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Extemporaneous Preparation and Stability Assessment of Omeprazole Suspension in a Teaching Hospital

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Research Article

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Abstract

Objective: To set up extemporaneous compounding and determine stability and quality of omeprazole suspension which is not commercially available in Iran.
Methods: We established a compounding service for preparation of oral liquid dosage forms at our center which is a tertiary care hospital. Omeprazole 2 mg/mL were prepared using sodium bicarbonate base, placed in 120 mL glass bottles and stored at 5°C for 28 days. Samples were collected on days 1, 7, 14, 21, and 28 after preparation for analysis by high performance liquid chromatography (HPLC) and assessment of appearance, odor, and pH.
Results: Omeprazole was stable for up to 28 days in the liquid formulations. No substantial changes in the appearance, odor, or pH of any liquid were observed.
Conclusions: Our extemporaneous unit is the first compounding service in Iran where oral liquids such as omeprazole suspension could be prepared according to standard protocols. We plan to extend extemporaneous knowledge in our country in order to prepare commercially unavailable dosage forms for patients.

Keywords: *Compounding, Education, Extemporaneous, Omeprazole, Pharmacy Pracice*

Introduction

Omeprazole is usually available as a delayed-release capsule containing enteric-coated granules to protect against acid degradation. Administration of enteric-coated omeprazole is problematic in paediatric patients, patients who are unable to swallow solid dosage forms, and patients who must receive medications via nasogastric or gastrostomy tubes. Recommendations for administration in these patients involve opening capsules and mixing the enteric-coated granules into soft acidic foods or flushing granules through nasogastric tubes with liquids. Such methods have significant drawbacks. Flushing granules through nasogastric tubes is time consuming and may lead to clogging of tubes.[1, 2] Moreover, oral administration of enteric coated granules to pediatric patients is fraught with problems. Children may be too young to swallow even soft foods, or they may chew the granules, which compromises the enteric coating and leads to drug inactivation.[1] Also, adjusting pediatric dosages of granule-containing omeprazole formulation by weight is difficult and not recommended.[3]

Alternative methods of delivery have been sought that allow an aqueous administration while simultaneously protect the intact drug from acid degradation. Published data support the use of an extemporaneous omeprazole suspension that retains drug stability during delivery.[4, 5]

Extemporaneous preparation is 'the manipulation by pharmacists of various drug and chemical ingredients using traditional compounding techniques to produce suitable medicines when no commercial form is available'.[6] Extemporaneous compounding is a big challenge in developing countries since pharmacies are generally not well equipped to carry out extemporaneous compounding of unavailable formulations. As well as they are limited by lack of resources such as ingredients and trained personnel.[7] Although dermatological preparations remain the most commonly compounded products even in the

community pharmacies, the biggest challenge comes to compounding of formulations for pediatric, elderly, or critically ill patients where no authorized preparations exist in the local market. In this study omeprazole suspension was prepared from commercially available capsules for first time in a teaching hospital in Iran. Stability and quality of the resulting preparation was determined.

Material and Method

Preparation of samples

Omeprazole suspension was prepared by emptying the contents of 60 capsules of omeprazole 20 mg into a 1000 mL Erlenmeyer flask. Using a volumetric flask, 600 mL of 8.4% sodium bicarbonate solution was added to achieve a final omeprazole concentration of 2 mg/mL. The mixture was magnetically stirred for 30 minutes. As the mixing process continued, the liquid preparation was drawn into six 120-mL amber-colored glass bottle to a total volume of 100 mL and stored in refrigerator (5 ºC).

All omeprazole glass bottles were inspected and tested in triplicate at days 1, 7, 14, 21, 28 following suspension compounding. Each sample was inspected for color and odor change, and the pH was measured and recorded at each time point. Prior to HPLC sample preparation, each bottle was shacked for one minute, then placed on a continuous rocker for three to five minutes to maintain a uniform dispersion of suspended drug particles since a lag time occurred from the preparation of the first HPLC sample to the last. An aliquot from each bottle was diluted to 50 µg /mL with acetonitrile /water (45:55 v/v), placed in separate l-mL plastic conical tubes, and vortexed for one minute. Three 0.5-mL samples were withdrawn from each conical tube and placed in HPLC autoinjector vials for analysis. Thus, each of the six bottles at each temperature was analyzed in triplicate, resulting in a total of eighteen data points for each time period.

High performance liquid chromatography

Omeprazole concentrations were determined by using a modified HPLC method.[8, 9] The liquid chromatographic system consisted of a multiple wavelength detector, autoinjector, liquid chromatograph, recorder, integrator, and column. Separation conditions for omeprazol were as follows: ultraviolet wavelength 285 nm, oven temperature 35°C, and mobile phase consisting of analytical-grade acetonitrile /water (45:55, v/v) adjusted to pH 7.5 with 1 M monobasic sodium phosphate salt. The injection volume was 150 µL and the flow rate 1 mL/min.

On each day a standard curves were prepared by serially diluting stock solutions of omeprazol in acetonitrile/water (45:55, v/v). Stock solutions were made from analytical- grade compound provided by the manufacturers. Calibration standards were prepared at concentrations of 0, 50, 100, 150, and 200 µg/mL. Plots of the omeprazole peak height against the concentration of omeprazole were linear over the range of 0 to 200 µg/mL, with r^2 values greater than 0.999. The variations for within-day and day-to-day reproducibility were 1.34% and 3.55% respectively.

