Devlopement and Evaluation of Mouth dissolving tablet of Zafirlukast using directly compressible excipients

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Abstract - *Mouth dissolving tablet serves as an alternative dosage form for patients who experience difficulty in swallowing. Further mouth dissolving tablets also have a faster onset of effects than tablets or capsules, and have the convenience of a tablet that can be taken without water. Zafirlukast is a leukotriene receptor antagonist (LTRA) and it is used for the maintenance treatment of asthma and to relieve the symptoms of seasonal allergies. It is generally administered orally. The present investigation is aimed to formulate mouth dissolve tablets of Zafirlukast to increase patient compliance. Fast dissolving tablet of Zafirlukast were successfully formulated and evaluated by using co-processed excipients method. The pre compression parameters such as angle of repose, tapped density, bulk density, Hausner's ratio, and compressibility index were evaluated for co-processed powder blend. The post compression evaluation parameters such as hardness, thickness, wetting time, disintegration time, and dissolution time were evaluated for all the formulations. The disintegration time of developed formulations were found in the range of 20 to 36 seconds, which revealed effectiveness of co-processed excipients in development of mouth dissolving tablets. It was concluded that the tablets made with co-processed excipients were have better compressibility and tablet characteristics in comparison to physical mixture.*

Key Words*: *Mouth dissolving tablets, co-processed excipients, Zafirlukast.

1. INTRODUCTION

A tablet is a pharmaceutical dosages form. Tablet defined as solid unit dosage form of drug or medicaments with or without suitable excipients and they are prepared either by compression or by molding process. The excipients are bulking agent, disintegrant or granulating agents. It consist of a mixture of drug substances and excipients (pharmaceutical aids), usually in powder form, pressed or compacted from a powder into a solid dose. Glidants and lubricants to ensure efficient tableting, the compressed tablet is the most popular dosage form is use today. A tablet can be formulated to deliver an accurate dosage to a specific site; and tablet dosage form available for child's, adults ad for pregnant women's , it usually taken orally, but can be administered Sublingually, Buccally, Rectally, or Intravaginally. According to Indian Pharmacopoeia, pharmaceutical tablets are solid, flat or biconvex, unit dosage form. About two-thirds of all prescriptions are dispensed as solid dosage forms, and half of these are compressed tablets.Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and an economical method of drug delivery having the highest patient compliance [1]. Tablet is most popular among all dosage forms existing today because of convenience of self administration, compactness and easy manufacturing [2]. Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in noncompliance and ineffective therapy [3]. To overcome this weakness, scientists have developed innovative drug delivery systems known as fast dissolving tablets [4]. United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as "a solid

dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed up on the tongue"[5]. Their characteristic advantages such as administration without water, patient compliance, rapid onset of action, increased bioavailability and good stability make these tablets popular as a dosage form of choice in thecurrent market [6].

"Co-processing method of excipients is a novel method used in the preparation of tablet dosage form, in which only a physical modification of excipients is done without changing their chemical nature. Co- processed excipient method enhance bioavailability, solubility , and dissolution rate of tablet" It is a combination of two or more excipients designed to physically modify their properties in a manner not achievable by simple physical mixing and without significant chemical change. [7]

1.1. CO-PROCESSING METHODOLOGY

Excipients selection on the basis of material characteristics

Selection of proportion of excipients

Homogenous dispersion or solution

Co-drying

Co-processed excipients are formulated on the bases of:

Solid state characterization**:**

1. Molecular level- Crystalline (polymorphic/ pseudo-polymorphic) & amorphous forms
2. Particle level -Particle shape, particle shape, particle size distribution, surface area, porosity, surface morphology
3. Bulk level- Flow properties, lubricant sensitivity, aggregation potential, bulk density, compressibility, hygroscopicity

1.2. PROPERTIES OF CO-PROCESSED EXCIPIENTS

- Absence of chemical changes, Improved flow properties. Reduced lubricant sensitivity
- Improved compressibility

1.3. METHODS OF CO- PROCESSING EXCIPIENTS:

- Granulation
- Spray drying

- Hot melt extrusion
- Solvent evaporation

1.4. CO-PROCESSED EXCIPIENTS ADVANTAGES:

Absence of chemical change, Improved flow properties, Improved compressibility,Better dilution potential,Weight variation, Reduced lubricant Sensitivity, Reduced the number of excipients in inventory, Improved organoleptic properties. Zafirlukast is chemically designated as Cyclopentyl N-[3-({2-methoxy-4-[(2 methylbenzenesulfonyl)carbamoyl]phenyl}methyl)-1-methyl-1H-indol-5-yl]carbamate, an orally administered drug of choice in the treatment used as an alternative to anti-inflammatory medications in the management and chronic treatment of asthma and exercise-induced bronchospasm (EIB). Zafirlukast inhibit CYP2C9 or CYP3A4 and is, therefore expected to affect the hepatic clearance of drugs metabolized by these enzymes. [8]

Major challenge for tablets manufacturing comes from the flow properties of the materials to be compressed. Most of the formulations (> 70%) contain excipients at higher concentration than active drug[8]. In recent years drug formulation scientists have recognized that single-component excipients do not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately[9]. Hence, there is a need to have excipients with multiple characteristics built into them such as better flow,
low/no moisture sensitivity, superior compressibility and rapid disintegration ability [10].
Excipients with improved functionality can be obtained by developing new chemical excipients, new grade of existing materials and new combination of existing materials [11]. Many patients express difficult to swallow tablets and hard gelatin capsules and thus does not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. Recent advances in novel drug delivery systems aim to enhance safety and efficacy of the drug molecules by formulating convenient dosage form for administration and to achieve better patient's compliance. One such approach is fast dissolving tablets) FDT)[12-15]. New combinations of existing excipients are an interesting option for improving excipients functionality because all formulations contain multiple excipients. One such approach for improving the functionality of excipients is coprocessing of two or more excipients. Coprocessing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual[16]. Co-processing excipients lead to the formulation of excipients granules with superior properties, compared with physical mixtures of components or individual components, like improved flow properties, improved compressibility, better dilution potential, fill weight uniformity, and reduced lubricant sensitivity [17].
Several co-processed superdisintegrants are commercially available: Ludipress (lactose monohydrate, polyvinyl pyrrolidone and crospovidone), Starlac (lactose and maize starch), Starcap 1500 (corn starch and pregelatinized starch), Ran Explo-C (microcrystalline cellulose (MCC), silica and crospovidone [CP]), Ran Explo-S (MCC, silica, Pactin, chitosan, guar gum, Aspartem, Manitol and sodium starch glycolate [SSG]), PanExcea MH300G (MCC, and CP)[18]. The widely used superdisintegrants are CP, croscarmellose sodium (CCS) and SSG. In the present investigation, the preparation and evaluation of Mouth dissolving tablets by using coprocessed superdisintegrants Zafirlukast and Mannitol , Guar gum ,co-processed superdisentragrantes , Chitosan , Pectin, Aspartame Cellulose microcrystalline, Crosscarmellose sodium in the ratios of 1:1, 1:2.5, 1:3, 1:5, 1:10.The reasons for selection of expients are high capillary activity, pronounced hydration capacity and little tendency to form gels. These expients are effective in wet granulation, dry granulation and direct compression in tablet processing[19]. CCS swells 4-8 folds in 10 sec.

The cellulose derivative swells in two dimensions readily[20]. In tablet formulations,it may be used in both direct compression and wet granulation processes. SSG was chosen because of its high swelling capacity[21]. Carbamazepine[22] tablets containing coprocessed superdisintegrants exhibit quick disintegration and improved drug dissolution. It can be concluded from the present work that coprocessed superdisintegrants of CP+CCS are superior to CP+SSG.

In the present work, In the present investigation, the preparation and evaluation of Mouth dissolving tablets by using coprocessed superdisintegrants Zafirlukast and Mannitol , Guar gum ,co-processed superdisentragrantes , Chitosan , Pectin, Aspartame Cellulose microcrystalline, Crosscarmellose sodium in the ratios of 1:1, 1:2.5, 1:3, 1:5, 1:10. Effect of coprocessed superdisintegrants on wetting time, disintegrating time, drug content, and *in-vitro* release have been studied.

2. MATERIAL AND METHODS:

Zafirlukast was procured as a gift sample from Macleod pharmaceutical private Limited, Baddi, Himachal Pardesh, India. expients like Mannitol , Guar gum ,co-processed superdisentragrantes , Chitosan , Pectin, Aspartame Cellulose microcrystalline, Crosscarmellose sodium purchased from S.D. Fine chem., Mumbai. All other materials were of analytical reagent grade. Preparation of Co-processed Superdisintegrants [23, 24]: The co-processed superdisintegrants were prepared by solvent evaporation method. A blend of (CCS + GG) and (CCS+ Pectin) (CCS+Chitosan) (in the ratio of1:1, 1:2.5, 1:3, 1:5, 1:10) was added to 10 ml of ethanol. The contents of the beaker (250 ml capacity) were mixed thoroughly and stirring was continued till most of ethanol evaporated. The wet coherent mass was granulated through # 44 mesh sieve. The wet granules were dried in a hot air oven at 60º C for 20 mins. The dried granules were sifted through # 44 mesh sieve and stored in airtight container till further use. Preparation of fast dissolving tablets by direct compression method [25, 26]: Mouth dissolving tablets of Zafirlukast were prepared by direct compression. All the ingredients (except granular directly compressible excipients) were passed through # 60 mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 200mg by direct compression method using 7 mm bi concave punches on a 16 station rotary compression machine. The composition of the tablets was given in Table 1

2.1. FORMULA OF MOUTH DISSOLVING TABLETS OF ZAFIRLUKAST

TABLE 1: Formula Table - (1)

S. NO	INGREDIENTS	F1	F2	F3	F4	F5
1	Zafirlukast	10mg	10mg	10mg	10mg	10mg
2	Croscarmellose sodium (CCS)	6mg	8mg	6mg	6mg	4mg
3	Guar gum (GG)	5mg	6mg	8mg	5mg	4mg
4	Co-processed superdisentragrantes (CCS + GG)	6mg	6mg	6mg	8mg	6mg
5	Cellulose microcrystalline	12mg	12mg	12mg	12mg	12mg

6	Aspartame	2mg	2mg	2mg	2mg	2mg
7	Mannitol	176mg	168mg	168mg	168mg	168mg

TABLE 2: Formula Table - (2)

S. NO	INGREDIENTS	F6	F7	F8	F9	F10
1	Zafirlukast	10mg	10mg	10mg	10mg	10mg
2	Croscarmellose sodium (CCS)	6mg	8mg	6mg	6mg	4mg
3	Pectin	5mg	6mg	8mg	5mg	4mg
4	Co-processed superdisentragrantes (CCS+ Pectin)	6mg	6mg	6mg	8mg	6mg
5	Cellulose microcrystalline	12mg	12mg	12mg	12mg	12mg
6	Aspartame	2mg	2mg	2mg	2mg	2mg
7	Mannitol	176mg	168mg	168mg	168mg	168mg

TABLE 3: Formula Table - (3)

S. NO	INGREDIENTS	F6	F7	F8	F9	F10
1	Zafirlukast	10mg	10mg	10mg	10mg	10mg
2	Croscarmellose sodium (CCS)	6mg	8mg	6mg	6mg	4mg
3	Chitosan	5mg	6mg	8mg	5mg	4mg
4	Co-processed superdisentragrantes (CCS+Chitosan)	6mg	6mg	6mg	8mg	6mg
5	Cellulose microcrystalline	12mg	12mg	12mg	12mg	12mg
6	Aspartame	2mg	2mg	2mg	2mg	2mg
7	Mannitol	176mg	168mg	168mg	168mg	168mg

Compatibility studies:IR Studies: IR spectra for pure drug Zafirlukast and formulations powdered tablets were recorded in Infrared spectrophotometer with KBr pellets.

