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Research

Formulation And *In Vitro* Characterisation Of Vilazodone Immediate Release Tablets

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Abstract

The aim present work is formulate and evaluate the Immediate release tablets of Vilazodone. The superdisintegrants were taken in different ratios. The formulations were prepared by direct compression technique. The pre compression and post compression parameters were in the IP limits. The FTIR studies showed no interaction between drug and superdisintegrants. Among all F5 was showed 96.57% and it was consider as a optimized Formulation.

Keywords: Vilazodone, Immediate release tablets

INTRODUCTION

Oral drug delivery is the most desirable and preferred method of administering therapeutic agent for their systemic effects. In addition, the oral medication is generally considered as the first avenue investigated in the discovery and development of new drug entities and pharmaceutical formulation, mainly because of patient acceptance, convenience in administration and cost-effective manufacturing process. For many drug substances, conventional immediate-release formulation provide clinically defective therapy while maintain the required balance of pharmacokinetic and pharmacodynamic profiles with an acceptable level of safety to the patient.

Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluents or carrier, which carrier or diluents does not prolong to an appreciable extent, the rate of drug relkease and/or absorption. This term excludes formulations which are adopted to provide for, “modified”, “controlled”, “sustained”, “prolonged” , “extended” or “deleyed ”release of drug.

Desired Criteria for Immediate release Drug Delivery System

- In case of the solid dosage it should dissolve or disintegrate in the stomach within a short period .
- In case of the liquid dosage form it should be compatible with taste making.
- Be portable without fragility concern.
- Have a pleasing mouth feel .
- It should not leave minimal or mo residence in the mouth after oral administration.
- Exhibit low sensitivity to environmental condition as humidity and temperature
- Be manufactured using conventional processing and packing equipment at low cost
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.

Merits of Immediate Release Drug Delivery System

- Improved compliance /added convenience
- Improved stability, bioavailability
- Suitable for controlled /sustained release actives
- Allows high drug loading
- Ability to provide advantages of liquid medication in the form of solid preparations.
- Adaptable and amenable to existing processing and packaging machinery
- Cost-effective.
- Improved solubility of the pharmaceutical composition.
- Decreased disintegration and dissolution times for immediate release oral dosage forms.

When an immediate release product is administered , the drug concentration in blood rises rapidly, peaks soon after administration and then declines .If the peak concentration is too high, the drug may exhibit undesirable side effects. If the decline in blood concentration isalso rapi, the product will have to be dosed frequently to maintain therapeutic blood levels. Such a large fluctuation in the blood concentration may not be suitable for some drugs, or may6 require dosing frequencies that are impractical. therapeutic .

Current technologies in oral delivery

Over the last 3 decades, many novel oral drug therapeutic systems have been invented along with the appreciable development of drug delivery technology. Although these advanced DDS are manufactured of fabricated in traditional pharmaceutical formulations such as tablets, capsules, sachets, suspensions, emulsions, they are superior to the conventional oral dosage forms in terms of their therapeutic efficacies, toxicities , and stabilities.

Based on the desired therapeutic objectives , oral DDS may ne sorted into three categories:

- immediate - release preparation,
- controlled- release preparation
- targeted- release preparation.

Immediate –Release Preparations

The preparations are primarily intended to achieve faster onset of action for drugs such as analgesics, antipyretics, and coronary vasodilators. Other advantages include enhanced oral bioavailability through transmucosal delivery and pregastric absorption, convenience in drug administration to dysphasic patients, especially the elderly and bedridden, and new business opportunities.

Conventional IR formulations include fast disintegrating tablets and granules that use effervescent mixtures, such as sodium carbonate (or sodium bicarbonate) and citric acid (or tartaric acid), and superdisintegrants such as sodium glycolate, crosscarmellose sodium, and crospovidone. Current technologies in fast-dispersing dosage form include modified tableting systems, shear from technology, which employs application of centrifugal force and controlled temperature, and freeze-drying.

Controlled –Release Preparations

The currently employed CR technologies for oral drug delivery are diffusion-controlled systems; solvent activated systems, and chemically controlled systems. Diffusion-controlled systems include monolithic and reservoir devices in which diffusion of the drug is the rate-limiting step, respectively , through a polymer matrix or a polymeric membrane. Solvent-activated systems may be either osmotically controlled or controlled by polymer swelling .Chemically controlled systems release drugs via polymeric degradation (surface or bulk matrix erosion) or cleavage of drug from a polymer chain. It is worth mentioning here that the so- called programmed-release (‘’ tailored-release’’) profile of a final CR product is rarely the outcome of a single pharmaceutical principle. Depending on the specific physiochemical properties of the drug in question and desired therapeutic objectives, different formulation and CR principle may be proportionally combined within the same dosage form. This task appears to be simpler when realized in term of appropriate selection of polymers and excipients that incorporate desired principles.

