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Formulation and evaluation of fast dissolving tablets of captopril

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Abstract

Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. The development of enhanced oral protein delivery technology by mouth dissolving Tablets which may release these drugs in the mouth are very promising for the delivery of high molecular weight protein and peptide. Good mouth feel property of MDDS helps to change the basic view of medication as "bitter pill", particularly for pediatric patients. To prepare mouth dissolving tablet using SSG & CCM by using Antihypertensive as model drug. Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme and it is a key component of the renin-angiotensin-aldosterone system. The ƛmax of Captopril was determined by scanning the 10µg / ml solution of drug using UV-Spectrophotometer and was found to be 271nm. The linear correlation was found to be 0.9995.The Fast dissolving tablets of captopril were prepared by direct compression method. Captopril can be successfully formulated as mouth dissolving tablets using various super disintegrate in different concentrations by direct compression method. The formulation containing 10% of crospovidone as super disintegrated was found to be outstanding than other formulations in terms of disintegration time and rate of dissolution.

Keywords: Captopril; Crospovidone; ƛmax; Compression; SSG; CCM

1. Introduction

Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance [1,2,3]. The development of enhanced oral protein delivery technology by mouth dissolving Tablets which may release these drugs in the mouth are very promising for the delivery of high molecular weight protein and peptide [4,5,6]. The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance [7,8,9,10]. FDDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. FDDTs, as a novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms [11,12]. Taste-masking is of critical importance in the formulation of an acceptable FDDT. The primary methods of taste-masking include adsorption onto or complexation with carriers and spray coating of solid dosage forms, which increase consumer choice, for the reason of rapid disintegrate/dissolve in oral cavity within seconds and swallowed without the need of water or chewing [13,14,15]. Fast dissolving drug delivery can be achieved various techniques like direct compression, wet granulation, compression moldings, volatization and freeze – drying. They involve different mechanisms like use of high amounts of hydrophilic disintegrating agents which allow the dosage forms to disintegrate quickly in the patient's mouth on contact with saliva [16,17].

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2. Material and methods

Table 1 Chemicals And Equipment's

Chemicals	Equipments
Captopril	Electronic Weighing Balance
Sodium starch glycolate	Single Punch Tablet Compression Machine
Crospovidone	UV- Visible Spectrophotometer
Croscarmellose sodium	Digital Tablet Dissolution Test Apparatus
Microcrystalline cellulose	Friability Test Apparatus
Mannitol	Hot Air Oven
Saccharin sodium	Disintegration Test Apparatus
Magnesium stearate	Tablets hardness tester (Monsanto)
Talc	Vernier Caliper

2.1. Captopril

Captopril is a potent, competitive inhibitor of angiotensin-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I (ATI) to angiotensin II (ATII).

- Molecular weight: A v e r a g e : 2 1 7 . 2 8 5
- Structure

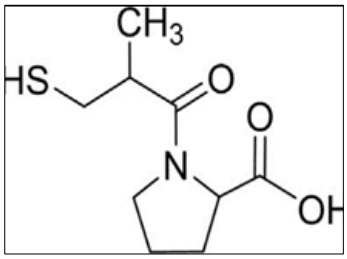

Figure 1 Structure of Captopril

2.2. Crospovidone

- Chemical Structure

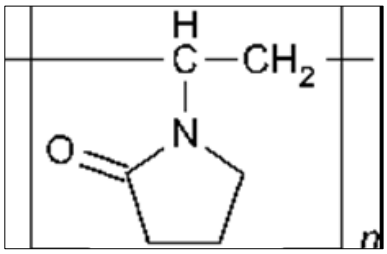

Figure 2 Structure of Crospovidone

2.3. Croscarmellose sodium

- Chemical Name: Cross linked carboxy methyl ether Cellulose sodium salt.
- Functional Category: Tablet and capsule disintegrant.

