MOUTH DISSOLVING TABLETS OF ZAFIRLUKAST BY EFFERVESCENT FORMULATION APPROACH

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ABSTRACT

In the present work, fast dissolving tablets of Zafirlukast were prepared by Effervescent method with a view to enhance the patient compliance. 10% Polacrilin Potassium (Kyron T314) is used as a superdisintegrant. Along with the superdisintegrant, sodium bicarbonate with anhydrous citric acid, tartaric acid and malic acid were used as effervescent agents in different ratios. The prepared batch of tablets were evaluated for hardness, friability, drug content uniformity and invitro dispersion time. All the formulations were tested for invitro drug release pattern in 0.5% Sodium lauryl sulfate. Among all the formulations Z-9 containing 10% Polacrilin Potassium and mixture of sodium bicarbonate and 20% malic acid emerged as the best($t_{50\%}$ 3min) based on the in-vitro drug release characteristics.

KEY WORDS: Zafirlukast, Fast dissolving tablets, Polacrilin Potassium, Citric acid, Malic acid, Tartaric acid, Effervescent method.

1.INTRODUCTION

Zafirlukast is chemically cyclopentyl N-[3-[[2-methoxy-4-[(2-methylphenyl)sulfonyl carbamoyl]phenyl]methyl]-1-methylindol-5-yl]carbamate. It is an oral leukotriene receptor antagonist widely used for the treatment of asthma (Dunn,2001). Zafirlukast blocks the action of the cysteinyl leukotrienes on the CysLT1 receptors, thus reducing construction of the airways, build-up of mucus in the lungs and inflammation of the breathing passages (Balzano,2002). Zafirlukast is a poorly water soluble drug and hence it is dissolution rate limited and thus delays the onset of action.

Tablet is most popular among all dosage forms existing today because of convenience of self administration, compactness and easy manufacturing. However many patients, especially elderly find it difficulty in swallowing tablets, capsules, fluids and thus do not comply with prescription which results in high incidence of non-compliance and ineffective therapy (Seager,1998; Habib,2000; Chang,2000). Patient convenience and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Rapidly disintegrating / dissolving tablet is one of such example. Fast disintegrating tablets are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a minute without the need of water or chewing (Sunada,1999; Reddy,2002; Kaushik,2004).

The main purpose of the present investigation is to increase the solubility of Zafirlukast by the preparation of complex with â-cd using kneading method, preparation and optimization of fast disintegrating tablets by incorporating different Effervescent agents at different concentration levels along with 10% Polacrilin Potassium as a superdisintegrant to enhance the safety and efficacy of the drug molecule, achieve better compliance, enhance the onset of action and provide stable dosage form.

2.MATERIALS AND METHODS

Zafirlukast sample was obtained from Dr. Reddy's Laboratories, Hyderabad, â-cyclodextrin was obtained from Roquette, France and Polacrilin Potassium was obtained from Corel pharma-chem, Ahmedabad. All other excipients used are of pharmaceutical grade.

Preparation of complex by kneading method:

Drug and â-cyclodextrin in 1:1 ratio were taken and triturated in a mortar with a small volume of methanol : water (3:2) solvent blend. The thick slurry was kneaded for 45 mins, and then the mass was further dried in a desiccator for 2 days. The dried product was crushed, pulverized and sieved through 100 mesh. The solid dispersions thus obtained were stored in a well closed container and kept in a desiccator.

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The prepared complex was tested for its drug content and it was found that the drug was within the compendial limits 95-101% w/w.

Preparation of tablets:

Effervescent method was used for the preparation of fast dissolving tablets .All the ingredients were accurately weighed and sifted through #44 mesh separately, sodium bicarbonate and anhydrous citric acid, tartaric acid and malic acid (separately) were preheated at a temperature of 80^0c to remove absorbed/ residual moisture and were thoroughly mixed in a mortar to get uniform powder and then added to other ingredients according to the formulae given in table 1. The blend obtained was directly compressed into tablets of 100mg weight on a 16-station rotary tablet machine. A minimum of 50 tablets were prepared for every batch.

Evaluation of blends:

The powder blend was evaluated for its flow properties such as angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio.

Evaluation of tablets:

Twenty tablets were selected at random and weighed individually. The individual weights were compared with average weight for determination of weight variation. Hardness and friability of the tablets were determined using PFIZER tablet hardness tester Roche friabilator (USP) respectively. The drug content was determined by taking the powder equivalent to 10mg, then it was dissolved in acetonitrile and liquid was filtered and Zafirlukast content was determined by measuring the absorbance at 238nm. The drug content was calculated using the standard calibration curve.

For the determination of invitro dispersion time, one tablet was placed in a beaker containing 10ml of 0.5% Sodium lauryl sulfate in water at 37± 0.5°C and the time required for complete dispersion was determined. Dissolution rate of Zafirlukast from all formulations was performed using LABINDIA DISSO 2000, an eight stage dissolution rate testing apparatus with paddle. The dissolution fluid was 900ml of 0.5% Sodium lauryl sulfate in water. A speed of 50 rpm and a temperature of 37±0.5°C were used in each test. Aliquots of 5ml were withdrawn at regular intervals of time i.e (5, 10, 20, 30, 45, min) and the sample is replaced with the fresh dissolution medium each time. The samples obtained were filtered through Whatman filter paper and the absorbance was measured at 238nm.

3.RESULTS AND DISCUSSION

Orodispersible tablets of Zafirlukast were prepared by effervescent method. kyronT-314 is used as a superdisintegrant, lactose as a diluent. The slight bitter taste of the drug has been masked by using sweetener (aspartame) and flavouring agent (strawberry flavour).A total of nine formulations were designed.

