International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 14, Issue 5, 2022

Original Article

FORMULATION, *IN VITRO* AND *IN VIVO* EVALUATION OF PALBOCICLIB SOLID DISPERSIONS

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Received: 26 Dec 2021, Revised and Accepted: 11 Jun 2022

ABSTRACT

Objective: The current research is aimed to enhance the dissolution and bioavailability of Palbociclib by formulating into solid dispersion

Methods: The Palbociclib solid dispersions (SD) prepared by adopting different methods: Surface solid dispersion technique (SSD1-SSD15), Melt granulation (MG1-MG15) and Liquisolid compacts (LSC1-LSC9). All formulations were evaluated for physico-chemical parameters followed by *in vitro* dissolution studies. The optimised formulation was subjected to bioavailability studies in rats.

Results: The results indicated that the prepared formulation satisfactory results for all the evaluated parameters. The SD formulations prepared by liquisolid compact and Melt Granulation technique (LSC1 and MG 3) displayed maximum dissolution of 99.64% and 99.58%. The FTIR of LSC1 displayed no interaction among drug and excipients while XRD, SEM displayed amorphous nature of drug in formulation. The stability study results indicated that LSC 1 was stable over 3 mo. The *in vivo* bioavailability studies conducted on rats indicate that at any time point, the drug plasma concentrations in animals administrated with the SD formulation was higher than pure drug. The C_{max} of the palbociclib SD was 970.76±1.22 ng/ml and was significant ($p<0.05$) when compared to pure drug suspension formulation (105.84±0.19 ng/ml). The T_{max} of both SD formulation and pure drug were 2.0±0.04 and 4±0.01 h, respectively. The $AUC_{0-\infty}$ for SD was higher 7816.61±1.37 ng. h/ml) than the pure drug suspension 2501.4±1.46 ng. h/ml indicating better systemic drug absorption from SD formulation prepared using Melt granulation technique.

Conclusion: A significant enhancement *in vitro* dissolution profile and bioavailability of the melt granules was observed compared to the pure Palbocicilib and marketed product.

Keywords: Palbociclib, Chemotherapeutic agent, Solid dispersion, Liquisolid compact technique, Melt granulation, *In vivo* bioavailability studies

DOI: https://dx.doi.org/10.22159/ijap.2022v14i5.43992. Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

An interminable confront in the pharmaceutical industry is associated with deprived solubility of the majority of drugs. This setback and be conquered with various technologies but none were proved to be a potent one. Solid dispersion (SD) is a solubilization technique accentuating basically on drug dispersion and its stability. Therefore, this technology has been realized as an extremely useful tool in improving the dissolution properties of poorly water-soluble drugs [1].

Solid dispersion (SD) is defined as "the dispersion of one or more active ingredients in inert carriers at solid state prepared by fusion, solvent or solvent fusion methods etc" [2].

On exposing to aqueous media, the carrier dissolve and the drug is released as the fine colloidal particle. This increases the surface area of dissolution rate and hence the bioavailability of poorly water-soluble drugs. Drug dispersed in hydrophilic carriers experience improved dissolution due to a reduction in particle size and increase in particle porosity, thus increasing bioavailability and reducing side effects [3, 4].

Palbociclib (Ibrance, PD-03329, France), the first-in-class oral, small molecular, reversible CDK4 and 6 inhibitors, was granted approval by USFDA in February 2015 following the Phase II (PALOMA-II/TRIO-18 trials) and regular approval on March 31, 2017, for treating hormone receptor (HR) positive, human epidermal growth factor receptor (HER2) negative advanced breast cancer in postmenopausal women [5, 6]. It acts by blocking the transition of cells from G1-S phase, thereby reducing the proliferation of oestrogen receptor-positive breast cancer cells. In humans, the PK of Palbociclib is characterized by slow absorption between 6 and 12 h and an elimination half-life of 29 (±5 h) [7].

Palbociclib possess a linear pharmacokinetic profile with peak plasma concentration of 6-12 h post-oral administration. The oral bioavailability was 46% with and only slightly soluble in water, so to improve the dissolution, a solid dispersion technique is selected [8, 9].

The present study deals with various preparation techniques of SD to improve the solubility dissolution and bioavailability of Palbociclib.

MATERIALS AND METHODS

Palbociclib was received as a gift sample from Hetero Drugs Ltd, Hyderabad, Cab–O–Sil M5, PEG 6000 was purchased from SDFCL, Mumbai. Kyron T-314, Inutec SP 1 was obtained from Gattefosse, Mumbai. Avicel PH 102, Fujicalin, Neusilin were purchased from Signet Chemical Corp. Pvt. Ltd. Gelucire 44/14 was purchased from BASF, Mumbai.

Solubility enhancement of palbociclib by surface solid dispersion technique

Solubility studies of palbociclib

Solubility studies of Palbociclib physical mixtures (Palbociclib and carrier in 1:1 ratios) in water was determined by the shake-flask method. The filtered solution was analysed for the concentration of Palbociclib by UV-VIS spectrophotometer at 220 nm [10].

