Drug Development and Industrial Pharmacy, 26(7), 777–779 (2000)

COMMUNICATION

Stability of Extemporaneous Norfloxacin Suspension

Prapaporn Boonme,* Narubodee Phadoongsombut, Parichat Phoomborplub, and Supavalee Viriyasom

Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat-Yai, Songkhla 90112, Thailand

ABSTRACT

The stability of norfloxacin as extemporaneous suspensions compounded from two brands of film-coated tablets (formulas I and II) was studied. The vehicle consisted of tragacanth, saccharin sodium, sorbitol solution, glycerin, paraben concentrate, peppermint spirit BP, purified water, and syrup USP. The final concentration of norfloxacin in the suspensions was 20 mg/ml. Formulas I and II were chemically stable for 28 days when stored in amber glass bottles at ambient temperature; however, their physical characteristics were different.
Key Words: *Norfloxacin; Stability; Suspension.*

INTRODUCTION

Norfloxacin is a synthetic antibacterial fluoroquinolone. It is effective in the treatment of urinary tract infections, gonococcal urethritis, and infectious diarrhea (1,2). In Thailand, norfloxacin is commercially available only as tablets and capsules (3). Many people have difficulty swallowing solid dosage forms. This problem could be overcome by preparing a liquid oral dosage form extemporaneously. Since norfloxacin is a solid and is slightly soluble in water (4), a suspension dosage form is the most suitable if the product is physically and chemically stable (5,6).

The purpose of this study was to formulate extemporaneous norfloxacin suspensions, which were prepared from two brands of norfloxacin 400 mg/film-coated tablets (formulas I and II) and to evaluate the physical and chemical stability of these formulas.

EXPERIMENTAL

Materials

All the chemicals were USP or BP quality and were used without further purification. They were purchased from the suppliers in Thailand. Two commercial film-

* To whom correspondence should be addressed.

Table 1

Formula for the Preparation of Norfloxacin Suspension

Ingredients	Amount Used
Norfloxacin tablets, 400 mg	50 tablets
Purified water	150 ml
Vehicle for norfloxacin suspension, qs to	1000 ml

coated tablets containing 400 mg of norfloxacin were bought in Thai pharmacies. Standard norfloxacin powder was purchased from Sigma (St. Louis, MO).

Formulation of Norfloxacin Suspension

A 1000-ml portion of norfloxacin suspension was prepared according to the formulas in Tables 1 and 2. The vehicle for norfloxacin suspension was first prepared. Tragacanth was mixed in a mortar with sorbitol solution and glycerin. A 10-ml portion of paraben concentrate containing 10% methylparaben and 2% propylparaben in propylene glycol was added to the mixture, followed by a solution of saccharin sodium in purified water, the peppermint spirit BP, and a 400-ml portion of syrup USP. After mixing, the contents of the mortar were transferred to a graduated cylinder, and syrup USP then was used to bring the volume to 1000 ml. A total of 50 norfloxacin tablets of each brand were crushed and triturated to a fine powder in the mortar. A 150-ml portion of purified water was added and mixed to dissolve the film and form a smooth paste. An 800-ml portion of vehicle prepared was slowly added and mixed, then the volume was adjusted to 1000 ml to obtain a drug strength of 20 mg/ml. Each product was prepared in triplicate. All samples were stored in glass containers protected from light at ambient temperature for 28 days to assess stability.

Table 2

Formula for the Preparation of Vehicle for Norfloxacin Suspension

Ingredients	Amount Used
Tragacanth	1g
Saccharin sodium	1g
Sorbitol solution	100ml
Glycerin	100ml
Paraben concentrate	10ml
Peppermint spirit BP	30ml
Purified water	300ml
Syrup USP, qs to	1000ml

Analysis of Samples

Each suspension was shaken thoroughly by hand immediately before assaying. A 1.0-ml sample was withdrawn and dissolved with 1% acetic acid to a volume of 25 ml. Of this solution, 0.125 ml was then withdrawn and diluted with distilled water to a volume of 10 ml, giving a 10 μg/ml concentration of norfloxacin. Each sample was assayed in duplicate. The analyses were performed immediately after preparation and at 7, 21, and 28 days by high-performance liquid chromatography (HPLC). The HPLC assay was modified from USP 23 (7) and the method of Parasrampuria and Gupta (8). The instrumentation included a Waters 600 E pump controller, Waters 486 UV light detector with the wavelength set at 275 nm, and Waters 746 Data Module (Waters Corp., Milford, MA). A Rheodyne injector model 7725I was used to load and inject the samples. A C_{18} column (Microbondapak by Waters, 30 cm × 3.9 mm) was the stationary phase. The mobile phase was a mixture of acetonitrile and solution of 2 ml of triethylamine in 1000 ml of 0.05 M KH_2PO_4 buffer solution at pH 7 (25:75 by volume), which was filtered and degassed before use. The flow rate was 1.25 ml/min. The retention times for norfloxacin and for vehicle were different by about 2 min. The drug concentrations were then calculated by comparing peak height of samples with peak height of standard norfloxacin solutions. The samples were also evaluated for visual appearance, sedimentation, pourability, and pH.

