Research Article
CODEN (USA): IJPLCP

ISSN: 0976-7126
Sharma *et al.*, 11(5):6580-6589, 2020

International Journal of Pharmacy & Life Sciences
Open Access to Researcher
©2010, Sakun Publishing House and licensed by IJPLS, This is Open Access article which permits unrestricted non-commercial use, provided the original work is properly cited.

Formulation and Evaluation of Sublingual Tablet of Solid Dispersion of Raloxifene Hydrochloride

Pravin Kumar Sharma*, Aparna Badoliya, Ravi Sharma and G.N. Darwhekar

Acropolis Institute of Pharmaceutical Education and Research, Indore (M.P.) - India

Article info

Received: 11/03/2020

Revised: 25/04/2020

Accepted: 18/05/2020

© IJPLS

www.ijplsjournal.com

Abstract

Raloxifene Hydrochloride is an oral selective estrogen receptor modulator (SERM) which is used to treat and prevent osteoporosis and breast cancer in postmenopausal women. It has very low oral bioavailability of approximately 2% due to extensive first pass metabolism and poor aqueous solubility. The present investigation was aimed to develop the sublingual tablet containing solid dispersion of Raloxifene Hydrochloride to improve its oral bioavailability. Solid dispersions of drug were prepared by using different hydrophilic polymer such as HPMC, Eudragit S100, PEG 6000 by solvent evaporation and physical mixing method. Solid dispersions prepared with HPMC (SD7) by solvent evaporation method found best based on improvement in aqueous solubility, % drug content and % yield. Sublingual tablet containing solid dispersion was prepared by direct compression method by using cross povidone as super disintegrating agent. Powder blend of all the formulation before compression was evaluated for bulk density, tapped density, Carr's index, Hausners ratio, angle of repose and was found to be free flowing.

Prepared tablets were evaluated for thickness, hardness, weight uniformity, friability, wetting time, water absorption ratio, % drug content, dispersion time, *in-vitro* drug release study and stability studies. Results of *in-vitro* drug release studies revealed improved i.e 97.12±59% drug release and dissolution up to 30 min.

Keywords: Raloxifene Hydrochloride, Solid Dispersion, Sublingual Tablet, Bioavailability

Introduction

Oral delivery of drugs is most popular and preferred method due to its convenience and ease of administration.[1] However, very low bioavailability has been observed for the drugs which have poor aqueous solubility and dissolution.[2] In addition, poor bioavailability has been observed for the drugs which suffers from extensive first pass metabolism.[3,4] Many techniques have been exploited to increase the water solubility of poorly soluble drugs such as particle size reduction, nanosuspensions, salt formation, use of surfactants, hydrotropy, co-solvency, solid dispersion, inclusion complexation, liquisolid technique and prodrug formation.[5]

However, solid dispersion method is most successfully used technique to improve the aqueous solubility, dissolution rates and subsequently the bioavailability of poorly water soluble drugs.[6,7]

***Corresponding Author**
E.mail: praveensharma910@gmail.com

On the other hand, sublingual tablet generally found to have a rapid onset of action in comparison with other conventional solid dosage forms. Moreover, absorption of drug through sublingual route bypass the process first pass metabolism.[4,8]

Raloxifene Hydrochloride has estrogenic actions on bone and anti-estrogenic actions on the uterus and breast. It is very well recommended for treatment of osteoporosis and breast cancer.[3,4] Raloxifene Hydrochloride belongs to BCS class II drugs and it has very low oral bioavailability due to poor aqueous solubility and extensive first pass metabolism in the liver by glucuronidation and enterohepatic cycling.[9,10] The objective of the present investigation was to formulate the sublingual tablets of solid dispersion of Raloxifene Hydrochloride for improving its oral bioavailability by enhancing its aqueous solubility and by avoiding problem of extensive first pass metabolism.

Material and Methods

Raloxifene Hydrochloride was obtained as gift sample from Cadila Pharmaceuticals Ltd. Ahmedabad (Gujarat). All other chemicals were purchased from Loba Chemie, Mumbai (Maharashtra).

