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Formulation, Development and Evaluation of Mouth Dissolving Tablet Containing Cyclodextrin as Taste Masker

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Abstract: Mouth dissolving dosage form is very important for geriatric patients who have difficulty in swallowing tablets or in situation where access of water is not possible. The present study was carried out to prepare Telmisartan mouth dissolving tablet that can used as an antihypertensive drug. To mask the bitter taste of the drug, the drug-polymer complex (DPC) were prepared in various ratio(1:1, 1:2, 1:3, 1:4, 1:5 & 1:6) by solvent evaporation method and the characterization of DPCs were carried out by determining Drug content , in-vitro evaluation of drug complex & Threshold value determination. The threshold value was determined at 200µg/ml and the DPC was selected which masked the taste of drug was 1:3 ratio. Selection of superdisintegrants like crosspovidone, sodium starch glycolate, crosscarmellose sodium was carried out. Tablets were prepared along with other additives by direct compression method was used for preparation of mouth dissolving tablets. Tablets were evaluated for various tests like weight variation, hardness, friability, content uniformity, wetting time, water absorption ratio, in-vitro disintegration time, in-vitro dispersion time & dissolution.

Keywords:Antihypertensive, Bitter Taste, , Superdisintegrants, Telmisartan, Threshold Value

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I. INTRODUCTION

Mouth dissolving table"The mouth dissolving tablets are defined as the solid dosage forms that rapidly get disintegrate and dissolve into saliva in the oral cavity, results into solution without the need of water for administration".

Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. Many patients have difficulty swallowing (dysphagia) tablets and consequently do not take medications as prescribed. The difficulty experienced in particular by pediatrics and geriatrics patients, but this also applies to the patients who are ill in bed or travelling. Other groups that may experience problems using conventional oral dosage form include the mentally ill, developmentally disable and patients who are uncooperative. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of noncompliance and ineffective therapy. For this reasons, tablets that can dissolve or disintegrate in oral cavity, have attracted a great deal of attention. Indeed, the **mouth dissolving tablet** is an important and attractive alternative to liquid dosage form. Mouth dissolving tablets are not only indicated for people having difficulty in swallowing but also ideal for unfavorable conditions of administration where water is not available. Syrups are best for pediatrics but they are bulky and drugs are not as stable in liquid form as in solid form like tablets.

Mouth dissolving tablets are also known as fast dissolving, rapid-dissolve, rapimelt, fast melts, porous tablets, EFVDAS or Effervescent Drug Absorption system, Orosolv, Zydis etc.

II. ANALYTICAL METHODS

2.1 Determination of λ max

50 mg of Telmisartan was dissolved in 5 ml methanol and volume was made upto 50 ml by using distilled water. Filter the solution by using whatman filter paper and the wavelength was determined by using UV-visible double beam spectrophotometer (UV- 1601 SHIMADZU) in the range of 200-400 nm.

2.2 Standard calibration curve of Telmisartane in pH 6.8 phosphate buffer

2.2.1 Preparation of standard calibration curve

Accurately weight 10 mg of Telmisartan was added in 10 ml volumetric flask and dissolve in sufficient quantity of methanol and lastly made the volume up to 10 ml using 6.8 phosphate buffer, take 1 ml from above

solution and dilute up to 100 ml with 6.8 phosphate buffer to make the stock solution of concentration 10µg/ml. further serial dilutions (1-5 µg/ml) were carried out with 6.8 phosphate buffer. The absorbance of the dilution were measured against 6.8 phosphate buffer as blank at 291.1 nm using double beam UV visible spectrophotometer.

III. PREPARATION OF DRUG-POLYMER COMPLEX (DPC)

Telmisartan is antihypertensive drug have intensive bitter taste. The objective of forming drug-β-cyclodextrin complex is to mask the bitter taste of telmisartan. As per the literature review (no), the complex of drug and β-cyclodextrin was prepared in different ratio as described.

Telmisartan and β-cyclodextrin complex was prepared using solvent evaporation method. Aqueous solution of β-cyclodextrin was added an alcoholic solution of Telmisartan in various ratio 1:1, 1:2, 1:3, 1:4, 1:5 and 1:6. Mixture was stirred for 1 hrs and evaporated at temperature of 45°C until dried. Then dried mass was pulverized in order to obtain a fine powder. These powder complexes were stored in a tightly closed container for further studies. The optimized ratio was selected on the basis of drug release in phosphate buffer pH 6.8 i.e. *in vitro* taste evaluation.

