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Research Article

IMPACT OF HPMC OPTIMIZATION ON RHEOLOGICAL BEHAVIOR OF MICROCRYSTALLINE CELLULOSE DURING WET GRANULATION

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ABSTRACT

The objective of this work was to investigate and optimize the influence of different variables on Hydroxypropyl methylcellulose binder solutions used as granulating agents during wet massing techniques prior to granulation step. Variables examined were the effect of polymer concentration, viscosity, addition of surfactant (Tween 80), addition of plasticizer (PEG 600), binder solution pH, and polymer grade. Mixing torque rheometer (MTR) was efficient in tracing and follow up of the interaction between liquid binder and the solid substrate providing us with the mean line torque of the wet mass and the optimum binder ratio required. The type of solid substrate (microcrystalline cellulose; Avicel PH-101) was kept constant while variations in the liquid binder grade and/or characteristics were tested. Full factorial design was used to study the possibility of combining more than one variable simultaneously on the same binder solution. Analysis of variance (ANOVA) was used for testing the significance of results. It was found that all HPMC concentrations were able to produce a mean line torque higher than that of the blank test. Increasing polymer molecular weight, concentration and/or viscosity caused increase in torque value of wet mass. The results showed the enhanced effect of plasticizer and surfactant on the spreading and diffusion of liquid binder inside solid substrate particles. The maximum torque amplitude of the wet mass was achieved using solution pH of about 7.5 and addition of 2.0 %v/v of surfactant. The results demonstrated the reliability of the tested variable to dictate the performance of the liquid binder solution differentially. From the current work it was found that many parameters are still needed to be evaluated

Keywords: Hydroxypropyl methylcellulose, Binders, Avicel, MTR, Wet granulation.

INTRODUCTION

Granulation technologies are of high interest in a wide range of industries including minerals processing, agricultural products, pharmaceuticals, detergents and foodstuffs [1]. Wet granulation is an important methodology of granulation, in which small particles are agglomerated together into large, semi-permanent aggregates with the aid of a liquid binder that serve as a glue holding individual particles as they are agitated in a tumbling drum, fluidized bed, high shear mixer or similar device [2]. Several studies have investigated the physics of interaction between the solid substrate and the liquid binders' solutions in granule systems to determine the real function of the binder and its effect on granule properties [3-7]. The liquid binder acts to get the particles together by a combination of capillary forces, surface tension and Vander Val's forces until solid permanent bonds are formed by subsequent drying or sintering [3].

The change in rheological properties of wet powder masses can be monitored using an instrument known as mixer torque rheometer (MTR) [8]. In MTR, two different parameters can be measured; firstly, the mean line torque that describes the mean resistance of the wet mass to mixing. Secondly, the binder ratio reflects the rheological heterogeneity of the mass and liquid volume per unit weight [9]. The variations in torque amplitudes obtained from MTR have been related to the different stages of liquid saturation of the mass [10, 11]. As the moisture content increases, the torque will increase as the liquid saturation goes from the pendular to the funicular stage [12]. A maximum mean line torque (Maximum torque) will be reached at complete liquid saturation known as the capillary stage [13]. Any further increase in the amount of liquid, results in the formation of slurry causing a fall in torque amplitude at a stage known as droplet phase indicating over-wetting of the processed mass [14]. MTR has been shown to be useful tool for predicting agglomeration properties of wet masses in different mixer granulators also it can be used to examine the effect of mixing time on the rheology of wet masses [13].

It was found that during production of pellets as special form of granules, the amount of liquid binder added at the maximum torque during pelletization steps was comparable with that found for the optimum production of pellets by spheronization [15] whereas another studies pointed out that pharmaceutical granules were formed at liquid saturations immediately prior to the torque maximum [12].

The rheological properties of wet samples drawn at different times from mixer granulators have been measured in MTR for monitoring batch variations during pharmaceutical production [16]. The degree of liquid binder spreading and wetting as well as the substrate binder interaction will determine peak positions and values of mean line torque on the produced MTR charts [17]. The passing between pendular, funicular and capillary phases are characterized by an increase in the network of liquid bridges between solid substrate particles causing an increase in cohesiveness of the powder mass and hence an increased agitation resistance and torque on the mixer blades of MTR manifested by increased power consumption [18].

