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Original Article

# DETERMINATION AND QUANTIFICATION OF NINE ADULTERANT LOCAL ANAESTHETICS IN ILLEGAL TREATMENTS FOR MALE PREMATURE EJACULATION BY GC-FID AND GC-MS

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**ABSTRACT**

**Objective:** A gas chromatography (GC) method using flame ionization (FID) and mass spectrometry (MS) was developed and validated for the determination of nine local anaesthetics in counterfeit drugs sold illegally as treatments for male premature ejaculation.

**Methods:** The GC-FID and GC-MS method validations demonstrated reliable specificity, selectivity, linearity, precision, and accuracy, and the validated methods were successfully applied to the analyses of collected samples.

**Results:** Approximately 60% of the samples contained, at least, one of the local anaesthetics, which included menthol, 2-phenoxyethanol, eugenol, lidocaine, prilocaine, and tetracaine. Lidocaine was the most frequently detected compound in the analysed samples and occurred in a wide concentration range (2.81–52.40 mg/g). The concentrations of the detected compounds varied greatly between 0.03–52.40 mg/g.

**Conclusion:** Continuous use of these counterfeit products, which contain high concentrations of local anaesthetics, can cause serious human health effects. Therefore, the continued screening of illegal products is required and our proposed methods could be used for the monitoring and quantification of local anaesthetics in counterfeit products.

**Keywords:** Local anesthetics, Premature ejaculation, GC/FID, GC/MS, Adulterants, Validation.



## INTRODUCTION

Premature ejaculation (PE) is a highly prevalent sexual dysfunction among men [1-5]. Local anaesthetics are used for the treatment of PE, and are available as prescription drugs in South Korea. However, the use of drugs containing local anaesthetics in commercial products and the distribution of prohibited imported drugs are strictly controlled by the Korean government. Nevertheless, many illegal products containing local anaesthetics are distributed online or through sex shops in South Korea. Furthermore, many countries have reported the use of prohibited local anaesthetics in creams for the treatment of PE [6-10].

Most people believe that these illegal products are safe because of incomplete product descriptions and insufficient information regarding their contraindications, and they deny that they have taken an illegal medicinal product [11]. Moreover, illegal products can contain high doses of prohibited ingredients [12]. The abuse of local anaesthetics can cause side effects, such as erectile dysfunction, hypersexuality, a decrease in arousal, numbness, dermatitis, and contamination of their partner's vagina [7]. These effects result in unpredictable risks to health and safety [11, 13]. Therefore, the increased use of illegal products containing local anaesthetics has necessitated the development of methods for simultaneous detection and continuous monitoring of these adulterants [13].

Few analytical methods for the determination of adulterated local anaesthetics have been described in the literature. Porra *et al.* developed a high-performance liquid chromatography (HPLC) method using solid-phase extraction for the identification of five local anaesthetics in commercial products [14]. An HPLC method using an ultraviolet diode array (UV-DAD) and electro spray ionization mass spectrometry (ESI-MS) was reported for the determination of prilocaine, procaine, benzocaine, and lidocaine in creams by Orsi *et al.* [6]. Additionally, the analysis of lidocaine as an adulterant in cocaine-based products was performed using HPLC-DAD [13]. Although some methods for the analysis of local anaesthetics have been proposed, none has described a validated method using GC-FID and GC-MS for the identification and quantification of local anaesthetic adulterants in seized creams that were sold illegally for the purpose of PE treatment.

Our aim was to develop and validate a method based on GC-FID and GC-MS for the monitoring of nine local anaesthetics in suspicious products. In addition, we assessed our validated method for its applicability in real samples of seized products that were advertised to strengthen male sexual function, especially PE, from online retailers and sex shops.

## MATERIALS AND METHODS

### Solvents and chemicals

Eugenol was purchased from Sigma-Aldrich Corp. (St. Louis, MO, USA). Lidocaine, 2-phenoxyethanol, menthol, procaine hydrochloride, benzocaine hydrochloride, bupivacaine hydrochloride, prilocaine hydrochloride, and tetracaine hydrochloride were obtained from U. S. Pharmacopeia (Rockville, MD, USA). Methanol (HPLC grade) was obtained from Merck (Darmstadt, Germany).

