1. INTRODUCTION:

Hypertension, elevated blood pressure, is a noteworthy public health concern worldwide due to its significant contribution to the global health burden and its role as a prominent risk factor for the development of a number of disease processes. In the year 2001, high blood pressure accounted for 54% of stroke, 47% of ischemic heart disease, 75% of hypertensive disease, and 25% of other cardiovascular disease worldwide. The negative impact of hypertension on health status is clear, especially taking into account the disability, decreased quality of life, and mortality associated with stroke and cardiovascular disease. In 2001, 7.6 million deaths (13.5% of all deaths) and 92 million disability life-years (6% of total) were attributable to systolic blood pressure greater than 115 mmHg (Lawes et al., 2008). It is saddening to note that such pervasive negative effects are related to such a modifiable cause.

Oral route has been the major route of drug delivery for the chronic treatment of many diseases. The purpose of the present work was to develop an optimized bilayer tablet for anti-hypertension patients using hypertensive agent as a model drug candidate by optimization technique.

Combination drug therapy is recommended for treatment of hypertension to allow medications of different mechanism of action to complement each other and together effectively lower blood pressure at lower than maximum doses of each.

This floating dosage form is well known as a hydrodynamically balanced system (HBS) (1–3). It has been suggested for the following instances that an active material should be formulated in the form of an HBS to enhance bioavailability: (i) having a dissolution and/or stability problem in the small intestine fluids, (ii) being locally effective in the stomach, (iii) being absorbed only in the stomach and/or upper part of the intestine.

The stomach is divided into 3 anatomic regions: fundus, body, and antrum (pylorus). The separation between stomach and duodenum is the pylorus. The part made of fundus and body acts as a reservoir for undigested material, whereas the antrum is the main site for mixing motions and act as a pump for gastric emptying by propelling actions. Gastric emptying occurs during fasting as well as fed states. The pattern of motility is however distinct for the two states.
During the fasting state an interdigestive series of electrical events take place, which cycle both through stomach and intestine every 2–3 h. This is called the interdigestive myoelectric cycle or migrating myoelectric cycle (MMC), which is further divided into following 4 phases.

- **Phase I (basal phase)** lasts for 40 to 60 min with rare contractions.
- **Phase II (preburst phase)** lasts for 40 to 60 min with intermittent action potential and Contractions. As the phase progresses the intensity and frequency also increases gradually.
- **Phase III (burst phase)** lasts for 4 to 6 min. It includes intense and regular contractions for short period. It is due to this wave that all the undigested material is swept out of the stomach down to the small intestine. It is also known as the housekeeper wave.
- **Phase IV** lasts for 0–5 min is a transition period of decreasing activity until the next cycle begins.

Food effects and the complex motility of the stomach play a major role in gastric retention behavior. Several approaches of non-effervescent and effervescent formulation technologies have been used and patented in order to increase gastric residence time of the GFDDS.

The rational for combination therapy is to encourage the use of lower doses of drug to reduce the patient’s blood pressure to goal to minimize dose dependent side effects and adverse reactions. When smaller doses of medication with different mechanism of action are combined synergistic or additive effects on blood pressure are achieved and dose dependent side effects are minimized.

Formulation & Evaluation of Bilayer Tablet of Antihypertensive Agent.

Bilayer tablet are compressed tablet made by more than one compression cycle. This process is best used when separation of active ingredient is needed for stability process, or mixing process inadequate to guarantee uniform distribution of two or more active ingredient. Bilayer tablet are prepared by compression addition tablet granulation on a previously compressed granulation. The operation may be repeated to produce bilayer tablet of two layers.