Journal of Carcinogenesis
Covering Genesis to Therapeutics
Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 5s, https://carcinogenesis.com/

Formulation And Evaluation Of Liquisolid Compact For Pazopanib

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ABSTRACT

Objective: The aim of the present investigation was to develop a liquisolid compacts to enhance the oral absorption of Pazopanibe by improving dissolution rate. Experimental work: the solubility of pazopanib in various liquid vehicles was determined. Liquisolid compacts were prepared using polyethylene glycol as a solvent, microcrystalline cellulose as carrier materials and silica as coating material. The interaction between drug and excipients were characterized by FTIR. The powder characteristics were evaluated by different flow parameters to comply with pharmacopoeial limits. The dissolution studies for liquisolid compacts and conventional formulations were carried out. Results and Discussion: liquisolid compacts showed significant higher drug release rates than conventional tablets. formulation F3 showed superior dissolution and are more effective carrier materials for liquid adsorption. Conclusion: it was concluded that liquisolid compacts would be a promising drug delivery system for poorly water-soluble drugs by the oral route..

Keywords: *Pazopanib, FTIR, Liquisolid compact, Evaluation, In-vitro drug release*

How to Cite: Raju R. Thenge, Vikas suresh shende , Gaffar Sayyed , Rahul S. Radke , Shivanand Karbhari Wagh , Nitin Motiram Gawai , Nilesh Dhanaji Zanzane , Ketakee Rajesh More, Shyam Mahadev Wankhede , Pratik Jadhao , (2025) Formulation And Evaluation Of Liquisolid Compact For Pazopanib, *Journal of Carcinogenesis*, *Vol.24, No.5s*, 585-598

1. INTRODUCTION

The oral route remains the preferred route of drug administration due to its convenience, good patient compliance and low medicine production costs. In order for a drug to be absorbed into the systemic circulation following oral administration, the drug must be dissolved in the gastric fluids. Thus, one of the major challenges to drug development today are poor solubility, as an estimated 40% of all newly developed drugs are poorly soluble or insoluble in water.[1] The dissolution rate of these drugs can be improved by decreasing particle size, decreasing crystallinity, and/or increasing the surface area. Liquisolid technique is novel and efficient approach for solubility enhancement in which the conversion of water insoluble drug takes place into dry looking, non-adherent, free flowing and acceptably compressible powder by incorporating into suitable non volatile solvents, carrier material and coating materials.[2] It is a novel “Powder Solution Technology” that involves absorption and adsorption efficiencies, making use of liquid medications, drug suspensions admixed with suitable carriers, coating materials and formulated into free flowing, dry looking, non-adherent and compressible powder forms. The design of liquisolid systems are mainly intended for enhancement of solubility, dissolution rate and bioavailability of poorly water-soluble and highly lipophilic drugs. Improvement in bioavailability may be due to increased surface area, increased aqueous solubility and increased the wettability of the drug. Pazopanib (PZB) is an anti-cancer drug which is

used in treatment of renal cell carcinoma, advanced soft tissue sarcomas and bone sarcoma. [3-5] . PZB is a potent and selective multi-targeted receptor tyrosine kinase inhibitor that blocks tumour growth and inhibits angiogenesis [6]. PZB primarily show its inhibitory effect on vascular endothelial growth factor receptor 1, 2 and 3, platelet endothelial growth factor receptor-α, and -β, and the stem-cell factor receptor c-kit [7,8] . It is a BCS class II drug exhibits low aqueous solubility ≤0.33mg/ml with log P value of 3.2 and low oral bioavailability[9,10]. Therefore present study reveals the formulation and evaluation of liquisolid compact of pazopanib to improve its solubility and dissolution rate and thus bioavailability

2. MATERIALS:

Materials Pazopanib was obtained as a gift sample from Aizant drug research solutions pvt. ltd. (Hyderabad), India, Microcrystalline Cellulose, Sodium Starch Glycolate, Crosspovidone, Propylene Glycol, Colloidal Silicon Dioxide, Magnesium stearate and talc.

3. METHODS:

A drug was initially dissolved in the suitable non volatile solvent system (Propylene glycol) having different drug solvent ratios. Then a suitable carrier material (microcrystalline Cellulose) was added in the above liquid preparation and triturated in the mortar. To the above blend suitable coating material (silica) was added to get fine absorptive particle. To the above mixture suitable superdisintegrants like sodium Starch Glycolate, crosspovidone, was added in the prepared mixture with continuous stirring in the mortar. The remaining additives like magnesium Stearate and talc was added and mix well. Then the dump mass was passed through the sieve no 20 to obtain Granules. These granules were dried at 60°C for 1 hour. After the drying of granules they were compressed by tablet punching machine.[11]

4. PREFORMULATION STUDIES:

Preformulation:

The first step in the rational design of dosage forms for a pharmacological substance is preformulation testing. It is the examination of the physical and chemical characteristics of a drug substance both by itself and in combination with excipients. Pre-formulation testing's main goal is to collect data that will help the formulator create stable, bioavailable dosage forms that are producible by humans.

Physical Characterization:

Organoleptic Evaluation:

The organoleptic evaluation was carried out by taking 1 g of drug sample in a dry petri dish and the sample was observed for the compliance with the specification.

Melting point determination:

Melting point determination of the Pazopanib hydrochloride drug sample was carried out as it is the first indication of the purity of the sample. It was measured by Thiele's tube apparatus by taking three readings.[12]

Solubility determination:

For the choice of best non volatile solvent solubility of Pazopanib Hydrochloride drug was carried out by preparing saturated solution of drug in different solvents, i.e. Propylene Glycol, PEG 400,PEG 200, Tween 80.