### Preparation of stock and standard solutions

Stock solutions of the nine compounds were prepared in methanol at concentrations of 1000 µg/ml and stored at 4 °C. Furthermore, the working standard solutions (100 µg/ml) were prepared daily by dilution of the stock solutions with methanol. Calibration standard solutions for GC-FID and GC-MS methods were prepared using working standard solutions in the concentration ranges of 5–100 µg/ml, i.e.,5, 10, 20, 40, 80, and 100 µg/ml, and 0.5–10 µg/ml, i.e., 0.5, 1, 2, 4, 8, and 10 µg/ml, respectively.

### Samples and extraction

The products advertised the ability to improve and strengthen male sexual capacity and were obtained from online retailers and sex shops. The 26 samples that were collected consisted of creams (17), gels (6), and sprays (3). The samples (1 g) were diluted in methanol (50 ml) and extracted using sonication for 30 min. All of the extracts were filtered through a 0.22 µm polytetrafluoroethylene (PTFE)

syringe filter (Whatman International Ltd., Maidstone, Kent, UK) before injection into the GC-FID and GC-MS systems.

**GC-FID operating conditions**

An Agilent 7890A GC system (Agilent Technologies Inc., Santa Clara, USA) equipped with a 7693 auto sampler and a flame ionization detector (FID) was used for the analysis. Separation was achieved using a J&W Scientific DB-5 column (length 50 m, internal diameter 0.25 mm, film thickness 0.25 µm) that was obtained from Agilent (CA, USA). The oven temperature was programmed to increase from 100–200 °C at a rate of 15 °C/min, then from 200–300 °C at a rate of 5 °C/min, where it was held constant for 8 min. The injection volume was 1 µl and a split (10:1) inlet mode was used. The inlet and detector temperatures were set to 250 and 300 °C, respectively. $N_2$ was used as the make-up gas and the carrier gas ($N_2$) flow rate was 1.0 ml/min.

**GC-MS operating and conditions**

An Agilent 7890A GC system (Agilent Technologies Inc., Santa Clara, USA) interfaced with a 5975C MSD, a 7683 auto sampler, and Agilent chem station software was used. The MS tuning was performed daily using a perfluoro-tributylamine (PFTBA) standard, which consisted of masses 69, 219, and 502 m/z. The temperature of transfer line was maintained at 280 °C. A 1 µl aliquot of a sample was injected using a split mode (10:1) at 250 °C. A DB-5 column (length 30 m, internal diameter 0.25 mm, film thickness 0.25 µm; J&W Scientific, Agilent, CA, USA) was used for the separation and the carrier gas was high-purity helium (99.9999%) at a flow rate 1.5 ml/min. The initial oven temperature was 100 °C, which was increased to 200 °C at a rate of 15 °C/min, and then increased to 300 °C at a rate of 5 °C/min, where it was held constant for 8 min. The samples were ionized in an electron ionization (EI) mode at 70 eV. The MS source and quad temperatures were set to 230 °C and 150 °C, respectively. The mass spectra were identified over the 50–500 m/z mass range in full scan (SCAN) mode. Quantitation was determined in selected ion monitoring mode (SIM mode) by the major ions for menthol, 2-phenoxyethanol, eugenol, benzocaine hydrochloride, tetracaine hydrochloride and bupivacaine hydrochloride at m/z 71, 94, 164, 120, 58 and 140. The major ions for prilocaine hydrochloride, lidocaine and procaine hydrochloride were m/z 86 (table 1).

