International Journal of Farmacia (IJF)

IJF |Vol.10 | Issue 4 | Oct - Dec -2024

www.ijfjournal.com

DOI : https://doi.org/10.61096/ijf.v10.iss4.2024.123-131

ISSN: 2231-3656

Research

Formulation development and *in vitro* evaluation of oral dispersible tablets of ramipril

Thatikanti Pravalika[1*], Dr. D. Venkata Ramana, J. Pravalika

[1]Department of Pharmaceutics, Holy Mary Institute of Technology & Science (College of Pharmacy), Bogaram Village, Keesara Mandal, Hyderabad, Telangana, India

*Author for Correspondence: Thatikanti Pravalika
Email: pravalikat55@gmail.com

Published on: 03 Oct 2024

Published by:
DrSriram Publications

Abstract

An attempt has been made for the development of orally disintegrating tablets of Ramipril prepared by direct compression method by using super disintegrants like Ac-Di-Sol, Poly plasdone XL, Tulsion339. Effect of different super disintegrants on disintegration behavior of tablets was evaluated. All the formulations were evaluated for pre compression, post compression parameters and *in vitro* dissolution. F6 showed short dispersion time with maximum drug release 99.57% in 30 minutes.

Keywords: Ramipril, Ac-Di-Sol, Poly plasdone XL, Tulsion339 and Oral disintegrating tablets.

INTRODUCTION

Formulation of drugs into a presentable form is the basic requirement and need of today. Dosage form is a mean of drug delivery system, used for the application of drug to a living body. Various type of dosage forms are available such as tablets, syrups, suspensions, suppositories, injections, transdermal and patches having different type of drug delivery mechanisms. These classical/modern dosage forms have some advantages and disadvantages therefore the development of an ideal drug delivery system is a big challenge to the pharmacist in the presence scenario. In order to get the desired effect the drug should be delivered to its site of action at such rate and concentration to achieve the maximum therapeutic effect and minimum adverse effect. For the development of a suitable dosage form a thorough study about the physicochemical principles that governs a specific formulation of a drug should be subjected [1].

During establishing dosage form for a drug, it requires knowledge about each ingredient i.e. physical, chemical and biological properties along with the compatibility with the active drug, so that the product formed should be palatable, stable and efficacious. Most drugs pass through the barrier by molecular diffusion, or through pores called pore diffusion. In pore diffusion the drug release rate is controlled by the crystal size, molecular size, pore size, pore structure and tortuosity of the polymers. In passive transport (Fick's first law) the drug moves from

high concentration to the low concentration, while in active transport energy is required for the movement of drug from low to high concentration region through one or more transport mechanisms. It requires energy or carrier such as enzyme, protein [2].

Need Of Innovative Drug Delivery System

The orally administered drug delivery is still considered as a standard system in pharmaceutics field and still considered safest, convenient and economical method of administration providing best route for patient compliance [3], however in case of tablet and capsule having a common drawback of difficulty in swallowing leading to poor compliance specially in geriatrics [4].

To improve compliance and making the administration convenient, design of new dosage forms gained significant importance. Conventional oral drug delivery present a drug with quick and full release that may go as such without producing the desired effect may be due to the presence of food, pH of the stomach, enzymatic degradation, change in GIT motility as so forth, giving not enough time to get absorbed [5]. Recently much light is being put on the area of designing drug delivery systems bearing organoleptic elegancy and maximum patient acceptability in pediatrics and geriatric groups [6,7 8]. A lot of innovative work is being done on drug delivery in which oral route is preferred because of ease of administration, cost effective therapy, self medication and noninvasive method leading to patient compliance to a higher level. Tablet coating is one of the parameter in drug delivery designing applied to minimize the bad tasting and side effects while enhancing elegancy and drug bioavailability [9].

Oral Disintegrating Tablets

Drinking water is mostly required for the oral administration of drugs, like tablet and capsules, in which some patients experience nuisance in swallowing bulky conventional dosage forms [10]. In order to prevent the dysphagia and improve patient compliance, orodispersible tablets are introduced as a substitute in oral DDS, designed to disintegrate in mouth without the aid of water. So they are useful in such conditions in which water is not available, or prohibited as before operation, in kinetosis, cough episodes due to neurological stimulation or chest infections. Different methods are adopted to manufacture the orodispersible tablets with the aim of giving fast disintegration to the dosage form as it gets in contact with saliva with good agreeable moth feeling [11]. These orodispersible tablets (ODT) can be administered to any patients having difficulty in swallowing. They are also recognized as mouth dissolvable, melt-in-mouth, fast dissolving, rapi-melts or porous tablets[12].

