# Formulation Challenges for Biopesticides

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# Formulation Challenges for Biopesticides: Overview

- Definitions
- Why Biopesticides?
- Market Trends
- Formulation Challenges
- How Are Biopesticides Being Formulated?
- Examples
- Conclusions and Discussion Points

# DEFINITIONS

# What Do You Think of as Biopesticides?

- Non-synthetic pesticides (define "non-synthetic")
- Natural pesticides (define "natural")
- Microbials
  - Bacteria, fungi, viruses, yeasts, nematodes, protozoans
- Biochemicals with non-toxic modes of action (define "non-toxic")
  - E.g. Plant extracts, fermentation products,
- Plant-incorporated products using GMO?

# US EPA Definition of Biopesticides

Biopesticides are certain types of pesticides derived from such natural materials as animals, plants, bacteria, and certain minerals.

- Microbial pesticides consist of a microorganism (e.g., a bacterium, fungus, virus or protozoan) as the active Ingredient
- Plant-Incorporated-Protectants (PIPs) are pesticidal substances that plants produce from genetic material that has been added to the plant.
- Biochemical pesticides are naturally occurring substances that control pests by non-toxic mechanisms.

http://www.epa.gov/pesticides/biopesticides/whatarebiopesticides.htm

# WHY BIOPESTICIDES?

# Why Biopesticides?

- Are they Green? (many interpretations of "Green")
- Better public safety image
- Low environmental impact
- Low to no chemical residues
- Quicker/Immediate harvest after treatment
- Fewer resistance issues
- Fast-track registration in USA (and EU…)

# MARKET TRENDS

# Trends – Biopesticides

| Year | Synthetic Pesticides $ billion | Biopesticides $ billion | % |
|---|---|---|---|
| 2005 | 36 | 0.26 | 0.7 |
| 2008 | 45 | 0.75 | 1.7 |
| 2010 | 44 | 1.0 | 2.3 |
| 2015 (forecast) | 50 | 2.5 | 5 |
| 2019 (BCC Forecast 2014) | 84 | 6.9 | 8.2 |
| Source: Knowles 2013, based on Phillips McDougall, AgroPages 2011. BCC 2014 | | | |

North America 40% (US EPA has 245 registered biopesticides)

Europe 25%

Asia 20%

Latin America 10%

# FORMULATION CHALLENGES

# Why Might Biopesticides Be Tricky to Formulate?

The term **"Biopesticides"** covers a wide range of chemical and biological entities for the formulator to consider, e.g.:

- Natural extracts – chemical entities or mixtures
- Biochemical entities – e.g. peptides, enzymes proteins
- Organisms – bacterial, fungal etc

| Type | Examples |
|---|---|
| Microbials | Bacillus thuringiensis, Beauveria bassiana, Metarhizium anisopliae, Baculoviruses |
| Biochemical extracts | Pyrethrum (pyrethrins) neem |
| Macrobials | Predators, parasitoids |
| Others | Nematodes, Pheromones, allelochemicals |

# Why Might Biopesticides Be Tricky to Formulate?

**Common challenges:**

- Stability (→ efficacy) on storage and in use
  - Natural extracts – chemical and physical stability
  - Stability to e.g. UV light, heat, environmental influences
  - Viability of organisms stored long-term - and in use
- Variability (frequently complex mixed systems of natural origin)
  - Season, source

# HOW ARE BIOPESTICIDES BEING FORMULATED?

# How Are Biopesticides Being Formulated? Formulation Types: Natural Products

| Type | % of total |
|---|---|
| Wettable/soluble powders (WP/SP) | 28 |
| Soluble liquid concentrates (SL) | 25 |
| Emulsion concentrates (EC) | 16 |
| Granules/microgranules (GR/MG) | 6 |
| Water dispersible/soluble granules (WG/SG) | 6 |
| Tablets (TB) | 3.5 |
| ULV | 3.5 |
| Others | 12 |