In a glass beaker, saturated solutions were made by adding an excess amount of drug to the non volatile solvent. For full 24 hours, the solution was shook sporadically to assist the undissolved drug particles reach equilibrium. After this the solutions were filtered through a 0.45 micronMilliporefilter and analyzed by UV Spectrophotometer at a wavelength of 273 nm against blank sample . Three determination were carried out to calculate the solubility of Pazopanib hydrochloride.[13]

5. EVALUATION OF LIQUISOLID POWDER SYSTEM:[14-16]

Bulk density was determined by USP method. A quantity of powder blend from each formulation was introduced into 250 ml measuring cylinder. Then the volume of powder measured directly from the graduation marks on the measuring cylinder as ml. The volume measured was called as bulk volume and the bulk density was calculated by following formula:

Bulk density = weight of the powder / bulk volume

After measuring the bulk volume the same measuring cylinder was set into tap density apparatus. The tap density apparatus was set to 300 taps drop per minute and operated for 500 taps. Volume was noted as Va and again tapped for 750 times and the volume was noted as Vb. If the difference between Va and Vb not greater than 2% then Vb is considered as final tapped volume and the tapped density was calculated by following formula:

Tapped density = weight of the blend / final volume

Angle of repose has been used as indirect method for quantifying powder flowability. Angle of repose for the blend of each liquisolid formulation was determined by fixed funnel method. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of the powder. The height and radius of the powder cone was measured at five different points and average was taken for calculating the angle of repose by using following formula.

$$\boldsymbol{Angle\ of\ Repose(\theta) = tan^{-1}\left(\frac{h}{r}\right)}$$

Where, h = height of the Liquisolid powder cone.

r = radius of the Liquisolid powder cone.

Carr's Index:

It is used to evaluate flowability of liquisolid powder by comparing the bulk density and tapped density of a liquisolid powder. The percentage compressibility of the Liquisolid powder was calculated by using following formula:

Compressibility Index = Tapped density – Bulk density / Tapped density ×100

Hausner's Ratio:

Hausner found that the ratio of tapped density/bulk density was related to inter particle friction as such could be used to predict powder flow properties. The powder with low inter particle friction had ratio of approximately 1.2, whereas more cohesive less free flowing powders have hausner's ratio greater than 1.6. Hausner's of less than 1.2 indicates good flow. It can be calculated by following formula for each liquisolid formulations.

Hausner's ratio = Tapped density / Bulk density.

Post compressional evaluation:

Tablet dimensions:

The thickness and diameter of prepared tablet from each liquisolid formulation were measured by using vernier caliper. Three tablets from each formulation were used and average values were calculated.[17]

Tablet hardness:

Tablets should be sufficiently hard to resist breaking during normal handling and yet soft enough to disintegrate properly after swallowing. The hardness of the Liquisolid compacts prepared was evaluated using Monsanto hardness tester. It is expressed in Newton (N). The mean of the hardness of each formulation was determined.

The weight of the liquisolid tablet was measured to ensure that the tablet contain proper amount of the drug. The test was performed as per Indian Pharmacopeia. Twenty liquisolid tablets of Pazopanib Hydrochloride were selected randomly and weighed. Then average of the tablet was determined. The percentage weight variation of the individual tablet should fall within the specified limits. Not more than the two of the individual weights deviate from the average weight by more than 5% percentage deviation.[17]

Friability Test:

Tablet hardness is not an absolute indicator of tablet strength, since some formulations compressed into very hard tablets tend to capon attrition losing their crown portions. Therefore another measure of tablet strength is its friability which is often measured. Roche friabilitor was used for testing the friability using following procedure. Twenty tablets were selected and their aggregate weight was measured as initial weight. The tablets were kept in a drum in friabilitor apparatus and then rotated at 100 rpm and then tablets were removed. Any loose dust from the tablets was removed and accurate weight was taken. Finally the friability of each liquisolid formulation was calculated by following formula:

$$\%\boldsymbol{Friability} = \frac{\boldsymbol{Initial\ weight\ of\ tablets - Final\ weight\ of\ tablets}}{\boldsymbol{Initial\ weight}} \times \mathbf{100}$$

Drug Content Uniformity:

The amount of active pharmaceutical ingredient is determined by the method described in assay and it is calculated. Since active ingredient of present work is not official in anyPharmacopeia, the following method was used for determination of drug content. Ten tablets were weighed and finely powdered. The drug content was determined by dissolving powder equivalent to 10mg of Pazopanib hydrochloride in 10ml of methanol and filter it using 0.45 µm whatman filter paper, diluted with 1.2 PH HCL buffer and analyzed by UV Spectrophotometer at 264 nm against buffer as a blank.[18]

Disintegration test:

For the tablets the first important step toward solution is the breakdown of the tablet into smaller particles or granules known as disintegration. The Pazopanib hydrochloride compact tablet was kept in every tube of the basket in the assembly. Then the assembly was suspended in the liquid mediumin a suitable vessel preferably in 1000 ml beaker. The volume of the liquid medium was adjusted such that the wire mesh at its highest point is at least 25 mm below the surface of the liquid

and it's lower point is at least 25 mm above the bottom of the beaker. A thermostatic arrangement was made for heating the liquid maintaining the temperature at37±2°C. Assembly was suspended in beaker containing the 1000 ml of distilled water and the apparatus was operated for specified time. Then the assembly was removed from the liquid. The tablet passes the test if all of them have disintegrated. If 1 or 2 tablets fail to disintegrate repeat the test for 12 additional tablets; not less than 16 of the total 18 tablets tested. Finally the disintegration time of tablets was observed.[19]

In vitro drug release study:

The USP rotating paddle apparatus II was used for all the in vitro dissolution studies of liquisolid formulations. The dissolution medium consists of 900 ml of HCL buffer pH 1.2 with 5% SLS. The release was performed at,37±2°Cat a rotation speed of 50 rpm. Sample (5ml) were withdrawn by using calibrated pipette at suitable time interval (5, 10, 15, 20, 25, 30, 45, 60, 90 and 120 minutes) and filtered through Whatman filter paper. Sink conditions were maintained throughout the study. The samples were analyzed at 264 nm by using UV visible spectrophotometer.[20]

6. PHARMACOKINETIC STUDY IN RATS

The pharmacokinetic parameters observed in the male Wistar rat following oral administration of pure Pazopanib hydrochloride and Pazopanib hydrochloride compact demonstrated the relationship between the *in-vivo* oral absorption and *in-vitro* drug release. The Pazopanib hydrochloride compact were showed better dissolution compared to Pazopanib hydrochloride therefore it was considered for the optimization and selected for the in-vivo study.[21]

