Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Issue 1, 2014

Research Article

FORMULATION AND EVALUATION OF TRIFLUOPERAZINE HYDROCHLORIDE ORODISPERSIBLE TABLETS

EBTIHAL A. DAKHIL*[1] AND NIDHAL K. MARAIE*[1]

[1]Department of pharmaceutics, Collage of pharmacy, Al-Mustansiriya University, Iraq. Email: ebtihalkazem@gmail.com

Received: 02 Oct 2013, Revised and Accepted: 01 Nov 2013

ABSTRACT

Objective: Trifluoperazine hydrochloride is an antipsychotic drug; it is widely used in the treatment of psychotic conditions, acute and chronic schizophrenia.

The objective of this study was to prepare trifluoperazine hydrochloride as orodispersible tablets to enhance the disintegration and dissolution of trifluoperazine hydrochloride, to improve the bioavailability of the drug through reducing 1st pass effect and to make easier administration for geriatric, mentally ill and dysphagic patients.

Methods: The tablets were made by direct compression and wet granulation methods using different superdisintegrants [sodium starch glycolate (SSG), croscarmellose sodium (CCS) and crospovidone (CP)]. Many variables were included such as glycine as disintegration enhancer at different concentrations, effervescent base in different ratios in addition the effect of different types of diluents, the effect of these variables had studied. The formulas were evaluated for flow properties, hardness, weight variation, friability, disintegration time, wetting time, content uniformity and in vitro drug release.

Results: the results showed that the formulas prepared by direct compression method gave shorter disintegration time than the formula which prepared by wet granulation method and the formula that contained 10% crospovidone (prepared by direct compression method) showed the best results regarding *In-vitro* disintegration time (14.6 seconds), *In-vivo* disintegration time (19seconds), hardness (3.8kg/cm^2), friability (0.73), weight variation within the limit (±7.5) and faster drug release rate of 80% within 2.02 minutes as compared with conventional marketed tablet which released 80% of drug within 21 minutes so it is considered as the optimum formula.

Conclusion: It can be concluded that the optimum formula is a good potential for preparation of orodispersible tablets of trifluoperazine hydrochloride with acceptable pharmaceutical properties that may be improved the patient compliance and the bioavailability of the drug.

INTRODUCTION

Oral route of drug administration is the most appealing route for the delivery of drugs, among the various dosage forms administered orally, tablets are the most preferred because of its ease of administration, manufacturing, accurate dosing & self medication, the main drawback of this dosage form for some patients, is the difficulty to sallow[1]. Difficulty in swallowing (dysphagia) can occur at any age but are particularly prevalent in the elderly and those with dementia, whereas refusal to swallow is often encountered in geriatric, pediatric, and psychiatric patients [2]. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as orally disintegrating tablets (ODTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water [3]. Orodispersible tablets are also called fast dissolving tablets; melt in mouth tablets, rapimelt, porous tablets and quick dissolving tablet [4]. Orodispersible tablets when put on the tongue disintegrate instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down in to the stomach, so the bioavailability of drug is significantly greater than those observed from conventional tablet dosage form [5].

The basic approach in development of orodispersible tablets (ODTs) is the use of superdisintegrants which provide instantaneous disintegration of tablets after putting on tongue [6]. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants were improved the compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose [7]. The primary application of trifluoperazine is for schizophrenia, it is also indicated for use in agitation and patient with behavioral problems, severe nausea and vomiting as well as severe anxiety [8]. It is readily absorbed from the gastrointestinal tract after oral doses but it has low oral bioavailability due to considerable first-pass metabolism [9, 10]. The aim of present study is to prepare orodispersable tablets of trifluoperazine hydrochloride using different types of superdisintegrants like (crospovidone (CP), croscarmellose sodium (CCS) sodium starch glycolate (SSG), to enhance the disintegration and dissolution of trifluoperazine hydrochloride. Different factors were studied to optimize the final formula which may be improved the patient compliance and the bioavailability of drug.

MATERIALS AND METHOD

Materials

Trifluoperazine HCl, iralizine®, croscarmelose sodium, microcrystalline cellulose (avicel ph 102), aspartame, talc, spray dried lactose, magnesium stearate, sodium bicarbonate, citric acid (Samara Drug Industry, Iraq). crospovidone, sodium starch glycolate and glycine were purchased from (Aladdin Chemistry co-Ltd,China). All other ingredients used were of analytical grade.