IV. CHARACTERIZATION OF DPC

4.1 Drug content

This was carried out to determine actual drug content per unit weight of the drug polymer complex (DPC). Pure drug Telmisartan and drug –β-CD complex equivalent to 20 mg of the drug was dissolve in 5ml methanol and volume was made up to 100 ml using pH 6.8 phosphate buffer. Further dilutions were made by using pH 6.8 phosphate buffer and absorbance was measured at 291.1 nm by using the solution.

4.2 Threshold value determination[27]

Accurately Weighed 20 mg of Telmisartan was taken in volumetric flask. 4ml of methanol was added and made volume up to 20ml by using simulated salivary fluid. Filter the solution and dilutions were prepared at different concentration as standard solutions 50, 100, 200, 400 µg/ml respectively. Then one drop of each dilution was tasted by human volunteer after each 10 min. interval. The threshold value was correspondingly selected from the different concentrations as the lowest concentration that had a bitter taste. The human volunteers were informed instruction regarding the oral toxicity of drug if any and obtained their consent form.

4.3*In vitro taste evaluation of drug complexes*

Drug-βcyclodextrin complex of various ratios equivalent to 20 mg of Telmisartan was taken in 25 ml volumetric flask. To this, 20 ml of simulated salivary fluid (SSF) was added and shaken for 60 sec. and then filter the solution. The appropriate concentration was made by dilutions. The amount of Telmisartan released was analyzed by UV visible spectrophotometer (Shimadzu 1601 Japan) at 291.1 nm.

V. FORMULATION AND PREPARATION OF MOUTH DISSOLVING TABLET (MDT)

Ingredients used in formulation of MDTs are mentioned in table no. (1)

Total ten formulations (F1-F4) were prepared containing varying concentration of superdisintegrants and diluents (Table 1). Direct compression method was used to compress powder blend using multitooling 12 station table press (CEMACH, Ahmadabad). The prepared MDTs were subjected to various evaluation tests.

VI. RESULT AND DISCUUSION

6.1 Evaluation of Mouth dissolving tablets

6.1.1 Hardness

Tablet hardness has been defined as, "the force required breaking a tablet in a diametric compression test". For each formulation, the hardness of three tablets were determined using Monsanto hardness tester.

6.1.2 Uniformity of weight

To study weight variation 20 tablets of each formulation were weighted using an electronic balance and the test was performed according to the official method in Indian Pharmacopoeia. The test passes if the weights of not more than 2 of tablets differ by more than the percentage listed in table no.(8) and no tablets differ in weight by more than double that percentage.

6.1.3 Friability

Six tablets from each batch were selected randomly and weighed. These tablets were subjected to friability test using Roche Friabilator for 100 revolutions. Tablets were removed dedusted and weighed again.

Following formula was used to calculate the friability:

F = (1- W/Wo) 100 (eq. 1)

Where,

Wo -Weight of tablet before test.
W - Weight of tablet after test.

6.1.4 Drug content

Ten tablets from each formulation were powdered. The powder equivalent to 10 mg of Telmisartan was weighed and dissolved in phosphate buffer pH 6.8 in 100 ml standard flasks. From this suitable dilution was prepared and the solution was analyzed at 291.1 nm using UV double beam spectrophotometer (UV-1601Shimadzu Japan) using pH 6.8 as blank.

6.1.5 Wetting time

Five circular tissue papers of 10 cm diameter are placed in a petri dish with a 10 cm diameter. 10ml of water containing amaranth (water soluble dye) is added to petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

6.1.6 Water absorption ratio

A piece of tissue paper folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the paper and time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R was determined using following equation.

R = 100(Wa- Wb)/ Wb (eq. 2)

Where,

Wb – Weight of tablet before absorption.
Wa – Weight of tablet after absorption.

Three tablets from each formulation were performed

6.1.7 *In vitro* disintegration test

The process of breakdown of a tablet in to 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. Place one tablet in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 phosphate buffer maintained at 37 ±2°C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 phosphate buffer 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.

