2.1 Tramadol Hydrochloride

1. **Deore R. K. et al. (2010)**[^1] prepared and evaluated sustained release matrix tablets of tramadol hydrochloride using glyceryl palmitostearate. The study showed that glyceryl palmitostearate (Precirol ATO 5) is an appropriate waxy matrix former for sustained release of a water-soluble drug such as tramadol hydrochloride. In this study, it was found that matrix tablets prepared by melt granulation technique were far superior to those prepared by direct compression of the physical mixture.

2. **Rao R. N. G. et al. (2009)**[^2] studied on formulation and evaluation of sustained release matrix tablets of tramadol hydrochloride. He concluded that carrageenan gum shown faster drug release within 6 hrs than formulations prepared with other polymers while formulations with Karaya Gum and HPMC K15M shown drug release in 8 hrs. With all three formulations, an initial burst release of the drug followed by a steady-state release was observed.

3. **Obaidat A. A. et al. (2001)**[^3] studied controlled release of tramadol hydrochloride from matrices prepared using glyceryl behenate. Different ratios of tramadol HCl, glyceryl behenate, and lactose or microcrystalline cellulose were used for tablet formulation. The study reveals that increasing the ratio of glyceryl behenate in the granules resulted in decreasing the release of the drug. Granules prepared with a ratio of 1:3 (tramadol HCl/glyceryl behenate) sustained release of the drug for 8 h. The matrices were prepared by physical mixture of drug and matrix forming agent and by hot fusion methods. Drug release was adjusted with release enhancers like MCC and lactose. A higher drug release was obtained with lactose. Drug release was observed to be independent of compression force and pH of dissolution medium and hot fusion method was effective in retarding drug release from matrices.

4. **Tiwari S. et al. (2003)**[^4] studied on controlled release formulation of Tramadol Hydrochloride using hydrophilic & hydrophobic matrix system. Hydrophilic matrix tablets were prepared by wet granulation and hydrophobic (wax) were prepared by
melt granulation technique. Hydrophobic matrix tablets resulted in sustained drug release (>20hrs.) as compared with hydrophilic (<14hrs.). Presence of ethyl cellulose prolonged release. Tablets prepared by combination of hydrophilic and hydrophobic polymers failed to prolong release beyond 12 hrs. Hydrophobic matrix tablets prepared using hydrogenated castor oil was found to be best suited for modulating the delivery of highly water-soluble drugs.

5. **US Pat. No. 5601842**[^5^]: prepared different sustained release formulations of tramadol hydrochloride. They used HPMC K100M, Eudragit RL30D, hydroxyethyl cellulose for sustaining release of drug upto 12 hrs.

6. **US Pat. No. 6306438**[^6^]: prepared extended release formulations by dispersed tramadol hydrochloride in a matrix of hydrophobic material containing wax like substance which was melted during preparation of matrix. They prepared different formulations using ethocel std 7, stearyl alcohol, cetostearyl alcohol, hydrogenated vegetable oil etc.

### 2.2 Metoprolol Succinate

7. **Augsburger et al. (1999)**[^7^] examined the influence of critical formulation and processing variables on extended release metoprolol tartrate matrix tablets using a hydrophilic polymer hydroxypropylmethylcellulose. Analysis of variance indicated that change in polymer level was the most significant factor affecting drug release. The drug release mechanism was predominantly found to be Fickian diffusion controlled.

8. **Deshmukh V. N. et al. (2009)**[^8^] studied on formulation and evaluation of sustained release metoprolol succinate tablet using hydrophilic gums as release modifiers. He concluded that as the time increase, swelling index was increased, because weight gain by tablet was proportional to rate of hydration up to 6hrs, later on it decreases gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The direct relationship was observed between swelling index
and gum concentration, as gum concentration increase swelling index increased. It was observed that the cumulative percent drug release decrease with increasing concentration of gum and swelling index.


10. Sandeep G et al. (2009) [10] formulated and optimized metoprolol succinate extended release matrix tablet using hydrophilic polymers like hydroxypropyl methyl cellulose, hydroxypropyl cellulose, ethyl cellulose, carbopol 934 by direct compression method and concluded that the formulation provide effective drug release for 20 hr. and it shows nearly zero-zero order drug release governed by diffusion through swollen matrix and erosion of the matrix, showing the anomalous diffusion or non-fickian transports.

