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Research Article

Liquid Solid Compaction Technique : Advances The Stability, Dissolving Rate And Oral Bioavailability Of Poorly Soluble Drug – Pioglitazone

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ABSTRACT
The aim of present study is to enhance the dissolution of poorly water soluble drug of Pioglitazone HCl by liquisolid compact technique. Liquid solid compact were prepared using PEG-400 as non-volatile solvent, Microcrystalline cellulose as carrier and cross povidone as superdisintegrant.The compatibility of excipients and drug was confirmed by FT-IR studies. The dissolution studies for prepared liquid solid tablet were distinctly higher as compared to directly compressed tablets which show significance increased in wetting properties and surface area of drug available for dissolution. The optimized formulation of liquid solid pioglitazone tablet shows higher drug release when compared to marketed formulation. The mechanism of drug release studied for best formulations where fitted in accordance with higuchi model and korsemeyer peppas model it is evident that a linear relationship was obtained showing that is an apparent first order process.

Keywords: Pioglitazone, Bioavailability, Liquid solid compaction.

INTRODUCTION

Pioglitazone is an anti-diabetic medication used to treat type 2 diabetes. It may be used with metformin, a sulfonylurea, or insulin. Use is recommended together with exercise and diet. It is not recommended in type 1 diabetes. It is taken by mouth. Common side effects include headaches, muscle pains, inflammation of the throat, and swelling. Serious side effects may include bladder cancer, low blood sugar, heart failure, and osteoporosis. Use is not recommended in pregnancy or breastfeeding. It is in the thiazolidinedione (TZD) class and works by improving sensitivity of tissues to insulin.

METHODOLOGY

Method of preparation of liquid solid compacts

1. Pioglitazone was initially dissolved as a liquid carrier for the creation of a pharmaceutical solution in the non-volatile solvent PEG-400.
2. The drug solution carrier material, microcrystalline cellulose, is then added to a continuous mixture in a fast blender granulator.
3. Add estimated quantity of coating matter, i.e. silica, to obtain fine and absorbent particles.
4. Before compressing, add the disintegrant necessary, such as Cross Povidone, add Cross carmellose sodium and mix completely.
5. Additional additives such as magnesiansterate lubricant and lactose (diluent) will be added and mixed for 10 to 20 minutes in a rapid mixer granulator.
6. When finished, the mixture is sieved.
7. The resulting fine powder is compressed using Tablet Press.

Drug content

Respective preparation was exactly weighed and powdered by three tablets. Powder corresponding to 100 mg of pioglitazone stood dissolved in 20 ml of alcohol, adjusted with 7.4 to 100 ml buffers. The solution was diluted by using a 207 nm UV spectrophotometer with the distilled water tested for the drug. The drug content is assessed by the absorption obtained by the calibration curve.

In – Vitro dissolution studies

Pioglitazone dissolving rate was achieved by dissolving test equipment for all formulations (paddle). The solubility of liquid 900ml Buffer PH 7.4 was used. Each test stood conducted at a speed of 50 rpm and at a temperature of 370.5 degrees Celsius. Five millilitre samples of the dissolution mediums (5ml) remained withdrawn at various time intervals (at 5, 10, 20, 30, 45, and 60 minutes), suitably diluted, and then analysed. using UV Pioglitazone spectrophotometers and

absorption detected at 207nm. Dissolution tests have been conducted three times.

In vitro Dissolution Studies of Tablets

Dissolution release profiles of the compressed tablets were analysed.

Dissolution parameters

Apparatus -- USP-II, Paddle Method
Dissolution Medium -- P^H 7.4 Phosphate Buffer
RPM -- 50
Samplingintervals(Mins)--2,4,6,8,10,12,16, 18 and 20 min
Temperature -- 37+ 0.5 °C

FTIR Spectroscopy studies

FTIR spectrums were examined on the optimised batches of Liquid solid Pioglitazone Compacts to test the API compatibility with excipients is a requirement. The FTIR (Brucker) spectrophotometer and the FTIR (Brucker) spectrophotometer were used to get FTIR potassium bromide pellet spectroscopy. scanning range used for the scan took between 4400 and 400 cm-1 for 1 minute.

DSC studies

The automatic thermal analyzer captured the best DSC thermogram for Liquid solid Compacts (10mg sample). Detection of Substrate Complexity (DSC) is used to examine how a medicine reacts with an excipient.

X-Ray Diffraction

Powder X-ray diffraction can remain used to qualitatively perceive long-range substantial by detecting its scattering patterns.More crystalline material appears on sharper peaks. The recently built X-ray systems are semi-quantitative.