Microbiological stability

Bacterial contamination of the suspensions was assessed at 1, 7, 14, 21, 28 days after preparation. Aliquots of 100 µL from each bottle were plated in duplicate on 5% sheep blood agar plates and stored aerobically at 37 ºC for 24 hours. Following the 24-hour incubation, agar plats were inspected for microbial grow and colony formation.

Patient overview

A questionnaire was given the parents of pediatric outpatients who received omeprazole suspension from the pharmacy. Questionnaire compromised four sections focusing on patient demographic, indication of drug usage, history of using omeprazole capsule and suspension, patient problems and overview regarding both dosage forms. 35% of questionnaires returned to the pharmacy in next visit.

Data analysis

Suspensions with ≤10% change from the initial drug concentration were considered stable.

Results

Visual/olfactory observations and pH measurements did not reveal any substantial changes during the study period. Chromatogram for omeprazole is shown in Figure 1. There were no significance changes in omeprazole concentrations during the 28 days at 5 ºC (Table1). Inspection of blood agar plates demonstrated no growth in all samples tested.

Table 1: Stability of omeprazole up to 28 days at 5°C

Day	%Initial concentration remaining (Mean±SD)
1	93.09±3.47
7	111.28±3.43
14	112.90±3.43
21	108.71±3.51
28	104.82±4.25

Pediatric outpatients who used omeprazole suspensions were aged 4-12 months. Omeprazole was indicated for gastrointestinal reflux for all of them. 43% of patients had no history of taking omeprazole. The remaining had problems for opening capsules and counting granules in order to dose adjustment and reported higher effectiveness of suspension compared with capsules. All of parents were satisfied with existence of liquid dosage form for their children. 28.6% of responders complained of unpleasant taste of suspension.

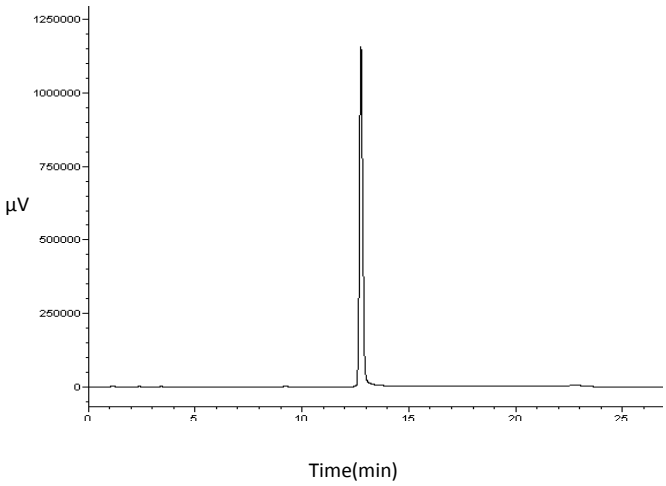

Fig 1: Chromatogram of omeprazole 2mg/mL

Discussion

Omeprazole is a high usage medicine in our hospital (a tertiary care, multidisciplinary teaching hospital) and its liquid dosage form is not commercially available in Iran. In this study we compounded omeprazole 2 mg/mL in sodium bicarbonate solution from commercially available capsules. The suspension was stable for 28 days at 5 ºC and patient were fulfilled with this new service.

While pharmacists are responsible for ensuring that drug use is safe and effective, in developing countries the emphasis is often on the technical aspects of pharmacy.[10] The movement of pharmacists towards professional practice should be occurred in different aspects. When drugs are not commercially available in appropriate dosage forms, patients and nurses crush tablets or open capsules to adjust dosage or prepare a liquid form. This action may cause toxicity or instability of the products. Pharmacists should educate and consult patients and nurses regarding proper use of medicines and prepare an extemporaneous formulation based on data in the literature or in consultation with peers.[11, 12]

Although compounding extemporaneous formulation is a significant portion of pharmacists' work in a health care setting, no extemporaneous service was available in our country before this study. We established an extemporaneous pharmacy for preparation of oral liquid dosage forms in our hospital. It was rational to start compounding from a highly usage and low risk product. The stability our product was in accordance with reported stability in the literature.[2,5] The information on the duration of drug stability enables patients to provide their medicine monthly and also allows pharmacists to compound batches during downtime in the pharmacy and store them for future usage.

The patients were pleased concerning availability of omeprazole suspension. The only complain was unpleasant taste. Since flavoring of suspension may cause instability of the product, it was recommended to mix unit dosage with milk.[13] Disseminating our results is useful for pharmacists especially in developing countries where pharmacists should be more acquainted with different aspects of their profession. We plan to compound extemporaneous formulation of other medications and train our pharmacists regarding this responsibility.

Conclusion

Omeprazole 2 mg/mL was compounded extemporaneously in a suspension which was stable for 28 days at 5 ºC. While extemporaneous compounding is a known practice for pharmacist profession, our experience could guide uneducated pharmacists to start compounding of unavailable dosage forms.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests