Research Article

Formulation and Evaluation of Naratriptan Hydrochloride Oral Disintegrating Tablets by Using Direct Compression Method

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ABSTRACT

The present study deals with the formulation and evaluation of Oral disintegrating tablets (ODT) of Naratriptan, a typical Antimigraine drug which is highly appropriate as it has ease of administration for mentally ill, disabled and uncooperative patients. ODTs have better patient acceptance, compliance, improved biopharmaceutical properties and efficacy compared with conventional oral dosage forms as they quickly disintegrate/dissolve/disperse in saliva. In the present research work, an attempt was made to design ODTs by addition of super disintegrants. Experimental design was run with four batches containing different concentration of super disintegrants. The optimization results revealed that the effect of super disintegrants result in good disintegration profile of 32sec (Ideal ODT should disintegrate within 1min), dissolution profile shows that more than 90% of the drug releases within 10 minutes, and good dispersion pattern. Crospovidone (8%) and Sodium starch glycolate (6%) are better super disintegrants. The formula F4 possesses good disintegration and dissolution profile with additions of super disintegrants. The prepared tablets by direct compression using super disintegrants pass all the quality control tests and FTIR studies reveal that there is no interaction between drug and excipients. This method can also be used to prepare ODTs of antiemetics, antiallergics, and cardiovascular agents etc which needs rapid onset of action. Thus, faster disintegration and dissolution of Naratriptan ODT may give better therapy for the treatments of Migraine.

Keywords: Oral Disintegrating Tablets, Naratriptan, Super disintegrants, Direct compression.

INTRODUCTION

Oral drug delivery is the largest and oldest segment of the total drug delivery market. It is the fastest growing and most preferred route for drug administration. Oral ingestion has been the most convenient and commonly employed route of drug delivery[1,2]. Moreover, the delay in onset of action by this route also calls for a delivery system which could provide a rapid onset and a quick relief. For the last two decades there has been an enhanced demand for more patient-compliant dosage forms. The demand for their technology also increased drastically. Orally disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts. Over a decade, the demand for development of orally disintegrating tablets (ODTs) has enormously increased as it has significant impact on the patient's compliance. Orally disintegrating tablets offer an advantage for population who has difficulty in swallowing. It has been reported that Dysphasia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting and motion sickness complications[2]. To overcome this weakness, scientists have developed innovative drug delivery system known as orally disintegrating tablets (ODTs). These are novel types of tablets disintegrates/dissolve/disperse in saliva. Their characteristic advantages such as administrating without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. Based on Migraine is a chronic, episodic, neurological disorder, which usually begins in childhood, adolescence or early adult life, characterized by unilateral headache often accompanied by nausea and vomiting, gastrointestinal disturbance and extreme sensitivity to light and sound. It affects 10-20% of the population during the most productive periods of their working lifes, women are affected up to four times more often than men. Naratriptan hydrochloride is approved for acute oral migraine therapy.

The drug is a selective agonist of 5 hydroxytryptamine1 (5-HT1) receptors, so it used in treatment of migraine attack and as well as in nausea, vomiting and headache[3,4].

MATERIALS AND METHODS

Materials

Naratriptan was obtained as gift sample from Natco pharma, sodium starch glycolate, Crospovidone, microcrystalline cellulose were obtained from SD fine chemical Ltd, Mumbai.

Method of Preparation

The naratriptan oral disintegrating tablets were prepared by direct compression technique. For each tablet formulation drug mannitol, sodium starch glycolate, cross povidone, aspartame and diluents were blended homogeneously for 8 min followed by addition of magnesium stearate. The resultant mixture was compressed into tablets in 8mm die cavities using Riddhi mini tablet press punching machine[5,6,7]. Nine formulations

were prepared by changing the amount of the ingredients.

Table 1: Formulation design of Naratriptan HCL oral disintegrating tablets

S. No.	Formulation code	Ratio of drug and S.D
1.	F1	1:1 (DRUG : CP)
2.	F2	1:2 (DRUG : CP)
3.	F3	1:3 (DRUG : CP)
4.	F4	1:4 (DRUG : CP)
5	F5	1:1 (DRUG : SSG)
6	F6	1:2 (DRUG : SSG)
7	F7	1:3 (DRUG : SSG)
8	F8	1:4 (DRUG : SSG)
9	F9	Without S.D

*S.D-super disintegrant, *C.P-cross povidone,*SSG-Sodium Starch Glycolate

Evaluation of Tablets

All the formulations were evaluated for the following parameters.

Weight variation test

20 tablets from each formulation were randomly picked up and weighed individually and the average weight was calculated. The individual weights were then compared with the average weight.

Friability

Ten tablets were weighed and placed in a Roche friabilator and rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated.

Hardness

The hardness of core tablets was measured using Monsanto hardness tester. A total of five tablets from each formulation were taken for the study and the average of the three is reported.

Uniformity of drug content

Drug content uniformity was determined by randomly selecting 5 tablets were powdered. The quantity equivalent to single dose of the drug was dissolved in HCL buffer solution, pH 0.1N HCL for 5 hours with occasional shaking and diluted to 50 ml with buffer. After filtration to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with the buffer[7,8]. The absorbance was measured at the required λmax 226 nm using a UV visible spectrophotometer. The experiments were carried out in triplicate for all formulations and average values were recorded.

