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FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLET OF TELMISARTAN USING NATURAL SUPERDISINTEGRANTS

Preeti Pokhariya *, G Ganarajan and Preeti Kothiyal

Department of Pharmaceutics, Shri Guru Ram Rai Institute of Technology & Science, Dehradun248001, Uttrakhand, India.

Abstract:

The aim of this research is to prepare and evaluate the Mouth dissolving tablet of Telmisartan introducing the use of newly arising natural excipient as a superdisintegrants .The applied Naturat superdisintegrants(chitosan and gellan gum) has versatile property in the Mouth disintegrating tablets using Telmisartan as model drug. Mouth disintegrating tablets are the useful formulations for pediatrics, geriatric, and physically and mentally disabeled patients resulting in improved patient compliance. Telmisartan is an antihypertensive drug which belongs to the class of Angiotensin Receptor II (Type- ATI) Antagonist. It is a poorly soluble drug (BCS class-II) and its absorption is dissolution rate limited. The oral bioavailability of Telmisartan is 45%. Hence, in this research an attempt was made to develop Mouth dissolving tablets of Telmisartan formulated with natural disintegrating agent and superdisintegrants(synthetic) combination with superior dissolution properties. The aim is to formulate various batches of mouth dissolving tablets of Telmisartan by using chitosan, gellan gum, microcrystalline cellulose, crospovidone and sodium starch glycolate with different concentrations by direct compression. The tablets were evaluated for the precompression parameters such as bulk density, compressibility, angle of repose etc and post compression parameters like hardness, weight variation, friability, disintegration time and in-vitro dissolution profiles . Among all the 5 formulation F4 is the best formulation because it show the high percentage of drug release in which was found to be 96.13% in 120 min and disintegration time was found to be 20 sec, as well as F4 formulation show the best results in every evaluation aspects.

Key words: *Telmisartan, chitosan, gellan gum, cross povidone, micro crystalline cellulose, sodium starch glycolate, Mouth dissolving tablets.*

Corresponding author:

Preeti Pokhariya ,

Department of Pharmaceutics,
Shri Guru Ram Rai Institute of Technology & Science,
Dehradun248001, Uttrakhand, India.

QR code

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INTRODUCTION:

Oral drug delivery has the platinum value in the pharmaceutical era as well as in the pharmaceutical production where it is regarded as the most simplest, beneficial and economical procedure of drug delivery. Oral drug delivery is having the maximum patient compliance with its safest site of drug delivery. Mouth dissolving tablets which can also called as fast Dissolving Tablets are usually beneficial for geriatric, pediatric and bedridden patients and for those active patients with busy schedule and traveling and when there is lack of water. Mouth dissolving Tablets are disintegrating or dissolve rapidly in the saliva without chewing or the need for water. Some tablets are formulated to dissolve in saliva within a minute without chewing and the requirement of water those are called as Mouth Dissolving Tablets. This tablet format is allow administering in the absence of water or fluid intake and also designed to dissolve or disintegrate readily in the saliva or oral cavity within a minute which may leave an easy to swallow residue.

Usually Applicable Areas or Fields of MDTs (Mouth Dissolving Tablets) includes-

1. Elderly patients having difficulties in taking other oral dosage forms like tablets, and capsules etc. This can be due to many reasons including hand tremors and dysphagia.
2. Now day's Young individuals commonly have problem in swallowing because of their underdeveloped muscular and nervous systems.
3. Other patients who may face problems in other oral dosage forms including the mentally ill, physically disabled, uncooperative patients, and those having decrease liquid-intake plans.
4. Other uses which extent the cause of production are – (i) unavailability or lack of water, (ii) difficulty in swallowing other solid dosage forms, (iii) nausea, (iv) motion sickness, (v)sudden allergic attack or coughing.

Recent advances in Novel Drug Delivery Systems (NDDS) are designed dosage forms, adequate and easy to be manufactured and administered and free of side effects. To achieve better patient compliance it offers immediate release and enhanced bioavailability,. Though oral drug delivery systems, preferably, tablets are the most widely accepted dosage forms, for being compact, offering uniform dose and painless delivery. Yet, dysphagia is the most common disadvantage of conventional tablets. This is seen to afflict nearly 35% of the general population and associated with a number of conditions, like Parkinsonism, mental disability, motion sickness, unconsciousness, unavailability of water etc. To overcome such problems, certain innovative

drug delivery systems, like, Mouth Dissolving Tablets‟ (MDT) have been developed. These are novel dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such MDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients. Development of a Mouth dissolving tablet is the most convenient and safe mode of drug administration with great patient compliance. Mouth dissolving tablet (MDTs) cover the limitations of other dosage form specially dysphagia (difficulty in swallowing) in geriatric, pediatric and disabled patients. Apart from the conventional methods of fabrication, this method used for the innovation and development of technologies like freeze drying, fast dissolving films, sublimation, tablet molding, direct compression, and cotton candy process, spray drying, along with their advantages and disadvantages.

Mouth Dissolving Tablet

Mouth dissolving Tablets (MDTs) are designed new generation of formulations which give benefits of both liquid and conventional tablet formulations, and added advantages over both the traditional dosage forms. MDTs show offer much more accurate dosing than the primary alternative, oral liquids. This format of drug delivery system is especially designed for dysphasic, pediatric and geriatric patients with swallowing problem. They do not require water for administration, thus are very beneficial for travellers and for bed ridden patients. They simply disappear by dissolving in saliva when placed in the mouth, so cannot be hidden in mouth by psychotic or uncooperative patients. These products not only increase the patient's compliance but also fetch the new revenue of production for manufacturer due to its product line extension.

In the recent past survey, new developed methods have been discovered for the manufacturing of mouth dissolving tablets (MDTs) which can have decreased disintegration time, amaze mouth feel and good taste masking. The technologies utilized for fabrication of MDTs include sthe innovation and development of technologies like freeze drying, fast dissolving films, sublimation, tablet molding, direct compression, cotton candy process, spray drying, along with their advantages and disadvantages. These methods are depend upon the basic concept of booming porosity or use of superdisintegrant and excipient which are soluble in the water. The formulations made by these methods might be deviating from each other depend upon the fact like drug and dosage form, mechanical potency of final product, formulation code , stability, mouth feel or after residue, taste, bioavailability, dissolution rate of the preparation and absorption rate.

