The Pharma Innovation Journal 2019; 8(3): 368-374

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2019; 8(3): 368-374

www.thepharmajournal.com
Received: 01-01-2019
Accepted: 05-02-2019

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Formulation and evaluation of curcumin Liquisolid tablets

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Abstract
The present study is an attempt to enhance the dissolution profile, absorption efficiency and bioavailability of water insoluble drugs, such as curcumin. A novel "Powder Solution Technology" or Liquisolid Compact Technology involves absorption and adsorption efficiency, which makes use of liquid medications, admixed with suitable carriers, coating materials and formulated into a free flowing, dry looking, Non-adherent and compressible powder forms. Formulations have been achieved by changing the proportion of carrier and coating material. Higher dissolution rates were observed in all liquisolid formulations, when compared with a conventional tablets and Pure Drug Mixture. The crystalline state of drug is changed to amorphous state; this transition occurs because the drug is in solution form and results of FTIR, revealed presence of all characteristics peaks of curcumin in formulations which confirm no drug excipient interactions. The amorphous form exhibited improvement in dissolution rates as well as apparent solubility was obtained because of the solubilization of Curcumin.

Keywords: Curcumin, liquisolid tablets, dissolution rate, solubility

1. Introduction
The progress in treatment of diseases has been evident with the upsurge in development of new drugs. An estimated 40% of these drugs are poorly water soluble. The enhancement of oral bioavailability of such poorly water soluble drugs remains one of the most challenging aspects of drug development [1, 2]. The development of Liquisolid Compact Technology as a practically viable method to enhance bioavailability of poorly water-soluble drugs overcome the limitations of previous approaches such as salt formation, solubilization by co solvents, and particle size reduction and other methods [3-5]. Much of the research that has been reported on Liquisolid Compact technologies involves drugs that are poorly water-soluble and highly permeable to biological membranes as with these drugs dissolution is the rate limiting step to absorption [6-8]. Liquisolid Compact technologies are particularly promising for improving the oral absorption and bioavailability of BCS Class II drugs [6-8].

1.2 Liquisolid Compact Technology
The new developed technique by Spireas liqui-solid system improves the dissolution properties of water insoluble or poorly soluble drugs. The term 'liqui-solid systems' (LS) is a powdered form of liquid drug formulated by converting liquid lipophilic drug or drug suspension or solution of water-insoluble solid drug in suitable non-volatile solvent systems, into dry looking, non-adherent, free-flowing and readily compressible powdered mixtures by blending with selected carrier and coating materials. Since drug dissolution is often the rate limiting step in gastrointestinal absorption, the significant increase in wetting properties and surface area of drug particles available for dissolution from Liquisolid compacts may be expected to display enhanced drug release characteristics and, consequently, improved oral bioavailability [10-12].

1.3 Components of Liquisolid Compact Formulation [13-14].
1. Nonvolatile solvent
2. Disintegrant
3. Carrier material
4. Coating material

2. Materials Used
Curcumin, Micro crystalline Cellulose, Starch, Silica, Lactose anhydrous, Talc, Magnesium stearate, Sodium Starch Glycolate, Propylene glycol.

3. Results and Discussions

3.1. Results

Table 1: Composition of different formulation of Curcumin liquisolid compacts

S. No	Ingredients in mgs	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Curcumin	50	50	50	50	50	50	50	50	50
2	Propylene glycol (ml)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
3	MCC	10	10	5	5	10	10	5	5	10
4	Starch	35	50	75	80	-	-	-	-	-
5	Lactose	-	-	-	-	35	50	75	80	200
6	Silica	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
7	Sodium Starch Glycolate	100	120	150	160	-	-	-	-	-
8	Cross Carmellose Sodium	-	-	-	-	100	120	150	160	25
9	Talc	50	40	10	-	50	40	10	-	5
10	Mg. Stereate	50	25	5	-	50	25	5	-	5
	Total Weight (mgs)	300	300	300	300	300	300	300	300	300

Table 2: Calibration Curve of Curcumin in pH 7.4 buffer at λ max 290nm

Concentration (µg/ml)	Absorbance
0	0
2	0.128
4	0.223
6	0.322
8	0.446
10	0.551
16	0.869
18	0.955

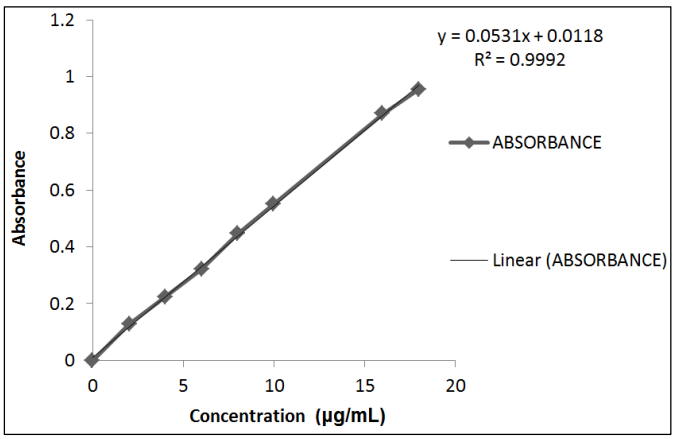

Fig 1: Calibration Curve of Curcumin in pH buffer 7.4 at 290nm

Table 3: Flow properties of Curcumin liquisolid compacts

Formulation Batch	Bulk density (g/cc)	Tapped Density (g/cc)	Carrs Index (%)	Hausners Ratio	Angle of Repose (Degrees)
F1	0.56	0.65	13.84	1.14	33
F2	0.66	0.74	10.8	1.12	34
F3	0.69	0.79	9.12	1.08	29
F4	0.55	0.64	13.16	1.15	26
F5	0.64	0.72	11.31	1.16	28
F6	0.68	0.76	12.34	1.08	22
F7	0.53	0.84	17.18	1.20	36
F8	0.62	0.96	16.78	1.12	38
F9	0.65	0.78	18.46	1.36	32

Table 4: Evaluation Studies of Curcumin Liquisolid Formulations

Formulation	Weight Variation (mg)	Hardness (Kg/cm^2)	Friability (percentage)	Disintegration Studies (mins)
F1	300±0.16	3.5±0.127	0.495±0.171	28.76
F2	300±0.10	3.7±0.132	0.365±0.121	25.45
F3	300±0.26	3.6±0.191	0.465±0.161	31.56
F4	299±0.16	3.9±0.221	0.410±0.151	21.68
F5	300±0.06	3.8±0.342	0.395±0.171	34.13
F6	300±0.18	3.4±0.342	0.315±0.112	18.53
F7	300±0.78	3.6±0.342	0.395±0.271	22.65
F8	299±0.26	4.1±0.342	0.422±0.122	21.98
F9	300±0.79	4.0±0.342	0.399±0.161	31.11

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

Batch Codes	Drug Content (%)
F1	100.13±0.88
F2	101.84±1.07
F3	99±1.2
F4	98.3±0.52
F5	97.5±0.21
F6	100.08±0.41
F7	93.9±0.34
F8	92.6±1.1
F9	99.9±0.7

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

Time (min)	Cumulative % Drug Dissolved ± SD (n=3)		
	F1	F2	F3
0	**0**	**0**	**0**
5	20.7±0.2	17.2±1	22.3±4
10	23±1.84	19.7±3	29.3±1.7
15	25.1±1.84	20.6±2.4	35.4±4.1
20	31.4±5	23.4±5	44.2±6
30	36.3±2.12	26.6±7.8	48±5.7
45	39.4±0.8	31.9±8.7	53.3±4.2
60	46.36±5.9	33.2±1.5	58.5±4.2
90	50.95±7.8	40±4.3	59.8±3.9
120	61.96±7.2	53.2±2.2	63.7±7.2

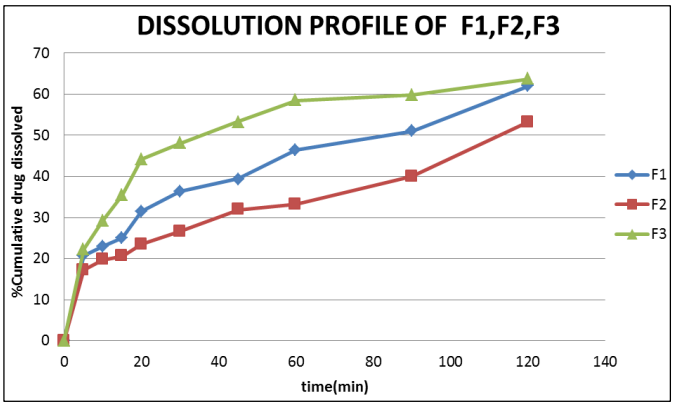

Fig 2: Dissolution profile of F1, F2, F3

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

Time (min)	Cumulative % Drug Dissolved ± SD (n=3)		
	F4	F5	F6
0	0	0	0
5	6.69±3.1	11.7±0.4	24.2±1.2
10	9.75±2.7	12.2±0.9	34.7±2.6
15	18.4±6.6	13.9±1.6	51.2±5
20	20.1±2.5	15.6±0.44	62.6±5.2
30	31.6±3.1	17.6±1.1	78.4±4.7
45	43.2±2.6	29.9±1	96.2±4.2
60	56.1±5.5	33.2±2.8	100.2±1.5
90	67.5±2.9	47.2±7.2	-
120	72.7±2.5	51.7±6.3	-