Preformulation Studies:

Determination of Melting Point

It was determined by using melting point apparatus. The drug sample was placed in a thin walled capillary tube. The tube was approximately 10-12 cm in length with 1mm in diameter and closed at one end. The capillary was placed in melting point apparatus and heated and when drug sample was melted the melting point of sample powder was recorded.[11]

Identification of drug sample by FTIR

FTIR spectrum was recorded of pure drug. The sample was analyzed by KBr pellet method using FTIR spectroscopy. About 10mg of Raloxifene Hydrochloride mixed with potassium bromide of equal weight. The spectrum was scanned over a frequency 4000 -400 cm $^{-1}$range.[12]

Determination of solubility of Raloxifene Hydrochloride in various medium

The solubility of Raloxifene Hydrochloride in various medium was determined by equilibrium solubility method. In this method 5 ml of each solvent was taken into a separate vial and excess amount of Raloxifene Hydrochloride was added in to vials containing distilled water and phosphate buffer pH 6.8. The vials put on mechanical stirrer at 37±2°C for 12 hrs. The solutions were allowed to equilibrate for next 24 hrs. The solution was transferred into eppendroff tubes and centrifuged for 5 min at 2000 rpm. And supernatants of each vial were filtered with 0.45µ membrane filter. Then made appropriate dilutions and analyzed by UV visible spectrophotometer (UV-1800, Shimadzu 1800, Japan) at 287nm.[13]

Drug-excipient interaction study

The compatibility of the drug with excipient was assessed by drug-excipient interaction study. The drug was mixed with various excipients in a 1:1 ratio in glass vials which were properly sealed and kept undisturbed at 40°C temperature for 14 days. After 14 days incompatibility (if any) was confirmed by TLC (William H et al 2012).[14]

Formulation and Development:

Preparation of solid dispersion

Solid dispersions of Raloxifene Hydrochloride with different polymers (HPMC, Eudragit S100 and PEG 6000) containing four different ratios (1:1, 1:2, 1:3, 1:4 w/w) were prepared by the solvent evaporation method and physical mixing.

Physical mixing method

Raloxifene Hydrochloride and polymers were weighed separately according to required ratio and passed through sieve no. 80. Sieved mass was collected, triturated in pestle and mortar for 5 min and then passed through sieve no. 80 and evaluated for drug content, % yield and *in-vitro* dissolution.[15]

Solvent evaporation method

Raloxifene Hydrochloride and the polymers were dissolved in 5 ml of methanol. Solution was stirred on magnetic stirrer for 30 min and dried at the temperature of 50°C in hot air oven. After drying, residue was ground in a mortar and sieved through mesh #60.[15]

Formulation of sublingual tablet of solid dispersion of Raloxifene Hydrochloride

It was found that the solid dispersion of Raloxifene Hydrchloride with HPMC in ratio of 1:3 (SD7) was more efficient as compared to ratios of same and different polymers. So SD7 was used in preparation of Sublingual tablets. Sublingual tablets were prepared by direct compression method. Microcrystalline cellulose

and cross povidone was used as superdisintegrants in different ratio. Polyvinyl pyrollidone and magnesium stearate was added as binding agent and glidant respectively. Since the dosage form is to be kept under tongue, tablet should contain such ingredients which makes dosage form more palatable so sweetening agents such as mannitol and saccharine were used in formulation. Overall details of formulation of sublingual tablet are shown in table 1. All the ingredients are passed through mesh #60 and were mixed according to their geometric dilution. Mixed blends were evaluated for pre granulation test such as bulk density, tapped density, angle of repose etc. Compress final blend using D-Tooling, multiple rotatory compression machine using 10mm round shaped punches and corresponding dies.[3,16,17]

Table 1: Formulation for sublingual tablet of solid dispersion Raloxifene Hydrochloride

Ingredients	Formulation Code					
	F1	F2	F3	F4	F5	F6
Selected solid dispersion of Raloxifene Hydrochloride (mg)	240	240	240	240	240	240
Mannitol (mg)	100	100	100	100	100	100
Sodium saccharine (mg)	8	8	8	8	8	8
Magnesium stearate (mg)	5	5	5	5	5	5
Cross povidone (mg)	-	2	4	8	12	16
Polyvinyl pyrollidone (mg)	7	7	7	7	7	7
Microcrystalline cellulose (mg)	90	88	86	84	82	80
Total Weight (mg)	450	450	450	450	450	450

Evaluation of pre compression parameter of sublingual tablets:[18,19]

Angle of repose

The angle of repose of powder blend was measured by the funnel method. The accurately weighed powder blend was taken in glass funnel. The height of the funnel was maintained in the funnel touches the heap of the powder blend. The powder blend was passed to flow through funnel and dropped onto the surface. The diameter of the powder cone was determined and angle of repose was calculated used the following equation.

