Slow Dissolving DBNPA Tablets

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Outline

- Background
- New Technology
- New Tablet Formulation
- Dissolution Testing
- Tablet Strength Testing
- Field Trials
- Conclusions

Background – Existing Technology

- DBNPA chemistry is ideal for biocontrol in small cooling water systems.
- Contain 40% active DBNPA in a matrix of hydroxypropyl methylcellulose (27%), octadecanoic acid (2.5%) with 30.5% proprietary inert ingredients.
- Dose of one 200 g tablet per 500 G for 2-3 weeks.

Challenges of Existing Tablets

- 40% active ingredient in a 200 g tablet.
  - Economics of buying 60% inert ingredients.
- Swell upon initial wetting.
  - Rules out the use with a floater or bypass feeder.
- Leave behind insoluble residue.
- Worker exposure

Outline of New Technology

- 97.5% active DBNPA in 100 g tablet.
  - Dissolution rate identical to existing 200 g tablets.
- Can be placed on a platform in sump or suspended in a net to avoid contact with metal.
- Non-swelling.
  - Suitable for use in a bypass feeder or sealed floater.
- No insoluble residues in tower sump.
- High tensile strength.
  - No splintering or dusting.

Dissolution Study Experimental Methods

- Dissolution rate measured by amount of DBNPA in solution over time.
- Correlated with the loss in weight of the tablet.
  - Mass balance confirmed.

Experimental Methods (cont)

- Based on DPD method for determining chlorine.
  - Allowed 3 min. reaction time before making measurement in a colorimeter.
  - Only 1 of 2 Br atoms in DBNPA respond to the DPD reagent.
  - The molecular weight of DBNPA is 241.9.
  - When Cl_2 meter is used, the number reported was multiplied by 3.4 because of the ratio of the molecular weight of DBNPA to Cl_2.

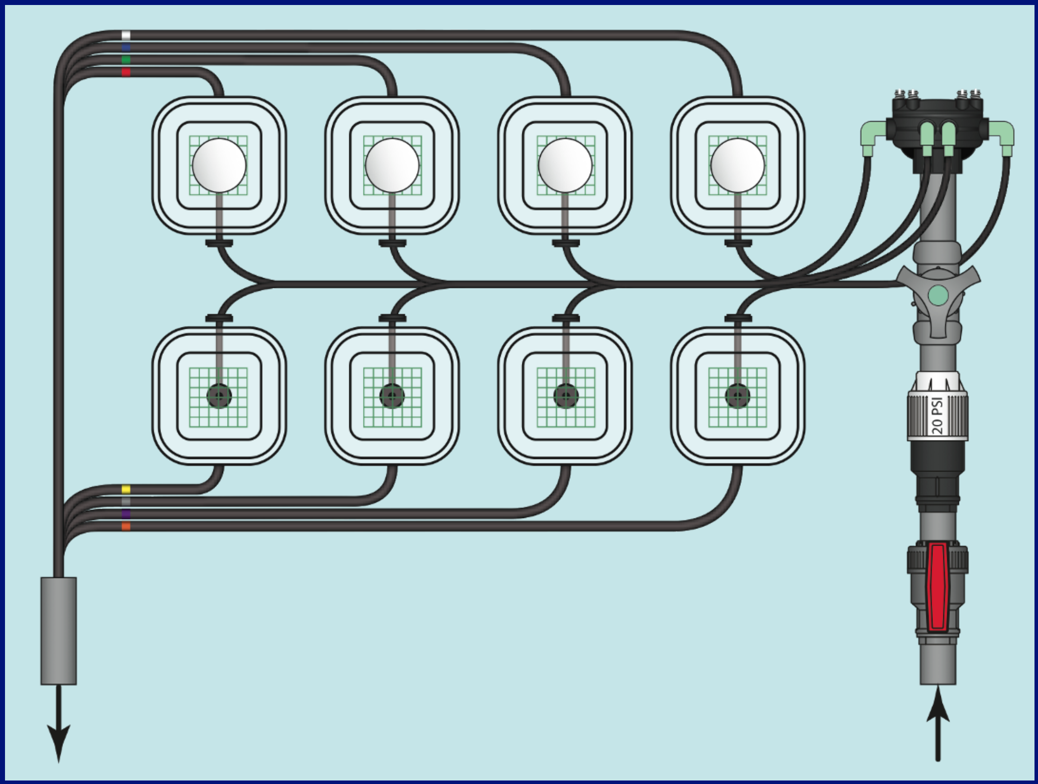
Tableting

- Tablets produced in-house on a custom-machined, stainless steel die and punch.
  - Cavity of the die measured 2.5”

Tableting (Continued)

– A manual hydraulic Carver Press Model 2626, with a max compression of 10,000 psi was used.

