International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.1, No.4, pp 840-850, Oct-Dec 2009

Formulation Evaluation of Mouth Dissolving Tablets of Fenofibrate Using Sublimation Technique

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ABSTRACT: Fenofibrate is a drug of the fibrate class. It is a widely used hypolipidemic drug. The poor aqueous solubility of the drug leads to variable dissolution rates. It is slightly soluble in water. The present investigation was to develop and characterize mouth dissolving tablets of fenofibrate using sublimation technique. Mouth dissolving tablets of Fenofibrate were prepared using different subliming agents like camphor, thymol, ammonium bicarbonate and different concentrations of menthol using direct compression method. The technique is to increase the porosity of the tablets whereby subliming material was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed in to tablets. Alternatively, tablets were first prepared and later exposed to vacuum. Since, these tablets can be swallowed in the form of dispersion; it is suitable dosage form for pediatric and geriatric patients. The drug and excipients were characterized using DSC and FTIR techniques. The blend was examined for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The prepared tablets were evaluated for general appearance, content uniformity, hardness, friability, taste evaluation, mouth feel, wetting time, *in vitro* and *in vivo* disintegration time, and *in vitro* dissolution studies. Tablets with menthol at 12.5% concentration have shown quick disintegrating features, i.e., within 20 s, which is very characteristic of oro-dispersible tablets. The *in vitro* drug release study revealed that menthol at a concentration of 12.5 % (F10) of the dosage form weight was able to fast the release of Fenofibrate within 10 minutes. These compressed tablets which have 12.5 % menthol (F10) rapidly dissolved within 22 seconds in saliva in the mouth. Further optimized formulations (F10) were subjected to stability testing for 3 months at temperatures 25±5ºC/60±5%RH and 40±5ºC/75±5%RH. Optimized tablets have shown no appreciable changes with respect to taste, disintegration, and dissolution profiles. In conclusion, the results of this work suggest that sublimation is a useful technique to enhance the solubility and dissolution rate of poorly water-soluble drug like fenofibrate.

Keywords: Mouth dissolving tablet, direct compression, Fenofibrate, Subliming agent, super disintegrant and Camphor.

INTRODUCTION

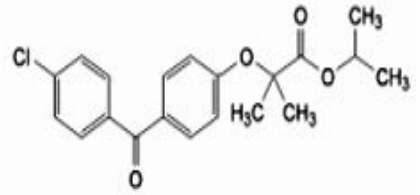
Pediatric and geriatric patients may have difficulties in swallowing or chewing pharmaceutical dosage forms for oral administration. Tablets that rapidly dissolve upon contact with saliva in the buccal cavity could present a solution to those problems and so there is an increased interest in fast dissolving dosage forms for buccal, sublingual and oral administration. Fast dissolving/ disintegrating tablet are perfect fit for these patients as these immediately release the active drug when placed on tongue by rapid disintegration/ dispersion, followed by dissolution of drug[1-2].

Fast dissolving tablets are dosage form, which disintegrate in patient's mouth within a few seconds without the need of water, or chewing, providing best remedy for the patient suffering from dysphasia. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down the stomach. In such cases the bioavailability is greater than those observed for conventional dosage form. The advantages of mouth

dissolving dosage form are increasingly being recognized in both industry and academia.

The basic approach used in the development of the fast-dissolving tablet is the use of superdisintegrants. Croscarmellose sodium, sodium starch glycolate, and crospovidone were screened in the present study, and the best one was used for further studies. Another approach used in developing MD tablets is maximizing pore structure of the tablets. Freeze-drying[3-4], vacuum-drying[5-7] and sublimation technique by using sublime agent like camphor, menthol[8-9]. However, as microcrystalline cellulose (MCC) and low-substituted hydroxyl propyl cellulose (L-HPC) were used as excipients in these tablets, patients, sometimes feel a rough texture in their mouth due to the incomplete solubilization of this type of tablet in saliva[10]. To eliminate such type of inconvenience in the mouth, we attempted to use a Perlitol SD200 as an excipient instead of crystalline cellulose and L-HPC, in the preparation of this type of tablet. However, use of Perlitol SD200 in tablet as water soluble excipient does not rapidly dissolve in saliva since it is difficult for water to penetrate into the tablets due to its low porosity. Above techniques have been tried by researchers to maximize the pore structure of tablet matrix. Freeze drying is cumbersome and it yields a fragile and hygroscopic product. Therefore, it was decided to adopt the vacuum-drying technique in the present investigation. Vacuum drying was adopted after addition of a subliming agent to increase porosity of the tablets. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly. Using Perlitol SD200 with subliming materials. We chose menthol, camphor, thymol and ammonium bicarbonate as a subliming material.