Method

Preparation of trifluoperazine HCl tablets

Different formulas were prepared as shown in table (1). (F1-F18)were prepared by direct compression technique where all the ingredients (except the lubricant and glidant) mixed for 15 minute in an air tight plastic container, after which the lubricant and glidant were added and blended for another 2 minutes. The final mixture then compressed directly using a 7 mm single punch and die tablet machine. Formula (F19) was prepared by wet granulation method where the drug and other ingredients were mixed together for 10 min. (except talc and magnesium stearate), then a sufficient quantity of alcoholic solution of PVP (10%w/v) was added and mixed to form a coherent mass. The wet mass was granulated using appropriate pore size mesh and re- granulated after drying (at 60ºC for 10 min. talc and magnesium stearate then were added to the granules and blended for 2 minutes, then compressed.

Table 1: Composition of trifluoperazine orodispersable tablets formulas

Material (mg)	Trifluoperazine HCl	MCC	CCS	SSG	CP	Glycine	Na-bicarbonate	Citric acid	lactose	Talc	aspartame	Mg-stearate	Mannitol Q.S to
F1	5	30	2%							1.5	4.5	1.5	150
F2	5	30	6%							1.5	4.5	1.5	150
F3	5	30	10 %							1.5	4.5	1.5	150
F4	5	30		2%						1.5	4.5	1.5	150
F5	5	30		6%						1.5	4.5	1.5	150
F6	5	30		10 %						1.5	4.5	1.5	150
F7	5	30			2%					1.5	4.5	1.5	150
F8	5	30			6%					1.5	4.5	1.5	150
F9	5	30			10 %					1.5	4.5	1.5	150
F10	5	30			10 %	7.5				1.5	4.5	1.5	150
F11	5	30			10 %	15				1.5	4.5	1.5	150
F12	5	30			10 %	22.5				1.5	4.5	1.5	150
F13	5	30					2.5%	1%		1.5	4.5	1.5	150
F14	5	30			10 %		2.5%	1%		1.5	4.5	1.5	150
F15	5	30			10 %		5%	2%		1.5	4.5	1.5	150
F16	5	30	5%		5%					1.5	4.5	1.5	150
F17	5	30		5%	5%					1.5	4.5	1.5	150
F18	5	30			10 %				92.5	1.5	4.5	1.5	150
***F19**	5	30			10 %					1.5	4.5	1.5	150

*Prepared by wet granulation method

Pre-compression evaluation of trifluoperazine hydrochloride formulas

Angle of repose (q)

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and horizontal plane. The frictional force in a loose powder or granules can be measured by angle of repose. It is determined by fixed funnel method. The powder mass is allowed to flow through the funnel kept on a stand at a fixed height. The powder is carefully poured through the funnel on the petri-dish until the apex of conical pile just reached the tip of the funnel. The height of the pile and radius of the conical pile is noted and the angle of repose is calculated by this equation

tan q = h / r, where, q is the angle of repose, h is height of pile; r is radius of the base of pile [11].

Compressibility (carr's) index

An accurately weighed quantity of the powder was carefully poured in to the graduated cylinder and volume (V_o) was measured then the graduated cylinder was closed with lid, then set into density determination apparatus, the density apparatus was set for 100 taps and after that the (V_f) was measured [12]. The compressibility index was calculated using this equation (Compressibility Index = (V_o - V_f) / V_o ×100).

Post-compression evaluation of the prepared orodispersible tablets

Wetting time

The wetting time of tablets was measured using a simple procedure. A piece of tissue paper folded twice was placed in a small petri-dish (internal diameter =6.5 cm) containing 6 ml of artificial saliva containing eosin (a water soluble dye). The dye solution is used to identify the complete wetting of the tablet surface. The method was slightly modified by maintaining artificial salvia at 37 ºC. A tablet was placed on the tissue paper and the time required for the complete wetting of the tablet was recorded as a wetting time. The mean of three determinations was used ± SD [13].

Tablet hardness

The hardness of the prepared ODTs was measured to study the ability of tablets to withstand breakage during transportation. The test is done using (Guoming hardness tester) in which the hardness was expressed as Kg/cm^2 required crushing the tablets [14].

Friability test

The friability of the tablet was determined using Friabilator (Erweka, Germany). It is expressed in percentage (%). Twenty tablets were initially weighed (W_o) and transferred into the friabilator. The friabilator was operated at 25 r.p.m for 4 minutes in which tablets are subjected to combined effect of shock and abrasion in a plastic chamber dropping the tablets at a height of 6 inch in each revolution. The tablets were de-dusted and weighed again (W). The % friability was then calculated by

% Friability = (W_o-W)/ W ×100 [15].

Weight variation

Weight variation test is done by weighing 20 tablets individually, calculating the average weight and comparing the individual weight to the average. The deviation from the average weight of the tablet should not exceed ± 7.5 [16].

***In-vitro* disintegration test**

In-vitro disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds was taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds. The disintegration tests were done for the prepared orodispersible tablets using the USP disintegration apparatus, the basket rack assembly containing six open ended tubes and 10- mesh screen on the bottom was used, and the six tubes are filled with artificial saliva

instead of water, in order to stimulate the in vivo environment as much as possible [17].

