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FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF METOPROLOL SUCCINATE

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Abstract:

In the present work efforts have been made to develop fast dissolving tablets of Metoprolol succinate using direct compression technique involving super disintegrants like cross povidone, sodium starch glycolate. The pre compression parameters like angle of repose, bulk density, true density, compressibility index are within the IP limit. The post compression parameters are acceptable and within the IP limit. In-vitro drug release at for all the formulations was found to be 95 to 99% and was satisfactory. The optimized formulation (F6,10%cross povidone) of drug release was found to be is 99% at 30 min.

Key words: *fast dissolving tablets, Mouth Dissolving Drug Delivery System and Metoprolol succinate*

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INTRODUCTION:

Fast dissolving tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed.

Desired Criteria for Mouth Dissolving Drug Delivery System [1-4]

Mouth Dissolving Tablet should-

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions as humidity and temperature.
- Allow the manufacture of tablet using conventional processing and packaging equipment at low cost

Salient Features of Mouth Dissolving Drug Delivery System[5-8]

- Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feel property of MDDS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.

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MATERIALS AND METHODS:

Materials:

Metoprolol succinate was obtained as a gift sample from Micro labs ltd Bangalore. Sodium starch glycolate and cross povidone were obtained from yarrow chemicals, Mumbai. Magnesium stearate and talc were obtained from S.D fines.

Methods:

Preparation of fast dissolving tablets: Metoprolol succinate and microcrystalline cellulose were mixed with super disintegrants for 15 minutes in mortar, passed through sieve no 60.this blend was mixed with talc ,and magnesium state for 5 min and processed for direct compression by using 8mm round flat faced of rotary tablet machine.

Evaluation of Pre-compression and Post-compression Parameters:

The prepared blend was evaluated by following tests.

- Angle of repose
- Bulk density
- Tapped density
- Carr's index

Angle of repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The diameter of the powder cone was measured and angle of repose was calculated using the following equation

$$\text{Tan } \theta = h/r$$

Where,

h and r are the height and radius of the powder cone.

Bulk Density

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

BD = Weight of the powder / initial Volume

Tapped Density

It was determined by placing a graduated cylinder, containing a known mass of drug-excipient blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals. The tapping was continued until no further change in volume was noted.

TBD = Weight of the powder / final volume

Compressibility Index

The Compressibility Index of the blends was determined by Carr's compressibility index.

Carr's compressibility index (%) =

[(initial volume-final volume) ×100] /initial volume

Evaluation of Tablets

All the formulated Metoprolol succinate fast dissolving tablets were subjected to the following

quality control tests:
1. Weight variation
2. Drug content uniformity
3. Friability
4. Hardness
5. Disintegration
6. Dissolution

Weight variation test
The U.S.P. weight variation test was run by weighing 20 tablets and then the average weight was determined.

Drug content uniformity
Twenty tablets were powdered and 10mg equivalent weight of Metoprolol succinate tablet powder was accurately weighed and transferred into a100 ml volumetric flask .initially 10 ml 0.01 n hcl was added and shaken for 10 minutes, then the volume was made up to 100ml with 0.01 n hcl . The drug samples were analyzed by measuring the absorption at 275 nm by using UV-visible spectrophotometer.

Friability test
The friability test was performed Ten tablets were taken and their weight was determined. Then they were placed in the Roche friabilator and allowed to make 100 revolutions. The tablets were then dedusted and reweighed. The percentage weight loss were calculated and given in table.no.3.

Hardness test
Monsanto hardness tester was used for measuring the hardness of the formulated Metoprolol succinate fast dissolving tablets. From each batch five tablets were taken and subjected to test.

Disintegration test
The U.S.P. device to test disintegration uses six glass tubes that are 3" long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is positioned in 1 liter beaker of distilled water at 37±2°C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker. The disintegration time was recorded.

Dissolution Studies
Dissolution was carried out by using Electrolab dissolution apparatus (USP XXI) by paddle method using 900ml of Ph 6.8 phosphate buffer as the medium and rotating the paddle at 50 rpm for 30 minutes. The temperature of dissolution medium was maintained at 37±2^{0}C. Aliquots were withdrawn at different time intervals of 0, 5, 10, 15, 20 minutes and it was replaced by adding equal volumes of fresh dissolution medium. The samples were suitably diluted and absorbance of the solution was determined at 275 nm by using UV-visible spectrophotometer.

