A Green Process for Innovative Cosmetic Ingredients

TeamWorks
March 21st, 2012
Agenda

- Defining Green
- What is Biocatalysis?
- Developing Anti-Aging Actives
- Emollient Esters
- GEM™ (Green Enzymatic Manufacturing)
- Environmental Footprint
- Formulating
- Industry Trends
So what is Green?

- **Natural**: having or constituting a classification based on features existing in nature; that has undergone minimal processing and contains no preservatives or artificial additives
- **Organic**: produced with the use of feed or fertilizer of plant or animal origin without employment of chemically formulated fertilizers, growth stimulants, antibiotics, or pesticides
- **Green**: concerned with or supporting environmentalism
EPA: Twelve Principles of Green Chemistry*

1. **Prevent waste**, rather than clean it up
2. **Maximize atom economy**
3. **Design less hazardous chemical syntheses**, for workers & the environment
4. **Design safer chemicals** and products, for end use applications
5. Use **safer solvents**, or eliminate them entirely
6. Increase **energy efficiency**
7. Use **renewable feedstocks**, whenever feasible
8. **Avoid chemical derivatization**, in the reaction process
9. **Use catalysts**, not stoichiometric reagents, more selective & **efficient**
10. Design products to **biodegrade** after use
11. Analyze reactions in real time, to **prevent by-products**
12. **Minimize** the potential for **accidents**, such as fire

How to Apply these Principles?

- **Biocatalysis**
  - the use of whole microbial cells or isolated enzymes to catalyze a chemical transformation.

- Biocatalysis is one of the oldest chemical transformations, but has been employed for man-made compounds in the past 30 years.
**BIOCATALYSIS**: Chemical and pharmaceutical makers seek more efficient and often cleaner routes to making old and new products

**Benefits**
- Chemoselectivity
- Lower Energy Required
- Mild Conditions
- No Side Reactions
- Biodegradable
- Minimal Waste

**Challenges**: Robust Catalyst to manufacture high Volumes and high Yield @Low Cost
Enzymatic Biocatalysis

- The covalent attachment of an enzyme to a solid matrix so that it cannot move but still act on its substrate
  - Enzyme selection and functionality
  - Substrate functionality
Anti-aging ingredients:

- retinyl esters
  - Chemical synthesis of retinyl esters can be harsh to the delicate functionality of the reactants and products.
  - Enzymatic esterification is a mild method, but requires the very unstable retinol.
  - Enzymatic inter-esterification is a preferred method.
Process comparison: retinyl esters

Twelve Principles of Green Chemistry were applied to the process
### Process comparison: Idebenone esters

<table>
<thead>
<tr>
<th></th>
<th>Biocatalytic Process 1</th>
<th>Biocatalytic Process 2</th>
<th>Biocatalytic Process 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product quality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yield</td>
<td>98%</td>
<td>98%</td>
<td>99%</td>
</tr>
<tr>
<td>Assay</td>
<td>98.4%</td>
<td>98.3%</td>
<td>98.3%</td>
</tr>
<tr>
<td>Residual idebenone</td>
<td>0.2%</td>
<td>0.4%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Residual acid</td>
<td>0.2%</td>
<td>0.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Reaction Solvent</td>
<td>2.87</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>(Liters /kg product)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation Solvent</td>
<td>7.47</td>
<td>3.37</td>
<td>0</td>
</tr>
<tr>
<td>(Liters /kg product)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total solvent</td>
<td>10.34</td>
<td>3.37</td>
<td>0.00</td>
</tr>
<tr>
<td>(Liters/kg product)</td>
<td></td>
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</table>
Cosmetic ingredients: Esters

Esters are a class of cosmetic ingredients represented across functional categories.

Actives are low volume ingredients

Additional functional ingredients can benefit from greener and sustainable manufacture
Cosmetic esters market

Estimate for “actives” is ~1 kMT

Regional demand for cosmetic esters:

<table>
<thead>
<tr>
<th>Emollient Esters</th>
<th>Volume (kMT)</th>
<th>Surfactant Esters</th>
<th>Volume (kMT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>19</td>
<td></td>
<td>31</td>
</tr>
<tr>
<td>Europe</td>
<td>32</td>
<td></td>
<td>39</td>
</tr>
<tr>
<td>Total</td>
<td>51</td>
<td></td>
<td>70</td>
</tr>
</tbody>
</table>

Worldwide market for all cosmetic esters

~500 kMT

Estimated greenhouse gas potential savings* based on product volume

*Difference between conventional and enzymatic processes.
Solvent-free biocatalysis

Reaction product is substantially pure, no further processing is required.

*Boaz & Clendennen, Cosmetics & Toiletries Magazine, 2009.*
Process comparison: Emollient esters

Conventional

- outputs
  - raw materials
  - volatiles
    - reaction
  - solid
    - filtration
  - by-products
    - bleaching
  - liquid
    - washing
  - liquid
    - drying
  - solid
    - filtration
    - packaging
    - Batch

GEM

- inputs
  - catalyst (re-used)
  - water oxidant
    - >150°C
    - 100-150°C
    - <100°C
  - water
  - filter aid
- outputs
  - liquid
  - packaging
  - Batch or Continuous
What can be Manufactured?

### Enzyme

<table>
<thead>
<tr>
<th>Property</th>
<th>Specification</th>
<th>Typical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identity</td>
<td>Consistent with structure</td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Clear, colorless liquid</td>
<td>Conforms</td>
</tr>
<tr>
<td>Assay</td>
<td>95% min.</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Acid number</td>
<td>2 max.</td>
<td>&lt;1.5</td>
</tr>
<tr>
<td>Pt-Co (APHA) color</td>
<td>25 max.</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Iodine value</td>
<td>1 max.</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Property</th>
<th>Typical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refractive index</td>
<td>1.4445-1.4465</td>
</tr>
<tr>
<td>Specific gravity at 25°C</td>
<td>0.85-0.865</td>
</tr>
<tr>
<td>Saponification value</td>
<td>150-160</td>
</tr>
</tbody>
</table>
Greenhouse Gas Reduction

52% Reduction
Energy Reduction

59% Reduction
Waste Comparison

93% Reduction
Batch Processing Water Usage

100% Reduction
GEM™ Summary

Batch Process Summary

- 52% GHG emission reduction
- 59% energy reduction
- 93% waste reduction
- 100% process water reduction

Continuous Production would further reduce environmental footprint
Can this impact a formulation?

Cosmetic Emollient & Emulsifier Esters

- Glyceryl Stearate
- Isopropyl Palmitate
- 2-Ethylhexyl Palmitate
- Isopropyl Myristate
- Myristyl Myristate
- Glyceryl Oleate
- Isononyl Isononanoate
- Isostearyl Linoleate
- Hexyl Laurate
- Cetyl Ricinoleate
- Cetyl Palmitate
- Isopropyl Isostearate

Skin Care Product

- Frag/Pres/Thickener (5%)
- Emulsifiers (7%)
- Emollients (18%)
- Water (70%)

Green your product by 7%

These ingredients are also used in color cosmetics and AP DEO Products
October 2011 release a report titled “Biotechnology and its Role in Sustainable Design”
The beauty is in the process