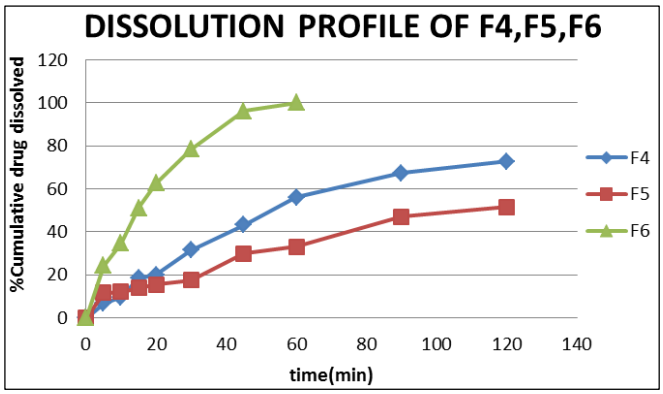

Fig 3: Dissolution profiles of F4, F5, F6

Table 8: Dissolution Profiles of F7, F8 and F9 in pH 7.4 buffer

Time (min)	Cumulative % Drug Dissolved ± SD (n=3)		
	F7	F8	F9
0	0	0	0
5	46.12±1.1	12±1.8	21±1
10	54.2±1.3	18.9±1.5	27.6±0.6
15	56.14±1.4	22.8±3.3	33.2±.4
20	59.2±1.8	24.6±4.7	37.9±1.5
30	60.4±2.1	28.6±4.5	40.3±3
45	61.3±1.7	36.2±3.8	43.1±3.8
60	62.7±2	43.9±6	45.3±6.1
90	63.2±3.4	52.5±1.6	48.2±7.1
120	66.2±3.3	63.9±1.5	55±5.5

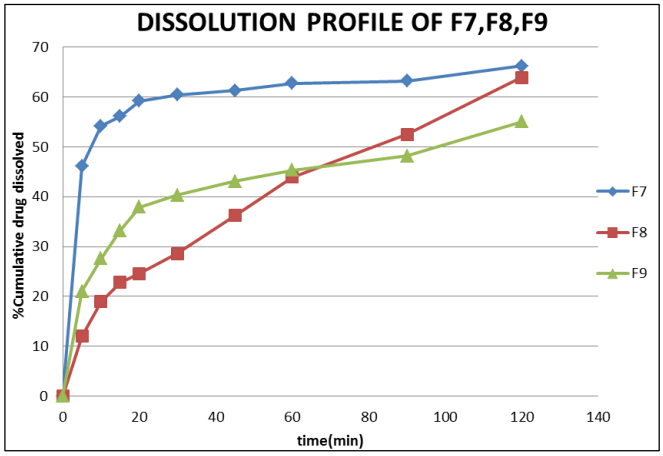

Fig 4: Dissolution profile of F7, F8, F9.

Table 9: Dissolution Profile of Curcumin Conventional tablets in pH 7.4 buffer

Time (min)	Cumulative % Drug Dissolved ± SD (n=3)
0	0
5	45.6
10	64.3
15	71.3
20	73.8
30	77
45	79.5
60	81.2
90	84
120	85

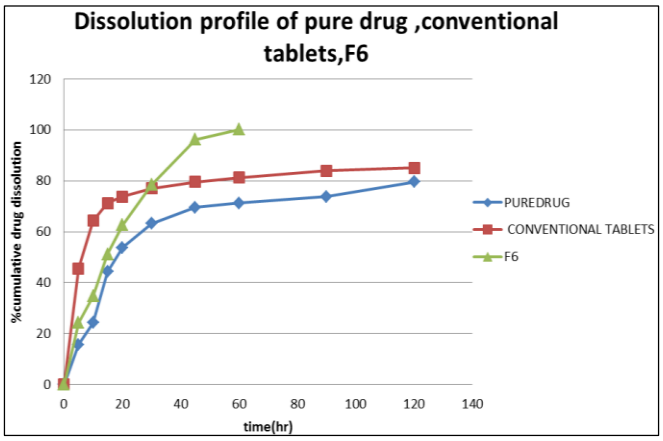

Fig 5: Dissolution profile of pure drug, conventional tablets, F6

Table 10: Dissolution Profile of Pure Drug in pH 7.4 buffer

Time (min)	Cumulative % Drug Dissolved ± SD (n=3)
0	0
5	15.6
10	24.3
15	44.3
20	53.8
30	63.2
45	69.5
60	71.2
90	73.8
120	79.6

Table 11: Dissolution profile of F6 formulation

Time (min)	F6
0	0
5	24.2±1.2
10	34.7±2.6
15	51.2±5
20	62.6±5.2
30	78.4±4.7
45	96.2±4.2
60	100.2±1.5
90	-
120	-

