

Isopropyl p-toluenesulphonic acid esters (IPTS) is a by-product that may be formed during synthesis of isopropyl palmitate (IPP) and isopropyl myristate (IPM). The synthesis route is via esterification of palm-based palmitic and palm kernel-based myristic acids, by reaction with isopropanol. Under certain reaction conditions (anhydrous, no base and high temperature) isopropyl alcohol may react with the catalyst, p-toluenesulphonic acid to form IPTS. These esters act as dry and soft non-greasy emollient, moisturisers, thickening and anti-static agents in cosmetic and personal care products. They are also used in many topical medicinal preparations including bath oils, baby oils, hair preparations, shaving preparations, creams, lotions, aftershaves, make-up foundations, lipsticks formulation, liniments, sunscreen products, anti-perspirants and cologne sticks. The structure of IPTS is shown in *Figure 1* and its physical properties are shown in *Table 1*.

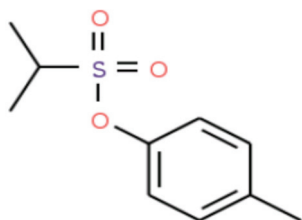


Figure 1. Structure of isopropyl p-toluenesulphonic acid ester (IPTS).

TABLE 1. PHYSICAL AND CHEMICAL PROPERTIES OF ISOPROPYL P-TOLUENESULPHONIC ACID ESTERS (IPTS)

Properties	Basic information
Molecular formula	C ₁₀ H ₁₄ O ₃ S
Molecular weight	214.28
Density	1.163 g cm ⁻³
Melting point	20°C
Boiling point	314.1°C at 760 mmHg
Flash point	143.7°C
Solubility	Very soluble in alcohol and acetone, not soluble in water

IPTS has been identified as a potential genotoxins (Glowienke *et al.*, 2005). Genotoxins are substances that can alter deoxyribonucleic acid (DNA), which may induce mutagenic, carcinogenic and teratogenic effects. The European Medicines Agency (EMA) and US Food and Drug Administration (FDA) had drafted guidelines for the pharmaceutical industry by proposing a threshold of toxicological concern (TTC) for genotoxic impurities, which was typically 1.5 µg per person per day (EMA, 2006; FDA, 2008). The use of IPP/IPM ester containing IPTS may cause contamination of the cosmetic products. Currently, there is no analytical method available to determine IPTS in cosmetic products.

OBJECTIVE

The method developed is to detect and quantify residual IPTS in cosmetic products.

METHODOLOGY

A sample of cosmetic product (0.2 g) is weighed and placed into a 10-ml screw capped vial, to which 5 ml of HPLC-grade acetonitrile is added. The mixture is stirred well using a vortex mixer for 1 min to extract the IPTS. Then, the mixture is filtered through a syringe filter disc prior to analysis by HPLC-diode array detector (DAD) (*Figure 2*). Quantification of IPTS is carried out by external calibration method using a six-point curve (0.5 µg ml⁻¹ to 50 µg ml⁻¹).

Recovery Study

This method involves spiking and recovery of IPTS at four levels of concentrations ranging from 25 µg g⁻¹ to 750 µg g⁻¹ of cosmetic sample. Recoveries of IPTS from cosmetic matrices ranges from 95% – 115% with relative standard deviation (RSD) of less than 6%. *Figure 3* shows the representative HPLC-DAD chromatograms of 1 µg ml⁻¹ IPTS standard, blank lotion and lotion spiked with 25 µg g⁻¹ of IPTS. *Table 2* shows the method validation parameters.



Figure 2. HPLC-DAD for determination of IPTS in cosmetic products.

