Tropical Medicine and International Health doi:10.1111/j.1365-3156.2010.02627.x

VOLUME 15 NO 11 PP 1340–1346 NOVEMBER 2010

High failure rate of the dissolution tests for 500-mg amoxicillin capsules sold in Cambodia: is it because of the product or the test method?

J. Okumura[1], M. Taga[2], S. Tey[3], Y. Kataoka[2], N. Nam[3] and K. Kimura[2]

1 *Department of International Health, Institute of Tropical Medicine, Nagasaki University, Nagasaki, Japan*
2 *Institute of Medical, Pharmaceutical, and Health Sciences, Kanazawa University, Ishikawa, Japan*
3 *National Health Product Quality Control Center, Ministry of Health, Phnom Penh, Cambodia*

Summary

OBJECTIVES During the survey of substandard medicines in Cambodia in 2007, it was found that more than 90% of 500-mg amoxicillin (AMPC) capsules failed the United States Pharmacopeia (USP) 30 TEST 1 dissolution test. In the USP, several monographs provide multiple methods for performing the dissolution test. By using the 500-mg AMPC capsule as an example, we aimed to identify the problems and implications of the USP methods adopted for the dissolution test as a global standard.

METHODS All AMPC samples were collected from the Cambodian market in 2007. For the quantitative test, we referred to USP 30. We performed the USP 28 and USP 30 TEST 2 dissolution tests and compared these results with those of the USP 30 TEST 1.

RESULTS All 500-mg AMPC capsules used for the comparison passed the quantitative test. Samples that passed the USP 28 and USP 30 TEST 2 dissolution tests were identical, and the pass rate was 97.1% (34/35), whereas the pass rate with the USP 30 TEST 1 was 8.6% (3/35). The difference in the dissolution results between the three methods was significant ($P < 0.0001$).

CONCLUSION This study revealed that many users would select the most stringent method when multiple methods exist in the USP. This may lead to a high failure rate of the tests. Because USP is a global standard, we recommend that it take into consideration the developing countries and create a more detailed user-friendly manual for selection for appropriate methods.

keywords dissolution test, quality assurance, substandard, amoxicillin, developing countries, United States Pharmacopeia

Introduction

As official guides to quality standards for pharmaceuticals, pharmacopoeias play an important role in ensuring the quality and safety of pharmaceutical products (USP 2009a). According to WHO (2006), there are 45 pharmacopoeias either published by governments or under official sanction worldwide. Most of the countries that publish or sanction pharmacopoeias are developed or intermediately developed nations; however, most developing countries have not yet published national pharmacopoeias. Therefore, developing countries often rely on the pharmacopoeias published by other countries for quality control. We believe that it is not incorrect to say that the United States Pharmacopeia (USP) is one of the most commonly referred to pharmacopoeias in developing countries.

In Cambodia, despite the enormous external and internal efforts, there are still problems related to the quality of medicines (McGinnis 2009). In 2006, we visited the National Laboratory for Drug Quality Control and found that it could not conduct dissolution tests because of severe budget constraints. Because the dissolution test is considered to be a minimal requirement to assure the quality of medicines (Cohen *et al.* 1990; Society of JP 2006a), we have major concerns regarding the quality of medicines sold in the Cambodian market. Therefore, we investigated the quality of medicines available in the Cambodian market, particularly in terms of the dissolution test.

In 2007, we collected 254 samples comprising amoxicillin (AMPC), ampicillin, cephalexin and acetaminophen and performed dissolution tests by referring to USP 30, the most up-to-date version at the time of the investigation.

J. Okumura and M. Taga contributed equally to this work.