Figure 1: Chemical structure of fenofibrate



Fenofibrate (FFA) (isopropyl ester of 2-[4-(4-chlorobenzoyl) phenoxy]-2-methylpropanoic acid) is a widely used hypolipidemic drug available as tablets for oral administration. Each tablet contains 40 mg or 120 mg fenofibrate. The empirical formula is $C_{20}H_{21}O_4Cl$ (figure 1) and the molecular weight is 360.83; fenofibrate is insoluble in water. The melting point is 79° to 82°C.Fenofibrate is a white solid which is stable under ordinary conditions. Its pharmacological activity consists in reducing triglyceride and cholesterol concentration in plasma. Solubility and permeability are the fundamental parameters controlling the rate and extent of drug absorption. According to the Biopharmaceutics Classification System (BCS), FFA is a Class II having low solubility and high permeability. Bioavailability of FFA solely depends on dissolution rate in the gastrointestinal tract. This drug is used mostly in lipid regulation as it decreases low-density lipoprotein (LDL) and very-low density lipoprotein (VLDL) levels, and increases high density lipoprotein (HDL) level[11].

In the present study, an attempt was made to develop mouth dissolving tablets of fenofibrate and to investigate the effect of various subliming agent on the disintegration time, wetting time and release profile of the drug in the tablets.

MATERIALS AND METHODS

Materials

Fenofibrate was supplied as a gift sample from Alembic Research Ltd (Vadodara, India). Aspartame (Ranbaxy, New Delhi, India). Sodium Laurel Sulphate (SLS), Camphor, ammonium bicarbonate, menthol, thymol, mannitol, polyvinyl pyrollidone (PVP), Lemon flavor (IFF), talc, aerosil and magnesium stearate were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals, solvents and reagents were used of either pharmacopoeial or analytical grade.

METHOD

Characterization of drug and excipients

1. Fourier transform infra red spectroscopy (FTIR)

FTIR spectra of pure fenofibrate and physical mixture of drug and excipients were recorded on Shimadzu Corporation, (Tokyo, Japan) Model-1601 PC. Potassium bromide pellet method was employed and background spectrum was collected under identical situation. Each spectrum was derived from single average scans collected in the region 400- 4000 cm^{-1} at spectral resolution of $2cm^{-2}$ and ratio against background interferogram. Spectra were analyzed by software supplied by Shimadzu.

2. Differential Scanning Calorimentry (DSC)

Thermal properties of the pure drug and the physical mixture of drug and excipients were analyzed by Shimadzu DSC-60, Shimadzu Limited Japan. The samples were heated in a hermetically sealed aluminum pans. Heat runs for each sample were set from 30 to 350^0C at a heating rate of 10^0C/ min, using nitrogen as blanket gas.

Formulation of mouth dissolving tablets of fenofibrate

The orodispersible tablets of fenofibrate were prepared using the subliming agents viz; camphor, menthol, thymol and ammonium bicarbonate. Crospovidone as superdisintegrant, mannitol as a diluent, aspartame as sweetening agent, alcoholic solution of PVP (10%w/v) as binder and magnesium stearate with talc as a flow promoter. The composition of the each batch shown in Table 1.

Table 1: formula of Mouth Dissolve fenofibrate Tablets

Ingredients (mg/tablets)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
fenofibrate	40	40	40	40	40	40	40	40	40	40
Camphor	15	--	--	--	--	--	--	--	--	--
Menthol	--	--	0	5	10	15	20	25	--	25
Ammonium bicarbonate	--	15	--	--	--	--	--	--	--	--
Thymol	--	--	--	--	--	--	--	--	15	--
Cross povidone	4	4	4	4	4	4	4	4	4	4
Aspartame	2	2	2	2	2	2	2	2	2	2
Treusil peppermint	2	2	2	2	2	2	2	2	2	2
Orange flavor	2	2	2	2	2	2	2	2	2	2
Aerosil	--	--	--	--	--	--	--	2	--	2
Talc	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	1	1	1	1	1	1	1	1	1	1
Mannitol q.s.to	200	200	200	200	200	200	200	200	200	200

All batches contained 10% polyvinylpyrrolidone in ethyl alcohol as a binder. Camphor/menthol/ammonium bicarbonate/thymol were sublimed from granules in Batches F1 to F9 and from tablets in Batch F10.

The mouth dissolving tablets of batch size one hundred (100) were prepared by direct compression process using camphor, thymol, ammonium bicarbonate and different proportions of menthol. The raw materials were passed through a 100-mesh screen prior to mixing. The drug and other ingredients were mixed together, and 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 sieve no. 12 and regranulated after drying through sieve no. 16. Granules of the formulations containing crospovidone as superdisintegrant but without any subliming agents (F3) were dried in a tray dryer (Tempo instruments and equipments, Mumbai) at 60^0C for 30 min. resulting in localized drying. Other granular formulations (F1, F2, and F4 to F9) contained a subliming agent and were dried at room temperature, 20-22 ^{0}C for 8hrs. The final moisture content of the granules was found to be between 1-2%, which was determined using an IR moisture balance. During drying the menthol, camphor, thymol and ammonium bicarbonate were sublimed with the formation of a porous structure on the surface of the granules.

Dried granules blend was evaluated for following precompression properties which includes;

EVALUATION OF GRANULE BLEND

Precompression parameters

Prior to compression into tablets, the blend was evaluated for properties such as;

1. Angle of repose

Angle of repose was determined by using funnel method. Powder was poured from a funnel that can be raised vertically until a maximum cone height, h, was obtained. Diameter of heap, D, was measured. The angle of repose, **Θ**, was calculated by formula

$$\tan \Theta = h / r$$

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

Where, Θ is the angle of repose, h is the height in cm and r is the radius.