Table 2: Formulation chart of Naratriptan HCL oral disintegrating tablets

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Naratriptan Hcl	2	2	2	2	2	2	2	2	2
Mannitol	50	50	50	50	50	50	50	50	50
Avicel pH 102	39.5	37.5	35.5	33.5	39.5	37.5	35.5	33.5	39.5
Cross povidone	2	4	6	8	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	-	2	4	6	8	-
Aspartame	5	5	5	5	5	5	5	5	5
Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Total weight (mg)	100	100	100	100	100	100	100	100	100

Drug-excipient Compatibility Studies

Fourier transform infra red spectroscopy (FT-IR)

In order to evaluate the integrity and compatibility of the drug in the formulation, drug-excipient interaction studies were performed. Pure drug and optimized formulations were analyzed by Fourier transform infra-red (FTIR) spectroscopy[9,10]. FTIR spectra of pure drug and its formulations were obtained by a FT-IR Bruker spectrophotometer. The samples were scanned from 400 to 4,000 cm^{-1} wave number.

Disintegration Time

The *in vitro* disintegration time was determined using disintegration test apparatus. Six tablets were placed in each of the six tubes of the apparatus. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Wetting Time

Wetting time was measured using a simple procedure. a piece of tissue paper cut circularly (6.5 cm diameter) and placed on a petric dish containing 6ml of water at room temperature. A tablet is placed on the surface of the tissue paper and the time required for complete wetting of the tablet was noted.

Water Absorption

A piece of tissue paper folded twice was placed in a small petridish (internal diameter = 6.5 cm) Containing 6 ml of water[11]. A tablet was placed on the paper, and allowed to wet completely. The wetted tablet was removed and reweighted. Water absorption was determined.

In-vitro dissolution study

The release rate of Naratriptan Hcl from oral disintegrating tablets was determined using *United States Pharmacopeia (USP)* 24 Dissolution Testing Apparatus II (paddle method). The dissolution test was performed using 500 ml of pH 0.1N HCL buffer, at 37±0.5°C and 50 rpm. A sample (5 ml) of the solution was with-drawn from the dissolution apparatus and the samples were replaced with fresh dissolution medium. The samples were diluted to a suitable concentration with pH 0.1 N HCL buffer[12,13]. Absorbance of these solutions was measured at λmax 226 nm using UV-Visible double-beam spectrophotometer.

RESULTS AND DISCUSSION

Drug-polymer interaction study

From the spectrum of Naratriptan Hcl[14], physical mixture of Naratriptan Hcl and polymers observed that all characteristic peaks of Naratriptan Hcl were present in the combination spectrum, thus indicating compatibility Naratriptan Hcl and superdisintegrant.

In-vitro drug release studies

The in-vitro drug release studies of Naratriptan hydrochloride oral disintegrating tablets were conducted in pH 0.1N HCL buffer for 15 min[15,16].

As the concentrations of cross povidone (superdisintegrant) increases in the formulations F1-F4 the percentage drug release was also found to be increased for these formulations as 79.8%, 86,44%, 89.27%, and 96.61% respectively (Fig:5).

Whereas the concentrations of Sodium Starch Glycolate (superdisintegrant) increases in the formulations F5-F8 the percentage drug release was also found to be increased for these formulations as 75.71%, 82.77%, 85.31%, and 87.01% respectively (Fig.5).

Without super disintegrants the percentage drug release was found to be 48.54% respectively.

F4 batch is selected as the optimized batch compared with other batches. And this optimised batch was compared with marketed formulation and percentage drug release found to be 94.53% respectively. It was revealed that the optimised formulation F4 shows better results than that of marketed formulation **(Table. 3&4)**

