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SUSTAINED RELEASE MATRIX TABLETS OF MIGLITOL: TECHNIQUES IMPLEMENTED AND PATENTS

Prabhjot Kour*, Ajay Bilandi, Mahesh Kumar Kataria, Himanshi Swami

Seth G.L. Bihani S.D.College of Technical Education, Sri Ganganagar (Rajasthan)

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For Correspondence:

Prabhjot Kour

Seth G.L. Bihani S.D.College of Technical Education, Sri Ganganagar (Rajasthan)

E-mail:

sonusdh57@gmail.com

ABSTRACT

Sustained drug delivery is defined as "any drug or dosage form modification that prolongs the therapeutic activity of the drug". It provides prolonged and reduces the need for repeated dosing. Sustained release tablets are formulated to dissolve slowly and release a drug over time. Matrix tablets may be defined as the "oral solid dosage forms in which the drug or active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices which serves as release rate retardants". Matrix drug delivery systems release the drug in continuous manner. These release the drug by both dissolution controlled as well as diffusion controlled mechanisms. Matrix systems are widely used for the sustained release dosages forms. Matrix system is a release system which prolongs and controls the release of the drug that is dissolved or dispersed. In other words, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. Miglitol is a second generation-glycosidase inhibitor with a chemical structure of 1-desoxynojiromycin. Miglitol acts as a potent competitive inhibitor the alpha glycosidase in the microvilli of the intestinal brush border, it retards the breakdown of disaccharides and polysaccharides (e.g. starch, sucrose, and other complex sugars) into monosaccharides such as glucose.In this review emphasized on the techniques implemented for the formulation of sustained release dosage form of miglitol with thier patents since last 20 years.

INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that has been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms, Oral route is the most oldest and convenient route for the administration of therapeutic agents because of low cost of therapy and ease of administration leads to higher level of patient compliance. Approximately 50% of the drug products available in the market are administered orally in which Tablets are the most commonly and widely used dosage form. This type of drug delivery system is called conventional drug delivery system and is known to provide an immediate release of drug. Such immediate release (IR) products results in relatively rapid drug absorption and onset of accompanying pharmacodynamic effects.[2] Sustained drug delivery is defined as "any drug or dosage form modification that prolongs the therapeutic activity of the drug". It provides prolonged and reduces the need for repeated dosing. Sustained release tablets are formulated to dissolve slowly and release a drug over time. The advantages of sustained-release tablets are that they can often be taken less frequently than conventional formulations of the same drug, and that they keep steadier levels of the drug in the bloodstream. Sustained-release tablets are formulated so that the active ingredient is embedded in a matrix of insoluble substance so that the dissolving drug has to find its way out through the holes in the matrix.[7, 9]

Matrix tablets may be defined as the "oral solid dosage forms in which the drug or active ingredient is homogeneously dispersed throughout the hydrophilic or hydrophobic matrices which serves as release rate retardants". Matrix drug delivery systems release the drug in continuous manner. These release the drug by both dissolution controlled as well as diffusion controlled mechanisms[1,3]. Matrix systems are widely used for the sustained release dosages forms. Matrix system is a release system which prolongs and controls the release of the drug that is dissolved or dispersed. In other words, a matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. In a sustained release method therapeutically effective concentration can be achieved in the systemic circulation over an extended period of time, thus achieving better compliance of patients. Numerous SR oral dosage forms such as membrane controlled system, matrices with water soluble/insoluble polymers or waxes and osmotic systems have been developed.[1]