**Table 1: Diagnostic ions and retention times of the local anaesthetics in the GC-MS**

| S. No. | Compound | Retention time (min) | Diagnostic ions (m/z) |
|---|---|---|---|
| 1 | Menthol | 3.671 | 71, 81, 95 |
| 2 | 2-Phenoxyethanol | 3.955 | 94, 77, 138 |
| 3 | Eugenol | 5.013 | 164, 149, 131 |
| 4 | Benzocaine hydrochloride | 6.827 | 120, 165, 92 |
| 5 | Prilocaine hydrochloride | 9.324 | 86, 106, 77 |
| 6 | Lidocaine | 9.733 | 86, 58, 87 |
| 7 | Procaine hydrochloride | 11.667 | 86, 99, 120 |
| 8 | Tetracaine hydrochloride | 14.455 | 58, 71, 176 |
| 9 | Bupivacaine hydrochloride | 15.065 | 140, 141, 84 |

**Validation method**

The two methods were validated using parameters, such as the specificity, selectivity, linearity, limits of detection and quantification (LOD and LOQ), precision, accuracy, recovery, and stability based on the International Conference on Harmonisation (ICH) [15-17]. Ten products (eight creams and two gels), which were not adulterated with local anaesthetics, were used as matrix-blank samples for the validation evaluation. Both matrix-blank sample types were assayed to confirm their specificity and selectivity. The linearity of the method was studied using an external standardization. The six calibration standard solutions were analysed in triplicate. The calibration curves were plotted using the peak areas corresponding to each compound versus their concentrations. The LODs and LOQs, calculated at signal-to-noise ratios of 3 and 10, respectively, were calculated using peak-to-peak signal-to-noise ratios across a concentration range of 0.1–1.0 µg/ml spiked into the matrix blank sample types. The precision, accuracy, recovery and stability were evaluated at three different (low, medium, and high) concentrations, i.e., 5, 40, and 100 µg/ml for GC-FID, and 0.5, 4, and 10 µg/ml for GC-MS. The precisions were determined by intra-and interday repeatability and expressed as their relative standard deviations (%RSD). The repeatability was evaluated by performing three replicate analyses at the three different concentrations during the same day. The intermediate precisions were evaluated using analyses at the three different concentrations in triplicate per day over three days. The accuracy was calculated by comparing the calculated and standard concentrations spiked into the matrix blank sample. The recoveries were evaluated using the matrix blank sample types that were spiked with the standards at three different concentrations. The average percent recoveries were calculated by comparing the peak areas of the spiked samples and the standard at their corresponding concentrations. The stability was evaluated using three replicate injections under the process conditions. A standard solution mixture was analysed every 24 h at ambient temperature for 48 h.

**RESULTS AND DISCUSSION**

**Identity**

Standard addition experiments were used for confirmation using GC-FID. The retention times, mass spectra, and m/z ratios of each analyte obtained from GC-MS in SCAN mode were compared for the identification of each analyte, and the spectrum match factors obtained from the NIST Identity Spectrum Search algorithm (NIST MS Search 2.0 ver. D) were used to evaluate the quality of the mass spectra of each analyte.

**Specificity and selectivity**

Matrix-blank sample types spiked with 5 µg/ml of the standard mixture were analysed. The results confirmed that the chromatograms generated from the GC-FID (fig.1) and GC-MS (fig.2) methods experienced no significant interference, nor the co-elution of any of the analytes. The mass spectra generated using the MS detection system was used for the chromatographic selectivity assessment. The similarities of the mass spectra of the analytes and from libraries were compared. Our method indicated that the similarity was >90% and it was considered selective.

**Linearity, LOD and LOQ**

The linearity of the method was evaluated in triplicate over linear concentration ranges of 5–100 µg/ml and 0.5–10 µg/ml at six different levels for the GC-FID and GC-MS methods, respectively. Calibration curves were obtained using the peak area responses of the standard solutions. The correlation coefficients ($R^2$) of each of the compounds obtained from both the GC-FID and GC-MS methods were>0.99 (table 2). The LOD and LOQ were considered to be three and ten times the signal-to-noise ratio, respectively, using matrix-blank samples spiked with the standards. The LOD and LOQ for the nine compounds from the GC-FID and GC-MS methods are given in table 2.

**Precision, accuracy and recovery**

The precision determined by intraday repeatability, the intermediate interday precision, and the accuracy values are reported in table 3. Intra-and interday assays were performed as nine analyses in the same day (three replications each for three concentrations) and as an independent analysis per day over 3 d, respectively. The %RSD ranged from 0.54–10.34% and 0.19–2.86% for inter-and intraday measurements, respectively, using the GC-FID

method. The RSD% values of GC-MS method were<11% for both the repeatability and intermediate precision. As seen in table 3, the accuracy ranged between 83.90–119.58% from intra and interday assays using the GC-FID and GC-MS methods. The average recoveries of the methods ranged between 80.13–118.89% and the %RSD of the average recoveries were<13% for all of the compounds (table 4).

