Biosciences, Biotechnology Research Asia Vol. **6**(2), 585-592 (2009)

Process optimization of pantoprazole sodium enteric coated tablets

V. RAVICHANDHRAN, S.K. UMADEVI, B. SENTHILNATHAN*, K. MASILAMANI, T. SARASWATHY[1], S. PADMAPRIYA and J. SRINIVASACHARI

Department of Pharmaceutics,Vels College of Pharmacy, Pallavaram, Chennai (India).
[1]Madras Medical College, Chennai - 3 (India).

(Received: July 1120, 2009; Accepted: September 02, 2009)

ABSTRACT

Pantoprazole is proton pump inhibitor, which prevent the production of acid in the stomach. Pantoprazole sodium enteric coated tablets were prepared by direct compression method. During this study the process parameters like granulation process, Compression process and Coating process are optimized by conducting the study with various blending time, blending speed, compression machine speed, pan speed, spray rate, spray gun distance to tablet bed, atomizing air pressure. Based on the evaluation results of various trials the optimum process parameters are selected (bending time-23min,blending speed- 6rpm, compression speed-30rpm, pan speed-9rpm, spray rate- 70ml/gun/min, spray gun distance to tablet bed- 24cm and atomizing air pressure-6kg/cm^2). By using this optimized parameters the final batch was prepared it was subjected to evaluation. The results are correlated with the standard specified limits.

Key words: pantoprazole sodium, process optimization, Granulation process, Compression process, Coating process.

INTRODUCTION

Optimization is the discipline of adjusting a process so as to optimize some specified set of parameters without violating some constraint. The most common goals are minimizing cost, maximizing output, and/or efficiency. This is one of the major quantitative tools in industrial decision making. It is a useful tools to quantitative a formulation that has been qualitatively determined. The development of formulation or process a series of logical steps are performed changening one variable at a time until a satisfactory and best formulation or process is produced.

The major objective of the present investigation is to optimize the process parameters during preparation of Pantoprozole sodium enteric coated tablets. This work involves two important steps. First step is to study the Granulation, Compression & Coating Processes and parameters. Second step is going to optimize those parameters to be effected by taking different trial batches.

MATERIAL AND METHODS

Pantoprazole sodium was prepared by direct compression method by using Hypromellose, Mannitol Crospovidone, Methacrylic acid co polymer

type 'c' USP, Polyethylene Glycol, Calcium stearate and Titanium dioxide. Optimization of granulation parameters at blending stage (Mixing speed and Mixing time), tablet compression parameters (Compression machine speed), tablet coating parameters (Spray rate, Pan speed, Spray gun distance to tablet bed, Atomizing air pressure)were optimized by conducting various trials(BI,BII,BIII)

Characterization of tablets

The properties of enteric coated tablet, such as thickness, hardness, friability, weight variation and content uniformity were determined using reported procedure.

In *vitro* release studies

The in *vitro* dissolution studies were performed using USP dissolution apparatus (paddle) type at 100 rpm. The dissolution medium consisted of 0.1 N hydrochloric acid for first 2h and subsequent 1h in phosphate buffer p^H 6.8

RESULTS AND DISCUSSION

The process optimization was determined by different parameters.

Granulation parameters

The optimum blending time was selected by carrying out blending at different duration of time i.e. 18min, 20min, 23min, and 25min, out of that optimum blending time was found to be 23min. During this study, the % drug content in 18min, 20min showed very lesser when compared to 23min and 25 minuts.There is no significant difference in % drug content in 23 and 25 minuts. So optimum blending is time 23min. The optimum blending speed was selected by carrying out blending at different rotation per minute (RPM) namely 4rpm, 6rpm, and 8rpm; out of these the optimum blending Speed was found to be 6rpm. The % drug content was very less with blending speed 4 rpm when compared to 6rpm and 8rpm.In the blending speed of 6rpm and 8rpm there was no significant changes in the % drug content. So optimum blending speed is 6rpm.