ADVANTAGES OF MATRIX TABLET

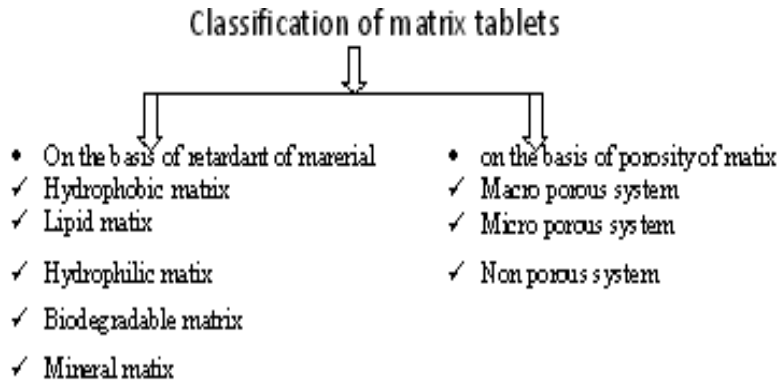
Advantages of matrix tablets are easy to manufacture and Versatile, effective and having low cost it can be made to release high molecular weight compounds. The sustained release formulations may maintain therapeutic concentrations over prolonged periods. The use of sustain release formulations avoids the high blood concentration. Sustain release formulations have the potential to improve the patient compliance. It reduce the toxicity by slowing drug absorption and Increase the stability by protecting the drug from

hydrolysis or other derivative changes in gastrointestinal tract. It minimize the local and systemic side effects by Improving in treatment efficacy and also Improve in the bioavailability of some drugs.

DISADVANTAGES OF MATRIX TABLET

Matrix tablets having High cost of preparations. The release rates are affected by various factors such as, food and the rate transit through the gut. The drug release rates vary with the square root of time. Release rate continuously diminishes due to an increase in diffusional resistance and/or a decrease in effective area at the diffusion front. However, a substantial sustained effect can be produced through the use of very slow release rates, which in many applications are indistinguishable from zero-order.

CLASSIFICATION OF MATRIX TABLETS:[1]



A. On the Basis of Retardant Material Used -

Matrix tablets can be divided in to 5 types

1. Hydrophobic Matrices (Plastic matrices):

The concept of using hydrophobic or inert materials as matrix materials was first introduced in 1959. In this method of obtaining sustained release from an oral dosage form, drug is mixed with an inert or hydrophobic polymer and then compressed in to a tablet. Sustained release is produced due to the fact that the dissolving drug has diffused through a network of channels that exist between compacted polymer particles. Examples of materials that have been used as inertor hydrophobic matrices include polyethylene, polyvinyl chloride, ethyl cellulose and acrylate polymers and their copolymers. The rate-controlling step in these formulations is liquid penetration into the matrix. The possible mechanism of release of drug in such type of tablets is diffusion. Such types of matrix tablets become inert in the presence of water and gastrointestinal fluid.

2. Lipid Matrices:

These matrices prepared by the lipid waxes and related materials. Drug release from such matrices occurs through both pore diffusion and erosion. Release characteristics are therefore more sensitive to digestive fluid composition than to totally insoluble polymer matrix. Carnauba wax in combination with stearyl alcohol or stearic acid has been utilized for retardant base for many sustained release formulation.

3. Hydrophilic Matrices:

Hydrophilic polymer matrix systems are widely used in oral controlled drug delivery because of their flexibility to obtain a desirable drug release profile, cost effectiveness, and broad regulatory acceptance. The formulation of the drugs in gelatinous capsules or more frequently, in tablets, using hydrophilic polymers with high gelling capacities as base excipients is of particular interest in the field of controlled release. Infect a matrix is defined as well mixed composite of one or more drugs with a gelling agent (hydrophilic polymer). These systems are called swellable controlled release systems. The polymers used in the preparation of hydrophilic matrices are divided in to three broad groups,

Cellulose derivative:

Methylcellulose400 and 4000cPs, Hydroxyethylcellulose, Hydroxypropylmethylcellulose (HPMC) 25, 100, 4000 and 15000cPs, and Sodium carboxymethylcellulose.

Non cellulose natural or semi synthetic polymers:

Agar-Agar, Carob gum, Alginates, Molasses, Polysaccharides of mannose and galactose, Chitosan and Modified starches.

Polymers of acrylic acid: Carbopol-9.

4. Biodegradable Matrices:

These consist of the polymers which comprised of monomers linked to one another through functional groups and have unstable linkage in the backbone. They are biologically degraded or eroded by enzymes generated by surrounding living cells or by nonenzymetic process in to oligomers and monomers that can be metabolized or excreted. Examples are natural polymers such as proteins and polysaccharides; modified natural polymers; synthetic polymers such as aliphatic poly (esters) and poly anhydrides.