11. US Pat. No. 20070053983: [11] prepared 24 hrs sustained release formulations of metoprolol succinate using one hydrophilic polymer and with one or more than that gum substance. In the formulations Methocel K15MCR, hydroxypropyl cellulose (HPC- LF), sodium alginate etc. were used.


2.3 Cyclobenzaprine Hydrochloride

14. Razaghi A. M. et al. (2002) prepared oral osmotic drug delivery systems containing PEO-swellable polymer and mannitol was used as osmotic agent. The release rates was independent of orifice size.

15. Razaghi A. M. et al. (2002) prepared osmotically rupturable systems and the release of cyclobenzaprine hydrochloride (model drug) from the systems was investigated. Systems were designed using mannitol (osmotic agent) and increasing amounts of polyethylene oxide (PEO, a water-swellable polymer) surrounded by a semipermeable membrane. When placed in an aqueous environment. Water imbibition into the systems distended and swelled the systems until the membrane ruptured and released the active compound to the outside environment. Tablets with increasing amount of PEO exhibited longer rupture times. This may be due to osmotic pressure-modulating properties of the polymer, changing the rate of water imbibition into the systems.

16. Jamunadhevi V. et al. (2011) prepared bilayer tablet of diclofenac potassium as IR part and cyclobenzaprine HCl as ER part. ER part was prepared using HPMC K 100 MCR. The effect of concentration of polymer was studied. The dissolution study of ER layer showed that an increasing amount of HPMC results in reduced drug release.

17. US Pat. No. 20100098832 prepared extended release (ER) formulations of Cyclobenzaprine HCl by coating inert particles with drug layer and then coating that polymer with polymer to make it ER beads.

2.4 Aceclofenac

18. Yadav I. et al. (2010) studied on formulation, evaluation and optimization of aceclofenac sustained release matrix tablets. He used EC and xanthan gum and concluded that high level of EC reduce drug release rate on account of formation of a strong matrix with reduced porosity. This increases diffusional path length
leading to reduced water penetration through the microspores resulting in slower drug release.

19. Kannan S. et al. (2010)\textsuperscript{[19]} studied formulation and evaluation of sustained release tablets of aceclofenac using hydrophilic matrix system. The study was undertaken with the aim to formulate and evaluate aceclofenac sustained release tablet using HPMC grade of polymer as retarding agent. From the study, it was concluded that the formulation of sustained release tablet of aceclofenac containing HPMC K100M, mannitol and lactose which are taken as ideal or optimized formulation of sustained release tablet for 24 hours.

20. Santanu et al. (2009)\textsuperscript{[20]} developed matrix tablets for oral controlled release of aceclofenac, using various viscosity grade hydrophilic polymer HPMC in two different proportions. Hydrophobic polymer ethyl cellulose and guar gum were prepared by wet granulation method and subjected to \textit{in vitro} drug release studies. Furthermore, the results of the \textit{in vitro} studies in pH 7.5 phosphate buffer medium showed that F7 tablets provided controlled release comparable with market sustained release formulation (aeroff-SR tablets). F7 tablets showed no change in physical appearance, drug content, or in dissolution pattern after storage at 40°C with 75%RH for 6 months. Based on the results of the \textit{in vitro} studies, it was concluded that the HPMC matrix tablets provided oral controlled release of aceclofenac.

21. Rao B. et al. (2011)\textsuperscript{[21]} studied sustained release formulation of aceclofenac based on monolithic matrix technology The tamarind seed polysaccharide (TSP) was extracted from tamarind kernel powder and this polysaccharide was utilized in the formulation of matrix tablets containing Aceclofenac by wet granulation technique and evaluated for its drug release characteristics. TSP is hydrophilic and rate controlling polymer. The \textit{in vitro} release study of matrix tablets were carried out in phosphate buffer pH 7.4 for 12 hr. Among all the formulations, F 5 showed 98.062% better controlled release at the end of 12 hr.
22. Mutalik S et al. (2007) \cite{22} have formulated once daily sustained release tablets of aceclofenac using HPMC K4M by direct compression method. The prepared tablets were evaluated for \textit{in vitro} drug release, stability studies, preclinical (anti-inflammatory, analgesic, pharmacokinetics and toxicity studies) and clinical pharmacokinetic studies and found identical pharmacokinetic parameters as compared with marketed tablet of aceclofenac. The pharmacokinetic study in healthy human volunteers indicated that B 7 tablets produced an extended drug release up to 24 h as that of marketed product with almost identical pharmacokinetic parameters.