2.4. Sodium starch glycolate

- Chemical Name: Sodium carboxymethyl starch
- Chemical structure

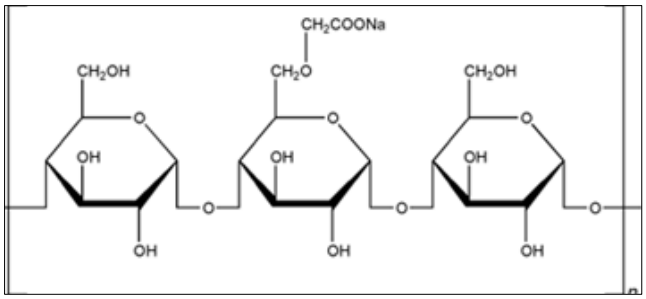

Figure 3 Structure of sodium starch glycolate

2.5. Magnesium stearate

- Synonyms: Magnesium octadecanoat.
- Chemical Name: Octadecanoic acid magnesium salt.
- Structural Formula: $[CH_3\ (CH_2)_{16}COO]_2Mg$

2.6. Mannitol

- Synonyms: Cordycepic acid.
- Chemical Name: D-Mannitol
- Empirical Formula and Molecular Weight: $C_6H_{14}O_6$ & 182.17
- Microcrystalline cellulose
- Synonyms: Avicel P^H

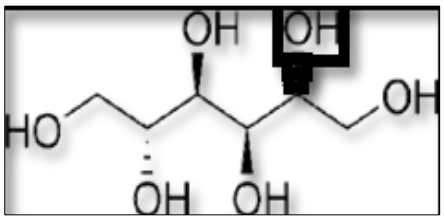

Figure 4 Structure of Mannitol

- Chemical Name: Cellulose
- Empirical Formula: $(C_6H_{10}O_5)$ n
- Molecular Weight: 36 000

2.7. Saccharin sodium

- Synonyms: 1,2-Benzisothiazolin-3-one 1,1-dioxide, sodium salt; Crystallose E954; sodium o-benzosulfimide; soluble gluside; soluble saccharin; sucaryl sodium.
- Chemical Name;
- 1, 2-Benzisothiazol-3(2H)-one 1, 1-dioxide, sodium salt for the dihydrate for the anhydrous material.
- Chemical structure

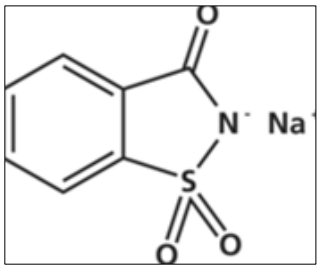

Figure 5 Structure of saccharin sodium

- Empirical Formula: $Mg_6(Si_2O_5)_4(OH)_4$

3. Results and discussion

3.1. Calibration of Captopril

The λ_{max} of Captopril was determined by scanning the 10µg / ml solution of drug using UV-Spectrophotometer and was found to be 271nm.The absorbance of the solution 5 to 25 µg/ml was measured in UV-Spectrophotometer at 271nm.(Table-1). The linear correlation was found to be 0.9995(Distilled water).

Table 2 Calibration of Captopril

Sr. No	Concentration(µg/ml)	Absorbance at 271nm (Avg ± S.D)
1	5	0.197 ± 0.0045
2	10	0.423 ± 0.004
3	15	0.611 ± 0.0024
4	20	0.804 ± 0.005
5	25	1.005 ± 0.0076
		r^2=0.9995

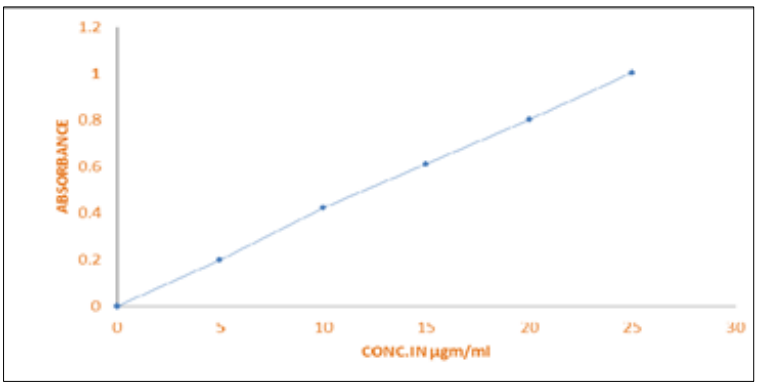

Figure 6 Calibration of captopril

3.2. Pre-formulation evaluations

3.2.1. Fourier Transmission Infra –Red (FT-IR) Studies

Before formulation, preformulation study was carried out by comparing FT-IR spectra of pure Captopril and its physical mixture with superdisintegrants using Fourier Transmission Infrared spectrophotometer. There was no difference in their spectra. It was observed that the drug remained intact in the presence of superdisintegrants.

