Introduction to Plastics and their Additives

Extractables and Leachables
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SGS Life Science Services

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Extractables und Leachables

- **Agenda**

  - **Introduction to Polymers**
    - Classification
    - Properties
    - Typical uses of Plastics
  
  - **Additives**
    - Relevant Additives / Chemical classes
    - Compendium Additives
  
  - **Examples / Applications**
    - LDPE / HDPE
    - Sterilization / Reaction Products
    - PVC
1. Introduction: -Polymers are typically classified by different Criteria

Polymers are classified by:

- **Origin:** Natural Polymers, Synthetic Polymers
- **Chemical composition:** Organic Polymers, Inorganic Polymers
- **Thermoelastic properties:** Elastomers, Thermoplastics, Thermosets
- **Route of synthesis:** Chain-growth and step-growth polymers
- **Number of monomers:** Homo-Polymer, Co-Polymer.
2. Overview: Classification of Polymers by its Origin and Chemical Composition

**Natural Polymers**

- Amylose (Starch)

**Synthetic Polymers**

**Organic**

- Polypropylene

**Inorganic**

- \([-\text{O-Si(CH}_3\text{)}_2\text{n-}\]

- Silicone
2. Overview: - Thermoplastic Properties

- The difference between **thermoplastics** and thermosettings plastics are, when heat is added:
  - thermoplastics become soft, remoldable and weldable

Associated by dipole-dipole (nylon) or Van der Waals forces (polyethylen)
2. Overview: -Thermoset

**Thermosetting** plastics however can not be welded or remolded when heated, simply burning instead.

- once a thermosetting is cured it tends to be stronger than a thermoplastic

Curing may be done by heat, irradiation or by electron beam
# 2. Overview: Plastic materials, classification

## List of Thermoplastics

<table>
<thead>
<tr>
<th>Material Type</th>
<th>Examples</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acrylonitrile butadiene styrene (ABS)</td>
<td>Ethylene-Vinyl Acetate (EVA)</td>
<td>Ethylene vinyl alcohol (EVAL)</td>
</tr>
<tr>
<td>Fluoroplastics (PTFE, along with FEP, PFA, CTFE, ECTFE, ETFE)</td>
<td>Polyacetal (POM or Acetal)</td>
<td>Polyacrylates (Acrylic)</td>
</tr>
<tr>
<td>Polyacrylonitrile (PAN or Acrylonitrile)</td>
<td>Polyamide (PA or Nylon)</td>
<td>Polyamide-imide (PAI)</td>
</tr>
<tr>
<td>Polyaryletherketone (PAEK or Ketone)</td>
<td>Polybutadiene (PBD)</td>
<td>Polybutylene (PB)</td>
</tr>
<tr>
<td>Polybutylene terephthalate (PBT)</td>
<td>Polycaprolactone (PCL)</td>
<td>Polychlorotrifluoroethylene (PCTFE)</td>
</tr>
<tr>
<td>Polyethylene terephthalate (PET)</td>
<td>Polycyclohexylene dimethylene terephthalate (PCT)</td>
<td>Polycarbonate (PC)</td>
</tr>
<tr>
<td>Polyhydroxyalkanoates (PHAs)</td>
<td>Polyketone (PK)</td>
<td>Polyester</td>
</tr>
<tr>
<td>Polyethylene (PE)</td>
<td>Polyetheretherketone (PEEK)</td>
<td>Polyetherimide (PEI)</td>
</tr>
<tr>
<td>Polyethersulfone (PES)- see Polysulfone</td>
<td>Polyethylenechlorinates (PEC)</td>
<td>Polymide (PI)</td>
</tr>
<tr>
<td>Polylactic acid (PLA)</td>
<td>Polymethylpentene (PMP)</td>
<td>Polyphenylene oxide (PPO)</td>
</tr>
<tr>
<td>Polyphenylene sulfide (PPS)</td>
<td>Pollyphthalamide (PPA)</td>
<td>Polypropylene (PP)</td>
</tr>
<tr>
<td>Polystyrene (PS)</td>
<td>Polysulfone (PSU)</td>
<td>Polyurethane (PU)</td>
</tr>
<tr>
<td>Polyvinyl acetate (PVA)</td>
<td>Polyvinyl chloride (PVC)</td>
<td>Polyvinylidene chloride (PVDC)</td>
</tr>
</tbody>
</table>
2. Overview: Plastic materials – Typical uses

