US 4,940,580 (Schering, Expired in 2006) claims a sustained release dosage form of labetalol hydrochlorid comprising the active ingredient in a polymeric matrix of hydroxypropylmethylcellulose and polyvinylpyrrolidone and a pharmaceutically acceptable organic acid.

US 7,731,989 (Depomed, Expiry: Oct 25, 2022) claims a dosage form, comprising between about 100 mg to about 4800 mg of gabapentin or pharmaceutically acceptable salt thereof, dispersed in a single polymer matrix comprising at least one swellable hydrophilic polymer that swells unrestrained dimensionally by imbibing water to increase its size to promote gastric retention of the dosage form in a stomach in a fed mode, wherein upon contact with water, gabapentin is released by diffusion from the dosage form over a period of at least five hours and at least 40 wt % of the gabapentin is retained in the dosage form 1 hour after administration.

US 5,591,454 (Alza, Expiry: Jan 7, 2014) claims a method for treating hyperglycemia in a patient, wherein the method comprises administering to the patient a dosage form comprising 2 mg to 750 mg glipizide that is administered at a therapeutically effective dose of 10 ng to 25 mg over 24 hours from the dosage form comprising 1 mg to 300 osmagent and a hydrogel selected from the group consisting of poly(ethylene oxide) having a 4,000,000 to 8,000,000 molecular weight and a carboxymethylcellulose having a 200,000 to 1,000,000 molecular weight to the patient to produce the intended effect in the patient.

US 5,948,437 (AstraZeneca, Expiry: May 28, 2017) relates to sustained release formulations comprising a gelling agent and quetiapine or a pharmaceutically acceptable salt thereof, together with one or more pharmaceutically acceptable excipients, to methods of treating psychotic states and hyperactivity utilizing the sustained release formulations and to a process for preparing the sustained release formulations.

US 5,334,392 (Adir et Compagnie, Expired in 2012) relates to matrix tablet for the sustained release of indapamide consisting of indapamide, polyvidone, methylhydroxyalkyalkylcellulose, and excipient, which exhibits linear sustained release for at least eight hours.
US 7,476,403 (Andrx, Expiry: June 16, 2014 + 548 days PTA) directed to a controlled release dosage form of clarithromycin. Hydroxypropyl cellulose or hydroxypropyl methylcellulose is used as a polymer. The controlled release formulation of present invention provides a therapeutic effect for at least 12 hours and wherein the maximum blood plasma concentration of the active drug (Cmax) when said dosage form is administered to a patient in a fed state is less than 50% higher or lower than the Cmax of said dosage form when administered in the fasted state, the area under the curve (AUC) when said dosage form is administered to a patient in a fed state in less than 20% higher or lower than the AUC of said dosage form when administered in the fasted state and the time to maximum blood plasma concentration (Tmax) when said dosage form is administered to a patient in a fed state is less than about 20% higher or lower than the Tmax of said dosage form when administered in the fasted state.

US 7,919,116 (Andrx, Expiry: Mar. 20, 2018) disclose sustained release formulation of metformin hydrochloride. The controlled release dosage form comprising (a) a core comprising: (i) an antihyperglycemic drug; (ii) optionally a binding agent; and (iii) optionally an absorption enhancer; (b) a semipermeable membrane coating surrounding the core; and (c) at least one passageway in the semipermeable membrane. The formulations provide therapeutic plasma levels of metformin hydrochloride to a human patient over a 24 hour period after administration.

WO/2009/117819 (Pharmascience Inc., Expiry: Mar. 26, 2029) relates to an extended release therapeutic drug delivery system comprising a controlled release core matrix composition comprising an active pharmaceutical ingredient such as a central nervous system stimulant (e.g., methylphenidate) and a release controlling agent (i.e., HPMC -K4M, HPMC-K 100M CR or HPMC-K 15 M CR) as well as a controlled release coating layer composition covering the core matrix composition, which comprises controlled release polymers such as Eudragit RL 30D.

