FORMULATION OF ATENOLOL ORALLY DISINTEGRATING TABLETS USING CROSPOVIDONE AS SUPERDISINTEGRANT

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INTRODUCTION

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Oral Delivery

Geriatric patient

- Physiological and neurological changing
- Difficulty in swallowing
- Hand tremors

Inconvenient to use conventional tablets

Poor patient compliance

Orally Disintegrating Tablets

INTRODUCTION

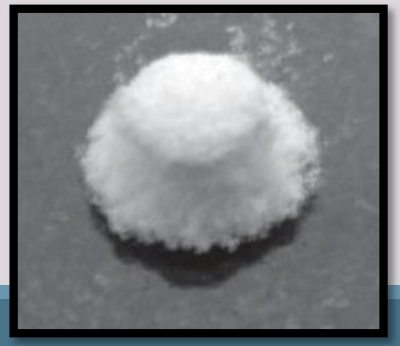
Hypertension in geriatric patients

Antihypertensives drugs

Atenolol

Competitive beta (1)-selective adrenergic antagonists, widely used in hypertension therapy

Orally Disintegrating Tablets of Atenolol



Superdisintegran

Rapid disintegration without gel formation on the surface of tablets

Crospovidone

FORMULA OF ATENOLOL ORALLY DISINTEGRATING TABLETS

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Material	Formula 1 (mg)	Formula 2 (mg)	Formula 3 (mg)
Atenolol	25	25	25
Crospovidone	-	30	60
Aspartam	9	9	9
Mg Stearat	4,5	4,5	4,5
Aerosil	1,5	1,5	1,5
Talk	3	3	3
Mint Flavour	3	3	3
Manitol DC	50,8	44,8	38,8
Avicel PH 102®	203,2	179,2	155,2
Bobot total per tablet	300	300	300

CPV 0% CONTROL

CPV 10%

CPV 20%

METHOD

Mixing of the drug and excipients

↓

Pre compression evaluation
(flowability, compressibility, Hausner ratio, moisture content)

↓

Compression

↓

Post compression evaluation
(% drug content, hardness, wetting time, water uptake ratio, in vitro dispersion time, friability, dissolution)

RESULT AND DISCUSSION

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PRE COMPRESSION EVALUATION

Flowability test

Compressibility test

Moisture content analyzer

RESULT AND DISCUSSION

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PRE COMPRESSION EVALUATION

Parameter	Formula			Specification
	Formula 1	Formula 2	Formula 3	
Flowability (g/detik)	9,31 ± 0,16	6.88 ± 0,32	7,37 ± 0,18	4-10 g/detik
Angle of repose (°)	32,15 ± 0,00	32,15 ± 0,00	35,54 ± 0,00	25°-35°
Compressibility index (%)	23,69 ± 0,50	19,67 ± 0,00	25,73 ± 0,00	<10% -20%
Hausner ratio	1,32 ± 0,006	1,24 ± 0,011	1,34 ± 0,006	< 1,25
Moisture content (%)	4,80 ± 0,24	5,52 ± 0,18	5,54 ± 0,07	3-5%

RESULT AND DISCUSSION

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POST COMPRESSION EVALUATION

Spectrophotometer UV-Vis

Erweka disintegration tester

Monsanto hardness tester

Friability tester

RESULT AND DISCUSSION

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POST COMPRESSION EVALUATION

Parameter	Formula			Spesification
	Formula 1	Formula 2	Formula 3	
Organoleptic	Round white tablet, sweet and mint odor	Round white tablet, sweet and mint odor	Round white tablet, sweet and mint odor	Round white tablet, sweet and mint odor
Drug content (%)	93,99 ± 0,13	100,21 ± 2,45	98,81 ± 2,31	90,0-110,0%
Hardness (kP)	2,85 ± 0,24	2,40 ± 0,52	2,75 ± 0,42	2-4 kP
Wetting time (seconds)	7,00 ± 1,00	4,00 ± 0,00	7,00 ± 0,00	
Water absorption ratio (%)	126,78` ±1,89	57,23 ± 1,18	60,47 ± 0,62	
Disintegration time (seconds)	4,00 ± 0,00	15,48 ± 1,16	19,85 ± 0,95	< 30 second
In vitro dispersion time (second)	15,00 ± 0,00	8,00 ± 1,00	13,00 ± 1,00	
Friabilility (%)	0,20 ± 0,09	0,61 ± 0,19	2,26 ± 0,66	< 1%
% Q (dissolution)	53,85	86,17	87,05	% Q > 85% in 30 minutes

