COMPARATIVE *IN VITRO* EVALUATION OF MARKETED AND FABRICATED TABLETS OF CHLOROQUINE PHOSPHATE

[1]V.P. Pandey*, [1]Venkateswara Reddy K., [2]R. Amarnath

[1]Department of Pharmacy, Annamalai University, Annamalainagar - 608 002. Tamil Nadu, India.
[2]Natco Pharma Limited, Kothur- 509 008. A.P. India.

*Corresponding author Email: vppnp@rediffmail.com

Summary

In the present investigation, performance of three marketed (MF1, MF2, MF3) tablet dosage forms are compared with one fabricated tablet dosage form (F) of chloroquine phosphate. F is studied in uncoated and coated forms both. F shows alteration in results in coated and uncoated forms for disintegration time and dissolution study. MF1 is uncoated tablets and MF2, MF3 are coated tablets. F is comparable to MF1 in uncoated form and comparable MF3 in coated form. Thus F is a successful tablet formulation and may be taken for commercial purpose.

Key Words: Chloroquine phosphate, croscarmellose sodium, tablets.

Introduction

The present drug chosen for study, chloroquine phosphate is antimalarial and is rapidly and almost completely absorbed from gastrointestinal tract [1]. 40 drug substances with proven or suspected bioavailability problems were reported. In many of examples cited, the product confirmed to label claims but drug simply was not available to the body [2, 3]. Levy studied on the comparative dissolution of different brands of tolbutamide and concluded that dosage form was responsible for the difference in therapeutic response [4]. Varley reported slower rate of dissolution to produce lower blood levels and to provide less hypoglycemic effect of tolbutamide [5]. Laboratories studies indicated that dissolution rate of drug from larger tablets was slower than from the smaller tablets [6]. Brice et.al. [7], showed nonequivalency of various brands of oxytetracycline produced by suppliers, certified by FDA. Generic equivalence and inequivalence of oral products are discussed by Wagner [8,9].

By observing the demand of chloroquine phosphate for treatment of malaria in India and having objective of studying importance of excipients used in manufacturing of tablet dosage form, the present investigation is taken. The present study is illustrative for selection of excipients for manufacture of tablet dosage form and a great help for new entrepreneur though the drug is old but still in high demand in tropical countries.

Materials

Chloroquine phosphate was procured from NATCO Pharma Ltd., Kothur, A.P. Lactose monohydrate (DMV International), Polyvinyl pyrrolidone K-30 (M/S B.A.S.F), aerosil (M/S Cabot Sanmer Ltd). Croscarmellose sodium (Signet Corporation), magnesium stearate (Dow chemicals), hydroxy propyl methyl cellulose E5 (Colorcon Asia Pvt. Ltd), polyethylene glycol 300 (Merck Inc.) and titanium dioxide (Ranbaxy Chemicals) were obtained from commercial sources and used as received.

Methods

Sl. No	Ingredients	mg per tablet
1	Chloroquine phosphate	250
2	Lactose monohydrate	84.1
3	PVP K-30	18.5
4	Aerosil	3.0
5	Croscarmellose sodium (Intragranular)	7.4
6	Magnesium stearate	7.0
7	Total tablet weight	370

Table 1. Formula of Fabricated Tablet Dosage Form F

Tablet formulation (F) was prepared by wet granulation technique. According to Table1, all ingredients were weighed accurately and passed through sieve number 40. Chloroquine phosphate, lactose monohydrate and croscarmellose sodium (disintegrant used intragranular) were mixed in a planetary mixer and thus powder blend was prepared. Binder solution of polyvinyl pyrrolidone K-30 (PVP K-30) was prepared by using demineralised water. Binding solution was placed in a sonicator for 2o minutes. Power blend was granulated with binding solution by slow addition in planetary mixer. Wet mass obtained was passed through sieve number 12. Granules were dried in tray drier for 1 hour. Dried granules were passed through sieve number 18. To the dried granules, glidant aerosol was added and mixed for one minute in planetary mixture. This mass was compressed using 11 mm punch and 12 KN compression force in Cadmach tableting machine.

Coating of Tablets F

Sl. No	Ingredients	mg per tablet
1	HPMC E5	11.1
2	PEG 300	2.22
3	Titanium dioxide	0.74

Table 2. Coating Materials for the Coating of Fabricated Tablets F

Hydroxypropyl methyl cellulose E5 (HPMC E5) was added to 100 ml of water and stirred with mechanical stirrer. Polyethylene glycol 300 (PEG 300) was added to above mixer and stirred for 20 minutes. Titanium dioxide was added to above preparation using mechanical stirrer. Quantities were taken according to Table 2. Tablets were coated with this mixture in a conventional pan coater.

Prior to compression, granules were evaluated for their flow and compressibility characters. The flow property of granules was assessed by determining angle of repose by the funnel method [10]. The compressibility index of granules was determined by Carr's compressibility index [11]. The prepared tablets were tested as per standard procedure for weight variation, thickness, hardness, friability, disintegration time and drug content.

The λ_{max} of choloroquine phosphate in distilled water was found at 343nm. standard calibration curve of drug was plotted in concentration range 5-25 µg/ ml with good correlation of r^2 value of 0.999, slope of 0.035378 and intercept of 0.001266. The *in vitro* dissolution studies were carried out using USP dissolution apparatus [12] type 2, paddle type at 100 rpm in 900 distilled water at 37 ± 0.5°C. Six samplings were done at 10 min, 15 min, 20 min, 30 min, 40 min, and 45 min (minutes) and analyzed by UV/VIS spectrophotometer at λ_{max} of 343 nm.

Results and Discussion

Sl. No	Parameters	Formulation				
		Uncoated F	Coated F	Uncoated MF1	Coated MF2	Coated MF3
1	Size in mm	11.02	11.08	10.06	9.10	9.62
2	Thickness in mm	4.2	4.4	4.26	4.66	4.28
3	Average weight in mg	372.7	373.5	353	300	310
4	Weight variation	Complies	Complies	Complies	Complies	Complies
5	Disintegration time in min. sec	1.50	3.10	5.50	9.10	10.15
6	Hardness in kg/cm^2	4.5				
7	Friability in %	0.16				
8	Assay in %	99.1	99.8	99.8	100.8	100.6

Table 3. Physicochemical Properties of Tablet Formulation

Preformulation characteristics of granules of F were studied. The values of Hausner's ratio, Carr's index and angle of repose were 1.10, 8.82% and 28.77 respectively. These values show that granules of F have good flow property and good compressibility.