Targeted- Release Preparations

Site-specific oral drug delivery requires spatial placement of a drug device at a desired site within the GI tract. Although it is virtually possible to localize a device within each part of GI tract, the attainment of site-specific delivery in the oral cavity and the rectum is relatively easier than the stomach and the small and large intestines. The latter requires consideration of both longitudinal and transverse aspects of GI constraints.

MATERIALS AND METHODS

Vilazodone Procured From Aurobindo Pharma Limited., Hyderabad. Provided by SURA LABS, Dilsukhnagar, Hyderabad., Cross Povidone from Nihar traders pvt Ltd, Crosscarmellose sodium from Nihar traders pvt Ltd, Sodium starch glycolate from Nihar traders pvt Ltd, Locust beam gum from Nihar traders pvt Ltd, Aspartame from Himedia Laboratories, Magnesium stearate from Nice chemicals Ltd, Talc from Nihar traders pvt Ltd, Microcrystalline cellulose from Finar chemicals Ltd.

Buffer Preparation

Preparation of 0.2M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.218 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000mL of distilled water and mixed.

Preparation of 0.2M sodium hydroxide solution: Accurately weighed 8 gm sodium hydroxide pellets were dissolved 10 1000ml of distilled water and mixed.

Preparation of pH 6.8 Phosphate buffer: Accurately measured 250ml of 0.2M potassium
Dihydrogen otho phosphate and 112.5 ml 0.2M NaOH was taken into the 1000ml volumetric flask. Volume was made up to 1000ml with distilled water.

Pre formulation Studies

Pre formulation involves the application of biopharmaceutical principles to the physicochemical parameters of drug substance are characterized with the goal of designing optimum drug delivery system.

Drug-Excipients compatibility studies

Drug Excipients compatibility studies were carried out by mixing the drug with various excipients in different proportions (in 1:1 ratio were prepared to have maximum likelihood interaction between them) was placed in a vial, and closed with rubber stopper and sealed properly.

Analytical method development for Vilazodone

a) Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400nm against the reagent blank to fix absorption maxima. The λmax was found to be 241nm. Hence all further investigation were carried out at the same wavelength.

b) preparation of Standard graph in pH 6.8 phosphate beffer

100 mg of Vilazodone was dissolved in method 5ml , volumetric flask make upto 100ml of Phospate beffer of pH 6.8., form primary stock 10ml was transferred to another volumetric flask made up to 100ml with Phosphate buffer of pH 6.8, from this secondary stock was taken separately and made up to 10 ml with Phosphate buffer of pH 6.8, to produce 2,4,6,8 and 10µg/ml respectively. The absorbance was measured at 241nm by using a UV spectrophotometer.

Formulation Development

- Drug and different concentrations for super Disintegrates and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass mortar for 15 minutes.
- The obtained blend was lubricated with Magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 minutes.
- The resultant mixture was directly compressed into tablets by using puch of rotary tablet compression machine. Compression force was kept constant for all formulations.

Table 1: Formulation of Immediate Release tablets

Ingrediants	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Vilazodone	10	10	10	10	10	10	10	10	10	10	10	10
Cross Povidone	10	20	30	-	-	-	-	-	-	-	-	-
Crosscarmellose sodium	-	-	-	10	20	30	-	-	-	-	-	--
Sodium starch glycolate	-	-	-	-	-	-	10	20	30	-	-	-
Locust beam gum	-	-	-	-	-	-	-	-	-	10	20	30
Aspartame	3	3	3	3	3	3	3	3	3	3	3	3
Mg stearate	6	6	6	6	6	6	6	6	6	6	6	6
Talc	6	6	6	6	6	6	6	6	6	6	6	6
MCC	85	75	65	85	75	65	85	75	65	85	75	65
Total weight	120	120	120	120	120	120	120	120	120	120	120	120

Total weight of tablets = 120mg

RESULTS & DISCUSSION

Determination of λ_{max}

The prepared stock solution was scanned between 200-400 nm to determine the absorption maxima . It was found to be 241 nm.

Calibration curve of Vilazodone

The standard curve of Vilazodone was obtained and good correlation was obtained with R^2 value of 0.998, the medium selected was pH 6.8 phosphate buffer.