6.1.8 *In-vitro* dispersion time

One tablet was placed in a beaker containing 10 ml of distilled water at 37 ±0.5°C and the time required for complete dispersion was determined.

6.1.9 *In vitro* dissolution studies

The dissolution study were carried out using USP paddle method at 50 rpm in 900 ml of pH 6.8 phosphate buffer as dissolution media, maintained at 37 ±0.5°C. 1 ml of samples, were withdrawn from the dissolution medium at the specified regular intervals, filtered through Whatmann filter paper and released of the drug was determined spectrophotometrically (UV-1601 Shimadzu Japan) at 291.1 nm. An equal volume of pre warmed (37°C) fresh medium was replaced into the dissolution medium each sampling, to maintain the constant volume of the dissolution medium throughout the test.

6.2Characterisation of drug-polymer complex

6.2.1 Drug content

The drug-polymer complexes prepared by solvent evaporation method in ratio of 1:1, 1:2, 1:3, 1:4, 1:5 & 1:6 were subjected to content uniformity. The percent of drug present in1:3 ratio was found 99.93. This indicated that, the drug contents are within limit of official compendia.

6.2.2 Threshold value determination

As per threshold value study, the numerical values for the inferences obtained by human volunteers are depicted in table no. (2). The concentrations used for the threshold value are shown in table (3). From the study by panel of volunteers, three volunteers found drug bitter in taste with concentration of 200mcg/ml. DPC of 1:3 ratio in same concentrations were administered to same volunteers and found drug very slightly bitter by four volunteers. Here we confirmed that the drug taste is masked. This might be happened due to imbibing effect of beta-cyclodextrin.

6.2.3 *In-vitro* taste evaluation of drug complexes

In-vitro taste evaluation study of drug complexes was done in simulated salivary fluid for approximate estimation of drug release in same fluid (pH 6.8). This method was used to select optimized drug-polymer ratio for DPC. % drug released in vitro in pH 6.8 was studied.

Drug-polymer complex in the ratio showed 62.53% drug released, which is less than the threshold concentration (91.23) that gives bitter taste with concentration of drug 200 µg/ml,

This study showed that the drug polymer ratio 1:3 was capable of producing a tasteless complex. Hence, the ratio 1:3 was selected as optimized drug polymer ratio for the preparation of drug polymer complex. The % of drug released from each ratio was shown in table no. (4).

6.3*In-vitro* Dispersion time:

One tablet was placed in a beaker containing 10 ml of distilled water at 37 ±0.5˚C and the time required for complete dispersion was determined.

6.4 In-vitro Dissolution study:

In vitro dissolution study of all the formulations of mouth dissolving tablets of Telmisartan were carried out in phosphate buffer pH 6.8. The drug release was calculated at various time intervals. Three different superdisintegrants and their combinations were used to prepare mouth dissolving tablet.

8. Tables and figures

Table No (1).: Composition of Mouth Dissolving tablet of Telmisartan.

Batches / **Ingredients (mg)**	**F 1**	**F 2**	**F 3**	**F 4**
DPC	80	80	80	80
Sodium starch Glycolate	_	_	_	3
Crospovidone	_	_	4.5	3
Crosscarmellose	9	18	4.5	3
Mannitol	60	60	60	60
Microcrystalline cellulose	139	130	139	139
Talc	6	6	6	6
Magnesium stearate	6	6	6	6

Table no. (2) : Standard calibration curve of Telmisartan in 6.8 phosphate buffer.

Sr. No.	Concentration (µg/ml)	**Absorbance**
1	0	0
2	1	0.0712
3	2	0.1256
4	3	0.1856
5	4	0.2541
6	5	0.3125

Table no. (3): Numerical scale representing taste

Rating	**Taste Inference**	**Concentration µg/ml**
0	Tasteless	----
1	Very slightly bitter	50
2	Slightly bitter	100
3	Bitter	200
4	Strong bitter	400

Table no. (4): In-vitro taste evaluation of drug complex

Sr. no.	Ratio	% Drug released	Threshold concentration for 200 µg/ml
1	1 : 1	82.24	91.23 %
2	1 : 2	73.86	
3	1 : 3	62.53	
4	1 : 4	62.61	
5	1 : 5	61.94	
6	1 : 6	61.87	