Dissolution Testing



- Testing apparatus designed so that 8 tablets could be tested on a side-by-side basis.

Dissolution Testing

Water flows up from bottom to an overflow outlet.

Detail of Dissolution Test Apparatus

Tablet supported on platform.

Properties of Modesto City Water Used in Dissolution Tests.

pH	8.0
Calcium Hardness (mg/L as $CaCO_3$)	172
Conductivity / μScm^{-1}	575
Total dissolved solids / mg/L	329
Total Chlorine / mg/L	0.7

Tablet Formula "Goals"

- >40% active DBNPA.
- Useable in a floater or bypass feeder.
  - Excipients do not swell in water.
- Useable in a delivery system that eliminates possibility of end user contacting DBNPA.
- High tensile strength that resists breakage.
  - When the tablet is deliberately broken, no splintering or excess dust.

Tablet Formula Optimization

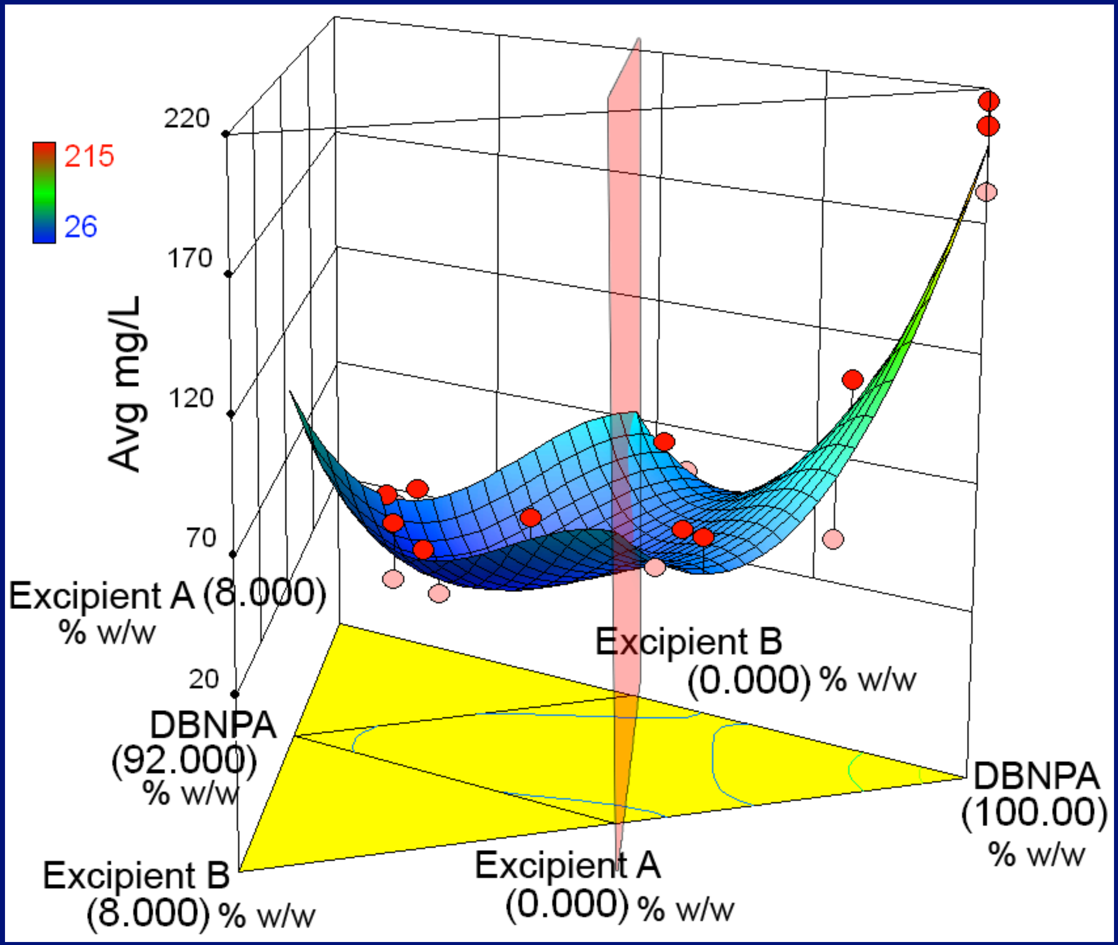
- Used data gathered in dissolution testing.
- Statistically designed mixture experiments used to optimize tablet formula.
  - Statease (Minneapolis, MN) Design Expert V.8
- Hypothesized that a blend of 2 tableting excipients would provide synergistic performance gains over those of either alone.