2. 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/ml and is given by

$$D_b = M / V_0$$

Where, M is the mass of powder and V_0 is the Bulk volume of the powder

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 and is given by

$$D_t = M / V_t$$

Where, M is the mass of powder and V_t is the tapped volume of the powder.

4. Powder flow properties

The flow properties were determined by

i) Carr's Index (I)

It is expressed in percentage and is expressed by

$$I = D_t - D_b / D_t$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

ii) Hausner ratio

It is expressed in percentage and is expressed by

$$H = D_t / D_b$$

Where, D_t is the tapped density of the powder and D_b is the bulk density of the powder.

Compression of tablet

After evaluation of granule blend were then blended with talc, magnesium stearate, aerosil and compressed into tablets using flat face round tooling on a Rimek-I rotary tablet machine (Karnavati Eng. Pvt. Ltd, Ahmedabad). Sublimation was performed from tablets instead of granules at 60º C in selected batch (F10). During drying the menthol sublimed with the formation of a porous structure on the surface of the tablet.

Evaluation of tablet[12-14]

All the tablets were evaluated for following different parameters which includes;

1. General appearance

Five tablets from different batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated.

2. Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated.

3. Hardness

For each formulation, the hardness of five tablets was determined using the Monsanto hardness tester (Cadmach).

4. Friability

The friability of a sample of 10 tablets was measured using a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated.

5. Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

6. *In vitro* Disintegration test

The disintegration time was measured using disintegration test apparatus. One tablet was placed in each tube of the basket. The basket with the bottom surface made of a stainless-steel screen (mesh no. 10) was immersed in water bath at 37 ± 2^0C. The time required for complete disintegration of the tablet in each tube was determined using a stop watch. To be complied with the pharmacopoeial standards, dispersible tablets must disintegrate within 3 min when examined by the disintegration test for tablets.

7. *In vitro* dispersion test

This test is performed to ensure disintegration of tablets in the salivary fluid, if it is to be used as an oro-dispersible tablet. *In vitro* dispersion time was measured by dropping a tablet in a measuring cylinder containing ml of simulated salivary fluid of pH 6.8. Five tablets from each formulation were randomly selected and *in vitro* dispersion time was performed.

8. Drug content

Twenty tablets were taken randomly and individual tablet were crushed, an amount of the powder equivalent to 40 mg of fenofibrate was dissolved in the 50 ml of 0.1M methanolic SLS was added. Shaken for 30 min and added sufficient 0.1 M methanolic SLS to produce 100 ml and filtered, diluted suitably and analyzed for drug content at 290 nm using UV-Visible spectrophotometer (UV 1601-Shimadzu, Japan)

9. Wetting time

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (Internal Diameter=9cm) containing 6 ml of simulated saliva pH 6.8. A tablet having amaranth powder on the upper surface was placed on the filter paper. Time required to develop red color on the upper surface of tablet was recorded as wetting time. Three tablets from each formulation were randomly selected and the average wetting time was noted. Wetting time corresponds to the time taken for the tablet to disintegrate when placed gently on the tissue paper in a petridish. This method will duplicate the *in-vivo* disintegration as the tablet is motionless on the tongue. Less is the wetting time indicates more porous the tablets

10. *In vivo* disintegration time[15]

Six healthy human volunteers were selected and their written consent was obtained. Each volunteer randomly took one tablet and kept on the tongue. The time taken for complete disintegration of the tablet on the tongue was noted. It is expressed in seconds. After the test, mouth was washed with distilled water. Three trials were performed with 2 days interval, between trials.

11. Mouth feel

The same human volunteers participated in taste evaluation test, were asked to give their opinion about the feeling of smoothness or grittiness of the dispersion soon after the tablet got disintegrated.

12. Taste evaluation[16]

Taste evaluation was done by a panel of six volunteers using time intensity method. One tablet was held in mouth for 10 s bitterness levels were recorded instantly and then at the end of 10 s, 30 s, 1 min, and 2 min, bitterness levels are again noted and recorded.

13. Dissolution Studies[17]

The release rate of fenofibrate from fast dissolving tablets was determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test was performed using 900 ml of 0.1 M SLS, at 37 ± 0.5^0C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus every 2 min. for 30 min, and the samples were replaced with fresh dissolution medium. The samples were filtered through Whatmann filter paper no. 41. Absorbance of these solutions was measured at 290 nm using UV spectrophotometer Shimadzu 1601. To increase the reliability of the observations, the dissolution studies were performed in triplicate.

14. Test for dispersion[18]

This test is carried out for dispersible tablets. Two tablets were placed in 100 mL of water and stirred gently until it was completely dispersed and smooth dispersion was obtained. The dispersed liquid was passed through sieve no. 22. No residue should remain over the sieve

Stability Studies

Stability studies were carried out on optimized formulation as per ICH specifications. The tablets were stored at 25 ± 2 ^{o} C / 60 ± 5% RH and 40 ± 2 ^{o} C / 75 ± 5% RH for duration of three month. After an interval of one month samples were withdrawn and tested for various physical tests and *in vitro* drug release.