5. Mineral Matrices:

These consist of polymers which are obtained from various species of seaweeds.

Example is Alginic acid which is a hydrophilic carbohydrate obtained from species of brown seaweeds (Phaephyceae) by the use of dilute alkali.

B. On the Basis of Porosity of Matrix:

Matrix system can also be classified according to their porosity and consequently,

Macro porous; Micro porous and Non-porous systems can be identified:

1. Macro porous Systems: In such systems the diffusion of drug occurs through pores of matrix, which are of size range 0.1 to 1 μm. This pore size is larger than diffusant molecule size.

2. Micro porous System: Diffusion in this type of system occurs essentially through pores. For micro porous systems, pore size ranges between 50 – 200 A°, which is slightly larger than diffusant molecules size.

3. Non-porous System: Non-porous systems have no pores and the molecules diffuse through the network meshes. In this case, only the polymeric phase exists and no pore phase is present.

POLYMERS USED IN MATRIX TABLET:

Hydrogels

Polyhydroxyethylemethylacrylate (PHEMA), Cross-linked polyvinyl alcohol (PVA), Cross-linked polyvinyl pyrrolidone (PVP), Polyethylene oxide (PEO), Polyacrylamide (PA)

Soluble polymers

Polyethyleneglycol (PEG), polyvinyl alcohol (PVA), Polyvinylpyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC)

Biodegradable polymers

Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone (PCL), Polyanhydrides, Polyorthoesters

Non-biodegradable polymers

Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), Polyvinyl chloride (PVC), Cellulose acetate (CA), Ethyl cellulose (EC)

Mucoadhesive polymers

Polycarbophil, Sodium carboxymethyl cellulose, Polyacrylic acid, Tragacanth, Methyl cellulose, Pectin

Natural gums

Xanthan gum, Guar gum, Karaya gum, Locust bean gum.[1,3]

Description of Miglitol

The use of oral antidiabetic drugs for the treatment of Type 2 diabetes is increasing rapidly. Miglitol is a second generation α-glycosidase inhibitor with a chemical structure of 1-desoxynojiromycin. Miglitol acts as a potent competitive inhibitor the alpha glycosidase in the microvilli of the intestinal brush border, it retards the breakdown of disaccharides and polysaccharides (e.g. starch, sucrose, and other complex sugars) into monosaccharides such as glucose. Miglitol is a Desoxynojirimycin derivative that delays the digestion of ingested carbohydrates, that resulting in a smaller rise in blood glucose concentration following meals. The generation and absorption of glucose are delayed. Miglitol has short biological half life (2 hrs) and bioavailability is greater than 90 percent the site of absorption of Miglitol is in the intestine. Absorption of miglitol is saturable at high doses a dose of 25 mg is completely absorbed, whereas a dose of 100 mg is 50percent – 70percent absorbed. For all doses, peak concentrations are reached in 2 to 3 hours. There is no evidence that systemic absorption of miglitol contributes to its therapeutic effect. The protein binding of miglitol is negligible less than 4.0percent. Miglitol has a volume of distribution of 0.18 L/kg, consistent with distribution primarily into the extracellular fluid .Miglitol is not metabolized in humans or in any animal species studied. No metabolites have been detected in plasma, urine or feces, indicating a lack of either

systemic or pre-systemic metabolism. Miglitol is eliminated by renal excretion as unchanged drug. Following a 25 mg dose, over 95 percent of the dose is recovered in the urine within 24 hours. At higher doses, the cumulative recovery of drug from urine is lower due to the incomplete bioavailability. The Miglitol belongs to Biopharmaceutical classification system 1 (BCS-1) having higher aqueous solubility and higher membrane permeability. It is practically soluble in water and ethanol and store at 4℃ in solid state power form. Miglitol having molecular weight of 207.22.