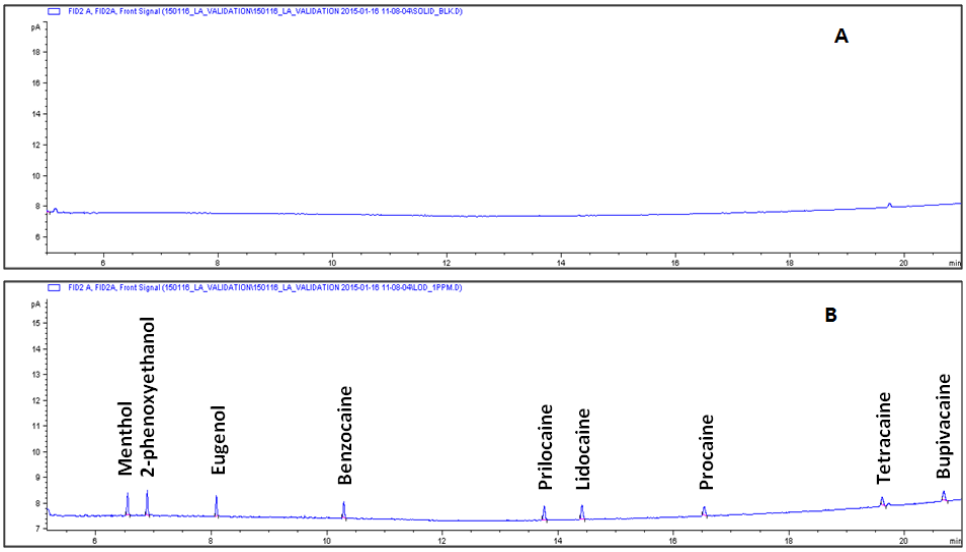


**Fig. 1: GC-FID chromatograms of (A) a matrix-blank sample and (B) a sample spiked with standard at the limit of quantification**

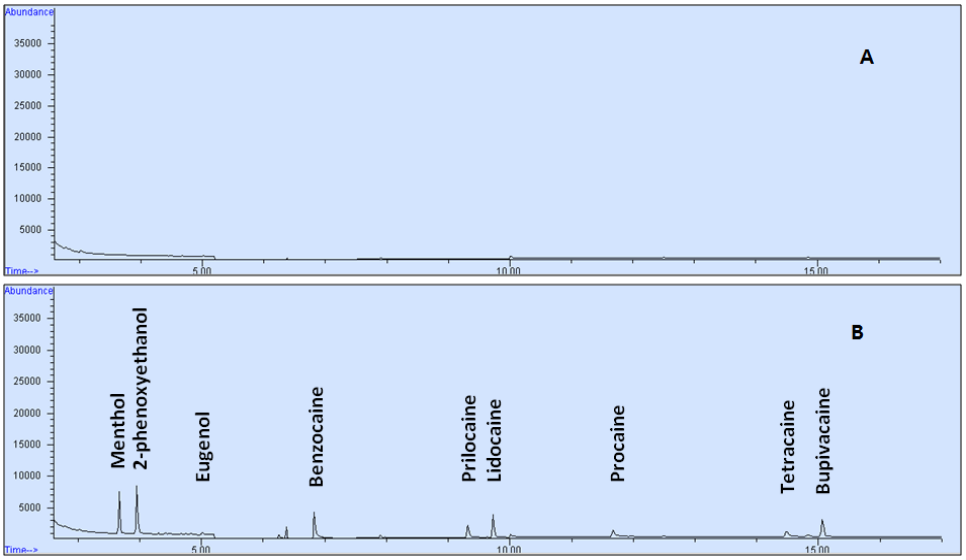


**Fig. 2: GC-MS extracted ion chromatograms of (A) a matrix-blank sample and (B) a sample spiked with standard at the limit of quantification**

