Pharmacists' and Community Knowledge on The Safety and Halal Status of Pediatric Medications Containing Alcohol

Putri Wulandari¹, Yunita Nur Aziza¹, Muhammad T. Ghozali², Marlyn Dian Laksitorini^{3,4} and Dwi Endarti^{3,5*}

- ^{1.} Undergraduate Program of Pharmacy, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia, 55281
- School of Pharmacy, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Yogyakarta, Indonesia
- ^{3.} Department of Pharmaceutics, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta Indonesia, 55281
- ^{4.} Institute of Halal and Industry System, Halal Center UGM, Universitas Gadjah Mada, Indonesia, Yogyakarta, 55281
- ^{5.} Research Center of Pharmacoeconomic and Health Technology Assessment, Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta Indonesia, 55281

Article Info	ABSTRACT
Submitted: 09-01-2024	Knowledge of the halal characteristics of products is crucial in
Revised: 13-08-2024	assessing product quality, particularly within societies where this
Accepted: 15-08-2024	consideration is highly significant. In this context, the presence of alcohol in
	medicinal substances may considerably influence consumer preferences, due
*Corresponding author	to potential implications for halal compliance and safety. This research aims
Dwi Endarti	to evaluate the awareness and understanding of these critical aspects among
	pharmacists and the wider community. This research employed a
Email:	convenience sampling method, drawing from 180 participants within the
endarti_apt@ugm.ac.id	Special Region of Yogyakarta, Indonesia. The sample included 100 community
	members with prior experience purchasing paediatric cough and flu syrups,
	alongside 80 community pharmacists. Data collection was conducted via a
	self-administered, paper-based questionnaire distributed between April and
	June 2023. Descriptive statistical methods were applied for data analysis. The
	research found that 76.1% of community participants demonstrated good
	knowledge regarding halal considerations for alcohol content in paediatric
	cough and flu syrups. Nonetheless, there was a notable gap in specific
	knowledge about the permissible alcohol levels for these medications to be
	deemed halal. Among community pharmacists, the findings revealed an
	average knowledge score of 73.88% concerning both health risks associated
	with alcohol in syrups and relevant halal criteria. However, pharmacists
	lacked sufficient understanding of the legally permitted alcohol limits in
	children's medications and the potential blood alcohol concentration in
	paediatric patients following consumption. This research underscores the
	urgent need for pharmacists to deepen their understanding of alcohol content
	in paediatric formulations and to proactively share this information with the
	community.
	Keywords: Alcohol, Halal, Knowledge, Paediatrics, Pharmacist

INTRODUCTION

Indonesia, notable for its large Muslim population, represents a significant market in the halal industry. As of 2022, the country is home to approximately 229 million Muslims, accounting for about 12.7% of the global Muslim population (Fathoni, 2020). Consequently, adherence to stringent halal standards is a crucial consideration for products marketed in Indonesia. This issue is particularly salient regarding food and medicine, as the consumption of halal products is an obligatory practice within the Muslim community (Rahmah &

Indonesian J Pharm 36(1), 2025, 187-195 | journal.ugm.ac.id/v3/IJP Copyright © 2025 by Indonesian Journal of Pharmacy (IJP). The open access articles are distributed under the terms and conditions of Creative Commons Attribution 2.0 Generic License (https://creativecommons.org/licenses/by/2.0/). Barizah, 2020). A key determinant of a product's halal status is the presence of alcohol (Rahmah, 2019). The Indonesian Ulema Council (MUI) has issued a fatwa advising against the use of alcohol in medications, except when no suitable alternatives are available. For food and beverages to be classified as halal, their ethanol concentration must not exceed 0.5% v/v. Furthermore, pursuant to National Law No. 33 of 2014, which focuses on Halal Product Assurance, any product entering, circulating, or being sold in Indonesia must possess a valid halal certificate (Rahmah & Barizah, 2020). In addition, the Indonesian Food and Drug Administration, through its decree No HK.03.1.23.06.10.5166 of 2010. mandates that manufacturers of drugs, traditional medicines, and dietary supplements must disclose the alcohol percentage in their products on the packaging if alcohol is used as an ingredient. This information must be prominently displayed and expressed as a percentage (% v/v). Failure to disclose alcohol content in medications is considered illegal under this law.

