

# Development of Home Preparation Instructions for Amoxicillin, Doxycycline, and Clindamycin for Pediatric Patients During a Public Health Emergency

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## Abstract

Amoxicillin, doxycycline, and clindamycin are among the commonly used antibiotics to treat bacterial infections. However, the federal government, including the Center for Disease Control (CDC), maintains limited stockpiles of pediatric formulations of these essential antibiotics. As such, it is anticipated that during a public health emergency, special instruction may need to be provided on home preparation and administration procedures to dose pediatric patients using available stockpiles of the oral capsule dosage forms. Mixing crushed tablets or capsule contents (i.e., the manipulated product) with soft- or liquid- foods is one of the most common home preparation procedures. For recommending safe and effective use of the manipulated drug product instead of the intended intact dosage form, the impact of manipulation of the dosage form needs to be studied. The suitability and compatibility of the possible soft- or liquid foods for home preparations and their use conditions for ensuring quality and effectiveness of the three antibiotics have not been evaluated, raising concern over readiness and appropriateness of an emergency use authorization during an emergency. The objective of this inter-agency collaboration is to understand the impact of the exposure of capsule contents to the selected soft- or liquid foods and stability of the antibiotics under study conditions for assessing the dosing accuracy of the antibiotics to patients.

## Introduction

Antibiotics are powerful medicines to treat certain infections and have saved countless lives. However, antibiotics can cause side effects ranging from minor to severe health problems and can also contribute to antibiotic resistance. Therefore, it's very important to use the right amount of antibiotics when necessary to protect the patients from the bacterial infections and combat harms caused by unnecessary antibiotics.

Amoxicillin, doxycycline, and clindamycin are some of the commonly used antibiotics to treat bacterial infections. They are not only important in everyday home use, but also important during public health emergencies. The stockpiled drug products in federal (Strategic National Stockpile) or local/state caches for preparation of public health emergencies are in oral capsule dosage forms and are well designed for adults. However, these capsule dosage forms are not age-appropriate for pediatric patients and adult patients with swallowing problems. Care providers often need to take necessary approaches to provide smaller doses and improved palatability to pediatric patients and to facilitate swallowing for adult patients unable to swallow the capsules.

Dividing the drug content and using foods and drinks to deliver the specific dose and to improve the taste of the administered drug is one of the commonly used approaches for care providers. However, there are knowledge gaps in the understanding of the effects of foods and drinks on the availability, stability, and dose accuracy of the drugs. In order to address these possible effects and to select appropriate food vehicles for the administration of the antibiotics, dissolution studies, stability studies, and homogeneity studies have been conducted on the capsule content of the three antibiotics, amoxicillin, doxycycline, and clindamycin, against 15 foods of choice.

## Materials and Methods

CDC had purchased and shipped 1700 capsules (500 mg strength) of Amoxicillin TH manufactured by Sandoz (NDC 0781-2613-05), 1700 capsules (100 mg strength) of Doxycycline H manufactured by Westward (NDC 00143-9803-05), and 1680 capsules (300 mg strength) of Clindamycin HCl manufactured by Sun Pharma (NDC 63304-693-62). Other chemicals including monobasic potassium phosphate, potassium hydroxide, sodium hydroxide, tetrabutylammonium hydrogen sulfate, disodium edetate, tertiary butyl alcohol, methanol, acetonitrile, phosphoric acid, hydrochloric acid, and triethylamine were purchased from the certified laboratory vendors.

A total of 16 commonly available soft- and liquid- foods were studied as potential vehicles to determine their compatibility with the three antibiotic drug products. A series of studies were conducted on intact capsules, including assay, content uniformity, and dissolution determinations using compendial methods, and additionally, for the capsule content-food mixtures, dissolution, and stability determinations and homogeneity assessments were made. The stability of the three antibiotic-food mixtures were assessed for 24 hours at 30°C. For preparation and use recommendations, homogeneity of antibiotic-food mixtures prepared in several types of containers, including cups, plates, and bowls, and mixing times (i.e., 0.5 min, 1 min, 2 min, and 5 min) were investigated by analyzing the drug recovery in each equally divided portion of the antibiotic-food mixture. Several HPLC techniques for quantifying the antibiotics were developed and applied to support the above-mentioned studies.

## Results and Discussion

The intact dosage units studied for all three antibiotics were within specification as labeled. Of the 16 studied soft- or liquid foods, peanut butter was found to be not suitable as vehicle (significantly reduced assay and dissolution of tested antibiotics) and hence omitted from the subsequent investigation. All other drug-food mixtures met the dissolution criteria, except for the amoxicillin-chocolate pudding mixture. In the preliminary stability assessments, all the antibiotics mixed with the 15 selected foods were stable for 24 hours at 30°C with more than 90% dose recovery under the test conditions suggesting the effectiveness of the home preparation of the drug-food mixtures. The compatibility chart (Figure 1) may further support the development of home preparation instructions for the drug-food mixtures. All three household containers were found to be sufficient to prepare uniform mixtures of the antibiotics and foods. For practical purposes, 1–2-minute stirring time was found to be sufficient for home preparation of drug-food mixtures.