The mean plasma concentration versus time profiles and other pharmacokinetic parameters of pure Pazopanib hydrochloride and Pazopanib hydrochloride compact after oral administration to Wister rats (male) were determined using PK solution 2.0 software. The plasma drug concentration was estimated by partially validated sensitive RP-HPLC method using UV absorbance detector at 210 nm. A chromatographic peak was observed at a retention time of 5.0 ± 0.2 min (Fig. 6.3.21) using the mixture of acetonitrile and water in the ratio of 45:55 v/v. The drug Pazopanib hydrochloride obeyed linearity in the concentration range from 20µg/ml to 200µg/ml. The plasma drug concentration of Pazopanib hydrochloride at predetermined time intervals was calculated from the linearity graph.[22-23]

7. REUSLT AND DISCUSSION

Preformulation studies:

Before planning to design the formula for the preparation of the liquisolid tablets, some necessary and laboratory based preformulation studies suchas Physical Characterization :organoleptic evaluation , determination of melting point, solubility determination; Spectral analysis: confirmation of drug by UV Spectroscopy and compatibility studies by FTIR Spectroscopy were carried out as mentioned below.

Physical Characterization:

Organoleptic Evaluation:

Organoleptic Evaluation of Pazopanib hydrochloride Liquisolid powder were performed and the result is as given in Table No.1.

Table No. 1 :Organoleptic Evaluation of Pazopanib hydrochloride liquisolid powder.

Sr. No.	Parameters	Observation/Result
1)	Colour	White
2)	Odour	Odorless
3)	Texture	soft

Determination of melting point:

Melting point determination of the Pazopanib hydrochloride drug sample was done as it is the first indication of the purity of the sample and the result of melting point is as given in Table No.2.

Table No. 2: Melting point of Pazopanib hydrochloride.

Sr. No.	Melting point of	Observation/Result
1)	Pazopanib Hydrochloride	389°C
2)	Pazopanib Hydrochloride	390°C
3)	Pazopanib Hydrochloride	391°C
	Average	390°C

Solubility study of PZH in different non volatile solvents:

The solubility of Pazopanib hydrochloride in propylene Glycol, PEG 400, Acetonitrile, PEG 200 is given in the table no. It is observed that, Pazopanib hydrochloride has the lowest solubility in PEG400. Solubility was found to be increased when polar solvents such as PG were used. The solvent being employed, and consequently the intermolecular interactions between pazopanib hydrochloride and the solvent, have a significant impact on the drug's solubility. As the polarity of solvents rises, so does the solubility of the medications. Solubility of the medications is therefore significantly influenced by the solvent's polarity. PG was chosen as a non-volatile solvent to prepare liquisolid compacts.

Table No. 3: Solubility data of Pazopanib hydrochloride.

Sr. No.	Solubility medium	Solubility (mg/ml)
1)	Propylene Glycol	1.070 mg/ml
2)	PEG 400	0.947 mg/ml
3)	PEG 200	0.962 mg/ml
4)	Tween 80	0.821 mg/ ml

Spectral Analysis of Pazopanib hydrochloride:

Spectral Analysis of Pazopanib hydrochloride includes the UV spectrum study for maximum absorbance, FTIR study etc.

Confirmation of drug by UV Spectroscopy:

A solution of 10µg/ml concentration containing Pazopanib hydrochloride was prepared in 0.1 N HCL buffer solution and scanned between 200 to 400 nm wavelength range for getting the maximum absorbance wavelength. The maximum wavelength was found to be 264 nm as shown in figure no. 9.1.2.1.1which is nearer to the reported wavelength.

Compatibility study by FTIR Spectroscopy:

The drug, excipients and mixture of both were subjected to Fourier Transform Infrared (FTIR) studies to check drug-excipients interaction using FTIR (Shimadzu).The sample preparation involved mixing of sample with potassium bromide, triturating in mortar and finally placing in a sample holder. Figure no. 1 to 7 shows the Infrared spectra of Pazopanib hydrochloride, Avicel PH 102, sodium starch glycolate, crosspovidone and physical mixture of drug and excipients.

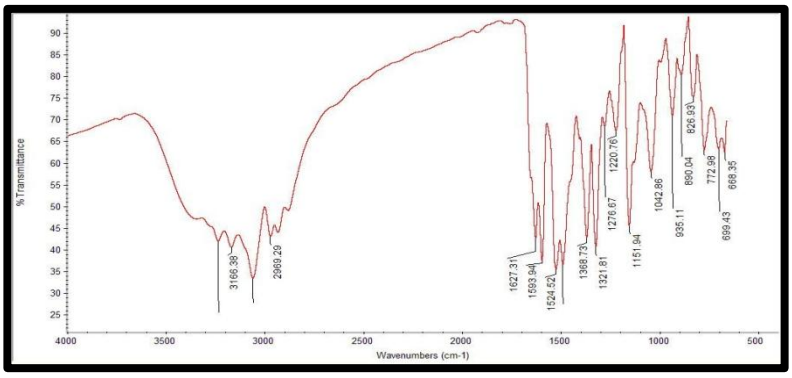

Fig. No. 1: Infra-red spectrum of Pazopanib hydrochloride.

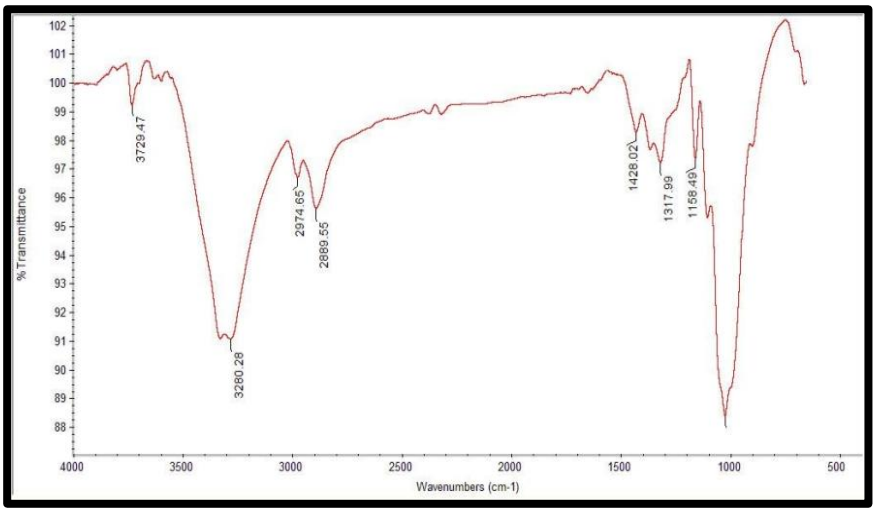

Fig. No. 2: Infra-red spectrum of Avicel PH 102.

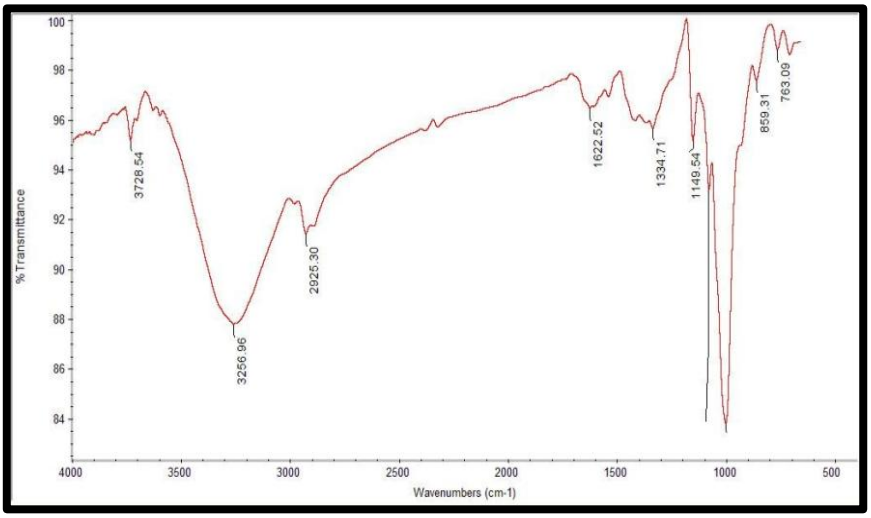

Fig. No. 3: Infra-red spectrum of Sodium Starch Glycolate

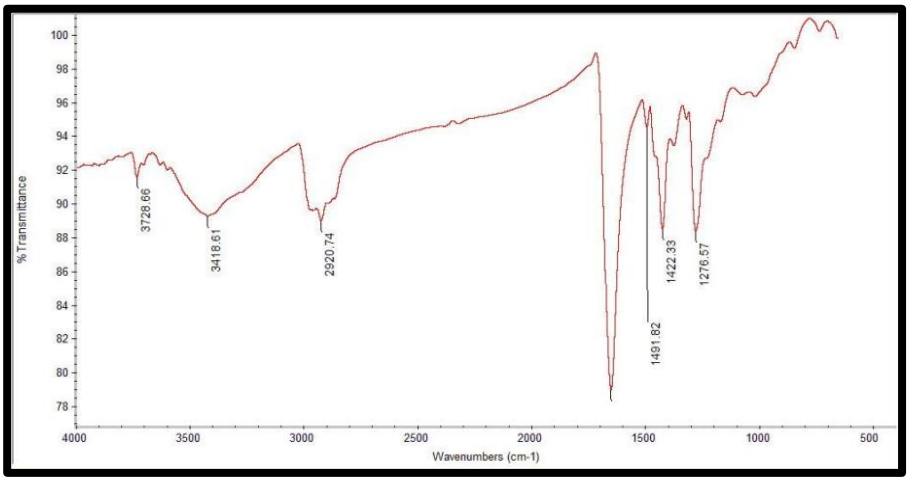

Fig. No. 4: Infra-red spectrum of Crosspovidone.

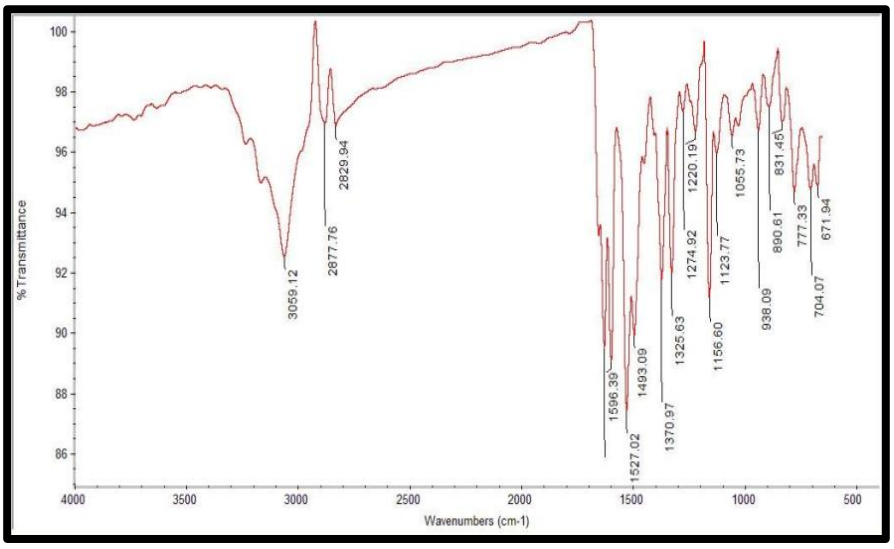

Fig. No. 5: Infra-red spectrum of mixture of PZH and Avicel PH 102.

