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Formulation and *In Vitro* Evaluation of Oral Disintegrating Tablets of Benralizumab

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ABSTRACT

In the present work, Oral disintegrating tablets of Benralizumab were prepared by direct compression method using superdisintegrants such as Crosspovidone lycoat, and Tulsion. Benralizumab has very long half-life and less bioavailability, so for enhancing the bioavailability of the drug it was formulated as oral disintegrating tablet. The dispersion time of tablets were reduced withincrease in the concentration of superdisintegrants like Crosspovidone, lycoat, and Tulsion . From the results obtained, it was concluded that Tulsion was found to be the best among the superdisintegrants, the highest drug release of F9 is 99.49% of the drug in 30 min.

Keywords: Benralizumab, Crosspovidone, lycoat, and Tulsion, Oral disintegrating tablets.

1. INTRODUCTION

Historically, the oral route of drug administration has been used most preferably for both conventional as well as for novel drug delivery because of the ease of administration and widespread acceptance by patients[1]. The term “direct compression” is employed to describe the procedure by which tablets are manufactured directly from the powder blends of active pharmaceutical ingredient/s and appropriate excipients[2]. Orally disintegrating tablets (ODTs) offer several advantages over the conventional oral dosage forms particularly in terms of patient compliance i.e. convenience and ease of use[3]. One negative aspect of solid oral dosage forms is dysphagia (difficulty in swallowing) and chewing in some patients particularly in geriatric and paediatric patients[4]. Orally disintegrating tablets (ODT) are well established dosage forms that disintegrate in the oral cavity leaving an easy-to-swallow residue. ODT’s disintegrate rapidly in saliva without the need of water, within few seconds to minute[5].

Benralizumab is a humanized recombinant monoclonal antibody of the isotype IgG1k immunoglobulin that specifically binds to the alpha chain of the interleukin 5 receptor (IL-5R) expressed on eosinophils and basophils. Subcutaneous administration of Benralizumab presented a dose-proportional pharmacokinetic profile. The administration of 20-200 mg presented an absorption half-life of 3.6 days with a bioavailability of 58%. So to improve its oral bioavailability and absorption Benralizumab was formulated as Oral disintegrating tablets using different super disintegrants.

2. MATERIALS AND METHODS

Benralizumab, Tulsion, Cross Povidone, Lycoat, Microcrystalline cellulose (Avicel), Talc, and Magnesium stearate were procured from the B.M.R. Chemicals, Hyderabad and SD Fine chemicals.

Formulation of Oral Disintegrating Tablets of Benralizumab

Oral disintegrating tablets of Benralizumab were prepared by direct compression according to the formulae given in the table 1. All the ingredients were passed through # 60 mesh sieve separately. The drug and micro crystalline cellulose (MCC) were mixed by adding small portion of each at a time and blending it to get a uniform mixture and kept aside. Then the other ingredients were mixed in geometrical order and

passed through coarse sieve (#44 mesh) and the tablets were compressed using hydraulic press. Compression force of the machine was adjusted to obtain the hardness in the range of 3-4 kg/cm2 for all batches. The weight of the tablets was kept constant for all formulations F1 to F9 (150 mg).

Preformulation Studies:[6-9]

a) Bulk Density
b) Tapped Density
c) Carr's compressibility Index
d) Hausner's ratio

Evaluation Studies of ODT'S of Benralizumab:[9-16]

a) Tablet Dimensions:

Thickness and diameter were measured using a calibrated vernier caliper. Three tablets of each formulation were picked randomly and thickness was measured individually.

b) Hardness:

The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2.

c) Friability test:

The friability of tablets was determined by using electrolab friabilator. It is expressed in percentage (%). The tablets were weighed again (WF).
The % friability was then calculated by –
%F = 100 (1-WI/WF)

% Friability of tablets less than 1% was considered acceptable.

d) Average weight of the Tablets:

Six tablets were selected randomly from each batch and weighed individually to check for average weight variation.

e) Test for Content Uniformity:

Tablet containing 30mg of drug was dissolved in 50ml of 6.8 pH buffer in volumetric flask. The drug was allowed to dissolve in the solvent. The solution was filtered, 2ml of filtrate was taken in 10ml of volumetric flask and diluted up to mark with distilled water and analyzed spectrophotometrically at 251nm. The concentration of Benralizumab was obtained by using standard calibration curve of the drug. Drug content studies were carried out in triplicate for each formulation batch.

f) In vitro Dispersion Time:

Tablet was added to 10ml of distilled water at 37±0.50C. Time required for complete dispersion of a tablet was measured.

g) In vitro Dissolution Study:

In vitro dissolution of Benralizumab Oral disintegrating tablets was studied in USP XXIV dissolution test apparatus. 900ml Phosphate buffer 6.8(simulated fluid) was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. One tablet was used in each test. Samples of dissolution medium (5ml) and analyzed for drug release by measuring the absorbance at 251nm

g) Data Analysis (Curve fitting analysis):

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:

1) Cumulative percentage drug released Vs time (*In-Vitro* drug release plots)
2) Log cumulative percentage drug remaining Vs Time (First order plots)

3. RESULTS AND DISCUSSION

The prepared oral disintegrating tablets were evaluated and the flow properties of Excipients and drug were good, FT-IR studies revealed that there is no chemical interaction between Benralizumab and the excipients used in the study.The tablets prepared were found to be good without any chipping, capping and sticking.Formulated tablets gives satisfactory result for various physico-chemical evaluation of tablets like tablet dimension, hardness, friability, weight variation, *in vitro* dispersion time, and drug content. The low values of standard deviation for average weight and drug content of the prepared tablets indicate weight and drug content uniformity within the batches prepared.

