INTRODUCTION

Congestive heart failure (CHF) is highly prevalent in our society and its incidence is increasing gradually especially in context with the growing aged population.\textsuperscript{1,2} Though understanding and development of new therapies for cardiovascular disorders have resulted in overall reduction of cardiovascular mortality, such benefits allow long standing stress to act upon an already weakened heart, resulting in CHF.\textsuperscript{3-6} With increasing longevity of the population of the developed countries, the number of patients suffering from cardiac insufficiency also increases, and CHF remains one of the leading cause of mortality in these countries and represents major medical problem. Over 5 million patients in the United States are affected by the disease with approximately 5,50,000 and high number of death each year.\textsuperscript{7,8}

As these figures appear to be increasing steadily, it is essential to continue with the quest for more effective CHF treatment. Despite important advances in the pharmacotherapy of heart failure over the past decade, the main challenge of cardiotonic research derives from the need of new drugs, which can not only manage CHF, but also underlying disease. Specially, the need follows from: a) the prevalence and mortality of heart failure in developed countries, b) the fact that the cardiac drugs available are clearly inadequate to restore health or even to minimize discomfort and disability and c) the condition that previous research efforts to provide drugs satisfying the above requirements have widely failed.\textsuperscript{9}

For nearly two centuries, cardiac glycosides have played a prominent role in the treatment of the CHF not withstanding their undesirable side effects.\textsuperscript{10-13} Among the thousands of analogs of glycosides that have been synthesized, no significant improvement in the therapeutic ratio has been achieved.\textsuperscript{14} The use of known sympathomimetics is limited by their positive chronotropic effect, their ability to adversely effect peripheral circulation and oral ineffectiveness.\textsuperscript{6} Although, the cardiac glycosides are the only orally effective agents, their use is limited mainly due to their propensity to cause life threatening arrhythmias.\textsuperscript{15-19}
This situation has initiated considerable research efforts devoted to the search for safer, orally active, non-glycoside 'digitalis replacement'.

Screening of several chemical classes of non-glycosides and non-catecholamine compounds resulted in the demonstration of positive inotropic properties in more than one class of drugs, e.g., pyridazinones, benzimidazoles etc. and led to the development of several novel cardiotonic agents such as levosimendan, pimobendan and sulmazole.

The current project is aimed at synthesis and study of some newer pyridazinone based cardiotonic agents with dual inotropic and vasodilatory properties, which may reduce preload and afterload on heart. Therefore it is in order to review the literature pertaining to various classes of drugs reported to possess cardiotonic effects and their perspectives in the treatment of congestive heart failure.