Determination of Serum Sodium Salicylate Concentrations in Swine Resulting from Administration through Water Medication Systems

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Summary and Implications

Aspirin is widely used in food animal production for pain relief and fever reduction due to the current lack of antiviral drugs, the inexpensive cost, and the over-the-counter availability. However, there is no reported information on dosage or achievable plasma or serum concentrations when acetylsalicylic acid or sodium salicylate products are administered via water medicator dosing systems typically used in swine production facilities.

Significant differences are reported in the solubility of aspirin and sodium salicylate in water. These differences potentially impact the amount of each product that can be provided to pigs via water medication systems. Additionally, dose data for the oral route of administration is based on the provision of a daily dose in a single oral gavage. This differs from the typical application in swine where a daily dose is consumed over a 24 hour period via the drinking water.

Reported differences in solubility were confirmed in the first phase of this trial. The second phase selected the most soluble product (sodium salicylate) and administered four concentrations to commercial swine for 72 hours. Serum plasma levels were analyzed by HPLC from 10 randomly selected pigs in each group including controls at 0, 24, 60, and 72 hours post administration. Sodium salicylate reached peak serum levels 24 hours post administration and exhibited a dose dependent trend.

This study provided information necessary to perform future challenge trials for dose determination.

Materials & Methods

Trial pens from a commercial nursery were plumbed with new pipes and equipment from the water nipple to the fresh water source. No previous medication had been administered through the system at study initiation. One-half inch internal diameter PVC pipe, 5/8" Swan® garden hose, Lixit® 1/2" nipple waterers, and 1/2" galvanized pipes were used. A water sample was taken from the site and tested for standard contaminants by the Iowa State University Diagnostic Laboratory.

A representative liquid sodium salicylate product and liquid acetylsalicylic acid product were chosen from those commercially available. The maximum solubility of each product in stock solution was determined by using the reported solubility.

To confirm the solubility calculation, each product was used to formulate a stock solution with equivalent concentration of active ingredients (11.2 mg/ml). These stock solutions were placed in the test nursery environment for 24 hours and sampled at 0, 8, 16, and 24 hours. The concentration of salicylate was determined by High Pressure Liquid Chromatography (HPLC). Due to the higher solubility of the sodium salicylate product it was used for the remainder of the trial.

Four groups of three pens in the commercial production nursery facility were plumbed with group specific water medicators and water meters. Three other pens, comprising a fifth control group, were plumbed with a water meter only. Pens were populated and managed according to the standard operating procedures of the facility. The use of animals in this study was approved by the Committee on Animal Care at Iowa State University.

When pigs were approximately forty pounds average weight, each set of pens received one of the four treatments for a period of 72 hours. Stock solutions were prepared at the following concentrations: 0.3 oz/gal (19.4 ppm), 0.7 oz/gal (38.9 ppm), 1.3 oz/gal (77.6 ppm), 2.66 oz/gal (155.3 ppm), respectively for treatments 1-4. Ten randomly selected pigs in each pen were tagged and bled at 0, 24, 60, and 72 hours after study initiation. Serum salicylate levels were measured using HPLC.

Results and Discussion

Water sample analysis yielded no significant quality concerns.

Under both laboratory and nursery conditions the acetylsalicylic acid crystallized and precipitated out of solution while the sodium salicylate remained in solution. HPLC analysis of the stock solutions (data not shown) confirmed observations of precipitation of acetylsalicylic acid in stock solutions. These results are consistent with published solubility data for acetylsalicylic acid (3.43g/L) and sodium salicylate (999.63 g/L). Acetylsalicylic acid concentrations were insufficient to achieve a recommended dose greater than 3.1 mg/kg.

Table 1 shows the mean serum concentration (µg/mL) (standard deviation in parenthesis) of sodium salicylate by treatment and time. The peak serum concentrations were

observed at 24 hours for all stock solution concentrations and show a dose dependent trend.

Only liquid aspirin products were used for this trial due to availability. Three manufacturers were found to produce all liquid aspirin and sodium salicylate products under various brand names at the time of this study. Labels claimed identical concentrations of active ingredient representing concentrations of sodium salicylate at 120 mg/ml and acetylsalicylic acid at 485.6 mg/ml.

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Table 1: Mean serum concentration (µg/mL) (standard deviation in parenthesis) of sodium salicylate by treatment and time.

T1 = stock solution concentration of 19.4 ppm, T2 = 38.9 ppm, T3 = 77.6 ppm, T4 = 155.3 ppm, T5 = 0 ppm

Sample time (hrs)	T 1	T 2	T 3	T 4	T5
0	0	0	0	0	0
24	0.41(0.31)	1.28 (1.03)	1.41 (0.64)	7.22 (2.31)	0
60	0.17 (0.15)	0.82 (0.77)	0.44 (0.50)	2.66 (2.41)	0
72	0.27 (0.20)	0.03 (0.07)	1.24 (0.79)	0.62 (0.48)	0