US 2005/0031546 A1 (Gruenenthal, Expiry: Oct 10, 2024) relates to an abuse-proofed, thermoformed dosage form containing, in addition to one or more active ingredients with abuse potential optionally together with physiologically acceptable auxiliary substances, at least one synthetic or natural polymer with a breaking strength of at least 500 N and to a process for the production thereof.
US 6,930,129 (Alza, Expiry: Jul 31, 2017) relates to methods and devices for maintaining a desired therapeutic drug effect over a prolonged therapy period are provided. In particular, oral dosage forms that release drug within the gastrointestinal tract at an ascending release rate over an extended time period are provided. The dosage forms may additionally comprise an immediate-release dose of drug.

US 6,149,940 (Synthelabo, Expiry: Aug 22, 2017) claims a pharmaceutical tablet for oral administration and for the controlled release of alfuzosin hydrochloride into the proximal segments of the gastrointestinal tract, the tablet comprising: a) a first layer having the property of swelling considerably and quickly on contact with aqueous biological fluids, the first layer being produced by compression of a mixture or of a granulate comprising a hydrophilic polymer constituting from 5.0 to 90% of the weight of the first layer, b) a second layer adjacent to the first layer containing the alfuzosin hydrochloride, the second layer being formulated with a hydrophilic polymer and with an auxiliary substance to give the preparation suitable properties of compressibility and in order to allow the release of alfuzosin hydrochloride within a predetermined time period, c) and optionally a third layer adjacent to the second layer comprising a hydrophilic polymer which gels and/or swells and which may optionally be broken down and has a barrier function which modifies the release of the alfuzosin hydrochloride from the second layer, the third layer being primarily highly impervious to passage of the active substance.

US 6,514,531 (Sanofi-Synthelabo, Expiry: Dec 1, 2019) claims a pharmaceutical controlled-release dosage form adapted to release zolpidem or a salt thereof over a predetermined time period, according to a biphasic in vitro profile of dissolution when measured in a type II dissolution apparatus according to the U.S. Pharmacopoeia in 0.01M hydrochloric acid buffer at 37 degree C., where the first phase is an immediate release phase having a maximum duration of 30 minutes and the second phase is a prolonged release phase, and wherein 40 to 70% of the total amount of zolpidem is released during the immediate release phase and the time for release of 90% of the total amount of zolpidem is between 2 and 6 hours.

US 5,914,131 (Alza, Expiry: Jul 7, 2014) claims a dosage form comprising a drug layer comprising 8 mg of hydromorphone, 67.8 mg of poly(ethylene oxide) of 200,000 molecular weight, 4 mg of poly(vinyl pyrrolidone), and 0.2 mg of a lubricant; a delivery layer comprising 37.8 mg of poly(ethylene oxide) possessing a 2,000,000 molecular weight, 18 mg of sodium chloride, 3 mg of hydroxypropylmethyl) cellulose of 9,200 molecular weight, 0.6
mg of a colorant, and 0.15 mg of a lubricant; a semipermeable wall comprising 27.2 mg of cellulose acetate of 39.8% acetyl content, and 0.275 mg of polyethylene glycol of 3,350 molecular weight; a passageway in the wall; and a controlled rate of release of 0.427 mg/hr for 17.3 hours.

**Barde RK et al., (2011)** developed optimized floating drug delivery system (GFDDS) of Labetalol Hydrochloride using Hydroxypropyl methyl cellulose K4M (X1), Carbopol 934P (X2), Sodium carboxymethylcellulose (X3) as independent variables and floating lag time, t50% and t80% as responses with combination of citric acid and sodium bicarbonate. They concluded that gastro retentive tablet of Labetalol hydrochloride can be prepared via floating mechanism to increase residence time of drug in stomach and thereby increasing its absorption and the present study demonstrates that use of simplex centroid design in development of floating tablets with minimum experimentation.