***In-vivo* disintegration test**

A measurement of disintegration time in the mouth was done for the best selected formulas were carried out in three healthy volunteers. After the mouth was rinsed with purified water, one tablet was held in the mouth until the tablet disintegrated without chewing. Then the disintegration time was recorded [18].

***In vitro* dissolution studies**

In vitro dissolution studies were performed only for the best selected formulas using (phosphate buffer pH 6.8) as a dissolution medium. The dissolution of the conventional tablet Iralizine® was compared with the optimum formula using 0.1N HCl as adissolution medium using type II (paddle) dissolution apparatus (Copley, UK) at 50 rpm, and 900 ml of dissolution medium. Temperature of dissolution medium was maintained at 37 ± 0.5°C. Five milliliters aliquot of the dissolution medium was withdrawn at specific time intervals for 30 minutes. Absorption of filtered solution was measured by UV–visible spectrophotometer at λ = 256 nm. The time required for 80% of drug to be released ($t_{80\%}$) and percent drug dissolved in 2 min ($D_{2\ min\ \%}$) were considered for comparing the dissolution results [19].

Content uniformity

This test was done to the optimum formula according to British pharmacopeia where one tablet is placed in a 100 ml graduated flask, add 50 ml of a mixture of 5 volumes of hydrochloric acid and 95 volumes of water, shake until the tablet has completely disintegrated, dilute to 100 ml with the same solvent, mix and filter, discarding the first 10 ml of filtrate and measure the absorbance spectrophotometrically [20].

Statistical analysis

The results of the experiments are given at least as a mean of triplicate samples ± standard deviation were analyzed according to the one way analysis of variance (ANOVA) at the level of ($P < 0.05$).

RESULTS AND DISCUSSION

The data obtained for pre-compression parameters for formulas F1-F19 such as carr's index and angle of repose are shown in table 2 found within acceptable limits according to USP. While post-compression parameters like hardness, friability, wetting time, and in vitro disintegration time are mentioned in Table 3. The tablets measured hardness was found to be in the range of 3.2 to 3.9 kg/cm^2. The percentage of friability was less than 1% for all formulations ensuring mechanical stability of the formulated tablets. All formulations then evaluated for variation in weight and the results indicated that all formulas exhibited very low weight variation which lies within the pharmacopoeial limit i.e. ± 7.5%. The percentage of the drug content of the optimum formula was found in the range of 92.5-107.5% which compliance with the British pharmacopeia limits.

Table 2: Angles of repose, compressibility index and flow character of ODTs

Formula code	Angle of repose	Carr's index	Flow character*
F_1	34.5	20.6	good and passable
F_2	35	20.5	good and passable
F_3	36	21.3	Fair and passable
F_4	34.3	19.3	Good and fair
F_5	32.9	21.8	Good and passable
F_6	35.2	22.7	Fair and passable
F_7	30	12.5	Excellent and good
F_8	31.3	15	Good and good
F_9	34	14.3	Good and good
F10	37.7	14.2	Fair and good
F11	41.6	13.2	Passable and good
F12	42.3	14.4	Passable and good
F13	32.1	17.2	Good and fair
F14	34.2	18.3	Good and fair
F15	35.8	22.5	Good and passable
F16	28.7	12.7	excellent and good
F17	31.6	13.8	good and good
F18	43.6	14.3	Passable and good
F19	33.9	19	Good and fair

*According to USP

Table 3: Physical properties of the prepared TFP ODTs (mean ±SD, n=3).

Formula No.	*In vitro* DT(sec)	Wetting time(sec)	Hardness(kg/cm^2)	Friability (%)
F1	35.6±1.1	41.3±1.5	3.6±0.2	0.65
F2	25.6±1.1	31.6±1.5	3.6±0.05	0.59
F3	32±1.7	32.3±2.5	3.6±0.2	0.66
F4	40.6±1.1	43.3±1.5	3.2±0.2	0.78
F5	33.3±1.1	41.6±2	3.2±0.2	0.73
F6	35.6±1.1	37±2.6	3.3±0.28	0.62
F7	22.6±0.5	23.3±1.5	3.7±0.2	0.67
F8	20±1.1	15.3±2.5	3.5±0.1	0.71
F9	14.6±1.1	9.3±0.5	3.8±0.2	0.73
F10	19±0	13.6±3.2	3.8±0.3	0.63
F11	21±1	12.6±4.6	3.7±0.1	0.67
F12	22.3±2	12.6±2.5	3.2±0.37	0.72
F13	42±2	52.3±2.5	3.3±0.26	0.85
F14	35.3±2.5	44.6±1.1	3.9±0.5	0.77
F15	24.3±2	25.6±4	3.4±0.17	0.73
F16	16±1.7	14.3±1.1	3.6±0.2	0.61
F17	17.6±1.5	15.6±3.2	3.8±0.2	0.58
F18	48.3±6.4	51±2.8	3.9±0.1	0.63
F19	48.3±6.4	51±2.8	3.9±0.1	0.63