Table 1: Optimization of blending time

Sample	% Drug content											
	BI Blending time				BII Blending time				BIII Blending time			
	18 min	20 min	23 min	25 min	18 min	20 min	23 min	25 min	18 min	20 min	23 min	25 min
1	92.8	95.9	98.3	98.2	92.6	95.4	98.4	98.2	92.7	95.7	98.4	98.6
2	92.9	94.8	98.6	98.8	92.9	95.5	98.4	98.4	92.8	95.3	98.6	98.7
3	92.7	95.2	98.8	98.7	92.6	95.6	98.5	98.6	92.7	95.5	98.5	98.3
Avg.	92.8	95.3	98.6	98.6	92.7	95.5	98.4	98.4	92.7	95.5	98.5	98.5

Table 2: Optimization of blending speed

Sample	% Drug content								
	BI Blending time			BII Blending time			BIII Blending time		
	4rpm	6 rpm	8 rpm	4 rpm	6 rpm	8 rpm	4 rpm	6 rpm	8 rpm
1	92.3	98.4	98.9	92.5	98.3	98.4	92.1	98.5	98.6
2	92.4	98.4	98.2	92.5	98.8	98.5	92.1	98.4	98.2
3	92.2	98.9	98.6	92.4	98.4	98.6	92.2	98.9	98.9
Avg.	92.3	98.6	98.6	92.5	98.5	98.5	92.1	98.6	98.6

Table 3: Optimization of compression speed in batch I

Parameter	Limit	Machine speed (RPM)							
		20		25		30		35	
		LHS	RHS	LHS	RHS	LHS	RHS	LHS	RHS
Appearance	White to off white coloured circular tablets with plain surfaces on both sides	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Average Weight 20 tablets(mg)	350mg ± 4% (336 mg -364 mg)	347	348	349	350	350	351	344	343
Thickness(mm)	3mm±0.2mm (2.80mm-3.20mm)	2.96	2.95	2.97	2.96	3.12	3.13	3.22	3.23
Hardness(kg/cm^2)	NLT 2.5 Kg/cm^2	4	4	4	4	5	5	3	3
Disintegration time(min)	NMT 12min	3'45"	3'50"	3'50"	3'55"	4'05"	4'07"	3'29"	3'31"

Table 4: Optimization of compression speed in batch II

Parameter	Limit	Machine speed (RPM)							
		20		25		30		35	
		LHS	RHS	LHS	RHS	LHS	RHS	LHS	RHS
Appearance	White to off white coloured circular tablets with plain surfaces on both sides	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Average Weight 20 tablets(mg)	350mg ± 4% (336 mg -364 mg)	348	348	349	350	351	352	343	343
Thickness(mm)	3mm±0.2mm (2.80mm-3.20mm)	3.0	2.98	3.02	3.05	3.13	3.13	3.22	3.24
Hardness(kg/cm2)	NLT 2.5 Kg/cm2	4	5	5	4	5	5	3	4
Disintegration time(min)	NMT 12min	3'43"	3'47"	3'51"	3'54"	4'04"	4'09"	3'30"	3'31"

Table 5: Optimization of compression speed in batch III

Parameter	Limit	Machine speed (RPM)							
		20		25		30		35	
		LHS	RHS	LHS	RHS	LHS	RHS	LHS	RHS
Appearance	White to off white coloured circular tablets with plain surfaces on both sides	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Average Weight 20 tablets(mg)	350mg ± 4% (336 mg -364 mg)	346	348	349	351	350	351	342	343
Thickness(mm)	3mm±0.2mm (2.80mm-3.20mm)	2.96	2.94	2.95	2.96	3.10	3.13	3.23	3.23
Hardness(kg/cm2)	NLT 2.5 Kg/cm2	5	4	4	4	5	5	3	3
Disintegration time(min)	NMT 12min	3'46"	3'48"	3'50"	3'52"	4'03"	4'06"	3'27"	3'29"

Table 6: Optimization of pan speed

Parameter	Limit	Pan speed (RPM)								
		Batch 1			Batch 2			Batch 3		
		8	9	10	8	9	10	8	9	10
Appearance	Off white to yellow	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Thickness (mm)	3.5mm±0.2mm (3.30mm-3.70mm)	3.31	3.52	3.50	3.2	3.54	3.52	3.39	3.53	3.50
Average Weight 20 tablets(mg)	375mg ± 4% (360mg - 390mg)	370	375	375	371	377	378	372	375	376

