Analytical Methods for the Determination of Mineral Oil Saturated Hydrocarbons (MOSH) and Mineral Oil Aromatic Hydrocarbons (MOAH)—A Short Review

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ABSTRACT: Mineral oils (such as paraffinum liquidum or white oil), which consist of mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH), are widely applied in various consumer products such as medicines and cosmetics. Contamination of food with mineral oil may occur by migration of mineral oil containing products from packaging materials, or during the food production process, as well as by environmental contamination during agricultural production. Considerable analytical interest was initiated by the potential adverse health effects, especially carcinogenic effects of some aromatic hydrocarbons. This article reviews the history of mineral oil analysis, starting with gravimetric and photometric methods, followed by on-line-coupled liquid chromatography with gas chromatography and flame ionization detection (LC-GC-FID), which still is considered as gold standard for MOSH-MOAH analysis. Comprehensive tables of applications in the fields of cosmetics, foods, food contact materials, and living organisms are provided. Further methods including GCxGC-MS methods are reviewed, which may be suitable for confirmation of LC-GC-FID results and identification of compound classes. As alternative to chromatography, nuclear magnetic resonance (NMR) spectroscopy has recently been suggested for MOSH-MOAH analysis, especially with the possibility of detecting only the toxicologically relevant aromatic rings. Furthermore, NMR may offer potential as rapid screening especially with low-field instruments usable for raw material control.

KEYWORDS: Mineral oil, hydrocarbons, chromatography, hyphenated techniques, magnetic resonance spectroscopy, sample cleanup

Introduction

Mineral oils are certain fractions from petroleum refining and may be traded under various designations such as paraffinum liquidum, paraffin, cera microcristallina, petrolatum (soft paraffin), mineral oil, paraffin wax, paraffin oil, ozokerite, or white (mineral) oil, depending on type (eg, liquid or solid) or field of application.[1–4] Highly refined mineral oils are practically tasteless and odorless even when warmed. Medicinally, they may be used as laxative or externally as protectant or lubricant; nonmedical uses include formulation aid in foods or in various consumer products as emollient.[2] Other areas of application for mineral oils include printing inks, cosmetic products, release agents (eg, for the bakery or confectionery industries), packaging materials for food (eg, wax paper, waxed cardboard), and various miscellaneous uses such as in technical products (eg, lubricating oil).[5–7]

Mineral oil contains open-chain hydrocarbons (paraffins), hydrocarbons with saturated ring systems (naphthenes) and aromatic hydrocarbons (Figure 1). Some of the compounds such as benzene hydrocarbons may be of potential health hazard, which specifically includes carcinogenic effects.[1] Although the health effects are not part of this review, they led to the considerable interest in developing and validating analytical methods to determine mineral oil hydrocarbons and their impurities in various consumer products.

This review is intended to provide an overview of the different detection methods of mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH).

A short history of mineral oil analysis

The interest in analyzing mineral oils and their components has increased considerably over the past decade. Historically, the methods up until the end of the 1990s[5,8,9] were purely focused on quality control of mineral oil products; eg, industry has established very early the standardized method IP 346, which gravimetrically determined the residue in a dimethyl sulfoxide (DMSO) extract. This method represents an initial test of the mineral oil industry for mineral oils that are later to be sold as highly refined pharmaceutical-grade mineral oils. Only mineral oil fractions containing less than 3% by weight of aromatics extractable with DMSO will be subjected to further processing preparation steps (eg, refining or hydrogenation). This level has been claimed by industry as a "certain threshold" to distinguish carcinogenic from noncarcinogenic products.[10] The threshold was empirically established based on animal testing data with various DMSO extracts. The European Union cosmetics regulation has implemented this method into law and demands that products for cosmetic use comply with the IP 346 limit. Even in the year 2018, the IP 346 method is still the current industry standard to assess carcinogenicity of mineral oil raw materials. In 2015, an interesting solid-phase microextraction method with gas chromatography–mass spectrometry (GC-MS) detection of benzo(a)pyrene in microcrystalline waxes was published. This method complements the nonspecific and time-consuming IP 346 method.[11]
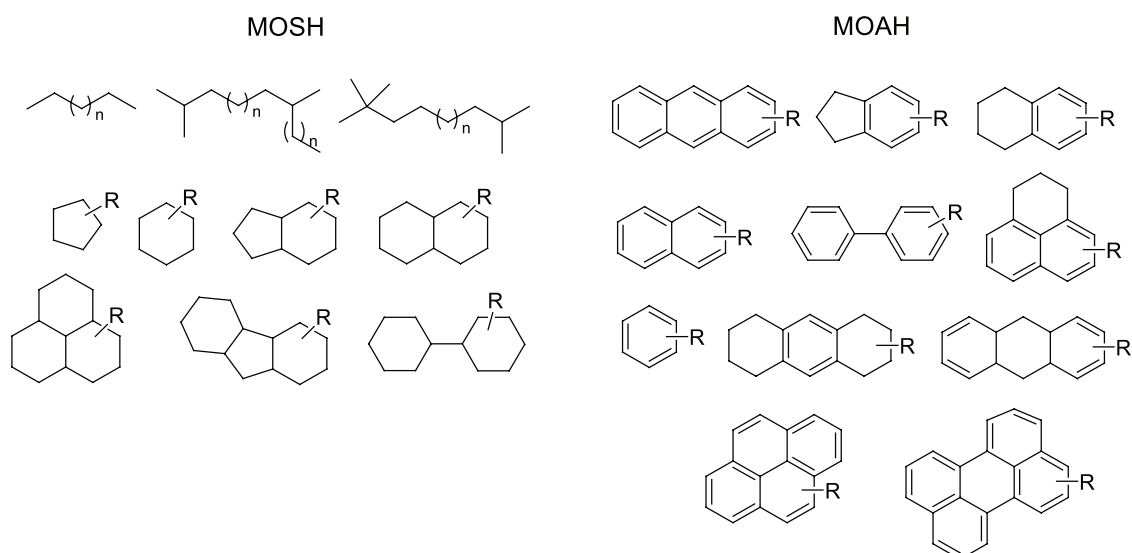
MOSH

MOAH

Figure 1. Chemical structures of representative compounds found in mineral oil saturated hydrocarbons (MOSH) and mineral oil aromatic hydrocarbons (MOAH).

The European pharmacopoeia has established a UV photometric procedure to more specifically determine carcinogenic constituents, namely, polycyclic aromatic hydrocarbons (PAHs). For this, a certain absorbance threshold has been defined, which may not be exceeded to put the product on the market as ingredient in medicinal products.[12] Some methods of higher specificity also exist to quantitatively determine PAH in mineral oil products.[13] It is important to differentiate between PAH and MOAH. The PAHs consist of a limited number of polycyclic aromatic hydrocarbons and can be analyzed as individual substances. In contrast, MOAH contain a multitude of compounds, usually highly alkylated (more than 98%).[9]

Mineral oil compounds may be contained as ingredients in cosmetic products, as well as additives or nonintended contaminants in food. Due to the wide application in technical products including food contact materials such as packaging materials, mineral oil products may migrate into foods, most easily into fat-containing foods such as chocolate or oil-containing foods. The first observations about this contamination led to considerable interest into this issue, increased by warnings from consumer magazines and nongovernmental organizations. The methods, suitable for pure mineral oil products mentioned above, were not able to detect trace contamination of mineral oil products migrated into foods. For this reason, development of new methods had to be conducted, and the first successful approach was reported from the lab of Grob in 1991 using a multidimensional chromatographic technique: on-line coupled liquid chromatography and gas chromatography (LC-GC).[14,15]

The first methods were designed only for the detection of the MOSH fraction. Often, an off-line solid-phase extraction (SPE) separation was used to isolate MOSH and then a GC-FID system was used for quantification. Biedermann et al[16] published in 2009 that the off-line separation of MOSH

and MOAH with activated silica gel is not complete. For the complete separation of cholestane (Cho) and tri-*tert*-butyl benzene (TBB), it is important to use a silver-impregnated silica gel SPE system, as described by Moret et al.[17] Detecting the MOAH fraction came into focus later. The first method was published by Moret et al in 1996 and described an LC-solvent evaporation (SE)-LC-GC-FID system for the analysis of edible oil or fatty food extract. On a silica phase using pentane/dichloromethane (90/10), a fraction ranging from saturated hydrocarbons to perylene was collected. Before transferring the solutes into the second LC system, the solvent was removed by concurrent evaporation.[18] On the second LC column, an amino-derived silica phase was used. Hydrocarbons were separated on the amino-silica phase according to their number of aromatic rings with pentane as eluent. For quantification, the fractions were transferred into the GC-FID part of the hyphenated system.[6]

Using this LC-GC-FID procedure, it was not possible to resolve the mineral oils into single components because they typically contain a complex mixture of alkanes and other compounds. Basically, LC-GC-FID only resolves 2 fractions: MOSH and MOAH. The 2 acronyms MOSH and MOAH gained high appreciation in the field and are currently used synonymously to mineral oil hydrocarbon analysis. The approaches later developed, based on GCxGC-MS or nuclear magnetic resonance (NMR) spectroscopy, also stuck with the terms MOSH-MOAH but provided more selective and specific identification.

Over the past decade, the LC-GC-FID method has been further refined and is today referred to as the method of choice or gold standard for detecting mineral oils in routine analysis.[14] The large variety of structurally similar single compounds makes it impossible to identify the individual compounds, but it is a common approach to increase the information about a sample, if found positive in LC-GC-FID, using additional

Table 1. Chromatographic methods to determine MOSH/MOAH in cosmetic products.

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION (REFERENCE IF PROVIDED)	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Lipstick, lip gloss, lip balm	MOSH/POSH	C14, C15	Hexane extraction, cleanup over aluminum oxide column[20,21]	GC-FID	—	DB-1 HT, 10 m × 0.25 mm × 0.1 μm	LOD: 30-1000 mg/kg	Niederer et al[19]
Lip balm, lip gloss, lipstick	MOSH/MOAH	Yes, but no details	Hexane extraction	LC-GC-FID	No information	No information	—	Niederer[22]
Cosmetics	MOSH/MOAH	CyCy, TBB, 1-MN, 2-MN, Cho, Per, 18B, DEHB	Hexane[16]	LC (off-line)-GCxGC-FID/TOF-MS[16,20,23]	LiChrospher Si 60, 250 × 2.0 mm × 5 μm Hexane/CH$_2$Cl$_2$ (gradient)	1st dimension: DB-17, 15 m × 0.15 mm × 0.15 μm 2nd dimension: PS-255, 3.2 m × 0.15 mm × 0.055 μm	—	Biedermann et al[14]

Abbreviations: FID, flame ionization detection; GC, gas chromatography; ID, inner diameter; LC, liquid chromatography; LOD, limit of detection; LOQ, limit of quantification; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon.
The underlined substances were used as quantification reference.

analytical methods, eg, GCxGC or, as recently proposed, quantitative NMR spectroscopy.[1] At this point, it should be noted that not all positive samples may require confirmation by the GCxGC coupling technique, whether or not it mostly depends on the matrix type. These analytical methods will be discussed in detail below.

As it was pointed out, the methodology applicable for mineral oil analysis is highly dependent on the field of application, so that we will structure the review according to matrix. For each field, we will tabulate the suggested methodologies and provide a critical review of the advantages and limitations.

Materials and methods

The scientific literature was searched for the keywords "MOSH," "MOAH," "mineral hydrocarbons," and "analysis." Systematic searches were carried out in September 2017 in the following databases: PubMed (US National Library of Medicine, Bethesda, MD, USA) and Google Scholar (Google Inc., Mountain View, CA, USA). References judged as suitable for inclusion into the review were obtained in full text and all reference lists were hand-searched for further articles not included in the databases. Inclusion criteria were the report of a novel analytical procedure or the advancement of an existing procedure. Pure application papers (ie, reports about analysis of products with an existing method) were excluded.

Results

The chromatographic methods to detect MOSH and MOAH were sorted according to sample matrix. Table 1 shows the applications for cosmetics, whereas Table 2 shows the methods for foods, and finally Table 4 shows the food contact materials. Quantitatively, the highest number of publications deals with foods, followed by food contact materials, whereas only very few applications were found for cosmetics. The focus in the area of cosmetics is also primarily restricted on lip care products because it is assumed that these are completely ingested orally and enter the gastrointestinal tract hence posing higher risks than topical cosmetics.[19]

In addition to these foods and consumer products, there are some publications regarding materials of living organisms such as certain tissues from humans or experimental animals (Table 3). Besides the chromatographic methods summarized in Tables 1 to 4, there are some few methods using another measurement principle, namely, NMR spectroscopy (Table 5).

Discussion

Sample preparation

The first step of MOSH-MOAH analysis is the necessity to obtain a solution usable for chromatography. In simple cases (e.g., for raw materials or dry food products), an extraction with hexane is sufficient, whereas for complex matrices such as fat-containing foods or cosmetic products (which also might contain other aromatic compounds), an efficient sample cleanup is

Table 2. Chromatographic methods to determine MOSH/MOAH in foods.

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Edible oils and fats	MOAH/PAH	C11, C13,CyCy, Cho, 5B, 1-MN, 2-MN, TBB, Per	Epoxidation	LC-GC-FID	Allure Si; 250mm×2.1mm×5µm Hexane/CH$_2$Cl$_2$ (gradient)	MXT-1, 15m×0.25mm×0.10µm	—	Nestola and Schmidt[24]
Vegetable oils	MOSH	C18, Cho, TBB, C14:1, Per	Hexane, SPE-cleanup (Ag-activated silica gel)	LVI-GC-FID	—	DB-5HT, 15m×0.25mm×0.10µm	LOQ: 2.5mg/kg	Liu et al[25]
Sunflower oil	MOAH (MOSH)	6B, 9B, BP, C12, C16, C14, Per, Cho	Hexane	LC (off-line)-GC×GC-FID/MS	LiChrospher Si 60, 25 cm×2.0mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	First dimension: PS-255, 20m×0.25mm×0.12µm Second dimension: SOP-50, 1.5m×0.15mm×0.075µm	LOD: 0.2mg/kg	Biedermann and Grob[26]
Pasta, rice, icing sugar	MOSH/MOAH	—	Hexane extraction; SPE-cleanup (Ag-activated silica gel)	LVI-GC-FID LC-GC-FID[27] GCxGC-FID/MS	— LiChrospher Si 60, 250mm×2.1mm×5µm[27] —	Cross-linked PS-255, 10m×0.25mm×0.15µm PS-255, 15m×0.25mm×0.15µm[27] First dimension: SLB-5ms, 30m×0.25mm×0.25µm Second dimension: Supelcowax-10, 1.0m×0.10mm×0.10µm	— — LOQ: 1.2mg/kg	Purcaro et al[28]
Pasta, rice	MOSH/MOAH	Cho, C11, C13,CyCy, 5B, 1-MN, TTB, Per	PLE in hexane or hexane/ethanol 1:1 (v/v)[20]	LC-GC-FID[16,29,30]	LiChrospher Si 60, 250mm×2.1mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	PS-255, 15m×0.25mm×0.12µm	LOQ: 0.1-0.2mg/kg	Moret et al[31]
Rice	MOSH/MOAH/POSH	Cho, TBB, C20, DPB	Hexane extraction[20]	LC-GC-FID LC (off-line)-GCxGC-FID/TOF-MS[32,33]	NP Hexane/CH$_2$Cl$_2$ (gradient)[20]	Biedermann and Grob[20] First dimension: DB-17, 15m×0.53mm×0.15µm Second dimension: PS-255, 2.5m×0.15mm×0.055µm	—	Biedermann and Grob[34]
Vegetable oils	MOSH	—	Hexane	LC-GC-FID	SUPELCOSIL LC-Si; 100mm×3.0mm×5µm; hexane (isocratic)	SLB-5ms, 15m×0.10mm×0.10µm	LOD: 0.6mg/kg; LOQ: 2mg/kg	Tranchida et al[35]
Olives, virgin olive oil	MOSH/MOAH/PAH	Cho, C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB, Per	Abencor extractor or MAE with hexane/ethanol 1:1 (v/v)	LC-GC-FID[16]	LiChrospher Si 60, 250mm×2.1mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	PS-255, 15m×0.25mm×0.15µm	LOQ: 1mg/kg	Gharbi et al[36]
Fats and oils, fatty foods with water content	MOSH/MOAH	Per, Cho, C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB	Liquid/solid fats and oils: hexane or extraction in CH$_2$Cl$_2$/hexane 3:7 (v/v) and SPE-cleanup Fatty foods with water content: ethanol- and hexane extraction Cleanup MOSH: aluminum oxide Cleanup MOAH: epoxidation	LC-GC-FID	LiChrospher, Si 60, 250mm×2.0mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	100% dimethylpolysiloxane or 95% dimethyl-5% phenylmethylpolysiloxane, 15m×0.32-0.25mm×0.25-0.10µm	—	DIN EN 16995[37]

Table 2. (Continued)

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Vegetable oils	MOSH	C18, Cho, TBB, C14:1	Hexane, SPE-cleanup (Ag-activated silica gel)	GC-FID	—	DB-5HT, 15m×0.25mm×0.10μm	LOQ: 2.5-12.5mg/kg	Li et al[38]
Pasta	MOSH/MOAH	Per, Cho, C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB	Hexane extraction	LC-GC-FID[16]	LiChrospher Si 60, 250mm×2.1mm×5μm; hexane/CH_2Cl_2 (gradient)	PS-255, 10m×0.25mm×0.15μm	LOD: 0.08mg/kg; LOQ: 0.25mg/kg	Barp et al[30]
Vegetable oils	MOSH/MOAH	Cho, C17, A, TBB	Hexane	LC-GC-FID/MS	SUPELCOSIL LC-Si, 150mm×3.0mm×5μm + SUPELCOSIL LC-Si, 250mm×2.1mm×5μm+Nucleosil SA, 150mm×1.0mm×5μm, lab-silvered; hexane/CH_2Cl_2 (gradient)	SLB-5ms, 30m×0.25mm×0.25μm	LOD: 0.1mg/kg; LOQ: 0.4mg/kg	Zoccali et al[39]
Vegetable oils	MOSH	Cho, TBB	Hexane, SPE-cleanup (Ag-activated silica gel)	GC-FID	—	PS-255, 10m×0.25mm×0.15μm	LOD: 5mg/kg; LOQ: 15mg/kg	Moret et al[17]
Vegetable oils, margarine, rice, chocolate, etc	MOSH/MOAH	6B, 9B, BP, C12, C14, C16, Per, Cho	Hexane, epoxidation, enrichment over silica gel column	LC-GC-FID	LiChrospher Si 60, 250mm×2.0mm×5μm; hexane/CH_2Cl_2 (gradient)	PS-255, 15m×0.25mm×0.13μm	LOD: 3mg/kg (oils) LOQ: 8mg/kg (oils); LOD: 1mg/kg (with off-line enrichment)	Biedermann et al[16]
Edible oils	MOSH/MOAH	C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB, Pyr	Hexane, cleanup over Ag-activated silica-gel/activated aluminum oxide column Cleanup MOAH: epoxidation	LC-GC-FID	Biedermann and Grob[40]	Biedermann and Grob[40]	LOD: 0.3mg/kg	Zurfluh et al[41]
Tea	MOSH/MOAH	—	Biedermann et al,[16] BfR[42] Cleanup MOSH: aluminum oxide Cleanup MOAH: epoxidation	LC-GC-FID GCxGC-TOF-MS	No information	No information First dimension:AB-5, 30m×0.25mm×0.5μm Second dimension: Rxi-17, 1.5m×0.1mm×0.1μm	—	Axel Semrau[43]
Cereals, chocolate, vegetable sausages, powder for cocoa based beverages	MOSH/MOAH	Per, Cho, CyCy, BP, C11, C12, 6B, TBB	hexane extraction, cold saponification, SPE-cleanup (Ag-activated silica gel)	LC-GC-FID[20,40] GC-MS	Phenomenex Luna Silica, 250mm×2.0mm×5μm; hexane/CH_2Cl_2 (gradient)	ZB5 MS, 15m×0.25mm×0.25μm Agilent HP5-MS, 30m×0.25mm×0.25μm	LOD: 0.6mg/kg (MOSH), 0.3mg/kg (MOAH)	Spack et al[44]
Risotto rice, polenta	MOSH/MOAH	C11, CyCy, 5B, 1-MN, 2-MN, TBB, C13, Cho, Per	Migration-experiments; hexane extraction	LC-GC-FID[20]	LiChrospher Si 60, 250mm×2.0mm×5μm; hexane/CH_2Cl_2 (gradient)	PS-255, 15m×0.25mm×0.13μm	LOD: 0.3mg/kg (MOSH); 0.1mg/kg (MOAH)	Lommatzsch et al[45]
Tea, rice, sugar, salt, pasta, wheat	MOSH/MOAH	—	Hexane extraction, SPE-cleanup (Ag-activated silica-gel)	LVI-GC-FID	—	PS-255, 10m×0.25mm×0.15μm	LOD: 0.05-0.12 μg/mL; LOQ: 0.16-0.40 μg/mL	Moret et al[46]

(Continued)

Table 2. (Continued)

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Dry foods (eg, baby product, biscuits, cereals, pasta, and rice)	MOSH/MOAH	C14, Cho, BP	Hexane extraction[33,47,48]	LC-GC-FID	Silica gel phase, hexane/CHCl$_2$ (gradient)[16]	Biedermann et al[16]	LOD: 0.5 mg/kg	Vollmer et al[49]
Rice	MOSH/MOAH	MOSH: C11, C13, CyCy, Cho MOAH: 5B, 1-MN, 2-MN, TBB, Per	Hexane extraction; SPE-cleanup (Ag-activated silica-gel) Modification MOSH-fraction: toluene[20]	GC-FID	—	PS-255, 10 m×0.25 mm×0.13 µm DB1-HT, 15 m×0.32 mm×0.1 µm	LOD: 0.5 mg/kg	Fiselier et al[50]
Dry foods (eg, polenta, noodles, and rice)	MOSH/MOAH/ POSH/DIPN photoinitiators/ phthalates	Phthalates: d$_4$-DiBP, d$_4$-DEHP	Hexane extraction[20,40] Photoinitiators/phthalates: QuEChERS-method	LC-GC-FID[20,40] GC-TOF-MS (phthalates)	Biedermann and Grob[20,40]	Biedermann and Grob[20,40]	LOD: 0.1-1 mg/kg 0.03 mg/kg (DIPN) 0.001 mg/kg (photoinitiators)	Biedermann et al[51]
Foods	MOSH/MOAH	CyCy, TBB, 1-MN, 2-MN, Cho, Per, 18B, DEHB	Hexane[16]	LC (off-line)- GCxGC-FID/ TOF-MS[16,20,23]	LiChrospher Si 60, 250×2.0 mm×5 µm hexane/CH$_2$Cl$_2$ (gradient)	First dimension: DB-17, 15 m×0.15 mm×0.15 µm Second dimension: PS-255, 3.2 m×0.15 mm×0.055 µm	—	Biedermann et al[14]

Abbreviations: d$_4$-DEHP, deuterated bis(2-ethylhexyl)phthalate; d$_4$-DiBP, deuterated diisobutylphthalate; FID, flame ionization detection; GC, gas chromatography; ID, inner diameter; LC, liquid chromatography; LOD, limit of detection; LOQ, limit of quantification; LVI, large volume injection; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon; SPE, solid-phase extraction. The underlined substances were used as quantification reference.

Table 3. Chromatographic methods to determine MOSH/MOAH in materials of living organisms.

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Human tissue (eg, fat, mesenteric lymph nodes, liver and kidney)	MOSH/MOAH	C11, CyCy, 5-B, 1-MN, 2-MN, TBB, Cho, Per[20]	Homogenization in ethanol; ethanol and hexane extraction[20]	LC-GC-FID[16,20]	LiChrospher Si 60, 250 mm × 2.0 mm × 5 μm; hexane/CH_2Cl_2 (gradient)	PS-255, 15 m × 0.25 mm × 0.13 μm	LOD: 0.7 mg/kg; LOQ: 2 mg/kg	Barp et al[52]
Human tissue[52]	MOSH	Biedermann and Grob[20]	Hexane and ethanol extraction	LC (off-line)-GCxGC-FID/TOF-MS	Biedermann and Grob[20]	First dimension: DB-17, 15 m × 0.25 mm × 0.15 μm Second dimension: PS-255, 2.5 m × 0.15 mm × 0.055 μm	—	Biedermann et al[32]
Tissues of female Fischer 344 rats (liver, spleen, adipose tissue)	MOSH	C11, CyCy, Cho, Per, C13[20]	Ethanol and hexane extraction[52]	LC-GC-FID[20] LC (off-line)-GCXxGC-FID/TOF-MS[34]	LiChrospher Si 69, 250 mm × 2.0 mm × 5 μm hexane (isocratic)[34]	PS-255, 15 m × 0.25 mm × 0.13 μm First dimension: DB-17, 15 m × 0.25 mm × 0.25 μm Second dimension: PS-255, 2.5 m × 0.15 mm × 0.055 μm	LOD: 0.5 mg/kg; LOQ: 1 mg/kg	Barp et al[23]

Abbreviations: FID, flame ionization detection; GC, gas chromatography; LC, liquid chromatography; LOD, limit of detection; LOQ, limit of quantification; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon.

necessary to reduce interfering compounds/carryover effects. Depending on the sample preparation used, different factors must be considered, eg, the achievement of complete extraction of a dry product is dependent on its permeability and its dispersion to undergo swelling with hexane. Biedermann et al[20] published in 2012 the detailed differences in the sample preparation of dry food, wet matrices, fatty matrices, paperboard, plastic films, and printing inks.

The importance of the sample preparation step in MOSH-MOAH analysis cannot be stressed enough: the LC-GC-FID method delivers only irregular humps of unresolved compounds (Figure 2). It takes a lot of experience to interpret the MOSH and MOAH humps correctly and to recognize potential false-positive results by simultaneous elution of interfering material from the sample matrix if cleanup has been incomplete. Such interfering groups may, e.g., be

1. Natural *n*-alkanes in plant materials or foods. They consist predominantly of *n*-alkanes with odd carbon numbers (in the range of C_{23}-C_{35}) and form well-shaped, isolated peaks. In large amounts, they may overload the GC so that MOSH detection is no longer possible.[20]
2. Polyolefin oligomeric saturated hydrocarbons (POSHs) are present in some food contact materials. They can be used in plastic bags, films, heat-sealable layers (eg, in aluminum bags). The POSHs elute from the high-performance liquid chromatography (HPLC) separation into the MOSH fraction because they largely consist of branched hydrocarbons. In most cases, it is possible to distinguish between MOSH and POSH by their chromatographic properties as described by Biedermann-Brem et al.[59]
3. Olefins such as squalene, their isomerization products, sterenes, carotenoids, terpenes and others. Because of their large polar band width, they elute in the MOSH or MOAH fraction.[20]
4. Lipids (eg, triglycerides) elute behind the MOAH fraction, but a huge amount may overload the LC column and reduces the capacity of the stationary phase for the MOSH/MOAH separation.[20]
5. Oligomers with aromatic rings, as occurring, eg, in adhesives.

Elimination of long chain n-alkanes by aluminum oxide activated at approximately 400°C. Aluminum oxide has a strong retention to *n*-alkanes beyond *n*-C_{23}. The method removes all *n*-alkanes above *n*-C_{23} but it seems not to be selective for linear alkanes. Biedermann et al described that with an increasing molecular mass, also a larger fraction of MOSH is retained (eg, 20% at C_{40}). The separation efficiency of aluminum oxide is irreversibly destroyed by more polar compounds (eg, lipids or humidity). A prior removal of such compounds is therefore required. It should be noted that the MOAH fraction is also

Table 4. Chromatographic methods to determine MOSH/MOAH in packaging and food contact materials.

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	DETECTION	LC COLUMN/MOBILE PHASE	GC COLUMN (LISTED AS LENGTH×ID×FILM THICKNESS)	LOD/LOQ	REFERENCES
Recycled paperboard	MOSH/MOAH	Per, Cho, C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB	Extraction with hexane/ethanol 1:1 (v/v)[20,48]	LC-GC-FID[53]	LiChrospher Si 60, 250mm×2.1mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	PS-255, 10m×0.25mm×0.15µm	LOD: 0.08mg/kg	Barp et al[30]
Cardboard	MOSH/MOAH	BP, CyCy, C11, C12, 6B, TBB, Per, Cho	extraction with hexane/ethanol 1:1 (v/v); SPE-cleanup (Ag-activated silica gel)	LC-GC-FID[20,40] GC-MS	Phenomenex Luna Silica, 250mm×2.0mm×5µm; hexane/CH$_2$Cl$_2$ (gradient) —	ZB5 MS, 15m×0.25mm×0.25µm Agilent HP5-MS, 30m×0.25mm×0.25µm	— LOD: 7mg/kg (MOSH), 8mg/kg (MOAH)	Spack et al[44]
For example, cardboard boxes, baking cups, and oven papers (recycled and virgin)	MOSH/MOAH	Cho, C11, C13, CyCy, 5B, 1-MN, 2-MN, TBB, Per	PLE with hexane	LC-GC-FID	LiChrospher Si 60, 250mm×2.1mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	PS-255, 10m×0.25mm×0.15µm	LOQ: 2mg/kg	Moret et al[54]
Cardboard packages	MOAH	C13	Cardboard: CHCl$_3$-extraction Packages: migration-experiments on Tenax; CHCl$_3$ extraction	GC-MS GC-FID	—	ZB-50. 30m×0.25mm×0.15µm	LOD: 72µg/kg (migration of MOAH to food)	Hauder et al[55]
Hot melt, cardboard	MOSH/MOAH	C11, CyCy, 5B, 1-MN, 2-MN, TBB, C13, Cho, Per	Hot melt: hexane extraction Cardboard: extraction with hexane/ethanol 1:1 (v/v)	LC-GC-FID[20] LC (off-line)-GCxGC-FID/ TOF-MS or GCxGC-FID/ TOF-MS[34]	LiChrospher Si 60, 250mm×2.0mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)[20]	PS-255, 15m×0.25mm×0.13µm First dimension: DB-17, 15m×0.25mm×0.15µm Second dimension: PS-255, 2.5m×0.15mm×0.055µm	LOD: 1-100mg/kg	Lommatzsch et al[45]
Cardboard (recycled and virgin)	MOSH/MOAH	—	Extraction with hexane/ethanol 1:1 (v/v); SPE-cleanup (Ag-activated silica gel)[48]	LVI-GC-FID	—	PS-255, 10m×0.25mm×0.15µm	LOD: 0.05-0.12 µg/mL; LOQ: 0.16-0.40 µg/mL	Moret et al[46]
Paperboard, plastic/paper bags	MOSH/MOAH	C14, Cho, BP	Extraction with hexane/ethanol 1:1 (v/v)[33,47,48]	LC-GC-FID	Silica gel phase, hexane/CH$_2$Cl$_2$ (gradient)[16]	Biedermann et al[16]	LOD: 5mg/kg	Vollmer et al[49]
Paperboard	MOSH/MOAH	MOSH: C11, C13, CyCy, Cho MOAH: 5B, 1MN, 2-MN, TBB, Per	Extraction with hexane/ethanol 1:1 (v/v), SPE-cleanup (Ag-activated silica-gel) Modification MOSH-fraction: toluene[20]	GC-FID	—	PS-255, 10m×0.25mm×0.13µm DB1-HT, 15m×0.32mm×0.1µm	LOD: 0.5mg/kg	Fiselier et al[50]
Plastic films, paperboard	MOSH/MOAH/ POSH/DIPN/ photoinitiators/ phthalates	Phthalates: d$_4$-DiBP, d$_4$-DEHP	Plastic films: hexane extraction Paperboard: extraction with hexane/ethanol 1:1 (v/v)[20,40] Photoinitiators/phthalates: acetonitrile extraction	LC-GC-FID[20,40] GC-TOF-MS (phthalates)	Biedermann and Grob[20,40]	Biedermann and Grob[20,40]	LOD: 1mg/kg (paperboard), 10mg/kg (plastic), 0.15mg/kg (photoinitiators)	Biedermann et al[51]
Plastic cap	POSH	Cho, C11, C13,CyCy, 5B, 1-MN, 2-MN, TBB, Per	Hexane extraction	LC-GC-FID[16]	LiChrospher Si 60, 250mm×2.1mm×5µm; hexane/CH$_2$Cl$_2$ (gradient)	PS-255, 15m×0.25mm×0.15µm	LOQ: 1mg/kg	Gharbi et al[36]

Abbreviations: FID, flame ionization detection; GC, gas chromatography; ID, inner diameter; LC, liquid chromatography; LOD, limit of detection; LOQ, limit of quantification; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon PLE, pressurized liquid extraction.
The underlined substances were used as quantification reference.

Table 5. Methods to determine MOSH/MOAH and related compounds using NMR.

MATRIX	ANALYTES	INTERNAL STANDARD	SAMPLE PREPARATION	SPECTROMETER FREQUENCY, MHZ	PULSE SEQUENCE	LOD/LOQ	REFERENCES
Hydrocarbon resins, polenta	"Aromatic protons"	D5, TMS	Resins: CDCl$_3$ polenta: migration experiment with cardboard and/or hot melt	500	Helling et al[56]	—	Lommatzsch et al[45]
FCC gasoline	PONA	TMS	CDCl$_3$	300	No details	—	Sarpal et al[57]
Mineral hydrocarbon raw material including vaseline	MOSH/MOAH	TMS	CDCl$_3$, syringe filters with polyester membrane	400	Bruker standard zg30 pulse sequence[58]	LOD: 100-4000 mg/kg	Lachenmeier et al[1]

Abbreviations: D5, decamethylcyclopentasiloxan; FCC, fluid catalytic crack; LOD, limit of detection; LOQ, limit of quantification; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon; NMR, nuclear magnetic resonance; TMS, tetramethylsiloxan.
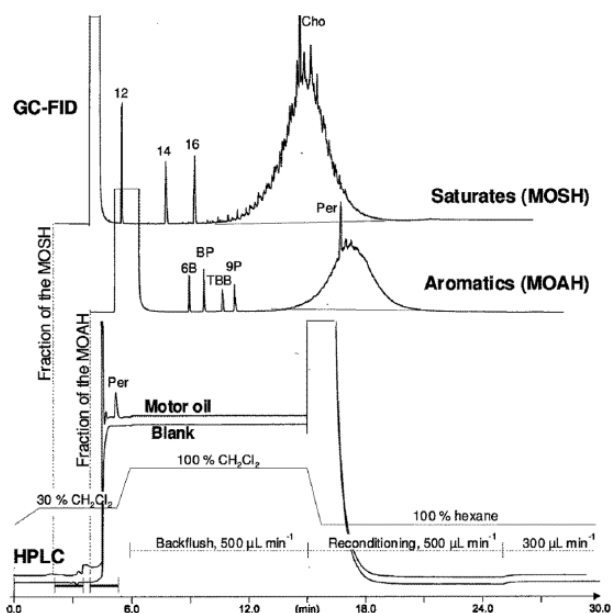The underlined substances were used as quantification reference.

Figure 2. Procedure for LC-GC-FID MOSH-MOAH analysis visualized by chromatograms of motor oil. Labeled peaks indicate internal standards for determining concentrations and verification of the performance. 6B indicates hexylbenzene; 9P=9B, nonylbenzene; 12, 14, 16, *n*-alkanes C$_{12}$–C$_{16}$; BP, biphenyl; cho, 5-α-cholestane; HPLC, high-performance liquid chromatography; LC-GC-FID, liquid chromatography with gas chromatography and flame ionization detection; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon; per, perylene; TBB, 1,3,5-tri-*tert*-butylbenzene.
Reprinted with permission from Biedermann et al.[16] Copyright (2009) American Chemical Society.

removed by activated alumina.[20] For further information, reference is given to the 2-part publication by Fiselier et al, which describes the selective retention of long-chain *n*-alkanes on alumina.[60,61]

Enrichment to lower the detection limit. The first possibility for enrichment are manual purification steps focused on the

MOSH fraction. McGill et al published in 1993 an off-line SPE-LC-GC-MS method for the MOSH detection in edible oils. The unpolar fraction of the edible oils was isolated by a silica gel-SPE step with *n*-hexane as eluent. In an additional LC purification step, the MOSH fraction was isolated and detected by GC-MS.[62] Another manual sample preparation for the MOSH fraction is performed by means of silver nitrate on a silica gel phase which was systematically optimized, as listed in Tables 2 and 3.[17,46]

For the MOSH fraction, the capacity of the silica phase column (LC) (250 mm × 2.1 mm) for retaining lipids is limited to 20 mg and thus the limit of quantification for MOSH in edible oil yielded above 0.6 mg/kg.[20] Grundböck et al published an off-line SPE enrichment for the MOSH fraction using silica gel and aluminum oxide in a double bed. After the SPE enrichment, the resulting MOSH fraction was reconcentrated and analyzed by off-line LC-GC. The limit of quantification yielded below 0.1 mg/kg edible oil.[63] Silica gel is widely used for the purification from triglycerides. This depends on its relatively strong retention power for triglycerides. The capacity of the silica phase for triglycerides depends on the solvent polarity. Grob et al published that the mobile phase reduces the capacity of the silica phase to retain triglycerides by the addition of a polar modifier to *n*-hexane as mobile phase.[64] For manual purification steps focused on the MOAH fraction, SPE purification with activated silica gel will help retain lipids and may reduce the detection limit by about a factor of 50.[63]

The amount of fat in a sample is a limiting factor for the sensitivity of the LC-GC method. Moret et al published a microwave-assisted saponification followed by an on-line LC-GC method for the determination of mineral oil in different cereal-based foodstuffs. It is a good solution for highly fat-containing samples.[65] The detection limit for the commonly used methods of the most food products is below 0.1 mg/kg. For fatty products, it is substantially higher, for the

reasons described above. Zurfluh et al published a method for the enrichment of the MOSH and MOAH fraction for fatty food products using a double-bed LC (the lower part consists of an activated aluminum oxide/silica gel with silver nitrate and activated silica gel; the upper part consists of activated silica gel). With this enrichment technique, the detection limit in edible oil reached below 0.3 mg/kg.[41] Another well-structured review of the mineral oils in oilseeds and vegetable oils was published in 2016 and also for hydrocarbon contamination in foods.[66,67]

Epoxidation step to remove naturally occurring olefins. Olefins can interfere with the chromatographic pattern. Removal of the olefins by epoxidation is necessary for samples containing them in amounts giving interference problems with the MOAH fraction (such as some fats) before analyzing the samples by LC-GC-FID. They can be converted into more polar derivatives by epoxidation and then they elute after the MOAH fraction. For epoxidation, the sample is reacted with 10% meta-chloroperoxybenzoic acid in dichloromethane. However, Biedermann et al determined that this epoxidation step leads to a loss of 20% to 40% of the MOAH fraction. The publication also contains a detailed description of the epoxidation step.[16] In 2017, the epoxidation was optimized in such an encouraging fashion, among other things, by the change of the solvent used (ethanol instead of dichloromethane), that 95% to 102% of the MOAH was recovered after epoxidation.[24]

Chromatographic LC-GC-FID methods

On-line-coupled LC-GC is ideal for the analysis of complex mineral oil matrices because it combines the high sample capacity and wide range of separation of the LC system and the high separation efficiency and a variety of selective detection methods of the GC system. In contrast to off-line techniques, the on-line-coupled LC-GC system has some advantages such as high reproducibility, high sample throughput, less susceptibility to carry over effects, a high level of automation, and robustness, as well as a higher sensitivity of the multidimensional chromatography (none of the sample material is wasted). For this analytical method, an FID is used because the large variety of chemical compounds within a mineral oil fraction requires an unselective detector for the detection of hydrocarbons. Flame ionization detection has virtually the same response per unit of mass for all hydrocarbons and thus the FID enables quantification without calibration by different compounds. In addition, the FID detector is characterized by its robustness and the detector signal is linearly proportional to the amount of the analyte over a wide concentration range. Biedermann and Grob[20] point to a rule of thumb for the detection limit of MOSH or MOAH of approximately 50 ng for the LC-GC-FID method. As a consequence, a large volume of sample must be injected into the GC. This assumes that all

compounds that can degrade the separation performance of the LC or GC column are previously eliminated or reduced by an off-line method prior to the LC-GC analysis (see sample preparation). In contrast to this, MS is more sensitive than FID, but calibration for mixtures of unknown composition is a problem for MS. Based on these facts, the LC-GC-FID method is called the method of choice for routine measurements in the field of mineral oil analysis.

The crucial instrumental difference between a simple GC analysis and an LC-GC coupling technique is the larger (1 μL to 1 mL) fraction volume in on-line LC-GC, which has to be transferred from LC to GC; thus, special techniques are required for the transfer (eg, on-column, loop-type, or vaporizer interfaces commonly used). The interface between LC and GC is the heart of the coupling system. The choice of the interface is largely dependent on the volatility of the analytes.[16,68]

In the multidimensional system (LC-GC), the role of the LC is to perform a fractionation of MOSH and MOAH as well as to perform a selective cleanup from interfering compounds. Figure 2 shows the principle of on-line coupling of LC with GC. A phase of high retention power is typically used as stationary phase (small pores/large internal surface area (eg, LiChrospher 60; Merck, Darmstadt, Germany; Allure Si; Restek, Bellefonte, PA, USA) and a gradient elution of *n*-hexane/dichloromethane. The strong retention power between the silica phase and the MOAH fraction requires a steep gradient of *n*-hexane/CH_2Cl_2 up to (70/30) to make the window of the MOAH fraction as narrow as possible. Dichloromethane is the ideal choice for the modifier, as it acts directly without any delay, as was observed with *tert*-butyl methyl ether. The column parameters (250 mm × 2.1 mm) and the volume flow 300 μL/min of the mobile phase are optimized for the LC-GC for a quantitative MOSH/MOAH separation. The focus is on the most efficient SE. To restore the separation efficiency of the column, the silica phase is backwashed with dichloromethane after each run.

The chromatographic windows of the MOSH and MOAH fractions are determined by the order of elution of specific chemical compounds (so-called markers). The elution behavior of different types of chemical structures of mineral oil hydrocarbons on a silica phase with small pores/large internal surface area is strongly influenced by size exclusion effects.[14,20] The elution sequence of the mineral oil compounds is schematically shown in Figure 3 by the used markers.[20]

The high molecular mass paraffins elute first (1.5-2.0 minutes), followed by the low-molecular-mass paraffins and the cyclic MOSH (such as cholestane and cyclohexyl cyclohexane [CyCy]) from the end of the MOSH fraction at 2.5 to 3 minutes. Cholestane is widely used as a marker to establish the end of the MOSH fraction.[20] Biedermann et al[16] published an update of the LC-GC analytical method, which was introduced in 2009. The group pointed out that the already
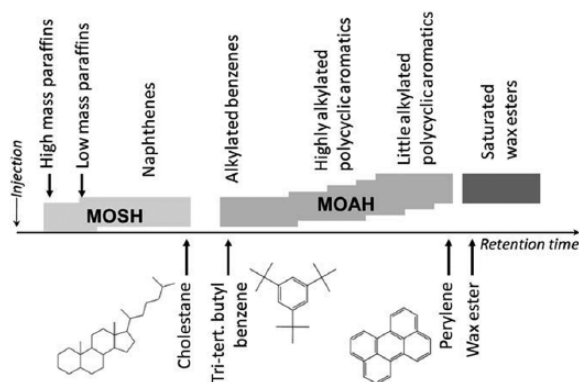
Figure 3. Elution sequence on the silica phase (LC) of MOSH and MOAH and the markers for establishing the fraction window. LC indicates liquid chromatography; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon.
Reprinted from Biedermann and Grob[20] with permission from Elsevier.

established markers for the determination of the MOSH and MOAH fraction windows should be reconsidered. Cyclohexyl cyclohexane elutes slightly later than cholestane (former marker for the end of the MOSH fraction) and is better suited to use because the elution is in the relatively little crowded early part of the GC. The aromatic compounds elute according to the size of their ring system and their steric demand. Thus, TBB is used as a marker to establish the start of the MOAH fraction window and perylene (5-5.5 minutes) for the end. The update of Biedermann et al included a new marker for the MOAH fraction, di(2-ethylhexyl) benzene (2.5-3 minutes) proposed as a highly alkylated benzene marker instead of tri-*tert*-butyl benzene (TBB). The elution behavior of TBB is predominated by size exclusion effects of the bulky *tert*-butyl groups, but highly alkylated benzenes eluted earlier by the mobile phase.[14] Wax esters eluted after the MOAH fraction. As a result, e.g., a selective cleanup of the MOAH fraction by the silica phase is possible. The detailed chromatographic conditions are listed in Table 2. Figure 4 shows typical application examples of such an LC-GC analysis of common food contact materials such as a fiber box and a tea bag.

Comparison of LC-GC interfaces. As mentioned before, the interface is the heart of the LC-GC FID system. For the on-line LC-GC method, basically 2 interfaces have been proposed, the Y-type interface (the on-column retention gap method) and the syringe-based programmed temperature vaporizer (PTV) interface. The Y-type interface avoids the memory effect, observed with the classical on-column interface.[53] The Y-type is characterized using long retention gaps (between 5 and 10 m) and a large inside diameter (ID of 0.53 mm). Thus, it is possible to handle large volumes of solvent and high gas flows, which is important for an efficient evaporation.[69] The PTV technique uses a packed liner which retains more liquid and is more stable than the retention gap. The comparison of these different interfaces for the LC-GC system has been

published by Purcaro et al.[70] The choice of the interface for LC-GC depends on the volatility range of the compounds of interest and on the dimension-transferred solvent fraction. There are several publications available reviewing the interface techniques.[20,71]

Standardization of LC-GC-FID. The standardized procedure as outlined in the European norm (EN) 16995 (see Table 2 for details) has been found satisfactory in interlaboratory trials to detect MOSH/MOAH concentrations of about 10 mg/kg in food matrices.[37] If interfering compounds from natural sources are expected, the fossil origin of MOSH/MOAH needs to be verified using GCxGC-MS, however. The peak area corresponding to mineral oil is determined following subtraction of the sharp peaks of *n*-alkanes (naturally occurring carbohydrates), terpenes, squalene and its isomerization products, sterenes, and olefins with carotenoid structure. MOSH and MOAH are quantified using an internal standard added before the procedure. Verification standards are added to control the correct HPLC fractionization and GC transfer. Mineral oil–contaminated food oil is almost exclusively constituted of branched compounds, which are not retained on activated aluminum oxide. The use of this agent for sample preparation therefore allows to remove plant-based paraffins. The EN contains a detailed sample preparation guideline for fat-containing foods.[37]

The EN[37] and Biedermann and Grob[26] are similar in the used LC-GC-FID methods. The EN method used a more polar gradient with *n*-hexane/dichloromethane (65/35) compared with Biedermann and Grob (70/30). Effectively, as far as it may be gathered from the published chromatograms, this difference does not lead to marked differences. From the literature, it appears that most groups actually use the established 70/30 ratio.

Limitations of LC-GC-FID. The EN 16995 and all similar LC-GC-FID methods are convention methods, which means methods that follow a well-defined procedure to obtain comparable results.[37] It is very important that all parameters of the standard operating procedure are strictly adhered to. Such convention methods are often used for official food control purposes.[72] The LC-GC-FID method is therefore a screening method with advantages and disadvantages, but positive screening results have to be complemented by a more specific and confirmatory method such as comprehensive GCxGC techniques, MS, or NMR methods.

The elution behavior of MOSH and MOAH is sometimes not completely specific to the aromaticity. The literature contains initial evidence that LC-GC may possibly overestimate MOAH compared with more specific methods such as NMR.[1] In general, it is not possible to gain more detailed knowledge about the composition of the sample using LC-GC-FID. A detailed identification of what is "hidden" inside the "humps" can only be achieved using a mass selective detector.[43]
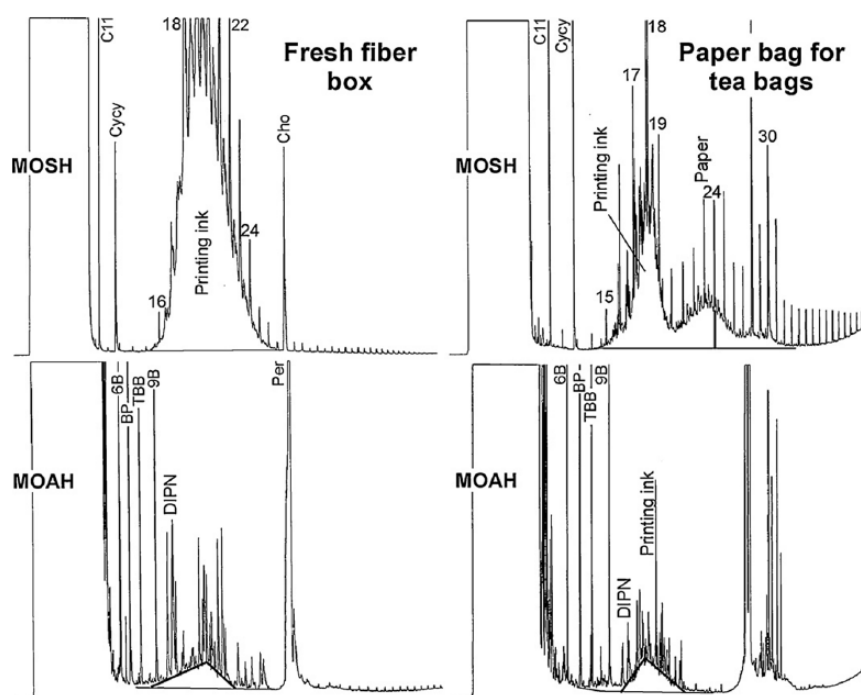
Figure 4. MOSH and MOAH chromatograms from a fresh fiber box for biscuits printed with a mineral oil containing ink (left) and a fresh fiber paper tea sachet with mineral ink oil and an oil probably used for paper making. CyCy, cyclohexyl cyclohexane; DIPN, diisopropyl naphthalene; MOAH, mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon.
Reprinted from Biedermann and Grob[40] with permission from Elsevier.

Further chromatographic methods including GCxGC

The LC-GC-FID method is a powerful method and the method of choice today for the quantitative determination of mineral oil hydrocarbons for routine measurements. Sometimes it is desirable to obtain more information about the type of hydrocarbons. The comprehensive 2-dimensional GC (GCxGC) is the technique which is then widely used.

With high retention power, the components are reconcentrated at the end of the first GC column. The peaks at the beginning of the second GC column get sharper. A preseparation of the mineral oil fraction by a LC, as used in the LC-GC-FID method, leads to an additionally improved separation efficiency in the field of naphthenic hydrocarbons.[34]

The basic principle of GCxGC is to combine columns with orthogonal separation properties. The order of the stationary phases is strongly dependent on the chromatographic target. Often, a nonpolar stationary phase (1D GC) is combined with a polar stationary phase (2D GC). For a higher resolution of the MOSH fraction and to achieve a good separation especially for the analysis of POSH,[34] the reversed arrangement is productive.[73] For more information, the publication of Vendeuvre et al shows the difference of GC and GCxGC for petrochemical matrices.[73]

Such a comprehensive GCxGC allows to systematically order the MOSH fraction into groups: *n*-alkanes, paraffins with low degree of branching and high degree of branching as well as cyclic systems with 1 to 4 rings. For example, such a 2-dimensional GC is able to achieve to detect residues of mineral oils in human tissues and hence gives information on the accumulation degree of different MOSH components.[32]

Other examples show the combination of LC-GC-FID followed by GCxGC-FID analyses to confirm positive LC-GC-FID results. The GCxGC also may provide additional information such as to differentiate between MOSH and POSH.

Nuclear magnetic resonance

There are only very few methods available that do not apply chromatography for MOSH-MOAH analysis. The only suitable direct spectroscopic option available appears to be NMR (Table 5).

Some methods quantified the sum of aromatic protons[45] or paraffins, olefins, naphthenes, and aromatics.[57] Only recently, our group suggested NMR to be used as convention method to quantify MOSH and MOAH, especially with the possibility of detecting only the toxicologically relevant aromatic rings, in a similar fashion to the LC-GC-FID approach.[1]

The major advantage of NMR over any chromatographic or mass spectrometric method is that—at least in ideal cases such as pure mineral oil hydrocarbon products—the sample can be directly measured without any need for sample preparation or pretreatment. This means that the sample can be measured "as it is" and does not need to be brought into a volatilized state as for GC or into a diluted liquid such as for LC.
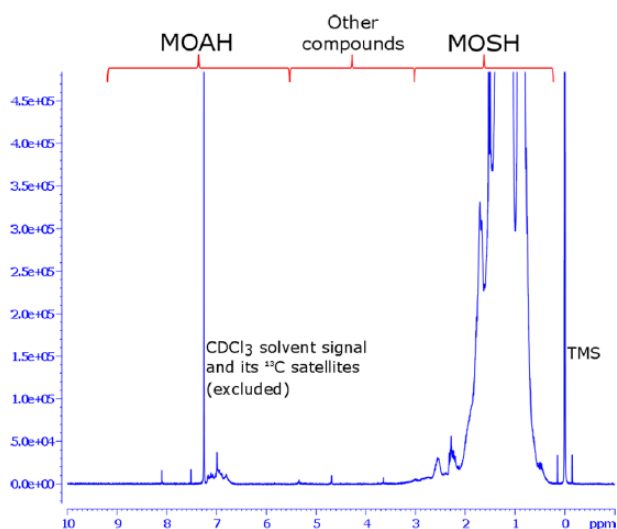
Figure 5. Representative high-field 400-MHz ^{1}H nuclear magnetic resonance spectrum of an authentic cosmetic product sample (bag balm) pointing out the spectral regions suitable for MOSH and MOAH quantification. MOAH indicates mineral oil aromatic hydrocarbon; MOSH, mineral oil saturated hydrocarbon; TMS, tetramethylsilane. Reprinted from Lachenmeier et al.[1] (No permission necessary. Creative Commons Attribution License 4.0 International (CC BY 4.0)).