Although, numerous technologies had been found and developed for the fabrication of these uniques dosage forms in last 3 decades, but so far, no

standardized technique has been developed or mentioned in pharmacopoeias for their evaluation except in European Pharmacopoeia (EP), which states Mouth Dissolving Tablets as "uncoated tablets intended to be placed in the mouth where they may disperse or disappear rapidly before being swallowed". EP also specifies that the Mouth Dissolving Tablets should disintegrate within 30sec -3 minutes when subjected to common disintegration test used for tablets and capsules. This article presents a detailed review regarding the evaluation measures available in literature to characterize the MDTs, which have been formulated keeping in view the special features of these novel drug delivery systems.

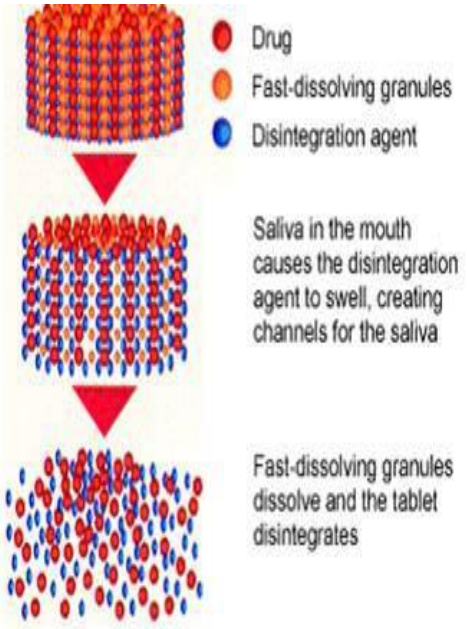


Fig 1: Basic mechanism of Mouth dissolving tablet

Ideal properties of mouth dissolving tablets

- It can dissolve or disintegrate in mouth in few second.
- It does not require water to swallow.
- It is compatible with excipients.
- It is portable and its transportion is easy.
- It allows high drug loading.
- It shows less sensitivity to environment condition.
- It leave a pleasant mouth feel.

Advantage of Mouth Dissolving Tablet

1. Skillful+ Dosing:

It provide bliss leisure distinct dosing and easy portability and manufacturing. It also includes the good physical and chemical stability. Being a unit solid dosage form it also used as an ideal substitute for pediatric and geriatric patients.

2. Enlarged bioavailability:

Drug bioavailability is increased due to absorption from oral cavity.

3. Quick action:

It shows rapid onset of therapeutic action when tablet gets disintegrated quickly along with fast dissolution and absorption in mouth.

4. Enhanced palatability:

Amaze mouth feel, with taste masking method that is applied to overcome the bitter taste of drug especially for pediatric patients.

5. Patient compliance:

As there is no need of water in swallowing of the Mouth Dissolving Tablets hence, it is also useful for patients that are traveling and do not have existence of water immediately.

6. Comfort of administration:

It is easy to administer, so convenient for geriatric, pediatric and disabled patients.

7. Affluence free:

There is no risk of suffocation or intruptment in airways due to its physical idleness when swallowed, thus exhibit developed safety and comforts.

Limitations of Mouth dissolving tablets

1. Handling:

The tablets mostly have insufficient mechanical strength so, careful handling is required.

2. Unpleasant taste:

The Mouth Dissolving Tablets may leave grittiness in mouth or may leave unpleasant taste if not formulated properly.

Disintegrating Agents

Disintegrating agents are very necessary elements of compressed Mouth dissolving Tablets because primarily they are the reasons for the fast disintegration in the oral cavity.In a Mouth dissolving Tablet System the elements which possess disintegrating property can be either a super disintegrant , natural super disintegrant or an effervescent system. Combination of different disintegrating agent are mostly preferred for good disintegration result, where the effervescent systems like combination of citric acid and sodium bicarbonate are usually possess broadly effective disintegrating Performa. When the effervescent agents come in touch with moisture the elimination of carbon dioxide helps to collapse the tablet matrix.The manufacturer should decrease amount of effervescent ingredients used in the formulation, if there any unpleasantness or unamze feeling arises in mouth owing to fizzing.

Super disintegrants:

In just out years, a number of newer agents have been discovered and manufactured known as super disintegrants. These disintegrants are having super quality of breaking the compact mass when the tablet is placed in a fluid environment. The

superdisintegrants possess the highbotel insertion and distribution in the tablet matrix. These superdisintegrants are very effective at less concentration with grater disintregating effiency and mechanical energy. When superdisintegrants come in touch with moisture, it boost up the size and produce a distracting change in the tablet and the volume of foam. Virtuous superdisintrigrents possess high compressibility, affinity with others and inertness to the mechanical potency of high dose formulations. In the most Mouth dissolving Tablets croscarmalose sodium,cross povidone and sodium starch glyconate are used as super disintegrants usually which are beneficial in a very less concentration of 2-5%. Increase amount of super disintegrants is not necessary for the faster disintegration. The Super-disintegrants are positively hygroscopic elements that allow the wicking water to enter from the saliva into the tablets. The Super disintegrants are easy to determine the effect of water so they are preferred over the effervescent system.

Natural Super disintegrants:

The natural superdisintegrants include number of natural elements like mucilages, gums, and other substances which are derived from natural resources . They are very beneficial at low concentrations which are having high disintegrating property and mechanical potency. Mucilage, gums and polymers of natural origin are preferred over synthetic or semi synthetic substances because of their abundantly availability, cheaper rates, nonirritating and nontoxic property. Agar, Karaya Gum and Starch already been used in the formulation of Mouth Dissolving Tablets. Gums and mucilage's arised from natural resources have been made its own name in the pharmaceutical industry. These are preferred as thickening agent, emulsifying agents, stabilizing agents, granulator, gelling agent, binding agent, suspending agent, in the formation of film, super disintegrating agents. Importance of these resources of natural origin is enhancing day by day as the new sources are being developed and discovered. Natural super disintegrates are being preferred because they are very cheap and easily available and non irritant in nature rather than synthetic and semi-synthetic disintegrants. They are having soothing action and also possess eco-friendly nature. Natural super disintegrants are useful for chemical modifications, capabilily degradable and having affinity with others due to their natural sources.

