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Assessment of Material and Process Related Attributes for a Desired Drug Release from Extended Release Film Coated Beads – A Design of Experimental Approach

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ABSTRACT

Aims: Extended Release (ER) film coated bead products are an effective way to achieve extended drug release. The ER film typically comprises both insoluble and soluble polymers and the drug release is influenced by both material and process attributes. The current study is aimed to evaluate the influence of material attribute (polymer viscosity) and process attribute (spray rate) on the drug release from ER beads.

Methodology: A full-factorial design was used to study the influence of HPC polymer viscosity and ER solution spray rate on drug release from ER beads. Based on the data obtained from the experiments, a mathematical equation and response surface plots were generated to predict the drug release from ER coated beads.

Results: The data demonstrated, the variability in drug release is observed with changes in the HPC viscosity and ER solution spray rate and the drug release is predominantly influenced by spray rate compared to viscosity. The polymer phase separation during the film formation process due to solubility differences of polymers creates either a bi-continuous or dis-continuous network within polymer films is hypothesized to the causative factor for observed differences in the drug release.

Conclusion: The results demonstrated the potential of the Design of Experiments in selecting the optimal material and process attributes for a desired drug release from ER beads.

Key Words: ER Beads, Wurster, Ethylcellulose, Hydroxypropyl cellulose, DoE, Drug release

1. INTRODUCTION

Oral modified drug delivery systems based on the multiarticulate (beads) dosage forms have gained immense advantages due to their ability to control drug release by facilitating more reproducible and desired pharmacokinetic profile and minimal intra-and inter subject variability compared to conventional (monolithic) dosage forms [1-4]. Beads or Pellets (such as sugar spheres, MCC beads, tartaric acid pellets) functions as inert cores for drug/functional coatings and are generally spheroidal in shape. In-soluble polymer film coatings on inert core beads are commonly used in oral controlled release systems to modify or extended the drug release profile[5, 6]. The drug release from the beads can be modified by selection of blends of polymers comprising both insoluble and soluble polymers [7, 8]. The water in-soluble polymers such as Ethyl Cellulose (EC) and water-soluble polymers such

as Hydroxypropyl cellulose (HPC) and Hydroxypropyl methyl cellulose (HPMC) are routinely used in the extended release (ER) coatings of the core beads to achieve a very broad range of release profiles[8, 9]. Since, the water permeability of in-soluble polymer (EC) is very low, the addition of water-soluble polymers (HPC or HPMC) is blended in the coating film to modify the drug release. When exposed with the aqueous environment, the HPC or HPMC in the ER film leads to polymer leakage and creates pores in the film facilitating the drug release from beads and the drug release is dependent on the extent of pores as well as their shapes[10, 11]. The ER film coating on the core beads can be produced by spraying the hydroalcoholic solution of polymer blends on the beads by bottom spray fluid bed (Wurster process) and the drug release is greatly influenced by film thickness and film coating process parameters [12, 13]. Wurster film coating is a bottom spray coating process in a fluidized bed system for a uniform and robust film coat and the spraying is done from below the product bed up into the product flow utilizing a Wurster column (Fig.1).

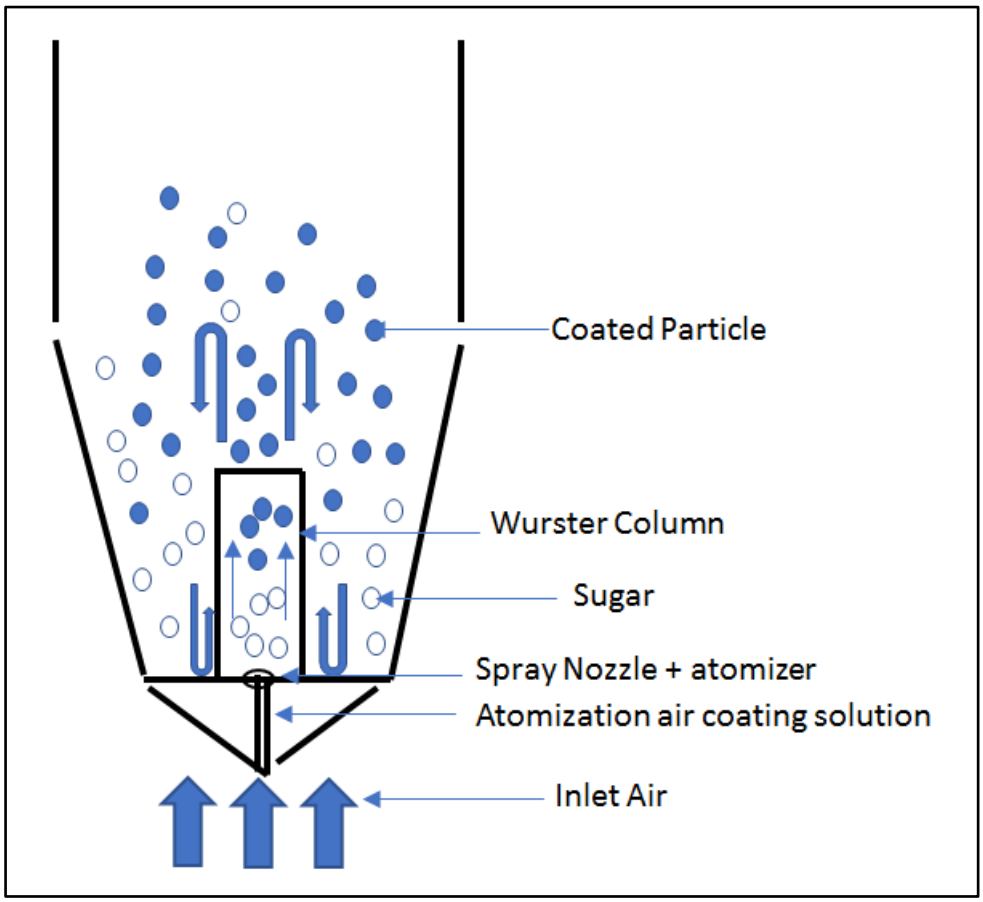

Fig.1. Schematic representation of Wurster coating process of beads

Since, the ER film coating solution consist of blend of polymers with different physicochemical properties and often completely immiscible and have tendency to phase separate during the solvent evaporation process to form polymer film [14] The polymer solution consisting of EC and HPC in ethanol upon spraying on the core beads, the solvent evaporation during the spray coating process suspectable for phase segregation leading to a film microstructure comprising distinct domains of enriched in either EC or HPC [15, 16]. The prior research has demonstrated that the drug release

from the EC/HPC polymer coated beads is influenced by multiple factors such as the molecular weight of EC and HPC and the film coating process parameters by formation of bi-continuous or dis-continuous network structures within the film structure during the manufacturing process [17-19]. At a fixed ratio of polymers, the extent of pores and shape of the pores can be controlled by the variabilities in the molecular weight of polymers along with the process parameters during the coating process. During the coating the dry and wet conditions can influence the phase separation thereby influencing the variability in the pore structures[20]. The dry conditions as attained by slower spray rate or increased product temperature and the wet conditions achieved by higher spray rate or lower product temperature influence the molecular mobility of the polymer during film formation and creates either bi-continuous or dis-continuous network [21].

Although, the influence of molecular weight of polymer and Wurster coating process parameters on drug release from beads is evaluated individually, per our understanding, no assessment was performed by studying the combined influence material and process attributes on drug release from ER film coated beads. Since, the drug release from beads is influenced by both material attributes and process attributes, it is critical to understand how these parameters are dependent each other and influence the drug release. In our current research, we have aimed at studying the interaction of material attributes of polymers and coating process parameters and its influence on the drug release characteristics. A design of experiments (DoE) based approach utilizing a full factorial study design was applied to evaluate the interaction of polymer properties and coating process parameters and its influence on drug release.

The DoE is a software-guided experimental design approach and provides information on the interaction of factors with a limited set of experiments. Full-factorial designs support linear responses and are particularly useful when the number of factors is as few as 2. Also, DoE fits the response data to mathematical equations and these equations serve as models to predict responses at desired parameter (factor) values. This approach is particularly relevant for identifying the parameter space relevant for a product with specific features [22, 23]

