Development of an Analytical Method for Lidocaine Identification in Magic Tissue Using Gas Chromatography Mass Spectrometry

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ABSTRACT / ABSTRAK

Antiseptic tissue to help clean the skin in men's sensitive areas (magic tissue) is a class I (low risk) health supplies product. Several marketed products are also claimed to have benefits for preventing premature ejaculation, which is suspected to be associated with the addition of lidocaine that is not disclosed on the product label. Lidocaine, an amide local anesthetic, is used in medicine to inhibit the sensation of pain. This research was conducted to determine the lidocaine content in magic tissue. The research method used is an experimental method, involving validation methods and testing samples. Lidocaine was identified using Gas Chromatography Mass Spectrometry, with test parameters of specificity, Limit of Detection, stability test, and resistance test. Sample preparation was carried out by dissolving one layer of tissue as a sample using methanol. The Standard Solution used is lidocaine compound with a concentration of 100 ppm. The results confirmed method specificity, as the sample and spiked solutions showed identical ion extracts, fragmentation, and intensity ratios to the standard solution. The LOD was determined to be 10 ppm, indicating sufficient sensitivity. Stability testing showed consistent mass-to-charge spectra between the first and fifth days, while resistance testing demonstrated that temperature variations affected peak retention times but not the mass spectra. Analysis of five different samples revealed positive results for lidocaine. Overall, these findings indicate that the developed GC-MS method meets validation parameters and can be reliably applied to identify lidocaine in magic tissue products.

Produk tisu antiseptik untuk pembersih area sensitif pria (magic tissue) dikategorikan sebagai perbekalan kesehatan kelas I (risiko rendah). Beberapa produk di pasaran dilaporkan mengklaim manfaat sebagai pencegah ejakulasi dini, yang diduga terkait dengan penambahan senyawa lidokain tanpa pencantuman pada etiket kemasan. Lidokain merupakan anestesi lokal golongan amida yang secara farmakologis berfungsi menghambat transmisi sensasi nyeri. Penelitian ini dilakukan untuk mengetahui kandungan lidokain dalam produk magic tissue yang beredar di Indonesia. Metode penelitian yang digunakan adalah metode eksperimental, dengan melakukan validasi metode dan pengujian sampel. Identifikasi lidokain dilakukan menggunakan Kromatografi Gas Spektrofotometri Massa, dengan parameter validasi metode berupa uji spesifisitas, Limit of Detection (LOD), uji stabilitas dan uji ketahanan metode. Selanjutnya, pengujian sampel dilakukan dengan melarutkan 1 lembar magic tissue menggunakan pelarut metanol. Larutan Baku sebagai kontrol positif yang digunakan adalah senyawa lidokain dengan konsentrasi 100 ppm. Hasil uji spesifisitas Larutan Sampel dan Larutan Spiked memiliki ekstrak ion, fragmentasi ion, dan perbandingan rasio intensitas ion yang sama dengan Larutan Baku. Nilai LOD adalah 10 ppm. Hasil uji stabilitas menunjukkan bahwa pada hari kelima, Larutan Sampel dan Larutan Baku memiliki spektrum massa per muatan yang sama dengan pengujian pada hari

pertama. Pada uji ketahanan metode, perubahan rentang suhu pengujian menyebabkan perubahan waktu retensi puncak namun spektrum massa per muatan masih sama dengan Larutan Baku. Pada penelitian ini dilakukan pengujian terhadap lima sampel yang berbeda dengan hasil positif mengandung lidokain. Metode uji yang dikembangkan memenuhi parameter validasi dan dapat digunakan untuk identifikasi lidokain dalam produk magic tissue.