Numerous studies have highlighted the presence of alcohol in pediatric medications, including cough and flu syrups, across various countries (Batista & Antoniosi Filho, 2020; Berlin et al., 2017; Christiansen, 2015; Kelber et al., 2017; Neo et al., 2014; Svirskis et al., 2013). The inclusion of alcohol in these medicinal formulations raises significant safety concerns, particularly for infants and toddlers, whose enzymatic systems for alcohol metabolism are not fully developed. This immaturity leads to distinctive pharmacokinetic characteristics and an increased risk of toxicity (Ieraci & Herrera, 2007; Laksitorini et al., 2021; Singh et al., 2007). Early exposure to alcohol has been shown to adversely affect neurogenesis and compromise the integrity of the blood-brain barrier. A study conducted on mice indicates that a single exposure to alcohol on postnatal day 7 correlates with a reduction in the pool of progenitor cells in the hippocampus (Ieraci & Herrera, 2007). Moreover, studies on young adults exposed to alcohol in utero demonstrate reduced volumes in critical brain regions, including the corpus callosum, caudate, putamen, and cerebellum (Inkelis et al., 2020). In addition, alcohol has been found to impair the blood-brain barrier by increasing its permeability, thereby undermining its typical restrictive function (Haorah et al., 2005, 2007, 2008; Laksitorini et al., 2021; Muneer et al., 2012). These findings underscore the detrimental effects of alcohol on early developmental processes.

Given that pediatric cough and flu syrups are often available over the counter, the knowledge possessed by caregivers and pharmacists is crucial for ensuring optimal therapeutic outcomes and mitigating potential adverse effects. Pharmacists must possess comprehensive knowledge about the medications they dispense (Bekele et al., 2020), while consumers should be adequately informed about the products they purchase (Taylor et al., 2023). This knowledge is particularly important, as few countries have established regulations concerning the maximum permissible alcohol content in pediatric medications. There is an urgent need for such regulatory measures to be implemented in developing nations, including Indonesia and Nigeria (Soremekun et al., 2019).

This research aimed to investigate underexplored areas in previous studies, specifically focusing on the knowledge possessed by pharmacists and the broader community regarding the halal and safety aspects of alcohol in preparations. pediatric and cough cold Furthermore, previous studies have not been conducted in regions where halal considerations are particularly significant (Barnes & Chappell, 1981).

Conducted in the city of Yogyakarta, Indonesia, this research aims to address this gap by assessing both the knowledge of pharmacists and the general awareness of the community regarding the safety and halal status of medications containing alcohol intended for children.

MATERIALS AND METHODS

This research employed a descriptive, observational, cross-sectional approach. This methodology primarily aimed to identify and elucidate the characteristics of a specific condition within a defined population at a single point in time.

Community Knowledge of Alcohol-Containing Pediatric Syrups for Cold and Cough

This reserach was conducted in Yogyakarta, Indonesia, following ethical approval from the Faculty of Medicine's Ethics Commission at Universitas Gadjah Mada (Approval No: KE/FK/0592EC/2023). The research utilized a convenience sample consisting of 100 participants from the Special Region of Yogyakarta, encompassing four regencies and one municipality. Eligible participants included males and females aged between 18 and 50 years, residing in Yogyakarta city, who had prior experience purchasing pediatric cold and cough syrups and expressed a willingness to participate in the research. Participants were recruited through Focus Group Discussions (FGDs) held during monthly parental community meetings (*Posyandu*), ensuring representation from all four districts and the municipality.

The data collection method employed a selfadministered, paper-based questionnaire specifically designed for this research. The questionnaire consisted of two distinct sections: the first section aimed to collect socio-demographic information and details related to cold and cough medications. Convenience sampling techniques were utilized, incorporating both online and offline avenues. Online platforms, including WhatsApp, Line, Telegram, and Instagram, were used in conjunction with offline distribution methods. Printed questionnaires were directly disseminated to pharmacists at pharmacies and distributed to community members in public spaces throughout the Special Region of Yogyakarta (Aziza, 2023).

