

Effectiveness of Alternative Antimicrobial Agents for Disinfection

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National Collaborating Centre for Environmental Health
EH Seminar Series
December 13, 2011



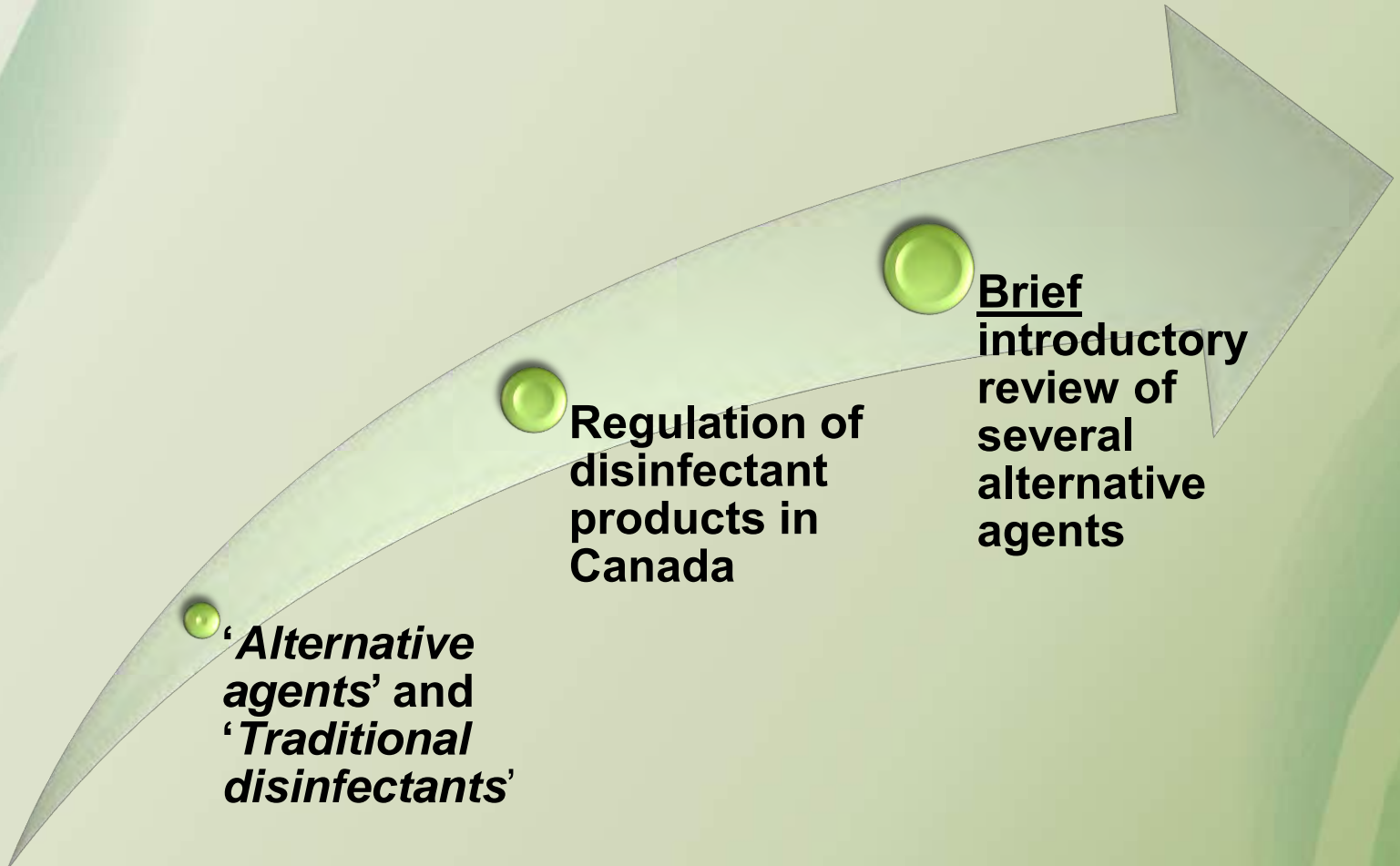
National Collaborating Centre
for Environmental Health

Centre de collaboration nationale
en santé environnementale



BC Centre for Disease Control
An Agency of the Provincial Health Services Authority

Outline



***'Alternative
agents' and
'Traditional
disinfectants'***

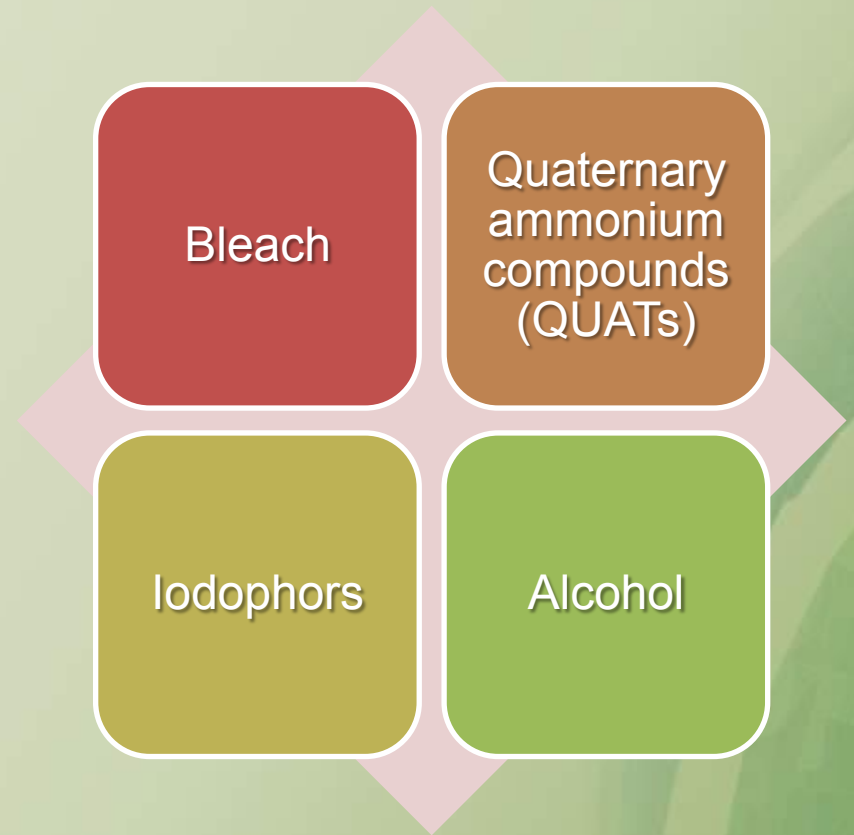
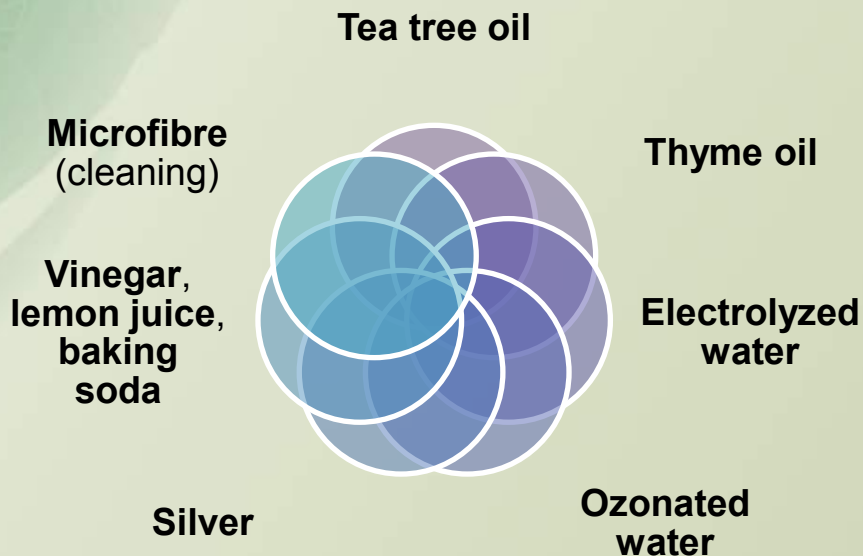
**Regulation of
disinfectant
products in
Canada**

**Brief
introductory
review of
several
alternative
agents**

What are they?

‘Alternative’ (in this presentation)