The current research work is aimed at studying the influence of HPC material properties such as viscosity and Wurster coating process parameters such as coating solution spray rate (factors) and their influence on the drug release (response) are assessed using a 2X2 full factorial design with a center point. The contour and surface response plots are created with a design space for selecting optimal properties for a desired drug release. Since, the characteristics of HPC material are critical determining the extent of pore formation in the ER film by phase separation phenomena, the viscosity of HPC material is selected as one factor in the study design along with spray rate of ER polymer solution is selected another factor. The dry and wet conditions during the film coating process are created by the changes in the spray rate conditions. The drug, Verapamil Hydrochloride, is selected as a model drug and the drug coated beads are prepared separately by coating the drug solution on inert core sugar beads. Verapamil HCl belongs to a calcium channel blocker class and is widely used in the treatment of high blood pressure. It is freely soluble in aqueous media and an extended-release dosage based on the beads is important for a controlled release of drug and also for minimization of absorption variability. The inert sugar spheres are used as core beads for drug coating and subsequent extended-release coating as guided by factorial design and the ER coated beads are assessed for drug release. Two grades of HPC polymer with different viscosity are selected for this study and the remaining materials are common in all the experimental studies. During the ER

film coating process, excluding the spray rate, all other conditions are maintained similar for all experiments.

2. MATERIALS AND METHODS

2.1 Materials

Inert sugar spheres (20/25 mesh, 710/850 micron) were obtained from Coloron Inc. The drug Verapamil HClwas provided by Mylan Pharmaceuticals, India. The excipient Hypromellose 2910 (Pharmacoat 606) was obtained from Shin Etsu chemical Co. and used for seal coat of the inert cores and also as binder in the drug coat solution. The extended release (ER) film materials, the Ethylcellulose (Ethocel standard 45 premium) was obtained from Dow chemicals. Only one grade of ER was used for all the studies and the viscosity of the Ethylcellulosewas 44.9 cps as referenced in the certificate of Analysis. The pore former in the ER film, the Hydroxy Propyl Cellulose (HPC) grades were supplied by Ashland Specialties. The grades of HPC utilized in the studies have the viscosity of 300 cps and 600 cps according to the manufacture's specifications. All other chemicals and reagents utilized in the study were of laboratory grade.

2.2 Design of Experiments

A 2X2 full-factorial design (Statgarphics Centurion 19 software, Statpoint Technologies, Inc.) was performed using viscosity of the HPC polymer (cps) and Spray rate (g/ml) during ER coating process as independent variables and drug release at 6 hr as the dependent variable. The high and low values of independent variables are given in the Table 1.

Table 1. Independent and dependent variables used in the full factorial design

Design	Independent variables (Factors)	Levels		Dependent variables (Responses)
		Low	High	
Full Factorial design	HPC polymer viscosity (cps)	300	600	% Drug release at 6hr
	Spray rate (g/min)	5	20	

A full factorial design was utilized to create the design space to achieve the desired release (responses) with variabilities of independent variables (factors)

The drug release at 6 hours was assessed as dependent variable. The full factorial was designed to study the effects in runs in a single block and with one center point. The order of the experiments has been fully randomized to provide protection against the effects of lurking variables. The contour, response surface and interaction plots were plotted and used to predict the drug release based on the variabilities observed with material attribute (HPC viscosity) and process attributes (spray rate).

2.3 Preparation of Drug Coated Beads

The Verapamil HCl coated sugar spheres were prepared to use as core beads for subsequent ER coating experimental studies. The qualitative and quantitative composition of seal/drug coated beads is presented in Table 2.

Table 2. Qualitative and quantitative composition of ER coated beads

Stage	Material	Quantity (kg)	% W/W
Seal Coat	Sugar Spheres (710-850 micron)	2.0	73
	Hypromellose 2910	0.12	4
	Purified Water	1.5	NA
Drug Coat	VerapamilHCl	0.5	18
	Hypromellose 2910	0.12	4
	Purified Water	5.0	NA
ER Coat	Seal /Drug coated Beads	2.6	87
	Ethylcellulose	0.3	10
	Hydroxypropyl cellulose	0.1	3

The preparation process involves sugar spheres (Inert core sugar spheres were first seal coated with aqueous solution of Hypromellose 2910) and then the seal coated beads were further drug coated with an aqueous solution of Verapamil HCl and Povidone (binder) utilizing a Wurster fluid bed. The Hypromellose 2910, a hydrophilic polymer was used for seal coat the sugar spheres prior to drug coating. The seal coat provides a smooth surface to facilitate efficient drug coating and mitigate the sugar spheres attrition during the drug coating.