Variables Affecting Dissolution Rate

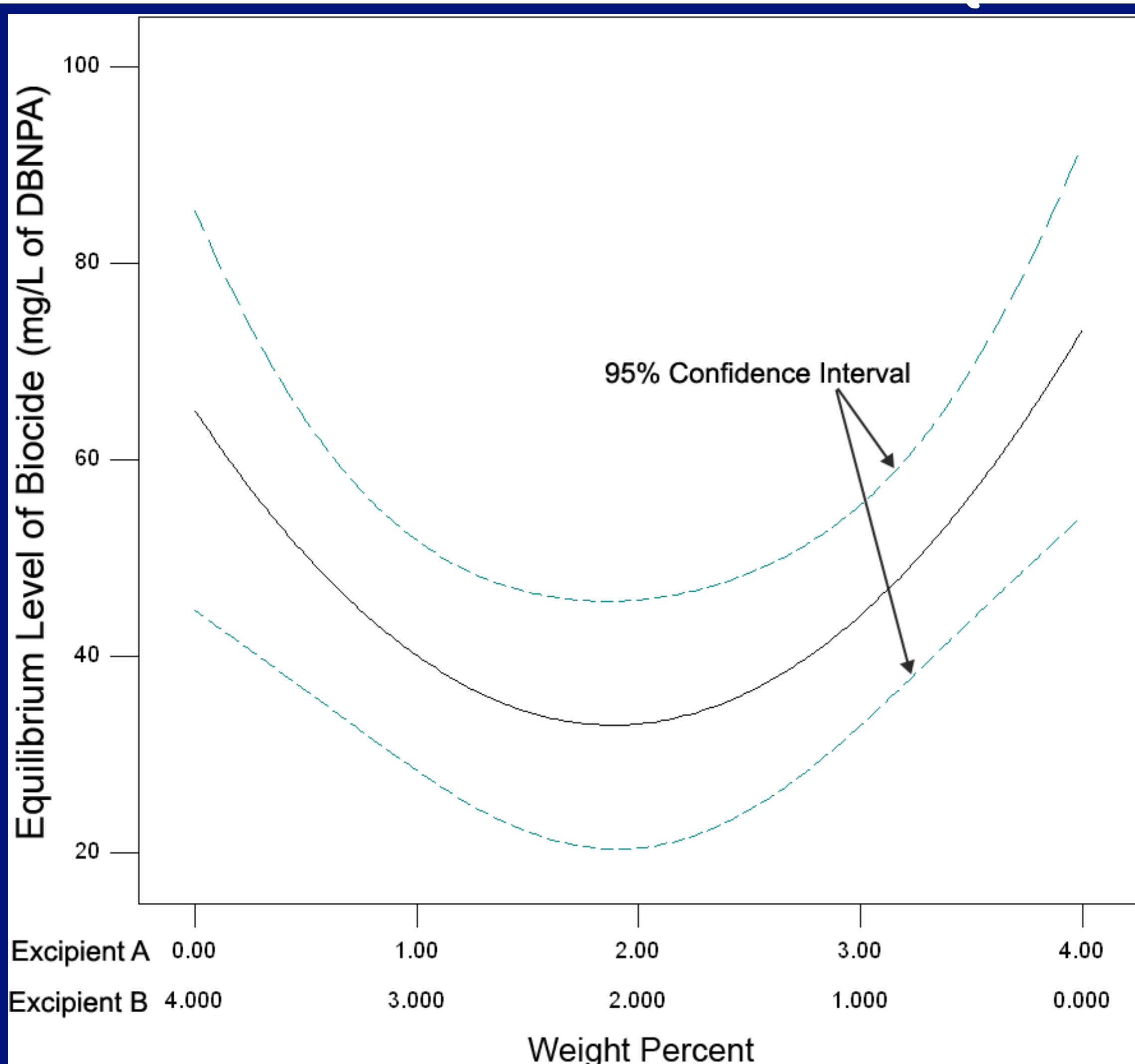
- Amount of excipient A
- Amount of excipient B
- Compaction pressure.