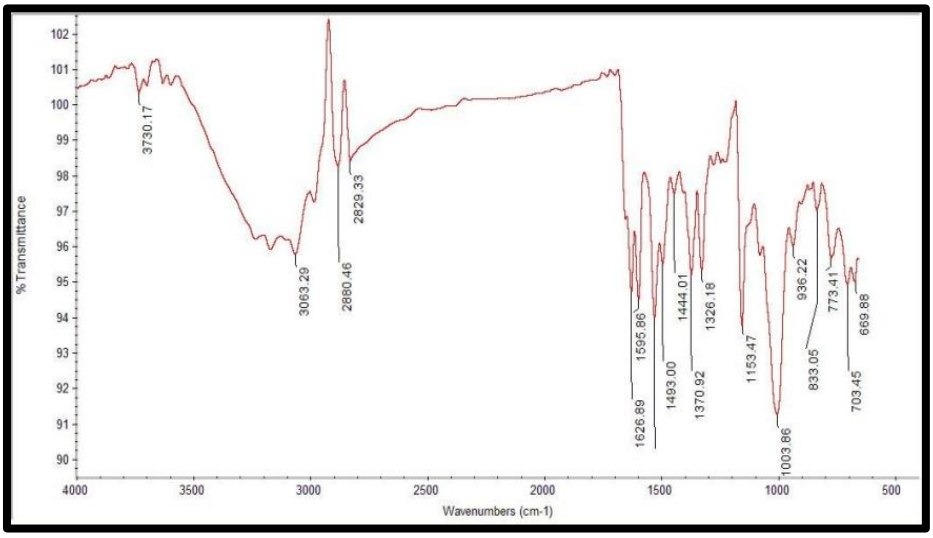

Fig. No.6: Infra-red spectrum of mixture of PZH and Sodium Starch Glycolate.

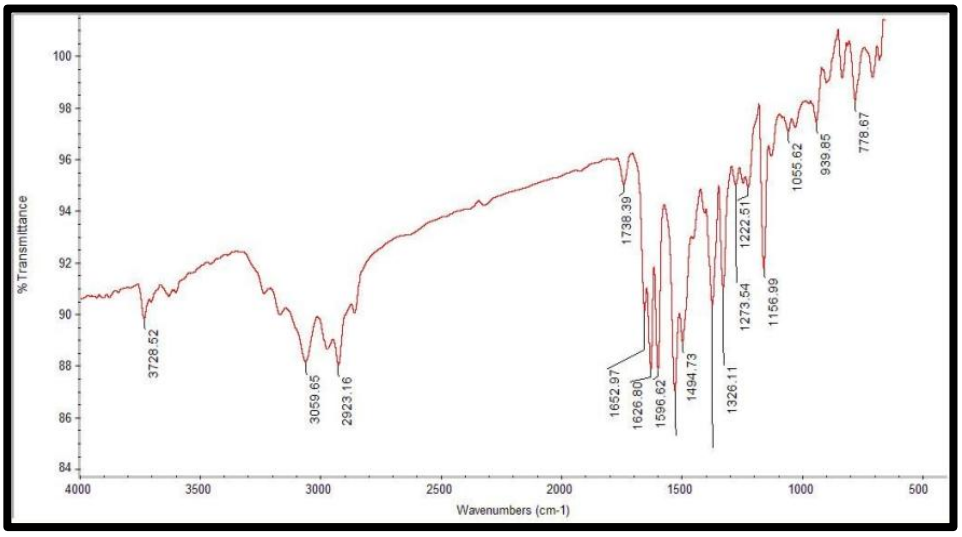

Fig. No. 7: Infra-red spectrum of mixture of PZH and Crosspovidone.

Precompressional evaluation:

The bulk powder's density, porosity, particle size, and shape all affect the flow property. An uneven powder flow from the hopper results in tablets with uneven weights. As a result, it is impossible to produce tablets with precise dose and content measurements. Therefore, prior to formulation, it is essential to determine the mass, tapped, angle of repose, Carr's index, and Hausner's ratio because they have an impact on compressibility, tablet porosity, and dissolving. In general, value of bulk density less than 1.2 g/cm^3 indicates good packing. The angleof repose greater than 40° has very poor flow properties whereas minimum angle closeto 20° correspond to very excellent flow property. Powders showing Carr's index up to21 are considered of acceptable flow property and Hausner's ratio values less than 1.25indicate good flow properties. Formulation LSC 3, LSC 4, LSC 8 and LSC 9 were proven to be excellent flowingproperty according to angle of repose, Carr's index and Hausner's ratio. Formulae LSC 1, LSC 2 and LSC 5 were proven to be acceptably flowing properties.

Table No. 4: Micromertitic properties of different liquisolid formulations.

Formulation code	Bulk density (g/ml)	Tapped density (g/ml)	Angle of repose	Carr's Index	Hausner's Ratio
LSC 1	0.5980	0.7475	30.10	20.00	1.25
LSC 2	0.5763	0.7044	30.18	18.18	1.22
LSC 3	0.5215	0.5650	30.14	07.69	1.08
LSC 4	0.6140	0.6822	30.31	10.00	1.11
LSC 5	0.6420	0.8025	30.02	20.00	1.25
LSC 6	0.5085	0.5933	30.14	14.28	1.16
LSC 7	0.6977	0.7850	30.31	11.11	1.12
LSC 8	0.4973	0.5738	29.98	13.33	1.15
LSC 9	0.5178	0.6061	29.94	14.28	1.16

Post compressional evaluation:

Tablet dimensions:

The thickness of Pazopanib hydrochloride liquisolid tablet ranged from 2.11 to 2.31 mm and diameter of all the Liquisolid tablets was found to be 8 mm. (Table 5)

Hardness:

Ideally, tablet formulation should aim to maximize tablet hardness without using excessive compression force, while also ensuring quick tablet disintegration and medication dissolution. In other words, a tablet must be strong enough to not break when handled normally, yet soft enough to dissolve properly when swallowed. This means the hardness of each liquisolid formulation was determined and presented in table 5.

Friability:

No tested formula showed a percentage loss in tablet weights that exceeded 1%, hence all liquid- solid compacts exhibited acceptable friability. (Table no.5) Friability below 1% is a sign of the tablets' strong mechanical resistance. As a result, tablets is ensured to be durable enough to endure pressure and shocks during handling, transit, and manufacturing operations.

Weight variation:

The tablets evaluated as under the range of Pharmacopoeial requirements based on weight variation. All formulas pass the test for weight variation.

Table No. 5: Result of evaluation of liquisolid tablets.

