FORMULATION AND *INVITRO* EVALUATION OF FAST DISSOLVING TELMISARTAN TABLETS USING DIFFERENT SUPERDISINTEGRANTS

A Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY,

CHENNAI- 600 032

In partial fulfilment of the award of the degree of

MASTER OF PHARMACY

IN

Branch-I -- PHARMACEUTICS

Submitted by

Name: SARANRAJ R

REG.No.261710256

Under the Guidance of

Mr. K. JAGANATHAN, M.Pharm.,

ASSOCIATE PROFESSOR

DEPARTMENT OF PHARMACEUTICS

J.K.K. NATTARAJA COLLEGE OF PHARMACY

KUMARAPALAYAM – 638183

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CERTIFICATES

EVALUATION CERTIFICATE

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"FORMULATION AND *INVITRO* EVALUATION OF FAST DISSOLVING TELMISARTAN TABLETS USING DIFFERENT SUPERDISINTEGRANTS", submitted by the student bearing **REG.No.261710256** to "**The Tamil Nadu Dr. M.G.R. Medical University – Chennai**", in partial fulfilment for the award of Degree of **Master of Pharmacy** in **Pharmaceutics** was evaluated by us during the examination held on.....

Internal Examiner **External Examiner**

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Associate Professor,
Department of Pharmaceutics

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DECLARATON

I do hereby declared that the dissertation **"FORMULATION AND *INVITRO* EVALUATION OF FAST DISSOLVINGTELMISARTAN TABLETS USING DIFFERENT SUPERDISINTEGRANTS",** submitted to "**The Tamil Nadu Dr. M.G.R Medical University - Chennai",** for the partial fulfilment of the degree of **Master of Pharmacy** in **Pharmaceutics,** is a bonafide research work has been carried out by me during the academic year 2019-2020, under the guidance and supervision of **Mr. K. Jaganathan, M.Pharm.,** Associate Professor, Department of Pharmaceutics, J.K.K. Nattraja College of Pharmacy, Kumarapalayam.

I further declare that this work is original and this dissertation has not been submitted previously for the award of any other degree, diploma, associate ship and fellowship or any other similar title. The information furnished in this dissertation is genuine to the best of my knowledge.

Place: Kumarapalayam **SARANRAJ R**

Date: **REG.No.261710256**

Dedicated to Parents,

Teachers&

My Family

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REG.No.261710256

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LIST OF ABBREVIATIONS USED

FTIR	Fourier Transform Infrared spectroscopy
ICH	International Conference for Harmonization
mg	Milligram
ODT	Orodispersible tablet
Rpm	Revolution per minute
hrs	Hours
min	Minutes
sec	Seconds
w/v	Weight/Volume
µg/ mcg	Micrograms
°C	Degree Centigrade
%	Percentage
% RH	Percentage relative humidity
FDDS	Fast dissolving drug delivery system
Mannitol DC	Direct compressible mannitol
B.P	British Pharmacopoeia
I.P	Indian Pharmacopoeia
MCC	Microcrystalline cellulose
CCS	Croscarmellose sodium

CP	Crospovidone
SSG	Sodium starch glycol
Nm	Nano meter
TBD	Tapped bulk density
LBD	Loose bulk density
SD	Standard deviation
U.S	United States of Pharmacopoeia

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INTRODUCTION

Solid dosage forms like tablet and capsule are most popular and preferred drug delivery system because they have high patient compliance, relatively easy to produce, easy to market, accurate dosing, and good physical and chemical stability[1].

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the food stuffs that are ingested daily. In fact, the development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology. Therefore, a fundamental understanding of various disciplines, including GI physiology, Pharmacokinetics, Pharmacodynamics and formulation design are essential to achieve a systemic approach to the successful development of an oral pharmaceutical dosage form. The more sophisticated a delivery system, the greater is the complexity of these various disciplines involved in the design and optimization of the system. In any case, the scientific frame work required for the

successful development of an oral drug delivery system consists of a basic understanding of the following three aspects:

1. Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug,
2. The anatomic and physiologic characteristics of the GIT, and
3. Physicochemical characteristics and the drug delivery mode of the dosage form to be designed.[2].

Drinking waterOrally disintegrating tablets are also called as oral disperse, mouth dissolving, rapidly disintegrating, fast melt and quick dissolve system. From past decade, there has been an increased demand for more patient-friendly and compliant dosage forms.As a result, the demand for developing new technologies has been increasing day by day.[3] US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the 'Orange Book' an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually with a matter of seconds, when placed upon the tongue.[4]

Many patient find difficulty to swallow tablet and hard gelatin capsule, consequently they do not take medication as prescribed. It is estimated that 50% of the population is affected by this problem which result high incident of incompliance and ineffective therapy[5].

The difficulty is experienced in particular by pediatric and geriatric patients, but it also applied to people who are ill in bed and those active working patients who are busy or traveling, especially those who have no access to water[6].

European Pharmacopoeia described orally disintegrating tablets as uncoated tablets intended the placed in the mouth where they disperse rapidly before being swallowed and as tablets which should disintegrate within 3 min[7].

To overcome this weakness, scientist have developed innovative drug delivery system known as fast dissolving "melt in mouth" or mouth dissolve (MD) tablet. These are novel type of tablet that disintegrate dissolve / disperse in saliva[8].

There are two different types of dispersible tablet which have to be distinguished, one dosage form disintegrates instantaneously in the mouth, to be swallowed without the need for drinking water, while other tablet formulation can readily be disperse in water, to form dispersion, easy to ingest by the patient[9].

In an effort to develop drug products that are more convenient to use and to address potential issues of patient compliance for certain product indications and patient populations, recent developments in technologies have come out with fast dissolving tablets (FDT) that can be ingested simply by placing them on the tongue. FDT is a solid dosage form that dissolves or disintegrates within a minute in the oral cavity without the need of water and has a pleasant taste. FDT is also

known as orally disintegrating tablet, fast-dissolving tablet, fast-melting tablet, mouth melting tablet or fast-disintegrating tablet[2].

Orally disintegrating tablets are also called as orodispersible tablet, quick disintegrating tablets mouth dissolving tablets. Fast integrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets and rapimelt. European pharmacopoeia has used the term orodispersible tablet for tablet that disperse readily and within 3 min in mouth before swallowing[10].

United State Food and Drug Administration (FDA) defined ODT as "a solid dosage form containing medicinal substance or active ingredients which disintegrate rapidly usually within a matter of second when placed upon the tongue[11].

Desired Criteria's for Fast Disintegrating Drug Delivery System[12,13]:

Fast dissolving tablets should:

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Should be compatible with taste masking.
- Should be potable without fragility concern.
- Leave minimal or no residue in the mouth after oral administration.

- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Allow the manufacture of tablet using conventional processing and packaging equipment at low cost.

Salient Features of Fast Dissolving Drug Delivery System[14]:

- Ease of administration to patients who refuse to swallow a tablet such as, pediatric, geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage form, which is highly convenient especially for patients who are traveling and do not have immediate access to water.
- Good mouth feel property of FDDS helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Rapid dissolution and absorption of drug, which may produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.

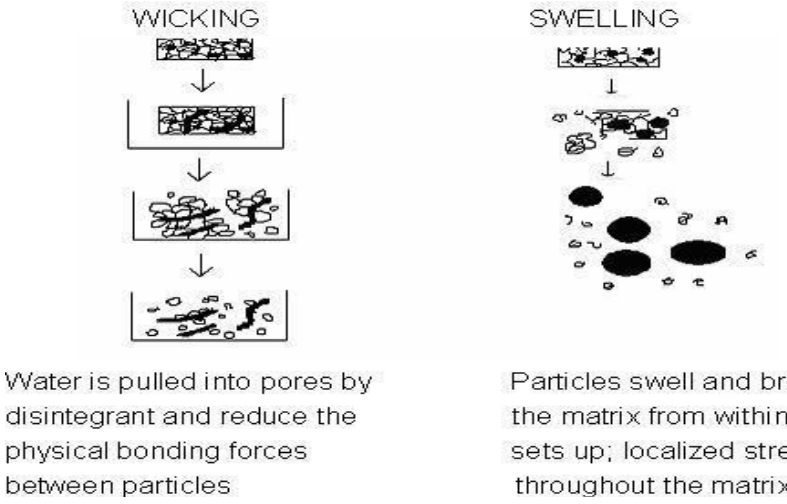
Mechanism of Superdisintegrants:[15]

I. Porosity and capillary action (Wicking)

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

II. Swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.



Disintegration of tablet by wicking and swelling

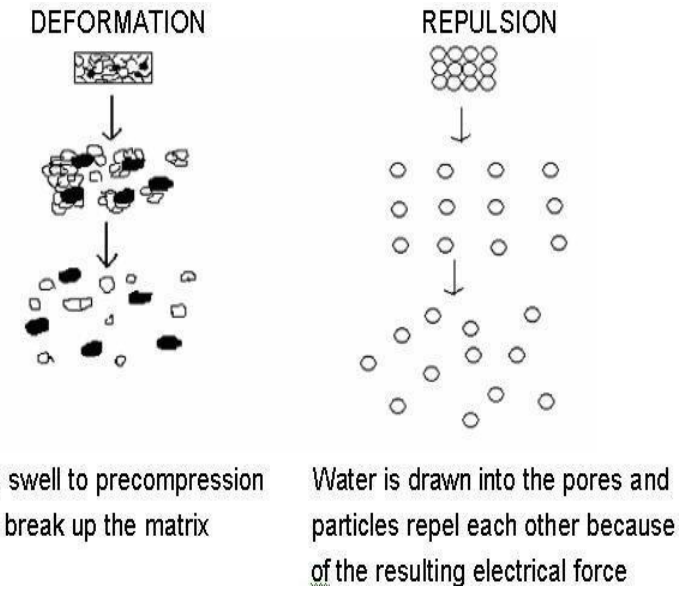
III. Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

IV. Due to deformation.

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a break up

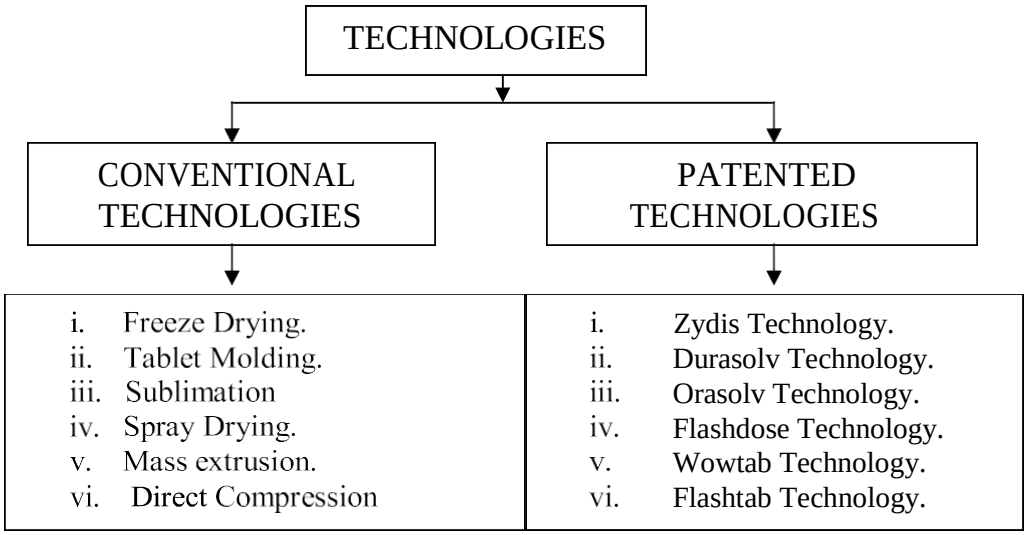
of the tablet. This may be a mechanism of starch and has only recently begun to be studied.



Disintegration by deformation and repulsion

Technologies Used to Manufacture Mouth Dissolving Tablets

The technologies used to manufacture mouth dissolving tablets can be classified



Conventional Technologies for Preparing Fast Dissolving Tablets[16-21]:

Freeze Drying:

A process in which water is sublimated from the product after freezing is called freeze drying. Freeze dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and some times to the drug, thereby enhancing the dissolution characteristics of the formulation. However, the use of freeze drying is limited due to high cost of the equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs.

A tablet that rapidly disintegrates in aqueous solution includes a partially collapsed matrix network that has been vacuum dried above the collapse temperature of the matrix. The matrix is partially dried below the equilibrium freezing point of the matrix. Vacuum drying of the tablet above its collapse temperature instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva.

Moulding:

Tablets produced by moulding are solid dispersions. Physical form of the drug in the tablets depends whether and to what extent it dissolves in the molten carrier. The drug can exist as discrete particles or microparticles dispersed in the

matrix. It can dissolve totally in the molten carrier to form solid solution or dissolve partially in the molten carrier and the remaining particles stay undissolved and dispersed in the matrix. Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion or dissolution. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, generally made from water-soluble sugars. Moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablet often occur during handling and opening of blister packs.

Sublimation:

Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed. Inert solid ingredients (E.g. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation generated a porous structure. Compressed tablets containing mannitol and camphor have been prepared by sublimation technique. The tablets dissolve within 10 -20 sec. and exhibit sufficient mechanical strength for practical use.

