

EVALUATION OF TIAMULIN AS A GROWTH-PROMOTING AGENT IN  
THE PIG BY MICROBIOLOGICAL CRITERIA  
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Since bacteria of the intestinal flora may, in particular, be carriers of resistance plasmids and may also, like higher organisms, change their properties through mutations, one should be sure that when an antibiotic is used as a growth promoter it will have no adverse effects on the therapy and prophylaxis of infectious diseases in man and animals.

In the light of the current status of knowledge on the onset of resistance in bacteria, the authorization, as a growth promoter, of a substance with anti-bacterial properties, such as tiamulin hydrogen fumarate (Dynamutilin, Feed Premix (extrudate formulation), E. R. Squibb & Sons, Inc.), hereafter referred to as tiamulin, calls for an answer to the following questions in the member countries of the EEC with the necessary investigations being carried out on representative species of the intestinal flora of the target animal.

1. What is the position regarding the selection of resistant mutants to the "new" substance?
2. If there is higher insensitivity to the new substance, is it associated with a corresponding resistance to a chemotherapeutic which may be used in the treatment of infectious diseases, due to a chemical relationship in structure, or through a similar mechanism of action?
3. Is the substance a selector of R-plasmids?

These questions must be answered both for gram-negative and gram-positive bacterial species for which phenomena of transmissible drug resistance are known.

In order to check on any possible adverse effects arising from the use of tiamulin (up to 30 ppm) as a growth promoter in the pig by the development of resistance in the species representative of the intestinal flora of the pig, and to answer the questions initially posed, two animal trials were carried out under practical conditions.

It has been confirmed that tiamulin, when used as a feed additive, is not a selector of R factors, probably because its anti-bacterial spectrum is concentrated on the gram-positive species, and proved inactive against porcine *E. coli*.

Since tiamulin is not active against *E. coli* and only partially active against gram-positive organisms of the intestinal flora of the pig, the intestinal flora is apparently not drastically changed by administration of this antibiotic at a nutritive dosage, so that it cannot promote the colonisation of pathogenic organisms which might become dominant.

It was also demonstrated that tiamulin, even in the highest dosage of 30 ppm, does not lead to the selection of *Lactobacilli* insensitive to tiamulin, so that the nutritive effect of tiamulin may be explained by a sustained reduction of these organisms, entering into competition with the host for nutrients and vitamins. Both the enterococci (group D streptococci) and the staphylococci, even after several weeks of use of tiamulin, proved sensitive to tiamulin.

The demonstrated resistance to chemotherapeutics in these organisms gave no hint of a direct or indirect effect of administration of tiamulin on the selection of representatives with deviations from the usual resistance patterns of these species. Tiamulin meets the requirements which a modern growth promoter has to satisfy. From the microbiological standpoint, there are no objections to the use of tiamulin as a growth promoting agent in the pig.