RESULTS AND DISCUSSION

Many patients, especially elderly find it difficult in swallowing tablets, capsules, fluids and thus do not comply with prescription, which results in high incidence of non-compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Rapidly disintegrating/dissolving tablet is one of such example, for the reason of rapid disintegration or even with saliva. Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms, ideal for paediatric and geriatric patients and rapid onset of action[19-25].

The mouth dissolving tablets are synonymous with Fast dissolving tablets, Melt in mouth tablets, Rapi-melts, Quick dissolving tablets, Rapidly disintegrating tablets, Porous tablets, Oro-dispersible tablets and Fast disintegrating tablets. Their characteristic benefits in terms of patient compliance, rapid on-set of action, increased bio-availability, (sometimes bi-pass first pass effect) and good stability make these tablets popular as a dosage form of choice.

Water insoluble diluents such as microcrystalline cellulose and dicalcium phosphate and L-HPC were omitted from the study as they are expected to cause an unacceptable feeling of grittiness in the mouth. Among the soluble diluents, mannitol was selected as a model soluble diluent considering its advantages in terms of easy availability, cost-effectiveness, negative heat of dissolution and relative moisture insensitivity.

Mouth dissolving tablets of fenofibrate were prepared by sublimation technique, with four subliming agents like menthol, thymol, camphor and ammonium bicarbonate.

Evaluation of precompression properties

For each designed formulation, blend of drug and excipients was prepared and evaluated for precompression properties shown in table 2. Bulk density was found to be between 0.52±0.04 to 0.58±0.01gm/cm^3 and tapped density between 0.67±0.01 to 0.730±0.03 gm/cm^3 for all formulations. From density data % compressibility was calculated and was found to be between 16.1±0.03% to 25.8±0.04 percent. Angle of repose was found to be in the range of 25.1±0.03 to 29.7±0.02. Hausner ratio was found below 1.22±0.02 to 0.35±0.05. Bulkiness was found to be in the range of 1.74±0.02 to 1.89±0.05. All the formulation shows the fair to good flow properties for direct compression and hence tablets were prepared by using direct compression technology.

Evaluation of post compression properties of fast disintegrating tablet

Tablets were prepared using direct compression technique. Since the powder material was free flowing, Tablets were obtained of uniform weight due to uniform die fill, tablets were obtained of uniform weight variations as per Pharmacopoeial specifications. All the tablets were exhibit in white color, odorless, convex in shape with smooth surface with zero defects. The drug content was found in the range of 97.15 – 100.21% (acceptable limit) and the hardness of the tablets between 3.8 – 4.0 kg/cm^2. Friability of the tablets was found below 1 % indicating a good mechanical resistance of tablets. Thickness of the formulations were varied from 2.8±0.02 to 3.2±0.02 mm, diameter of the formulations were varied from 9.7±0.01 to 10.2±0.01 mm. All the parameters were found well within the specified limit (table 3).

Characterization of drug and excipients

The formulation additives in concentrations used did not affect the stability and Ultraviolet absorbance of the drug.

Fourier transform infra red spectroscopy (FTIR)

IR spectra of fenofibrate and its physical mixture with formulation excipients were determined using FT-IR. and are presented in Figure2. Pure fenofibrate spectra showed sharp characteristic peaks at 2990, 1740, 1660, and 1600cm^{-1}.FTIR-spectra of fenofibrate and its physical mixture with excipients are exactly same, and there is no shift of peaks or disappearance of principle peaks or modification of the principle peaks indicating that there is no interaction between the drug and excipients.

Differential Scanning Calorimentry (DSC)

The DSC analysis (Figure 3) of pure fenofibrate showed a characteristic, sharp endotherm peak at 82°C corresponding to its melting point and indicates the crystalline nature of the drug. The DSC analysis of physical mixture of drug and excipients revealed negligible change in the melting point of fenofibrate in the presence excipients, indicating no modification or interaction between the drug and excipients.

On the basis of the results obtained in the preliminary screening studies, the batch containing crospovidone showed the fastest disintegration. Hence, it was selected for further studies. Polyvinylpyrrolidone was used as a binder at a concentration of 10% wt/vol, considering its widespread applicability in the industry.

Subliming agents such as menthol, camphor, thymol and ammonium bicarbonate were used to increase porosity of the tablets in the preliminary tablet formulations. Menthol containing tablets exhibited faster disintegration as compared with tablets containing camphor, thymol and ammonium bicarbonate.

The batches F3 to F8 were prepared using menthol at different concentrations to study its effect on disintegration time. The sublimation time (6-12 hours)

depended on the amount of menthol present initially (0%, 2.5%, 5.0%, 7.5%, 10% and 12.5%). Batch F8 containing 12.5 % menthol showed the least disintegrating time. The results shown in figure 3 to 5 indicate that concentration-dependent disintegration was observed in batches prepared using menthol as a subliming agent. The porous structure is responsible for faster water uptake; hence it facilitates wicking action of crospovidone in bringing about faster disintegration.