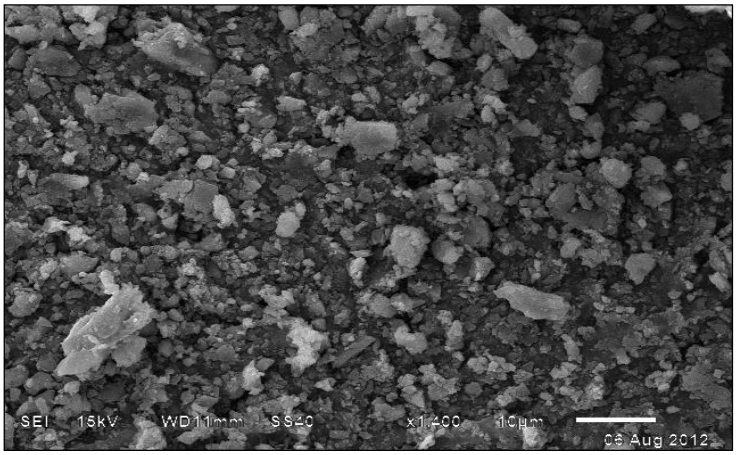

Fig 6: SEM Image of Optimized formulation F6

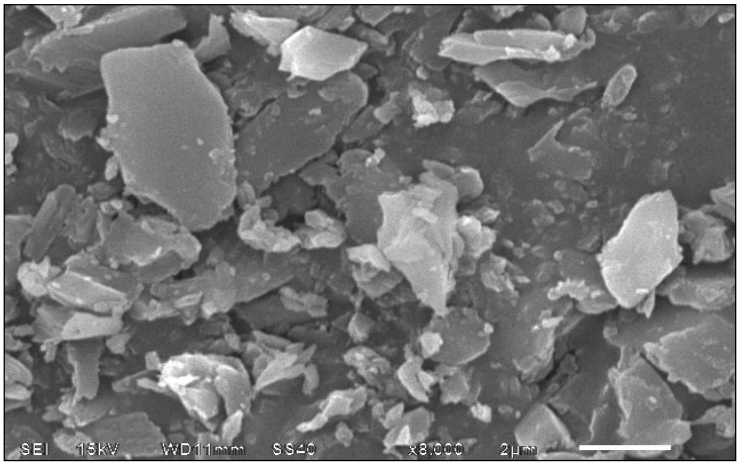

Fig 7: SEM Image of Curcumin pure drug