Typical pharmaceutical uses of various plastics and associated materials

<table>
<thead>
<tr>
<th>Material</th>
<th>Abbreviation</th>
<th>Typical Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyethylene</td>
<td>PE</td>
<td>Tubing, catheters, connectors, bottles, container/packaging systems</td>
</tr>
<tr>
<td>Poly (vinyl chloride)</td>
<td>PVC</td>
<td>Tubing, container/packaging systems</td>
</tr>
<tr>
<td>Polypropylene</td>
<td>PP</td>
<td>Disposable syringe, bottles, container/packaging systems, connectors, membranes</td>
</tr>
<tr>
<td>Polyethylene terephthalate</td>
<td>PET</td>
<td>Blow-molded components, bottles, containers</td>
</tr>
<tr>
<td>Polysulfone</td>
<td>-----</td>
<td>Membrane for dialysis or ultrafiltration, oxygenator</td>
</tr>
<tr>
<td>Polyurethane</td>
<td>PU</td>
<td>Tubing, adhesives, pump, balloon and/or valve materials, prostheses</td>
</tr>
<tr>
<td>Polycarbonate</td>
<td>PC</td>
<td>Housings, connectors, packaging materials, bottles, syringe barrels</td>
</tr>
<tr>
<td>Poly(methyl methacrylate)</td>
<td>PMMA</td>
<td>Dental materials, bone replacement, lenses, membranes for dialysis or ultrafiltration, container material</td>
</tr>
<tr>
<td>Polyamide</td>
<td>PA</td>
<td>Container/packaging material, drug release systems</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>PS</td>
<td>Container/packaging materials, tubing</td>
</tr>
<tr>
<td>Cellophane</td>
<td>-----</td>
<td>Secondary packaging</td>
</tr>
<tr>
<td>Natural or synthetic rubber</td>
<td>----</td>
<td>Shunts, catheters, tubing, prostheses, closures, drug-release systems, container/packaging systems</td>
</tr>
<tr>
<td>Paper/cardboard</td>
<td>-----</td>
<td>Secondary packaging, labels</td>
</tr>
</tbody>
</table>
2. Overview: Plastic materials, classification

Some examples of thermostets are:

- Vulcanized rubber
- Bakelite, a phenol-formaldehyde resin (used in electrical insulators and plasticware)
- Urea-formaldehyde foam (used in plywood, particleboard and medium-density fibreboard)
- Melamine resin (used on worktop surfaces)
- Epoxy resin (used as an adhesive and in fibre reinforced plastics such as glass reinforced plastic and graphite-reinforced plastic)
- Polyimides (used in printed circuit boards and medical tubing)
2. Overview: -Plastic materials, classification

The following properties define polymers as an Elastomer:

- An elastomer is a polymer with the property of elasticity
- Must be amorphous when unstretched
- Must be above their glass transition temperature to be elastic

A: is a schematic drawing of an unstressed polymer
B: is the same polymer under stress. When the stress is removed, it will return to the A configuration.
2. Overview: Plastic materials, classification

- **Crosslinked elastomers** consists of:
  - Base elastomeric polymer
  - Property modifying additives
  - A reactive cross linking agent

- **Thermoplastic elastomer** consists of:
  - Base elastomeric polymer in which the neat polymer has inherently elastomeric properties
  - It can be formed like thermoplastic but the final object has elastomeric behavior
2. Overview: Plastic materials, classification

- The material properties of natural rubber make it an elastomer and a thermoplastic.