Spray Drying:

Highly porous and fine powders can be produced by spray drying, as the processing solvent is evaporated rapidly during spray drying. Spray drying technique is based upon a particulate support matrix and other components to form

a highly porous and fine powder. This is then mixed with above ingredients and compressed to tablet. The fast dissolving tablets prepared form Spray drying technique disintegrated within 20 sec.

Mass Extrusion:

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

Direct compression:

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water-soluble excipients and effervescent agent. Disintegrant efficacy is strongly affected by tablet size and hardness. Large and hard tablets have disintegration time more than that usually required. As consequences, products with optimal disintegration properties often have medium to small size and/or high friability and low hardness. Breakage of tablet edges during handling and tablet rupture during the opening of blister alveolus, all result from insufficient physical resistance.

Various commercially available superdisintegrants along with their properties.[15]

Sr. no.	Name	Type	Properties	Brand name
1.	Crospovidone	Polyvinyl-pyrrolidone	Crossed linked Poly vinyl pyrrolidone Rapidly disperses and swells in water	Polyplasdone XL, Kollidon CL
2.	Croscarmellose Sodium.	Modified cellulose	Cross linked sodium carboxy methylcellulose. Excellent swelling and water wicking properties.	Ac-di-sol, Primellose, Solutab.
3.	Sodium starch Glycolate	Modified Starch	Sodium salt of carboxy methyl ether of starch. High swelling capacity and rapid water uptake	Primogel, Explotab, Glycolys.

Patented Technologies for Fast Dissolving Tablets[16,18]:

ZYDIS Technology:

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength during handling, polymers such as gelatin, dextran

or alginates are incorporated. These form a glossy amorphous structure, which imparts strength.

To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze drying process or long term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

Durasolv Technology:

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring small amounts of active ingredients.

Orasolv Technology:

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet

machine is used to prepare the tablets. The tablets prepared are soft and friable and packed in specially designed pick and place system.

Flash Dose Technology:

This technology is based on the preparation of sugar based matrix known as floss, which is made from a combination of excipients either alone or in combination of drugs. Two platform fuisz technologies called Sheaform or Ceform are currently being utilized in preparation of wide range of oral disintegrating product.

Flash dose has been patented by Fuisz. Nurofen meltlet, a new form of Ibuprofen as melt-in-mouth tablets; prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consists of self-binding shearform matrix termed as "Floss". Shearform matrices are prepared by flash heat processing.

Wowtab Technology:

Wowtab Technology is patented by Yamanouchi Pharmaceutical Company WOW means "Without Water". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet.

Flashtab Technology:

Prographarm laboratories have patented the Flashtab technology. Tablets prepared by this system consist of an active ingredient in the form of microcrystals. Drug microgranules may be prepared by using the conventional techniques like coacervation, microencapsulation, and extrusion-spheronisation. All the processing utilized conventional tableting technology.

Ceform Technology:

In this, microspheres containing active ingredient are prepared. The manufacturing process involves placing a dry powder, containing either substantially pure drug material or a special blend of drug materials plus other pharmaceutical compounds, and excipients into precision engineered, and rapidly spinning machine. The centrifugal force throws dry blend at high speed through small, heated openings. The resultant microburst of heat liquifies the drug blend to form sphere. The microspheres are blended or compressed into preselected oral delivery dosage form. The microspheres can be incorporated into a wide range of fast dissolving dosage forms such as flash dose, or spoon dose, EZ chew.

Shearform Technology:

Shearform technology is based on preparation of floss that is also known as "Shearform Matrix", which is produced by subjecting a feedstock containing a sugar carrier to flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which raises the

temperature of the mass to create an internal flow condition, which permits part of it to move with respect of the mass. The flowing mass exits through the spinning head that flings the floss. The floss so produced is amorphous in nature so it is further cropped and recrystallised by various techniques to provide uniform flow properties and then facilitates blending. The recrystallised matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablet. The active ingredient and other excipients can be blended with floss before carrying out recrystallisation. The Shearform floss, when blended with the coated or uncoated microspheres, is compressed into tablets or EZ chewable tablets from standard tableting equipment.

Cotton candy:

Cotton candy process is known as candy floss process .this technique forms the basis of flash dose (Fuisz technologies, Chantilly,VA) In this technology , saccharides or polysaccharides are processed into amorphous floss by a simultaneous action of flash melting and centrifugal force. The floss is then partially recrystallised to impart a good flow properties and compressibility The floss then can be milled and blended with active ingredient and other excipients and finally that compressed into MDT. Advantages of this process are that the tablet can be accommodate high doses and posses satisfactory mechanical strength .The candyfloss are hygroscopic, hence , their manufacturing requires control of humidity conditions.

Comparison of some patented technologies for fast dissolving tablets

Technology	Novelty	Handling/storage	Drug release/ bioavailability
Zydis (R.P. Scherer, Inc.)	First to market. Freeze Dried	Do not push tablet through foil. Do not use dosage form from damaged package. Sensitive to degradation at humidities >65%	Dissolves in 2 to 10 sec. May allow for pre-gastric absorption leading to enhanced bioavailability
Orasolv (CIMA Labs, Inc.)	Unique taste masking. Lightly compressed	Packaged in patented foil packs	Disintegrates in 5 to 45 sec. depending upon the size of the tablet. No significant change in drug bioavailability
Durasolv (CIMA Labs, Inc.)	Similar to Orasolv, but with better mechanical strength	Packaged in foil or bottles. If packaged in bottles, avoid exposure to moisture or humidity	Disintegrates in 5 to 45 sec. depending upon the size of the tablet. No significant change in drug bioavailability
Wowtab (YAMANOUCHI Pharma Technologies, Inc.)	Compressed dosage form. Proprietary taste masking. Smoothmelt action gives superior mouth feel	Package in bottles. Avoid exposure to moisture or humidity	Disintegrates in 5 to 45 sec. depending upon the size of the tablet. No significant change in drug bioavailability

List of commercially available orodispersible tablets

Trade Name	Active Drug	Manufacturer
Feldene Fast Melt	Piroxicam	Pfizer Inc., USA
Calritin Redi Tab	Loratidine	Schering Plugh Corp, USA
Maxalt MLT	Rizatriptan	Merck & Co. USA
Zyprexia	Olanzapne	Eli Lilly, Indianapolis, USA
Pepcid RPD	Famotidine	Merck & Co., NJ, USA
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
Tempra Quiclets	Acetaminophen	Bristol Myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateauneuf, France
Nimulid MDT	Nimesulide	Panacea Biotech, New Delhi, India
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, USA

CHAPTER-2

OBJECTIVES

Aims and Objectives:

In the present work, fast dissolving tablets of telmisartan are planned to prepare with an intention to improve disintegration, dissolution rate and bioavailability of the drug**.** The fast dissolving tablet will be prepared by direct compression method are evaluated for various quality control tests for tablets such as hardness, friability, weight variation, drug content uniformity, disintegration and dissolution.

Need for the Study:

Telmisartan is a antihypertensive. Commercially available in the form of plain tablet in the market. Literature reveals that after oral administration of telmisartan tablets. This decreased bioavailability (42%) is mainly due to disintegration and dissolution process. The efficacy of the drug may be improved by number of techniques such as complexation, salt formation, solid dispersion and by formulating/preparing into a dispersible tablet.

Fast dissolving tablets are formulated with an objective improving disintegration and dissolution rate of the drug. Fast dissolving tablets are planned

to prepare by using some super disintegrutes.

Objectives

Fast dissolving tablets have number of advantages in comparison to conventional tablets such as ease of administration

1. Increased bioavailability (rapid absorption)
2. Convenient for such patients
3. Reduce patient compliant
4. Improved safety due to low risk of choking or suffocation during oral administration.

CHAPTER-3
REVIEW OF LITERATURE

Chaudhari PD et. al,[19] Studied the bitter taste of famotidine was masked using Eudragit in different ratio. The different superdisintegrants like Ac-di-sol and polyplasdone with their varying concentration used for disintegration of tablet in mouth. After dissolution study he concluded that all formulation showed faster release rate than marketed formulation.

Ritika Malik et al.,[51]The present research aims to enhance the dissolution profile of Telmisartan through formulation of its fast disintegrating tablets using a super-disintegrant Ac-Di-Sol. The effect of super-disintegrant Ac-Di-Sol was studied mainly on disintegration time and in-vitro drug release. A 22 factorial design was employed in formulating the fast disintegrating tablets. The selected independent variables Ac-Di-Sol and microcrystalline cellulose showed significant effect on dependent variables i.e. disintegration time and percent drug dissolved. The disintegration time and percent drug dissolved decreased with increase in the concentration of Ac-Di-Sol and decrease in the concentration of microcrystalline cellulose in the tablet. The optimized formulation was compared with the conventional marketed formulation for the same dependent variables. It showed about 62% increase in dissolution rate. The study concluded that dissolution rate of Telmisartan could be enhanced using Ac-Di-Sol as a super-disintegrant.

Venkateswara Rao. S et al.,[52] The present research was carried out to develop mouth dissolving tablets using superdisintegrants and improve the solubility ultimately bioavailability of Telmisartan by encapsulating it inside the cavity of β-cyclodextrin. Mouth dissolving tablets improve the oral bioavailability by enhancing the drug disintegration and release of drug particles from the dosage form, which enable quick and direct delivery into the circulatory system by avoiding first pass metabolism. Total nine batches of mouth dissolving tablets were prepared using superdisintegrants like Crosscarmellose sodium (CCS), Sodium Starch Glycolate (SSG) and Crosspovidone (CP) by direct compression method. Precompression parameters (Angle of repose, Carr's index and Hausner ratio) were in acceptable range as per the specifications given in IP. Prepared tablets were evaluated for thickness, uniformity of weight, hardness, friability and the results were well within IP limits. Out of the nine formulations developed, the F7 – F9 formulations containing CP as super disintegrant had exhibited the gratifying results when compared with the other two. The results conclude that F9 is the best formulation containing 40 mg of CP. It showed the superlative results in terms of disintegration time, wetting time and *In vitro* drug release. F9 had low wetting time 8.22 sec, low *in vitro* disintegration time (5 sec), high water absorption ratio (180%) and highest drug release profile (99.81%) which releases the drug within 12 minute. The different kinetic models revealed that drug release followed zero order and diffusion mechanism. It was concluded from the results that prepared mouth dissolving tablets might decrease dosing frequency, enhance bioavailability, improves patient compliance, rapid onset of action and avoid first pass metabolism, which was the objective of the present work.

Takao M et. al.,[20] Tried to developed novel fast-disintegration tablet as a user friendly dosage form for the aged. Used mannitol, lactose, glucose, magnesium stearate as excipient. Prepared many formulations using different exicipients in different formulation, various parameters checked and compare. They concluded that tablet contain mannitol, glucose and lactose showed quick disintegration time, but very low hardness and tablet contain maltose and mannitol having high hardness but slow disintegration time

Zhao N et. al.,[21] Compared disintegration efficiency and to developed a discriminating model for 3 classes of superdisintegrants represented of AC-Di-Sol, primoses and polyplasdone X L 10. The study were thus provides a closer look at the functionality of superdisintegrants in promoting tablet disintegration and development of model formulation with examinated by videography and dissolution profile. AC-Di-Sol was found to disintegrate tablet rapidly intoapparently primary particles. 3 disintegrants representing each of the 3 main classes of superdisintegrants differed in their ability to disintegrate model tablets into their primary particles.

Desai SA et. al.,[22] Prepared orodissolving tablets of promethazine hydrochloride were prepared by using superdisintegrant sodm starch glycolate and cross carmellose sodium by direct compression method. The prepared tablets were evaluated for uniformity of weight, tensile strength, content uniformity, hardness, friability, wetting time, invitro and invivo dispersion time and invitro drug release.

Nandgude TD et. al.,[23] Prepared diphenhydramine tannate fast dissolving

tablet by wet granulation method after incorporating superdisintegrants like sodium glycolate and crospovidone in different concentration. The tablets are subjected to evaluation with post compressional parameters like weight variation, hardness and friability, tensile strength, water absorption ratio, *in-vitro* dispersion time, *in vivo* dispersion time. Concluded that conventional tablet show 100% release after 7 hrs where as mouth disintegration tablet achieved maximum release 3-4 hrs. Tablet containing SSG show superior organoleptic properties along with excellent *in-vitro* dispersion time.

Uddhav S et. al.,[24] Described manufacturing technologies for mouth dissolving tablets showing that incorporation of an existing medicine into a new drug delivery system can significantly improve its performance in terms of efficacy, safety and improved patient compliance. In these studies they had described different types of technologies employed for the formulation of mouth dissolving tablets i.e. freeze drying, spray drying, sublimation and comparison of sugar based excipients with their dissolution rate and compressibility.

Shisu et. al.,[25] Prepared taste masked granules using aminoalkyl methacrylate copolymer by the extrusion method and formula rapidly disintegrating tablet by direct compression method. The tablet prepared by using microcrystalline cellulose and sodium starch glycolate ate as disintegrant. Concluded that tablet had a good taste and rapidly disintegrated in the mouth were useful and practical for pediatric and geriatric population.

Sharma S et. al.,[26] Formulated promethazine theoclate solid dispersion with PEG 4000 by using optimized amount of superdisintegrant.A phase solubility

method was used to evaluate the effect of various water-soluble polymers on aqueous solubility of promethazine theoclate.PEG 4000 was selected and solid dispersion were prepared by method of fusing.