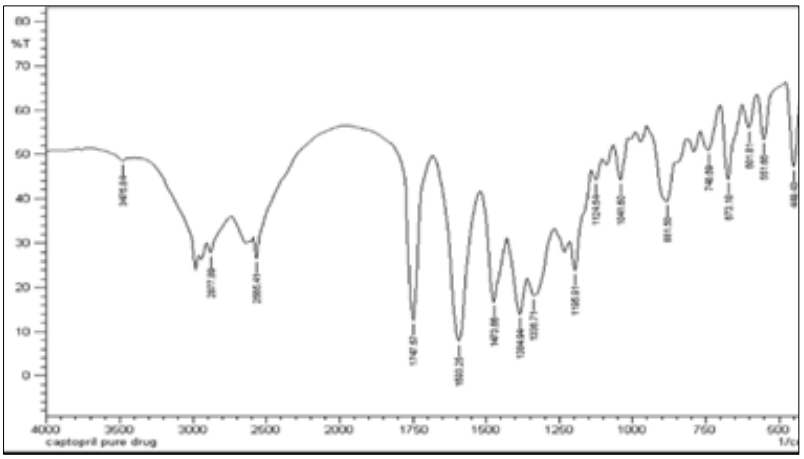

Figure 7 FT-IR Spectrum of CaptopriL

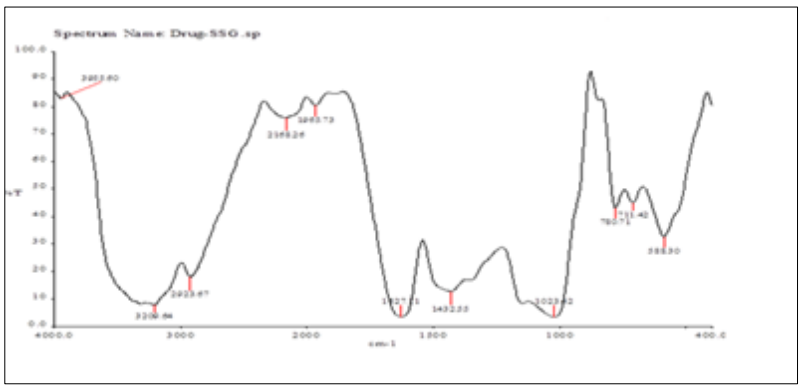

Figure 8 FT-IR Spectrum of Sodium starch glycolate

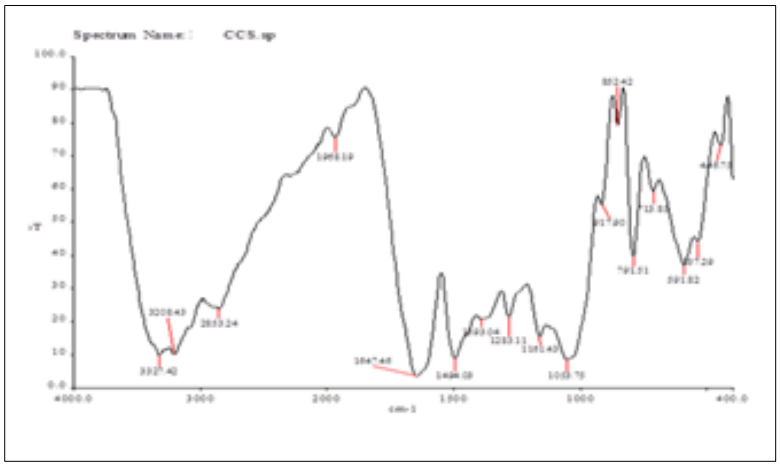

Figure 9 FT-IR Spectrum of captopril + CCS

3.3. Formulation of Fast Dissolving Tablets of Captopril

The individually weighed powder blends of each formulation were compressed in to tablets in a single punch tablet compressing machine. Fifty tablets for each formulation were obtained. The tablets were white in colour and round in shape. The contents for tablets of each formulation were shown in Table -03.

Table 3 Formulation of Fast Dissolving Tablets of Captopril

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Captopril	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Croscarmallose sodium	4	8	12	16	20	-	-	-	-	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	-	-	4	8	12	16	20	-	-	-	-	-
Crospovidone	-	-	-	-	-	-	-	-	-	-	4	8	12	16	20
Mannitol(27.5%)	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
Magnesium stearate(2%	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Sodium Sacharrin%	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Talc (0.5%)	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Micro Crystalline Cellulose	96	92	88	84	80	96	92	88	84	80	96	92	88	84	80
Total weight of tablet	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200

3.4. Precompression evaluations for the powder blend

Precompression evaluations were done to ensure the flow properties of the powder blend .Good flow properties of the powder blend will yield the tablets of desired quality and ease the tableting process. So it was mandatory to assess the flow ability of the blend before compression.