Tablets with lower friability (≤0.5%) may not break during handling on machines and/or shipping. The use of a sublimation agent resulted in increased friability probably due to increased porosity. It was decided to incorporate aerosil, extra granularly, at a level of 1% to decrease the friability of the tablets (batches F8 and F10). Addition of aerosil resulted in appreciable decrease in friability and marginal decrease in disintegration time. Aerosil helps to restore the bonding properties of the excipients.

In the first few attempts (F4 to F8), sublimation of menthol was performed from granules prior to compression into tablets. In Batch F10, sublimation was performed after compression rather than directly from granules. The results shown in figure 3 to 5 reveal that sublimation of menthol from tablets resulted in faster disintegration. The compaction process might have caused breakage of porous granules and subsequent reduction in porosity. The low value of wetting time and disintegration time indicate that the porosity of tablets of batch F10 would be greater than batches F3 to F8. The granules required 3 hours of vacuum drying, whereas the tablets required 12 hours of vacuum drying. The longer drying time was required in the case of tablets probably because of the decreased surface area and porosity.

In vitro release studies were carried out using USP tablet dissolution test apparatus paddle method at 37±0.5 ^{o}C, taking 900 ml of 0.1M SLS as dissolution medium. Speed of rotation of the paddle was set at 50 rpm. Aliquots of 5 ml were withdrawn at different time interval and analyzed spectrophotometrically at 290 nm. The *in vitro* dissolution profile (Figure 6 and 7) indicated faster and maximum drug release from formulation F10. Formulation F10 prepared by direct sublimation of menthol from final tablets showed release 95 % drug at the end of 10 min when compared to tablets prepared by sublimation of menthol from granules (F8). The rapid drug dissolution might be due to easy breakdown of particles due to porous structure formation after sublimation of camphor and rapid absorption of drugs into the dissolution medium, and slope values signify that the release rate follows first order kinetics.

Based on *in vitro* release, *in vitro* and *in vivo* disintegration time and wetting time formulation F10 having menthol as sublimating agent in the concentration of 12.5 % was selected as the optimized formulation.

Taste evaluation

Panel of healthy human volunteers for taste masking evaluation using time intensity method, none of the formulation show any bitter taste when tablets are held in the mouth by using time intensity method, which shows excellent taste masking effect of the aspartame and flavors.

Mouth feel

The healthy human volunteers participated in taste evaluation test, were asked to give their opinion about the feeling of smoothness or grittiness of the dispersion soon after the tablet got disintegrated. All the formulations show smooth and pleasant mouth feeling, thus fulfill the requirements of oro-dispersible tablets.

Stability study

The optimized formulation F10 were charged on accelerated stability and monitored for appearance, hardness, friability, drug content, *in vitro* dispersion time, *in vivo* disintegration time, wetting time and dissolution profile study at 1,2 and 3 month. The stability study reveals no significant variation in appearance, color, odor, taste, hardness, friability, drug content, *in vitro* dispersion time, *in vivo* disintegration time, wetting time and *in-vitro* dissolution study up to three months stability studies for F10 formulations at different temperatures. The formulation was stable under accelerated conditions of temperature and humidity (figure 8). The different stages of swelling of fast dissolving tablets are shown in figure 9.

CONCLUSION

In the present investigation we developed mouth dissolving tablets of fenofibrate by using sublimation technique using menthol, camphor, ammonium bicarbonate and thymol as sublimating agent. Sublimation technique using vacuum oven would be an effective alternative approach to use of more expensive adjuvant and sophisticated instruments in the formulation of mouth dissolving tablets. The wetting time or simulated saliva penetration was observed to be very fast with batch F10 tablets. The total drug from the optimized batch was found to be released within the first ten minutes of dissolution study. These tablets rapidly dissolved (within 10-20 sec) in saliva. The prepared tablet gives benefit in terms of patient compliance, low dosing, rapid onset of action, increased bio-availability, low side effect and good stability which make these tablets popular as a dosage form for the treatment of hyperlipidemia.

Table 2: Results of precompression properties

Formulation code	Angle of repose(°)*	Bulk density (gm/cm^3)*	Tapped density (gm/cm^3)*	Carr's index (%)*	Hausner ratio (H_R)*	Bulkiness (cc/g)*
F1	28.0±0.01	0.57±0.01	0.69±0.01	17.6±0.05	1.24±0.04	1.74±0.02
F2	29.7±0.02	0.55±0.02	0.73±0.02	24.7±0.04	1.22±0.05	1.80±0.04
F3	25.1±0.03	0.56±0.03	0.71±0.02	21.1±0.04	1.27±0.04	1.76±0.04
F4	26.1±0.01	0.53±0.02	0.72±0.02	25.8±0.04	1.35±0.05	1.85±0.04
F5	27.5±0.02	0.57±0.02	0.67±0.02	20.8±0.03	1.26±0.04	1.89±0.05
F6	25.1±0.03	0.52±0.04	0.68±0.01	16.1±0.03	1.29±0.04	1.75±0.04
F7	27.5±0.04	0.57±0.03	0.67±0.01	21.6±0.02	1.30±0.02	1.89±0.04
F8	26.1±0.01	0.58±0.01	0.73±0.01	21.1±0.02	1.32±0.01	1.75±0.04
F9	26.0±0.02	0.55±0.01	0.73±0.03	17.6±0.01	1.24±0.01	1.74±0.04
F10	25.1±0.02	0.56±0.02	0.71±0.03	24.7±0.04	1.22±0.02	1.80±0.01