Preparation of palbociclib surface solid dispersions (SSD)

About 125 mg of the drug was dissolved in the required amount of methanol to get a clear solution. Carrier was added to this clear drug solution and dispersed. The solvent was removed by continuous trituration until a dry mass was obtained. The obtained mass was further dried at 50 °C for 4 h in an oven. This product was crushed, pulverized and sifted through a 60# sieve. The obtained product was stored in desiccators containing CaCl2 and evaluated [11] (table 1).

Table 1: Formulation of palbociclib SSD's

Formulation code	Palbociclib (mg)	Ratio of drug: carrier	Kyron T-314 (mg)	Florite R (mg)	Cab–o–Sil M5 (mg)	SSG (mg)	CPV (mg)
SSD1	125	1:1	125				
SSD2	125	1:2	250				
SSD3	125	1:3	375				
SSD4	125	1:1		125			
SSD5	125	1:2		250			
SSD6	125	1:3		375			
SSD7	125	1:1			125		
SSD8	125	1:2			250		
SSD9	125	1:3			375		
SSD10	125	1:1				125	
SSD11	125	1:2				250	
SSD12	125	1:3				375	
SSD13	125	1:1					125
SSD14	125	1:2					250
SSD15	125	1:3					375

Note: Methanol was added Qs

Evaluation of palbociclib surface solid dispersions

Solubility studies of Palbociclib SSD, Percentage practical yield [8], % Drug content [9] were performed accordingly as mentioned in referred procedures.

***In vitro* drug dissolution of palbociclib SSD's**

In vitro dissolution study was conducted for Palbociclib pure drug, using a USP dissolution Apparatus II (Lab India DS 8000, Mumbai, India) using 900 ml of pH 1.2 0.1 N HCl at 37±0.5 °C and the speed of the paddle was set at 75 rpm. The sample powder containing 125 mg of drug was mixed with a dissolution medium. About 5 ml of eluted sample was withdrawn at specified time intervals, filtered, and replaced with an equivalent amount of buffer into the vessel. The samples were suitably diluted and analyzed for Palbociclib using UV method spectrophotometrically at 220 nm [14].

Solubility enhancement of palbociclib by melt granulation technique

Preparation of palbociclib solid dispersions by melt granulation technique

Palbociclib (125 mg) was added to the molten base comprising carrier with its quantities as listed in table 2. The blend was heated 10 °C above the melting point of each carrier for 5 min with continuous magnetic stirring. The mass was crushed, ground gently with a mortar and pestle and passed through a 500 µm sieve. The final solid dispersion formulation was obtained by continuous blending for 10 min [15].

Table 2: Composition of palbociclib MG's

Formulation code	Palbociclib (mg)	Ratio of drug: carrier	Poloxamer 188 (mg)	Poloxamer 407 (mg)	Gelucire 44/14 (mg)	Inutec SP 1 (mg)	PEG 6000 (mg)
MG 1	125	1:0.5	62.5				
MG 2	125	1:1	125				
MG 3	125	1:1.5	250				
MG 4	125	1:0.5		62.5			
MG 5	125	1:1		125			
MG 6	125	1:1.5		250			
MG 7	125	1:0.5			62.5		
MG 8	125	1:1			125		
MG 9	125	1:1.5			250		
MG 10	125	1:0.5				62.5	
MG 11	125	1:1				125	
MG 12	125	1:1.5				250	
MG 13	125	1:0.5					62.5
MG 14	125	1:1					125
MG 15	125	1:1.5					250

Evaluation of palbociclib solid dispersions prepared by melt granulation technique

Percentage practical yield, % Drug content, *In vitro* drug dissolution of Palbociclib Melt granules, were performed in a similar manner as mentioned under SSD technique.

Solubility enhancement of palbociclib by liquisolid compact technique

To select the best non-volatile solvent for dissolving Palbociclib, solubility studies of the drug were carried out in different non-volatile solvents; PEG 600, Tween 80, Solutol HS 15, Cremophor EL, Transcutol HP, Glycerine and Propylene glycol. Saturated solutions were prepared by adding the excess drug to the vehicles and shaking on the incubator shaker for 48 h at 25 °C±1 °C. After this period, the solutions were filtered through a 0.45 µm Millipore filter, diluted with distilled water and analyzed by a double beam UV-Visible spectrophotometer (Systronics, Hyderabad) at a wavelength of 220 nm against a blank (blank sample contained the same concentration of specific solvent used without drug).

Binding capacity of adsorbents for the solvents

Binding capacity is defined as the capacity of different excipients (carrier material) to hold liquid and behave like dry powder. This was determined by following a simple technique. The constant weights of (5 g) of the different powder excipients were taken and a non-volatile solvent was added in an increment of 0.01 ml. The mixture was triturated after each addition to help distribution of the liquid throughout the powder particles. The addition of the vehicle and the trituration was continued until mortar contents start to look like dry powder [16].

