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STUDIES ON DILUENTS FOR FORMULATION OF TABLETS

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ABSTRACT

Lactose monohydrate, dibasic calcium phosphate (DCP) and microcrystalline cellulose phosphate (MCCP) were studied as diluents in the same quantity for manufacture of chloroquine phosphate tablet using polyvinyl pyrrolidone K-30 (PVP K-30) as binding agent and sodium starch glycolate (S.S.G.) as disintegrating agent. In the present study, it was found that lactose monohydrate was suitable diluent for chloroquine phosphate tablets considering hardness and disintegration time. There were not much variations in other parameters like Hausner's ratio, compressibility index, angle of repose and friability for all the three diluents.

Key words: Diluent, Chloroquine phosphate, Lactose, PVP K – 30.

INTRODUCTION

Tablet remains popular as a dosage form because of the advantages afforded both to the manufacturer (e.g. Simplicity and economy of preparation, stability and convenience in packing, shipping, and dispensing) and the patient (accuracy of dose, compactness, baldness of taste and ease of administration). Excipients are inert substances used as diluents or vehicles for a drug. In pharmaceutical industry, it comprises of diluents or fillers, binders or adhesives, disintegrants, lubricants, glidants or flow promoters, colors, flavors, fragrances and sweeteners. Diluents are fillers, which comprise of heterogeneous group of substances, designed to make up the required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Tablet formulation may contain diluent to provide better tablet properties such as improved cohesion, direct compression manufacturing and to promote flow properties. Okafor et. al. [1]conducted a comparative study of modified starches for chloroquine phosphate. They found the hardness of the chloroquine tablets generally decreased to a minimum with modified starch at 40% concentration and increased to a maximum at 80% concentration. Chloroquine phosphate is an antimalarial drug, which is

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absorbed rapidly and almost completely through gastrointestinal tract[2]. The main objective of present study is to select a suitable diluent among lactose monohydrate, DCP and MCCP for manufacture of chloroquine phosphate tablets on basis of physico-chemical parameters and dissolution study.

EXPERIMENTAL

Materials and methods

Materials

Chloroquine phosphate was procured from Natco Pharma Limited, Kothur, A.P., lactose monohydrate, DCP, MCCP (Prakash & Company), PVP K-30 (Signet Pharma Agencies), aerosil (Cabbot Samnol Pharma Agencies), SSG (D.M.B. international) and magnesium stearate (Sinai Pharma, Bangalore) were obtained from commercial sources and used as received.

Methods

Different tablet formulations (F1-F3) were prepared by wet granulation technique (Table 1). All ingredients were weighed accurately and passed through sieve number 40. Chloroquine phosphate and lactose monohydrate (F1), DCP (F2) and MCCP (F3) were mixed in planetary mixer and thus, powder blend was prepared. Binder solution of PVP K-30 was prepared by using demineralised water. Binding solution was placed in a sonicator for 20 minutes. Powder 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 aerosil and disintegrating agent SSG were added externally and mixed well in a planetary mixer for 3 minutes. Lubricant, magnesium stearate was mixed with it in a planetary mixer for 1 minute. Thus, this mass was compressed using 11 mm punch and 12 KN compression force in Cadmach tabletting machine.

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[3]. The compressibility index of the granules was determined by Carr's compressibility index[4]. The prepared tablets were tested as per standard procedure for weight variation, thickness, hardness, friability, disintegration time and drug content. The λ_{max} of chloroquine phosphate in distilled water was found at 343 nm. 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[5] type 2, paddle type at 100 rpm in 900 mL 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 and analysed by UV/VIS spectrophotometer at λ_{max} of 343 nm.

Table 1: Formula of fabricated tablets

S. No	Ingredients in (mg/tablet)	Formulation		
		F1	F2	F3
1	Chloroquine phosphate	250	250	250
2	Lactose monohydrate	84.1		
3	DCP		84.1	
4	MCCP			84.1
5	PVP K - 30	18.5	18.5	18.5
6	Aerosil	3.0	3.0	3.0
7	SSG	7.4	7.4	7.4
8	Magnesium stearate	7.0	7.0	7.0
	Total tablet weight	370.0	370.0	370.0

RESULTS AND DISCUSSION

The results of Hausner's ratio, compressibility index and angle of repose are depicted in Table 2. All three formulations (F1-F3) are having almost the same value for Hausner's ratio, Carr's index and angle of repose for its granules (Table 2). So granules characteristic may be considered for good flow and good compressibility but may not be considered for selection of any one formulation's granules superior to others. Thus, tablet characteristics may only be considered for selection of one diluent among three.

