

Original Research

Prevalence of pharmacist knowledge on beyond-use date (BUD) of various non-sterile compounding drugs in Indonesia

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Abstract

Objective: In extemporaneous compounding, drugs' stability is indicated by beyond-use date (BUD), which is different from the expiration date determined by manufacturers, hence, pharmacists are required to provide proper BUD information to patients. A recent study showed that BUD knowledge in the North Jakarta community is low, therefore, this study aims to examine the prevalence of Indonesian pharmacists' BUD knowledge regarding various non-sterile dosage forms. **Methods:** This cross-sectional study involved Indonesian pharmacists' knowledge of serving extemporaneous prescriptions. Recruitment was carried out through the purposive and snow-balling sampling method, while data were obtained by filling out a validated authors' designed questionnaire, with total 34 questions, and collected in September 2021 and then analyzed using the chi-square test. **Results:** Among the 221 total respondents, 93.7% had BUD knowledge, while 12.7% responded that BUD and expiration date are similar. Regarding BUD for crushed tablets, dry syrup without preservatives, and ointment without moisture, there were 13.1%, 82.8%, and 29.4% responded rightly, respectively. Furthermore, there was no correlation between BUD knowledge and respondents' characteristics, including health-care workplace and location, as well as gender, and age with $p > 0.05$. **Conclusion:** Based on the results, the Indonesian pharmacists were considered to have inadequate BUD knowledge, specifically on crushed tablets and ointment, and this might affect drugs' safety.

Keywords: Cross-Sectional Studies; Drug Compounding; Drug Stability; Indonesia; Pharmacists

INTRODUCTION

Beyond-use date (BUD) reflects drugs' stability of both sterile and non-sterile extemporaneous compounding.¹ According to the United States Pharmacopeia (USP) and Good Manufacturing Practices (GMP), when the primary packaging has been torn off, drug stability is indicated by BUD rather than the expiration date labeled by the manufacturer due to non-equality of protection risk or non-compatibility of the container with the preparation.^{2,3}

Drug stability is a crucial aspect that can alter the efficacy and/or safety, according to the standard of pharmaceutical services and drug use mentioned in the National Hospital Accreditation Standard Edition 1 (SNARS), extemporaneous drugs are to

be prepared and delivered in a safe and clean environment, and drugs must be labeled with important information including BUD.⁴ Meanwhile, based on the cross-sectional study conducted by Pramestutie et al. (2020), which included 322 samples, 30% of respondents in Malang City received BUD information from pharmacists or other health workers, while others received the information from various sources, e.g., magazine/book/leaflet/poster, drug labeling, electronic media, and family or friends.⁵ Therefore, information on drug stability needs to be well comprehended by pharmacists to rightly deliver BUD information to patients for rational and optimal use of drugs. According to the recent study by Cokro et al. (2021), the comprehension of BUD among the North Jakarta community in Indonesia is extremely low, as only 3% have sufficient knowledge, and none of the respondent mentioned pharmacists as a source of BUD information.⁶ This study aims to examine the prevalence of Indonesian pharmacists' knowledge of BUD of various non-sterile compounding drugs since this problem has not been previously investigated.

METHODS

Study design

This study was conducted using a cross-sectional design to obtain general information about respondents' knowledge on BUD of various non-sterile compounding as well as the characteristics that might contribute to it.

Study setting

This study included pharmacists working in healthcare facilities, including community and hospital-based practice, since

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compounding practice could be implemented in all healthcare setting, especially in Indonesia.

Population and sample

The population used was Indonesian pharmacists screened to become samples using the purposive and snow-balling sampling method. Based on the National Pharmacist Committee data in 2016, there are 32,386 pharmacists in Indonesia with a population ratio of = 1:7, 700; therefore, according to Charan et al, the minimal sample size needed for this study ranges from 15 with 5% absolute error to 380 with 1%.^{7,8} Based on power calculation using G*power 3.1 application, 145 sample is needed to acquire 95% power, with effect size $w = 0.3$; alpha error probability = 0.5; and $df = 1$; using chi-square family test. The inclusion criteria include Indonesian pharmacists willing to fill out the questionnaire, and those with the experience of serving patient prescriptions, specifically crushed tablets, dry syrup, and/or ointment extemporaneous dosage forms. Before filling out the questionnaire, prospective respondents were informed about the objectives of this study, identity confidentiality, and the use of data for publication. Non-registered pharmacist and pharmacy technicians were excluded from the study.

