



Analysis of Potential Drug's Interaction In Prescription Compounded at Arbai Pharmacy From January to March 2024

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ARTICLE INFO

Article history

Received : 20 Dec 2025

Revised : 23 Dec 2025

Accepted : 31 Dec 2025

Keywords

Compounded Prescriptions

Drug Interaction

Pharmacy

Pharmaceutical compatibility

ABSTRACT

Based on the prescription preparation process, prescriptions are divided into compounded and non-compounded prescriptions. Compounded prescriptions are often written for pediatric patients. Methods in the research use a descriptive, non-experimental study of compounding prescriptions from January to March 2024 at Arbai Pharmacy. Analysis of drug interactions with mechanisms of action in terms of pharmacokinetics, pharmacodynamics, and severity based on the Medscape Drug Interaction Checker software and the Pharmaceutical Codex Twelfth Edition to analyze interactions in terms of pharmaceuticals. The results are based on pharmaceutical interactions; 2 prescriptions were found to have the potential for photolysis and hygroscopicity, and 103 prescriptions were compatible. Drug interactions were found in 21 prescriptions (20%) with the potential interaction. There are 15 forms of combination. Mechanisms of interaction in terms of pharmacokinetics in 7 prescriptions (46.67%), 8 prescriptions in terms of pharmacodynamics with a minor severity level in 4 cases (26.67%), 11 cases (74.33%) moderate and none major. Based on The Pharmaceutical Codex Twelfth Edition, the drug is photolytic and hygroscopic in terms of pharmaceutical properties. Based on the Medscape Drug Interaction Checker, the drug interacts through pharmacokinetic and pharmacodynamic mechanisms. To prevent drug-drug interactions in compound prescriptions, there must be good collaboration between pharmacists..

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INTRODUCTION

Pharmacies function as facilities for pharmaceutical services and as places where pharmacists practice their profession (Permenkes, 2017). Pharmaceutical services are defined as direct services provided to patients related to pharmaceutical preparations with the primary goal of improving patients' quality of life (Permenkes, 2016). To ensure the quality of pharmaceutical services delivered to the community, the Ministry of Health of the Republic of Indonesia issued Regulation No. 73 of 2016 concerning Standards for Pharmaceutical Services in Pharmacies, which serves as a guideline for pharmaceutical personnel in professional practice.

Pharmaceutical services in pharmacies begin with prescription review, which includes administrative, pharmaceutical, and clinical assessments conducted by pharmacists. One of critical component of prescription review is the identification of potential drug–drug interactions. Such interactions may occur in prescriptions containing two or more drugs, with the risk is increasing substantially in polypharmacy prescriptions involving five or more medications. Polypharmacy is commonly encountered among elderly patients, pediatric patients, and critically ill patients (Nego and Gayatri, 2023). In addition, compounded prescriptions are particularly susceptible to drug–drug interactions due to the combination of multiple active ingredients and dosage forms.

Drug–drug interactions arise when drugs are administered concurrently, leading to synergistic, antagonistic, or other undesirable effects (Amarullah et al., 2025). Drug–drug interactions arise when drugs are administered concurrently, leading to synergistic, antagonistic, or other undesirable effects (Amarullah et al., 2025). These interactions may result in various clinical consequences, including reduced therapeutic efficacy, enhanced pharmacological effects, or drug toxicity. Drug interactions are generally classified into three mechanisms: pharmaceutical, pharmacokinetic, and pharmacodynamic. Pharmaceutical interactions, also referred to as incompatibility or immiscibility interactions, occur outside the body and involve physical or chemical changes such as precipitation, crystallization, or alterations in pH that affect drug solubility and stability. Hygroscopic and photolabile drugs may further compromise the stability of compounded preparations.

Compounded prescriptions are frequently prescribed for pediatric patients due to the lack of appropriate commercial dosage forms and the need for individualized dose adjustments based on body weight. Although compounding is practical and economical, it also increases the risk of pharmaceutical incompatibility, particularly when coated tablets are used in compounded formulations. (Rochjana et al., 2019) Therefore, careful evaluation of compounded prescriptions is essential to prevent potential drug–drug interactions.