‘Traditional’ *

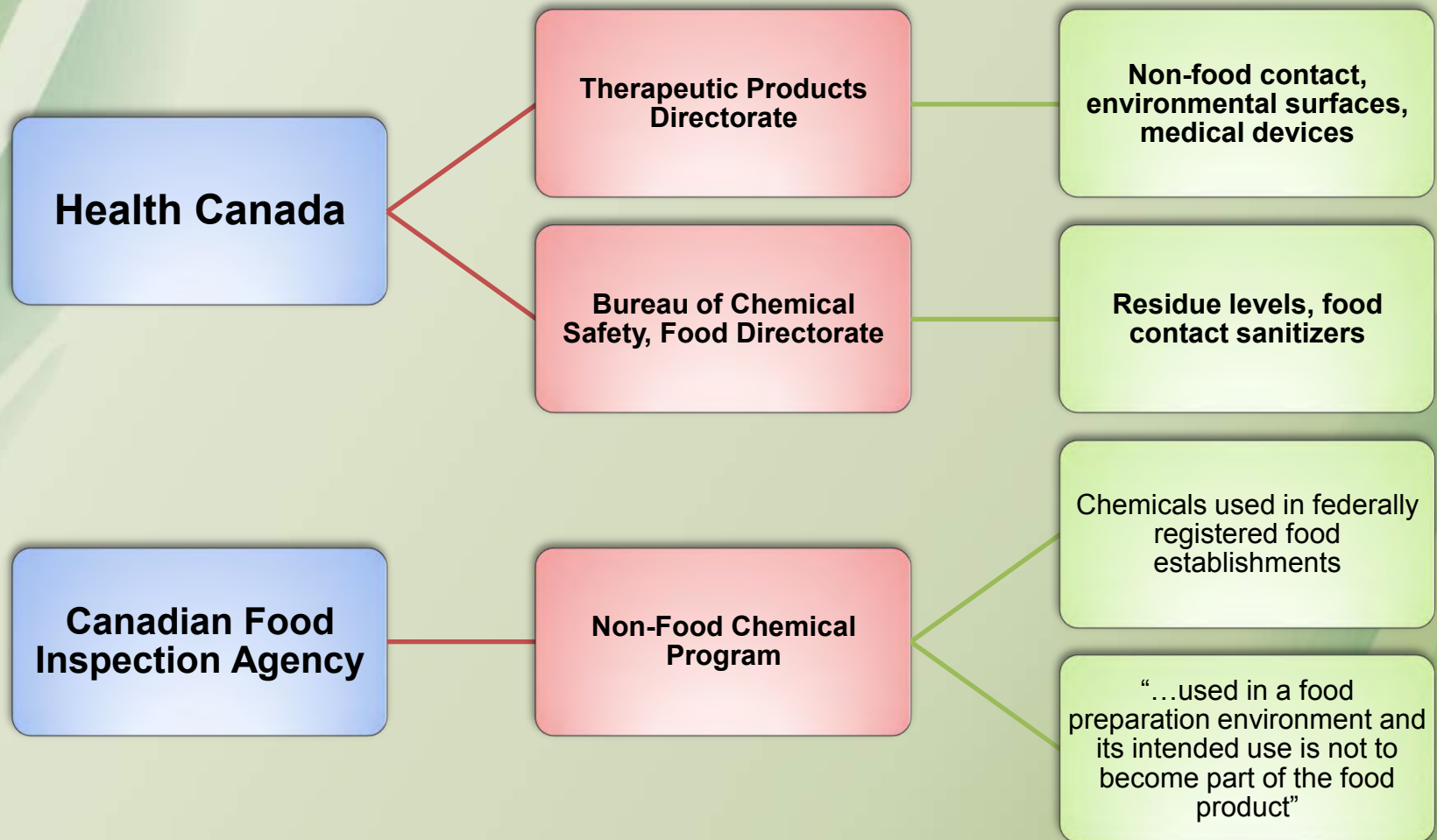


*For more on „traditional’ disinfectants please see: NCCEH evidence review on ***Disinfectants and Sanitizers for Use on Food Contact Surfaces*** (http://www.ncceh.ca/en/practice_policy/ncceh_reviews/food_contact_sanitizers)

Regulation of Disinfectants in Canada

- „Disinfectants’ are “drugs” defined by the *Food and Drugs Act*
 - *any substance or mixture of substances manufactured, sold or presented for use in:
[...] disinfection in premises where food is manufactured, prepared or kept*
- IF the product has „disinfectant claims’, must have a Drug Identification Number (DIN)
 - Not all *sanitizers* have „disinfectant claims’, hence no DIN; they may still have substantial antimicrobial properties

Regulation of Disinfectants in Canada





Health
Canada Santé
Canada

Your health and
safety... our priority.

Votre santé et votre
sécurité... notre priorité.

Drug Identification Number (DIN)

What is a DIN?

A Drug Identification Number (DIN) is a computer-generated eight digit number assigned by Health Canada to a drug product prior to being marketed in Canada. It uniquely identifies...

Canada

Health Canada - Drug Product Database

<http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php>

Product Name: BENEFECT BOTANICAL DISINFECTANT

DIN: 02242474 Electronic Product Monograph is not available

Company: SENSIBLE LIFE PRODUCTS
34 7 Innovation Drive
Flamborough
Ontario
Canada L9H 7H9

Class: Disinfectant

Dosage Form(s): Spray

Route(s) of Administration: Disinfectant (Domestic)
Disinfectant (Food Premises)
Disinfectant (Hospital/Hc Facilities)
Disinfectant (Institutional/Industrial)

Number of Active Ingredient(s): 1

Schedule(s): OTC

American Hospital Formulary Service (AHFS): ? 38:00.00 DISINFECTANTS (FOR AGE

Anatomical Therapeutic Chemical (ATC): ? V07AV TECHNICAL DISINFECTANTS

Active Ingredient Group Number: ? 0101107005

Active Ingredient(s)
THYMOL (THYME OIL)

Strength
0.23 %

[Food > Reference Listing](#)

About the CFIA

[Overview](#)
[Acts and Regulations](#)

Subjects


Food

Reference Listing

- [Using the Reference Listing](#)
- [Frequently Asked Questions](#)
- [Guidelines for Submission](#)

Animals

Plants

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[Proactive Disclosure](#)

Reference Listing of Accepted Construction Materials, Packaging Materials and Non-Food Chemical Products

Use of "marketing claims" as advertising related to the Canadian Food Inspection Agency (CFIA) or other government agencies:

Please note that any references related to CFIA logo, Agriculture and Agri-Food Canada or Health Canada certifying acceptance, approval, evaluation, registration, homologation or a category in the CFIA's reference listing, e.g. : sub-category N1, are not acceptable and should not be used as marketing tools on a private label and or any advertising tools. This is also applicable to any other communication mediums with the clientele, e.g. : website, catalogue, brochure etc., in regards to the mandatory pre-market evaluation of non-food chemicals, construction materials and packaging materials by the present program prior to their use in registered food establishments in Canada.

Therefore our policies do not permit the use of the CFIA's name or any other government agencies as mentioned above by a commercial entity. This practice may be considered as an endorsement from our Agency or other government agencies and consequently should be deleted from any marketing tools used by a Canadian or a foreign manufacturer.

[Using the Reference Listing](#)

Last Update: 2011/12/05

Search by Category and Sub-category

To view the list of companies and their products, please select a category and a sub-category.

Categories

Disinfectants

Sub-Categories

--- Select All ---

No entry in any field will return the entire list.

SUBMIT

Regulation of Disinfectants in Canada

“Intended Use”

General criteria in evaluation:

- Efficacy
- Safety
- Quality

Application-specific

- Hospital, institutional, food premise, residual activity, target organisms
- *Need to read and understand labels and manufacturer instructions*

HOUSEHOLD ALLERGENS: Pre-clean (heavily) soiled surfaces. Discard wipe. Use a fresh wipe to remove dust mite debris, pet dander, pollen particles, dust, dirt and hair that may cause sneezing. Unplug small appliances before cleaning. NOT recommended for polished or bare wood surfaces. NOT intended for personal hygiene. DO NOT use on utensils, dishes or glasses.

→ **To Sanitize (Kill 99.9%):** *Salmonella enterica*, *Escherichia coli* (E. coli), *Staphylococcus aureus* (Staph), *Streptococcus pyogenes* (Strep), Methicillin Resistant *Staphylococcus aureus* (MRSA), *Campylobacter jejuni*, *Listeria monocytogenes*, and *Enterobacter aerogenes*, allow surface to remain wet for 30 seconds.

→ ***To Disinfect (Kill 99.99%+):** *Salmonella enterica*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, Respiratory Syncytial Virus, Swine Influenza A (H1N1) virus allow surface to remain wet for 10 minutes. Allow surface to air dry.

→ **For surfaces that come in contact with food:** Use only on hard non-porous surfaces and rinse thoroughly with water.

→ **To Disinfect Toys:** Use only on hard non-porous surfaces. Use enough fresh wipes to thoroughly wet surfaces. Wipe surface and allow to remain wet for 10 minutes. Allow surface to air dry. Toss dirty wipe away. Rinse thoroughly with water after use.

FOR CHILDREN

Criteria Test Organisms for Disinfectants

- **Spores:**
 - *Bacillus subtilis* and *Clostridium sporogenes*
- **Mycobacteria:**
 - *Mycobacterium bovis*
- **Virus:**
 - Poliovirus, Type 1 (Sabin)
- **Fungi:**
 - *Trichophyton mentagrophytes*
- **Bacteria:**
 - *Salmonella choleraesuis* (*S. enterica*), *Pseudomonas aeruginosa*, and *Staphylococcus aureus*

Performance Criteria for Microbicidal Efficacy

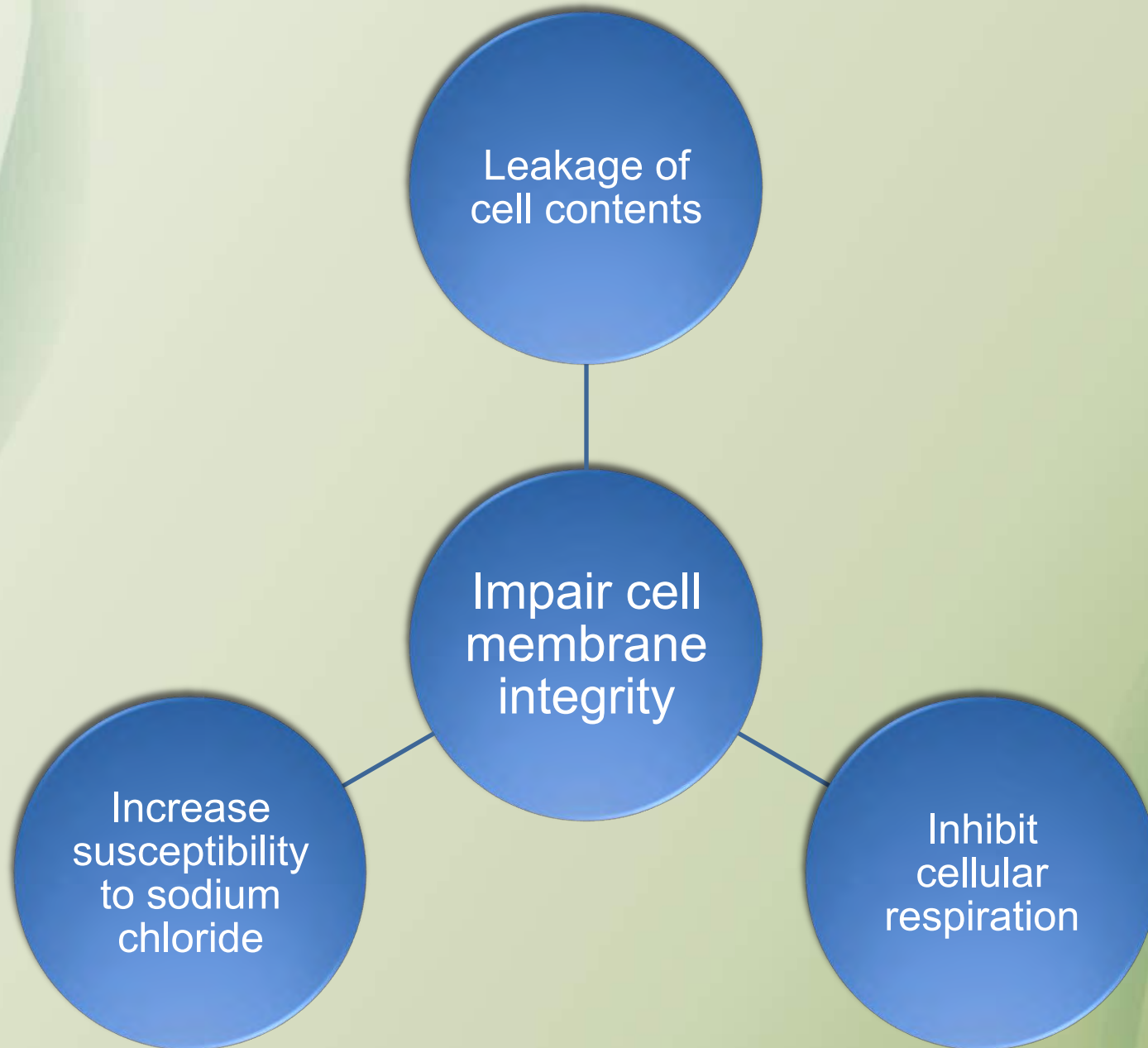
Type of organism (claim)	Level of Disinfection	Reduction Criteria
Bacterial spores (sporicide)	Chemosterilization (CS), high level disinfection (HLD)	$\geq 6 \log$ (99.9999%)
Mycobacteria (mycobactericide)	CS, HLD Intermediate level disinfection	$\geq 6 \log$ (99.9999%) $\geq 4 \log$ (99.99%)
Virus (virucide)	Disinfection (general)	Viral "infectivity titer must be reduced by at least 3 \log_{10} beyond the level of cytotoxicity"
Fungi (fungicide)	Disinfection (general)	$\geq 4 \log$ (99.99%)
Bacteria (bactericide)	Disinfection (general)	$\geq 5 \log$ (99.999%)