Table no. (5): Preliminary evaluation of mouth dissolving tablet:

Formulation	Hardness ±SD (kg/cm^2)	Thickness ±SD (mm)	Diameter ±SD (mm)	Weight variation ±SD (mg)
F 2	3.13±0.362	3.41±0.246	10.1±0.00	300±0.00
F 2	3.3±0.280	3.52±0.301	10.1±0.00	300±0.00
F 3	3.19±0.127	3.32±0.189	10.1±0.00	300±0.00
F 4	3.38±0.152	3.45±0.268	10.1±0.00	300±0.00

Table no. (6): Evaluation test of Mouth dissolving tablet:

Formulation	Friability (%)	Disintegration time (sec)	Wetting time (sec)	Water absorption ratio	Drug content (%)
F 1	0.38	24±0.021	57±0.998	95±0.213	97.28
F 2	0.33	19±0.23	52±1.207	98±0.205	98.93
F 3	0.51	37±0.026	63±0.917	91±0.223	94.81
F 4	0.39	30±0.019	58±1.224	94±0.214	97.54

Table no. (7): *In-vitro* Dispersion time

Formulation	F 1	F 2	F 3	F 4
In-vitro dispersion time (sec)	27	24	26	25

Table No. (8): Cumulative percent drug dissolved

Time (min)	F 1	F 2	F 3	F 4
2	42.97	46.65	37.04	41.45
5	51.84	55.53	42.97	47.39
10	62.20	67.36	54.78	59.21
20	74.04	79.21	67.35	68.84
30	85.89	88.86	78.46	80.69
60	93.34	98.52	84.43	95.49

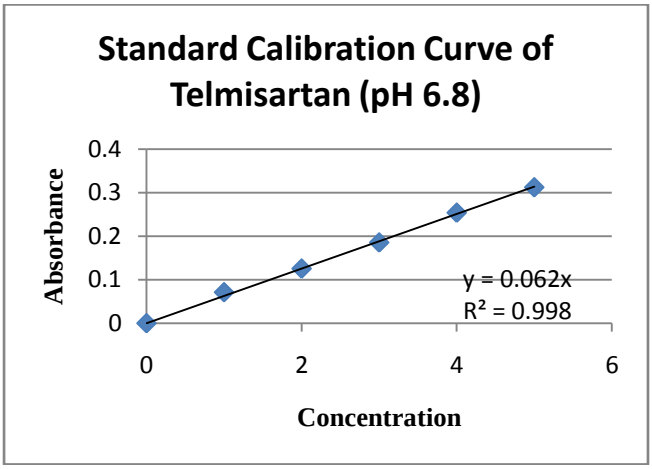


Figure no. (1): Calibration curve of Telmisartan in 6.8 phosphate buffer.

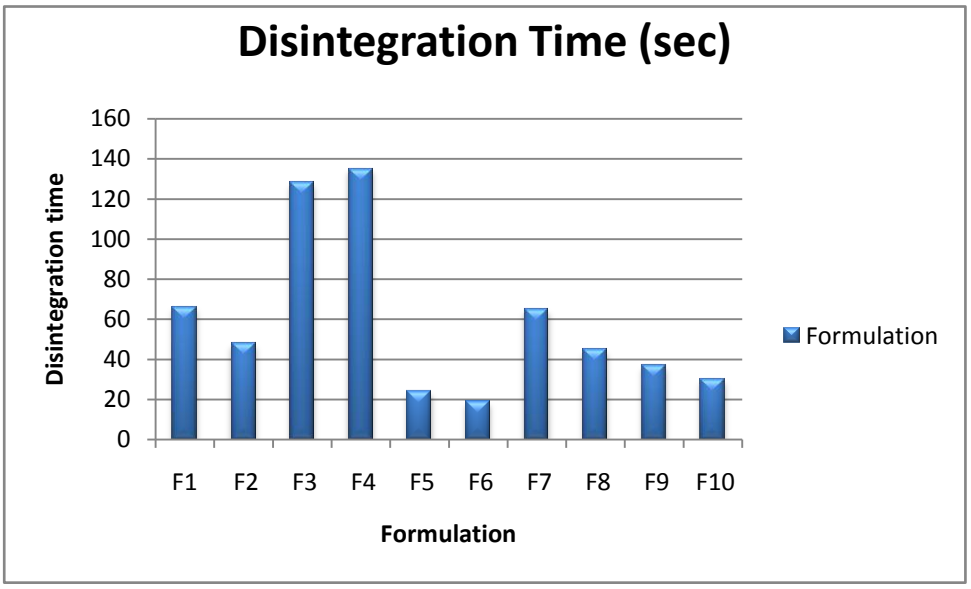


Figure no. (2): Disintegration time graph.