Calculation of load factor

In liquisolid system, the carrier and coating materials can retain only certain amounts of liquid while maintaining acceptable flow and compression properties depending on the excipients ratio used. The excipients ratio R (R = Q/q) of powder is defined as the ratio between the weights of the carrier (Q) and coating (q) materials present in the formulation. Preparation of a liquisolid system with acceptable flowability and compressibility is possible if the maximum liquid on the carrier material is not exceeded. This characteristic amount of liquid is termed the liquid load factor (Lf). The Lf is defined as the weight ratio of the liquid medication (W) and carrier powder (Q) in the system (i.e., Lf = W/Q) [18]. To calculate the loading factor, non-volatile solvent (liquid medication without drug) was added to 10 g of carrier material and blended for 1 min. To this coating, the material was added and triturated.

Pre-compression parameters

The lubricated blend was evaluated for Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's Ratio [17].

Characterization for final optimised formulation

Characterization was done using Fourier transforms infrared spectroscopic analysis, X-Ray Diffractometer (XRD) and SEM studies procedures as referred [18, 19].

Stability studies

The Palbociclib Capsules were placed in a stability chamber (Thermo Lab, India) at 75%±5% RH and 40 °C±2 °C for accelerated stability studies as mentioned in ICH guidelines. Samples analyzed at the specified time [20].

***In vivo* pharmacokinetic analysis**

Animals

Eighteen healthy Wistar rats were (Weighing 150-180 g) were made to maintain the animals under controlled environmental conditions (Temperature 25 °C, Relative Humidity 45% and 12 h light/dark cycles) with 100 % fresh air exchange and uninterrupted supply of power and water. Rats provided with a standard diet and water ad libitum and the study *was* approved by the institutional animal ethics committee (IAEC NO: 1447/PO/Re/S/11/CPCSEA/35/A).

Study design

Rats were divided in to three groups at random; each group contain 6 rats. The rats were fasted for 24 h prior to the experiments. After 4 h of dosing, foods were reoffered. First group was administered with pure Palbociclib (as such) made suspension with 0.5% methocel and the second group was administered with prepared Palbociclib optimized solid dispersion formulation by oral route at a dose of 1.95 mg. Third group was kept as control. Then, 500 µl blood samples taken out from the femoral artery at certain times 0-24h post dose and transferred into Eppendorf tubes containing heparin to retard blood clotting. Plasma was isolated by centrifugation of samples at 5000 rpm for 5-10 min and stored at −20 °C [21].

Pharmacokinetic analysis

The pharmacokinetic parameters employed to evaluate were maximum plasma concentration (C_{max}), time to attain C_{max} i.e., T_{max} and t ½ values, area under plasma concentration-time curve from zero to the last sampling time ($AUC_{0\text{-}t}$), area under plasma concentration-time curve from zero to infinity ($AUC_{0\text{-}\infty}$).

The analysis was carried out using Win Nonlin 3.3® pharmacokinetic software (Pharsight Mountain View, CA USA).

RESULTS AND DISCUSSION

Solubility studies of palbociclib

The solubility studies indicated that pure drug solubility is 0.0192±0.63 mg/ml in water. Physical mixture of Palbociclib with Kyron T 314 shown the highest drug solubility i.e., 2.80±0.36 mg/ml.

Table 3: Solubility studies of palbociclib physical mixtures (1:1 ratio)

S. No.	Composition	Solubility (mg/ml)
1	Pure drug	0.00152±0.17
2	Drug+Pregelatinised Starch	1.049±0.27
3	Drug+Sodium Starch Glycolate	1.55±0.28
4	Drug+Crospovidone	1.40±0.82
5	Drug+Cab–o–Sil M5	1.75±0.73
6	Drug+Avicel PH 102	1.12±0.69
7	Drug+Kyron T 314	2.80±0.36
8	Drug+Florite R	1.63±0.72

Data is given as mean±Standard Deviation; (n=3)

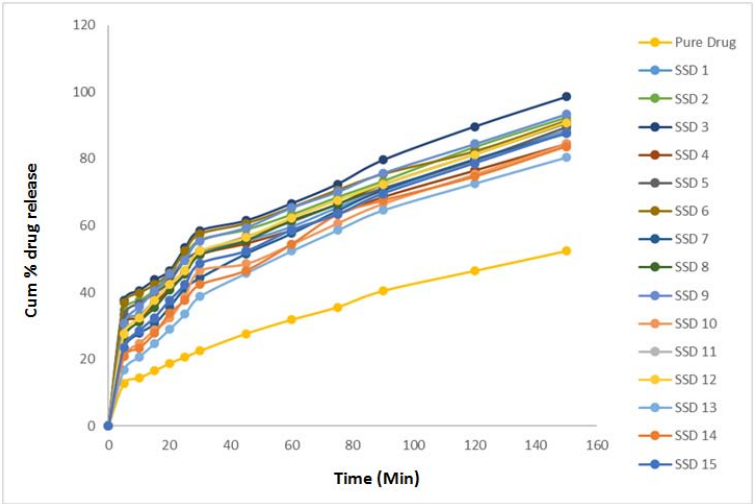


Fig. 1: *In vitro* drug dissolution of pure palbociclib and palbociclib surface solid dispersions SSD1-SSD15

Percentage practical yield (PPY) determination and drug content of palbociclib SSD

All the formulations contained active ingredients within the general limit of 90-110%.