2.2. EVALUATION OF FAST DISSOLVING TABLETS OF ZAFIRLUKAST:

Pre-compression Parameters: EVALUATION OF PRE-FORMULATION STUDIES: [27].

Preformulation study:

I) Pre-compression evaluation parameters:

a) Angle of repose. b) Bulk density. c) Tapped density. d) Hausner'sratio. e) Compressibility index (%).

II) Drug polymer interaction study:

a) FTIR studies. b) DSC studies.

Pre compression evaluation parameters:

Micromeritic properties:

Angle of Repose (θ):

The frictional strength in a movable powder or granules can be determined through the angle of repose and that is the most angles possible among the outside of a quantity of powder or granule and the flat plane.

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

Where, θ = angle of repose, h = height, r = radius.

Method: A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on a graph sheet was taken to measure the area of pile, there by evaluating the flow ability of the granules. Height ofthepilewas also measured.

Bulk Density:

Bulk density is defined as the mass of a powder divided by the bulk volume. The bulk density of a powder depends primarily on particle size distribution, particle shape and the tendency of the particles to adhere to one another.

Method: Together Loose Bulk Density (LBD) and Tapped Bulk Density (TBD) were determined. A quantity of accurately weighed powder (bulk) from each formula, previously surprised to break some agglomerates shaped was introduced into a 25ml measuring cylinder. After the early quantity was experiential, the cylinder was allowable to drop below it's possess weight on to a solid outside from the height of 2.5cm at 2 sec interval. The taping was sustained pending no additional alter in amount was noted.

LBD (Loose Bulk Density) = Weight of the Powder/Volume of Packing

TBD (Tapped Bulk Density) =Weight of the Powder/ Tapped Volume of Packing

Tapped density:

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (λt) was calculated using thefollowing formula t = m/v

Hausner's ratio:

Hausner's ratio is a not direct catalog of ease of powder flow. It is measured through the following method

Hausner's ratio = t/d

Where t = tapped density, d = bulk density

Lower H (<1.25) indicate improved flow property than superior ones (>1.25)

Percentage Compressibility:

Percentage compressibility of mixed powder was determined by Carr's compressibility index calculated by following formula.

Carr's Index % = TBD – LBD/TBD x 100

Where, LBD = Loose Bulk Density, TBD = Tapped Bulk Density.

Post - compression parameters: [28].

Tablets were subjected to evaluation of properties including drug content uniformity, weight variation, tablet hardness, friability, and thickness, and in-vitro drug release with different media.

Weight variation:

The tablet weight being complete was regularly determined to make sure that tablets contain the appropriate quantity of drug. The USP weight difference test is done by weighing 20 tablets separately, the average weight calculated and the individual weight compared to the average weight. The tablets meet the USP requirement that not supplementary than 2 tablets are exterior the proportion limits and no tablet differ through more than 2 times the proportion limit. USP official limits of percentage deviation of tablet are presented in the Table 2.

Sr. No.	Average weight of tablet (mg)	Maximum % difference allowed
1	130 or less	10
2	130-324	7.5
3	324<or more	5

TABLE 4: WEIGHT VARIATION LIMITS

Tablet hardness:

The confrontation of tablets to delivery or under breakage condition of the storage, carrying and handling earlier than custom depends on its rigidity. The rigidity of each lot of tablet was checked by using the apparatus (Monsanto hardness tester). The rigidity was calculated in conditions of kg/cm^2. 3 tablets were chosen at random and tested for rigidity. The standard rigidity of 3 determinations was recorded.

Friability:

Friability usually refers to weight loss of the tablets in the containers outstanding to elimination of fine from the tablet exterior. Friability usually reflects deprived consistency of tablet ingredients.

Method:

20 tablets were weighing and the weight of these tablets was recorded and placed in apparatus (Roche friabilator) and rotate at the velocity of 25 rpm for 100 revolutions and then tablets were detached from the apparatus, dusted rancid the fines and weighed again. The recorded the weight.

$$\% \text{ Friability} = \frac{\text{Initial Wt. of tablet - Final Wt. of Tablet}}{\text{Initial Wt. of tablet}} \times 100$$

Tablet thickness:

Thickness of the tablet is important for uniformity of tablet size. Thickness was measured using Vernier Calipers. It was determined by checking the thickness of ten tablets of each formulation.

Content Uniformity:

The tablets were tested for their drug content uniformity. At random 20 tablets were weighed and powdered. The powder equivalent to 500 mg was weighed accurately and dissolved in 100ml of phosphate buffer of pH 6.8. The solution was shaken thoroughly. The undissolved matter was removed by filtration through Whattman's filter paper No.41. Then the serial dilutions were carried out. The absorbance of the diluted solutions was measured at 263 nm. The concentration of the drug was computed from the standard curve of the RC in phosphate buffer of pH 6.8.

Disintegration time:

Tablet disintegration is an important step in drug absorption. The test for disintegration was carried out in Electro Lab USP disintegration test equipment. It contains 6 glass tubes which are 3 inches extended, open at the top, and held against a 10 mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tablets, one tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker containing pH 1.2 Buffer solution at 37°C ± 1°C such that the tablet remains 2.5 cm under the outside of the liquid. The disintegration time of the tablet was noted.