**Table 2: Correlation coefficients and the limits of detection and quantification (LOD and LOQ) for local anaesthetics by GC-FID and GC-MS**

| S. No. | Compounds | GC-FID | | | | | GC-MS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | $R^2$ | Cream | | Gel | | $R^2$ | Cream | | Gel | |
| | | | LOD[a] (ppm) | LOQ[a] (ppm) | LOD[a] (ppm) | LOQ[a] (ppm) | | LOD[a] (ppm) | LOQ[a] (ppm) | LOD[a] (ppm) | LOQ[a] (ppm) |
| 1 | Menthol | 0.999 | 0.17 | 0.52 | 0.17 | 0.52 | 0.997 | 0.03 | 0.10 | 0.04 | 0.13 |
| 2 | 2-Phenoxyethanol | 0.999 | 0.23 | 0.69 | 0.46 | 1.37 | 0.995 | 0.04 | 0.11 | 0.05 | 0.14 |
| 3 | Eugenol | 0.999 | 0.33 | 1.00 | 0.17 | 0.50 | 0.993 | 0.18 | 0.54 | 0.09 | 0.27 |
| 4 | Benzocaine hydrochloride | 0.999 | 0.35 | 1.05 | 0.35 | 1.05 | 0.993 | 0.09 | 0.26 | 0.13 | 0.38 |
| 5 | Prilocaine hydrochloride | 0.998 | 1.02 | 3.07 | 0.34 | 1.02 | 0.994 | 0.10 | 0.31 | 0.26 | 0.77 |
| 6 | Lidocaine | 1.000 | 0.34 | 1.02 | 0.34 | 1.02 | 0.991 | 0.09 | 0.26 | 0.09 | 0.26 |
| 7 | Procaine hydrochloride | 0.999 | 1.04 | 3.13 | 0.69 | 2.08 | 0.992 | 0.17 | 0.51 | 0.09 | 0.26 |
| 8 | Tetracaine hydrochloride | 0.999 | 1.04 | 3.13 | 0.69 | 2.08 | 0.991 | 0.17 | 0.50 | 0.17 | 0.50 |
| 9 | Bupivacaine hydrochloride | 1.000 | 1.03 | 3.10 | 0.69 | 2.07 | 0.991 | 0.08 | 0.25 | 0.08 | 0.25 |

[a] LOD, limit of detection; LOQ, limit of quantification, *n*=3.