Hydroxypropyl methylcellulose (HPMC) is a versatile polymer has different uses as a binder or control drug release rate by gelling behavior as a matrix system that depends on HPMC amount and its molecular weight [19, 20]. Behavior of HPMC as binder in wet granulation up till now is not fully investigated using MTR to view the influence of different variables. During production of pharmaceutical products, several variables are needed to be optimized; some of which may be maximized while others may have to be minimized [21]. All the responses that may affect the quality of product should be taken into consideration [22].

Central composite design and analysis of response surfaces were used because they are systematic and efficient methods to simultaneously study the effect of multiple variables and to find an optimum formulation [23-25] The main objective of the present study was the optimization of the liquid binder solution under the influence of different controlling factors that may affect on the degree of interaction between binder solution (HPMC) and the solid substrate (Avicel) aiming to get more detailed understanding about the wet granulation technique via changing some variables. To achieve this goal many parameters were studied such as; binder solution concentration, viscosity, pH value, surfactant level, plasticizer level and polymer grade.

MATERIALS AND METHODS

Materials

The following materials were used as received: microcrystalline cellulose (Avicel PH-101), lot. No. P10982/003 was kindly donated by (FMC International, Wallingstown, Little Island Co. Cork, Ireland). Hydroxypropyl methylcellulose (Hypermellose) was kindly donated from JRS Pharma (Germany). Polyethylene glycol 600 (PEG 600) with n; 11 – 12.5 was purchased from BDH chemicals Ltd. (Poole, England). Tween 80 was purchased from AVONCHEM (Cheshire, UK). All other chemicals used in this investigation were of high purity analytical grade and were purchased from Fisher Scientific UK Ltd. (Loughborough, UK).

Methods

Binder solution characterization

Viscosity determination

The dynamic viscosity in centipoises (cP) was determined using rotatory viscometer at constant temperature (20 ± 0.5°C) using Brookfield viscometer model DV-11T connected to a Brookfield temperature controller TC-202 (Brookfield engineering laboratories, Inc.).

Surface *tension by the drop-weight method*

At constant temperature (22 ± 0.5°), surface tension of the test solution was determined relative to that of distilled water [26, 27].

pH adjustment

Using pH-meter (METTLER TOLEDO GMBH, ANALYTICAL CH8603, Switzerland), pre-calibrated as manufacturer instructions. Volumetric solutions of 1.0 normal (N) hydrochloric acid and 1.0 N sodium hydroxide prepared according the monograph of USP 30 – NF 25 and were used for pH adjustment procedure.

Wet massing studies using mixer torque rheometer (MTR).

The MTR used in the present study was of a 135-mL capacity stainless steel bowl inside which two rotating blades with rotational speed ranging 0-150 rpm (MTR-3, Caleva, Dorset, UK).

Mixing procedure in MTR

An accurately weighed 15.0 g of Avicel PH-101 was used in the wet massing studies. Five milliliters of liquid binder were added manually in multiple additions over predetermined wet massing intervals. Each wet massing interval consisted of a 60-s mixing period and a 20-s data logging (collection) period with the MTR operating at 50 rpm at room temperature. A 40-s period was allowed for the MTR to auto-zero when empty and also on the dry powder before liquid addition. Data were collected as a relation between the mean line torques versus the binder ratio during the granulation process at specific time intervals.

Experimental design

A full factorial design was constructed to study the optimum combination of some variables simultaneously. The first independent variable was designed for binder solution pH-value and indicated as A, the second independent variable was designed for surfactant level and indicated as B and the response (dependent) variable was designed for maximum torque and indicated as Y (Table 2).

Statistical analysis of results

The following second order general polynomial equation was used:

$$Y = b_0 + b_1A + b_2B + b_{11}A^2 + b_{22}B^2 + b_{12}AB$$

Response surface plots resulting from equations were drawn by STATGRAPHICS plus 4.1-professional version (Statistical Graphics, Corp.). Other curves and statistical analysis were performed using Graph Pad, PRISM® 5.01 (Graph Pad software, Inc.) using one way ANOVA (Table 4).

RESULTS AND DISCUSSION

Different binder solution formulations were made of different components serving our aims for the present study (Table 1). The whole ranges of the used binder solution concentrations were compared with that of distilled water as a binder and avicel as a solid substrate due to its versatility as a solid excipient in almost all solid dosage forms. Two main parameters were used for evaluation of the interaction between the solid substrate and the liquid binder. The first parameter was the amplitude of the mean line torque in Newton-meter (Nm) unit, developed in the wet mass inside the MTR due to blades resistance passing through the 4-phases of the wetting mechanisms that are characterized by unique arrangement of liquid bridges between solid substrate particles and the maximum torque characterizes the capillary phase of interaction [28, 13]. The second parameter was the binder ratio in (ml/g) unit, that reflect the volume of liquid in milliliter corrected to the unit weight in gram of dry solid weight.

