

QUALITY OF PHARMACEUTICAL ITEMS AVAILABLE FROM DRUGSTORES IN PHNOM PENH, CAMBODIA

Daravuth Yang¹, Pinyupa Plianbangchang², Nuwat Visavarunroj¹ and Soravoot Rujvivipat¹

¹Department of Pharmaceutical Technology, ²Pharmacy Practice Research Unit, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, Thailand

Abstract. Drugstores and drug outlets are the main sources of care for the majority of Cambodian citizens because of the availability of drugs, short waiting time, and ability to control the cost of treatment. Unfortunately, no enforcement of pharmacy regulations and little consumer and drugstore personnel education contribute to a potential harmful unregulated drug market resulting in high costs and prolonged illness. No study has looked at the quality of over-the-counter drugs, which would have the highest impact on the people. In this study, we were interested in exploring the quality of commonly used pharmaceutical items available from drugstores in Phnom Penh, Cambodia, using uncoated aspirin tablets as a case study. Factors relating to quality of the drug were also examined. This study was conducted by means of drug fishing method to obtain uncoated aspirin tablet samples from 96 drugstores in Phnom Penh. The quality of the samples was examined in six aspects: percent label amount, weight variation, hardness, percent friability, disintegration time, and dissolution rate. We found that only seven (7.3%) of the total 96 samples passed all six quality criteria. Dissolution test appeared to be the most critical step in determining aspirin quality. Factors that were statistically related to the quality of the sample were type of packaging. All the drugs that passed the six criteria were in bottles. Source of the medications was also significantly related to their quality. Among seven samples that passed the test, six were from Vietnam. Our study revealed that the quality of uncoated aspirin tablets was a serious problem. The vast majority of the samples did not meet the standard requirements. Type of packaging and source of medications were related to the quality of samples. This study has important implications for the Cambodian government regarding the control of the quality of pharmaceutical items available in drugstores.

INTRODUCTION

Civil war and brutality have characterized the past 30 years of Cambodian history. After liberation from the genocide under the rule of Pol Pot in 1994, the country has been facing many difficulties in re-establishing its health care system. Among the problems are the low availability of health care facilities, insufficient health care personnel, and low accessibility to health services (Heng and Key, 1995; Chareonkul *et al*, 2002; Gollogly, 2002).

The information from the National Public Health and Research Institute, Cambodian Min-

istry of Health (1998) indicated that average monthly health expenditure of Cambodian citizens was 22.1% of their total household expenditure. The figure increases when the total household income decreases. In addition, 49% of this health expenditure was utilized by the private sector. A study found that a number of Cambodian people sold their land to pay for health care: most of this money was spent on inappropriate or dangerous treatment provided by unlicensed healers, or unofficial fees collected in government hospitals (Heng and Key, 1995).

The majority of Cambodian people seek care in the private sector since oftentimes when they visit government settings, unofficial fees are requested for services that should be given free of charge. In addition, Cambodian people reported low level of trust in government hospitals for lack of medications and long waiting time. For this reason, the majority of Cambodian citizens turned to the private sector, mostly purchasing medicines

Correspondence: Pinyupa Plianbangchang, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok 65000, Thailand.

Tel: 66-5526-1000 ext 3620; Fax: 66-5526-1057

E-mail: pinyupa@nu.ac.th, plianbangchang@hotmail.com

from drugstores and drug outlets. The main reasons are availability of drugs, short waiting time, and ability to control the cost of treatment (National Public Health and Research Institute, 1998). Unfortunately, with no enforcement of pharmacy regulations and little drug consumer education on the potentially side effects and limitations of modern drugs, people are not protected from a potentially harmful unregulated drug market with resulting in high costs and prolonged illness (The Committee for Research and Study on Counterfeit Drugs, 2001).

Drugstores, the main outlet of medications in Cambodia, are categorized into two main types: legal and illegal drugstores. Legal drugstores are further divided into three groups: Legal A stores which are the responsibility of registered pharmacists; Legal B stores which the responsibility of pharmacist assistants; and Legal C stores which are the responsibility of retired nurses. Regarding illegal drugstores, the government also categorized them into three groups: Illegal A stores which should be responsible to pharmacists but never have any pharmacist on duty; Illegal B stores or 'the doctor's cabinet' which are stores selling medications in front of the doctor's house along with providing illegal treatment; and Illegal C stores which are grocery stores illegally selling medications. According to the Cambodian Ministry of Health, there were approximately 892 legal drugstores and 2,800 illegal drugstores nationwide (The Committee for Research and Study on Counterfeit Drugs, 2001).