Table 7: Optimization of Atomization air pressure

Parameter	Limit	Spray rate (ml/gun/min)								
		Batch 1			Batch 2			Batch 3		
		50	60	70	50	60	70	50	60	70
Appearance	Off white to yellow	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Thickness (mm)	3.5mm±0.2mm (3.30mm-3.70mm)	3.2	3.3	3.5	3.3	3.3	3.6	3.3	3.4	3.6
Average Weight 20 tablets (mg)	375mg ± 4% (360 mg -390 mg)	371	373	375	372	374	375	371	374	375

Table 8: Optimization of of spray rate

Parameter	Limit	Pan speed (RPM)								
		Batch 1			Batch 2			Batch 3		
		50	60	70	50	60	70	50	60	70
Appearance	Off white to yellow	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies
Thickness (mm)	3.5mm±0.2mm (3.30mm-3.70mm)	3.2	3.3	3.5	3.3	3.3	3.6	3.3	3.4	3.6
Average Weight 20 tablets (mg)	375mg ± 4% (360 mg -390 mg)	371	373	375	372	374	375	371	374	375

Table 9: Optimization of spray gun distance

Parameter	Limit	Pan speed (RPM)											
		Batch 1			Batch 2			Batch 3					
		22	23	24	22	23	24	22	23	24			
Appearance	Off white to yellow	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies	Complies			
Thickness (mm)	3.5mm±0.2mm (3.30mm-3.70mm)	3.9	3.9	3.6	4.0	3.9	3.6	3.9	3.8	3.5			
Average Weight 20 tablets(mg)	375mg ± 4% (360 mg -390 mg)	381	380	375	383	381	376	379	379	375			

Compression parameters

The optimum compression machine speed was selected by running the machine at varying speed from 20 to 35 rpm. It was found that 30 rpm was the optimum speed because above that quality of product is not consistent.

Table 10: Dissolution profile pantoprazole sodium enteric coated tablets BI

S. No.	% Cumulative Drug release Time interval(min)				
	15	20	30	45	60
1	35.1	46.5	63.2	79.3	98.1
2	35.2	46.9	63.2	79.3	98.8
3	35.5	46.5	63.5	79.9	98.6
4	35.3	46.6	63.3	79.5	98.6
5	35.5	46.3	63.4	79.6	98.5
6	35.9	46.4	63.9	79.9	98.3

Table 11: Dissolution profile pantoprazole sodium enteric coated tablets BII

S. No.	% Cumulative Drug release Time interval(min)				
	15	20	30	45	60
1	37.2	48.1	64.2	80.1	98.3
2	37.4	47.9	64.5	79.8	98.4
3	37.7	47.8	64.4	80.2	98.6
4	37.2	48.2	64.7	80.5	98.2
5	37.6	47.8	64.3	79.9	98.5
6	37.5	48.1	64.4	80.1	98.6

Table 12: Dissolution profile pantoprazole sodium enteric coated tablets BIII

S. No.	% Cumulative Drug release Time interval(min)				
	15	20	30	45	60
1	36.5	49.1	66.2	78.1	98.2
2	36.7	49.9	66.4	79.2	98.6
3	36.4	49.3	66.7	79.2	98.4
4	36.6	49.4	66.7	79.1	98.6
5	36.2	49.8	66.3	79.9	98.7
6	36.5	49.4	66.4	79.1	98.9

Coating parameters

The optimum coating pan speed was selected by running the coating pan at varying rpm from 8 to 10 rpm. When it was subjected to 8 rpm, it showed the differences in average weight in all the three batches. Where as in 9 rpm and 10 rpm, the results were correlated with the specification. So optimum coating pan speed is 9 rpm. The optimum atomizing air pressure was selected by continuously changing the air pressure from 5 to 7 kg/cm^2, out of these optimum atomization air pressures was found to be 6 kg/cm^2. In 5kg/cm^2 and 7 kg/cm^2 atomizing air pressure, the average weight of tablet showed significant differences.