Pharmacokinetic drug interactions involve processes related to drug absorption, distribution, metabolism, and excretion, whereas pharmacodynamic interactions occur at the level of drug–receptor interactions, resulting in altered pharmacological effects. Based on drug interaction checker applications, the severity of drug interactions is classified into three categories: minor, moderate, and major. Minor interactions generally cause mild effects and do not require changes in therapy, moderate interactions may lead to clinically significant effects requiring therapeutic adjustment, and major interactions have the potential to cause serious or fatal outcomes and therefore require immediate intervention. Previous research by (Amarullah et al., 2025) which analyzed the potential for drug interactions in pharmacy services using Stockley's Drug Interactions (Preston, 2015), identified 17 interaction cases and 5 unidentified cases. Pharmacokinetic interactions were the most frequently observed (45.4%), followed by pharmacodynamic interactions (31.8%). Most interactions were classified as minor (40.9%) or moderate (36.3%), and no major interactions were reported.

In addition, several studies in Indonesia have reported persistent administrative, pharmaceutical, and clinical inadequacies in prescription practices, particularly in pediatric patients (Febrianti et al., 2018) found that deficiencies in pediatric cough prescriptions included missing patient weight, prescription date, and age. From a pharmaceutical perspective, powder formulations were most commonly prescribed, while information on dosage strength was rarely provided. Clinically, although most



prescriptions had appropriate dosing and frequency, a small proportion still exhibited potential drug–drug interactions.

A study conducted at pharmacies in the Umbulharjo District of Yogyakarta City from January to December 2015 reported several administrative, pharmaceutical, and clinical inadequacies in pediatric cough prescriptions. The most frequently unmet administrative requirements were patient weight (99.7%), prescription date (50.4%), and patient age (35.4%). From a pharmaceutical perspective, powder formulations were the most commonly prescribed (71.4%), followed by syrups (15.5%) and tablets (13.1%), while information on dosage strength was available in only 0.3% of prescriptions. Clinically, most prescriptions had appropriate dosages (84.2%) and correct administration frequency (100%), with no cases of polypharmacy and only 0.3% showing potential drug–drug interactions.

Based on these findings, this study aims to analyze the potential for drug–drug interactions in prescriptions dispensed at Arbai Bandar Lor Pharmacy in 2024.

METHOD

This study employed a non-experimental descriptive design using retrospective data collected from January to March 2024. The study population consisted of all outpatient prescriptions dispensed at Arbai Bandar Lor Pharmacy during the study period.

Samples were selected using purposive sampling based on predefined inclusion and exclusion criteria. The inclusion criteria were outpatient prescriptions covered by the Health Insurance Administration Agency (BPJS) that contained compounded medications and were complete and legible. Prescriptions that were incomplete, illegible, or non-compounded were excluded from the study. A total of 105 prescription sheets met the inclusion criteria and were analyzed.

Data were obtained from original BPJS outpatient prescription records. The selected study period was chosen to provide a representative snapshot of routine pharmacy practice while ensuring the availability and completeness of prescription data for analysis.

RESULT

Arbai Pharmacy is a pharmacy store located at Jl. Bandar Lor Gg. II no. 34 B Kediri. It provides services to general patients and BPJS patients. This study used BPJS patient prescriptions from January to March 2024. There were 3,319 prescription sheets, and using the Slovin formula with a margin of error of 0.05%, a minimum sample of 98 prescription sheets was required. Based on purposive sampling, 105 prescription sheets were obtained, with the following data

Table 1 List of medications compounded for patients

Drug Name	Dosage Form	Therapy Class	Quantity	Percentage (%)
Acyclovir	Tablets	Antivirus	2	0.54
Alphamol	Caplets	Antipyretic Analgesic	1	0.27
Alpara	Caplets	Antihistamine	1	0.27
Ambroxol	Tablets	Expectorant	28	7.52
Amoxicillin	Caplets	Antibiotic	24	6.45
Antasida	Chewable tablets	Anti-reflux, anti-ulcer	1	0.27

