Presentation & Publication
Application of Placket Burman Screening Design for Preparing Glibenclamide Nanoparticles for Dissolution Enhancement

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Purpose
This study is to improve the dissolution characteristics of a poorly water-soluble drug glibenclamide (GLB), by preparing nanoparticles through liquid anti solvent precipitation.

Methods
A Placket Burman screening design was employed to screen the significant formulation and process variables. Total 12 experiments were generated by Minitab 16 for screening 5 independent variables namely amount of poloxamer 188 (PX) (X1), amount of PVP S 630 D (PD) (X2), solvent to antisolvent volume ratio (S/AS) (X3), amount of GLB (X4) and speed of mixing (X5). Particle size (Y1), saturation solubility (Y2) and % DE5min (Y3) were selected as response variables.

Results
All of the regression models yielded a good fit with high determination coefficient and F value. The pareto chart (Figure 1) depicted that all the independent variables except amount of drug had a significant effect on the response variables. The mathematical model for particle size generated from the regression analysis was given by $PS = 830 - 8.14\cdot PX + 12.8\cdot PD - 11.1\cdot S/AS + 1.42\cdot Drug\ Conc. - 0.676\cdot Speed$ ($R^2=93.5$, $F_{ratio} = 17.28$, $p<0.001$). The optimum batch of prepared nanoparticles had a particle size of 205 nm (Figure 2) and showed a significant ($p < 0.05$) improvement in the release as compared to pure GLB (Figure 3) releasing almost all drug within first five minutes. X ray diffraction studies concluded that the crystallinity of nanoparticles of optimum batch was intact and the increased dissolution could be ascribed to conversion of unmilled drug to nanosized drug.

Conclusion
GLB nanoparticles were prepared by nanoprecipitation, Placket Burman screening design helped in identifying the significant parameters that affected the response variables. The optimized formulation maintained the crystallinity of GLB and showed improved dissolution as compared to pure drug.
Studies in formulation development and process optimization for preparing glibenclamide nanocrystals to improve dissolution characteristics
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Purpose
This study is to improve the dissolution characteristics of a poorly water-soluble drug glibenclamide (GLB), by engineering nanocrystals using wet milling by zirconia beads.

Methods
Various formulation and process variables were identified and optimized by employing a $3^2$ factorial design at two stages. Based on preliminary studies the formulation variables selected were polymer to drug ratio and surfactant to drug ratio. The process variables selected were milling speed and milling time. The particle size, zeta potential, saturation solubility and % drug released at 10 minutes were selected as dependent variables at both stages.

Results
Statistical evaluation suggested that the predetermined response parameters were significantly dependent on the independent variables. As shown in figure 1 an optimum desirability of 0.9925 was achieved using response profiler by Statistica 8.0. The optimized formulation prepared as per levels obtained through desirability showed a close agreement between the predicted and expected values. X ray diffraction studies concluded that the crystallinity of prepared nanocrystals was intact and as shown in figure 2 the increased dissolution could be ascribed to conversion of un milled drug to nanocrystals.

Conclusion
GLB nanocrystals were prepared and the optimized formulation showed better dissolution as compared to pure drug. All the predetermined independent variables were found to affect the dependent variables from the resultant nanocrystals. The factorial design at two levels employed helped in understanding the process of nanocrystal formation. The optimized formulation maintained the crystallinity of GLB and released almost all the drug within 10 minutes.
Self nanoemulsifying drug delivery system of glimepiride: Design, development and optimization.
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**Purpose**
The objective of the present investigation was to develop and characterize the self nanoemulsifying drug delivery system (SNEDDS) of glimepiride (GMP) a poorly soluble drug, for improving its dissolution characteristics.

**Methods**
Solubility of GMP in various vehicles was determined and ternary phase diagrams were constructed using a suitable oil, surfactant and cosurfactant system to find out the efficient self emulsification system. A three factor three level Box Behnken statistical design (BBD) was employed to explore the main and interaction effect of independent variables namely X1 (amount of Capmul MCM), X2 (amount of Acrysol K 140), and X3 (amount of Transcutol P), % Transmittance value (Y1), droplet diameter (Y2) and % drug released at 5 minutes (Y3) were the dependent variables. Formulation optimization was carried out to optimize the droplet diameter and % drug dissolved at 5 minutes.

