Pharmaceutical and Biomedical Sciences Journal
Volume 6(2), 2024, 118-123

A retrospective descriptive cross-sectional study of Oral Dosage Form Administered in The Form of Suspension to ICU Patients at Hospital X

Nelly Suryani[1*], Vidia Arliani Anwar[2], Yardi Saibi[1], Estu Mahanani Dhilasari[1], Sabrina Dahlizar[1], Ofa Suzanti Betha[1], Ismiarni Komala[1], Afifah Nurnishrina Azzahra[1]
[1]Departement of Pharmacy, Faculty of Health and Sciences, Syarif Hidayatullah State Islamic University, Jakarta, Indonesia
[2]Stikes IKIFA East Jakarta, Indonesia

**corresponding author: nelly.suryani@uinjkt.ac.id*

Received: 17 September 2024; Accepted: 18 December 2024

Abstract: Patients in the intensive care unit were often very sick and had lost consciousness. Because they had trouble swallowing, individuals with reduced awareness frequently depended on enteral tubes (NGT) for their daily medical and nutritional requirements. Since not all medications were accessible in parenteral forms, patients who relied on enteral tubes often had issues, including drug stability. Many problems arose in clinical usage when the medication was crushed or suspended and put into the NGT, including drug obstruction in the enteral tube and a reduction in drug stability as a result of the dose form being altered, making the drug unstable. Thus, this study aimed to ascertain the stability of oral suspension medications given to intensive care unit patients. The medical records of intensive care unit patients who had received oral medication therapy at X Hospital in Jakarta were examined retrospectively using a cross-sectional, descriptive approach. According to the statistics, coated tablets accounted for 68% of the most frequently used oral medication preparations. It was highly likely that crushing the coated tablets and administering them via NGT had resulted in tube obstruction. Additionally, 59.26% of the medications used had exhibited hygroscopic qualities, and several had been readily hydrolyzed. Based on these findings, it was concluded that oral medications, particularly crushed-coated tablets, could negatively affect drug stability. Active substances with hygroscopic properties and those prone to hydrolysis were also identified as potential contributors to instability.

Keywords: Enteral Tube, Hygroscopic, ICU, Oral Medicine, Stability

DOI: 10.15408/pbsj.v6i2.41341

1. INTRODUCTION

The Intensive Care Unit (ICU) was a part of the hospital that served patients with acute or chronic illnesses requiring immediate intervention that could not be provided in general care rooms (Ananta and Fitri, 2020). During the swallowing process, most ICU patients experienced a decrease in consciousness. Patients in this condition typically relied on a nasogastric tube, also known as an NGT. The NGT was used to provide nutrition and daily care (Sigmon and An, 2021).

Oral solid medications administered via an NGT were crushed or triturated with 10-20 milliliters of water using a mortar and pestle. Tube blockage during administration was one of the many issues associated with the clinical use of this technique. In 6-45% of cases, nasogastric tubes could become clogged (Kunieda *et al.,* 2021). This could impact the stability of medications used in ICU patients and was a major risk factor (Rahmawati *et al*., 2018). If a product retained the same characteristics and quality as when it was manufactured and could be stored within certain limits, it was referred to as stability.

The stability of active ingredients, the manufacturing process of dosage forms, packaging methods, and environmental factors such as temperature, or formulation factors like pH, solubility in water, and particle size were some factors that could affect the stability of pharmaceutical preparations. The case of drug instability in intravenous catheters was typically caused by pH precipitation (Hanifah, 2015). When a drug was prepared in solution form, it was important

to determine the ideal pH of the preparation, as the solution's pH significantly impacted its stability (Banker and Rhodes, 2011).

The study conducted by Bernardus et al. (2013) found that 100% of compounded drugs underwent physical changes due to their hygroscopic or moisture-retaining properties, which led to alterations in the stability of the drugs. In the study conducted by Thong *et al.* (2018), it was found that an assessment of medication loss among 24 commercially available medication-crushing devices revealed that medication loss, without rinsing, ranged from 1.9% to 13.3%, depending on the crushing device. All devices, except for six, resulted in significant drug loss.

In addition to pH, drugs containing ester and amide groups often underwent degradation pathways. Drug instability could lead to decreased or lost efficacy, conversion of the drug into a toxic form, or changes in the appearance of the preparation (such as color, odor, taste, and consistency), which could be detrimental to the user. x This drug instability had the potential to endanger the patient's condition. As a result, it delayed the therapeutic process and increased therapy costs. Research related to drug stability and compatibility remained very limited. This study aimed to ascertain the stability of oral suspension medications given to intensive care unit patients. The medical records of intensive care unit patients undergoing oral medication therapy at X Hospital in Jakarta were reviewed retrospectively using a descriptive, cross-sectional method.

