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RESEARCH ARTICLE

PREPARATION AND EVALUATION OF POLYMERIC NANOPARTICLES OF GLIBENCLAMIDE

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*Corresponding Author E-mail: anupnaha@gmail.com**ABSTRACT**

Simple, reliable and reproducible method was used for the preparation of polymeric nanoparticles of Glibenclamide. The formulation was prepared by solvent evaporation method using magnetic stirrer with overnight stirring and the same was then evaluated for its particle size, drug content and *in vitro* dissolution studies. The above mentioned method showed similar particle size and exhibited an improvement in the drug entrapment efficiency. The ultraviolet spectrophotometric method was used to analyze Glibenclamide at 300 nm in different buffers. The study demonstrated the successful preparation of sustained release polymeric nanoparticles of Glibenclamide.

Keywords: Glibenclamide, polymeric nanoparticles, solvent evaporation

INTRODUCTION

Solubility is an important criterion for drug efficacy, independent of route of administration. It also poses a major challenge for pharmaceutical industries, which are developing new pharmaceutical products, since 40% of the active substances being identified are either insoluble or poorly soluble in aqueous media¹. A limiting factor for *in vivo* performance of poorly water soluble drugs, following oral administration, is their resistance to being wetted and being dissolved into the fluid in the gastrointestinal tract¹. Increasing the dissolution rate of poorly water soluble drugs is thus important for optimizing bioavailability¹. To overcome these problems, various formulation strategies are reported in the literature including the use of surfactants (e.g. tween 80, gelucire), cyclodextrins (e.g. beta-cyclodextrin, hydroxypropyl beta-cyclodextrin), solid dispersions, micronization, lipid based systems^{2,3,4,5}. However, these approaches are successful in only selected cases.

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000 nm⁶. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed⁶. Glibenclamide is one of the most widely used anti hyperglycemic drug. However, glibenclamide's low bioavailability has been attributed to its poor dissolution properties⁷. Hence, in the study it is planned to formulate polymeric

nanoparticles of Glibenclamide to improve its dissolution and absorption.

METHODS**Preparation of polymeric nanoparticles of glibenclamide:**

Weighed amount of drug was dissolved in dichloromethane, and weighed amount of Eudragit RLPO polymer was dissolved in methanol (Table 1). Drug-polymer solution was prepared by mixing the solutions, followed by vortexing. The drug-polymer solution was homogenized at 10000-13000 rpm and sonicated. The solution was then evaporated using a rotary evaporator, until there were no traces of the organic solvent. The resulting solution was centrifuged and the solution was frozen at -80°C and then lyophilized, after the addition of required quantity of mannitol.

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Table 1: Formulation of various batches of polymeric nanoparticles

Ingredient	Drug polymer ratio			
	1:5	1:10	1:20	1:40
Drug(mg)	5	5	5	5
Polymer(mg)	25	50	100	200

Optimized batches of the ratios 1:5 and 1:40 were prepared using the same procedure stated above.

Evaluation of polymeric nanoparticles:

Particle size

The particle sizes of the different formulations were measured using Malvern Zeta Sizer (Nano ZS), before and after lyophilization.

Drug content

5mg of the lyophilized sample of each of the optimized formulations was weighed, dissolved in 5ml of the methanol, and the absorbance was measured spectrophotometrically at 300 nm. The percentage entrapment was calculated.

In vitro release

The dissolution study was carried out using Type 2 dissolution with 900ml of phosphate buffer (pH 6.8) for 6 hours, first at intervals of 30 minutes, and then at intervals of an hour. The dissolution medium was kept in a thermostatically controlled water bath, maintained at $37 \pm 0.5^{\circ}C$. The pre-weighed formulation was filled in a capsule, and then introduced into the dissolution jar. The paddle was rotated at 75rpm. At different time intervals the samples were withdrawn and analyzed spectrophotometrically at 300nm for drug release.

RESULTS AND DISCUSSION

Particle size

The particle sizes of the formulations were measured before and after lyophilization, and the results showed that particles were within the desired size range (Table 2,3).

Table 2: Particle size of formulations

Drug polymer ratio	Particle size(nm)	
	Before lyophilization	After lyophilization
1:5	154	2929
1:10	95.4	2793
1:20	100.4	1267
1:40	133	1503

Table 3: Particle size for Optimized Formulations

Drug polymer ratio	Particle size(nm)	
	Before lyophilization	After lyophilization
1:5	741.6	626.2
1:40	554.5	683.6

Drug content

The drug content of the optimized formulations was calculated, after measuring the absorbance at wavelength 300nm. The drug content of the formulation had a percentage entrapment in the range of 50-60%.

In vitro drug release

Drug release profile of 1:4 and 1:5 drug polymer ratios was calculated. Dissolution study was performed for 1:4 and 1:5 drug polymer ratio and percentage cumulative drug release was calculated (%CDD). The drug polymer ratio showed an increase in drug release with time. Formulation exhibited a complete drug release at the end of 6hrs (Figure 1)

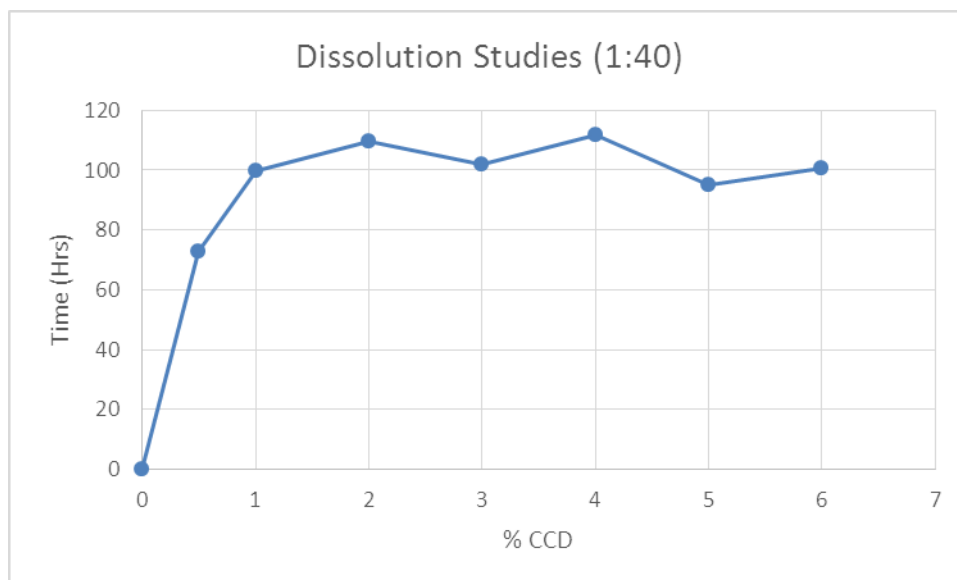


Figure 1: Drug release profile

CONCLUSION

The drug Glibenclamide was prepared by solvent evaporation method using magnetic stirrer with overnight stirring and the nanoparticles produced were evaluated. The optimized formulation prepared showed similar particle sizes and exhibited an improvement in

the drug entrapment efficiency. Formulation exhibited a complete drug release at the end of 6hrs. The present study demonstrated the successful preparation of sustained release polymeric nanoparticles of Glibenclamide.

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