Formulation Code	Tablet dimensions		Hardness	Friability (%)	Weight variation (g)
	Thickness (mm)	Diameter (mm)			
LSC 1	2.11	8 mm	7.33	0.4166	0.199
LSC 2	2.22	8 mm	7.63	0.3636	0.207
LSC 3	1.94	8 mm	6.89	0.3424	0.198
LSC 4	1.84	8 mm	8.35	0.7812	0.217
LSC 5	1.83	8 mm	8.56	0.3676	0.224
LSC 6	2.27	8 mm	5.34	0.3389	0.199
LSC 7	2.15	8 mm	8.23	0.3787	0.202
LSC 8	2.31	8 mm	9.22	0.6644	0.219
LSC 9	2.33	8 mm	7.50	0.5988	0.200

The necessity for a steady dosage of medicine between each tablet is a key need for all the pharmaceutical preparations. It was observed that formulae LSC 3, LSC 6, LSC 5, LSC 9 and LSC 7 compiled with the test of Pazopanib hydrochloride content uniformity according to Indian Pharmacopeia specification (90% - 110%), having the average Pazopanib hydrochloride content of 92.97 %, 94.18 %, 92.31 %, 94.30 % and 95.94 % w/w respectively. In each of the mentioned formula, no more than one tablet is outside this limit nor is one individual outside the limits of 90 – 110%.

Disintegration time:

The liquisolid tablet formulation disintegrated in 15 minutes, according to the Indian Pharmacopoeia's criteria for uncoated tablets, according to the results of the disintegration time test. The disintegration property of microcrystalline cellulose may aid in the breakdown of drugs and the disintegration of tablets. Delay in disintegration time is anticipated since the liquisolid formulation contains a non-volatile solvent serving as a binding agent. Because it can quickly absorb a lot of water when exposed to an aqueous environment, sodium starch glycolate is also used to speed up pill disintegration. Tablets break due to water absorption, hastening the disintegration process.

Table No. 6: Disintegration time and drug content uniformity.

Formulation Code	Mean disintegration time	Drug content (%)
LSC 1	4.18	91.46
LSC 2	4.34	93.58
LSC 3	4.30	93.57
LSC 4	4.37	94.70
LSC 5	4.11	90.49
LSC 6	4.33	90.12
LSC 7	3.43	92.18
LSC 8	3.22	94.31
LSC 9	2.48	90.97

Table No. 7: Solubility study of different liquisolid formulations:

Formulation Code	Solubility (mg/ml)
PZH	0.0433
LSC 1	0.65
LSC 2	0.59
LSC 3	1.51
LSC 4	0.99
LSC 5	0.70
LSC 6	0.67
LSC 7	0.55
LSC 8	0.63
LSC 9	0.54

In vitro dissolution study of PZH Liquisolid tablets:

The results of in vitro percentage amount of drug released at different time intervals plotted against time to obtain the release profiles. All the liquisolid tablets showed higher drug release than the marketed preparation. The enhanced dissolution rates of liquisolid tablets compared to marketed preparation This occurs may be due to the drug is already in the PG solution, while at the same time it is carried by the powder particles (MCC and SiO2).Thus it's release is accelerated due to the addition of non volatile solvent. The dissolution rate enhance by PG by facilitating wetting of drug particles by decreasing interracial tension between dissolution medium and tablet surface.

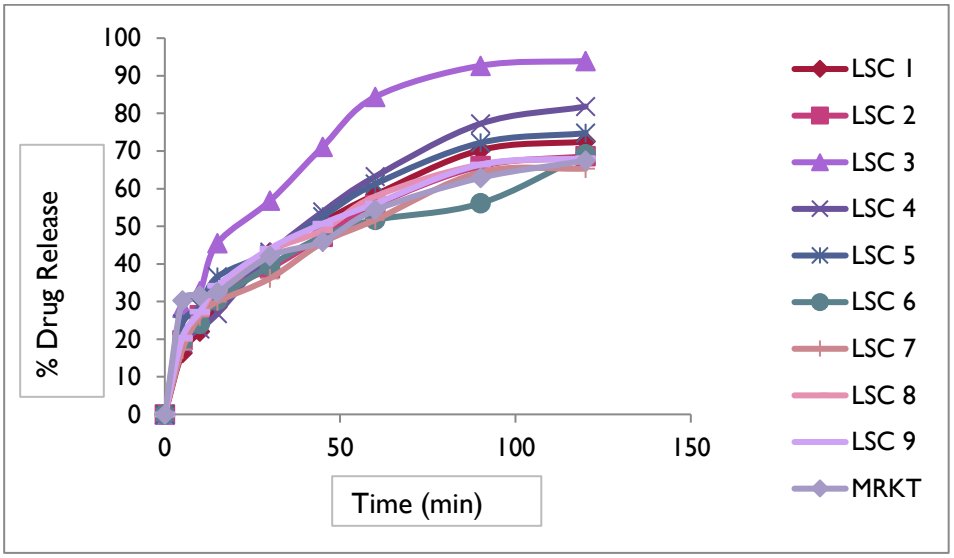

Fig No. 8: % Drug Release for Pazopanib Liquisolid compacts Formulation

Liquisolid tablets with greater smaller values of carrier and coating material could be directly associated with enhanced disintegration and wicking properties. Therefore it was observed that liquisolid formulations with higher quantity of carrier material and lower quantity of coating material shows higher dissolution as compared to lower quantity of carrier material and higher quantity of coating material.

All the liquisolid formulations had higher drug dissolution rate and larger amount of drug dissolved than the commercial preparation of PZH tablet. Due to significant increased wetting properties and increase surface area available for dissolution, liquisolid formulations shows enhanced drug release characteristics and as a result improved bioavailability. From all the evaluation test carried out for the each liquid solid formulation of PZH is conclude that, the formulation LSC 3 in the view of solubility enhancement, drug contain uniformity and percentage drug release over 120 minutes was found

to be optimize batch.