2. MATERIALS AND METHOD

2.1 Study Design

A retrospective descriptive cross-sectional method was used in this study. Medical records of ICU patients at Hospital X in Jakarta who received oral medication as part of their therapy were reviewed. .The study findings were presented in narrative or illustrative form.

a. Inclusion Criteria

1. Complete medical records containing (medical record number, gender, and age) that were clearly legible.
2. The research subjects were medical record data of patients who received oral therapy in suspension form in the ICU of RS Pelabuhan Jakarta.
3. Patients who received therapy with ≥ 5 oral medications.

b. Exclusion Criteria

1. Medical records that were incomplete, unclear, or illegible and could not be evaluated.
2. Patients who received treatments in forms other than oral preparations.
3. Patients who received therapy with ≤ 5 oral medications.

2.2 Study Subjects

The sample for this study comprised all medical records of ICU patients who were administered solid oral medication at Hospital X Jakarta from July to December 2021. A total of 34 patients were included in the study, consisting of 20 men and 14 women.As secondary data were used, no sampling technique was applied in this study.

2.3 Data Analysis

To determine the prevalence of incompatibility and stability issues with oral preparations in the ICU, univariate analysis was conducted using Microsoft Excel 2010.

3. RESULTS AND DISCUSSION

3.1 Patient Characteristics

There were 34 ICU patients, including 20 male and 14 female patients. The largest age group consisted of 17 patients over 65, followed by eight patients aged 56 to 65. According to a 2011 study by Vera at Immanuel Hospital Bandung, the age group 60-69 years accounted for 46% of the population, and those over 80 years represented 18%. This was considered a risk factor due to the association between age and the aging process, which led to decreased organ function in elderly patients. The mortality rate for critically ill patients increased with age (Root *et al*., 2011). The percentage of patient characteristics is shown in Table 1.

Table 1. Characteristics of ICU Patients Based on Gender and Age for the Period July – December 2021

Characteristics	Number of Medical Records (n=34)	Percentage (%)
Gender		
Male	20	58.8
Female	14	41.2
Age		
5-11	1	3.1
36-45	4	11.7
46-55	4	11.7
56-65	8	23.5
>65	17	50

3.2 Types of Oral Solid Dosage Forms.

The results showed that ICU patients at Hospital X Jakarta commonly used film-coated and enteric-coated tablets, with 15 frequently used medications. These included isosorbide dinitrate for 21 patients (12.96%), bisoprolol for 17 patients (10.49%), and simvastatin for 10 patients (6.17%).

The most commonly used enteric-coated tablet was aspirin, administered to 16 patients (10%). This could lead to drug instability due to the variety of coated tablet formulations administered through enteral tubes. If these drugs were intended to be swallowed whole, they should not have been chewed, crushed, split, or broken, as per the IAI guidelines (2014). Table 2 presents this data.

References such as Martindale 36th Edition, Indonesian Pharmacopoeia VI Edition, Handbook on Injectable Drugs 17th Ed, and journal articles were used to process data on the physicochemical properties and stability of drugs administered to ICU patients at Hospital X Jakarta.

Table 2. Frequency Distribution of Oral Solid Drugs Based on Preparation Type

Name of Drugs	Frequency	Percentage %
Film Coated Tablets		
ISDN	21	12.96
Bisoprolol	17	10.49
Simvastatin	10	6.17
KSR	9	5.56
Amlodipine	7	4.32
Furosemide	6	3.70
Atorvastatin	6	3.70
Ethambutol	4	2.47
Isoniazid	4	2.47
Azithromycin	4	2.47
Euphilin	4	2.47
Metformin	3	1.85
Cefixime	3	1.85
Spironolactone	2	1.23
Cetirizine	2	1.23
Enteric Coated Tablets		
Aspirin	16	10
Sugar Coated Tablets		
Bicnat	5	3
Uncoated Tablets		
Candesartan	7	4.32
Paracetamol	6	3.70
Alprazolam	4	2.47
Digoxin	3	1.85
Glimepiride	3	1.85
Capsule		
N-Acetyl Cysteine	7	4
Caplet		
BECOM C	5	3.09
Ramipril	4	2.47
Total	**162**	**100**

The hygroscopic properties of drugs presented in Table 3 were referenced to estimate potential instability. The data showed that some drugs were hygroscopic. Hygroscopicity is the ability of a substance to absorb moisture from its environment. Evaluating the hygroscopicity of pharmaceutical solids was crucial, as absorbed moisture could impact pharmaceutical products' physical and chemical stability (Allwood and Kearney, 1998)

(Gayatricitraningtyas and Abidjuli, 2012) (Benardus, 2013)

Hygroscopic drugs should have been stored in tightly sealed containers to slow the degradation of their powders (Allada *et al.*, 2016). Hygroscopic or moisture-sensitive drugs, such as salts like HCl, HBr, and maleate, complicated tablet manufacturing (Allada *et al.*, 2016). The hygroscopic nature of an active pharmaceutical ingredient affected the stability of the drug itself and impacted the moisture level of other drugs when combined (Allada *et al.*, 2016). Moisture in powders led to microbial growth reduced aesthetic quality, and degradation of active ingredients, including color, odor, and clumping upon mixing (Allada *et al.*, 2016).