These are tablets which get dispersed or disintegrate when gets in a contact with saliva with the release of active drug, providing maximum drug bioavailability as compared to conventional dosage form. This dispersible property is given by the addition of superdisintegrants to the dosage form, that releases the drug in mouth increasing the bioavailability [13]. Three different methods for the addition of disintegrants are used, they are intra granular (within the granules), extra granular (addition after granulation) and combination of both processes [14].

The best time for an orodispersible tablet to get disperse is considered to be less than a minute. Mostly the disintegration times varies from 5 to 30 seconds and are prepared applying; direct compression, solid dispersion, lyophilization or molding techniques. In all these methods direct compression is preferred because of its effortlessness, quick procedure and cost effectiveness [15]. ODTs are developed by the addition of super disintegrants like cross linked cellulose derivative; carboxymethyl cellulose, sodium starch glycolate, polyvinylpyrollidone, which gives burst disintegration when gets in contact with water or salivary secretions. Bioavailability of drugs may rise due to oral and pregastric absorption, reducing first pass metabolism in gastrointestinal tract[16]

Oral drug delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, the most convenient and most economical method of drug delivery with the highest patient compliance [17]. Oral route is the most preferred route of administration and tablet and capsules are the most preferred dosage forms, but several limitations of that kind of dosage forms like chocking and swelling discomfort in geriatric and pediatric patients [18,19]. Orally disintegrating tablets have been developed and new ODT technologies compensate many pharmaceuticals and patients' needs, ranging from enhanced life-cycle management to convenient dosing for pediatric, geriatric, and psychiatric patients with dysphasia . Over the past three decades, orally disintegrating tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance [20]. ODTs are being named as orodispersible, rapid-dissolving, mouth-dissolving, rapid-disintegrating tablets. There are some definitions that made by pharmacopeias and agency as follows: Orodispersible tablets have been placed in the mouth where they disperse fast before being swallowed and they are uncoated tablets. Orodispersible tablets disintegrate within 180 seconds when the disintegration tests have been conducted up to the test for disintegration of tablets [21,22]. Orally disintegrating tablets are intended to disintegrate fast in the mouth to provide dispersion before being swallowed where the active ingredient is intended for gastrointestinal delivery and/or absorption. A solid dosage form containing active ingredients which disintegrates fast, usually within seconds, when put on the tongue. In addition to those definitions, FDA

recommends that, orally disintegrating tablets should be considered as solid oral preparations that disintegrate fast in mouth, with an in-vitro disintegration time of approximately less than or equal to 30 seconds, when the disintegration test conducted to the United States Pharmacopeia (USP) disintegration test method or alternative [23].

Bioequivalence

Bioequivalence of ODTs has some challenges but in this part basic solutions to overcome these challenges were given. Active pharmaceutical ingredients that are formulated as ODTs should be dispersed or dissolved in the saliva, then directly absorbed via oral mucosa and/or absorbed through the gastrointestinal system. When defining the dissolution test conditions to prove both of the in-vitro and in-vivo bioequivalence of two formulations, the physiological conditions of the mouth should be considered. pH, flow rate, volume of the saliva and targeted population are the important factors that should be considered. There are several in-vivo studies for ODTs that conducted to prove bioequivalence of the ODTs, nevertheless BCS based biowaiver is also being considered for especially the active pharmaceutical ingredients are not absorbed via oral mucosa, but must be absorbed through the gastrointestinal system. But if this cannot be demonstrated, bioequivalence must be evaluated via in-vivo studies. If the ODT test product is an extension to another oral formulation, a 3-period study is recommended in order to evaluate administration of the orodispersible tablet both with and without concomitant fluid intake. However, if bioequivalence between ODT taken without water and reference formulation with water is demonstrated in a 2-period study, bioequivalence of ODT taken with water can be assumed. If the ODT is a generic/hybrid to an approved ODT reference medicinal product, the following recommendations regarding study design apply:

- If the reference medicinal product can be taken with or without water, bioequivalence should be demonstrated without water as this condition best resembles the intended use of the formulation. This is especially important if the substance may be dissolved and partly absorbed in the oral cavity. If bioequivalence is demonstrated when taken without water, also bioequivalence can be assumed with ODT taken with water.
- If the reference medicinal product is taken only in one way (e.g. only with water), bioequivalence should be shown in this condition (in a conventional two-way crossover design).
- If the reference medicinal product is taken only in one way (e.g. only with water), and the test product is intended for additional ways of administration (e.g. without water), the conventional and the new method should be compared with the reference in the conventional way of administration (3 treatment, 3 period, 6 sequence design).