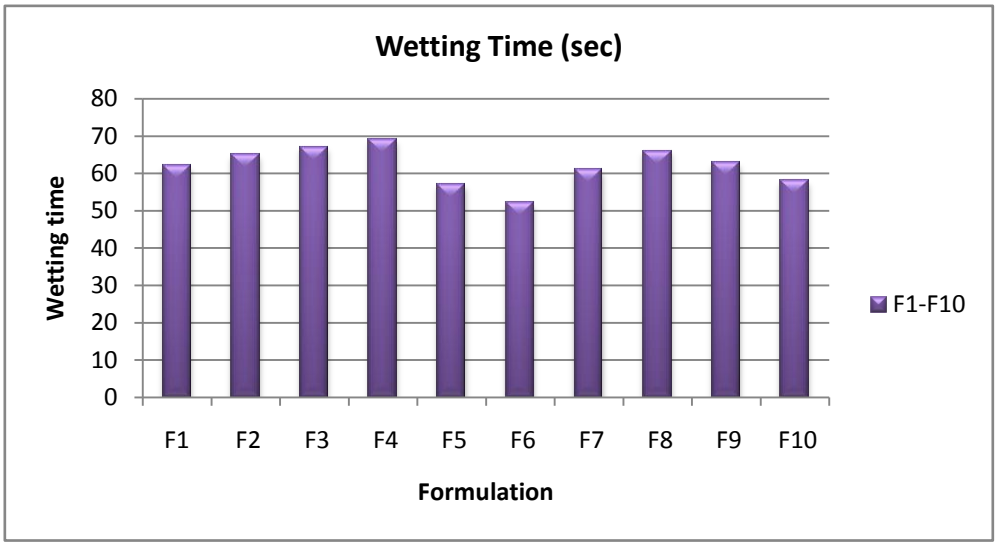


Figure no.(3): Wetting Time Graph

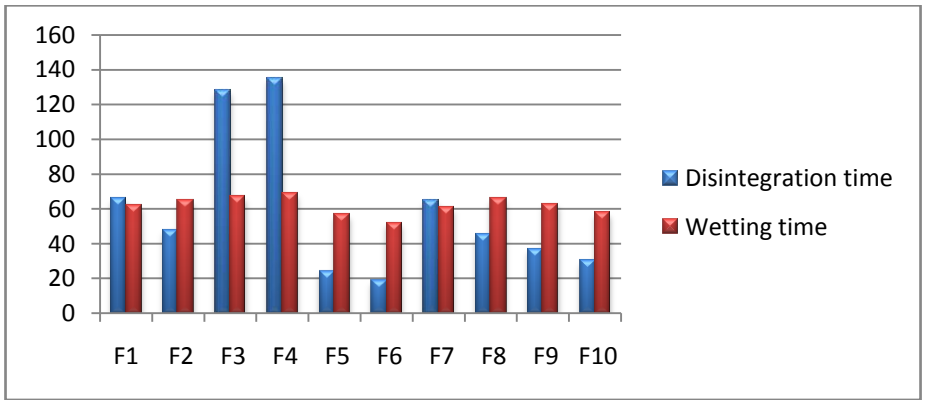


Figure no. (4): Comparison between Disintegrating and Wetting time.