*All values are expressed as mean ± SD, n=3

Table 3: Results of Post Compression Properties of fenofibrate Tablets

Formulation code	Diameter (mm)*	Thickness (mm)*	Hardness (kg/cm^2)*	Friability (%)***	Drug content (%)**	Weight variation (mg)**
F1	10.0±0.01	3.0±0.01	4.0±0.1	0.32±0.01	98.12±0.04	199±0.01
F2	9.8±0.01	3.1±0.02	3.9±0.12	0.45±0.02	98.35±0.05	200±0.01
F3	9.7±0.01	3.2±0.02	4.0±0.05	0.45±0.01	97.15±0.05	198±0.01
F4	10.0±0.02	2.8±0.02	3.9±0.09	0.55±0.04	99.15±0.02	197±0.02
F5	10.1±0.02	2.9±0.02	4.0±0.08	0.61±0.03	100.12±0.03	201±0.02
F6	10.2±0.01	3.0±0.01	3.8±0.01	0.71±0.03	99.45±0.02	202±0.02
F7	10.0±0.02	3.0±0.02	4.0±0.02	0.61±0.03	99.98±0.03	200±0.03
F8	10.0±0.02	2.9±0.01	3.9±0.03	0.38±0.05	101.21±0.02	198±0.03
F9	10.1±0.03	3.0±0.02	4.0±0.04	0.45±0.01	97.56±0.02	198±0.03
F10	10.0 ±0.01	2.8±0.03	4.0±0.06	0.31±0.01	98.32±0.03	197±0.03

*All values are expressed as mean ± SE, n=5; **All values are expressed as mean ± SE, n=20; ***All values are expressed as mean ± SE, n=10.

Figure 1: FTIR spectra of pure fenofibrate and physical mixture of drug and excipients