Table 3. Hygroscopic Properties of Drugs

No	Name of Drugs	Number of Prescriptions Containing Drugs
		Hygroscopic
1	ISDN (Isosorbid Dinitrat)	21
2	Aspirin	16
3	Simvastatin	10
4	KSR	9
5	Candesartan	7
6	Furosemide	6
7	Becom C	5
8	Ethambutol	4
9	Ramipril	4
10	Digoxin	3
11	Metformin	3
12	Glimepiride	3
13	Cefixime	3
14	Spironolactone	2
15	Paracetamol	0
16	Cetrizin	0
17	Alprazolam	0
18	Bisoprolol	0
19	Amlodipine	0
20	N-Acetyl cysteine	0
21	Isoniazid	0
22	Bicnate	0
23	Azithromycin	0
24	Atorvastatin	0
25	Euphilin	0
Total		96
Instability percentage		59,26%

Instability also occurred when certain drugs were co-prescribed, such as metformin and ethambutol. Both salts had hygroscopic properties, meaning they could absorb and retain moisture at various temperatures and humidity levels (Allada *et al.*, 2016). Thus, when these two drugs were combined and administered through an enteral tube, drug instability could occur, causing the medication to become sticky and adhere to the tube, leading to blockages in the enteral tube (Allada *et al.*, 2016).

Table 4. Drugs Not Available in Parenteral Preparations

No.	Name of Drugs
1.	Bisoprolol
2.	Aspilet
3.	Simvastatin
4.	KSR (Potassium chloride)
5.	Amlodipine
6.	Candesartan
7.	Atorvastatin
8.	Becom C
9.	Alprazolam
10.	Rapimpril
11.	Isoniazid
12.	Ethambutol
13.	Metformin
14.	Cefixime
15.	Glimepiride
16.	Spironolactone
17.	Cetrizin

3.3 Solid Oral Dosage Forms

Data regarding medications that were unavailable in parenteral forms was presented in Table 4. Out of the 25 drugs surveyed, 17 of them were not accessible orally because these medications were transformed into suspensions administered via nasogastric tubes (NGT) before being given to patients. Consequently, researchers were more interested in understanding how the stability of these drugs changed after being converted into suspensions.

According to Ruzikova (2014), crushing or grinding coated tablet medications were not recommended as they altered the drug's stability. Crushing solid oral dosage forms impacted the stability of the active pharmaceutical ingredient. If tablets were broken to remove the enteric coating that protected the drug from the acidic gastric environment, the degradation of the drug in vivo increased, resulting in a minimal amount of active drug available to produce the desired clinical effect (Root *et al.*, 2011).

Crushing enteric-coated tablets and administering them via enteral feeding tubes was likely to cause tube blockages. This occurred because, prior to inserting enteric-coated tablets through the enteral feeding tube, the enteric coating had to be broken or removed. As a result, the drug was likely to degrade in the stomach. Thus, the amount of drug that could be absorbed decreased, and patients needed to be monitored regularly (Valentovic, 2007)

One example of a prodrug, simvastatin, was administered in an inactive lactone form and was processed by the liver into the beta-hydroxy acid metabolite by carboxylesterase enzymes. Subsequently, the active plasma inhibited HMG-CoA reductase (hydroxymethylglutaric acid coenzyme A reductase) (Sinaga, 2013) (Li *et al*., 2019). Hydrolysis of simvastatin to simvastatin acid could increase plasma concentration, affecting simvastatin's efficacy and adverse reactions (Basusarkar, 2013) Simvastatin is also hydrolyzed at basic pH.

Moreover, spironolactone was easily hydrolyzed due to its lactone ring (cyclic ester) and thioester group. The degradation resulted from hydrolysis of the thioacetate group to produce 7α-thiospironolactone (as an intermediate), followed by S-methylation to generate 7α-thiomethylspironolactone. The lactone ring in 7α-thiomethylspironolactone was also hydrolyzed to produce canrenone. (WHO, 2001). The effect of this hydrolyzed drug caused the drug to degrade in the stomach, leading to a decrease in drug levels in the body (Root *et al*., 2011).By changing the dosage form from tablets to suspensions, the stability of the drug changed, especially for coated tablet medications.