Chaudhari PD et. al.,[28] Formulated and evaluated taste masked orodispersible dosage form of levocetirizine. An attempt was made to mask the taste, by complexation technique using ion-exchange resin, tulsion 335 formulate in to a orodispersible dosage form. The drug loading onto ion exchange resin was optimized for concentration of resin, swelling time of resin, stirring time, pH of resin solution, stirring temperature. Shows bitter drug successfully taste masked using suitable ion exchange resin. The drug resin complex orodispersible tablets were formulated and the evaluated for drug content, content uniformity, weight variation, hardness, friability, water absorption ratio, *in-vitro* and *in-vivo* drug release

Prabhu NB et. al.,[28]Studied on taste masking of drotaverine hydrochloride by the complexation technique. The drug loading process was optimized for taste masking and drug: resin ratio, the resinate was evaluated for bulk density, tap density, taste and characterization was done using DSC. The taste masked drotaverine complex was incorporated into palatable melt in mouth tablet and evaluated various quality control parameters. The mouth dissolve tablets had optimum physiochemical property with complete release of drug with 30 min.

Swamy PV et. al.,[29] Developed or dispersible tablet of meloxicam using different superdisintegrants. Combinations of sodium starch glycolate-croscarmellose sodium or sodium starch glycolate–crospovidone were used along

with directly compressible mannitol. The prepared batches evaluated for hardness, friability, wetting time, water absorption ratio like various parameters. He concluded that the formulation prepared using 2% w/v sodium starch glycolate and 15% croscarmellose sodium was found better formulation compare to conventional tablet.

He X et. al.,[30] Developed the rapidly dispersing tablet of a poorly wettable compound–formulation DOE and mechanistic study of effect of formulation excipient on wetting of celecoxib. In this work a tablet was placed in water and the turbidity of the resulting "dynamic" suspension was measured. They describe the novel method to enhance the dissolution rate for poorly soluble compounds by reduction in particle size, with screening formulation statistical design of experiments, mechanistic studies, optimization design of experiments and analytical methods like turbidity test, contact angle analysis, microscopic test.

Adamo F et. al.,[31]Developed eight formulations containing Ibuprofen in the form of orally disintegrating tablets. To prevent bitterness of drug he masked the taste of drug using taste masking agents. Aspartame used as a sweeter in formulation, mannitol used as a binder and explotab were added as superdisintegrant and compacted under low compression force. Dissolution profile suggest that the combined action of hydrophobic lecithin and coating delay the release of the drug from tablets with respect to when it is free or in the form of simple granules.

Setty CM et. al.,[32] Developed fast dispersible Aceclofenac tablets and study the effect of superdisintegrants on wetting time, disintegration time, drug

content, *in-vitro* release and stability parameter using direct compression technique. The parameters were tested for significance by using analysis of variance (ANOVA: Single factor). The stability study showed that tablet containing superdisintegrants were sensitive to high humidity condition. He also concluded that although functional differences existed between the superdisintegrants, the fast dispersible aceclofenae tablets could be prepared by using any of the superdisintegrants used.

Mulla JA et. al.,[33]Prepared promethazine hydrochloride mouth disintegrating tablet that have been used for prevention of emesis and nausea using disintegrants like Ac-di-sol, explotab, polyplasdone and MCC along with other additives by directly compression techniques. It was observed that the concentration of the superdisintegrants had an effect on disintegration time and *in-vitro* dissolution time and *in-vitro* dissolution characteristics. Ac-di-sol was found to be better as compared to other superdisintegrants used in study.

Rao TV et. al.,[34] Prepared mouth dissolving tablet of simavastatin by effervescent technique. Used sodium bicarbonate and citric acid a effervescent agent with mannitol, Magnesium stearate used as exicipient. Four formulation prepared simavastatin tablet improve the patient compliance and palatability moisture activation was successfully employed in tablet. Having a balance over the hardness and disintegration time of tablet using economic lab feasible method.

Rampure MV et. al.,[35] Prepared rapidly disintegrating tablet at Alfuzosin by effervescent method using sodium bicarbonate and citric acid. Crospovidone, sodium starch glycolate and croscarmellose sodium used as superdisintegrants.

The prepared tablet evaluated for different parameters and compare market product. He showed that the formulation containing crospovidone along with mixture at 24% w/w of sodium bicarbonate and 18% w/w citric acid as over all best formulation.

Swamy PV et. al.,[36] formulated amoxycilline trihydrate Concluded that formulation contain crosspovidone show good dissolution rate as compare to market product. They also concluded that croscarmellose sodium can be used for enhancing the *in-vitro* dissolution rate of poorly water soluble drug amoxycilline trihytrate.

Jeong SH et. al.,[37]Developed fast dissolving tablet using various polymer coated ion-exchange resin complexes. Complex of ion exchange resin and model drug prepared using different particle size of the resin. A high shear granulation method was used to prepare the granules containing coated resin particles. The tablets were examined using SEM. He concluded that as the resin particle becomes smaller. The time needed to reach equilibrium was shorter than of bigger particles and drug release rate increased due to the increased surface area of the resin complexes.

Patel DM et. al.,[38] Prepared fast dissolving Etoricoxib tablet by sublimation method using camphor as a subliming agent along with the exicipients. The tablets were evaluated for percentage friability and disintegration time and 3^2 full factorial designs were applied to investigate the combine effect of 2 formulation variables. The optimized tablet formulation was compared with conventional marketed tablets for percentage drug dissolved in 30 min. From the

result they concluded that fast dissolving tablet with improved etoricoxib dissolution could be prepared by sublimation containing suitable subliming agent

Rao NG et. al.,[39] formulated fast dissolving tablets of poorly soluble carbamazepine by direct compression technique with < -cyclodextrin complexes using various superdisintegrants like Indion-414, croscarmellose sodium, crosspovidone and sodium starch glycolate. The prepared tablets were evaluated for hardness, friability, drug content, weight variation, disintegration time, wetting time, *in-vitro* dissolution studies and were characterized by DSC, FTIR and stability studies. Concluded that the formulation containing 10% of crosscarmellose sodium is over all the best formulation.

CHAPTER-4

METHODOLOGY

Materials:

Table 1: Materials Used

Sl. No.	Material	Source
1.	Telmisartan	Cipla Pharma R & D, Vikhroli
2.	Croscarmellose sodium	HiMedia Laboratories Ltd, Mumbai
3.	Crospovidone	HiMedia Laboratories Ltd, Mumbai
4.	Sodium starch glycolate	HiMedia Laboratories Ltd, Mumbai
5.	Microcrystalline cellulose	Merck Specialties' limited., Mumbai
6.	Magnesium stearate	Oxford Laboratory., Mumbai.
7.	Talc	NR Chem, Mumbai.
8.	Lactose	Merck Specialties' limited., Mumbai

Equipment:

Table 2: Equipment Used

Sl. No.	Equipment	Make / Model
1.	Tablet compression machine	Rimek, minipress 10 station rotary machine
2.	Hardness tester	Pfizer hardness tester, Servewell instruments and equipments pvt. ltd., Bangalore.
3.	Friability Test Apparatus	Dolphin ,Bombay
4.	Tablet Dissolution Test Apparatus	Campbell electronics, DR-6 Dissolution Appratus
5.	UV visible spectrophotometer	PG Instruments limited, T-80 UV-VIS Spectrometer
6.	Single pan digital Balance	Shimadzu, Shimadzu corporation, JapanL
7.	pH meter	Hanna Instruments, Ranchi.
8.	FT-IR Spectrometer	Perkin Elmer Instruments, USA

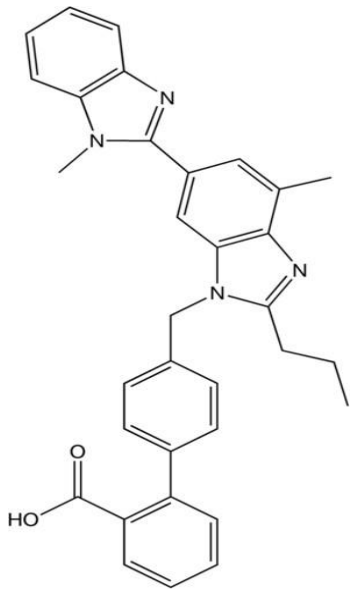
4.2 Drug Profile[40]:

Telmisartan:

Chemical formula:

2-(4-{[4-methyl-6-(1-methyl-1*H*-1,3-benzodiazol-2-yl)-2-propyl-1*H*-1,3-benzodiazol-1-yl]methyl}phenyl)benzoic acid

Chemical structure:



Empirical Formula : $C_{33}H_{30}N_4O_2$

Molecular weight : 514.617 g/mol

Solubility: Slightly soluble in chloroform and 0.1mol/L NaOH Liquor and very lightly soluble in methanol and acetonitrile and hardly soluble in water.

Bioavailability : 42%

Protein Binding : 99.5%

Half-life : 24 hour

Therapeutic category: Telmisartan is an angiotensin II receptor antagonist (angiotensin receptor blocker, ARB) used in the management of hypertension.

Indication: Telmisartan is indicated in the treatment of essential hypertension

Contraindication: Telmisartan is contraindicated during pregnancy. Like other drugs affecting the renin-angiotensin system (RAS), telmisartan can cause birth defects, stillbirths and neonatal deaths It should not be taken by breastfeeding women since it is not known whether the drug passes into the breast milk.

Adverse effect: Side effects are similar to other angiotensin II receptor antagonists and include tachycardia and bradycardia (fast or slow heartbeat), hypotension (low blood pressure), edema (swelling of arms, legs, lips, tongue, or throat, the latter leading to breathing problems), and allergic reactions.

Administration: The usually effective dose telmisartan is (20–)40–80 mg once daily. Some patients may already benefit at a daily dose of 20 mg. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80 mg once daily

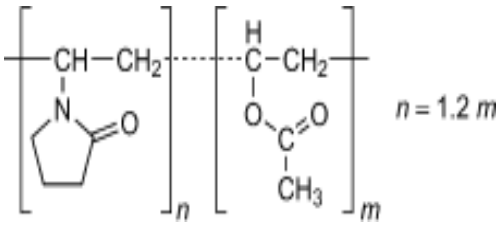
Contraindication: Telmisartan is contraindicated during pregnancy. Like other drugs affecting the renin-angiotensin system (RAS), telmisartan can cause birth defects, stillbirths, and neonatal deaths. It should not be taken by breastfeeding women since it is not known whether the drug passes into the breast milk.

Mode of action: Telmisartan is an angiotensin II receptor blocker that shows high affinity for the angiotensin II receptor type 1 (AT_1), with a binding affinity 3000 times greater for AT_1 than AT_2. It has the longest half-life of any ARB (24 hours) and the largest volume of distribution. In addition to blocking the RAs, telmisartan acts as a selective modulator of peroxisome proliferator-activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose metabolism. It is believed that telmisartan's dual mode of action may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease (CVD).

Excipient Profiles[41, 42,43]

CROSPOVIDONE:

1. Nonproprietary names	:	BP : Crospovidone PhEur : Crospovidonum USPNF: Crospovidone\
2. Synonyms	:	Crosslinked povidone, polyvinyl polypyrrolidone, PVPP,
3. Chemical name and CAS registry number	:	1-Ethenyl-2-pyrrolidinone homopolymer [9003-39-8]
Empirical formula and molecular weight	:	The USPNF 23 describes crospovidone as a water-insoluble synthetic crosslinked homopolymer of *N*-vinyl-2-pyrrolidinone.

$(C_6H_9NO)_n$>1 000 000		An exact determination of the molecular weight has not been established because of the insolubility of the material
Structural formula	:	
Functional category	:	Superdisintegrant.
Description	:	Crospovidone is a white to creamy-white, finely divided, free-flowing, practically tasteless, odorless or nearly odorless, hygroscopic powder.

Applications in pharmaceutical formulation or technology:

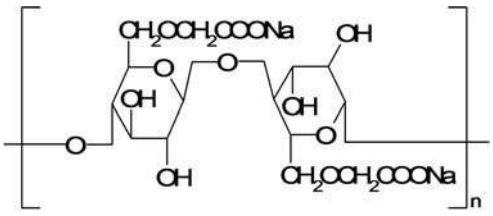
Crospovidone is a water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods. It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels. Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets. Larger particles provide a faster disintegration than smaller particles. Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence

of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.

Croscarmellose sodium:

Nonproprietary Name	:	USPNF: Croscarmellose sodium.
Synonyms	:	Ac-Di-sol; cross-linked carboxy methylcellulose Sodium; Primellose
Functional category	:	Tablet and capsule disintegrants
Chemical name	:	Cellulose, carboxymethyl ether, sodium salt, cross- linked
CAS Registry Number	:	74811-65-7.
Description	:	Croscarmellose sodium occurs as an odourless, white-coloured powder.

Structural formula:

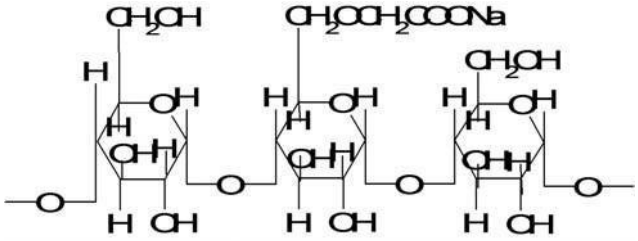


Molecular weight	:	90000-700000.
pH (1% w/v dispersion)	:	5.0-7.0.