Source: Knowles 2013 – Agrow – New Trends in Crop Protection Formulations

# How Are Biopesticides Being Formulated? Formulation Types: Living Systems

| Type | % of total |
|---|---|
| Wettable/soluble powders (WP/SP) | 33 |
| Granules/microgranules (GR/MG) | 13.5 |
| Water dispersible/soluble granules (WG/SG) | 17 |
| Suspension concentrates (SC) | 12 |
| Oil flowables (OF) | 10 |
| Seed treatments (WS/DS) | 4.5 |
| Emulsifiable suspensions (ES) | 2 |
| Others | 8 |

Source: Knowles 2013 – Agrow – New Trends in Crop Protection Formulations

# How Are Biopesticides Being Formulated?

- In general, as conventional formulations
  - consider the physical and chemical properties of the active and the target application and choose formulation type accordingly
- Examples:
  - Abamectin (low water solubility, $K_{OW}$ 4.4) formulated as EC
  - Emamectin benzoate (water solubility 24mg/l, $K_{OW}$ 5) formulated as EC, SG
- Obvious limitations, e.g. living systems will not be dissolved (in EC/SL)
- Living systems – often formulated as dry granules/powders – low water activity will prevent organism growth on storage

# Potential Solutions to Challenges

- Additives
  - UV Stabilisers
  - Also adjuvants or surfactant systems
- Protection
  - Encapsulation
    - Polymers
    - Natural solutions
- “Gentler” Formulation types
  - Minimise intensive processing (temperature, time, shear)

# UV Stabilisers

- Benzophenone
- Octyl methoxycinnamate
- 4-aminobenzoic acid (PABA)
- Stilbene
- Inorganic oxide dispersions
- Acyl glycerols, modified soya bean

# EXAMPLES

# Some Examples of Approaches

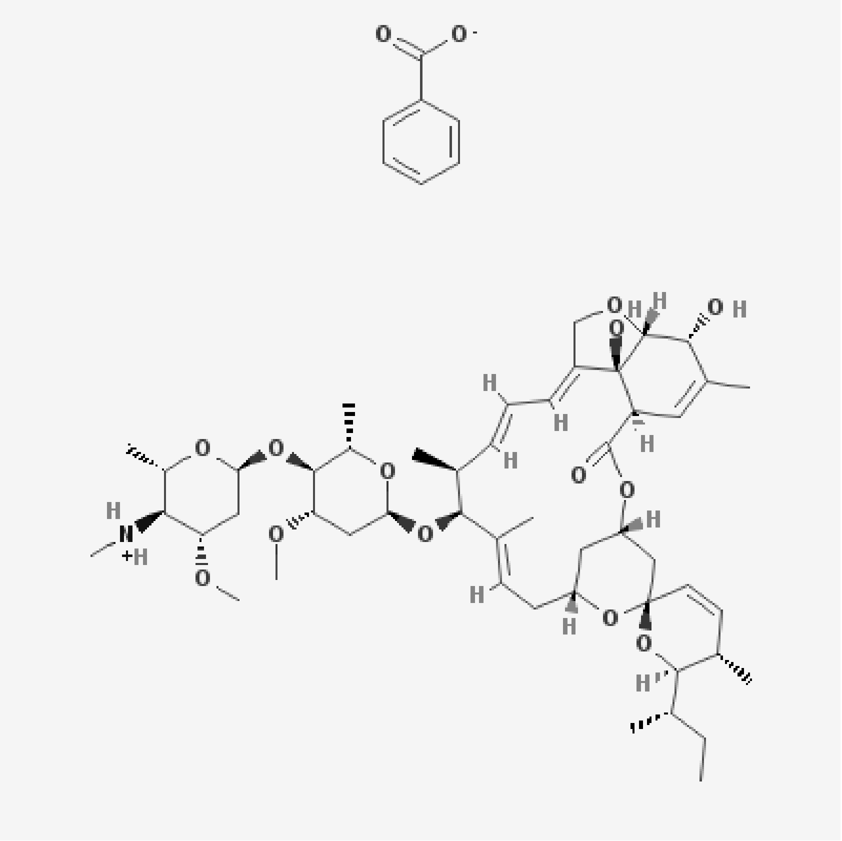
(summarised in Agrow Formulations Report 2016)