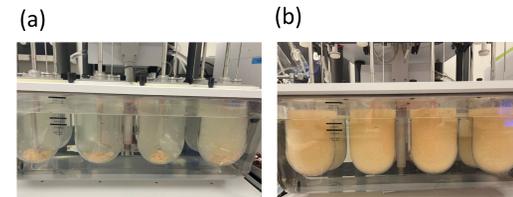


Figure 1. Amoxicillin capsule content-peanut butter dissolution at (a) 5 min and (b) 60 min.

	Amoxicillin	Doxycycline	Clindamycin
Apple Juice	✓	✓	✓
Apple Sauce	✓	✓	✓
Baby Food (Banana)	✓	✓	✓
Chocolate Milk	✓	✓	✓
Chocolate Pudding	✗	✓	✓
Chocolate Syrup	✓	✓	✓
Cranberry Juice	✓	✓	✓
Enfamil	✓	✓	✓
Grape Jelly	✓	✓	✓
Low Fat Milk	✓	✓	✓
Orange Juice	✓	✓	✓
Rice Pudding	✓	✓	✓
Similac	✓	✓	✓
Soy Milk	✓	✓	✓
Yoghurt	✓	✓	✓

Amoxicillin	Fail < 80%	Pass 80% - 100%
Doxycycline	Fail < 85%	Pass 85% - 105%
Clindamycin	Fail < 80%	Pass 80% - 100%

Figure 2. Dissolution results for the capsule content-food mixtures. Cells in green means the drug-food mixture passes the USP dissolution acceptance criteria. A cell in red indicates the specific drug-food mixture does not pass the dissolution acceptance criteria.



Figure 5. Preparation procedure of capsule content-food mixtures

## Disclaimer

The contents in this poster reflect the views of the authors and should not be construed to represent FDA's views or policies.

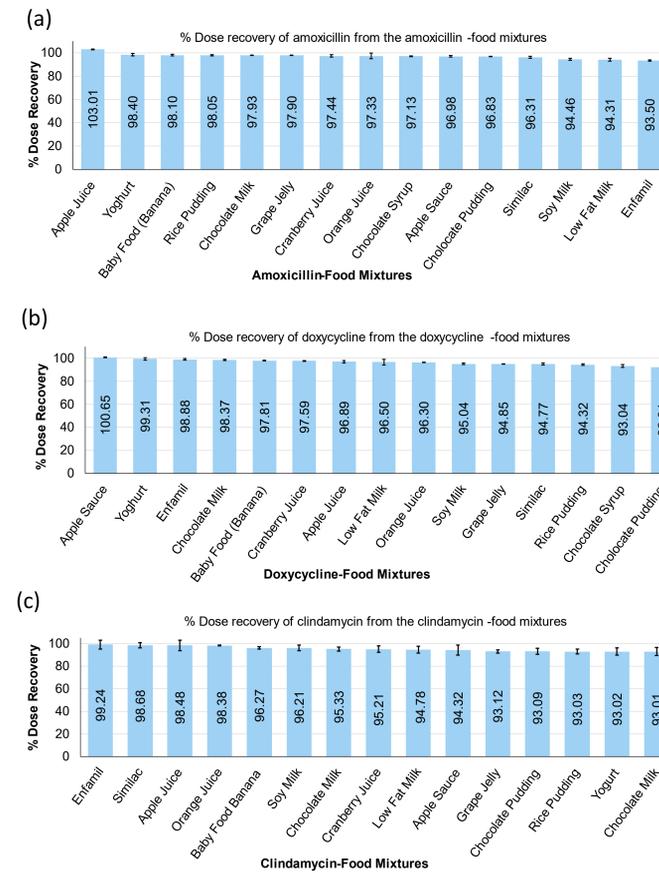


Figure 3. The dose recovery of (a) amoxicillin, (b) doxycycline, and (c) clindamycin from the capsule content-food mixtures.



Figure 4. The homogeneity of the antibiotics mixed with (a) liquid foods, and (b) soft foods prepared by a variety of combinations of containers and mixing times.

## Conclusions

The presented studies provide information on potential interactions between the antibiotics and the studied soft- or liquid foods. Ideally, the drug-food mixtures are recommended to be used immediately that is within a 2-hour window after its preparation when microbiological studies are not carried out. The screening experiments with additional in vitro studies are informative in providing basic recommendations for preparedness against public health emergencies caused by bacteria, and are crucial for pediatric patients and patients with swallowing difficulties, who are equally vulnerable to the threatening agents.

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