Community Pharmacist Knowledge of Alcohol-Containing Pediatric Syrups for Cold and Cough

This research examined pharmacists' knowledge regarding the halal status and safety aspects of pediatric cold and flu syrups containing alcohol. Conducted in Yogyakarta in April 2023, the research received ethical approval from the Ethics Commission of the Faculty of Medicine at Gadjah University (Approval Mada No: KE/FK/0617/EC/2023). participants Eligible included pharmacists employed in health facilities and pharmacies within Yogyakarta who were willing to participate in the study. The second section of the questionnaire was specifically dedicated to assessing participants' knowledge concerning the halal status and safety considerations associated with alcohol-containing medications (Wulandari, 2023).

Data analysis

This research presents the demographic characteristics of the sample, providing a general overview of the entire group. The demographic characteristics were analyzed using descriptive statistics. In addition, the level of knowledge was described based on the distribution of responses to individual questionnaire items. Respondents were categorized into 'high' or 'low' knowledge groups, with the median scores of each group serving as cutoff points for classification.

RESULTS AND DISCUSSION

Community Knowledge of Halal and Safety Aspects of Pediatric Cold and Cough Syrups Containing Alcohol

Provides an overview of the characteristics of the community participants, presenting the demographic profile of the study cohort (Table I). The majority of participants, 83 individuals or 83%, were women. The educational levels of the participants varied, with the highest level of education being a high school diploma, represented by 29 participants (29%). Participants with doctoral degrees were the least represented, with only one individual (1%) in this category. In terms of occupation, the largest group consisted of civil servants, totaling eight participants (8%). Conversely, the least represented occupations were freelancers, researchers, and engineers, each comprising only one participant (1%).

For the community's knowledge (Table II) level about ethanol content in these syrups in Yogyakarta City, the analysis revealed a range of scores from 20% to 100%, with a median value of 76.1% and an average score of 80%. The majority of the participants demonstrated a high level of knowledge (50-75%), accounting for 95% of the respondents, while 5% were categorized as having low knowledge (25-50%).

Among pharmacists in Yogyakarta City, the highest frequency and percentage of knowledge fell into the good category (\geq 75-100%), with 45 participants (56.3%). This was followed by the adequate knowledge category (60-75%), which included 25 participants (31.3%), and the low knowledge category (\leq 60%), which comprised ten participants (12.5%) (Table III).

The findings from the research revealed that approximately 50% of the participants were unaware of the presence of alcohol in pediatric medications. In addition, around 66% of participants lacked information regarding the permissible limit of alcohol concentration in medications to be considered halal. However, a significant proportion (78%) expressed a strong interest in verifying the alcohol content in pediatric medications prior to purchase. The most widely acknowledged statement, receiving 96% agreement, was that the halal label should be prominently displayed on the packaging of cold and cough syrups. Conversely, the least recognized aspect concerning the MUI standard related to the definition that medications with an alcohol content below 0.5% v/v are deemed halal.

No	Variable	Category	N (%)
1	Sex	Male	17 (17%)
		Female	83 (83%)
2	Education	Junior high school	3 (3%)
		High school	29 (29%)
		Vocational high school	12 (12%)
		Vocational school	13 (13%)
		Bachelor degree	29 (29%)
		Master degree	11 (11%)
		Doctoral degree	1 (1%)
3.	Occupation	Freelance	1 (1%)
		Engineer	1 (1%)
		Pharmacy Assistant	4 (4%)
		Faculty member	3 (3%)
		College students	5 (5%)
		Housewife	34 (34%)
		Government officer	8 (8%)
		Self-Employed	34 (34%)
		Researcher	1 (1%)
		Teacher	6 (6%)
		Pharmacist.	1 (1%)

Table I. Demographic Description of Pharmacist Community Respondents(n=100)

Table II. Public Community Members' Responses to Perceptions of Alcohol Content in Pediatric Cough and Flu Syrup Preparations

