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Original Research Article

# Determination of methylparaben in some cosmetics and pharmaceutics using liquid-liquid extraction and spectrophotometric technique

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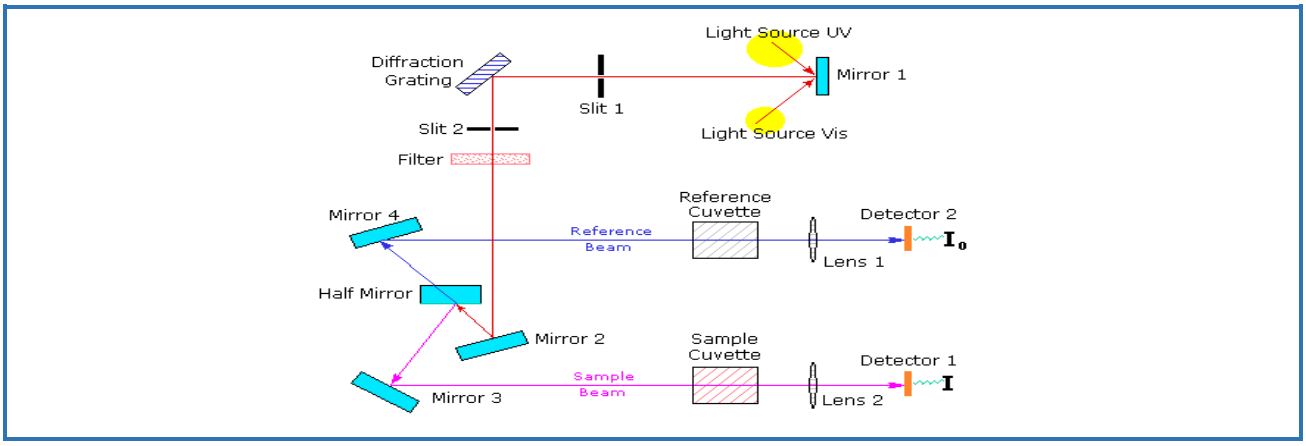
**ABSTRACT**

Parabens are compounds often added to cosmetics and pharmaceutics as preservatives for fungi and bacterial growth, but, recent studies have linked these compounds to several adverse side-effects such as cancer, miscarriage and infertility. The extraction of methyl paraben from (hand cream, body lotion, blusher, body cream, and bath foam) was studied using liquid-liquid extraction with ethyl acetate as a solvent, and double beam UV-spectrophotometer at wave length 282 nm. Calibrations are linear (correlation coefficient r>0.997) and the limit of detection was 2.358 µg/mL The concentrations of methyl paraben for the selected cosmetic samples were ranged from 0.077% to 0.451%.



## Graphical Abstract

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## Introduction

Parabens are chemical compounds of esters of para-hydroxybenzoic acid, from which the name is derived, with the general formula $C_7H_5O_3R$ (Where R is an alkyl group). Scheme 1 illustrates the general chemical structure of parabens [1].

Commonly parabens include methylparaben, ethylparaben, propylparaben, butylparaben and heptylparaben whereas less common parabens include isobutylparaben, isopropylparaben, benzylparaben and their sodium salts [2].

### *Methylparaben*

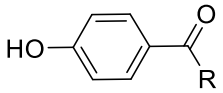
One of the parabens compounds with the chemical formula $C_8H_8O_3$ is the methyl ester of *p*-hydroxybenzoic acid as the IUPAC name is methyl 4-hydroxy benzoate. Scheme 2 shows the chemical structure of methyl paraben [3].

It is available in the form of white crystals, but industrial use grades may be light grey or light tan. Contacting with air and light causes oxidation and darkening of colour. Methyl paraben is soluble in water, methanol, and ether and slightly soluble in chloroform [4]. However the chemical and physical properties of methyl paraben are shown below in Table 1.