- Quickly became apparent that compaction pressure had no influence, so emphasis placed on other two variables.

Mathematical Model fit to equilibrium biocide concentration vs. composition data.

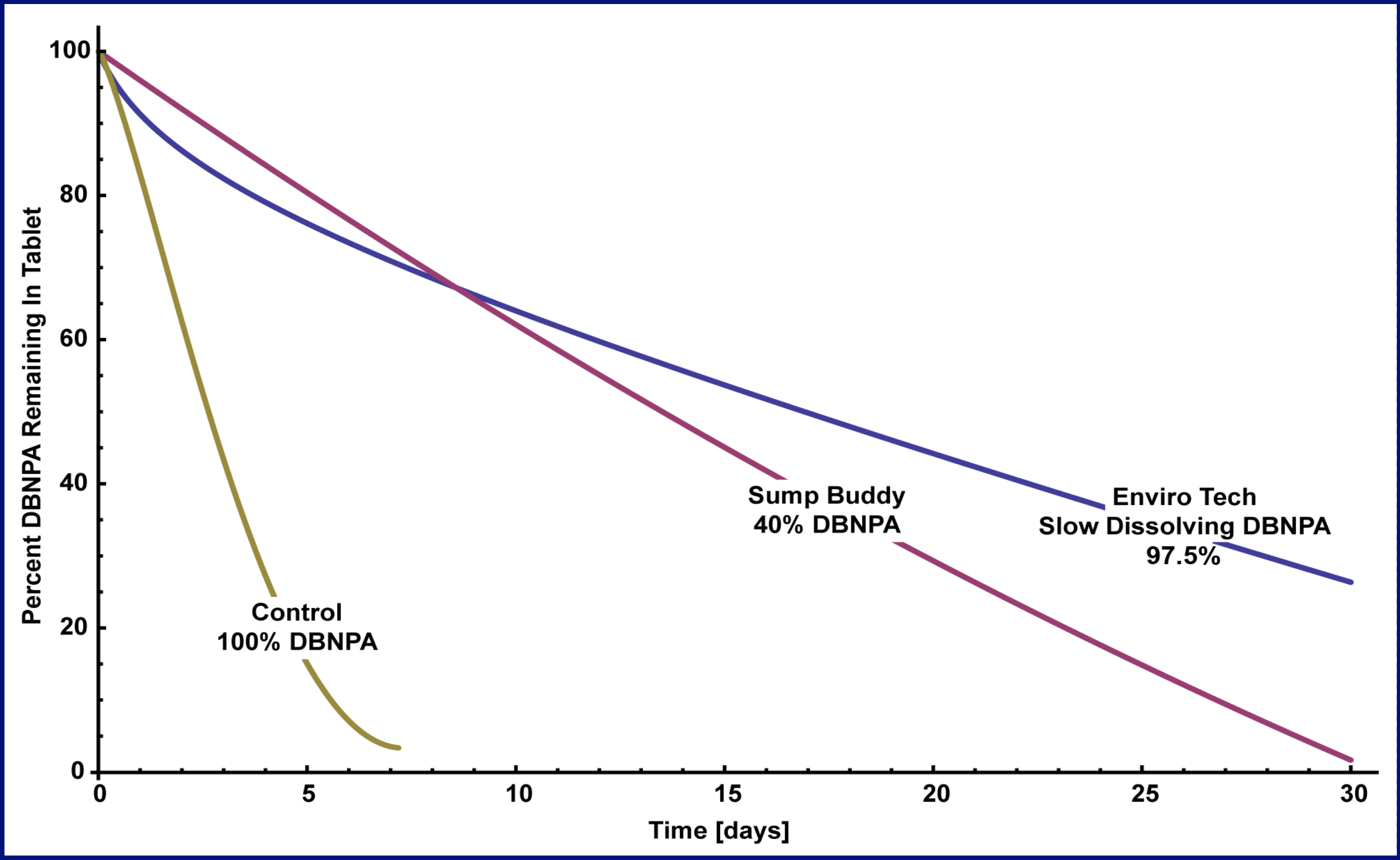


Mathematical Model (cont.)