Drug Name	Dosage Form	Therapy Class	Quantity	Percentage (%)
Betamethasone	Cream	Corticosteroid	2	0.54
Bromhexin	Tablets	Expectorant	13	3.49
Cefadroxil	Capsule	Antibiotic	11	2.96
Cetirizin	Film-coated tablet	Antihistamine	13	3.49
Ciprofloxacin	Film-coated tablet	Antibiotic (Quinolone)	1	0.27
Cotrimoxazole	Tablets	Antibiotic (Sulfonamida)	3	0.81
CTM	Tablets	Antihistamine	7	1.88
Dexymox	Caplets	Antibiotic	6	1.61
Demacolin	Tablets	Antihistamine	21	5.64
Dexametasone	Tablets	Corticosteroid	49	13.17
Domperidon	Tablets	Antiemetic	1	0.27
Flucadex	Caplets	Cough and Fever	3	0.81
Gentamicin	Ointment	Antibiotic (Aminoglikosida)	1	0.27
Grafachlor	Caplets	Non-steroid Anti-inflammatory(NSID)	10	2.69
Grantusif	Caplets	Antifungal	8	2.15
GG	Tablets	Expectorant	8	2.15
Heptasan	Film coated tablet	non-steroidal anti-allergic	17	4.57
Ibuprofen	Film coated tablet	NSID	4	1.07
Ketoconazole	Tablet	Antifungal	1	0.27
Mecobalamin	Capsul	Hematopoietic Agent – Nootropic	1	0.27
Metil Prednisolon	Tablet	Corticosteroid	21	5.64
Metronidazole	Tablet	Antibiotic	2	0.54
Miconazole	Cream	Antifungal	1	0.27
Neurodex	Film coated tablet	Vitamin	1	0.27
Ondancetron	Film coated tablet	Antiemetic – Serotonin receptor antagonist	3	0.81
Paracetamol	Caplets	Antipyretic Analgesic	27	7.26
Ranitidin	Film-coated tablet	H2 receptor antagonist	9	2.42
Salbutamol	Tablets	Adrenoreceptor - bronchodilator	10	2.69
Teosal	Tablets	Anti-asthma	1	0.27
Tera F	Tablets	Cough and Fever	13	3.49
Vesperum	Tablets	Antiemetic	1	0.27
Vitamin B6	Tablets	Vitamin	1	0.27
Vitamin B Complex	Tablets	Vitamin	20	5.38
Vitamin C	Tablets	Vitamin	16	4.3
Zink	Dispersible Tablet	Electrolyt	9	2.42



Drug Name	Dosage Form	Therapy Class	Quantity	Percentage (%)
	Amount		372	100

Table 1 shows that the most commonly prescribed drugs at Arbai Pharmacy are dexamethasone, ambroxol, paracetamol, and amoxicillin. Dexamethasone accounted for 49 prescriptions with a percentage of 13.17%, ambroxol accounted for 28 prescriptions with a percentage of 7.52%, paracetamol accounted for 27 prescriptions with a percentage of 7.26%, and amoxicillin accounted for 24 prescriptions with a percentage of 6.45%

Table 2 Pharmaceutical Interactions Reviewed from Stability and Compatibility Perspectives

Pharmaceutical Interactions	Amount of Prescriptions			
	There are		There are none	
	Amount	Percentage (%)	Amount	Percentage (%)
Stability	2	1.90	103	98.10
Compatibility	103	98.10	2	1.90

According to Table 2, pharmaceutical interactions in terms of stability to light (photolysis) and hygroscopicity show that 2 prescriptions (1.90%) have the potential for photolysis and hygroscopicity, while 103 prescriptions (98.10%) are compatible.

Table 3 Potential for drug interactions

Potential for drug interactions	Amount of Prescriptions			
	There are		There are none	
	Amount	Percentage (%)	Amount	Percentage (%)
Drug – drug interaction	21	20	84	80

According to Table 3, it can be seen that the results of the analysis of potential drug-drug interactions were found in 21 prescriptions (20%).

Table 4 Drug-Drug Interactions

Drug Combination	Mechanism of action and severity	Detail	Quantity
Cefadroxil + Ibuprofen	Pharmacokinetics Minor	Cefadroxil will increase the levels or effects of ibuprofen through competition with acidic (anionic) drugs for renal tubular clearance.	1
Chlorpheniramine (tera f) + Salbutamol	Pharmacodynamics Moderate	Chlorpheniramine increases sedation and albuterol decreases it.	1

