THE VALUE OF CARBADOX[a] (METHYL 3-(2-QUINOXALINYLMETHYLENE) CARBAZATE N^1, N^4DIOXIDE) IN THE DIETS OF WEANER PIGS IN THE HUMID TROPICAL ENVIRONMENT

By

G.M. BABATUNDE, B.L. FETUGA
and F.O. AMUBODE
Department of Animal Science,
University of Ibadan, Nigeria.

SUMMARY

Two experiments were carried out with 108 weaner pigs of the Large White and Large X Landrace breeds, to determine the effects of feeding graded levels of Carbadox (Mecadox), a relatively new synthetic feed medicant with bactericidal and growth-promotion properties, to weaner pigs on their levels of performance and their nutrient utilization abilities in the hot humid tropical environment. Two management conditions, a clean and an untidy conditions were tried. The basal diet was a 19% crude protein diet to which were added 0.0, 10.0, 25.0 and 50.0 ppm levels of Carbadox to give a total of our diets which were fed either individually or in groups to the piglets within each of the four treatment groups. Digestibility trial was carried out in the middle of experiment 1 only. In both experiments, pigs on the 50 ppm diet grew at a faster rate than the pigs on the other diets, but significantly faster in experiment 2 only. Feed consumption was slightly stimulated by the presence of Carbadox, though not significantly, while the efficiency of feed utilization was significantly improved in experiment 2, being best for the 50 ppm diet and worst for the control Carbadox-free diet. The digestibility trial in experiment 1 showed no significant differences in the nutrients digestion coefficients and nitrogen retention, all of which were close for all treatments, with no consistent trends.

[a]A Pfizer International Product.

INTRODUCTION

Carbadox is a relatively new synthetic chemical compound made by Pfizer International Incorporated, New York. Its chemical name is Methyl 3-(2-quinoxalinylmethylene) Carbazate N, N^4 diozide, and its generic name is "Carbadox." Pfizer markets it under the trade name "Mecadox." Its molecular formula is $C_{11}M_{10}N_4O_4$, and its molecular weights is 262.23. This synthetic chemical compound classified as quinozaline di-N-oxide has both anti-bacterial and growth promoting properties, and it is supposed to be unique in its efficacy against swine dysentery and has inhibitory action against a very wide range of Gram-positve and Gram-negative bacterial specie. It is usually recommended for pigs below the weight of 35kg., with the warning that withdrawal of the compound should take place at least 10 weeks prior to slaughter.

Before the compound was put in the market, Pfizer International commissioned a large number of research stations in different parts of the world to investigate the effects of using this compound on growth rate, feed/gain ratio, nutrient digestion coefficients and the prevalence of vibrio-like organism and salmonella spp. in the faecal swabs of pig and the results of these are summarized in Pfizer Technical Bulletins on Mecadox (Anon, 1970 & 1971). Other than the extensive information summarized in this Bulletin, one does not often find information on this compound in the literature. The few available on weaner pigs showed significant improvements on growth rates and efficiency of feed utilization through the use of carbadox (Trasher *et al* 1969, 1970), as well as better digestion and retention of nutrients (Yen *et al,* 1976).

The studies reported here were carried out to evaluate the relative merits of feeding graded levels of Carbadox to weaner pigs in a humid tropical environment which was not one of the climatic environments covered by the Pfizer studies using this product.

MATERIALS AND METHODS

The studies reported here were carried out in Ibadan, Nigeria, with a hot, humid tropical climate, Ibadan city is located at Latitute 07° 20 N and longitude 03° 50 E, with an altitude of 212 metres. average maximum and minimum temperatures during the period of experimentation were 33° and 24°C respectively, and the average relative humidity at 10.00 and 16.00 hrs. were 85 and 68% respectively while the total hours of bright sunshine average 170 per month. The average monthly precipitation was about 108 mm.

These studies involved 108 weaner pigs of the Large White and the Large White X Landrace crossbreeds randomly assigned to various treatments as described below. Experiment 1.

