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In vitro evaluation of marketed antimalarial chloroquine phosphate tablets

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Background & objectives: The aim of the present study is to investigate the physicochemical equivalence of seven brands of tablets containing chloroquine phosphate, an antimalarial purchased from different retail pharmacy outlets.

Methods: The quality and physicochemical equivalence of seven different brands of chloroquine phosphate tablets were assessed. The assessment included the evaluation of uniformity of weight, friability, crushing strength, disintegration and dissolution tests as well as chemical assay of the tablets.

Results: All the seven brands of the tablets passed the British Pharmacopoeia (BP) standards for uniformity of weight, disintegration and crushing strength. One of seven brands failed the friability test. One of the brands did not comply with the standard assay of content of active ingredients. Dissolution test passes the pharmacopoeial standards for chloroquine phosphate tablets. There were no significant differences in the amounts of chloroquine phosphate released from the different brands.

Interpretation & conclusion: Out of the seven brands of anti-malarial chloroquine phosphate tablets only one brand fails to meet BP quality specifications which shows constant market monitoring of new products to ascertain their equivalency to pharmacopoeial standards.

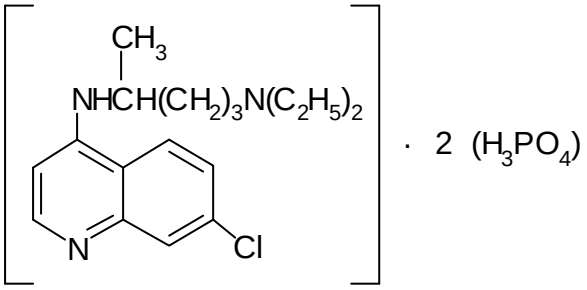
Key words Chemical equivalence – chloroquine phosphate tablets – friability

The increase in the number of generic drug products from multiple sources has placed people involved in the delivery of health care in a position of having to select one among several seemingly equivalent products. For instance, in 1975 approximately 9% of all prescription drugs dispensed in the United States were generic versions[1]. This figure rose to 20% in 1984 and 40% in 1991[2]. Over 80% of the approximately 10,000 prescription drugs available in 1990 were obtained from more than one source and variable clinical responses to these dosage forms supplied by two or more drug manufacturers is documented[2]. These variable responses may be due to formulation ingredients employed, methods of handling, packaging and storage and even the rigours of in-process quality control. Thus, there is need to determine their pharmaceutical and therapeutic equivalence in order to ensure interchangeability.

However, many developing countries do not have an effective means of monitoring the quality of generic drug products in the market. This results in widespread distribution of substandard and/or counterfeit drug products. It was in view of this fact that the World Health Organization issued guidelines for global standard and requirements for the registration, assess-

ment, marketing, authorisation and quality control of generic pharmaceutical products[3]. Generic drug products must satisfy the same standards of quality, efficacy and safety as those applicable to the innovator products. Preliminary physicochemical assessment of the products is very important and *in vitro* dissolution testing can be a valuable predictor of the *in vivo* bioavailability and bioequivalence of oral solid dosage forms[4].

Chloroquine phosphate is a 4-aminoquinoline compound for oral administration. It is 7-chloro-4-{[4-(diethyl amino)-1-methylbutyl] amino]} quinoline phosphate (1:2) and has the following structural formula:



Chloroquine is rapidly and almost completely absorbed from the gastrointestinal tract. It is indicated for the suppressive treatment and for acute attacks of malaria due to *Plasmodium vivax, P. malariae, P. ovale,* and susceptible strains of *P. falciparum.* The drug is also indicated for the treatment of extraintestinal amoebiasis.

Thus, in the present study the equivalence of seven brands of chloroquine phosphate tablets sourced from retail pharmacies from North Gujarat were determined using *in vitro* methods. This preliminary study is aimed at obtaining baseline data towards the establishment of bioequivalence of the tablets.

Material & Methods

Seven brands of chloroquine phosphate tablets (A to G) were obtained from different retail outlets in north Gujarat. All the products were manufactured within six months from the date of study.