2.3.1 Seal Coating Solution Preparation

With a continuous agitation, 150 gms of Hypromellose 2910 (Pharmacoat 606) was added to the 1.5 kg of purified water and mixed with a stirrer. The mixing was continued approximately 30 mins to ensure the Hypromellose is completely dissolved. The final seal coat solution was clear, and the final concentration was 10 %w/v.

2.3.2 Drug Solution Preparation

With a continuous agitation, 150 gms of Hypromellose 2910 (Pharmacoat 606) was added to 5.0 kg of purified water and mixed with a stirrer. The mixing was continued approximately 30 mins to ensure the Hypromellose 2910 is completely dissolved. While stirring, 500 gms of Verapamil HCl was added to the above solution and mixing was continued for 30 minutes to ensure a clear solution was obtained. The final drug coat solution was clear that contains 13% w/v of solids.

2.3.3 Seal Coating And Drug Coating

The inert core sugar spheres (2.2 kg) were added to 7" Wurster column (Glatt GPCG3) and the process parameters such as air flow, inlet temperature, and exhaust temperature were adjusted as presented in the Table 3 to ensure a good fluidization and movement of the beads in the Wurster.

Table 3. Process parameters for seal and drug coating

Parameter	Seal Coat	Drug Coat
Bowl Charge (kg)	2.2	2.2
Inlet Temperature (^{o}C)	70	70
Product Temperature (^{o}C)	37	37
Air Flow (CFM)	90	95
Atomizing air Pressure (PSI)	30	30
Spray Rate (g/min)	10	12
Partition Height	10	10
Exhaust Temperature (^{o}C)	40	40

After the beads attained the defined product temperature (37^{o}C), the beads were coated by spraying seal coat solution and dried for 5 minutes at 70^{o}C. Then, drug coat solution was sprayed on seal coated beads at a spray rate of 12 g/min. During the drug coating process, the coating parameters were monitored to ensure no agglomeration and spray drying of the drug solution. Once the drug coat solution was completely sprayed, the drug coated beads were dried for 5 mins and then discharged. The seal and drug coated beads obtained from six separate batches were then pooled to obtain seal/drug coated beads for subsequent ER coating studies. The samples were collected from the pool to characterize the beads for bead size distribution (PSD) and % assay. The theoretical drug load of the seal/drug coated beads was 183 mg/gram of beads.

2.4 Preparation of Extended Release Coated Beads

The ER film coated beads are prepared by using the seal/drug coated beads as starting core beads and sprayed with ER solution in a Wurster fluid bed. The experiments (EB1-5) were executed as defined by DoE. The process parameters and level of independent factors are given in Table 4.

Table 4. Process parameters for ER coating (Wurster coating)

Parameter	Exp 1	Exp 2	Exp 3	Exp 4	Exp 5
HPC Viscosity (cps)	**450**	**300**	**300**	**600**	**600**
Spray Rate (g/min)	**12.5**	**5**	**20**	**5**	**20**
Bowl Charge (kg)	2.5	2.5	2.5	2.5	2.5
Inlet Temperature (^{o}C)	65	65	65	65	65
Product Temperature (^{o}C)	35	35	35	35	35
Air Flow (CFM)	100	100	100	100	100
Atomizing air Pressure (PSI)	30	30	30	30	30
Partition Height	10	10	10	10	10
Exhaust Temperature (^{o}C)	40	40	40	40	40

2.4.1 Extended Release Coating Solution Preparation

The ER solution was an alcoholic solution of HPC and EC at a ratio of 25 :75. The solution is prepared by adding 6.0 kg of alcohol to a suitable stainless container and with continuous agitation 150gms of HPC is added and continued mixing for 30 minutes to ensure the HPC is dissolved completely. To the solution, 350gms of EC is added and mixed for 30 minutes. At the end of the mixing, it is verified for both the components are dissolved completely. The theoretical concentration of the solution 6.7%w/v.

2.4.2. Extended Release Coating

The drug coated beads (2.6 kg) are added to 7" Wurster column (Glatt GPCG3) and the process parameters such as air flow, inlet temperature, and exhaust temperature were adjusted as presented in the Table 4. The spray rate was varied for each study as defined by design of experiments. While varying the spray rates, the inlet temperatures were adjusted to ensure no agglomeration of the beads during the coating process. After the specified coating solution (6.4kg) was sprayed, the beads were dried for 5 minutes, and the coated beads were discharged. Based on the above studies and data obtained, a confirmatory batch (CB) was executed with HPC polymer viscosity of 450cps and at a

spray rate of 8 gm/min. The remaining process parameters were maintained similar to all other studies.

