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Formulation and evaluation of fast dissolving tablets of Chlorpromazine HCl

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Abstract

Chlorpromazine HCl is a potent anti-emetic, act by blocking D_2 receptors in the Chemoreceptor trigger zone (CTZ), and antagonize apomorphine induced vomiting. In the present study an attempt has been made to prepare fast dissolving tablets of Chlorpromazine HCl in the oral cavity with enhanced dissolution rate. The tablets were prepared with five superdisintegrants eg: Sodium starch glycolate , Crospovidone ,Croscarmellose, L-HPC, Pregelatinised starch , The blend was examined for angle of repose, bulk density, tapped density , compressibility index and hausners ratio. The tablets were evaluated for hardness, friability, disintegration time, dissolution rate, drug content, and were found to be within 1 min. It was concluded that the fast dissolving tablets with proper hardness, rapidly disintegrating with enhanced dissolution can be made using selected superdisintegrants.

Key Words: Fast dissolving tablets, Chlorpromazine Hcl, Superdisintegrants.

Introduction

Many patients, especially elderly find it difficulty in swallowing tablets, capsules ,thus do not comply with prescription , which results in high incidence of non-compliance and in effective therapy convince and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems[1]. Fast dissolving tablets is one of such example, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva. Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms ideal for pediatric and geriatric patients and rapid onset of action[2].

Chlorpromazine HCl is chemically {3-(2-chlorophenothiazin-10yl)} dimethylamine Hcl. A potent anti-emetic, act by blocking D_2 receptors in the Chemoreceptor trigger zone (CTZ), and antagonize apomorphine induced vomiting. In the present study, an attempt had been made to prepare fast dissolving tablets of Chlorpromazine HCl in the oral cavity with enhanced dissolution rate & hence improved patient compliance[3].

Mareials and Methods

Chlorpromazine Hcl was obtained as gift sample sodium starch glycolate, Crosscarmellose sodium, crospovidone, microcrystalline cellulose, L-HPC, Pregelatinised starch were produced from FMC, Ahmedabad and all other chemicals/ Solvents used were of analytical grade.

Preparation of Mixed Blend of Drug and Excipients

All the Ingredients were passed through mesh 60. Required quantity of each ingredient was taken for each specified formulation (depicted in the table II) and all the ingredients were co grind in a mortar and pestle. The powder blend was evaluated for flow properties such as Bulk density, Tapped density, Compressibility index, Hausner ratio.

Compression of Tablets

The ingredients depicted in Table I (except magnesium stearate) were mixed homogenously and co grind in a mortar and pestle .Finally magnesium stearate was added and mixed for 5 min. The mixed blend of drug and excipients was compressed using cadmach single punch tablet punching machine to produce convex faced tablets weighing 150 mg each with a diameter of 8mm. a minimum of 50 tablets were prepared for each batch.

Table 1: Composition of nine compressed tablets of different formulations.

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Chlorpromazine HCl	10	10	10	10	10	10	10	10	10
2	Microcrystalline cellulose	61	58	61	58	61	58	55	58	54
3	Mannitol	69	69	69	69	69	66	68	69	68
4	Crospovidone	2	5	--	--	--	--	--	--	--
5	Croscarmellose sodium	--	--	2	5	--	--	--	--	--
6	Sodium starch glycolate	--	--	--	--	2	8	--	--	--
7	L-HPC	--	--	--	--	--	--	9	--	--
8	Pregelatinized starch	--	--	--	--	--	--	--	5	10
9	Aerosil	2	2	2	2	2	2	2	2	2
10	Aspartame	4	4	4	4	4	4	4	4	4
11	Magnesium stearate	2	2	2	2	2	2	2	2	2
12	Strawberry flavor	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
	Average weight	**150 mg**	**150 mg**	**150 mg**	**150 mg**	**150 mg**	**150 mg**	**150 mg**	**150 mg**	**150 mg**

Physical characterization of fast dissolving tablets

The thickness was measured using vernier caliper. Weight variation was conducted as per specifications. Hardness test was performed using a mansanto hardness tester. Friability was performed using a roche friability testing apparatus. The physical characteristics of tablets were showed in table 2.

Estimation of drug content in fast dissolving tablets

Powder one tablet, shake 1 ml of dilute Hcl and 401 ml of water for 15 min, and add sufficient water to produce 100 ml and mix. Centrifuge about 15 ml and to 10 ml of the clear, supernatant liquid add 2 ml of 1M Hcl and sufficient water to produce a solution containing about 0.005 % w/w concentrated Hcl .Measure the absorbance of the resulting solution at the max. at about 254 nm. Calculate the content of $C_{17}H_{19}Cl\ N_2S$ .HCl in the tablet.