Physical measurements: Twenty tablets selected at random were weighed individually and their average weight calculated to determine the weight uniformity[5] and percentage deviation of each tablet from the average weight was determined. The pre-weighed twenty tablet sample was placed in the friabilator (HICON) and weight loss was determined as a percentage of the initial weight. Crushing strength of each of nine tablets per brand was performed by using Pfizer hardness tester [Pfizer-HICON hardness tester]. The disintegration test ((DT-HICON)), dissolution test [Electrolab (USP, TDT-06T)] and assay (Spectrophotometry Shimadzu 1700) of all tablets were carried out as per USP'2002[6].

Data analysis: Data for weight uniformity test, friability, crushing strength and the disintegration and dissolution times of the tablets were analysed by determining the mean ± standard deviation.

Results & Discussion

The results of the physicochemical properties of the various brands of chloroquine phosphate are presented in Table 1. All brands showed acceptable uniformity of weight as none had percent deviation in weight > 5% as stipulated by the British Pharmacopoeia 1998[5]. The significance of this test is to ensure that the tablets in each lot are within the appropriate size range.

The crushing strength of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling before storage. The results showed that the brands examined had mean crushing strength within the range of 4.87–8.45 kg/cm^2.

Another tablet property related to crushing strength is friability, which is designed to evaluate the ability of the tablet to withstand abrasion during packaging, handling and shipping. For compressed tablets, percentage loss in weight of less than 1% is usually con-

Table 1. Physicochemical properties of seven brands of chloroquine phosphate tablets

Parameter	Weight uniformity (mg) (Mean ± SD)	Friability percentage (Mean ± SD)	Crushing strength (kg/cm^2) (Mean ± SD)	Disintegration time (min) (Mean ± SD)	Content percentage (Mean ± SD)	Dissolution at 30 min percentage (Mean ± SD)
A	315.8 ± 5.2	0.16 ± 0.1	7.13 ± 0.2	8.42 ± 0.5	96.93 ± 0.1	95.23 ± 2.4
B	370.6 ± 3.6	0.34 ± 0.1	5.77 ± 0.1	5.2 ± 0.5	98.69 ± 0.1	96.86 ± 1.9
C	328.8 ± 2.5	0.41 ± 0.1	5.1 ± 0.4	6.56 ± 0.3	95.15 ± 0.1	98.47 ± 3.9
D	297.4 ± 8.9	0.23 ± 0.1	4.87 ± 0.3	4.46 ± 0.2	101.67 ± 0.1	92.86 ± 4.8
E	347.5 ± 11.5	1.1 ± 0.1*	6.89 ± 0.9	5.89 ± 1	92.1 ± 0.1*	90.68 ± 5.3
F	319.8 ± 9.3	0.43 ± 0.1	8.45 ± 0.6	7.84 ± 0.8	99.89 ± 0.1	91.13 ± 3.4
G	348.6 ± 8.5	0.36 ± 0.1	6.38 ± 0.6	6.15 ± 0.3	102.68 ± 0.1	94.58 ± 2.9

*Failed to meet BP specifications.

sidered acceptable[7]. The results showed that brands A, B, C, D, F and G conformed to the required standard for friability, while brand E failed to comply. This failure could have resulted from the use of inadequate or insufficient amount of binding agent during formulation, inadequate moisture content during compression or insufficient compression pressure during tableting.

The disintegration test measures the time required for tablets to disintegrate into particles. This is a necessary condition for dissolution and could be the rate-determining step in the process of drug absorption. The BP 1998 stipulates a disintegration time of not more 15 min for uncoated tablets. The results of the disintegration test are presented in Table 1. The results showed that all the brands passed the disintegration test.

The results of the assays of chemical content to determine the amount of chloroquine phosphate present in each formulation are presented in Table 1. Except brand E all the brands contain between 92.5 and 107.5% of the labeled amount specified for chloroquine phosphate. Low content in brand may be due to poor preparation techniques during formulation and subsequent manufacturing.

The dissolution test is a measure of the amount of the drug released into the dissolution medium with time. The United States Pharmacopoeia stipulates that at 30 min, all tablets should have released into the dissolution medium an amount not less than 60% of the labeled amount of chloroquine phosphate. All the brands passed the dissolution test.

Conclusion

Only one brand of antimalarial chloroquine phosphate failed to meet the requirement according to pharmacopoeia and all other brands of chloroquine phosphate passed the standards. This study highlights the need for constant market monitoring of new products to ascertain their equivalency to pharmacopoeial standards.

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