IJP (2024), Vol. 11, Issue 11 **(Research Article)**

Received on 12 October 2024; received in revised form, 22 November 2024; accepted, 26 November 2024; published 30 November 2024

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLET CONTAING METOPROLOL TARTRATE

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Keywords:

Fast dissolving, Super disintegrants, Direct compression, Pre-compression, Post-compression

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ABSTRACT: In the present work, fast dissolving tablets of metoprolol tartrate, were prepared using sodium starch glycolate, sodium croscarmellose and crospovidone as superdisintegrants, by the direct compression method. The tablets prepared were evaluated for various parameters including Bulk density, Tapped density, Angle of repose, Carr's index, Hauser's ratio, weight variation, hardness, friability, *in-vitro* dispersion time, drug content water absorption ratio, wetting time, *in-vitro* drug release. The tablet prepared by the direct compression method had a weight variation in the range of 198mg to 204mg which is below ±6.5%, Hardness of 3.7kg/cm^2 to 4.3kg/cm^2 , Percentage friability of 0.56% to 0.61%, *in-vitro* dispersion time of 18 sec to 24 sec, Wetting time of 33 sec to 51 sec and *in-vitro* drug release of 45.04% to 97.63% within 15 min. Fast dissolving tablets of metoprolol tartrate have enhanced dissolution and will lead to improved bioavailability and more effective therapy. The release rate of drugs from fast dissolving tablets intensifies with a rise in the concentration of super disintegrants and the metoprolol tartrate formulations reaches the peak levels.

INTRODUCTION: The usual practice for oral pharmaceutical dosage forms, such as conventional tablets and capsules, is to swallow them or chew them according to the instructions provided [1]. Fast-dissolving tablets dissolve or disintegrate in the mouth within a minute, resulting in significantly higher bioavailability compared to traditional tablet forms [2]. Despite significant advancements in drug delivery methods, the oral route continues to be preferred for administering therapeutic agents because it offers precise dosing, cost-effectiveness, ease of self-administration, and simplicity in use, all of which contribute to high patient adherence [3]. The main objective of drug delivery systems is to ensure the effective administration of medication, with nearly 90% of drugs being delivered via what is widely regarded as the safest, most convenient, and cost-effective method, thereby maximizing patient compliance [4].

It is especially beneficial for patients who face difficulties with swallowing, such as pediatric and geriatric populations, as well as for bedridden individuals and those prone to vomiting, diarrhea, sudden allergic reactions, or coughing [5]. Super disintegrants are essential for developing fast disintegrating tablets. Various techniques for manufacturing FDTs have been developed, including vacuum drying, direct compression, lyophilization, and molding.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.IJP.11(11).609-16

Article can be accessed online on: www.ijpjournal.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.IJP.11(11).609-16

Among these, direct compression is particularly notable for its cost-effectiveness and ease of producing tablets with the necessary mechanical strength [6]. A range of formulations has been developed to enhance the drug's palatability, thereby improving its effectiveness and suitability. Various technologies have been utilized to make the drug formulation more agreeable to taste. A range of formulations has been developed to enhance the drug's palatability, thereby improving its effectiveness and suitability [7]. Various technologies have been utilized to make the drug formulation more agreeable to taste. The development of solid dispersions relies on the disintegration rate, which can be enhanced by increasing the surface area to prevent precipitation within the carrier and improving wetting properties through direct interaction with a hydrophilic polymer carrier, resulting in the formation of a metastable crystalline structure [8].

MATERIALS AND METHODS:

Materials: The materials used for Metaprolol tartrate fast dissolving tablets are Crosscarmellose sodium; Sodium starch glycolateare collected in Aditya chemicals Ahmedabad. Crospovidone in Shreeji chemicals, Mumbai, Microcrystalline cellulose in LOBA Chemie, Starch, Povidone, Aspartame, Talc, Magnesium stearate and D-mannitol in S D fine chemicals. All the materials and instruments used in the work were sourced from various sources.

Method:

Preparation of Metaprolol Tartrate Fast Dissolving Tablet: Choosing and adjusting the concentrations of super disintegrants are crucial for developing fast-dissolving tablets. These tablets are formulated to dissolve or disintegrate in the mouth within 15-60 seconds without the need for water and should have an enjoyable taste. In this formulation, CCS and sodium starch glycolate were used as super disintegrants.

