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Evaluation of the anticoccidial efficacy of quinfamide alone and in combination with carbopol in rabbits at weaning

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Abstract

This study aimed to evaluate the anticoccidial activity of quinfamide in rabbits during the weaning period, which is considered a particularly vulnerable time for the clinical presentation of coccidiosis. Thirty-day-old New Zealand rabbits were included in this trial and were divided into the following groups: randomized control, non-randomized control, quinfamide (30 mg/kg) + carbopol; quinfamide (30 mg/kg); quinfamide (60 mg/kg) + carbopol and quinfamide (60 mg/kg). Treatments were administered orally by mixing the drugs with the rabbits' standard feed. Weight, daily weight gain, feed intake, conversion, and oocyst shedding were recorded for 14 days. The groups treated with quinfamide and quinfamide (60 mg/kg) + carbopol showed a clear improvement in the evaluated parameters compared to the control groups, and there was an increase in the duration during which oocysts in feces could not be detected. The group treated with quinfamide (30 mg/kg) + carbopol also presented better results than the control groups. In contrast, the group treated with quinfamide (30 mg/kg) alone, did not show any differences compared to control groups. Based on these results, it can be considered that quinfamide may present a useful anticoccidial effect, similar to the one obtained with other anticoccidial drugs in rabbits, but only when pharmaceutically prepared with carbopol as quinfamide retentive polymer in the gastrointestinal tract.

Keywords: Rabbit; Quinfamide; Carbopol; Coccidia; Treatment.

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Additional information and declarations can be found on page 11

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Study contribution

A new drug as an alternative for treating coccidiosis in rabbits evaluated under production-specific conditions. Increasing treatment alternatives aims to prevent or reduce the development of resistance.

Introduction

Recently, rabbit medicine has advanced due to various economic and productive benefits. Rabbits can be regarded as companion, laboratory, or meat-producing animals. Aside from an epistemic shift that increasingly views animal foods through moralistic lenses, rabbit meat production is increasingly relevant in developing countries.[1, 2] As such, coccidiosis is the main parasitic disease in production animals and generates important economic losses due to the reduction in feed consumption, presence of diarrhea, weight loss, and alterations in their metabolism. Coccidiosis is caused by the protozoan microorganisms of the genus *Eimeria*.[1, 3, 4] In rabbits, various species of *Eimeria* are known, of which the majority are located at the intestinal level and only *Eimeria stiedai* exclusively colonizes the liver, and biliary tract.[5] *E. coecicola*, *E. exigua*, *E. flavescens*, *E. intestinalis*, *E. irresidua*, *E. magna*, *E. media*, *E. perforans*, *E. piriformis*, *E. stiedai* and *E. vejdovskyi* affect the gastrointestinal (GI) tract.[1] Diagnosis can be made by identifying the parasites' oocysts in feces and correlating the lesions with the site of infection and the present clinical signs. Also, other tests such as ELISA and PCR are available.[1, 5, 6]

The prevalence of coccidiosis is related to several environmental factors, nutritional deficiencies, and production stress.[7] Transmission is oro-fecal occurring through fomites and contaminated feed containing feces from infected animals.[8] Affected rabbits exhibit poor growth rates, reduced feed consumption, abdominal pain, prostration, and diarrhea.[6] There is no difference in the clinical signology or change in the prevalence associated with sex, so it must be considered that this disease can occur in all animals.[2] However, rabbits are more susceptible to coccidiosis between the first and third months of life, especially at weaning (28-32 days). However, rabbits under 21 days are less susceptible to this disease.[3, 6, 9] Morbidity and mortality are estimated from 60 to 90 % in 30 to 70-day-old rabbits.[1]

There are various pharmacological options for the treatment and prevention of coccidiosis, such as ionophore antibiotics (monesin, narasin, salinomycin) and compounds such as toltrazuril, sulfonamides, robenidine, and decoquinate. They are administered in their feed throughout their productive period.[8, 10, 11] Also, other preventive measures are recommended, such as continuous cleaning of their habitats, disinfection with dry heat (> 40 °C), and/or use of chemical disinfectants such as formalin, cresol, sodium hypochlorite, quaternary ammonium, among others.[6]