Effect of super disintegrants types and concentrations

F1-F9 were used to study the effect of different superdisintegrant types (CCS, SSG, CP) with different concentrations (2%, 6% and 10%) on the flowability of the powder blend and the physical properties of the prepared TFP orodispersible the results showed that CP with a concentration 10% (F9) gave faster disintegration time and wetting time compared with the CCS and SSG (as shown in figure 1) since crospovidone quickly wicks saliva into tablets to generate volume of expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth, so the major mechanism of CP is wicking while SSG, CCS are swelling, crospovidone particles under a scanning electron microscope appear to be granular and highly porous this unique, porous nature facilitates wicking of liquid into the dosage systems and causes rapid disintegration. And because of its high crosslink density, it swells rapidly in water without gel formation [21].there for crospovidone use a combination of mechanisms to provide rapid disintegration(wicking and swelling) [22]. The optimum concentration of superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration the tablet disintegration time is inversely proportional to the concentration ofsuperdisintegrant. If the concentration of superdisintegrants incorporated in tablet is above the critical concentration, the disintegration time remains approximately constant or even increases [23, 24].

Effect of glycine concentration (disintegration enhancer)

Formulas (F10-F12) were prepared to study the effect of glycine addition as disintegration enhancer with different concentrations (5%, 10% and 15%) on the flowability of powder blend and physical properties of the prepared ODTs. All formulas had acceptable flow characters as well as had acceptable hardness and friability. The addition of glycine especially at concentration 5% was improved the disintegration time and wetting time in comparison with other formulas other than (F9). Due to its polar surface free energy which comprises about 75 % of its component. The polar glycine has a strong affinity to water and create aqueous channels that accelerated the wetting of tablet. However the addition of glycine gave a significant increase ($p>0.05$) in disintegration time and wetting time compared with formula F9 which contain CP alone this due to that glycine decreases the rate of water penetration to the tablet and has less water holding capacity i.e it has lower and slower swelling nature [25, 26].

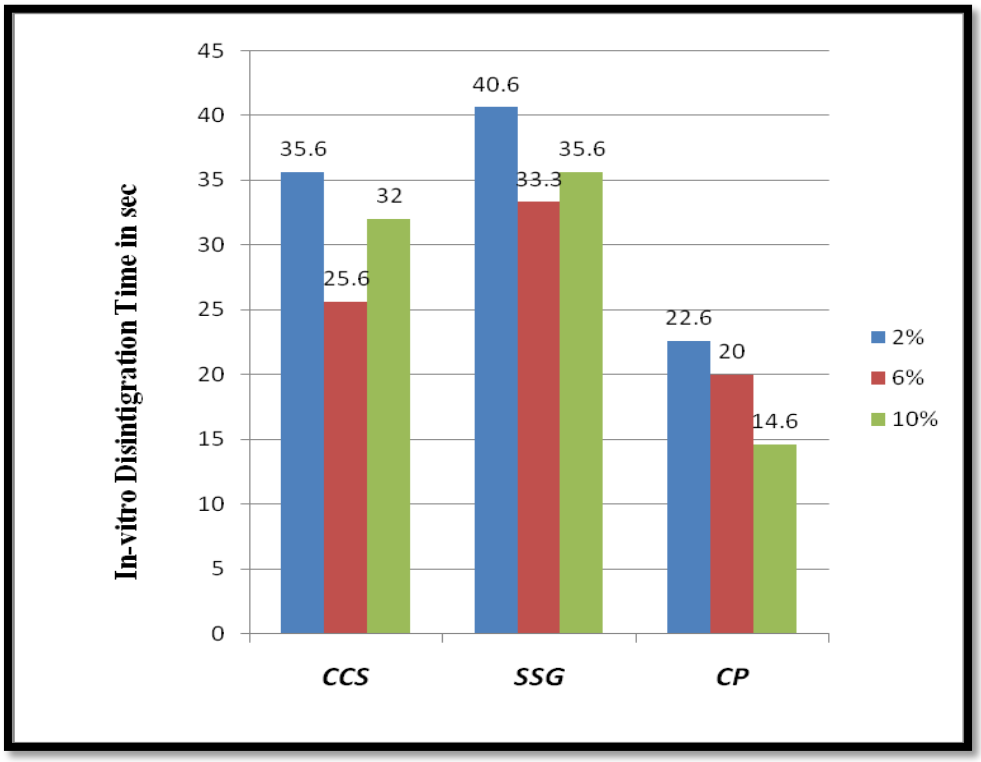

Fig. 1: *In-vitro* disintegration time of prepared ODTs containing CCS, SSG and CP in artificial saliva at 37±0.5ºC

