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THE COMBINED EFFECTS OF  
ETHANOL AND FENMETAZOLE (DL-524)  
IN ANIMALS AND MAN

by

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## SUMMARY

Experiments were conducted with DL-524, 2[(3,4-dichlorophenoxy)methyl]-2-imidazoline HCl, to study its possible antagonism of ethanol's depressant effects. The intraperitoneal (ip) administration of DL-524 significantly shortened the sleeping time induced by ethanol in mice and rats. The brain concentration of ethanol was determined in DL-524 (10 mg/kg) and saline treated mice at various times after ethanol (4.5 g/kg ip). The disappearance of ethanol from DL-524 and control mice was the same. In other studies, the brain ethanol concentration was determined when an animal regained the righting reflex and mice pretreated with 5-20 mg/kg DL-524 had significantly higher concentrations than controls. The antagonism of ethanol by DL-524 was not due to an alteration of ethanol's disappearance rate and DL-524 treated mice were less sensitive to the ethanol's depressant effects. DL-524 (5-20 mg/kg) did not increase locomotor activity in mice and resulted in no amphetamine-like stimulation. Pretreatment with DL-524 did not change the LD50 of ethanol but did result in a slight antagonism of ethanol's impairment of rotorod performance.

The effect of DL-524 on ethanol-induced narcosis was not attenuated by prior administration of agents which specifically deplete the CNS of norepinephrine (NE), dopamine (DA), or 5-hydroxytryptamine (5-HT). Specific blockers of DA and 5-HT receptors did not attenuate DL-524's activity but the stimulation of NE receptors could not be eliminated as a possible mechanism of action.

Eight male volunteers ingested 0 or 200 mg DL-524 1 hr before drinking either 0 or 50 ml/70 kg ethanol. Drugs were administered in a double-blind manner and all treatments were assigned to each subject in a randomized complete block design. The mean blood ethanol concentration was 53 mg% and was unaltered by DL-524. Tests designed to measure mental and motor performance indicated that DL-524 did not antagonize ethanol's impairment of performance. In combination, the subjective symptoms caused by DL-524 and ethanol were additive but DL-524 did not enhance the psychomotor impairment induced by this dose of ethanol.