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Optimization dissolution rate by Inclusion complexation of repaglinide using β-cylclodextrin.

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ABSTRACT

In the current research, Repaglinide is a carbonoyl methyl benzoic acid derivatives insulinotropic agent used for treatment of NIDDM (non insulin dependent diabetes mellitus) and belongs to class II BCS drugs. The present research work is an attempt to enhance the solubility of the poorly soluble drug, Repaglinide(RPG). The drug also having poor flow properties, which is significantly enhanced by complexation with beta cyclodextrin (BCD). Micromeritics study of pure drug (Repaglinide) measured by tapped density, bulk density, angle of repose, carr's index , hausner's ratio which found to be 0.1742,0.2632,33.82%,1.52,33.52 respectively. After complexation it optimized to 0.294,0.384,23.43%,30.064°,1.306 of above parameters respectively. The calibration curve of RPG with 0.1N HCL and distilled waters with enhanced ratio calibrated a straight line with regression value of 0.999 at 242 nm. solubility study with solvents distilled water and 0.1N HCl found as 15.78, 84.29mg/100mL respectively. Dissolution of pure drug was found to 20.18%DR after 30min. Complexation made by physical mixture (PM) and kneading method (KM). Phase solubility study shown 5.76,6.24,6.88,7.74, 7.06, 5.54 mg/100ml with molar concentration of BCD 0.5,1,1.5,2.0,2.5,3 respectively. Which was optimized at 1:2. In PM and KM % drug content found 83.82 and 85.62 respectively. The kneading method was optimized by altering solvents at various temperature which shown 15ml ethanol at 45°C was the maximum. The complexation was confirmed by XRD and dissolution carried out at IMMT, BBSR . The fuse peak confirmed the complexation. The optimized dissolution rate found to be 86.43% compared to pure RPG of 20.18 at 30min.

Keywords: Repaglinide, β-cyclodextrin, XRD, Complexation.

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INTRODUCTION

In the present research, Repaglinide is a carbonyl methyl benzoic acid derivative. It is an insulinotropic agent used for treatment of NIDDM (Non-Insulin Dependent Diabetes Mellitus) and belongs to class-II BCS drugs. Poor solubility and wettability of drug leads to poor dissolution and hence, shows variation in bioavailability. So, this research work is an attempt to enhance the solubility of the poorly soluble drug, Repaglinide (RPG).

OBJECTIVE

Repaglinide has poor flow properties. Cyclodextrine plays an important role in formulation development due to its effect on solubility, dissolution rate and absorption of drug. So, the solubility of Repaglinide is significantly enhanced by forming complex with β-cyclodextrin (BCD).

EXPERIMENTAL METHOD

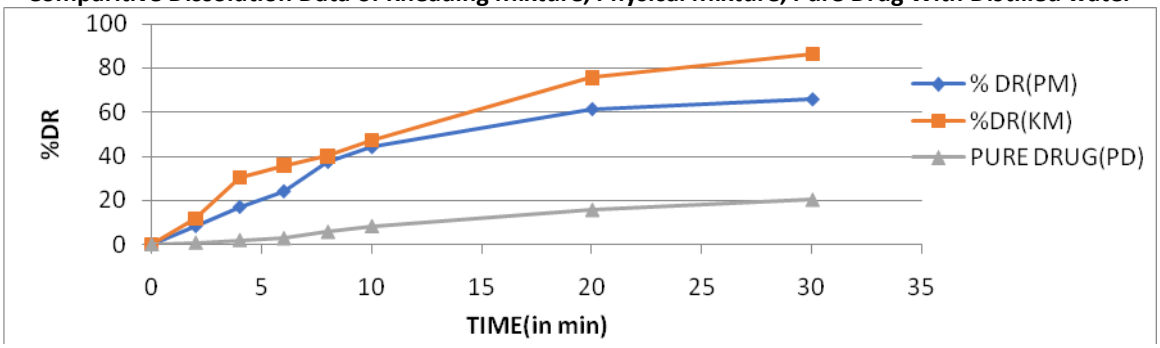
Micromeritics study of pure drug (Repaglinide) measured by tapped density, bulk density, angle of repose, carr's index , hausner's ratio which found to be 0.1742,0.2632,33.82%,1.52,33.52 respectively. After complexation it optimized to 0.294,0.384,23.43%,30.064°,1.306 of above parameters respectively. The calibration curve of RPG with 0.1N HCL and distilled waters with enhanced ratio calibrated a straight line with regression value of 0.999 at 242 nm. solubility study with solvents distilled water and 0.1N HCl found as 15.78, 84.29mg/100mL respectively. Dissolution of pure drug was found to 20.18%DR after 30min. Complexation made by physical mixture (PM) and kneading method (KM). Phase solubility study shown 5.76,6.24,6.88,7.74, 7.06, 5.54 mg/100ml with molar concentration of BCD 0.5,1,1.5,2.0,2.5,3 respectively. Which was optimized at 1:2. In PM and KM % drug content found 83.82 and 85.62 respectively. The kneading method was optimized by altering solvents at various temperature which shown 15ml ethanol at 45° C was the maximum. The complexation was confirmed by XRD and dissolution carried out at IMMT, BBSR . The fuse peak confirmed the complexation. The optimized dissolution rate found to be 86.43% compared to pure RPG of 20.18 at 30min.

RESULT AND DISCUSION

Comparative Dissolution Data of Kneading Mixture, Physical Mixture, Pure Drug With Distilled water

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

Comparitive Dissolution Data of Kneading Mixture, Physical Mixture, Pure Drug With Distilled water



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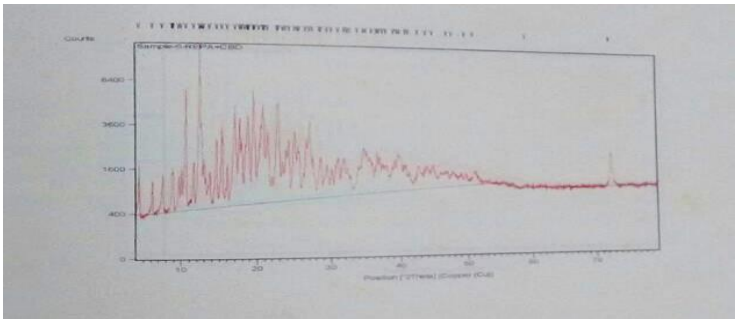

(XRD of β-CD and Repaglinide mixture indicating peaks below 2500 conforming the complexation)

CONCLUSION

After making complexation with BCD at the dissolution rate was found to be 86.43. the XRD report of complex showing it fused peak below 2500 shows its amorphous characteristics. It was concluded with high dissolution rate and better micromeritics property.

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