Procedure: Fast dissolving tablet were prepared using various ratios of superdisintegrants by direct compression method. The superdisintegrants like criscrormellose sodium, crospovidone and sodium starch glycolate were used in various concentration to formulate 200 mg of fast dissolving tablets of Metoprolol tartrate tablets.

- Drug, mannitol and micro crystalline cellulose were mixed thoroughly. Mannitol is used as diluent and MCC is used as binder.
- Then the superdisintegrants were incorporated individually into the powder mix.
- Add magnesium stearate and talc to powder mix which are used as lubricant and glidant respectively.
- Weigh individually and punched into tablets using rotary punch tableting machine.

TABLE 1: FORMULATION DETAILS FOR METAPROLOL TARTRATE IRTS

Ingredients (mg/tab)	FD1	FD2	FD3	FD4	FD5	FD6
Metaprolol tartrate	25	25	25	25	25	25
Croscarmellose sodium	4	8	-	-	-	-
Sodium starch glycolate	-	-	4	8	-	-
Crospovidone	-	-	-	-	4	8
Microcrystalline cellulose	50	50	50	50	50	50
Starch	15	15	15	15	15	15
Aspartame	4	4	4	4	4	4
Talc	2	2	2	2	2	2
Magnesium stearate	2	2	2	2	2	2
Povidone	8	8	8	8	8	8
D-mannitol	90	86	90	86	90	86

Evaluation of Fast Dissolving Tablet:

Pre Compression Parameters [9, 10]:

Angle of Repose: The angle of repose (θ) measures the friction forces in loose powder and indicates its flow properties. It is defined as the maximum angle between the surface of the powder pile and the horizontal plane.

$$\tan(\theta) = h / r$$

$$\theta = \tan^{-1}(h / r)$$

Where, ɵ is the angle of repose, h is the height in cm, r is the radius in cm.

TABLE 2: STANDARDS OF ANGLE OF REPOSE

S. no.	Angle of repose	Type of flow
1	<20	Excellent
2	20-30	Good
3	30-40	Passable
4	>34	Very poor

Bulk Density: Bulk density was determined by pouring the blend into a Graduated cylinder. The bulk volume (V) and weight of the powder (M) was determined. The bulk density was calculated by using the below mentioned formula,

Bulk density = mass of granules / volume of granules.

Tapped Density: The measuring cylinder with a known mass of blend was tapped for a specified duration. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the following formula,

Tapped density = weight of the blend / volume occupied in cylinder (Vt).

Carr's Compressibility Index: The easiest method to measure the free flow of powder is compressibility, which indicates how readily a material can flow. The compressibility index, known as Carr's index, is calculated using the following formula.

Carr's compressibility index = (Tapped density -Bulk density) / (Tapped density) × 100

Hausner's Ratio: Hausner's ratio serves as an indirect measure of powder flow ease and is calculated using the following formula.

Hausner's Ratio = ρ_t / ρ_o

Where ρ_t is tapped density and ρ_o is bulk density.

Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (> 1.25).

TABLE 3: STANDARDS OF CARR'S INDEX AND HAUSNER'S RATIO

Carr's index (100%)	Flow character	Hausner's ratio
≤10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
38	Very, very poor	≥1.60

Post-compression Parameters [11, 12, 13, 14, 15]: The tablets from each batch were evaluated for both in process and finished product quality control tests, including thickness, weight variation, hardness, friability, drug content, wetting time, disintegration time and *in-vitro* drug release studies.

Tablet Hardness and Thickness: This test was applied with a tablet hardness tester (Monsanto, tablet hardness tester) on 10 tablets for each formulation. It is usually expressed in Kg/cm^2. The thickness of the tablet calculated by using screw gauge which indicates the strength of with stand compression force applied.

Friability test: This test assesses the tablets' ability to endure abrasion during packing, handling, and transport. The initial weight of 20 tablets is recorded, and they are placed in a Roche friabilator rotating at 100 rpm for 4 minutes. Afterward, the tablets are removed, dedusted, and weighed again. The weight difference is noted and expressed as a percentage.

$$\% F = (1 - W/W^*) \times 10$$

Where, W* is the original weight of tablet, W is the final weight of tablet after test, Acceptance limit of friability is: 0.5 – 1%

Drug Content Uniformity: Twenty tablets were crushed and powder equivalent to weight of one tablet was dissolved in phosphate buffer 6.8. Then suitable dilutions were made and absorbance at 276 nm wavelength was taken by using a UV visible spectrophotometer.