Table 2: Standard graph values of Vilazodone at 241nm in pH 6.8 phosphate buffer

Concentration (µg/ml)	Absorbance
0	0
2	0.144
4	0.307
6	0.464
8	0661
10	0.823

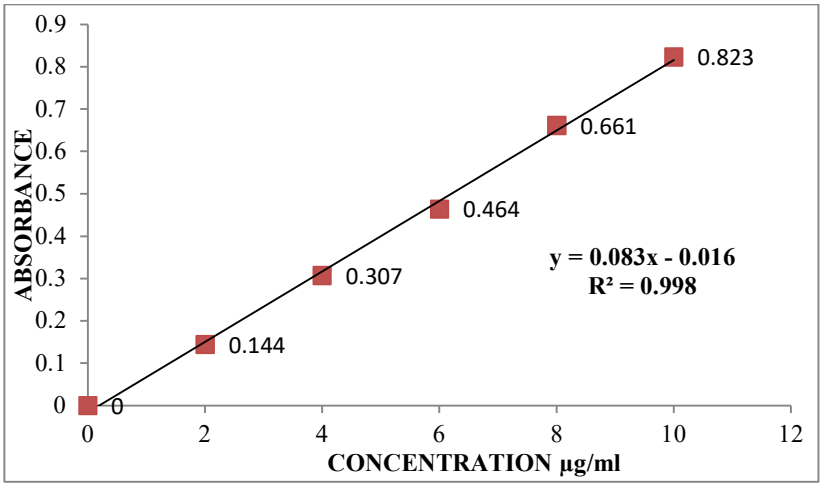

Fig 1: Standard curve of Vilazodone

Drug-Excipient compatibility studies by FTIR studies

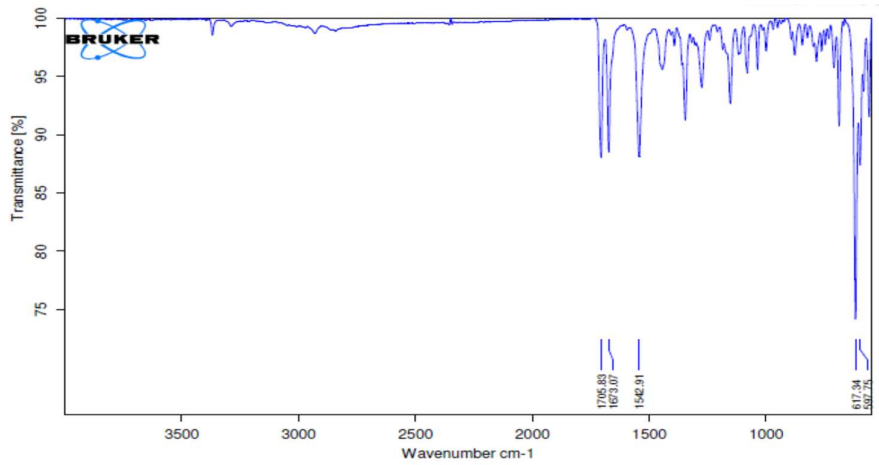

Fig 2: FTIR spectra of pure drug

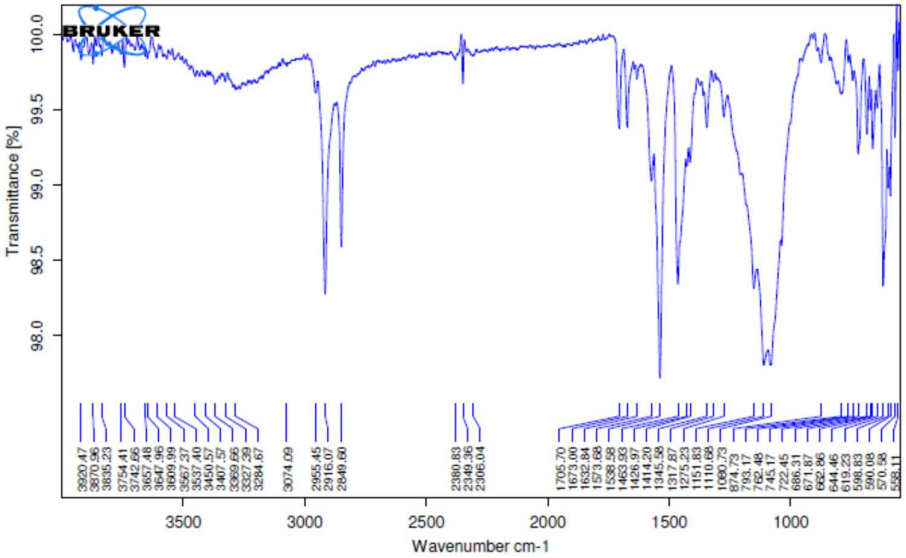

Fig 3: FTIR spectra of optimized formulation

Vilazodone was mixed with various proportions of excipients showed no colour change at the end of two months, providing no drug –excipient interactions.