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

Where, h= height of the cone.
r = radius of the cone.

Bulk Density

Bulk density ρ_b is defined as the mass of the powder divided by the bulk volume and is expressed as g/cm^3. Accurately weighed quantity of powder blend from each formulation was taken in a measuring cylinder and the initial volume of the powder blend (V_b) in the measuring cylinder was noted. This was calculated by using below given formula.

$$P_b = M / V_b$$

Where,
ρ_b - Bulk density
M - Weight of the sample in g
V_b- volume of the blend in ml

Tapped Density

It is the ratio of total weight of the powder to the tapped volume of powder. The volume was measured by tapping the powder blend for 50 times and the tapped volume was noted. Tapped density of powder was calculated using the following formula:

$$P_t = M / V_t$$

Where,
ρ_t-Tapped density,
M - Weight of the sample in g
V_t - Tapped volume of blend in ml

Compressibility index and Hausners ratio

The compressibility index of the powder blend was measured by Carr's index and the Hausner's ratio is calculated by using the formula

Hausner's Ratio = Tapped density / Bulk density

Carr's compressibility index (%) = [(Tapped density-Bulk density/Tapped density) × 100]

Evaluation of solid dispersion of Raloxifene Hydrochloride:

Solubility determination

The sample of solid dispersion equivalent to 10 mg of Raloxifene Hydrochloride was added to 10 ml of distilled water and phosphate buffer pH 6.8. It is shaken well and kept for 24 hrs. The solution was filtered and analyzed using UV-Visible spectrophotometer (UV-1800, Shimadzu, Japan) after suitable dilution at 287nm.[20]

% Drug content of solid dispersion

Solid dispersion equivalent to 10 mg of Raloxifene Hydrochloride was weighed and dissolved in 10 ml of methanol. The solutions were filtered through filter paper and diluted suitably. The drug content in solid dispersion was calculated by using UV-Visible spectrophotometer (UV-1800, Shimadzu, Japan) at 287nm.[3,21]

Evaluation of post compression parameter of sublingual tablet:

Thickness

Twenty tablets were randomly selected from formulation and thickness was measured individually by screw gauge. The result was expressed in millimeters.[22]

Hardness

The crushing strength of tablet was measured using a Monsanto Hardness Tester. Tablets to be placed were held between a fixed and a moving jaw of Monsanto hardness test apparatus. The screw knob was moved clockwise until the tablet breaks and the force required breaking the tablet was noted. Three tablets of each formulation batch were taken randomly, tested and the average reading was recorded.[18]

Weight uniformity

Twenty tablets were randomly taken from each batch and their average weight was determined. Then individual weight was compared with average weight. The weight was measured using weighing balance.[22]

Friability

Friability test was performed by using Roche friabilator. Ten tablets were weighed and place in the friabilator, which was then operated for 25 rpm. After 4 min (100 revolutions) the tablets were dusted and reweighed. Then percentage friability was calculated.[18]

Wetting time

The tablet was placed at the center of two layers of tissue adsorbent paper fitted into a petri dish. After the paper was wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.[22]

Water absorption ratio

The piece of tissue adsorbent paper was folded twice was placed in a small petri dish containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wetting. The wetted tablet was again weighed. Water absorption ratio, R was determined using following equation

$$R = 100 \times (W_a - W_b)/W_a$$

Where,

W_a = Weight of tablet after water absorption

W_b = Weight of wetted tablet before water absorption.[22]