Weight Variation: The formulated tablets were tested for weight uniformity. For this 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated. Each tablet's weight was compared to the average weight to determine if it fell within permissible limits.

% Weight variation = Average weight-Individual weight/average weight × 100

TABLE 4: STANDARD OF WEIGHT VARIATION (IP)

Average weight of Tablet	% Deviation
80mg or less	±10
More than 80mg but less than 250mg	±7.5
250mg or more	±5

Wetting Time and Water Absorption Ratio: A double-folded tissue paper was placed in a Petri dish, and 6 mL of water containing a water-soluble dye (eosin) was added. A pre-weighed tablet was carefully positioned on the tissue paper's surface. The time it took for the water to reach the upper surface of the tablet was recorded as the wetting time. After the tablet was wetted, it was weighed again, and the water absorption ratio (R) was calculated using the following equation:

$$R = 100 (Wb - Wa) / Wb$$

Where Wa and Wb are the weights of tablet before (dry weight) and after water absorption (wet weight) respectively.

***In-vitro* Disintegration Test:** The disintegration time for the batches of tablets was determined using the BP tablet disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus. Phosphate buffer of pH 6.8, used as the disintegration medium was maintained at 37 ± 0.5ºC and the time taken for the entire tablet to disintegrate completely was measured in seconds.

***In-vitro* Dissolution Studies:** *In-vitro* dissolution rate study was done by using USP Type II apparatus which was rotated at 50 rpm. Phosphate buffer pH 6.8 (900 ml) was taken as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5°C.

Aliquots of dissolution medium were withdrawn at specific time interval and it was filtered. Absorbance of filtered solution was determined by Spectrophotometer (Systronicsuv Double beam spectrophotometer-2101) at 275.4 nm and drug concentration was determined from standard calibration curve.

RESULT AND DISCUSSION:

Melting Point Determination:

TABLE 5: MELTING POINT METOPROLOL TARTRATE

Reported	Method	Observed
121-124℃	Thiel's tube	122°C
	DSC	122°C

Solubility: It is very soluble in water and freely soluble in chloroform, methylene chloride and alcohol. It is slightly soluble in acetone and insoluble in ether.

TABLE 6: DATA FOR STANDARD CALIBRATION CURVE OF METOPROLOL TARTRATE

Sl. no.	Conc. in µg/ml	Absorbance at nm			Mean absorbance	Standard Deviation (SD)
		Trial-1	Trial-2	Trial-3		
1	0	0	0	0	0	0
2	6	0.18	0.176	0.168	0.174	0.004
3	12	0.338	0.343	0.343	0.347	0.01
4	18	0.556	0.545	0.55	0.548	0.006
5	24	0.714	0.769	0.72	0.734	0.024
6	30	0.891	0.906	0.893	0.896	0.006

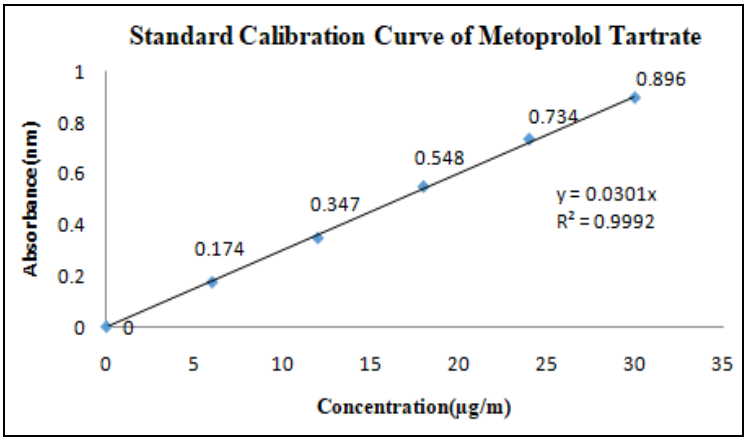

FIG. 1: STANDARD CALIBRATION CURVE OF METOPROLOL TARTRATE

Pre-compression Parameters:

TABLE 7: MICROMERITICS CHARACTERS OF FAST DISSOLVING TABLETS

Code	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Hauser's ratio	Carr's index (%)	Angle of repose (^{0})
F1	0.53	0.64	1.19	16	28.22
F2	0.51	0.63	1.20	17	29.06
F3	0.53	0.65	1.21	17	30.08
F4	0.52	0.62	1.20	18	28.52
F5	0.54	0.65	1.25	15	28.38
F6	0.55	0.64	1.23	17	29.54

Preformulation studies such as angle of repose, bulk density, tapped density, carr's index and Hauser ratio were performed and the results showed that all the parameters are within the acceptable limits.

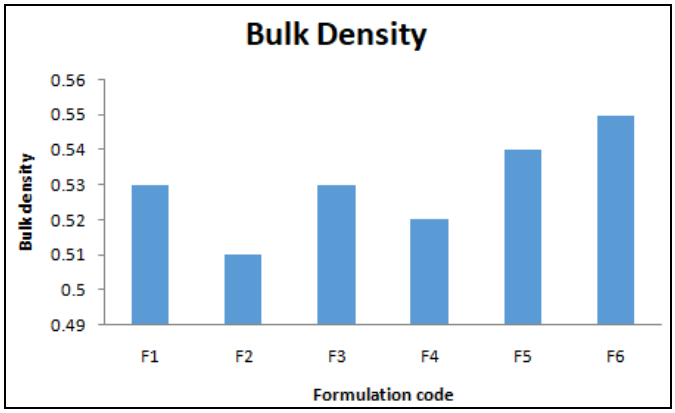

FIG. 2: BULK DENSITY OF FORMULATIONS CONTROL-F6

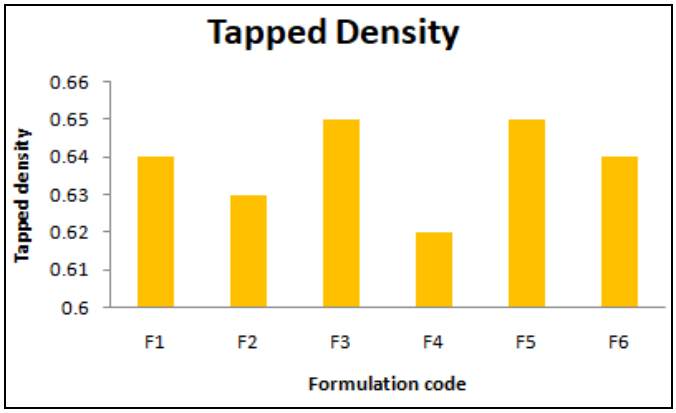

FIG. 3: TAPPED DENSITY OF FORMULATIONS CONTROL-F6

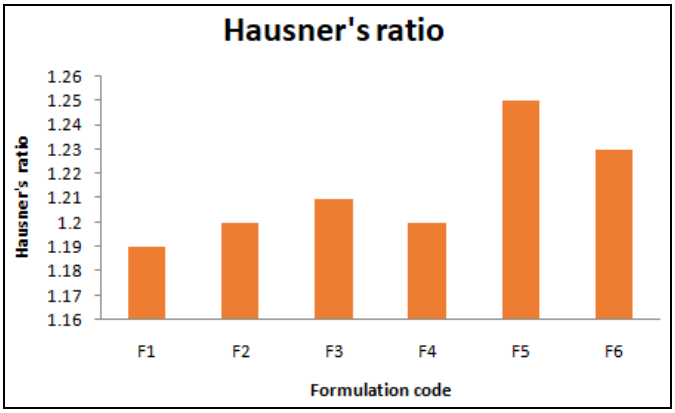

FIG. 4: HAUSNER'S RATIO OF FORMULATIONS CONTROL-F6

