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Solubility Enhancement of poorly water soluble drug by Solid dispersion using sugar carriers

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Abstract

The drug allopurinol is in crystalline form which is converted to amorphous form to enhance the solubility by solid dispersion .This might be due to solubilising effect of carriers or amorphous state of the drug in solid dispersion or entrapping the drug in molecular state by the carrier.Maltose and Sucrose are used as a carrier in the formulation of solid dispersion in different concentration such as 1:1, 1:3, 1:5. As the concentration of the carriers increased, it also improved the solubility of the drug. The nature and amount of carrier used plays an important role in the enhancement of the dissolution rate. The increased solubility and dissolution rate of allopurinol provided the rapid onset of action .The carrier used is easily available , feasible to use and have low cost .Thus the formulation will be the cost effective.

From the above study it was concluded that the kneading technique is useful for the preparation of solid dispersion of allopurinol.

Keywords: Solid dispersion, Solubility, Evaluation

Introduction

The drug Allopurinol is a Xanthine Oxidase Inhibitor and is used to treat gout and certain types of kidney stones. It is conjointly accustomed stop redoubled acid level s in patients receiving cancer therapy. These patients will have redoubled acid levels because of unharness of acid from the dying cancer cells. Allopurinol works by reducing the quantity of acid created by the body but Allopurinol shows poor-water solubility. The enhancement of the bioavailability of poorly water-soluble drugs is one of the greatest challenges of drug development and several pharmaceutical technologies have been investigated.

Solid dispersion is one in all these ways, that was most generally and with success applied to boost the solubility, dissolution rates and consequently the bioavailability of poorly soluble medicine. Some drugs are poorly water soluble and it is difficult to formulate dosage form which gives maximum bioavailability. So the important product not reaching the market.

Many of the techniques are there which enhance the solubility of the poorly water soluble drugs, solid dispersion is one of that fruitful technique which enhance solubility, dissolution rates and the bioavailability of poorly soluble drugs

Hence, In this project work an attempt will be made to increase the solubility of Allopurinol by solid dispersion using sugar carrier.[1-3]

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Material and Methods

The drug Allopurinol and the carriers, Maltose and Sucrose were mixed and wetted with double distilled water and kneaded thoroughly for 45 mins in the mortar pestle. The paste formed was dried for 24 hours. Dried powder was passed through sieve no.40 and kept in the dessicator until further evaluation. [4-5]

Table 1: Composition of solid dispersion

Formulation Code	Drug (in mg)	Maltose (in mg)	Sucrose (in mg)	Net weight
F1	100	100	-	200
F2	100	300	-	400
F3	100	500	-	600
F4	100	-	100	200
F5	100	-	300	400
F6	100	-	500	600

Evaluation [6-7]

Bulk characterization of solid dispersion

Flowability is an important bulk powder characteristic. The term "Flowable" means an irreversible deformation of a powder to make it flow due to the application of external energy or force. Various parameters such as angle of repose, Carr's index, Hausner ratio, flow function (ff) are used to express flowability of powders.

Determination of saturation solubility

Solubility study was performed according to method reported by Higuchi and Connors. To evaluate the increase in solubility of allopurinol in solid dispersion F1,F2,F3,F4,F5,F6 were added 10 ml distilled water taken in stoppered conical flask and were shaken for 8 hrs at37°C in incubator shaker. And solution were kept for 24 hrs, after shaker to achieve equilibrium, two ml aliquots were withdrawn at 1 hr intervals and filtered through whatman filter paper. The filtered were solution analysed spectrophotometrically at 250 nm against blank.

Drug content in solid dispersions

An amount equivalent to 10 mg of allopurinol was weighed from each resultant solid dispersion (with different carriers) and dispersed in 50 mL 0.1 N sodium hydroxide using a 100 mL volumetric flask and then was stirred for 10 min. The volume obtained was completed to 100 mL with 0.1 N sodium hydroxide and shaken well. 2ml from the previous solution were taken and were completed to 10ml with 0.1N sodium hydroxide.The absorbance was measured using a UV spectrophotometer at 250nm ,using 0.1N sodium hydroxide as a blank.

