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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" 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 marketed product (Doctors Best). 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.

Key words: curcumin, liquisolid tablets, dissolution rate, solubility.

1. INTRODUCTION

One of the major concerns of present pharmaceutical research is how to enhance the dissolution profile, absorption efficiency and bioavailability of water insoluble drugs. During the past few years many techniques have been developed such as drug micronization, solid dispersions, co- precipitation, lyophilization and micro–encapsulation, use of pro-drug, drug derivatization processes and inclusion of drug solutions into soft gelatin capsules[1].

Micronization is the most common method used to increase the surface area of a drug, but this becomes less effective, when the drug is formulated as tablets or capsules[2-4]. In case of soft gelatin capsules, Ebert's review stated that these products demonstrated most efficient bioavailability since the drug was already in solution form[5]. The formulation of soft gelatin capsules is expensive and requires sophisticated technology; better approaches are still available to prepare the liquid oily medications and drug solutions of water insoluble solid drugs. A novel "Powder Solution Technology" makes use of liquid medications admixed with suitable carriers, coating materials and formulated into a moderately flowing, dry looking, non adherent and compressible powder forms with increased drug dissolution rates was employed in this study. Liquisolid compacts are formulated using non volatile oils as vehicles to produce liquid medications such as oily liquid drugs, solutions or suspensions of water insoluble solid drugs[6].

The quantities of various excipients required for powder solution formulations are determined in accordance with a new mathematical model expression[7]. The absorbate molecules diffuse inside the absorbent and are eventually captured by the powder particles within their bulk and thus absorption of the liquid occurs. Adsorption is the phenomenon in which liquid is not truly absorbed and instead of being dispersed through out the interior of the solid, the molecules only cling to its available surface, internal and external. Depending on the sorbent properties, both of these processes can occur simultaneously, thus referred to as sorption. Initially the liquid is absorbed into the interior of the particles and captured by its internal structure after saturation of this process then adsorption of the liquid onto the internal and external surfaces of the porous carrier particles occurs[8].

Curcumin (Figure 1) is also known as diferuloylmethane is a yellow polyphenol extracted from the rhizome of turmeric (*Curcuma longa*). Curcumin is a main constituent of the Indian spice turmeric, is of growing interest due to its wide ranging pharmaceutical properties[9]. Curcumin compound has a great pharmaceutical activity, has an effective antioxidant as well as has free radical scavenger properties. This compound has potency against many diseases such as cough, diabetes, anorexia, Alzheimer disease, rheumatism and hepatic disorders[10]. Besides it is extensively used in food industries. Raw materials itself will have variation in composition in term of colour, flavour and aroma compounds due to different harvesting time, size and growing site of the product. Curcumin has poor bioavailabity, low aqueous solubility and chemically unstable under acid and alkaline condition as well as light sensitivity[11].

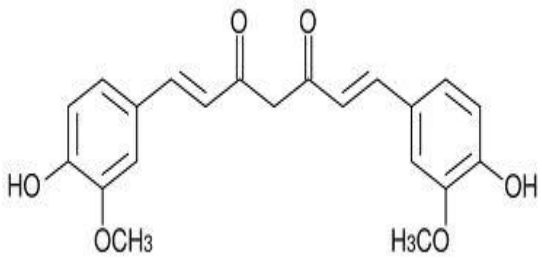

Figure 1. Stucture of curcumin.

2. MATERIALS AND METHODS

Curcumin (Aldrich, USA), Microcrystalline Cellulose 200 (Avicel) and Colloidal Silicon Dioxide (Aerosil) were procured from Cadilla Pharmaceuticals (Ahmedabad, India). Crospovidone was obtained as a gift sample from Alred (Roorke, India) and Poly Ethylene Glycol 400 (PEG 400) was procured from S.D. Fine Chem. Ltd. (Mumbai, India).

2.1 Calculation of the load factor (Lf)

In the present study, Polyethylene glycol 400 (PEG 400) was used as a non volatile solvent. Avicel PH 102 and Aerosil were used as carrier and coating materials respectively. To calculate the loading factor, 20 g of Avicel PH 102 and Aerosil in 2:1 (w/w) ratio were added to the PEG 400 and blended for 15 min, using a flow meter higher than $10cm^3/s$ was considered as an acceptable flow rate and the step was repeated to achieve optimum flow property. According to new mathematical model expression of liquisolid systems, liquid load factor is the ratio of the weight of liquid medication (W) and the weight of the carrier system (Q)

$$Lf = W/Q$$

Depending on the carrier and coating material ratio different carrier and coating material ratios ranging from 1, 3, 5 were taken[12] (Table 1).