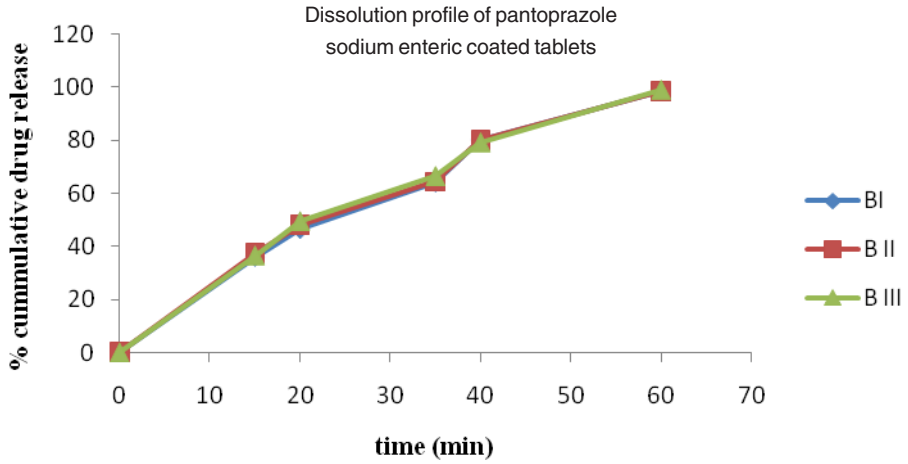

Fig. 1: Dissolution profile pantoprazole sodium tablets(BI,BII,BIII)

When it was subjected at 6kg/cm^2 atomizing air pressure, the results are correlated with the specifications. The optimum spray rate was selected by changing the spray rate from 50 to70 (ml/gun/min), out of these optimum spray rate was found to be 70 ml/gun/min. Since the results (physical parameter evaluation) obtained with 70 ml/gun/min correlated with the specification when compared to the results obtained with 50 (ml/gun/min) and 60 ml/gun/min. By using the above optimized parameters, the Pantoprazole sodium enteric coated tablets were prepared. Then it was subjected to dissolution study. The dissolution data obtained with all the three batches correlated with the standard specified limits.

CONCLUSION

The process optimization for the preparation of pantoprazole sodium enteric coated tablets was done and the Optimum blending time 23min, Optimum blending speed 6 rpm, Optimum compression speed 30 rpm, Optimum coating pan speed 9 rpm, Optimum coating spray rate 70 ml/gun/min, Optimum coating spray gun distance to tablet bed 24 cm, Optimum coating atomizing air pressure 6 kg/cm^2 were selected as optimized parameters for the production of Pantoprazole sodium enteric coated tablets . The dissolution data obtained with all the three batches correlated with the standard specified limits which were prepared by using the optimized parameters.

REFERENCES

1. Leon Lachman, Herbert A.Liberman Lachman, Joseph L, Kaning "theory and practice of industrial pharmacy", 171-198, 293-373.
2. Liberman Lachman "Tablets Dosage forms" **1-2**: 274-348.
3. Liberman Lachman "pharmaceutical dosage forms" **2**: 366-368.
4. JVV MCGINITY Aqeous polymeric coating for pharmaceutical dosage forms 81-95,227-267 (1997).
5. Www. Wikepedia.com
6. Devault G., Chassary O., Schmitt H., "international validation of health- related quality of life questionnaire in patients with erosive gastro-oesophageal reflux disease" Aliment pharmacoltger. **15**.29 (6) (2009).
7. KD.Bardhan., Stanghellini.V., Gatz G., "international validation of request in patients with endoscopy negative gastro-oesophageal reflux disease (2007).
8. Unsalan.S., Rollas.S., "Determination and validation of ketoprofen, pantoprazole and valsartan together in human plasma by high perforanceliquid chromatography".
9. Raffin Rp., Guterres SS., Jornada DS., "pantoprazole sodium effect of scale of production and validation".
10. Filipe A., Almedia S., Franco., Spinola AC., "Bioequilence study of two enteric coated formulation of pantoprazole sodium" Arzneeimittel forschung (2008).
11. Howden CW., Ballard ED., Koch FK., "Release rate of pump inhibitors in patients with GERD" J Clin Gasstroenterol, 43(4) (2009).
12. Hoggan D., Pratha V., Riff D., "Oral pantoprazole in the form of granules or tablets are pharmacodynimically eqivalent in supressing acid output in patients with gasstro-oesophageal reflux disease".
13. Pohlmann AR., Guterres SS., "Prepartion, characterisation and in vivo anti-ulcer evaluation of pantoprazole –loaded micropaticles".
14. Santos SR., Mrrtins VL., Araujo MC., "A flow-injection biamperometric method for determination of pantoprazole in pharmaceutical tablets"