From the *in vitro* dissolution data, it was found that the drug release study from formulations containing Cross povidone as super disintegrant (F1-F3) was 61.24, 86.83, 88.32% drug release respectively at the end of 30mins. Formulations containing lycoat as super disintegrant (F4-F6) showed 92.3, 90.93, 97.52% of drug release respectively at the end of 30 mins. Formulations containing Tulsion as super disintegrant (F7-F9) showed 94.62, 96.26, 99.49% of drug release respectively at the end of 30mins.

Table 1: Formulation table of oral disintegrating tablets of Benralizumab:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Benralizumab	30	30	30	30	30	30	30	30	30
Cross povidone	7.5	-	-	10	-	-	12.5	-	-
lycoat	-	7.5	-	-	10	-	-	12.5	-
Tulsion	-	-	7.5	-	-	10	-	-	12.5
M.C.C	50	50	50	50	50	50	50	50	50
Lactose	50.5	50.5	50.5	48	48	48	45.5	45.5	45.5
Magnesium stearate	6	6	6	6	6	6	6	6	6
Talc	6	6	6	6	6	6	6	6	6
Total weight	150	150	150	150	150	150	150	150	150

Table 2: Pre-Compression Parameters of all Formulations

FC	Bulk density* (g/cc)	Tapped density* (g/cc)	Angle of repose* (θ)	Hausner's ratio	Compressibility Index (%)
F1	0.516	0.611	28.33′	1.18	15.54
F2	0.533	0.622	26.70′	1.16	14.30
F3	0.471	0.544	25.14′	1.15	13.41
F4	0.468	0.543	27.01′	1.16	13.81
F5	0.516	0.611	28.33′	1.18	15.54
F6	0.521	0.592	28.65′	1.13	11.9
F7	0.516	0.611	28.33′	1.18	15.54
F8	0.533	0.622	26.70′	1.16	14.30
F9	0.471	0.544	25.14′	1.15	13.41

Table 3: physical properties of tablets of all formulations

FC	Diameter* (mm)	Thickness* (mm)	Average Weight* (mg)	Hardness* (kg/cm2)	Friability (%)	*Invitro* dispersion time(secs)	Drug content (%)
F1	8.02±0.049	3.79±0.007	150.2±1.47	3.22±0.5	0.395	56±1.2	87.95±0.54
F2	8.01±0.043	3.81±0.059	146.8±1.13	3.10±0.1	0.393	50±0.57	90.55±0.65
F3	8.04±0.043	3.80±0.006	147.8±1.83	3.41±0.1	0.332	38±1.15	93.4±0.247
F4	8.01±0.036	3.80±0.011	150.1±1.49	3.18±0.3	0.333	27±1.732	96.7±0.344
F5	8.01±0.043	3.77±0.010	149.8±1.22	3.31±0.5	0.263	51±0.57	82.9±0.493
F6	8.00±0.024	3.79±0.008	149.7±1.25	3.23±0.3	0.632	46±0.52	89.52±0.16
F7	8.01±0.041	3.79±0.007	150.4±2.16	3.44±0.2	0.197	23±1.02	93.6±0.42
F8	8.00±0.033	3.80±0.009	149.5±3.47	3.35±0.1	0.263	19±0.57	98.34±0.5
F9	8.01±0.048	3.79±0.004	149.8±1.47	3.51±0.2	0.291	18±0.57	99.89±0.16

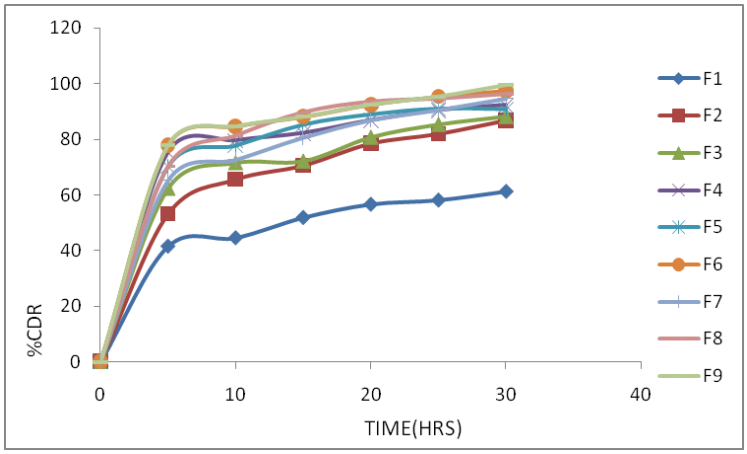

Fig.1: *In vitro* dissolution graphs of Benralizumab oral disintegrating tablets

4. CONCLUSION

From the present study, it was concluded that the Oral disintegrating tablets of Benralizumab prepared by direct compression method using superdisintegrants like Crosspovidone, lycoat, and Tulsion. Totally nine formulations were prepared among them F9 formulation containing Tulsion was found to be the best among the superdisintegrants, the highest drug release of F9 is 99.52% of the drug in 30 min.

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