23. Manda R. et al. (2010) \cite{23} prepared a sustained release matrix tablet of aceclofenac using different natural polymers (Guargum, Xanthan gum, Chitosan) in various proportions as release controlling factor by direct compression. The in vitro release study showed that only F9 formulation was releases the drug in a sustained manner for 11 hours. From this study, a decrease in release kinetics of the drug was observed when the polymer concentration was increased. The drug release from these formulations was satisfactory after 3 months storage in 40C and 75% RH. Besides, this study explored the optimum concentration and effect of polymer(s) on acelofenac release pattern from the tablet matrix for 11 hour period.

24. Shivhare U. D. et.al. (2009) \cite{24} developed “once daily” sustained release tablets of aceclofenac by wet granulation using carboxypolymethylene polymer. The drug excipient mixtures were subjected to preformulation studies while the tablets were subjected to physicochemical studies, \textit{in vitro} drug release, stability studies and validation studies. The physicochemical properties of tablets were found within the limits. Formulation F2 & F9 containing Carbopol 971P and Carbopol 974P were found to release the drug in sustained manner upto 24 hour and were stable under accelerated conditions of temperature for 6 months since there were no significant changes in drug content and physical parameters.
25. EP 2393486: prepared single layer and double layer tablet of aceclofenac to achieve release of drug in controlled manner. Immediate release part consists of drug, water soluble additives, pH controlling agent (sodium hydrogen carbonate), disintegrant; while controlled release part consists of polymer of HPMC and carbomer.

2.5 Biopharmaceutics Classification System

26. Lennernas H. et al. (2005) explained about BCS classification system to provide a scientific approach for classifying drug compounds based on solubility and intestinal permaeability. BCS acts as simple tool to early drug development.

27. Lindenberg M. et al. (2004) explained about BCS system has became an increasingly important tool for regulation of drug products world wide. They have classified model list of essential medicines of the WHO on the basis of BCS classification.

28. Reddy B. B. K. et al. (2011) discussed in their work and concluded Biopharmaceutics Classification System (BCS) is the result of continuous effort in mathematical analysis for elucidation of the kinetics and dynamics of the drug process in the gastrointestinal tract for NDA and ANDA filings and biowaiver. This step reduces timeliness in the new drug development process.

29. Varma M. V. et al. (2004) explained about significance of biopharmaceutics, solubility and permeability in new drug discovery. Classification system for drugs based on BCS provides drug design an opportunity to manipulate structure or physicochemical properties of lead candidates to achieve better deliverability.

2.6 Sustained Release Matrix System using Hydrophilic Polymer

30. Saravankumar et al. (2010) developed once daily sustained release matrix tablets of Stavudine using hydrophilic matrix materials such as hydroxyl propyl methyl cellulose (HPMC) K4M and carbopol 974P. The prepared extended release
tablets were then evaluated for various physical tests. The results of all these tests were found to be satisfactory. This finding reveals that above a particular concentration, HPMC K4M and carbopol 974P are capable of providing almost zero order drug release.

31. Dhopeshwarkar V. et al. (1993)\textsuperscript{[31]} studied on evaluation of xanthan gum in the preparation of sustained release matrix tablets. He concluded that release of a soluble drug (chlorpheniramine maleate) and an insoluble drug (theophylline) from tablets containing low concentrations of xanthan gum was mainly via diffusion and erosion, respectively. Drug release from tablets containing xanthan gum was slightly faster in acidic media due to more rapid initial surface erosion than at higher pH. After hydration of the gum, drug release was essentially pH-independent. The amount released was directly proportional to the loading dose of drug and inversely proportional to gum concentration in tablets.