### *Occurrence of methyl paraben in nature*

Methyl paraben serves as a pheromone for a variety of insects and is a component of queen mandibular pheromone. Some plants produce methyl paraben *i.e.,* thale cress. Naturally-occurring parabens have similar preservation properties as synthetic parabens; indeed, they are present in these plants to help them defend themselves against various micro-organisms. Not all plants have been tested for naturally-occurring parabens, so it is impossible to know if all plants contain these molecules or not. Most plants that have been tested for the presence of naturally-occurring parabens specifically contain methyl paraben and sometimes ethyl paraben (remember parabens are a family of various molecules). Honeysuckle can be regarded as one of those plants which are richest in naturally-occurring methyl paraben. Other plants known to contain naturally-occurring parabens include: blueberries, carrots, olives, strawberries [5]. The % of naturally-occurring parabens in plants tends to be extremely low. In this sense, while in a cosmetic preparations parabens might make up to 0.3% of the formula; naturally-occurring methyl paraben in blueberries is less than 0.003%.

**Scheme 1.** General chemical structures of parabens



**Scheme 2.** Chemical structure of methyl paraben

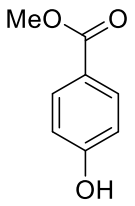



**Table 1.** Chemical and physical properties of methyl paraben

| Property | Result |
|---|---|
| Physical properties | Crystalline solid |
| Colour | White |
| Odour | Odourless |
| Melting point | 125-128 °C |
| Boiling point | 265.5 °C |
| Flammability | Non flammable |
| Solubility | Soluble in water, alcohol, ether, acetone, slightly soluble in benzene and carbon tetrachloride |
| $PK_a$ | 9.96 |
| Density/Specific Gravity | 1.209 g/cm$^3$ |
| Molecular weight | 152.15 g/mol$^{-1}$ |

*Uses of methyl paraben*

Parabens have been safely used for almost 100 years as preservatives in the food, drug, personal care and cosmetic industries [6]. Parabens (including methylparaben, ethylparaben, propylparaben, butylparaben, isopropylparaben, and isobutylparaben) may be used in products such as makeup, moisturizers, hair care and shaving products. Contrary to some reports, most of the major brands of deodorants and antiperspirants contain parabens [7]. Preservatives like methylparabens may be used in cosmetics to protect against microbial (*e.g.,* bacteria, fungus) growth, both to protect consumers and to maintain product integrity.

*Regulatory exposure limits*

A number of commonly used parabens have had the U.S. Food and Drug Administration's (FDA) Generally Recognized as Safe (GRAS) classification since the early 1970s. The GRAS designation means that the substance is generally recognized among qualified experts, as it has been adequately shown to be safe under the conditions of its intended use [8].

In 1984, CIR reviewed the safety of parabens used in cosmetics and concluded that they were safe, even in extremely large doses. Typically parabens are used at levels ranging from 0.01 to 0.3 percent, and the CIR concluded that they were safe for use in cosmetics at levels up to 25 percent.

In 2012, the CIR reopened its safety report on parabens in order to consider all new data. As it did in 1984, the expert panel reaffirmed the safety of cosmetic products in which parabens preservatives are used [9].

*Toxicity of parabens*

Parabens can enter the human body through the skin and parenterally. The average daily total personal parabens exposure is estimated to be 76 mg, with cosmetics and personal care products accounting for 50 mg, 25 mg from pharmaceutical products, and 1 mg from food [10]. Parabens applied to the skin are metabolized by keratinocyte carboxyl esterases and conjugated metabolites and are excreted in the urine. Oral or intravenous parabens are metabolized by esterase within the intestine and liver [11]. Parabens have been detected in urine, serum, breast milk and seminal fluids, but most worrisome has been the detection in breast tissue from patients with breast cancer. Some have hypothesized that the higher concentration in the upper lateral breast near the axilla correlates with the exposure from underarm deodorant and an increased incidence of breast cancer development in the area. Still absolute concentrations indicate that levels of parabens within human fluids and tissues are low with average urine concentrations reported in the US ranging from 0.5 to 680 ng/mL and breast tissue concentrations ranging from 0 to 5100 ng/g of breast tissue.