In studies evaluating ODTs without water, it is recommended to wet the mouth by swallowing 20 ml of water directly before applying the ODT on the tongue. It is recommended not to allow fluid intake earlier than 1 hour after administration.[24]

Advantages of ODTs

The major advantage of the ODT formulation is that it combines the advantages of both liquid and conventional tablet formulations. It provides the convenience of a tablet formulation, and also allows the ease of swallowing as the liquid formulation. Others are:

- ✓ Not requirement of water or other liquid to swallow.
- ✓ Easily dissolution or disintegration in saliva within a few seconds.
- ✓ Pleasing taste.
- ✓ Leave in trace amount or no residue in the mouth when administered.
- ✓ Being portable and easy to transport.
- ✓ Being able to be manufactured by direct compression method with low cost.
- ✓ Can be easily administered to children, old and mentally disabled patients.
- ✓ Accurate dosing as compared to liquids.
- ✓ Dissolution and absorption of drug is fast, offering rapid onset of action.
- ✓ Bioavailability of drug is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva transferring
- ✓ down into the stomach.
- ✓ First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- ✓ Free from risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- ✓ Suitable for sustained/controlled release actives.
- ✓ Allows high drug loading [25-28].

Challenges and Limitations for ODTs

Drugs with relatively larger doses are difficult to formulate into ODTs e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug. The application for technologies used for ODTs is limited by the amount of drug into each unit dose. The drug dose must be lower than 400mg for insoluble drugs and 60mg for soluble drugs[29]. However Flashdose technology can accommodate larger drug doses and offers improved mechanical strength. Orasolv® technology can accommodate a wide range of active pharmaceutical ingredient from 1 mg to 500 mg.

MATERIALS

Ramipril-Procured From Torrent Pharmaceuticals Limited, Gujarat, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad. Ac-Di-Sol-SD Fine Chemicals Ltd,Poly Plasdone Xl-SD Fine Chemicals Ltd,Tulsion339-SD Fine Chemicals Ltd, Sodium saccharin-SD Fine Chemicals Ltd,Talc-SD Fine Chemicals Ltd,Magnesium stearate-SD Fine Chemicals Ltd, Microcrystalline cellulose-SD Fine Chemicals Ltd

Methodology

Characterization of Ramipril

Organoleptic properties

Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

Determination of Ramipril Melting point

The melting point of Ramipril was determined by capillary tube method according to the USP. A sufficient quantity of Ramipril powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Ramipril in the tube passed into liquid phase**.**

Determination of Ramipril Solubility

Determination of solubility of drug by visual observation. An excess quantity of Ramipril was taken separately and adds in 10 ml of different solutions. These solutions were shaken well for few minutes. Then the solubility was observed and observations are shown in the Table.

Buffer preparation

Preparation of 0.2 M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.128 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 ml of distilled water and mixed.

Preparation of 0.2 M sodium hydroxide solution: Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed.

Preparation of pH 6.8 phosphate buffer: Accurately measured 250 mL of v0.2 M potassium dihydrogen orthophosphate and 112.5 mL of 0.2 M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Analytical method development for Ramipril

Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400 nm against the reagent blank to fix absorption maxima. The λmax was found to be 210nm. Hence all further investigations were carried out at the same wavelength.

Construction of standard graph

100 mg of Ramipril was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL) 10 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.1 mg/ml (100µg/ml). From this stock solution aliquots of 0.5 ml, 1 ml, 1.5 ml, 2.0 ml, 2.5 ml, were pipette out in 100 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 5,10,15,20 and 25µg/ml respectively. The absorbance of each concentration was measured at respective (λmax) i.e., 210 nm.