Sodium starch glycolate:

Synonyms:	:	Explotab, Primogel.
Non proprietary Name	:	BP: Sodium starch glycolate USPNF: Sodium starch glycolate
Functional category	:	Tablet and capsule disintegrant.
Chemical names	:	Sodium carboxymethyl starch.
CAS Registry Number	:	9063-38-1
Description	:	Sodium starch glycolate is a white to off-white, odourless, tasteless, free flowing powder. It consists of oval or spherical granules, 30-100 μm in diameter with some less spherical granules ranging from 10-35 μm in diameter.

Structural formula:



Solubility: : Practically insoluble in water; sparingly soluble in ethanol (95%). In water it swells up to 300 times its volume

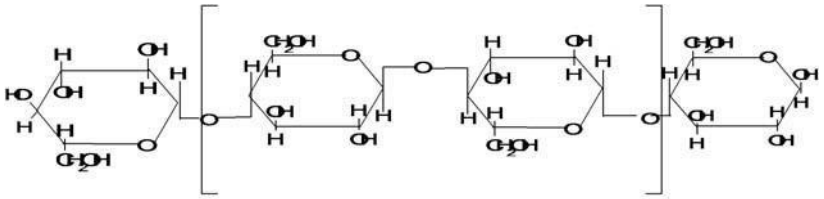
Stability andstorage conditions	:	It is a stable material. It should be stored in a well closed container to protect from wide variations in humidity and temperature that may cause cracking.
Incompatibilities	:	Incompatible with ascorbic acid.
Safety	:	It is generally regarded as a non-toxic and non-irritant material. However, oral ingestion of large quantities may be harmful.
Applications	:	As a disintegrant in tablet (wet granulation and direct compression) and capsule formulation in 2-8% concentration.

Microcrystalline cellulose (AVICEL PH 102):

Nonproprietary name	:	NF :Microcrystalline cellulose. USP : Microcrystalline cellulose.
Functional category	:	Tablet and capsule diluents, tablet disintegrant, suspending and/or viscosity increasing agent.
Synonyms	:	Cellulose gel: Crystalline cellulose: Avicel PH101, 102,
Chemical names	:	Cellulose
CAS Registry number	:	9004-34-6
Empirical formula	:	(C6H10O5)n n=220

Molecular weight : 36,000(approx)

Structural formula:



Microcrystalline Cellulose

Description: : Purified, partially depolymerized cellulose occurs as a white, odorless, tasteless, crystalline powder composed of porous particles.

Density: : Apparent density - 0.28g/cm^3

Tap density - 0.43g/cm^3

Solubility: : Insoluble in water, dilute acids and most organic solvents, slightly soluble in 5% w/v NaOH solution.

Stability and storage conditions : Stable, hygroscopic. Store in a well closed container

Incompatibilities: : Nonecited in the literature.

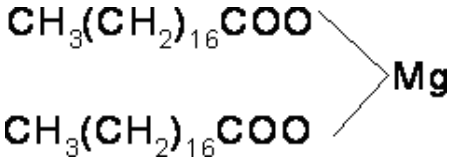
Safety: : Generally regarded as safe

Applications:	:	Tablet binder/diluents (wet or dry granulation) 5 to 20%
		Tablet disintegrant 5 to 15%
		Tablet glidant 5 to 15%
		Antiadherent 5 to 20%

Magnesium stearate:

Nonproprietary name	:	NF: Magnesium stearate. BP/EP: Magnesium stearate
Synonyms	:	Metallic stearic; Magnesium salt.
Functional category	:	Tablet and capsule lubricant.
Chemical names	:	Octadecanoic acid; Magnesium salt; Magnesium stearate
CAS Registry number	:	557-04-0
Empirical formula	:	$C_{36}H_{70}MgO_4$
Molecular weight	:	591.3

Structural formula:



Description	:	It is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint characteristic odour and taste. The powder is greasy to touch and readily adheres to the skin. Density (He) : 1.03-1. g/cm^3 Bulk volume : 3.0-8.4 ml/g Tapped volume : 2.5-6.2 ml/g
Solubility	:	Practically insoluble in ethanol, ethanol (95%), ether and water, slightly soluble in benzene and warm ethanol (95%).
Stability andstorage conditions	:	Stable, non-self polymerizable. Store in a cool, dry place in a well closed container
Incompatibilities	:	Incompatible with strong acids, alkalies, iron salts and with strong oxidizing materials

LACTOSE:

Synonyms: Fast-Flo, Microlose, milk sugar, Pharmatose, Tablettose.

Functional Category: Tablet and Capusle diluent.

Applications: As filler or diluent in tablets (wet granulation and direct compression) and capsules, in lyophilized products and infant fed formulas.

Description: White to off-white crystalline particles or powder, odourless and slightly sweet-tasting.

Solubility: Freely soluble in water, practically insoluble in chloroform, ethanol and ether.

Stability: Under humid conditions (80% RH and above) modl growth may occur.

Storage conditions: Lactose should be stored in a well-closed container in a cool, dry place.

Incompatbilities: A Maillard-type condensation reaction is likely to occur between lactose and compounds with a primary amine group to form brown colored products.

Safety: Adverse reactions to lactose is largely attributed to lactose intolerance, which occurs in persons with a deficiency of the intestinal enzyme lactase.

Talc:

Non proprietary name	:	Purified talc
Synonym	:	Powdered talc.
Empirical formula	:	$Mg_6(Si_2O_5)_4(OH)_4$.
Specific surface area	:	2.41-2.42 m^2/g
Description	:	Talc is very fine, white to greyish-white colored, odorless, hydrophobic, crystalline powder. It adheres readily to the skin, is soft to touch, and free from grittiness.

Functional category	:	Anticaking agent, glidant, tablet and capsule diluent, tablet and capsule lubricant
Pharmaceutical applications	:	It is commonly used as a lubricant in tablet and capsules.

Concentrations of talc to be used in various applications

Use	Concentration (%)
Dusting powder	90-99
Glidant and tablet lubricant	1-10
Tablet and capsule diluent	5-30

Stability and storage conditions	:	Talc is a stable material. It should be stored in a well-closed container in a cool, dry place.
Incompatibilities	:	Incompatible with quaternary ammonium compounds
Safety	:	Following oral ingestion talc is not absorbed systemically and may be thus regarded as an essentially nontoxic material

4.4 Method

A) Construction of calibration curve in 0.1 N HCL[44, 45]

Spectroscopic Method for Estimation of Telmisartan:

The standard calibration curve for telmisartan was prepared in 0.1N HCl.

Standard Solution: 100mg of pure drug transferred into 100ml of 0.1 N HCl in a volumetric flask to give a concentration of 1 mg/ml.

Stock Solution: From the standard solution a stock solution was prepared to give a concentration of 100 mcg/ml in 0.1 N HCl.Aliquots of 0.2,0.4, 0.6, 0.8, 1.0, 1.2 ml of stock solution was pipette out in 10 ml volumetric flasks. The volume was made up to mark with solvent. The dilution gives 2μg/ml, 4μg/ml, 6μg/ml, 8μg/ml, 10μg/ml, 12μg/ml, of telmisartan respectively.

The absorbance of prepared solution of telmisartan in HCl was measured at 296 nm in PG instruments UV\visible spectrophotometer against 0.1N HCl as blank. The absorbance data for standard data for calibration curve yields a straight line, which shows that drug obeys Beer's law in the concentration range of 4 -14 mcg\ml. The results are given in table-1 and figure-1

Table 3: Standard calibration curve of Telmisartan in 0.1 N HCL at λ_{max} 296nm

Sl. No.	Concentration (mcg/ml)	Absorbance
1.	00	0.000
2.	02	0.178
3.	04	0.270
4.	06	0.365
5.	08	0.466
6.	10	0.55
7.	12	0.65

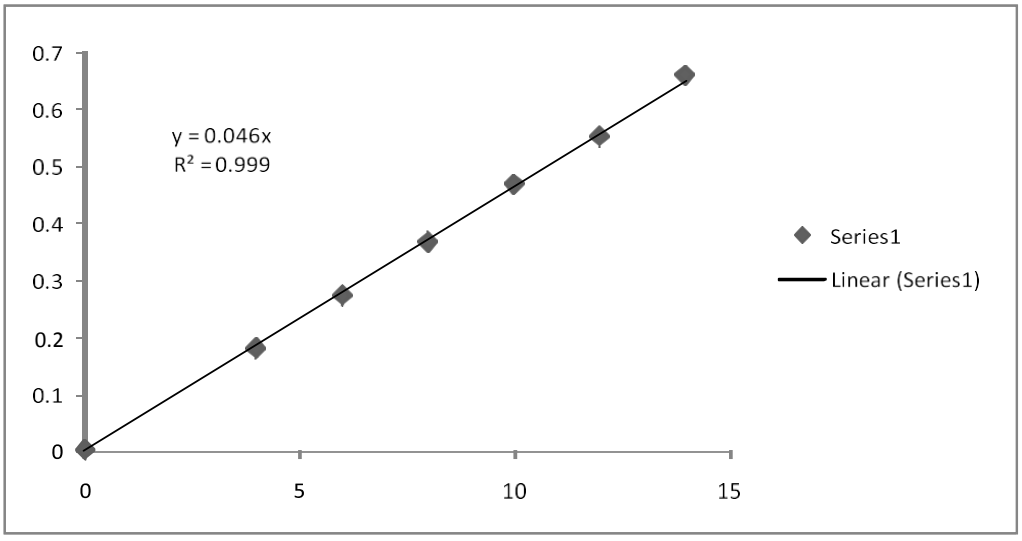


Figure 1: Standard calibration curve of Telmisartan in 0.1N HCl at λ_{max} 296nm

B) Preparation of Telmisartan Fast dissolving tablet[45]

Telmisartan fast dissolving tablet F_1 to F_{12} were prepared by direct compression method and the detailed tablet composition was given in table-1. A total of tablets were prepared in every batch and the quantity for 60 tablets were given in table-06.

Method:

- All the ingredients were passed through 60 mesh sieve separately.
- Then drug and diluents separately taking small portion of both each time and blending it thoroughly to get uniform mixture.
- The granules were compressed using 8 mm size to get a tablet of 150 mg tablet weight using Rimek mini press machine

Table-4: Materials used in the study with their property

Sl. No.	Materials	Property
1.	Telmisatan	Antihypertensive
2.	Crospovidone	Disintegrant
3.	Croscarmellose sodium	Disintegrant
4.	Sodium starch glycolate	Disintegrant
5.	Microcrystalline cellulose	Diluent
6.	Lactose	Diluent
7.	Talc	Glidant
8.	Mg stearate	Lubricant

Table-5: Parameters fixed for the fast dissolving tablets

Sl. No.	Test	Limit
1.	Physical apperance	white,circular
2.	Average weight	150 mg
3.	Diametr	7 mm
4.	Thickness	3mm
5.	Hardness	2-4 Kg
6.	Friability	NMT 1%
7.	Disintegrantion time	NMT 180 Sec

C) PRECOMPESSION STUDY[46, 47,48]:

Angle of repose (θ) [46,48]:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose.

$\tan \theta = h / r$

$\theta = \tan^{-1} (h/r)$

Where, θ is the angle of repose

h is height of pile

r is radius of the base of pile

Different ranges of flow ability in terms of angle of repose (Table No. 9) are given below.

Relationship between angle of repose (θ) and flow properties.

Angle of Repose (θ) (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Method:

A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, thereby evaluating the flow ability of the granules. Height of the pile was also measured.

Bulk density:

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape, and the tendency of the particles to adhere to one another.

Method:

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of accurately weighed powder (bulk) from each formula, previously shaken to break any agglomerates formed was introduced into a 25 ml

measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec interval. The taping was continued until no further change in volume was noted. LBD and TBD were calculated using following formula;

$$LBD = \frac{\text{Weight of powder}}{\text{Volumeof packing}} \quad \text{--------- (a)}$$

$$TBD = \frac{\text{Weight of powder}}{\text{Tapped packing}} \quad \text{---------- (b)}$$

True density:

True density of granules is carried out by using specific gravity bottle:

- First take the empty bottle weight i.e., W1
- Then add 3/4th of liquid in it, that the weight of that i.e., W2
- Add 1/4th quantity of powder then take the weight i.e., W3
- Finally take the weight of bottle., powder and liquid., W4

It is calculated by using the formula:

$$\text{True Density} = \frac{(w_3 - w_1)}{\frac{(w_2 - w_1) - (w_4 - w_3)}{\rho}}$$

Percentage Porosity: This can be calculated by taking the value of bulk density and true density

$$\text{Percent Porosity} = 1 - \frac{\text{Bulk desnity}}{\text{True density}} \times 100$$

Post-Compression parameters:

All the formulation of telmisartan prepared were evaluated for the following physical and chemical parameters

Physical Parameters:

Size and shape: The tablet formulated were circular in shape with 7 mm diameter.

Organoleptic Characters:

Colour: Telmisartan fast dissolving tablets were found to be white in colour.

Tablet Properties:

Hardness test:

Tablets require a certain amount of strength, or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated.

Friability test:

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition.

The friability of tablets was determined by using Veego Friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The percentage friability was then calculated by,

$$F = \frac{\text{Initial weight} - \text{Finalweight}}{\text{Initial weight}} x100 \qquad \text{---------- (d)}$$

% Friability of tablets less than 1% is considered acceptable.