In vitro dissolution of allopurinol from solid dispersions

The rotating basket dissolution apparatus was used for the determination of dissolution rates of allopurinol solid dispersions. An accurately weighed amount of each solid dispersion equivalent to 100 mg of allopurinol was placed into the basket of the dissolution test apparatus. The basket was rotated at 50 rpm in 900 mL of the dissolution medium (0.1 N HCl) and maintained at a constant temperature (37 ± 0.5°C). Each of 5 mL, were withdrawn from the dissolution medium at time intervals of 5, 15, 30, 45 and 60. The same volume of 0.1 N HCl was used to replace the withdrawn samples. The samples were suitably filtered, diluted, and measured spectrophotometrically at 250 nm.

Powder X-ray diffractometry

Powder X-ray diffraction (PXRD) patterns were traced employing Xray diffractometer for the all samples, using Ni filter, CuK (α) radiation, a voltage of kV, a current of 20 mA and receiving slit of 0.2 in. The samples were analyzed over 2θ range of 5° to 60°, with scan step size of 0.020° (2θ) and scan step time of 1 second.

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Results and Discussion

Table 1: Bulk characterization and flow properties of formulation

Formulation Code	Bulk Density	Tapped Density	Hausner's Ratio	Carr's Index	Angle of repose
F1	0.34	0.58	1.70	41.37	26.4°
F2	0.51	0.71	1.39	28.16	30.06°
F3	0.70	0.95	1.35	26.31	25.4°
F4	0.33	0.55	1.66	40.00	26.95°
F5	0.55	0.79	1.43	30.37	27.6°
F6	0.69	0.95	1.37	27.36	26.3°

Determination of saturation solubility

Saturation solubility studies were carried out to select the best solvent for the formulation of solid dispersion. The figure shows the result of solubility studies.

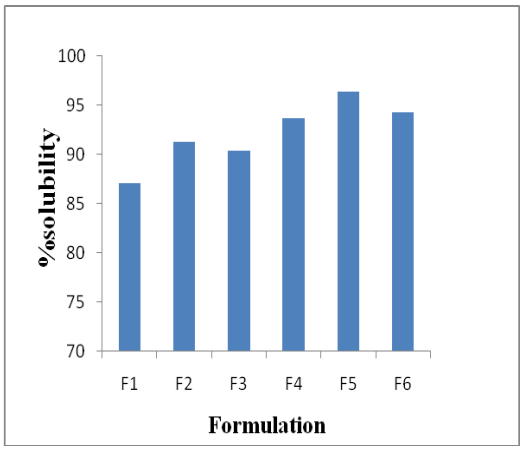

Fig. 1 Comparison of solubility of pure drug with formulations

Drug content in solid dispersions

The drug content estimation was performed to ensure uniform distribution of drug. The drug content of solid dispersion of Allopurinol was performed for all the prepared formulations. The result indicates that the drug content in all the formulations was found uniform between 87% to 96% which was analysed spectrophotometrically at λmax 250nm.

Table 2: Drug content of various formulation

Formulation Code	%Drug Content
F1	87.09%
F2	91.20%
F3	90.30%
F4	93.60%
F5	96.30%
F6	94.26%

In vitro dissolution of allopurinol from solid dispersions

The in vitro drug release profile of pure drug Allopurinol, solid dispersion in dissolution medium are shown in figure (8.1, 8.2).Solid dispersion of Allopurinol showed a significant increase in the drug release as compared with pure Allopurinol. In the formulations F1 and F2 showing 96.18% and 95.6% drug release, F3 and F4 showing 89.43%and 97.31% drug release, and F5 and F6 showing 98.43% and 98.43% drug release respectively. All the formulation showed improved drug release rate as compared to pure Allopurinol.