Table 1: Formulation table showing various compositions

INGREDIENTS	FORMULATION CODE								
	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
Ramipril	5	5	5	5	5	5	5	5	5
Ac-Di-Sol	10	20	30	-	-	-	-	-	-
Poly plasdone Xl	-	-	-	20	40	60	-	-	-
Tulsion339	-	-	-	-	-	-	15	30	45
Sodium saccharin	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Magnesium stearate	6	6	6	6	6	6	6	6	6
Microcrystalline cellulose 102	84	74	64	74	54	34	79	64	49
Total weight (mg)	120	120	120	120	120	120	120	120	120

All the quantities were in mg

RESULTS AND DISCUSSION

Organoleptic properties

Table 2: Organoleptic properties

S No.	Properties	Results
1	State	Solid
2	Colour	white
3	Odour	Odorless
4	Melting point	105-112 °C

Solubility studies

Table 3: Solubility studies of drug in different solvents

S NO.	Solvents	Solubility of Ramipril
1	Water	Sparingly soluble
2	Methanol	Freely soluble
3	Polar substances and buffered aqueous solutions	Soluble

Preparation of calibration curve of Ramipril

The regression coefficient was found to be 0.999 which indicates a linearity with an equation of y=0.025x=0.004. Hence Beer-Lmbert's law was obeyed.

Table 4: Calibration curve data of Ramipril in pH 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
5	0.129
10	0.264
15	0.377
20	0.515
25	0.625