Characterization of precompression blend

The precompression blend of Vilazodone were characterized with respect to angle of repose , bulk density, tapped density, Carr's index and Hausner's ratio. Angle of repose was less than 28˚, Carr's index values were less than 11 for the precompression blend of all the batches indicating good to fair floability and compressibility . Hausner's ratio was less than 1.25 foe all batches indicating good flow properties .

Table 3: Physical properties of precompression blend

Formulation code	Angle of repose (Θ)	Bulk density (gm/cm^3	Tapped density(gm/cm^3)	Carr's index (%)	Hausner's ratio
F1	30.48±0.02	0.515±1.47	0.610±0.01	15.57±1.4	1.18±0.01

F2	31.24±0.04	0.523±0.45	0.612±0.01	14.95±0.66	1.17±0.02
F3	30.86±0.03	0.518±0.25	0.613±0.02	15.35±0.3	1.18±0.01
F4	33.28±0.01	0.517±1.05	0.617±0.03	15.66±0.10	1.185±0.15
F5	32.19±0.02	0.525±0.99	0.611±0.01	14.91±0.33	1.175±0.03
F6	31.10±0.02	0.522±0.36	0.623±0.02	14.56±0.20	1.170±0.01
F7	39.23±0.01	0.527±0.45	0.618±0.01	16.53±1.6	1.198±0.21
F8	32.21±0.01	0.516±0.24	0.622±0.05	14.96±0.15	1.186±0.03
F9	33.54±0.04	0.522±0.25	0.615±0.04	15.64±0.26	1.175±0.02
F10	34.65±0.08	0.526±0.65	0.614±0.01	15.62±0.72	1.187±0.13
F11	36.27±0.06	0.522±0.34	0.621±0.04	14.87±0.35	1.185±0.06
F12	35.24±0.07	0.525±0.11	0.619±0.02	15.32±0.09	1.197±0.07

All the values represent n=3

Evaluation of tablets

Physical evaluation of Vilazodone Immediate release tablets

The results of the weight variation, hardness, thickness, friability, and drug content of tablets are given in table. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limit. The hardness of the tablets ranged from 2.28±86 - 2.96±68 kg/cm^2 and the friability values were < than 0.39±66 % indicating that the tablets were compact and hard. The thickness of the tablets ranged from 2.01±22 - 2.08±57. All the formulations satisfied the content of the drug as they contained 98-100% of Vilazodone and good uniformity in drug content was observed. Thus all physical attributes of the prepared tablets were found to be practically within control limits.

Table 4: Evaluation of Vilazodone Immediate release tablets

Formulation code	Average Weight (mg)	Thickness (cm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity(%)	*In Vitro* Disintegration time (Minutes)
F1	198.18	2.02±98	2.65±25	0.42±95	99.18	4.3
F2	196.68	2.05±84	2.84±96	0.56±64	97.27	4.4
F3	199.25	2.01±22	2.82±88	0.38±84	100.68	4.6
F4	197.37	2.06±31	2.90±76	0.51±72	101.85	4.8
F5	200.99	2.08.14	2.55±22	0.63±38	96.39	2.8
F6	201.76	2.02±96	2.28±86	0.54±99	99.47	3.3
F7	199.55	2.01±65	2.47± 65	0.48±57	98.25	4.1
F8	198.68	2.06±77	2.96±68	0.56±75	96.44	3.6
F9	199.91	2.08±57	2.87±46	0.39±66	98.19	3.1
F10	200.77	2.03±28	2.64±33	0.41±38	99.27	5.0
F11	202.38	2.04±71	2.94±75	0.46±24	100.69	5.2
F12	199.43	2.05±27	2.72±68	0.53±38	99.48	5.4