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Table 3: In vitro dissolution of allopurinol from various formulations

Time (min)	F1	F2	F3	F4	F5	F6	Drug
5	15.18	6.75	10.12	12.93	16.87	14.06	9.56
10	16.87	28.12	19.68	27.00	23.62	21.37	18.00
15	28.12	30.37	28.12	29.81	32.62	33.75	32.62
30	51.75	66.37	46.12	51.75	57.93	63.56	51.75
45	75.37	79.31	77.62	77.62	81.0	78.75	79.31
60	96.18	95.06	89.43	97.31	98.43	97.43	95.66

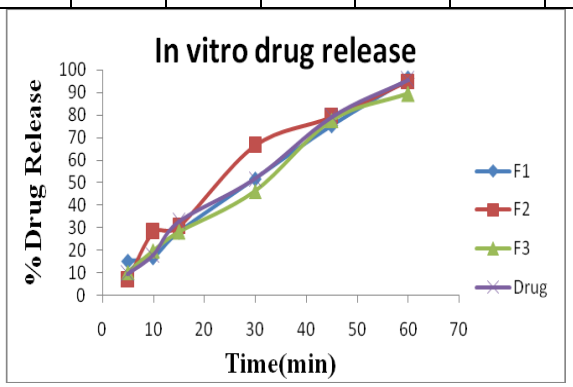

Fig. 2:Comparison of drug release profile of pure Allopurinol & F1,F2,F3 Batches

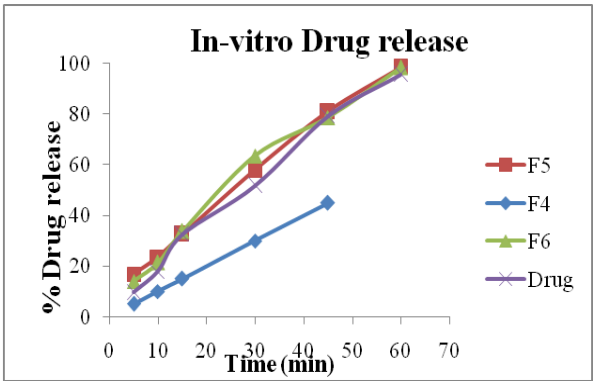

Fig. 3:Comparison of drug release profile of pure Allopurinol & F4,F5,F6 Batches

Powder X-ray diffractometry

The X-ray diffraction of pure drug, Maltose and Sucrose are shown in figure. It shows that the crystalline form of the drug was converted in the amorphous form.

