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Der Pharmacia Lettre, 2021, 13 (9): 11-18
(http://scholarsresearchlibrary.com/archive.html)

ISSN 0975-5071
USA CODEN: DPLEB4

Inclusion Complexation of Curcumin with Beta Cyclodextrin to Improve Solubility

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ABSTRACT

Curcumin is an antidiabetic, anti-bacterial, anti-inflammatory, antioxidant drug having low solubility due to its crystalline nature. Drug is coming under class II BCS classification [1]. Here it is an attempt to improve solubility by inclusion complexation method. For this research work cyclodextrin was used. Cyclodextrin is derived from starch. It of different types alpha, beta and gamma cyclodextrin. Depending upon number of sugar moiety cyclodextrins is classified. β Cyclodextrin used in research work for complexation with Curcumin [2]. X ray Diffraction study was conducted for both pure drug and complex. The pure drug shows sharp peaks in graph which reflects nature of crystallinity. Inclusion complexation was done by Physical mixture and kneading method. Volume, temperature and solvent were optimised. After complexation micromeritics and in vitro dissolution tests were conducted, this gave satisfactory results. Calibration curve was done with distilled water. Phase solubility study was conducted [3].

Key words: FTIR, Phase solubility, BCS, Crystallinity, Amorphous.

INTRODUCTION

Curcumin is a drug used for multiple purpose. It also helps to prevent nerve problem, blindness, kidney damage. It keeps blood sugar low. More than 400 million people across the world under the threat of diabetes [4]. It's having anti-inflammatory effect. The solubility of drug is least in aqueous medium and under BCS class II. Effects of curcumin for diabetic patients are needful and helpful. So combined therapy for diabetes is effective. The study is designed to improve the aqueous solubility by different techniques. Both drugs having challenges for formulations. Solid dispersion can improve the solubility of curcumin [5]. The curcumin can be enhanced its solubility by complexation. It can be formulated by enhancing its dissolution rate. As there as not still studied the combined formulation of complexed formulation with the said techniques, it is important to study the comparative study of drug with complexation and non-complexed active ingredients the successful study may lead to cost effective formulations with an effective formulation for mankind [6].

MATERIALS AND METHODS

Materials

The list of apparatus and instruments used in this research are listed below (Table 1).

SL. No.	Apparatus	Source
1	Analytical balance	Adair Dutta, AD-50 B, Kolkata
2	Glass wares, beakers, separatory funnel	Borosil
3	Magnetic stirrer	Remi magnetic stirrer
4	Syring	Dispovan
5	Sonicator	Probe Sonicator
6	UV/VIS. Spectroscopy	Systronic double beam 2203 smart spectrophotometer
7	Powdered – XRD	Phillip analytical X-ray BV (PW3710) X-ray Diffractometer
8	Dissolution Apparatus	USP 8 basket Digital Test Apparatus Lab India (Disso-2000) Mumbai
9	Sieve set	ASTM Standard Sieves, SISSO, India
10	Distillation apparatus	Borosil
11	Shaker water bath	Remi shaker water bath
12	Incubator	Thermoline laboratory incubator

Table 1: Apparatus and instruments.

Micromeritics study-density measurement

Bulk density: First 1 gm drug is weighed accurately and kept in a clean dry graduated measuring cylinder. Then after pouring the dug in to the cylinder, the granular bed made uniform without disturbing much [7]. The volume map measured directly from the granulation. Measured volume is called as bulk volume. The density is called as bulk density.

$$\text{Bulk density} = \frac{\text{weight of the drug}}{\text{Bulk volume}}$$

Tapped density: After measuring bulk volume of the same measuring cylinder is subjected to tap really 200 times by hand. Then volume was detected. This volume is called as tapped volume.

$$\text{Tapped density} = \frac{\text{Weight of the granules}}{\text{Tapped density}}$$

Flow properties

Angle of repose: A glass funnel having tip cut horizontal to the surface was fixed at constant height around 2 cm with the help of a stand and on the tip one graph paper was placed 2 gm of the drug was weighed and directly poured at a time through the funnel [8]. So the granules formed a conical structure having a height. The weight of the firmed core way measured with the help of scale and the perimeter of the core was marked with the help of marker [9]. From this average radius of the formed circle was measured by drawing various diameter through the center, the angle of repose was calculated by the following formula [10].

$$\theta = \tan^{-1} h/r$$

Where,

θ=Angle of repose.

h=height of the formed cone.

r=radius of the circular base on the formed cone (Table 2).