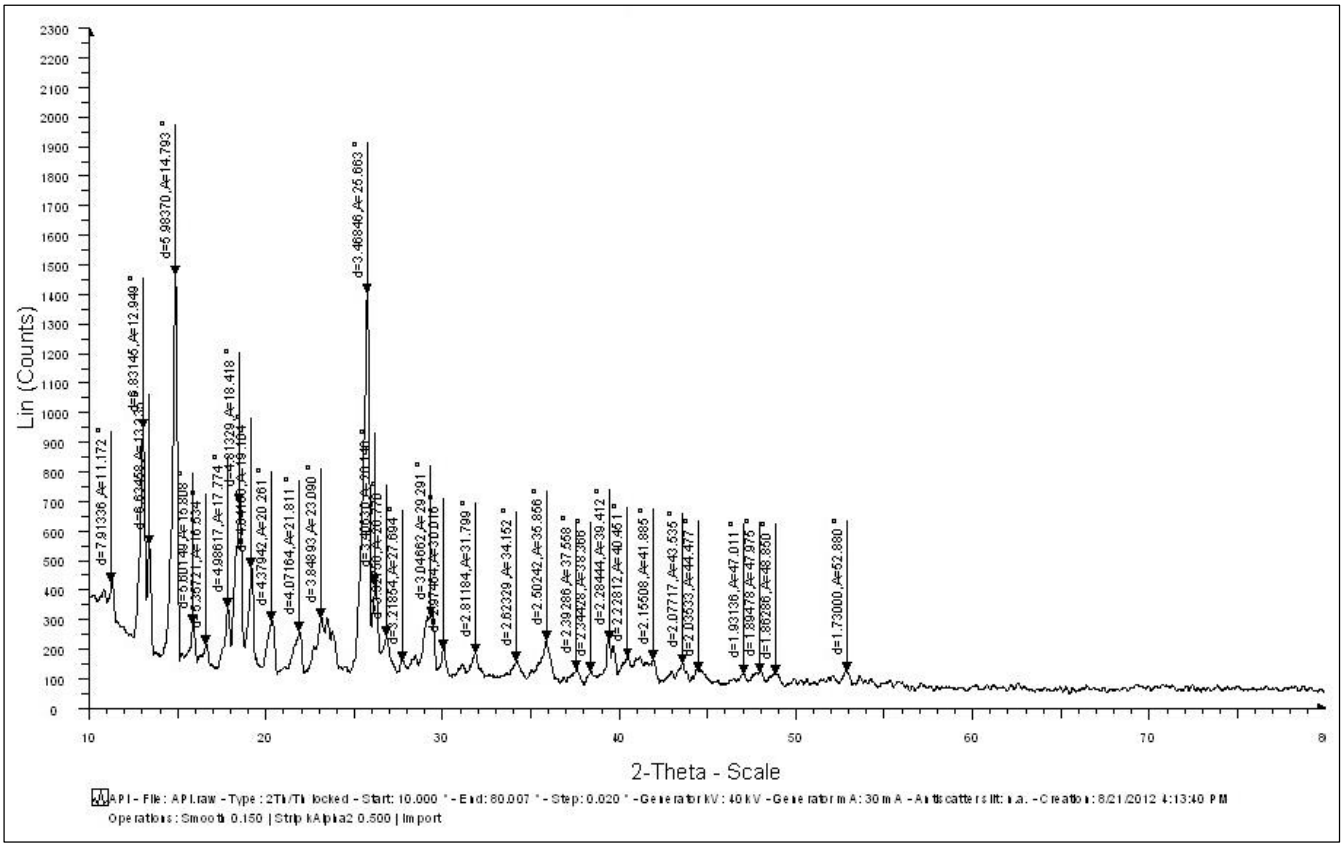

Fig 8: XRD of Curcumin pure drug

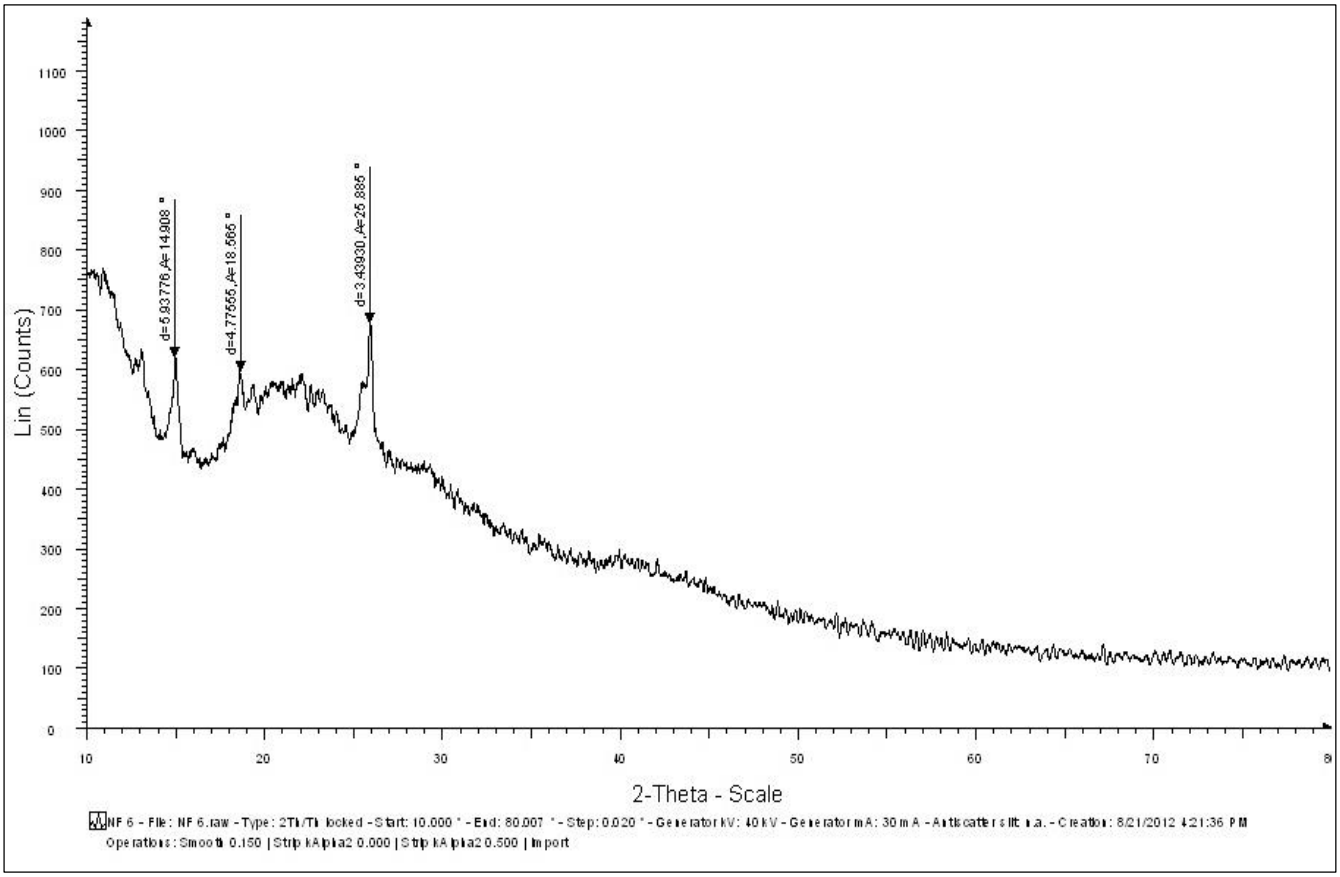

Fig 9: XRD of Optimized formulation F6