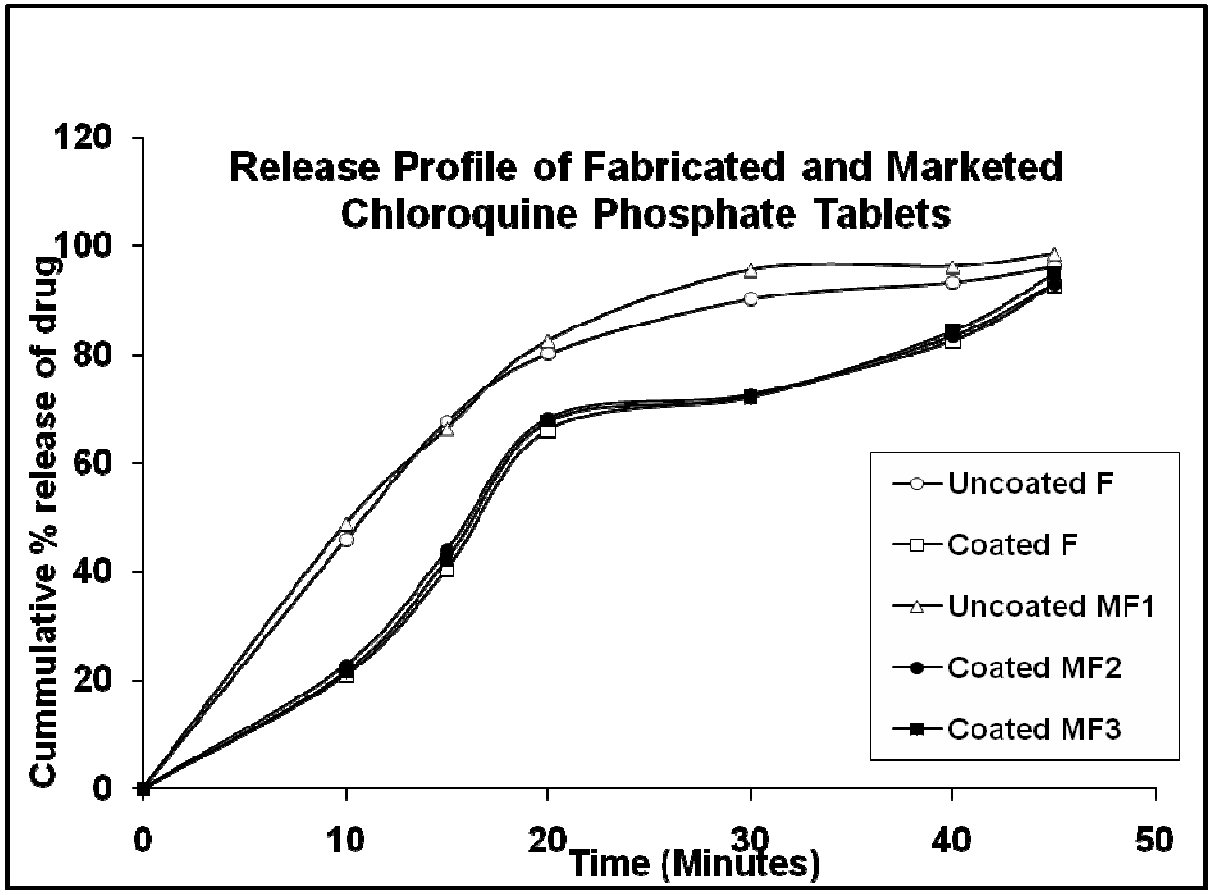

Figure 1. Release Profile of Fabricated and Marketed Chloroquine Phosphate Tablets

Physicochemical properties of fabricated uncoated and coated tablet formulation F are depicted in Table 3. In all the respect fabricated coated and uncoated tablet formulation F are suitable and all the parameters are meeting official and unofficial requirement for fabricated tablets F (Table 3 and Fig 1). Physicochemical properties of marketed MF1, MF2 and MF3 are depicted in Table 3. MF1 is uncoated marketed tablet formulation and MF2, MF3 are coated marketed tablet formulation. These marketed tablet formulations MF1, MF2 and MF3 are meeting all official and unofficial requirements (Table 3 and Fig. 1). If F is compared for physicochemical properties, its disintegration time of 1 minute 50 seconds in uncoated form is less than coated F, MF1, MF2 and MF3. Low disintegration time of F may be due to croscarmellose sodium (Table 1) Fig.1 shows that drug release of uncoated F is comparable to marketed uncoated MF1 and better than coated F, MF2 and MF3. Coated F is comparable to MF3 (Fig.1) Coated F shows 3 minute 10 seconds of disintegration time (Table 3) more than 1 minute 50 seconds of uncoated F and slow in release characteristic (Fig.1). This may be due to HPMC E5 used in coating material (Table 2). Thus F in coated and uncoated both forms are comparable to the best uncoated marketed and coated marketed tablet dosage form. If disintegration time (Table 3) is considered for superiority, F is superior to MF1, MF2 and MF3. Thus F may be taken successful tablet dosage form (Table 3, Fig.1)

References

1. R.S.Satoskar, S.D. Bhandarkar, Nirmala M. Rege. 'Pharmacology and Pharmacotherapeutics' revised 19th edition, p.765.
2. Schnellar, G.H., J.Am. Pharm. Ass. NS **9**: 455-459, 1969.
3. Chenellar, G.H. Proc. 8th Pan-Am. Congr. On Pharmacy and Biochemistry, Carcas, 1969.
4. Levy, G. Gan-Med Ass. J. **90**: 878 - 979, 1964.
5. Varley, A.B.J., Am. Med. Ass., **206**: 1745-1748, 1968.
6. Lozinski, E. Can. Med. Ass. J. **83**: 177-178,1960.
7. Brice, G.W. and Hammer, H.F.J., Am. Med. Ass. 268: 1189-1190.
8. Wagner, J.G., Drug Intell. Clin. Pharm, **5**: 115-128, 1971
9. Wagner J.G., J.Pharm. Sci, **50**: 359-387, 1961.
10. Carter, S.J., Eds; In: Cooper and Gunn's: Tutorial Pharmacy, 6th Edn., CBS Publishers and Distributors, Delhi, p.228, 1986.
11. Aulton, M.E., Eds; In: Pharmaceutics, The Science of Dosage Form Design, Ist Edn., Churchill Livingstone, London, p.247, 1998.
12. The United States Pharmacopeia 24, The United States Pharmacopeial Convention, Rockville, MD. P.1942, 2002.