Homogeneity and stability of a flubendazole oral suspension in drinking water

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Introduction

Flubendazole is a benzimidazole compound active on digestive pig nematodes including an ovicidal effect. Its efficacy in pigs via feed has been reported (1). Nevertheless medication in drinking water would be a valuable alternative (no constraint of medicated feed manufacture, flexibility of treatment implementation), provided that a reliable and easy to use formulation would be available. Thus a new 10% flubendazole oral formulation has been developed, allowing treatment in water over 4 h per 24 h without stirring of medicated water required, followed by an easy cleaning of water equipment (Flimabo®/Flimabend®, Virbac/Krka).
Efficacy of this formulation has been reported on *Ascaris suum* (2). Objective of this study was to test homogeneity and stability of the formulation in drinking water from stock suspension to drinkers delivery.

Materials and Methods

In a first step, a stock suspension containing 2.4 g/l of flubendazole was prepared for either the tested *suspension (A) or a control 10% flubendazole emulsion* (B). Following initial stirring, the stock suspension was either left unstirred (products A and B) or stirred every 30' (product B) for 4 h. Water samples were taken every hour on the top and the bottom of the stock suspension, with or without stirring for product B.
In a second step, a stock suspension was prepared with product A and left unstirred for 4.5 h during which a dosing proportioner incorporated the medicated water through a pipeline to nipples (either pig or poultry model) at the rate of 1.13% (theoretical end flubendazole concentration : 85 mg/l). Water samples were taken every 15' at the nipple level.
In both studies, flubendazole was assayed in water samples by High Performance Liquid Chromatography.

Results

Concentration in stock suspension ranged between 91% and 102% of theoretical one for product A without stirring over 4 h. For product B, when the stock suspension was stirred every 30', concentrations below 90% of theory were measured at bottom level before each stirring. When the suspension prepared from product B was left unstirred, the phenomenon was enhanced, with concentration decreasing from 97% to 55% over 4 h (Figure 1).
Concentrations at nipple level ranged between 94% and 115% of theoretical one for product A without stirring over 4.5 h (Figure 2).

Discussion

As flubendazole is not soluble in water, medication through this vehicle requires a formulation allowing homogeneity and stability of the medicated water suspension during the whole treatment period. The tested formulation (A) fulfilled these criteria from the stock suspension to the end drinkers without requiring any stirring over 4 h. For the control formulation (B), a demixing was observed in the stock suspension, even according to the recommended way of use (stirring every 30'), possibly leading to heterogeneity of medicated water distributed to animals and concern on treatment efficacy

Conclusion

This study confirms that the tested formulation allows a reliable and practical way of flubendazole medication in water.

Fig. 1: Flubendazole stock suspension concentrations (bottom level)

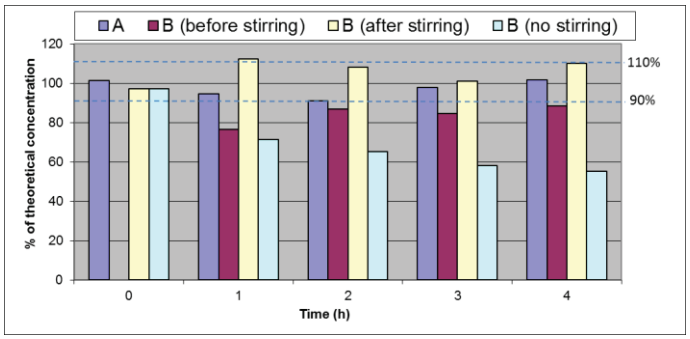
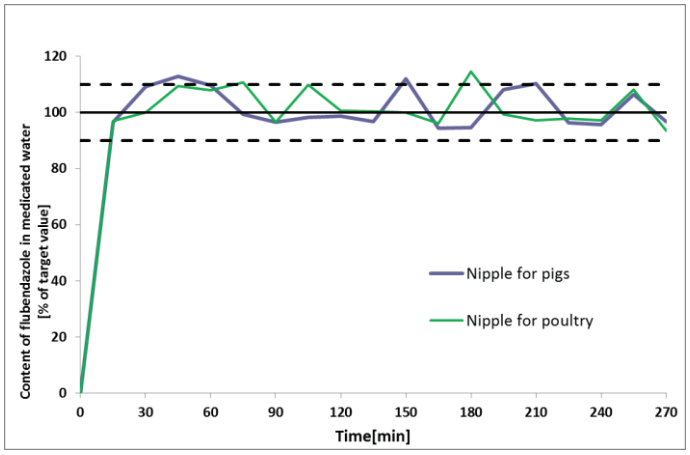


Fig. 2: Flubendazole concentrations at nipple level



References

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