Next Generation Chemical Preservatives:
Protecting People, Products, and our Planet

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Preservatives are necessary in liquid products

All water-based consumer products require preservation

Preservatives prevent growth of bacteria, yeast, and mold
  ◦ Odor issues
  ◦ Product performance
  ◦ Pathogens

Image source: soapqueen.com
Conventional preservatives can be hazardous to human health and the environment

Preservatives are bioactive molecules by design

Human health risks:
- Skin and eye irritation
- Skin and respiratory sensitization
- Endocrine activity
- Cancer
- Reproductive toxicity

Environmental risks:
- Not degraded by sewage treatment
- Acute toxicity
- Bioaccumulation and bioconcentration
- Persistence

Image sources: Mayo Foundation; usresponserestoration.wordpress.com
Goal:
Recommend safer preservatives for home and personal care products
How we approached this challenge

Partner organizations

From biomimicry to industrially relevant chemicals

Evaluation of alternatives

Beyond “drop-ins” – formulation strategies

Concluding thoughts and recommendations
Partnerships with industry support actionable research

BEAUTYCOUNTER
Cosmetics
FDA-regulated
Acidic pH
Replace phenoxyethanol

SEVENTH GENERATION
Home and personal care
EPA-regulated
Basic pH
Replace isothiazolinones

Safer, effective, biodegradable alternatives
Inspiration from biology translates into functional themes

Membrane disruption
- Fatty acids (human skin)
- Terpenes (Douglas fir tree)
- Cationic peptides (Chungan frog skin)

Synergistic formulation
- Peptide mixture (American dog tick)
- Nonanal, indole (Reticulated giraffe)

Iterative evaluation...

Inspiration from Biology

- Biomimetic Strategies (structural and functional themes)

- Physical/Chemical Properties
  - (volatility, pKa, water solubility)

- Antimicrobial Potency
  - (minimum inhibitory concentration, mechanism of action)

- Health Hazards
  - (acute, chronic, ecotoxicity)

Existing Product Formulations
...takes us from biology to biomimetic design

Terpenes

Peptides

Flavonoids

Fatty Acids

Image sources: en.wikipedia.org, examiner.com, naturesbounty.ca
Terpenes: a diverse natural toolkit

Over 74,000 known small molecule terpenes are known.

Cyclization of simple precursors generates enormous diversity.

Functions range from hormones to structural components:
- Antimicrobials are among the most common.

Precedent for use in home and personal care products

Common in perfumes, aromatherapy, cleaning products

Added as pure compounds or essential oils

Antimicrobial peptides are safe food preservatives

Chemically or biosynthetically prepared
- Usually expensive

Sensitive to enzyme hydrolysis

Limited use against Gram-positive bacteria

Two examples used in food
- Inexpensive
- FDA approved GRAS (Generally Recognized as Safe)
- Used in formulations and packaging

Polylysine

Nisin

Image source: en.wikipedia.org
Flavonoids have diverse functions in plants

Secondary plant metabolites
Found in fruits, vegetables, nuts, seeds, flowers, and plant-based products

Functions:
- Pigments in flowers
- UV-B radiation protection agents in leaves
- Antimicrobials against fungal pathogens
Precedents for use

Common in household and cosmetics products
  ◦ By-products in plants extracts and essential oils

Possible pharmaceutical use
  ◦ Synthetic modifications for new antimicrobials in medicine

Antimicrobial lipids are multifunctional ingredients

Advantages
- Naturally derived from vegetable oils
- Inexpensive
- Naturally abundant on human skin
- Common ingredients in cosmetics
  - Emollient, emulsifier, surfactant

Disadvantages
- Limited activity against Gram-negative bacteria
Proposed alternatives have comparable efficacy to conventional preservatives

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<tr>
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<th>Terpenes</th>
<th>Peptides</th>
<th>Flavonoids</th>
<th>Fatty Acids</th>
<th>Parabens</th>
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<td><strong>Gram-positive Bacteria</strong></td>
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+ low efficacy  
++ moderate efficacy  
+++ high efficacy
Hazards might be avoided at low concentrations

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1: low hazard  
2: medium hazard  
3: high hazard  
DG: data gap
Take advantage of multifunctional ingredients

Common ingredients can be exploited for their diverse properties

Advantages:
- **Cost**
- **Ease of formulation**
- **Consumer acceptance**
- **Regulatory compliance**

1. **Monoglycerides**
   - Surfactant
   - Emollient
   - Emulsifier
     - *Preservative*

   ![Glyceryl caprylate](image)

2. **Chelators**
   - Water softener
     - *Preservative booster*

   ![GLDA](image)

3. **Plant extracts**
   - Antioxidant
     - *Preservative*

   ![Epigallocatechin](image)

4. **Terpenes**
   - Fragrance
     - *Preservative*

   ![Carvacrol](image)
Mixtures can operate synergistically or antagonistically

Antimicrobials may act **synergistically, additively** or antagonistically

Improve understanding for more efficient formulation

What is the optimal way to target a microbe’s biochemistry?

1. Fractional inhibitory concentration (FIC) = (A/MIC A) + (B/MIC B)

2. Synergy

   menthol + geraniol

   FIC (B. cereus): 0.06

3. Antagonism

   carvacrol + eugenol

   FIC (B. cereus): 4

Functionally similar isomers avoid undesired qualities

Effective antimicrobials may have potentially undesirable properties (e.g. scent)

Isomers may avoid these undesirable attributes

Derivatization obviates unfavorable characteristics

Microbial activation of a chimeric antimicrobial

*In vivo enzymatic ester cleavage* has been shown to deliver and trap molecules in the interior of cells.

Antimicrobial derivatives may likewise be *activated in vivo by microbial enzymes*.
Host-guest encapsulation improves volatility, solubility

Noncovalent inclusion of an antimicrobial in a host molecule or polymer may:

1. **Decrease volatility, scent**
2. **Increase solubility**
3. **Increase guest stability**
Concluding thoughts and recommendations

As drop-in replacements, terpenes, polypeptides, flavonoids, and fatty acids may be safer, effective, and biodegradable preservatives

- Subject to *data limitations, consumer perception,* and *regulation*

A longer view should include new chemical and non-chemical approaches

- Synergy, encapsulation, microbial hydrolysis, chimera complexes
- Innovative packaging

**Industry-academia collaborations** leverage expertise of both sectors

Industry players have an opportunity to *work together to protect people, products, and our planet*
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Questions?