1. Chitin and chitosan

It is a polysaccharide of natural origin. Which is arised from crab or from shrimp shells? Chitosan possesses free amino group as compared to chitin which possess amino group linked covelalently to acetyl group. Chitosan is developed by the deacetylation of chitin, which is the exoskeleton's structural element of crustaceans or cell walls of fungi. Bruscato et al 1978 researched that when chitin or chitisan was used in the commonly standard tablets, the tablets get disintegrated or break within 5 -10 minutes. The wetting time of the drug in the oral cavity can be analysed by surface free energy. Chitosan has been known for the best versatile nature in the pharmaceutical excipients.

2. Gellan gum

Gellan gum is a deacetylated exocellular polysaccharide which is produced by fermentation of a pure culture of a bacterium *Pseudomonas elodea*, having a tetrasaccharide repeating unit of one α-L-rhamnose, one β-D-glucuronic acid and two β-D-glucose residues.Gellan gum is anionic and water soluble in nature. Antony et al 1997 discovered that the Gellan gum is having disintegrant property and its efficiency was compared with other common disintegrants. It is found that the disintegration property of gellan gum might be due to the directly rapid swelling property , when it come in touch with moisture and owe to its great water solublility. The overall biffussion or disintegration of Mouth Dissolving Tablet has proved Gellan Gum as super disintegrant.

Mechanism of fast dissolving Tablet

1. Wicking (porosity capillary action):

Replacement of air absorbed by the liquid media into the tablet resulted as lowering the potency of intra-molecular bond and breaking down of tablet into small particles.

2. Swelling:

The broadly known mechanism of tablet disintegration is swelling. Due to absence of which having high swelling force tablets show poor disintegration. Where there is enough or accurate force tablet shoe low porosity. If the packing fraction is very high, fluid cannot lead to penetrate in the tablet and disintegration again get lower down.

3. Due to particle repulsion forces:

Guyot-Hermann clarifies the particle repulsion concept by giving the example of mechanism of swelling of tablet made with non-swellable disintegrants. Water is required for the mechanism of electric repulsive forces between particles.

4. Due to dislocation

Sometimes disintegrated particles become deformed during the compression of tablet. These deformed particles come into their general shape

when they come in touch with liquid media or water.

Techniques for Preparing Mouth dissolving Tablets

Current techniques been reported to be used commonly for the formulation of Mouth dissolving tablets.

Direct Compression*:*

It is the most common and most convenient method of manufacturing. It is the most simplest and economical method. This technique is used in the formulation of Mouth Dissolving Tablet because of the application of different effaceable excipients like Super disintegrants and Sugar based excipients.

Freeze-Drying or lyophilization:

The first step of this method is zydis delivery system invented by R.P. Scherer. This system is compossed of gelatin, sugars, and other excipients poured into depression of pack of blister. Water is magnifying away in lyophilization which retain an increase in porosity and relatively soft solid. The retained wafers diffuse on the tongue quickly in about 3-5 seconds. These freeze dried wafers shows some limitations as solubility of drug and sensitivity to water . They require special packaging due to weakness in strength.

Tablet Molding:

This process possess its two types.-

(a)Solvent method:- this technique include moisten up the powder blend with hydro alcoholic solvent and then it is firmning of small pressure in molded plates to make a wetted mass. The solvent then aparted by air drying.

(b)Heat method:- This technique include formation of a suspension that carry a drug ,agar and sugar and then pouring the suspension into the blister walls and solidifying agar into the jelly at the room temperature and then it is dried at 30^0C under vacuum. The mechanical strength can be boost up by the addition of binding agents.

Spray drying:

It is the process depends upon a support matrix, prepared by spray drying, which is an aqueous composition and other substances to form an extremely porous and fine powder which are then mixed and compressed into tablets. Then the other excipients are involved. Tablet compressed after the spray dried powder disintegrated within 20 seconds, when come in contact with a liquid media.

Sublimation

Different ingredients are used in the manufacturing of the formulation to make a porous medium. This tablet includes the compression of highly volatile substances like Urea, Ammonium bicarbonate, Camphor, Ammonium carbonate, Benzoicacid, Naphthalene, Urethane and Phthalicanhydride and with other excipients .These highly volatile substances is then eliminated by sublimation leaving after a highly porous matrix. Tablet made by this procedure can disintegrate with in10-60 sec.

Mass-extrusion:

This method includes lightening of the active solvent mixture of hydrophilic polyethylene glycol and methanol and successive banishment of lighter mass of extruder or syringe to achieve a barrel of the compound into equal parts with the use of fierce knife to make tablet. The drained barrel can be used for housing the granules for masking the bitter taste.

Cotton Candy Process:

The FLASHDOSE is a MDDDS manufactured using Shearform technology to eliminate the bitter taste of the medicament. The Shearform technology is employed in the preparation of a matrix known as ‘floss’, made from a combination of excipients, either alone or with drugs.

The manufacturing process can be alienated into four steps as detailed below.

- Floss Blend
- Floss Processing
- Floss Chopping and Conditioning
- Blending and Compression

Nanonization

Nanomelt is a recently developed technology involves decrease in the particle size of drug to nanosize by milling. The nano size crystals of the drug were stabilized beside agglomeration by surface adsorption on chosen stabilizers, which are then incorporated into MDTs. This technique is especially beneficial for poorly water soluble drugs.

METHODOLOGY:

UV-Visible Spectroscopy:

In order to confirm max of Telmisartan, 100µg/ml solution was analyzed at spectrum measurement by double beam spectrophotometer against methanol as a blank in the range of 200-400nm.The UV spectrum is shown in Telmisartan showed maximum absorption at 242 nm.

Preparation of calibrationcurve of Telmisartan

100mg of Telmisartan is accurately weighed and taken in a volumetric flask (100ml). Then made the volume upto 100ml with pH 6.8 phosphate buffer.Different concentration like2, 4, 6, 8,10, 12 and 14mg/ml of these solutions were checked for their absorbance using UV – Visible

spectrophotometer at λmax 242 nm using distilled water as blank and a standard graph was plotted.