WETTING TIME AND WATER UPTAKE TEST

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Formula 1
(Control)

Formula 2
(10% crospovidone)

Formula 3
(20% crospovidone)

IN VITRO DISPERSION TIME TEST

Formula 1
(Control)

Formula 2
(10% crospovidone)

Formula 3
(20% crospovidone)

MECHANISM FOR TABLET DISINTEGRATION

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- Swelling
- Wicking
- Recovery energy of elastic deformation
- Repulsion
- Heat of wetting

Kanig and Rudnic , 1984; Hahm and Augsburger, 2008.

MECHANISM FOR TABLET DISINTEGRATION

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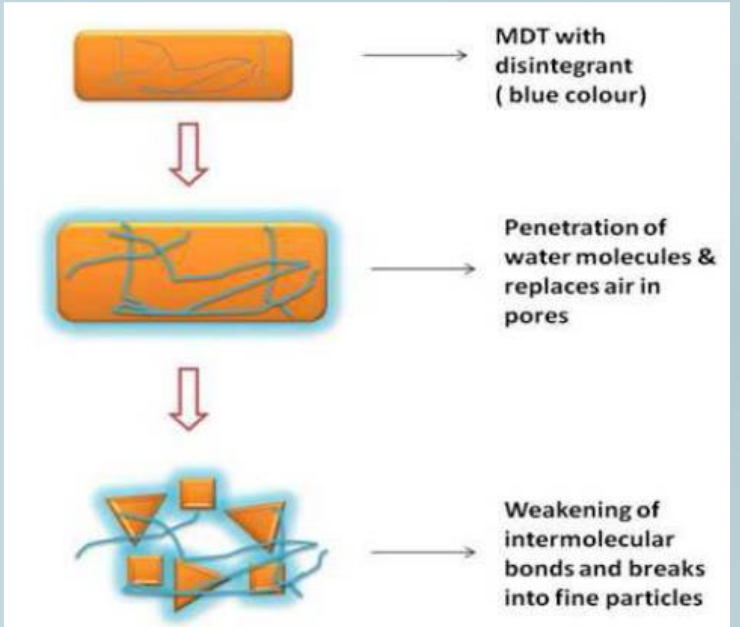
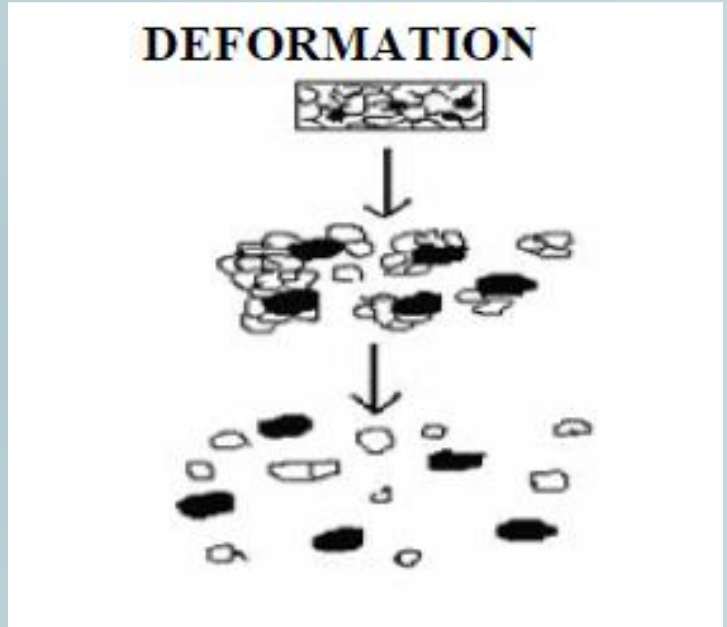
Crospovidone