RESULTS:

Table 1: Formulation of Fast Dissolving Tablets of Metoprolol succinate

Ingredients	F1	F2	F3	F4	F5	F6
Metoprolol succinate	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
Sodium starch glycolate	24 mg	36 mg	48 mg	---	---	---
Crosspovidone	--	---	--	24 mg	36 mg	48 mg
Micro crystalline cellulose	66 mg	54mg	42mg	66 mg	54mg	42mg
Magnesium stearate	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Talc	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
Total Tablet weight (Mg)	**180 mg**	**180 mg**	**180 mg**	**180 mg**	**180 mg**	**180 mg**

Preparation of fast dissolving tablets:
Metoprolol succinate and microcrystalline celluiose were mixed with super disintegrants for 15 mins in mortar, passed through sieve no 60.this blend was mixed with talc ,and magnesium state for 5 min and processed for direct compression by using 8mm round flat faced of rotary tablet machine.

Drug and Exicipient compatibility studies:
The FTIR spectra of pure Metoprolol succinate (fig-1) and FTIR spectra of cross carmellaose sodium , FTIR spectra of sodium starch glycolate ,mixture of FTIR spectra of Metoprolol succinate and cross carmellaose sodium,(fig-2, FTIR spectra of Metoprolol succinate and sodium starch glycolate (fig-3).The same characteristic mixture ,indicating that no chemical interaction.