Forty-eight newly-weaned piglets of both sexes were selected. They weighed 10kg. on average, at the time of selection. The males had earlier been castrated and their wounds had healed about three weeks before the trial started. They were randomly divided into four equal treatment groups of 12 pigs, each group having equal breed ratios, equal average initial liveweight, and equal sex ratios, although the females slightly outnumbered the males (7:5, females to males). Before they were selected for the trial, they were all on the standard weaners' diet containing 24% crude protein. At the start of the trial, the pigs were placed on one of the four test diets formulated to contain approximately 19% crude protein (basal) to which were added 0.0 10.0, 25.0 or 50.0 ppm., Carbadox. These diets were also randomly assigned to the treatment groups. In this trial, all pigs were individually fed four times per day at 08.00hr., 12.00hr., 15.00hr. and 18.00hr., each feeding lasting one hour, after which the pigs were led out into the play pens where they drank water freely until the next feeding period. This feeding arrangement was the only way we could get accurate individual feed intake of the pigs. The composition of the diets used appear in table 1. Records were taken weekly of body weights and consumption.

After the pigs had been on the trial for three weeks, three pigs were randomly selected from each treatment group and placed in the pig metabolism cages designed and described by Oyenuga (1961). In these cages, the pigs were given weighed quantities of their previous feeds daily as well as liberal quantities of water in feeding and watering compartments of these cages. The first four days were used for acclimatization, while faeces and urine were collected for the next six days, using chromic oxide powder as marker to signal the times to start and stop faecal collections. They were returned to their various groups after the metabolism trial, and their records of feed consumption and weight gained were all considered along with the rest throughout the trial. All the analyses of feed, faeces and urine were carried out in accordance with the AOAC methods of Analysis (A.O.A.C., 1971). This trial lasted 8 weeks under what is hereby described as 'clean management conditions' in which the pens were regularly cleaned thrice per day with water.

Experiment 2.

This involved 60 weaner pigs of the same breeds as those in experiment 1, although they were heavier (approximately 15kg., average initial weight) at the start of the trial. They were randomly divided into four equal treatment groups of 15, each group having equal sex and breed ratios. Each group of 15 was further subdivided into three equal replicated groups of 5 pigs, the three replicate groups being fed the same diets *ad libitum* according to their treatments. The four diets which were also randomly assigned to each main treatment group were the same as those for the pigs in experiment 1, and hence their composition are the same as in Table 1. Watering was also *ad libitum* throughout the day.

TABLE 1

Composition of Experimental Diets (Expts. 1 and 2)

Ingredients (%)	*Diets*			
	1	2	3	4
Yellow maize	40.90	40.90	40.90	40.90
Groundnut meal	20.00	20.00	20.00	20.00
Blood meal	5.00	5.00	5.00	5.00
Fish meal	1.50	1.50	1.50	1.50
Brewers' yeast	1.50	1.50	1.50	1.50
Dicalcium phosphate	2.50	2.50	2.50	2.50
Oyster shell	0.50	0.50	0.50	0.50
Palm Oil	2.50	2.50	2.50	2.50
Carbadox premix	0.00	5.00	12.30	24.70
Wheat offals[a]	24.70	19.70	12.40	0.00
Pfizer's Agricare mix[b]	0.40	0.40	0.40	0.40
Salt	0.50	0.50	0.50	0.50
Totals	100.00	100.00	100.00	100.00
Analysed crude protein	18.97	18.84	18.68	18.89
Concentration of mecadox (pmm) ...	0.00	10.00	25.00	50.00

(a) Wheat offals was added to balance the amount present in the Mecadox premix.

(b) A Pfizer Livestock Feeds products supplying the following per kg of finished diets. Vitamin A, 9823 IU; D_3, 1965 IU; Vit. E, 69 IU; K, 20mg; B_{12}, 10mg/ton; Riboflavin, 41mg; Nicotinic acid, 246mg; Iodine, 20mg; Maganese, 341mg; Zinc, 100mg; Iron, 100mg: Oxytetracycline hydrochloride, 20g/ton.

In this trial, the cleaning of the pens was done only once a day (at 07.00hr.) in contrast to the thrice per day cleaning in experiment 1 to stimulate a "dirty condition." Metabolism trial was not carried out on these pigs because the results of the first metabolism trial showed no statistically significant differences among treatments. Records of weight gains and feed consumption were taken for all the pigs. This trial lasted only 28 days because the pigs were getting to the heavier weight not recommended for Carbadox medications by the manufacturers.

All the data on growth rate, feed consumption, feed efficiency ratios and nutrient digestion coefficients were subjected to the analysis of variance followed by Dunca's Multiple Range Test (Steel and Torrie 1960) to isolate the significant treatment means.

RESULTS

Tables 2 and 3 show the summaies of the performance characteristics and nutrient digestion cofefficients for the pigs in trials 1 and 2 respectively.

