

Amoxicillin, stability and solubility

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Amoxicillin dissolves fast, has a high solubility and a good stability if the pH can be buffered at 8. These objectives were met with Octacillin®. Several studies were done to evaluate the stability of amoxicillin in its different presentations, as well as its stability after dissolution in tap water. These studies are briefly discussed.

Drinking water contaminated with 3000 CFU *Pseudomonas aeruginosa* and *Flavimonas oryzae* per ml reduced amoxicillin concentration to zero if a bacterial growth promoting agent was used as a carrying agent for the antibiotic. In case of Octacillin® this was not the case, as the product does not contain a growth promoting agent.

0.150 g amoxicillin per litre drinking water with pH 8.00, temperature 19.0°C, hardness 13.0 °d (therapeutic solution for continuous application) was tested for solubility and stability. No major differences were seen between the different products, except one product which showed increased degradation products.

When 4.2 g amoxicillin was dissolved in 1 litre drinking water with pH 8.04, temperature 19.5°C, hardness 13.1 °d, conductivity 584 µS/cm (concentrated solution for pulse medication) the results were different. Some products did not dissolve at all, some showed free particles, but some were clear colourless solutions free from particles.

In this colourless group free of particles the stability of amoxicillin ranged from 54 % to 100 % after 24 hours, showing a proportionate increase of degradation products.

Products which showed visibly improved solubility after adding solubility enhancers, were not always stable solutions at 6 or 24 hours after dissolving.

It can be concluded that the visible solubility is not in relation with the in water stability of concentrated forms of amoxicillin used for pulse medication. Details of solubility and stability tests are shown.

Keywords: Amoxicillin 1; stability 2; solubility 3; pulse 4; Octacillin® 5

Introduction

Amoxicillin is an extended spectrum penicillin. Amoxicillin penetrates more easily from the bacterial cell surface to the peptidoglycan structure than penicillin G. This partly explains the broader spectrum of amoxicillin. Amoxicillin is mainly used for necrotic enteritis treatment, dysbacteriose and respiratory infections in broilers (Jansegers L., 2006). Therefore drinking of medicated water is advised.

Materials and methods

In a first study, the stability of amoxicillin when dissolved in drinking water, contaminated with 3000 CFU *Pseudomonas aeruginosa* and *Flavimonas oryzae*, was investigated. Amoxicillin was diluted at 60 mg per l water. Octacillin, without lactose in its formula, was used and Product A (United Kingdom / Ireland), a growth promoting containing amoxicillin water-soluble powder, as reference. The amount of amoxicillin and amoxicillin degradation products were measured by HPLC at 0 and 24 hours.

In a second trial 0.150 g amoxicillin per litre drinking water with pH 8.00, temperature 19.0°C, hardness 13.0 °d was tested for solubility and stability. The products used were: product B (France), product C (France), product D (Belgium), product E (Belgium), product F (Belgium), product G (the Netherlands), product H (the Netherlands), Octacillin® – Eurovet Animal Health, product I (France). The pH and the amoxicillin concentration was determined at t = 0, 6 and 24 hours. At each time point, 5 ml water was sampled 5 cm below the surface and immediately after sampling the solution was filtered through a 1.0 µm filter. The amoxicillin concentration was determined in the filtered solution

In a third trial 4.8 g amoxycillin trihydrate of the same products was added to glass containers, filled with 1 litre water (pH 8.04 temperature 19.5°C, hardness 13.1 °d, conductivity 584 µS/cm) and equipped with a magnetic stirrer. The pH and the amoxicillin concentration was determined at t = 0, 6 and 24 hours. At each time point, 5 ml water was sampled 5 cm below the surface and immediately after sampling the solution was filtered through a 1.0 µm filter. The amoxicillin concentration was determined in the filtered solution.

Results and discussion

The results of the first trial indicated that products without growth promoting agents, had a much better stability. (*Table 1*) Water-soluble powders often contain a sugar as excipient. Sugars however are an excellent nutritional source for germs. When an antibiotic together with a sugar are added to the drinking water, the antibiotic will kill susceptible bacteria that are present in the pipe system. Yeasts and fungi however may survive and, thanks to the sugar, overgrow the system. In a few days this may result in slimy obstructive debris, which is very hard to remove. Bacteria that are resistant to the antibiotic may also multiply thanks to the sugar and even inactivate the antibiotic.

Table 1: Amoxicillin concentration in drinking water contaminated with 3,000 CFU *Pseudomonas aeruginosa* and *Flavimonas oryzihabitans* per ml

Concentration	Octacillin	Reference product with bacterial growth promoting agent
t = 0 hours	100%	100%
t = 24 hours	73%	0%

In the second trial no major differences were seen between the different products for stability, except one product showed decreased amoxicillin amounts. (*Table 2*). Solubility at this low concentration was good for all products. Product G showed reduced stability.

Table 2 Amoxicillin concentration in % of administered amount of 0.15 g /l

Amoxicillin concentration in % of administered amount of 0.15 g /l			
	t=0	t=6	t=24
Product B	100	98.0	97.0
Product C	100	98.0	97.0
Product D	100	100.0	99.0
Product E	100	100.5	99.0
Product G	100	99.2	95.9
Product H	100	100.5	100.7
Octacillin® - Eurovet Animal Health	100	100.7	100.4
Product I	100	100.4	98.0

In the third trial product D, product E and product H were not dissolvable at 4.8 g /l amoxicillin trihydrate. Products E and H went in solution after adding a solubility enhancer. No specific solubility enhancer for product D is known. (*Table 3*). This results show impaired stability product E plus solubility enhancer and product G.

Table 3 Amoxicillin concentration in % of administered amount of 4.8 g /l

Amoxicillin concentration in % of administered amount of 4.8 g /l			
	t=0	t=6	t=24
Product B	100	102.3	97.6
Product C	100	100.0	100.0
Product E with solubility enhancer	100	80.9	52.3
Product F	100	100.0	97.6
Product G	100	80.0	55.0
Product H with solubility enhancer	100	97.5	95.0
Octacillin – Eurovet Animal Health	100	100.0	97.5
Product I	100	100.0	97.5

Drinking water medication can only be effective if the antimicrobial drug is available to the animals in a sufficiently high concentration in the drinking water for a sufficiently long period. The characteristics of the water-soluble preparation and the mode of administration to the drinking water are major factors influencing this availability.

References

JANSEGGERS L., (2006) , WVPA study day, Ghent, Belgium