RESULTS AND DISCUSSION

The results of HPLC analysis are presented in Table 3. The range of 95% and 104% of the mean initial norfloxacin concentrations remained in formula I and formula II, respectively. Assuming that drug concentrations equal to or greater than 90% of the initial value indicate stability, the results indicate that these suspensions, stored in amber glass bottles at ambient temperature, were chemically stable for 28 days. In addition, at each time interval, chemical stability of formulas I and II was not significantly different. The data, however, showed high standard deviations since the heterogeneous property of the suspensions might cause an error in taking samples.

There was no apparent change in color in any of the samples during the study period. The suspended particles

Table 3

Stability of Norfloxacin Suspensions

Formula	Actual Initial Concentration[a] (mg/ml)	Initial Concentration Remaining[a] (%)		
		Day 7	Day 21	Day 28
I	18.48 ± 1.40	95.00 ± 7.55	104.69 ± 12.41	103.99 ± 14.95
II	19.83 ± 2.51	98.80 ± 12.31	104.93 ± 7.80	100.44 ± 12.82

[a] Reported as mean ± SD. $n = 6$.

settled more rapidly in formula I than in formula II. At day 27, it was found that sedimentation volumes (ratios of final volume of sediment and initial volume of suspension) were 0.19 and 0.97 for formula I and formula II, respectively. However, the sediment in formula I could be redispersed on shaking, and the preparation could be poured easily. In contrast, formula II was gel-like and too viscous to pour. This could be due to the gellation of the excipients in tablets of formula II with the vehicle. Therefore, when extemporaneous norfloxacin suspensions from tablets are required, the suitable vehicle for each brand of tablets must be assessed.

The initial pH (mean ± SD, $n = 6$) in formula I and in formula II were 6.82 ± 0.09 and 6.73 ± 0.07, respectively. At the end of the study period, the pH was 6.93 ± 0.02 for formula I and 6.89 ± 0.02 for formula II. No appreciable change in pH was identified in any sample.

CONCLUSIONS

The general observations made in this study regarding percentage of drug remaining and physical properties of suspensions in each formula support the following conclusions: (*a*) Both formulas in this study are stable for 28 days under the conditions used; (*b*) although the vehicle used in this study gives a good chemical result for both formulas, it shows a poor physical result for formula II. Therefore, it has to be considered that the properties of extemporaneous suspensions also depend on the kind and amount of excipients in tablets used in preparation.

ACKNOWLEDGMENT

A grant for this study was provided by the Faculty of Pharmaceutical Sciences and the Prince of Songkla University.

REFERENCES

1. C. Mazuel, Norfloxacin, in *Analytical Profiles of Drug Substances*, Vol. 20 (K. Florey, Ed.), Academic, San Diego, CA, 1991, pp. 557–600.
2. D. W. Sifton, *Physicians' Desk Reference (PDR)*, 49th ed., Medical Economics, New York, 1995, pp. 1600–1602.
3. H. Hor, MIMS, Medi Media, 27(1), 204–210 (1998).
4. S. Buduvari (Ed.), *The Merck Index*, 12th ed., Merck and Company, Rahway, NJ, 1996, p. 1150.
5. H. C. Ansel, *Introduction to Pharmaceutical Dosage Forms*, 4th ed., Lea and Febiger, Philadelphia, PA, 1985, pp. 207–222.
6. J. G. Nairn, Solutions, Emulsions, Suspensions and Extracts, in *Remington: the Science and Practice of Pharmacy*, 19th ed. (A. R. Gennaro, Ed.), Mack Publishing, Easton, PA, 1995, pp. 1515–1521.
7. U.S. Pharmacopeial Convention, *The United States Pharmacopeia*, 23rd rev., Author, Rockville, MD, 1995, pp. 1103–1104.
8. J. Parasrampuria and V. D. Gupta, *Drug Dev. Ind. Pharm.*, 16(9), 1597–1604 (1990).