CHAPTER I

Introduction
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The splendid discovery of digitalis by William Wuthering in the year 1785 has enriched the field of medical science with regard to cardiovascular disorders, thus saving and prolonging the lives of those suffering from such disorders.


Initially the mechanism of positive inotropic action was controversial as was evident from the works of Hass and Hartfelder, G.(1968), Akera, T. and Brody, T.M. (1978), Lee,
K.S. and Klans, W. (1971), Schwartze, A. (1976). The major controversial issue was the inhibition of the Na\(^+\)K\(^+\) pump by digitalis which causes increased intracellular Na\(^+\) and decreased intracellular K\(^+\) concentrations. The constant levels of these ions in the intracellular fluid are maintained by the active movement of these ions against electrochemical potential gradient across surface membrane of cells. Schatzmann, H.J. (1976) established the hypothesis of inhibition of Na\(^+\) and K\(^+\) ions by digitalis in red cells. Sokou, J. (1957) indicated that active movement of ions is related to ATPase. It has now been well proved that Na\(^+\)K\(^+\) ATPase activity is specifically inhibited by digitalis in many tissues - Akera, T. (1981), Glynn, I.M. (1964), Schwartze, A. et al (1975), Skou, J.C. (1965). Thus with an adequate knowledge about the mechanism of action of digitalis, it has been used in different cardiovascular disorders like congestive heart failure, prophylaxis of heart failure, Atrial fibrillation, Atrial flutter, Paroxysmal atrial tachycardia, sick sinus syndrome with gratifying results.

Another remarkable discovery in the allied field is the function of Ca\(^+\)\(^+\) in myocardial contractility by Sidney Ringer in 1882 that has brought a new light in the treatment of myocardial diseases. Though this concept was first introduced 100 years back, it was studied systematically by Hass and Hartfelder in 1962 and subsequently by Rougier et al (1969) and Fleckenstein (1984). With the knowledge gained from the above studies it was first used in clinical medicine by Japanese and European cardiologists in the year 1970.
According to their pharmacological proportion Calcium Channel Blockers can broadly be classified in three groups:

(i) Verapamil (ii) Nifedipine and (iii) KB-9447 Mayer, H. (1984). The mechanism of action of all the three types of drugs vary and accordingly they are used in different cardiovascular disorders. Amongst the above mentioned three groups of drugs, Diltiazem and Nifedipine have got an unique effect on heart. They act primarily by increasing coronary resistance, oxygen uptake of myocardial tissue and epicardial artery size, on the other hand decreasing aortic pressure and altering the heart rate which further depends upon the pathophysiology - Richard et al (1984).

Thus digitalis and Calcium channel blockers combined with sophisticated investigations and monitoring facilities like continuous E.C.G. monitoring, echocardiogram, angioram, scincitogram, enzymatic and electrolyte estimations have brought a tremendous achievement in the management of all types of cardiovascular disorders.

Both the drugs decrease the systolic blood pressure but Diltiazem increases diastolic blood pressure at the same time. Thus, Nifedipine is superior to Diltiazem as it can also be used in the case of hypertension. Calcium Channel blockers are superior to Beta blockers in the sense that it causes vasodialatation whereas the latter causes vasoconstriction in smooth muscles. Calcium channel blockers have got antianginal effect without negative inotropic effect whereas Beta blockers have negative inotronic effect which is an intrinsic part of their antianginal effect - Jce and Opie (1984).
In cases of Myocardial ischaemia there is increased density of $\alpha$ (alpha) receptor which are responsible for malignant arrhythmias - Korr and Sharma (1984). Naturally Beta blockers have no effect whereas Calcium channel blockers have an excellent action because of the $\alpha$ (alpha) antagonistic activity. Thus the latter are superior to Beta blockers in myocardial ischaemia with malignant arrhythmias.


In the present study both these drugs, Digitalis and Nifedipine have been an automatic choice because of their immense value in clinical and experimental in cardiovascular disorders. Again, Potassium chloride and Calcium chloride have also been incorporated into the study because these drugs are always advocated in any clinical condition where infusions are needed. Moreover, the concentration of Calcium and Potassium ions have got some definite role in the action of these drugs.

Though these drugs have been used for a long time in different cardiovascular disorders, their effects and side effects after immediate infusion and their inter relation with potassium and calcium ions have not been well established in our routine clinical practice because of the lack of sophisticated investigations and monitoring facilities like
continuous E.C.G. monitoring, Echocardiogram, scintigram, angiogram and so on. Naturally we are practically devoid of such beneficial knowledge which has not immense clinical value regarding the proper management and outcome of patients.

The present study is aimed at a simultaneous experimentation on animals and clinical investigation on patients in Pediatric age group with cardiovascular disorders. Firstly, the knowledge of experimental findings that give a mechanistic approach of the drug to some extent and specify the field of application, help us immensely in clinical application. On the other hand the clinical observations that are usually associated with the application of drug, its side effects and restriction of its application can better be understood with the allied experimental findings on animal. Therefore, the present investigation will enrich us with vivid and scrupulous information on the treatment of cardiovascular disorders.