Effect of binder solution concentration

Different concentrations of HPMC binder solution were used and the corresponding maximum torque and binder ratio were determined from the obtained MTR chart. Distilled water used as a blank was found to produce a relatively high maximum torque of about 1.335 ± 0.11 Nm at binder ratio of about 1.333 ml/g that reflect the intrinsic binding capability of avicel that will be affected with the used binders either increasing or decreasing to be used as the main source of our current evaluation.

HPMC K15M was studied at different concentration levels in the range of 1–5%, w/v (Fig. 1) forming solutions of different viscosities those increased with the increase in polymer concentration. It was found that all HPMC concentrations were able to produce a mean line torque higher than that of the blank test. The mean line torque increased as binder ratio was increased due to an increase in cohesiveness and agitation resistance of the wet mass, and hence an increased torque on the mixer until reaching the maximum torque after which a gradual decline in torque was noticed that was due to reaching the droplet or slurry phase. Results were in agreement with that obtained with [17].The maximum torque ranged from 1.449 ± 0.064 to 2.100 ± 0.038 Nm (Table 1). The optimum binder ratio required to cause maximum torque was also increased with all HPMC concentrations and ranged from 1.200 to 1.333 ml/g that is relatively similar to that of the blank test. A direct proportion relationship was noticed between HPMC concentration and the maximum torque and had the equation $y = 0.151x + 1.336$ (x; indicate for concentration and y; indicate for maximum torque) with correlation coefficient; $R^2 = 0.984$. These findings could generally refer to the high binding ability of HPMC.

Effect of binder solution pH-value

Binder solution pH value is the least parameter investigated in the literature depending on just dissolving the polymer binder generally in distilled water and controlling another parameter like the concentration, viscosity or the polymer grade for wet granulation. In the current work a general investigation for the influence of the pH value of HPMC binder solution demanding to optimize the binder solution was done. Changing pH of binder solution in industry should be preceded by preliminary investigation of stability, bioavailability and other important parameters affecting on the formulation processing or medicinal effect so the current study is designed to point out importance of controlling the binder solution pH-value as a general investigation.

HPMC K15M 3%, w/v solution was used for investigating the different pH-values covering both the acidic and alkaline ranges from pH 2.58 to pH 11.35 (Table 1). All MTR curves showed the same pattern of rapid increase in torque with increase in binder volume until reaching the maximum torque that was followed by rapid decline in the mean line torque. Unique results were obtained with this polymer especially the sharp MTR peaks (Fig. 2). Consistency of the optimum binder ratio was noticed at about 1.067 ml/g while the great change of the maximum torque in the range of 1.729 ± 0.038 to 2.198 ± 0.028 ml/g with every change in binder solution pH-value. The maximum value of torque was attained with binder solution has pH 6.4 indicating the higher binding activity towards the neutral side of the acidic range that may be due to facilitated solvent penetration into the polymer structure and consequently ease wetting of solid particles that is in agreement with results of [29]. Extreme pH-values had the same effect of minimizing the torque value so it is advisable to adjust the HPMC solution at about neutral pH.

Effect of plasticizer on binder solution efficacy

Some literature investigations were done about studying the effect of plasticizers on the binding solution characterization and suitability of film coating using HPMC [30] but more details were needed. In the current study investigation made on the possible affection of changing binder solution plasticity on the wet massing technique measured using MTR. Polyethylene glycol 600 (PEG 600) as a liquid plasticizer, was selected for our study due to its versatility and lower toxicity and that is the cause of its wide selection in many dosage forms [31].

HPMC 3%, w/v solution was the selected concentration for investigation of the plasticizer effect in the range of 0 - 5%, v/v (Table 1). A noticeable change in the maximum torque value was produced with change in plasticizer concentration ranged from 0.555 ± 0.048 to 1.143 ± 0.085 Nm. However, all are lower than that of the blank solution that produced about 1.675 ± 0.028 Nm. The result indicates a general notice about the decrease in the wet mass torque with plasticizer addition but this might not exclude the other beneficial effects of plasticizers in wet granulation. Concerning the effect of plasticizer on the optimum binder ratio required for the maximum torque, consistency was noticed at about 1.333 ml/g (Fig. 3) except that of the 1%, v/v plasticizer concentration that required about 1.667 ml/g to reach its maximum. These findings may be attributed to the differential effect of plasticizer on the spreading and diffusion power of binder solution between solid substrate particles reflecting the change in torque value.