1. Tea Tree oil

Description

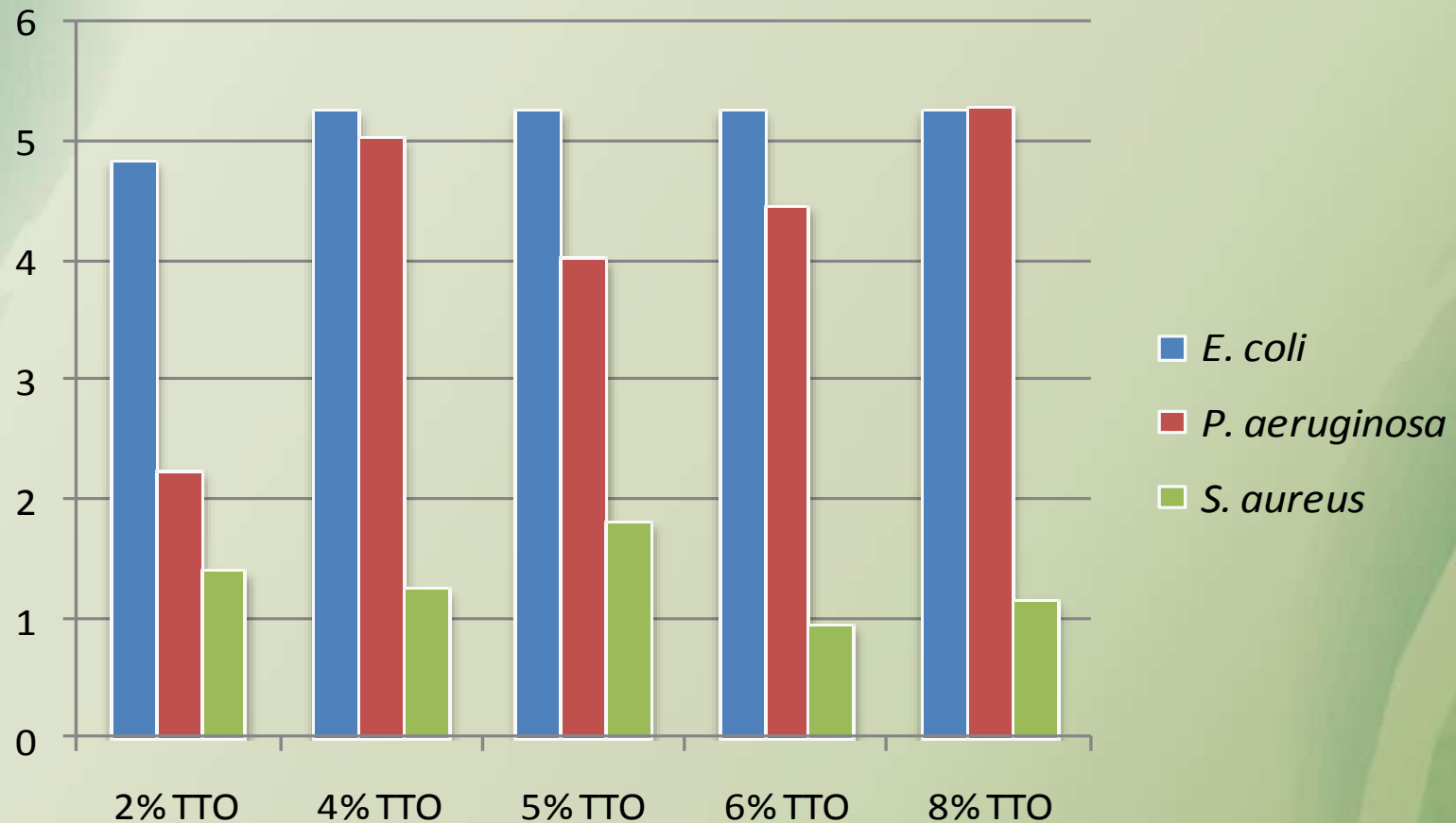
- Essential oil extracted from leaves of a plant (*Melaleuca alternifolia*)
- Present in cosmetic products
 - Deodorants, shampoos, hair products, skin products,
- Often used as topical anti-inflammatory:
 - skin infections, acne, ringworm, scabies, and athlete's foot
- Int. standards for chemical composition (ISO 4730)





Tea Tree Oil – antimicrobial efficacy

Log reduction, 5 min contact time



Data from: Messenger et. al., 2005

Tea Tree Oil – antimicrobial efficacy

Organism	MIC (% v/v)	MBC/MFC (% v/v)
<i>Bacillus cereus</i>	0.3	–
<i>Escherichia coli</i>	0.08 – 2	0.25 – 4
<i>Pseudomonas aeruginosa</i>	1– 8	2– >8
<i>Staphylococcus aureus</i>	0.5–1.25	1–2
MRSA	0.04–0.35	0.5
<i>Aspergillus flavus</i>	0.31–0.7	2–4
<i>A. niger</i>	0.016–0.4	2–8
<i>Trichophyton mentagrophytes</i>	0.11–0.44	0.25-0.5

MIC = Minimum inhibitory concentration (inhibit growth/replication)

MBC/MFC = Minimum bactericidal/fungicidal concentration (kills microbe)

Data from: Carson et al., 2006

Tea Tree Oil – toxicity

- Ingestion of undiluted TTO
 - Confusion, inability to walk, disorientation, ataxia, unconsciousness, coma
- Dermal exposure (cosmetic products)
 - Allergic skin reactions, irritation



Tea Tree Oil – endocrine disruptor?

- Clinical report:
 - 3 cases of prepubertal gynecomastia (abnormal growth of breast tissue)
 - Age 4, 7, and 10 yrs
 - Otherwise healthy boys
 - All had exposure to cosmetic products w/ lavender oil and/or TTO.
 - Discontinued use resolved condition

Tea Tree Oil – endocrine disruptor?

Human cell culture study (Henley et al., 2007)

- Both lavender and TTO induced “*estrogenic and antiandrogenic activities*”



Bioavailability of TTO components known to penetrate skin (Nielson, 2008)

- “The estrogenic potency of TTO was confirmed, but none of the bioavailable TTO constituents demonstrated estrogenicity.”
- “[...] cautions *in vitro* to *in vivo* extrapolations from the mixtures of constituents with potentially varying bioavailabilities.”

Highlights - TTO

Substantial antimicrobial properties

- Inhibits growth of variety of bacteria, fungi

Oral and dermal toxicity may limit use

- Accidental ingestion by children
- Skin sensitizer

Low solubility in water

- Issues with formulation and use on surfaces?

2. Thyme Oil

Description

- Essential oil from herb, *Thymus spp.*
 - Thymol, carvacrol
 - GRAS status (US)
- Uses
 - Food additive
 - Mouthwash (thymol)
 - Other (insufficient evidence to support effectiveness):
 - sore throat, cough, bronchitis
 - **Disinfectant (thymol, carvacrol)**



Thyme Oil – antimicrobial efficacy

- Primary active ingredient in several registered disinfectants
 - At least one has been accepted for use in federally registered food establishments (issued ***no objection letter***)