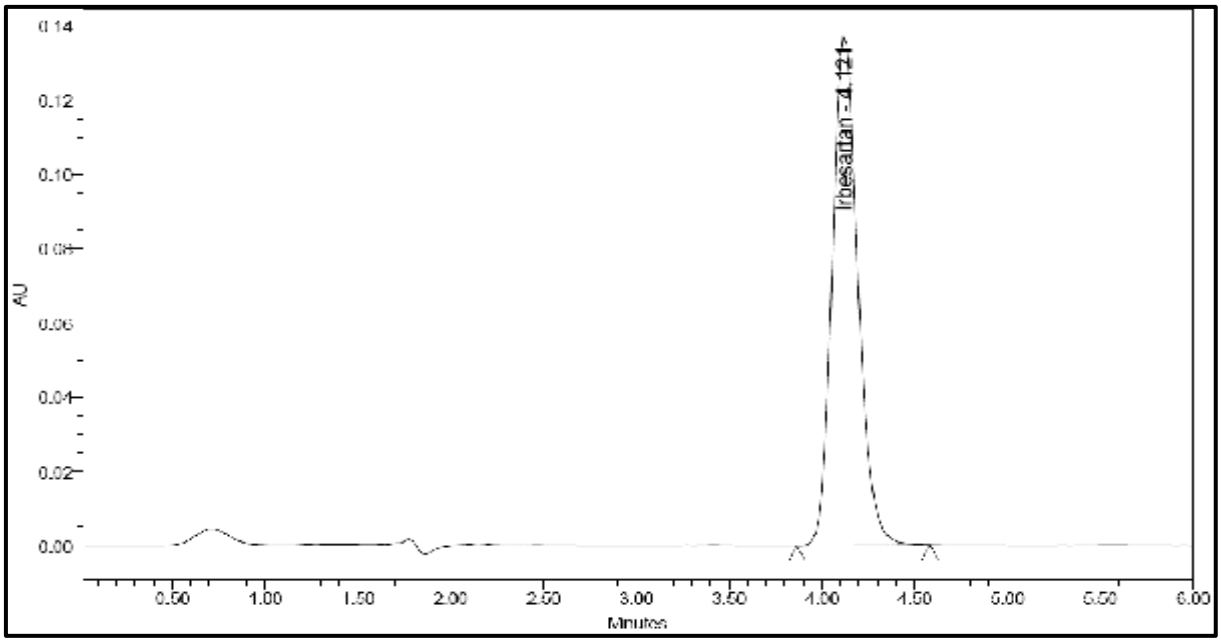

Figure 9: HPLC Chromatogram for Pure Pazopanib hydrochloride

The drug concentration of each plasma samples were determined by extrapolating the linearity graph with peak area at above said predetermined time interval (0, 0.5, 1, 2, 3, 4, 5). The plasma drug concentration-time curve of Pazopanib hydrochloride pure drug and Pazopanib hydrochloride Liquisolid compacts were plotted and presented in Figure 6.3.22-6.3.24 and other pharmacokinetic parameters (Table 8) were calculated by non compartmental model using PK solution 2.0 software.

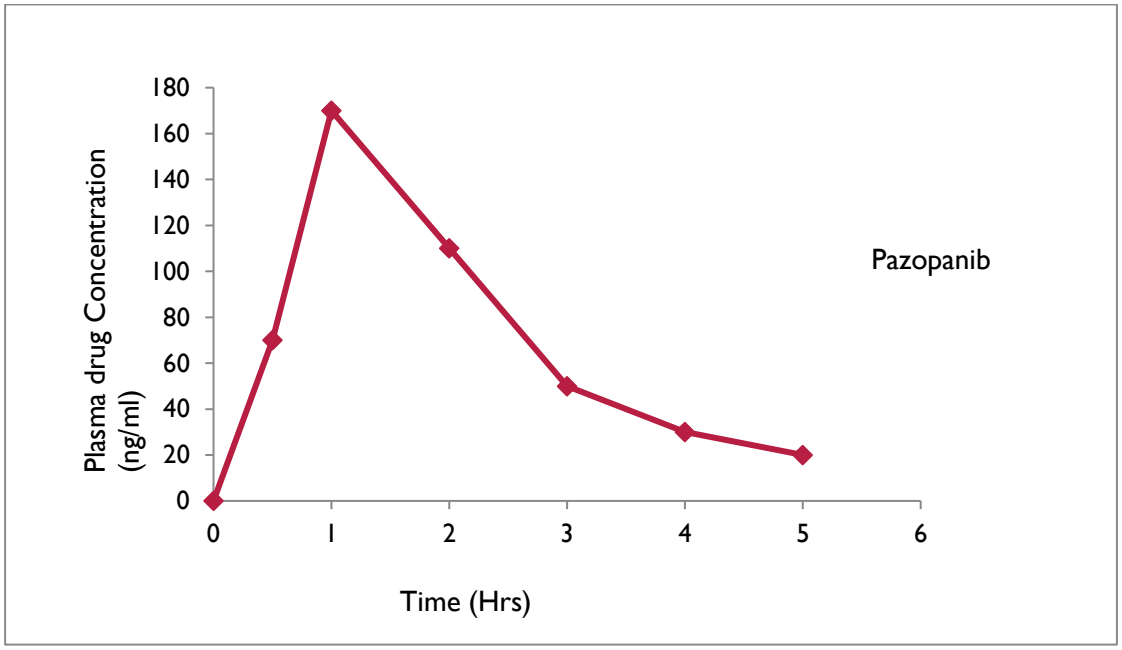

Figure 10: Mean plasma concentration-time profile of Pazopanib hydrochloride after single oral administration of pure drug.

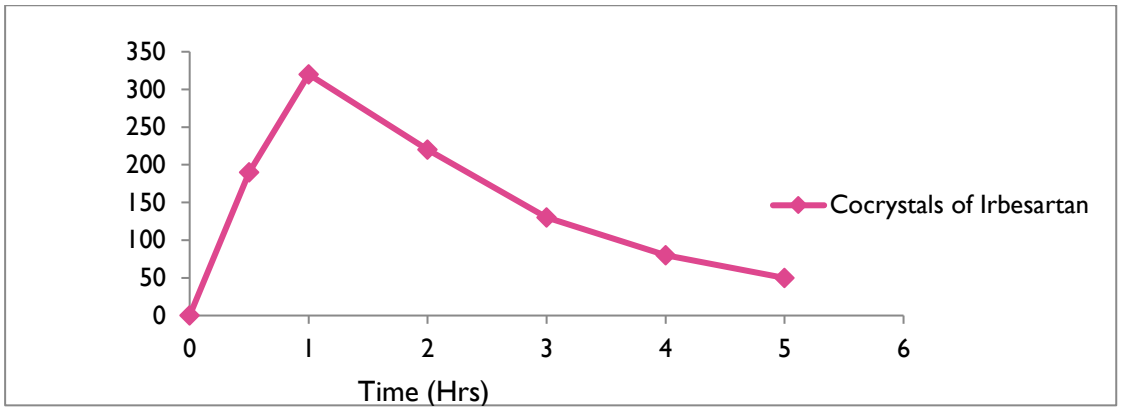

Figure 11: Mean plasma concentration-time profile of Pazopanib hydrochloride liquisolid compact after single oral administration.