**Results**
The results clearly indicated that Acrysol K 140 showed the highest emulsification efficiency; amongst the various cosurfactant assorted Transcutol P showed most promising results. Box Behnken statistical design revealed that the observed responses showed a large variation, suggesting that the independent variables had a significant effect \((p<0.05)\) on the selected dependent variables. A final formulation was prepared as per levels obtained in optimization as shown in figure 1, and as shown in figure 2 the droplet diameter of the optimized formulation was found out to be 34.10 nm, which was in close agreement with expected value, while as shown in figure 3 the optimized batch showed significantly \((p<0.001)\) higher drug release as compared to pure GMP.

**Conclusion**
BBD was effectively employed to optimize the dissolution of GMP, from SNEDDS containing Capmul MCM - Acrysol K 140 - Transcutol P. The optimum formulation prepared by response optimizer through desirability function provided a final formulation with \(D = 0.9943\) which released 79.85% of GMP within 5 minutes.
Application of Plackett–Burman screening design for preparing glibenclamide nanoparticles for dissolution enhancement

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A R T I C L E   I N F O
Article history:
Received 19 May 2012
Received in revised form 15 September 2012
Accepted 27 October 2012
Available online 2 November 2012

Keywords:
Glibenclamide
Liquid antisolvent precipitation
Dissolution enhancement
Plackett–Burman screening design

A B S T R A C T
This study is to improve the dissolution characteristics of a poorly water-soluble drug glibenclamide (GLB), by preparing nanoparticles through liquid anti solvent precipitation. A Plackett–Burman screening design was employed to screen the significant formulation and process variables. A total of 12 experiments were generated by Minitab® 16 for screening 5 independent variables namely the amount of poloxamer 188 (PX) (X1), amount of PVP S 630 D (PD) (X2), solvent to antisolvent volume ratio (S/AS) (X3), amount of GLB (X4) and speed of mixing (X5). Mean particle size (Y1), saturation solubility (Y2) and % dissolution efficiency (%DE5min) (Y3) were selected as response variables. All the regression models yielded a good fit with high determination coefficient and F value. The Pareto chart depicted that all the independent variables except the amount of GLB had a significant effect (p < 0.001) on the response variables. The mathematical model for mean particle size (PS) generated from the regression analysis was given by PS = 830 + 1.42 GLB Conc. – 12.8 PD – 11.1 S/AS + 1.42 GLB Conc. – 0.676 speed of mixing (R² = 93.5, F ratio = 17.28, p < 0.001). Prepared GLB nanoparticles exemplified a significant improvement (p < 0.05) in the release as compared to pure GLB with the optimum formulation releasing almost 80% drug within first 5 min. The X-ray diffraction studies concluded that the crystallinity of nanoparticles from the optimum batch was intact and the increased dissolution could be ascribed to conversion of unimilled GLB to nanoparticles.

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1. Introduction

According to the food and drug administration nanoparticulate drug is not a generic drug rather is considered as “newdrug” molecule and is not bioequivalent to its microcrystalline or solubilized form administered at the same dose and therefore it can be patented [1]. Nanosuspensions are liquid dispersion consisting of solid drug nanoparticles, stabilized by polymer and/or surfactant offering, fewer side effects, lower doses and faster onset of action [2]. Extensive review has been done on the various approaches for the development and characterization of nanoparticles, nevertheless briefly it has been classified into two basic approaches i.e. top down technology and bottom up technology. The top down approach relies on mechanical attrition to render large crystalline particles into nanocrystals and their reduced size and increased surface area lead to an increased dissolution rate which may offer an increased bioavailability [3]. However, breaking large crystalline drug particles to nanoparticles with size below 100 nm is extremely difficult with these methods since these methods are very time consuming and require significant energy, which might generate a large amount of amorphous particles, and contamination from milling media or homogenization chamber [4]. The
Subject: PDA/2012/002162 -- Manuscript Decision
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MS ID#: PDA/2012/002162
MS TITLE: Self nanoemulsifying drug delivery system of glimepiride: Design, development and optimization.

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