% Drug content determination

5 tablets from each of the formulations were taken and triturated. Triturated powders equivqlent to 10mg of Raloxifene Hydrochloride were weighed and dissolved in 10ml of methanol. The solutions were filtered through filter paper and diluted suitably. The drug content in solid dispersion was calculated by using UV-Visible spectrophotometer (UV-1800, Shimadzu, Japan) at 287nm and the % drug content was calculated.[3]

***In-vitro* Dispersion Time**

Tablet was added to 10ml of phosphate buffer pH 6.8 at 37±0.5°C. Time required for complete dispersion of a tablet was measured.[23]

***In-vitro* drug release study**

The *in-vitro* drug release study of formulated sublingual tablets F1-F6 was carried out using USP dissolution apparatus type II (Electro Lab Dissolution Tester USP II) at 50 rpm. A temperature of 37±0.5 ^{0} C was maintained throughout the study. The dissolution test was carried out using 300ml of saline phosphate pH 6.8. A sample (5 ml) of the aliquot was withdrawn from the dissolution apparatus at 2, 4, 6, 8, 10, 12 and 14min. The samples were replaced with fresh dissolution. The samples were filtered through Whattman filter paper and analyzed using UV-Visible spectrophotometer (UV-1800, Shimadzu,

ISSN: 0976-7126
Sharma *et al.*, 11(5):6580-6589, 2020

Japan) at 287nm and the percentage drug release was calculated.[3]

Stability studies

The stability studies were carried out for a period of 1 month in the stability chamber. The tablets were stored under the conditions as prescribed by the ICH guidelines (40°C±2°C and 75±5% RH, Q1C). The tablets were withdrawn periodically with an interval of 30 days and analyzed for weight uniformity, hardness, % drug content, wetting time and dispersion time.[22]

Results and Discussion

Preformulation Study:

Melting point determination

Melting point of Raloxifene Hydrochloride was determined using capillary tube method and found to be 180±3^{0}C.

Identification of drug sample by FTIR

The prominent FTIR peak of Raloxifene Hydrochloride is shown in table 2 and FTIR spectrum of Raloxifene Hydrochloride and its solid dispersion is shown in figure 1 and 2 respectively. Results indicated that all the peaks matched with that of standard FTIR of Raloxifene Hydrochloride. There was no incompatibility found in solid dispersion form of drug.

Table 2: Prominent peaks of FTIR Spectrum of Raloxifene Hydrochloride

S. No.	FTIR Absorption peak	Chemical group
1	1597	C-O-C stretching
2	1643	C=O stretching

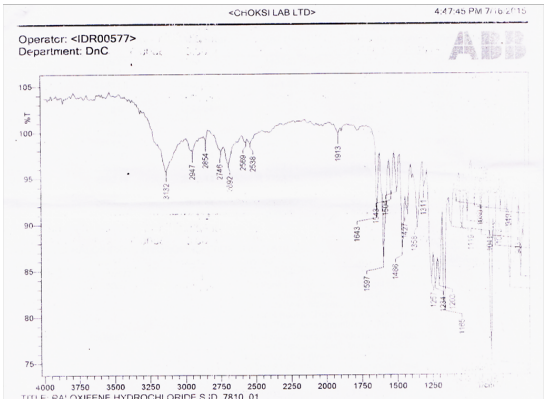

Fig. 1: FTIR Spectrum of Raloxifene Hydrochloride

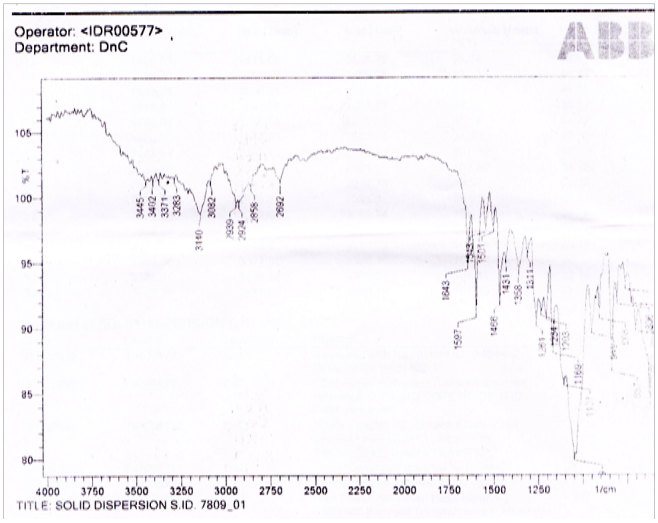

Fig. 2: FTIR Spectrum of solid Dispersion of Raloxifene Hydrochloride

Determination of solubility in various mediums

The solubility of Raloxifene Hydrochloride in various mediums was studied and the results of study are shown in table 3. Results indicated the poor aqueous solubility of drug.