Effect of polymer grade on binder solution efficacy

It was of importance to investigate impact of changing the polymer grade on the attitude of the liquid binder on the used solid substrate. Polymer grades selected were HPMC K3M, HPMC K5M, HPMC K15M and HPMC K100M (Table 1). MTR curves were of sharp peaks (Fig. 4) and had the same optimum binder ratio of about 1.20 ml/g except that of HPMC K100M that required a smaller volume of binder solution about 1.067 ml/g to reach the maximum torque that may be due to its high viscosity. Results of the maximum torque amplitude were logical as it increased steadily with increasing the molecular weight and viscosity of the polymer binder 1.450 ± 0.042 for HPMC K3M, 1.671 ± 0.029 for HPMC K5M, 1.798 ± 0.077 for HPMC K15M and 1.817 ± 0.047 HPMC K100M. Results were in agreement with Parker [13]. These results could be explained by the effect of increasing the molecular weight on the viscosity at constant concentration and subsequent increase in wet mass resistance against mixer blades producing an increase in torque value.

Effect of surfactant on binder solution efficacy

Some articles in the literature referred to the effect of surface tension on effect of surfactant addition on the attitude of HPMC polymer [30]. Here we tried to get some results to approve this relation by eliciting the effect of different concentrations of a widely used surface active agent (SAA); Tween 80 as a model surfactant added to HPMC solution then wet massing of the solid substrate (Avicel PH-101) tracing the interaction using the MTR. HPMC K15M as 3%, w/v concentration was used as a stock solution to which serial concentrations of Tween 80 (1 – 5%, v/v) were added (Table 1). The interaction between the modified binder solution and solid substrate was traced with MTR (Fig. 5). The solid substrate requirement from the liquid binder was variable and ranged from 1.067 ml/g to 1.333 ml/g. All curves showed a rapid increase in torque amplitude then a slow decline after the maximum torque forming sharp peaks. The maximum torque amplitude ranged from 1.299 ± 0.037 to 2.016 ± 0.043 Nm. The highest torque value was obtained with the 2% v/v of surfactant concentration and was higher than that obtained with the blank test solution followed by gradual decline in maximum torque amplitude with an increase in surfactant concentration. This may be due to higher surfactant concentration that fastens reaching to the droplet phase. Results were in agreement with that of Parker [6] and came to prove the positive effect of surfactant on the torque amplitude when adding specific surfactant concentration to binder solution for wet massing of avicel PH-101, which may be of some importance or of valuable impact on the subsequent formulation processing.

Optimizing formulations using factorial design

After a general screening of specific variables that highly affecting the results, a central composite design was used to study the effect of two formulation variables simultaneously affecting the liquid binder solution on one response variable. The two formulation independent variables studied were the surfactant concentration, and binder solution pH-value, while the response dependent variable was the maximum torque.

General screening of HPMC K15M using MTR on avicel PH-101 showed that the most prominent factors affected on the torque amplitude were binder solution pH-value and surfactant level added to the binder solution so, factorial design was constructed to study the optimum combination of both variables (Table 3). The first independent variable was designed for binder solution pH-value and indicated as A, the second independent variable was designed for surfactant level and indicated as B and the response (dependent) variable was designed for maximum torque and indicated as Y (Table 2). The second order polynomial equation resulted from the statistical software for the response was:

$$\left[Y_{(HPMC)} = -0.355838 + 0.537154A + 0.307996B - 0.0327248A^2 - 0.0370027B^2 + 0.0206579AB \right]$$

Analysis of variance (ANOVA) (Table 4) indicated that the assumed regression models were significant at $P \leq 0.05$ and valid for the considered response variable. The three-dimensional response surface plots resulted from the above equation was drawn to estimate the effects of the independent variables on the proposed response (Fig. 6). As shown in (Fig. 6), the effect of binder solution pH-value (A) on the maximum torque (Y) was more pronounced than that of the surfactant level (B). Therefore, according to the best points of desired dependent variable, the most suitable area for optimum formulation was found. The optimum combination of both variables A and B deduced from the response surface diagram and its related statistical data showed that it could be at about pH 7.5 of variable A and about 2.0%, v/v of variable B which may maximize the torque amplitude to about 1.991 Nm. The optimum formulation was reproduced and tested using the MTR (Formulation 11, Table 3). (Fig. 7) shows the effect of the optimum formulation on the relation between the binder ratio and the mean line torque with maximum torque about 1.762 ± 0.044.