Data collection and instrument

Data collection was conducted by distributing the questionnaire through various social media platforms, including Instagram and Facebook as well as communication applications, mainly through Indonesian Pharmacists Association (IAI) Whatsapp groups, where members of IAI across regions of Indonesia were contacted. To ensure that all respondents are pharmacists, we asked for IAI membership number as confirmation to the respondents. The process of filling out the questionnaire was carried out in September 2021 with 34 questions, including sociodemographic and BUD knowledge of three common non-sterile compounding drugs found in Indonesia, namely crushed tablets, dry syrup without preservatives, and ointment without moisture. Before distribution, the questionnaire had passed face and content validity through peer-review process with clinical pharmacist expertise. Moreover, this questionnaire passed validity and reliability tests on 30 non-sample respondents using Pearson's Correlation (correlation coefficient greater than R table) and Cronbach's Alpha (with cutoff of 0.6) respectively.

Variables

This study mostly describes the profiles of BUD knowledge among Indonesian pharmacists. However, the probability of a correlation between respondents' characteristics and BUD knowledge was also analyzed. Dependent variables include the type of health facility and location where respondents work, as well as gender, and age groups, which were all analyzed in relation to BUD knowledge. Good BUD knowledge is derived as knowledge of the right drug storage, where the storage time for the powder mixture is 180 days, syrup without preservative is 14 days, and ointment without water content is 90 days. This definition follows United States Pharmacopeia (USP) since up to date, there is no specific BUD determination in Indonesian

Pharmacopeia.

Data analysis

The Chi-square test was used to measure the significant correlation between respondents' characteristics and BUD knowledge using the SPSS Base version 22 application. This type of analysis is suitable for measuring nominal data between two independent samples.

Ethics

This study was implemented following the Helsinki Declaration of 1975, the design was approved by the ethics committee, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia in May 2021.

RESULTS

A total of 221 respondents were included and filled out the questionnaire, 202 have experience serving crushed tablet extemporaneous dosage form prescriptions, while 139 and 150 have experience of serving dry syrup and ointment, respectively. Respondents' characteristic data are shown in Table 1. Regarding the workplace, there were similarities between hospital and community-based pharmacists. However, in terms of location, there were no significant differences between respondents' working within and outside Jabodetabek namely Jakarta and its surrounding. Respondents were mostly female and adults.

Table 1. Demographic data of pharmacist respondents

Characteristics of Pharmacist Respondents	Frequencies (n (%))
Health facility workplace	
Hospital-based	93 (42.1%)
Community-based	128 (57.9%)
Workplace location	
Jabodetabek*	118 (53.4%)
Outside Jabodetabek	103 (46.6%)
Gender	
Male	43 (19.5%)
Female	178 (80.5%)
Age	
Adult (21-46 years old)	199 (90%)
Middle-aged (≥ 46 years old)	22 (10%)

*) Jakarta and its surrounding

In the questionnaire, questions related to extemporaneous drug forms were developed to examine respondents' BUD knowledge. Regarding extemporaneous preparations, among the 221 respondents, 93.7% admitted to have knowledge about BUD, while approximately 12.7% claimed that BUD and expiration date are similar. Furthermore, 13.1%, 82.8%, and 29.4% responded rightly about BUD for crushed tablets, dry syrup without preservatives, and ointment without moisture, respectively. Confirmation questions were also provided to ascertain respondents' knowledge about BUD, and only 15.4% responded rightly, as shown in Table 2.