Table 3: Solubility study data of Raloxifene Hydrochloride in various mediums

S. No.	Solvent	Solubility of Raloxifene Hydrochloride (µg/ml)
1	Distilled water	5.06µg/ml
2	Phosphate buffer (pH) 6.8	474.19µg/ml

Drug-excipient interaction study

Results of drug-excipient interaction study are shown in table 4. Raloxifene Hydrochloride was found to be compatible with various excipients which were selected for formulation of sublingual tablets. The compatibility was assessed by TLC and the retention factors of all ratios found similar.

Table 4: Data of drug-excipients interaction study

S. No.	Drug/ drug+ Excipient Ratio (1:1)	Present Day (Rf)	After 8 Days (Rf)	Inference
1	Drug (Raloxifene HCL)	0.551	0.551	No Change
2	Drug + HPMC	0.543	0.543	No Change
3	Drug + Sodium Saccharine	0.530	0.530	No Change
4	Drug + Cross Povidone	0.548	0.548	No Change
5	Drug + Polyvinyl Pyrollidone	0.550	0.550	No Change
6	Drug + Microcrystalline Cellulose	0.566	0.566	No Change
7	Drug + Mannitol	0.616	0.616	No Change
8	Drug + Magnesium Stearate	0.583	0.583	No Change

Formulation and Development

Preparation of Solid dispersion

It was attempted to improve the aqueous solubility of Raloxifene Hydrochloride by solid dispersion technique. Based on the results of solubility, % yield and drug content, HPMC (1:3 drug to polymer ratio using solvent evaporation method) shown remarkable increase in aqueous solubility and highest drug content. Thus HPMC (1:3 drug to polymer ratio) was selected as best carrier for preparation of solid dispersion of Raloxifene Hydochloride using solvent evaporation method.

Formulation of sublingual tablets of solid dispersion of Raloxifene Hydrochloride

The different formulation of sublingual tablet of selected solid dispersion of Raloxifene Hydrochloride was prepared by direct compression method.

Evaluation of pre compression parameter of sublingual tablets

The bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose of selected formulations were performed and results are shown in table 5. All the results show that the final formulations possess a good flow property.

Table 5: Various flow properties of formulation (n=3)

Evaluation	F1	F2	F3	F4	F5	F6
Bulk density	0.418±0.3	0.452±0.5	0.456±0.4	0.463±0.6	0.459±0.2	0.461±0.5
Tapped Density	0.584±0.4	0.668±0.3	0.672±0.3	0.632±0.2	0.663±0.4	0.658±0.2
Carr's Index	27.20±0.02	29.97±0.04	31±0.06	29.32±0.02	25.30±0.03	26.3±0.05
Hausner's Ratio	1.42	1.45	1.43	1.43	1.41	1.38
Angle of Repose	40±0.42	39.2±0.16	36.4±0.57	37.2±0.76	35.2±0.45	34±0.73

Evaluation of solid dispersion of Raloxifene Hydrochloride:

Solubility and % drug content determination

Results of solubility studies and drug content are shown in table 6 and it revealed remarkable increase in the aqueous solubility of Raloxifene Hydrochloride (Rlx) in SD7 batch.