Table no. 1- LIST OF BRANDS OF MIGLITOL[24,25]

S.NO	BRAND NAME	MANUFACTURER
1.	Diamig (25mg)	DTF(Micro lab ltd)
2.	Diamig (25mg)	Micro lab ltd (DTF)
3.	Diamig (50mg)	Micro lab ltd(DTF)
4.	Diamig (50mg)	DTF(Micro lab ltd)
5.	Eltox (50mg)	Cardiovascular (Ranbaxy laboratorios ltd.)
6.	Eltox (50mg)	Ranbaxy laboratories ltd (cardiovascular)
7.	Euglitol(25mg)	Abbot health care pvt.ltd(AHPL)
8.	Euglitol (50mg)	Piramal healthcare
9.	Glock	Unichem laboratories
10.	Miglit	Biochen limited
11.	Mignar	Heonealth(Glenmark pharmaceuticals ltd.
12.	Migset	Cipla ltd.
13.	Migtor	Torrent
14.	Misobit	Lupin

METHODS FOR TABLET PREPARATION

1. Granulation method

Wet granulation

Dry granulation.

2. Direct compression method

Table no- 2 LIST OF METHOD OF PREPRATION[21]

Name of method	Procedure	Advantages	Disadvantages
Direct compression	Weighing ↓ Mixing ↓ Blending ↓ Compression	Simple economical process. No need for moisture ,so good for unstable compounds	Not suitable for all compounds Limited for lower dose compounds Expensive excipients
Wet granulation	Weighing	Suitable for all	Expensive

	↓ Sieving ↓ Dry mixing ↓ Wet mixing ↓ Drying ↓ Screening ↓ Fluid bed ↓ V-blender ↓ Compression	formulations Imparts flowability and elasticity to a formulations	Time consuming process Stability issue for moisture sensitive preparation
Wet granulations(non aqueous)	--	Suitable for moisture sensitive preparation	Expensive equipment Needs organic facility Solvent recovery problem Health and environment issues
Dry granulation(slugging and roll compaction	Weighing ↓ Mixing ↓ Compression in to slugs ↓ Size reduction of slugs ↓ Sieving ↓ Mixing of granules With pharmaceutical aids	Eliminate exposure to moisture and drying	Dusty procedure Slow process Not suitable for all compounds

Evaluation of sustained release matrix tablets[1]

a. Diameter and Thickness.

b. Hardness and Friability.

c. Weight uniformity.

d. Content uniformity.

e. *In- vitro* drug release studies

SUSTAINED RELEASE MATRIX TABLET OF MIGLITOL

J Ashtamkar et al 2013 designed the controlled release tablets of miglitol (25 mg) by combination of hydrophilic polymers like Hydroxypropylmethylcellulose, Hydroxypropylcellulose and Hydroxyethylcellulose using their varying concentration that was 10,15 or 25 percent by direct compression method. The release kinetic study was performed by using USP type 2 dissolution apparatus (paddle) at 50 rpm in 900 ml of acidic dissolution medium (pH 1.2) for 2 hours, and also followed by 900 ml alkaline dissolution medium (pH 7.4) up to 12 hour at 625 rpm. The in vitro release study revealed that formulation showed sustained release of 90% up to 12 hrs. In this formulation the combination of polymers produce a more linear release from matrix tablets with low standard deviation. The release studies were conducted in triplicate.

Rangasamy Manivannan et al. formulated and evaluated Miglitol (50 mg) sustained release tablet by wet granulation method using polymers like HPMC K15M, Hydroxyl Methyl Cellulose E5, Micro Crystalline Cellulose, Lactose and Sodium starch glycolate. The Miglitol sustained release tablets were evaluated for hardness, friability, weight variation, drug content and *In-vitro* dissolution study. The Miglitol sustained release tablets showed drug release from 28.68 to 97.43% of drug at the end of 24^{th} hr by *in-vitro* dissolution study.