Drug Combination	Mechanism of action and severity	Detail	Quantity
Ciprofloxacin + Piridoksin (vit. B Complex)	Pharmacokinetics	Ciprofloxacin will decrease the levels or effects of pyridoxine by altering the intestinal flora. This only applies to the oral forms of both agents.	1
	Minor		
Ciprofloxacin + Tiamin (vit. B Complex)	Pharmacokinetics	Ciprofloxacin will decrease thiamine levels or effects by altering the intestinal flora. This only applies to the oral forms of both agents	1
	Minor		
Dexamethasone + Ibuprofen	Pharmacodynamics	Both increase the toxicity of the other through pharmacodynamic synergism. Increased risk of GI ulceration	1
	Moderate		
Dexamethasone + Metronidazole	Pharmacokinetics	Metronidazole will increase the levels or effects of dexamethasone by affecting the metabolism of the liver/intestinal enzyme CYP3A4	1
	Moderate		
Dexamethasone + Ondansetron	Pharmacokinetics	Dexamethasone will decrease the levels or effects of ondansetron by affecting the metabolism of the liver/intestinal enzyme CYP3A4. No adjustment of the ondansetron dose is recommended for patients taking this drug.	2
	Moderate		
Heptasan + Chlorpheniramine (CTM)	Pharmacodynamics	Both increase sedation	1
	Moderate		
Heptasan + Chlorpheniramine (demakolin)	Pharmacodynamics	Both increase sedation.	1
	Moderate		
Heptasan + Diphenhydramin (grantusif)	Pharmacodynamics	Both increase sedation.	2
	Moderate		
Heptasan + Salbutamol	Pharmacodynamics	Cyproheptadine increases sedation and albuterol decreases it.	4
	Moderate		
Metilprednisolon + Theophyllin (Teosal)	Pharmakoninetic	Methylprednisolone will decrease the levels or effects of theophylline by affecting the metabolism of the CYP3A4 enzyme in the liver/intestines.	1
	Moderate		



Drug Combination	Mechanism of action and severity	Detail	Quantity
Ondancetron + Metronidazole	Pharmacodynamics Moderate	They both increase the QTc interval. Caution should be exercised when metronidazole is administered concomitantly with IV ondansetron or higher doses of IV ondansetron (do not exceed 16 mg IV)	1
Paracetamol + Metronidazole	Pharmacokinetics Minor	Metronidazole will increase the levels or effects of acetaminophen by affecting the metabolism of the liver enzyme CYP2E1	2
Salbutamol + Diphenhydramin (grantusif)	Pharmacodynamics Moderate	Diphenhydramine increases sedation and salbutamol decreases it.	1

Table 4 indicates that there were 15 types of drug interactions in the combination therapy. The most common drug interaction occurred with Heptasan + Salbutamol, with 4 prescriptions. The mechanism of interaction was pharmacokinetic in 7 (46.67%) combinations and pharmacodynamic in 8 (53.33%) combinations, with a minor severity level in 4 (26.67%) cases and a moderate severity level in 11 (74.33%) cases, based on the Medscape Drug Interaction Checker reference.

DISCUSSION

During the process of mixing powders and ointments, the medicine must be removed from its packaging and crushed using a mixer or mortar and pestle. Several things to note are ensuring homogeneous mixing, maintaining humidity, room temperature, and light in the mixing area, as these factors can affect the stability of the drug. The assessment of drug stability in this study is based on several literature sources such as Martindale's 38th edition, Pharmacopeia Edition VI, the Handbook of Vitamins (Zempleni et al, 2007), and The Pharmaceutical Codex.

Hygroscopicity is the ability of a substance to absorb moisture from the environment. According to Martindale's 38th edition, acyclovir must be protected from moisture and light. Ciprofloxacin is slightly hygroscopic, containing varying amounts of water (Brayfield et al., 2014). According to the Indonesian Pharmacopoeia Edition VI, mecobalamin in anhydrous form is highly hygroscopic, absorbing approximately 12% water when exposed to air. Neurodex, which contains thiamine mononitrate, is hygroscopic (Zempleni et al., 2007). In the Pharmacopoeia Edition V 2014 literature, ranitidine is sensitive to light and moisture. According to Pharmaceutical Codex, the wetness of powder formulations is caused by certain drugs that are hygroscopic or moist, such as salt forms (HCl, HBr, maleate, etc.). Meanwhile, Vitamin B Complex is also hygroscopic because it contains the active ingredients Vitamin B1 and Vitamin B2, which

are hygroscopic, as well as calcium pantothenate, which is slightly hygroscopic. (Kemenkes RI, 2020). This is in line with the research by (Syamsuddin & Purnamasari, 2024) on compatibility and stability studies.