*Principles of spectroscopic measurements*

Spectroscopists use the interactions of radiation with matter to obtain information about a sample. Several of the chemical elements were discovered by spectroscopy. The sample is usually stimulated in some way by applying energy in the form of heat, electrical energy, light, particles, or a chemical reaction. Prior to applying the stimulus, the analyte is predominately in its lowest energy or ground state. The stimulus then causes some of the analyte species to undergo a transition to a higher energy or excited state. We acquire information about the analyte by measuring the electromagnetic radiation emitted as it returns to the ground state or by measuring the amount of the absorbed electromagnetic radiation.

*Liquid-liquid extraction techneque*

Liquid-liquid extraction is a mass-transfer operation in which a liquid solution (The feed) is contacted with an immiscible or nearly immiscible liquid (Solvent) that exhibits preferential affinity

or selectivity towards one or more of the components in the feed. Liquid-liquid extraction (or more briefly, solvent extraction) is a useful method to separate components (Compounds) of a mixture. The success of this method depends on the difference in solubility of a compound in various solvents [13].

In the practical use, usually one phase is water or water-based (Aqueous) solution and the other an organic solvent which is immiscible with water. Solvent extraction is used in nuclear reprocessing, ore processing, the production of fine organic compounds, the processing of perfumes and other industries. In solvent extraction, a distribution ratio is often quoted as a measure of how well extracted a species is. The distribution ratio (D) is equal to the concentration of a solute in the organic phase divided by its concentration in the aqueous phase. Figure 1 illustrates the common used extraction solvents [14].

Liquid-liquid extraction (LLE) technique has been introduced for the analysis of organic compounds, inorganic analytes and various types of analytes from different matrices such as water, tissue, biological fluids, and food matrices. LLE which is designed using volumes of extraction solvent is based on the equilibrium distribution process of the target analytes between the sample solution and the extraction solvent. Ethyl acetate which is the most suitable solvent, as compared to the available solvents, is lighter than water and produces the maximum coverage extraction E% [15].

The advantage of this method offers simplicity of operation, rapidity, low cost, high recovery, high enrichment factor, and environmental benignity with wide application prospects in trace analysis. In conventional LLE application, the density of extraction solvent should be higher than water. The high density extraction solvents, being mostly halogenated, are generally hazardous to laboratory personnel and are not often compatible with UV-spectrophotometer equipment. There has been much research focused on parabens because they are so widely used. *Devon C. Zimmerman*, *Henry F. Rossi*, *Daniel W. Keating*, at west Chester University USA (2013), used solid-supported liquid-liquid extraction (SLE) and liquid-liquid extraction (LLE) for the extraction of parabens from a shampoo/body wash samples followed by high performance liquid chromatography (HPLC) [15].

In this work we present a simple technique of liquid-liquid extraction to extract methyl paraben in cosmetics and pharmaceutics. In addition, the sample preparation step was employed for the extraction of target analyte in cosmetics before LLE and thus reducing the matrix effect.

## Experimental

### *Materials and methods*

Methyl paraben for analysis (99%), methanol, acetone, sodium chloride, *n*-propanol, ethyl acetate, magnesium sulfate. Standard solutions of methyl paraben were prepared in methanol by dilution of

the stock solutions at nominal concentrations of 1000, 500, 100, 50, 25, 10, and 1 ppm. Appropriate dilutions were made, whenever necessary with methanol.

*Instrumentation and equepiments*

A double beam spectrophotometer is used for determination of methyl paraben absorbance. The pH meter Jenway 3150 was made in the U.K. The weight of the compounds was determined using electronic balance Mettler-Toledo (AB54-S) (max, 51.00 g/min, 10.00 mg).

*The sampling*

Eleven different trademarks of cosmetic products were randomly selected from Benghazi markets. The method recommended by (*Devon C. Zimmerman*, 2009) was used to analyze the presence and precise concentration of paraben. For the samples, about accurately 1 g of each sample was dissolved in 2.5 mL of acetone and 1.25 mL of sodium chloride and vortex for 30 sec in a water bath. This solution was filtered with a filter paper. The concentration of paraben was detected using a double beam UV spectrophotometer at a wavelength of 282 nm and quartz cuvette.