Phnom Penh, the capital of Cambodia, has a population of approximately 1,100,000. The city is located on the banks of three rivers (the Mekong, the Tonle Sap and the Tonle Bassac), and is divided into seven districts. Four districts; Chamcar Mon, Makara, Daun Penh, and Tuol Kok, are in the city area. The other three districts; Mean Chey, Russey Keo, and Dang Korv, are in the outskirts area of the city. As of 2002, there were approximately 400 Legal drugstores and about the same number of Illegal outlets in the city.

Aspirin (acetyl salicylic acid) is one of the world's safest and least expensive pain relievers with over 100 years of proven and effective treatment for a variety of illnesses. Nowadays, aspirin is widely used as an analgesic, antipyretic, and

anti-inflammatory agent (Gennaro, 1995). Aspirin is also the only over-the-counter pain reliever approved by the US Food and Drug Administration for prevention of cardiovascular diseases in persons who have suffered a first heart attack or a transient ischemic attack (TIA stroke) or who have unstable angina (US FDA, 1998). The entity is easily hydrolyzed into salicylic acid and acetic acid by exposing to moisture and/or high temperature. In Cambodia, aspirin is widely utilized for its availability and cheap price. Given its easily decomposed nature due to inappropriate storage, we chose this drug to be an example of commonly used drugs that people purchase from drugstores. The quality of aspirin tablets was assessed in six aspects: percent label amount, percent weight variation, hardness, percent friability, disintegration time, and dissolution rate.

The objective of this study was to examine the quality of commonly used pharmaceutical items available from drugstores in Phnom Penh, Cambodia, using uncoated aspirin tablets as a case study. We were also interested in assessing the factors relating to quality of the drug.

MATERIALS AND METHODS

This study was conducted between October 2002 and February 2003. We randomly selected drugstores, both legal and illegal, proportionately from the seven districts of Phnom Penh to be included in the sample. The sample size was 96 (from the total of approximately 800 drugstores).

The study was divided into two phases. Phase one was the sample collection by means of drug fishing method. One of the investigators (DY), who is native to the area, presumed the role of an orchard landlord. He went into each drugstore and requested a hundred tablets of uncoated aspirin. The reason for buying, if asked by drugstore personnel, was for his orchard workers for their muscle pain and fever. Immediately after leaving the store, DY recorded condition of the store, appearance of the seller, and detailed information of the sample in the Report Form (available upon request). In addition, the sample was instantly transferred to a proper container with desiccant to prevent further degradation prior to analysis.

Phase two comprised of quality determination of the samples in six aspects: percent label amount, weight variation, hardness, percent friability, disintegration time, and dissolution rate. Except for hardness testing, all analyses were in compliance with USP XX (1980) and USP XXV (2002). Each sample must pass all the tests to be considered acceptable quality. In addition, any sample that failed in percent label amount or weight variation test would not be subject to dissolution test. Further information on the analysis procedure is available upon request.

The data from this study were analyzed using SPSS version 10.0. The level of significance was set at 0.05.

RESULTS

The presentation of this section is divided into three parts. Part 1 describes the characteristics of the drugstores and aspirin sample. Part 2 shows the results of quality determination. Part 3 analyzes the factors relating to the drug quality.

Characteristics of the drugstores and aspirin sample

From 96 drugstores surveyed, 66 (68.7%) were located in the city area. The majority of them were legal drugstores (76, 79.2%). Pharmacists were identified by means of the question, 'Are you the pharmacist?' We found that, among 96 drugstores, only nine sellers (9.4%) were registered pharmacists. All of them were in Legal A stores. Only one was a nurse in Legal C store, and the rest were drug sellers without professional training.

About half of the sellers (55, 57.3%) did not ask any questions when the research confederate requested 100 tablets of aspirin. Among those who asked, the only question was 'For whom is this medication?' Furthermore, the majority of the sellers (79, 82.3%) did not give any advice accompanying their dispensing procedure. Among the advice given were, 'Take the medication immediately after meal,' and 'Follow by plenty of water'. There was no statistical difference in giving advice across types of drugstores. All pharmacists in this sample were found to give at least one piece of advice.

With regard to the condition of the stores,

only two (2.1%) were air-conditioned. Even though all stores were found to have appropriate cabinets in which the drugs are kept, most of the stores (87, 90.6%) did not arrange their items appropriately, *ie*, the drugs were not organized pharmacologically. The information regarding characteristics of the drugstores is shown in Table 1.