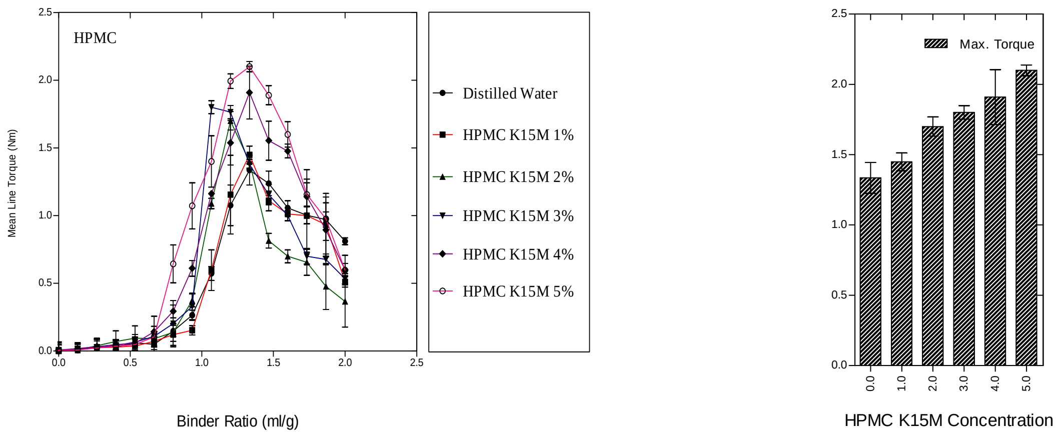

Fig. 1: MTR curve showing the relation between binder ratio (ml/g) of HPMC K15M solution of different concentrations 0–5% (w/v) and the mean line torque (Nm) developed in Avicel PH-101. The related histogram showing the relation between HPMC K15M concentration and the peak maximum torque (mean + SD, n = 3)

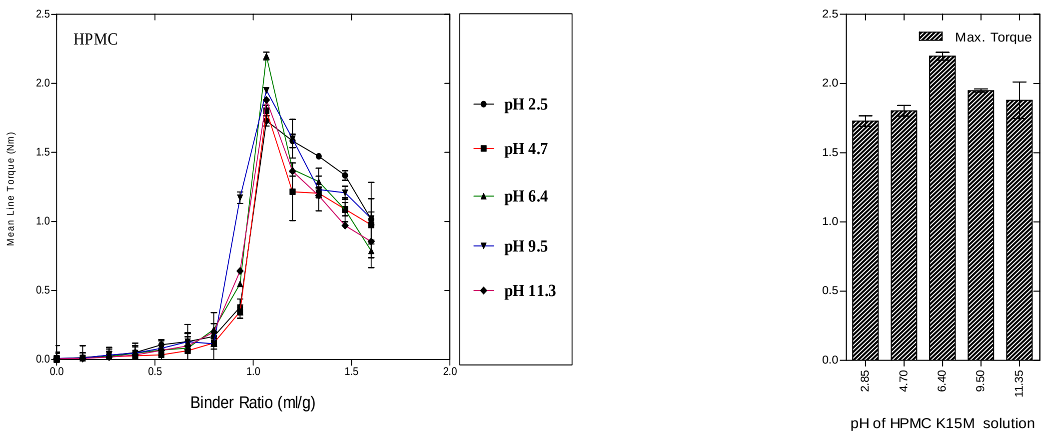

Fig. 2: MTR curve showing the relation between binder ratio (ml/g) of HPMC K15M 3% (w/v) solution at different pH values and the mean line torque (Nm) developed in Avicel PH-101. The related histogram showing the relation between HPMC K15M solution pH and the peak maximum torque (mean + SD, n = 3)