The PPY for all Palbociclib SSD's lie within 95.03±0.21%-98.95±0.39%. Maximum yield of 98.95±0.39% observed.

The % drug content of all Palbociclib SSD's lie within 95.07±0.42–99.76±0.24%.

***In vitro* dissolution of SSD's of palbociclib**

The pure drug showed only (31.82±0.94%) in one hour. The drug release with SSD on Kyron T314 showed greater results when compared to other carriers. As the carrier concentration is increased, the dissolution of drug got increased. The release of the drug with 1:3 drug: Kyron T314 SSD was more when compared to 1:1 drug: Kyron T-314 SSD due to the availability of more carrier for coating the drug. Formulation SSD3 containing a high amount of Kyron T-314 showed the highest dissolution rate of 66.65±1.63% in one hour (fig. 1).

Kyron T-314 being a super rapid disintegrant with high porosity and swelling index compared to other polymers [22], pose an equal advantage for the drug to exhibit higher solubility and hence greater dissolution.

Solubility enhancement of palbociclib by melt granulation technique

Percentage practical yield (PPY) determination and drug content of Palbociclib MG

All the formulations exhibited content uniformity within the IP limits between 90%-110%

The PPY for all Palbociclib SD's lie within 94.01±0.23 %-98.26±0.74%/.

The % drug content of all Palbociclib SD's lie within 95.01±0.28–99.64±0.29 %.

***In vitro* dissolution studies**

Among all, formulations Drug with Poloxamer 188 exhibited greater dissolution. Formulation MG 3 containing a high amount of Poloxamer 188 showed more dissolution rate of 92.34±0.72 % in one hour (fig. 2).

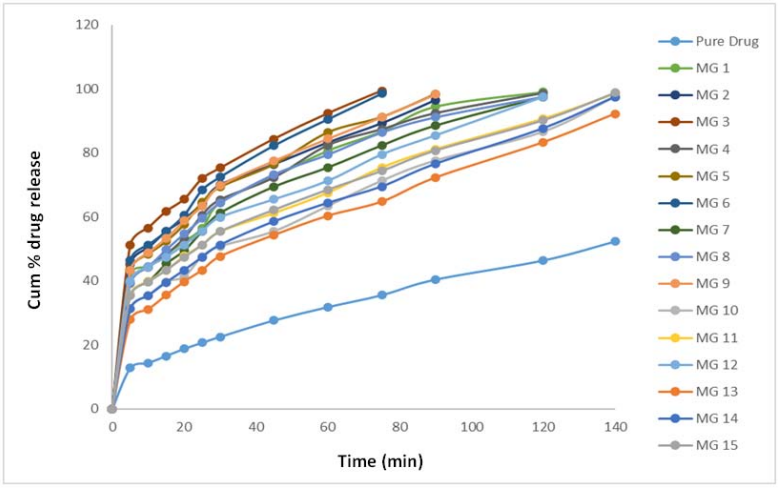


Fig. 2: *In vitro* drug dissolution of pure palbociclib and palbociclib melt granules MG 1-MG 15 solubility enhancement of palbociclib by liquisolid compact technique

Solubility studies of palbociclib

The solubility of Palbociclib in different non-volatile solvents is given in table 4. The table shows that the Palbociclib has highest solubility in Solutol HS 15.

Table 4: **Solubility studies of palbociclib in non-volatile solvents**

S. No.	Non-volatile solvent	Solubility (mg/ml)
1	Drug+Solutol HS 15	1261±0.48
2	Drug+Tween 80	1150±0.47
3	Drug+Cremophor EL	875±0.66
4	Drug+Transcutol HP	645±0.58
5	Drug+PEG 600	545±0.75
6	Drug+Propylene Glycol	315±0.45
7	Drug+Glycerine	205±0.68

Data is given as mean±Standard Deviation, n=3

Binding capacity of adsorbents for the solvents

Binding capacity of different amounts of carriers were evaluated and are given in table 5. From the table it is evident that as the amount of carrier is increasing, the amount of liquid that can be loaded onto it is decreasing. Thus, 100 mg of carrier (Neusilin) was selected for further study at an Excipient ratio of 5:1.

Micrometric properties of palbociclib lubricated blend

The powder mixtures of different formulations were evaluated for angle of repose and Carr's index. The results of angle of repose<30 and compressibility index<15 indicates excellent flow properties of the powder mixture containing Neusilin as carrier material.

Percentage practical yield (PPY) determination and drug content of Palbociclib liquisolid compact

The practical percentage yield (PPY) for all Palbociclib LSC's was found to be within 95.16±0.47%-99.60±0.86%.