Product Name: BENEFECT BOTANICAL DISINFECTANT

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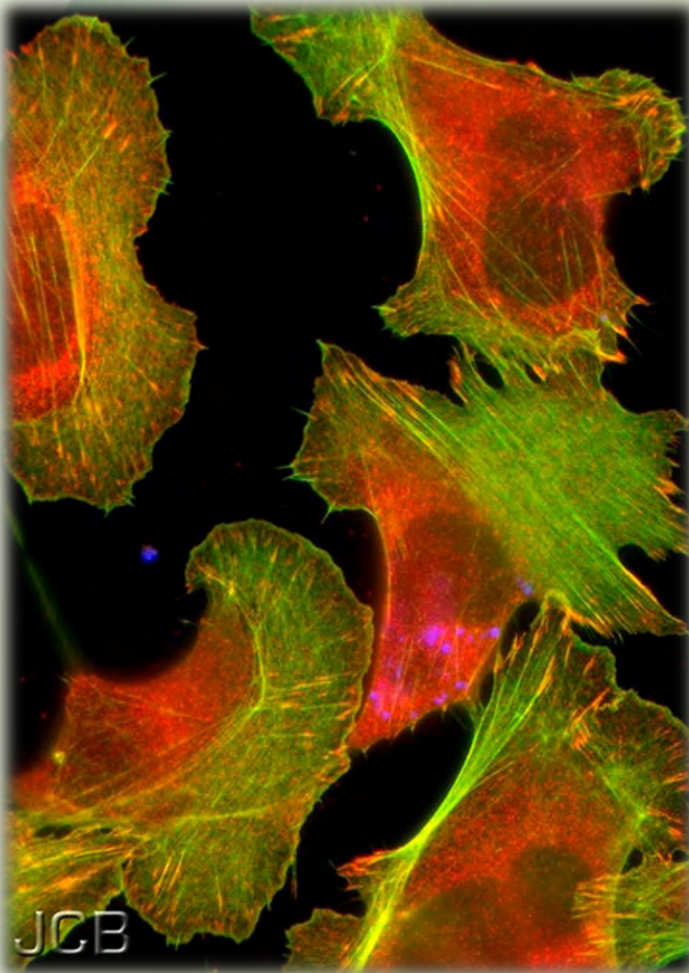
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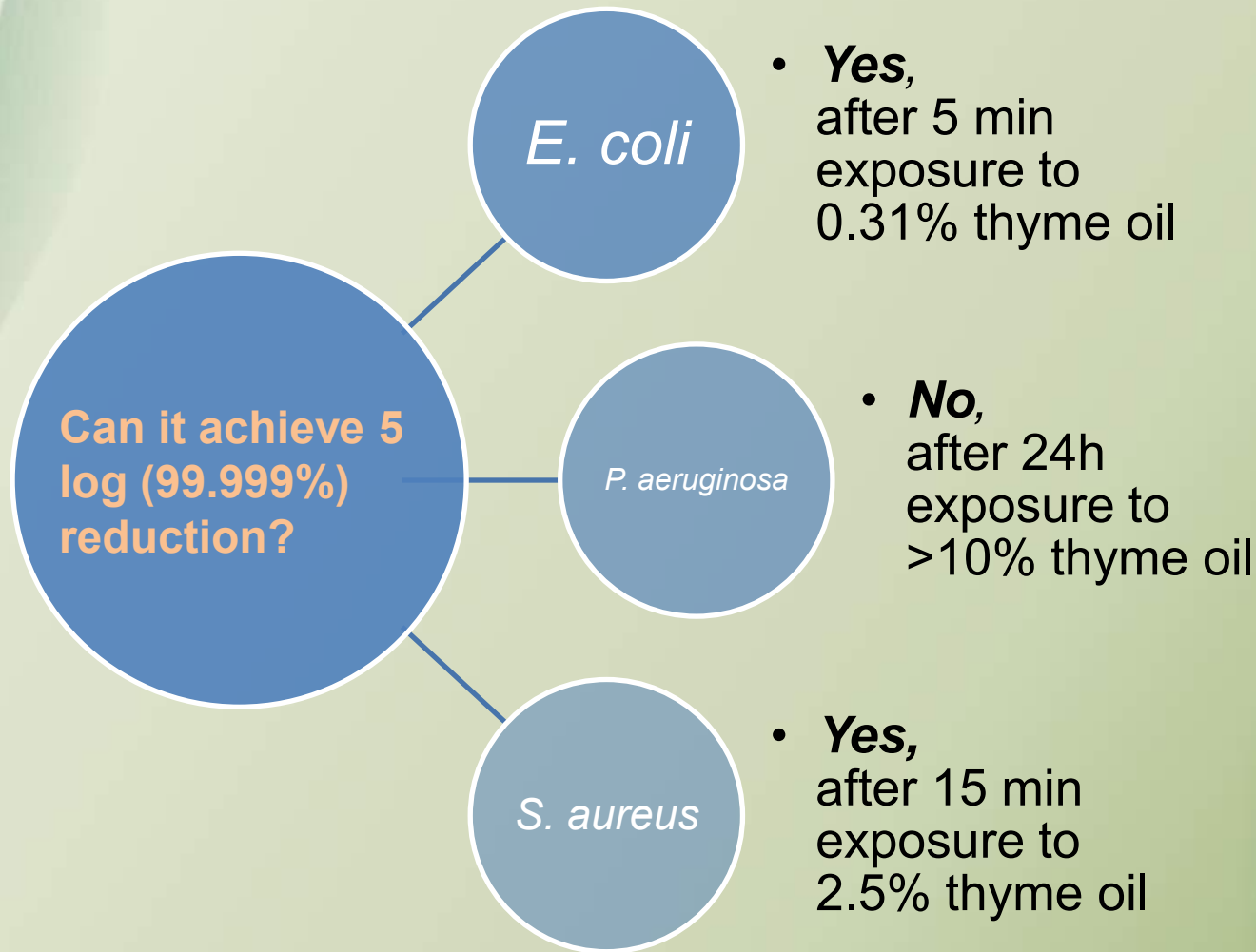
Thyme Oil



Mechanism of action

- Impair cell membrane integrity
 - Leaky cell
 - Decrease in ATP (molecule that drives chemical reactions in cell)
 - Reduction in proton motive force (generates ATP)

Thyme Oil – antimicrobial efficacy



Thyme Oil – antimicrobial efficacy

Organism	MIC (% v/v)	MBC (% v/v)
<i>Escherichia coli</i>	0.045–0.35	0.31
<i>Listeria monocytogenes</i>	0.0156–0.62	0.62
<i>Pseudomonas aeruginosa</i>	>10	>10
<i>Salmonella spp.</i>	0.045– >2	–
<i>Staphylococcus aureus</i>	0.02–0.29	–
<i>Aspergillus flavus</i>	9.35	25
<i>A. niger</i>	9.35	22.5
<i>Stachybotrys chartarum</i>	6.2	12.6

MIC = Minimum inhibitory concentration (inhibit growth/replication)

MBC/MFC = Minimum bactericidal/fungicidal concentration (kills microbe)

Data from: Burt, 2007; Hammer et al., 1999; Mayaud et al., 2008; Segvic Klaric et al., 2007

Highlights – Thyme oil

Primary active ingredient in disinfectant

- Use in at least one HC registered disinfectant

Minimum Risk Pesticide
(US EPA)

- Low oral and dermal toxicity, GRAS status
- Exempt from certain pesticide registration requirements

Listed as a sensitizer and
asthmagen by the
*Association of Occupational
and Environmental Clinics*
(AOEC)

- Concerns with occupational exposure?

3. Electrolyzed Water

FYI

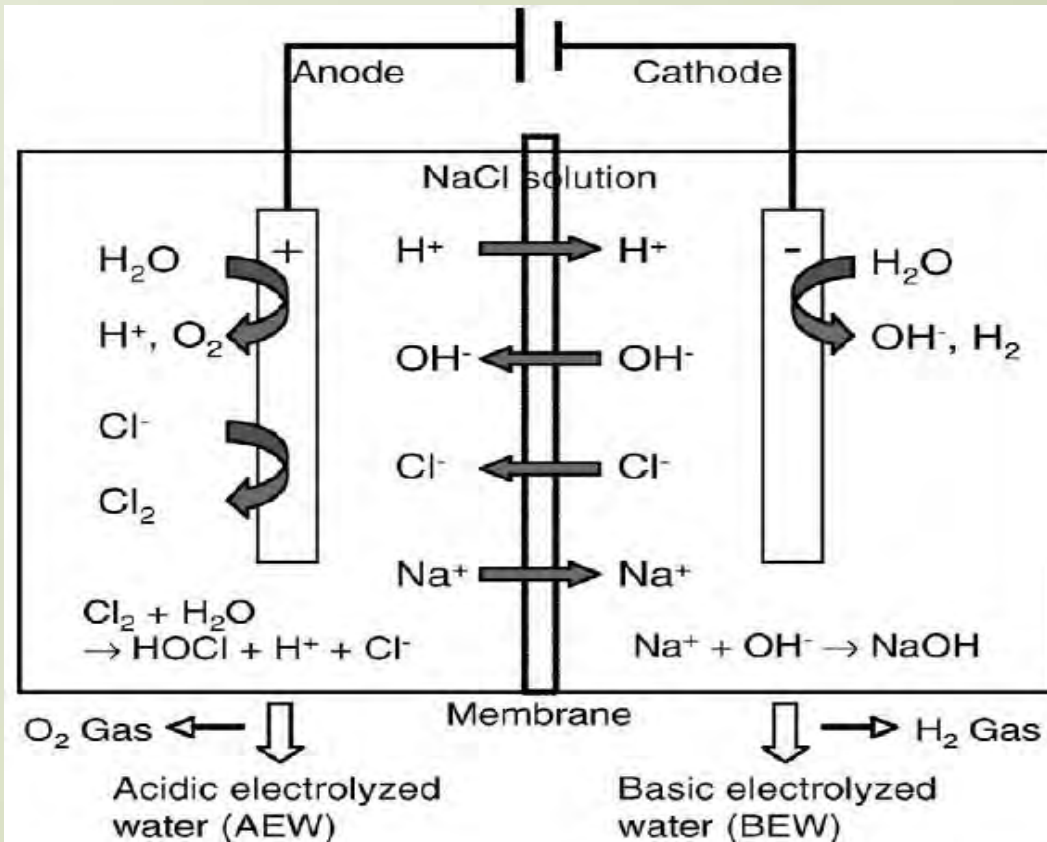


FIGURE 1. Schematic of electrolyzed water generation. The basic chemical reactions at the anode can be summarized as follows: $2\text{H}_2\text{O} \rightarrow 4\text{H}^+ + \text{O}_2\uparrow + 4\text{e}^-$, $2\text{NaCl} \rightarrow \text{Cl}_2\uparrow + 2\text{e}^- + 2\text{Na}^+$, and $\text{Cl}_2 + \text{H}_2\text{O} \rightarrow \text{HCl} + \text{HOCl}$. At the cathode, the main chemical reactions are $2\text{H}_2\text{O} + 2\text{e}^- \rightarrow 2\text{OH}^- + \text{H}_2\uparrow$ and $2\text{NaCl} + 2\text{OH}^- \rightarrow 2\text{NaOH} + \text{Cl}^-$.

Source: Hricova et al., 2008

Electrolyzed Water

- Bottom line...