*Procedure of liquid-liquid extraction*

Transfer the ready sample to the extraction funnel and add about 20 mL of ethyl acetate and 5 mL of NaCl of (0.1 M) solution, shake well, let the gases outlet, and decant the water. Then, dry it with 0.5 gr of $MgSO_4$. Figure 2 illustrates the procedure of extraction for methyl paraben.

| Name | Formula | Density[1] (g / mL) | bp (°C) | Comments |
|---|---|---|---|---|
| | | ***LIGHTER THAN WATER:*** | | |
| diethyl ether | $(CH_3CH_2)_2O$ | 0.7 | 35 | highly flammable, toxic |
| petroleum ether | - | ~0.7 | 30 - 60 | flammable |
| hexanes | - | ~0.7 | >60 | flammable |
| benzene | $C_6H_6$ | 0.9 | 80 | flammable, toxic, carcinogenic |
| toluene | $C_6H_5CH_3$ | 0.9 | 111 | flammable |
| ethyl acetate | $C_4H_8O_2$ | 0.9 | 78 | flammable, irritant |
| | | ***HEAVIER THAN WATER:*** | | |
| methylene chloride (dichloromethane) | $CH_2Cl_2$ | 1.3 | 41 | toxic |
| chloroform | $CHCl_3$ | 1.5 | 61 | toxic |
| carbon tetrachloride | $CCl_4$ | 1.6 | 77 | toxic, cancer suspect agent |

**Figure 1.** Illustrates the common extraction solvents

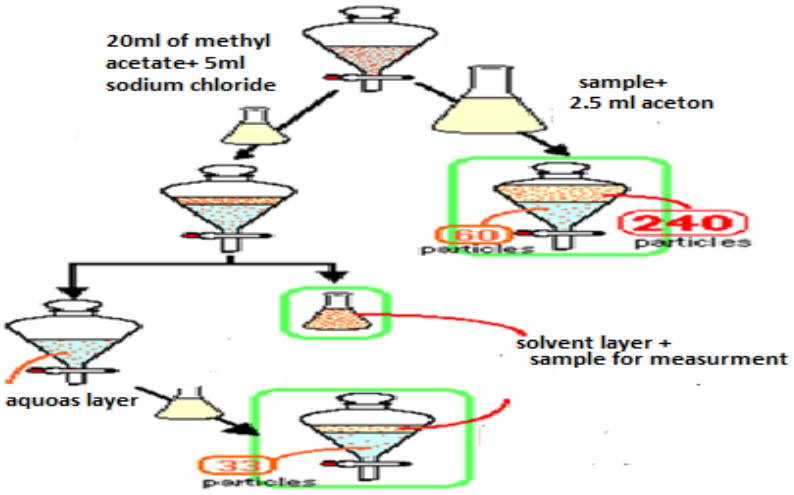



**Figure 2.** Shows the sample preparation of liquid-liquid extraction for methyl paraben

*Estimation of ƛmax (Maximum absorption of methyl paraben)*

To determine the maximum absorption, standard solutions of methyl paraben in concentration of 40 ppm were prepared. Scanning of the methyl paraben in a wavelength range from 250 nm to 320 nm showed a maximum absorbance (ƛmax) at 282 nm.

*Calibration curve*

After determination of the maximum absorption of methyl paraben (282 nm), using double beam UV-spectrophotometer, the absorbance was then taken at a wavelength of 282 nm and traced on the calibration curve to give the concentration methyl paraben in each sample. The calibration curve was obtained from methyl paraben standard by serial dilutions of concentrations 0, 2, 4, 6, 8 and 10 µg/mL.

Under the best experimental conditions, a good linear correlation was obtained between the absorbance and methyl paraben concentration in the range from 0 to 10 µg/mL. The calibration curve of methyl paraben standard solution has been shown in Figure 3.