Effect of combining the superdisintegrant with the effervescent base

The formulas (F13-F15) were utilized to study the effect of combination of crospovidone (CP) with effervescent base citric acid in concentration (1% and 2%) and sodium bicarbonate in concentration (2.5% and 5%) on pre and post characters of the prepared TFP ODTs. The results showed that the addition of effervescent base to the powder blend gave acceptable angle of repose and compressability index which indicated good flow property as well as had acceptable hardness and friability. F14 contain 10%CP and 3.5% mixture of (sodium bicarbonate and citric acid) gave disintegration time (35.3 sec) while F13 which contain effervescent base without superdisintigrant has disintegration time (42 sec) due to the presence of CP as disintigrant. As the concentration of effervescent base is increased (from 3.5% in F14 to 7% in F15 the disintegration time is decreased (24.3 sec) as shown in figure (2) which was indicated the disintigrant activity of the effervescence base. The combination between the superdisintegrant and effervescent base (F14and F15) caused significant enhancement ($P<0.05$) in disintegration time compared with the formula (F13) which contain effervescent base alone. Therefore the effervescent base can be regarded as a disintegrant in the ODT formulation but it is less efficient than using combination of superdisintigrant and effervescent base this agreed with reported data [27]. It found that the combination of superdisintigrant and effervescent base is much less efficient than using superdisintigrant CP alone (F9) this might be due to the competition between CP and effervescent base on the disintegration medium which lead to decrease the amount of the medium that reached to CP and so the wicking action of superdisintigrant decreased and lead to increase in disintegration time and wetting time.

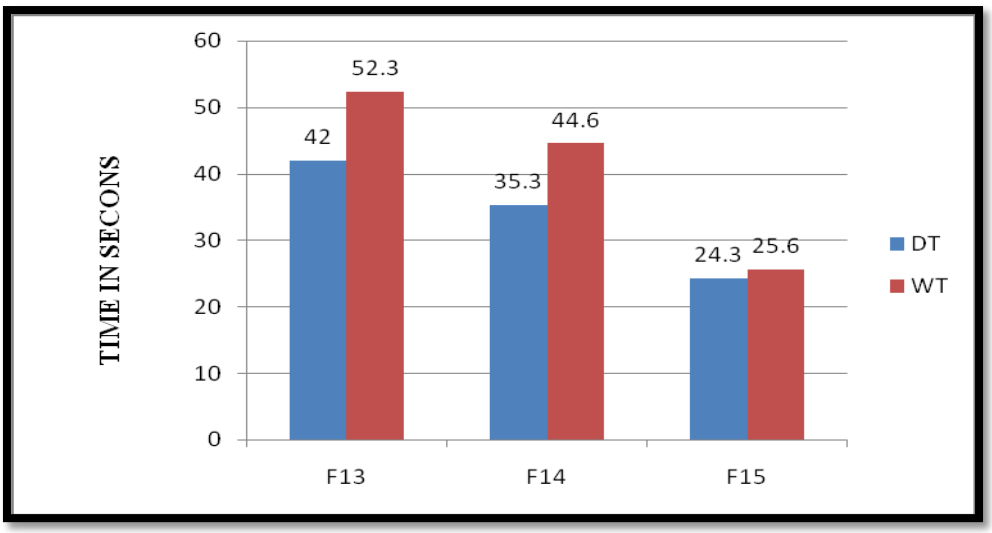

Fig. 2: Effect of effervescent base on disintegration time and wetting time of the prepared trifluoperazine HCl ODTs

Effect of combination of CP with other superdisintegrants

Formulas (F16 and F17) were utilized to study the effect of combination of CP with (CCS and SSG) in 1:1ratio. The results showed that the flowability of the powder blends and compressibility characters were within acceptable limit, the hardness and friability of the prepared ODTs within acceptable limit. Regarding the disintegration time and wetting time the results showed that the formulas F16 and F17 which contain combination of CP: CCS and CP: SSG gave a significant enhancement ($P<0.05$) in disintegration time compared with the formulas which contain CCS and SSG alone (F1-F6). The faster disintegration of tablets containing combination of CP with other superdisintigrants is attributed to the rapid capillary activity and pronounced hydration of crospovidone with little tendency to gel formation, so using wicking type of disintigrant enhanced the disintegration time. These results are in agreement with the reported data [28, 29]. Due to highly porous structure of crospovidone, it draw large amount of water by water wicking mechanism into porous network of tablet and thus crospovidone swells very little, yet rapidly absorbs water into its network. Due to this property, CP is improved water uptake and lead to reduction in disintegration time [30].

