INTERNATIONAL JOURNAL OF PHARMACY AND ANALYTICAL RESEARCH

ISSN:2320-2831

IJPAR |Vol.7 | Issue 3 | July - Sep -2018
Journal Home page: www.ijpar.com

Research article *Open Access*

Formulation and evaluation of paliperidone HCL oral disintegrating tablets

Mohit Kumar, Vandana Arora (Guide)

Department of Pharmacy, lloyd institute of management & technology, Greater Noida

***Corresponding Author: Mohit Kumar**
Email: mohit18789@gmail.com

ABSTRACT

Paliperidone HCL is atypical antipsychotic agent which blocks D2, 5HT2, α2, α1 and H1 receptor. It is derivative of Resperidone having better efficacy in treatment of Schizophrenia. When compared with other atypical antipsychotics (eg. Chlorpromazine), it having broad spectrum activity and reduces both positive and negative symptoms of Schizophrenia. It undergoes an extensive hepatic first pass metabolism leads to low oral bioavailability (28%). ODT can overcome this problem through improving its bioavailability with an immediate drug release.In the present work, Oral disintegrating tablets of Paliperidone HCL were prepared by direct compression method using superdisintegrants such as Crosspovidone lycoat, and Tulsion. Paliperidone HCL has very long half hife and less bioavailability, so for enhancing the bioavailability of the drug it was formulated as a oral disintegrating tablet. The dispersion time of tablets were reduced with increase 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 99.45% of the drug in 30 min.

Keywords: Paliperidone HCL, Crosspovidone, Lycoat, and Tulsion, Oral disintegrating tablets.

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. 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. 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 One negative aspect of solid oral dosage forms is dysphagia (difficulty in swallowing) and chewing in some patients particularly in geriatric and paediatric patients. 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.

Paliperidone HCL is atypical antipsychotic agent which blocks D2, 5HT2, α2, α1 and H1 receptor. It is derivative of Resperidone having better efficacy in treatment of Schizophrenia. When compared with other atypical antipsychotics (eg. Chlorpromazine), it having broad spectrum activity and reduces both positive and negative symptoms of Schizophrenia. It undergoes an extensive hepatic first pass metabolism leads to low oral bioavailability (28%). ODT can overcome this problem through improving its bioavailability with an immediate drug release.

In the present work, Oral disintegrating tablets of Paliperidone HCL were prepared by direct compression method using superdisintegrants such as Crosspovidone lycoat, and Tulsion. Paliperidone HCL has very long half hife and less bioavailability, so for enhancing the bioavailability of the drug it was formulated as a oral disintegrating tablet.

MATERIALS AND METHODS

Paliperidone HCL was procured from Aurbindo pharma Ltd., Hyd. Tulsion,cross povidone,Lycoat, Microcrystalline cellulose (Avicel),Talc, Magnesium stearate, were purchased from Signet Chemical Corp., Mumbai.

FORMULATION OF ORAL DISINTEGRATING TABLETS OF PALIPERIDONE HCL: 29

Oral disintegrating tablets of Paliperidone HCL 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 (100 mg).

EVALUATION OF ORAL DISINTEGRATING TABLETS

Preformulation studies

Angle of Repose, Bulk Density, Tapped Density, Carr's Index, Hausner's ratio were evaluated to determine the flow properties.

Shape of Tablets

Directly compressed tablets were examined under the magnifying lens for the shape of the tablet.

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.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm2. Three tablets were randomly picked and hardness of the tablets was determined.

Friability test

The friability of tablets was determined by using electrolab friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (WI) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. 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.

Weight Variation Test

Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. A little variation was allowed in the weight of a tablet according to U.S. Pharmacopoeia.

Test for Content Uniformity

Tablet containing 3mg 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 236nm. The concentration of Paliperidone HCL was obtained by using standard calibration curve of the drug. Drug content studies were carried out in triplicate for each formulation batch.

In vitro Dispersion Time

Tablet was added to 10ml of distilled water at 37±0.5^{0}C. Time required for complete dispersion of a tablet was measured.

In vitro Dissolution Study

In vitro dissolution of Paliperidone HCL Oral disintegratingtablets 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) were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 236nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent Paliperidone HCL released was calculated and plotted against time.

