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FORMULATION AND EVALUATION OF IMMEDIATE RELEASE OF IRBESARTAN TABLETS

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ABSTRACT

The aim of the present study is to formulate and evaluate immediate release tablets of Irbesartan by using direct compression method. It is a water insoluble oral anti-hypertensive agent, belongs to class-II drugs according to BCS system. Irbesartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively binding to the AT1 angiotensin II receptor. The oral bio availability of irbesartan is 60% and having half-life 11-15h. The aim of the present study is to prepare immediate release tablet of irbesartan with increase rate of dissolution, which leads to increased bio availability. In order to obtain acceptable product several trials were conducted using sodium starch glycolate, croscarmellose sodium, micro crystalline cellulose, crospovidone as super disintegrants by direct compression.

INTRODUCTION:

In the present study and research, novel drug delivery systems are developed for expanding Markets/indications, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly patient compliance. [1]

The concept of immediate release drug delivery system emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence, they do not comply with prescription, which results in high incidence of oncompliance and ineffective therapy. [2] Irbesartan is an angiotensin II receptor antagonist used in the treatment of hypertension. It may also delay progression of diabetic nephropathy and also indicated for the reduction of renal disease progression in patients with type II diabetes. According to BCS classification irbesartan belongs to class II . Since it has poor solubility in water, methods has been developed for enhancement of solubility by using different types and concentrations of surfactants and super disintegrates by which the solubility and finally dissolution profile of irbesartan has been increased. [3]

MATERIALS AND METHOD:

Irbesartan was gift sample from CDLT (Central Drug Testing Laboratory, Mumbai). Vanilla flavour, Magnesium Stearate was purchased from S.D. Fine Chem. Ltd. Sodium Starch gycolate, Microcrystalline Cellulose was purchased from Signet Chemical Corporation, Mumbai.

METHODOLOGY:

Preparation of standard Calibration Curve of Irbesartan:

100 mg of Irbesartan was accurately weighed and dissolved in 100 ml of methanol into a volumetric flask (1000 mcg/ml). 10 ml of this solution was taken and made up to 100 ml with methanol, which gives 100 mcg/ml concentrations (Stock solution).

From this stock solution, sample of 0.5, 1.0, 1.5. 2.0, 2.5 & 3.0 ml withdrawn and diluted to 10ml it makes solution of concentration 5

µg/ml, 10µg/m, 15µg/ml, 20µg/ml, 25µg/ml & 30µg/ml in methanol were prepared. The absorbance of the diluted solution was measured at 277 nm and a standard plot was drawn using the data obtained.

Determination of ƛ max in Methanol:

100mg of pure drug transferred into 100 ml of methanol in a volumetric flask. Withdrawal 10ml from this solution and diluted to 100ml it make 100 mcg/ml (stock solution). Again 10ml from this solution withdrawn and diluted to 100ml with methanol and absorbance is taken between 400nm-200nm.

Determination of ƛ Max in phosphate buffer 6.8:

100 mg of pure drug transferred into 100ml of phosphate buffer 6.8 in a volumetric flask. Withdrawn 10ml from this solution and diluted to 100 ml it make 100mcg/ml (stock solution). Again 10 ml from this solution withdrawn and diluted to 100ml with phosphate buffer and absorbance is taken between 400nm-200nm.

Compatibility studies of drug and polymers:

Prior to the development of the dosage forms the compatibility study was carried out. Hence infrared spectra of the physical mixture of the Irbesartan and the polymers were taken. Also the infrared spectra of formulation design.

Preparation of tablets:

Direct compression method: [4]

The drug was mixed with proper portion of superdisintegrants. Care should be taken to confirm the proper mixing of drug and superdisintegrants. Then other excipients were added. Then the mixture is passed through sieve No.44. The mixture is blended with colour, lubricating agent (magnesium stearate) and filler. Finally the blend is subjected for compression using 10mm on clit pilot press 10 station machines.