The % drug content of all Palbociclib LSC's lie within 95.60±0.72–99.75±0.23%

***In vitro* dissolution studies of palbociclib LSC**

A significant increase in drug dissolution rate is observed in all the formulated LSCs of Palbociclib when compared to the pure drug (31.82±0.84%) in one hour. Three carriers (Neusilin, Fujicalin and Avicel PH102) and three solvents (Tween 80, Solutol HS 15 and Cremophor EL) were used in the formulation of Palbociclib LSC's. Formulations containing Neusilin (LSC1-LSC3) exhibited a greater dissolution rate when compared to Fujicalin andAvicel PH 102

(LSC4-LSC9). Among all, formulation LSC1 containing Neusilin as carrier and Solutol HS 15 as solvent showed the highest dissolution rate of 92.23±1.38% in one hour.

The increased dissolution rate was found to be for the LSC1, where Palbociclib is molecularly dispersed in solvent Solutol HS which enhances solubility, and due to the increased wettability of the drug molecules by the Solutol HS than other solvents [23], the carrier (neusilin) effect and also carrier to coating material ratio (5:1) may be a reason as they adsorb the drug molecules and thus, they make the drug exposed to the dissolution media [24, 25] (fig. 3).

Table 5: Determination of optimum concentration of carriers and loading factors

Amount of carrier 100 mg							
Solvent	**Excipient ratio**	**Volume of liquid consumed**			**Liquid loading factors**		
		Neusilin	**Fujicalin**	**Avicel**	**Neusilin**	**Fujicalin**	**Avicel**
Solutol HS 15	5	0.43	0.41	0.38	3.58	3.41	3.16
	10	0.39	0.35	0.34	3.57	3.2	3.09
	15	0.38	0.32	0.31	3.56	3.0	2.90
	20	0.37	0.30	0.29	3.52	2.85	2.76
Cremophor EL	5	0.41	0.35	0.33	4.78	4.08	3.85
	10	0.37	0.31	0.29	4.70	3.94	3.69
	15	0.32	0.26	0.28	4.20	3.41	3.67
	20	0.30	0.25	0.27	4.00	3.33	3.6
Tween 80	5	0.35	0.29	0.27	3.09	2.56	2.38
	10	0.30	0.24	0.21	2.89	2.31	2.02
	15	0.28	0.22	0.16	2.78	2.18	1.59
	20	0.27	0.20	0.13	2.72	1.98	1.31
Amount of Carrier 200 mg							
Solvent	Excipient Ratio	Volume of liquid consumed			Liquid loading factors		
		Neusilin	Fujicalin	Avicel	Neusilin	Fujicalin	Avicel
Solutol HS 15	5	0.49	0.46	0.40	3.50	1.91	1.66
	10	0.46	0.43	0.37	2.09	1.95	1.68
	15	0.44	0.40	0.35	2.06	1.87	1.64
	20	0.43	0.39	0.34	2.04	1.85	1.61
Cremophor EL	5	0.47	0.44	0.33	2.74	2.56	1.925
	10	0.43	0.40	0.29	2.73	2.54	1.84
	15	0.40	0.38	0.28	2.62	2.49	1.83
	20	0.37	0.37	0.27	2.46	2.46	1.80
Tween 80	5	0.40	0.32	0.29	1.76	1.41	1.28
	10	0.32	0.29	0.24	1.54	1.39	1.15
	15	0.29	0.27	0.20	1.44	1.23	0.99
	20	0.28	0.26	0.18	1.41	1.31	0.09

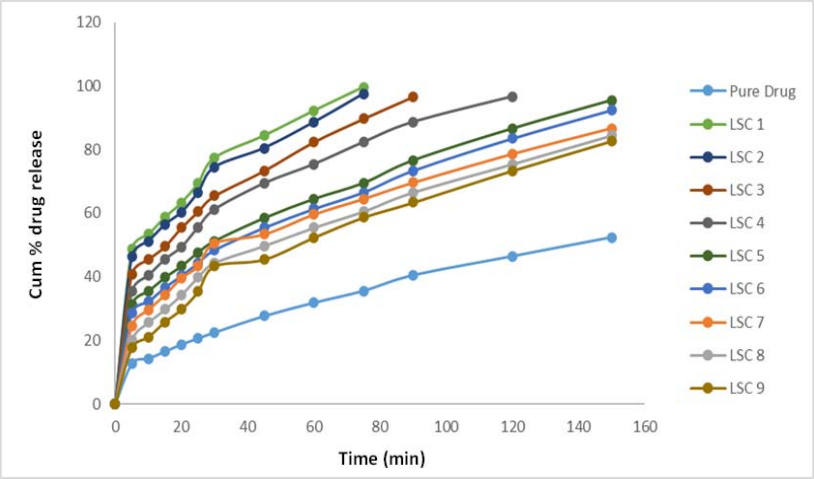


Fig. 3: *In vitro* drug dissolution of pure palbociclib and palbociclib liquisolid powders LSC 1-LSC 9, data is given as the mean of triplicate

Comparative dissolution profiles of optimised formulations of three preparation techniques and marketed product

Fig. 4 depicts the comparative drug release of SSD 3, MG 3 and LSC 1. Palbociclib prepared by Melt Granulation technique was found to be the best formulation (MG 3) with the highest drug release of 92.34±1.38% in 1 h.

