Literature review:

1. **Shaji Jessy et.al (2007)** developed a multiple-unit, floating-pulsatile drug delivery system. The system developed consists of drug containing core pellets prepared by extrusion-spheronization process, which were coated with an inner pH-dependent layer of Eudragit S100 and outer effervescent layer of sodium bicarbonate and HPMC K100M.

2. **Andrea Gazzaniga, et.al (2008)** these authors in their review article discussed pulsatile release, various design strategies have been proposed, chiefly including reservoir, capsular and osmotic formulations and role water-swellable polymers.

3. **Andrei Dashevsky ,et.al (2006)** developed and evaluated a pulsatile multiparticulate drug delivery system (DDS), coated with aqueous dispersion Aquacoat® ECD.

4. **Bin Li, JiaBi Zhu, et.al (2008)** developed a novel system for three-pulse drug release based on “tablets in capsule” device based on a matrix tablet. This system which consists of a water-soluble cap, impermeable capsule body, and two multi-layered tablets. Types of materials for the modulating barrier and its weight can significantly affect the lag time. Polymers were chose sodium alginate and hydroxy-propyl methyl cellulose (HPMC E5) as the candidate modulating barrier material.

5. **M. Efentakis, et.al (2006)** studied comparative evaluation of various structures in polymer controlled drug delivery systems and the effect of their morphology and characteristics on drug release. Swellable polymers used such as hydroxypropylmethyl cellulose (Methocel E 50 LV, Methocel K 100M), polyethylene oxide (Polyox), and cellulose acetate propionate as a hydrophobic, impermeable material.

6. **Srisagul Sungthongjeena, et.al (2004)** developed pulsatile release tablets with swelling and reputable layers. System consisting of cores coated with two layers inner layer of swelling layer containing superdisintegrants crosscarmellose sodium and rupturable layer of ethyl cellulose coatings was prepared and evaluated as pulsatile drug delivery system.

7. **Yan Zhang, et.al (2003)** developed a novel pulsed-release system based on osmotic pumping mechanism bilayer coated tablets containing an osmotically active agent is presented. This system consists of Terbutaline sulphate and sodium chloride was coated
with the mixture of Eudragit RS and RL different ratios were applied as the swelling layer and semipermeable outer coat, respectively.

8. **H. Zou, et al. (2008)** developed a floating-pulsatile drug delivery system intended for chronopharmacotherapy. Floating pulsatile concept was applied to increase the gastric residence of the dosage form having lag phase followed by burst release. To overcome limitations of various approaches for imparting buoyancy, they generate the system which consist of three different parts a core tablet containing the active ingredients, an erodible outer shell, and a top cover buoyant layer. The buoyant layer, prepared with methocel K4M, Carbopol, 934P, and sodium bicarbonate, provides buoyancy to increase the retention of the oral dosage form in the stomach.

9. **Bodmeie R. et al. (2004)** developed the pulsatile release tablets with swelling and rupturable layers. Cores containing buflomedil HCl as model drug were prepared by direct compression of different ratios of spray-dried lactose and microcrystalline cellulose and were then coated sequentially with an inner swelling layer containing a superdisintegrant (croscarmellose sodium) and an outer rupturable layer of ethylcellulose. The lag time of the pulsatile release tablets decreased with increasing amount of microcrystalline cellulose.

10. **Lin. et al. et al. (2004)** studied hydrophilic excipients like HPMC, Spray-Dried Lactose modulate the time lag of time-controlled disintegrating press-coated tablet. They reported that the lag time markedly dependent on the weight ratio of Ethylcellulose (EC) /spray dried lactose or EC/HPMC in the outer shell. Different time lags of the press coated tablets from 1 to 16.3 hours could be modulated by changing the type and amount of excipients.

11. **Lin. et al. et al. (2001)** also studied the formulation design of double layer in the outer shell of Dry-coated tablet to modulate lag time and time-controlled Dissolution Function using micronizes Ethylcellulose. Different compositions of EC powder with a coarse particle (167.5 μm) and several fine particles (<6 μm), respectively, were mixed to formulate the whole layer of the outer shell of dry-coated tablets. The formulations containing different weight ratios of coarse/fine particles of EC powders or 167.5 μm EC
powder/excipient in the upper layer of the outer shell to influence the release behavior of sodium diclofenac from dry-coated tablet were also explored.

12. Conte U. et al. (1993) studied the mechanism of drug release from the press coated tablet using various grades of HPMC and concludes that the delay in release start is not influenced by the core composition and depends only on the shell formulation. Except for the lag time, the release kinetics of the drug contained in the core are not significantly influenced by the presence of the erodible barrier, but can be widely modulated using a sellable polymeric shell.