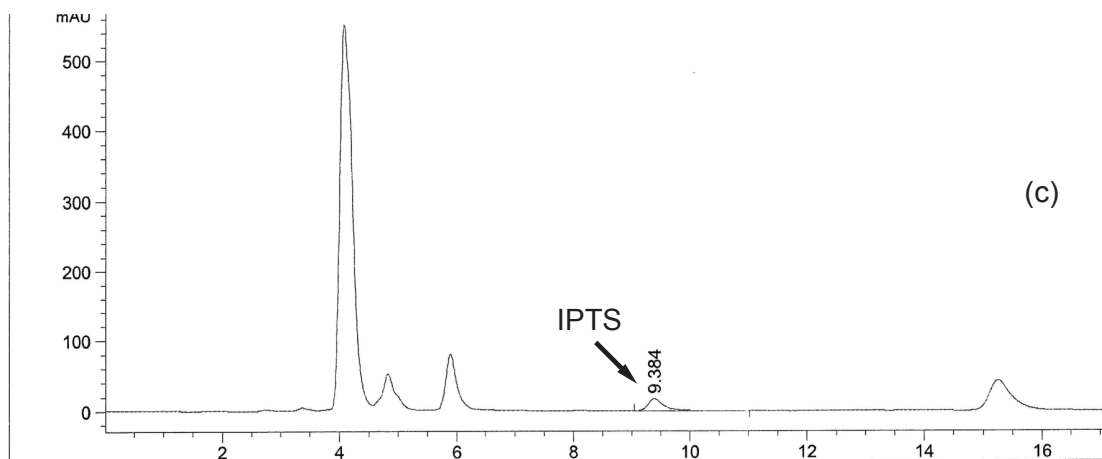
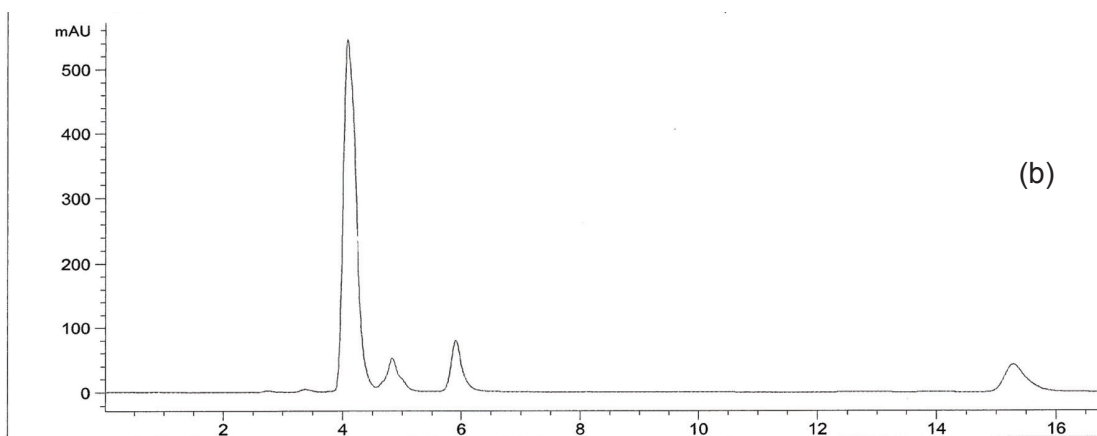
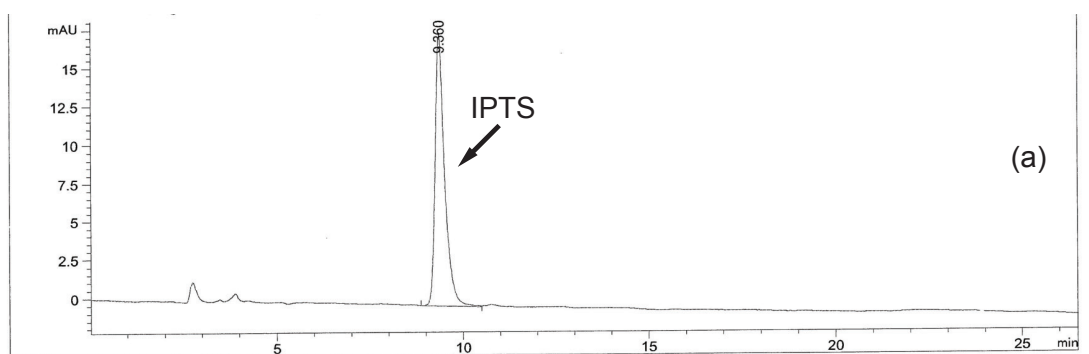


Figure 3. HPLC-DAD representative chromatograms of (a) $1 \mu\text{g ml}^{-1}$ IPTS standard, (b) blank lotion and (c) spiked lotion (with $25 \mu\text{g g}^{-1}$ of IPTS).

TABLE 2. METHOD VALIDATION PARAMETERS

Parameters	Validation data
Calibration curve (0.5 – 50 µg ml ⁻¹)	Linear, correlation coefficient of 0.999
Limit of detection	12.5 µg g ⁻¹
Limit of quantification	25 µg g ⁻¹
Accuracy (recovery)	95% -115%
Precision (relative standard deviation)	< 6%
Specificity	Applicable to cosmetic products containing IPP/IPM

BENEFIT

An accurate, reliable and simple method for monitoring the presence of IPTS in cosmetic products.

CLIENT

Producers of cosmetic products who are using IPP and IPM in their formulations.

SERVICE OFFERED

Service for determining IPTS in cosmetic products using HPLC-DAD method with the following terms:

- Sample (about 2 - 3 g)
- Test results, in the form of a Certificate of Analysis.

COST OF ANALYSIS

The indicative cost for one to five types of cosmetic samples is RM 235 per sample (subject to change). For more than five types of cosmetic samples is RM 200 per sample (subject to change).

REFERENCES

EMEA (2006). *Committee for Medicinal Products for Human Use Guidelines on the Limits of Genotoxic Impurities*. <http://www.emea.europa.eu>, accessed in January 2015.

FDA (2008). *Guidance for Industry Genotoxic and Carcinogenic Impurities in Drug Substances and Products: Recommended Approaches*. US Food and Drug Administration. <http://www.fda.gov/cder/guidance/index.htm>, accessed in November 2014.

GLOWIENKE, S; FRIEAUFF, W; ALLMENDINGER, T; MARTUS, H; SUTER, W and MUELLER, L (2005). Structure-activity considerations and *in vitro* approaches to assess the genotoxicity of 19 methane-, benzene- and toluenesulfonic acid esters. *Mutat. Res.* 581: 23 -24.

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