Identification of drug through FTIR
Identification of the sample drug is done through FTIR.FTIR spectra of standard drug is compare with the FTIR spectra of sample drug. FTIR of standard Telmisartan is shown in Figure and FTIR spectrum of sample Telmisartan in Figure

Compatibility study of drug with polymer:
KBr Pellet Method
This method shows that the property of alkali halide converted to plastic when subjected to a particular pressure and result in the form of sheet that show transparent behaviour in IR region. Potassium bromide (KBr) is the most common alkali halide above all which are used in the pellet cesium iodide (Csi) is also sometime used to measure the IR spectrum in 400-250nm in low wave no. region. The 13mm diameter pellet prepared by this method is describe below.
200-250mg fine alkali halide mixed with approximately 0.1-1% of drug sample after that pellet takes from a pellet forming die by pulverized.
The transparent pellet is formed by exerting a force which is approximately 7-8 tones when applied. Beneath a vacuum several mm/hg for numerous minutes. Designing process is accomplished to remove air and moisture from powder KBr. Easily broken pellets are the result of the insufficient vacuum supplied with further result in scattering of light. When the measurement are performed the background is measured with an empty pellet holder introduce to the sample channel.

Nujol Method
This is the method for measuring powder sample with sample pretreatment. The sample is distributed in a liquid of approximately equal refractive index, and the infrared spectrum is measured. Generally, the powder is dispersed in non-volatile liquid paraffin (Nujol) that has low absorption in infrared region. To prepare a sample, pulverize approximately 10 mg sample powder in mortar and pastel. Add one or two drops of liquid paraffin. Apply the paste to a liquid cell (KBr crystal plate etc) and sandwich it under another cell plate. The spectra obtained for Telmisartan, polymers and physical mixtures of Telmisartan with polymers were compared. FTIR spectrum are shown in Figure

Preformulation Studies:
Organoleptic characteristics: The organoleptic and physical characteristics like description, taste, odour and colour werestudied carefully and the results were obtained.

Melting Point Determination: Melting point of drug was determined by capillary method. The small quantity of drug is take in a a capillary tube sealed at one end and was placed in melting point apparatus and temperature range at which the drug melts was noted.

Solubility: The solubility of drug was checked with water, 0.1N HCL, Phosphate buffer pH 6.8, Phosphate buffer pH 7.4 The parameter used for solubility is given in Table 1.

Table 1: Parameters of solubility

Descriptive Term	Pats of solvents required for 1 part of solute
Practically insoluble	10000 and more
Very slightly soluble	From 1000 to 10000
Slightly soluble	From 100 to 1000
Sparingly soluble	From 30 to 100
Soluble	From 10 to 30
Freely soluble	From 1 to 10
Very soluble	Less than 1

Partition Coefficient:
The partition coefficient of the drugs was determined by taking equal volumes of n-octanol and aqueous phases in a separating funnel .A drug solution was prepared and drug 1ml of the solution was added to octanol:water(20:20) was taken in a separating funnel and shaken for 10 minutes and allowed to stand for 1h and is continued for 24h., then aqueous phase and octanal phase was separated,centrifuged for 10 min at 2000rpm. The aqueous phase and octanol phase were assayed before and after partitioning using uv-spectrophotometer at their respective max to get partition coefficient. The partitioncoefficient of Dicyclomine Hydrocloride was calculated from the ratio between the concentration of Di-cyclomine Hydrocloride in organic and aqueous phase using following equation.
Po/w = (C oil /C aqueous) equilibrium

Preparation of mouth dissolving Tablet of Telmisartan:
Telmisartan (20 mg) was prepared using different ratio of superdisintegrants by direct compression. The superdisintegrants such as sodium starch glycolate, microcrystalline cellulose, crospovidone, gillan gum and chitosan were used in different amounts. All the ingredients were passed through sieve number 60 and were subjected for drying to remove the moisture content at 40-45° C. Weighed amount of drug and excipients were mixed for 15 min manually in mortar pastle. The mixed portion of drug and the excipients was subjected to compressed on single punching machine.

Table 2: formula for mouth dissolving tablet with different concentration of superdisintigrants:

Ingredients	Formulation code				
	F1	F2	F3	F4	F5
Telmisartan	20	20	20	20	20
Crospovidone (mg)	10	10	10	8	8
Saccharin Sodium (mg)	5	5	5	5	5
Sodium Starch Glycolate (mg)	10	7	6	5	4
Menthol (mg)	3	3	3	3	3
Talc (mg)	2	2	2	2	2
Gellan Gum(mg)	10	8	8	6	6
Micro Crystalline Cellulose (mg)	70	75	80	85	90
Chitosan(mg)	15	15	11	11	7
SLS (mg)	2	2	2	2	2
Magnesium stearate(mg)	3	3	3	3	3

Evaluation parameter of mouth dissolving tablets:

Pre-compression evaluation parameter of powder mixture:

Angle of repose (θ):

There is an empirical relationship between angle of repose and the ability of the powder to flow. It was determined using fixed funnel method. The funnel height was maintained in such a way so that the tip of the funnel should just come in contact with the apex of the pile which is the combination of powders Precompression mixture. The mixture combination of powders was allowed to flow freely by such way that drops in the funnel on top of the surface. The diameter units and radius of the cone or the pile of powder combination mixture and calculation of angle of repose is done by the equation given below.

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

Where h = height of the tip of powder from the base

r = radius of the cone

Bulk Density:

Apparent bulk density was determined by pouring pre-sieved drug excipient blend into a graduated cylinder and measuring the volume and weight "as it is". It is expressed in g/cm^3.

Tapped Density:

It was determined by placing a graduated cylinder, containing a known mass of drug excipient blend, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to constant volume. It is expressed in g/ml.

Cars Index (I):

It is expressed in percentage and is expressed by

$$I = (Dt - Db)/ Dt .$$

Where, Dt is the tapped density of the powder Db is the bulk density of the powder.

Hausners Ratio:

It is expressed in percentage and is expressed by

$$H = Dt/ Db \times 100.$$

Where, Dt is the tapped density of the powder Db is the bulk density of the powder.