13. Fukui. et al. (2000) studied the applicability of Press-coated tablets, containing diltiazem hydrochloride (DIL) in the core tablet and coated with hydroxypropylcellulose (HPC) as the outer shell as timed-release tablets with a predetermined lag time and subsequent rapid drug release phase. The results indicated that tablets with the time drelease function could be prepared, and that the lag times were prolonged as the viscosity of HPC and the amount of the outer shell were increased.

14. Sirkiä T. et al. (1994) studied on development and biopharmaceutical evaluations of a press-coated prolonged-release salbutamol sulphate tablet. The aim of the study described was to develop prolonged-release press-coated tablets of salbutamol sulphate from which drug release would increase with time. The tablets, each consisting of a core and a coat, were prepared using a compression-coating technique. Different viscosity grades and amounts of HPMC were used in the coat.

15. Lin S Y. et al. (2001) studied on Micronized ethylcellulose used for designing a directly compressed time-controlled disintegration tablet. The drug release from dry-coated tablet exhibited an initial lag period that was dependent on the particle size of the EC powder, followed by a stage of rapid drug release. The smaller the EC particle size used the longer the lag time obtained.

17. Ozeki Y.et.al. (2004) investigate novel one-step dry-coated tablets (OSDRC) manufacturing method and evaluated the possibility of its application to delayed-release tablets. The effects of different outer layer thicknesses and various compression pressures were examined using HPMC to evaluate OSDRC applicability to delayed-release tablets.

18. T.Y. Fan, S.L. Wei, W.W. Yan et.al.(2002) evaluate of pulsatile release tablets with ethylcellulose and Eudragit L as film coating materials and cross-linked polyvinylpyrrolidone in the core tablets. They develop new pulsatile release tablets, which can suppress drug release in stomach and release the drug rapidly after a predetermined lag time of about 3 h in intestine, the use of tablets with ethylcellulose / Eudragit L as a coating film and cross-linked polyvinylpyrrolidone in the core tablets was investigated. The release of diltiazem hydrochloride (DIL) as a model drug in the core tablets was investigated in vitro.

19. Krogel et al. (1999) developed a floating-pulsatile drug delivery systems based on a reservoir system consisting of a drug-containing effervescent core and a polymeric coating. Preliminary studies identified important core and coating properties for the two systems. For the floating system, a polymer coating with a high elongation value and high water- and low CO₂ permeability’s was selected (Eudragit® RL: acetyltributyl citrate 20%, w:w), while for the pulsatile DDS, a weak, semi permeable film, which ruptured after a certain lag time was best (ethyl cellulose : dibutyl sebacate 20%, w:w). A polymer (cellulose acetate or hydroxypropyl methylcellulose) was added to the core to control the drug release.

20. S. Sharma et al. (2006) developed a floating-pulsatile drug delivery system using porous calcium silicate (Florite RE) and sodium alginate. Meloxicam was adsorbed on the Florite RE (FLR) by fast evaporation technique. Drug adsorbed FLR powder was used to prepare calcium alginate beads by ionotropic gelation method, using 3² factorial designs.

21. Usha Yogendra Nayak et al. (2009) prepared system contained swellable polymer (L-hydroxypropyl cellulose (L-HPC), xanthan gum, polyethylene oxide or sodium alginate) together with drug tablet and erodible tablet (L-HPC or guar gum) in a pre-coated capsule.

22. M.E. Sangalli et al. (2004) develop system is composed of a drug-containing core and a hydrophilic swellable polymeric coating capable of delaying drug release through slow
interaction with aqueous fluids. An optional external gastroresistant film is applied to overcome gastric emptying variability, thus allowing colon delivery to be pursued according to the time-dependent approach by using various grades of HPMC.

23. **Ahmad Mohamad, ET al. (2006)** develop a rupturable, capsule-based pulsatile drug delivery system with pH-independent properties prepared using aqueous coating. The drug release is induced by rupturing of the top-coating, resulting by expanding of swellable layer upon water penetration through the top-coating.

24. **Shan-Yang Lin, ET al. (2001)** design a novel dry-coated tablet with time-controlled drug release. This dry-coated tablet, containing a core tablet of sodium diclofenac and an outer coating layer of EC, was prepared by direct compression. The drug release from dry-coated tablet exhibited an initial lag period that was dependent on the particle size of the EC powder, followed by a stage of rapid drug release.

25. **Raimar Lo benberg, et al. (2005)** investigate differences in the pharmacokinetic patterns between a pulsatile drug delivery system using a pulsatile capsule, an immediate release tablet and a controlled release tablet. Metoprolol was chosen as a model drug because of its high solubility and high permeability pattern throughout the GI tract.

26. **Jonathan C.D., et al. (2003)** investigated the coating-dependent release mechanism of a pulsatile capsule using NMR microscopy. Nuclear magnetic resonance microscopy was used to elucidate the internal mechanisms underlying this behaviour by studying the routes of internal water transport and the timescale and sequence of events leading to the pulse.