Fig. 5 depicts the comparative drug release of Palbociclib Melt granule formulation and Marketed product Ibrance 125 mg. Marketed product showed a drug release of 99.98 % within one hour and prepared formulation displayed a profile of 92.67 % within 1 h.

Characterization of palbociclib formulation

FTIR spectroscopy

The characterization of pure drug Palbociclib by FTIR studies was shown in fig. 6A. The N–H stretching of Palbociclib observed at 3396.76 cm^{-1}, N–H bending at1587.47 cm-^{1}. A broad peak was observed at 1228.70 cm^{-1} a sharp peak was observed in 1741.78 cm^{-1}. The FTIR of optimised formulation of Palbociclib LSC11 showed all peaks for Palbociclib, suggesting no significant interaction observed between them [26] (fig. 6B).

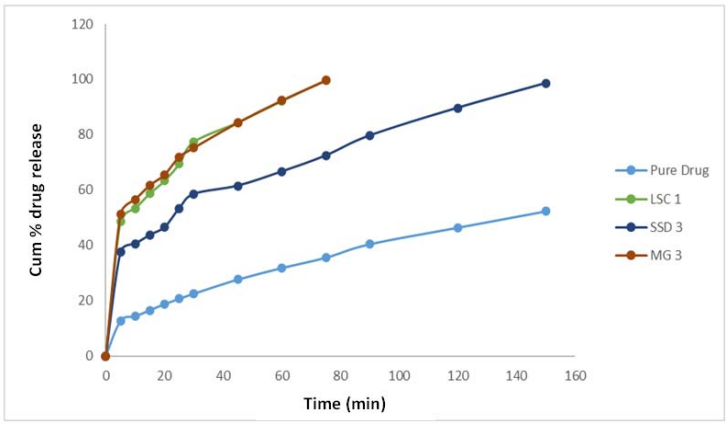


Fig. 4: Comparative dissolution profiles of palbociclib pure drug and palbociclib solid dispersions, data is given as mean of triplicate

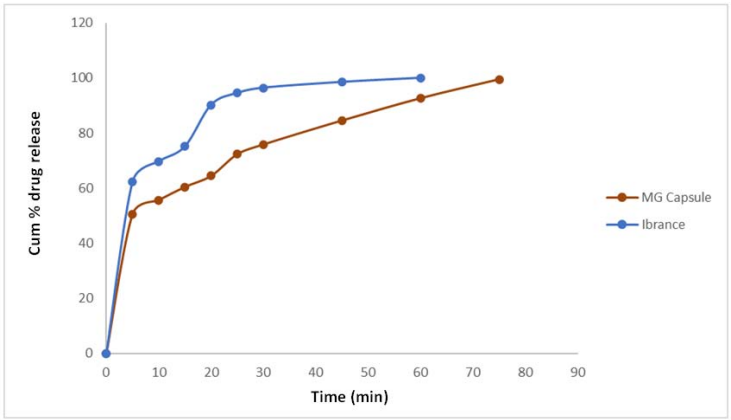


Fig. 5: Comparative dissolution profiles of palbociclib melt granule formulation and marketed product, data is given as mean of triplicate

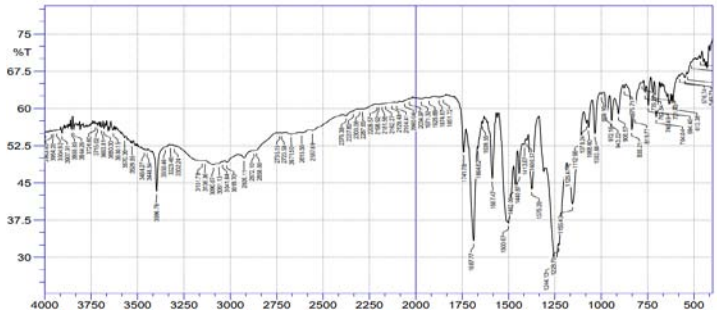


Fig. 6A: FTIR of pure drug palbociclib

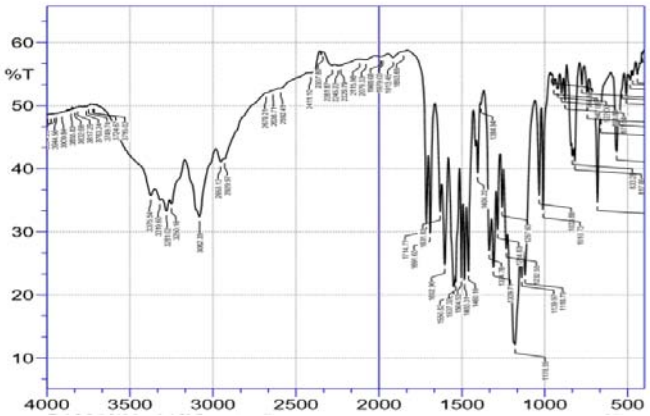


Fig. 6B: FTIR spectrum of optimized formulation of palbociclib MG 3

3.5.2. XRD

The XRD pattern depicted in fig. 7 by pure drug (A), optimised formulation LSC 1 (B) and optimised formulation MG 3 (C) reveals a decrease in the number of peaks which probably represents a decrease in crystallinity [27].