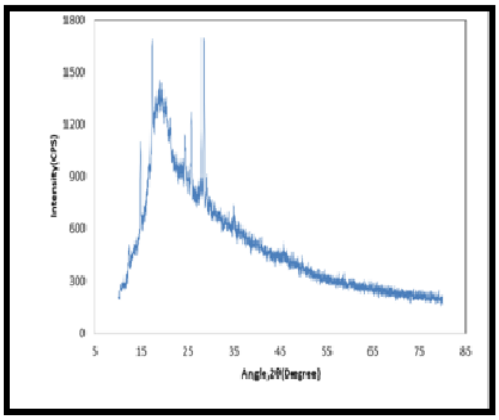

Fig. 4:X-Ray diffraction of Allopurinol

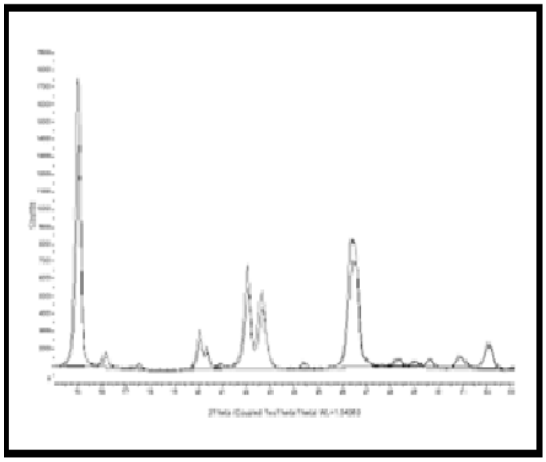

Fig. 5X-Ray diffraction of Maltose

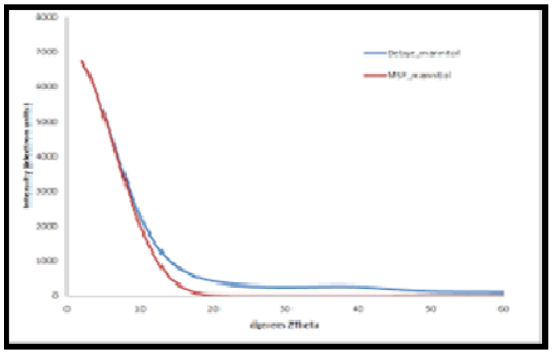

Fig. 6:X-Ray diffraction of Sucrose

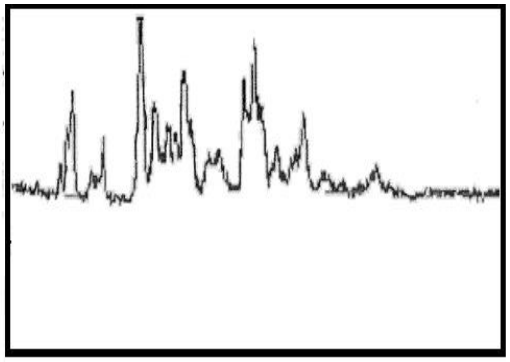

Fig. 7: X-Ray diffraction of formulation F5

Conclusion

Allopurinol is a Xanthine Oxidase Inhibitor and is used to treat gout and certain types of kidney stones. It is conjointly accustomed stop redoubled acid level s in patients receiving cancer therapy. These patients will have redoubled acid levels because of unharness of acid from the dying cancer cells. Allopurinol works by reducing the quantity of acid created by the body but the major drawback of the drug is low water solubility. Different solubility enhancement techniques have been developed till present but now a days researchers are mainly focusing on novel solubility enhancement techniques to improve solubility of the drug.

In the present research work the aim is to formulate and evaluate the Allopurinol by solid dispersion technique.

Various formulation of Allopurinol solid dispersion F1, F2, F3, F4, F5, F6 was formed. In solid dispersion formulation F1, F2, F3 are prepared using Maltose as a carrier and F4, F5, F6 are prepared using Sucrose as a carrier.

The prepared solid dispersion powder was evaluated for different parameters like bulk density, angle of repose , tapped density, carr's index, hausner's ratio. In vitro drug release of the developed formulation was carried out using Dissolution test apparatus (Rotating paddle type II) at the speed of 50 RPM with 0.1N HCL, as dissolution medium for 1 hr. All the formulation showed improved dissolution over pure drug Allopurinol. In solid dispersion formulation F1, F2, F3 are prepared using Maltose as a carrier shows 96.1% , 95.06%, and 89.43% respectively and F4, F5, F6 are prepared using Sucrose as a carrier shows 97.31%, 98.43% and 97.43% respectively.

Drug content of the formulation was determined using 0.1N NaOH at 250nm. The drug content was maximum at formulation F5 (96.30%) and minimum with formulation F1 (87.09%).

The X-ray diffraction patterns were traced employing Xray diffractometer for the all samples, using Ni filter, CuK (α) radiation, a voltage of kV, a current of 20 mA and receiving slit of 0.2 in. The samples were analyzed over 2θ range of 5° to 60°, with scan step size of 0.020° (2θ) and scan step time of 1 second.The formulation F5 shows characteristic peak of Allopurinol.

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