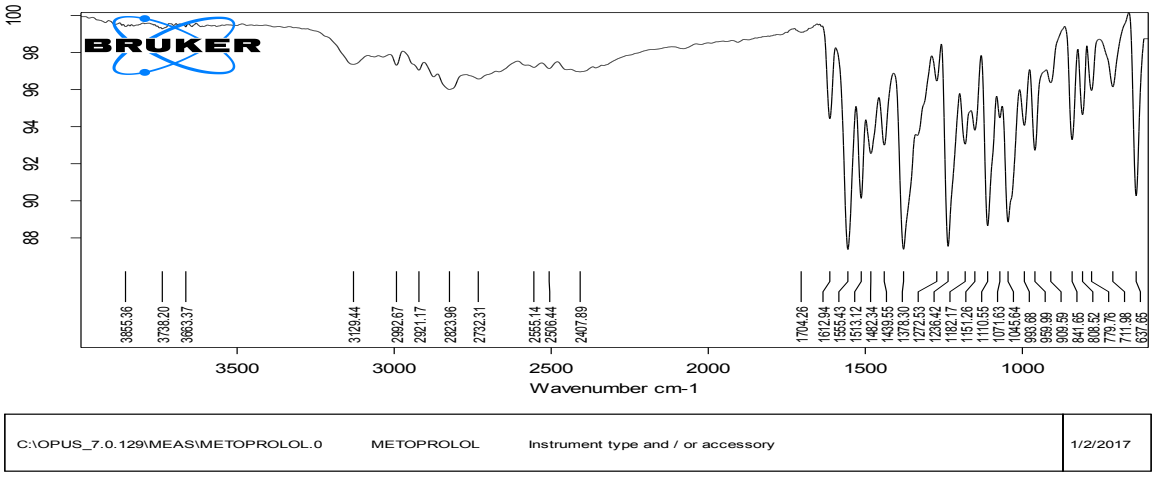

Fig 1: FTIR Spectra of Pure Drug

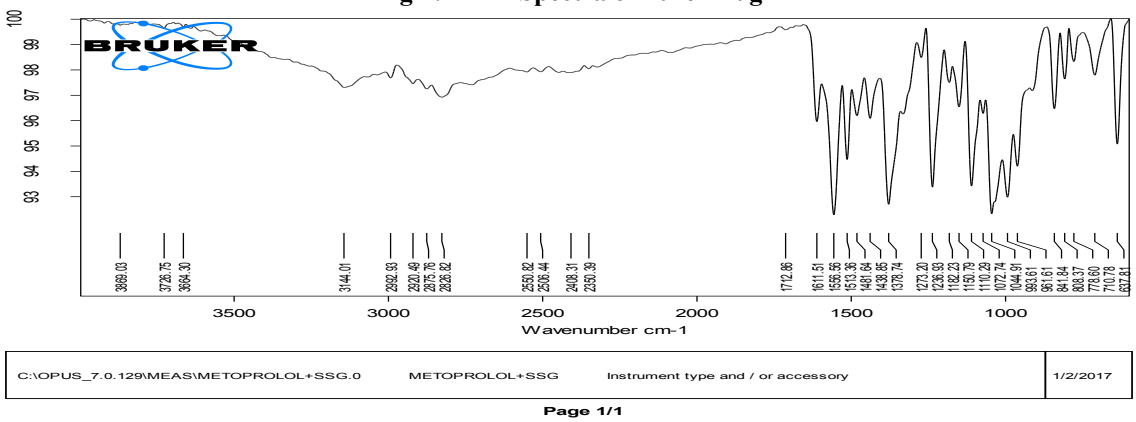

Fig 2: FTIR Spectra of Physical Mixture

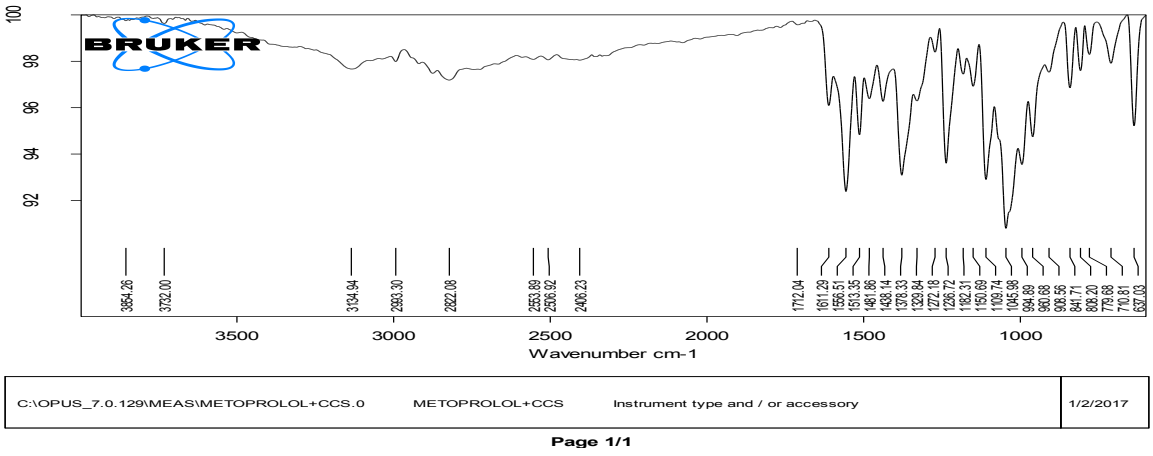

Fig 3: FTIR Spectra of Physical Mixture

Table 2: Evaluation of pre compression parameters of fast dissolving tablets of Metoprolol succinate

Formulation Code	Angle of Repose (^{0}) ±S.D* (n=5)	Bulk density (gm/cc) ±S.D* (n=5)	True density (gm/cc) ±S.D* (n=5)	Carr's index (%) ±S.D* (n=5)
F1	$25^0$12' ±0.02	0.433±0.02	0.52±0.02	16.66±0.03
F2	$29^0$59' ± 0.03	0.371±0.04	0.43±0.01	14.28±0.05
F3	$28^0$27' ±0.02	0.406±0.03	0.49±0.01	17.18±0.03
F4	$26^0$27' ±0.01	0.433±0.01	0.50±0.01	13.33±0.04
F5	$29^0$35' ±0.02	0.382±0.01	0.47±0.02	14.70±0.03
F6	$28^0$20' ±0.03	0.317±0.02	0.43±0.02	14.28±0.03

Table 3: Evaluation of Post Compression Parameters of fast dissolving tablets of Metoprolol Succinate

Formulation code	Weight variation (mg) **	Thickness (mm) *	Hardness (kg/cm^3) *	Friability (%) ***	Drug content uniformity (%) **	Disintegration time (sec)
F1	182±0.01	1.5±0.01	4.11±0.18	0.469±0.02	98±0.02	20±0.02
F2	185±0.01	1.5±0.01	4.76±0.12	0.412±0.03	99±0.03	18±0.03
F3	180±0.01	1.6±0.02	4.01±0.05	0.414±0.04	97±0.02	28±0.02
F4	178±0.02	1.5±0.02	3.96±0.09	0.353±0.05	98±0.02	24±0.02
F5	183±0.02	1.6±0.03	4.12±0.08	0.409±0.03	98±0.03	29±0.03
F6	179±0.02	1.4±0.02	4.05±0.08	0.353±0.02	99±0.04	24±0.04

Table 4: *In Vitro* Drug Release Studies:

Time (Min)	Cumulative Percentage of Drug Release ± S.D. *(n=3)*					
	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	70±0.26	75±0.76	78±0.12	72±0.51	70± 0.11	75±0.72
10	82±0.55	85±0.54	84±0.46	84±0.56	82 ±0.35	88 ± 0.33
15	88±0.17	89±0.47	89±0.61	89±0.95	85 ±0.62	90 ± 0.36
20	90±0.54	92±0.73	90±0.85	92±0.71	90 ±0.76	92 ± 0.77
25	92±0.27	94±1.00	93±0.26	95±0.78	92 ±0.57	95 ± 0.86
30	95±0.86	96±0.51	97±0.53	97±0.56	98 ±0.85	99 ± 0.74

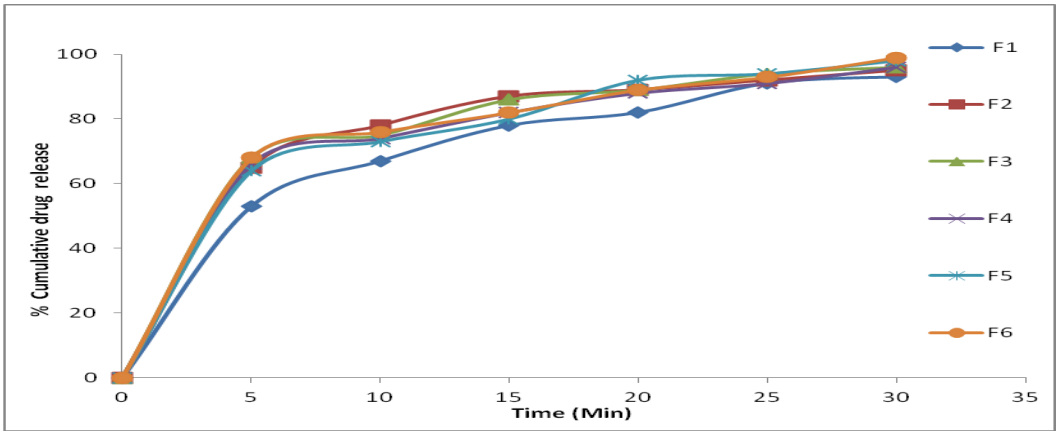

Fig 4: Comparison Graph of Immediate Release Formulations F1-F6

DISCUSSION:

In the present work efforts have been made to develop fast dissolving tablets Metoprolol succinate using direct compression technique involving Super Disintegrants like cross carmellose sodium, sodium starch glycolate.

IR spectrum of physical mixture of drug with polymers revealed that there was no appreciable change in position & intensity of peak with respect to IR spectrum of metoprlol succinate.. Hence, IR analysis revealed that there was no known chemical interaction between drug and polymers.

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All the prepared powdered blends were evaluated for Angle of repose, Bulk density, Tapped density, Compressibility index. The angle of repose for all the formulations F1-F6 was found to be 25^0-$28^0$and indicates good flow property of powder blends. The bulk density, true density, Carr's index for all the formulations F1-F6 was found to be 0.52-0.43 gm/cc and 16.66-14.28% and · Indicating all the values were within the limits as per IP.

The weight variation for all the formulations was found to be 182-179 mg and was satisfactory.

The thickness for all the formulations was found to be 1.5-1.4 mm and was satisfactory. The hardness for all the formulations was found to be 4.11-4.06 Kg/cm^2 and was satisfactory. The friability for all the formulations was found to be 0.49-0.32and was satisfactory. The drug content for all the formulations was found to be 98.8-99.0% and was satisfactory. The disintegration for all formulation was found to be 20-24 sec and was satisfactory.

In-vitro drug release at for all the formulations was found to be 95 to 99% and was satisfactory. The optimized formulation (F6) of drug release was found to be is 99% at 30 min.

CONCLUSION:

Metoprolol succinate tablets were formulated by using direct compression method using micro crystalline cellulose as diluents, crospovidone and sodium starch glycolate as super disintegrating agent with magnesium stearate,talc as lubricant.

Compatibility studies were carried out by means of physical mixture and the drug was found to be compatible with all the excipients used in different formulations.

The pre compression and post compression parameters are satisfactory and within the limit.

In-vitro drug release at for all the formulations was found to be 95 to 99% and was satisfactory. The optimized formulation (F6) of drug release was found to be is 99% at 30 min.

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