Ashtamkar Joel1 et al 2013 designed miglitol 25 mg controlled release matrices were prepared by direct compression method by using hydrophobic polymers like- Hydroxypropyl methylcellulose phthalate (HPMCP), polyvinyl acetate (PVA) and their combination were used as rate controlling polymers. Effects of addition of hydroxypropyl methylcellulose phthalate and polyvinyl acetate on in-vitro drug dissolution were studied. Tablets were formulated using total polymer content as 20, 30 and 40 percent. In-vitro drug release was carried out using USP Type II at 50 rpm in 900 ml of acidic dissolution medium (pH 1.2) for 2 hours, followedby 900 ml alkaline dissolution medium (pH 7.4) up to 12 hours The drug content was estimatedby measuring the absorbance of both standard and sample solutions at 625 nm using UV/Vis spectrophotometer.

Anudeep kalikonda et al designed sustained release formulations by inclusion of drugs into interpolymer complex for controlling the drug release. The interpolymer complexes were formed by association of poly(carboxylic acids) and non-ionic polymers in solutions via hydrogen bonding. These complexes can potentially be used for design of novel mucoadhesive dosage forms, development of solid drug dispersions and solubilisation of poorly soluble drugs, encapsulation technologies, preparation of nanoparticles, hydrogels, in situ gelling systems and electrically erodible materials. The most commonly used poly

(carboxylic acids) for preparing interpolymer complexes are poly(acrylic acid) (PAA) and poly(methacrylic acid) (PMAA). These inter polymer complexes affect the release of drug from the matrix tablet. By selecting suitable polymer extended release of drug can be achieved. The interpolymer complexes such as chitosan-alginate complex, cationic guar gum and xanthan gum complexes are readily available in market.

Singh kanchan et al designed bilayer tablets of miglitol and valsartin in which first layer released drug immediately. The second layer designed to release drug later. This release immediate after oral administration, the upper layer of the `bilayer tablets, disintegrates first to release valsartan in stomach and gets absorbed thereby reduces hypertension. Simultaneously, the sustained release layer will start to release miglitol, which gets absorbed hence it maintains normal blood glucose level in severe hyperglycemia for longer duration. Due to shorter half -life of miglitol (antidiabetic) and multiple dosing frequencies, it was aimed to formulate and evaluate bilayer sustained release tablets of valsartan and miglitol for the treatment of diabetic hypertensive patients.

Yadav Narendra et al 2014 designed a patent of sustained release matrix tablet of miglitol by the direct compression method .polymer used in this prepration like microcrystalline cellulose as the directly compressible vehicle HPMC-K-4, HPMC-K-15 and HPMC-K-100 were used as the retardant materia Other excipients were magnesium stearate as a lubricant and talc as a glidant using in performed in -vitro drug dissolution study.The in vitro release study revealed that formulation showed sustained release of drug after 12hrs.

B Senthilnathan, & V Suba (2013) designed a press coated tablet of miglitol for the pulsatile drug delivery system for anti-diabetic drug miglitol to control the increased blood glucose level after food consumption in diabetic patient by allowing the drug to release immediately after meals. Press coated tablets of miglitol were prepared by compression coating immediate release miglitol core tablets with hydrophilic and hydrophobic polymer in different ratios. The ideal concentrations of hydrophilic and hydrophobic polymers are used on basis of in vitro drug release profile and desired lag time of 4 hrs. The Invitro release studies were carried out for the formulated miglitol press coated tablets using different buffer solutions such as pH 1.2,7.4 and 6.8.The invitro drug release profile of miglitol press coated tablets containing 25mg of glyceryl behenate and 175 mg of L-HPC exhibited a time period of 4 hrs without drug release (lag time) followed by a rapid release of drug. Hence the developed formulation was found to be suitable for the diabetic patient to manage the blood glucose levels which are high after food consumption.

Mahmut Bilgic (2012) designed a stable acarbose formulation of alpha glycoside inhibitor by using dry blending method. The polymer used to prepare tablet was microcrystalline cellulose. The binder and lubricant used were starch, corn starch and magnesium stearate respectively.

John amtruda et al 2013 designed a sustained release formulation of alpha glycosidase by suitable manufacturing methods like direct compression, compression following a granulation step, formation of pellets using extrusion/spheronization or generated by a fluidized bed process (Wurster process e.g.). The tablets were compressed as monolayer tablets, bilayer tablets or coat core tablets and the polymers used were HPMC, HPC, HEC, xanthan gum , chitosan, alginic acid. The floating excipients were also used that were HPMC, HEC, MC. The CO2 formimg excipients used was sodium carbonate. The dissolution study was performed upto 4 hrs.