Salt



Water



Electricity

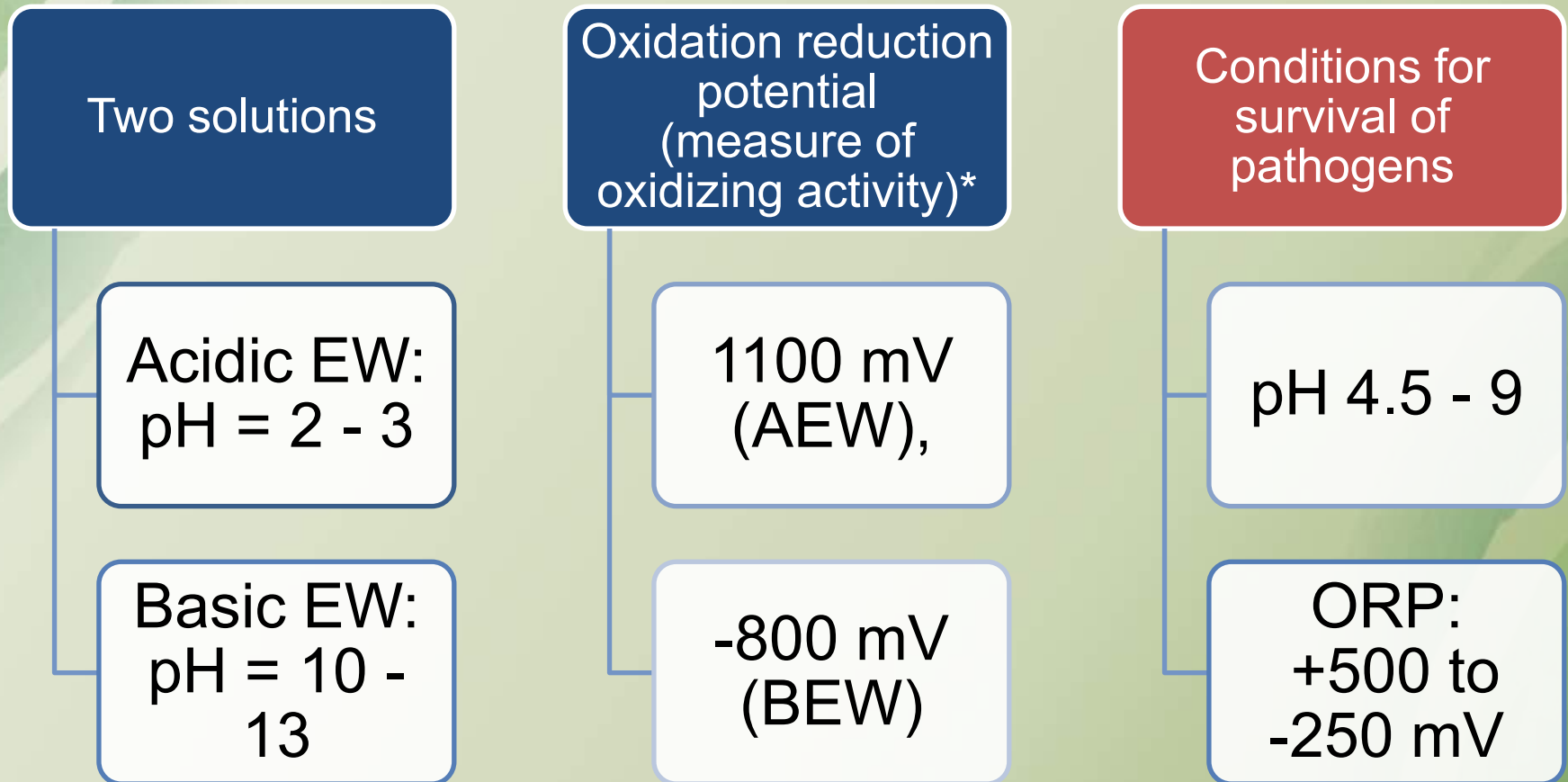


HOCl

Electrolyzed Water

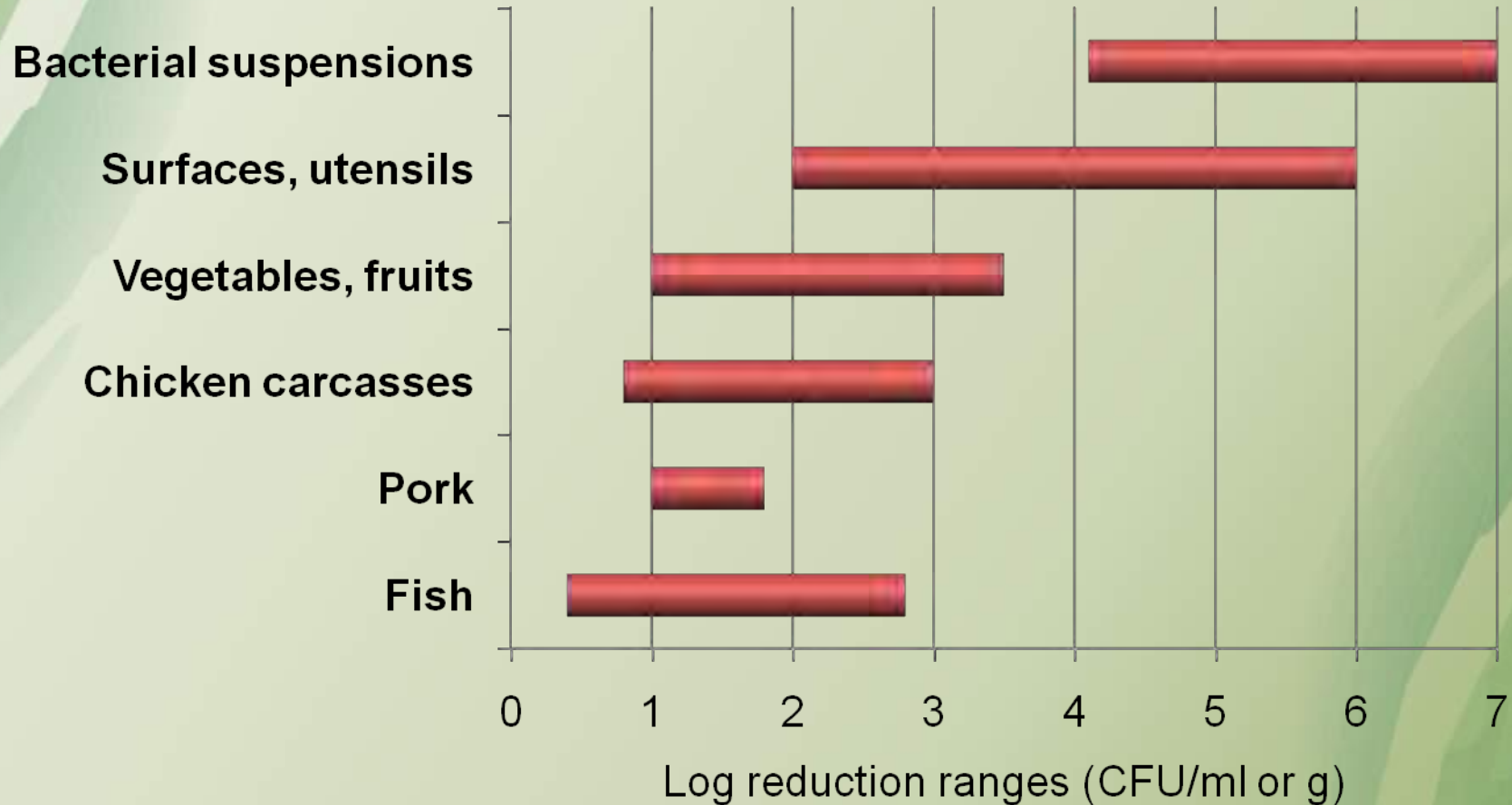
- HOCl (hypochlorous acid)
 - Strong oxidizing agent with antimicrobial activity
 - Active agent in household bleach, pool disinfectant (e.g., sodium hypochlorite)
 - Typically 10-90 ppm
- Why not just use bleach?
 - EW has other properties...

Electrolyzed Water – typical properties



*For comparison, Hydrogen peroxide ORP = 1.77 V; Ozone gas ORP = 2.07 V

Electrolyzed Water – antimicrobial efficacy



Data from: Huang et al., 2008; Hricova et al., 2008; Park et al., 2002; Venkitanarayanan et al., 1999; Vorobjeva et al., 2004; Deza et al., 2005

Electrolyzed Water

- Other applications
 - Sanitizer (AEW, HOCl)
 - Degreaser (BEW, NaOH)
 - Decontamination of cattle hides
 - 47% reduction in hides positive for *E. coli* O157:H7 (Bosilevac et al., 2005)
 - Decontamination of shell eggs
 - >6 log reduction in *S. enteritidis* in 1 min (Cao et al., 2009)

Highlights – Electrolyzed Water

Promising
alternative
agent

- Many potential applications
- Reviews available

Low oral toxicity,
but may be
corrosive

- Lower concentrations of HOCl
- No special handling of hazardous chemicals
- Acidic EW vs. Neutral EW

Rapid loss of
antimicrobial
activity

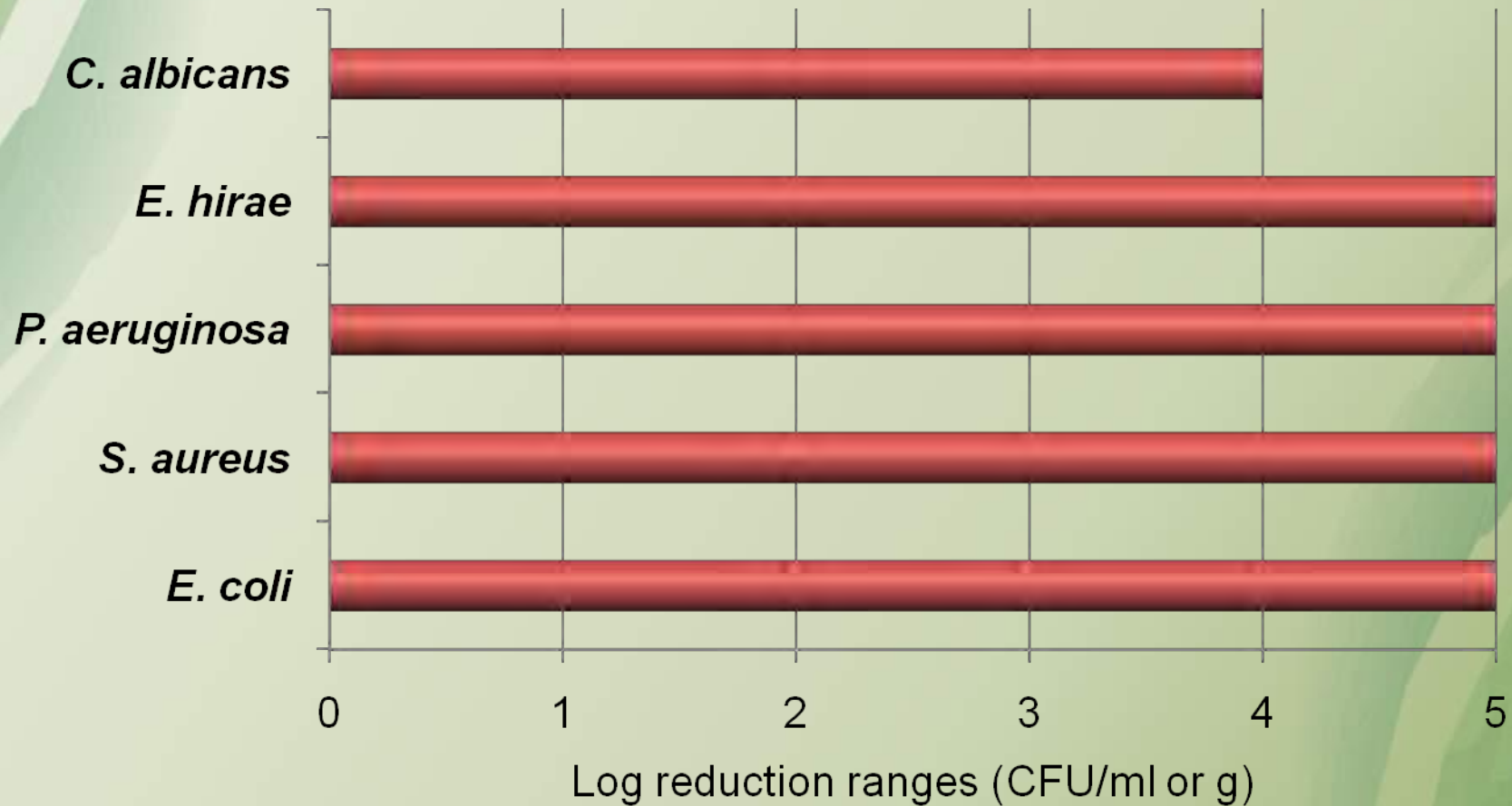
- Hours to days

4. Ozonated Water

- Ozone gas dissolved in water
 - unstable (30 min half life)
- US FDA approved
 - Antimicrobial agent
 - Treat, store, process foods
- NSF registered devices
 - Food processing areas
- CFIA
 - acceptable use in food establishment