SEM studies

The shape and diameter of the exterior surface of Liquid solid Compacts were investigated. using electron microscope scanning. Under a scan microscope, the Liquid solid Compacts were spotted. The two-sided stickband remain placed directly on the SEM sampled stub and coated by gold foil (200nm thick) at low pressure (0.0001 mm Hg).

Disintegration test

The mounting tablet is suspended to 1000 ml of 37±2°C Water Beaker and is operated until there is no residue on the device screen in the test tablet. Reiteration the test on 12 added tablets if 1 or 2 pills do not totally dissolve. If the requirement has not been met, less than 16 of the 18 tablets examined are dissolved.

RESULTS AND DISCUSSION

Solubility Studies

Table 1: Solubility Data of Pioglitazone in Various Solvents

Solvent	Solubility(mg/ml)
Water	0.06±0.42
Tween 20	22±1.64
Tween 80	27±1.22
PG	38±1.56
Glycerine	54±3.86
PEG 200	68±1.65
PEG 400	83±2.29

Table 2: Calibration Curve of Pioglitazone in 0.1N HCl at 207nm

Concentration (μg/ml)	Absorbance
0	0
10	0.041
20	0.08
30	0.116
40	0.152
50	0.191
60	0.224

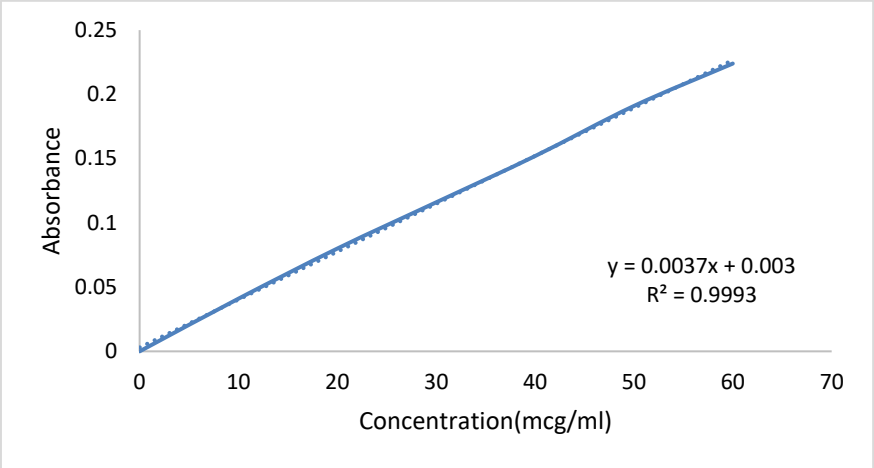


Fig.1: Calibration Curve of Pioglitazone in 0.1N HCl

Table 3: Flow properties of Different Formulations

Formulation Batch	Bulk density (g/cc)	Tapped Density (g/cc)	Carrs Index (%)	Hausners Ratio	Angle of Repose
F1	0.426	0.499	16.6	1.21	7.27
F2	0.37	0.72	45.13	1.86	19.21
F3	0.385	0.72	45.92	1.85	16.43
F4	0.26	0.382	34.2	1.6	17.3
F5	0.46	0.56	18.19	1.21	18.9
F6	0.52	0.715	29.98	1.42	15.4
F7	0.415	0.52	16.82	1.22	11.28
F8	0.52	0.54	9.04	1.12	13.38
F9	0.39	0.52	24.2	1.2	20.12

Table 4: Evaluation Studies of Different Formulations

Formulation	Weight Variation(mg)	Hardness (Kg/cm^2)	Friability	Disintegration Studies (mins)
F1	499±1.12	3.6±0.12	0.582±0.11	2.58
F2	498±0.04	3.23±0.24	0.52±0.18	3.2
F3	498±0.02	3.32±0.32	0.48±0.14	3.42
F4	498±0.16	3.64±0.22	0.46±0.28	3.82
F5	499±0.24	3.9±0.24	0.48±0.56	3.8
F6	498±0.28	3.5±0.32	0.42±0.28	3.92
F7	501±0.12	3.8±0.28	0.38±0.28	3.64
F8	498±0.14	3.2±0.38	0.461±0.26	3.92
F9	499±0.24	3.8±0.94	0.38±0.68	4.21

Table 5: Assay Values of Different formulations (n=3±sd)

Batch Codes	Drug Content (%)
F1	101.14±0.68
F2	98.82±2.08
F3	89.32±2.4
F4	78.32±0.48
F5	98.51±0.46
F6	83.16±0.24