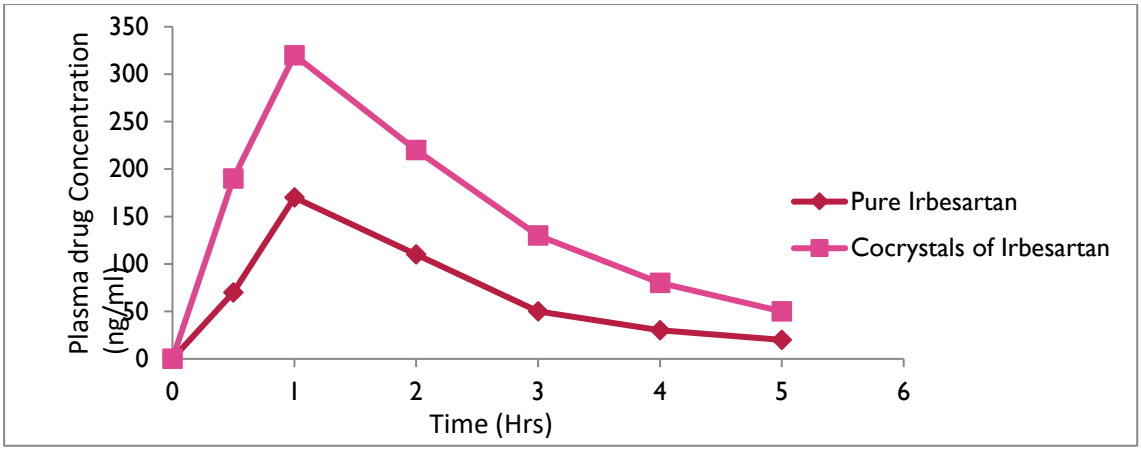

Figure 12: Mean plasma concentration-time profile of pure Pazopanib hydrochloride and Pazopanib hydrochloride liquisolid compact after single oral administration.

Table 8: Pharmacokinetic Parameter for Pure Pazopanib hydrochloride and Pazopanib hydrochloride Liquisolid Compacts

Pharmacokinetic Parameter	Pure Pazopanib hydrochloride	Pazopanib hydrochloride compact
AUC $_{0-t}$(ug/ml * hr)	165.16±24.2	374±22.5
AUC $_{0-\infty}$(ug/ml * hr)	570.23 ± 19.11	1217.8 ±25.46
Cmax (ug/ml)	170 .24 ±4.6	320.43± 2.8
Tmax (hrs)	2.0±0.0 hr	1.5±0.0hr
$t_{1/2}$(hrs)	4.3.±0.2 hr	5.5±0.2 hr
K_e(hrs)	0.35±	0.43±
Relative Bioavalability	--	2.5

The *in vivo* pharmacokinetic parameters of Pazopanib hydrochloride and Pazopanib hydrochloride Liquisolid compact were studied in Wistar rats. The measured mean Pazopanib hydrochloride plasma concentrations versus time after single oral administration in male Wistar rats using 0.5% oral Solution are depicted in (Fig. 12). The pharmacokinetic parameters calculated from the non-compartment model using linear trapezoidal method are described in (Table 8).

Relative bioavailability was calculated by using the following formula:

Relative bioavailability (%) = AUC_{test}/ $AUC_{reference}$× $Dose_{reference}$/ $Dose_{test}$

The pharmacokinetic parameters of Pazopanib hydrochloride obtained from non-compartmental analysis using a linear trapezoidal method after a single oral dose of 10 mg/kg of Pazopanib hydrochloride to Wistar rats. The t1/2, Tmax and Cmax of the drug was found to be about 4.3.±0.2 hr, 2.0±0.0 hr, and 170 .24 ±4.6 ng/ml respectively along with AUC_{0-t} of 165.16±24.2 ng/mL*h. In contrast, the Pazopanib hydrochloride liquisolid compact demonstrated higher Cmax and AUC_{0-t} as compared to pure Pazopanib hydrochloride (Cmax= 320.43± 2.8 ng/ml, AUC_{0-t} = 374±22.5). Conversely, the Tmax of the Pazopanib hydrochloride liquisolid compact was 1.5 hr where as it was 2.00 hrs for pure Pazopanib hydrochloride . The relative bioavailability of Pazopanib hydrochloride liquisolid compact formulation was found to be about 2.5 folds higher, which may be due to conversion of drug into its new solid phase which is having high internal energy that promotes quick dissolution and hence higher bioavailability was observed.

8. CONCLUSION:

PZH's solubility was improved by dispersing the medication in propylene glycol, which increased the drug's surface area and wetting property, improving the drug's oral bioavailability and dissolution. The Preformulation study like flow properties, UV analysis of PZH werecomplied with Indian Pharmacopoeial standards. The FT-IR spectra revealed that, there was no interaction between the drug and excipients. The excipients used were compatible with the PZH and hence with formulation also. The PZH liquisolid tablet's in-vitro drug release demonstrated an increase in PZH's rate of dissolving when compared to commercial tablets. As a cost-effective alternative, propylene glycol may be used as a dissolution-enhancing agent. The most innovative and potentially effective method for accelerating the dissolving of poorly water-soluble pharmaceuticals and the creation of instant release solid dosage forms is the liquisolid approach.

9. ACKNOWLEDGEMENT:

Authors are thankful to Glenmark Generic Ltd. Goa, India for providing gift sample of ciprofloxacin. Authors are also thankful to Principal and Management of DRGCOP, Malkapur for providing research and instruments facilities to carry out the research work..

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