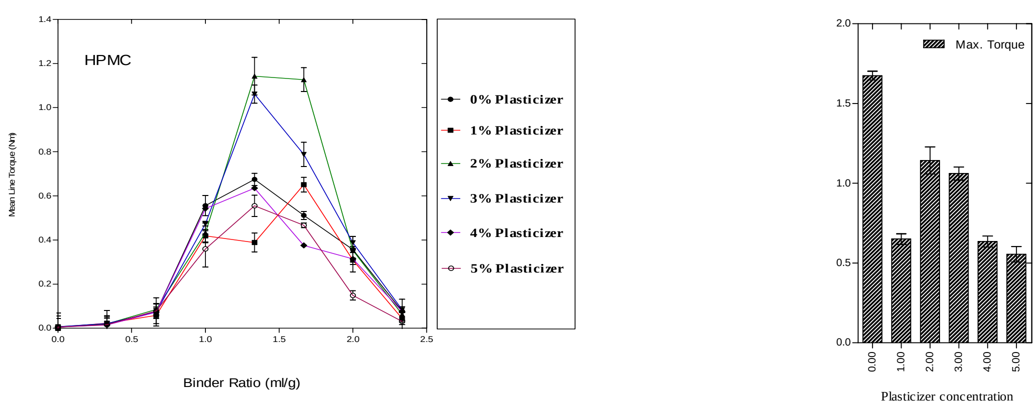

Fig. 3: MTR curves showing the relation between binder ratio (ml/g) of HPMC K15M 3% (w/v) solution plasticized with PEG 600 at different concentrations 0–5% (w/v) and the mean line torque (Nm) developed in Avicel PH-101. The related histogram showing the relation between plasticizer concentration and the peak maximum torque (mean + SD, n = 3)

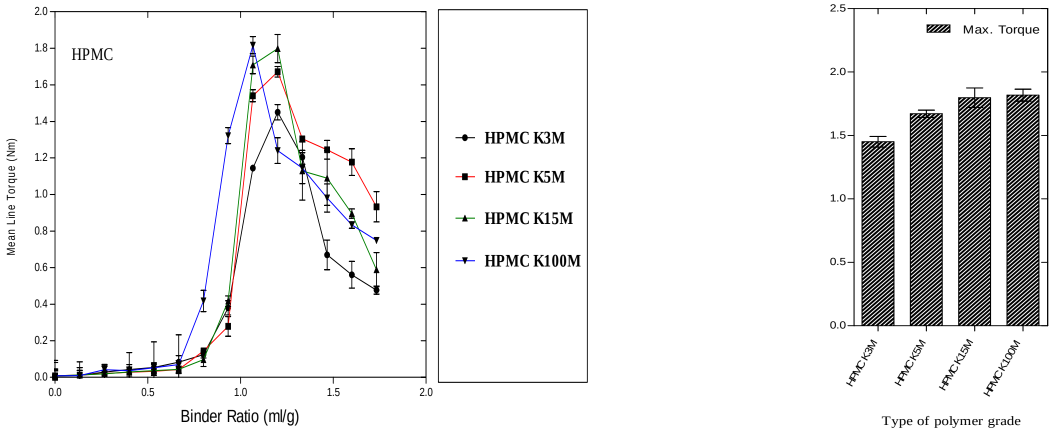

Fig. 4: MTR curve showing the relation between binder ratios (ml/g) of HPMC 3% (w/v) solution of different grades and the mean line torque (Nm) developed in Avicel PH-101. The related histogram showing the relation between polymer grade and the peak maximum torque (mean + SD, n = 3)