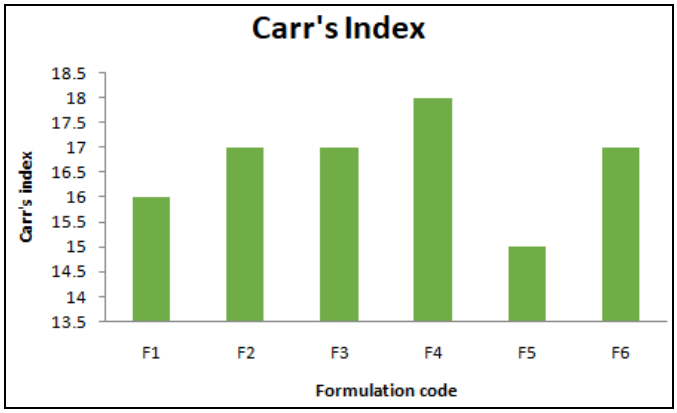

FIG. 5: CARR'S INDEX OF FORMULATIONS CONTROL-F6

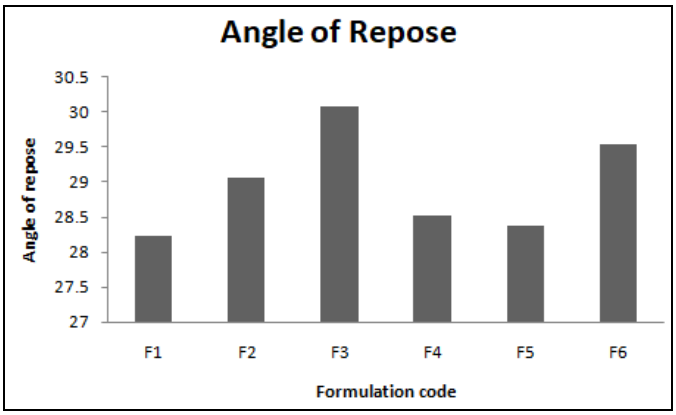

FIG. 6: ANGLE OF REPOSE OF FORMULATIONS CONTROL-F6

Post Compression Parameter of Fast Disintegrating Tablets:

TABLE 8: RESULTS OF HARDNESS, THICKNESS, FRIABILITY, AND WEIGHT VARIATION FORMULATIONS F1 – F6

Formulation batches	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation
F1	4.2	3.8	0.56	203
F2	4.4	3.7	0.61	199
F3	4.6	4.2	0.59	204
F4	4.7	4.3	0.60	202
F5	4.4	4.1	0.56	198
F6	4.3	4.3	0.59	201

Post formulation studies such as Thickness, hardness, friability and weight variation were performed and. To be good appearance without showing any chipping, capping and sticking defects and all other parameters were passed the test. The results showed that all the parameters are within the acceptable limits.