Effect of diluents type

F18 containing spray dried lactose was used to investigate the effect of diluent on the flowability of powder blend and physical properties of the prepared orodispersible tablets. Mannitol was selected as a diluent considering its advantages in terms of easy availability and negative heat of dissolution [31], it is water-soluble, non-hygroscopic, and produces a semi-sweet, smooth, and cool taste. Because of its low hygroscopicity, mannitol is potentially an excellent excipient since it is compatible with the majority of active pharmaceutical ingredients [32]. Pre-compression evaluation parameters showed satisfactory flow properties for both formulas (F9 and F18). But the disintegration time for mannitol containing formula (F9) and spray dried lactose containing formula (F18) were 14.6 and 48.3 second respectively which indicates that using mannitol as a diluent gives shorter disintegration time, This may be due to the fact that mannitol has slower dissolution kinetics, that is to say; lactose tends usually to dissolve rather than disintegrate, forming a sticky layer due the dissolution of lactose and subsequent hindrance in the further ingress of water into the tablet [33].

Effect of preparation method

F19 was prepared by wet granulation method. It contains the same ingredients and concentrations in comparison to F9 (prepared by direct compression method) to study the effect of method type on the physical properties of the prepared ODTs. The disintegration time for (F9) and (F19) were 14.6 and 48.3 seconds; respectively. Statistically, a highly significant difference ($p<0.05$) was found between the results obtained for the two preparation methods. This is due to the fact that in direct compression method, the tablet disintegrates to primary drug particles rather than granules associated with wet granulation and this provide faster disintegration time [34]. So direct compression is more effective than wet granulation in production of fast disintegration tablet [35].

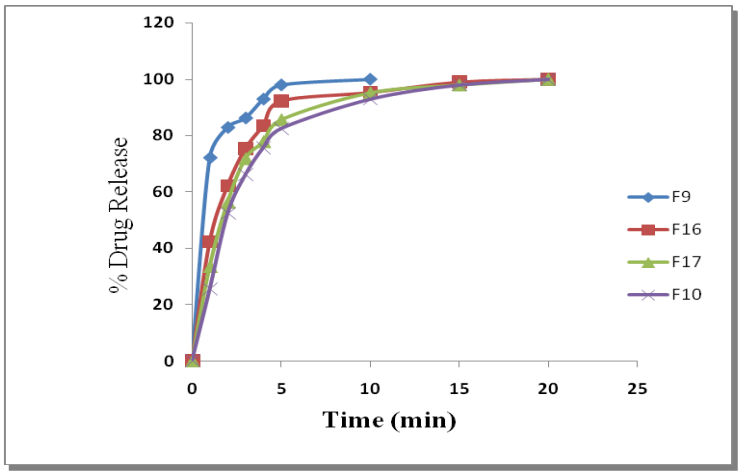

Fig. 3: Dissolution profile of the selected formulas in phosphate buffer pH 6.8 at 37±0.5ºC

***In-vitro* dissolution studies**

The release profile of the selected formulas (F9, F13, F14 and F24) were shown in figure (3) using phosphate buffer (pH 6.8), also the comparison of release profile of conventional reference tablet with the optimum formula. The time required for 80% of the drug to be released ($t_{80\%}$) from the tablet and percent drug dissolved in 2 minutes ($D_{2\ min}$ (%)) were considered for the comparison of the dissolution results (36). The results indicated that the formula (F9) has the lowest $t_{80\%}$ and highest $D_{2\ min\ (\%)}$ (1.93 minutes and 82.88%) respectively. So the formula F9 gave faster dissolution rate when compared to other formulas (F16, F17 and F10). From these results formula F9 considered as the optimum formula because of its lowest disintegration time and wetting time (14.6±1.1, 9.3±0.5), good pre and post compression properties also it has fastest dissolution rate.

Comparison of optimum formula with conventional (Iralizine®) tablets

Comparison of optimum formula F9 with conventional marketed tablet (Iralizine®) for drug release profile in 0.1 N HCl as dissolution medium is shown in figure (4). The results indicated a significant difference ($p<0.05$) in the percent of trifluoperazine hydrochloride released in 0.1N HCl (at 37±0.5^{0}C) between prepared formula (F9) and conventional tablets, these results showed that the selected formula (F9) has the higher $D_{2\ min\%}$ (79.12) than Iralizin® (20.18%) . For t80%, the formula F9 has the lower value (2.02 minutes) compared with Iralizine® (21minutes) which indicated that F9 gave faster dissolution rate compared with conventional marketed tablets.