No	Statement	Correct Answer
1	Halal-certified drug products have met cleanliness, quality, and safety	86 (86%)
2	The halal logo on the packaging of drug products is one of many factors that consumers consider when choosing a product.	90 (90%)
3	Drug products with halal certification assure their cleanliness, quality, and safety.	93 (93%)
4	Halal certification in syrup products aims to provide assurance of their safety.	87 (86%)
5	The halal status of the drug product can be identified based on the availability of the halal label on the packaging.	70 (70%)
6	Some pediatric syrups contain alcohol as an ingredient	50(50%)
7	According to the Indonesian Ulema Council, a drug product with an alcohol content of less than 0.5% v/v can be categorized as halal.	34 (34%)
8	Children are more prone to experience adverse effects from alcohol in pediatric syrup compared to adults.	79 (79%)
9	A halal label on the packaging of pharmaceutical products is a must.	96 (96%)
10	Information on the percentage of alcohol in the product can be used as an alternative approach to assess the halal status of pediatric syrups when buying the product.	78 (78%)

Variable	Number of respondents	Minimum	Maximum	Mean	Median	SD
Knowledge	100	20	100	76.1	80	6.31

No.	Variable	Category	n(%)
1.	Age	21-25 y.o.	5 (6.3%)
		26-30 y.o.	36 (45.0%)
		31-35 y.o.	17 (21.3%)
		36-40 y.o.	10 (12.5%)
		41-45 y.o.	6 (7.5%)
		46-50 y.o.	4 (5.0%)
		51-55 y.o.	1 (1.3%)
		66-70 y.o.	1 (1.3%)
2.	Sex	Male	15 (18.8%)
		Female	65 (81.3%)
3.	Education	Pharmacist (Undergraduate)	73 (91.3%)
		Pharmacist (Master Program)	7 (8.8%)
4.	Work experience	<1 year	3 (3.8%)
		1-5 years	37 (46.3%)
		6-10 years	22 (27.5%)
		11-15 years	10 (12.5%)
		16-20 years	5 (6.3%)
		>20 years	3 (3.8%)
5.	Job description in	Pharmacist as a Pharmacy Manager	51 (63.8%)
	pharmacy	Pharmacist work in community pharmacy	27 (33.8%)
		Pharmacist work in Drug Information in Pharmacy	2 (2.5%)

Table III. General Description of Pharmacist Respondents

Table IV. Pharmacist Respondents' Knowledge of Ethanol Content in Pediatric Cough and Flu Syrup

Variable	Number of correct answer (%)
Blood alcohol concentration (BAC) is a parameter that indicates the toxicity of alcohol to individuals	75 (93.75%)
Blood alcohol concentration (BAC) of 180 mg/dL is associated with impaired vision, coordination, and emotional lability	58 (72.5%)
Alcohol in pediatric medication requires greater attention due to its neurotoxic properties	74 (92.5%)
Alcohol is added to oral medication to reduce the solubility of the drugs.	69 (86.25%)
A Blood alcohol concentration (BAC) above the normal level can impair the blood-brain barrier (BBB).	74 (92.5%)
The consumption of pediatric medications containing alcohol should not result in a blood alcohol concentration above 0,25 g/L (25 mg/dL).	48 (60%)
The adverse effect of alcohol in the blood, exceeding the legal blood alcohol concentration, may include impairment in vision, coordination, speech, emotional liability, ataxia, sweating, nausea, vomiting, and unconsciousness.	77 (96.25%)
The Indonesian Ulema Council released a fatwa in 2018 stating that alcohol content above $5\% \text{ v/v}$ is unlawful.	42 (52.5%)
To protect the pediatric population, the European health authorities have established a limit where children aged 6 years should not consume than 6mg/kg BW of alcohol in medications, and resulting in the blood alcohol concentration of less than 1 mg/dL	27 (33.75%)
Many drugs in Indonesia contain alcohol levels exceeding those permitted by the Indonesian Ulema Council.	47 (58.75%)

Variable	Number of respondents	Minimum	Maximum	Mean	Median	SD
Knowledge	80	30	100	73.88	80	15.39

Table V. Respondents' Knowledge Categories Based on Interval

Interval	Knowledge Levels	n(%)	
≥75% - 100%	Good	45 (56.3%)	
60% - 75%	Sufficient	25 (31.3%)	
≤60%	Lack	10 (12.5%)	

