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It has become increasingly evident that Ca$^{2+}$ channels, such as the voltage-dependent calcium channels (VDCC) are subject to regulatory influences. These influences may be of physiological, pathological or pharmacological nature (Ferrante and Triggle, 1990).

Three distinct types of VDCC (T, L and N) have been described based on their electrophysiological properties and sensitivity to various pharmacological substances (Tsien et al, 1987). Membrane potential constitutes the primary signal to which VDCCs respond, activating and inactivating according to potential range and duration. However, these potential-dependent channels are also modulated in their activities by a variety of receptor-initiated events (Hockberger and Swandulla., 1987; Hofmann et al., 1987; Levitan 1988; Rosenthal and Schultz, 1987; Siegelbaum and Tsien, 1983).

The type of ligand, agonist or antagonist may dictate how a receptor system will regulate. Generally chronic administration of agonist or antagonist receptor ligands results in decrease (down-regulation) and increase (up-regulation) respectively in ligand-binding densities (Hollenberg, 1985a; Pastan and Willingham, 1981).

Prolonged treatment with beta-adrenoceptor blocking agent propranolol can lead to an increase in beta-receptor number in various tissues, which may contribute to the
development of withdrawal symptoms if discontinuation of drug therapy is abrupt (Lefkowitz et al., 1984).

However, beta - adrenoceptor up - regulation is not an automatic consequence of antagonist exposure and in some systems beta - adrenoceptor number decreases (Hughes et al., 1988). This down-regulation may contribute to the pharmacological activity of these agents, but the mechanism of action remains to be defined (Ferrante and Triggle, 1990).

Receptor changes occur also as a result of chronic administration of drug. Some antidepressant agents, including desipramine also produce a decrease in the number of beta-adrenoceptor and this is likely to be related to their mechanism of action. A decrease in the myocardial beta-adrenoceptor number has been implicated in the pathophysiology of congestive heart failure (Lefkowitz et al., 1984; Smith and Katovich 1985). In hyperthyroidism the number of cardiac beta-adrenoceptors is increased. Additionally changes in the cardiac VDCCs have also been observed (Hawthorn et al., 1988; Kim et al., 1987).

Thus membrane receptor or channel regulation has important therapeutic and pathological consequences along with the various factors that may alter the properties and turnover of VDCCs.

The present study attempts to investigate the interactions of calcium channel blockers (CCBs) and antagonists with various agonists. It is known that different
agonists produce their effects by using different sources of calcium (Richard et al., 1993). The experimental design had to be restricted to recording of pharmacological responses. This was necessitated on account of the lack of facilities for measuring calcium ion movements and for radioligand binding assays. The experiments were conducted on the isolated right ventricle and isolated aorta of albino rats treated chronically with CCBs, agonists and antagonists. Responses of these two tissues were recorded to several common agonists most of which are present in the body and have been assigned a physiological role in relation to the cardiovascular system. The tissues were obtained from normal rats, hypertensive rats (DOCA-saline model) and hyperthyroid rats.