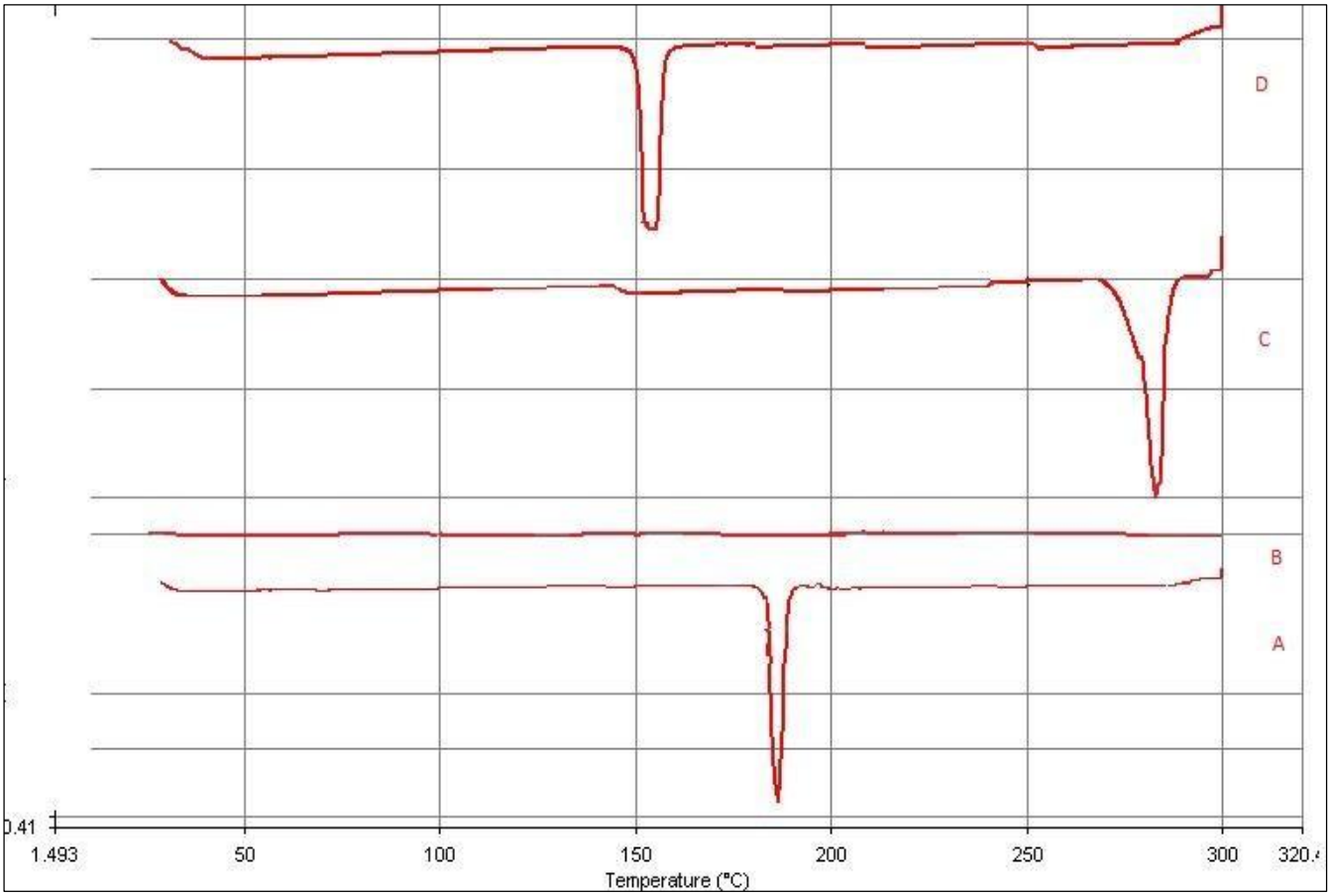

Fig 10: DSC Thermograms of A- Curcumin, B- Aerosil, C- Avicel PH 102, D- Liquisolid Preparation (F6)