Post compression evaluation parameter of tablets:

Tablet Hardness: - Hardness of the tablets was determined by using a Monsantohardness tester. Three tablets from each batch were selected randomly and tested. The percentage deviation was calculated. (Lachman *et al*., 1987)

Uniformity of Weight: - The weight variation test was done by taking twenty tabletsweighed individually and collectively and the average weight was determined. The percentage deviation was calculated and checked for weight variation. (Lachman *et al*., 1987)

Friability Test: - The friability of the tablets was measured according to European Pharmacopoeia (1997) method. i.e. using the Roche friability apparatus for 4 min with the drum rotating at a speed of 25 rpm. Twenty tablets were weighed before and after the measurement and the weight loss was calculated (n = 1). The percentage deviation was calculated and checked for friability testing. Percentage friability was calculated for each batch by using following formula-

Percentage friability = (initial weight-finalweight/initial weight) × 100 (Lachman*et al*., 1987)

Disintegration Test: In the disintegration test for Mouth Dissolving Tablets, the disintegration apparatus is used without closing the mouth of plastic disks, and the acceptable time limit is 2 min for tablet disintegration. So all of our formulations meet the requirement for disintegration. The rapid and desired disintegration of tablets is due to the presence and good proportion of MCC, SSG, CP, Gellan Gum and Chitosan and can be explained with following reasons. MCC has good wicking and absorbing capacities. Tablets of MCC disintegrated rapidly due to the rapid passage of water into the tablets resulting in the instantaneous rupture of the hydrogen bonds.

Wetting time: A circular tissue paper of 10 cm diameter was placed in threepetridish with a 10cm diameter, one in each after folding. 10 ml of simulated salivary solution (phosphate buffer pH 6.8) was poured into the tissue paper placed in the petridish. A tablet was placed carefully on the tissue paper surface. The time needed for the solution to arrive the upper surface of the tablet was recorded as the wetting time. The percentage deviation was calculated and results were tabulated.

Tablet Thickness: Five tablets were taken and their thickness was measured usingVarnier calliper. The thickness was measured by placing tablet between two arms of the Varnier calipers. The percentage deviation was calculated and results were tabulated. (Lachman *et al*., 1987)

Water absorption ratio:-A circular tissue paper of 10cm diameter was placed inthree petridish with a 10cm diameter, one in each after folding. 10 ml of simulated salivary solution (phosphate buffer pH 6.8) was poured into the tissue paper placed in the petridish. Three tablets were weighed individually and placed one in each petridish. Fully wetted tablets were weighed individually. The water absorption ratio was calculated for every batch. The percentage deviation was calculated and results were tabulated.
The water absorption ratio R was determined according to the following formula.

R = (Wa – Wb) / Wa x 100.

Where Wb is the weight of the tablet before keeping in the petridish and Wa is weight of Fully wetted tablet.

RESULT AND DISCUSSION:

A total 5 formulations of fast dissolving tablet of Telmisartan were made bydirect compression method using super-disintegrants such as sodium starch glycolate, micro crystalline cellulose and crospovidone and Natural superdisintegrant like gellan gum and chitosan in different ratios. During the preparation, the lubricating agent and sweetening agent were kept constant to avoid any possible influence by these ingredients. Saccharine sodium which is used as sweetening agent to mask the bitter taste of drug may be helpful for increasing the patient compliance.
The frictional force in powder blends can be measured by angle of repose. The angle of repose for the powder blend was found to be in the range 22º41"±42"to 32^{0}37"±54
Interparticulate interactions influence the bulking properties of powder. A comparison of bulk density and tapped density can give a measure of relative importance of the interaction in a given powder; such a comparison is often used as an index of ability of the powder to flow. The bulk density of powder formulation was in range of 0.50±0.005 to 0.58±0.001. The tapped density was in range of which indicate that powder was not bulky. The carr's index was found to be in range of 11.2±0.533 to 20.22±0.163 indicate the good compressibility of powder .Weight variation of the powder was performed as per Indian Pharmacopoea 2001 (IP); the test ensured that the fill in the die cavity was uniform for all the batches. Deviation within the IP allowed limit of 7.5% is permissible. Improvements were done through the compression of tablet to get uniform weight. The percent deviation calculated was less than 7.5% of the average weight of the tablet. Hence all batches comply with the test for weight variation as per IP. The average thickness of tablets was recorded as 0.3±0.05. The friability of all the batches was found less than one percent, thereby all the batches were found to pass the test for friability of the tablet. The hardness of all the batches found to be 2.5-3.7 kg/cm$^{2.}$
The disintegration test was performed as per IP. The disintegration time range for all batches was found to be 15±0.316 to 44±0.348. Among the various batches, formulation made with the combination of crospovidone, micro crystalline cellulose, chitosan, gellan gum and sodium starch glycolate. F5 formulation has the least disintegration time of 15±0.316 s. whereas, formulation F4 had less amount of micro crystalline cellulose showed increased disintegration time 20±0.540 s. formulation F3 showed an increased in disintegration time due to the presence of starch in formulation and also due to absence of crospovidone. Formulation F2 lacked in micro crystalline cellulose the disintegration time is found to be greater than the disintegration for the formulation F3 because of the presence of micro crystalline cellulose which enhanced the disintegration time. Formulation F1 has the highest disintegration time of 44±0.348 s. because

of the smallest amount of Micro crystalline cellulose. The disintegration time of the various formulations have been mentioned in Table.

Wetting time test was performed to find out the time taken for the water to wet the whole tablet and the wetting time range for all batches was found to be in the range of 18±1.41 to 40±1.82

All the formulations were to subject to in-vitro dissolution studies and the percentage of the drug release was calculated and fig represents the in-vitro release profile for formulation F1 to F5. Among the 5 formulation high percentage of drug release in F5 and F4 formulation was found to be 98.84% and 96.13% respectively in 120 min and disintegration time was found to be 15 and 20 sec respectively. The formulation f2 containing less amount of superdisintegrant micro crystalline cellulose show low percentage of drug release when compare to F3 formulation. In presence of dry binder starch the formulation F3 showed low percentage of drug release 92.87% as compare to F4 formulation. The result from the formulation F1 to F5 are not encouraging when compare to the formulation F5 and F4 but due to less percentage of chitosan F5 has less binding property so it found to b less stable as compared to F4. So we took F4 as a best formulation. Regression value of the formulation F4 for first order kinetic (0.678) is higher than zero order kinetics (0.413). This confirms that drug release kinetics follow first order kinetics.

Pre-formulation study results:

Organoleptic characteristics:

The Organoleptic physical characteristics were studied carefully and the results are shown in the table 3.