From Table 2, the parameters of the methyl paraben concentration-absorbance straight line were calculated by the least-squares method. The regression equation of the calibration line has the following form:

$$A = 0.022\ C + 0.007\ (R^2 = 0.997)$$

Where C is the concentration of methyl paraben (µg/mL), A is the absorbance. The correlation coefficient ($R^2$) is 0.997. Statistical evaluation of the regression line using standard deviation about

the regression ($S_r$), the standard deviation of intercept ($S_a$) and standard deviation of the slope ($S_b$), gave the following values: $1.60\times10^{-2}$, $4.53\times10^{-4}$, and $1.14\times10^{-2}$, respectively. The values of the regression and the intercept are small and point out to the low scattering of the point around the calibration curve and to the high precision of the method.

The limit of detection (LOD) was determined by establishing the minimum level at which the analyte can be detected. The LOD was found to be 2.358 μg/mL. According to the 3s/m definition, where *s* is the standard deviation (n=6) of the signal from 30 μg/mL methyl paraben aliquots, *m* is the slope of the calibration graph. The limit of quantification (LOQ) was determined by establishing the lowest concentration which was measured with acceptable accuracy and precision and was found to be 7.858 μg/mL.

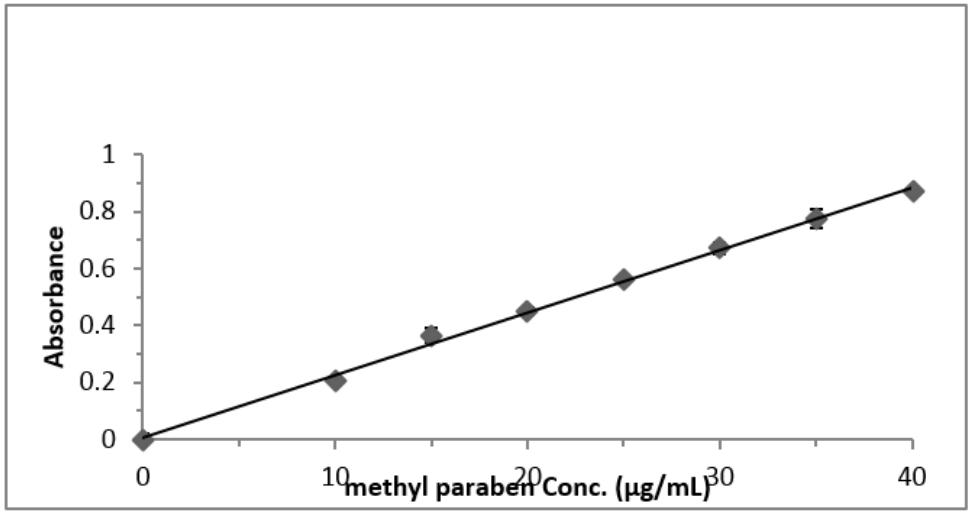



**Figure 3.** Calibration curve of standard solution of methyl paraben methanol solution at 282 nm. The linear regression equation is A=0.022 C+0.007 ($R^2$=0.997)

**Table 2.** Analytical data and the optical characteristics for the determination of methyl paraben

| Parameter | Analysis of methyl paraben |
|---|---|
| $\lambda_{max}$ | 282 nm |
| Linear range | 0-10 μg/mL |
| Linear regression equation (A=mC+a) | |
| Intercept (a) | 0.007 |
| Slope (b) | 0.022 |
| Correlation coefficient ($R^2$ ) | 0.997 |
| Limit of detection | 2.358 μg/mL |
| Limit of quantification | 7.858 μg/mL |

*Practical application*

After estimation and identifying the maximum wavelength for absorption measurement and obtaining the best working range for methyl paraben in standard solution, the method was applied for quantitative determination of methyl paraben in some body-care products and cosmetics.