Only 34% of participants accurately identified this criterion, while 16% provided incorrect responses, and 50% indicated the need for further information or clarification on this specific point. The assessment of the community's knowledge level regarding the alcohol content in paediatric cold and cough syrups within Yogyakarta City demonstrated considerable variability in scores, ranging from a minimum of 30% to a maximum of 100%. The median and mean scores were recorded at 80% and 76.1%, respectively. The average total score of 80% suggests that the community in Yogyakarta generally possesses good knowledge regarding the halal status of alcohol in paediatric cough and flu syrups (Table II). However, it is noteworthy that approximately 5% of participants fell into the low knowledge category, scoring between 25-50%.

This research aimed to assess the knowledge of pharmacists in Yogyakarta regarding the alcohol content in paediatric cold and cough syrups. The statement items, along with the number of participants providing correct responses, were analysed. The results indicated that the highest level of awareness among pharmacists pertained to the side effects of alcohol in paediatric formulations, with 96.25% of participants acknowledging the potential for various adverse effects when blood alcohol concentration (BAC) limits are exceeded (Table IV). In contrast, the aspect least understood by participants was the European regulation concerning BAC limits (1 mg/dL) and the maximum permissible alcohol content (6 mg/kgBW) in paediatric doses for children aged six years. Only 33.75% of participants correctly answered this question, while 43.6% admitted to a lack of knowledge, and 22.5% provided incorrect responses. These findings highlight a significant knowledge gap among participants regarding BAC regulations, as evidenced by the limited number of correct answers and the substantial proportion of participants either lacking awareness or offering incorrect responses.

The findings from this research indicate several key points: (1) Both pharmacists and the community demonstrate a sufficient level of knowledge regarding the halal status and safety aspects of paediatric medications containing alcohol; (2) Community awareness regarding the presence of alcohol in certain paediatric medications is limited; (3) Knowledge related to the maximum permissible alcohol content in medications, as established by the Indonesian Ulema Council (MUI), is notably low across both groups studied; (4) Pharmacists exhibit a restricted understanding of the maximum allowable alcohol content in paediatric medications as determined by international regulatory bodies such as the FDA, WHO, and EMA; (5) There is a lack of awareness among pharmacists regarding the fact that some paediatric medications exceed the alcohol level thresholds defined by the Indonesian Ulema Council. The novelty of this research lies in its focus on pharmacists' knowledge of the halal and safety aspects of alcohol in paediatric medications.

A study surveyed 309 pharmacists from various metropolitan areas in Canada and revealed a concerning deficiency in knowledge, with respondents achieving an average score of less than Notably. the findings 50%. highlighted pharmacists' inability to answer questions of considerable practical importance. This gap in knowledge included a lack of understanding of the interactions between alcohol and medications such as probenecid, salicylic acid, chlorpromazine, and penicillin. While another study has primarily focused on the role of pharmacists in advising or intervening with patients experiencing alcoholrelated issues, there has been limited investigation into their awareness of halal pharmaceuticals, particularly those containing alcohol (Alserhan et al., 2020; McCaig et al., 2011; Sheridan et al., 2008).

From a halal perspective, it is recommended to avoid alcohol in medications whenever possible. The Indonesian Ulema Council (MUI) suggests that the ideal maximum alcohol content in medications should be less than 0.5% v/v. Notably, this religious guideline aligns with the thresholds established by the Food and Drug Administration (FDA) and the World Health Organization (WHO), both of which advocate for a maximum alcohol concentration of 0.5% v/v in paediatric medications intended for children under six years of age (Alserhan et al., 2020). This globally recognized standard is designed to prevent alcohol intoxication among the paediatric population, a demographic particularly vulnerable due to their incomplete development of alcohol-metabolizing enzymes. This developmental immaturity increases the susceptibility of paediatric patients to the adverse effects associated with alcohol consumption.