RESULTS & DISCUSSION

The flow properties of polymer and drug were good.FT-IR studies revealed that there is no chemical interaction between Paliperidone HCL 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 evaluations 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). F1 formulation shows maximum drug release at the end of 95.5% at the end of 30mins. Whereas F2 formulation shows maximum drug release at the end of 98.07% at the end of 30mins, while F3 formulation shows maximum drug release at the end of 97.4% at the end of 25mins.

While the Formulations containing lycoat as super disintegrant (F4-F6) showed 92.7, 97.19, 96.66% of drug release respectively at the end of 30, 25 and 20 mins respectively.

Wheras the Formulations containing Tulsion as super disintegrant (F7-F9) showed 99.78, 98.91, and 99.45% of drug release respectively at the end of 30, 25 and 20mins.

From the in vitro dissolution studies it was observed that the increase in the super disintegrant concentration proportionally decreases the time taken for the dissolution.

It was observed from the results that, formulations containing Tulsion as super disintegrant showed maximum dissolution rate 99.45% of drug release in F9 in 20 min.

This shows that effectiveness of superdisintegrants are in the order of Tulsion> Lycoat > Cross povidone. The concentration of superdisintegrants in the formulations also increased the dissolution rates. It was observed from the results that, formulations containing Tulsion as super disintegrant showed maximum dissolution rate 99.45% of drug release in F9 in 20 min.

From the present study, it may be concluded that the Oral disintegrating tablets of Paliperidone HCL can be prepared by direct compression method using superdisintegrants. Among Crosspovidone, lycoat, and Tulsion, Tulsion was found to be the best among the superdisintegrants. The highest drug release of F9 is 99.45% of the drug in 20 min.

TABLE.1: Formulation table of Paliperidone HCL Oral Disintegrating Tablets:

Ingredients(mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Paliperidone HCL	3	3	3	3	3	3	3	3	3
Cross povidone	3	-	-	3	-	-	3	-	-
lycoat	-	5	-	-	5	-	-	5	-

Tulsion	-	-	7.5	-	-	7.5	-	-	7.5
Aspartame	12	12	12	12	12	12	12	12	12
Mannitol	30	30	30	30	30	30	30	30	30
M.C.C	Q.S	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Magnesium stearate	6	6	6	6	6	6	6	6	6
Talc	6	6	6	6	6	6	6	6	6
Total weight(mg)	100	100	100	100	100	100	100	100	100

Table: Pre Compression parameters

FC	Tapped density	Bulk density	Angle of Repose	Carr's Index	Hausner's rat
F1	0.48±0.01	0.56±0.015	26.38±0.30	14.28±1.02	1.16±0.06
F2	0.46±0.01	0.52±0.02	27.42±0.39	11.53±1.26	1.13±0.03
F3	0.42±0.04	0.48±0.01	24.02±0.68	12.58±2.08	1.14±0.05
F4	0.46±0.02	0.54±0.015	26.26±0.96	14.81±1.28	1.12±0.02
F5	0.52±0.6	0.60±0.03	30.68±0.73	13.33±1.86	1.17±0.04
F6	0.49±0.2	0.58±0.006	29.26±0.36	15.51±1.96	1.18±0.05
F7	0.42±0.08	0.48±0.04	24.02±0.68	12.58±2.08	1.14±0.05
F8	0.52±0.12	0.60±0.03	30.68±0.73	13.33±1.86	1.17±0.04
F9	0.42±0.06	0.48±0.01	24.02±0.52	12.58±1.08	1.14±1.05

FC	Avg. Wt (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Disintegration time(secs)	Drug content (%)
F1	100.12	3.34	3.41	0.23	86	87.95
F2	101.97	3.12	3.69	0.41	63	90.55
F3	100.56	3.30	3.97	0.77	47	93.4
F4	100.56	3.20	3.55	0.54	79	96.7
F5	99.23	3.33	3.36	0.63	58	82.9
F6	102.78	3.45	3.64	0.70	39	89.52
F7	101.89	3.36	3.40	0.19	71	93.6
F8	102.55	3.55	3.39	0.35	53	98.34
F9	98.41	4.02	3.77	0.48	30	99.89