AVERAGE DAILY GAIN (ADG).

In both trials, the pigs on the 50 ppm Carbadox diet outgained the pigs on all the other diets. In experiment 1, although there were no significant differences in the ADG for the treatments, the growth improvement index showed that pigs on 50 pmm Carbadox outgained the pigs on the control, zero Carbadox diet by 22%, while those on 25 ppm level outgained the control pigs by 17%. All the pigs on the Carbadox diet by 22%, while those on 25ppm level outgained the control pigs by 17%. All the pigs on the Carbadox-medicated diets were supperior gainers than to those given the control diet.

In experiment 2, (Table 3) the pigs on the 50 ppm Carbadox diet grew at a significantly faster ($P < 0.05$) rate than the pigs on the control diet only, having a

growth improvement index of 27% over the control pigs. Pigs on the 25 ppm. and 10 ppm Carbadox diets also outgained the control pigs by 17 and 15% respectively but the differences were not significant. Overall, the pigs in trial 2 were superior gainers to those in experiment 1, although their average starting weight was heavier.

TABLE 2

Performance Characteristics and Nutrients Digestion Coefficient of Pigs fed Graded Levels of Carbadox: Experiment 1

Characteristics	*Dietary Treatment Means 1/*				
	1	2	3	4	
Levels of Carbadox (ppm)	0.00	10.00	25.00	50.0	ppm
Average number of pigs	12.00	12.00	12.00	12.00	
Average initial liveweight (kg)	10.00	9.55	10.09	8.86	
Average final liveweight (kg)	33.04	34.75	36.97	36.86	
Average daily gain (kg)	0.41	0.45	0.48	0.50	
Growth improvement index	1.00	1.10	1.17	1.22	
Average daily feed consumed (kg) ...	0.96	1.04	1.09	1.13	
Average feed/gain ratio	2.34	2.31	2.27	2.26	
Feed efficiency index	1.00	1.01	1.03	1.04	
Crude protein digestibility (%) ...	88.50	88.08	87.20	87.69	
Ether extract digestibility (%)	89.54	91.58	90.86	89.77	
Crude fibre digestibility (%)	65.61	70.73	70.79	66.81	
Nitrogen retained (%)	55.51	54.73	53.03	55.09	
Apparent Biological Value	67.04	67.36	67.86	71.79	

1/ There were no significant differences in the treatment means for all the characteristics investigated in this trial. (P. 0.05).

TABLE 3

Performance Characteristics of Pigs fed Graded Levels of Carbadox: Experiment 2

Characteristics	*Dietary Treatment Means*			
	1	2	3	4
Levels of Carbadox (ppm)	0.0	10.0	25.0	50.0
Number of pigs	15	15	15	15
Average initial liveweight (kg)	15.32	15.73	14.86	15.59
Average final liveweight (kg)	29.88	32.25	31.94	34.07
Average daily gain (kg)	0.52a	0.59ab	0.61ab	0.66b
Growth improvement index	1.00	1.13	1.17	1.27
Average daily feed (kg)	1.70	1.83	1.77	1.81
Average feed/gain ratio	3.27a	3.10ab	2.90ab	2.74b
Feed Efficiency index	1.00	1.05	1.13	1 . 1 9

a,b..... Treatment means in the same horizontal columns not underscored by the same surfix are significantly different from each other (P. 0.05).

AVERAGE DAILY FEED INTAKE (ADF)

As the data in Tables 2 and 3 show for both trials, there was a general tendency towards improved feed intake as the levels of Carbadox increased in both trials but the differences in ADF data in both experiments were not significant. It was observed that pigs in experiment 2 also consumed much larger quantities of feed than those in experiment 1, most probably because they were on *ad libitum* feeding regime unlike those in experiment 1 that were slightly restricted. Average Efficiency of Feed Conversion (EFC).

A direct comparison of this parameter for both trials 1 and 2 showed that pigs in experiment 1 had much better EFC than those in experiment 2. In trial 1, although there was a trend of better efficiency of feed utilization as the Carbadox levels increased, with the pigs on the 50 ppm Carbadox having the best conversion efficiency and the control pigs the worst converters, the differences in treatment means were not significant. In experiment 2, however, while a similar improvement in feed conversion efficiency was found as the Carbadox levels increased, the pigs on the Control, unmedicated diet (P 0.05) but were not significantly better than the other medicated diets. Similarly, the differences in the EFC ratios for the pigs on the control, 10 ppm and 25 ppm Carbadox diets were not significant. The feed efficiency improvement index was very much higher for pigs in trial 2 than those in experiment 1, with the pigs on the 50 ppm Carbadox diet being 19% and 4% more efficient than the pigs on the control diet for experiments 2 and 1 respectively. Nutrient Digestion Results.

