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Correlation analysis of heat stability of veterinary antibiotics by structural degradation, changes in antimicrobial activity and genotoxicity

Hsieh MK, Shyu CL, Liao JW, Franje CA, Huang YJ Chang SK, Shih PY, Chou CC:

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[fulltext]

The relationship between the structural degradation of veterinary antibiotics, their antimicrobial activity, and possible mutagenicity after heating have not been well investigated sequentially. This study aimed to evaluate the heat stability of 14 veterinary antibiotics under a short-term heating scenario by characterization of their structural degradation and their relationship to resultant changes in antimicrobial activity. Mutagenicity was also examined in four representative antibiotics after 15-min-heat treatments at two temperatures (100 °C and 121 °C). Differential heat stabilities of antibiotics between drug classes, between

temperature levels, and among the same class of drugs were discovered. Heat treatment resulted in the reduction of the main peak and the production of new peaks in certain antibiotics, contributing to minimum inhibitory concentration increases of 2- to 1024-fold. Ranking of heat stability by antibiotic classes at 121 °C was highest for sulfonamides, followed by lincomycin, colistin, tetracyclines and β-lactams while at 100 °C sulfonamides equaled lincomycin and and was greater than colistin but variability was observed within different tetracyclines and β-lactams. Correlation analysis suggested that except for doxycycline (DC), structural degradation of the drugs was in good agreement with the reduction in antimicrobial activity, suggesting that degradation also diminished antimicrobial activity. Furthermore, the markedly variable heat stabilities within the classes of tetracyclines and β-lactam antibiotics highlighted the fact that heat stability within these two classes can be very different despite their structural similarity; hence, it is not appropriate to predict heat stability simply by antibiotic class. Mutagenicity (Ames) tests on heated

6-fold revertant changes in *Salmonella typhimurium* TA98 and TA100. The combined results suggest that correlation analysis of structural degradation and antimicrobial activity offers dual evaluation of a drug's heat stability but gives little advantage over assessment of the resultant toxicity.

Keywords:

capillary electrophoresis; minimum inhibitory concentration; mutagenicity; Ames test; thermodegradation

[fulltext]