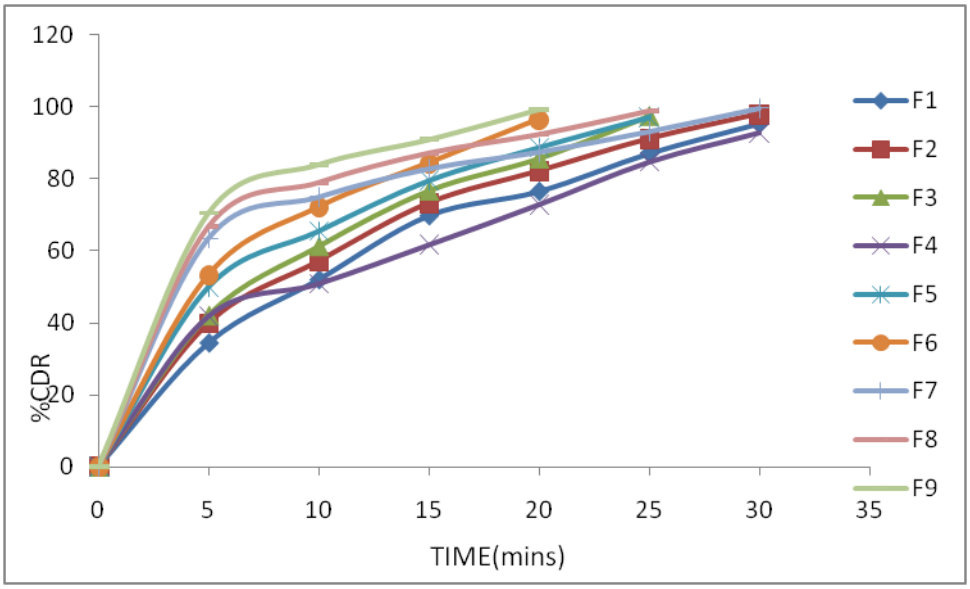

Fig1: Cumulative percentage drug release of core formulation F1 – F9

CONCLUSION

In the present work, Oral disintegrating tablets of Paliperidone HCL were prepared by direct compression method using superdisintegrants such as Crosspovidone lycoat, and Tulsion. From the results obtained, it can be concluded that Among Crosspovidone, lycoat, and Tulsion, Tulsion was found to be the best among the superdisintegrants. The highest drug release of F9 is 99.45% of the drug in 20 min.

REFERENCES

[1]. Seager H. Drug delivery products and the zydis fast dissolving dosage forms. J. Pharm. Pharmacol. 50, 1998, 375-382.
[2]. Chang RK, Guo X, Burnside BA, Couch RA. Fast dissolving tablets. Pharm. Tech. 24(6), 2000, 52-58.
[3]. Dobetti L. Fast melting tablets: Developments & Technologies. Pharm. Tech. 44(1), 2001.
[4]. Kuchekar BS, Aruagam V. Fast dissolving tablets. Indian J. Pharm. Edu. 35, 2001, 150-152.
[5]. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. Pharma. Times, 35, 2003, 7-9.
[6]. Bradoo R, Shahani S, Poojary S, Deewan B, Sudarshan S. An observer blind, randomized controlled clinical trial to compare the onset of action, efficacy and safety of cetrizine flash tablets with oral Loratidine and cetrizine conventional tablets in allergic rhinitis. JAMA India, 4(10), 2001, 27-31.
[7]. European Directorate for quality of medicines (www.pheur.org) Pharmeuropa, 10(4), 1998, 547.
[8]. Udupa N, Venkatesh, Srinivas M, Venugopal K. Nimesulide dispersible tablets from 'Direct compression' method. 38(4), 2001, 208-10.
[9]. Luca Dobetti. Fast melting tablets: Developments & Technologies. Pharmaceutical Technology, 11, 2001.
[10]. Reddy LH, Ghosh B, Rajneesh. Fast dissolving drug delivery systems: A review of the literature. Indian J. Pharm. Sci, 7, 2002, 331-336.
[11]. Lindgreen S, Janzon L. Dysphagia: Prevalence of swallowing complaints and clinical findings. Med. Clin. North Am. 77, 1993, 3-5.