The final blend of drug and excipients were evaluated for flow properties and was found that the blends were free flowing (angle of repose<30^oc, carr's index, 15%).The tablets obtained were of uniform weight with acceptable variation as per I.P specifications i.e., below 7.5%.Drug content was found to be in the range of 95 to 101% within the acceptable limits. Hardness of the tablets was found to be 2.4 to 2.9 kg/ cm^2.Friability was below 1% which was an indication of good mechanical resistance of the tablets. The results were shown in Table 2.

Among all the formulations Z-9 containing 10% Polacrilin Potassium along with mixture of sodium bicarbonate 20% w/w and malic acid 20% w/w was found to be promising and has shown an in vitro dispersion time of 13 s which facilitates their faster dispersion in the mouth. The results were shown in figure 1.

CONCLUSION

In vitro dissolution studies of all the formulations were carried out in water with 0.5% Sodium lauryl sulfate. The dissolution data revealed that the formulation Z-9 has more dissolution efficiency with $t_{50\%}$ 3min. The study shows that the dissolution rate of Zafirlukast can be enhanced to a great extent by the effervescent method, which facilitates faster dispersion in mouth there by faster dissolution.

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Formulation ingredients	Z-1	Z-2	Z-3	Z-4	Z-5	Z-6	Z-7	Z-8	Z-9
Drug and β-cyclodextrin(1:1) complex	20	20	20	20	20	20	20	20	20
Lactose Anhydrous (SuperTab 21AN)	59.5	54.5	44.5	59.5	54.5	44.5	59.5	54.5	44.5
Polacrilin Potassium(Kyron T314)	10	10	10	10	10	10	10	10	10
Citric acid + Sodium bicarbonate(1:1)	5	10	20	-	-	-	-	-	-
Tartaric acid + Sodium bicarbonate(1:1)	-	-	-	5	10	20	-	-	-
Malic acid + Sodium bicarbonate(1:1) Malic acid + Sodium bicarbonate(1:1)	-	-	-	-	-	-	5	10	20
Talc	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Magnesium stearate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Colloidal Silicon Dioxide (Aerosil 200)	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Color	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Strawberry flavor	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25

Table1: Formulation of Orodispersible tablets of Zafirlukast

Table 2: Evaluation of Oro dispersible tablets of Zafirlukast

Formulation code	Average weight (mg) ±SD	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Percent drug content ±SD	In vitro Dispersion time (s) ±SD
Z-1	98.5 ±0.20	2.78±0.03	2.59±0.05	0.38±0.17	98.42±1.01	20±0.68
Z-2	99.5±0.24	2.86±0.09	2.67±0.06	0.28±0.12	99.74±0.88	18±0.45
Z-3	99.8±0.36	2.90±0.07	2.87±0.05	0.48±0.17	98.44±0.62	16±1.32
Z-4	96.5±0.42	2.55±0.04	2.45±0.67	0.52±0.15	100.06±0.68	28±0.36
Z-5	98.5±0.21	2.68±0.12	2.74±0.02	0.28±0.08	98.25±0.58	25±0.68
Z-6	101±0.12	2.92±0.02	2.76±0.01	0.32±0.21	97.49±0.88	22±1.54
Z-7	97.8±0.26	2.96±0.02	2.68±0.14	0.54±0.11	99.96±0.62	18±0.91
Z-8	97.6±0.21	2.47±0.01	2.49±0.17	0.48±0.16	100.08±049	15±0.62
Z-9	99.8±0.10	2.89±0.01	2.69±0.04	0.30±0.12	99.86±1.03	13±0.21

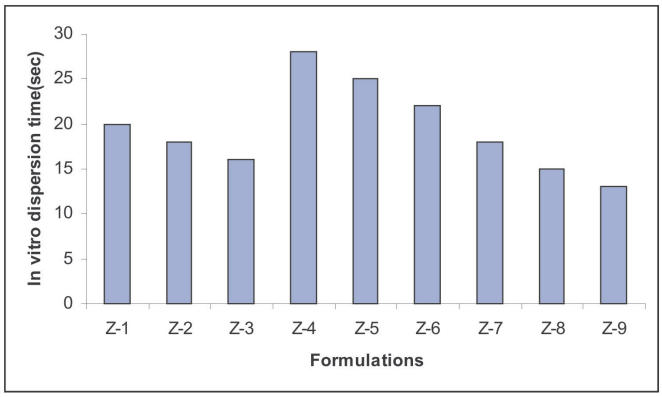

Fig 1: Effect of Effervescent agents on In vitro dispersion time of Zafirlukast tablets

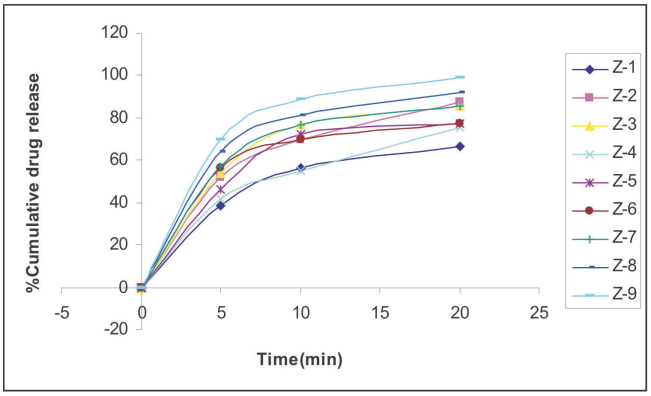

Fig 2: In vitro Dissolution profile of prepared Zafirlukast formulations

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