The findings of this research indicate that the community recognizes the necessity of halal labelling on the packaging of cold and cough syrup medications. However, regarding the safety of alcohol-containing medications, respondents demonstrate a lack of awareness that children under six years old should avoid medications with alcohol concentrations exceeding 0.5% v/v. The Indonesian Ulema Council allows the use of alcohol medications only under emergency in circumstances. However, there is ongoing debate about whether the current situation qualifies as an emergency, particularly given the increasing presence of pharmaceutical scientists and advancements in pharmaceutical technology that can provide alternatives to alcohol in drug formulations. This research suggests a pressing need for the pharmaceutical industry to explore methods for eliminating alcohol from liquid medications. Various techniques have already been investigated to develop more suitable formulations for children (Attebäck et al., 2022; Laksitorini & Purnomo, 2023; Zahálka et al., 2018).

The current research also emphasizes that pharmacists demonstrate a solid awareness of the potential side effects associated with medications containing alcohol. However, it was observed that pharmacist respondents were not fully aware of the specific considerations required when selecting alcohol-containing medications for children under six years old. Moreover, pharmacists showed limited recognition of the thresholds and recommendations established by international health agencies regarding the maximum permissible alcohol content in pediatric

medications (European Medicines Agency, 2010; Neo et al., 2014; Soremekun et al., 2019; Zuccotti & Fabiano, 2011). These previous studies underscore the necessity for ongoing educational programs specifically designed for pharmacists to enhance their understanding of safety considerations related to children's medications. Pharmacists play a vital role in providing information and guidance on selecting safe products for paediatric patients, particularly with regard to those containing alcohol.

This exploration is essential for fostering a deeper understanding of this multifaceted issue. Furthermore, the anticipated findings of this research are expected to encourage stakeholders to consider the implementation of regulations advocating for limitations on alcohol content in pediatric formulations.

CONCLUSION

Both communities and pharmacists exhibit good knowledge of the safety implications associated with alcohol in medications. However, the community's knowledge of the permissible percentage of alcohol considered halal and safe for children appears to be inadequate. In addition, community pharmacists demonstrate a lack of awareness regarding global regulatory guidelines that restrict alcohol content in paediatric medications. It is essential for pharmacists to enhance their understanding of alcohol content in paediatric formulations. Equally important is their proactive dissemination of this knowledge within the community.

ACKNOWLEDGMENTS

The authors extend their heartfelt gratitude to Gadjah Mada University for generously supporting this research through the Final Project Recognition Grant (*Hibah RTA*) Number 2920/UN1/DITLIT/Dit-Lit/PT.01.05/2022.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

Alserhan, B. A., Bayirli, M., & Zakzouk, F. (2020). Awareness towards Halal pharmaceuticals: an analysis of pharmacists' views. International Journal of Islamic Marketing and Branding, 5(1), 43. https://doi.org/10.1504/ijimb.2020.10906 5

- Attebäck, M., Hedin, B., & Mattsson, S. (2022). Formulation optimization of extemporaneous oral liquids containing naloxone and propranolol for pediatric use. *Scientia Pharmaceutica, 90*(1). https://doi.org/10.3390/scipharm9001001 5
- Aziza, Y. (2023). Alcohol profile in medication and community perception on halalness of cold and cough pediatric syrup. (Undergraduate Thesis, Universitas Gadjah Mada, Indonesia).
- Barnes, G. E., & Chappell, N. L. (1981). Pharmacists' knowledge in the area of alcohol, and alcohol and drug interactions. Social Science & Medicine. Part A: Medical Psychology & Medical Sociology, 15(5), 649–657. https://doi.org/10.1016/0271-7123(81)90088-2
- Batista, L. R., & Antoniosi Filho, N. R. (2020). Ethanol content determination in medicine syrups using headspace and multidimensional heart-cut gas chromatography coupled to mass spectrometry. Journal of the Brazilian Chemical Society, 31(2), 394-401. https://doi.org/10.21577/0103-5053.20190193
- Bekele, K. M., Abay, A. M., Mengistu, K. A., Berhanemeskel, Atsbeha, W., Demeke, C. A., Belay, W. S., & Yimenu, D. K. (2020). Knowledge, attitude, and practice on overthe-counter drugs among pharmacy and medical students: a facility-based crosssectional study in Punjab, Pakistan. *Latin American Journal of Pharmacy*, *9*, 135–146. https://doi.org/doi: 10.2147/IPRP.S266786
- Berlin M, Shaniv D, Mendelson Mastey C, Zins I, Ainbinder D, Schwartzberg E (2017). Ethanol content in pediatric preparations registered in Israel: address the excess. 2017. Available from: <u>https://www.researchgate.net/publication</u> /318129183
- Christiansen, N. (2015). Ethanol exposure through medicines commonly used in paediatrics. *Archives of Disease in Childhood: Education and Practice Edition, 100*(2), 101–104. https://doi.org/10.1136/archdischild-2013-305671
- European Medicines Agency. (2010). European Medicines Agency. Ethanol Content in Herbal Medicinal Products and Traditional Herbal Medicinal Products Used in Children.