Table 4 Precompression Evaluation

Formulation code	Angle of repose(°)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility index (%)	Hausner's ratio	Drug content (%)
F1	30.50	0.3368	0.4440	24.14	1.31	96.92
F2	31.40	0.3614	0.4436	18.53	1.22	96.69
F3	30.69	0.3760	0.4655	19.22	1.23	96.92
F4	30.54	0.3624	0.4660	22.23	128	96.45
F5	30.25	0.3621	0.4656	22.22	1.28	96.69
F6	30.66	0.3906	0.4650	16	1.19	96.21
F7	30.56	0.3760	0.4444	15.39	1.18	96.69
F8	30.54	0.3913	0.4658	15.99	1.19	95.98
F9	30.46	0.3916	0.4663	16	1.19	96.92
F10	30.72	0.3915	0.4661	16	1.19	96.21
F11	30.72	0.3914	0.4659	15.9	1.19	96.45
F12	30.43	0.3914	0.4660	16	1.19	96.92
F13	30.59	0.3915	0.4661	16	1.19	96.21
F14	30.52	0.3913	0.4659	16	1.19	96.21
F15	30.06	0.3914	0.4660	16	1.19	96.69

3.5. Post compression evaluations

The tablets obtained after compression were evaluated on various parameters to determine their quality and to ensure that the resultant product meets all necessary criteria's required for the fast dissolving tablets

Table 5 Post Compression Evaluations of Fast Dissolving Tablets of Captopril

Formulation code	Hardness (kg/cm$^{3)}$	Thickness (mm)	Diameter (mm)	Drug Content (%)	Weight variation(mg)	Friability (%)	Wetting time (sec)	Water Absorption ratio in (%)	Disintegration time (sec)	% drug release in 5 minutes
F1	3	3	8	95.74	184.1 - 214.04	0.51	15	75.22	623	19.27±0.56
F2	3	3	8	96.21	184.47-214.27	0.72	90	113	173	77.60±0.76
F3	3	3	8	96.69	185.04-214.84	0.55	103	131	179	88.55±0.50
F4	3	3	8	96.21	184.5 - 214.5	0.56	36	144	42.6	95.34±0.64
F5	3	3	8	97.16	184.26-214.12	0.53	151	59.6	311	83.06±0.42
F6	3	3	8	95.98	185.06-215.06	0.71	70	86.3	217	95.98±0.67
F7	3	3	8	96.21	184.82-214.78	0.54	74	110.8	91	90.71±0.66
F8	3	3	8	96.45	184.7 - 214.64	0.52	88	119.8	171	93.24±0.28
F9	3	3	8	96.21	184.63-204.49	0.52	57	105.9	120	92.26±0.43
F10	3	3	8	96.69	185 - 214.98	0.66	100	110.3	150	93.06±0.29
F11	3	3	8	95.74	184.76-214.72	0.65	74	129.6	72	90.21±0.24
F12	3	3	8	96.45	184.92-214.9	0.66	30	108.7	87	92.41±0.15
F13	3	3	8	95.74	184.88-214.86	0.48	25	107.5	29	93.37±0.18
F14	3	3	8	96.21	184.85-214.81	0.50	24	126	21	96.24±0.15
F15	3	3	8	96.69	184.88-214.86	0.70	19	129.6	4	97.19±0.28

4. Conclusion

It was concluded, that captopril can be successfully formulated as mouth dissolving tablets using various superdisintegrants in different concentrations by direct compression method. The formulation containing 10% of crospovidone as superdisintegrants was found to be outstanding than other formulations in terms of disintegration time and rate of dissolution.

Compliance with ethical standards

Acknowledgments

The satisfactions, which accomplish a successful completion of any task, are incomplete without the mentioning of the names of those people who makes it possible. I would like to thank those sailors who have kept my spirits up to sail

in…even through the stormy sea making difficult to end up safely on the shore of success. I am thankful to Dr. P R. Patil, Principal, KYDSCTS . College of Pharmacy, Sakegaon , for his help and motivation.

Disclosure of conflict of interest

Author don't have conflict of interest.

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