2.5 Characterization of Beads (Seal/Drug Coated and ER coated)

2.5.1 Bead Size Distribution

The seal and drug coated beads are characterized for bead size distribution utilizing mechanical agitation sieving method as defined by USP <786>. Briefly, each test sieve (#16mesh, #18 mesh, #20 mesh, #25 mesh, #30 mesh and Pan) are tared to the nearest 0.1 g and then accurately weighed 100gm of beads are placed on the top (#16 mesh) sieve, and the lid was replaced. The nest of sieves is agitated for 5 minutes. Then each sieve id removed carefully without loss of material and reweighed with the beads to determine the quantity of beads retained on each mesh. The % of beads retained on each mesh from the total quantity of beads used for test were calculated.

2.4.2 % Assay

The theoretical drug load of the seal /drug coated beads is 183 mg / gram of coated beads. Accurately, 100mg equivalent of drug (545 mg of beads) are weighed to a 100 ml volumetric flask and approximately 75 ml of aqueous solvent mixture of water and acetonitrile (75:25) is added and sonicated for 30 minutes. Then, was allowed to cool to room temperature and diluted to 100 ml with aqueous solvent mixture and mixed. From the stock solution, 25 ml of solution is centrifuged, and 10 ml of supernatant is diluted to 100 ml with aqueous solvent mixture and mixed. The drug concentration was estimated using a UV spectrometer with a 0.2 cm flow ell and the ultraviolet absorbance is measured at a maximum absorbance of 280nm.

2.4.3 % Drug Release

The drug release from beads is measured using USP apparatus Type 2 dissolution apparatus. The dissolution media is 900ml of 0.1 N HCl. Accurately weighed ER beads equivalent to 100 mg of drug (600 mg ER beads) are transferred into dissolution vessel containing 900 ml of 0.1 N HCl warmed to 37^{o}C. The 10ml of sample is collected at 60 minutes of the start and the drug content is measured using UV spectrophotometer as discussed above. The drug content is measured at 280 nm absorption maximum. The drug content is estimated using a standard linear curve plotted with standard samples.

3. RESULTS AND DISCUSSION

3.1 Seal/Drug Coated Beads

The inert sugar spheres (710-850 micron) were utilized as core beads for drug coatingand then subsequently for ER coating studies. The inert sugar spheres were large enough providing a suitable surface for subsequent application of drug layer. The core sugar spheres were first seal coated with Hypromellose 2910, a hydrophilic polymer, as a seal coat to ensure the sugar spheres have a smooth surface for efficient adhesion of drug layer. The seal coated beads were further drug layered with drug layer solution comprising drug and Hypromellose 2910 as a binder. The seal/drug layer studies were iterated for six separate times with a bowl load of 2kg each time and with the similar process parameters as defined earlier. The results of assay and bead size distribution characterization of drug coated beads are summarized in Table 5.The seal/drug layered beads have demonstrated an assay value of 98.6% of the total theoretical drug load indicating a good adhesion of drug and the bead size

distribution indicates that there were no agglomerates and fines generated (0% on 16 mesh and on Pan). The seal/drug coated beads were subsequently used ER coating studies.

Table 5. Results of characterization of seal/drug coated beads

Parameters	Value
% Assay	98.6
#16 mesh (1.18 mm) retained (%)	0
#18 mesh (1.00 mm) retained (%)	0
#20 mesh (850 micron) retained (%)	93.2
#25 mesh 710 micron) retained (%)	6.8
#30 mesh 600 micron) retained (%)	0
Pan retained (%)	0