Tabl3. No. 1. Different prepared formulations of Curcumin

Formulation	Curcumin conc. in PEG 400	carrier and coating material ratios
F1	5 %	1:1
F2		3:1
F3		5:1
F4	10 %	1:1
F5		3:1
F6		5:1
F7	20 %	1:1
F8		3:1
F9		5:1

2.2 Load factor preparation of liquisolid tablets

Specific quantities of previously weighed solid drug were mixed with PEG 400 and constantly stirred until homogeneous liquid medications were obtained for 5%, 10% and 20% amount of drug in PEG. Calculated amounts of carrier (Avicel PH 102) (Q) was added to the liquid medication and blended for 15 minutes. The resulting mixture was blended with the calculated amounts of coating material (Aerosil) (q). Crospovidone (2%) was added as a super disintegrate to the mixture of carrier and coating materials and blended thoroughly (Table 2). The prepared liquisolid systems were compressed into tablets.

2.3 Pre compression studies of the liquisolid powder systems

Pre-compression studies may play a key role in dose variations, to get a uniform filling of tablet dies and acceptable flow properties for the proposed liquisolid powder systems. Flow properties of the powders were evaluated by determining the angle of repose. Static angle of repose was measured according to the fixed funnel and freestanding cone method. A funnel with the end of the stem cut perpendicular to the axis of symmetry is secured with its tip 10 cm height, H, above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the conical pile so formed just reaches the tip of the funnel. The mean diameter, 2 R, of H, base of the powder cone, was determined and the tangent of the angle of repose was given by:

$$\tan \theta = h/r$$

Where θ is the repose angle

Angle of repose, Carr's Index and Hausner's Ratio were calculated.

Table No.2. Evaluation of flow properties

Sr. No	code	Carrier and coating material ratio	Tan (θ)	Carr's Index	Hausner's ratio
1	F2	3:1	31.2	13.7	1.21
2	F4	1:1	32.1	13.1	1.17
3	F8	3:1	31.5	12.2	1.13

2.4 Fourier Transform Infrared Spectroscopy (FTIR)

Infrared spectroscopy was performed on FTIR. Different formulations were analyzed in FTIR and the range from 400 to 4000 nm was selected. The results obtained from FTIR, revealed presence of all characteristics peaks of curcumin in formulations which confirm no drug excipient interactions.

2.5 Differential Scanning Calorimetry (DSC)

The DSC thermograms were recorded using a differential scanning calorimeter (DSC 823E, Mettler Toledo, Japan). About 2.5 mg of each sample was heated in a pierced aluminum pan from 30 to 2000C at a heating rate of 10°C /min under a stream of nitrogen at a flow rate of 50 ml/min. Thermal data analysis of the DSC thermograms were conducted using STARe software (version 5.21).

2.6 *In-Vitro* Dissolution studies

The *in vitro* drug release studies were performed using 900 mL of 0.1 N HCl with paddle rotation of 50 rpm at 37^0c ± 0.5°c. The samples were withdrawn at specific time intervals and replaced by the fresh medium. Obtained samples were filtered on a 0.45µm filter paper and analyzed at 425 nm by using a UV visible spectrophotometer (UV 1800 shimadzu).