The results of the nutrient digestion and retention (trial 1 alone) appear at the bottom of Table 2. For the major fractions studied, crude protein, either extract, and crude fibre, there were no significant differences among the treatment means and in fact, the figures were similar with no trends except in the apparent Biological Value which slightly increased non-significantly with increases in the Barbadox levels.

DISCUSSION

This synthetic chemical compound can be likened to any one of the major, well known, antibiotics since it has anti-bacterial and growth-promoting properties. It is unique in view of its efficiency against those micro-organisms that cause swine dystentery or bloody scours and swine enteritis.

The claim that the compound promotes better growth and feed efficiency in pigs has been vindicated in these trials even though the growth improvement was significant in one trial and not so in the other one. In virtually all the experiments summarized in the Mecadox Technical Bulletins (Anon, 1970, 1971) and more recently by Trasher *et al* (1969, 1970) and Yen *et al* (1976) the growth-promoting ability of Carbadox was demonstrated, and in all of them, the recommended level of 50 to 55 ppm Carbadox gave the best results as obtained in the trials described here. The differences in the growth responses between the two trials could be attributed to a number of reasons, the most significant one being the differences in the feeding regimes. The pigs in trial 2 were on *ad libitum* regime and hence they consumed much more feed which enabled them to grow faster than those pigs in trial 1 that were on a semi-restricted feeding regime. However, a comparison of the growth improvement indices in thetwo trials shows higher indices for pigs in trial 2 than those in trail 1. While the *ad libitum* regime of feeding could be a contributing factor, it was possible that the Mecadox was more effective in the medicated versus non-medicated diet in this trial because their

environment was "dirtier" than those in the first trial. This finding further confirms those of Braude, Wallace and Cunha (1953), and Cunha, Burnside, Meadows, Edwards, Benson, Pearson and Glasscock (1950), among others who had earlier said that under conditions of stress, such as poor sanitation and low quality rations, the improvement in growth and feed utilization are much greater when antibiotics are feed than under sanitary conditions. Furthermore, the finding is in line with those of Carpenter (1951), Catron *et al* (1950), Speer *et al* (1951, 1950) and Wallace, Hay and Cunha (1951), who claimed that in swine nutrition, the degree of effectiveness of antibiotic feeding is largely determined by the level of sanitation and hence disease level in the feed-lot. The absolute levels of improvement indices in the growth and feed conversion efficiency of our pigs were not as great as many of those summarized in the Mecadox Technical Bulletins (Anon, 1969, 1970) probably because we used higher protein diets which would tend to mask the differences in the inadequacies of the diets as had earlier been indicated by Braude *et al* (1953, 1955) who found significant differences in the performance characteristics of their pigs when they fed Carbadox to pigs on low protein diets but not so when the diets were high in protein.

The nutrient digestibility data were, however, contrary to what most workers had reported for pigs on various levels of antibiotics in the past. Yen *et al* (1976) also obtained mixed results with respect to nutrient digestibility and retention but overall, they confirmed the findings of previous workers who obtained significant improvements in nutrient utilization as a result of antibiotics therapy. Catron *et al* (1952), Braude *et al* (1953, 1955), and Coates *et al* (1955) obtained significant improvements in nutrient utilization by the pigs or chicks fed antibiotics and postulated that the animals on antibiotics generally developed more efficient digestive enzyme system as well as a thinner intestinal lining that absorbed nutrients more readily than the thicker walls of those animals on the antibiotic free diets. The pigs in our studies did not show any significant differences in their nutrient digestion and retention abilities, but a possible reason could be the high protein intake levels and the high level of fibrous feed incorporation due to the need to equalize the fibre levels in all the diets, since the Carbadox was supplied premixed with wheat offals.

In conclusion, these studies have shown that in the humid tropical environment, the feeding of Carbadox at 50 ppm level would improve growth rate, feed consumption and the feed conversion efficiency of weaner pigs, but its effects on the nutrient digestion and retention abilities of the pigs is still inconclusive, although the level of dietary protein used in the basal diet might be a major factor to consider.

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