**Kramar A et al., (2003)** evaluated three formulation parameters i.e. the concentration of plasticizer (triethyl citrate), methacrylate polymers ratio (Eudragit RS:Eudragit RL) and the quantity of coating dispersion for the application of polymethacrylic films from aqueous dispersions in order to obtain multiparticulate sustained release of diclofenac sodium.

**Siddique S et al., (2010)** prepared sustained release capsule containing coated matrix granules of metoprolol tartrate using hydrophilic hydroxypropyl methyl cellulose (HPMC K100M) and hydrophobic ethyl cellulose (EC) polymer as matrix builders and Eudragit® RL/RS as coating polymer and studied its in vitro release and in vivo absorption. The results suggested that wet granulation with subsequent coating by fluidized bed technique, is a suitable method to formulate sustained release capsules of metoprolol tartrate and it can perform therapeutically better than conventional immediate release dosage form.

**Lakshmana PS et al., (2010)** prepared sustained release microspheres of rosin containing aceclofenac using o/w emulsion solvent evaporation technique and found that appropriate variation in the proportions of drug; polymer and stabilizer can lead to a product with the desired controlled release features.

**Lakade SH et al., (2008)** developed hydrophilic polymer (HPMC) and hydrophobic polymer (Ethyl cellulose) based Nicorandil matrix sustained release tablet which can release the drug up to time of 24 hrs in predetermined rate.

**Shanthi CN et al., (2010)** reviewed sustained/controlled release formulations of captopril and suggested that all the controlled release dosage forms available for captopril claims to
release the drug upto 8h. These need the drug administration for two to three times a day which is not feasible to for once a formulation. In some cases, the optimum release of drug was shown but with in vitro data only. The in vivo release was studied under animals only. Further clinical studies are needed to assess the utility of these systems for patients suffering from hypotension.

Chitta SK et al., (2008) developed matrix tablets of Aceclofenac with Prosophis juliflora gum and to study its functionality as a matrix forming agent for once daily sustained release tablet formulations. The result revealed that Prosophis juliflora gum appears to be suitable for use as a release retardant in the manufacture of once daily sustained release matrix tablets because of its good swelling, good flow and suitability for matrix formulations.

Hirlekar RS et al., (2008) studied the effect of post-compression curing on Floating Kollidon® SR (KSR) matrix tablets containing Labetalol HCl and concluded that the gastroretentive tablets of Labetalol HCl can be prepared successfully with desired release pattern, negligible FLT and FT of about 24 h using Kollidon® SR as polymer and lactose and PEG 6000 as channelling agent.

Gummudavelly S et al., (2008) formulated extended release matrix tablets of metoprolol succinate using hydrophilic polymers like Hydroxy Propyl Methyl Cellulose (HPMC K100M), Hydroxy Propyl Cellulose (HPC), Ethyl Cellulose, Carbopol 934 and found the nearly zero order release of metoprolol succinate for 20 hrs.

Emami J et al., (2004) formulated sustained-release lithium carbonate matrix tablets and studied the influence of hydrophilic materials on the release rate. The results concluded that Na CMC, CP, and HPMC can be used to modify release rates of lithium carbonate in hydrophilic matrix tablets.


Tiwari SB et al., (2003) prepared controlled release formulation of tramadol hydrochloride using hydrophilic and hydrophobic matrix system and studied the effect of concentration of hydrophilic (hydroxypropyl methylcellulose [HPMC]) and hydrophobic polymers (hydrogenated castor oil [HCO], ethylcellulose) on the release rate of tramadol. The study revealed that hydrophobic matrix tablets prepared using HCO is to be best suited for modulating the delivery of the highly water-soluble drug, tramadol hydrochloride.
Genc L et al., (1999) prepared controlled release tablets of dimenhydrinate with different polymers as EC, HEC, Carbopol 934, Eudragit RLPM and Eudragit NE 30 D at different concentrations (2.5–10%). Using Direct compression (DC) and wet granulation (WG) techniques. The result shows that the diffusion release mechanism in a matrix system comprising an insoluble hydrophobic and a hydrophilic gel-forming part depends greatly on the wettability of the added drug. Furthermore, with wettable and water soluble drug, the matrix swells and release is mainly achieved.