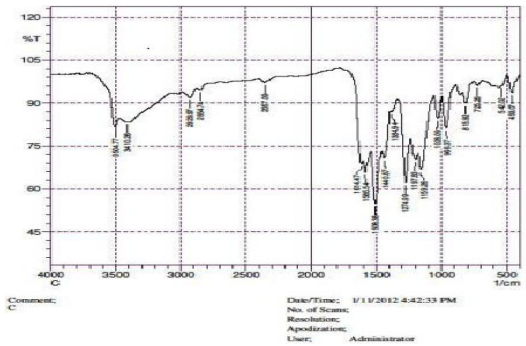

Figure 2. FTIR of Curcumin

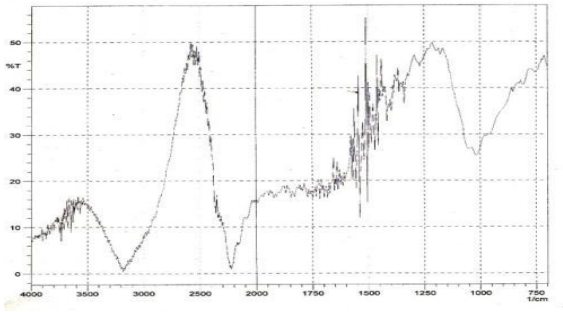

Figure 3. FTIR of formulation F2

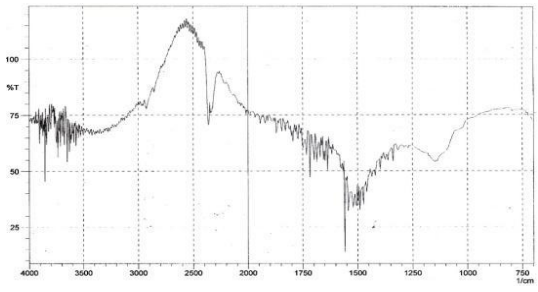

Figure 4. FTIR of formulation F4

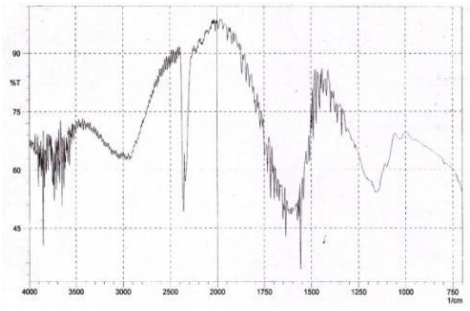

Figure 5. FTIR of formulation F8

3. RESULTS AND DISCUSSION

Angle of repose, Carr's index and Hausner's ratio were performed for all the Curcumin liquisolid formulation. Among those F2, F4 and F8 exhibited better flow properties (θ=31.2, 32.1, 31.5; Carr's Index =13.7, 13.1, 12.2 and Hausner's ratio=1.21, 1.17, 1.13 respectively) when compared to other formulations. These liquisolid tablets also showed acceptable friability and percentage loss in weight not more than 1% and exhibited acceptable durability and resisted abrasion during handling. Thus these formulations considered optimized and selected for further evaluations. Loading factor was calculated and was found to be 115 for F2, 55 for F4 and 40 for F8. Formulations F2, F4 and F8 also showed good dissolution profile (Figure 7), but F2 showed higher drug release as compared to other probably due to the higher amount of PEG 400, which might have contributed to the increase in the saturation solubility of the drug at the microenvironment. At this microenvironment, it may be possible that the infinite amounts of PEG 400 diffusing with the drug molecules out of a single liquisolid particle and excessive amount of avicel may be responsible for its disintegration property.

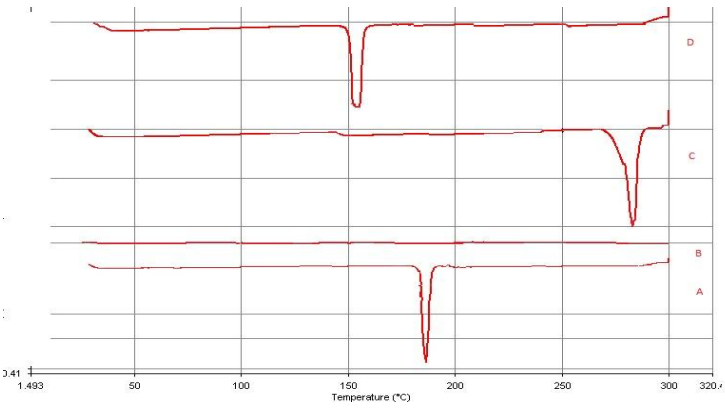

Figure 6: A- Curcumin, B- Aerosil, C- Avicel PH 102, D- Liquisolid Preparation

The FTIR spectra for curcumin and its formulations were showed in Figure 2-5. The prominent spectrum of curcumin are as follows; 3512, 1627, 1508, 1429, 1281, 1206, 1153, 1026, 963, 856 and 814 cm^{-1}. Generally, the stretching region of hydroxyl group, O-H was showed at the band range of 3200-3600 cm^{-1}. The band at 3510 cm^{-1} indicates the presence of hydroxyl group in the curcumin; sharp peak was noticed for carbonyl in curcumin. The band of alkanes (C-H) is shown at 1350-1512 cm^{-1}. Stretching bands at 1000-1260 cm^{-1} indicated the presence of ether group (C-O). The results obtained from FTIR, revealed presence of all characteristics peaks of curcumin in formulations which confirm no drug excipient interactions. Curcumin constructive peak points out that Curcumin has almost entirely converted from crystalline to the amorphous state. This transition is due to Curcumin solubilization in the liquid vehicle that was absorbed into the carrier such as avicel and adsorbed on to the coating material such as aerosil.

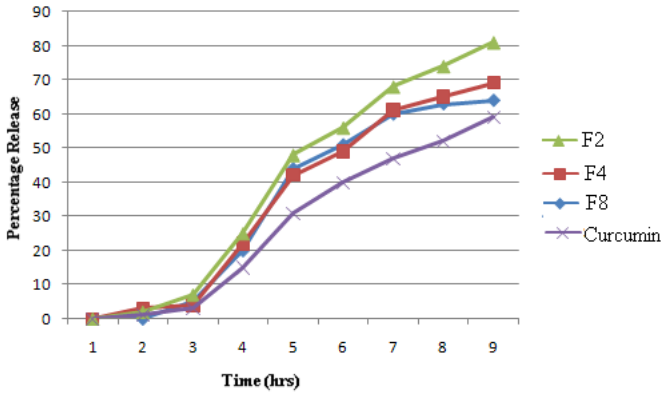

Figure 7. Dissolution profile of different optimized formulations.

