Benefits & Challenges of Alternative Preservative Blends

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Overview

Recent market trends and regulations have driven traditional chemistries or legacy preservatives out of use or to the margins of brand offerings.

Alternative blends are becoming more popular as consumers demand more natural or sustainable raw materials with demonstrable safety profiles.

As traditional preservatives come under increasing regulatory scrutiny and social networking stigma, many formulators have ingredient requirements dictated by highly individualized lists of preferred ingredients.

The Good Old Days - Remember when you reached on the bench and got:

- ✓ broad-spectrum activity
- ✓ single-component preservative
- ✓ long-standing performance (peace of mind)
- ✓ inexpensive and stable formulation cost
- ✓ extensive substrate compatibility
- ✓ wide global acceptance and regulatory compliance
- ✓ safety profile well-established and unchallenged by consumers
- ✓ robust data packages
- ✓ well-inventoried and readily-available
- ✓ easily incorporated into formulations

The New Challenge of Market Demands: The dreaded list of "NO's"

"I am in need of a preservative for my new application. I cannot use: propanediol, IPBC, DMDM hydantoin, MIT, CIT, butylparaben, benzyl alcohol, hexylene glycol, chlorphenesin, sorbic acid, pentylene glycol, imidazolidinyl urea, parabens, triclosan.

I would love to use something natural derived, but not necessary as long as it avoids my list.

It needs to be compatible between pH 5-8, It also needs to be compatible with anionics and nonionic surfactants and CMC right now.

Would you be able to help?"

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The Formulation Environment

Then

- Bench selection criteria focused largely on product stability and ease of formulation only
- Raw materials came in well-preserved with Formalin or CIT/MIT
- Facilities more resistant to latent pathogens
- More synthetic ingredients with initial lower bio-burden potential
- More flexible manufacturing & scale-up options.
- Fewer market demands for transparency into product profile

Now

- Raw materials often unpreserved or more weakly preserved using high activity and pH
- Processing no longer simple; each step must be evaluated for biostability
- Increased chance of biofilm forming pathogens in plant
- Higher initial bio-burden from natural ingredients
- Less flexibility to chemically irradiate raw materials
- More market demand for transparency into the raw material profile
- Formulation Angst!

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The Raw Material Environment:

Unseen benefits of background preservation and synthetic processing

- Raw materials were also often well-preserved in background. Formalin or formaldehyde donors and CIT/MIT were in widespread use.
- Strong background preservation affords added benefit of keeping the manufacturing plant biologically stable.
- More synthetic ingredients with narrow specifications and fewer naturals with lower bio-burdens were typical.
- Less emphasis on minimally-processed raw materials.
- More freedom to chemically purify or irradiate raw materials when needed, even though not common due to cost.

Preservation Strategies

- Selection needs to take into consideration the packaging and use environment
- Overcoming plant hurdles and potential contamination sites thru better manufacturing procedures
- Control of bio-burden thru raw material assessment and selection

- Some smaller manufacturing plants lack the resources to effectively guarantee antimicrobial performance.
  - SOP's
  - QA Personnel
  - Manufacturing Controls
  - Internal testing resources

Alternative Preservative Blends

- Multiple components
- Often on GRAS listing or naturally derived with a widely-established safety profile
- Often with low skin irritation potential
- Containing components that individually have lower efficacy but are effective when combined
- Additionally, blends make use of “Potentiators” - ingredients that contribute some synergy to the kill power of a system as a whole.

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Multifaceted Regulation of Preservatives

Governmental Jurisdiction US:

FDA

- Used in or on living animals or humans

FIFRA / EPA

- Inanimate surfaces; most often claims driven; specific label requirements

Both (dual jurisdiction)

- Direct or indirect food uses
- Use on food contact surfaces

Material Preservatives TSCA/EPA

- Chemicals added during industrial processes
    - paints, coatings, adhesives, textiles, paper, cosmetic ingredients
- State Regulations requiring labeling: CA Proposition 65 (initially a groundwater standard)