Fan TY et al., (2001) developed new pulsatile release tablets with ethylcellulose and Eudragit L as film coating materials and cross-linked polyvinylpyrrolidone in the core tablets, which can suppress drug release in stomach and release the drug rapidly after a predetermined lag time of about 3 h in intestine. They concluded that the pulsatile release tablets may be considered to be suitable for the use in drugs which are expected to exhibit therapeutic effects several hours after taking sysmedicine, e.g., from midnight to daybreak.

Siepmann F et al., (2008) studied the use of polymer blends as coating materials for controlled drug delivery systems and teach that for the future a thorough understanding of the polymeric structures on a molecular level as well as of the underlying drug release mechanisms is highly desirable to reduce time-and cost intensive series of trial-and-error experiments.

Tsai T et al., (1998) were granulated lactose and dibasic calcium phosphate (DCP) with various concentrations of film-forming polymers by a stepwise spraying method to prepare a directly compressible matrix excipients and suggested that conventional excipients can be modified by a simple granulating procedure to provide better physical properties for being used as a matrix material.

Sahib MN et al., (2008) formulated prednisolone-modified release tablets (coated matrix) using a wet granulation method as a potential colon delivery system and found that Avicel for use, as it provided a reasonable dissolution rate compared to other types, Eudragit S 100 is more suitable for colonic targeting in comparison to other types of coating formulas (Eudragit L100 and cellulose acetate phthalate), and Polyvinylpyrrolidone (PVP) at a concentration of 10% was an excellent binder.

Takka S et al., (2001) incorporated anionic polymers, namely Eudragit S, Eudragit L 100-55, and sodium carboxymethylcellulose into hydroxypropylmethylcellulose (HPMC K100M) to modify the drug release from HPMC matrices and examined the effects of changing the ratio...
of HPMC to anionic polymers in water and in media with different pH. They concluded that blends of HPMC and Eudragit L 100-55 in 1:1 ratio succeeded in producing pH-independent extended-release tablets; however, the blends of HPMC and other anionic polymers (Eudragit L 100-55, Eudragit S, and NaCMC) in various other ratios did not produce pH-independent extended-release tablets in water, 0.1 N HCl, and phosphate buffer with pH 6.8.

Hardy IJ et al., (2006) investigated Compression and compaction properties of plasticised high molecular weight hydroxypropylmethylcellulose (HPMC) as a hydrophilic matrix carrier and suggested a useful improvement of HPMC compaction and matrix properties by PG plasticisation, with lowering of Tg resulting in improved deformation and internal bonding and the deformation characteristics of this HPMC in the solid state is dominated by hydroxyl mediated bonding, rather than by hydrophobic interactions between methoxyl-rich regions.

Chavanpatil MD et al., (2006) developed novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin using various release retarding polymers like psyllium husk, HPMC K100M and a swelling agent, crosspovidone in combinations and evaluated for in vitro drug release profile, swelling characteristics and in vitro bioadhesion property.

Conti S et al., (2007) used hydroxypropylmethylcellulose (HPMC) and sodium carboxymethylcellulose (NaCMC) as polymeric carriers to improve controlled release performances of matrix tablets containing a soluble drug and evaluated the effect of the dissolution medium pH, on the drug release performance, release tests were conducted at pH 1, 4.5 and 6.8. In vitro release studies demonstrated that the mixture of the two cellulose derivatives enables a better control of the drug release profiles at pH 4.5 and at 6.8 both in term of rate and mechanism.

