FORMULATION DEVELOPMENT AND IN - VITRO EVALUATION OF MOUTH DISSOLVING TABLETS OF PROPONOLOL TABLETS

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Abstract : ***The objective of the study was to formulate and evaluate Mouth Dissolving Tablets Of Proponolol.Direct compression method was used to formulate orally disintegrating tablet of Proponolol by employing different super disintegrants, polymers, and magnesium stearate (lubricant), Talc. These prepared formulations were then evaluated. Dissolution and drug content tests were performed using USP apparatus II and ultraviolet spectrophotometry, respectively. All formulations showed compliance with pharmacopeia standards. The effect of super disintegrants concentration and direct compression method on drug release profile was studied. Release profile of F4 were found to be satisfactory comparing to other formulations. F4 Formulation as processed excipient was found to be the best super disintegrants for the preparation of Proponolol orally disintegrating tablets formulations. Due to it has exhibited faster disintegration time and best dissolution profile when compared to other formulations.***
Keywords: Proponolol, super disintegrants, polymers, direct compression technique, in-vitro drug release studies.

I.INTRODUCTION

Solid dosage forms also present significant administration challenges in other patient groups, such as children, mentally challenged, bed ridden and uncooperative patients[1]. Pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control[2]. Moreover, patients traveling with little or no access to water, limit utility of orally administered conventional tablets or capsules. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as orally disintegrating tablets (FDTS)[3].

These dosage forms are preferable alternative for oral medication in improving Sthe quality of life and patient acceptability. FDTS are also known as oro dispersible tablets, mouth dissolving tablets, rapimelts, melt-in-mouth tablets, fast disintegrating tablets and rapid dissolving tablets. FDTS are the solid unit dosage forms/entities containing medicinal substances which disintegrate[4] or dissolve rapidly in oral cavity usually within a few seconds even without the need of water or chewing. FDTS also combine the advantages of both liquid and conventional tablet formulations allowing the ease of swallowing in the form of liquid[6]. The advantages of these dosage forms are continuously and increasingly being identified in both pharmaceutical industries as well as in academia. The objective of present work is to highlight the development of FDTS, their significance, ideal characteristics, various techniques and aspects related to design and formulation, marketed preparations and future prospectives[7].Solid oral dosage forms are most convenient from patient as well as from manufacturing chemist's perspective[8]. Fast dissolving tablets are required to disintegrate within 3 mins in water at 15-25°C.The aim of this study is development and characterization of proponolol hcl fast dissolving tablets. Propranolol is a competitive antagonist of beta-1-adrenergic receptors in the heart. It competes with sympathomimetic neurotransmitters for binding to receptors, which inhibits sympathetic stimulation of the heart.The objective of present study is to design and develop a stable solid oral dosage form of proponolol hcl fast dissolving tablets to deliver with optimum concentration of drug at desired site at specific time comparable to the innovator product with better stability, high production feasibility, and excellent patient compatibility[9].

II. MATERIALS AND METHOD

2.1 MATERIALS

Proponolol was collected as a gift sample from Hetero labs,Hyd , polymers and other excipients were purchased from Vijaya Chemicals, Hyd.

2.2 METHODODOLOGY

Drug excipient compatability[10]

Compatibility studies of proponolol hcl and the disintegrants were carried out by using Fourier Transform Infrared Spectroscopy (FTIR). Fourier transform infrared spectra of the samples were obtained in the range of 4000 to 450 cm-1 using a FTIR by the KBr disc method

Formulation table:

Table-1: Formulation table

S.No	Ingredient	F1	F2	F3	F4
1	proponolol hcl	60	60	60	60
2	Crosspovidone	5	10	-	-
3	Sodium starch glycolate	-	-	5	10
4	Lactose Monohydrate	30	25	30	25
6	Magnesium stearate	2	2	2	2
7	Talc	3	3	3	3
8	Total wt	100	100	100	100

Procedure

Direct compression technique

Fast dissolving tablets of proponolol hcl were prepared by direct compression. All the ingredients were passed through 40- mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 100mg using 6mm round flat punches on 10- station rotary tablet machine (Rimek).