Weight variation test[49]:

The tablets were selected randomly from each formulation and weighed individually to check for weight variation. The U.S Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

Percentage deviation in weight variation

Average weight of a tablet	Percentage deviation
130 mg or less	10
More than 130 mg and less than 324 mg	7.5
324 mg or more	5

In all the formulations the tablet weight was more than130mg and less than 324 mg, hence 7.5% maximum difference allowed.

Drug content uniformity[50]:

Twenty tablets were weighed and crushed in a mortar. Then weighed powder contain equivalent to 100mg of drug transferred in 100ml of 0.1 N HCL. Its concentration 1000 mcg/ml. 10ml from this stock solution taken and diluted to 100ml of 0.1N HCL, it makes 100µg/ml. Then 0.6ml from stock solution and diluted to 10ml. Absorbance measure at 296nm.

***In vitro* disintegration time:**

The process of breakdown of a tablet into smaller particles is called as disintegration. The *in-vitro* disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications.

I.P. Specifications: Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using 0.1 N HCL maintained at 37°±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the 0.1 N HCL maintained at 37°±2°C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded. The results are given in table 11.

***In vitro* dissolution studies:**

Dissolution rate was studied by using USP type-II apparatus , Dissolution Test Apparatus at 50 rmp) using 900ml of 0.1 N HCl as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C, aliquot of dissolution medium was withdrawn at every 1 min interval and filtered. The

absorbance of filtered solution was measured by UV spectrophotometric method at 296 nm and concentration of the drug was determined from standard calibration curve. The results are given in table 17 to 28 and figures from 2 to 13.

***In vitro* drug release studies details:**

Apparatus used	:	USP II dissolution test apparatus
Dissolution medium	:	0.1 N HCl
Dissolution medium volume	:	900 ml
Temperature	:	37 ± 0.5°C
Speed of basket paddle	:	50 rpm
Sampling intervals	:	1 min
Sample withdraw	:	5 ml
Absorbance measured	:	296 nm

Drug polymer interaction studies:

FTIR STUDIES:

IR spectra for pure drug, formulations Telmisartan,Crospovidone and F6 were recorded in a Fourier transform infrared (FTIR) spectrophotometer (Shimadzu corporation 8600, Japan) with KBr pellets.

Table-6
Formulation of Telmisartan fast dissolving tablets prepared by direct compression method

Ingredient (mg)	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**	**F_{10}**	**F_{11}**	**F_{12}**
Telmisatan	20	20	20	20	20	20	20	20	20	20	20	20
Croscarmellose sodium	4	8	12	----	----	----	----	----	----	----	6	6
Crospovidone	----	----	----	4	8	12	----	----	----	6	6	----
Sodium starch glycolate	----	----	----	----	----	----	4	8	12	6	----	6
Microcrystalline cellulose	36	32	28	36	32	28	36	32	28	28	28	28
Lactose	80	80	80	80	80	80	80	80	80	80	80	80
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Mg stearate	5	5	5	5	5	5	5	5	5	5	5	5
Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

Table-7
Formulation of Telmisartan fast dissolving tablets prepared by direct compression method (60 tablets)

Ingredient (mg)	**F_1**	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**	**F_{10}**	**F_{11}**	**F_{12}**
Telmisatan	1200	1200	1200	1200	1200	1200	1200	1200	1200	1200	1200	1200
Crospovidone	240	480	720	----	----	----	----	----	----	360	360	360
Croscarmellose sodium	----	----	----	240	480	720	----	----	----	----	----	----
Sodium starch glycolate	----	----	----	----	----	----	240	480	720	360	360	360
Microcrystalline cellulose	2160	1920	1680	2160	1920	1680	2160	1920	1680	1680	1680	1680
Lactose	4800	4800	4800	4800	4800	4800	4800	4800	4800	4800	4800	4800
Talc	300	300	300	300	300	300	300	300	300	300	300	300
Mg stearate	300	300	300	300	300	300	300	300	300	300	300	300
Total	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**	**9000**

CHAPTER-5

RESULTS

Results of Granule Parameter Evaluation:

Table-:8 Granule Parameters for Telmisartan Formulation

Formulation Code	Bulk Density gm/cc	True Density	Angle of Repose θ=h/r	Percentage Porosity
F_1	0.53	1.27	28.32	56
F_2	0.52	1.45	29.08	57
F_3	0.55	1.23	30.21	56
F_4	0.54	1.09	30.11	56.5
F_5	0.51	1.23	28.43	57
F_6	0.50	1.87	30.38	56.8
F_7	0.53	1.45	31.03	56.9
F_8	0.54	1.78	28.10	56
F_9	0.52	1.67	26.28	56.4
F_{10}	0.54	1.25	29.78	56.2
F_{11}	0.52	1.76	26.89	56.3
F_{12}	0.51	1.24	26.45	56.8

Hardness Test Result

Table-9: Hardness Test for Telmisartan Formulation

Formulation code	Hardnesss in* Kg/cm^2 ±SD
F_1	3.22±0.12
F_2	3.23 ±0.28
F_3	3.34 ±0.12
F_4	3.23 ±0.24
F_5	2.9 ±0.36
F_6	2.84±0.32
F_7	3.17±0.12
F_8	2.91 ±0.01
F_9	2.95 ±0.14
F_{10}	4.0±0.00
F_{11}	3.7±0.12
F_{12}	3.7±0.28

*** Average of three diterminations**

Friability Test Results

Table-10: Friability test for Telmisartan Formulation

Formulation code	Friability (%)
F_1	0.54
F_2	0.54
F_3	0.57
F_4	0.62
F_5	0.64
F_6	0.59
F_7	0.60
F_8	0.64
F_9	0.70
F_{10}	0.87
F_{11}	0.78
F_{12}	0.56

In Vitro Dispersion Test Result

Table-11: *In Vitro* Dispersion Time for Telmisartan Formulation

Formulation code	Time in seconds ±SD
F_1	75.0±2.5
F_2	60.0±1.4
F_3	35.0±1.8
F_4	55.0±0.7
F_5	38.0±0.4
F_6	15.0±0.5
F_7	110.0±1.1
F_8	85.0±1.4
F_9	68.0±0.7
F_{10}	87.0±0.9
F_{11}	64.0±0.7
F_{12}	45.0±0.6

Table-12: Weight Variation of Telmisartan Formulation

Sr. No.	F1			F2			F3		
	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation
1	151	1.3	0.81	154	4.4	2.7	153	2.2	1.36
2	152	2.3	1.4	152	2.4	1.49	152	1.2	0.74
3	149	0.7	0.43	148	2.4	1.49	152	1.2	0.74
4	154	4.3	2.69	150	0.4	0.24	150	0.8	0.49
5	147	2.7	1.69	148	2.4	1.49	150	0.8	0.49
6	148	1.7	1.06	148	2.4	1.49	153	2.2	1.36
7	150	0.3	0.187	149	1.4	0.87	152	1.2	0.74
8	148	1.7	1.06	150	0.4	0.24	149	1.8	1.11
9	150	0.3	0.187	152	2.4	1.49	147	3.8	2.36
10	148	1.7	1.06	153	3.4	2.11	150	0.8	0.49
	Average of 10 Tablets 149.7 mg			Average of 10 Tablets 150.4 mg			Average of 10 Tablets 150.8mg		

Table-13: Weight Variation of Telmisartan Formulation

Sr. No.	F4			F5			F6		
	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation
1	152	1.1	0.68	150	0.7	0.43	152	0.8	0.49
2	155	4.1	2.54	152	1.3	0.80	153	1.8	1.11
3	148	2.9	1.80	154	3.3	2.05	151	0.2	0.12
4	150	0.9	0.55	152	1.3	0.80	152	0.8	0.49
5	152	1.1	0.68	152	1.3	0.80	152	0.8	0.49
6	153	2.1	1.30	151	0.3	0.18	153	1.8	1.11
7	153	2.1	1.30	149	1.7	1.05	148	3.2	1.98
8	147	3.9	2.42	148	2.7	1.68	149	2.2	1.36
9	149	1.9	1.18	147	3.7	2.30	150	1.2	0.74
10	150	0.9	0.55	152	1.3	0.80	152	0.8	0.49
	Average of 10 Tablets150.9 mg			Average of 10 Tablets 150.7mg			Average of 10 Tablets151.2 mg		

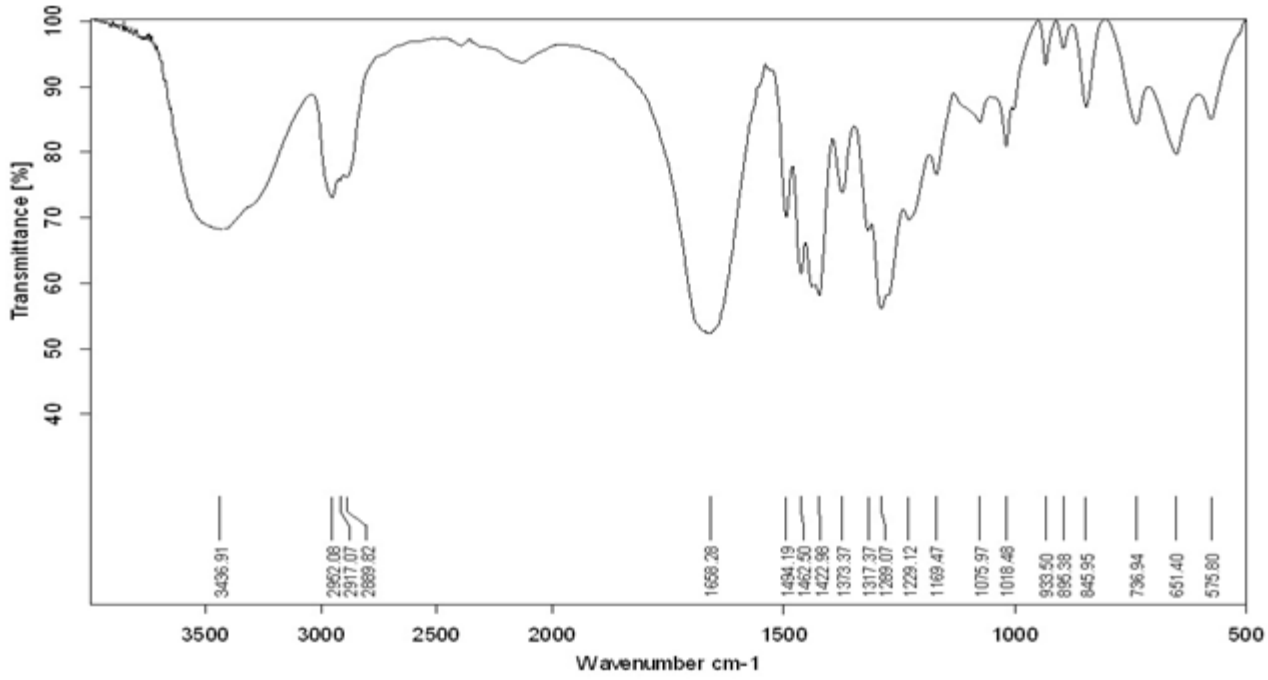
Table-14: Weight Variation of Telmisartan Formulation

Sr. No.	F7			F8			F9		
	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation
1	151	0.8	0.49	150	0.1	0.06	152	1.3	0.80
2	152	1.8	1.12	149	1.1	0.68	153	2.3	1.43
3	153	2.8	1.74	147	3.1	1.93	149	1.7	1.05
4	149	1.2	0.74	152	1.9	1.18	148	2.7	1.68
5	148	2.2	1.37	153	2.9	1.81	152	1.3	0.80
6	147	3.2	1.99	149	1.1	0.68	153	2.3	1.43
7	149	1.2	0.74	147	3.1	1.93	148	2.7	1.68
8	150	0.2	0.12	149	1.1	0.68	149	1.7	1.05
9	151	0.8	0.49	153	2.9	1.81	151	0.3	0.18
10	152	1.8	1.12	152	1.9	1.18	152	1.3	0.80
	Average of 10 Tablets 150.2 mg			Average of 10 Tablets 150.1 mg			Average of 10 Tablets 150.7 mg		

Table-15: Weight Variation of Telmisartan Formulation

Sr. No.	F10			F11			F12		
	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation	Weight in mgs	Difference in weight	Percent Deviation
1	151	0.5	0.31	151	0.9	0.56	152	1.9	1.18
2	152	1.5	0.93	152	1.9	1.18	152	1.9	1.18
3	153	2.5	1.55	153	2.9	1.81	151	0.9	0.56
4	148	2.5	1.55	149	1.1	0.68	149	1.1	0.68
5	149	1.5	0.93	148	2.1	1.31	147	3.1	1.93
6	152	1.5	0.93	150	0.1	0.06	148	2.1	1.31
7	153	2.5	1.55	148	2.1	1.31	152	1.9	1.18
8	148	2.5	1.55	148	2.1	1.31	153	2.9	1.81
9	149	1.5	0.93	149	1.1	0.68	149	1.1	0.68
10	150	0.5	0.31	153	2.9	1.81	148	2.1	1.31
	Average of 10 Tablets150.5 mg			Average of 10 Tablets 150.1mg			Average of 10 Tablets 150.1mg		