The obtained result for the selected measuring concentration of methyl paraben is given in Table 3 equation (i) illustrates the converting methyl paraben from µg/ml to %.

$$\%\ \text{methylparaben} = \frac{g\ amount\ of\ methyl\ paraben\ found}{weight\ of\ sample}\ X\ dil.factor\ X100 \qquad \text{(i) [15]}$$

*Analysis of cosmetics*

Various cosmetic products (Hand cream, body lotion, face powder, shower gel) were collected from local markets. The concentrations of methyl paraben in the selected cosmetic samples were ranged from 0.077% to 0.451% as shown in Table 3.

**Table 3.** Analysis of methyl paraben in some cosmetics by the spectrophotometric method

| Preparation | $A_{282}$ | Found (µg/mL)[a] | Found (g%)[b] |
|---|---|---|---|
| Vaseline Eva cosmetic Co. Egypt. | 0.343 | 5.090 | 0.073 |
| Life buoy Hindustan Unilever Limited brand, India | 0.844 | 12.524 | 0.310 |
| Perfect glycerene | 0.331 | 4.911 | 0.017 |
| Mac | 0.09 | 1.335 | 0.053 |
| Deborah | 0.369 | 5.475 | 0.0077 |
| Clean and clear | 0.151 | 2.240 | 0.14 |
| Matte blusher | 0.677 | 10.045 | 0.081 |
| Blusher | 1.08 | 16.025 | 0.451 |

[a] The values obtained from the calibration curve

[b] The values obtained by applying in equation (2.1)

## Conclusions

The results show that the LLE technique offers an effective method for the extraction of methyl paraben from a shampoo/body wash matrix. The impurities that were extracted from the matrix together with the parabens were minimal and did not interfere with the quantitation of the methyl paraben. The advantage of this method is low cost and simple procedure for determination of methyl paraben in cosmetic and pharmaceutics products.

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**Orcid**

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**References**

[1]. Zhang Q., Lian M., Liu L., Cui H. *Anal. Chim. Acta*., 2005, **537**:31

[2]. Dabra P.D., Aljarrah A., Miller W.R. *J. Appl. Toxicol*., 2004, **24**:5

[3]. Routledge E.J., Parker J., Odum J., Ashby J., Sumpter J.P. *Toxicol. Appl. Pharmacol*., 1998, **153**:12

[4]. Maeda Y., Yamamoto M., Owada K., Sato S., Masui T., Nakazawa H., Fujita M. *Chromatogr*, 1987, **410**:413

[5]. North M., Tandon V.R. *PLoS ONE*, 2011, **6**:e24205

[6]. McGregor D. *Critical Rev. Toxicol.,* 2007, **37**:887

[7]. Kari F.W., Bucher J., Eustis S.L., Haseman J.K., Huff J.E. *Food Chem. Toxicol.*, 1992, **30**:737

[8]. Hiraku Y., Kawanishi S. *Cancer Res.*, 1996, **56**:5172

[9]. Kang, S.H., Kim H. *Journal of Pharmaceutical and Biomedical Analysis*, 1997, **15**:1359

[10]. Soni M.G., Burdock G.A., Taylor S.L. Greenberg N.A. *Food Chemical Toxicology*, 2002, **40**:1335

[11]. Carcia P.L.G., Santoro M.I.R.M., Singh A.K., Kedor-Hachmann E.R.M. *Brazilian J. Pharm. Sci.,* 2007, **43**:397

[12]. Mincea M.M., Lopsa I.R. *J. Serb. Chem. Soc*., 2009, **74**:669

[13]. Leong M.I., Huang S.D. *Journal of Chromatography A*, 2008, **1211**:8

[14]. Jamali M.R., Rahimpour S., Rahnama R. *Applied Chemistry*, 2012, **23**:21

[15]. Darbe P.D., Aljarrah A., Miller W.R., Coldham N.G., Sauer M.J., Pope G.S.
*J. Appl. Toxicol*., 2004, **24**:5

[16]. Odumasu P.O., Elkwe T.O. *African J. Pharm. Pharm*., 2010, **4**:231

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