**Table 3: GC-FID and GC-MS precisions and accuracies for the local anaesthetics**

| S. No. | Compounds | Conc. [a] (ppm) | GC-FID | | | | GC-MS | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Intra-day[b] | | Inter-day[b] | | Intra-day[b] | | Inter-day[b] | |
| | | | Accuracy (%) | Precision (%RSD[c]) | Accuracy (%) | Precision (%RSD[c]) | Accuracy (%) | Precision (%RSD[c]) | Accuracy (%) | Precision (%RSD[c]) |
| 1 | Menthol | low | 117.08 | 0.50 | 108.82 | 7.39 | 95.54 | 5.55 | 98.47 | 2.21 |
| | | medium | 99.80 | 0.65 | 102.77 | 7.40 | 88.41 | 3.05 | 89.31 | 3.68 |
| | | high | 99.09 | 0.92 | 103.15 | 7.05 | 98.42 | 5.32 | 97.75 | 5.56 |
| 2 | 2-Phenoxyethanol | low | 110.28 | 0.51 | 107.64 | 5.53 | 96.50 | 3.69 | 99.33 | 2.24 |
| | | medium | 98.48 | 0.47 | 98.87 | 4.32 | 86.32 | 2.53 | 87.72 | 2.98 |
| | | high | 98.66 | 0.99 | 100.17 | 3.75 | 100.43 | 5.77 | 99.74 | 4.24 |
| 3 | Eugenol | low | 84.04 | 1.30 | 89.59 | 10.34 | 97.63 | 2.17 | 101.14 | 1.05 |
| | | medium | 90.29 | 0.65 | 88.02 | 2.34 | 83.79 | 1.83 | 84.01 | 4.26 |
| | | high | 96.06 | 0.80 | 94.98 | 1.24 | 104.07 | 5.83 | 101.53 | 3.63 |
| 4 | Benzocaine hydrochloride | low | 102.86 | 0.61 | 100.16 | 6.78 | 95.79 | 3.94 | 96.97 | 5.42 |
| | | medium | 96.03 | 0.82 | 97.47 | 6.21 | 85.76 | 0.83 | 85.34 | 3.13 |
| | | high | 96.05 | 1.14 | 98.40 | 5.68 | 105.56 | 4.63 | 102.46 | 3.37 |
| 5 | Prilocaine hydrochloride | low | 90.92 | 2.86 | 119.23 | 6.91 | 98.16 | 2.16 | 95.23 | 5.89 |
| | | medium | 111.16 | 0.27 | 107.61 | 3.51 | 84.65 | 0.68 | 84.81 | 7.81 |
| | | high | 115.27 | 1.07 | 111.99 | 4.23 | 97.86 | 4.72 | 97.38 | 7.33 |
| 6 | Lidocaine | low | 89.27 | 1.39 | 86.97 | 4.71 | 96.68 | 3.59 | 99.66 | 3.54 |
| | | medium | 93.66 | 0.36 | 96.10 | 4.84 | 85.47 | 0.98 | 85.08 | 3.59 |
| | | high | 95.14 | 1.07 | 98.63 | 4.61 | 106.61 | 5.32 | 103.55 | 3.60 |
| 7 | Procaine hydrochloride | low | 116.08 | 1.70 | 114.60 | 2.25 | 96.78 | 3.74 | 90.48 | 10.98 |
| | | medium | 98.47 | 1.01 | 99.10 | 0.58 | 83.90 | 1.13 | 84.09 | 8.13 |
| | | high | 96.72 | 0.24 | 96.84 | 0.57 | 98.37 | 3.86 | 97.30 | 8.54 |
| 8 | Tetracaine hydrochloride | low | 113.69 | 1.46 | 110.19 | 5.66 | 98.42 | 4.16 | 93.78 | 6.45 |
| | | medium | 93.40 | 0.99 | 93.82 | 0.54 | 84.17 | 1.28 | 84.62 | 7.94 |
| | | high | 91.41 | 0.30 | 91.48 | 0.61 | 95.85 | 3.27 | 96.61 | 8.79 |
| 9 | Bupivacaine hydrochloride | low | 118.76 | 1.42 | 119.58 | 0.77 | 99.71 | 1.97 | 97.77 | 4.63 |
| | | medium | 97.77 | 1.06 | 100.12 | 2.16 | 87.07 | 0.83 | 86.84 | 4.30 |
| | | high | 95.11 | 0.19 | 96.62 | 1.37 | 99.66 | 3.83 | 99.35 | 6.08 |

[a] Conc, concentration, [b] *n*=9, [c] %RSD, percentage relative standard deviation.