The DSC of pure Curcumin, excipients and formulation are shown in Figure 6. The thermogram of pure curcumin showed a sharp endothermic peak at 178.46 °C due to drug melting. The sharp endothermic peak indicated that the curcumin was in crystalline state. The liquisolid formulations showed the little shif in a peaks, which indicates that there is change in crystalline form to amorphous form of drug and formation of drug solution in the liquisolid powdered system, i.e., the drug is molecularly dispersed within the liquisolid matrix and there is no interaction between drug and excipients (figure 8). From above finding it can be concluded that the enhanced dissolution rate of curcumin liquisolid compacts is due to the formation of amorphous form of the drug. We believe that, therefore, in the present study due to significantly improved wetting properties of liquisolid compacts and drug particles, liquisolid compacts display enhanced drug dissolution characteristics.

These results confirm that improvement in dissolution rates as well as apparent solubility was obtained because of the solubilization of Curcumin.

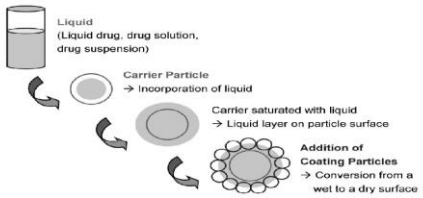

Figure 8 : Schematic presentation of Liquisolid systems

4. CONCLUSION

Powder solution technology is one of the promising approaches to increase dissolution rate and is confirmed by the experimental results. Rationale of the present study suggesting that the use of avicel can provide good flow properties and hardness. Curcumin liquisolid tablets prepared with PEG 400 showed highest dissolution rate. This was due to increase in wetting properties and surface area of drug available for dissolution media. Accordingly, choosing a suitable liquid vehicle, depending on its different properties for a particular drug is important to prepare a successful liquisolid tablets Thus study concluded that liquisolid technology can be used effectively for the poorly soluble drugs.

5. ACKNOWLEDGEMENT

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REFERENCES

1. Kapsi SG, Ayreys JW. Processing factors in development of solid solution formulation of itraconazole for enhancement of drug dissolution behavior of water insoluble drugs. J. Pharm. Sci. 2001; 76: 74-752.

2. Aguiar AJ, Zelmer AJ, Kinkel AW. Deagglomeration behavior of relatively insoluble benzoic acid and its sodium salt. J. Pharm. Sci. 1979; 56: 1243-1252.

3. Finholt P, Solvang S. Dissolution Kinetics of drugs in human gastric juice the role of surface tension. J. Pharm. Sci. 1968; 571: 322-1326.

4. Lin SL, Menig J, Lachman L. Interdependence of physiological surfactant and drug particle size on the dissolution behavior of water insoluble drugs. J. Pharm. Sci. 1968; 57: 2143-2146.

5. Ebert WR. Soft gelatin capsules: unique dosage form. Pharm. Tech. 1977; 1: 44-50.

6. Spireas S. Liquisolid systems and methods of preparing same, United State Patent 6, 423, 339 (B1), 2002.

7. Liao CC. Physicochemical properties of selected powdered drug solutions, Ph.D. thesis, St.John's University, Jamaica, 1983. 27-30

8. Martin AN, Swarbbrick J, Cammarata A. Physical chemical principles in the pharmaceutical sciences. In: Martin, (Ed.) Physical pharmacy. Philadelphia: Lea & Febiger. 1983; 445-468

9. Kristin N, Patricia B, Boland G. and Brian D.W. Fluorescence enhancement of curcumin upon inclusion into parent and modified cyclodextrins. J. Photochem. Photobiol. A–Chem., 2005; 173: 230–237.

10. Ono K, Hasegawa K, Naiki H and Yamada M. Curcumin have potent anti-amyloidogenic effects for Alzheimer's bamyloid fibrils *in vitro.* J. Neurosci. Res., 2004; 75: 742–750.

11. Regina AO, Jan NMC, Barbara VL and Nico PEV. Inhibition of human recombinant cytochrome P450s by curcumin and curcumin decomposition products. J. Toxicol., 2007; 235: 83–91.

12. Javadzadeh Y, Mussalrezaei L, Nokhodchi A. Liquisolid technique as a new approach to sustain propranolol hydrochloride release from tablet matrices. Int. J. Pharm. 2008; 362: 102- 108.