A bivariate analysis was conducted to determine the correlation



BUD Knowledge Profile	Frequencies (n (%))
Have you ever heard about BUD? Yes, I have No, I have not heard before	207 (93.7%) 14 (6.3%)
Is BUD the same as the expiration date stated on drug packaging? Yes No	28 (12.7%) 193 (87.3%)
How long can we keep crushed tablets? Right answer* Wrong answer	29 (13.1%) 192 (86.9%)
How long can we keep dry syrup without preservatives? Right answer** Wrong answer	183 (82.8%) 38 (17.2%)
How long can we keep ointment without moisture? Right answer*** Wrong answer	65 (29.4%) 156 (70.6%)
Knowledge confirmation question: If a doctor prescribed an extemporaneous acetaminophen "X" crushed-tablet on 9 July 2021, and the expiration date of the drug written on the packaging is 15 November 2021, when is BUD that should be written on the patient's drug label? Right answer Wrong answer	34 (15.4%) 148 (81.3%)

*) Based on USP 2019 recommendation, 180 days is the correct answer

**) Based on USP 2019 recommendation, 14 days is the correct answer

***) Based on USP 2019 recommendation, 90 days is the correct answer

#) Total respondents for this question was 182 pharmacists, while 39 did not finish the questionnaire.

between general BUD knowledge and four components of respondents' characteristics, including health facility workplace, location, gender, and age. The chi-square analysis results showed that there are no correlations between these aspects, with $p > 0.05$ for every analytic measurement, as shown in Table 3.

DISCUSSION

According to the United States Pharmacopeia (USP), the appropriate BUD for non-aqueous formulations is below 6 months. Meanwhile, water containing oral and topical formulations without moisture have BUD of 14 days and 90 days, respectively. Table 2 shows that the majority of respondents seemingly had inadequate BUD knowledge on crushed tablets and ointment formulations. Moreover, only a few achieved the right answer on confirmation question, which

means that the actual number of pharmacists with adequate BUD knowledge is low. To enhance Indonesian pharmacists' competency, in 2013, the Association of Indonesian Pharmacy Higher Education composed an Academic Script containing the core curriculum of pharmacist education as a standard that must be followed to ensure the quality of graduates. Based on the academic script, pharmacists are required to adequately prepare non-sterile extemporaneous compounding, determine its storage and labeling, as well as inform patients about the rational use of drugs by implementing effective communication.^{9,10} Consequently, Indonesian pharmacists are expected to be acquainted with the steps on gathering and delivering BUD information by making legible labeling and communicating effectively to patients. However, a previous study on BUD knowledge of the North Jakarta community found that approximately 50% of the informants consider BUD and the expiration date similar.⁶ This result shows that there is

BUD Knowledge Item	Health facility workplace	Workplace location	Gender	Age
BUD knowledge related to the difference with expiration date	0.929	0.101	0.778	0.413
BUD knowledge related to maximum duration of keeping crushed tablets	0.935	0.315	0.184	0.555
BUD knowledge related to maximum duration of keeping dry syrup without preservatives?	0.072	0.645	0.530	0.897
BUD knowledge related to maximum duration of keeping ointment without water content?	0.622	0.702	0.174	0.794



a need to promote Indonesian pharmacists on having sufficient BUD knowledge and delivering the information to patients. This study emphasizes the importance of repeating and updating BUD information through various education development programs regulated by The Indonesia Pharmacist Association. Without proper BUD knowledge, drug labeling might be misleading, thereby causing misinformation to patients which might lead to unsafe use of medications. However, similar studies which focused on pharmacist comprehension of BUD were rare.

The possible limitation of this study is the relatively broad variation of respondents, due to the use of only a few exclusion criteria. However, each aspect of respondents' characteristics was analyzed in relation to BUD knowledge. Characteristics such as workplace location and health care facility type showed similarities, but gender and age had discrepancies as female adults dominated this study and might be one of its limitations. This is because adulthood is considered to be a productive period compared to the older age group. Regarding gender, the number of female pharmacist graduates is more than male, specifically in Indonesia.¹¹ However, there was no significant correlation between all aspects of respondents' characteristics towards pharmacist knowledge.

CONCLUSION

Based on the results, Indonesian pharmacists have a low

BUD knowledge about various non-sterile extemporaneous compounding. Therefore, policy-maker involvement, such as The Indonesian Pharmacist Association, is strongly needed in updating BUD knowledge.

CREDIT AUTHOR STATEMENT

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Sherly Tandi Arrang: Methodology, Investigation, Resources, Writing – Review and Editing

Monika Arvia Chiara: Validation, Investigation, Formal Analysis, Investigation

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CONFLICTS OF INTEREST

This research has no conflicts of interest.

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