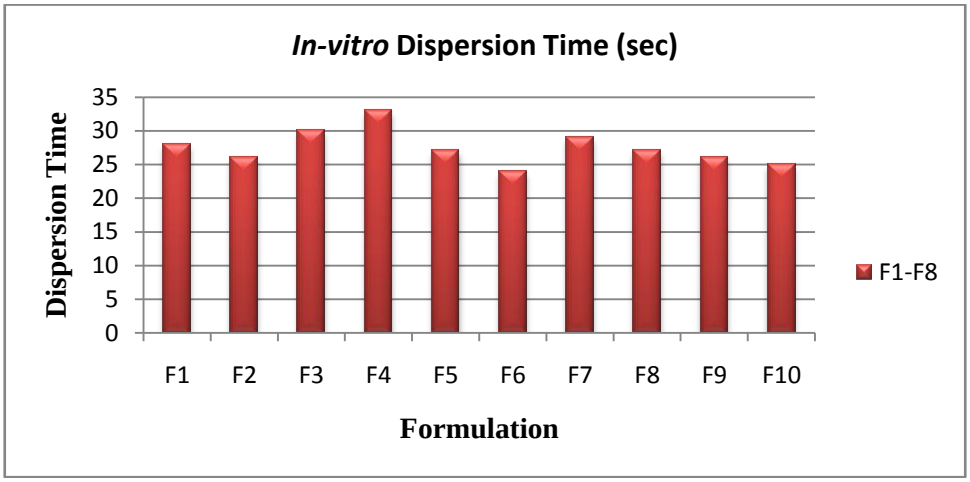


Figure no. (5): *In-vitro* dispersion time graph.

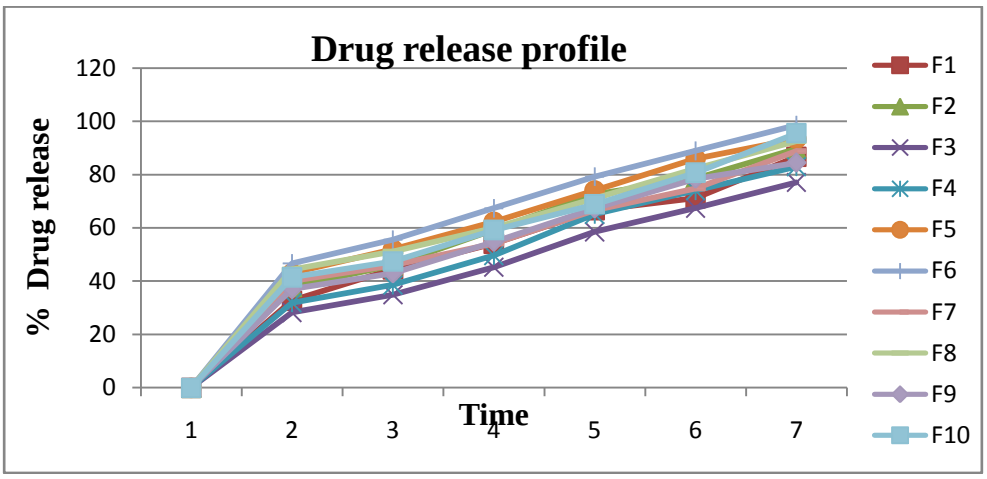
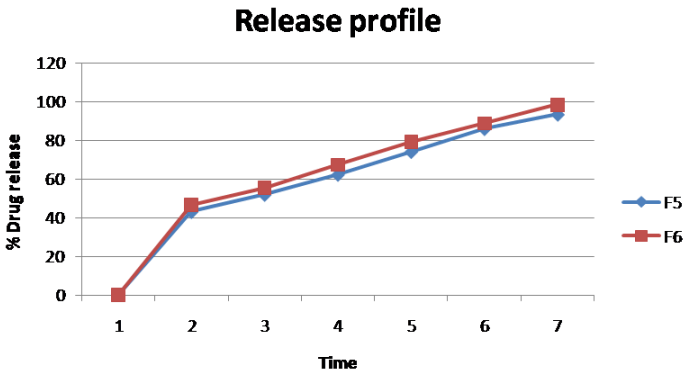
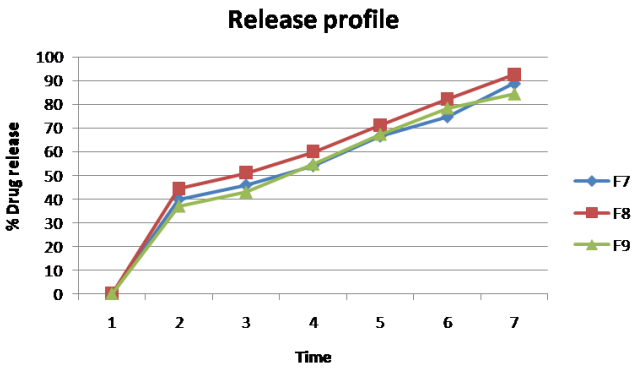


Figure no. (6): *In-vitro* Dissolution Time Graph.