**Table 4: GC-FID and GC-MS recoveries (%) of the local anaesthetics in the matrix-blank samples**

| S. No. | Compounds | | GC-FID | | | | GC-MS | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Conc. [a] (ppm) | Cream Recovery[b] | %RSD[c] | Gel Recovery[b] | %RSD[c] | Cream Recovery[b] | %RSD[c] | Gel Recovery[b] | %RSD[c] |
| 1 | Menthol | low | 116.53 | 1.06 | 113.94 | 0.47 | 94.09 | 6.58 | 86.91 | 6.33 |
| | | medium | 111.13 | 0.62 | 111.49 | 0.74 | 95.03 | 4.25 | 94.10 | 3.63 |
| | | high | 110.20 | 0.42 | 108.63 | 0.41 | 98.74 | 9.15 | 101.75 | 10.42 |
| 2 | 2-Phenoxyethanol | low | 116.98 | 1.10 | 111.08 | 1.44 | 119.97 | 6.61 | 99.40 | 5.50 |
| | | medium | 108.68 | 0.60 | 108.44 | 0.64 | 102.72 | 3.18 | 104.97 | 2.98 |
| | | high | 106.81 | 0.45 | 105.54 | 0.38 | 104.34 | 9.76 | 111.04 | 11.77 |
| 3 | Eugenol | low | 97.87 | 1.20 | 101.35 | 0.41 | 111.67 | 4.06 | 97.01 | 2.52 |
| | | medium | 91.72 | 0.59 | 96.72 | 0.78 | 117.52 | 4.27 | 107.51 | 4.08 |
| | | high | 89.93 | 0.42 | 93.81 | 0.39 | 99.47 | 7.78 | 96.07 | 13.00 |
| 4 | Benzocaine hydrochloride | low | 116.06 | 1.05 | 114.04 | 1.07 | 102.67 | 3.73 | 118.89 | 6.24 |
| | | medium | 108.69 | 0.60 | 111.92 | 0.86 | 100.01 | 3.91 | 97.26 | 4.61 |
| | | high | 107.11 | 0.38 | 108.14 | 0.64 | 108.09 | 9.24 | 108.97 | 12.32 |
| 5 | Prilocaine hydrochloride | low | 111.43 | 1.25 | 112.85 | 0.89 | 96.71 | 3.23 | 91.23 | 0.65 |
| | | medium | 102.97 | 0.53 | 107.60 | 0.83 | 94.87 | 1.17 | 96.23 | 2.32 |
| | | high | 99.19 | 0.41 | 101.21 | 0.75 | 100.07 | 10.55 | 92.85 | 12.03 |
| 6 | Lidocaine | low | 109.46 | 1.22 | 112.90 | 0.53 | 96.86 | 2.25 | 92.88 | 0.72 |
| | | medium | 104.83 | 0.64 | 109.54 | 0.91 | 95.73 | 1.41 | 97.63 | 3.10 |
| | | high | 103.74 | 0.37 | 105.62 | 0.74 | 106.77 | 10.93 | 91.33 | 12.29 |
| 7 | Procaine hydrochloride | low | 99.01 | 4.15 | 86.54 | 4.77 | 98.92 | 4.61 | 112.38 | 9.25 |
| | | medium | 98.02 | 1.20 | 80.13 | 2.84 | 96.33 | 0.83 | 101.18 | 9.11 |
| | | high | 101.67 | 0.12 | 88.44 | 0.57 | 105.78 | 9.39 | 107.08 | 12.20 |
| 8 | Tetracaine hydrochloride | low | 104.40 | 0.80 | 107.79 | 1.13 | 104.70 | 2.91 | 104.96 | 4.01 |
| | | medium | 97.08 | 0.72 | 101.09 | 0.93 | 97.52 | 0.74 | 98.38 | 1.56 |
| | | high | 95.31 | 0.37 | 96.45 | 0.76 | 101.40 | 8.07 | 102.56 | 11.79 |
| 9 | Bupivacaine hydrochloride | low | 112.69 | 3.41 | 113.51 | 1.85 | 95.83 | 2.22 | 89.24 | 0.50 |
| | | medium | 107.40 | 1.42 | 113.54 | 0.15 | 95.99 | 0.33 | 93.31 | 1.80 |
| | | high | 105.96 | 0.28 | 108.64 | 1.19 | 98.54 | 8.46 | 100.47 | 11.16 |

[a] Conc, concentration, [b] *n*=3., [c] %RSD, percentage relative standard deviation.

**Stability**

The stabilities of the standard solutions, which were stored at 4 °C, were evaluated by their comparison with the peak areas detected from freshly prepared standard solutions. The stability experiments were performed in the auto sampler (20 °C) at three concentrations over 48 h. Table 5 summarizes that an averaged %RSD of the stabilities were within 13%. Therefore, all of the stock solutions were considered to have reliable stability under normal working conditions.