John R. et al 2011 designed extended release tablet of highly soluble drug substances by using direct compression method,wet and dry granulation method.The formulation were designed by using suitable polymer like hypromellose KJ100,sodium alginate ,carrageenan,or chitosan,MCC,Colidal silica or Mg srerate by using USP apparatus 2,RPM speed 50 and maintaining the temperature at 37℃.

Gregory E. Amidon et al 2004 designed a sustained release formulation of highly soluble drug substances by using following ingredients: HPMC 2208, pegelatinized starch, colloidal silicon dioxide, magnesium stearate, ethyl cellulose based coating material.

Table no. 3: LIST OF METHOD OF PREPRATION

S.NO.	FORMULATION	METHODS OF PREPARATION	POLYMERS USED	REFERENCES
1	Sustained Release Tablets	Wet granulation	HPMC K15M, Hydroxyl Methyl Cellulose E5, Micro Crystalline Cellulose, Lactose and Sodium starch glycolate.	Rangasamy Manivannan et al.
2	Controlled release Tablets	Direct compression	Hydroxypropyl methylcellulose, Hydroxypropyl cellulose and Hydroxy ethyl cellulose(hydrophilic polymer)	J Ashtamkar et al 2013
3	Controlled release Tablets	Direct compression	Hydroxypropyl methylcellulose phthalate and Polyvinyl acetate(hydrophobic polymer)	Ashtamkar Joell et al
4	Sustained release Matrix tablets	Direct compression	Microcrystalline cellulose, HPMC-K-4, HPMC-K-15 and HPMC-K, Magnesium stearate and Talc	Yadav Narendra et al 2014
5	Press coated tablet	---------	Glyceryl bentate, core of hydrophilicand hydrophobic polymer L-HPC	Yadav Narendra et al 2014

6	Controlled release interpolymer complexes	Compression coating	Polyacrylic acid(PAA), Polymethacrylic acid(PMAA), Polycarboxlic acid (PCA),Guargum ,xanthan gum,chitosin alginate	Singh kanchan
7	Bilayer tablets	----------	Hydrophilic and hydrophobic polymers	senthinathanet B et al (2013)

Table no.4 - LIST OF PATENTS

S.NO.	PUBLICATION NO.	APP NO.	TOPIC NAME	INVENTORS	YEAR
1	WO2013115746A1	PCT/TR2013/000050	Pharmaceutical compositions or comprising alpha glycosidase inhibitors	Mahmut Bilgic	2013
2	WO2013115746A1	PCT/TR2013/000055	A production method for (effervescent) pharmaceutical composition comprising an alpha glycosidase inhibitor (Miglitol and Metformin)	Mahmut Bilgic	2013
3	CN103070842A	CN 201310043951	Preparation method of miglitol sustained release tablet	-------	2013
4	W02013115745A1	PCT/TR2013/000054	A processcess for production of pharmaceutical composition Comprising alpha glycosidase inhibitors	Mahmut Bilgic	2013
5	EP2379060-A2	EP20090837968	Extend–release pharmaceutical formulation	John.R caedinal, jack Lawarence, james elastic mels opp,david M.oakleg	2011
6	US7976871B2	US11/134,631	Modified release composition of highly soluble drugs	Navin vaya, Nadkarni, Vinod Kumar Gupta	2011
7	CN1679550-A	CN-200510037785	Sustained preparation of miglitol and its preparing agents	----------	2005
8	WO199026606A2	PCT/EP1998/007198	Sustained release formulations comprising alpha glycosidase inhibitors	John Amatruda, Patrick Bosche, ErichBrendel, Davidgodman, Carola Poertner	1992