In-vitro Dissolution time:

In-vitro dissolution studied of center and encrusted drug of HMG-COA reductase inhibitor was carried out using Electro lab TDT-08L USP dissolution test equipment. The particulars be known as below:

Electro lab TDT-08L USP dissolution test apparatus:

Medium: pH 1.2 buffer solution and pH 6.8 buffer solution, RPM: 50

Time: 2hrs in pH 1.2 followed by dissolution in pH 6.8 buffer solutions.

Procedure:

Tablet was introduced into the basket of the Electro Lab TDT-08L USP dissolution test equipment and the equipment was put in activity, 5 ml of test was reserved for 1st half hour at 10 min intervals and after that at 15min intervals and replace by the personal buffer solution. Reserved sample are analyze through UV spectrophotometer for presence of drug using buffer solution as blank.

3. RESULT AND DISCUSSION:

Co-processed superdisintegrants were prepared by solvent evaporation using (CCS + GG) and (CCS+ Pectin) (CCS+Chitosan) (in the ratio of1:1, 1:2.5, 1:3, 1:5, 1:10). In the present study the FTIR spectra for pure drug Zafirlukast and its formulations like F1,F2,F3,F5 with various polymers and other excipients is taken to establish the physical characterization of drug and its formulations (Fig 1). The drug-excipients study was done by Fourier transform infrared (FTIR) spectroscopy study.