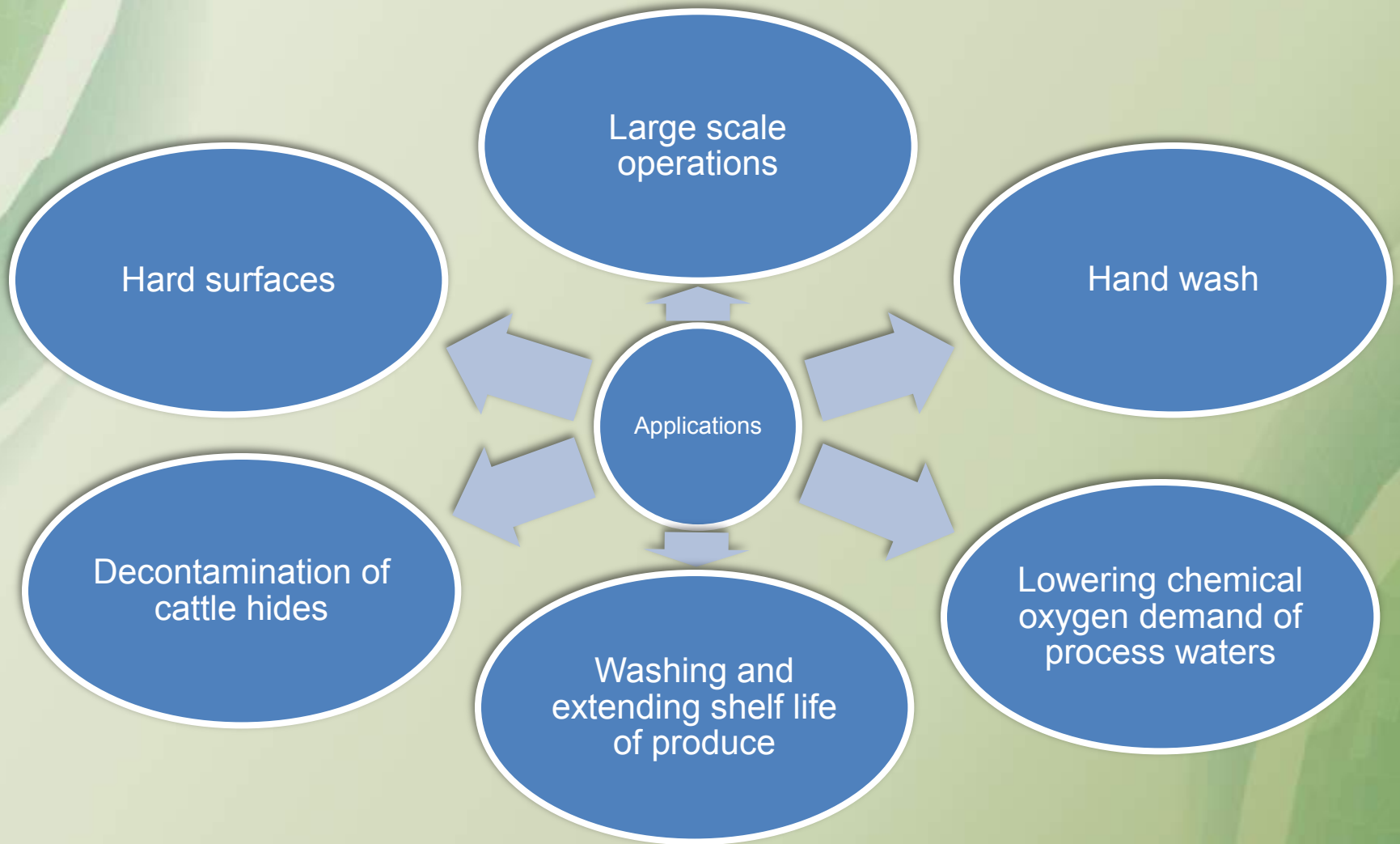
Ozonated Water – antimicrobial efficacy



3 ppm ozone, 30s

Data from: Bialoszewski et al., 2010

Ozonated Water



Highlights – Ozonated Water

Promising
alternative agent

- Many potential applications
- Devices recognized by NSF, U.S. FDA, CFIA

No toxic residues

- No special handling of hazardous chemicals

High start up and
operating cost

- Corona discharge, high energy UV

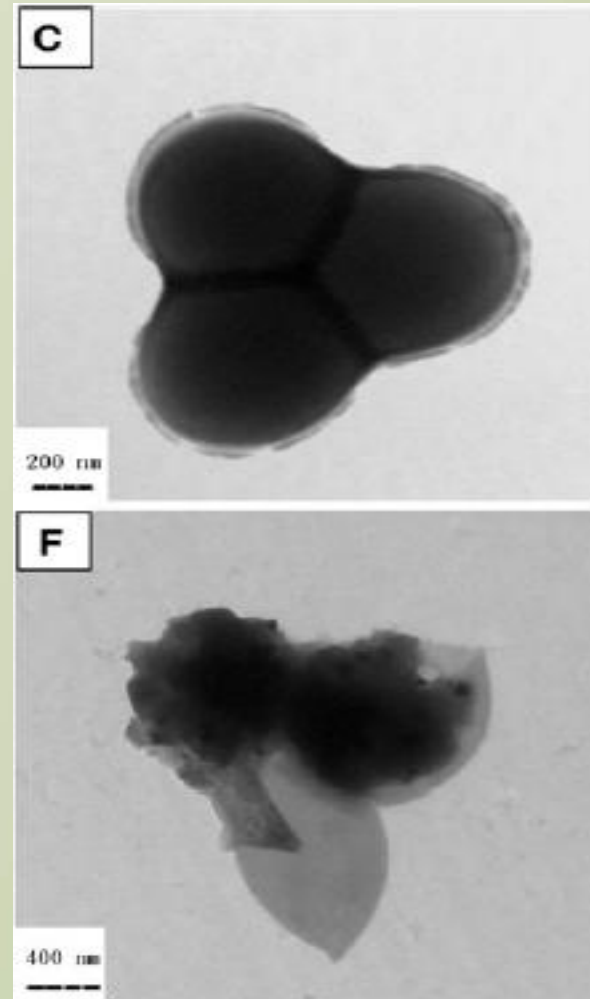
Rapid loss of
antimicrobial activity

- Minutes

5. Silver

Description

- Silver ion (Ag^+)
 - Interfere w/ cellular respiration
 - Interacts with DNA
 - Disruption of proteins
- **Disinfectant**
 - Silver dihydrogen citrate
 - **Residual** antimicrobial activity

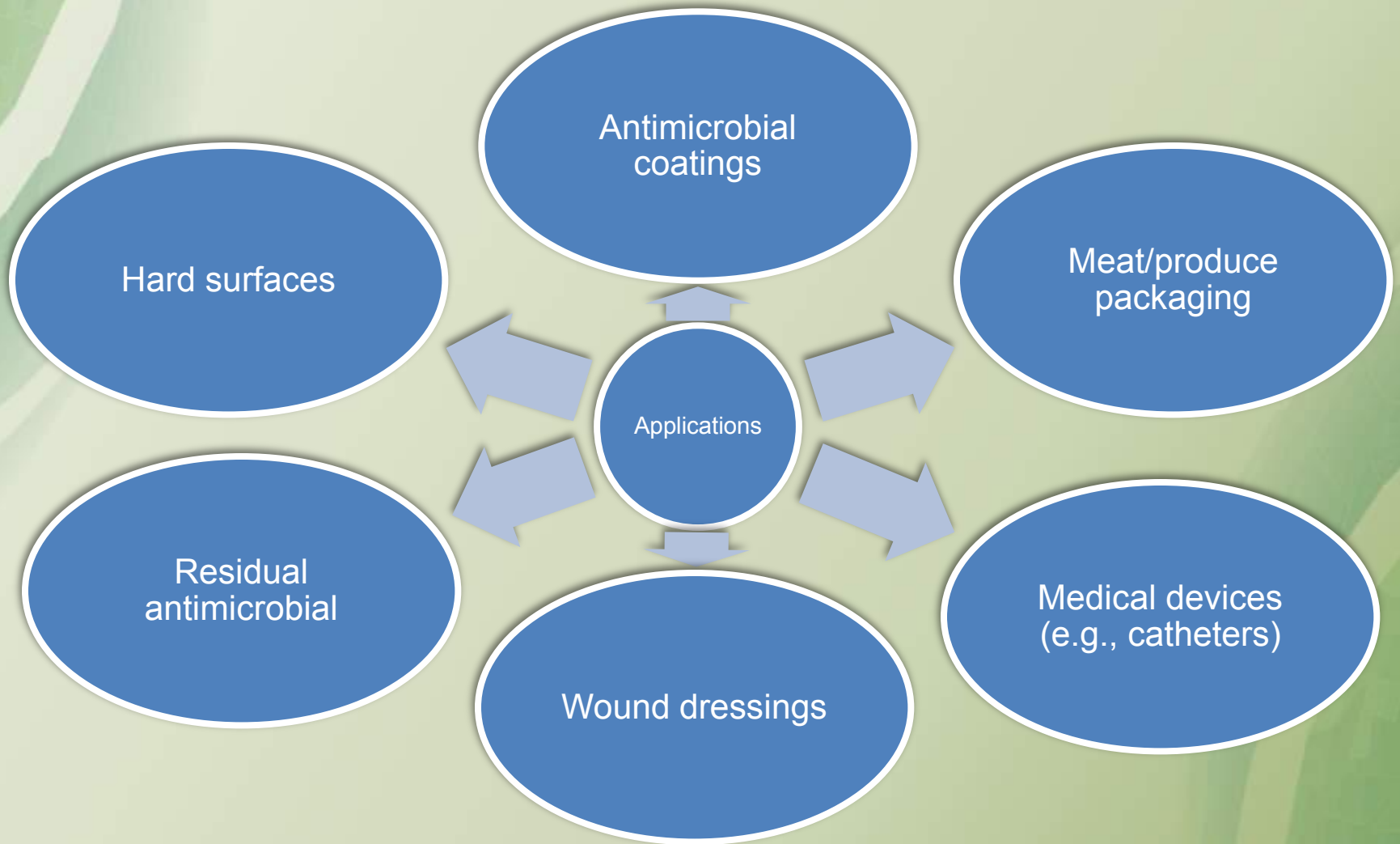


Untreated,
12hrs

Ag-NP,
50µg/ml,
12hrs

Li et al., 2011

Silver



Silver – antimicrobial efficacy

- Silver impregnated meat/melon liners
 - 1 log reduction (meat)
 - 3 log reduction (melon)
- Silver-zeolite coatings
 - 5 log reduction in 24 hours (*S. aureus*, *E. coli*, *P. aeruginosa*, and *L. monocytogenes*)
 - *B. cereus* were reduced by 3 logs after 24h, but spores viable at 48 h

Silver – Concerns?