Cross section through plane shows minimum dissolution rate and synergistic effects using a 1:1 blend of excipients A & B.

Dissolution Rate Comparison



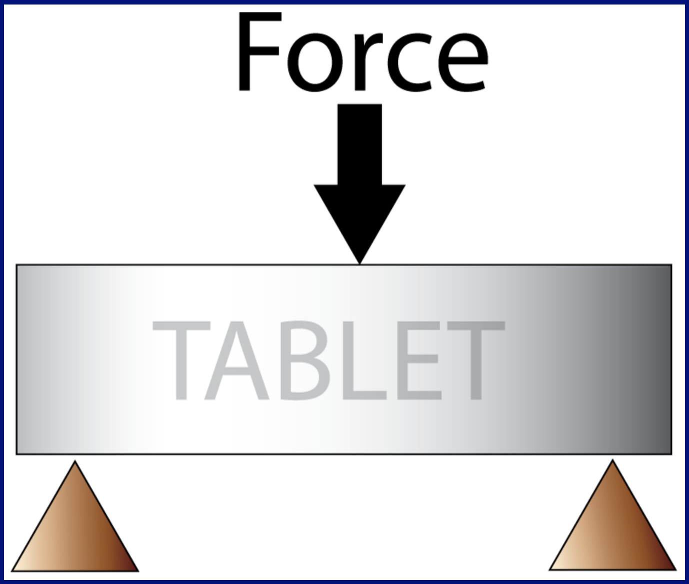
Optimized tablet design for comparable dissolution rate with existing product.

Tablet Strength Testing

- How well tablets can take abuse in manufacturing and shipping process.
- Criteria for a good tablet:
  - High tensile strength.
  - Doesn’t splinter/shatter or create excessive dust and powder upon fracture

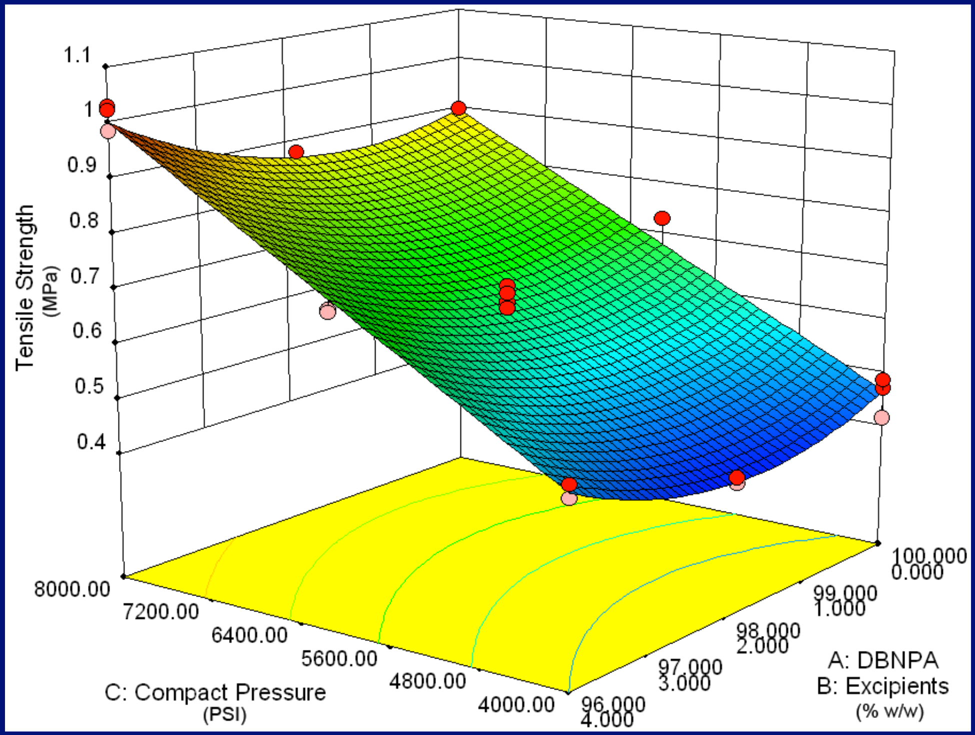
Tablet Strength Testing (cont)

- Easily determined for brittle materials through a three-point bend test as the point at which the material "yields", or snaps in half.