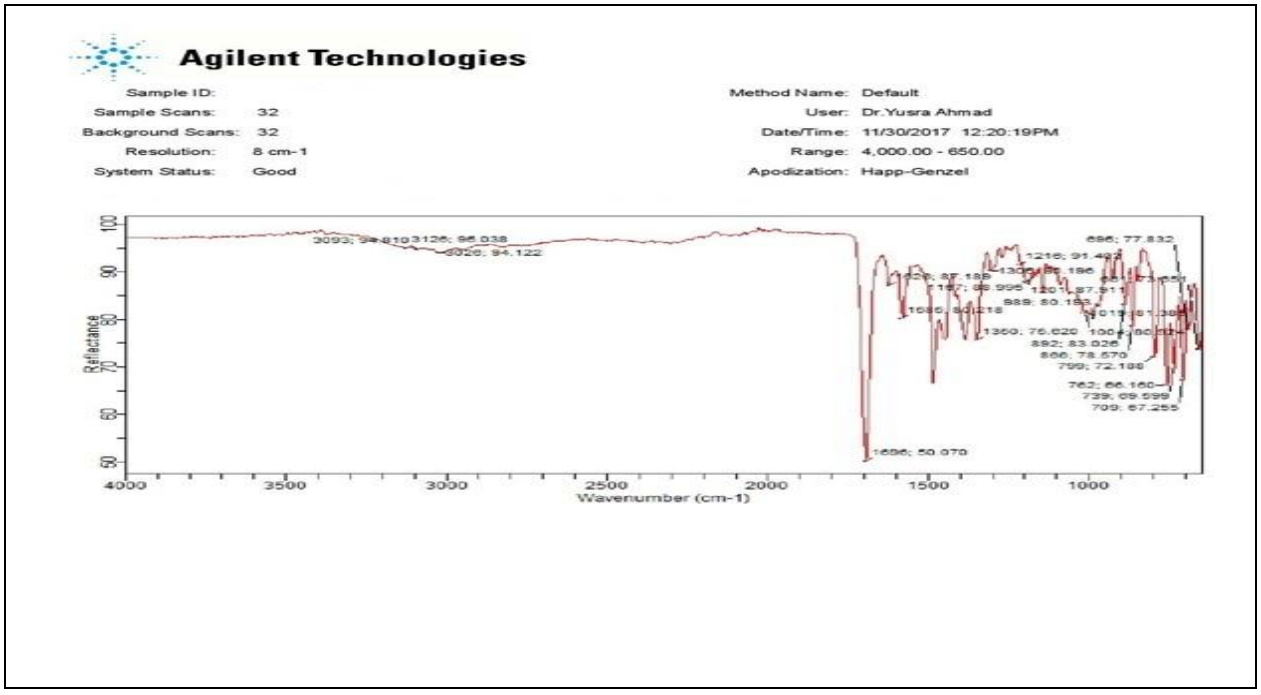

FIG 1: FTIR SPECTRA OF PURE DRUG ZAFIRLUKAST AND FORMULATION

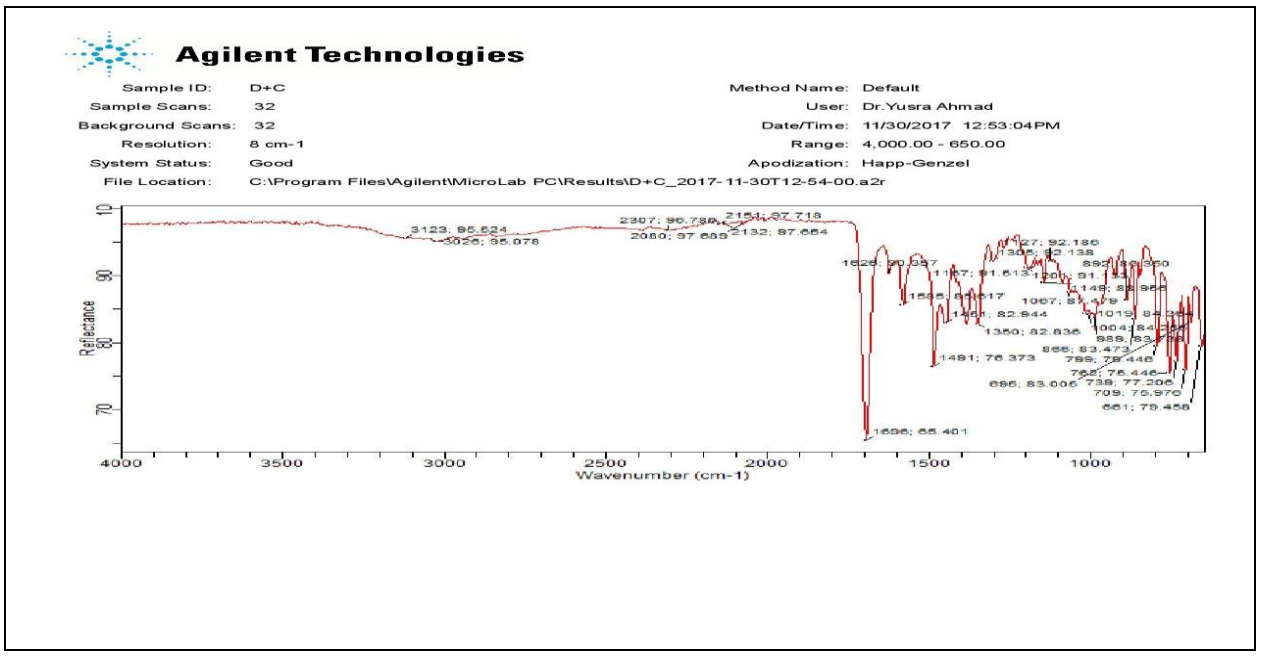

FIG 2: FTIR SPECTRA WITH ZAFIRLUKAST AND CHITOSAN

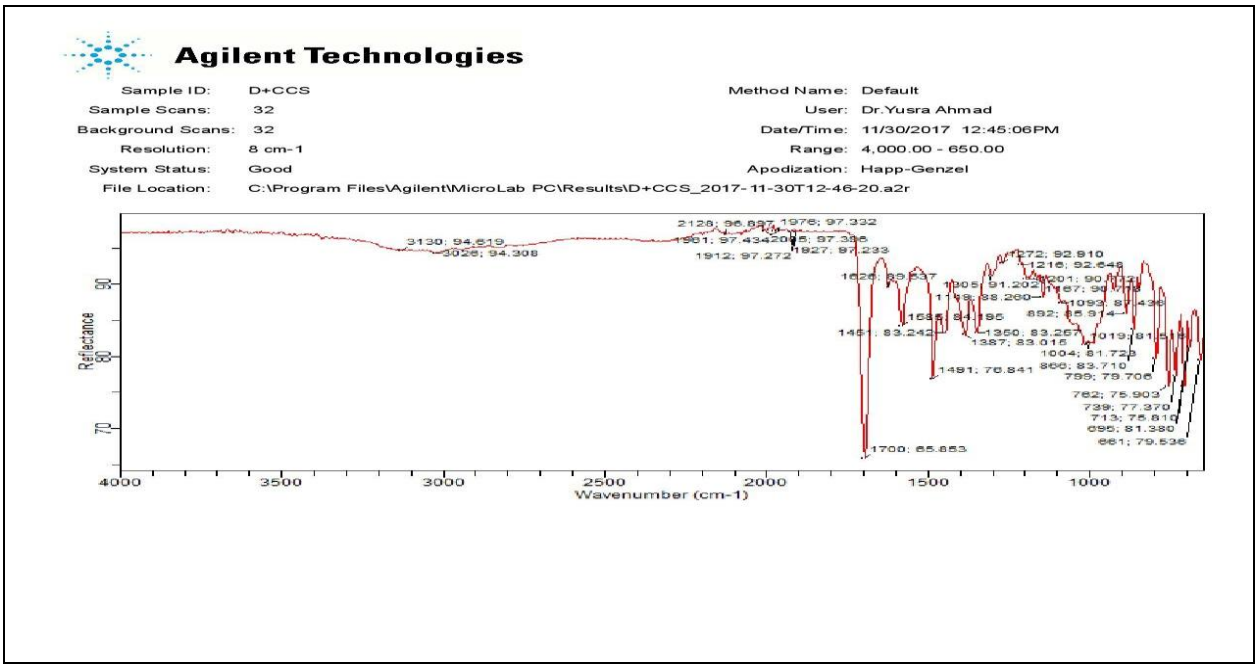

FIG 3: FTIR SPECTRA WITH ZAFIRLUKAST AND CROSSCARMILLOS SODIUM

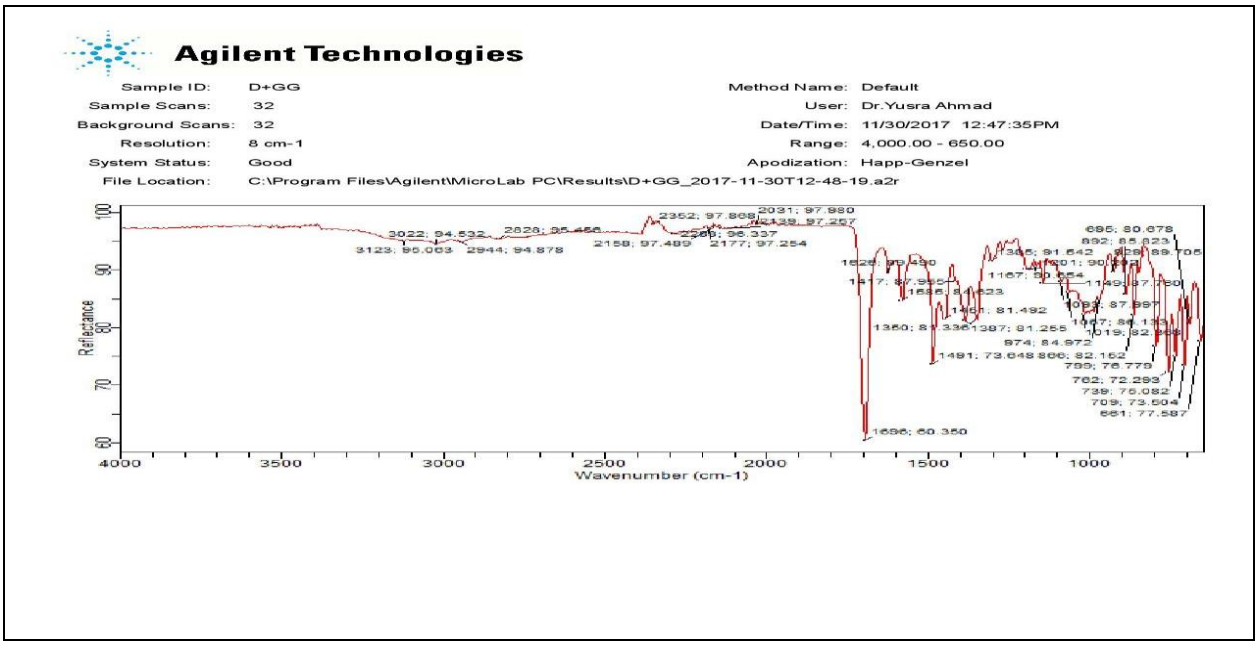

FIG 4: FTIR SPECTRA WITH ZAFIRLUKAST AND GUAR GUM

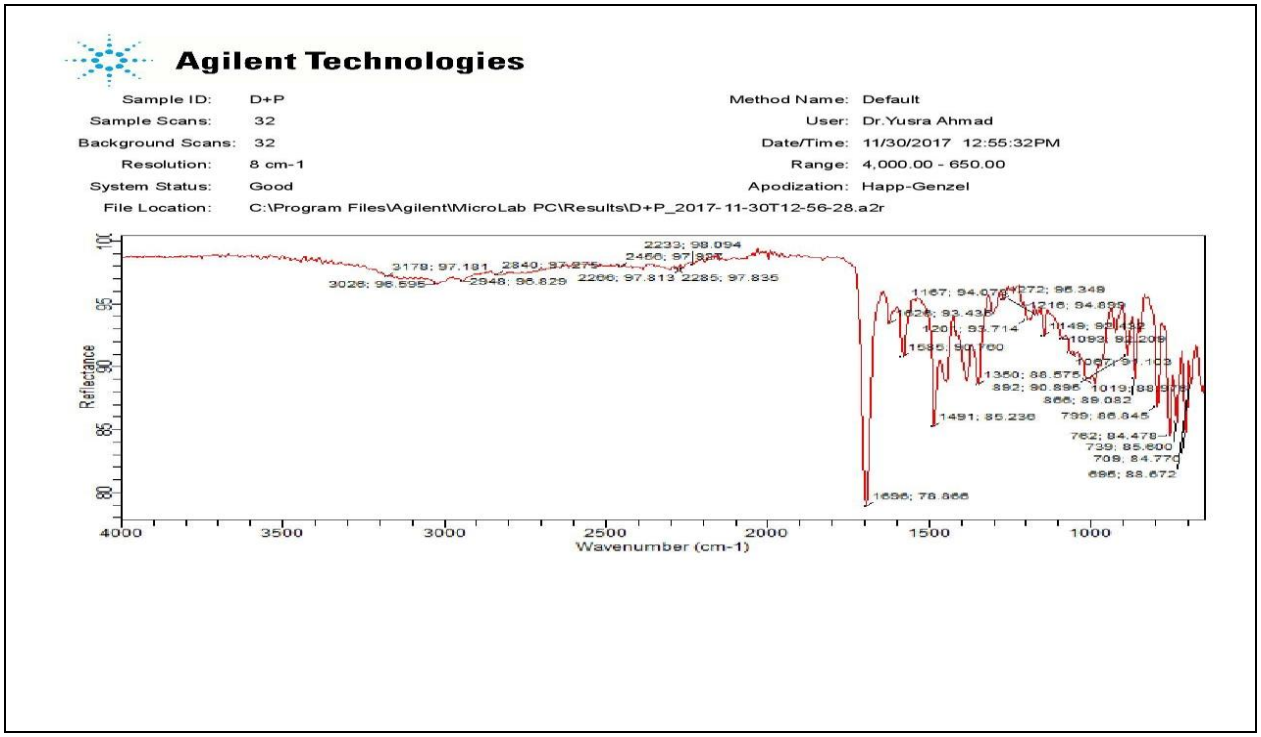

FIG 5: FTIR SPECTRA WITH ZAFIRLUKAST AND PECTINE

The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property (Table 3).

Table 3: Pre-compression parameters of mouth dissolving **Zafirlukast** tablets by direct compression and co-process method:

TABLE 5: ALL THE POST-COMPRESSION PARAMETERS ARE EVALUATED WERE PRESCRIBED LIMITS AND RESULTS

FORMULATION	PARAMETERS				
	Angle of Repose(θ)	Tapped Density (gm/ml)	Bulk density (gm/ml)	Hausner's ratio	Compressibility index (%)
F1	16.37	0.8243	0.7530	1.06	16.32
F2	16.46	0.8432	0.7308	1.03	18.21
F3	15.47	0.8334	0.7902	1.07	18.01
F4	14.19	0.7304	0.7660	1.12	16.22
F5	15.08	0.8301	0.7198	1.01	16.23
F6	16.28	0.8324	0.7309	1.03	16.22

F7	17.45	0.8435	0.7322	1.13	16.02
F8	17.65	0.7423	0.7936	1.03	18.32
F9	16.34	0.8425	0.7098	1.04	17.12
F10	16.54	0.9232	0.7638	1.12	16.32
F11	1756	0.8432	0.7578	1.02	15.99
F12	18.55	0.8425	0.7726	1.06	16.43
F13	14.43	0.8423	0.7624	1.03	16.32
F14	15.18	0.8233	0.7453	1.08	14.13
F15	17.08	0.8423	0.7325	1.07	16.31