- Examples of saturated Rubbers that cannot be cured by sulfur vulcanization:
  - Silicone rubber (SI, Q, VMQ)
  - Fluorosilicone Rubber (FVMQ)
  - EPM (ethylene propylene rubber, a copolymer of ethylene and propylene) and EPDM rubber (ethylene propylene diene rubber, a terpolymer of ethylene, propylene and a diene-component)
2. Overview: Plastic materials, classification

However it should be noted that as the rubber is vulcanized it will turn into a thermoset.
2. Overview: Plastic materials, classification

- Examples of **unsaturated rubbers** that can be cured by sulfur vulcanization:
  - Synthetic Polyisoprene (IR)
  - Butyl rubber (copolymer of isobutylene and isoprene, IIR)
  - Halogenated butyl rubbers (Chloro Butyl Rubber: CIIR; Bromo Butyl Rubber: BIIR)
3. Additives – Advantages / Drawbacks of Plastic materials

- Light materials
- Rigid or flexible
- Mouldable
- Reasonable inert
- Printable
- Transparent or colored
- Combinable with other materials

- Ageing by UV or Oxygen impact
- Tread groove cracking
- Damage to the environment
- Migration of plastic components
3. Additives: Improvement of selected Properties

**Typical classes of additives**

I. Antioxidants

II. Plasticizers

III. Antidegradants
   a. Photostabilizer
   b. Antiozonants

IV. Coupling agents

V. Flame retardants

VI. Lubricants

VII. Acid scavengers

VIII. Peroxides / Crosslinking agents

IX. Blowing agents

X. Pigments / colorants

XI. Antistatic agents

XII. Barrier forming additives

XIII. Metall chelators

XIV. Adhesives

XV. Bacterizides

XVI. Clarifying agents

XVII. Antifogging agents
3. Additives: - I. Antioxidants (antidegradant)

- Assure protection against thermal and oxidative degradation during processing and during environmental exposure.

Chemical classes are:
- Sterical Hindered phenols BHT (radical scavengers)
- Organic phosphites / phosphonates (peroxides decomposers)
- Thioethers
- Thiocarbamates
- Mercaptobenzimidazoles
- Thiobisphenols …..and others

More than 380 patents dealing with new compounds acting as antioxidants are recorded each year!!!
3. Additives: -I. Antioxidants (Phenolic)

- Irganox 1010 (secondary antioxidant)
3. Additives: -I. Antioxidants (Phenolic)

- **Irganox 1010 break down products I**
3. Additives: -I. Antioxidants ( Phenolic)

- Irganox 1010 break down products II
3. Additives: -I. Antioxidants (Phosphites)

- Irgafos 168 (primary antioxidant)
3. Additives: -I. Antioxidants (Phosphites)

- Irgafos 168 break down products II
3. Additives: -II. Plasticizer

- gives the plastics flexibility and durability.
- Some requirements for plasticizer should be:
  - Low extractability by water and solvent
  - Stability to heat and light
  - Low odor, taste and toxicity

Chemical classes are:
- Phthalates (esters)
- Fatty acids (Stearic acid, Palmitinic acid)
- Oils such as epoxidized linseed oil, tall-oil
- Adipates, azelates, sebacates
- Derivates of glycols and aliphatic dicarboxylic acids
3. Additives: -III. Antidegradants

- Stops the degradation of the finished plastic product.

- Antiozonants (ozone protection, barrier):
  - Alkylphenylamines

- UV-Stabilizers (UV protection against discoration):
  - Benzophenones
  - Benzotriazoles
  - Salicylate eters
  - Cyanoacrylates
  - Malonates
  - Benzilidenes
  - Polimeric sterically hindered phenols
3. Additives: -IV. Coupling agents

- Are substances that are capable of bonding organic polymer systems to inorganic substrates such as glass, mineral fillers and metals

Chemical classes are:

- Silanes
  - Aminoalkyl silanes
  - Alkyl-alkoxy silyl-sulfides
  - Epoxy-alkyl-silanes
  - Vinyl-alkoxy-silanes
3. Additives: -V. Flame Retardants

- Added to inhibit ignition or flammability of the end-use product and used in thermoplastics:
  - Polystyrene, polyesters, polyolefins...