F7	94.92±0.22
F8	98.61±1.4
F9	90.93±0.6

Table 6: Dissolution Profiles of F1, F2 and F3 in pH 7.4 buffer

Time (mins)	% Cumulative drug release		
	F1	F2	F3
0	0	0	0
2	10.7±0.2	7.2±1.4	5.3±4
4	20.3±0.8	16.7±3,7	9.3±1.7
6	30.1±1.8	24.6±2.4	15.4±4.1
8	45.4±5.7	36.4±5.8	24.2±6
10	66.3±2.1	56±7.8	38±5.7
12	99.4±0.8	74.9±8.7	53.3±4.2
14	-	83.2±1.5	68.5±4.2

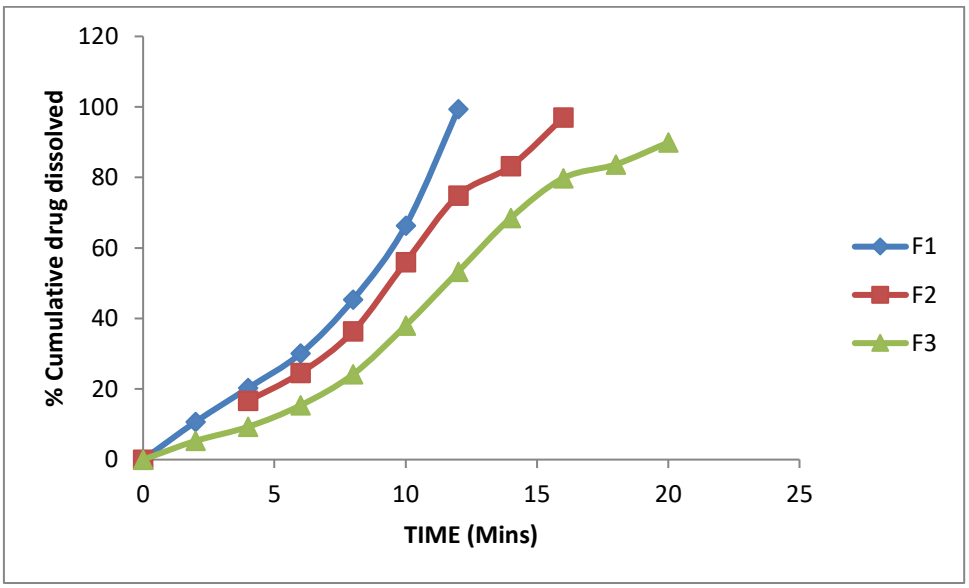


Fig.2: Dissolution profile of F1, F2, F3

Table 7: Dissolution Profiles of F4, F5, and F6 in pH 7.4 buffer

Time (mins)	% Cumulative drug release		
	F4	F5	F6
0	0	0	0
2	7.76±2.8	9.8±1.2	9.6±0.9
4	8.79±1.8	13.3±1.6	13.9±2.8
6	17.6±5.4	14.2±2.4	19.6±0.44
8	20.1±2.5	15.6±0.44	26.6±1.1
10	31.6±3.1	17.6±1.1	39.9±1
12	43.2±2.6	29.9±1	43.2±2.8
14	56.1±5.5	33.2±2.8	57.2±7.2
16	67.5±2.9	47.2±7.2	61.7±6.3
18	72.7±2.5	51.7±6.3	67.2±7.2
20	78.8±2.5	57.2±7.2	71.7±0.4