TABLE 6: IP ACCEPTABLE LIMITS. RESULTS OF POST COMPRESSION PARAMETERS POST COMPRESSION PARAMETERS OF TABLETS PREPARED BY CO-PROCESSED SUPER DISINTEGRANTS METHOD

FORMULATION CODE	THICKNESS (mm)	DIAMETER (mm)	HARDNESS (kg/cm2)	WETTING TIME(sec)	WATER ABSORPTION RATIO	DISINTEGRATION TIME(sec)
F1	3.3	9	1.5	55	0.005	36
F2	3.6	9	1.5	31	0.018	22
F3	3.3	9	1.5	27	0.028	20
F4	3.6	9	1.5	50	0.006	29
F5	3.6	9	1.5	55	0.005	30
F6	3.3	9	1.5	50	0.006	22
F7	3.5	9	1.5	28	0.025	21
F8	3.6	9	1.5	28	0.025	30
F9	3.3	9	1.5	30	0.02	23
F10	3.3	9	1.5	33	0.015	21
F11	3.5	9	1.5	30	0.02	20
F12	3.5	9	1.5	24	0.05	33
F13	3.3	9	1.5	28	0.025	30
F14	3.6	9	1.5	31	0.018	21
F15	3.6	9	1.5	31	0.018	20

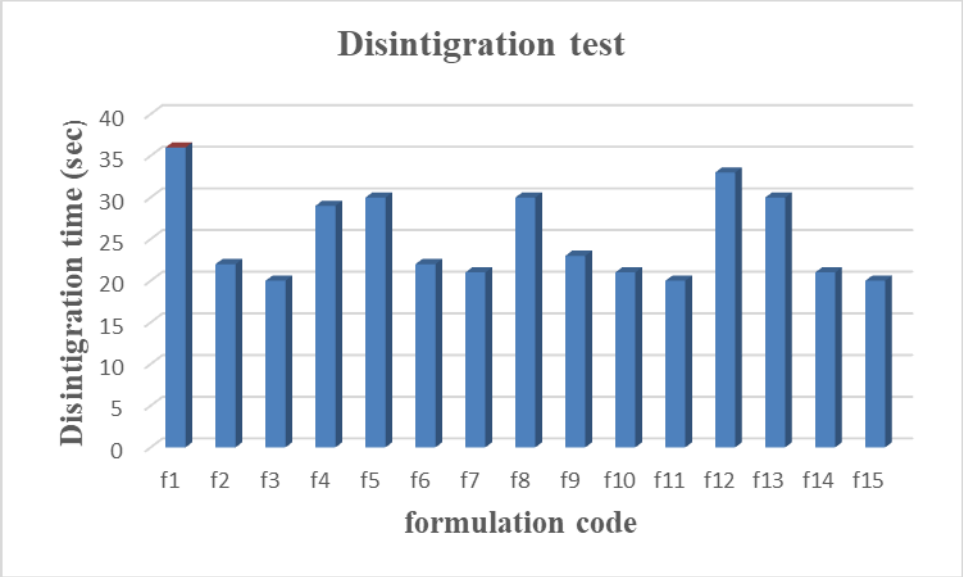

FIG 6: DISINTEGRATION TIME VS FORMULATION

TABLE 7: RELEASE PROFILE OF FORMULATIONS

Time interval	% Dissolution				
	F1	**F2**	**F3**	**F4**	**F5**
0	0	0	0	0	0
1	73.2	73.5	85.5	97.689	89
5	74.4	77.6	94.8	104.7	99.9
10	83.8	81	102.5	105.7	104.7
15	95.1	82.4	104.4	106.1	105.5
20	99.2	85.5	107.4	106.8	105.1
25	100.3	86.4	108.2	107.1	105.1

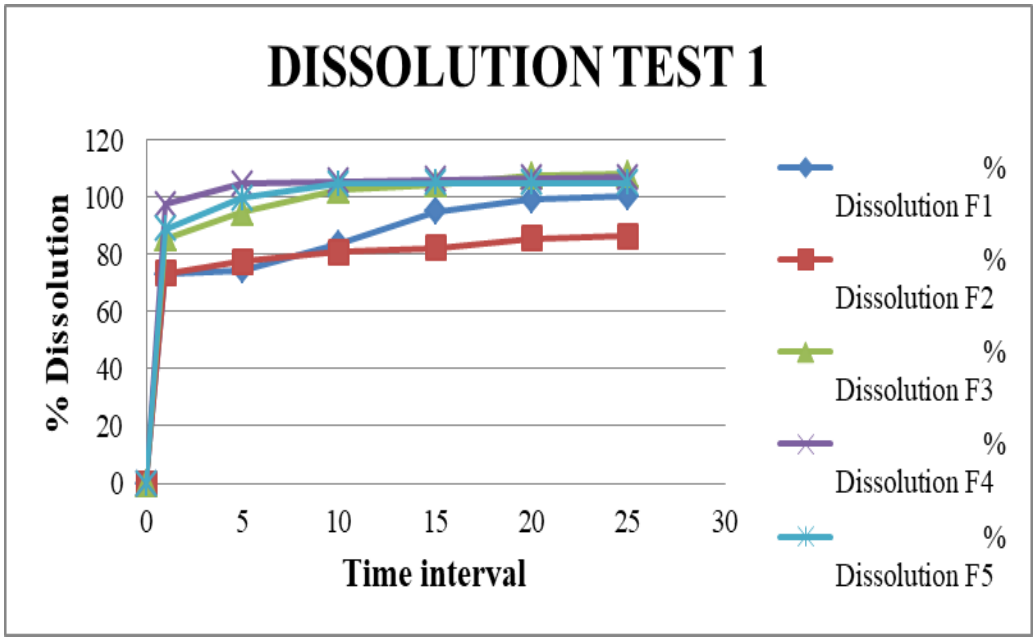

FIG 7: DISSOLUTION TEST 1

TABLE 8: RELEASE PROFILE OF FORMULATIONS

Time interval	% Dissolution				
	F6	**F7**	**F8**	**F9**	**F10**
0	0	0	0	0	0
1	71.0	62.1	87.6	77.1	81.2
5	71.2	67.7	93.2	82.9	82.2
10	75.4	82.4	100.2	91.0	83.9
15	83.2	83.3	101.2	102.1	84.0
20	84.4	85.4	102	103.0	90.2
25	84.8	89.9	102.1	100.3	92.9