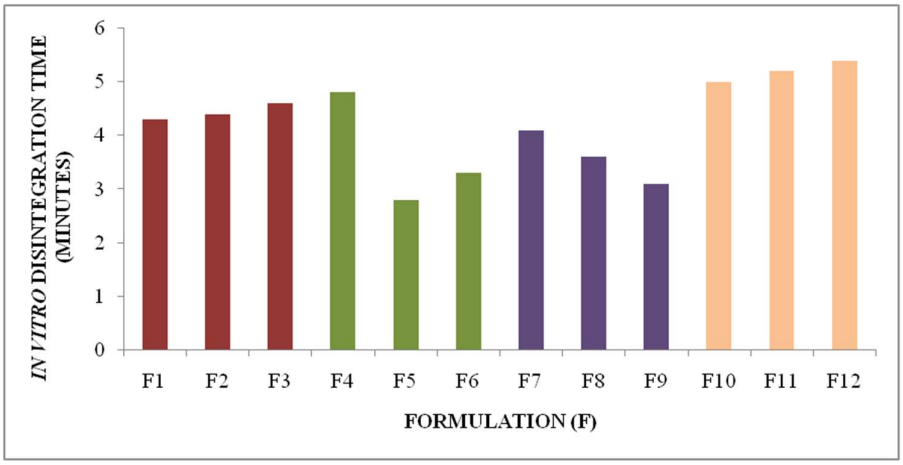

Fig 4 : *In vitro* disintegration time Graph

***I*n vitro Dissolution**

The drug release rate from tablets was studied using the USP type II dissolution test apparatus . The dissolution medium was 500 ml of pH 6.8 phosphate buffer at 50 rpm at a temperature of 37±0.5 ˚C . Samples of 5 ml were collected at different time intervals up to 1 hr and has analyzed after appropriate dilution by using UV spectrophotometer at 241nm

Table 5: *I*n vitro data for formulation F1- 12

TIME (MINUTES)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
5	16.28	12.26	15.33	18.12	18.15	22.28	20.48	22.71	24.37	20.85	20.22	18.45
10	39.42	25.38	27.57	27.38	34.93	34.58	28.63	31.94	36.39	33.62	28.31	36.69
15	43.15	39.99	45.36	39.27	47.69	45.35	37.28	42.37	45.47	43.68	36.18	45.76
20	57.75	47.62	59.75	52.85	62.26	64.88	44.94	48.54	52.69	55.25	48.85	60.54
25	64.74	69.75	68.33	66.85	74.88	72.74	62.22	63.33	79.66	68.99	55.91	68.37
30	72.28	75.31	79.18	78.43	96.57	87.63	70.99	86.27	93.54	84.14	76.88	72.41

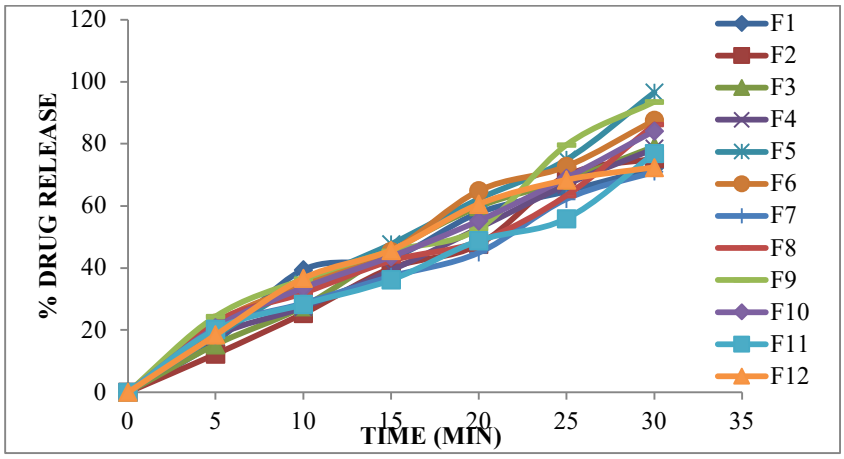

Fig 5: *In Vitro* dissolution data for formulations F1-F12

Among all the formulations F5 formulation containing drug and explotab showed good result that is 96.57 % in 30 minutes, at the concentration of 20 mg and F5 Formulation showed Less Disintegration time (2.8Minutes). Hence from all the formulations it is evident that F5 formulation is the better formulation.

CONCLUSION

In the present study, Vilazodone 10 mg tablets have been formulated and developed using direct compression technique, to provide a safe, highly effective method for treating severe Depression while reducing undesirable adverse effects. The results suggest that suitably formulated immediate release tablets of Vilazodone with a superdisintegrants (Cross Povidone, Crosscarmellose sodium, Sodium starch glycolate and Locust beam gum) can be achieved. Pre formulation studies of Vilazodone Were performed. The FTIR analysis revealed that the superdisintegrants and excipients used were compatible with Vilazodone. Immediate release tablets Vilazodone is to be prepared by direct compression technique using superdisintegrants namely Cross Povidone, Crosscarmellose sodium, Sodium starch glycolate, Locust beam gum. Among all the formulations, formulation containing Crosscarmellose sodium as a superdisintegrants is fulfilling all the parameters satisfactorily. It has shown excellent(Less) *in vitro* disintegration compared to other superdisintegrants. A part from all formulations F5 formulation showed maximum drug release 96.57 % at end of 30 min.

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