International Regulations

- (EU) 2017/1224 Limiting CIT to 15 ppm vs.100
- (EU) 2016/1121 of 11 July 2016 amending Annex V to Regulation (EC) No 1223/2009 limiting Ethyl Lauroyl Arginate HCl should be allowed for use as a preconcentration of 0.15 % w/w in mouthwashes, except for children under the age of 10

Commonly Accepted Raw Material Standards that are driving the Market

- Whole Foods Compliance
- EWG (Environmental Working Group)Score
- NPA (Natural Products Association)
- Ecocert/COSMOS Approved
- CleanGredients Listed
- ISO Cosmetic Standard

Trending Market Requirements

- Non GMO
- Vegan
- “Preservative Free” trending claims
- Gluten Free
- Non-petroleum derived
- Minimally processed

Alternative Standards and Third Party Verification

- USDA Organic / NSF ANSI 305 Cosmetic compliance
- Leaping Bunny /Non animal tested
- Free Trade
- Rain Forrest Alliance

Involves a multi-step process for approval:

- ❑Application
- ❑Inspection
- ❑Review
- ❑Resolution
- ❑Certification

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Criteria for Evaluating Blends

- Suitability for your product/market focus
- Spectrum of activity
- Impact on scent and color
- Impact on viscosity
- Long-term stability
- Safety and adverse reactions
- Product oackaging e.g., aerosol restrictions
- Solubility characteristics
- Compatibility with other ingredients
- Application dosage and cost
- MOQ and shelf life
- Sustainability and ethical sourcing
- Public opinion

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Common Blend Ingredients

- Caryll Glycol
- Phenoxyethanol
- Phenethyl Alcohol
- 1,3 Propane diol
- Ethylhexyl Glycerin
- Glycerin
- Pentylene Glycol
- Benzoic Acid/Sodium Benzoate
- Potassium Sorbate
- Sorbic Acid
- Organic oils: Basil, Lemongrass
- Salycilic Acid/Sodium Salycilate
- Ethanol
- Iodopropynyl butylcarbamate
- BIT benzyl Isothiazilanone
- Glyceryl Undecylinate

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Product Benefits

- Reduce risk of formulation interactions:
  - odor
  - color
  - viscosity
- Easily incorporated, tend to migrate quickly to the solvent interfaces
- Most can survive common process temps and are cold-processable
- Lower toxicity profiles than older single-component preservatives
- Potential co-functions of ingredients (multifunctional)
  - emolliency
  - moisturization
  - humectancy
  - solvency

Product Challenges

- Individual marketing department concerns
- Formulation costs
- Higher usage levels
- Interference with sensory aspects and viscosity profile
- Color interactions
- Long-term stability
- Latent bio-burden of raw materials must be considered

Example 1: Ingredient Profile

1,3 Propanediol, EWG Score 1

- ✓ Co-Function: humectant/moisturizer; co-solvent

Ethylhexylglycerin, EWG Score-1

- ✓ Co-Function – Skin conditioning agent, Enhances the activity of other preservatives
- ✓ Antimicrobial – Strong against bacteria, weak against fungal

Potassium Sorbate, EWG Score-3

- ✓ pH control and stability in formulations.

Physical form: Clear Liquid

Solubility: Water Soluble

Example 1: Efficacy

- "Low Solids Baby Wash Type Formulation"

Mixed Inoculum Initial Control Counts

Mixed Bacterial Inoculum 1.3 x 106 Mixed Fungal Inoculum 9.8 x 105

Mixed Bacteria Counts	Lincoln ID	Sampling Intervals				
Low Solids Baby Wash		Day 0 Count (cfu/mL)	Day 7 Count (cfu/mL)	Day 14 Count (cfu/mL)	Day 21 Count (cfu/mL)	Day 28 Count (cfu/mL)
1.5% Preservative #1	110314S	6.3 x 10^4	<10	<10	<10	<10

Mixed Fungal Counts	Lincoln ID	Sampling Intervals				
Low Solids Baby Wash with		Day 0 Count (cfu/mL)	Day 7 Count (cfu/mL)	Day 14 Count (cfu/mL)	Day 21 Count (cfu/mL)	Day 28 Count (cfu/mL)
1.5% Preservative #1	110314S	3.3 x 10^5	<10	<10	<10	<10