Angle of repose in degree	Flow property
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Table 2: Flow properties with angle of repose.

Carr's index: It is one of the most important parameter to characterize the nature of powder and granules **(**Table 3).

$$\text{Carr's index}(\%) = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

Carr's index	Types of flow
5-15	Excellent flow
12-16	Good flow
18-21	Fair to passable flow
23-35	Poor flow
33-38	Very poor flow
>40	Extremely poor flow

Table 3: Carr's index and flow property relationship**.**

Hausner's ratio: It is an important character to determine the flow property of powder and granules.

$$\text{Hausner's ratio} = \frac{\text{Bulk density}}{\text{Tapped density}}$$

Value less than 1.25 indicates good flow and greater than 1.25 indicates poor flow.

RESULTS AND DISCUSSION

Illuriation on micromeritics study of pure drug

Micromeritics of the study of the pure drugs and their results were reported in the (Table 4).

Experiment	Result
Bulk density	0.1742 gm/ml
Tapped density	0.2632 gm/ml
Carr's index	33.82%
Hausner's ratio	1.51
Angle of repose	33.52°

Table 4: Accurate experimental results of the micromeritics study-density measurement.

Sieve analysis: An accurate weighed 2 gm quantity of drug was subjected to granulometric study using sieves 22, 30, 44, 60, 80, 100 and 120 using a sieve shaker. Drug is sieved nearly around 10 minutes than the sieves are removed from the sieve shaker and powder retained in each sieves was calculated in percentage form using initial weight taken. The results were given below (Tables 5-7, Figures 1 and 2).

Sieve no.	Retained amount of drug (in mg)	Percentage retained (%)
22	0.926	46.3
30	0.33	16.5
44	0.176	8.8
60	0.168	8.4
80	0.016	0.8
100	0.101	5.05
120	0.01	0.5
Total	1.727	86.35

Table 5: Sieving analysis.

Concentration (mcg/ml)	Absorbance
0	0
5	0.076
10	0.191
15	0.298
20	0.396
25	0.492
30	0.611
35	0.728
40	0.836
45	0.939
50	1.043

Table 6: Calibration curve of drug with pH 7.4 buffer solution.

Sl.NO.	Time	%DR
1	0	0
2	2	0.76
3	4	1.9
4	6	2.75
5	8	5.63
6	10	8.25
7	20	15.6
8	30	20.18

Table 7: Dissolution data of pure drug in distilled water.

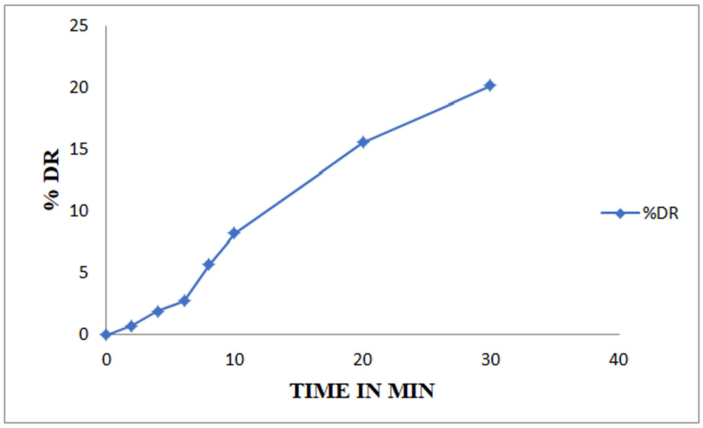

Figure 1: Dissolution of pure drug in distilled water. —♦—: %DR.