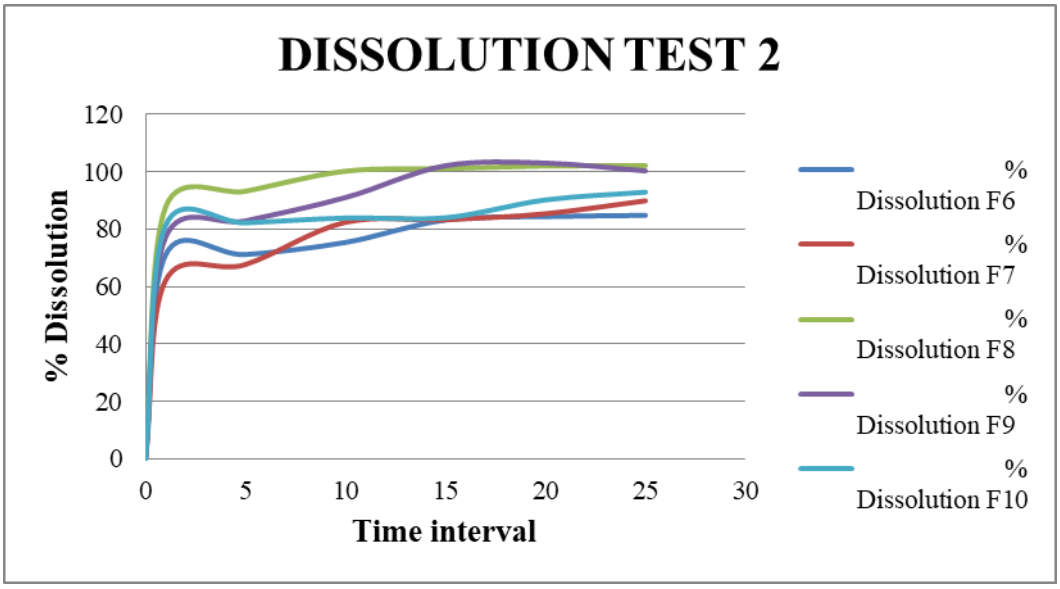

FIG 8: DISSOLUTION TEST 2

TABLE 9: RELEASE PROFILE OF FORMULATIONS

Time interval	% Dissolution				
	F11	**F12**	**F13**	**F14**	**F15**
0	0	0	0	0	0
1	72.0	79.4	72.3	81.0	99.8
5	72.2	86.8	97.3	99.3	99.9
10	72.8	91.2	98.8	101.6	100.3
15	82.3	93.4	99.7	101.8	100.9
20	87.2	93.8	102.2	103.2	101
25	91.1	104.3	104.3	103.7	124.8

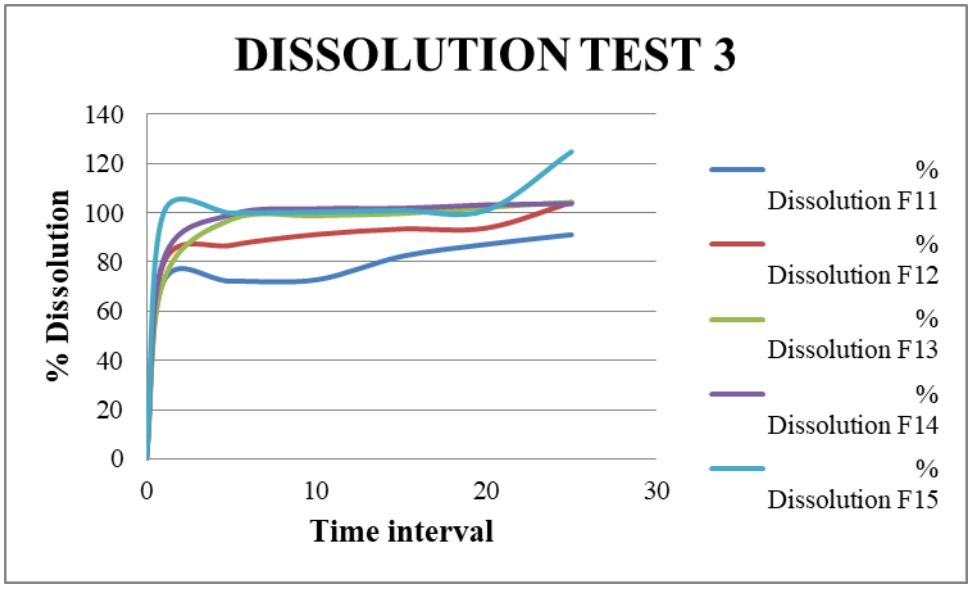

FIG 9: DISSOLUTION TEST 3

4. Conclusion:

The present work is aimed to formulate the Mouth dissolving tablet of Zafirlukast. Drug Zafirlukast is widely used in the management of Asthma. Although conventional tablets are available in market but may have difficulty in swallowing by critically ill patients and geriatric patients. So to increase the patient compliance present work is designed to develop mouth dissolving tablet by using directly co-processed compressible excipients. It was concluded that the tablets made with cp-processed excipients were have better compressibility and tablet characteristics in comparison to physical mixture.

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