

ORIGINAL RESEARCH ARTICLE

Formulation and Evaluation of Mouth Dissolving Tablets of Chlorpromazine Hcl

Amitesh Kumar Palo*¹, Satyendra Kumar¹, A Asish Kumar Patro¹, Abhilash Panda¹,
Arun Kumar Dash²

¹College of Pharmaceutical Sciences, Mohuda, Berhampur, Odisha.

²Royal College of Pharmacy and Health Sciences, Andhapasara Road, Berhampur, Odisha.

Received 20 May 2011; Revised 05 Aug 2011; Accepted 12 Aug 2011

ABSTRACT

Chlorpromazine HCl is a potent anti-emetic, act by blocking D2 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 noncompliance 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 Hydrochloride is chemically {3-(2-chlorophenothiazin-10yl)} dimethylamine Hydrochloride. It is a potent anti-emetic, which acts by blocking D2 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 Hydrochloride with enhanced dissolution rate & hence improved patient compliance^[3].

MATERIALS AND METHODS

Chlorpromazine Hydrochloride 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. Mannitol, Camphor, Sodium saccharine, Ammonium Bicarbonate, Talc, Polyvinyl Pyrolidone used were procured from Loba Cheme.

Preparation of Mixed Blend of Drug and Excipients:

All the ingredients were passed through mesh 60. The required quantity of each ingredient was taken for each specified formulation (Table I) and all the ingredients were co-grinded in a mortar and pestle. The powder blend was evaluated for flow properties such as bulk density, tapped density, Compressibility Index and Hausner ratio.

Compression of Tablets:

All the ingredients (except magnesium stearate) were mixed homogenously and co-grinded 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 150mg

*Corresponding Author: Amitesh Kumar Palo, Email: amiteshpalo@live.com, Phone No: +91-7205429804

each with a diameter of 8mm. A minimum of 50 tablets were prepared for each batch.

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.

In vitro Drug release 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 °c 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

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 C₁₇H₁₉Cl N₂S .HCl in the tablet.

RESULTS AND DISCUSSION

Four formulations of Chlorpromazine Hydrochloride 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. 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

Table 1: Composition of the Four Different Formulations.

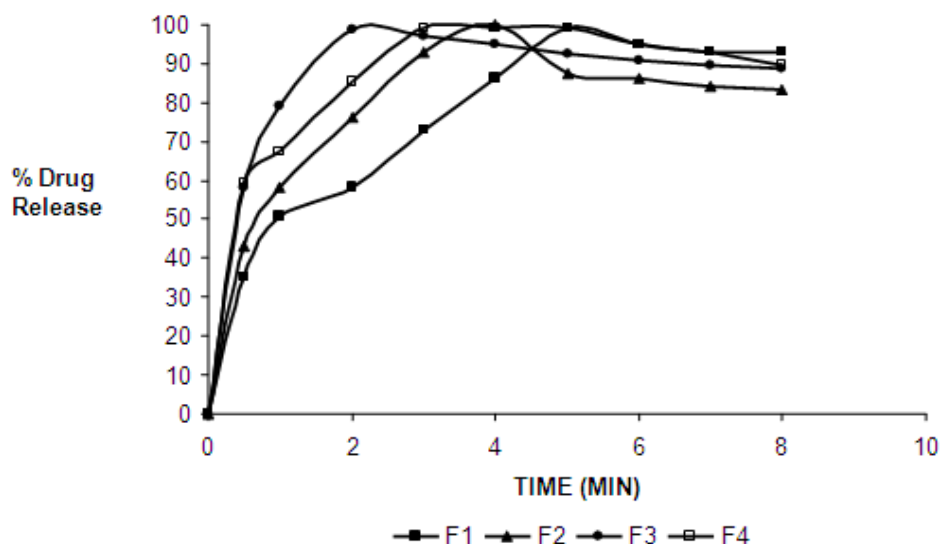
S.No	Ingredients	F1	F2	F3	F4
1	Chlorpromazine HCl	10	10	10	10
2	Microcrystalline cellulose	51	48	51	48
3	Mannitol	59	59	59	59
4	Camphor	20	20	20	20
5	Crospovidone	2	5	--	--
6	Croscarmellose sodium	--	--	2	5

technique. The bulk density was found in the range of 0.390-0.511 g/cm³ and the tapped density between 0.0450-0.603 g/cm³. Using these values the Hausner's ratio and Compressibility Index was calculated. The Hausner's ratio of the powder blends of all formulations was found to be less than 1.25 which indicates better flow property. The compressibility index was found to be in between 13.3-19.1 which indicates a fairly good flowability of the powder blend. The good flowability of the powder blend was also evidenced with angle of repose (26- 31°) 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 *in vitro* disintegration time of the tablets was found to less than 40 sec. All the formulations showed enhanced dissolution rate as compared to pure Chlorpromazine Hydrochloride. 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 in 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 Hydrochloride can be successfully prepared by using the selected superdisintegrants in order to improve disintegrants/dissolution of the drug in oral cavity & hence better patient's compliance & effective therapy.