3.2 Extended Release Coated Beads

The experiments are executed per full factorial design with the variabilities of HPC viscosity and spray rate. The ER coated beads were characterized for bead size distribution, % assay and drug release at 6 hr. The analytical and physical characteristics of ER coated beads were presented in Table 6. A total of five separate ER coating studies (EB1-5) were executed. The ER film comprises Ethylcellulose(45cps), an ER polymer, and Hydroxypropylcellulose, a pore former, at a weight ratio of 75:25 in alcohol. The HPC grades utilized in the studies are 300 and 600 cps and only one grade of Ethylcellulose was used in all studies. Along with the HPC viscosity, another variability in the current assessment was spray rate of ER solution during Wurster ER coating process. The remaining process parameters were uniformly maintained for all studies. The inlet temperature was adjusted with the change in spray rate to ensure a consistent product temperature of 35^{o}C. The bead size distribution data suggests there were no agglomerates (0% retained on #16mesh) and no fines (0% retained on Pan) in all the studies. The ER coated beads were mostly retained on #20 mesh (850 micron) and a very little proportion of larger beads (%retained on #18 mesh, 1.00 mm) was noticed. Although, 3.4% beads were retained on #18 mesh with EB3 and it was hypothesized to be higher spray rate causing few agglomerations. The % assay of these beads was ranged from 99.1-99.8 % of total theoretical drug load indicating there was no drug shredding from the beads during the ER coating process. The drug release at 6 Hr from the ER coated was determined using a USP type 2 apparatus. The data suggests variability in the drug release with the changes in the HPC viscosity and Spray rate. The data obtained from these studies was analyzed statistically.

Table 6. Results of ER beads characterization

Parameter	**Exp 1**	**Exp 2**	**Exp 3**	**Exp 4**	**Exp 5**
Drug Release % (at 6 HR)	68	80	63	72	55
% Assay	99.4	99.5	99.1	99.8	99
#16 mesh (1.18 mm) retained (%)	0	0	0	0	0
#18 mesh (1.00 mm) retained (%)	0.8	1.2	3.4	0.7	2.9
#20 mesh (850 micron) retained(%)	97.2	95.5	95.3	96.2	96.1
#25 mesh 710 micron) retained (%)	2	3.3	1.3	3.1	1
#30 mesh 600 micron) retained (%)	0	0	0	0	0
Pan retained (%)	0	0	0	0	0

The experiments (Exp 1-5) are executed per full factorial design with the independent variables of HPC viscosity and spray rate and the drug release as dependent variables. The data obtained is analyzed statistically to create the design space and to predict the drug release with variabilities in factors.

3.3 Optimal Parameters for Desired Drug Release by Full-Factorial Design

A 2X2 full factorial design was applied to create a design space and to identify the optimal process and material attributes for a desired drug release from ER beads. The relation of independent variables on dependent response was studied by contour plot (Fig.2).

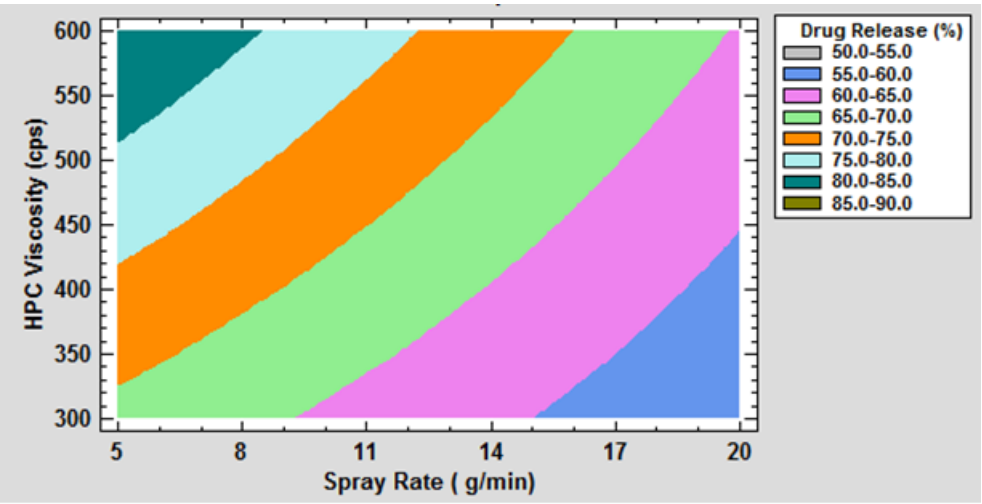

Fig.2. Contour plot

The response surface plot as shown in Fig.3. wasplotted and used for the selection of HPC polymer viscosity and spray rate for a desired drug release