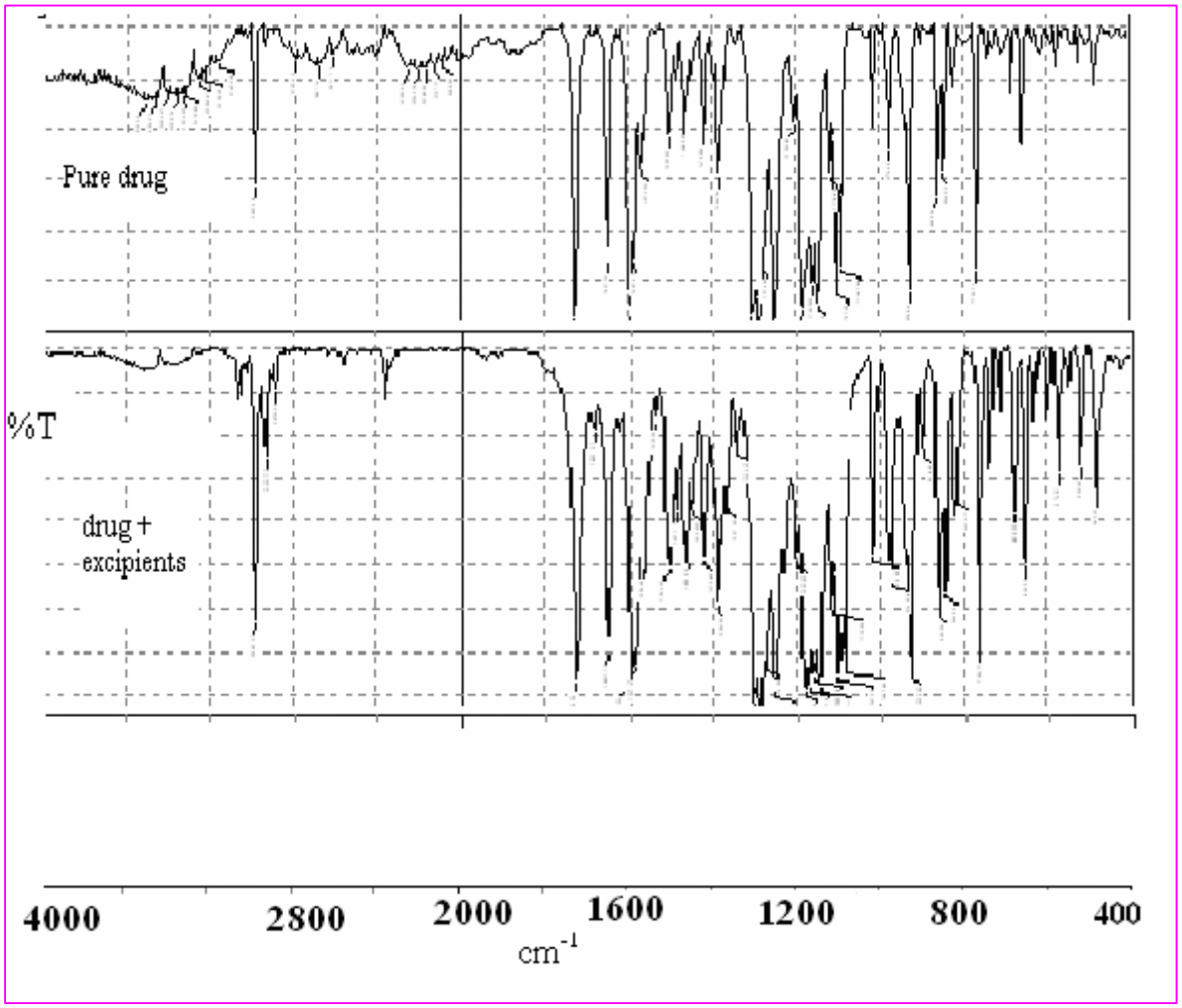


Figure 2: DSC thermograms of pure fenofibrate and physical mixture of drug and

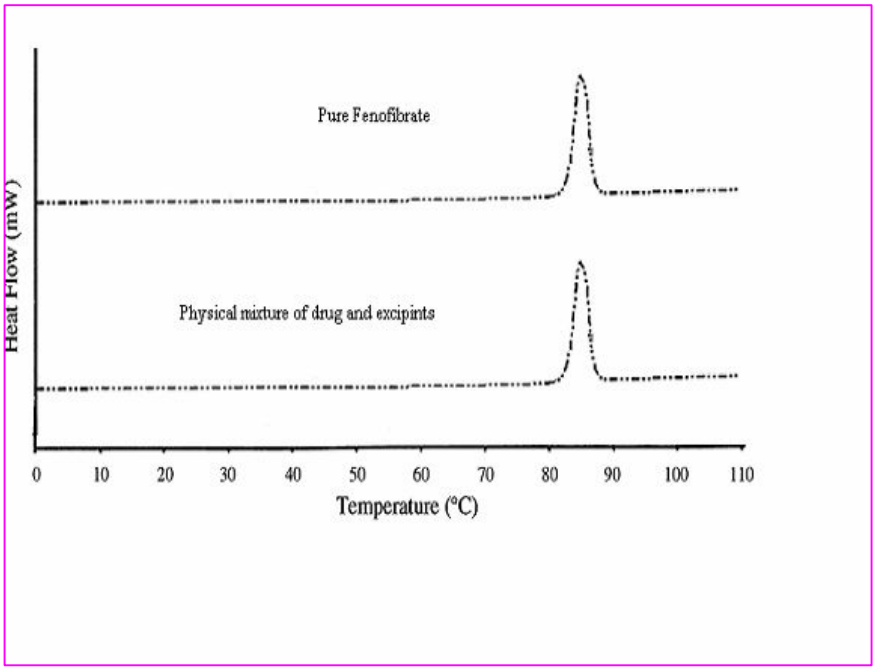


Figure 3: Comparison of *In vitro* disintegration time of various formulations

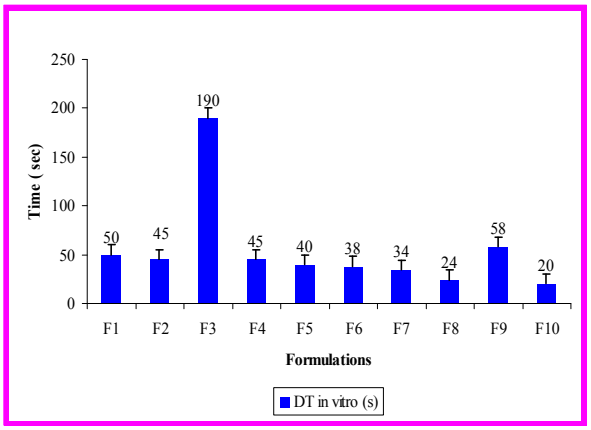


Figure 4: Comparison of wetting time of various formulations

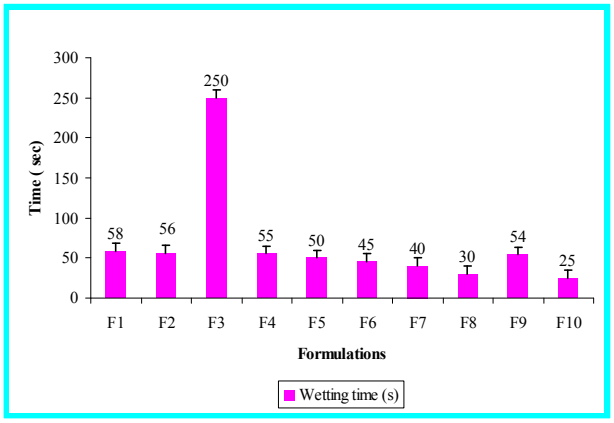


Figure 5: Comparison of *In vivo* disintegration time of various formulations

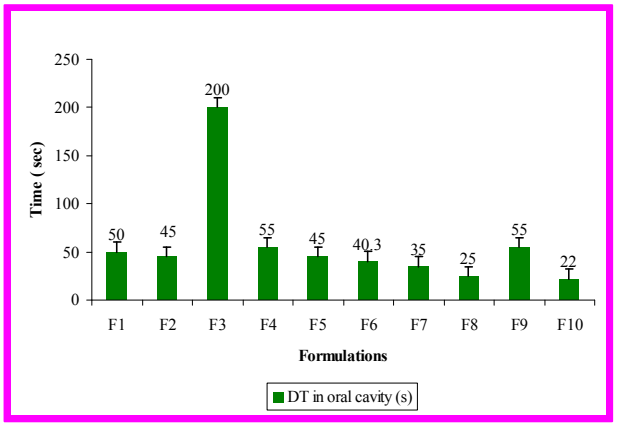


Figure 6: Comparison of *In vitro* release profile of various formulations

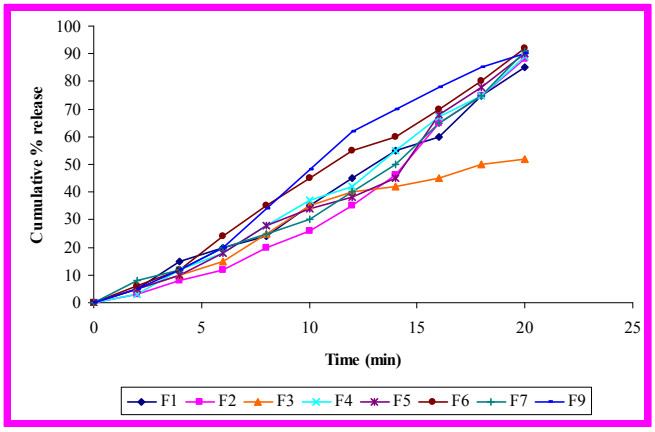
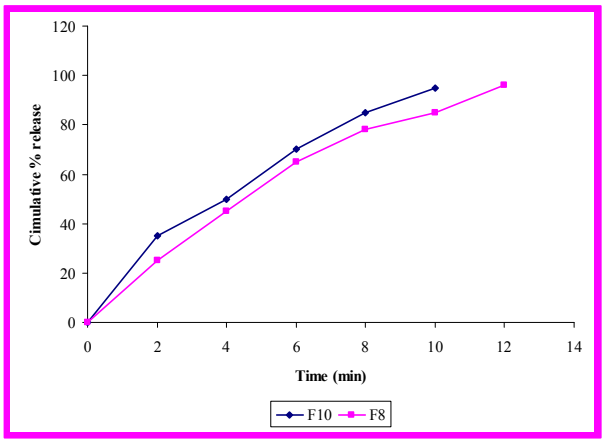


Figure 7: Comparison of *In vitro* release profile of F8* and F10**