32. Mishra B. et al. (2005)\textsuperscript{[32]} studied on development and in vitro evaluation of hydrophilic matrix tablets of diltiazem hydrochloride. Tablets having HPMC K15M gave more sustained release than other hydrophilic polymers studied. Amount of HPMC K15M and presence of different diluents significantly affected the drug release. It was observed that all the fabricated tablets delivered the drug following Higuchi diffusion mechanism.

33. Vidyadhara S et al. (2004)\textsuperscript{[33]} formulated and evaluated propranolol HCl oral controlled release matrix tablets using HPMC K4M along with electrolytes. The in vitro results indicated that the drug was released at a controlled rate which is due to differential swelling rate, matrix stiffening and provided a uniform gel layer. These findings indicated that the swelling and gel formation in the presence of ionisable species within the hydrophilic matrices provides an attractive alternative for controlled drug delivery from a simple monolithic system.
34. Ragavendra et al. (2009) \cite{34} developed sustained release matrix tablets of water soluble tramadol hydrochloride using different polymers viz. Hydroxy propyl methyl cellulose (HPMC) and natural gums like karaya gum (KG) and carrageenan (CG). Varying ratios of drug and polymer like 1:1 and 1:2 were selected for the study. After fixing the ratio of drug and polymer for control the release of drug up to desired time, the release rates were modulated by combination of two different rates controlling material and triple mixture of three different rate controlling material. After evaluation of physical properties of tablet, the in vitro release study was performed in 0.1N HCl pH 1.2 for 2 hrs and in phosphate buffer pH 6.8 up to 12 hrs. The effect of polymer concentration and polymer blend concentration were studied. Different ratios like 80:20, 60:40, 50:50, 40:60 and 20:80 were taken. Dissolution data was analyzed. It was observed that matrix tablets contained polymer blend of HPMC/CG were successfully sustained the release of drug upto 12 hrs.

35. Maghsoodi M.et al. (2008) \cite{35} studied on effect of formulation variables on Phenobarbital release from HPMC matrices. He concluded that higher drug release rate was found for formulations with lower HPMC/lactose ratios and lower HPMC viscosity grades. The viscosity of HPMC polymer has a large influence on the erosion rate of matrix tablet. Use of low viscosity grade of HPMC polymer is desired for drugs that are poorly water soluble such as Phenobarbital since the erosion rate of tablet matrix is the controlling factor for drug release. As the proportion of EC or NaCMC in admixture with HPMC increased, the release rates gradually increased.

36. Sasidhara RLC et al. (2007) \cite{36} formulated oral CR matrix tablets of verapamil HCl using poly (ethylene oxides) \{Polyox WSR 303 and Polyox WSR 301\}. In this study, the matrix tablets were prepared by direct compression method. The drug release from the formulations followed first order kinetics and were linear with Higuchi plots. The in vitro drug release studies for different formulations were also compared with drug release studies of commercially available products. The results
indicated that the formulations containing drug and polymer ratio 1:0.5 for Polyox WSR 303 and 1:1 for Polyox WSR 301 for Verapamil HCl were linear with drug release rates of marketed products. The formulations containing drug and polymer ratio 1:1, 1:1.5 for Polyox WSR 303 and 1:1.5 for Polyox WSR 301 showed greater inhibition on release rate of Verapamil HCl from the tablet matrix.

37. Goyal K. et al. (2009) [37] studied on formulation and evaluation of oral sustained drug delivery system for Venlafaxine Hydrochloride using hydrophilic gums and polymers such as Xanthan [Xgum], Guar gum [Ggum] and HPMC. The Matrix tablets of Venlafaxine Hydrochloride were prepared by direct compression method. No drug excipients incompatibility was seen. All the physical characteristics of the fabricated tablets were found to be within the acceptable limits. Guar gum alone or in combination with Xanthan gum could not efficiently retard the drug release, while Xanthan gum along with HPMC could retard the release of Venlafaxine Hydrochloride.

38. Reza et al. (2003) [38] to investigate effect of plastic, hydrophilic and hydrophobic types of polymers and their content level on release profile of drug from matrix system. Polymers used were Kollidon SR, HPMC, carnauba wax. Higher polymeric content in matrix decrease release rate of drug because of increase tortuosity and decrease porosity. Carnauba wax found to cause strongest retardation of drug.