Crospovidone not swell as much on contact with water





DISSOLUTION PROFILE

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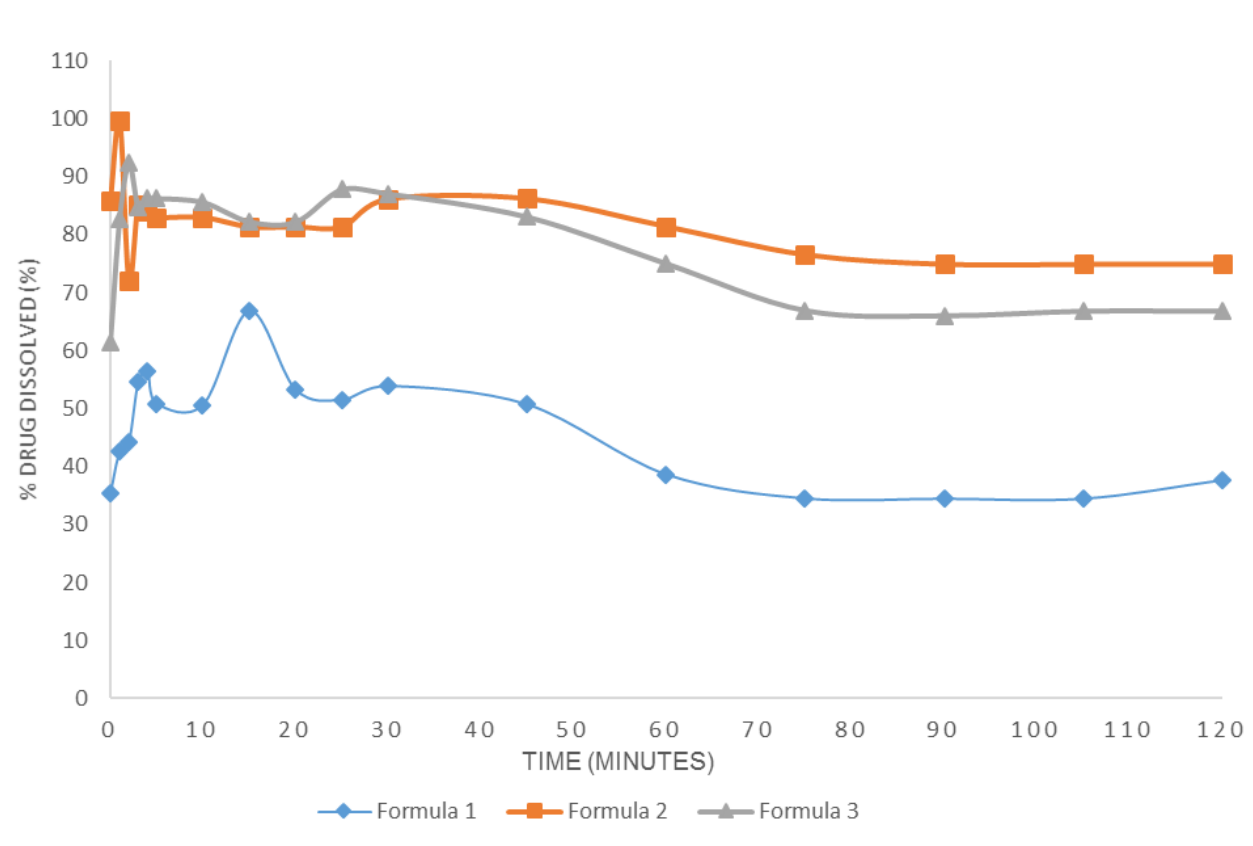

DISSOLUTION PARAMETER	F1	F2	F3
AUC	4384,32±195,95	9650,99±76,89	7693,65±47,19
Dissolution efficiency (ED) (%)	36,54±1,63	80,43±0,64	64,11±0,35

There was a significant difference of dissolution efficiency (ED) between formula 1, formula 2, and formula 3

Formula 2 (10% CPV) showed the highest dissolution efficiency. Dissolution efficiency of formula 2 fold approximately 2,2 compare to formula 1 (control)

CONCLUSION

- The difference of crospovidone concentration in atenolol orally disintegrating tablet affect the physicochemical characteristics of orally disintegrating tablet.
- The optimum formula was formula 2 (10% crospovidone)