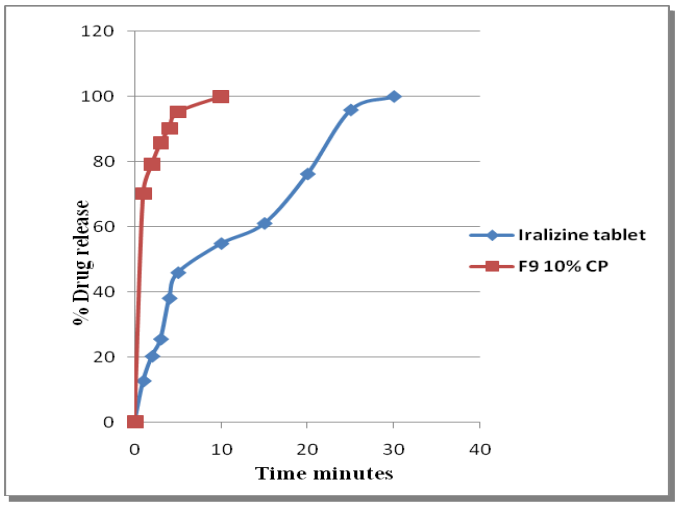

Fig. 4: Dissolution profile of the optimum formula (F9) and conventional marketed tablet (Iralizine®) in 0.1N HCl at 37±0.5ºC

CONCLUSION

The overall results showed that TFP can be prepared as ODTs with good pharmaceutical properties that enable packaging, storage and marketing so the selected formula that is quickly disintegrated and gave faster drug release leading to easy administration of the drug without need water so it is improved the patient compliance and improved the bioavailability of the drug because the drug may readily absorbed from the oral cavity which reducing the 1st pass effect.

REFERENCES

1. Anjankumar PB, Najmuddin M,Upendra K and Hariprasanna RC. Formulation and evaluation of lornoxicam fast dissolving tablet. International Research Journal of Pharmacy 2011; 2(4): 130-133.
2. Saurabh S, Rajni B, Baibhav J, Rana AC and Vikas S. Mouth dissolving tablets: a future compaction. International Research journal of Pharmacy 2012; 3 (8): 98-109.
3. Sagar N, Goswami L and Kothiyal P. Orally disintigrating tablets: a review. International Journal of Advances in Pharmaceutical Research 2012; 3(10): 1222 – 1228.
4. Kulkarni SD, Pawar SP, Bakliwal SR, Rane BR and Gujrathi NA. Mouth dissolving tablet: an overview. International Journal of Research in Ayurveda and Pharmacy 2011; 2(4): 1117-1123.
5. Ritika S, Menu R, Pawan P and Saurabh S. Fast Dissolving drug delivery system-a review. International Research Journal of Pharmacy 2011; 2(11):21-29.
6. Nitan B, Neeraj B, Pooja S and Kulwinder S. Fast dissolving tablets: a new era in novel drug delivery system. International Research Journal of Pharmacy 2012; 3(9):59-64.
7. Konapure SA, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV and Chorage TV. Mouth dissolving tablets an innovative technology. International Journal of Applied Biology and Pharmaceutical Technology 2011; 2(1): 496-503.
8. Reddy CMB, Reddy GVS and Reddy NAK. Development and validation of UV spectrophotometric method for determination of trifluoperazine hydrochloride in bulk and pharmaceutical dosage form. International journal of scientific and research publication 2012; 2(8):1-5.
9. Sweetman SS, Martindale: The Complete Drug Reference. 36th edition; London: Pharmaceutical Press 2009. P. 1034.
10. Gahiwade HP, Patil MV, Tekade BW, Thakare VM and Patil VR. Formulation and in vitro evaluation of trifluoperazine hydrochloride bilayer floating tablet. International Journal of Pharmacy and Biological Sciences 2012; 2(1):166-172.
11. Sahib AS, Abdul Rassol A A, Abd al hammid S N. Preparation and evaluation of phenobarbital orodispersable tablets. Int J Pharm Pharm Sci, 2013; 5(1): 193-197
12. PriyaVA, Rao CS, Reddy DS and Reddy VP. The effect of different superdisintegrants and their concentration on the dissolution of topiramate immidate release tablets. International Journal of Pharmaceutical Sciences and Nanotechnology 2009; 2 (2): 531-536.
13. Malik K, Arora G and Singh I. Locust bean Gum as superdisintegrant– formulation and evaluation of nimesulide orodispersible tablets. Polimery w Medycynie 2011; 41(1):17-28.
14. Chirag J P, Rajesh A, Dhruv M, Harish R and Kanu p. Formulation and evaluation of orodispersible tablets of diazepam using different superdisintegrants. International Research Journal of Pharmacy 2012; 3 (3):298-301.
15. Jasem A M and Ghareeb M M . Preparation and characterization of orodispersible tablets of candesartan cilexetil by direct compression method. Int J Pharm Pharm Sci. 2013 ; 5(1): 328-333.