39. Peppas et al. (2002) [39] investigated the swelling behavior of four cellulose ethers such as HPMC K4M, HPMC K15M, HEC and HPC that differ in their type and degree of substitution and also elucidated the network structure of the swollen matrices under dynamic and equilibrium conditions [27].

40. Maggi et al. (2000) [40] compared the performance of PEO and HPMC polymers when employed in the geomatrix technology, a versatile, well-known method to achieve extended release of drugs at a constant rate. Four core formulations were prepared, containing soluble drug (Diltazem) and, alternatively, PEO or HPMC of
two different viscosity grades, particularly polyox WSR N60 K and polyox WSR 303, which are believed to be comparable to HPMC K4M and HPMC K100M. The results show slower release rate from matrices containing HPMC compared to PEO.

2.7 Sustained Release Wax Matrix Tablet

41. Basak S. et al. (2008) \[41\] studied on design and release characteristics of sustained release tablet containing metformin HCl concluded that tablet matrices containing cetyl alcohol gave better release of the drug than other materials studied. However, the rate of release varied with amount of cetyl alcohol in the matrix. Release of drug observed by diffusion.

42. Kamble R.N. et al. (2004) \[42\] has studied melt solidification technique. He used higher amount of wax in ibuprofen beads prepared by melt solidification technique. He observed better integrity and prolonged drug release by using a combination of waxes, it was concluded that waxes for the combination should be selected on the basis of their erosion and solidification behaviour.

43. Li F. Q. et al. (2006) \[43\] studied \textit{in vitro} controlled release of sodium ferulate from Compritol 888 ATO-based matrix tablets, This study showed that Compritol 888 ATO is an appropriate waxy material that can be utilized as a matrix-forming agent to control the release of a freely water-soluble drug sodium ferulate. Matrix tablets prepared from solid dispersions were more effective than those from physical mixtures in controlling the drug release rate. The release rates of SF from Compritol 888 ATO-based matrix were retarded effectively.

44. Ozyazıcı M. et al. (2006) \[44\] prepared lipid matrix tablets of Metronidazole using Carnauba wax, Beeswax, Stearic acid, Cutina HR, Precirol ATO 5, and Compritol ATO 888 by hot fusion method. Among these, Stearic acid matrix tablets showed the highest and Carnauba wax matrix tablets showed the least release rates. These workers also investigated the effect of swelling and relaxation properties of lipid
matrix on diffusional exponent. Swelling ratios were in decreasing order for Cutina HR > Beeswax > Precirol ATO 5 > and Compritol ATO 888, respectively. They concluded that the diffusion mechanism was probably pure Fickian for stearic acid and Carnauba wax and coupling of Fickian and relaxation for Cutina HR, Beeswax, Compritol ATO 888, and Precirol ATO 5 tablets.

45. Paradkar A. R. et al. (2004) \cite{45} prepared matrices of metformin hydrochloride and glycercyl behenate by direct compression and melt granulation. Melt granulation method was found to be more effective in retarding release of drug as compared to physical mixture. The effect of release enhancers such as lactose and microcrystalline cellulose on release profile of drug was investigated. They found increased release of drug from lactose containing matrix than from MCC containing matrix.

2.8 Effect of excipients on release profile of drug

46. Albhar K. G. et al. (2012) \cite{46} studied on effect of gums and excipient on drug release and swelling of Ambroxol Hydrochloride sustained release matrices. He concluded that Xanthan gum and κ-Carrageenan gum retarded the drug release more than Guar gum. Avicel 102 and lactose enhanced the dissolution rate whereas dicalcium phosphate retarded the drug release.

47. Levina M. et al. (2004) \cite{47} investigated the effect of commonly used excipients like spray dried lactose, microcrystalline cellulose and starch 1500 on release profile of drug from HPMC matrix system. They found starch 1500 produced significant reduction in drug release as compared to MCC or spray dried lactose when used.

48. Bravo S. A. et al. (2002) \cite{48} studied the effect of MCC, starch and lactose on release of drug from HPMC matrix tablet. They found release of drug is influenced by presence of these excipients.
49. **Jannin V et al. (2006)**[^49] studied on influence of Poloxamers on the dissolution performance and stability of controlled release formulation containing Precirol ATO 05 and concluded that, the addition of these hydrophilic polymers (Lutrol) in the lipid matrix increased the amount of theophylline released due to the swelling of the hydrophilic polymer and the creation of a porous network into inert lipid matrix.