EVALUATION STUDIES

Evaluation parameters

Determination of bulk density and tapped density

a) Bulk Density[11]

Bulk density is defined as the mass of powder divided by bulk volume.

It is calculated using the following equation:

Bulk density = weight of sample taken /volume noted

b) Tap density[11]

An accurately weighed quantity of the powder (W) was carefully poured into the graduated cylinder and the volume (vo) was measured.

Tapped density = weight of sample taken / tapped volume

Where,

Vo = initial volume

Vf = final volume.

Compressibility index[12]

Based on the apparent bulk density and the tapped density, the percentage Compressibility of the bulk drug was determined by the following formula.

Carr's index = Tapped density - Bulk density / Tapped density X 100

Hausner's ratio[12]

It indicates the flow properties of the powder. The ratio of tapped density to the bulk density of the powder is called Hausner ratio.

Hausner's ratio = Tapped density / Bulk density

Angle of repose[13]**:**

The flow characteristics are measured by angle of repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

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

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

Where

h = height of pile

r = radius of the base of the pile

θ = angle of repose

Evaluation of tablet[14,15,16]

Weight variation

Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more then two of the individual tablet weight deviate from the average weight by more than the percentage.

Thickness

Twenty tablets were randomly selected form each batch and there thickness was measured by using vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Pfizer hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets were determined.

Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed. Compressed tablets should not loose more than 1% of their weight.

The percentage friability was measured using the formula,

$$\% F = \{1-(Wo/W)\} \times 100$$

Where,

% F = friability in percentage

Wo = Initial weight of tablet

W = weight of tablets after revolution

Content Uniformity

Powder equivalent of proponolol hcl was dissolved in phosphate buffer pH 6.8. Sufficient dilutions were made to obtain 10 mcg/ml solution. Absorbance of the resulting solution was measured using a T60 model UV/VIS spectrophotometer. From the absorbance values, amount of drug present in the given tablet was calculated. Procedure was repeated by using four more tablets from the same formulation and the average value of all five tablets was calculated.

In- Vitro Release study

The release rate of proponolol hcl from fast dispersible tablets was determined using dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.5oC and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at different time interval (minutes). The samples were filtered through a 0.45m membrane filter. Absorbance of these solutions was measured using a instrument T60 model UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The prepared disintegration tablets of proponolol hcl were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2oc and refrigerator 2-8oc for a period of 90 days.

III.RESULTS

FT-IR Spectrum of Proponolol hcl

All the formulations were uniform in drug content and the FTIR spectra of proponolol hcl and its fast disintegrating tablets are identical. The principle FTIR absorption peaks of proponolol hcl fast disintegrating tablets were observed and found to be identical with the spectra of proponolol hcl pure drug. Thus from the spectra it was understood that there was no interaction between proponolol hcl and the disintegrants used in the preparation of tablets.

