MOSH and MOAH: occurrence and toxicological evaluation

Koni Grob
Kantonales Labor Zürich
The issues

• MOSH/MOAH measurements are wrong
  – no standardized method available
• MOSH and MOAH are naturally formed by plants
• Environmental contamination is inevitable
• Olive pomace oils contain 250-400 mg/kg MOSH
  – and nobody complains
• Present MOSH and MOAH reference values have no toxicological base…
  – …and are far exaggerated
Measurements are wrong

• MOSH/MOAH analysis is demanding!
  – battery of methods required
  – experience in interpretation of chromatograms

• Socialism in chemical analysis: Do the weakest laboratories determine whether the analysis is possible?

• Standardization ensures that all do the same - same errors?
  – interpretation of chromatograms cannot be standardized

• Is the quality of the data limited by the price the customer is willing to pay?
  – often additional steps would clarify – but are considered too expensive
Components of MOSH/MOAH analysis

- Extraction of the sample (solid samples!)
- HPLC preseparation
  - isolation from sample matrix, e.g. fat
  - separation of MOSH and MOAH
- GC-FID analysis (virtually equal response)
  - large volume GC injection/transfer
- Auxiliary methods
  - enrichment to achieve more reliable data
  - removal of natural n-alkanes (aluminum oxide)
  - removal of natural olefins (epoxidation)
  - GCxGC for confirmation, e.g. distinction from POSH
- Correct interpretation of chromatograms
HPLC isolation, MOSH/MOAH separation

UV 230 nm

Verification standards → determination of start and end of fractions
- 2-ethyl hexyl benzene (MOSH-MOAH separation)
- perylene (end of MOAH)

normal phase HPLC: e.g. Lichrospher Si 60 (250 x 2 mm i.d.)
Example for MOSH fraction: couscous

- homogeneous distribution of n-alkanes → MOSH
- natural waxes, terpenes → no MOSH
Example for MOAH fraction: couscous

- similar molecular mass distribution of MOSH and MOAH
- MOAH concentration smaller than MOSH
Limit of quantification without enrichment

Possible reconcentration of food extracts is limited by the capacity of the HPLC column for triglycerides: 20 mg

Referring to amount of sample; 100 µl injections into HPLC:

- low fat (≤4 %) samples (e.g. rice, corn, noodles)
  - 10 times (10 g food to 1 mL hexane) → LOQ ca. \(0.1 \text{ mg/kg}\)

- medium fat (~20 %) samples (e.g. cereals, muesli, biscuits)
  - no reconcentration (1 g to 1 mL) → LOQ ca. \(0.5 \text{ mg/kg}\)

- high fat (~40 %) samples (e.g. chocolate)
  - only half amount/concentration (0.5 g to 1 mL) → LOQ ca. \(1 \text{ mg/kg}\)

- vegetable oils
  - 20 % solutions → LOQ ca. \(2.5 \text{ mg/kg}\)
Reconcentration of extracts

**MOSH**
- 1.4 mg/kg
- 10 x concentrated

**MOAH**
- 0.3 mg/kg
- 10 x concentrated
Interferences: MOSH in sunflower oil

MOSH: ≤3.8 mg/kg

→ Enrichment and removal of long-chain n-alkanes
Removal of natural n-alkanes

Aluminum oxide activated at about 400 °C retains n-alkanes above about C24 using n-hexane as eluent – no retention with iso-octane. Prerequisite: no humidity or polar solvents.

Performed off-line (SPE-style) or on-line LC (SiO2) – LC (alox), with backflush of the alox by iso-octane


Enrichment + removal of n-alkanes

MOAH eluent:
25 % dichloromethane/
0.25 % toluene/74.75 %
hexane

8 g activated silica gel

10 g activated aluminum oxide and 7 g silica gel/
0.3 % silver nitrate

→ Equivalent of 200 mg oil/fat can be injected into
   LC-GC
   → enrichment by factor 10
Example: sunflower oil

Direct on-line HPLC-GC

HPLC-GC after enrichment and preseparation by alox

diesel oil  lub oil

oil extracted from manually collected seeds

total MOSH content: 1.4 mg/kg

rate: 25 °/min

Calarene

65 °C 350 °C

23 25 29 31 35 37
Examples needing epoxidation

Epoxidation renders olefins more polar → retention on LC beyond MOAH

Aromatic hydrocarbons of mineral oil origin in foods: method for determining the total concentration and first results
M. Biedermann, K. Fiselier and K. Grob
Epoxidation not always needed: Panettone

MOSH C16-C35: 13.1 mg/kg

MOAH fraction before epoxidation

MOAH fraction after epoxidation

MOAH: <0.2 mg/kg
Epoxidation: the best presently available

Epoxidation of olefins is faster than that of most MOAH, but
- partial loss of MOAH
- removal of interferences may remain incomplete
The two methods for epoxidation

Biedermann et al. (2009)
- Reaction in dichloromethane
- Fast \(\rightarrow\) requires cooling
- Reaction stopped by polyunsaturated fats/oils

Nestola/Schmidt (2017)
- Reaction in ethanol: far slower!
- No cooling required (autosampler!)
- Reaction kinetically stopped
- No evaporation step

We prefer the Nestola/Schmidt method:
- more convenient, particularly for automated preparation
- MOAH losses are same
- peracid is not stable in ethanol: fresh solutions
The peracid is not stable in ethanol

The solution of 3-chloro-perbenzoic acid in ethanol needs being
- fresh
- cooled
Incomplete removal of interferences

MOSH

Olive pomace (sansa) oil

MOAH

Safe recognition of interference may be more important than efficient removal!
Characterization by comprehensive two-dimensional GC (GCxGC)
GCxGC-FID of mineral oil hydrocarbons

Mixture of crude mineral oil fractions + 16 EPA PAHs, column set: polar – apolar, FID

- n- and iso-alkanes
- alkyl-cyclopentanes/hexanes
- steranes (4R)
- hopanes (5R)
- multibranched alkanes
- alkyl-benzenes

Temperature conditions:
- 80 °C to 320 °C
- 5 °/min
Plants produce MOSH and MOAH???

Characteristic MOSH pattern
- markers: steranes, hopanes etc.

Not produced by plants or microorganisms:
- C-C bonds are not easily rearranged at RT
- fermentation of olive pomace did not produce MOSH or MOAH
MOAH fraction, FID
Rice 1: contamination with batching oil

**MOSH**
- m/z 184+198+212+226
- 20.2 mg/kg

**MOAH**
- m/z 184+198+212+226
- 8.7 mg/kg
Rice 2: MOH and POSH

MOH fraction:
- C11 cycy
- C13
- C13
- C13
- C13

MOSH fraction:
- Pristane
- C21:1 PP oligomers
- C11/12 cyclo C5/6
- C7 decalins
- C3 perhydro 3R
- C1 perhydro pyrens

MOAH fraction:
- 5B tbb
- MNs
- sq
- per
- DIPN

MOSH fraction: 5.4 mg/kg
MOAH fraction: 1.8 mg/kg
Rice 3 and 4: LDPE/LLDPE oligomers (POSH)

MOSH fraction

1.2 mg/kg

2.1 mg/kg
Recognition of interferences in MOAH fraction

- No interferences from carotenes
- Hump at the position of squalene/sterenes
- Hump more narrow than for MOAH
- Characteristic fields in GCxGC
Refined hazelnut oil
Environmental input

White shirts get gray when left outdoor for some days – plants are left outdoor for more than a few days!

Hydrocarbons $\leq$ C24 mainly in gas phase
Hydrocarbons $\geq$ C24 mainly in the particulates
Leaves from beech in Zürich over seasons:

<table>
<thead>
<tr>
<th>Date</th>
<th>Concentration (mg/kg dry weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 May 2001 (leaves few days old)</td>
<td>4.7</td>
</tr>
<tr>
<td>1 July</td>
<td>4.0</td>
</tr>
<tr>
<td>28 September</td>
<td>4.5</td>
</tr>
<tr>
<td>12 November (leaves freshly dropped)</td>
<td>4.8</td>
</tr>
</tbody>
</table>
MOSH in sunflower oil
Enrichment + removal of n-alkanes

Manually picked kernels; concentrations related to oil

On-line HPLC-GC-FID after enrichment and removal of natural n-alkanes
Oil from mechanically harvested kernels

**Sample A** after drying

**Sample C** before unloading

**Sample G** from harvester

**Sample B** from harvester

60 °C

350 °C

20 °/min

12

14

16

18

21

27

38

a

te

ui

3

12

15

17

22

27

38

Diesel oil

Lubricating oil

Diesel + fuel oil

21

Lubricating oil

3.5 mg/kg

0.7 mg/kg

2.4 mg/kg

after drying

41 mg/kg
Toxicological evaluation

History of errors
Difficulties in better evaluation
The “old” toxicological evaluation

• Based on experiments with entire mineral oil products
  – mixtures with little information about composition (mainly viscosity)
  → no information about which components produced which effect

• End points considered pivotal:
  – granuloma formation for MOSH
  – MOAH are genotoxic

• Increased organ weights in rats
  – repeatedly observed…
  – …but not adequately investigated, probably since human exposure was grossly underestimated

• Measured half-life in rats seemed moderate…
  – …but accumulation of minor parts cannot be excluded in this way

→ SCF and JECFA 2002: very high tolerance for MOSH >C25
# 2002 JECFA classification of white mineral oils

![Table showing classification criteria for white mineral oils](http://whqlibdoc.who.int/trs/WHO_TRS_913.pdf)

<table>
<thead>
<tr>
<th>Name</th>
<th>ADI (mg/kg bw)(^a)</th>
<th>Viscosity at 100 °C (mm(^2)/s)</th>
<th>Average relative molecular mass</th>
<th>Carbon number at 5% distillation-point</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Microcrystalline wax</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-melting-point wax</td>
<td></td>
<td>≥ 11</td>
<td>≥ 500</td>
<td>≥ 25</td>
</tr>
<tr>
<td><strong>Low-melting-point wax</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-melting-point wax</td>
<td>Withdrawn(^c)</td>
<td></td>
<td>No specification</td>
<td></td>
</tr>
<tr>
<td><strong>Mineral oil (high viscosity)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P100</td>
<td>0–20(^a)</td>
<td>≥ 11</td>
<td>&gt; 500</td>
<td>&gt; 28</td>
</tr>
<tr>
<td><strong>Mineral oil (medium and low viscosity) class I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P70</td>
<td>0–10(^d)</td>
<td>8.5–11</td>
<td>480–500</td>
<td>≥ 25</td>
</tr>
<tr>
<td>Medium-viscosity liquid petroleum</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>P70(H)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Mineral oil (medium and low viscosity) class II</strong></td>
<td></td>
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</tr>
<tr>
<td>N70(H)</td>
<td>0–0.01(^e,f)</td>
<td>7.0–8.5</td>
<td>400–480</td>
<td>≥ 22</td>
</tr>
<tr>
<td><strong>Mineral oil (medium and low viscosity) class III</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P15(H)</td>
<td>0–0.01(^e,f)</td>
<td>3.0–7.0</td>
<td>300–400</td>
<td>≥ 17</td>
</tr>
<tr>
<td>N15(H)</td>
<td></td>
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</tbody>
</table>

C\(^{34}\)=478 Da
However…

- Frequent occurrence of MOH granulomas in human tissues, reported in about 1950-1990
  - remained unexplained
- 2003, Scotter et al.: strong accumulation of MOSH >C25 (those with the very high ADI!) in rat tissues
  - no follow-up
- Long-term accumulation of MOSH not adequately investigated
  - little data on tissue concentrations (demanding analysis!)

Presently used reference values from German Ministry

- German values were originally derived from JECFA evaluation from 2002 for class III oils: ADI of 0.01 mg/kg body weight
  - 60 kg person, 1 kg food/d → 0.6 mg/kg food
  - 25 % MOAH → 0.15 mg/kg food
- This ADI was withdrawn in 2012
- Limits later increased to 2 mg/kg/0.5 mg/kg
  - no toxicological justification
More recent evaluations

• 2003, 2008: MOSH in human milk and body fat
  – milk: mean ~ 50 ppm, maximum 1300 ppm/fat

• 2012: Evaluation by EFSA
  – no ADI or TDI owing to lack of data primarily on accumulation
  – present exposure to MOSH considered «of potential concern»
    • based on the old (inadequate!) data (low melting wax)
    – “MOAH with three or more, non- or simple-alkylated, aromatic rings may be mutagenic and carcinogenic, and therefore of potential concern”

• 2012: WHO/JECFA withdraws ADI for Class II/III oils

• 2014: Measurement in human tissues reveals
  – strong accumulation of a probably small part of the MOSH
  – no accumulation of MOAH

• 2017: EFSA project with Fischer 344 rats
  – source of granuloma formation, increased organ weights
2011: BfR evaluation by accumulation

- BfR: potential adverse effects are from the accumulated MOSH limits related to accumulation
  - 12 mg/kg C10-C16 (not accumulated)
  - 4 mg/kg C16-C20 (low accumulation)
  - anticipated lower limit for >C20

In conflict with JECFA evaluation!
2014: Concentrations in human tissues
Samples from Pathology Wien, 37 subjects, mean age: 67 y

Calculated human body burden

Quarter of subjects: >5 g MOSH
Human tissues

- Fat tissue ≈ MLN
- Liver ≈ spleen
- Composition in all subjects ± equal

Liver
- Fat tissue
- 122 mg/kg
- 122 mg/kg

Fat tissue
- 205 mg/kg
- 20 mg/kg

Liver
- 20 mg/kg
- 16

Lung
- 3.5 mg/kg
- 65 °C

Heart
- 8 mg/kg
- 19

Kidney
- 6.4 mg/kg
- 21

MLN
- 48 mg/kg
- 42

Spleen
- 27
- 24
- 29

on-line HPLC-GC-FID
Selective accumulation

- Only C18-C35 efficiently accumulated
  - more volatiles exhaled
  - higher masses not absorbed (or no exposure?)
- Metabolisation within this range
- Human milk transfers most accumulating MOSH to babies
Selective accumulation also by structure
HPLC GCxGC-FID

78 y old female, 56 kg bw

Paraffin oil

GC-FID

Unresolved hydrocarbons

Baseline

GCxGC-FID

110 °C  →  5 °/min  →  270 °C
First dimension separation

Second dimension separation [sl]

GCxGC-FID

MLN (1390 mg/kg)

Spleen (1400 mg/kg)

Pristane

Cyclopentyl-Cyclohexyl-

Multibranched paraffins

n-Alkanes and little branched paraffins

31 33

20
EFSA project on MOSH 2014-2017

• Data gaps identified in EFSA-Opinion from 2012:
  – Classification of MOSH according to composition rather than products
  – Effect of MOSH accumulation: comparison of animal data with human tissue data (internal exposure)

• ♂ Fischer 344 rats (considered as most sensitive)

• Phase 1: broad MOSH-mixture (C14-C50)
  – 40, 400, 4000 mg/kg added to feed, 30-120 days

• Phase 2: specific MOSH mixtures:
  – Oil mostly <C25 (S-C25; “bad” MOSH according to JECFA)
  – Oil mostly >C25 (L-C25; “good” MOSH according to JECFA)
  – Oil (L-C25) + wax 1:1 (L-C25W)
  – 400, 1000, 4000 mg/kg feed, 120 days
Accumulation of n-alkanes in F344 rats

n-Alkanes are generally considered as readily metabolized, but some are strongly accumulated by Fischer 344 rats.

Liver and spleen of Fischer 344 rats:
- n-alkanes <C24 eliminated
- strong accumulation centered at C30
- none >C38 (not absorbed).

Crystallization prevents metabolization?
Melting point of n-C25: 54 °C
F344 rats: granulomas from n-alkanes

Occurrence of granulomas in livers of Fischer 344 rats:
- MOSH largely <C25: some granulomas at high dose
  - test mixture contained some n-alkanes C25-C30
- MOSH >C25: hardly any granulomas
  - no n-alkanes C25-C30
- MOSH >C25 + wax: very many granulomas, even at low dose

→ Granuloma formation correlated with wax components

Crystal formation triggers granuloma formation?

Accumulation of n-alkanes in humans?

Human liver and spleen contain hardly any n-alkanes.

Potential explanations:
- efficient elimination
- negligible exposure

Exposure to mineral waxes is low…
…but exposure to plant waxes (odd-numbered n-alkanes) is high (single apple ≈ 25 mg!)

Humans probably readily eliminate n-alkanes
If granuloma formation in F344 rats is due to crystallization of n-alkanes, granuloma formation should not be of concern for humans.

however:

- What caused then the wide-spread granulomas in human tissues in the past?
  - was the exposure to MOSH that high that even oils precipitated and formed granulomas?

- Open questions:
  - are there still granulomas in human tissues?
  - uptake of MOSH depends on physical and matrix properties
    - are crystalline waxes (e.g. from apples) not absorbed?
### Extrapolation from animal data

<table>
<thead>
<tr>
<th>Rat, 120 days</th>
<th>Dose (mg/kg feed)</th>
<th>Concentration (mg/kg)</th>
<th>Liver</th>
<th>Spleen</th>
<th>Fat tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
<td>40</td>
<td>220</td>
<td>32</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>400</td>
<td>1604</td>
<td>202</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4000</td>
<td>5511</td>
<td>383</td>
<td>274</td>
<td></td>
</tr>
</tbody>
</table>

Human exposure 1998-2010 according to EFSA (2012):
- 0.03-0.3 mg/kg body weigh/day
- ≈ 1.8-18 mg/day
- ≈ 1.8-18 mg/kg food (mean of all)

Rats feed ~10 times more per body weight than humans eat

<table>
<thead>
<tr>
<th>Humans</th>
<th>Concentration (mg/kg)</th>
<th>Liver</th>
<th>Spleen</th>
<th>Fat tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measured data (n=37)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>131</td>
<td>93</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>901</td>
<td>1400</td>
<td>493</td>
<td></td>
</tr>
<tr>
<td>Extrapolated from animal data</td>
<td>1.8 mg/d</td>
<td>2.5</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td></td>
<td>18 mg/kg</td>
<td>24.8</td>
<td>1.7</td>
<td>1.2</td>
</tr>
</tbody>
</table>

**Liver:** maximum (n=37) >100 times higher than extrapolated

**Spleen:**
- Maximum >1000 times higher
- Higher than in rats

**Fat tissue:** 100-1000 times higher
Reasons for the underestimation

1. Certain MOSH accumulate over very long periods
   – possibly decades instead of, e.g. 120 days in rats (factor >100)

2. Rats: tissue concentrations do not increase linearly with dose: higher absorption at low concentration

<table>
<thead>
<tr>
<th>Rats, 120 days</th>
<th>linear extrapolation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mg/kg feed)</td>
<td>Concentration (mg/kg)</td>
</tr>
<tr>
<td></td>
<td>Liver</td>
</tr>
<tr>
<td>40</td>
<td>220</td>
</tr>
<tr>
<td>400</td>
<td>1604</td>
</tr>
<tr>
<td>4000</td>
<td>5511</td>
</tr>
</tbody>
</table>

3. Humans exposed to pre-digested MOSH (enriched accumulating MOSH)?
Basic safety assessment

- Standard safety assessment based on No Observed Adverse Effect Level (NOAEL) in animals:
  - most sensitive animal, except effect is known to be irrelevant for humans
- Standard safety margin for extrapolating animal tox data to humans; for solid data set: factor 100
  - factor 10 for inter-species differences
  - factor of 10 for variable sensitivity within species
- In case of accumulation: comparison of internal doses (tissue concentrations) rather than external doses (exposures)

2. Underestimated accumulation
Safety margin for MOSH

- Human tissues (n=37)
- Concentrations in Fischer 344 rats at maximum dose (4000 mg/kg feed), mixture >C25 free of n-alkanes (no granulomas)

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Rat (mg/kg)</th>
<th>Man (mg/kg)</th>
<th>Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Max</td>
<td>Mean</td>
</tr>
<tr>
<td>Liver</td>
<td>3805</td>
<td>131</td>
<td>901</td>
</tr>
<tr>
<td>Spleen</td>
<td>419</td>
<td>93</td>
<td>1400</td>
</tr>
<tr>
<td>Adipose tissue</td>
<td>36</td>
<td>130</td>
<td>493</td>
</tr>
</tbody>
</table>

Margin far <100; human tissue concentrations may even exceed those in test animals (red)
Increased weight of liver and spleen in rats

Is the maximum tissue concentration in F344 rats really a NOAEL?

Increased organ weights indicate struggling with an extra-task

Data from EFSA project:

<table>
<thead>
<tr>
<th>Dose (mg/kg)</th>
<th>Weight after 120 days (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>0</td>
</tr>
<tr>
<td>MOSH largely &lt;C25</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>4000</td>
</tr>
<tr>
<td>MOSH largely &gt;C25</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>4000</td>
</tr>
<tr>
<td>MOSH largely &gt;C25 + wax 1:1</td>
<td>400</td>
</tr>
<tr>
<td></td>
<td>4000</td>
</tr>
</tbody>
</table>

→ Affected organ performance as relevant end point?
• doubled spleen weight already at an internal dose 3 times below maximum in human spleen?
New evidence from EFSA Project 2017

1. Granuloma formation in Fischer 344 rats is correlated with n-alkanes C25-C35
   - n-alkanes probably not accumulated in humans → might be an exceptional feature of Fischer 344 rats

2. MOSH concentrations in human tissues are far higher than extrapolated from animal experiments
   - maximum concentrations (n=37): 1.4 ‰ (spleen and lymph nodes)
   - insoluble in water → concentrations in lipids (membranes?) many %!
   → safety margins far smaller than assumed (or inexistent)

3. Increased organ weight as most relevant end point?

4. Maximum accumulation in human liver and spleen: C27-C28
   - JECFA classification is fundamentally wrong
Mislead evaluations for MOSH

• SCF/JECFA 2002: focused on granulomas, not noting that these are due to accumulation of n-alkanes (only) in F344 rats
  – oils >C25 are well deparaffinated → no n-alkanes → no granuloma formation → oils >C25 considered of little concern → high ADI
  – oils of lower mass tested contained n-alkanes → granulomas → considered of concern → very low ADI of Classes II and III oils and waxes
  – underestimated human exposure → no other end points considered

• EFSA 2012
  – margin of exposure (MoE) still based on granuloma formation
    • lowest NOAEL from a low melting wax (high content of n-alkanes)
  – “old” classification by molecular mass distribution no longer confirmed
    • but not corrected
  – insufficient safety margin not noted (unknown human data)
  – no comment on increased organ weights
MOAH

- EFSA: “of potential concern” for MOAH with >2 aromatic rings
  - known genotoxic MOAH have >2 aromatic rings
  - fraction <2 aromatic rings was Ames-negative
- Most mineral oils used in the context of food contain virtually no MOAH >2 aromatic rings
  - exception: jute and sisal bags
- Analytical method should separate ≤2 from >2 aromatic rings
- Environmental contaminants ± free of MOAH
  - apparently degraded (to what?)

→ MOAH might not be of main concern
  - MOAH are automatically low if MOSH are regulated adequately
Outlook

- JECFA 2002 and EFSA 2012 evaluations need to be revised
  - high limits must be withdrawn
- Classification (Class I with <5 % below C25) is perverse
  - MOSH <C20 hardly accumulated and probably not of concern
  - main part in Class I (C25-C35) is of most concern
- Granulomas are not the pivotal end point
  - to be investigated, see increased organ weights
- Insufficient safety margin: exposure must be strongly reduced
  - high exposure according to EFSA 2000-2010: 18 mg/kg food
    → maximum MOSH concentration across all foods 10 times lower?
Conclusions

- Oils and waxes should be evaluated separately
  - Oils contain strongly accumulating constituents, waxes probably not
- Tox evaluation must be based on human tissue data
  - what are the levels from present exposure?
  - is only oral exposure relevant? Were the highest tissue concentrations only from contaminated food?
    - problem: relationship exposure – concentrations in human tissues
- Environmental contribution, almost exclusively of (predigested!) MOSH, is already in the range of the limit and difficult to avoid
- Use of mineral oil products should not longer be authorized
  - at least until adequate safety assessment is achieved
- Synthetic hydrocarbons (e.g. polyolefin oligomers) should be considered more critically
Publications


• Accumulation of mineral oil saturated hydrocarbons (MOSH) in female Fischer 344 rats: Comparison with human data and consequences for risk assessment
Science of the Total Environment 575 (2017) 1263–1278

• 445 Mineral oil saturated hydrocarbons (MOSH) in female Fischer 344 rats; accumulation of wax components; implications for risk assessment.

• Mineral oil saturated hydrocarbons (MOSH) in female Fischer 344 rats; accumulation of wax components; implications for risk assessment
Science of the Total Environment http://dx.doi.org/10.1016/j.scitotenv.2017.01.071

• Toxic effects of MOSH and relation to accumulation in rat liver
Food and Chemical Toxicology 123 (2019) 431-442.

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