**Table 5: Stability of the standard stock solutions**

| S. No. | Compounds | Conc. [a] (ppm) | GC-FID (%RSD[b]) | GC-MS (%RSD[b]) |
|---|---|---|---|---|
| 1 | Menthol | low | 1.56 | 2.11 |
| | | medium | 2.21 | 2.28 |
| | | high | 1.52 | 1.42 |
| 2 | 2-Phenoxyethanol | low | 7.13 | 1.02 |
| | | medium | 2.19 | 2.29 |
| | | high | 1.80 | 1.69 |
| 3 | Eugenol | low | 4.17 | 3.06 |
| | | medium | 2.15 | 3.93 |
| | | high | 1.78 | 2.00 |
| 4 | Benzocaine hydrochloride | low | 12.42 | 8.46 |
| | | medium | 2.01 | 3.61 |
| | | high | 1.99 | 1.56 |
| 5 | Prilocaine hydrochloride | low | 7.31 | 10.81 |
| | | medium | 1.35 | 6.40 |
| | | high | 1.97 | 3.14 |
| 6 | Lidocaine | low | 2.77 | 6.28 |
| | | medium | 2.26 | 3.51 |
| | | high | 2.04 | 1.25 |
| 7 | Procaine hydrochloride | low | 10.98 | 8.52 |
| | | medium | 1.68 | 12.34 |
| | | high | 3.15 | 4.55 |
| 8 | Tetracaine hydrochloride | low | 9.34 | 14.09 |
| | | medium | 1.34 | 4.92 |
| | | high | 2.85 | 6.08 |
| 9 | Bupivacaine hydrochloride | low | 3.72 | 8.70 |
| | | medium | 2.06 | 5.22 |
| | | high | 2.15 | 1.37 |

[a] Conc, concentration., [b] %RSD, percentage relative standard deviation; *n*=3.

**Analysis of the seized samples**

The developed and validated GC-FID and GC-MS methods were applied to the screening for the presence of local anaesthetics and their quantification in 26 products collected from online retailers or sex shops in South Korea. Approximately 60% (16/26) of the samples were adulterated with some of the local anaesthetics (table 6). The local anaesthetics that were detected in the samples were menthol, 2-phenoxyethanol, eugenol, prilocaine, tetracaine, and lidocaine. The most frequently detected adulterant was lidocaine, which was found in 58% (15/26) of the samples. Its concentration ranged between 2.81–52.40 mg/g. Eugenol and prilocaine were only detected in each samples. Three of the samples (12%) contained both menthol and 2-phenoxyethanol. Also, more than one local anaesthetic was detected in some of the analysed products. Menthol (0.03–0.16 mg/g) and 2-phenoxyethanol (0.20–0.21 mg/g) were found in combination with lidocaine (2.81–9.68 mg/g) in two samples, and menthol (7.89 mg/g) and 2-phenoxyethanol (3.19 mg/g) were in combination with eugenol (3.45 mg/g) in one sample. Tetracaine (52.20 mg/g) and lidocaine (33.00 mg/g) were detected in combination with prilocaine (12.80 mg/g) in one sample, and tetracaine (18.30 mg/g) was found in combination with lidocaine (34.80 mg/g) in another sample. However, three of the compounds (benzocaine, procaine, and bupivacaine) were not detected in any of these illegal products.

**CONCLUSION**

There was limited preliminary literature regarding the analysis of local anaesthetics in creams. However, a study on the presence of adulterant local anaesthetics in products advertised for strengthening male sexual function using GC-FID and GC-MS has never been published.

In this study, we validated a GC-FID method for the identification and quantification of local anaesthetics in illegal product samples. This method allowed the clear separation of each suspected compound and provided stable values during the analysis procedure. It could be routinely performed in most laboratories. Further study using GC-MS allowed for the confirmation of the trace local anaesthetics by their mass spectra, and it would be possible to screen suspicious compounds including local anesthetics in counterfeit products.

Our suggested methods were applied to the detection of seized illegal products that included local anaesthetics, and more than half of the analysed samples contained illegal local anaesthetics whose concentrations were quite high. We consider the screening and identification of adulterants in illegally distributed products important because the undeclared components of illicit creams or counterfeit products can cause health problems.

We anticipate that the proposed combination of methods used in this study would facilitate the screening of local anaesthetic adulterants, which are included in numerous unknown products advertised as treatment or improvements for PE. These studies in the field of forensic science will contribute to the strict regulations of these illegal products and the public health.

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**CONFLICT OF INTERESTS**

Declared none

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