- Antimicrobial resistance
- Chronic ingestion of silver (gram amts)
 - Argyria:
 - Irrev. blue discolouration
 - condition is not currently associated with pathological effects
 - Unproven health claims
 - Lifetime NOAEL 10 g
 - Levels in water is thousands, if not millions lower



Highlights – Silver

Primary active ingredient in disinfectant

- Silver dihydrogen citrate

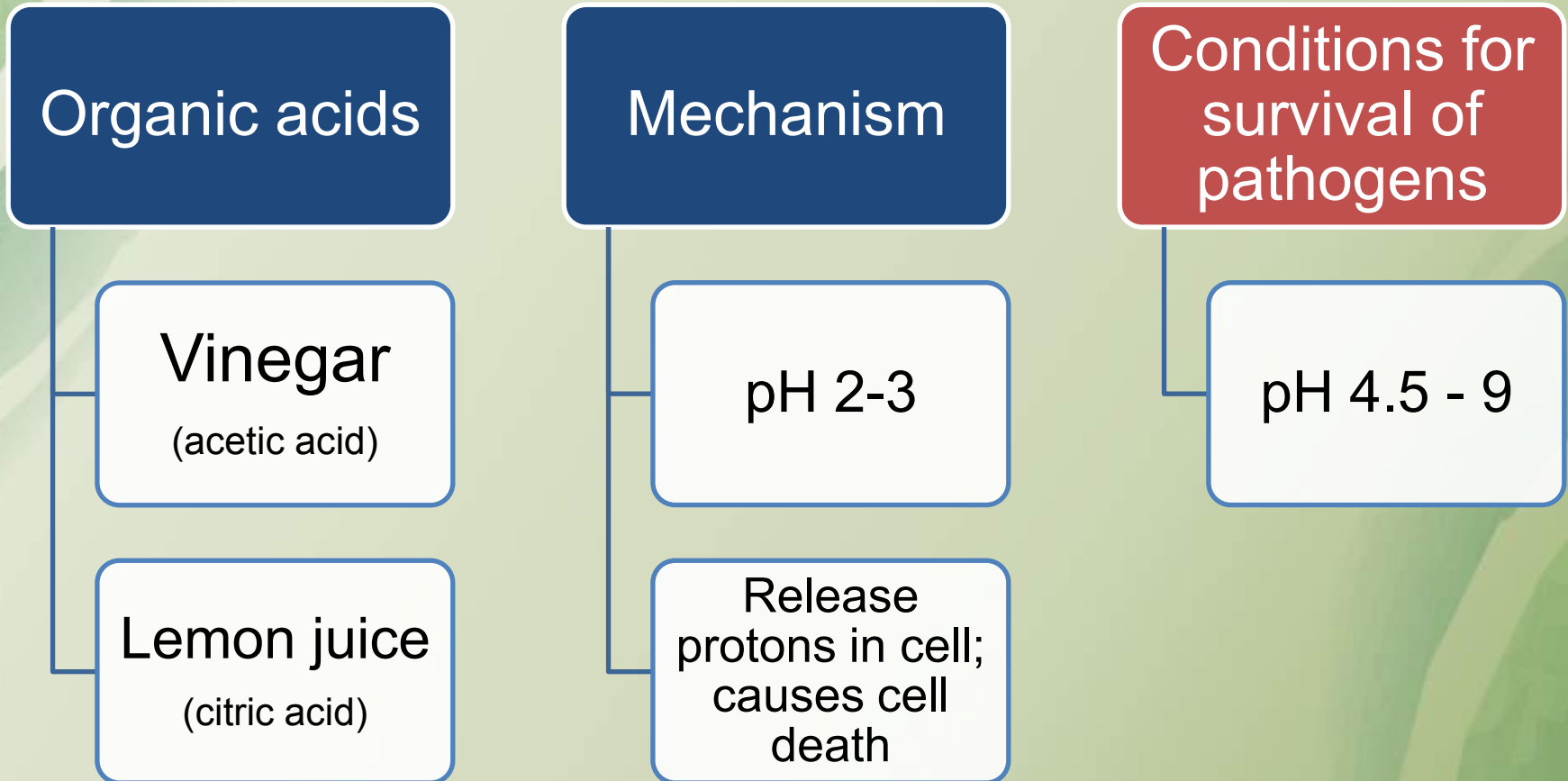
Residual antimicrobial activity

- Many potential applications
- Silver coatings/nanotechnology

Silver impregnated materials

- May lose antimicrobial activity once all Ag ions released

6. Vinegar, lemon juice, baking soda



Baking Soda



- Mechanism

- Unclear...
- pH 8.34...unlikely inhibits growth of pathogens

Vinegar, lemon juice, baking soda – antimicrobial efficacy

Organic acids

- Some efficacy against *Shigella*, *Salmonella*, *E. coli*, *P. aeruginosa*, *Y. enterocolitica*
- Less against *S. aureus*, *L. monocytogenes*

Baking Soda

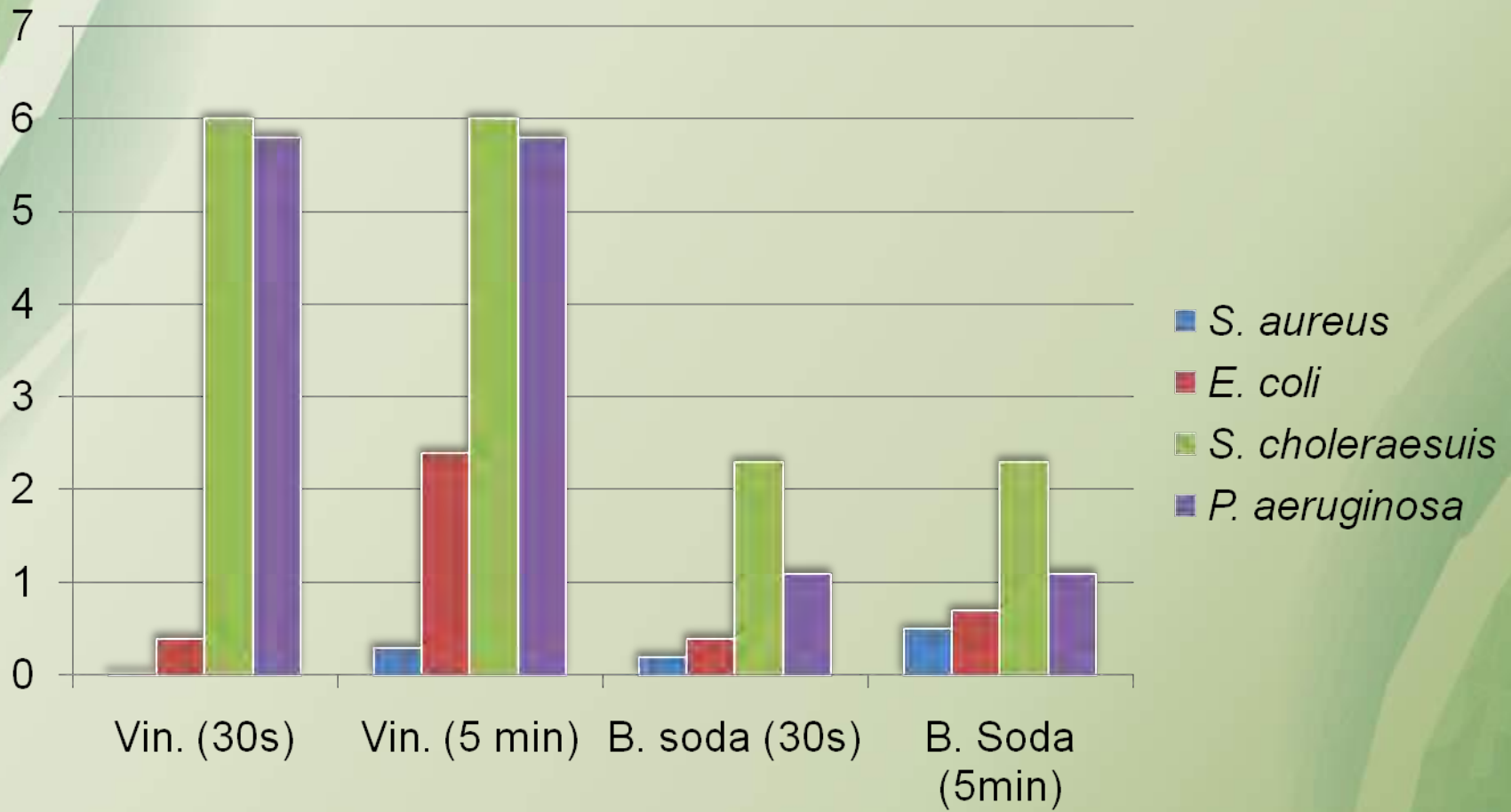
- Notable virucidal activity against feline calicivirus (norovirus surrogate)
- Ineffective against *E. coli*, *P. aeruginosa*, *S. aureus*, *Salmonella*



Please see NCCEH evidence review for tabulated data

Log reductions

Vinegar, Baking Soda



Data from: Rutala et al., 2000

Highlights – Vinegar, lemon juice, baking soda

Applications are limited

- Poor antimicrobial efficacy, difficult to compare
- **Household** vs. commercial