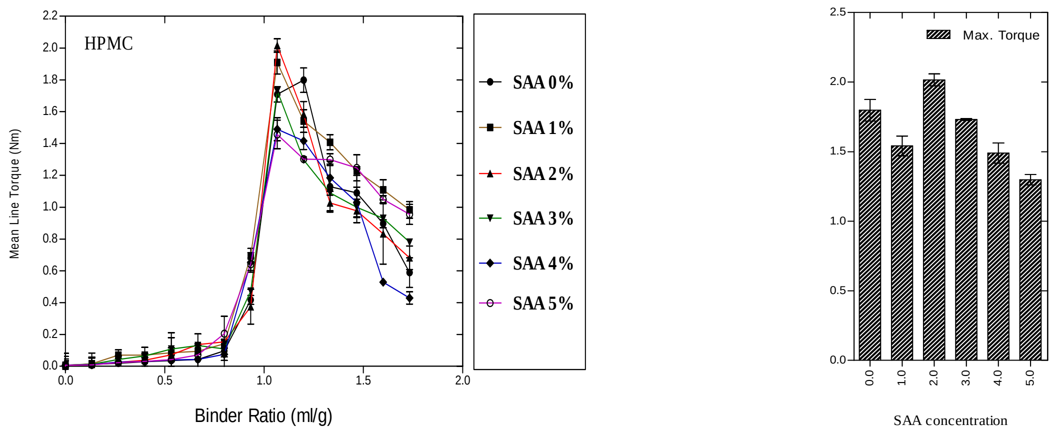

Fig. 5: MTR curve showing the relation between binder ratio (ml/g) of HPMC K15M 3% (w/v) solution with different concentrations of Tween 80 as surface active agent (SAA) 0–5% (w/v) and the mean line torque (Nm) developed in Avicel PH-101. The related histogram showing the relation between Tween 80 concentration and the peak maximum torque (mean + SD, n = 3)

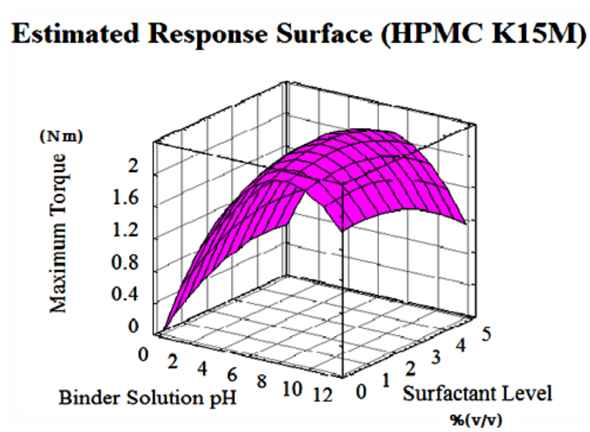

Fig. 6: Surface plot for Hydroxypropyl methylcellulose (HPMC) K15M

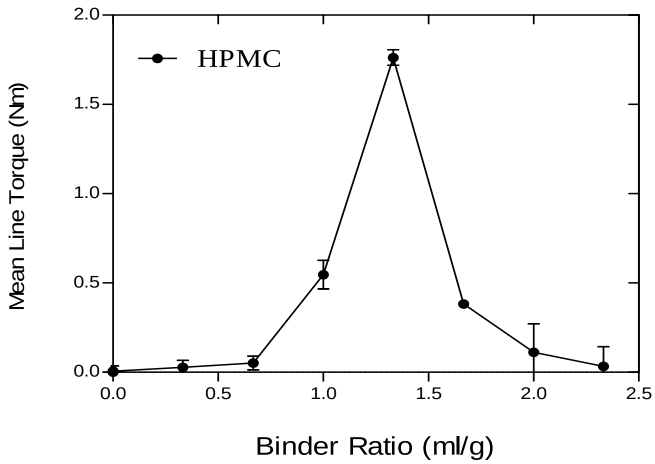

Fig. 7: MTR curve of optimum formulation HPMC as predicted from surface methodology, showing the relation between binder ratio (ml/g) and the mean line torque (Nm) developed in Avicel PH-101(mean + SD, n = 3)

Table 1: Formulations made of Hydroxypropyl methylcellulose (HPMC) for avicel PH-101 wet massing in MTR and the related results (Formulation 1 – 24)