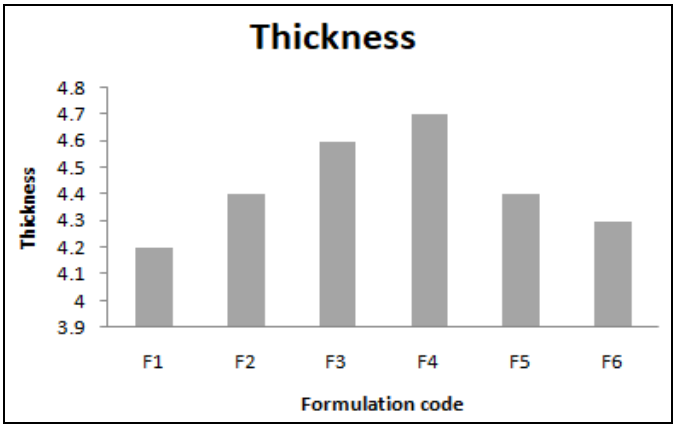

FIG. 7: THICKNESS OF FORMULATIONS CONTROL-F6

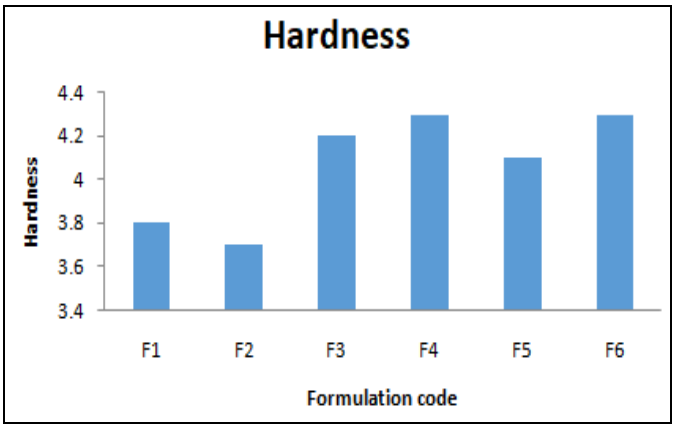

FIG. 8: HARDNESS OF FORMULATIONS CONTROL-F6

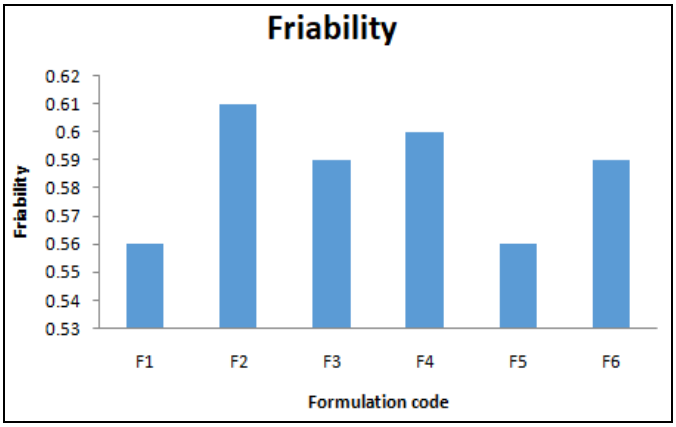

FIG. 9: FRIABILITY OF FORMULATIONS CONTROL-F6

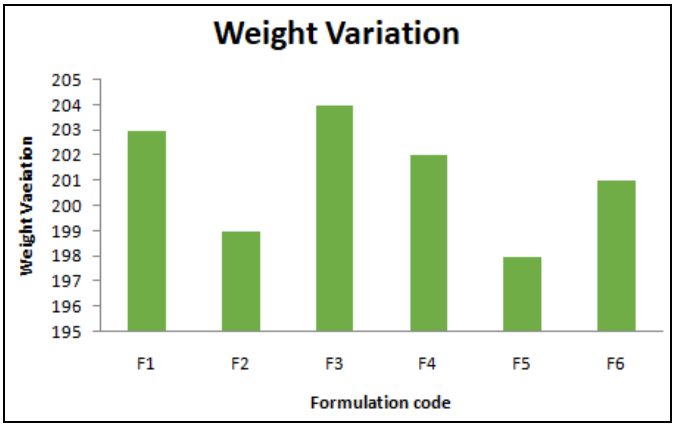

FIG. 10: WEIGHT VARIATION OF FORMULATIONS CONTROL-F6

TABLE 9: RESULTS OF WETTING TIME AND DISINTEGRATION TIME OF F1 – F6

Formulations	Disintegration time (sec)	Wetting Time (sec)
F1	18	41
F2	21	39
F3	16	51
F4	18	48
F5	22	33
F6	24	35

Tablets were prepared by direct compression method and evaluated for wetting time, disintegration time. All the formulations were showed that all the parameters are within the acceptable limits.