FTIR Spectrum
IR Spectrum of Drug + Mixture



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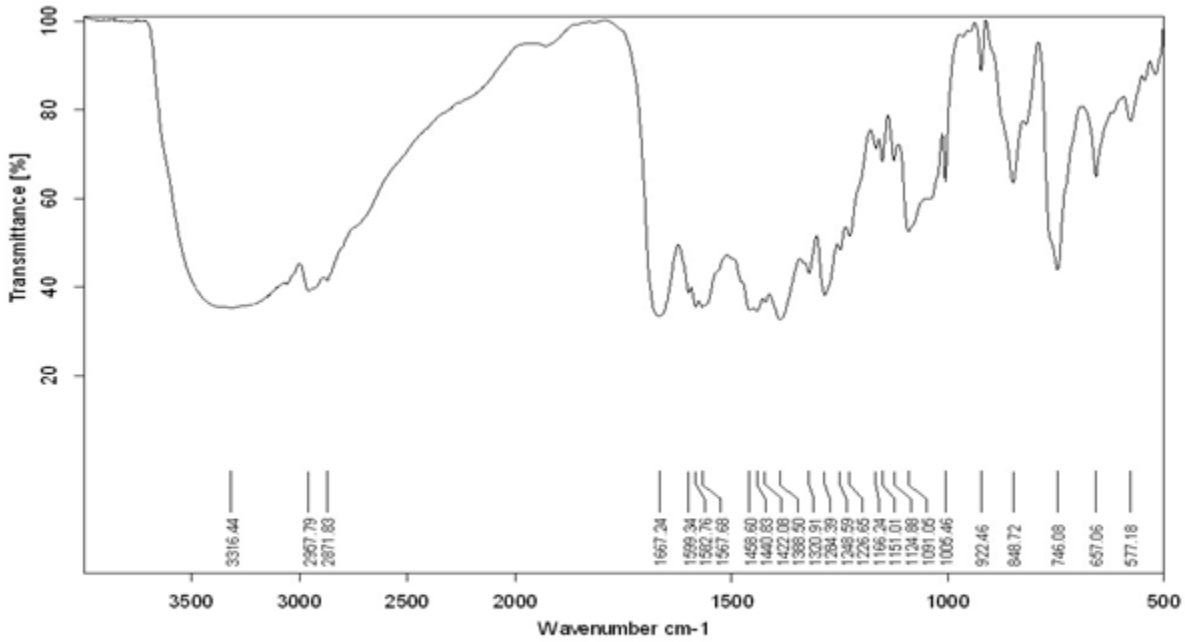
FTIR Spectrum
IR Spectrum of Pure Drug Telmisartan



FTIR Spectrum

IR Spectrum of Formulation F_6

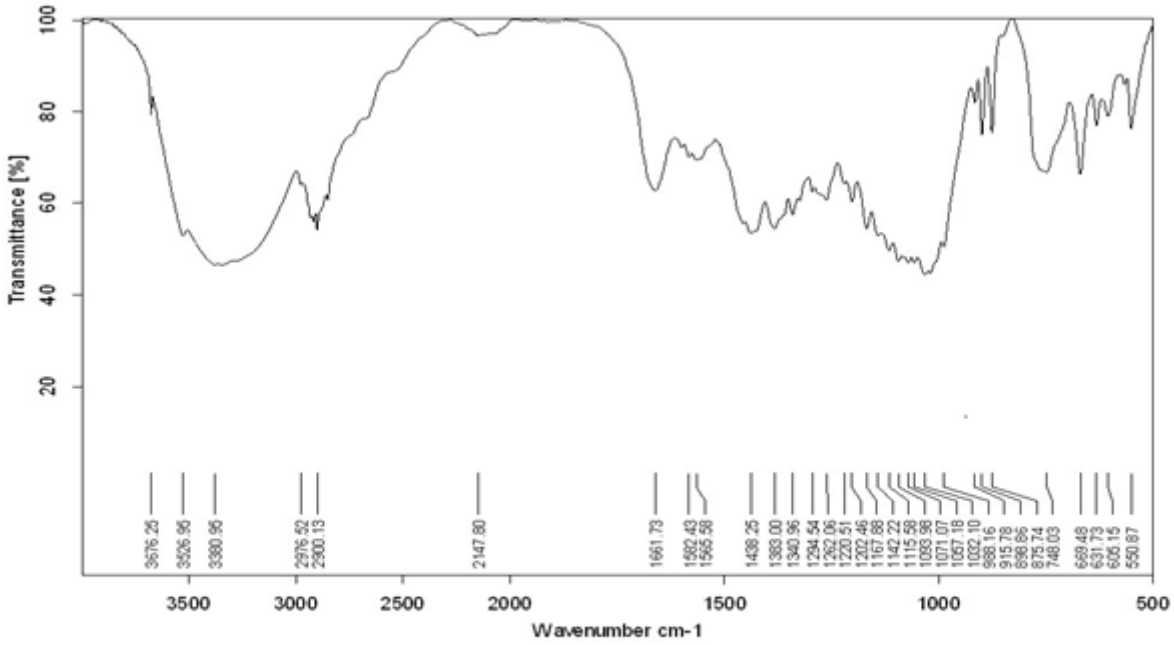


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Table 16: Drug Content of Telmisartan Formulation

Sr. No.	Formulation code	Absorbance	Concentration in mcg/ml	Average Content (%)±SD
1	F1	1.202	19.9	99.5 ± 0.175
2	F2	1.205	20	100.0 ± 0.275
3	F3	1.173	19.4	97.0 ± 0.175
4	F4	1.162	19.2	96.0 ± 0.436
5	F5	1.209	20.06	99.3 ± 0.354
6	F6	1.205	20	99.0 ± 0.154
7	F7	1.153	19.1	95.5 ± 0.265
8	F8	1.202	19.9	99.5 ± 0.241
9	F9	1.173	19.4	97.0 ± 0.156
10	F10	1.162	19.2	96.0 ± 0.123
11	F11	1.209	20.06	99.3 ± 0.432
12	F12	1.165	19.3	96.5 ± 0.143

Table-17: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_1

Time in Minute	Absorbance	Concentration in mg	% Drug Release ± SD
01	0.085	3.06	15.3 ± 0.12
02	0.150	5.4	27.0 ± 0.32
03	0.221	7.95	39.78 ± 0.12
04	0.272	9.79	48.95 ± 0.32
05	0.335	12.02	60.12 ± 0.21
06	0.405	14.58	72.90 ± 0.16
07	0.455	16.38	81.9 ± 0.55
08	0.510	18.36	91.8 ± 0.34
09	0.525	18.9	94.5 ± 0.16
10	0.539	19.40	97.02 ± 0.44

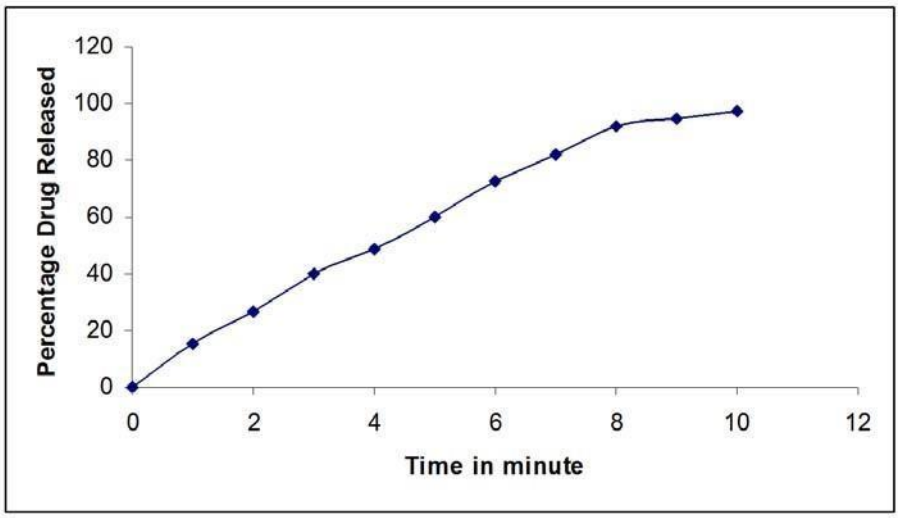


Figure –2: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_1

Table-18: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_2

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.080	2.88	14.4 ± 0.12
02	0.160	5.76	28.8 ± 0.34
03	0.222	7.92	39.6 ± 0.56
04	0.268	9.648	48.24 ± 0.45
05	0.340	12.24	61.2 ± 0.66
06	0.400	14.40	72.0 ± 0.68
07	0.460	16.56	82.8 ± 0.43
08	0.520	18.72	93.6 ± 0.12
09	0.539	19.404	97.02 ± 0.13
10	0.545	19.62	98.1 ± 0.01

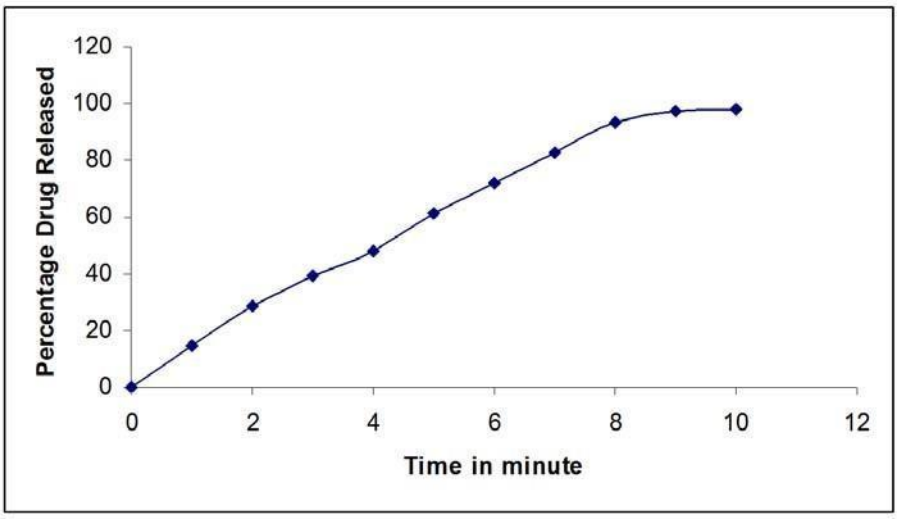
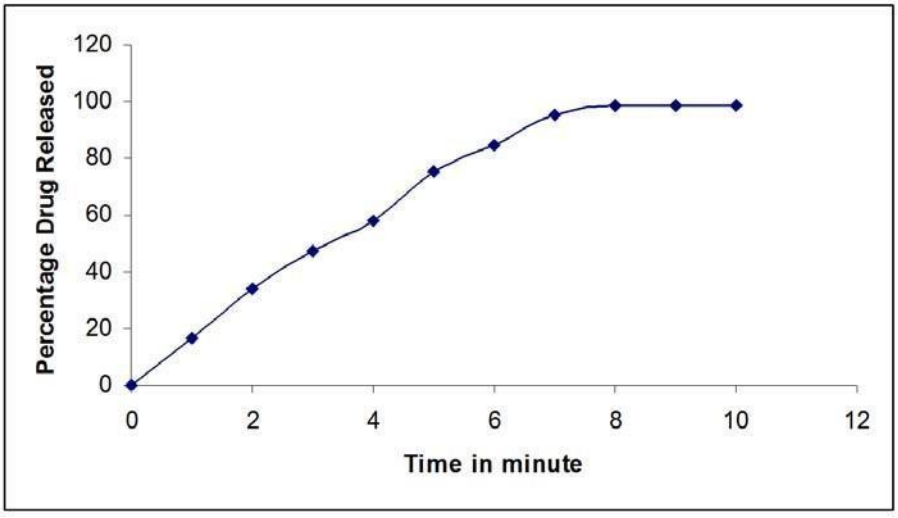


Figure –3: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_2

Table-19: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_3

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.91	3.276	16.56 ± 0.32
02	0.190	6.84	34.2 ± 0.12
03	0.262	9.432	47.16 ± 0.32
04	0.321	11..55	57.78 ± 0.44
05	0.420	15.12	75.60 ± 0.45
06	0.469	16.884	84.42 ± 0.43
07	0.531	19.11	95.58 ± 0.23
08	0.549	19.76	98.82 ± 0.72
09	0.549	19.76	98.82 ± 0.12
10	0.549	19.76	98.82 ± 0.10



Figure–4: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_3

Table-20: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_4

Time In Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.112	4.032	20.66 ± 0.22
02	0.231	8.316	41.58 ± 0.23
03	0.321	11.550	57.78 ± 0.55
04	0.400	14.40	72.0 ± 0.45
05	0.460	16.56	82.80 ± 0.88
06	0.482	17.35	86.76 ± 0.12
07	0.500	18.00	90.00 ± 0.14
08	0.520	18.72	93.60 ± 0.16
09	0.543	19.548	97.74 ± 0.12
10	0.551	19.828	99.74 ± 0.12