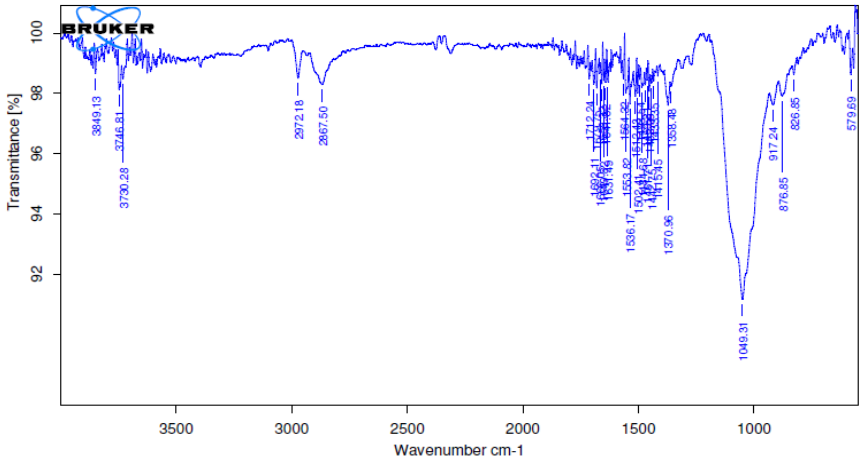

Fig-:1 FTIR Studies of Proponolol hcl

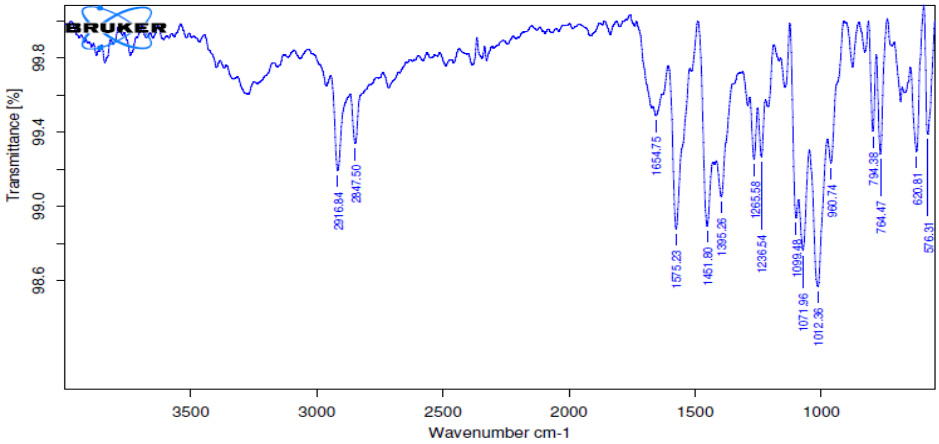

Fig-: 2 FTIR Studies of physical mixture of drug

Evaluation studies

Pre compression parameters

Average Weight variation of tablets was found in range 391.57- 397.36 mg. Hardness of the tablets was found in the range 3.0- 3.3 Kg/cm^2.

a) Bulk Density: The Bulk density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The bulk density was found in the range 0.215-0.253gr/ml.

b) Tapped density: The Tapped density of various powder mixed blends prepared with different super disintegrants, was measured by graduated cylinder. The Tapped density was found in the range 0.308-0.342 gr/ml.

c) Angle of repose: The angle of repose for the formulated blend was carried out. It concludes that all the formulations blend was found to be in the range of 26 to31^0

c) Compressibility index: The Compressibility index of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, compressibility index was calculated. It was found in the range 26.02-31.56%.

d) Hausner's ratio: The Hausner's ratio of various powder mixed blends, prepared with different super disintegrants, using bulk density and tapped density data, Hausner's ratio was calculated. It was found in the range 1.35- 1.46.

The flow properties of powder blend in all formulations exhibit good flow and passable characteristics.

Characterization of Formulation

Table-: 2 Pre compression parameters of Proponolol hcl Mouth dissolving tablets

S. no	**Bulk density**	**Tapped density**	**Compressibilty index**	**Hausner ratio**	Angle of repose(0)
F1	0.253	0.342	26.02	1.35	27^0c
F2	0.242	0.332	27.10	1.37	25^0c
F3	0.219	0.320	31.56	1.46	28^0c
F4	0.231	0.326	29.14	1.41	30^0c

Post compression parameters

Weight variation:

All the formulated (F1 to F4) tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values.

Thickness:

Tablets mean thickness were uniform in F1 to F4 formulations and were found to be in the range of 2.0 mm to 2.6 mm.

Hardness:

The measured hardness of tablets of each batch ranged between 4.19to 4.50 kg/cm^2. This ensures good handling characteristics of all formulations.

Friability:

Tablets were evaluated by using Roche friabilator and friability of tablets was observed in the range 0.31-0.88%

Content Uniformity:

The proponolol hcl tablets were tested for drug content by UV method, the percentage drug content was found to be in between 98 to 101.37%

Disintegration Time:

Tablets were evaluated for disintegration time in the disintegration apparatus. The disintegration time was found in the range 12- 56 sec.

Wetting Time:

Tablets were evaluated for wetting time test. The wetting time was found in the range 54 – 59 sec.