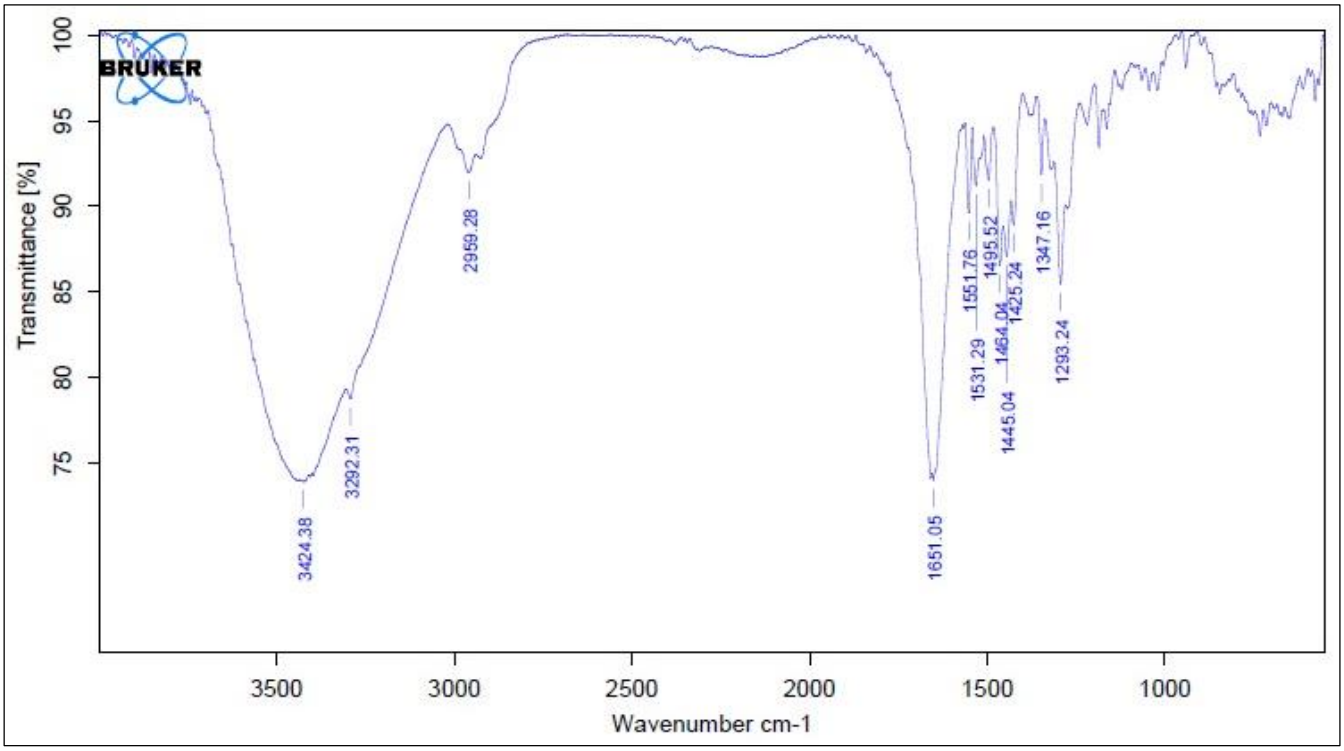

Fig 11: FT-IR Spectrum of Pure Drug Curcumin

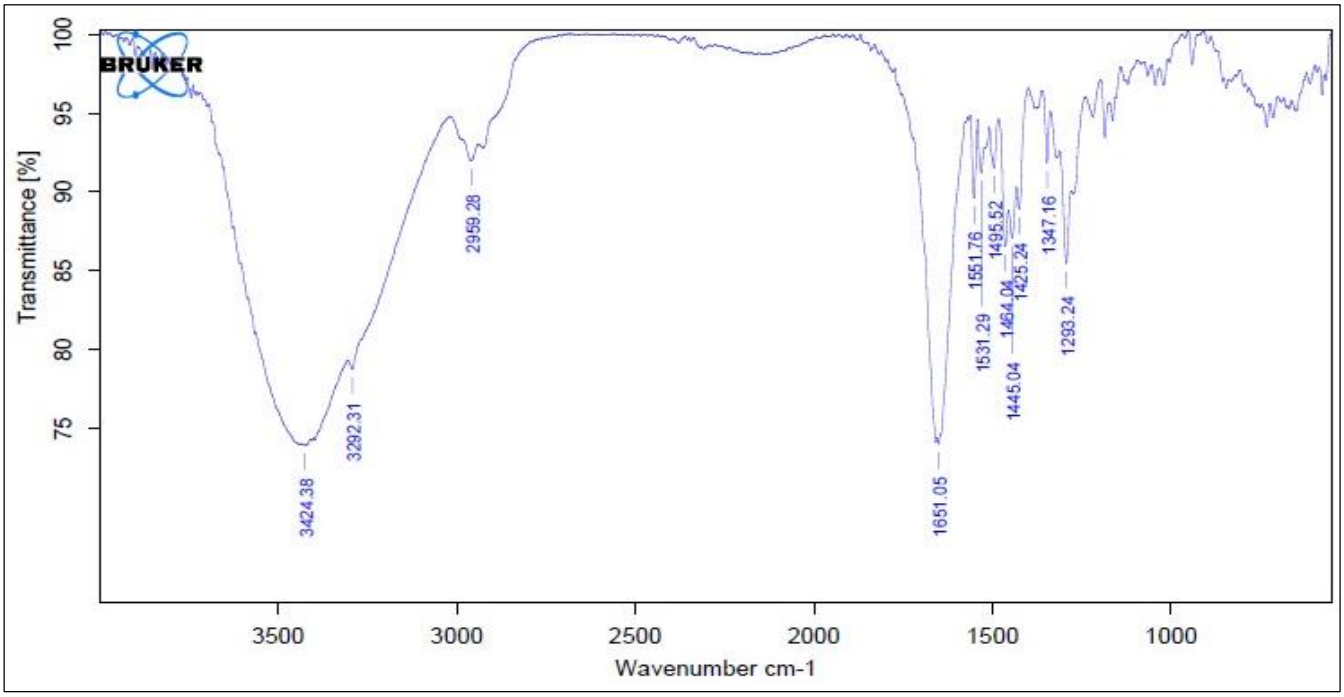

Fig 12: FT-IR Spectrum of Optimized formulation F6

3.2. Discussion

The present research work was aimed to prepare and evaluate liquisolid compacts using PEG 400 as a Non-volatile solvent and Curcumin as a drug. Totally Nine batches of formulations were prepared by liquisolid technique with different Carrier, Coating materials and Super disintigrants. For F1-F4 formulations varying concentrations of microcrystalline cellulose is used as a Carrier material, Silica and Starch as a coating material and sodium starch glycol ate is super disintigrant. For F5-F9 formulations varying concentrations of Microcrystalline Cellulose is used as Carrier material, Silica and Lactose as a coating material and cross Carmellose sodium as superdisintigrant. All the formulations were prepared by normal direct compression method. Solubility of Curcumin in Distilled water, propylene glycol, polyethylene glycol 400 and Tween 80 were performed. Its solubility was very poor in Distilled water. Propylene glycol (PG), the solubility of Curcumin was found to be slightly greater than that of water. This slight increase in solubility was probably through hydrogen bonding. Curcumin drug was very highly soluble in PEG 400 as compared to others. PEG 400, with a large polar part and several hydroxyl groups is responsible for the enhanced solubility. Thus, among the solvents tested, PEG400 could be a better choice as a solvent. In Pre formulation studies,

it was found that, the wavelength of Curcumin by spectroscopic method at 290 nm in Distilled water. This complied with IP standards thus indicating purity of obtained drug sample and plot graph of absorbance V/s concentration between 2-18 µg/ml ranges. The IR value of Curcumin pure drug was observed as no difference between the IR patterns of the liquisolid compact of Curcumin and polymer and with pure drug it indicates there is no drug and Excepient interactions. The flow properties of the liquisolid granules are vital for the performance of the tablet. Hence the flow properties were