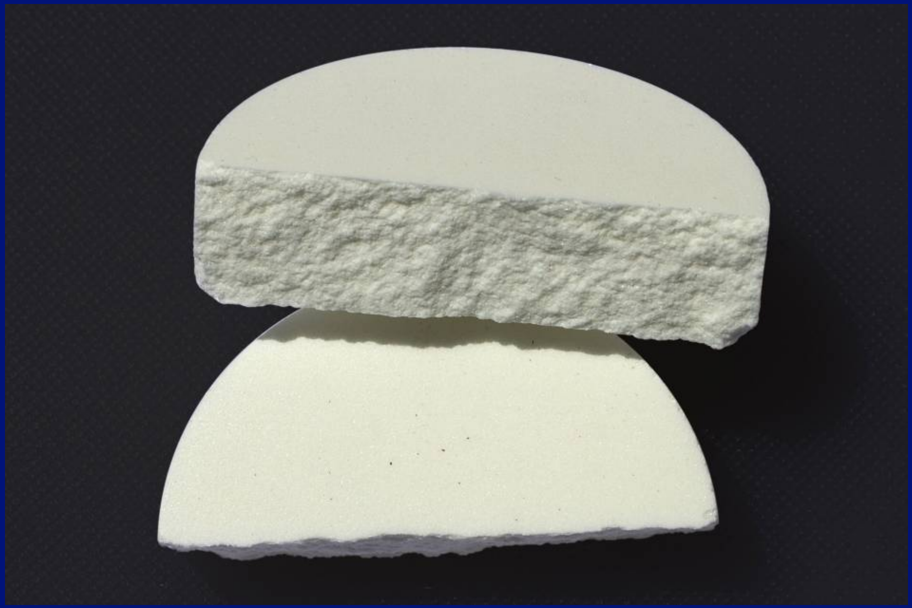


Model for Tensile Strength

- Tensile strength found to be weakly quadratic function of composition and a strongly linear function of compaction pressure.



Deliberately Broken Tablets



Detail showing fracture surface after a 3 point bend test.

Very little material was lost as powder or splintering.

Field Trials

- Two sites were selected, and relevant tower characteristics were recorded.
- Data gathered 3x/week.
  - DBNPA residual present in the cooling water.
  - Weight of the floater measured so that the amount of DBNPA remaining could be gauged.
  - Aerobic bacteria count in the tower water.

Field Trial

- Floater tared and filled with 6 x 100 g, 2.5 in DBNPA tablets.
- Adjusted for minimum flow (one available slot exposed)

Field Trial #1

Water Chemistry

	pH	Cond. (mS/cm)	Calcium Hardness (ppm as $CaCO_3$)
Makeup	7.67	1.21	0
Recirculated Water	9.18	3.70	30