Table-: 3 Evaluation parameters of Proponolol hcl mouth dissolving tablets

F. No.	**Weight variation (mg)***	**Thickness (mm)***	**Hardness (kg/cm^2)***	**Friability (%)**	**Drug content (%)**	**Disintegration time(sec)**	**Wetting time (sec)**
F1	99	1.9	3.92	0.49	93.96	25	152
F2	100	2.4	3.58	0.45	92.35	31	160
F3	98	2.6	3.21	0.38	95.33	20	155
F4	100	2.4	3.55	0.35	98.25	19	163

Dissolution studies

All the four formulation of Proponolol hcl mouth dissolving tablets were subjected to in vitro release studies these studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period of time.

Table-: 4 Drug release studies of all formulations

Time	F1	F2	F3	F4
0	0	0	0	0
5	23.72	26.36	25.18	28.98
10	35.42	37.89	37.82	35.16
15	53.56	54.59	52.95	50.92
20	70.42	69.86	71.53	75.88
25	81.93	82.63	83.91	85.52
30	93.52	94.28	95.86	97.69

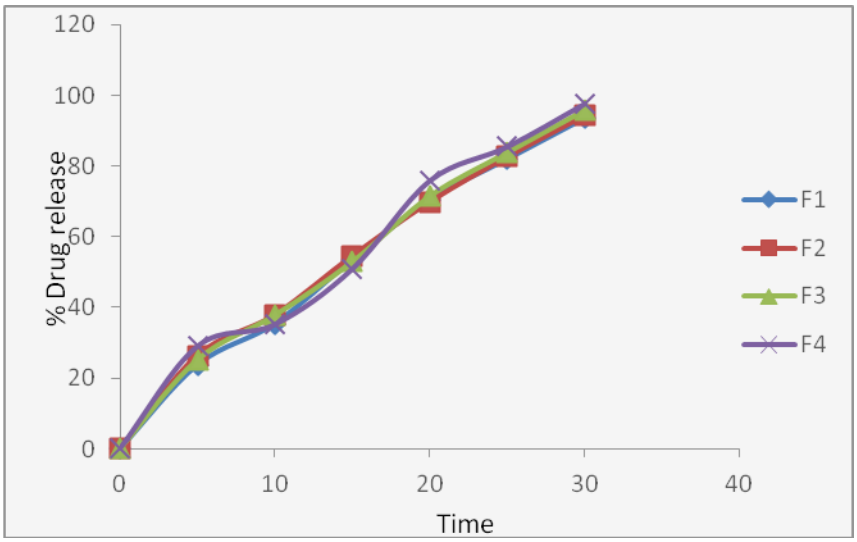

Table-:3 Dissolution Profile of F1 to F4 formulations

Stability Study

There was no significant change in physical and chemical properties of the tablets of formulation F-4 after 3 months. Parameters quantified at various time intervals were shown.

Table-:5 Stability studies of all formulations

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-4	**25^0C/60%RH % Release**	97.69	96.98	95.99	94.15	**Not less than 85 %**
F-4	**30^0C/75% RH % Release**	97.69	96.85	95.84	93.98	**Not less than 85 %**
F-4	**40^0C/75% RH % Release**	97.69	96.78	94.98	93.56	**Not less than 85 %**

IV.CONCLUSION

The aim of the present study was to develop an optimized formula for Mouth dissolving tablet containing Proponolol hcl. After pre-formulation studies it was decided to prepare fast dissolving tablets prepared by direct compression method. In the formulation of sodium starch glycolate and crosspovidone were used as super

disintegrants. Prior to compression the granules were evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. The compressed tablets were also evaluated for weight variation, hardness, friability, drug content, disintegration time and in vitro drug release. Mouth dissolving tablet is a promising approach with a view of obtaining rapid action of the drug and would be advantageous in comparison to currently available conventional dosage forms. The selection of an ideal batch of Mouth dissolving tablets was made after consideration of the evaluation parameters by dissolution study, disintegration time and wetting time. From the data obtained, it is observed from the formulation containing sodium starch glycolate in Formulation F4, shows Disintegration time in 19 seconds and the Percentage drug release is of 97.69 % at the end of 30 min which satisfied all the tablet evaluation parameters for Mouth dissolving tablet Hence looking at all the satisfactory parameters F4 formulation is selected as the optimized formulation.

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