Keywords: Magic tissue, Lidocaine, Gas Chromatography Mass Spectrometry, Validation Method
Kata Kunci: *Tisu magic, Lidokain, Kromatografi Gas Spektrofotometri Massa, Validasi Metode*

1. Introduction

Lidocaine is an amide-type local anesthetic commonly used in medical practice to inhibit pain sensation (Karnina et al., 2021). Its chemical formula is C14H22N2O. The compound consists of a lipophilic subunit (tertiary amine) and a hydrophilic subunit (unsaturated aromatic ring) (Vardanyan & Hruby, 2006). The lipophilic portion determines the local anesthetic activity (Johansson, 2012). Lidocaine is widely used in medical practice, ranging from minor surgery to local anesthesia. Its topical use has also been applied in certain products for preventing premature ejaculation in men (Hisasue, 2016). For some patients, topical therapy with local anesthetics, including lidocaine and/or prilocaine, may be an effective treatment option (Hisasue, 2016; Shah et al., 2023). Topical anesthetics such as lidocaine and/or prilocaine in the form of creams, gels, or sprays are known to be effective in delaying ejaculation. They act by reducing glans sensitivity and are thought to inhibit spinal reflexes responsible for ejaculation (Hisasue, 2016).

Magic tissue is an antiseptic tissue product used for cleansing sensitive areas in men and preventing sexually transmitted diseases, thereby helping to maintain hygiene and health. Magic tissue is categorized as a health supply product, typically containing ingredients such as ethyl alcohol (ethanol), polyethylene oxide, benzalkonium chloride, and fragrance. Some products may also include natural ingredients, such as aloe vera extract, for skin softening, or other additives, like triclosan and cocamidopropyl betaine.

According to Law Number 17 of 2023 on Health, health supplies refer to all materials and equipment necessary for health efforts. Based on the Regulation of the Minister of Health of the Republic of Indonesia Number 62 of 2017 on Distribution Permits for Medical Devices, In Vitro Diagnostic Devices, and Household Health Supplies, magic tissue falls under class I (low risk) health supplies, which, in its use, does not cause significant adverse effects such as irritation, corrosiveness, or carcinogenicity.

In the market, magic tissue is also known for its claimed benefit in preventing premature ejaculation in men. It is often preferred over modern herbal remedies due to its lower cost, immediate effect, and relatively mild side effects, typically including numbness in the genital area (Hardon et al., 2015). It is suspected that lidocaine, as an active substance, is added to the magic tissue to provide this effect. However, the presence of lidocaine in these products is often not declared on the label, making such an addition “illegal.”

Traditionally, the analysis of lidocaine in known pharmaceutical preparations has been performed using High-Performance Liquid Chromatography (HPLC) (Ministry of Health, 2020). However, since the type of active ingredient added to the magic tissue is unknown, this study employed Gas Chromatography-Mass Spectrometry (GC-MS) equipped with a compound database for identification. This research aimed to develop a method for lidocaine

identification in magic tissue products using GC-MS, with a simple sample preparation process to facilitate routine laboratory testing.

2. Methodology

2.1. Time and Place of Study

This research was conducted at the Laboratory of Pharmaceutical Chemistry, Active Pharmaceutical Ingredients, Narcotics, Psychotropics, Precursors, and Addictive Substances, Center for National Quality Control Laboratory of Drugs and Food (PPPOMN), The Indonesian Food and Drug Authority, from July to August 2022.

2.2. Materials and Instruments

The materials used in this study included magic tissue suspected of containing lidocaine, obtained as case samples from law enforcement authorities who collected them from the market and submitted them to The Indonesian Food and Drug Authority for testing of hazardous substances, methanol (MS grade) as the solvent for the GCMS system (Agilent, Germany) (Huber, 2010), and lidocaine reference standard obtained from the Reference Standard Laboratory, PPPOMN.

The instrument used was a GC-MS system (Agilent 7890B) equipped with a DB-5MS column (30 m in length, 0.25 mm internal diameter, and a 5% phenyl–95% methyl polysiloxane stationary phase). The chromatographic system specifications are presented in Table 1 (The Indonesian Food and Drug Authority, 2021).