EVALUATION:

Hardness:

Tablet crushing strength, the critical parameter was controlled as the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage, depends on its hardness. Hardness of the tablet in formulation containing 75 mg of Irbesartan shows the range within acceptable limit. Hardness of tablets prepared by direct compression was 3.81 ± 0.5 to 4.187 ± 0.13 kg/cm2 in formulation F1 TO F9.

Friability:

To achieve % friability within limits for an immediate release tablet is a challenge to the formulator since all methods of manufacturing of immediate release tablets are responsible for increasing the % friability values. The % friability value for all formulation batches prepared was found to be >1.0%. This was also observed due to constant tablet press setting across all batches.

Average weight:

As material was free-flowing, tablets were obtained of uniform weight due to uniform die fill with acceptable variation as per L.P. standards. The weight was found in all designed formulations in the range 250 mg. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopoeial limits

Thickness:

The thickness of the tablets was determined by using Vernier callipers. Randomly 10 tablets selected were used for determination of thickness that expressed in Mean ± SD and unit is mm.

Disintegration Test:

The USP device to rest disintegration was six glass tubes that are long, open at the top, and held against 10” screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is positioned in 1 liter beaker of distilled water at 37± 2 degree Celsius, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5 cm from the bottom of the beaker. Disintegration time is very important for immediate release of irbesartan tablets which is desired to be less than 60 seconds. The formulations showed disintegration time less than 60 seconds.

Table 1: Composition of Irbesartan Immediate release tablets

Ingredients (mg/tab)	Formulation Codes								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Irbesartan	75	75	75	75	75	75	75	75	75
Microcrystalline cellulose	139	137	135	139	137	135	139	137	135
Mannitol	25	25	25	25	25	25	25	25	25
Croscarmellose sodium	6	8	10	-	-	-	-	-	-
Crospovidone	-	-	-	6	8	10	-	-	-
Sodium starch glycolate	-	-	-	-	-	-	6	8	10
Aspartame	2	2	2	2	2	2	2	2	2
Vanilla flavour	1	1	1	1	1	1	1	1	1
Magnesium Stearate	2	2	2	2	2	2	2	2	2
Total weight	250	250	250	250	250	250	250	250	250

Fig 1: FTIR Spectra of Irbesartan

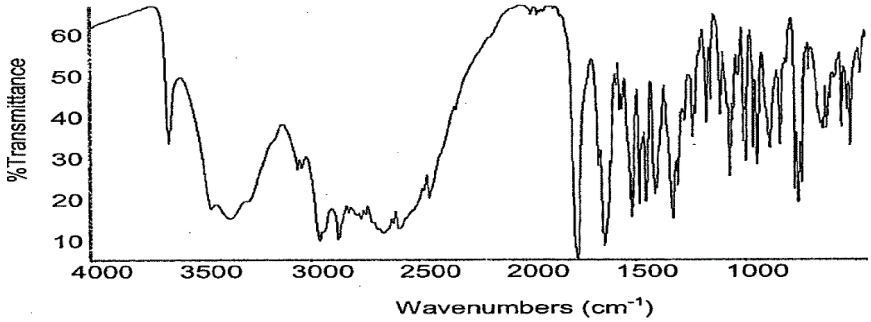

Table 2: Standard calburation curve of irbesartan in phosphate buffer PH 6.8

S.no	Concentration	Absorbance
1	0	0
2	4	0.113
3	8	0.224
4	12	0.329
5	16	0.456
6	20	0.570