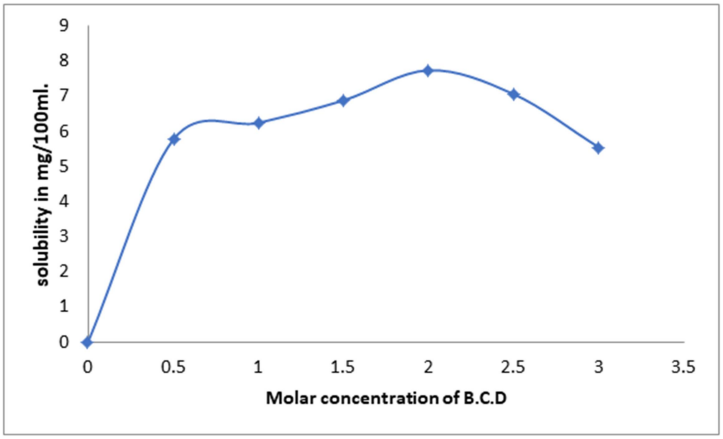

Figure 2: Phase solubility studies of drug and β -CD.

Methodology optimization

Physical mixture method: Drug and beta-cyclodextrin in the ratio 1:2 was taken and were mixed thoroughly with constant trituration, passed through sieve no. 100 and stored in a desicator.

Kneading method: Drug and beta-cyclodextrin in the ratio 1:2 was taken and to it 20 ml methanol was added and were mixed till a thick slurry was obtained with constant trituration, then it was dried at 45°C, passed through sieve no.100 and stored in a desicator (Tables 8-11, Figures 3 and 4).

Method	% Drug content
Physical mixture method	83.82
Kneading method	85.62

Table 8: Drug content in pH 7.4 buffer.

Sample	Volume of methanol	Percentage
A	25	55.12
B	20	85.62
C	15	85.05

Table 9: Estimation of drug content of drug complex in pH 7.4 buffer.

Parameters	Complex	Pure drug
Bulk density	0.294 gm/ml	0.1742 gm/ml
Tapped density	0.384 gm/ml	0.2632 gm/ml
Compressibility index	23.43%	33.82%
Angle of repose	30.068	33.52
Hausner's ratio	1.306	1.51

Table 10: Physicochemical characterization of complex.

Time(min)	%DR(PM)	%DR(KM)	Pure Drug(PD)
0	0	0	0
2	8.3	11.58	0.76
4	17	30.29	1.9
6	24.1	35.89	2.75
8	37.5	40.09	5.63
10	44.21	47.2	8.25
20	61.48	75.74	15.6
30	65.94	86.43	20.18

Table 11: Comparative dissolution data of kneading mixture, physical mixture, pure drug with distilled water.

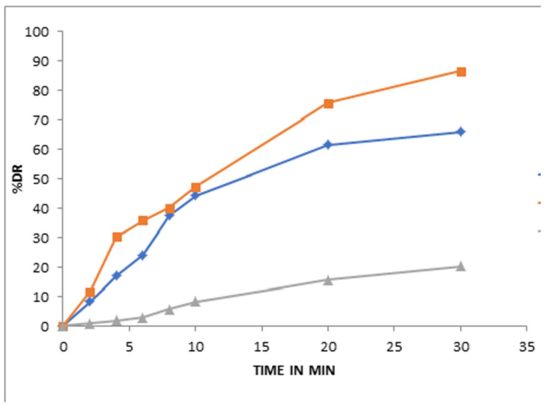

Figure 3: Comparitive dissolution data of kneading mixture, physical mixture, pure drug with distilled water.

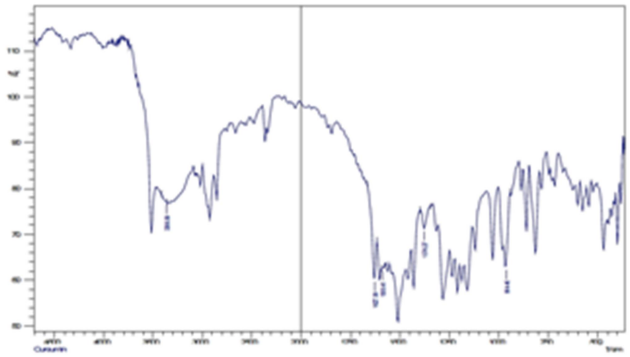

Figure 4: FTIR study.

CONCLUSION

According to World Health Organization (WHO) reports from 1980 to 2016 the people of diabetes rose from 108 million to 422 million. Between 2000 to 2016 death rates below the age of 18 increased to 5%. Diabetes plays an important role in failure of kidney, blindness, Heart attack. According to WHO diabetes is the seventh leading cause of death. The potent drug curcumin may plays an important role if it will more soluble. The result is satisfactory and it can be formulated in new dosage form along with anti-diabetic drug.

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