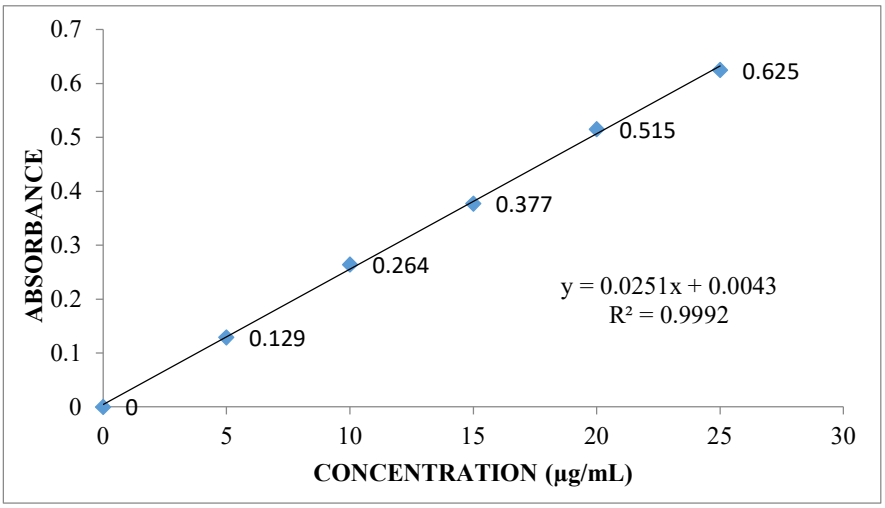

Fig 1: Calibration curve data of Ramipril in pH 6.8 phosphate buffer

FTIR RESULTS

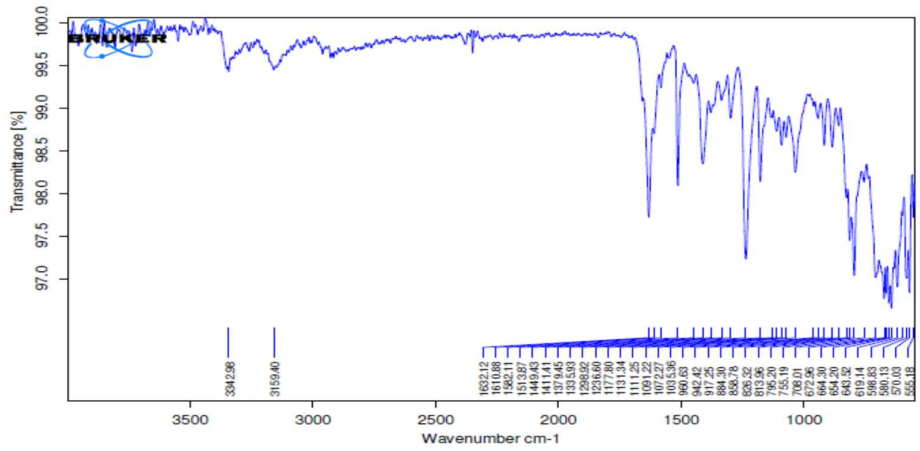

Fig 2: FTIR of Ramipril Pure Drug

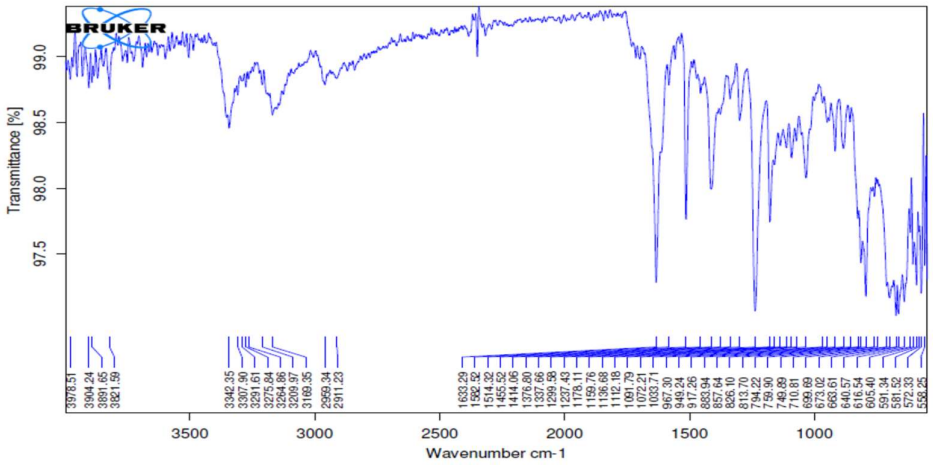

Fig 3: FTIR of Ramipril optimized formulation

From the above studies it was found that there was no shifting in the major peaks which indicated that there were no significant interactions occurred between the Ramipril and excipients used in the preparation of different Ramipril Oral disintegrating tablets formulations. Therefore the drug and excipients are compatible to form stable Formulations under study, The FTIR spectra of Ramipril and physical mixture used for optimized formulation were obtained and these are depicted in above figures. From the FTIR data it was evident that the drug and excipients does not have any interactions. Hence they were compatible.

Evaluation Of Pre-Compresion Parameters Of Powder Blend

Table 5: Evaluation of pre-compression parameters of powder blend

Formulation code	Angle of repose	Bulk density (gm/mL)	Tapped density (gm/mL)	Carr's index (%)	Hausner's ratio
F1	26.2	0.45	0.55	18.1	1.22
F2	25.4	0.47	0.55	14.5	1.17
F3	26.8	0.50	0.58	13.7	1.16
F4	24.8	0.46	0.55	16.3	1.19
F5	24.3	0.50	0.58	13.7	1.16
F6	26.3	0.47	0.55	14.5	1.17
F7	26.4	0.50	0.58	13.7	1.16
F8	24.3	0.41	0.50	18.6	1.21
F9	28.4	0.41	0.50	18.8	1.21

- For each formulation blend of drug and excipients were prepared and evaluated for various pre compression parameters described earlier in methodology chapter.
- The bulk density of all formulations was found in the range of 0.41 to 0.50 and tapped density was in the range of 0.50 - 0.58.
- The Carr's index and Hausner's ratio was calculated from tapped density and bulk density.

Evaluations of Post Compression Parameters of Ramipril Odts

Table 6: Evaluation of post compression parameters of Ramipril Oral Disintegrating Tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)	*In vitro* disintegration Time (sec)
F1	120.1	4.0	0.63	2.8	98.20	31
F2	119.5	4.5	0.55	2.5	96.19	26
F3	118.1	3.6	0.50	2.2	99.99	18
F4	119.2	4.1	0.49	2.9	97.56	35
F5	120.2	4.2	0.34	2.4	99.14	20
F6	120.3	4.0	0.59	2.7	100.1	15
F7	120.0	3.5	0.41	2.3	98.05	46
F8	120.5	4.0	0.38	2.6	96.25	38
F9	118.1	4.8	0.40	2.5	98.56	25

Weight variation and Thickness

All the formulations were evaluated for uniformity of weight using electronic weighing balance and the results are shown above. The average tablet weights of all the formulations were noted down.

Hardness and friability

All the ODT formulations were evaluated for their hardness using Monsanto hardness tester and the results are shown above. The average hardness for all formulations was found to be between (3.5 - 4.8) kg/cm^2 which was found to be acceptable. Friability was determined to evaluate the ability of the tablets to with stand the abrasion during packing, handling and transporting. All the ODT formulations were evaluated for their percentage friability using Roche friabilator and the results are shown above. The average percentage friability for all the formulations was between 0.34-0.63 which was found to be within the limit.