Table 6: Evaluation of Solid Dispersion (n=3)

S. No.	Composition	Ratio	Method	% yield	Percent drug content	Aqueous Solubility (µg/ml)
SD1	Rlx:HPMC	1.1	Physical Mixing	63.1±1.7	65±2.3	14.8±0.9

ISSN: 0976-7126
Sharma *et al.*, 11(5):6580-6589, 2020

SD2	Rlx:HPMC	1:2	Physical Mixing	56.5±1.5	67±1.5	207.6±1.7
SD3	Rlx:HPMC	1:3	Physical Mixing	68.3±2.1	66±3.3	209.6±1.9
SD4	Rlx:HPMC	1:4	Physical Mixing	65.1±1.3	62±.90	0.570±0.8
SD5	Rlx:HPMC	1.1	Solvent Evaporation	86.2±1.9	86±2.7	152±1.02
SD6	Rlx:HPMC	1:2	Solvent Evaporation	91.23±0.9	91.0±3.4	309.6±0.7
SD7	Rlx:HPMC	1:3	Solvent Evaporation	93.5±1.2	92.67±1.5	317.6±2.1
SD8	Rlx:HPMC	1:4	Solvent Evaporation	89.8±0.7	89±1.7	1.382±0.6
SD9	Rlx:Eudragit S100	1.1	Solvent Evaporation	70.6±0.9	83.26±1.8	78.4±1.1
SD10	Rlx:Eudragit S100	1:2	Solvent Evaporation	75.2±1.3	86.6±2.7	95.8±0.9
SD11	Rlx:Eudragit S100	1:3	Solvent Evaporation	82.1±0.8	89.7±4.1	160.4±1.5
SD12	Rlx:Eudragit S100	1:4	Solvent Evaporation	79.7±1.2	84.1±0.98	199.8±1.7
SD13	Rlx:PEG 6000	1.1	Solvent Evaporation	83.1±0.8	82.6±0.62	104.6±0.7
SD14	Rlx: PEG 6000	1:2	Solvent Evaporation	85.6±1.5	83.9±1.6	147.6±1.2
SD15	Rlx: PEG 6000	1:3	Solvent Evaporation	87.6±0.7	85.6±5.2	181.6±0.8
SD16	Rlx: PEG 6000	1:4	Solvent Evaporation	85.2±0.9	88.3±3.6	194.8±1.1

Evaluation of sublingual tablets of Raloxifene Hydrochloride

The results of various evaluated parameters like weight variation, thickness, friability, hardness, % drug content, wetting time, water absorption ratio and dispersion time are shown in table 7.

Table 7: Post compression evaluation of parameters sublingual tablets of Raloxifene Hydrochloride (n=3)

Formulation	F1	F2	F3	F4	F5	F6
Weight uniformity (mg)	450±3.2	450±4.5	446.8±2.3	450.3±4.8	452±3.9	447±4.3
Thickness (mm)	4.27±0.07	4.25±0.6	4.26±0.05	4.24±0.06	4.24±0.04	4.26±0.05
Friability %	0.69±0.02	0.36±0.03	0.68±006	0.42±0.04	0.46±0.03	0.43±0.04
Hardness (kg/cm^2)	3.6±0.14	3.6±0.16	3.2±0.2	3.5±0.16	3.2±0.22	3.2±0.24
Wetting time(sec)	95±5	97±4	93±2	92±7	94±4	89±3

ISSN: 0976-7126
Sharma *et al.*, 11(5):6580-6589, 2020

Water Absorption Ratio (%)	70±2.6	72±1.2	74±2.4	73±2.4	71±1.9	69±1.4
Dispersion Time (sec)	55±1.23	44.5±0.76	42.3±1.32	51±0.94	45±0.82	39±0.24
Drug Content (%)	92.35±0.65	92.57±0.40	91.13±0.11	92.87±0.59	91.38±0.92	93.56±0.19

In-vitro drug release study

Result of *in-vitro* drug release study is shown in figure 3. It revealed that the formulation F6 showed highest drug release of 97.12±59% up to 30 min. It suggested increase in the drug release with increasing the concentration of cross povidone. All other formulation also showed more than 90% drug release up to 30min.