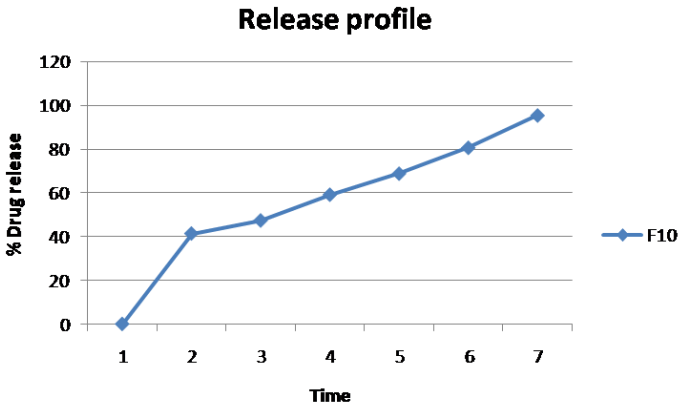
Figure no. (7): Release profile of all formulation batches. (F1-F10)



Time (min)	F5	F6
2	42.97	46.65
5	51.84	55.53
10	62.20	67.36
20	74.04	79.21
30	85.89	88.86
60	93.34	98.52



Time (min)	F7	F8	F9
2	39.98	44.40	37.04
5	45.91	51.07	42.97
10	54.06	59.95	54.78
20	66.62	71.05	67.35
30	74.79	82.17	78.46
60	88.85	92.56	84.43



Time (min)	F10
2	41.45
5	47.39
10	59.21
20	68.84
30	80.69
60	95.49

VII. SUMMARY AND CONCLUSION

The present study was carried out to prepare Telmisartan mouth dissolving tablet that can used as an antihypertensive drug. To mask the bitter taste of the drug, the drug-polymer complex (DPC) were prepared in various ratio (1:1, 1:2, 1:3, 1:4, 1:5 & 1:6) by solvent evaporation method and the characterization of DPCs were carried out by determining Drug content , in-vitro evaluation of drug complex & Threshold value determination. The threshold value was determined at 200µg/ml and the DPC was selected which masked the taste of drug was 1:3 ratio.

Thus, from result it was concluded that formulations of mouth dissolving tablets containing Telmisartan were prepared by direct compression using various superdisintegrants are very effective.

REFERENCES

[1]. Lachman L. & Liberman H.A, The theory and practice of industrial pharmacy; Varghese publishing house, third edition. 1990, 329-335.
[2]. Aulton M.E; Aulton's pharmaceutics, The design and manufacture of medicines; third edition; 2007,441-482.
[3]. Ansel H.C; Ansel's pharmaceutics dosage forms & drug delivery system; edition 9th; 2011, 225-256.
[4]. Prabhakar V., Agarwal S., Chauhan R., Sharma S: Fast dissolving tablet –an overview; International journal of pharmaceutical science review and research; 2012, 16(1), 17-24.
[5]. Gupta A., Mittal A. & Prof. K. K. Jha; Fast dissolving tablet- A Review; The Pharma Innovation, 2012, 1(1), 1-7.
[6]. Bera A. & Mukherjee A.; A Detailed study of mouth dissolving drug delivery system; Acta Chim. Pharm. Indica: 2013, 3 (1), 65-93.
[7]. Arora P., Arora Sethi V.; Orodispersible Tablets: A Comprehensive review; Int. J. Res. Dev. Pharm. L. Sci., 2013, 2(2), 270-284.
[8]. Bandari S, Mittapalli RK, Gannu R, Rao YM.; Orodispersible tablets: An overview. Asian J Pharm,2008, 2(1): 2- 11.