***In vitro* Dissolution studies**

The *in vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (Electrolab, India) .The dissolution medium consisted of phosphate buffer (pH 6.8).An amount of 900 ml of the dissolution fluid was used at 37±0.5 ºc with stirring speed of 50 RPM Samples were withdrawn at 1, 2, 4, 6, 8, and 10 minutes time intervals by replacing with same dissolution medium and samples were analyzed by measuring the absorbance at 254 nm by UV spectrophotometer.

Table 2: Evaluation data of compressed tablets of different formulations.

S.No	Evaluation	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Weight variation (mg)	150 ±2	150± 1	151 ±1	150 ±2	150 ±1	149± 2	150±2	151± 1	150± 2
2	Thickness (mm)	3.53 ± 0.08	3.49± 0.04	3.51 ± 0.04	3.53 ± 0.02	3.76 ± 0.03	3.63± 0.02	3.57± 0.06	3.62± 0.05	3.57± 0.05
3	Friability (%)	0.60	0.48	0.64	0.57	0.62	0.51	0.63	0.56	0.51
4	Hardness ($Kg/cm^{2)}$)	3.3± 0.2	3.6± 0.2	3.1± 0.4	3.4± 0.2	3.6± 0.4	3.3± 0.3	3.5± 0.4	3.4± 0.3	3.6± 0.3
5	Disintegration time (sec)	26± 1.15	17± 2.1	32± 1.16	23± 2.15	41± 2.27	30± 1.19	50± 2.41	57± 3.16	49± 2.18
6	Content uniformity (%)	96.1 ± 0.8	99.1± 1.3	93.2 ± 1.6	97.4 ± 2.1	94.3 ± 2.4	96.1± 1.31	95.1± 1.31	94.3± 1.1	95.5± 1.9
7	Assay(%)	98.1	99.3	97.3	98.1	96.9	97.1	93.2	94.3	95.2

Results and Discussion:

Nine formulations of Chlorpromazine Hcl were prepared with varying concentration of five superdisintegrants: Sodium starch glycolate, Crospovidone, Crosscarmellose, L-HPC, Pregelatinised starch and microcrystalline cellulose, and mannitol were used as diluents (Table 1). For each formulation, blend of drug and excipients were prepared and evaluated for various parameters as explained earlier. The powder blend was compressed using direct compression technique. Bulk density, was found in the range of 0.390-0.511 g/cm^3 and the tapped density between 0.0450-0.603 $g/cm^{3.}$ Using these two density data hausner's ratio and compressibility index was calculated. The powder blends of all formulations had hausner's ratio less than 1.25 indicates better flow property. The compressibility index was found between 13.3-19.1 which indicates a fairly good flowbility of the powder blend. The good flowability of the powder blend was also evidenced with angle of repose (range of 26-31) which is below 40^o indicating good flowability. Tablets were prepared using direct compression technique. Since the powder material was free flowing, tablets were obtained of uniform weight due of uniform die fill, with acceptable weight variations as per I.P. The drug content was found in the range of 93.2 % - 99.1% (acceptable limit) and the hardness of the tablets were fond below 1% indicating a good mechanical resistance of the tablets, and the parameters were found well within the specified limit for uncoated tablets. The *invitro* disintegration time (DT) of the tablets was found to less than 60 sec. Tablets containing 5% Pregeatinised starch (F8) should Disintegration time of 57 sec. While rest of the tablets around 30 sec only. All the formulations showed enhanced dissolution rate as compared to pure Chlorpromazine Hcl, the results were shown in Table 2.The maximum increase in the dissolution rate was observed with 5% Crospovidone

amongst the superdisintegrants. The order of enhancement of the dissolution rate with various superdisintegrants was found to be Crospovidone>Crosscarmellose>Sodium starch glycolate>L-HPC>Pregelatinized starch. The preparation process in direct compression tablets includes co grinding of all the excipients before compression, resulting the increase in the solubility due to the reduction in the effective particle size of the drug following increase in the wetting of drug particle by the excipients and improved dissolution of drugs. It was concluded that fast disintegrating tablets of Chlorpromazine Hcl. can be successfully prepared selected superdisintegrants in order to improve disintegrants/dissolution of the drug in oral cavity & hence better patient's compliance & effective therapy.

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