Maeda A et al., (2011) prepared the sustained-release microparticles of tamsulosin hydrochloride for orally disintegrating tablets. Microparticles were prepared from an aqueous ethylcellulose dispersion (Aquacoat®), and an aqueous copolymer based on ethyl acrylate and methyl methacrylate dispersion (Eudragit® NE30D), with microcrystalline cellulose as core particles with a fluidized bed coating process. The microparticles were evaluated for in vitro drug release and in vivo absorption to assess bioequivalence in a commercial product, Harnal® pellets. They concluded that this development produces microparticles in single-step
coating that provided a sustained-release of tamsulosin hydrochloride comparable to Harnal® pellets.

Qui Y et al., (2003) designed and evaluated Controlled release hydrophilic matrix formulations of divalproex sodium via in vitro and in vivo studies against the commercial enteric tablet dosed twice-daily in a multiple dose study, and shown to provide desired nearly constant therapeutic plasma concentrations over the entire 24-h dosing interval. Preliminary linear relationships between in vitro dissolution and in vivo absorption were observed in both the animal model and in humans.

Lamoudi L et al., (2012) evaluated physical properties and release from matrix tablets containing different ratios of HPMC 15 M and Acryl-EZE. A further aim is to assess their suitability for pH dependent controlled release. The obtained results revealed that the presence of Acryl-EZE in the matrix tablets is effective in protecting the dosage forms from release in acid environments such as gastric fluid. In pH = 6.8 phosphate buffer, the drug release rate and mechanism of release from all matrices is mainly controlled by HPMC 15 M. The model of Korsmeyer–Peppas was found to fit experimental dissolution results.

Santos JV et al., (2012) developed directly compressed matrices of zidovudine (AZT) comprised different ratios of hydroxypropylmethylcellulose K15M and K100M, ethylcellulose, and methacrylic acid (Eudragit® RS PO and Eudragit® RL PO). The results showed that the simultaneous application of both hydrophilic and hydrophobic polymers can modulate the drug release process, leading to an improved efficacy and patient compliance. All AZT formulations studied were found to be cytotoxic against Caco-2 cells, F19 being the most effective one.

Ma D et al., (2012) developed hydroxypropyl methylcellulose (HPMC) based controlled release (CR) formulations via hot melt extrusion (HME) with a highly soluble crystalline active pharmaceutical ingredient (API) embedded in the polymer phase. The dissolution results showed sustained release profiles without burst release for the HPMC K4M, K15M, and K100M formulations. The extrudates have good dissolution stability after being stressed for 2 weeks under 40°C/75% RH open dish conditions and the crystalline API form did not change upon storage. Overall, the processing windows were established for the HPMC based HME-CR formulations.

Yadav K et al., (2012) formulated and evaluated sustained release matrix tablets using different hydrophilic, hydrophobic and waxy materials as matrix formers. The developed
matrix tablet formulations with HPMC and cetyl alcohol provided sustained release profiles for prolonged periods than commercial formulations.

Fujisaki Y et al., (2006) developed sustained-release tablets containing Sodium Valproate using membrane-controlled system and found a relatively good correlation was observed between the absorption profiles and the dissolution profiles of the drug.

Karmarkar AB et al., (2010) evaluated in vitro dissolution profile comparison methods of sustained release tramadol hydrochloride liquisolid compact formulations with marketed sustained release tablets and found that these methods provide an acceptable model approach that indicates the true relationship between percent drug release and time variables, including statistical assumptions.

Kibria G and Reza-Ul-Jalil (2008) studied the effect of the ratio of two acrylic polymers Ammonio Methacrylate Copolymer Type A (Eudragit RL 30 D) & Ammonio Methacrylate Copolymer Type B (Eudragit RS 30 D) on the in vitro release kinetics of ketoprofen from pellets prepared by extrusion and spheronisation technique. The results generated in this study showed that proper selection of polymeric materials based on their physicochemical properties is important in designing sustained release pellets dosage form with suitable dissolution profile.