50. **Amaral et al. (2001)**[^50] studied effect of concentration of hydrophilic and hydrophobic polymer i.e. HPMC and Hydrogenated castor oil, fillers (lactose and dicalcium phosphate) on Naproxen release. Matrix tablet prepared using HPMC and hydrogenated castor oil with increase in their concentration decrease the rate of drug release. Drug release modulated by adding suitable diluents. Lipid matrices forming material is suitable for sustained release dosage formulation or modulating the delivery of highly water soluble drug.

51. **Patel N. M. et al. (2008)**[^51] prepared extended release formulation of venlafaxine hydrochloride using glyceryl behenate as matrixing agent. They studied the effect of release liner like PEG 6000, lactose and MCC. They found the faster release of drug from matrix containing PEG 6000.

52. **Killen B. U. et al. (2006)**[^52] prepared sustained release wax matrix tablet using stearic acid and studied effect of concentration of lactose. They found that increase in concentration of lactose increase release of drug, may be due to erosion mechanism.

### 2.9 Three Layer and Tablet in Tablet Technology

53. **Phaecamuda T. et al. (2008)**[^53] studied the drug release of model drug propranolol using various polymers like Xanthan gum, chitosan. A tri-layer matrix tablet system was designed in which the upper and lower layer consisted of Xanthan gum and chitosan as barrier layers and the middle layer consisted of drug, Xanthan gum, Chitosan and lactose. Barrier layers successfully retard the drug...
dissolution. Near zero-order kinetic could be achieved for drug release from the three layer tablets. Swelling and erosion behaviors corresponded to the drug release characteristics of the three-layered tablet in different dissolution fluids

54. Al-Saidana S.M. et al. (2004) [54] studied oral controlled release tri-layer matrix tablets prepared using guar gum and Metaprolol Tartarate. Guargum 50% was used as release retardant. In this 75 mg of guar gum granules on both sides acted as rate controlling layers and it was found to provide the required release rate. A mixture of talc and magnesium stearate was used as lubricant and HPMC was added as a diluents. The upper and lower layer contained guar gum and the middle layer consisted of metoprolol and guar gum. *In vivo* performance of the guar gum-based three-layer matrix tablet for a highly water-soluble drug (metoprolol tartrate) was studied in healthy human volunteers.

55. Chavda H. et al. (2012) [55] in their work have designed an oral controlled drug delivery system for sparingly soluble diclofenac sodium (DCL) using guar gum as triple-layer matrix tablets. Matrix tablet granules containing 30% (D1), 40% (D2) or 50% (D3) of guar gum were prepared by the conventional wet granulation technique. The upper layer consists of guar gum, HPMC, starch and middle layer contained drug, guar gum. HPMC, starch, and the lower layer contains guar gum. The in vitro drug release by Hopfenberg model indicated that the release of drug from tablets displayed heterogeneous erosion. The batch containing 87% of guar gum in guar gum layers and 50% of guar gum in middle layer matrix granule layer was found to provide the release rate for prolonged period of time.

56. Krishnaiah Y.S.R. et al. (2002) [56] prepared oral controlled drug delivery systems for highly water-soluble drugs using guar gum as a carrier in the form of a three-layer matrix tablet. Metoprolol tartrate was chosen as a model drug because of its high water solubility. Three-layer matrix tablets were prepared by compressing 50 mg of granules containing 87% of guar gum on both sides of matrix granules containing either 30, 40 or 50% of guar gum (coded as TL1M1, TL1M2 or TL1M3,
respectively). The other three-layer tablets were prepared by compressing 75 mg of granules containing 87% of guar gum on both sides of matrix granules containing either 30, 40 or 50% of guar gum (coded as TL2M1, TL2M2 or TL2M3, respectively). The three-layer matrix tablet with 75 mg of guar gum layers on both sides of the metoprolol tartrate matrix formulation containing 50% of guar gum was found to provide the required release rate matching with the theoretical release rate constants calculated on the basis of pharmacokinetic properties of the drug, for metoprolol tartrate tablet formulations meant for twice daily administration. The results clearly indicate that guar gum in the form of three-layer matrix tablet is a potential hydrophilic carrier in the design of oral controlled drug delivery systems for highly soluble drugs.