[9]. Shet N, Vaidya I.: Taste masking: A pathfinder for bitter drugs. Int. J. Pharm. Sci. Rev. Res. 2013, 18(2), 1-12.
[10]. Dhiraj A. K., Sanjay P., Chetan S. C., Ashish B.V.: Orodispersible tablet-An overview: International journal of pharmaceutical research & bioscience; 2013,2(6): 305-331.
[11]. Vishnumurthy Vummaneni, Nagpal D.; Taste Masking Technologies: An Overview and Recent Updates. International Journal of Research In Pharmaceutical and biomedical science, 2012, 3(2), 510-524.
[12]. Goyal R., Baghel S. S., Pathak A., Sharma K., Tiwari G., Shivhare R.: A review on formulation and evaluation of mouth dissolving tablet; World journal of pharmaceutical research; 2012, 1(3): 576-590.
[13]. Chaudhary K. P. R., Aishwarya K.V.N.R.: Recent research on fast dissolving tablets- a review: Journal of Global Trends in Pharmaceutical Sciences 2013, 4(1):940-954.
[14]. Bhowmik D., Krishnakanth C. B., Chandire R. M.; Fast dissolving tablet- an overview, Journal of chemical and pharmaceutical research, 2009, 1(1); 163-177.
[15]. Ahire S. B., Bankar V. H., Gayakwad P. D., Pawar S. P.; A Review: Taste masking tachniques in pharmaceuticals. An Int. J. Pharm. Sci., 2012 3(3), 68-82.
[16]. Shukla D, Teipathi R, Mishra B.; Taste masking in oral drug delivery system: A Technological Update. 73-82.
[17]. Anisree G.S; Anu V; Rauof P; Megha V; Jouhara O.P; Abeera C.H; Design and evaluation of mouth dissolving tablet of levocetrizine hydrochloride; Scholars academic journal of pharmacy,2014,3(1),45-49.
[18]. Mahanthesha M.K; Nagaraja T.S; Lakshmi R.G; Geni A.B; Formulation and evaluation of mouth dissolving tablet of antibacterial agent; International journal of advanced research 2013;1(6),465-470.
[19]. Sharma V; Singh L; Saxena P; Kumar J.A; Formulation and evaluation of mouth dissolving tablet of cefixime; International research journal of pharmacy 2011;2(5),171-174.
[20]. Tiwari N; Formulation and evaluation of fast dissolving tablet; International journal of advanced research in pharmaceutical & bio science 2013;3(1),60-69.
[21]. Jonwal N; Mane P; Mokati S; Meena A; Preparationand in vitro evaluation of mouth dissolving tablet of domperidone; International journal of pharmacy and pharmaceutical science 2010;2(3),170-172
[22]. Bhanushali A. K; Chaudhari P.M; Sonawane T.D; Solanki N.D; Formulation and evaluation of mouth dissolving tablet of isosorbide mononotrate; International research journal of pharmacy 2011;2(3),149-153.
[23]. Thakur R. R; Sharma M; Formulation and evaluation of mouth dissolving tablet containing quetiapine fumarate; International research journal of pharmacy 2012,3(5),438-443.
[24]. Ashish P; Harsoliya M.S; Pathan J.K; Shruti S; Formulation of mouth dissolving tablet; International journal of pharmaceutical & clinical science 2011;1(1),1-8.
[25]. N.G. Raghavendra Rao; Patel T; Kumar R; Development of fast dissolving carbamazepine tablet ; International journal of pharmaceutical science and nanotechnology 2010,3(1),824-833.
[26]. Sharma A; Jain A; Purohit A; Jatav R; Sheorey R.V; Formulation and evaluation of aceclofenac fast dissolving tablet; International journal of pharmacy and life sciences 2011,2(4),681-686.
[27]. Saroha K; Kumar G; Paul Y; Formulation and evaluation of fast dissolving tablet of amoxicillin trihydrate; International journal of pharma and bio science 2013,4(1),254-262.
[28]. Singh S; Shaha D; Development and characterization of mouth dissolving tablet of zolmitriptan; Asian pacific journal of tropical disease 2012;S457-S464.
[29]. Gupta S.C; Gurjar R; Khambete H; C.K.Sudhakar; Jain S; Formulation and evaluation of mouth dissolving tablet of dicyclomine HCl; Journal of chemical & pharmaceutical research 2011,3(4),55-61.
[30]. Birhade S.T., Bankar V. H., Gaikwad P. D., Pawar S. P.; Preparation and evaluation of cyclodextrin based binary system for taste masking: International Journal of Pharmaceutical Sciences and Drug Research; 2010, 2(3): 199-203.

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