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The emergence of clonidine, as a centrally acting antihypertensive agent conferred a new dimension to the pharmacological research. Clonidine, chemically related to naphazoline, was originally developed as a decongestant drug, but was later found to possess potent antihypertensive action, which was discovered by chance. This apparently paradoxical action of an alpha adrenoceptor agonist, attracted the attention of investigators to explore the underlying mechanism of action, responsible for the clinically useful antihypertensive effect. Subsequent studies, using various alpha adrenoceptor agonists and antagonists revealed the presence of two types of alpha adrenoceptors, which differed in their topographic localization (Langer, 1974; Starke et al., 1975b). The terms $\alpha_1$ and $\alpha_2$, analogous to $\beta_1$ and $\beta_2$ were loosely suggested (Delbarre and Schmitt, 1973) to describe post- and presynaptic alpha adrenoceptors, respectively. The discovery of these auto-
regulatory presynaptic alpha\textsubscript{2} adrenoceptors
(Langer, 1974; Starke, 1972b; 1977) opened a new
era of research in neurotransmitter pharmacology.
The presynaptic receptor concept has now been extended
to other putative neurotransmitter systems as well
(Raiteri et al., 1978; Vizi, 1979; Drew, 1977a;

In recent years, alpha\textsubscript{2} adrenoceptors have
also been found to occur postsynaptically in certain
peripheral tissues. It has been suggested that the
classification of alpha adrenoceptors into subtypes
be based on pharmacological effects rather than on
their pre- or postsynaptic location (Wikberg, 1979).
Receptors more sensitive to clonidine than to phenylephrine
and more susceptible to blockade by yohimbine
than by prazosin have been designated as alpha\textsubscript{2} and
receptors at which the effectiveness of these drugs
is in reverse order designated as alpha\textsubscript{1}. It has
been shown that vascular smooth muscle of the rat
(Docherty et al., 1979; Timmermans and Van Zwieten,
1980), dog (Constantine et al., 1980) and humans
(Docherty and Hyland, 1985) possessed both types of
alpha adrenoceptors as mediators of pressor response.
A comparative account of pre- and postsynaptic effects
of alpha adrenergic agonists on in vivo and in vitro preparations has been extensively reviewed (Table I, II). More recently, Drew (1985) has suggested, on the basis of $\text{PA}_2$ values obtained for yohimbine and prazosin (Table II) that alpha adrenoceptors may fall into more than the well established two ($\alpha_1$ and $\alpha_2$) categories.

The classification of alpha adrenoceptors into subtypes has clinical significance. Clonidine, guanfacine and alpha methyldopa owe their antihypertensive effect to their central $\alpha_2$ agonistic properties. The same holds good for some of their side effects such as sedation and dry mouth (inhibition of cholinergic transmission). Furthermore, an analgesic effect has been observed upon intravenous administration of clonidine to patients with postoperative pain (Gordh and Tamsen, 1983). Clonidine has also been shown to improve the memory of patients with Korsakoff's psychosis (McEntee and Mair, 1980). Further, clonidine is fast becoming an accepted drug for opiate withdrawal syndrome (Gold et al., 1978).

More recently, the beneficial action of antidepressant drugs is proposed to be mediated through down regulation of $\alpha_2$ adrenoceptors (Finberg and Tal, 1985; Doxey
et al., 1985). If depression involves diminished transmission through central noradrenergic synapses, alpha$_2$ antagonists might have a salutary effect in depression by virtue of their facilitatory effect on noradrenergic transmission. In fact, the antidepressant activity of mianserin has been attributed to its alpha$_2$ blocking property.

Clonidine, a prototype alpha$_2$ agonist may serve as an investigational tool by virtue of its several psychopharmacological actions (Fielding and Lal, 1980; Kulkarni et al., 1984). The present investigation was undertaken to explore this possibility. The role of alpha$_2$ adrenoceptors in behavioral depression, EEG synchronization, analgesia and hyperalgesia has been investigated. The potential of alpha$_2$ agonists in alleviating alcohol abstinence syndrome is also assessed. Clonidine was employed as a prototype alpha$_2$ agonist in all these studies and its effects were compared with two other more selective alpha$_2$ adrenoceptor agonists viz. guanfacine and B-HT 920, which incidentally belonged to different chemical classes.