Table 3: Organoleptic characteristics of Telmisartan

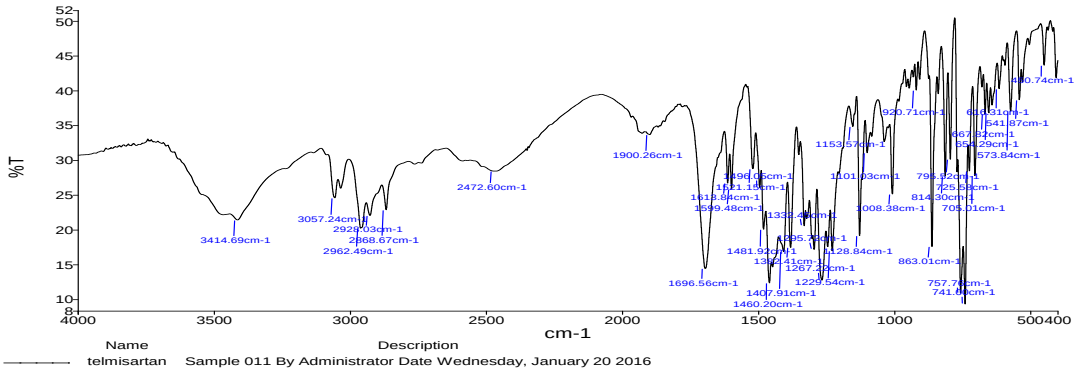
S.No.	Properties	Results
1	Description	Amorphous powder
2	Taste	Bitter
3	Odour	Odourless
4	Colour	White powder

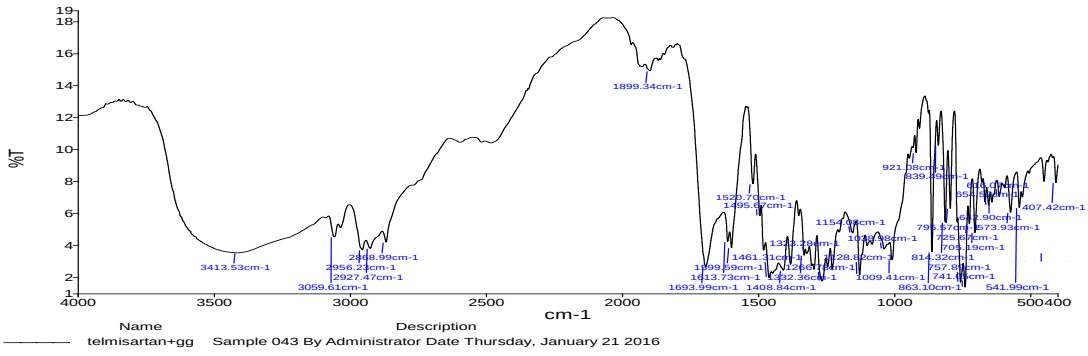
2. Solubility:

Table 4: Solubility profile:

S. No.	Solvents	Mg/ml	Remarks
1	Water	10000	Insoluble
2	Ethanol	110	Soluble
3	0.1 N HCL	9	Freelysoluble
4	Phosphate Buffer pH 6.8	0.6	Very Soluble
5	Phosphate Buffer pH 7.4	0.9	Very soluble

Drug and Excipients Interaction Study:





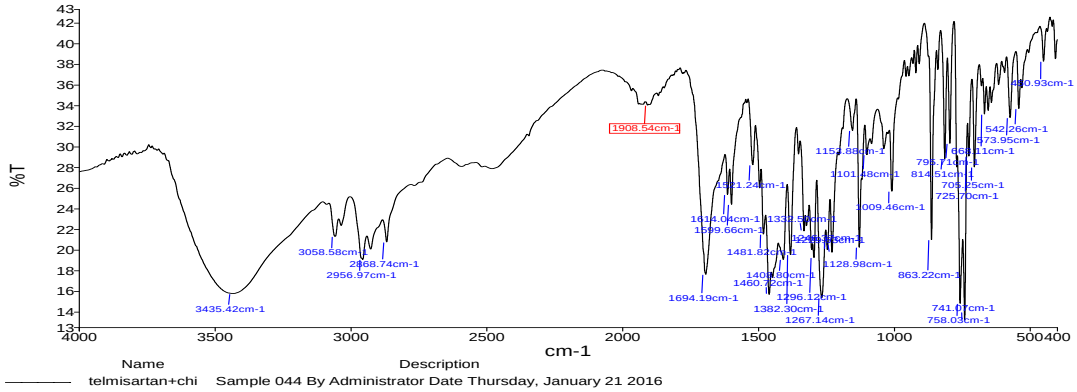


Fig 2: Fourier Transform Infra-Red Spectrum of a) Telmisartan, b) Telmisartan with gellan gum and c) Telmisartan with chitosan

Melting Point:
By open capillary method: The melting point of Telmisartan was determined by using open capillary method. The milting point was found to be 261 ℃.

Partition coefficient: Partition coefficient of drug was found to be 3.5

Calibration Curve:

Table 5: calibration curve of Telmisartan:

Concentration (mg/ml)	Absorbance (nm)
0	0.000
2	0.164
4	0.311
6	0.455
8	0.592
10	0.764
12	0.879
14	0.946

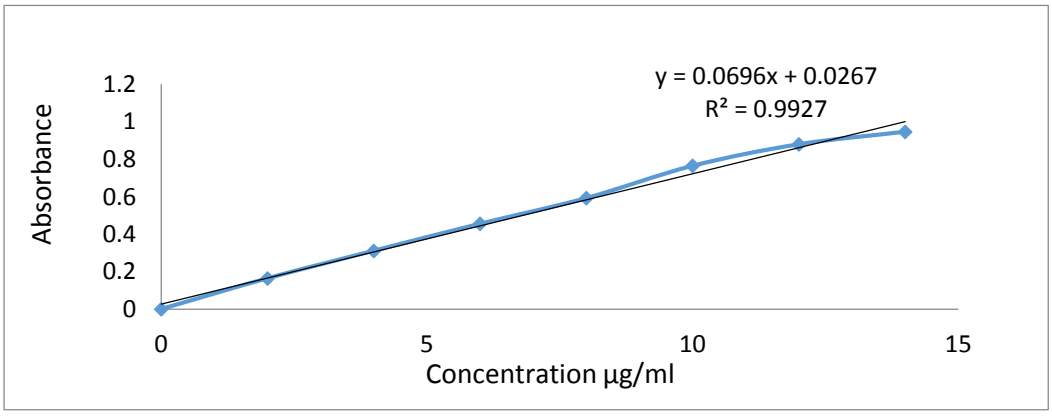


Fig 3: Standard Curve of Telmisartan

Line of equation:y= 0.069x + 0.026
Beer's range: 4-16µg/ml
R^2 value:R^2= 0.992
λ_{max}: 242nm

