CHAPTER I

INTRODUCTION

Nifedipine, a dihydropyridine derivative, is one of a group of compounds thought to act by blocking the transmembrane inward movement of calcium; a calcium-channel blocker, slow-channel blocker or calcium entry blocker. Nifedipine often referred to as antagonist, has been used frequently as tools for the elucidation of calcium dependent regulatory mechanisms.

Calcium ion flux from the extracellular space through the slow channel of the cell membrane plays an importance role in several fundamental physiological processes in myocardial and vascular smooth muscle cells. Nifedipine blocks this influx of calcium into the cell that confers on it potent coronary and peripheral arteriodilator properties that is useful in various clinical areas. It is used in the treatment and prophylaxis of angina pectoris particularly when a vasospastic element is present, and in the treatment of hypertension and Raynaud's syndrome.

Nifedipine is rapidly and almost completely absorbed from the whole length of gastrointestinal tract [Raemsch and Summer, 1983], close to 100% of an oral dose is absorbed largely in the small intestine although the bioavailability from capsules is 45% to 68% [Foster et al., 1983]. Following admistration by mouth, peak blood concentrations occurred after 30 to 120 minutes. It is about 92 to 98% bound to plasma protein. It has been theorized that substantial first-pass metabolism is

responsible for the lower bioavailability of the drug, the biological half-life is in the range of 2 to 5 hours [Kleimbloesm et al., 1984]. The elimination half-life of nifedipine is apparently dependent upon the dosage from in which it is administered, with half-lives of 6 to 11 hours, 2 to 3.4 hours and 1.3 to 1.8 hours measured after oral tablet, oral capsule and intravenous administration respectively [Foster et al.,1983; Klembloesm et al., 1984].

Nifedipine undergoes almost complete hepatic oxidation to 3 pharmacological inactive metabolites which are excreted in the urine. It has been reported that following oral administration 30% to 40% of the amount absorbed is metabolized during the first-pass through the liver. Two of these metabolites, an hydroxy carboxylic acid derivative, contain 95% of the total amount of nifedipine undergoes biotransformation, only traces of unchanged parent drug are excreted in the urine [Kondo et al. 1980]. The total systemic clearance of nifedipine from plasma ranges from 27 to about 66 liters per hour.

Nifedipine may be administered sublingually or buccally by directing the patient to bite the capsule for a more rapid effect. It may be given as a sustained-release tablet in a dose of 10 to 40 mg. twice daily in hypertension. It may also be given concomitantly with beta blockers in the treatment of angina or hypertension and with nitrates in angina. In the mean time various sustained release preparations of nifedipine have been developed with the purpose of reducing the frequency of administration and the incidence and intensity of side effect. The recent development in transdermal drug delivery system using skin as a route of drug

administration has become the most interesting route. By this route, the first-pass effect can be avoided so the efficacy of drug is increased.

In the development of the preparations of drug, especially transdermal drug delivery system, the study of the *in vitro* release of drug products has been the basis protocol [Barry, 1985]. This study has been purposed to investigate the *in vitro* release of nifedipine from matrix gel preparations containing various types and concentrations of surfactants.

Objectives of This Study :

On the basis of the rational mentioned above, the objectives of this research are,

1. To study the effect of types of surfactants on release of nifedipine from matrix gel by *in vitro* study.

2. To study the effect of concentrations of surfactants on release of nifedipine from matrix gel.

3. To study the effect of surfactants and its concentration on the physical appearances of matrix gel.

4. To be the guidelines of development of transdermal drug delivery of nifedipine in matrix diffusion controlled type.