Strong odour/taste

- May damage organoleptic properties of foods

Low toxicity

- Food additives

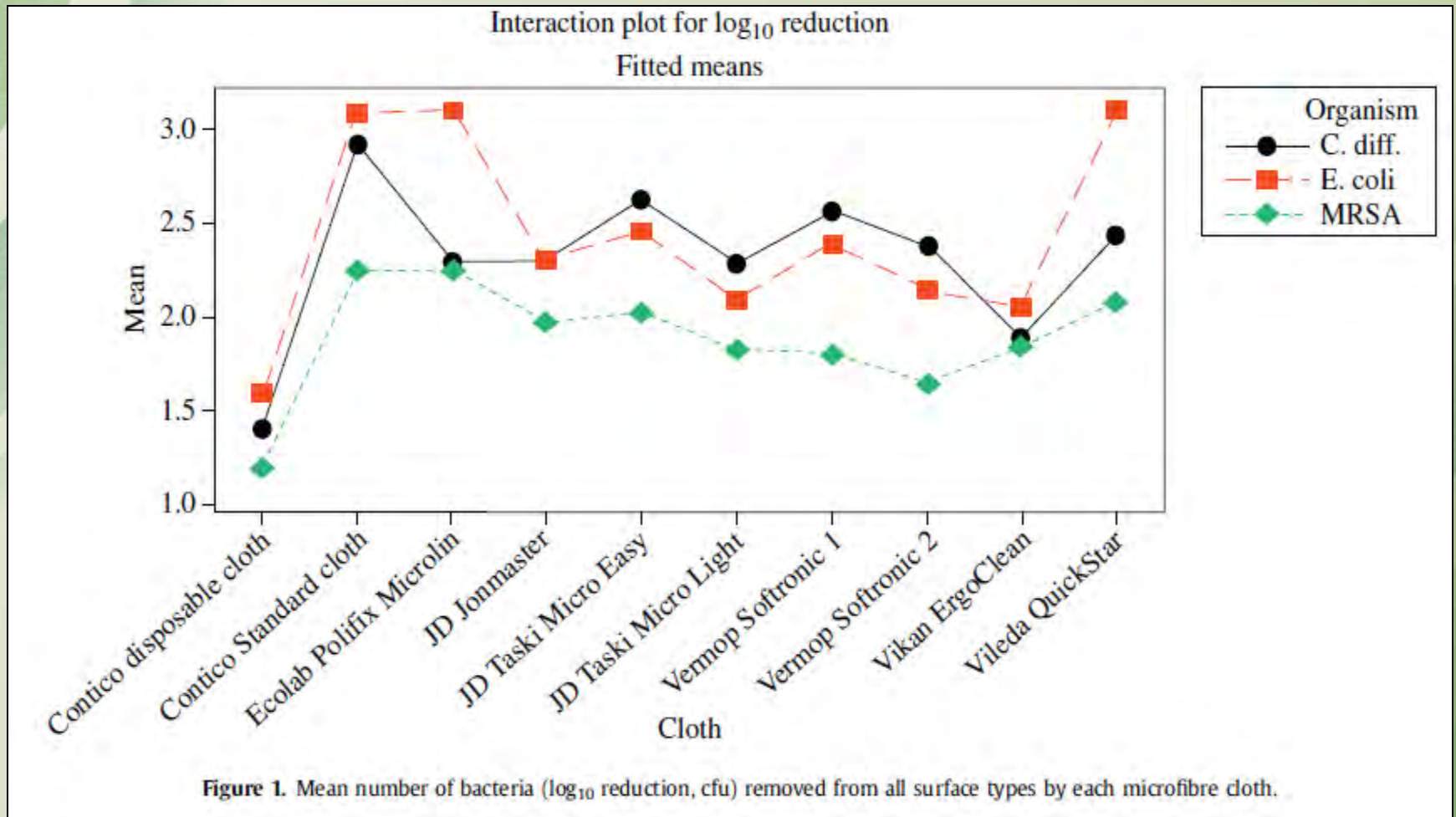
7. Microfibre

Description

- Fibres with extremely small weight to length ratio
- <1 g per 9000 m; $1/16^{\text{th}}$ thickness of human hair
- Unique structure, electrostatic, capillary effect
 - Used without detergents
 - 40X more surface area than cotton

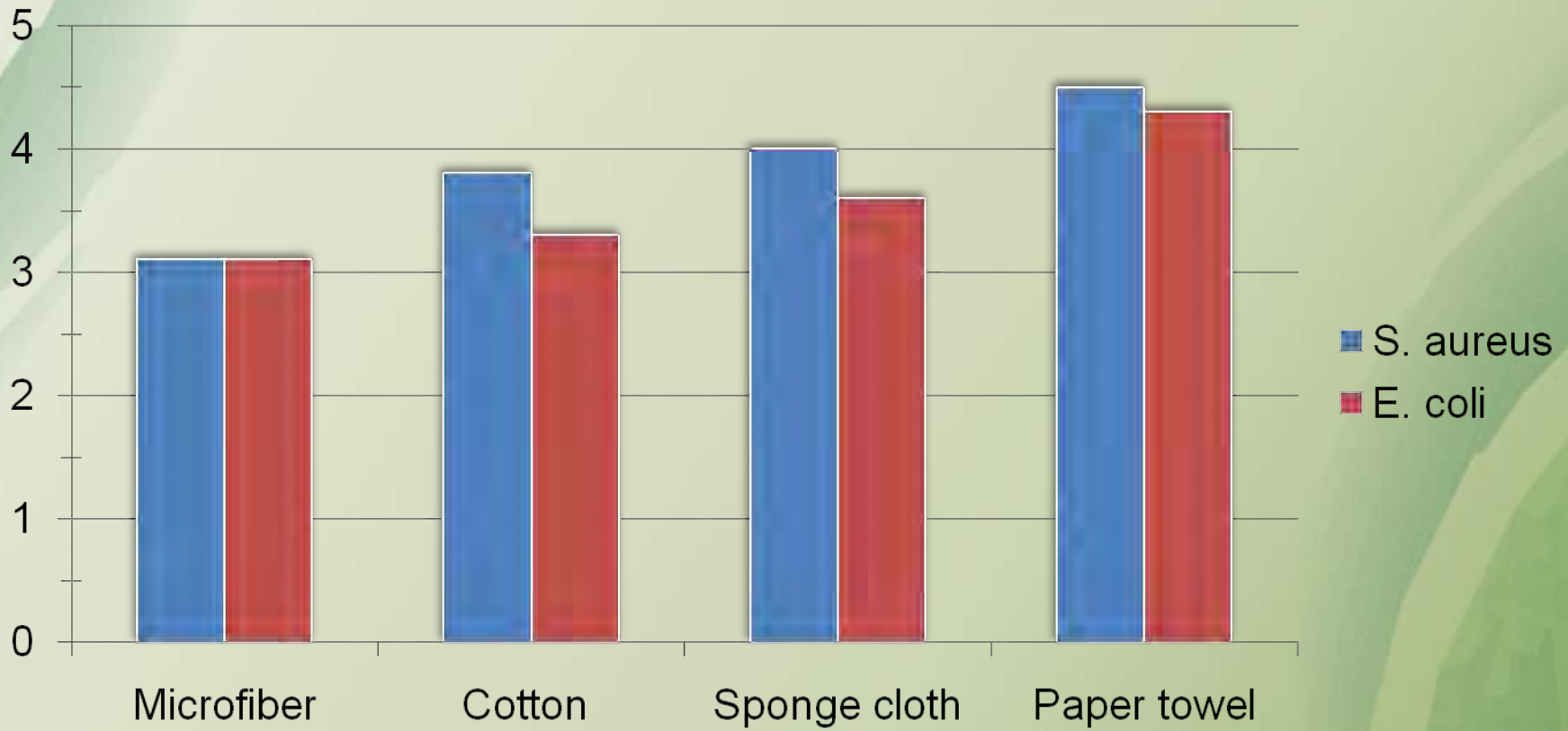


Microfibre – cleaning efficacy



“...no significant difference
in the decontamination efficacy...”

***S. aureus* or *E. coli* log CFU remaining on test surface
after decontamination with different cloth types**



Data from: Diab-Elschahawi et al., 2010

Microfibre – economical?

- University of California Davis Medical Center (UCDMC) in Sacramento, CA
 - study compared between using conventional cotton mops vs. microfibre mop system (U.S. Environmental Protection Agency, 2002)

>> Total Costs <<	
\$468 to \$470 per 100 rooms per day	\$497 per 100 rooms per day
>> Microfiber mops use 95% less water and chemicals <<	

Source: U.S. Environmental Protection Agency, 2002

Microfibre – economical?



Microfibre

Program Results

UCDMC first used the microfiber mops in a pilot test beginning in summer 1999, and within one year it completely replaced conventional loop mops with the microfiber alternative in all patient care areas. The program resulted in three measurable economic benefits:

- 60% lifetime cost savings for mops
- 95% reduction in chemical costs associated with mopping tasks
- 20% labor savings per day

Highlights – Microfibre

Unique properties

- Effective for cleaning
- Lighter material
- Reduce use of water, chemicals

No active antimicrobial properties

- Issues with cross contamination if used with water only

Damaged by heat, chlorine

- Special laundry procedure
- Compatibility with cleaning agents/disinfectants?

Overall impressions...

- **Electrolyzed water and Ozonated water**
 - Potential for many applications
- **Silver**
 - Unique residual antimicrobial activity
- **Thyme oil**
 - Can be an alternative, but costly?
- **Tea tree oil**
 - Oral and dermal toxicity concerns
- **Vinegar, Lemon juice, Baking soda**
 - Perhaps use in household setting, but not commercial
- **Microfibre**
 - Potential for cost-effective cleaning alternative, economical?

Thank You

Questions?
Comments?

www.ncceh.ca | www.ccnse.ca

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BC Centre for Disease Control
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Acknowledgements

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Additional Resources

- Disinfectants:
 - NCCEH - Disinfectants and Sanitizers for Use on Food Contact Surfaces (http://www.ncceh.ca/en/practice_policy/ncceh_reviews/food_contact_sanitizers)
 - NCCEH - Summary of cleaning and disinfection at Personal Service Establishments (http://www.ncceh.ca/en/major_projects/personal_service_establishments)
 - BCCDC Laboratory Services - A Guide to Selection and Use of Disinfectants (http://www.bccdc.ca/NR/rdonlyres/EAA94ACF-02A9-4CF0-BE47-3F5817A25669/0/InfectionControl_GF_DisinfectntSelectnGuidelines_nov0503.pdf)
- Registration of Disinfectants in Canada:
 - Health Canada - Drug Product Database (<http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php>)
 - Health Canada - Guidance Document: Disinfectant Drugs (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demanded/guide-ld/disinfect-desinfect/disinf_desinf-eng.php)
 - Health Canada - Frequently Asked Questions related to Health Canada's Guidance Document: Disinfectant Drugs (http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demanded/guide-ld/disinfect-desinfect/notice_faq_disinfec_avis_faq-eng.php)
 - CFIA - Reference Listing of Accepted Construction Materials, Packaging Materials and Non-Food Chemical Products (<http://www.inspection.gc.ca/english/fssa/reference/refere.shtml>)

References

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