Stability of antibiotic trimethoprim-sulfamethoxazole in three different rodent water formulations

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Advantages of antibiotic administration in drinking water

Administration of medications in the drinking water is desirable for several reasons, including:

- Low stress to the animal
- Efficient in time for researchers and other personnel
Medication administration in the drinking water of mice

Potential limitations:

- Drug stability in the water
- Mouse consumption of water
- Systemic absorption
Previous studies

• Previous studies evaluated the efficacy of various antibiotic in water bottle formulations with variable results

• Mean plasma concentrations measured for the antibiotics were below the lower range of the minimal inhibitory concentration (MIC) for many pathogens
200 mg of sulfamethoxazole (SMX) and 40 mg of trimethoprim (TMP) per 5 ml
MediDrop® Sucralose

- Sweetened water gel formulation that can be used for medication delivery
- Maintains medications in suspension
- Facilitates consistent delivery
Specific Aims

- Test the stability of trimethoprim (TMP)-sulfamethoxazole (SMX) in reverse osmosis (RO), acidified (AW), and sweetened water gel (SWG; MediDrop) water bottle formulations
Materials & Methods

- Water bottles suspended in empty mouse cages for 7d
- Water was collected to mimic the water the mice would be drinking from the end of the sipper tube.
- Starting concentrations
  - 0.8 mg SMX & 0.16 mg TMP per mL
  - 0.4 mg SMX & 0.08 mg TMP per mL

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Quantity (ml)</th>
<th>Sulfu-trim quantity (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RO water</td>
<td>490</td>
<td>10</td>
</tr>
<tr>
<td>Acidified water</td>
<td>490</td>
<td>10</td>
</tr>
<tr>
<td>MediDrop</td>
<td>495</td>
<td>5</td>
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</tbody>
</table>
Experimental design

- High-performance liquid chromatography (HPLC) analysis

- 0 h, 4 h, 8 h, 24 h, 48 h, 72 h and 7 d time points
Results - RO water group

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</thead>
<tbody>
<tr>
<td>TMP (ug/ml)</td>
<td>19.80±0.42</td>
<td>19.8±2.04</td>
<td>19.84±2.36</td>
<td>21.62±0.50</td>
<td>20.20±3.21</td>
<td>19.90±3.23</td>
<td>21.92±3.32</td>
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<tbody>
<tr>
<td>SMX (ug/ml)</td>
<td>59.5±10.76</td>
<td>31.08±1.25</td>
<td>28.62±3.05</td>
<td>31.22±3.13</td>
<td>33.06±3.63</td>
<td>30.77±2.80</td>
<td>37.47±4.52</td>
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### Results - acidified water group

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<th>day7</th>
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<tbody>
<tr>
<td>TMP</td>
<td>50.9±18.21</td>
<td>45.65±4.02</td>
<td>45.73±3.09</td>
<td>43.87±1.58</td>
<td>44.29±1.80</td>
<td>44.60±3.85</td>
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<th>day7</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMX</td>
<td>116.43±15.62</td>
<td>103.07±7.83</td>
<td>101.08±8.73</td>
<td>79.22±5.55</td>
<td>83.51±7.83</td>
<td>84.66±10.46</td>
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## Results-MediDrop group

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</thead>
<tbody>
<tr>
<td>TMP</td>
<td>93.01±1.14</td>
<td>91.32±0.66</td>
<td>91.95±0.82</td>
<td>93.02±0.75</td>
<td>93.31±1.28</td>
<td>94.56±2.21</td>
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<tr>
<td>SMX</td>
<td>336.39±1.32</td>
<td>333.85±3.28</td>
<td>343.73±7.82</td>
<td>340.96±5.52</td>
<td>348.83±8.05</td>
<td>346.92±8.04</td>
<td>344.69±10.44</td>
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Discussion points

- Concentration of trimethoprim remained steady in all three groups
- Sulfamethoxazole precipitated out in RO & AW group, however levels of both constituents were steady in MediDrop® Sucralose
In vivo experiment - SMX levels
**In vivo experiment - TMP levels**

- **Concentration (ng/ml)**
  - **Trimethoprim (ng/ml)**
    - 3d
    - 7d

- **Samples**
  - RO water
  - Acidified water
  - MediDrop (low dose)
  - MediDrop (high dose)
References

Acknowledgements

- Trinka Adamson, MS, DVM, DACLAM
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  - Marie Perez, LATG
- ClearH2O