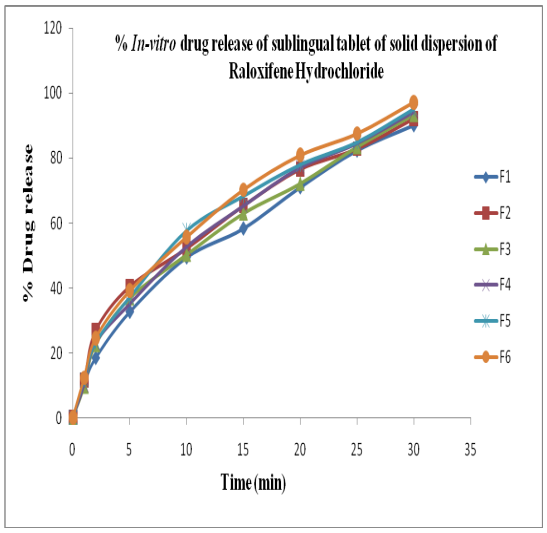

Fig. 3: Percentage drug release from sublingual tablets formulation

Stability studies

Results of the stability studies are shown in table 8.The stability studies F6 Formulation were carried out for a period of 1 month in the stability chamber. The tablets were stored under the following condition as prescribed by the ICH guidelines (40°C±2°C and 75±5%RH, Q1C). The tablet were withdrawn periodically with an interval of 30 days and analyzed for weight uniformity, hardness, % drug content, wetting time and dispersion time. Overall result of the study suggested the good stability of the formulation.

Table 8: Stability study for fast dissolving tablet of Formulation batch (F6)

Parameter	0 days	15 days	30 day	Result
Weight uniformity (mg)	447.1±0.39	447.1±0.39	447.1±0.39	No change
Hardness (kg/cm^2)	3.2±0.15	3.2±0.15	3.2±0.15	No change
Drug content (%)	93.56±0.24	93.54±0.24	93.50±0.20	Some change
Wetting time (sec)	89±1	88±1	88±1	No change
Dispersion time (sec)	39±3	39±3	40±3	No change

Conclusion

The present investigation was aimed to develop the sublingual tablet of solid dispersion of Raloxifene Hydrochloride. Solid Dispersions of Raloxifene Hydrochloride were prepared with different hydrophilic polymer and method, out of which HPMC (SD7) was selected as best polymer and solvent evaporation method as found be best based on the results of % yield, % drug content and solubility. Sublingual tablet containing solid dispersion was prepared by direct compression method and evaluated for pre compression and post compression evaluation parameters. It revealed that the formulation F6 showed highest drug release of 97.12±59% up to 30 min. It suggested increase in the drug release with increasing the concentration of cross povidone. Stability study also suggested good stability of the formulation.

References

1. Patil A. and Kumar S. (2017). Formulation and evaluation of solid dispersions of an anthelmintic drug for enhancement of dissolution rate, Journal of Innovations in Pharmaceutical and Biological Sciences, 4(3): 71-74.
2. Pandya B.R., Chotai N.P., Suthar R.M. and Patel H.K. (2017). Formulation, *in-*

vitro evaluation and optimization of nanoemulsion of Raloxifene Hydrochloride, International Journal of Pharmaceutical Research, 9(2): 38-48.