44(January), 1–8. http://www.ema.europa.eu/ema/index.jsp ?curl=pages/regulation/general/general co ntent 000402.jsp. Accessed Feb 21st 2022.

- Fathoni, M. A. (2020). Potret industri halal Indonesia: Peluang dan tantangan (Portrait of the Indonesian halal industry: opportunities and challenges.). *Jurnal Ilmiah Ekonomi Islam*, 6(3), 428. https://doi.org/10.29040/jiei.v6i3.1146
- Haorah, J., Heilman, D., Knipe, B., Chrastil, J., Leibhart, J., Ghorpade, A., Miller, D. W., & Persidsky, Y. (2005). Ethanol-induced activation of myosin light chain kinase leads to dysfunction of tight junctions and bloodbrain barrier compromise. *Alcoholism: Clinical and Experimental Research*, 29(6), 999–1009.

https://doi.org/10.1097/01.ALC.00001669 44.79914.0A

- Haorah, J., Knipe, B., Gorantla, S., Zheng, J., & Persidsky, Y. (2007). Alcohol-induced blood – brain barrier dysfunction is mediated via inositol 1,4,5-tripjosphate receptor (IP3R)gated intracellular calcium release. *Journal of Neurochemistry*, *100*(2), 324–336. https://doi.org/:10.1111/j.1471-4159.2006.04245.x
- Haorah, J., Schall, K., Ramirez, S. H., & persi. (2008).
 Activation of protein tyrosine kinases and matrix metalloproteinases causes bloodbrain barrier injury: novel mechanism for neurodegeneration associated with alcoholabuse. *Glia*, 56(1), 78–88. https://doi.org/10.1002/glia
- Ieraci, A., & Herrera, D. G. (2007). Single alcohol exposure in early life damages hippocampal stem/progenitor cells and reduces adult neurogenesis. *Neurobiology of Disease*, *26*(3), 597–605. https://doi.org/10.1016/j.nbd.2007.02.011
- Inkelis, S. M., Moore, E. M., Bischoff-Grethe, A., & Riley, E. P. (2020). Neurodevelopment in adolescents and adults with fetal alcohol spectrum disorders (FASD): A magnetic resonance region of interest analysis. *Brain Research*, *1732*(January), 146654. https://doi.org/10.1016/j.brainres.2020.14 6654
- Kelber, O., Steinhoff, B., Nauert, C., Biller, A., Adler,
 M., Abdel-Aziz, H., Okpanyi, S. N., Kraft, K., &
 Nieber, K. (2017). Ethanol in herbal medicinal products for children: Data from pediatric studies and pharmacovigilance

programs. *Wiener Medizinische Wochenschrift*, 167(7–8), 183–188. https://doi.org/10.1007/s10354-016-0474-x