Table 2 exhibits the characteristics of 96 aspirin samples. The majority of aspirin samples were imported from Thailand (62 from 96, 64.6%), followed by Vietnam (21, 21.9%). The rest were imported from India (9, 9.4%), Malaysia (3, 3.1%) and USA (1, 1.0%). None of the sample was locally made. The average price of 100 tablets was $3,993.75 \pm 486.62$ Riels (approximately US\$1). The average recency of drug manufacturing (calculated in January 2003) was 17.18 ± 8.47 months.

About half (53, 55.2%) of the samples were packed in blister strips. The rest were stored in bulk bottles. For the latter, we found that the medications were kept inappropriately; that is, all were in plastic containers without any desiccant. Moreover, more than half of these bottles (33 of 43,

Table 1
Characteristics of the drugstores.

Variable	Number (%)
Location of the store	
City area	66 (68.7)
Out-skirt area	30 (31.3)
Type of the store	
Legal drugstore	76 (79.2)
Legal A	54 (56.3)
Legal B	12 (12.5)
Legal C	10 (10.4)
Illegal drugstore	20 (20.8)
Illegal A	9 (9.4)
Illegal B	3 (3.1)
Illegal C	8 (8.3)
Type of seller	
Pharmacist	9 (9.4)
Nurse	1 (1.0)
Non-professional seller	86 (89.6)
Drugstores with air-conditioning	2 (2.1)
Drugstores with appropriate cabinets	96 (100.0)
Drugstores with appropriate item categorization	9 (9.4)

76.7%) were presented without caps. When dispensed, the vast majority of drugstore personnel did not use medicine trays (39 of 43, 90.7%). The most frequently found method was pouring the drugs directly onto hands, and transferring them to small clear plastic bags (not medicine pouches). If not enough, the sellers then used their fingers to reach into the bottle and take more tablets. For sealing, all drugstores used rubber bands to wrap around to plastic bags.

Quality determination

The results of quality determination of aspirin tablets are shown in Table 3. Overall, only seven (7.3%) of the total sample passed all six criteria. The dissolution test appeared to be the most critical step in determining aspirin quality.

Eighty samples passed the percent label amount test. Among those that failed (16, 16.7%), all but one failed in the upper direction, *ie*, the tablets were found to contain more than 110% of the active ingredient claimed on the label.

Table 2
Characteristics of the aspirin sample.

Variable	Number (%)
Source of the medication	
Thailand	62 (64.6)
Vietnam	21 (21.9)
India	9 (9.4)
Malaysia	3 (3.1)
USA	1 (1.0)
Type of packaging	
Blister packed	53 (55.2)
Bottle packed	43 (44.8)

Table 3
Sample that passed the quality determination criteria.

Criteria	Number (%)
Percent label amount	80 (83.3)
Percent weight variation	95 (99.9)
Hardness	94 (97.9)
Percent friability	64 (66.7)
Disintegration	80 (83.3)
Dissolution (n = 66)	7 (7.3)
Overall test	7 (7.3)

Factors relating to the quality of aspirin tablets

Five factors were hypothesized to be related to the quality of aspirin tablets. They were type of the drugstores, location of the drugstores, type of packaging, source of the drugs, and recency of drug manufacturing.

The results indicated that all of the quality samples were from Legal drugstores. In addition, the majority of them were in the city area. However, no statistical difference was found for these two factors at p-value 0.05. Likewise, the recency of drug manufacturing did not statistically differ between the samples that passed and those that failed the tests.

Type of packaging was statistically related to the quality of the samples. All the drugs that passed six criteria were stored in bottles. Source of the medications was also significantly related to their quality. Among seven samples that passed the test, six were from Vietnam.

DISCUSSION

Before the discussion, we would like to point out three limitations of this study. First, this study was conducted only in Phnom Penh. Therefore, generalizability of the findings to other parts of the country is limited. However, Phnom Penh could be regarded as highly developed in the country. The results, therefore, could be used as a lower estimate of the real situation of the country. Second, the nature of our survey hindered us from observing the appropriateness of lighting and moisture level in the stores. This precluded two variables that could determine the quality of aspirin samples. Further study using other techniques such as in-depth interview and observation, which allowed the researcher more time in the store, is warranted to better understand these factors. Last, our study demonstrated that any sample which was not in the range of the United State Pharmacopoeia, was defined as substandard. However, whether this was intentionally a fraudulent product, incompetently made, or caused by inappropriate storage cannot be determined by the present data alone.