Drug content

All formulations were evaluated for drug content according to the procedure described in methodology section and the results were shown above. The assay values for all formulations were found to be in the range of (96.19 -100.1). According to IP standards the tablets must contain not less than 95% and not more than 105% of the stated amount of the drug. Thus, all the ODT formulation complies with the standards given in IP.

***In vitro* Disintegration time**

In vitro disintegration studies showed from 15-46 Sec. The F6 formulation showed *in vitro* disintegration time i.e. 15 sec.

***In Vitro* Drug Release Studies Of Orally Disintegrating Tablets**

Table 7: Dissolution data of Ramipril

Time (MIN)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	22.12	26.31	20.35	15.41	18.24	27.67	20.38	17.59	21.28
10	45.36	45.53	47.77	39.15	35.62	53.89	41.66	35.23	45.96
15	65. 95	62.85	63.05	60.87	54.14	67.95	57.98	48.91	63.84
20	70.42	73.15	75.12	78.98	79.39	75.91	67.97	58.67	75.37
25	73.84	84.72	76.33	89.75	85.96	88.22	82.18	71.42	88.93
30	78.96	86.48	90.95	96.21	95.49	99.57	90.88	83.61	97.69

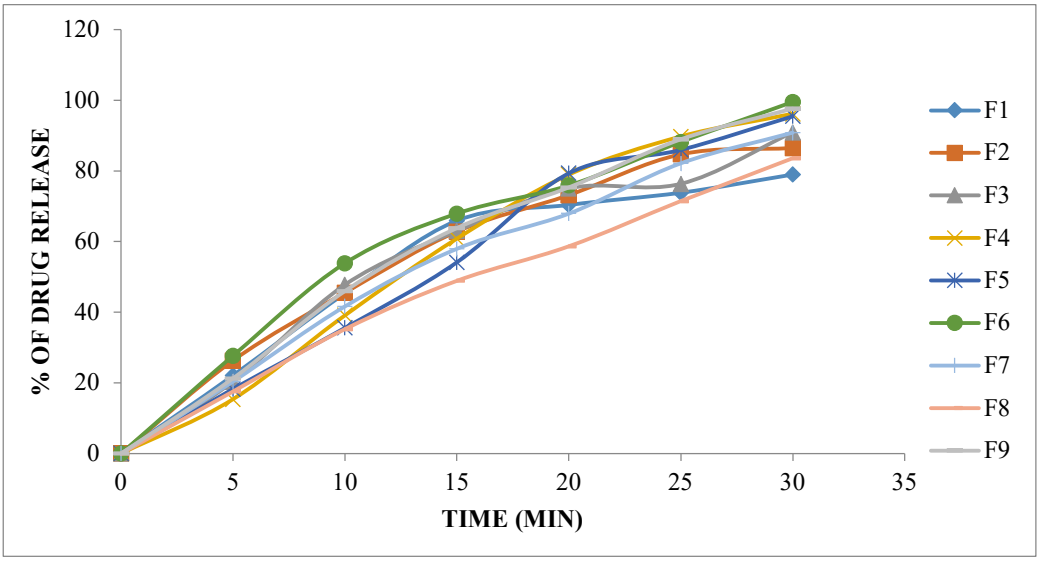

Fig 4: Dissolution profile of all formulations F1-F9

From the Table it was evident that the formulations prepared with Ac-Di-Sol powder were showed good drug release i.e, 90.95 % (F3 Formulation) in higher concentration of blend i.e. 30mg. Formulations prepared with Poly plasdone Xl showed good drug release i.e., 99.57 % (F6 Formulation) in 60 mg concentration when increase in the concentration of Poly plasdone Xl drug release was retarded. Formulations prepared with Tulsion339 showed maximum drug release i.e., 97.69% (F9 Formulation) at 30 min in 45 mg of blend. Among all formulations F6 formulation considered as optimised formulation which showed maximum drug release at 30 min. i.e. 99.57 %. Poly plasdone XL were showed good release when compared to other disintegrating. Finally concluded that F6 formulation (Contains Polyplasdone XL) was optimised better formulation.