2.3. Identification Using GC-MS

The identification test of lidocaine in magic tissue was performed using a GC-MS instrument with the specifications listed in Table 1, which represents the development of an internal method by PPPOMN. The preparation of the standard solution was carried out by weighing approximately 5 mg of lidocaine, obtained from the Indonesian Pharmacopeia Reference Standard (BPFI), which was then placed into a 10 mL volumetric flask. Five milliliters of methanol were added, and the solution was sonicated for 2 minutes. Afterward, the solution was diluted with methanol to volume. A 200 µL aliquot of the standard solution was transferred to a vial and diluted with 800 µL of solvent, resulting in a concentration of 100 ppm.

The sample solution was prepared by weighing one sheet of tissue, which was placed in a 100 mL Erlenmeyer flask and extracted with 25.0 mL of methanol by sonication for 15 minutes. A 200 µL aliquot of the sample solution was transferred to a vial and diluted with 800 µL of solvent. Both the standard and sample solutions were each pipetted 500 µL into separate vials and mixed to create a spiked solution.

Before sample testing was conducted, the analytical method to be used was first validated with the following test parameters: selectivity/specificity, Limit of Detection (LOD), stability test, and method robustness test. The selectivity/specificity test was performed by comparing the standard solution, sample validation solution, and spiked solution by observing the retention time of the target analyte peak (lidocaine) and the spectrum showing the fragmentation pattern of the compound. The test was carried out twice. The Limit of Detection (LOD) was determined by observing the signal-to-noise ratio produced by the standard solution with six repetitions. The stability test was performed by observing the test

results from the standard solution, sample validation solution, and spiked solution that had been stored for 5 days under the specified storage conditions, in accordance with the standard operating procedure applied at the research location.

The robustness test was performed by testing temperature variations and evaluating five different brand samples (The Indonesian Food and Drug Authority, 2010). Sample testing was conducted using five different samples with three repetitions for each sample.

Table 1. GC-MS Chromatographic System

GCMS System	Explanation
Column	DB-5 MS, 30 m × 0.25 mm i.d., 5% phenyl–95% methyl polysiloxane
Detector	Mass Spectrophotometer
	Injector temperature 290 °C
	Column temperature 100 °C (held 2 min)
	ramp 10 °C/min to 290 °C (held 10 min)
	MS Source 230°C
	MS Quard 150°C
Carrier gas	Helium Ultra Pure
Flow rate	1,5 mL/min
Flow Control Mode	Linear Velocity
Split ratio	10:1
Injection volume	1 µL
Solvent Cut Time	2,5 min
MS mode	Scan
m/z range	40-550

3. Results and Discussion

In this study, the identification method was designed to be as simple as possible, with straightforward sample preparation, to facilitate its application in routine laboratory testing. Gas Chromatography Mass Spectrometry (GC-MS) was chosen due to its high sensitivity and the availability of a compound library in the instrument, which significantly aids in the detection of analytes. The validation results obtained in this study are described as follows:

3.1. Selectivity/Specificity

Chromatograms of solvent, standard solution, sample solution, and spiked solution are presented in Figure 1. The chromatograms show no interfering peaks at the retention time of lidocaine (tr 12.994–13.658 min). No peaks from the solvent overlapped with the retention time of the target analyte peak in the standard solution.

Specificity was demonstrated by the fact that the sample and spiked solutions showed the identical mass spectra per charge (m/z) as the standard solution (Figure 2). Furthermore, the sample and spiked solutions exhibited identical extracted ions to the standard solution, with at least three fragment ions (87, 58, and 72). The ion intensity ratios were calculated and compared against the acceptable tolerance limits (Table 2).

For peaks with relative intensities ≤10% of the base peak, the tolerance for relative ion intensity in mass spectrometry is ±50% (Ferrer & Thurman, 2003). The ion intensity ratio results confirmed that the peaks detected in the sample and spiked solutions corresponded to lidocaine, as confirmed by the standard solution.

