Full thickness, excisional wounds a) 20 × 20 mm and b) 15 × 15 mm were made on the left flank in male (250-300 g) (M) and female (F) (200-250 g) Hooded Lister rats. The wounds were covered for 48 hrs with Tegaderm and then allowed to heal with full air exposure. Wound areas were traced on acetate sheets immediately after infliction and daily for a max. of 16 days. The tracings were photocopied, digitised (DIGIT. Institute of Ophthalmology, University of London) and expressed graphically as log wound area versus time. From these graphs the specific rate of contracture (Billingham and Russel, 1956) was calculated. The effects of two anti-inflammatory agents on the specific rate of contracture were investigated, drug treatments began on the second day after wound infliction. The following specific rates were calculated as:-

The data suggests that the specific rate of wound contracture is a reproducible and simple constant to derive and may be predictive in leading to the discovery of drugs capable of usefully modifying wound contracture.

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Evaluation of the irritation and contact-sensitizing potential of fenticonazole

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Fenticonazole (F) is an imidazole derivative with antimycotic and antibacterial activity and it is indicated in the treatment of fungal infections, including candidiasis and pytiriasis versicolor (Veronese, 1984; Wiest, 1987).

The identification of contact allergens by means of safety studies is essential in the correct development of any drug to be administered topically like F (Kligman, 1967).

The aim of this study was to evaluate the irritation and the contact –sensitizing potential of fenticonazole both as dermatological and gynaecological formulations.

With regards to dermatological formulations a double-blind, randomized clinical trial was performed on twelve healthy volunteers to evaluate the irritation and contact-sensitizing potential of fenticonazole 2% cream and spray versus miconazole 2% cream and econazole 1% spray. The study period for each subject was 72 hours irritation test, 5 days wash-out and 2 weeks contact-sensitizing test.

An open clinical trial with gynaecological formulations was performed on twenty-four healthy volunteers. During the irritation test, the first group (12 subjects) was treated with F 200 mg ovules, once a day for three days and the second group (12 subjects) was treated with F 600 mg ovules in single administration. Contact-sensitizing test was performed with F 200-600 mg ovules and its excipients according to the method described by Kligman, 1967.

There was no evidence of irritation after treatment with fenticonazole cream, its excipients, miconazole cream and fenticonazole spray excipients, whereas signs of irritation were observed in four cases after treatment with the spray formulations (two after fenticonazole, two after econazole). Neither spray nor cream formulations of fenticonazole showed evidence of sensitization in any of the twelve subjects.

There was no evidence of irritation after treatment with fenticonazole 200 mg and 600 mg ovules. After performing the contact-sensitizing test, two subjects (one in the F 200 mg ovules group and one in the F 600 mg excipients group) presented signs of mild sensibilization.

No systemic adverse reactions were noted and no subject had to be withdrawn from these studies.

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Analgesic and anti-pyretic effect of cyproheptadine

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Cyproheptadine has both strong anti-serotonine effect and anti-histamine effect. It has also slight central depressing effect and anti-choline effect. It is clinically applied mainly in allergic diseases. Treatment of Cushing's disease, prolactinoma and hyperprolactinemia has been also reported. Its anti-inflammatory effect has been already reported by the author. In this report the analgesic and anti-pyretic effect of cyproheptadine was investigated.

Cyproheptadine-HCl raised the pain threshold in hot plat test and writhing test in mice and tail flick test in rats, strenthened the hypnotic action by subthreshold dosage of sodium phenobarbital and chloral hydrate. The ED50 of analgesia was 4.4(3.2-5.7) mg/kg 30 min after ip cyproheptadine in mice. The ED50 of analgesia was 0.14(0.12-0.18) mg/kg 90 min after icv cyproheptadine in mice. The ED50 of analgesia was 12.4(8.4-18.2) mg/kg 30 min after ip cyproheptadine in rats. Cyproheptadine po 20, 40 mg/kg and ip 10, 20 mg/kg showed significant anti-pyretic effect on yeast-induced pyrexia in rats.

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Differences in analgesic effects of ibuprofen (acid) and ibuprofen lysinate using an experimental evoked potential pain model

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Maximal plasma concentrations are reached sooner in case where ibuprofen is administered (p.o.) as the lysinate than when administered in acid form (Geisslinger G. et al., Int. J. Clin. Pharmacol. Ther. Tox 27(7): 324–328, 1989). The aim of the present study was to test, whether the analgesic effects of these two preparations are also different. 16 young and healthy volunteers (8 female, 8 male) participated in the study, which followed a controlled, randomized, double-blind, 3-fold cross-over design (ibuprofen acid 600 mg, ibuprofen-lysinate 1000 mg, and placebo). Measurements were performed before, 30, 60, and 90 min after administration of the test medication. 30 phasic CO_2-stimuli of two painful concentrations were applied to the left nostril and 20 tone bursts were presented to the left ear. A continous cool and dry air stream was used in order to study the effects on responses to tonic pain stimuli. The EEG was recorded from 8 sites of the 10/20 classification. Following are the main results of the experiments: No changes in acoustic evoked potentials and cardiovascular parameters (heart rate and blood pressure) were observed. A short lasting decrease in the alpha-band of the EEG 30-60 min after administration of both ibuprofen preparations was found when compared with placebo ($p < 0.05$), as well as a decrease in intensity estimates to tonic pain stimulation which was more pronounced for ibuprofen lysinate than for ibuprofen acid ($p < 0.05$). Estimates of the tonic pain stimuli did not differ after administration of both test medications. Latencies of pain-related responses obtained 30 min after ibuprofen lysinate administration increased more than after ibuprofen acid and placebo administration ($p < 0.05$). Plasma concentrations mainly correlated with amplitudes of the pain-related potentials from the frontal leads. Based on the data of this experiment it can be assumed that ibuprofen lysinate occasioned a better/sooner