Alternative IV Lipid Emulsions

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• Provide brief background on lipids and their function

• Discuss the evolution of IVLEs

• Discuss the IVLEs approved in the US and their component oils

• Introduce a new alternative lipid emulsion available on the US market
**LIPIDS: WHAT ARE THEY?**

- Biological substances that are soluble in organic solvents but insoluble in water

**Where are they found?**

- Soybeans/Vegetables
- Walnuts/Peanuts
- Fish
- Avocado/Olives
- Coconuts
- Eggs, milk, animal meats
LIPIDS: PURPOSE

• Dense source of energy
• Provides essential fatty acids\(^1,2\)
• Important in structural components of cell membranes\(^1\)
• Carry lipid soluble vitamins
• Involved in hormone and enzyme production
• Important in immune and inflammatory responses\(^1\)

Triglycerides

• The most abundant lipids in the body
• Fatty acids: the fundamental building blocks of lipids

Phospholipids

• The components of the lipid bilayer of cell membranes

Saturated fatty acids: No double bonds between carbon atoms

Stearic acid (18:0)

Unsaturated fatty acids

1 double bond = Monounsaturated Fatty Acids (MUFAs)

Oleic acid (18:1\(\omega\)-9)

2 or more double bonds = Polyunsaturated Fatty Acids (PUFAs)

Alpha-Linolenic acid (18:3\(\omega\)-3)
METABOLIC PATHWAYS OF ω-3, ω-6, ω-9 FATTY ACIDS

**PARENT Essential Fatty Acid**

**Omega-3 Fatty Acids**

- Alpha-Linolenic Acid (ALA) 18:3 ω3
  - delta-6-desaturase
  - Octadecatetraenoic Acid 18:4 ω3
  - elongase
  - Eicosatetraenoic Acid 20:4 ω3
  - delta-5-desaturase
  - Eicosapentaenoic Acid (EPA) 20:5 ω3
  - elongase
  - Docosapentaenoic Acid 22:5 ω3
  - elongase
  - 24:5 ω3
  - delta-6-desaturase
  - Docosahexaenoic Acid (DHA) 22:6 ω3

**Omega-6 Fatty Acids**

- Linoleic Acid (LA) 18:2 ω6
  - delta-6-desaturase
  - Gamma-Linolenic Acid 18:3 ω6
  - elongase
  - Dihomo-Gamma-Linolenic Acid 20:3 ω6
  - delta-5-desaturase
  - Arachidonic Acid (AA) 20:4 ω6
  - elongase
  - Docosatetraenoic Acid 22:4 ω6
  - 24:4 ω6
  - 24:6 ω3
  - Delta-6-desaturase
  - Docosahexaenoic Acid (DHA) 22:6 ω3

**Omega-9 Fatty Acids**

- Oleic Acid (OA) 18:1 ω9
  - Octadecadienoic Acid 18:2 ω9
  - elongase
  - Eicosadienoic Acid 20:2 ω9
  - elongase
  - Eicosatrienoic Acid (Mead Acid) 20:3 ω9
  - Tetraene
  - Triene

METABOLIC FUNCTIONS OF LIPIDS

- Triglyceride (Energy Depot)
- High-Energy Substrate

FATTY ACID

- Membranes
- Physical Changes
  - Fluidity
  - Receptors
  - Ion Channels

- Membrane-Bound Receptors

- Enzymes
  - Eicosanoids
    - Prostaglandins
    - Leukotrienes
    - Thromboxanes
    - Protectins
    - Resolvins
    - Lipoxins

- Signal Transduction Pathways

- Gene Expression Regulation

- Cytokines
  - Immune Cell and Other Cell Types
    (Various Functions)

**ESSENTIAL FATTY ACID (EFA)**

**What is an EFA?**
- An EFA cannot be synthesized by the human body and must therefore be acquired in diet\(^1\)
- Essential for growth, development, and function\(^2\)
- Utilized primarily in 3 metabolic pathways\(^3\):

\[\text{Elongation of Free Fatty Acids} \quad \text{Energy Conversion} \quad \text{Incorporation in Cell Membrane}\]

**Which fatty acids are essential?**
- Alpha-Linolenic Acid 18:3\(\omega-3\)
- Linoleic Acid 18:2\(\omega-6\)

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Evolution of IVLEs

IVLE=intravenous lipid emulsions; PN=parenteral nutrition; MCT=medium-chain triglyceride; LCT=long-chain triglyceride
MCT = medium-chain triglyceride; TG = triglyceride
IVLEs Available in the US
### FDA APPROVED IVLEs

<table>
<thead>
<tr>
<th>FDA Approved in USA</th>
<th>Intralipid¹,²</th>
<th>Nutrilipid³</th>
<th>Clinolipid²,⁴</th>
<th>Smoflipid⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td>Fresenius Kabi/Baxter*</td>
<td>B. Braun Medical</td>
<td>Baxter</td>
<td>Fresenius Kabi</td>
</tr>
<tr>
<td>Oil Source</td>
<td>Soybean Oil</td>
<td>Soybean Oil</td>
<td>Olive Oil 80% Soybean Oil 20%</td>
<td>Soybean Oil 30% MCT 30% Olive Oil 25% Fish Oil 15%</td>
</tr>
</tbody>
</table>

