INTRODUCTION

Chlorpromazine (diemthylaminopropyl-N-chlor-phenothiazine hydrochloride) like promethazine is a phenothiazine derivative and possesses some of its actions to a greater degree, but it has negligible antihistaminic properties. Courvoisier and her associates (1953) have described an amazingly large number of pharmacological actions for this drug. These authors were the first to describe the inhibitory effect of chlorpromazine on the pressor responses to adrenaline and noradrenaline. Since then chlor-promazine has been repeatedly shown to exert an anti-adrenaline and sometime an antinoradrenaline effect in a number of animal species (dogs, cats, rats and rabbits).

Recently Martin, Riehl and Unna (1960) observed considerable and prolonged inhibition of the responses of the rabbit aortic strip to adrenaline and noradre-nalinenaline following chlorpromazine, and characterized the drug as a long acting adrenergic blocking agent. However, a secure pharmacological characterization of chlorpromazine as an adrenergic blocking agent has been continuously plagued by the inability of the drug consi-stently to block the pressor effect of noradrenaline. Thus a review of the literature shows that in cats anaesthetized with chloralose and in spinal and spinal

vagotomized cats chlorpromazine markedly and consistently reduces the pressor effect of adrenaline whereas the pressor effect of noradrenaline is either unaffected or actually potentiated (Kopera and Armitage, 1954; Martin and Riehl, 1956, Martin, Riehl and Unna,1960; Gokhale, Gulati and Kelkar, 1963). Moreover, the exact mechanism and the precise nature of the adrenergic blocking action of chlorpromazine has not still been fully elucidated.

In addition to its adrenergic blocking action, chlorpromazine has many interesting and rather complex effects on a variety of adrenergic mechanisms. The drug seems to exert a central depressant effect on vasomotor tone and reflex activity. Thus, intracisternal injection of chlorpromazine in the rhesus monkey lowers blood pressure and suppresses carotid sinus reflexes. Pressor responses to electrical stimulation of hypothalamic and medullary pressor areas and the sciatic pressor reflex are abolished by chlorpromazine in decorticate cats (Dasgupta and Werner, 1954). Chlorpromazine blocks the pressor responses to phenylethylamine, tyramine, bretylium and guanethidine drugs whose effects are probably due to release of amines from tissue stores (Vane, 1960; Gokhale et al., 1963). Ehringer, Hornykiewicz and Lechner (1960) and Pletscher and Gay (1960) have suggested that chlorpromazine reduces the outflow of amines from storage sites by decreasing

membrane permiability. Chlorpromazine also inhibits the uptake of noradrenaline at these sites (Hertting, Axelrod and Whitby, 1961).

The present experiments were undertaken with a view to precisely characterize and quantitate the adrenergic blocking action of chlorpromazine. Experiments were also designed to elucidate the selective blockade of adrenaline pressor effects by chlorpromazine.