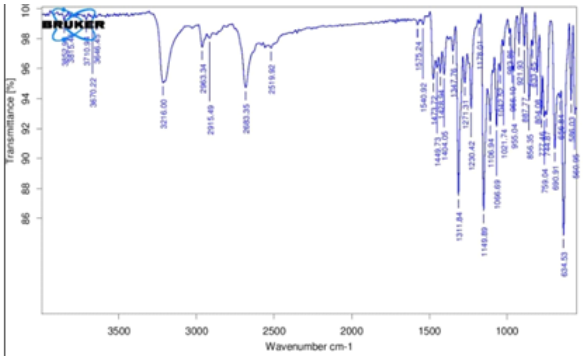

Figure 1: IR Spectrum of Naratriptan Hcl

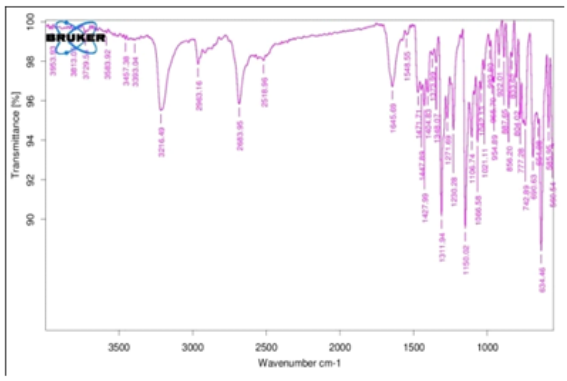

Figure 2: IR Spectrum of mixture of Naratriptan and cross povidone

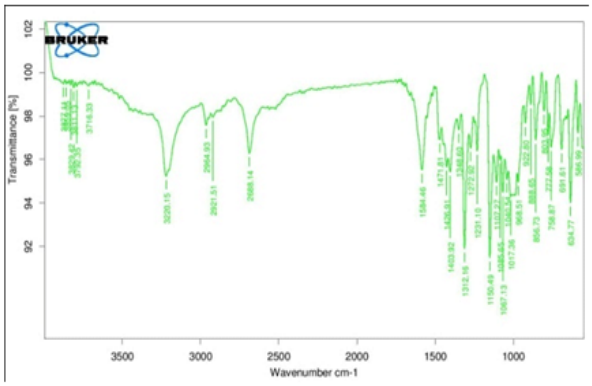

Figure 3: IR Spectrum of mixture of Naratriptan Hcl

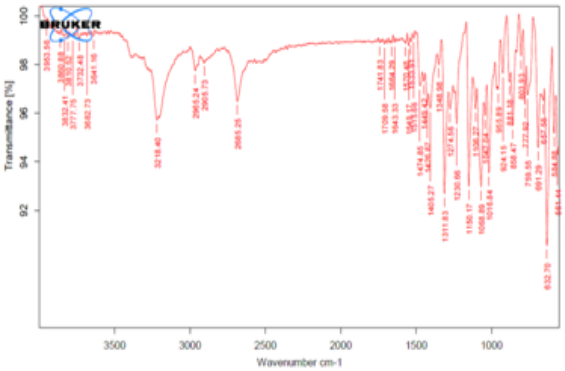

Figure 4: IR spectrum of Naratriptan HCl and sodium starch glycolate and mannitol

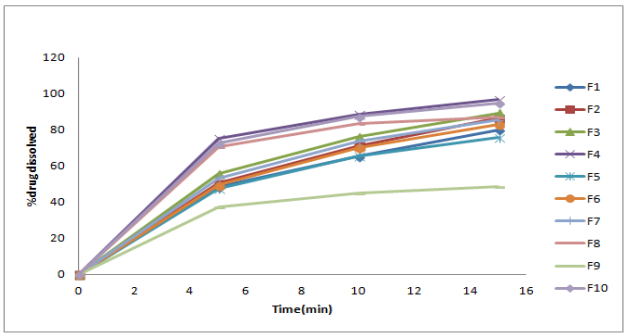

Figure 5: Comparative *in vitro* release profile of F1 toF10 and Marketed formulation.

Table 3: Post-Compression Parameters of Designed Formulations.

Formulation	Weight Variation (%)	Hardness (kg/cm^2)	Friability (%)	% Drug content	Wetting time(sec)	Water absorption Ratio	Disintegration time (sec)
F1	2.35	3	0.678	89.92	23	68.7	58
F2	2.65	3.5	0.420	92.03	21	62.2	51
F3	2.78	4	0.399	95.56	20	71.7	45
F4	3.12	3.5	0.606	87.95	18	79.4	32
F5	3.56	3	0.455	93.29	38	62.3	150
F6	3.26	4	0.504	95.0	35	59.8	68
F7	4.5	2.5	0.367	97.25	33	55.3	60
F8	2.3	2.5	0.84	98.81	31	52.9	54
F9	2.35	3	0.359	93.75	41	48.5	180

Table 4: Drug release kinetics data

TIME (min)	% Drug dissolved									
	F1	F2	F3	F4	F5	F6	F7	F8	F9	Marketed Formulation (F10)
0	0	0	0	0	0	0	0	0	0	0
5	48.5	50.56	55.93	74.86	47.74	49.43	53.39	70.62	37.29	72.45
10	65.42	71.19	75.99	87.29	63.56	70.34	73.16	83.33	44.35	87.26
15	79.8	86.44	89.27	96.61	75.71	82.77	85.31	87.01	48.59	94.53

CONCLUSION

From the results of the study, we conclude that formula F4 (Mannitol, Crospovidone, Micro crystalline cellulose, Magnesium stearate, Aspartame.) processes good disintegration and dissolution profile with additions of super disintegrants (Crospovidone, Sodium Starch Glycolate). On comparing with their respective batches the prepared tablets by DC they passing all the quality control test viz., friability, disintegration time dispersion time, wetting time. FTIR studies reveal that there is no interaction between drug and excipients[17]. The addition of super disintegrants method can be used to prepare ODTs of several categories of drug such as antiemetics, antiallergics cardiovascular agent's analgesic neuroleptics which need rapid onset of action. Faster disintegration of orally disintegrating tablets of above mentioned pharmacological categories improves the availability of drug for absorption in a faster rate. This may enhance the bioavailability. Faster disintegration and dissolution of Naratriptan ODT may give better therapy for the treatment of Migraine.

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