Chemical classes are:
- Inorganic
  - Aluminium trihydrate
  - Antimony oxide
  - Boron compounds
- Organic
  - Brominated and chlorinated compounds
  - Brominated diphenyl ethers (PBDE)
3. Additives: -XX. Other Components of Interest

- **Cross linking agents** are used to form links between molecular chains
  - Sulfur
  - Thiazoles

- **Processing aids** lower the viscosity, provide additional stability, prevent attack bacteria, etc.
  - Amides (Erucamide)

- **Retarders slow** down the reaction process
  - Phatalic anhydride
4. Additives: -Compendium Additives – Ph. Eur. 3.1.13

3.1.13. PLASTIC ADDITIVES

Note: the concentration given is according to the IUPAC ratio. The percentage given in bold corresponds to the same given in the body of Chapter 5. The percentage corresponding to the ratios of “Additives Abroad” is also given.

Additiv 07 ≤ 0,125%
2,6-di-tert-butyl-4-methylphenol (BHT)

Additiv 08 ≤ 0,3%
ethylen bis[3,3-bis[3-(1,1-dimethylethyl)-4-hydroxy-phenyl]butanoate] (Hostanox 19)

Additiv 09 ≤ 0,3%
pentaerythrityl tetrakis[3-(3,5-di-tert-butyl-4-hydroxy-phenyl)propionate] (Irganox 1010, Ethanox 310)

[...]

General Notice (I): relating to all monographs and other texts
Typical Compendium „bushwa“:

- *polyolefin's may contain a certain number of additives ... to adapt them for their intent of use. All additives are chosen from an appended list which specifies for each product a maximum allowable content.*

- *Polyolefin's may contain a most three antioxidants, one of several lubricants or antiblocking agents ....*

😊 Pharmaceutical products could be contaminated by additives and particularly by their reaction products!
### 4. Examples: Polyolefines I – Extractables from LDPE and HDPE

<table>
<thead>
<tr>
<th>Component</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aliphatic hydrocarbons</td>
<td>Not polymerized monomers</td>
</tr>
<tr>
<td>Branched aliphatic hydrocarbons</td>
<td>Mould release agents</td>
</tr>
<tr>
<td>Irganox 1010, 1076, Irgafos 168</td>
<td>Antioxidants</td>
</tr>
<tr>
<td>Tetra-methyl succinonitrile</td>
<td>Catalyst</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>----</td>
</tr>
<tr>
<td>Alcohols</td>
<td>Hydrolyze product of DEHP</td>
</tr>
</tbody>
</table>

DEHP: Di-(2-ethylhexyl) phtalate
4. Examples: Polyolefines – Extractables / Extractables from LDPE / HDPE

- Carbonic acids: $C_1$, $C_2$, $C_3$ etc.
- $C_2 – C_5$ - Aldehydes
- Ketones
- BHT derived from Irganox 1010, 1076
- 2,5-di-tert-butyl benzene and 2,5-di-tert-butyl phenol from Irgafos 168

BHT: 3,5-di-tert-butyl-4-hydroxytoluol
4. Examples: Polymers and Additives can degrade during Processing and upon Sterilization

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Classification</th>
<th>Polymer</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABS</td>
<td>1</td>
<td>Polyimide</td>
<td>1</td>
</tr>
<tr>
<td>Acetyl</td>
<td>4</td>
<td>Polymethylmethacrylate</td>
<td>2</td>
</tr>
<tr>
<td>Aliphatic polyamide</td>
<td>2-3</td>
<td>Polymethylnpentene</td>
<td>4</td>
</tr>
<tr>
<td>Aromatic polyamide/polyimide</td>
<td>1</td>
<td>Polypropylene</td>
<td>3</td>
</tr>
<tr>
<td>Butyl rubber</td>
<td>4</td>
<td>Polytetrafluoroethylene</td>
<td>4</td>
</tr>
<tr>
<td>Cellulosic</td>
<td>2</td>
<td>Polystyrene</td>
<td>1</td>
</tr>
<tr>
<td>EPDM rubber</td>
<td>1-2</td>
<td>Polysulfone</td>
<td>1</td>
</tr>
<tr>
<td>Epoxy</td>
<td>1</td>
<td>Polyurethane</td>
<td>1</td>
</tr>
<tr>
<td>Flexible PVC</td>
<td>2</td>
<td>Radiation resistant rigid</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>polyvinyl chloride</td>
<td></td>
</tr>
<tr>
<td>Fluorinated ethylene propylene</td>
<td>4</td>
<td>Radiation stable</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>polypropylene</td>
<td></td>
</tr>
<tr>
<td>Phenolic</td>
<td>1</td>
<td>Rigid polyvinyl chloride</td>
<td>3</td>
</tr>
<tr>
<td>Polycarbonate</td>
<td>2</td>
<td>Silicone</td>
<td>1</td>
</tr>
<tr>
<td>Polyester</td>
<td>1</td>
<td>Styrene-butadiene rubber</td>
<td>3-4</td>
</tr>
<tr>
<td>Polyethylene</td>
<td>1</td>
<td>Nitrile rubber</td>
<td>2</td>
</tr>
</tbody>
</table>