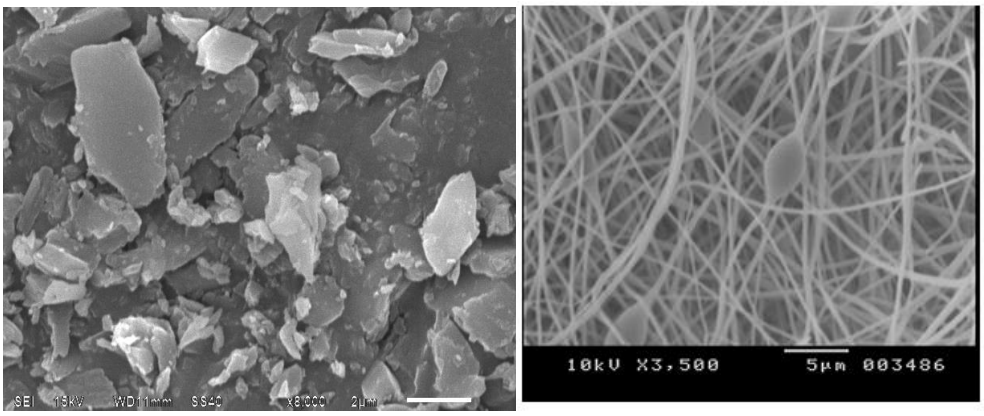
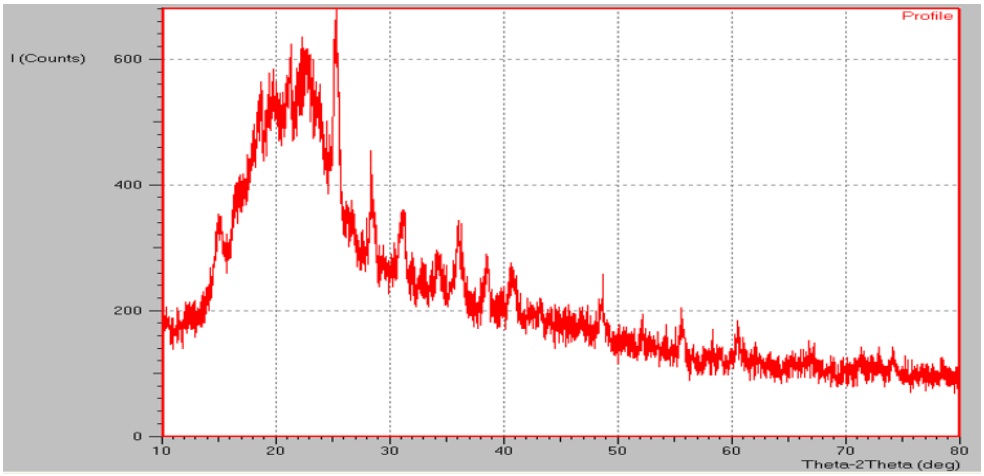


Fig.3: SEM Image of Pioglitazone
(a) pure drug mixture without Liquid (b) Best Formulation

XRD of pure drug



XRD of optimized formulation

SUMMARY AND CONCLUSION

The research focused on the preparation and assessment of liquid compacts in 400 concentrations utilising various PEG (polyethylene glycol) as non-volatile solvents and pioglitazone as medicine. Completely Nine packages of formulations have been produced utilising a liquid technique with diverse carrier, coating materials, super disintegrants and gliding agents. Variable quantities of microcrystalline cellulose are used for F1-F9 formulations as carriers, different levels of Silica gel as coating components. Different levels

of sodium cross-carmellose are practiced in preparations F1-F4 as a superdisintegrating agent. In F5–F9 formulae and as a gliding magnesium stereate different quantities of Crosspovidone are used as a superdisintegrant. All formulations were created using the traditional direct compression method. Tween 80, propylene glycol, polyethylene glycol 400, and distilled water were compared to see which would work best in pioglitazone solutions. Very little of it may be dissolved in pure water. Pioglitazone solubility was somewhat higher in polyethylene glycol 400 (PEG) than that of water. Hydrogen bonding was probably a slight increase in solubility. When compared to other solutions, pioglitazone was more soluble in PEG 400. PEG 400, which has a substantial polar component as well as numerous hydroxyl groups, remains accountable for the increased solubility. As a solvent, PEG400 could therefore be a superior choice among solvents studied. U.V. Pioglitazone with maximal absorption was scanned in the region of 400nm - 200nm, at 207nm, and the IP standards demonstrate the purity of the collected pharmaceutical sample and the graph of the V/s absorption chart in between 10-60 µg/ml. The FT-IR value of pure drug pioglitazone has been noticed since there was no change between the compact liquid and polymer patterns of Pioglitazone FT-IR and no drug and Exceptant interaction is shown for pure pharmaceutical. In order for the tablet to be effective, the flow qualities of the liquisolid granules must be considered. The flow properties were therefore determined before the tablets were compressed, as a result of this.The Carrs index is 20, but the Hausner ratio is just 0.25 and the remainder of the angle 0.25 revealed that the granular flow capacity is rather decent. The granules were free to flow owing to homogenous substantial in the die. Hardness is 2-4 kg/cm2 and friction is 0.35-0.7% showing strong mechanical strength. In dissolving media the release of a regular Pioglitazone pill is below 68.9% in 20 minutes. The synthesization of compact liquid molecules led to the enhancement of this poorly soluble medication. Drug release from a Liquisolid compact Pioglitazone tablet was greater than 99.4 percent in a dissolution medium of 12 minutes. The dissolution investigation shows that the F1 formulation displayed good pharmaceutical release than other formulations.

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