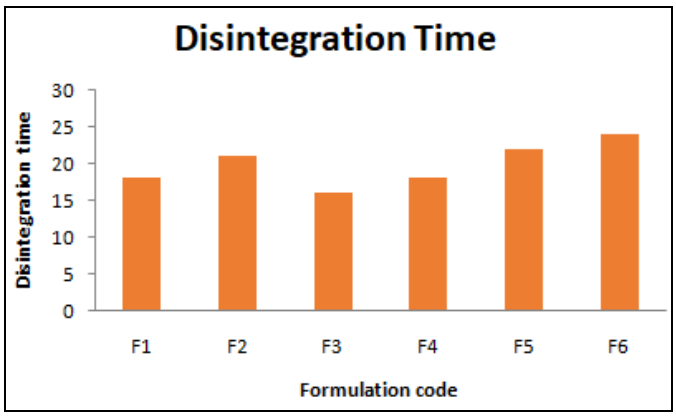

FIG. 11: DISINTEGRATION TIME OF FORMULATIONS CONTROL-F6

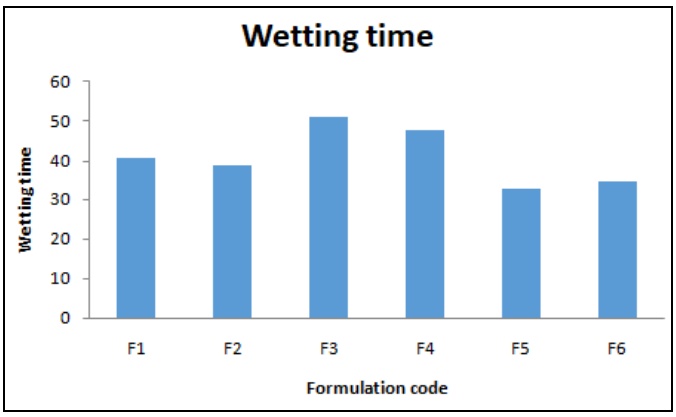

FIG. 12: WETTING TIME OF FORMULATIONS CONTROL-F6

TABLE 10: *IN-VITRO* DRUG RELEASE STUDY OF FORMULATIONS F1 – F6 IN PHOSPHATE BUFFER PH 7.4

	Percentage of drug release					
Time (min)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
3	51.03	49.56	45.04	47.01	52.43	53.72
6	65.26	63.00	58.06	59.87	66.03	66.94
9	75.66	75.98	69.05	70.12	76.25	77.09
12	86.53	88.60	78.47	77.86	91.28	93.06
15	94.46	95.35	84.38	83.76	96.79	97.63

When comparing all the formulation, F6 shows a better drug release of 97.63% at the end of 15 min.

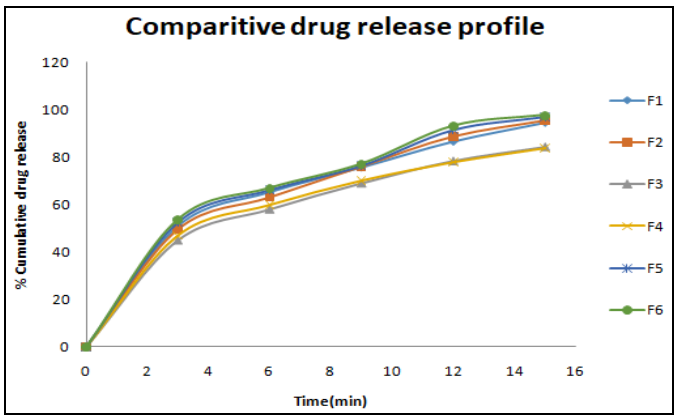

FIG. 13: COMPARITIVE DRUG RELEASE OF FORMULATIONS CONTROL-F6

CONCLUSION: In the present study fast dissolving tablets of metoprolol tartrate were prepared by direct compression methods using superdisintegrants such as sodium starch glycolate, croscarmellose sodium and crospovidone.

All the tablets of metoprolol tartrate were subjected to tests for weight variation, hardness, friability, *in-vitro* dispersion, drug polymer interaction, drug content uniformity, water absorption ratio, wetting time, and *in-vitro* drug release.

Based on the above studies, the following conclusions can be drawn:

- Tablets prepared by direct compression methods were found to be good and free from chipping and capping.
- The low values of the standard deviation of average weight of the prepared tablets indicated weight uniformity within the batches prepared.
- The hardness of the prepared tablet was found to be 3.5kg/cm^2 to 4.3kg/cm^2. The friability values of the prepared tablet was found to be less than 1%.
- IR spectroscopic and DSC studies indicated that the drug is compatible with all the excipient.
- The *in-vitro* dispersion time of metoprolol tartrate prepared by direct compression method was found to be in the range of 18 sec to 24 sec fullfilling the official requirements.
- Based on the *in-vitro* disintegration time cover formulation F6 was found to be promising and

showed a dispersion time of 22 sec. And wetting time of 33 sec, Facilitating faster dispersion in the mouth.

- The drug release from the optimized batch (F6) was about 97.63% at 15 min.

ACKNOWLEDGEMENT: Nil

CONFLICT OF INTEREST: Nil

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How to cite this article:
Raj PG, Ranjeetha AR, Bhavya G, Vardhana MGH and Gowda HUJ: Formulation and evaluation of fast dissolving tablet containg metoprolol tartrate. Int J Pharmacognosy 2024; 11(11): 609-16. doi link: http://dx.doi.org/10.13040/IJPSR.0975-8232.IJP.11(11).609-16.