- Emamectin benzoate (abamectin derivative) – Syngenta examples
- Avermectin nanocomposites  with layers of surfactant
- Alginate/bentonite encapsulation of fungal bioinsecticide
- Wax Encapsulation of Insect Viruses (Lancaster University with Exosect)
- Superabsorbent polymers: BASF example
- Eden Research – naturally occurring capsules for biopesticides

# Emamectin Benzoate

Example from A. Heming (Syngenta), from the Informa Conference, Berlin 2015

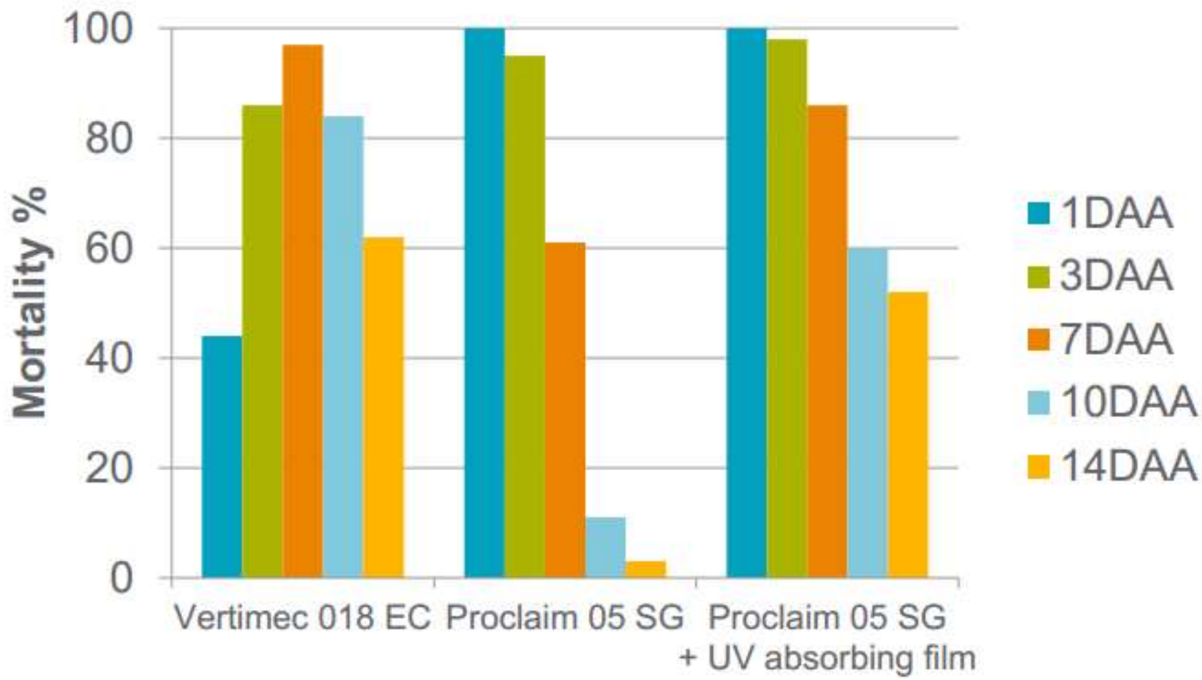
- Derivative of naturally occurring abamectin, which is produced by the fermentation of the soil bacteria (Streptomyces avermitilis)
- Usually seen as benzoic acid salt → emamectin benzoate
- More water soluble than abamectin
- Used in controlling lepidoptera (larvae are caterpillars → butterflies, moths etc)