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Example 1: Toxicology Testing

Propanediol, Ethylhexylglycerin, Potassium Sorbate

HET-CAM (Eye Irritation Potential)

1.5% Preservative Blend #1 Gentle Baby Shampoo

INCI List of Ingredients: Cocamidopropyl Hydoxysutaine;

Sodium Coco Sulfate; Disodium Lauroamphodiacetate

Ocular Irritation:

10% test solution of the shampoo scored 0.25 compared to industry standard baby shampoo which scored 1.75.

Results: little or no ocular irritation potential *in vivo*.

Example #2 (Good EWG Compliance) Ingredient Profile

Typical Use Levels/pH range 0.5% - 2.0%
Optimal formulation pH range 3 – 10

Pentylene Glycol - EWG Score – 0

- •Co-Function – Skin conditioning
- •Antimicrobial activity– Strong against bacteria and yeast, weak against molds

Caprylyl Glycol, - EWG Score 0

- •Co-Function – Emollient, skin and hair conditioning agent
- • Antimicrobial activity– Strong against bacteria and medium against fungi

1,3 Propanediol- EWG Score – 1

- • Co-Function – Humectant and Moisturizer

Ethylhexylglycerin, EWG Score-1

- •Co-Function – Skin conditioning agent, Enhances the activity of other preservatives
- •Antimicrobial – Strong against bacteria, weak against fungal

Example #2 Efficacy: Shampoo

Pentylene Glycol; Capryly Glycol;1,3 Propanediol; Ethylhexylglycerin

Shampoo pH 7.5	**Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Fungi (*A. niger* & *C. albicans*)**				
	Day 0	**Day 7**	**Day 14**	**Day 21**	**Day 28**
0.65% Preservative Blend #2	1-3x10^5	<10	<10	<10	<10
Unpreserved Shampoo – pH 7.5	1-3x10^5	1-3x10^5	1-3x10^5	1-3x10^5	1-3x10^5

Shampoo	**Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Bacteria (*P. aeruginosa, E. coli and S. Aureus & B. Cepacia)***				
	Day 0	**Day 7**	**Day 14**	**Day 21**	**Day 28**
0.65 % Preservative Blend #2	1-3x10^6	<10	<10	<10	<10
Unpreserved Shampoo –pH 7.5	1-3x10^6	1-3x10^6	1-3x10^6	1-3x10^6	1-3x10^6

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Example #2 Efficacy: Emulsion

Pentylene Glycol; Capryly Glycol;1,3 Propanediol; Ethylhexylglycerin

Skin Care Emulsion pH 7.0	**Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Fungi (*A. niger* & *C. albicans*)**				
	Day 0	**Day 7**	**Day 14**	**Day 21**	**Day 28**
0.8% Preservative blend #2	**$1\text{-}3x10^5$**	**<10**	**<10**	**<10**	**<10**
Unpreserved Emulsion – pH 7	**$1\text{-}3x10^5$**	**$1\text{-}3x10^5$**	**$1\text{-}3x10^5$**	**$1\text{-}3x10^5$**	**$1\text{-}3x10^5$**

Skin Care Emulsion pH 7.0	**Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Bacteria (*P. aeruginosa, E. coli and S. Aureus & B. Cepacia)***				
	Day 0	**Day 7**	**Day 14**	**Day 21**	**Day 28**
0.8% Preservative Blend Example #2	**$1\text{-}3x10^6$**	**<10**	**<10**	**<10**	**<10**
Unpreserved Emulsion – pH 7	**$1\text{-}3x10^6$**	**$1\text{-}3x10^6$**	**$1\text{-}3x10^6$**	**$1\text{-}3x10^6$**	**$1\text{-}3x10^6$**

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Example #3: Whole Foods

Compliant cost-effective blend

Typical Use Levels/pH range 0.5% - 1.5%
Optimal formulation pH range 3 – 10

Ingredient Profile:

Phenoxyethanol CAS# 122-99-

Caprylyl Glycol CAS#1117-86-8

Ethylhexylglycerin CAS# 70445-33-9

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Example #3: Challenge testing

Skin Care Emulsion Preservative Blend #3	**Double Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Fungi (*A. niger* & *C. albicans*)**					
	Day 7	**Day 14**	**Re Challenge Day 7**	**Re Challenge Day 14**	**Re Challenge Day 21**	**Re Challenge Day 28**
0.75% Preservative	<10	<10	<10	<10	<10	<10
Unpreserved Emulsion – pH 7	1-3x10^5	1-3x10^5	1-3x10^5	1-3x10^5	1-3x10^5	1-3x10^5

Skin Care Emulsion Preservative Blend #3	**Double Challenge Data – Colony Forming Units per Gram (cfu/g) Mixed Bacteria (*P. aeruginosa, E. coli and S. Aureus & B. Cepacia*)**					
	Day 7	**Day 14**	**Re Challenge Day 7**	**Re Challenge Day 14**	**Re Challenge Day 21**	**Re Challenge Day 28**
0.75% Preservative	<10	<10	<10	<10	<10	<10
Unpreserved Emulsion – pH 7	1-3x10^6	1-3x10^6	1-3x10^6	1-3x10^6	1-3x10^6	1-3x10^6

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Example #4: All Natural Blend

-Phenethyl alcohol

-Natural Derivation: Corn based.

- Co-Functions – Fragrance Ingredient, not listed as a preservative in EU;
- Antimicrobial – Strong against bacteria and moderate against fungi(yeast/mold)
- EWG (Environmental Working Group) score – 1

-Pentylene Glycol

- Natural Derivation: Sugar Cane/Corn cobs.
- Co-Function – Skin Conditioning
- Antimicrobial – Strong against bacteria and yeast, weak against molds
- EWG Score – 0

-Propanediol, CAS# 504-63-2, all natural from corn.

- Function – Humectant and Moisturizer
- Antimicrobial –Boosts efficacy against fungi and bacteria
- EWG (Environmental Working Group) score – 1

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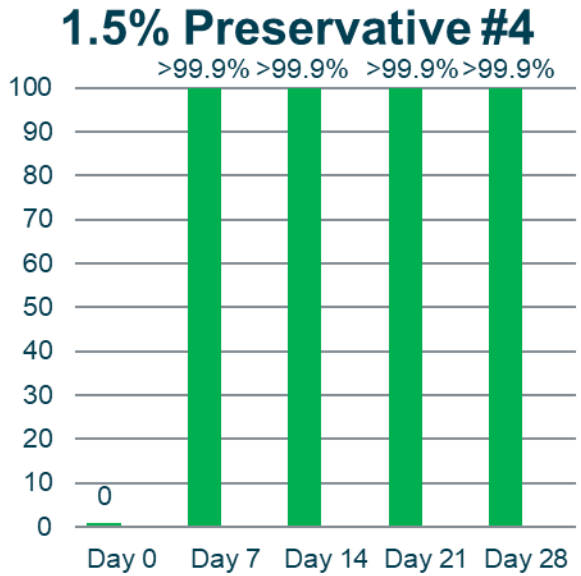
Example #4: Natural Blend
Physical properties and safety

- Physical form: clear, water, white liquid
- Low odor
- Minimal impact on viscosity
- Solubility in water <1.2%
- Typical Use Level 0.5% - 2.0%
- Effective pH range 3 – 10

- **Toxicology Testing**
- Repeated Insult Patch Test Results: Preservative in skin cream on 50 subjects showed No Dermal Irritation or Sensitization

Example #4: Natural Blend Challenge Testing in skin cream

% Reduction against mixed bacteria (starting inoculum 1-3x10^6) and mixed fungi (starting inoculum 1-3x10^5)



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Conclusion: Benefits of Preservative Blends

- Effective preservation across most personal care platforms
- Ease of manufacture
- Customized combinations meet many market demands.
- Most ingredient listings address perceived health concerns
- Standard rations afford quicker development
- Ease of development combined with predictable scale up
- Inventory cost and complexity reduced

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Questions

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