Formulation	Polymer grade	Polymer concentration (% w/v)	Tween 80 (% v/v)	PEG 600 (% v/v)	Adjusted-pH value	Viscosity (cP)	Surface tension (dyne/cm)	Optimum binder ratio (ml/g)	Maximum Torque (Nm) ±SD
1	HPMC K15M	——	——	——	——	1.0	——	1.000	1.335 (0.110)
2	HPMC K15M	1.0	——	——	——	6.0	——	1.333	1.449 (0.064)
3	HPMC K15M	2.0	——	——	——	14.0	——	1.200	1.700 (0.068)
4	HPMC K15M	3.0	——	——	——	33.0	——	1.067	1.798 (0.077)
5	HPMC K15M	4.0	——	——	——	64.0	——	1.333	1.909 (0.195)
6	HPMC K15M	5.0	——	——	——	112.0	——	1.333	2.100 (0.038)
7	HPMC K15M	3.0	——	——	2.58	——	——	1.067	1.729 (0.038)
8	HPMC K15M	3.0	——	——	4.70	——	——	1.067	1.803 (0.039)
9	HPMC K15M	3.0	——	——	6.40	——	——	1.067	2.198 (0.028)
10	HPMC K15M	3.0	——	——	9.5	——	——	1.067	1.949 (0.012)
11	HPMC K15M	3.0	——	——	11.35	——	——	1.067	1.879 (0.132)
12	HPMC K15M	3.0	——	1.0	——	——	——	1.667	0.651 (0.033)
13	HPMC K15M	3.0	——	2.0	——	——	——	1.333	1.143 (0.085)
14	HPMC K15M	3.0	——	3.0	——	——	——	1.333	1.061 (0.041)
15	HPMC K15M	3.0	——	4.0	——	——	——	1.333	0.635 (0.035)
16	HPMC K15M	3.0	——	5.0	——	——	——	1.333	0.555 (0.048)
17	HPMC K3M	3.0	——	——	——	6.0	——	1.200	1.450 (0.042)
18	HPMC K5M	3.0	——	——	——	10.0	——	1.200	1.671 (0.029)
19	HPMC K100M	3.0	——	——	——	230.0	——	1.200	1.817 (0.047)
20	HPMC K15M	3.0	1.0	——	——	——	1.683	1.200	1.541 (0.071)
21	HPMC K15M	3.0	2.0	——	——	——	1.609	1.067	2.016 (0.043)
22	HPMC K15M	3.0	3.0	——	——	——	1.500	1.067	1.731 (0.007)
23	HPMC K15M	3.0	4.0	——	——	——	1.327	1.067	1.490 (0.072)
24	HPMC K15M	3.0	5.0	——	——	——	1.166	1.333	1.299 (0.037)

Table 2: Independent and dependent variables and the levels used for factorial design of HPMC K15M

	Factors (independent variables)	Levels used			Response (dependent variables)
HPMC K15M		1	0	-1	
	A: Binder Solution pH	12	6.0	2	Y = Maximum Torque
	B: Surfactant Level	5%	2.5%	0%	
	$Y_{(HPMC)} = -0.355838 + 0.537154A + 0.307996B - 0.0327248A^2 - 0.0370027B^2 + 0.0206579AB$				

Table 3: Formulations of experimental design of HPMC K15M (Formulations 25 – 35)

	Formulation	Binder solution pH-value	Surfactant level (%v/v)	Maximum Torque (Nm)
HPMC K15M	25	6.75	2.00	2.256
	26	2.00	1.00	1.210
	27	11.5	1.00	1.800
	28	2.00	5.00	0.988
	29	11.5	5.00	0.793
	30	2.00	3.00	0.677
	31	12.0	3.00	1.100
	32	6.75	0.17	1.322
	33	6.75	5.82	1.688
	34	6.75	3.00	1.937
	35	7.50	2.00	1.762

Table 4: Analysis of variance (ANOVA) of dependent variables included in the factorial design of HPMC K15M

	Source	Sum of Squares	Degree of Freedom	Mean Square	F-Ratio	P-Value
HPMC K15M	A:Binder Solution pH	0.15574	1	0.15574	0.82	0.4151
	B:Surfactant Level	0.09318	1	0.09318	0.49	0.5211
	AA	1.28062	1	1.28062	6.67	0.0598
	AB	0.15405	1	0.15405	0.82	0.4174
	BB	0.10394	1	0.10394	0.55	0.4993
	Total error	0.75518	4	0.18879		
	Total (corr.)	2.45191	9			

CONCLUSION

The present results indicate that it is possible to control and optimize the degree of interaction between the granulating agent and the solid substrate during wet massing by introduction of specific variables to the liquid phase. Increasing HPMC concentration and viscosity were reflected as increased maximum torque values. The maximum torque value was attained with binder solution has pH 6.4 indicating the higher binding activity towards the neutral side although it should be about 7.5 when combining with 2%, v/v Tween 80 as deduced from response surface methodology. Extreme pH-values had negative effect on the torque value so it is advisable to adjust the HPMC solution at about neutral pH. The wet mass torque decrease as plasticizer level increased but this could not exclude the other beneficial effects of plasticizers in wet granulation. Results of the maximum torque amplitude were logical as it increased steadily with increasing the molecular weight of the polymer binder. Higher viscosity HPMC grades require smaller volume of binder solution. The highest torque value was obtained with the 2% v/v of surfactant concentration. Results came to prove the positive effect of surfactant on the torque amplitude which may be of some importance on subsequent formulation processing. Response surface methodology was generally efficient methodology in evaluating the impact of different variables simultaneously on the same binder solution.

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