3. Kakde M.G. (2013). Formulation and evaluation of sublingual tablets of Raloxifene Hydrochloride, JPR:BioMedRx: An International Journal, 1(8): 826-832.
4. Maghraby G.M.E. and Ghanem S.F. (2016). Preparation and evaluation of rapidly dissolving tablets of Raloxifene Hydrochloride by ternary system formation, International Journal of Pharmacy and Pharmaceutical Sciences, 8(1): 127-136.
5. Alam A., Das S.S., Hussain A. and Faruk A. (2018). Formulation and evaluation of solid dispersion and inclusion complex of poorly aqueous soluble Diacerein, Juniper Online Journal Material Science, 5(1): 001-009.
6. Chowdhury R., Anjum R., Siddiqui S.A., Rahman M.Z., Sharmin T. and Rashid M.M.O. (2017). Formulation and evaluation of Aceclofenac solid dispersion for improving the solubility and dissolution rate, International Journal of Pharmaceutical Science Invention, 6(10): 30-34.
7. Krishnan S.K., Ashwini G. and Ahmed M.G. (2015). Formulation and evaluation of matrix tablets of Verapamil Hydrochloride by solid dispersion method, World Journal of Pharmaceutical Research, 4(9): 1088-1107.
8. Madhagi W.A., Albarakani A.A., Alhag A.K., Saeed Z.A., Noman N.M. and Mohamed K. (2017). Formulation and evaluation of new Glimepiride sublingual tablets, Journal of Pharmaceutics, doi.org/10.1155/2017/3690473: 1-5.
9. Patil P.H., Belgamwar V.S., Patil P.R. and Surana S.J. (2013). Enhancement of solubility and dissolution rate of poorly water soluble Raloxifene using microwave induced fusion method, Brazilian Journal of Pharmaceutical Sciences, 49(3): 571-578.
10. Prasanthi N.L., Manikiran S.S. and Rama R. N. (2010). Formulation and characterization of fast-dissolving tablets of Raloxifene Hydrochloride, International Journal of Pharmaceutical Sciences and Drug Research, 2(1): 55-57.
11. Kala S. and Juyal D. (2016). Preformulation characterization studies of Aceclofenac active ingredients. The Pharma Innovation Journal, 5(9): 110-119.
12. Kaur L., Bala R., Kanojiya N. and Nagpal M. (2014). Formulation development and optimization of fast dissolving tablet of Aceclofenac using natural superdisintegrants, Hindawi Publishing Corporation ISRN Pharmaceutics, dx.doi.org/10.1155/2014/242504: 1-10.
13. Jain D.K. and Darwhekar G.N. (2013). Osmotically regulated asymmetric capsular system for sustained delivery of Indomethacin, Journal of Pharmaceutical Investigation, 43:27-35.
14. William H., Devi B.P., Kurien J., Valsalakumari P.K. and Mohandas C.K. (2014). validated high performance thin layer chromatographic estimation of Aceclofenac in bulk and pharmaceutical dosage forms, International Journal of Science and Research, 3(6): 2613-2617.
15. Sridhar I. and Doshi A. (2013). Solid Dispersions: an Approach to enhance solubility of poorly water soluble drug, Journal of Scientific and Innovative Research, 2(3): 685-694.
16. Parmar T.B. and Prajapati T.K. (2014). Formulation and evaluation of sublingual tablet of Valsartan, International Journal of Pharmaceutical Research and Bio-Science, 3(2): 969-989.
17. Patel R.J. and Patel B.N. (2014). Formulation and evaluation of Felodipine sublingual tablet, World Journal of Pharmacy and Pharmaceutical Sciences, 3 (6): 850-864.
18. Manorama P., Trivikram B.M., Kumar K. and Bala K. (2012). Formulation and evaluation of Aceclofenac fast disintegrating tablets in the design

hordeum vulgari hull, Journal of pharmacy research., 5(1): 657-660.
19. Michael E. Aulton (2007). Pharmaceutics "The design and manufacture of medicine"3 rd edition, page no.355.
20. Deshmukh R.K. and Jain K.S. (2012). Development of Aceclofenac mouth dissolving tablet using solid dispersion technique: *In-vitro* evaluation, Indian Journal of Pharmaceutical Education and Research, 46(2): 97-104.
21. Kothawade S.N., Kadam N.R., Aragade P.D. and Baheti D.G. (2010). Formulation and characterization of Telmisatan solid dispersions, International Journal of PharmTech Research, 2(1): 341-347.
22. Dave V., Yadav R.B., Ahuja R., Yadav S. **(**2017). Formulation design and optimization of novel fast dissolving tablet of Chlorpheniramine maleate by using lyophilization technique, Bulletin of Faculty of Pharmacy, Cairo University, 55(1): 31-39.
23. Aher S.B. and Gahide K.S. (2015) Fast dissolving tablets: Review, Indo American Journal of Pharmaceutical Sciences, 2(4): 815-826.

Cite this article as:
Sharma P.S., Badoliya A., Sharma R. And Daewhekar G.N. (2020). Formulation and Evaluation of Sublingual Tablet of Solid Dispersion of Raloxifene Hydrochloride**,** *Int. J. of Pharm. & Life Sci.,* 11(5): 6680-6689.
Source of Support: Nil
Conflict of Interest: Not declared
For reprints contact: ijplsjournal@gmail.com