We found that much needed to be improved in terms of the condition of the drugstores and

Table 4
Factors relating to the quality of aspirin tablets.

Hypothesized variable	Number of sample		Statistics ^a
	Passed	Failed	
Type of the drugstores			
Legal	7	69	Chi-square 1.987 ^{ns}
Illegal	0	20	
Location of the drugstores			
City	6	60	Chi-square 1.011 ^{ns}
Out-skirt	1	29	
Type of packaging			
Blister	0	53	Chi-square 9.307*
Bottle	7	36	
Source of the drugs			Chi-square 18.047*
Thailand	1	61	
Vietnam	6	15	
India	0	9	
Malaysia	0	3	
USA	0	1	
Recency of the drug manufacturing (months)	17.29 ± 5.56 ^b	17.18 ± 8.69 ^b	Independent t 0.033 ^{ns}

Note: ^aFor Chi-square test of 2 by 2 tables, the significance was assessed by Fisher's exact test.

^b $\bar{X} \pm SD$; ^{ns} $p > 0.05$; * $0.001 < p < 0.005$

their personnel. Even though most of the drugstores had appropriate cabinets in which the drugs were kept, very rarely did we find appropriate item categorization. Mostly we found all the drugs kept together without arrangement according to pharmacological properties. This practice potentially led to mistakes in drug dispensing. In addition, from 54 Legal A-type drugstores surveyed, only in six were registered pharmacists available. This is a violation of the regulation that this type of drugstore needs to have a pharmacist on duty throughout the business hours. In Legal B and C, likewise, we found mostly non-professional sellers on duty. This raises a flag for Cambodian authority to monitor the availability of drugstore personnel to be in accordance with the regulations.

Quality determination analyses revealed that the dissolution test was the criteria which most samples failed. The dissolution test is an important indicator of bioavailability of the drugs in human body. Therefore, the study indicated the fact that the aspirin that people purchased might not be beneficial for their ailments. In addition, we found that 15 of 16 samples that failed the

percent label amount test did so in the upper direction, *ie*, the tablets contained much more of the active ingredient than claimed in the label. Fortunately, aspirin has a wide therapeutic window so the danger of ingesting too much may not be as serious. However, this finding can be used as an example for the authorities to exert more caution when it comes to drugs with narrow therapeutic window.

We found two factors that were significantly correlated with the quality of aspirin samples. The first factor was source of the medications. We found that six of seven samples that passed the standard criteria came from Vietnam. Special caution, then, should be placed on imported drugs from other countries. Unfortunately we could not collect any sample that was locally produced. Therefore, a comparison could not be made.

Packaging was another factor correlated with the quality of the samples. Aspirin tablets that were packed in bottles were significantly of better quality than those in blister packs. This finding somewhat contradicts a lay belief that blister packages should better preserve the items than

bottles. However, there are many types of blister packs with different permeability. Considering that the blistered samples in this study were only two brand names, it could fairly be assumed that the quality of blister package materials utilized by these particular manufacturers was compromised. In addition, the storage condition highly affected the quality of the medication. There is a false belief held by drugstore personnel that drugs kept in blister packages should be more durable to heat and moisture than drugs in bottles. This might influence them to fail to pay attention to proper storage conditions for blister packed drugs.

The location and type of drugstore were not statistically correlated with quality of medication in this study. However, a trend emerged. Samples from legal drugstores and city area were more likely to meet the standard criteria than the samples from illegal drugstores and outskirt area. Fortunately, the Cambodian government has made a strong intention to eliminate illegal drugstores. From this effort, the number of illegal drugstores in Phnom Penh has been reduced from approximately 400 in 2000 to 67 stores in May 2003 (Ministry of Health, 2003). This is promising that the substandard drugs that are available predominantly in illegal drugstores will be subsequently diminished.

Interestingly, recency of manufacturing did not exhibit relationship with quality of the medication. This finding is in the opposite direction to the theory that the drugs should be decomposed over time. Further research into this issue is highly warranted.

Overall, this study revealed that the quality of uncoated aspirin tablets in Phnom Penh was a serious problem. The vast majority of the samples in this study (89 of 96, 92.7%) did not meet the standard requirements. Compared with a study in Cambodia in 1997 (Giminez *et al*, 1997), where 36 of 128 (28.125%) of anti-infective drugs analyzed were substandard, the finding from our study posed a more serious situation concerning quality of the drugs.