F8* camphor (12.5%) sublimed from granules; F10** camphor (12.5%) sublimed directly from the tablet

Figure 8: *In vitro* release profile of optimized formulation (F10) after stability study

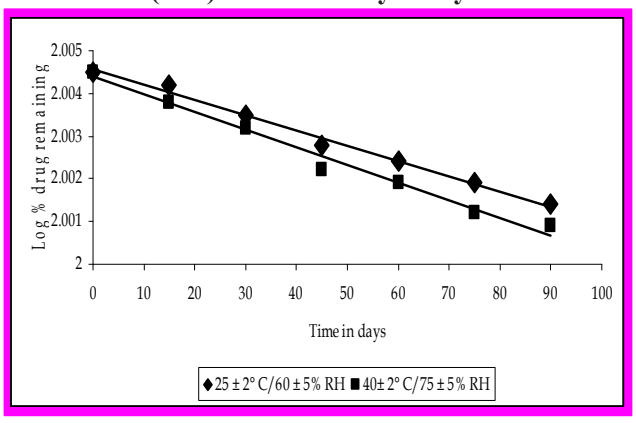
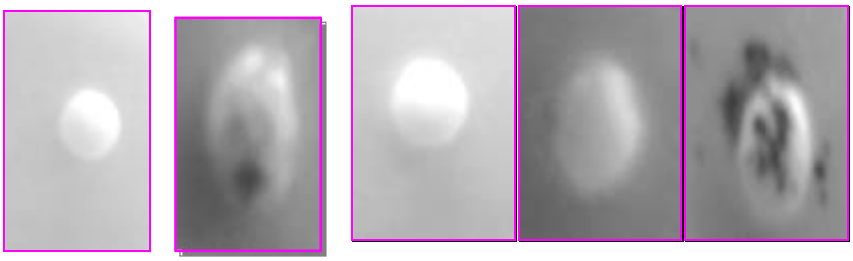


Figure 9: Different stages of Swelling of Fast Dissolving Tablet



ACKNOWLEDGMENT

The authors would like to thank Alembic Research Ltd Vadodara, India for providing gift sample of fenofibrate. The authors also thank Dr.M.B.Patil, Principal, KLES college of Pharmacy, Ankola for providing all the facilities and encouragement for the research work.

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