57. Krishnaiah YSR et al. (2002) prepared oral controlled drug delivery systems for highly water-soluble drugs using guar gum as a carrier in the form of three-layer matrix tablets. Trimetazidine dihydrochloride was chosen as a model drug because of its high water solubility. Matrix tablet granules containing 30%, 40% or 50% of guar gum were prepared. Three-layer matrix tablets of trimetazidine dihydrochloride were prepared by compressing on either side of guar gum matrix tablet granules of trimetazidine dihydrochloride, guar gum granules containing either 65% of guar gum (Guar gum, starch paste, HPMC, talc and magnesium stearate), 75% of guar gum or 85% of guar gum as release retardant layers. The three-layer guar gum matrix tablet provided the required release rate on par with the theoretical release rate for guar gum formulations meant for twice daily administration. The three-layer guar gum matrix tablet (T3M3) showed no change either in physical appearance, drug content or in dissolution pattern after storage at 40 8C/RH 75% for 6 months. The DSC study did not show any possibility of interaction between trimetazidine dihydrochloride and guar gum/other formulation excipients used in the study. The results indicated that guar gum, in the form of three-layer matrix tablets, is a potential carrier in the design of oral controlled drug delivery systems for highly water-soluble drugs such as trimetazidine dihydrochloride.
2.10 Bilayer Tablet Technology

58. Rao NGR et al. (2010) studied controlled release glipizide bilayered matrix tablets using different grades of HPMC as novel release modifier along with Xanthan gum, guar gum and karaya gum as release retardants. Bilayered matrix tablets were prepared by wet granulation method. He found all above said polymers gave zero order release of glipizide.

59. Vijaya Kumar B. et al. (2010) developed bilayer tablet of guaifenesin using superdisintegrant sodium starch glycolate for the fast release layer and metalose 90 SH and Carbopol 934 for the sustaining layer. The formulations gave an initial burst effect to provide the loading dose of the drug followed by sustaining release for 12 hr from the sustained layer of matrix tablets.

60. Patra C. N. et al. (2007) developed bilayer tablet of propranolol hydrochloride using superdisintegrant sodium starch glycolate for the fast layer and water immiscible polymers such as ethylcellulose, Eudragit RLPO and Eudragit RSPO for the sustaining layer. The formulations gave an initial burst effect to provide loading dose of the drug followed by sustained release for 12 hrs.

61. Karwa P. et al. (2011) developed bilayer tablets comprising two layers, i.e. immediate release and controlled release layer. The immediate release layer comprised croscarmellose sodium as a super disintegrant and the controlled release layer comprised HPMC K100M as the release retarding polymers. Direct compression method was used for formulation of the bilayer tablets. In vitro dissolution studies were carried out in a USP apparatus I, basket method. HPMC K100M extended the release of drug from the extended release layer for 6 hr.

62. Shirwaiker A. A. et al. (2004) designed sustained release bi-layered tablets of diltiazem HCl using ethylcellulose or rosin as matrix materials in various quantities to study their ability to retard the drug release. The formulations gave an initial burst effect followed by sustained release for 12 h which indicates bimodal release of diltiazem HCl from matrix tablets. The kinetics of drug release involved both diffusion and dissolution mechanism.
2.11 REFERENCES

Tramadol Hydrochloride

Metoprolol succinate
CHAPTER 2


Cy clobenzaprine Hydrochloride


Ace clofenac


**Biopharmaceutics Classification System**


**CHAPTER 2**

**Sustained release (Modified Release) hydrophilic polymer matrix system**


**Sustained release (Modified Release) wax matrix system**


**Effect of excipients on release profile of drug**


51. Patel N. M., Soniwala M. M., Influence of release enhancers on release of venlafaxine hydrochloride from glyceryl behenate matrix tablet, Indian Drugs, 2008; 45 (2), 98-104.


**Three layer tablet technology**


**Bilayer Tablet System**