All tablet formulations (F1-F3) complied weight variation test of Indian Pharmacopoeia 1996. The size of all tablet formulations was 11.06 mm and thickness ranged between 4.1 mm to 4.3 mm. The average weight to tablets ranged between 369.00 mg to 374.00 mg. According to Table 3, all formulations (F1-F3) complied the test for friability, disintegration time (D.T) and assay. Tablet characteristics like dissolution, hardness and disintegration time (D.T) are considered for selection of suitable diluent used in present

study. According to Fig. 1, F3 is showing highest drug release of 92.96% in 45 minutes. According to Table 3, hardness of F3 is 3.9 kg/cm^2, lowest among all, as well as it may not be suitable to withstand stress. Thus, F3 may not be considered as suitable tablet formulation due to less value of hardness though D.T. is 3.45 min. sec lowest to the other two formulations (F1 & F2). Now if F1 is compared to F2, F1 bears appropriate hardness value of 4.9 kg/cm^2, a little more than of F2 (4.6 kg/cm^2), 6.30 min. sec of D.T., lower than F2 of 8.50 min. sec and drug released in 45 minutes for F1 is 87.12% better than 83.56% of F2. Thus, F1 is a choice of tablet formulation. F1 contains lactose monohydrate (Table 1) as diluent. In the present study, lactose monohydrate is the most suitable diluent for tablet formulation of chloroquine phosphate.

Table 2: Preformulation characteristics of granules

S. No	Parameters	Formulation		
		F1	F2	F3
1	Hausner's ratio	1.18	1.18	1.18
2	Carr's index (%)	15.38	15.87	15.62
3	Angle of repose (°)	28.11	27.56	28.77

Table 3: Physico - chemical properties of tablet formulations

S. No	Parameters	Formulation		
		F1	F2	F3
1	Size (mm)	11.06	11.06	11.06
2	Thickness (mm)	4.1	4.2	4.3
3	Average weight (mg)	370.5	374.0	369.0
4	Weight variation	Complies	Complies	Complies
5	D.T. (min. sec)	6.30	8.50	3.45
6	Hardness (kg/cm^2)	4.9	4.6	3.9
7	Friability (%)	0.36	0.30	0.42
8	Assay (%)	98.5	99.2	97.5

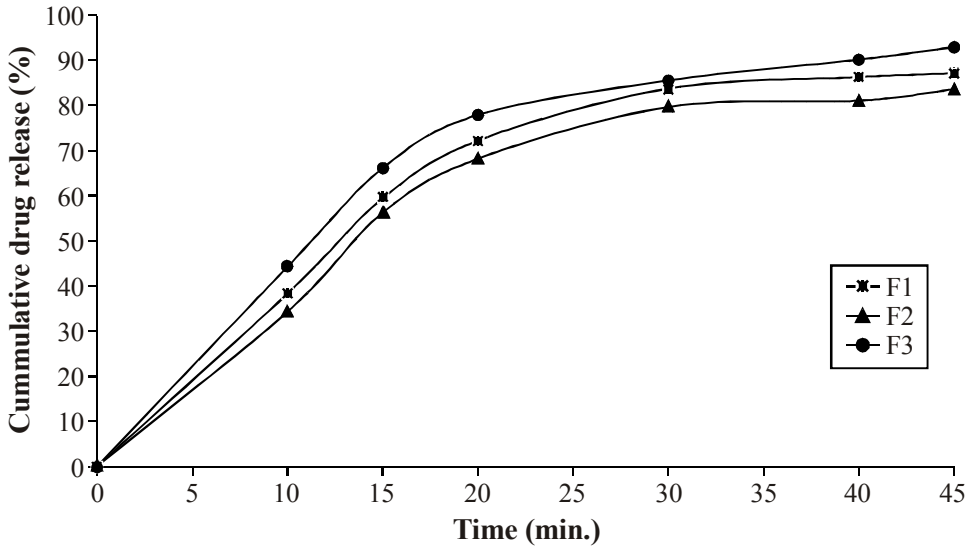

Fig. 1: Dissolution release profile of chloroquine phosphate

In the present study, most common diluents, lactose monohydrate, DCP and MCCP are studied for suitable tablet formulation of chloroquine phosphate. Thus, the present investigation is highly illustrative and useful for selection of diluent for new drug or entrepreneur to develop suitable tablet formulation.

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