This study has important implications for the Cambodian government regarding the following issues:

The control of imported drugs. This study

showed that drugs imported from different countries were of different quality. Since most of the drugs utilized in the country are imported, strict investigation of imported drugs before they can enter the distribution system is highly important. The current law and regulation regarding imported drugs require that importers file for an importing visa, which demands extensive documents proving the quality of drug manufacturing process as well as final product. In addition, such visa requires a renewal every five years. This measure should be theoretically effective in assuring the quality of pharmaceutical items entering the country. Unfortunately, the problem of drug smuggling along the Cambodian border has been prevailing. We highly believe that the findings of this study were the result of such problem. Therefore, the Cambodian government should pay close attention to this issue.

The condition of drugstores. Poor storage condition leads to degradation of medication, sometimes to the extent that it can harm the consumer. We found that most drugstores in our sample still needed much improvement in terms of storage condition. A countrywide surveillance and the implementation of law enforcement regarding the condition of drugstores are crucial. This measure could be incorporated into the 'Quality Drugstores Program' which is the current attempt of the Department of Drug and Food, Ministry of Health, in recognizing drugstores that comply to appropriate standard.

Training of health professionals and/or non-professional sellers in the drugstores. We found that drugstore personnel with professional training such as pharmacists and nurses performed far better than their lay personnel counterparts for their better knowledge in pharmacology and pharmacotherapeutics. This phenomenon occurs even though the government currently provides training for drugstore personnel every fortnight, with reportedly high attendant rate. More attention, therefore, should be paid to the cognitive, attitude and behavioral outcomes of such training to assure good quality training that could actually be translated into good practice in the community. In addition, emphasis should be made on notification of the

personnel of harm that can be caused by procuring substandard pharmaceutical items, both legally to their stores, and clinically to the health of their patients.

In summary, our study revealed that the quality of uncoated aspirin tablets was a serious problem. The vast majority of the samples did not meet the standard requirements. Type of packaging and source of medications were related to the quality of samples. Even though this study utilized only one drug as a case study, and surveyed only in one city, the results could be taken as the lower limits of the real problem occurring in the country. This is because aspirin is a relatively safe drug and Phnom Penh is considered a highly developed city in Cambodia. The Cambodian authorities, therefore, should strive to control and improve the quality of drugstores throughout the country, which serve as the main source of medications for Cambodian people. In addition, the quality of imported pharmaceutical items should also be closely monitored.

ACKNOWLEDGEMENTS

We would like to thank the Faculty of Pharmaceutical Sciences, Naresuan University for funding this study. Sincere appreciation goes to Assistant Professor Anong Visavarungroj, Department of Medicinal Chemistry and Pharmacognosy, Faculty of Pharmaceutical Sciences, Naresuan University, for her kind assistance in sample analysis procedure.

REFERENCES

Chareonkul C, Khun VL, Boonshuyar C. Rational drug

use in Cambodia: study of three pilot health centers in Kampong Thom Province. *Southeast Asian J Trop Med Public Health* 2002; 33: 418-24.

Gennaro AR. Remington: the science and practice of pharmacy. 19th ed. Baltimore, MD: Lippincott Williams & Wilkins. 1995: 1209-10.

Giminez F, Bruneton C, Narongrith DY. Étude de la qualité des médicaments vendus et dispensés au Cambodge. *Med Mal Infect* 1997; 271: 541-4.

Gollogly L. The dilemmas of aid: Cambodia 1992-2002. *Lancet* 2002; 360: 793-8.

Heng MB, Key PJ. Cambodian health in transition. *Br Med J* 1995; 311: 435-7.

Ministry of Health, Department of Drug and Food. Nombé de Pharmacies, Dépôt de Pharmacies A et B à Phnom Penh et Province Du 01-05-2003 au 31-05-2003. Phnom Penh: Ministry of Health, Cambodia, 2003.

National Public Health and Research Institute, Ministry of Health, Kingdom of Cambodia. The demand for health care in Cambodia. Phnom Penh: Ministry of Health, 1998.

The Committee for Research and Study on Counterfeit Drugs. Study report on counterfeit and substandard drugs in Cambodia. Phnom Penh: Ministry of Health, 2001.

The United States Pharmacopoeia (USP) XX. Rockville, MD: United States Pharmacopoeial Convention, Inc. 1980: 57.

The United States Pharmacopoeia (USP) XXV. Rockville, MD: United States Pharmacopoeial Convention, 2002: 168.

US Food and Drug Administration, Center for Drug Evaluation and Research. New prescribed uses for aspirin: questions and answers, 1998 [accessed 03 August 2001]. Available at <http://www.fda.gov/cder/news/aspirin/aspirinQA.htm>