#### Fat Composition (%, mean values)¹-⁵

<table>
<thead>
<tr>
<th></th>
<th>Intralipid</th>
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</thead>
<tbody>
<tr>
<td>Linoleic</td>
<td>53</td>
<td>53</td>
<td>17.9</td>
<td>19.5</td>
</tr>
<tr>
<td>α-Linolenic</td>
<td>7.5</td>
<td>7.5</td>
<td>2.4</td>
<td>2.5</td>
</tr>
<tr>
<td>Eicosapentaenoic (EPA)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.3</td>
</tr>
<tr>
<td>Docosahexaenoic (DHA)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2.3</td>
</tr>
<tr>
<td>α-Tocopherol (mg/L)</td>
<td>38</td>
<td>n/a</td>
<td>32</td>
<td>163-225</td>
</tr>
</tbody>
</table>

IVLE=intravenous lipid emulsion; MCT=medium chain triglyceride

*Distributed

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1. Intralipid Prescribing Information, 2015.
5. Smoflipid Prescribing Information 2016.

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2. Fresenius Kabi, Data on File.

MCT = medium chain triglyceride

* Not approved in the US
SOYBEAN OIL: $\omega$-6

• Only available IVLE source in the U.S. from 1970 to 2016

• Soybean oil contains an average of:
  
  • 50% Linoleic Acid (LA)
  
  • 7% $\alpha$-linolenic acid (ALA)$^1$

  - Prevents EFAD

• High $\omega$-6 fatty acid content: precursors to pro-inflammatory eicosanoids$^{2,3}$

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• IVLE with MCT available outside the U.S. since the mid-1980s

• MCT is found in coconut oil and palm kernel oil

• Good source of energy (8 kcal/g)
  - Provides rapidly available energy

• Efficient triglyceride clearance from bloodstream

• Have been added to some IVLEs to decrease ω-6 fatty acid
  - Are always mixed with soybean oil for IVLE

OLIVE OIL (OO): ω-9

• IVLE with OO available outside the U.S. since 1990s\(^1\)

• Provides MUFA, primarily oleic acid\(^1\)

• Less prone to peroxidation than PUFA\(^2,3\)

• Not converted into active mediators of inflammatory processes\(^4\)

• Provides small amounts of linoleic and α-linolenic acid for EFA

FISH OIL (FO): ω-3

• IVLE with FO available outside the U.S. since mid-1990s

• Very rich in omega-3 fatty acids

• Provides “conditionally essential” fatty acids\(^1-3\)
  – EPA and DHA

• Provides precursors to less inflammatory eicosanoids and specialized pro-resolving mediators\(^4\)

IVLEs BASED ON RELATIVE SYSTEMIC INFLAMMATORY ACTIVITY

Note: This is a relative (not absolute) figurative scale to demonstrate relative inflammatory activity
Smoflipid is a new lipid IVLE option for adults in the United States

- IV lipid emulsion product made with four different types of oils: Soy, MCT, Olive and Fish
- Provides energy and EFAs
- Safe, well tolerated, and has demonstrated efficacy
<table>
<thead>
<tr>
<th>Oil Source</th>
<th>Characteristics</th>
</tr>
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</table>
| Soy Oil (ω-6) | • Source of essential fatty acids  
• Provides energy |
| MCTs | • Source of rapidly available energy\(^1\)  
• Clears faster from the bloodstream than other fatty acids\(^2\) |
| Olive Oil (ω-9) | • Contains small amount of linoleic acid and α-linolenic acid  
• Immune neutral\(^3\) |
| Fish Oil (ω-3) | • Source of conditionally essential fatty acids EPA & DHA\(^4\)  
• Precursors to less inflammatory eicosanoids\(^5\) |

## SMOFLIPID COMPOSITION

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<th>Smoflipid&lt;sup&gt;5&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Oil Source</td>
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### Notes:

- IVLE = intravenous lipid emulsion; MCT = medium chain triglyceride
- *Distributed

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INDICATIONS AND USAGE

• Smoflipid is indicated in adults as a source of calories and essential fatty acids for parenteral nutrition when oral or enteral nutrition is not possible, insufficient, or contraindicated

Limitations of Use

• The omega-6:omega-3 fatty acid ratio and Medium Chain Triglycerides in Smoflipid have not been shown to improve clinical outcomes compared to other intravenous lipid emulsions

• The usual daily dosage is 1 to 2 grams/kg per day and should not exceed 2.5 grams/kg per day

CONTRAINDICATIONS

• Known hypersensitivity to fish, egg, soybean, or peanut protein, or to any of the active ingredients or excipients

• Severe hyperlipidemia or severe disorders of lipid metabolism with serum triglycerides > 1,000 mg/dL
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Limitations of Use
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For intravenous infusion only into a peripheral or central vein.

The usual daily dosage in adults is 1 to 2 grams/kg per day and should not exceed 2.5 grams/kg per day.
Thank You!
### IVLES: AVAILABILITY

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