Table 3: Post compression parameters of tablets of formulations F1 TO F9

Formulation Code	Hardness (kg/cm2)	Thick-ness (mm)	Weight variation	Friability %	Wetting Time	Water absorption Ratio
F1	3.87 ±0.21	3.4	0.201±0.1	0.6±0.05	42.86±1.14	66.78±1.027
F2	3.81±0.5	3.4	0.198±0.33	0.4±0.01	46.66±0.23	62.5±2.106
F3	3.95±0.1	3.4	0.199±1.5	0.4±0.02	44.33±0.1	61.0±1.001
F4	4.15±0.1	3.4	0.199±1.4	0.9±0.02	32.86±0.6	57.98±0.1
F5	4.25±0.02	3.4	0.197±1.8	0.6±0.05	36.56±0.04	60.52±0.52
F6	4.06±0.5	3.4	0.201±0.89	0.2±0.04	38.33±0.28	56.52±0.042
F7	4.21±0.21	3.4	0.192±1.23	0.4±0.02	38.5±0.3	56.4±0.541
F8	4.125±0.4	3.4	0.199±1.08	0.5±0.08	36.43±0.25	57.9±0.009
F9	4.187±0.13	3.4	0.201±0.98	0.3±0.07	36.36±2.9	59.72±0.05

Table 4: *In-vitro* disintegrating time, Drug content and % Drug release of formulation F1 to F9

Formulation	Disintegrating time (sec)	% drug release	Drug content uniformity
F1	34.4±0.56	81.53	99.02±0.25
F2	31.3±0.96	90.13	97.87±0.57
F3	35.6±0.46	85.44	97.35±0.87
F4	38.73±0.16	85.82	98.23±0.44
F5	34.36±0.5	94.66	99.45±0.66
F6	29.93±0.35	98.63	99.84±0.11
F7	39.36±0.22	81.58	97.22±0.22
F8	38.83±0.3	86.19	97.45±0.90
F9	34.3±0.36	86.19	98.65±0.57

Among the three superdisintegrants used, Crospovidone showed less disintegrating time followed by croscarmellose sodium and sodium starch gycolate. The probable reason may be high gelling tendency of croscamellose sodium and sodium starch gycolate than Crospovidon which causes swelling of tablet mass with subsequent retardation of disintegration (5). Besides the type, the concentration of superdisintegrants used also affected the disintegration time. In case of the tablets containing crospovidon and croscarmellose sodium, an increase in concentration of superdisintegrants resulted in definite decrease in disintegration time(6). The same result was found for tablets containing Sodium starch gycolate up to 4%. At 5% concentration, it resulted in slight increase in disintegration time from 31 sec. to 34 sec, for formulation containing 75 mg of Irbesartan. This delay in disintegration time might have occurred due to probable blockade of capillary pores in tablet mass as result of formation of viscous plug by Sodium starch gycolate, which subsequently, prevented free access of fluid into tablets.(7)

Wetting Time:

In formulation containing 75mg of Irbesartan (F1 to F9) observed that wetting time of tablets was in the range of 32.86 to 46.66 seconds. It was observed that type of the disintegrant affected the wetting of the tablets. On comparing superdisintegrants the formulation containing Sodium starch gycolate take more wetting time than croscamellose sodium and Crospovidone. Hence wetting is related to the inner structure of the tablets and hydrophobicity of the components. This may be due to the fact that sodium starch gycolate is disintegrated by swelling mechanism leading to longer wetting time.

Water absorption ratio: Water absorption ratio ranged from 56.4 to 66.78 in formulation containing 75 mg of Irbesartan.

Drug content Uniformity: The drug content in different formulation was highly uniform and in the range of 97.22% to 99.45% was seen in the formulation from F1 to F9.

Weight variation: Weight variation for prepared tablets was found within specifications of Indian Pharmacopoeia for formulation containing 75 mg of Irbesartan.

CONCLUSION:

The formulations were successfully developed using various disintegrates like crosscarmellose sodium, sodium starch glycolate and Crospovidone. From the executed experimental results, it could be confirmed that croscamellose sodium, sodium starch glycolate and crospovidone are suitable carriers for Irbesartan, FTIR studies revealed that there are incompabilities between the drug and excipients used in the formulations. The pre compression evaluation studies have shown that the powder blend has good flow properties and are suitable for direct compression. Post Compression evaluation studies have shown that all the parameters were within the specifications for immediate release formulations. Of all the formulations developed formulation F6 was optimized based on the results of disintegration time, wetting time, water absorption ratio and in vitro dissolution profiles. It releases maximum of drug within 30 minutes there by the objective of increasing dissolution has been met by this formulation.

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