CONCLUSION

The present investigation of this study was undertaken with an aim to formulate and characterize fast disintegrating tablets of Ramipril using direct compression method with the addition of super disintegrating agents. FTIR study reveals that there is no drug-excipients interaction between Ramipril and excipients. It is observed that the formulation F6 containing 60 mg (w/w) of Poly plasdone Xl was found to be promising showing disintegration time of 15 sec, and highest dissolution rate (99.57%) in 30 min when compared to other Formulations. It was concluded that superdisintegrant, Poly plasdone XL showed better disintegrating time and dissolution property than the Ac-Di-Sol and Tulsion339 combination with Poly plasdone XL in the formulation of fast disintegrating tablets. By employing commonly available pharmaceutical excipients such as Ac-Di-Sol, Poly plasdone XL, Tulsion339 and microcrystalline cellulose a fast disintegrating tablet of Ramipril can be developed which can be commercialized. The developed formulation of Ramipril ODT showed good efficacy, rapid onset of action, better patient compliance.

REFERENCES

1. P. A. Hannan, J. A. Khan, A. Khan, and S. Safiullah. Oral Dispersible System: A New Approach in Drug Delivery System. Indian J Pharm Sci. 2016 Jan-Feb; 78(1): 2–7.
2. Mahato RI, Narang AS. Pharmaceutical Dosage Forms and Drug Delivery. 2nd ed. New York: CRC Press; 2011. Drug delivery systems; pp. 217–34.
3. Parul S, Anoop K, Pankaj S, Sharad V. Fast disintegrating oral films: A recent trend of drug delivery. Int J Drug Dev Res. 2012;4:80–94.
4. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery – A review. Pharm Sci Technolo Today. 2000;3:138–45. [PubMed].
5. Reddy PD, Swarnalatha D. Recent advances in novel drug delivery systems. Int J Pharm Technol Res. 2010;3:2025–7.
6. Bhushan SY, Sambhaji SP, Anant RP, Mahadik KR. New drug delivery system for elderly. Indian Drugs. 2003;37:312–18.
7. Bradoo R, Shahani S, Poojary S, Deewan B, Sudarshan S. Fast dissolving drug delivery systems. JAMA India. 2001;4:27–31.
8. Wadhwani A, Prabhu NB, Nandkarni MA, Amin PD. Consumer friendly mucolytic formulations. Indian J Pharm Sci. 2004;7:506–7.
9. Pahwa R, Piplani M, Sharma PC, Kaushik D, Nanda S. Orally disintegrating tablets-Friendly to pediatrics and geriatrics. Arch Appl Sci Res. 2010; 2:35–48.
10. Ishikawa T, Mukai B, Shiraishi S, Utoguchi N, Fujii M, Matsumoto M, et al. Preparation of rapidly disintegrating tablet using new types of microcrystalline cellulose (PH-M series) and low substituted-hydroxypropylcellulose or spherical sugar granules by direct compression method. Chem Pharm Bull (Tokyo) 2001;49:134–9. [PubMed]
11. Ghosh T, Ghosh A, Prasad D. A review on new generation orodispersible tablets and its future prospective. Int J Pharm Pharm Sci. 2011;3:1–7.
12. Bi Y, Yonezawa Y, Sunada H. Rapidly disintegrating tablets prepared by the wet compression method: Mechanism and optimization. J Pharm Sci. 1999;88:1004–10.
13. Masareddy RS, Kadia RV, Manvi FV. Development of mouth dissolving tablets of clozapine using two different techniques. Indian J Pharm Sci. 2008;70:526–8.
14. Sekar V, Chellan VR. Immediate release tablets of telmisartan using superdisintegrant-formulation, evaluation and stability studies. Chem Pharm Bull (Tokyo) 2008;56:575–7.
15. Abdelbary G, Prinderre P, Eouani C, Joachim J, Reynier JP, Piccerelle P. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm. 2004;278:423–33.
16. Bhowmik D, Chiranjib B, Pankaj Fast dissolving tablet: An overview. J Chem Pharm Res. 2009;1:163–77.
17. Abay FB and Ugurlu T. Orally Disintegrating Tablets: A Short Review. June 25, 2015.
18. Kaushik D, Dureja S, Saini TR (2003) Mouth Dissolving Tablets - A Review. Indian Drugs 41: 187-93.
19. Sreenivas SA, Dandagi PM, Gadad AP. Orodispersible tablets: New - fangled drug delivery system – A Review. Indian J Pharm Edu Res. 2005; 39: 177-81.
20. Ganesh NS, Deshpande KB. Orodispersible Tablets: An Overview of Formulation and Technology. Int J Pharma Bio Sci. 2011; 2: 726-34.