REFERENCES

1. Patel Harnish, Dhrupesh R. Panchal, Upendra Patel, Tushar Brahmbhatt, Mayur Suthar. Matrix type drug delivery system, Journal of pharmaceutical science and bioscientific rearch (JPSBR) JPSBR: Volume 1, Issue 3: Nov Dec 2011 (143-151)
2. Gedar Sushma, Kataria Mahesh Kumar, Bilandi Ajay An Overview On Techniques Implemented For Sustained Release Matrix Tablet Of Glipizide International Journal Of Advanced Pharmaceutics Vol 4 | Issue 2 | 2014 | 93-98.
3. Jain N.K., Controlled and novel drug delivery, CBS Publishers and distributors, first edition 1997, New Delhi, page no. 27-49.
4. Singh kanchan, formulation and in vitro evaluation of sustained release bilayer tablet of valsartin and miglitol 2013,page no-5-10.
5. Manivannan Rangasamy Kotha Aravind Kumar, Bandaru Lakshmi Narayana Rao and Palnati Venkata Krishna Reddy, Formulation and evaluation of miglitol sustained release tablets, asian Journal of pharmaceutical science & Technology vol-3 ,issue-2.
6. J.Asthmakar S. Nangude and N. Chugh 2013, Formulation and evaluation of controlled release tablets of miglitol using combination of hydrophilic polymers, international journal of pharmaceutical science and rearch ,IJPSR Vol,4 issue 2
7. Raja challa redy 2013,formulation and in vitro evaluation of sustained release tablets of ante diabetic drug,department of pharmatechnology pes college of pharmacy,bangaluru.
8. J.asthmakar,chug naresh et al 2013 formulation and evaluation of contolled release tablets of miglitol using combination of hydrophobic polymers, journal of drug discovery and thearapeutics,1(5),04-08.
9. John Amatruda, Patrick Bosche, ErichBrendel, Davidgodman, Carola Poertner(1992), Sustained release formulations comprising alpha glycosidase inhibitors, publication no-WO199026606A2,appno- PCT/EP1998/007198.
10. John.R caedinal,jack Lawarence,james elastic mels opp,et al (2011) Preparation method of miglitol sustained release tablet, Pub no CN103070842A ,App no- EP20090837968.
11. Mahmut Bilgic(2013), Pharmaceutical compositions or comprising alpha glycosidase inhibitors,Pub no- WO2013115746A1,App no PCT/TR2013/000050.
12. Mahmut Bilgic (2013),A processcess for production of pharmaceutical compositionComprising alpha glycosidase inhibitors ,Pub no- W02013115745A1,App no- PCT/TR2013/000054

13. Navin vaya,Rajesh Singh Karan, Sunil Sadanand Nadkarni, Vinod Kumar Gupta Modified release composition of highly soluble drugs (2011),Pub no- US7976871B2,App no- US11/134,631.
14. Mahmut Bilgic(2013), A production method for (effervescent) pharmaceutical composition comprising an alpha glycosidase inhibitor (Miglitol and Metformin),Pub no- WO2013115746A1,Appno- PCT/TR2013/000055.
15. Sustained prepration of miglitol and its preparing agents(2005),Pub no- CN1679550-A,Appno- CN-200510037785.
16. Preparation method of miglitol sustained release tablet(2013),Pub no- CN103070842A,Appno- CN 201310043951.
17. Anudeep kalikonda, Controlled release interpolymer complexes.
18. Senthilnathanet B et al (2013), Press coated tablets, Inventi Impact - Pharm Tech.
19. Gregory E. Amidon et al(2004), sustained release formulation of highly soluble drug substances
20. https://encrypted.google.com/search?q=tablet+preparation+steps&sa=X&biw=1360&bih=667&tbm=isch&tbo=u&source=univ&ei=x-N6VKuzN9iSuAT-s4LACQ&
21. Martindale,'The complete Drug reference'34th edition,2005Published by the pharmaceutical press,page no-343.2.
22. The Merc index,'An encyclopedia of chemicals Drug and biological,12th edition 1995,Published by Merck Research Laboratories of Merck & co,in Page no-6274.
23. http://www.medindia.net/drug-price/miglitol.htm
24. http://www.medlineindia.com/endocrine/miglitol.htm