27. **Srisagul Sungthongjeen et al. (2008)** develop floating multi-layer coated tablets were designed based on gas formation. The system consists of a drug-containing core tablet coated with a protective layer (hydroxypropyl methylcellulose), a gas forming layer (sodium bicarbonate) and a gas-entrapped membrane, respectively. The mechanical properties of acrylic polymers (Eudragit_ RL 30D, RS 30D, NE 30D) and ethylcellulose were characterized by the puncture test in order to screen a suitable film for the system.

28. **HAO ZOU, et al. (2008)** Design and Evaluation of a Dry Coated Drug Delivery System With Floating–Pulsatile Release. the system which consisted of three different parts, a core tablet, containing the active ingredient, an erodible outer shell and a top cover
buoyant layer. The dry coated tablet consists in a drug-containing core, coated by a hydrophilic erodible polymer which is responsible for a lag phase in the onset of pulsatile release.


30. T. Bussemer et al (2003) develop and evaluate a rupturable pulsatile drug delivery system based on soft gelatin capsules with or without a swelling layer and an external water-insoluble but permeable polymer coating, which released the drug after a lag time (rupturing of the external polymer coating). The swelling of the gelatin capsule itself was insufficient to rupture the external polymer coating, an additional swelling layer was applied between the capsule and the polymer coating.

31. Anil K. Anal et al (2007) review Time-Controlled Pulsatile Delivery Systems for Bioactive Compounds. This review describes the recent patents related to preprogrammed delivery systems, such as systems with eroding, soluble or rupturable barrier coatings, and systems with capsular structures.

32. Sachin Survase et al (2007) review current scenario of pulsatile drug delivery. Various technologies present in the market based on the various methodologies..like delivery systems with rupturable coating layer or with erodible coating layers or with release controlling plug, stimuli induced PDDS less temperature induced and chemical stimuli induced systems and externally regulated system.

34. **Patel Gayatri C. et al** (2009) studied explores the comparative utility of the enteropolymers (enteric-coated polymers) such as acrycoat L-100, acrycoat S-100, ethyl cellulose (EC) and cellulose acetate phthalate (CAP) in developing a suitable dosage form, exhibiting a minimum drug release in the upper regions of the gastrointestinal tract (GIT) on order to provide site specificity as well as time controlled formulation.

35. **Manivannan Rangasamy** (2010) review Colon Specific Drug Delivery System, Advantages, Approaches. These are pressure controlled colon delivery capsules, CODESTM, colon drug delivery systems based on pectin and galactomam coating, hydrogels, osmotic controlled drug delivery system, pulsincap system, time clock system, chronotropic system, enterion capsule technology

36. **Asim Sattwa Mandal, et al** (2010) review Drug delivery system based on chronobiology. This review on chronopharmaceutics gives a comprehensive emphasis on potential disease targets, revisits the existing technologies in hand and also addresses the theoretical approaches to emerging discipline such as genetic engineering and target based specific molecules.

37. **Rajan K et al.** (2001) review Current Status of Drug Delivery Technologies and Future Directions. This article discussed drugs can be delivered to a patient by many different delivery systems, including oral, transdermal, injection, implants, etc. Most of the drugs are amenable to these types of delivery systems

38. **Alessandra Maroni, et al** (2010) review Rationale and chronopharmaceutical formulations. This article discussed chronotherapeutic approaches and a growing awareness of the impact of patient compliance are likely to strengthen the research efforts towards the design, preparation and evaluation of such devices.


such as type of plug (powder or tablet), plug thickness and the formulation of fill material on the release pattern of diltiazem HCl, a model drug, was investigated.

41. **Anuradha K. Salunkhe, Remeth J. Dias et al. (2011)** developed floating pulsatile drug delivery system of metoprolol tartrate. The prepared floating pulsatile delivery system consisted of three different parts: a core tablet, containing the active ingredient, an erodible outer shell and a top cover buoyant layer. The rapid release core tablet (RRCT) was prepared by using superdisintegrants along with active ingredient. Dry coating of optimized RRCT was done by using different grades of hydroxy propyl methyl cellulose (HPMC) E5, E15, and E50 and upper most buoyant layer was prepared with HPMC K15M and sodium bicarbonate.

42. **J.Kausalya, J.Lakshmi Eswari, et al. (2011)** developed multiparticulate system consisting of drug –loaded cellulose acetate cores encapsulated within Eudragit S-100 microspheres was designed for chronotherapeutic delivery of flurbiprofen. Drug –loaded cellulose acetate cores were prepared by emulsion solvent evaporation technique in an oily phase at different drug: polymer ratios (1:1, 2:1 and 3:1). These cores were successfully microencapsulated with Eudragit S-100 following the same technique at the core: coat ratio of 1:5.