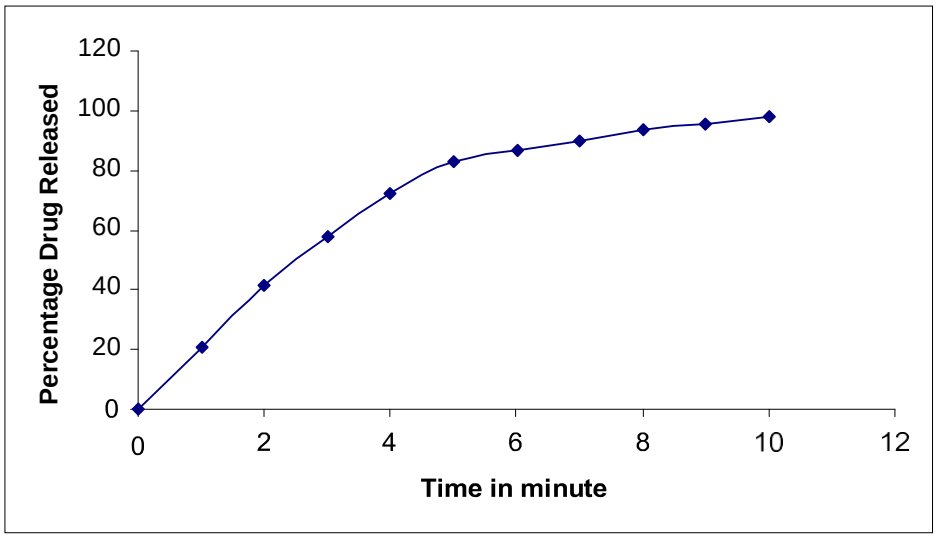


Figure –5: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_4

Table-21: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_5

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.121	4.356	21.78 ± 0.22
02	0.233	8.388	41.94 ± 0.23
03	0.333	11.988	59.94 ± 0.22
04	0.409	14.724	73.62 ± 0.36
05	0.462	16.632	83.16 ± 0.24
06	0.491	17.676	88.38 ± 0.14
07	0.511	18.396	91.98 ± 0.16
08	0.549	19.792	99.46 ± 0.01

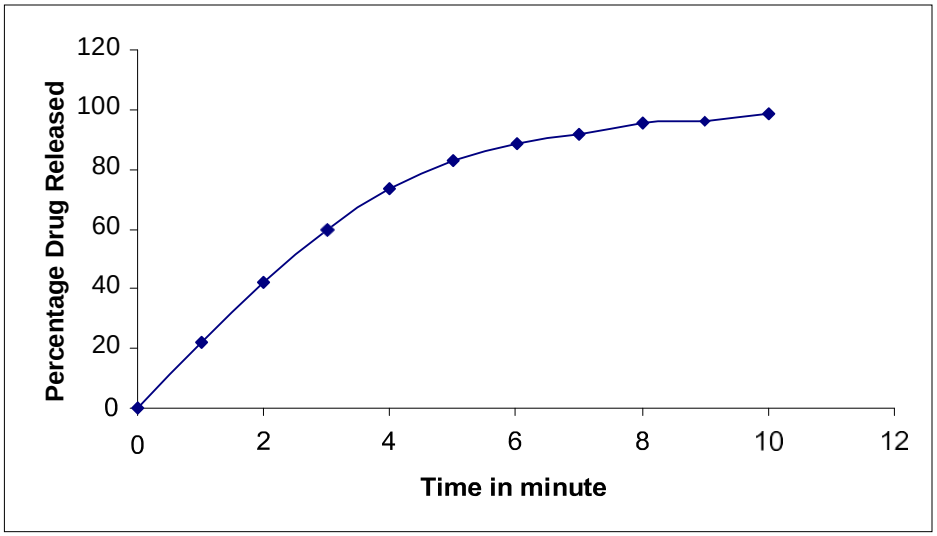


Figure –6: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_5

Table-22: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_6

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.144	5.184	25.92 ± 0.44
02	0.289	10.404	52.02 ± 0.46
03	0.415	14.904	74.52 ± 0.12
04	0.518	18.648	93.24 ± 0.11
05	0.555	19.98	99.9 ± 0.00

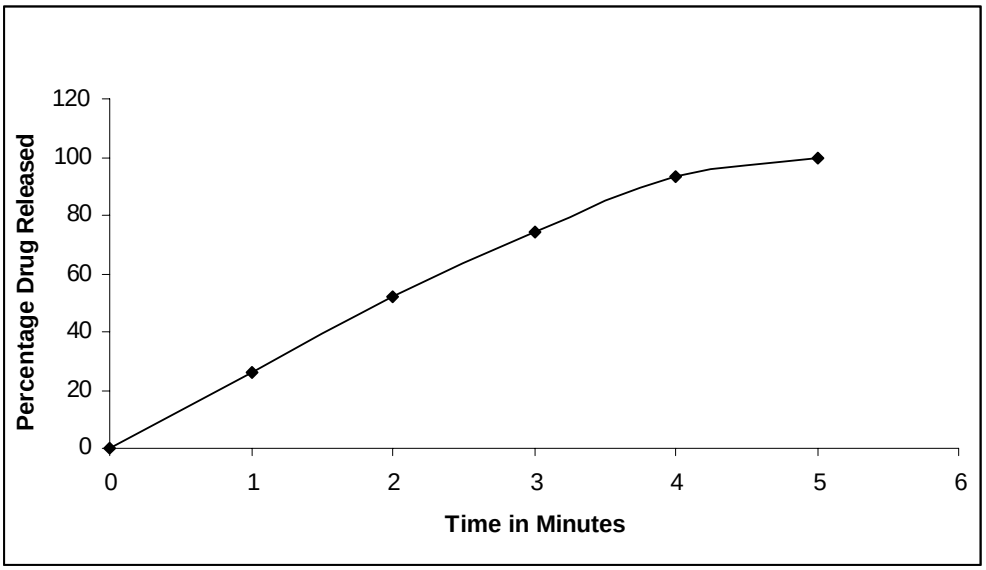


Figure –7: In-vitro Drug Release of Telmisartan Fast Dissolving Tablet TF_6

Table-23: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_7

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.77	2.772	13.86 ± 0.13
02	0.145	5.22	26.10 ± 0.43
03	0.243	8074	43.74 ± 0.65
04	0.310	11.16	55.80 ± 0.24
05	0.327	11.772	58.86 ± 0.64
06	0.355	12.78	63.90 ± 0.12
07	0.422	15.19	75.96 ± 0.24
08	0.494	17.78	88.92 ± 0.42
09	0.518	18.64	93.24 ± 0.31
10	0.523	18.82	94.14 ± 0.52

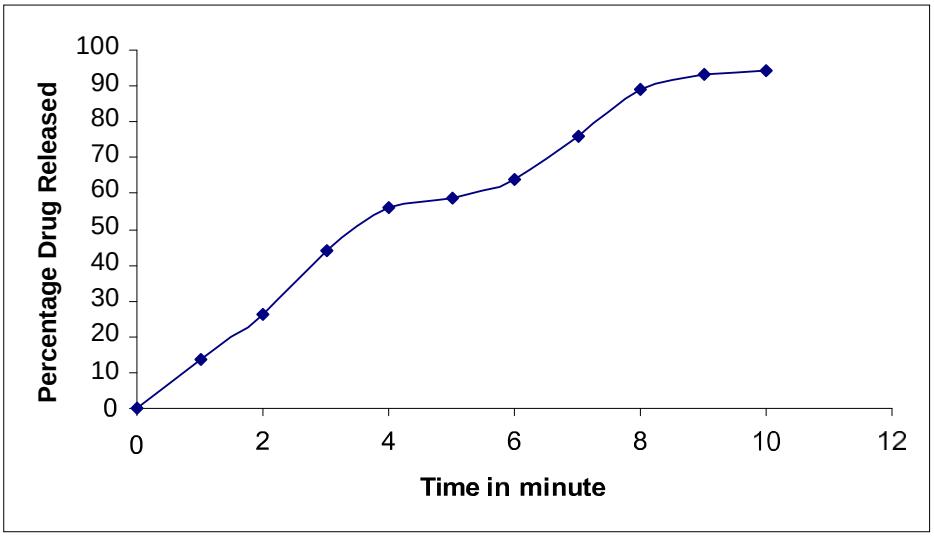


Figure –8: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_7

Table-24: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_8

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.065	2.34	11.88 ± 0.78
02	0.133	4.788	23.94 ± 0.64
03	0.193	6.948	34.74 ± 0.44
04	0.262	9.432	47.16 ± 0.22
05	0.314	11.304	56.52 ± 0.42
06	0.378	13.608	68.04 ± 0.12
07	0.441	15.876	79.38 ± 0.14
08	0.478	17.172	85.86 ± 0.16
09	0.506	18.216	91.08 ± 0.99
10	0.526	18.936	94.68 ± 0.11

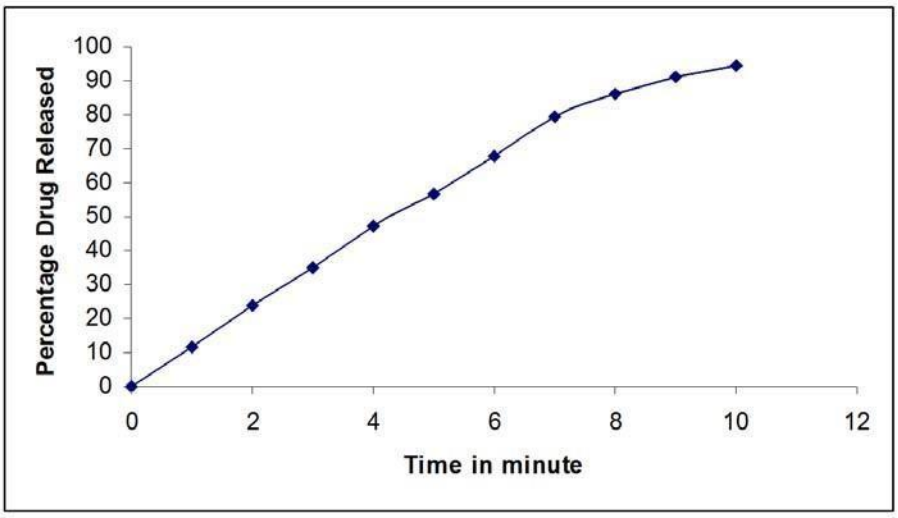


Figure –9: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_8

Table-25: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_9

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.072	2.592	12.96 ± 0.33
02	0.144	5.184	25.92 ± 0.36
03	0.232	8.352	41.76 ± 0.23
04	0.298	10.728	53.64 ± 0.12
05	0.378	13.608	68.04 ± 0.12
06	0.441	15.876	79.38 ± 0.24
07	0.499	17.964	89.82 ± 0.16
08	0.521	18.756	93.78 ± 0.18
09	0.524	18.864	94.32 ± 0.03
10	0.506	18.216	91.08 ± 0.03

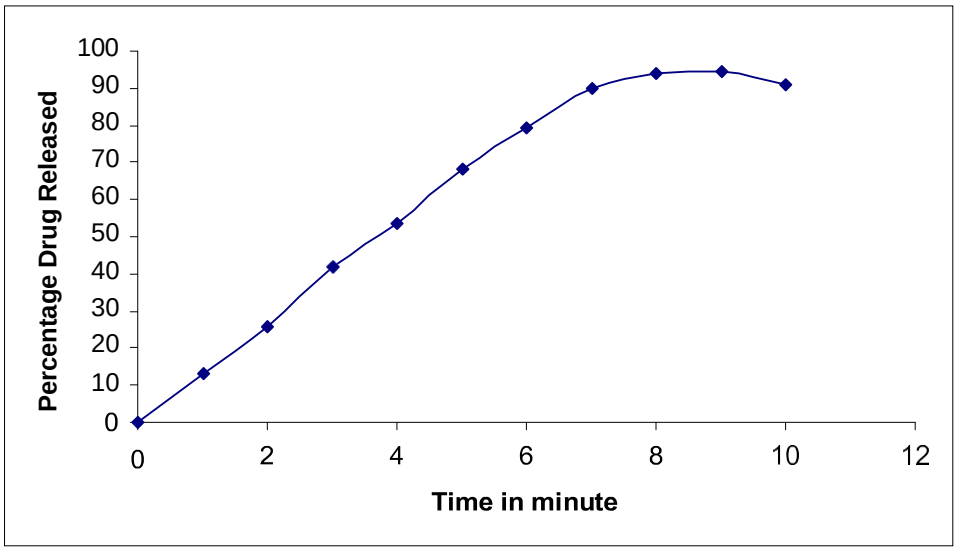


Figure –10: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_9

Table-26: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_{10}

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.076	2.736	13.68 ± 0.09
02	0.136	4.896	24.48 ± 0.08
03	0.177	60372	31.86 ± 0.05
04	0.244	8.784	43.92 ± 0.08
05	0.303	10.908	54.54 ± 0.12
06	0.365	13.14	65.70 ± 0.30
07	0.432	15055	77.76 ± 0.24
08	0.481	17.316	86.58 ± 0.12
09	0.509	18.324	91.62 ± 0.38
10	0.528	19.008	95.04 ± 0.11