analyzed before compression of the tablets. The Hausner's ratio is ≤1.15 and angle of repose ≤25.00 values indicated a fairly good flow ability of granules. As the granules was free flowing, due to uniform filling in the die. Hardness is from 3.4-5.6kg/cm^2 and friability values are 0.35-0.7% indicated that tablets had a good mechanical strength. The drug release from a conventional Curcumin tablet is less that is only 65.6% and 79.78% drug was released in dissolution media in 40 and 60 min respectively. The dissolution enhancement of such poorly soluble drug was carried out by formulating liquisolid compacts. The drug release from a Liquisolid compact Curcumin tablet is more that is 96.2 to 100.2% drug was released in dissolution medium in a 40 to 60 min respectively. From the dissolution study it is clear that F6 formulation showed good drug release then that of other respective formulation batches.

4. Conclusion

In the present work totally nine formulations of Curcumin tablets were successfully developed by using liquisolid compact technique. Dissolution of Curcumin tablets were improved by liquisolid compact technique. Curcumin tablets were prepared by liquisolid technique with different concentrations of Carrier and Coating materials. Starch, Silica and Lactose are used as coating materials and Micro crystalline cellulose was used as carrier material. For F1-F4 formulations varying concentrations of microcrystalline cellulose is used as a Carrier material, starch, Silica as a coating materials and sodium starch glycolate is superdisintigrant. For F5-F9 formulations varying concentrations of microcrystalline cellulose is used as Carrier material, starch, Silica as coating materials and cross Carmellose sodium as superdisintigrant. The F6 formulation was found to be best of all the formulations showing that with an increased rate of dissolution rate and solubility. The *in- vitro* drugs release of Curcumin compacts showed an increase in dissolution rate. It is concluded that the Liquisolid compact technique can be used for increasing the dissolution rate of Curcumin tablets.

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