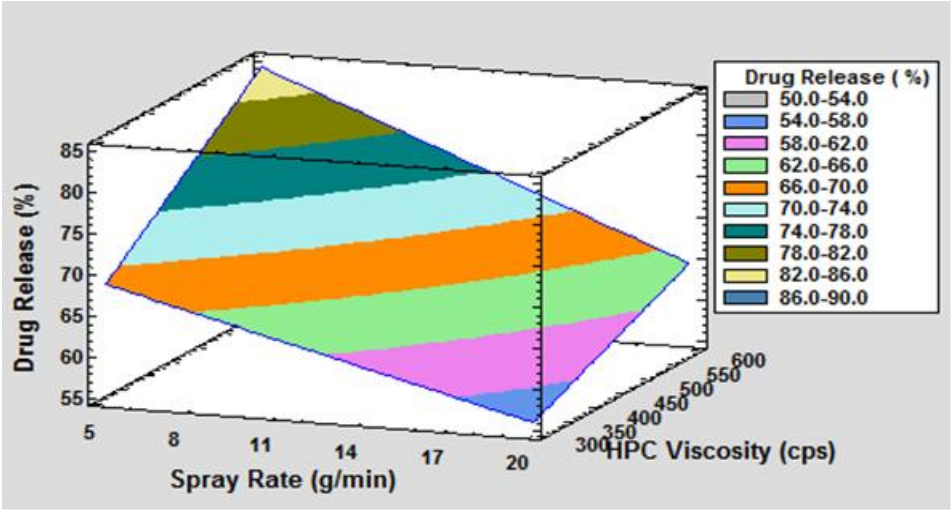

Fig.3. Response surface plot

Also, an interaction plot (Fig.4.) was used to understand the interaction of both viscosity and spray rate on dug release from ER beads.

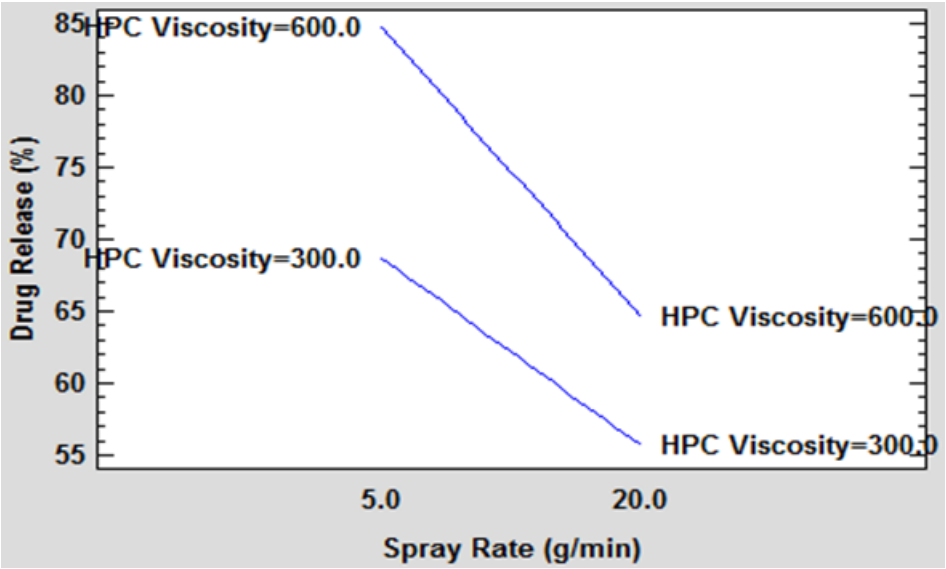

Fig.4. Interaction Plot

The mathematical equation relating the influence of the HPC viscosity (and ER solution spray rate to the drug release) is given in following equation.

Drug Release (%) = 54.65 - 0.4*Spray Rate + 0.0611111*HPC Viscosity - 0.00155556*Spray Rate*HPC Viscosity

The coefficient values and contour plots indicate the effect of the HPC viscosity (cps) and ER solution spray rate (g/min) on drug release. The positive coefficient value for HPC viscosity indicates that drug release expedites with an increase in viscosity. The negative coefficient for spray rate indicates that drug release is slows down with an increase in the spray rate. The higher coefficient value for spray rate (0.4) compared to viscosity (0.06) indicates that spray rate has a greater influence on drug release. A term comprising product of 2 factors represents an interaction term. Based on the response surface and contour plots, the desired drug release from ER beads can be predicted with the variabilities in the HPC viscosity and ER solution spray rate.