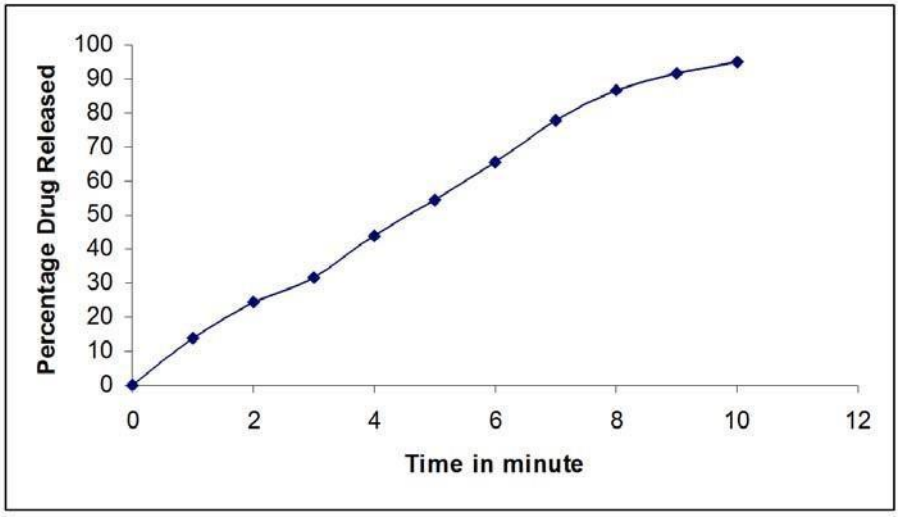


Figure –11:*In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_{10}

Table-27: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_{11}

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.079	2.844	14.22 ± 0.32
02	0.144	5.184	25.92 ± 0.23
03	0.204	7.344	36.72 ± 0.80
04	0.249	8.964	44.82 ± 0.05
05	0.322	11.592	57.96 ± 0.12
06	0.371	13.356	66.78 ± 0.07
07	0.436	15.696	78.48 ± 0.00
08	0.489	17.64	88.02 ± 0.00
09	0.515	18.54	92.70 ± 0.01
10	0.530	19.08	95.40 ± 0.02

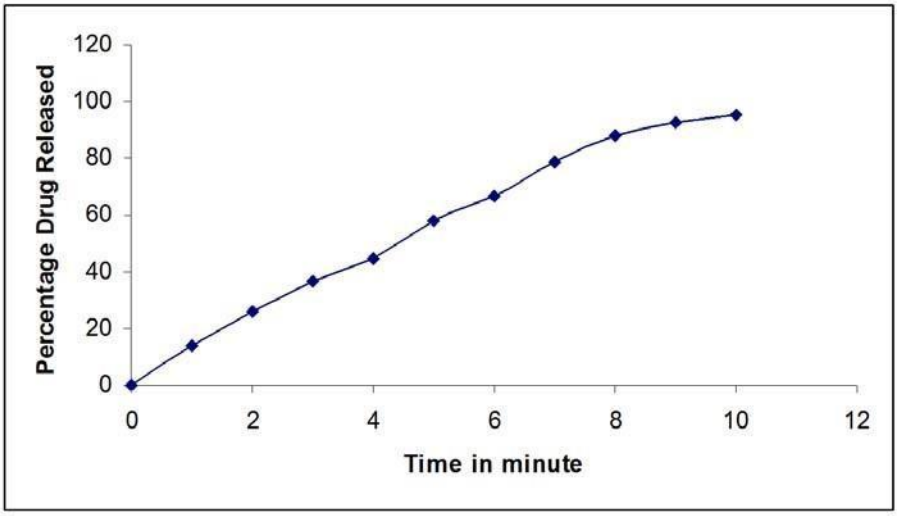


Figure –12: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_{11}

Table-28: *In-vitro* Drug Release of Telmisartan Fast dissolving Tablet F_{12}

Time in Minute	Absorbance	Concentration in mg	% Drug Release ±SD
01	0.117	4.212	21.06 ± 0.12
02	0.179	6.444	32.22 ± 0.22
03	0.244	8.784	43.92 ± 0.11
04	0.323	11.628	58.14 ± 0.09
05	0.363	13.068	65.34 ± 0.08
06	0.428	15.408	77.04 ± 0.06
07	0.481	17.316	86058 ± 0.14
08	0.506	18.216	91.08 ± 0.8
09	0.525	18.90	94.50 ± 0.08
10	0.535	19.26	96.30 ± 0.09

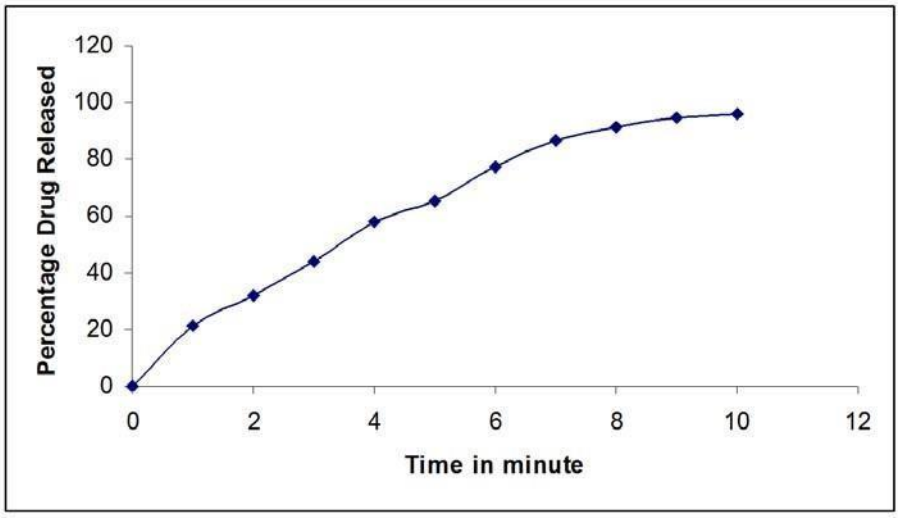


Figure –13: *In-vitro* Drug Release of Telmisartan Fast Dissolving Tablet F_{12}

Accelerated Stability Study

The formulation F_6 was selected for stability studies on the basis of their *in vitro* dispersion time, percent drug release. The stability studies were carried out at 40 ± 2°C / 75 ± 5%RH up to 30 days. At the end, tablets were analyzed for physical appearance, percentage drug content, *in vitro* dispersion time. The results obtained were shown in Tables 29. *In vitro* drug release studies were conducted and the results are shown in Table 30.

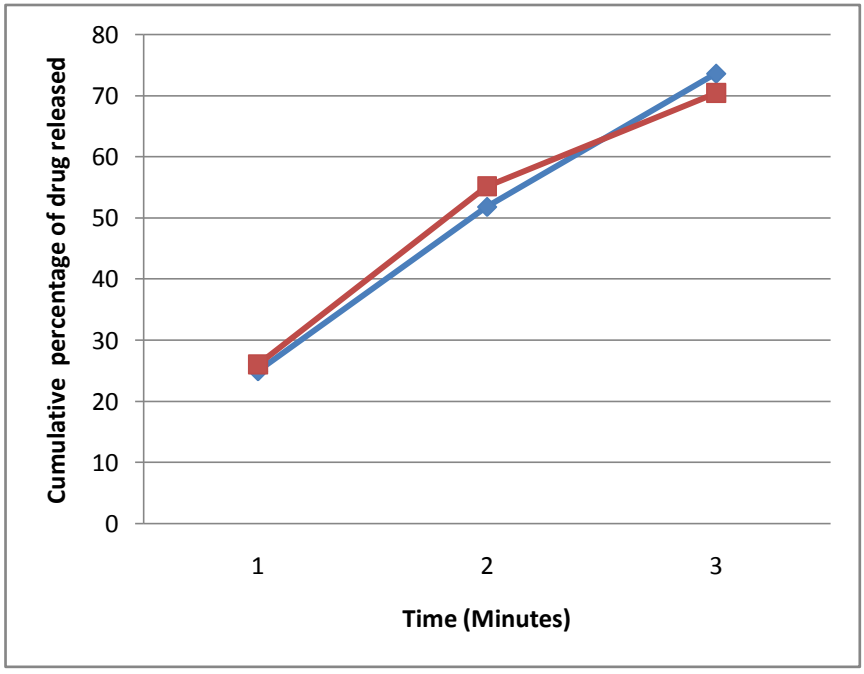
Table 29: Evaluation for Percentage Drug Content, *In vitro* Dispersion time after Stability Studies of Drug Release of Telmisartan Fast dissolving Tablet F_6

Time	% Drug Content*	*In vitro* Dispersion Time* (seconds)
Tablets of 15th day	98.6 ± 0.134	15.0±0.53
Tablets of one month	98.9 ± 0.120	15.0±0.61

*Each value is an average of three determinations.

Table 30: Evaluation for *In vitro* Drug Release of Telmisartan Fast dissolving Tablet F_6 after Stability Studies

Time (Minutes)	Cumulative Percentage of drug released* AM ± SD	
	Tablets of 15 days	Tablets of 30 days
01	24.92 ± 0.32	26.02 ± 0.24
02	51.82 ± 0.51	55.12 ± 0.35
03	73.62 ± 0.13	70.42 ± 0.25
04	92.64 ± 0.15	94.60 ± 0.27
05	98.23 ± 0.20	99.2 ± 0.13



CHAPTER-6

DISCUSSION

Telmisartan is a new angiotensin II receptor antagonist and used for the treatment of essential Hypertension only. Croscarmellose sodium, Crospovidone and Sodium starch glycolate alone and in combination were used in different concentration to prepare Fast dissolving tablets.

All the formulations prepared were evaluated for pre compression parameters like Bulk density, True density, Angle of Repose and Percentage porosity and are given in table. The angle of repose for the all formulation was found to be less than 30° indicating free flowing granules. All the Fast dissolving tablets were found to be elegant without any chipping, capping and sticking.

Fast dissolving tablets so prepared were evaluated for post-compression parameters like Hardness, Friability, Drug content uniformity, weight variation, *In-Vitro* Dispersion, Drug intactness and *In-Vitro* Drug release studies, etc. Hardness of the three tablets of each batch were checked by using Monsanto hardness tester and the results were shown in the table 9. The results showed that the hardness of the tablet is in the 2.8-4.0.Kg/cm^2. Tablets of each batch were evaluated for percentage friability and the results were given in table 10. The results suggests that the friability will withstand the rigors which occurred during packing, transportation and shipping etc. Because of their low percentage friability

is less than one.

Drug content uniformity study was carried out on the tablets of every batch and the results were shown in the Table 15. The results were showed that there was uniform distribution of the drug throughout the batch.

Drug Polymer Interaction Study

The probability/possibility of drug polymer interaction was studied by Infrared Spectroscopy using KBr pellet method. The Infrared Spectra of Pure drug Telmisartan shows a characterstic peak at different frequencies which are as follows.

- Peak at 1667.24cm^{-1} is due to C=O stretching.
- Peak at 1422 cm^{-1} is due to C=N stretching.
- Peak2957.79cm^{-1} is due to C-H stretching.
- Peak at 1582.76 cm^{-1} is due to C=C stretching.

The spectra of the formulation scanned showed following peaks.

- Peak at 1661.73 cm^{-1} is due to C=O stretching.
- Peak at 1438.25 cm^{-1} is due to C=N stretching.
- Peak at 2976.52 cm^{-1} is due to C-H stretching.

When the peaks of the formulation spectra compared with the peak of Telmisartan Pure Drug Spectra, the characteristic peak of Pure Drug were retained indicating the intactness of the drug in the formulation prepared.

Tablets of every batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet were shown in the table 12 to 15.

The average weight of the tablet is approximately 150mg. So the permissible limit is ± 7.5%. The results the test showed that, the tablets were weighing in the range of within the limit.

Three tablets of each batch were evaluated for *In-Vitro* Dispersion time test. The results showed that the tablets prepared were disintegrating and dispersing in the time range of 15 to 110 seconds. The tablets of the batch F_6 prepared using 12mg of Crospovidone showed Faster disintegration is within 15 seconds.

Finally, the tablets were evaluated for *In-Vitro* drug release studies for a period of 10 minutes and the results were shown in the table 17-28. In all the cases a minimum of 91% of the drug was released within 10 minutes, among the various formulation prepared the batch/tablets of the composition drug Telmisartan and Crospovidone (12mg) F_6 released 99% of the drug within 5minute.

The improved drug release was mainly due to the increased *In-Vitro* dispersion which is due due to the addition /inclusion of super disintegrant.

CHAPTER-7
CONCLUSION

The concepts of formulating Fast Dissolving Tablets of Telmisartan offers a suitable an practical approach in serving desired objectives of faster disintegration and dissolution characteristics.

In the present work, Fast dissolving tablets of Telmisartan were prepared by Direct Compression Technique using Crospovidone, Croscarmellose sodium Sodium starch glycolate as Super disintegrants. All the Fast dissolving tablets of Telmisartan prepared were subjected to Drug content Uniformity, weight vaiation, Hardness, Thickness, Friability, Disintegration and Dissolution studies.

- Pre Compression parameters like Bulk density, True density, Porosity Angle of repose. The result of angle of repose indicates free flowing characteristics of granules.
- Hardness of the tablet of every batch was in the range of 2.8 to 4.0Kg/cm^2
- Friability of all the tablets were less than 1%.
- Weight variation test results of every batch showed that the weight of each tablet of the batch tested was within the range ±7.5%.
- All the tablets formulated using Croscarmellose sodium, Crospovidone and Sodium starch glycolate disintegrated within 3minutes fulfilling the official limits of the Fast dissolving tablets.

- IR Spectral analysis suggests that the characteristic peaks of the Pure drug Telmisartan exist in the Spectra of Formulation prepared indicting the intactness of the drug is in intimate contact with the additives. It has not undergone any chemical interaction with the excipients used in the development of Telmisartan Fast dissolving tablets.
- Drug content uniformity study results showed that the drug Telmisartan was uniformly distributed throughout the formulation of every batch.
- Finally, we can conclude that, among various formulations prepared, the Fast dissolving tablets prepared, using Crospovidone (12mg) F_6, disintegrated rapidly and gave highest dissolution of Telmisartan within a short period of time.

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