Pre-compression parameters of Telmisartan:

Table 6: Pre compression parameter of Telmisartan:

Formulation code	Angle of repose ±SD	Bulk density (g/ml)±SD	Tapped density (g/ml)±SD	Compressibility index(%)	Hausner ratio
F1	22º41"±42	0.50±0.005	0.63±0.002	11.2±0.533	1.11±0.007
F2	24º18"±51	0.52±0.006	0.64±0.004	15.1±0.116	1.14±0.002
F3	26º45"±56	0.52±0.003	0.64±0.003	16.06±0.183	1.17±0.003
F4	28º87"±65	0.54±0.004	0.65±0.009	19.43±0.465	1.19±0.009
F5	32^{0}37"±54	0.58±0.001	0.67±0.006	20.22±0.163	1.26±0.006

Post-compression parameters of Telmisartan:

Table 7 Post compression parameter of Telmisartan:

Formulation code	Weight variation (mg)±SD	Thickness (mm)±SD	Hardness (kg/cm^2)±SD	Friability (%)
F1	152±0.684	3.23±0.21	3.7±0.9	0.60
F2	154±0.753	3.26±0.14	3.6±0.4	0.66
F3	150±0.993	3.31±0.32	3.5±0.2	0.65
F4	151±1.063	3.41±0.14	3.2±0.3	0.77
F5	153±0.740	3.45±0.20	2.2±0.7	0.85

***In-Vitro* evaluation studies:**

Table 8: *In-Vitro* studies:

Formulation code	In-vitro disintegrationtime (sec) ±SD	Wetting time (sec) ±SD	Water absorption Ratio ±SD
F1	44±0.348	40±1.82	45±1.34
F2	41±0.316	33±1.34	50±1.25
F3	34±0.316	25±1.49	60±1.12
F4	20±0.540	20±1.90	65±1.18
F5	15±0.316	18±1.41	70±1.33

***In-Vitro* Drug Release Study**

In-vitro drug release of the sample was carried out using USP type 2 dissolution apparatus (paddle type). One Telmisartan tablet was subjected in each flask of dissolution apparatus. The dissolution apparatus was permitted to run for 120 min. Sample measuring 5 ml were withdrawn after every 5 minute and the time units considered are 5, 10, 20, 40, 60, 90, 120 min. The new dissolution medium was replaced every time with the equal quantity.

Table 9: *In-vitro* dissolution study of Telmisartan for F1 formulation

S.N.	Time (min)	√T	log time	Cumulative % drug release	Cumulative % Drug remain	Log Cumulative % drug release	Log cumulative % drug remain
1	5	2.23	0.348	43.78	56.22	1.64	1.75
2	10	3.16	0.499	55.17	44.83	1.74	1.65
3	20	4.47	0.65	65.45	34.55	1.81	1.54
4	40	6.32	0.8	68.88	31.12	1.84	1.49
5	60	7.74	0.888	76.25	23.75	1.88	1.38
6	120	10.95	2.07	82.56	17.44	1.92	1.24

Table 10: *In-vitro* dissolution study of Telmisartan for F2 formulation

S.N.	Time (min)	√T	log time	Cumulative % drug release	Cumulative % Drug remain	Log Cumulative % drug release	Log cumulative % drug remain
1	5	2.23	0.348	50.35	49.65	1.7	1.69
2	10	3.16	0.499	59.23	40.77	1.77	1.61
3	20	4.47	0.65	70.75	29.25	1.85	1.47
4	40	6.32	0.8	78.45	21.55	1.89	1.33
5	60	7.74	0.888	82.05	17.95	1.91	1.25
	120	10.95	2.07	87.56	12.44	1.94	1.09

Table 11: *In-vitro* dissolution study of Telmisartan for F3 formulation

S.N.	Time (min)	√T	log time	Cumulative % drug release	Cumulative % Drug remain	Log Cumulative % drug release	Log cumulative % drug remain
1	5	2.23	0.348	55.59	44.41	1.74	1.65
2	10	3.16	0.499	62.81	37.19	1.79	1.57
3	20	4.47	0.65	76.25	23.75	1.88	1.38
4	40	6.32	0.8	80.55	19.45	1.91	1.29
5	60	7.74	0.888	84.29	15.71	1.93	1.20
6	120	10.95	2.07	92.87	7.13	1.97	0.85

Table 12: *In-vitro* dissolution study of Telmisartan for F4 formulation

S.N.	Time (min)	√T	log time	Cumulative % drug release	Cumulative % Drug remain	Log Cumulative % drug release	Log cumulative % drug remain
1	5	2.23	0.348	61.24	38.76	1.79	1.59
2	10	3.16	0.499	70.41	29.59	1.85	1.47
3	20	4.47	0.65	83.71	16.29	1.92	1.21
4	40	6.32	0.8	88.25	11.75	1.95	1.07
5	60	7.74	0.888	92.47	7.53	1.97	0.88
6	120	10.95	2.07	96.13	3.87	1.98	0.59

Table 13: *In-vitro* dissolution study of Telmisartan for F5 formulation

S.N.	Time (min)	√T	log time	Cumulative % drug release	Cumulative % Drug remain	Log Cumulative % drug release	Log cumulative % drug remain
1	5	2.23	0.348	63.85	36.15	1.81	1.56
2	10	3.16	0.499	76.29	23.42	1.88	1.37
3	20	4.47	0.65	84.12	15.88	1.92	1.20
4	40	6.32	0.8	90.79	9.21	1.96	0.96
5	60	7.74	0.888	95.11	4.89	1.98	0.67
6	120	10.95	2.07	98.84	1.16	1.99	0.64

Table 14: Regression value for formulation F1-F5

Formulation	Zero Order	First order	Highuchi	Korsmeyer and Peppas	Mechanism of release	Best fit model
F1	0.013	0.893	0.667	0.576	Non fickian	First order
F2	0.001	0.879	0.681	0.616	Non fickian	First order
F3	0.007	0.952	0.732	0.527	Non fickian	First order
F4	0.057	0.773	0.748	0.507	Fickian	First order
F5	0.062	0.904	0.775	0.621	Non fickian	First order