Since, the drug release from ER film coated beads is influenced by multiple factors and combined with a need for optimal and consistent drug release from the beads, in the current study, we have attempted to evaluate the influence of HPC polymer viscosity and ER solution spray rate during Wurster film coating and their combination. The response surface and contour plots provide the prediction of drug release with the changes in both spray rate and HPC polymer viscosity. These plots facilitate the selection optimal parameters for a desired drug release. The use of mathematical equation was verified by substituting the values of independent variables, HPC polymer viscosity and ER solution spray rate, from all the experimental runs in the previously mentioned mathematical equation to predict the responses. The predicted values were in good agreement with observed values as indicated by small residual values. The precited model and mathematical equation was further validated by executing a separate confirmatorystudy (CB) by selecting HPC polymer viscosity of 450cps and ER solution spray rate of 8gm/min. The actual drug release value (75.3%) from this batch was proximity to the predicted value of 73.4%. This demonstrated the applicability of the DoE procedure to select the optimal parameters to obtain a desired drug release.

The results from experimental design were consistent to previous findings in which the drug release is highly dependent on HPC polymer viscosity and spray rate during the Wurster ER film coat

process [17, 24]. These attributes predominantly influence the ER film characteristics by formation of bi-continuous and dis-continuous networks within the ER film. The HPC, soluble polymer, in the ER film upon contact with the aqueous media solubilizes and creates pores for drug release through the ER film. At a fixed combination along with the Ethylcellulose polymer, the viscosity of the HPC largely influence the extent and shape of the pores in the ER film under similar process conditions. Due to solubility differences of HPC and EC polymer in ethanol, phase separation of polymer happens during the ER solution spray/drying process depending on the viscosity of the HPC polymer [15, 16, 24]. The results from the high viscosity grade HPC polymer solution demonstrated higher drug release and are mainly interpreted to formation of a bi-continuous structure in the ER film. The low viscosity HPC polymer due to their highly mobility produces a phase separated film in which distinct high HPC rich pockets can be formed thereby by slower water permeability. Whereas the higher viscosity HPC increases the water permeability by formation of inter connectivity of both HPC and EC polymer (bi-continuous structure) by slower movement of HPC polymer and locking of film structure before phase separation happens. However, apart from viscosity of polymer, the film formation process conditions largely influence the phase phenomena in the HPC/EC film network [21]. The wet and dry conditions during the Wurster coating process could influence the film formation network and thereby impacts the drug release. When the spray rate is increased, it allows longer time to dry the film allowing the phase separation of HPC polymer and forms high EC and HPC rich domains causing the lower permeability and a slower release. Similarly, upon slower spray rate conditions, the film gets dried faster and due to increase of ER solution viscosity, the mobility of EC and HPC polymers is reduced and forms an interconnected polymer network i.e., a bi- continuous network. As seen through the experimental data, the variability in drug release is observed with changes in the HPC viscosity and ER solution spray rate. Through the analysis, it is observed that the drug release is predominantly influenced by spry rate compared to viscosity. A bi-continuous network with the minimal phase separation in the ER film can be created by optimization of viscosity and spray rate and their combination. The full factorial study design and the contour plots have shown the optimal conditions for a desired drug release.

Using DoE, we were able to identify process conditions suitable for preparing ER beads with a desired drug release, irrespective of the HPC polymer viscosity and spray rate conditions. The findings are particularly important for obtaining a desired drug release from ER film coated beads considering the complexity of the ER beads manufacturing.

4. CONCLUSION

The drug release from ER beads is a critical quality attribute for ER film coated bead products and the desired drug release performance consistently was influenced by multiple factors including the material and process attributes. The current study assessed the influence of material attribute (HPC viscosity) and Process attribute (spray rate) and their combination on the drug release performance. The usefulness of full factorial design was demonstrated by the selection of optimal HPC viscosity and spray rate conditions for a desired drug release. The quantitative effects of the HPC polymer viscosity and spray rate during Wurster coating process, on a measured response (drug release) was predicted by mathematical linear equation and contour plots. In a nut shell, application of DoE identified process parameters for successful development of ER coated beads of Verapamil HCl.

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Declaration of interest

The authors declare no potential conflict of interest.

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