Some drugs that undergo photolysis are ambroxol, bromhexine, cetirizine, chlorpheniramine maleate, dexamethasone, methylprednisolone, metronidazole, ondansetron, paracetamol, salbutamol, and vitamin C because the stability of these drugs is affected by light. Ambroxol, methylprednisolone, and salbutamol must be protected from light according to The Pharmaceutical Codex Twelfth Edition.

Metronidazole becomes darker when exposed to light (Kemenkes RI, 2020). Bromhexine is stored in light-protected containers (Kemenkes RI, 2020). The aqueous solution of chlorpheniramine maleate has a pH between 4 and 5. It must be stored in an airtight container and protected from light (Brayfield et al., 2014). Dexamethasone in solid form is stable in air but must be protected from light. Storage at relatively high humidity levels also has a detrimental effect on tablet stability, as does paracetamol, which requires protection from light. In dry conditions, pure paracetamol is stable up to a temperature of 45°C. It absorbs an insignificant amount of moisture at 25°C at a relative humidity of up to 90% (The Pharmaceutical Codex Twelfth Edition).

Incompatibility occurs when a drug cannot be mixed properly, either physically or chemically, which can result in a loss of therapeutic effectiveness and an increased risk of toxicity or unwanted side effects. At the Arbai Pharmacy, an incompatibility was observed between Demacolin and Vitamin B Complex. According to Martindale, 36th Edition, pseudoephedrine (an ingredient in Demacolin), along with Vitamin B1, Vitamin B2, and Ca Pantothenate (ingredients in Vitamin B Complex), increases the hygroscopicity of the preparation when mixed. As a result, the mixture does not blend well, as supported by research. Incompatibility occurs when a drug cannot be mixed properly, either physically or chemically, which can result in a loss of therapeutic effectiveness and increase the risk of toxicity or unwanted side effects. Regarding the incompatibility of prescription drugs at the Arbai pharmacy, there was incompatibility between Demacolin and Vitamin B Complex. According to the Martindale 36th Edition literature, pseudoephedrine (an ingredient in Demacolin) and Vitamin B1, Vitamin B2, and Ca Pantothenate (ingredients in Vitamin B Complex) increase the hygroscopicity of the preparation when mixed, so that the mixture cannot blend well, according to research by (Syamsuddin & Purnamasari, 2024) Drug interactions can occur due to the combination of several drugs that can cause interactions between one drug and another, resulting in toxicity or side effects. The severity of drug interactions that occur in prescribed drugs consists of 4 cases of minor interactions, 11 cases of moderate interactions, and no cases of major interactions. There are two mechanisms of drug interactions: pharmacokinetic and pharmacodynamic. Of the 15 cases of drug interactions, 8 involved pharmacokinetic interactions and 7 involved pharmacodynamic interactions.

CONCLUSION

This study found that, based on pharmaceutical properties related to photolysis and hygroscopicity, 2 prescriptions (1.90%) had the potential for pharmaceutical instability, while the majority of prescriptions (98.10%) were considered compatible. Analysis using the Medscape Drug Interaction Checker revealed that 21 out of 105 prescriptions (20%) had the potential for drug–drug interactions.



Most potential interactions were classified as moderate in severity (74.33%), followed by minor interactions (26.67%), with no major interactions identified. In terms of interaction mechanisms, pharmacodynamic interactions accounted for 53.33% of cases, while pharmacokinetic interactions accounted for 46.67%. These findings indicate that although most compounded prescriptions were pharmaceutically compatible, a considerable proportion still posed a risk of clinically relevant drug–drug interactions. Recommendation is Pharmacists should strengthen prescription review and routinely screen compounded prescriptions for potential drug–drug interactions using reliable interaction-checking tools. Attention to the stability and compatibility of hygroscopic and photolabile drugs during compounding is essential. Enhanced collaboration between pharmacists and prescribers is recommended to reduce the risk of clinically significant drug–drug interactions.

ACKNOWLEDGMENT

The Arbai Pharmacy, located in Bandar Lor, which provided the venue, facilities, and infrastructure for the research. Ghouzul Muna, who conducted the sampling, and the research team, who collaborated and contributed to the implementation of this research.

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