*Classification: 1 = Excellent 2 = Good 3 = Problematic 4 = Not Advisable*
### 4. Examples: Extractables from PVC I

<table>
<thead>
<tr>
<th>Component</th>
<th>Origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethylenoxide</td>
<td>Sterilization residue</td>
</tr>
<tr>
<td>Di-(2-Ethylhexyl)phtalat (DEHP)</td>
<td>Plasticizer</td>
</tr>
<tr>
<td>Phthalic acid</td>
<td>Hydrolysis of DEHP</td>
</tr>
<tr>
<td>Mono-(ethylhexyl)phtalat (MEHP)</td>
<td>Hydrolysis of DEHP</td>
</tr>
<tr>
<td>Dibutyl phthalate</td>
<td>Impurity of DEHP</td>
</tr>
<tr>
<td>2-Ethyl-1-hexanol</td>
<td>Hydrolysis of DEHP</td>
</tr>
<tr>
<td>Vinyl chloride monomer</td>
<td>PVC</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>Oxidation of PVC</td>
</tr>
<tr>
<td>Formic acid</td>
<td>Oxidation of PVC</td>
</tr>
<tr>
<td>Cyclo hexanone</td>
<td>Residue solvent</td>
</tr>
<tr>
<td>9,10-Epoxy stearic ester</td>
<td>Impurity</td>
</tr>
</tbody>
</table>

### 4. Examples: Extractables from PVC II

<table>
<thead>
<tr>
<th>Component</th>
<th>Orign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>Residue solvent</td>
</tr>
<tr>
<td>Toluene</td>
<td>Residue solvent</td>
</tr>
<tr>
<td>1,1 –Dimethylethyl-4-methoxyphenol (BHA)</td>
<td>Antioxidant</td>
</tr>
<tr>
<td>Bisphenol A</td>
<td>Antioxidant</td>
</tr>
<tr>
<td>3,5-di-tert-butyl-4-hydroxytoluene (BHT)</td>
<td>Antioxidant</td>
</tr>
<tr>
<td>t-Butyl cyclohexanol</td>
<td>Inks</td>
</tr>
</tbody>
</table>

### 4. Examples: Different Plastics – Metals / Minerals

<table>
<thead>
<tr>
<th>Material</th>
<th>Analytics / Extract</th>
<th>Component / Level [ppm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE</td>
<td>ICPMS, ICP-OES microwave digestion</td>
<td>Mg / 0,5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Si / 16,0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca / 32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zn / 1,8</td>
</tr>
<tr>
<td>LDPE</td>
<td>ICPMS microwave digestion</td>
<td>Mg / 2,3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Al / 8,9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mn / 0,01</td>
</tr>
<tr>
<td>PVC</td>
<td>ICP-OES /Extraction with 5% acetic acid 2h 122°C</td>
<td>Al / 0,2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ca / 0,4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Si / 0,9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zn / 0,4</td>
</tr>
<tr>
<td>Perfluoro elastomer</td>
<td>ICP-MS, IC /water 4 weeks 80°C</td>
<td>F / 1,1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metals &lt; 0,1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TOC 1,54</td>
</tr>
</tbody>
</table>
5. Discussion

Questions?

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