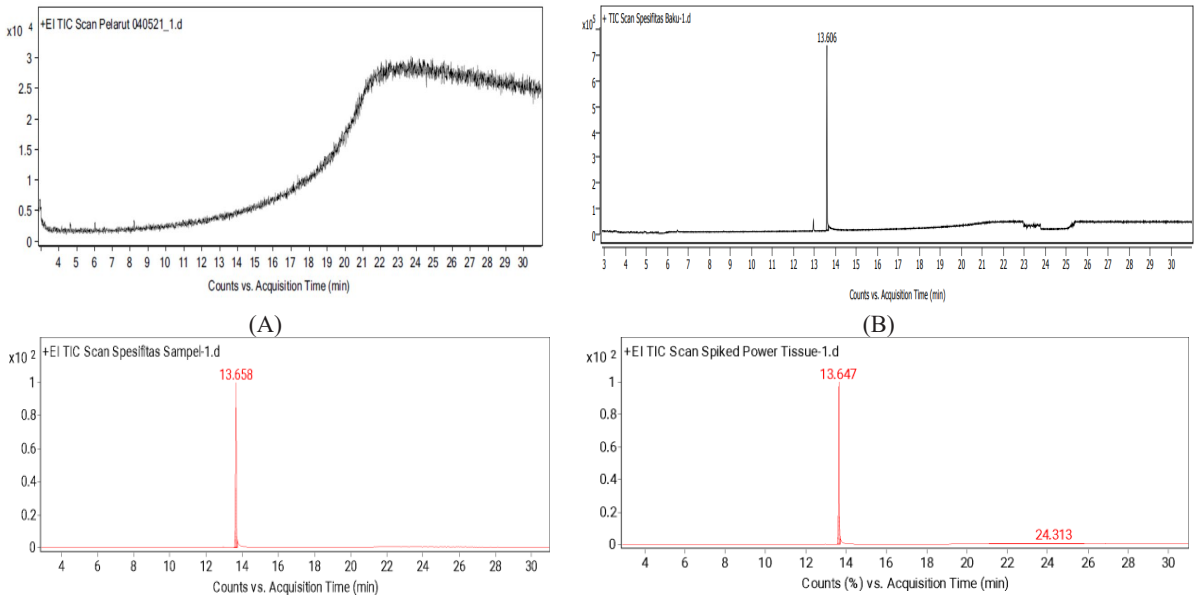

Figure 1. Chromatograms of lidocaine in solvent (A), standard solution (B), sample solution (C), and spiked solution (D)

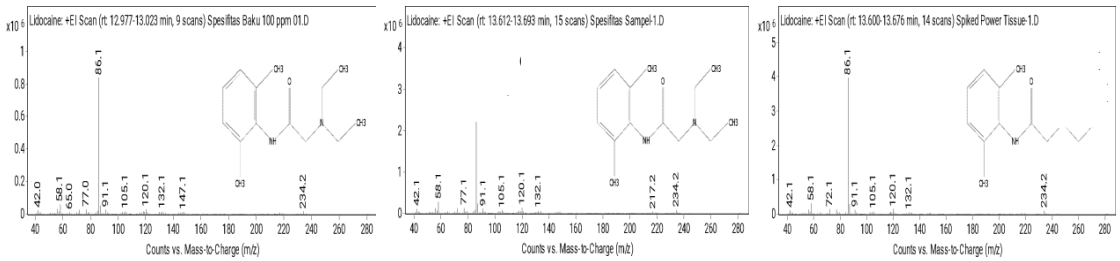

Figure 2. Ion fragmentation of lidocaine in standard solution (A), sample solution (B), and spiked solution (C)

Table 2. Comparison of ion intensity ratios

Solution	Mass-to-Charge ratio (m/z)	Relative Value	Acceptance Range (*Relative Deviation*)	Conclusion
Standard Solution	87	6,11	3,06 – 9,17	
(Lidocaine)	58	6,89	3,44 – 10,33	-
	72	2,85	1,42 – 4,27	
Sample Solution	87	6,98		Accepted
	58	8,20	-	
	72	3,32		
Spiked Solution	87	6,60		Accepted
	58	7,51	-	
	72	3,14		

3.2.Limit of Detection (LOD)

The LOD is the minimum concentration of analyte that can be reliably detected (Gandjar & Rohman, 2007). In this study, several concentrations of the standard solution, near the expected detection limit, were prepared, and the signal-to-noise (S/N) ratios were observed.