SEM studies

Morphological characteristics of pure drug Palbociclib, Optimised melt granule formulation MG 3, were studied using SEM. The photomicrograph of the pure drug Palbociclib (fig. 18A) showed that the drug is crystalline in nature and Optimised melt granule formulation MG 3 (fig. 8B), showed a more amorphous molecularly dispersed form.

Stability studies

Results indicate that the optimized formulation (MG 3) is stable with no variations in its drug content and *in vitro* dissolution profile [28] (table 6).

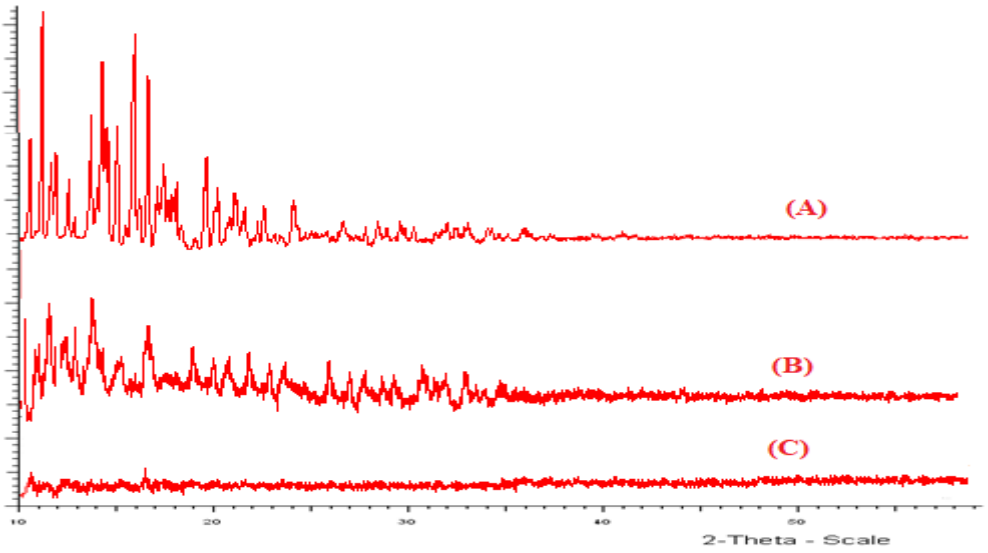
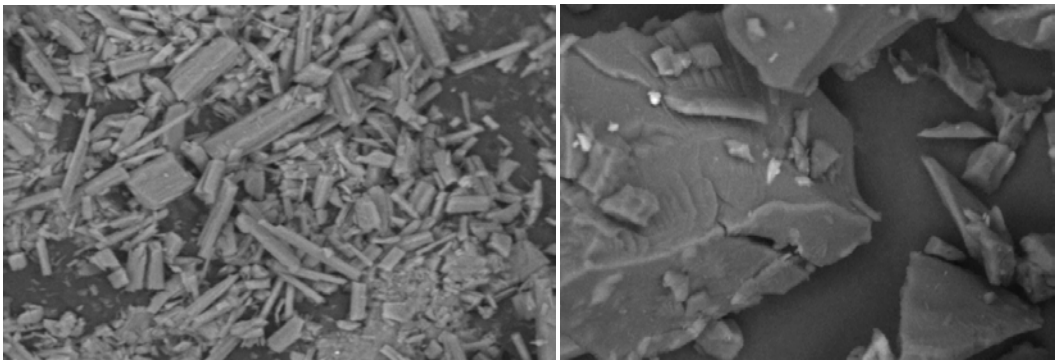


Fig. 7: XRD of (A) Pure drug (B) Optimised liquisolid formulation LSC 1 (C) Optimized formulation of palbociclib MG 3



(A) **(B)**

Fig. 8A and 8B: SEM images of (A) Pure drug and (B) Optimized formulation of palbociclib MG 3

Table 6: Stability studies of MG 3 stored at 40±2 °C/75±5% RH

Retest time for optimized formulation MG 3	*Drug content (%)	*_In vitro_ drug release profile (%)
0 d	99.75±0.23	99.98±0.17
30 d	99.54±0.73	99.90±1.83
60 d	99.52±1.85	99.89±0.13
90 d	99.25±0.73	99.82±0.27

*Data is given as mean±standard deviation; (n=3)

Pharmacokinetic parameters comparison for palbociclib pure drug and solid dispersions

Fig. 9 indicates the plasma concentration-time curve recorded post single oral dose of Palbociclib SD formulation in comparison to Palbociclib pure drug suspension. At any time point, the drug plasma concentrations in animals administrated with solid SD was higher than that of pure drug.