# Photodegradation

Example from A. Heming (Syngenta), from the Informa Conference, Berlin 2015

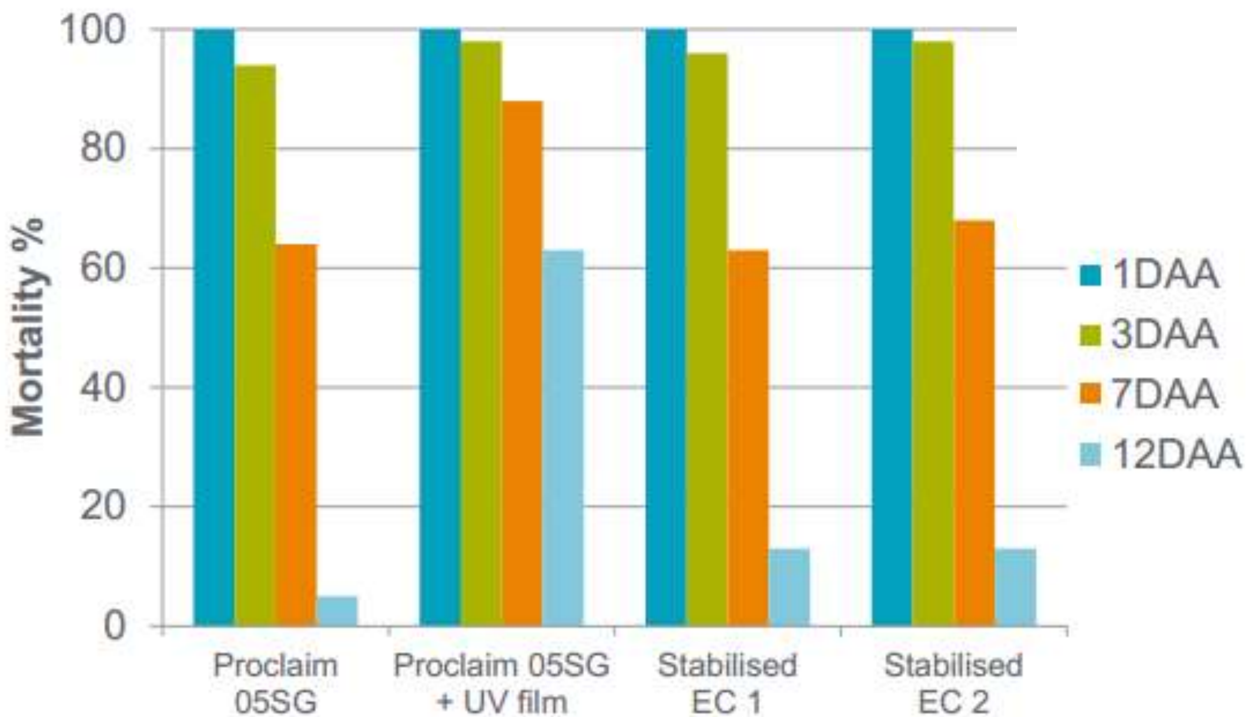
- Vertimec 018 EC is standard EC formulation of abamectin
- Proclaim 05 SG is granule formulation of emamectin benzoate
- Tested with and without UV absorbing film present