7	Sodium starch glycolate	--	--	--	--
8	L-HPC	--	--	--	--
9	Pregelatinized starch	--	--	--	--
10	Aerosil	2	2	2	2
11	Aspartame	4	4	4	4
12	Magnesium stearate	2	2	2	2
	Final weight	150 mg	150 mg	150 mg	150 mg

Table 2: Evaluation of Various Parameters of the Compressed Tablets of Different Formulations

S.No	Evaluation	F1	F2	F3	F4
1	Weight variation (mg)	150±2	150±1	150±1	150±2
2	Thickness (mm)	3.53±0.08	3.49±0.04	3.51±0.04	3.53±0.02
3	Friability (%)	0.08	0.11	0.09	0.13
4	Hardness (Kg/cm ²)	3.5	3.0	2.75	3.25
5	Disintegration time (sec)	26±1.15	17±2.1	23±2.15	32±1.16
6	Content uniformity (%)	96.1±0.8	99.1±1.3	94.3±2.4	97.4±2.1
7	Assay(%)	98.2	96.4	97.6	97.3

Fig 1: Invitro Drug Release Profile of Different Formulations

CONCLUSION

Fast dissolving tablets constitute an innovative dosage form which overcomes the problem of swallowing and provides a quick onset of action. The pediatric and geriatric populations are the primary targets, as both the groups found difficulty to swallow conventional tablets. The basic approach followed by all the currently available technologies engaged in the formulation of fast dissolving tablets is to maximize the porous structure of the tablet matrix by incorporates super disintegrating agent in optimum concentration so as to achieve rapid disintegration and instant dissolution of the tablet along with good taste masking properties and excellent mechanical strength. Fast dissolving drug delivery system can provide a unique alternative in product life cycle management of existing drug in general and novel approach in

particular for the treatment of acute disorders .The availability of the various technologies and the manifold advantages of the fast dissolving tablets will surely increase its popularity in the near future.

REFERENCES

1. Abu-lazza, Khawla, A., Li, Vincent, H., Look, Jee, L., Parr, Graham, D., Schineuer, and Matthew, K.; "Fast dissolving tablet", US Patent 6733781, May 11, 2004.
2. Blank, R. G., Mody, D. S., Kenny, R. J., and Avenson, M. C.; "Fast dissolving dosage form", US Patent No. 4946684, Aug 7, 1990.
3. Sweetman, S. C.; Martindale, The Complete Drug Reference, Thirty third

- edition, Pharmaceutical Press, London, Chicago, 2002, 660-664, 1241-1244.
4. Dollery, C.; Therapeutic Drugs, Second edition, Churchill Livingstone, Vol I & II, 1999, baD196-D199,
 5. Mosby's; The Complete Drug reference, seventh Edition, II 443-48, II 1581-1586.
 6. Lachman, L., Liberman, H. A., and Kanig, J. L.; "The Theory and Practice of Industrial Pharmacy", Third edition, Varghese Publishing House, Bombay, 1987, 293-342.
 7. Yunxia, B., Hisakazu, Yurinobu, Y., Kazumi, D., Akinobu, O., and Kotaro, I.; "Preparation and evaluation of compressed tablet rapidly disintegrating in the oral cavity", Chem. Pharm. Bull., 1996,44(11),2121-2127.
 8. Makino, T., Yamada, M., and Kikuta, J.; "Fast-Dissolving tablets and its production", US Patent No. 5501861, Mar 26, 1996.
 9. Vandana B Patravale, Namita B Prabhu, Indian Journal of Pharmaceutical Sciences, Mar-Apr.2005,233-235.
 10. M.M.Patel and D.M.Patel, Indian Journal of Pharmaceuticals sciences, March-April 2006, 222-226.
 11. Amin, A. F., Shah, T. J., Bhadani, M. N., and Patel, M. M.; "Emerging trends in the development of orally disintegrating tablet technology", Jan-2006.
 12. www.pharmainfo.net/exclusive/reviews/emerging_trends_in_the_development_of_orally_disintegrating_tablet_technology/