C_{max} of the Palbociclib solid dispersions optimized formulation was 970.76±1.22 ng/ml and was significant ($p<0.05$) as compared to the pure drug suspension formulation 105.84±0.19 ng/ml. T_{max} of both

solid dispersions formulation and pure drug was 2.0±0.04 and 4±0.01 h, respectively. $AUC_{0-\infty}$ infinity of SD formulation was higher 7816.61±1.37 ng. h/ml) than the pure drug suspension 2501.4±1.46 ng. h/ml (table 7)

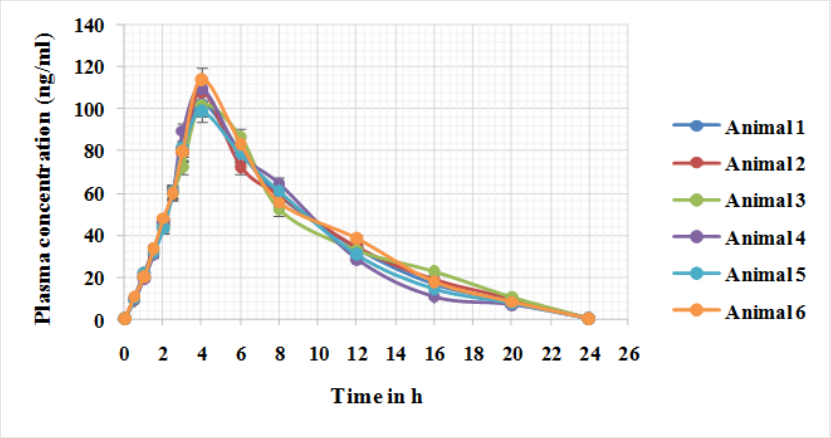


Fig. 9A: Plasma concentration-time profile of the palbociclib pure drug in rat plasma, data is given as mean±standard deviation; (n=6)

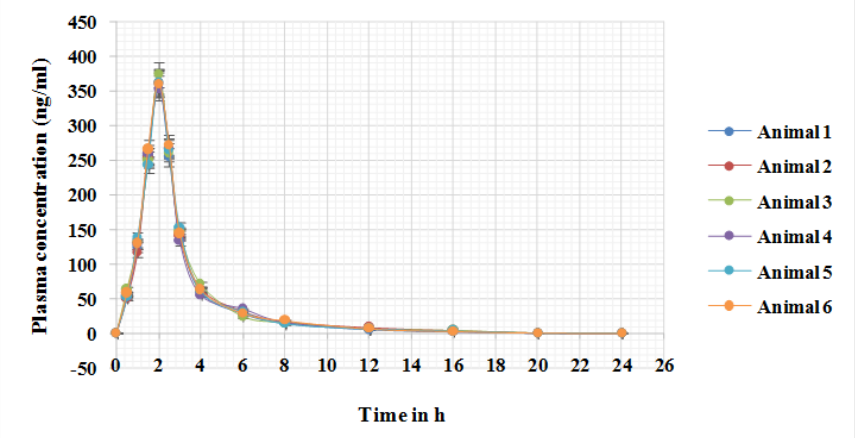


Fig. 9B: Plasma concentration-time profile of palbociclib optimized solid dispersions in rat plasma, data is given as mean±standard deviation; (n=6)

Table 7: Pharmacokinetic parameters of palbociclib melt granule formulation and pure drug

	Palbociclib pure drug	Palbociclib melt granules
C_{max} (ng/ml)	105.84±0.19	362.76±1.84
AUC_{0-t} (ng. h/ml)	1512.6±1.49	4861.23±1.09
AUC_{0-inf} (ng. h/ml)	2501.4±1.46	7816.61±1.37
T_{max}(h)	4±0.01	2.0±0.04
$t_{1/2}$ (h)	23.044±0.02	20.02±0.04

CONCLUSION

Solid dispersions of Palbociclib were formulated for enhancing the drug solubility and dissolution rates. Out of all formulations when compared, SSD3 formulation prepared by surface solid dispersion technique exhibited drug release of 66.65%, MG3 prepared by melt granulation showed 92.34% and LSC1 prepared by liquisolid compact technique of 92.23%. Hence the pecking order for the preparation techniques based on dissolution can be given as MG>LSC>SSD. FTIR studies for the optimised formulation MG 3 showed no significant interactions and XRD, SEM studies revealed a non-crystalline form. In conclusion, it can be stated that the objective of the study was achieved in improving the solubility and dissolution of the Palbociclib using Melt granulation Technique in comparison to the traditional solid dispersion method.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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