# Field Trials: with Photostabiliser

Example from A. Heming (Syngenta), from the Informa Conference, Berlin 2015

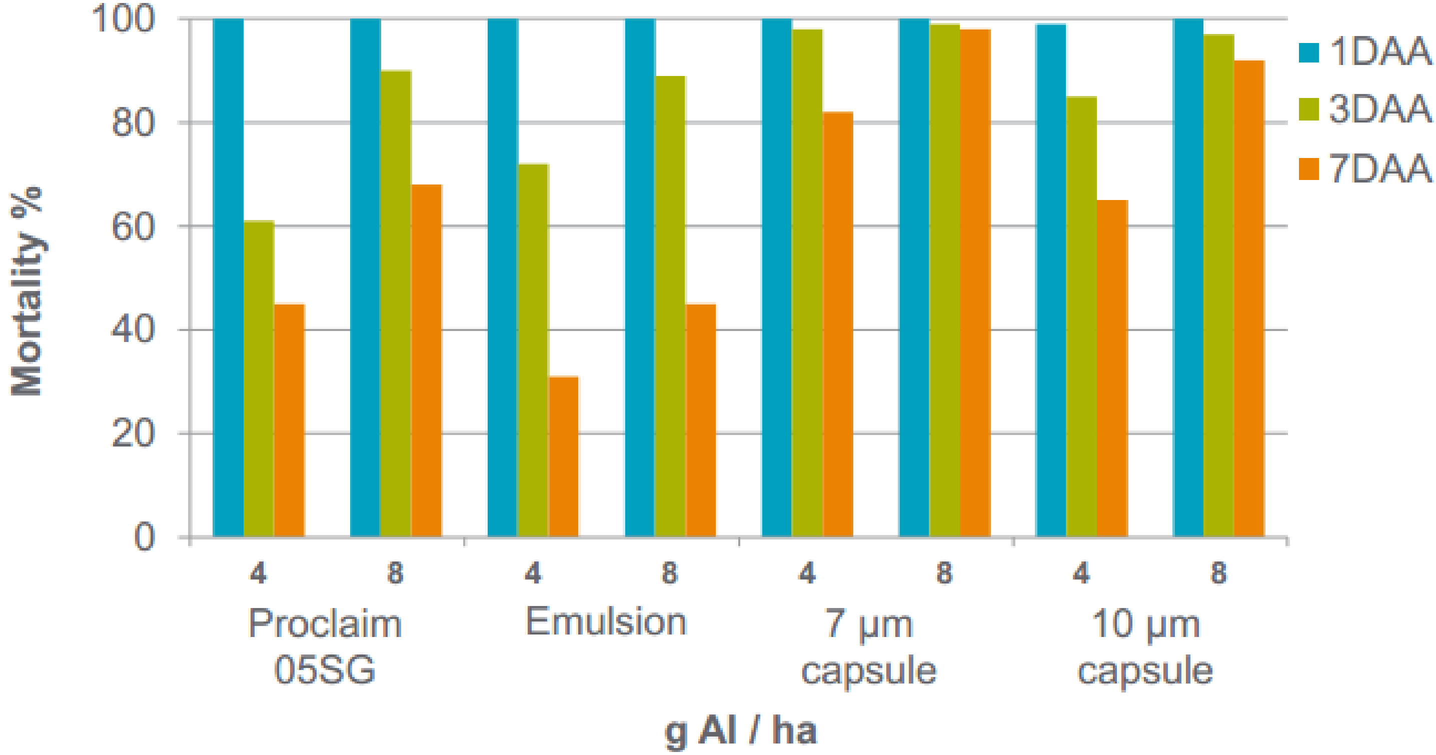
- Tested photo-stabilised EC formulations