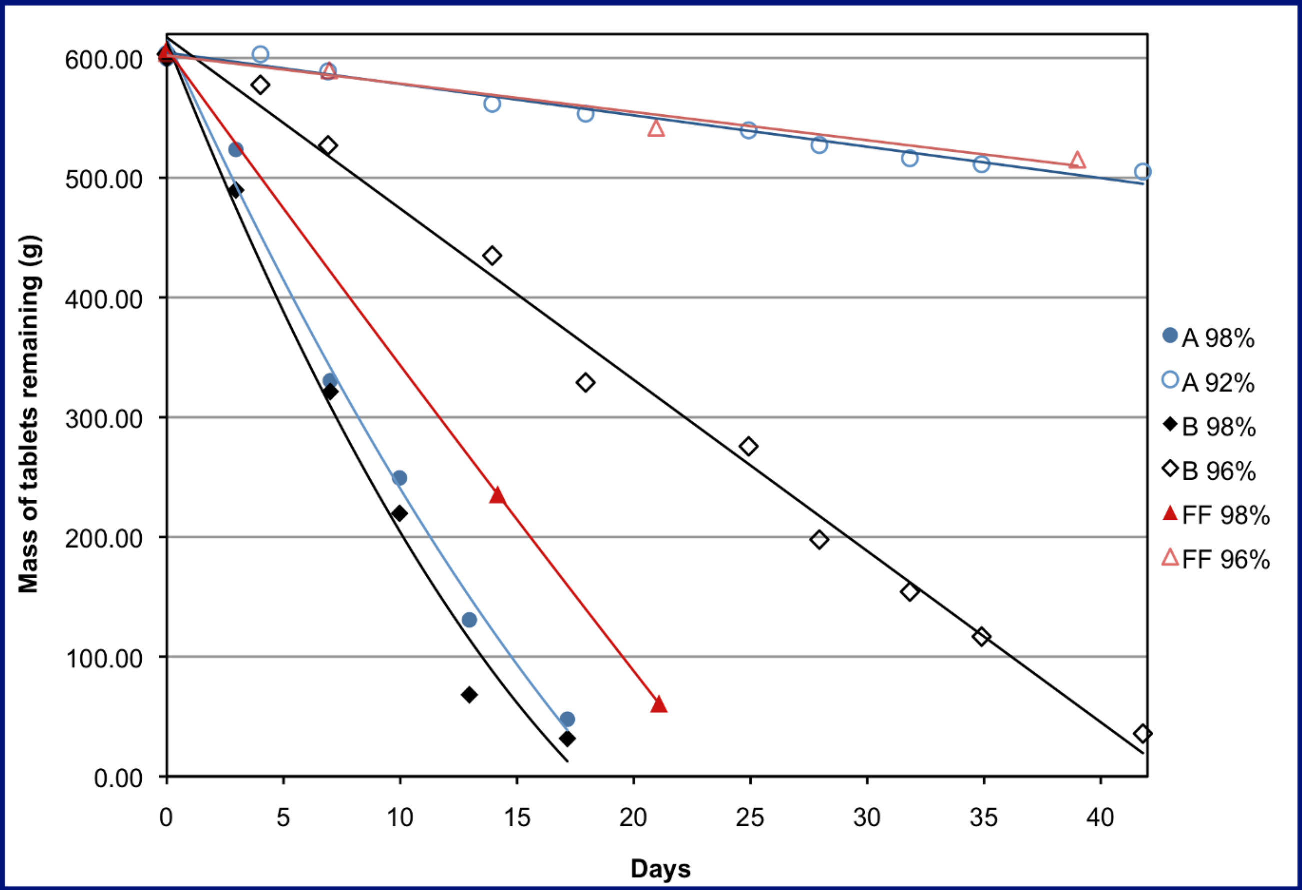
Tower Characteristics

TSCV (gal)	ΔT (°F)	Cycles (based on σ)	Prev. Biocide Program	Aerobic (init.) (Log_{10} CFU/mL)
4400	15	3.06	BCDMH	2.89

Makeup water softened using ion-exchange resin, regenerated with NaCl as needed.

Field Trial Results

Two formulation tested in each tower basin. Tablet weight remaining vs. time is plotted below for all tests.



Field trial results. A: Trial 1, Basin 1 B: Trial 1, Basin 2 FF: Trial 2.

Detailed results for Trial 1

Formulation	Avg Residual (ppm as DBNPA)	Avg. Aerobic Count (log$_{-10}$ CFU/mL)	Lifespan (days)
A 98%	0.27	3.12 (± 0.17)	19
B 98%	0.27		20
A 96%	0.27	2.95 (± 0.12)	45
B 92%	0.20		~270

Detailed results for Trial 2

Formulation	Avg Residual (ppm as DBNPA)	Avg Aerobic Count ($\log_{10}$ CFU/mL)	Lifespan (days)
FF 98%	0.44	3.09 (± 0.35)	23
FF 96%	0.17	3.20 (± 0.30)	~265

- Utilized only 1 x 100g DBNPA tablet because of low system volume.
- The lifespan for the 96 % formulation (2% Excipient A and 2% Excipent B) is an extrapolated estimation.

Conclusions

- Use of 4% excipient A and 4% excipient B (92% DBNPA) results in a tablet with an unacceptably low dissolution rate.

- A tablet between 96% and 98% DBNPA with the balance a 1:1 blend of excipents A and B achieves the target dissolution rate.

- The three week replacement rate is achievable with a tablet consisting of 97.5% DBNPA with 1.25% each of excipients A & B.

Conclusions

- Preferred tablet formulations released sufficient DBNPA to maintain aerobic plate counts below
- 4 $\log_{10}$ CFU/mL.

- Slow dissolving, 100 g DBNPA tablets of high tensile strength have been developed so that one tablet is used for every 500-1000 G of recirculating water to be treated.

- New tablets have a comparable dissolution rate to a commercially-available 200 g DBNPA tablet.

Acknowledgements

Brad McGhee and James Shaw of Triton Chemical Services (a member of the AWT) are thanked for identifying and making available the two cooling water trial sites.