INTRODUCTION

Cardiovascular diseases are the leading cause of death worldwide. The therapy and treatment for these disorders have undergone dramatic changes since 1950s. Although the advances in drug therapy have significantly reduced overall cardiovascular morbidity and mortality, these ailments affect a better segment of society and therefore remains the most pressing health problem. Globally this insidious health problem accounts for almost 50% of total mortality from all causes (Atlas of Heart Disease and Stroke, WHO, Sept. 2004). To combat with this, various heart disorders such as hypertension, angina, arrhythmias etc. are widely investigated over past few decades and derived much benefits from the development of various compounds such as thiazide diuretics, α-agonists, α and β-antagonists, calcium channel blockers, Angiotensin Converting Enzyme (ACE) inhibitors etc. in the past 20 years.\(^1\)\(^-\)\(^3\) Now a days, among the armamentarium against heart disorders, calcium channel blockers occupy a prominent position and have revolutionized the cardiovascular therapy for the treatment of essential hypertension and several other disorders at different stages of severity.\(^4\)

The drugs classified as calcium channel blockers or calcium antagonists were introduced into clinical medicine in 1960s and are now among the most frequently prescribed drugs for the treatment of cardiovascular disorders.\(^5\) The increase in the number of available calcium antagonists, either as new formulations of pre-existing drugs or new chemical entities, over recent years has contributed to an ever-changing scenario regarding their appropriate use.\(^6\) Their wide appeal can be attributed to several features, including their well documented antihypertensive efficiency, metabolic neutrality and a clean side effect profile.\(^7\) Although these agents share a similar mechanism of action as they all inhibit the influx of extracellular calcium through the L-type channel resulting in relaxation of vascular smooth muscle and reduction in vascular resistance and are therefore assumed to be a homogeneous family of drugs but are, in fact, an extremely heterogeneous group of compounds with marked differences in chemical structure, binding sites, tissue selectivity and consequently clinical activity and therapeutic indications.\(^8\)\(^,\)\(^9\) This chemical and pharmacodynamic heterogeneity of calcium antagonists is also related with the
location of the calcium channels that they can block with more intensity. Some agents act more on calcium channels of heart than on the vascular ones, e.g., phenylalkylamines; others act more on the channels of the myocyte membranes of the resistance vessels, e.g., dihydropyridines and still others act proportionally at the level of heart and of the arterioles, e.g., benzothiazepines.

Besides the chemical and pharmacodynamic heterogeneity, there is also relevant pharmacokinetic heterogeneity. This is originated not only in the intrinsic properties of the substance but also in the galenic characteristics of different oral formulations.\textsuperscript{10,11} The newer developments like the availability of second and third generation calcium channel blocking agents and also the synthesis of new structures active against different classes of channels have increased the roles of these agents and expanded their use beyond the cardiovascular system. Simultaneously these agents have also proved to be valuable molecular tools to determine the localization, properties and structures of voltage dependent calcium channels.\textsuperscript{12}

Such interesting observations about this class of drugs, their vast heterogeneity, prompted the present investigator to undertake research work on calcium channel blockers and this is in order to review the literature on various facets of this particular class of cardiovascular agents.