At 10 ppm, the standard solution consistently produced detectable signals across six replicate injections, with an average signal-to-noise ratio (S/N) of 5.7 (Table 3). This indicates that the minimum detectable concentration of lidocaine using this GC-MS method is 10 ppm. The LOD value depends on the instrument sensitivity, detector performance, column resolution, and instrument noise. Generally, an S/N ratio of ≥3:1 is considered acceptable for the LOD. In this experiment, reproducibility was confirmed by consistent signals across repeated injections.

Table 3. Limit of Detection (LOD) for Lidocaine

Solution	Concentration (ppm)	Area	Signal/Noise (S/N)
Standard Solution Lidocaine 01	10	64489,95	5,9
Standard Solution Lidocaine 02	10	68055,43	7,3
Standard Solution Lidocaine 03	10	68055,43	5,5
Standard Solution Lidocaine 04	10	54893,00	6,1
Standard Solution Lidocaine 05	10	53856,28	5,0
Standard Solution Lidocaine 06	10	47247,30	4,3
			Average: 5,7

Lidocaine testing in pharmaceutical preparations is typically performed using HPLC, as outlined in official monographs, such as the Indonesian Pharmacopoeia VI Edition (2020). However, this method is generally intended for the detection of pharmaceutical dosage forms containing relatively high concentrations of lidocaine, making them easily detectable and quantifiable. In contrast, this study revealed the presence of lidocaine in wet tissues, which was previously unknown, as it was not declared in the product composition. Therefore, the use of GC-MS in this method aimed to detect any active substances present in the product, with lidocaine being identified as one of them.

The LOD value helps determine the smallest amount of analyte in a sample that the instrument can still detect. The detection limit of 10 ppm obtained in this study was determined based on the signal-to-noise (S/N) ratio. The analyte signal at the LOD must be significantly distinguishable from instrument noise. In general, an S/N ratio of at least 3:1 is acceptable for LOD determination. At the LOD concentration, the method must demonstrate adequate reproducibility, meaning that detection at this level must be consistent when the analysis is repeated under the same conditions. In the experiment, six replicate injections yielded consistent signal-to-noise (S/N) ratios (greater than 3). The LOD value also depends on the instrument's sensitivity, specifically the detector's performance, column separation efficiency in GC, and instrument noise.

3.3.Stability Test

Stability testing was performed on standard, sample, and spiked solutions after five days of storage at room temperature. The results (Table 4) demonstrated that all solutions maintained the identical mass spectra per charge (m/z) as on day one, indicating that lidocaine remained stable under the tested conditions for up to five days.

Table 4. Stability test results of lidocaine

Solution	Mass-to-Charge Ratio (m/z)	
	Day 1 Testing	*Day 5 Testing*
Standard Solution	87	87
	58	58
	72	72
Sample Solution	87	87
	58	58
	72	72
Spiked Solution	87	87
	58	58
	72	72

3.4.Robustness Test

In robustness testing, temperature variations of ±1 °C from the setpoint (9 °C and 11 °C deviations) caused slight shifts in retention time for lidocaine in the standard, sample, and spiked solutions. However, the mass spectra per charge remained consistent with the standard solution (Table 5). This indicates that minor temperature changes did not affect compound identification.

Table 5. Robustness test results with temperature variation

Solution	Retention Time (minute) dan Mass-to-Charge Ratio (m/z)					
	10°C		*9°C*		*11°C*	
Standard Solution	12,994	87	13,845	87	12,271	87
		58		58		58
		72		72		72
Sample Solution	13,658	87	13,979	87	12,382	87
		58		58		58
		72		72		72
Spiked Solution	13,641	87	13,973	87	12,376	87
		58		58		58
		72		72		72

Robustness was further confirmed by testing five different brands of magic tissue from the market. Lidocaine was positively identified in all samples (Table 6). These results demonstrate that the developed method is robust and suitable for routine application.