16. The United State Pharmacopoeia, The united states pharmacopoeia convention, Rockville, MD, 2006.
17. Dekivadia M, Gudigennavar A, Patil C and Umarji B. Development & optimization of fast Dissolving tablet of levocetirizine HCl. International Journal of Drug Development & Research 2012; 4 (2): 237-246
18. Gosai AR, Patil SB and Sawant KK. Formulation and evaluation of orodispersible tablets of ondansetron hydrochloride by direct compression using superdisintegrants, International Journal of Pharmaceutical Sciences and Nanotechnology, 2008; 1(1):106-111
19. Khalid K, Ghareeb M M, and Abdulrasool A A. Formulation and optimization of orodispersible tablets of diazepam. AAPS PharmSciTech. 2010; 11(1): 356-361.
20. British Pharmacopoeia. London: Crown Inc. London UK; 2010.
21. Shihora H, and Panda S, Superdisintegrants, utility in dosage forms: a quick review. Journal of Pharmaceutical Science and Bioscintific Researarch 2011; 1(3): 148-153.
22. Mangal ST, Goswami M and Ghai P. Superdisintegrants: an updated review. Int. J. Pharm. Pharm. Sci. Research 2012 2 ;(2): 26-35.
23. Jagdale SC, Fernandes NC, Kuchekar BS, Shah TP and Chabukswar AR, Selection of superdisintegrant for famotidine rapidly disintegrating tablets. Journal of Chemical and Pharmaceutical Research 2010; 2(2):65-72.
24. Ashwini G, Kumar CA., Kumar SU, Dayal GR, Mansi S, and Prateek S. Fast disintegrating tablets: a never-ending trend. Novel Science International Journal of Pharmaceutical Science 2012; 1(5):245 -253.
25. Goel H, Kaur G, Tiwary AK and Rana V. Formulation development of stronger and quick disintegrating tablets: a crucial effect of chitin. Journal of the Pharmaceutical Society of Japan. 2010; 130(5):729- 735.
26. Fukami J, Ozawa A, Yoshihashi Y, Yonemochi E and Terada K. Development of fast disintegration compressed tablets using amino acid as disintegration accelerator: evaluation of wetting and disintegration of tablet on the basis of surface energy. Chem. Pharm. Bull., 2005; 53(12): 1536-1539.
27. Shirsand SB , Swamy PV , Kusum Devi V and Suresh S, Formulation design and optimization of fast dissolving effervescent tablets of clonazepam. RGUHS Journal of Pharmaceutical Sciences 2011; 1(3):202-208.
28. Sravanthi CH, Swamy SK, Lakshmi GNA and Goud BA. Formulation and evaluation of taste masked oro-dispersible tablets of ondansetron hydrochloride, Journal of Advanced Pharmaceutical Sciences 2013; 3(1):394- 414.
29. Panigrahi R, Chowdary KA, Mishra G, Bhowmik M and Behera S. Formulation of fast dissolving tablets of lisinopril using combination of synthetic superdisintegrants. Asian J. Pharm. Tech. 2012; 2(3): 94-98.
30. Kolhe S, Deshpande A and More D. Formulation and evaluation of taste masked cetrizine dihydrochloride orally disintegrating tablets: a research. International Journal of Drug Development & Research 2013; 5(1): 357-365.
31. Anilkumar J, Arun N, Amol P and Harinath N. Development and characterization of oral fast dissolving tablet of nifedipine using camphor as a subliming material. Research Journal of Pharmaceutical Biological and Chemical Sciences. RJPBCS, 2010; 1(1):46-50.
32. Daraghmeh N, Rashid I, Mahmoud M H Al omari, Leharne SA, Chowdhry BZ and Badwan A. Preparation and characterization of a novel co-processed excipient of chitin and crystalline mannitol. AAPS PharmSciTech 2010; 11(4): 1558–1571.
33. KhanS., Kataria P., Nakhat P.,and Yeole P, Taste Masking of Ondansetron Hydrochloride by Polymer Carrier System and Formulation of Rapid-Disintegrating Tablets, AAPS PharmSciTech 2007; 8 (2):1-6.
34. Mohamed EA and Abd Al hammid SN. Formulation and evaluation of rosuvastatin orodispersable tablets. International Journal of Pharmacy and Pharmaceutical Sciences 2013; 3: 339-346.
35. Patel H, Patel J, Patel K and Patel R. Studies on formulation and in vitro evaluation of fast dissolving trablets of domperidone. Int. J. Ph. Sci. 2010; 2(1):470- 476.
36. Swamy P, Shahidulla S, Shirsand S, Hiremath S and Ali M. Orodispersible tablets of carbamazepine prepared by direct compression method using 3 full factorial designs. J. Pharm. Sci. 2008, 7(1): 1-5.