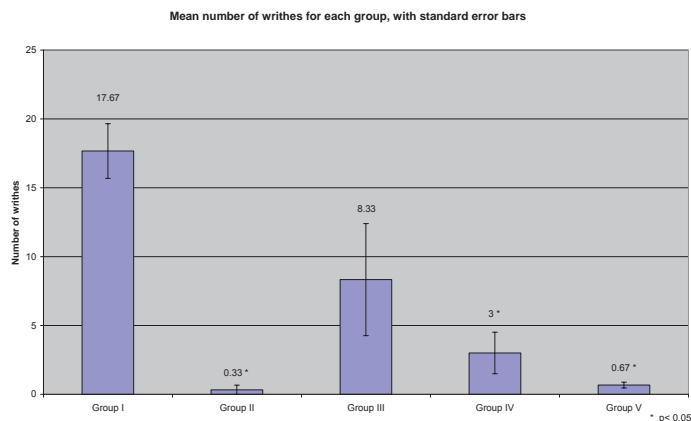


Figure 1. The mean number of writhes for each group. Group I Control (saline)- 17.67±1.99 writhes/5 minutes. Group II: pure DMSO, 11 g/kg bw - 0.33±0.33 writhes/5 minutes. Group III: DMSO:saline 1:1 vol/vol (5 g/kg bw DMSO)- 8.33±4.07 writhes/5 minutes. Group IV: metamizole sodium 500 mg/kg bw + saline - 3.00±1.51 writhes/5 minutes. Group V: metamizole sodium 500 mg/kg bw+ DMSO:saline 1:1 vol/vol bw (2.5 g/kg bw DMSO) - 0.67±0.21 writhes/5 minutes.

ances. Thus a nonparametric test, Kruskal Wallis test, was performed. It showed the existence of a statistically significant difference between groups. Data computation using a multiple comparison test which didn't presume the variances' homogeneity, showed statistically significant differences between groups I and II, between groups I and IV and between groups I and V.

Discussion.

In the present experiment, administration of the same volume of solution was preferred and an interval of 2 hours between i.p. injection of the substances and test was chosen. The interval is adequate for observing the onset of the effect for DMSO as showed in reference [2], and also for metamizole sodium. [3] [4].

The results showed significant analgesic effects for groups II, IV and V. The analgesic effect at 2 hours after pure DMSO administration was almost complete. The effect of DMSO:saline 1:1 vol/vol (group III) was not statistically significant. This result was similar to that described in reference [2]. In this reference the dilution 1:1 DMSO:distilled water had an analgesic effect smaller than that of pure DMSO even if the same doses of DMSO in mg/kg were used. The significant analgesic effect obtained for metamizole sodium demonstrated the validity of the data we obtained. Although it was not statistically significant ($p=0.726$), the effect of the association of metamizole sodium 500 mg/kg

bw with DMSO:saline 1:1 vol/vol (group V) was greater than that of metamizole sodium 500 mg/kg bw with saline (group IV).

Conclusions.

1. DMSO had an analgesic effect in the writhing test in mice.
2. The analgesic effect was present only for the pure DMSO and not for the diluted DMSO 1:1 in saline.
3. DMSO associated to metamizole sodium had a nonsignificant tendency to increase the analgesic effect of metamizole in the writhing test.
4. These results raise the question of a possible interference of DMSO, used as vehicle, on the analgesic effects of other substances assayed in the writhing test.

References

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