- Laksitorini, M., & Purnomo, H. (2023). Application of hildebrand solubility parameter to identify ethanol-free co-solvent for pediatric formulation. *Indonesian Journal of Pharmacy*, 34(2). https://doi.org/10.22146/ijp.6627
- Laksitorini, M., Yathindranath, V., Xiong, W., Parkinson, F. E., Thliveris, J. A., & Miller, D. W. (2021). Impact of Wnt/β-catenin signaling on ethanol-induced changes in brain endothelial cell permeability. *Journal of Neurochemistry*, *157*(4), 1118–1137. https://doi.org/10.1111/jnc.15203
- McCaig, D., Fitzgerald, N., & Stewart, D. (2011). Provision of advice on alcohol use in community pharmacy: A cross-sectional survey of pharmacists' practice, knowledge, views and confidence. *International Journal of Pharmacy Practice*, *19*(3), 171–178. https://doi.org/10.1111/j.2042-7174.2011.00111.x
- Muneer, P. M. A., Alikunju, S., Szlachetka, A. M., & Haorah, J. (2012). The mechanisms of dysfunction cerebral vascular and neuroinflammation by MMP-mediated degradation of VEGFR-2 in alcohol ingestion. Arteriosclerosis, Thrombosis, and Vascular Bioloav. 32(5). 1167-1177. https://doi.org/10.1161/ATVBAHA.112.24 7668
- Neo, M. S., Gupta, S. M., Khan, T. M., & Gupta, M. (2014). Quantification of ethanol content in traditional herbal cough syrups. *Pharmacognosy Journal*, 9(6), 821–827. https://doi.org/10.5530/pj.2017.6.128
- Rahmah, M., & Barizah, N. (2020). Halal certification of patented medicines in Indonesia in digital age: A panacea for the pain? *Systematic Reviews in Pharmacy*, *11*(12), 210–217. https://doi.org/10.31838/srp.2020.12.34
- Rahmah, R. (2019). Alcohol and Khamr in Fiqh Based on Science Perspective. *IJISH* (*International Journal of Islamic Studies and Humanities*), 2(1), 1–10. https://doi.org/10.26555/ijish.v2i1.859
- Sheridan, J., Wheeler, A., Chen, L. J. H., Huang, A. C.
 Y., Leung, I. N. Y., & Tien, K. Y. C. (2008).
 Screening and brief interventions for alcohol: Attitudes, knowledge and

experience of community pharmacists in Auckland, New Zealand. *Drug and Alcohol Review*, 27(4), 380–387. https://doi.org/10.1080/09595230802093 760

- Singh, A. K., Jiang, Y., Gupta, S., & Benlhabib, E. (2007). Effects of chronic ethanol drinking on the blood-brain barrier and ensuing neuronal toxicity in alcohol-preferring rats subjected to intraperitoneal LPS injection. *Alcohol and Alcoholism*, 42(5), 385–399. https://doi.org/10.1093/alcalc/agl120
- Soremekun, R., Ogbuefi, I., & Aderemi-Williams, R. (2019). Prevalence of ethanol and other potentially harmful excipients in pediatric oral medicines: Survey of community pharmacies in a Nigerian City. *BMC Research Notes*, 12(1), 1–5. https://doi.org/10.1186/s13104-019-4486-7
- Svirskis, D., Toh, M., & Ram, S. (2013). The use of ethanol in paediatric formulations in New Zealand. European Journal of Pediatrics, 172(7), 919–926. https://doi.org/10.1007/s00431-013-1972-0
- Taylor, J. G., Ayosanmi, S., & Sansgiry, S. S. (2023). Consumer impressions of the safety and effectiveness of OTC medicines. *Pharmacy*, *11*(2), 51. https://doi.org/10.3390/pharmacy110200 51
- Wulandari, P. (2023). Blood alcohol prediction (BAC) prediction and pharmacist knowledge on ethanol-containing medication: Cold and Cough Syrup. (In Undegraduate thesis, Universitas Gadjah Mada, Indonesia). https://doi.org/10.1201/9780849378812. ax2
- Zahálka, L., Klovrzová, S., Matysová, L., Šklubalová,
 Z., & Solich, P. (2018). Furosemide ethanolfree oral solutions for paediatric use: formulation, HPLC method and stability study. *European Journal of Hospital Pharmacy*, 25(3), 144–149. https://doi.org/10.1136/ejhpharm-2017-001264
- Zuccotti, G. V., & Fabiano, V. (2011). Safety issues with ethanol as an excipient in drugs intended for pediatric use. *Expert Opinion on Drug Safety*, *10*(4), 499–502. https://doi.org/10.1517/14740338.2011.5 65328

Indonesian Journal of Pharmacy

VOL 36 (1) 2025: 187–195 | RESEARCH ARTICLE