One aspect that had to be considered when administering medications through enteral tubes was the type of drug selected, which should always have been tailored to the needs of local healthcare facilities. The aspect of bioequivalence of drugs had to be considered when converting drugs to another formulation, as it could lead to changes in efficacy and safety. Variations in the amount of drug that reached systemic circulation due to changes in drug formulation could impact efficacy and the likelihood of side effects, particularly for drugs with a narrow therapeutic index, such as digoxin and theophylline (Root *et al.,* 2011).

4. CONCLUSION

The study showed that the most commonly used oral drug preparations were coated tablets, accounting for 68%. Crushing coated tablets and administering them through NGT had a high likelihood of causing tube blockages. Additionally, 59.26% of the drugs used exhibited hygroscopic properties, and several were prone to hydrolysis. The findings concluded that solid oral drugs, particularly crushed-coated tablets, could negatively affect drug stability, and active drug substances with hygroscopic and easily hydrolyzed properties had the potential to cause instability.

5. REFERENCES

Allada, R., et al. (2016) ‘Hygroscopicity Categorization of Pharmaceutical Solids by Gravimetric Sorption Analysis: A Systemitic Approach’, Asian Journal of Pharmaceutics, p. 279.

Allwood, M.C., & K.M.C.J. (1998) Compatibility and Stability of Additives in Parenteral Nutrition Admixtures. 9th edn.

Ananta, T.B. and Fitri, A.L.D. (2020) ‘Mobilisasi Dini Pada Pasien Kritis Di Intensive Care Unit (Icu)’, Case Study. J Keperawatan Widya Gantari Indones, 4(1), pp. 59–66.

Banker GS and Rhodes CT (2011) ‘Karakteristik Pasien Usia Lanjut di Ruang Rawat Intensif Rumah Sakit Immanuel Bandung’, JKM, 10(2), pp. 110–119.

Basusarkar, A., Kandimalla, A., Dudley, R., et al. (2013) ‘Chemical Stability of Compounded Spironolactone Suspension in Proprietary Oral Mix’, J.Pharm Sci, 23(1), pp. 67–70.

Bernardus, R., and Kurniawan (2013) ‘Stabilitas Resep Racikan yang Berpotensi Mengalami

Inkompatibilitas Farmasetika yangg Disimpan pada Wadah Tertutup Baik', Jurnal Ilmiah Mahasiswa Universitas Surabaya, 2(2).

Gayatricitraningtyas and Abidjulu, J. (2012) 'Pengaruh Suhu Terhadap Stabilitas Serta Penetapan Kadar Tablet Furosemida Menggunakan Spektrofotometer Uv-Vis', Pharmacon, 1(2), pp. 93–97.

Gupta, A.K., et al. (2018) 'Update on Current Approaches to Diagnosis and Treatment of Onychomycosis', Pubmed, pp. 929–938.

Hanifah, S. (2015) 'Identifikasi pH Obat-Obat yang Digunakan di Pediatric Intensive Care Unit (PICU) untuk Pencegahan Inkompatibiltas Intravena', Ilm Farm, 11(2), pp. 55–64.

Kunieda, K., et al. (2021) 'A Safe Way to Administer Drugs Through a Nutrition Tube—The Simple Suspension Method', Dysphhagia, 37(2), pp. 318–322.

Li, Z., et al. (2019) 'Role of Esterase Mediated Hydrolysis of Simvastatin in uman and Rat Blood and Its Impact on Pharmacokinetic Profiles of Simvastatin and Its Active Metabolite in Rat', J Pharm Biomed Anal, 168, pp. 13–22.

Madden, A. (2007) Handbook of Drug Administration Via Enteral Feeding Tubes. 2nd edn.

Rahmawati, R., et al. (2018) 'Problem Kompatibilitas dan Stabilitas Pencampuran Sediaan Intravena Pada Pasien Anak di RSUP Dr. Sardjito', Intravenous Drug Compatibility and Stability Problem in Pediatric Patient at RSUP Dr. Sardjito, p. 7.

Remington, J.P. (2021) Remington - The Science and Practice of Pharmacy. 21st ed.

Root, T., et al. (2011) 'Pharmaceutical Issues when Crushing , Opening or Splitting Oral Dosage Forms', R Pharm Soc, 1, pp. 1–7.

Sigmon, D.F., and An, J. (2021) 'Nasogastric Tube', Petunjuk Teknis Penyelenggaraan Pelayanan Intensive Care Unit di Rumah Sakit , p. 53.

Sinaga, E. (2013) Strategi Meningkatkan Penghantaran Obat Di Dalam Tubuh. Edited by UNAS Press.

Thong, M.Y., Manrique, Y.J., & and Steadman, K.J. (2018) 'Drug Loss While Crushing Tablets: Comparison of 24 Tablet Crushing Devices', PLoS ONE, 13.

Valentovic, M. (2007) 'Simvastatin', xPharm Compr Pharmacol Ref, 1, pp. 1–4.