# Encapsulation with Photostabiliser

Example from A. Heming (Syngenta), from the Informa Conference, Berlin 2015

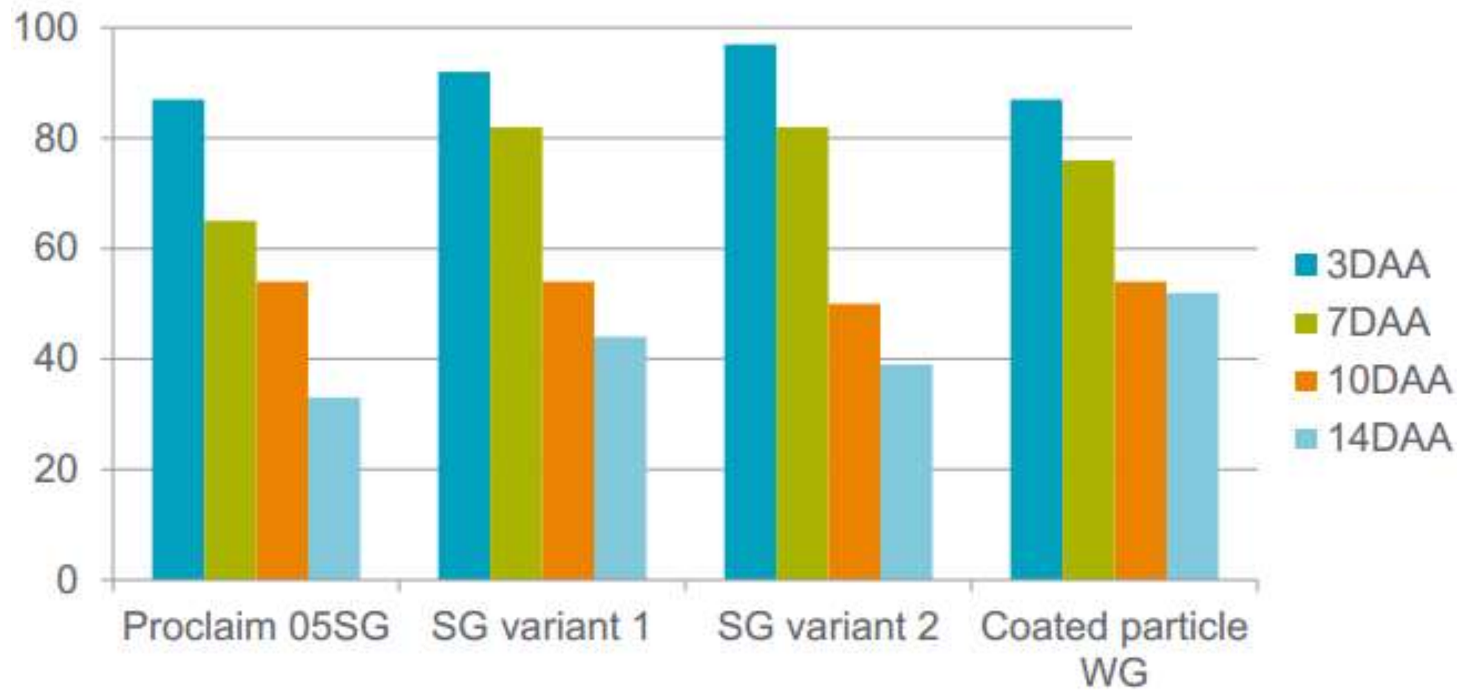
- Comparison of SG with photostabilised emulsion as well as photostabilised capsule formulations



# Spray Dried Granule with Photostabiliser

Example from A. Heming (Syngenta), from the Informa Conference, Berlin 2015

- Powder coating technique used – novel Syngenta technology
- Further enhanced performance was seen



# Nanocomposites: Avermectin with Surfactant

- *"Sodium dodecyl sulfate was utilized to modify the avermectin-layered double hydroxide nanohybrids for the preparation of water dispersible nanocomposites, resulting in the successful conversion of hydrophobic surfactant monolayer structure on the solid surface to hydrophilic bilayer.*
- *It was found that the prepared materials could well control the release of avermectin, and the prepared nanocomposite would be a promising candidate for water dispersible controlled release formulation."*

- From "Water dispersible avermectin-layered double hydroxide nanocomposites modified with sodium dodecyl sulfate", Jikuan Zhao, Xiaomei Fu, Shouzhi Zhang, Wanguo Hou, Applied Clay Science Volume 51, Issue 4, March 2011, Pages 460–466.

# Polymer Nanocomposites: Encapsulation of a Bioinsecticide Fungus

- Alginate encapsulation modified by addition of bentonite
- Formulate as suspension and then extrude
- From “Polymer/Layered Silicate Nanocomposite as Matrix for Bioinsecticide Formulation”; Batista, D.P.C. et al; Macromol. Symp Vol 344 Pages 14-21, 2014