Table 6. *Robustness test results with various commercial samples*

Solution	Mass-to-Charge Ratio (m/z)	Relative Value	Acceptance Range (Relative Deviation)	Conclusion
Standard Solution	87	6,11	3,06 – 9,17	
	58	6,89	3,44 – 10,33	-
	72	2,85	1,42 – 4,27	
Sample 1	87	8,68		Accepted
	58	9,19		
	72	4,09		
Spiked 1	87	7,21		Accepted
	58	7,78		
	72	3,42		

Table 6 (Continued).

Solution	Mass-to-Charge Ratio (m/z)	Relative Value	Acceptance Range (Relative Deviation)	Conclusion
Sample 2	87	8,86		Accepted
	58	9,24		
	72	4,17		
Spiked 2	87	7,61		Accepted
	58	8,04		
	72	3,57		
Sample 3	87	7,93		Accepted
	58	8,37		
	72	3,70		
Spiked 3	87	6,64		Accepted
	58	7,61		
	72	3,08		
Sample 4	87	7,66		Accepted
	58	8,33		
	72	3,61		
Spiked 4	87	6,71		Accepted
	58	7,54		
	72	3,14		
Sample 5	87	7,62		Accepted
	58	8,31		
	72	3,54		
Spiked 5	87	7,54		Accepted
	58	7,94		
	72	3,53		

3.5. Sample Testing

Sample testing using the developed analytical method was performed on five different brands of magic tissue. The test was conducted to determine whether an active substance, lidocaine, had been added to the product. The results showed that the samples were positively detected to contain lidocaine (Table 7).

Table 7. Sample testing results

Solution	Retention time (minutes)	m/z	Conclusion
Standard Solution	12,994	87 ; 58 ; 72	Positive for Lidocaine
Sample 1	13,676	87 ; 58 ; 72	Positive for Lidocaine
Sample 2	13,670	87 ; 58 ; 72	Positive for Lidocaine
Sample 3	13,670	87 ; 58 ; 72	Positive for Lidocaine
Sample 4	13,659	87 ; 58 ; 72	Positive for Lidocaine
Sample 5	13,658	87 ; 58 ; 72	Positive for Lidocaine

The validation results demonstrated that lidocaine can be identified using GC-MS with acceptable specificity, detection limit, stability, and robustness. Previously, lidocaine

identification and quantification were performed using HPLC. Compared to HPLC, GC-MS provides higher sensitivity and selectivity due to its integrated compound library and lower detection limit. Additionally, GC-MS enables compound identification without requiring a reference standard for every analysis.

The detection of lidocaine in all five commercial magic tissue products confirms the suspicion that lidocaine was deliberately added. According to regulations, antiseptic tissue products must clearly declare their composition on the product label. If lidocaine is added, the product is reclassified as a medicinal product requiring the Indonesian Food and Drug Authority registration, since lidocaine is a prescription-only drug under the Ministry of Health Regulation No. 3 of 2021 on Drug Classification. Therefore, accurate labeling of lidocaine is critical for both manufacturers and regulators, and it is necessary to conduct monitoring and supervision of magic tissue products circulating in Indonesia.

Lidocaine is an anesthetic drug used to inhibit pain sensation, consisting of a lipophilic subunit (tertiary amine) and a hydrophilic subunit (unsaturated aromatic ring) (Vardanyan & Hruby, 2006). The lipophilic part determines the local anesthetic activity (Johansson, 2012). Lidocaine works by blocking sodium ion channels, thereby reducing cell membrane permeability and preventing depolarization, which in turn blocks the conduction of electrical impulses that cause pain (Fozzard et al., 2011). Lidocaine can be used for the treatment of premature ejaculation as it reduces gland sensitivity and is believed to inhibit the spinal reflex responsible for ejaculation (Hisasue, 2016; Shah et al., 2023).

4. Conclusion

The validation results of the analytical method demonstrated that the method used fulfilled the requirements for selectivity/specificity, limit of detection (LOD), stability, and robustness. Gas Chromatography Mass Spectrometry (GC-MS) met the validation criteria and can therefore be applied for the identification of lidocaine in magic tissue samples.

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