It was found that the typical NMR solvent $CDCl_3$ easily solubilizes liquid as well as solid mineral oil hydrocarbons, and the resulting solution can be directly transferred to an NMR measuring tube. This direct measurement in $CDCl_3$ allows to quantify the proportion of MOSH and MOAH in the sample, as well as of other compounds not belonging to these structural categories.[1]

A typical example of an NMR spectrum of a mineral hydrocarbon–based cosmetic product is shown in Figure 5. The spectral range of 6.5 to 7.2 ppm includes the MOAH compounds; above 7.3 ppm resonances of PAHs are expected. The region of 6.5 to 3.0 ppm includes other compounds besides MOSH and MOAH, and the low-field region of 3 to 0.2 ppm finally contains the MOSH fraction. Due to the direct structural relationship of the resonances in NMR, a higher specificity of MOSH and MOAH is expected than in LC-GC.[1] Using the so-called PULCON quantification method (see Monakhova et al[74]), there is no need to apply an internal standard unlike any of the LC-GC methods.

Although the NMR method is not widely applied so far, research has shown that the method can be fully validated and is fit for routine testing use of pure mineral oil products and related cosmetic products such as vaseline.[1]

A limitation of direct NMR is the possible occurrence of other aromatic ingredients in the mixture that may have resonances in the MOAH region (such as BHT [3,5-Di-*tert*-butylhydroxytoluene], which is widely applied as additive in Vaseline). If this refers to known compounds, the resonances can be excluded from the integration window, and it is still possible to achieve an accurate quantification. More complicated are cases of complex mixtures (such as in lip care products or cosmetic creams, which may contain a multitude of compounds with potential aromatic groups such as UV filters or coloring agents). In these cases, a sample preparation has to be conducted similar to LC-GC, eg, a silica gel column cleanup with cyclohexane elution. Any other sample preparation mentioned in the LC-GC sections above also appears suitable if the resulting solution contains the compounds above the detection limit of NMR (which typically is higher than that for LC-GC; the concentrations should be above 0.01% to be detectable in NMR). Solvent suppression in the NMR pulse program may be necessary if the solution contains nondeuterated solvents to increase the sensitivity.

Another limitation of high-field NMR (400 MHz) as applied in the work by Lachenmeier et al[1] is the comparably high investment cost for an NMR spectrometer compared with an LC-GC system (while the actual cost per sample might be much lower due to less personnel and consumable costs). Nevertheless, the investment could be too high for small- and medium-sized enterprises. For this reason, the authors have evaluated a low-field NMR instrument basically with the same method as published previously.[1] Low-field benchtop NMR instruments are considerably cheaper than LC-GC systems and do not require coolant gases. Initial measurements (Spinsolve Ultra 60 MHz; Magritek, Aachen, Germany) have provided spectra with less resolution but still quantifiable for MOSH-MOAH contents (Figure 6). An excellent correlation between NMR high-field and low-field results was found (R = 0.9948 for MOAH). Low-field NMR is therefore suggested as an efficient alternative for quality control of pure hydrocarbon products.

Conclusions

While there appears not to be much innovation in the field of quality control of pure mineral hydrocarbons and some normative procedures have been in use since the 1980s, there is currently much development work for analysis of trace concentrations in foods and other consumer products. The first European normative procedure for this purpose has only been published in 2017 during writing of this review.[37] The analysis of trace contaminants is challenging not only due to the need for sample preparation and enrichment but also due to the need of complex multidimensional chromatography. In the more recent chromatographic approaches, a positive LC-GC-FID value is verified by a GCxGC-MS assay. The major result of the review appears to be a need for increased specificity during MOSH-MOAH analysis, as otherwise there is a considerable option for overquantification, especially when part of MOSH may be counted as MOAH.

From the reviewed methods, NMR appears to be best suitable to provide a rapid screening of products. The advantages of NMR are that the sample preparation is easier than for chromatography, the measurement is very quick (20 minutes), and the assignment of MOSH and MOAH is more specific than with LC-GC-FID. Low-field NMR methods appear to
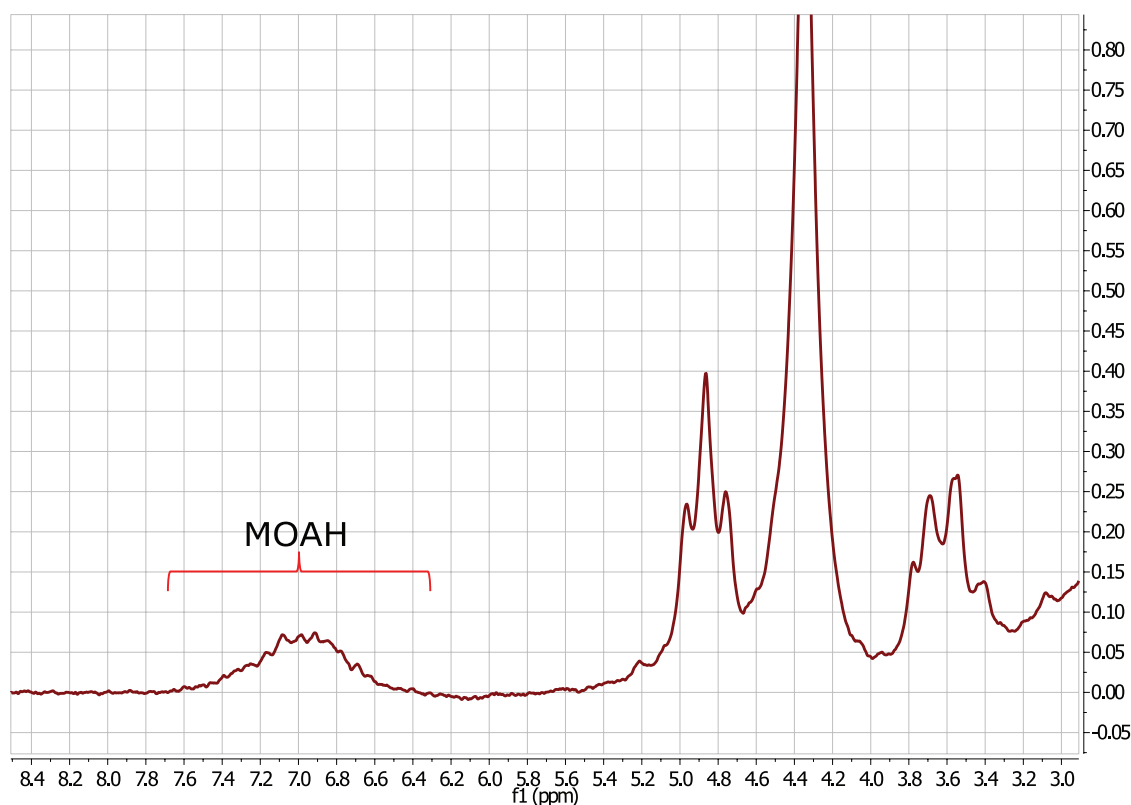
Figure 6. Representative low-field 60 MHz ¹H nuclear magnetic resonance spectrum of an authentic product sample (coal tar cream with 1.6% MOAH) (original data by the authors). MOAH indicates mineral oil aromatic hydrocarbon.

have the potential to be a substitute for the rather obsolete IP 346 procedure.

Following NMR, all suspicious samples above a certain threshold (which needs to be established based on toxicological risk assessments) should be further characterized because the NMR MOAH value currently does not provide information about the degree and position of alkylation (it is expected that only 2 vicinal H-atoms on an aromatic ring would be toxicologically relevant because they may be metabolized to epoxides). The characterization could be conducted with one of the chromatographic procedures pointed out: LC-GC-FID, LC-MS, GC-MS, or GCxGC-MS.

Author Contributions

DWL conceived and designed the article. SW and KS analyzed the data. SW, DWL, and KS wrote the first draft of the manuscript. GM, TK, and SGW contributed to the writing of the manuscript. SW, KS, GM, TK, SGW, and DWL agree with manuscript results and conclusions and made critical revisions and approved final version. SW and DWL jointly developed the structure and arguments for the paper. All authors reviewed and approved of the final manuscript.

Disclosures and Ethics

As a requirement of publication, authors have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following:

authorship and contributorship, conflicts of interest, privacy and confidentiality, and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. The authors declared no potential conflicts of interest with respect to research, authorship, and/or publication of this article. The external blind peer reviewers report no conflicts of interest.

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