**Stability of Encapsulated Products at 25°C (0 = no growth, 1 – germination delay 72hrs, 2 – germination delay 24hrs, 3 – germination similar to fresh product**

| Sample | Month 1 | Month 2 | Month 3 | Month 4 | Month 5 | Month 6 | Month 7 |
|---|---|---|---|---|---|---|---|
| Alginate alone | 3 | 3 | 1 | 0 | 0 | 0 | 0 |
| Alginate + 0.5% Bentonite | 3 | 3 | 2 | 2 | 1 | 0 | 0 |
| Alginate plus 1.0% Bentonite | 3 | 3 | 2 | 1 | 1 | 0 | 0 |
| Alginate plus 2% Bentonite | 3 | 3 | 2 | 1 | 1 | 0 | 0 |
| Alginate plus 4% Bentonite | 3 | 3 | 3 | 3 | 3 | 2 | 2 |

# Wax Encapsulation of Insect Viruses

- UK Research Grant - Lancaster University with Exosect
- Use of chemically inert carnauba wax blends
- *"By combining the biopesticide active ingredients (baculoviruses) with Entostat waxes, we aim to enhance field efficacy and increase persistence over existing formulations, so reducing the cost of using biopesticides and increasing their attractiveness to users, so making them a more viable replacement for disappearing chemical pesticides"*
- *"This proof of concept project, by determining that insect viruses can be effectively encapsulated with Entostat waxes and co-formulated with other chemicals such as UV blockers, opens a whole new avenue of research on biopesticide product development that could be applied to improving the acceptability and cost-effectiveness of a wide range of biopesticides both currently used and under development."*
- From http://gtr.rcuk.ac.uk/projects?ref=BB/P004970/1

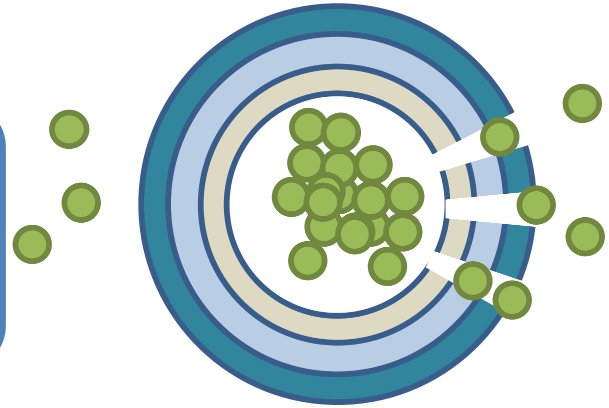
# Superabsorbent Polymers

BASF US Patent Application US20160316759A1

- Formulate and apply the biopesticide (typically a microorganism) with a superabsorbent polymer (SAP)
  - SAP can be peptide based, polysaccharide, polyacrylate etc
- Efficacy benefits claimed – related to water binding of SAP, e.g.:
  - enhance the water storage capacity of the soil
  - improve the water use efficiency and drought resistance
  - prevent nutrient leaching and improve the nutrient use efficiency
  - improve the delivery of the biopesticide to the plant
  - prolong the availability of biopesticides to the plants

# Encapsulation of Biopesticides: Further Example

**Dry conditions: Pores close and prevent release of biopesticide**



**Damp conditions: Pores open and release biopesticide**

*"The terpenes continue to diffuse out of the carrier by the addition of more moisture from rainfall, dew or mist…A similar effect is achieved in the soil when the encapsulated product is applied as a soil drench or via irrigation systems. After soaking into the soil, the free terpenes loosely adhering to the carrier particles kill nematodes and disease-causing microbes.* ***As the soil dries out, activity slows or stops. However, when the soil becomes wet again due to rainfall or irrigation, activity restarts.*** *As a result, the efficacy of the terpenes is maintained over an extended period and controls the re-emergence of disease or pests"*

- Natural capsules are based on yeast cells
- Up to 4-fold efficacy increase
- Can also plug pores with e.g. alginate, chitosan for further control

**Eden Research.** See http://www.edenresearch.com/html/technology/EDS.asp

# SUMMARY

# Conclusions and Discussion Points

- Biopesticides –stability challenges are being addressed
  - The nature of the active component dictates formulation type
  - Use of photostabilisation is common
  - Many approaches depending on new encapsulation and controlled release technologies

- Discussion points
  - What do you see as the trickiest challenges in biopesticide formulation?
  - What approaches do you see as most promising?