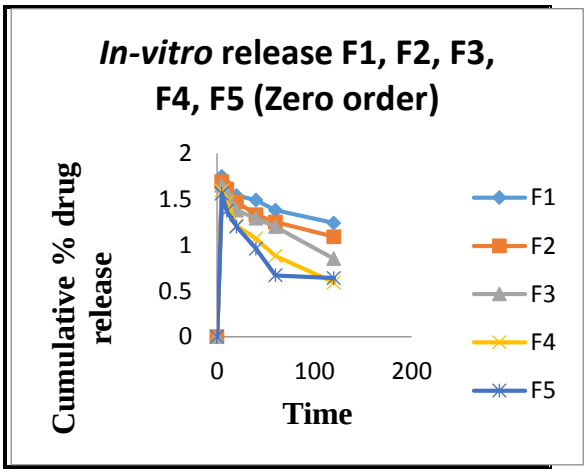


Fig 4: zero order plot of F1, F2, F3, F4, F5 Formulations

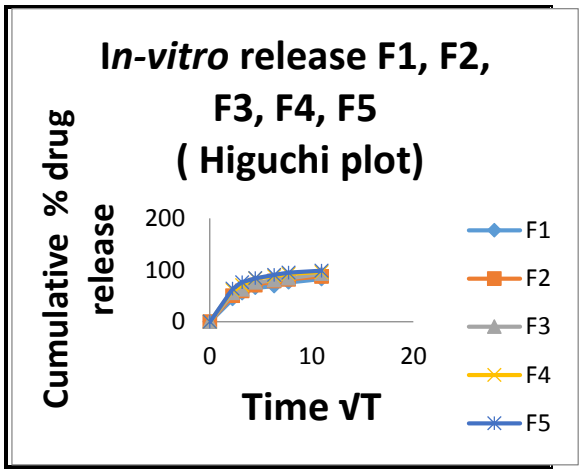


Fig 6: Higuchi Plot of F1, F2, F3, F4, F5 Formulations

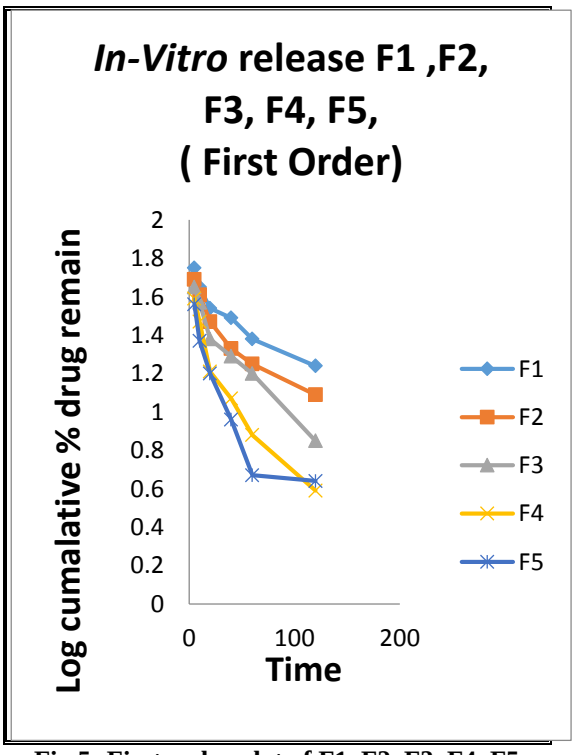


Fig 5: First order plot of F1, F2, F3, F4, F5 Formulations

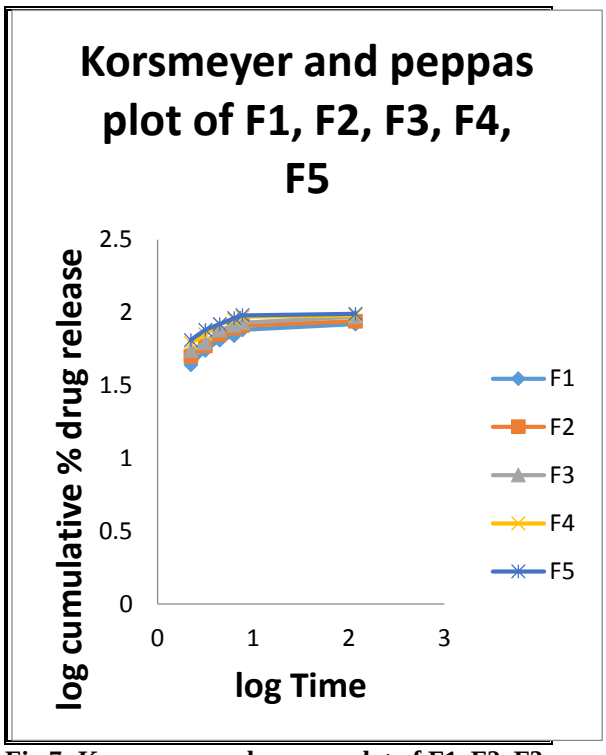


Fig 7: Korsmeyer and peppas plot of F1, F2, F3, F4, F5 Formulations

CONCLUSION:

A total 5 formulations of mouth dissolving tablet of Telmisartan (20mg) were prepared by direct compression method using super-disintegrants such as microcrystalline cellulose, sodium starch glycolate and crospovidone andnatural superdisintigrant as chitosan and gellan gum in different ratios. The study was performed with the aim to formulate and evaluate Fast dissolving tablet of Telmisartan. .The bulk density of powder formulation was in range of 0.50±0.005 to 0.58±0.001. The tapped density was in range of which indicate that powder was not bulky. The carr's index was found to be in range of 11.2±0.533 to 20.22±0.163 indicate the good compressibility of powder . The The average thickness of tablets was recorded as 0.3±0.05.The hardness of all the batches found to be 2.9-3.7 kg/cm^{2}.The disintegration time range for all batches was found to be 15±0.316 to 44±0.348. Wetting time test was performed to find out the time taken for the water to wet the whole tablet and the wetting time range for all batches was found to be in the range of 18±1.41 to 40±1.82

The tablets of Telmisartan (20mg) were prepared by direct compression method using super-disintegrants such as microcrystalline cellulose, sodium starch glycolate and crospovidone andnatural superdisintigrant as chitosan and gellan gum. The wetting time and disintegration time found to be less in F4 formulation and F4 formulation had high in-vitro release among all the formulation and satisfied best results in each evaluation. Therefore F4 is a best formulation.

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