The development of coccidia resistance to anticoccidial drugs has been reported and the assessment and development of new therapeutic options are important.[9, 12, 13] In this trial, quinfamide is being evaluated. It is commonly used to treat amoebic dysentery in human medicine. Also, its anticoccidial efficacy has been reported in broiler chickens and sheep when administered orally.[12] Quinfamide, a derivative of dichloro-acetyl-quinolinol, has low toxicity, and its anticoccidial efficacy can be enhanced by prolonging its intestinal residence time by adding suitable pharmaceutical vehicles.[14, 15] Hence, in this trial, the anticoccidial activity of

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quinfamide was evaluated in rabbits considering the weaning period as a susceptibility factor to the clinical presentation of the disease.

Material and methods

Ethical statement

This study was approved by the institutional committee for the research, care, and use of experimental animals (CICUA) of the Faculty of Veterinary Medicine and Husbandry of the National Autonomous University of Mexico, with protocol number 706.

Animals and housing

Forty-two 30-day-old New Zealand white rabbits from the same farm, located in Iztapalapa, Mexico City (19.358912, -99.092584), were used. The farm had a clinical history of being affected by coccidiosis and the mothers were previously diagnosed to confirm coccidiosis by the McMaster technique. A maximum of six animals per battery-type cage of 90 cm long × 40 cm high × 60 cm wide, were housed. The airflow was adjusted with curtains and fans to maintain a room temperature ranging from 16 to 23 °C; the temperature was measured with a digital room thermometer near the cages. A commercial food was provided *ad libitum* (V-ital conejos, Purina® México), considering 138 g per rabbit per day, plus an extra 20 %. The commercial feed was free of antibiotics, anthelmintics, and growth promoters, and the content analysis was moisture 12 %, protein 15 %, fat 2 %, fiber 12 %, ash 10 %, nitrogen-free extract 42.5 %, calcium 1 % and 0.5 % phosphorus. Water was available *ad libitum* through automatic drinkers. The inclusion criteria were rabbits from mothers positive for coccidiosis, without diarrhea or another sign related to enteric or respiratory disease, and the exclusion criteria were rabbits from mothers with clinical coccidiosis or another digestive or respiratory disease.

Treatments

The chosen rabbits did not receive any treatment before the commencement of this experiment. A litter of seven animals was assigned as a non-random control group (NRC) and which did not receive treatment with anticoccidials from day 1 to day 14 of the study, the rest of the animals were randomly divided into 5 groups (n = 7/group), as follows: a second control group (random control group) that did not receive anticoccidials from day 1 to day 14 (RC); group Q30 that received quinfamide treatment at a dose of 30 mg/kg on days 1, 2 and 3 of the study; group QC30 receiving a treatment based on quinfamide plus carbopol at a dose of 30 mg/kg on days 1, 2 and 3 of the study; group Q60 treated with quinfamide at a dose of 60 mg/kg on days 1, 2, 3, 7, 8 and 9, and group QC60 treated as the former one but with quinfamide/carbopol.

Quinfamide (1 %) and quinfamide/carbopol (also 1 % in both cases) treatments were prepared with alfalfa flour and cornflour as pellets at the Department of Physiology and Pharmacology, School of Veterinary Medicine, National Autonomous University of Mexico. They were given to rabbits as in-feed medication in their

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standard diet. Ninety-seven percent pure quinfamide was obtained from Megafarma Laboratories SA de CV.

Sampling and processing

To assess the efficacy of the administered treatments, body weight (BW), daily weight gain (DWG), feed intake (FI), feed conversion ratio (FCR), and oocyst count per gram of feces (OPG) were measured. Each parameter was recorded from day 1 to day 14 (FDA, 2011). Stool samples to evaluate OPG were collected individually. Five grams of feces were obtained, labeled, and stored at 4 °C until processing within the next 48 h employing the flotation technique aided by an optic microscope (Amscope®) and a McMaster plate.[8]

Statistical analysis

This was performed by one-way analysis of variance (ANOVA). First OPG results were normalized by natural log transformation and then were compared using the Bonferroní test. All significant differences set at $P < 0.05$. The analyses were performed using the IBM SPSS Statistics 27 program.

Results

Weight

The groups with the highest mean weight on day 1 were Q60 (821.6 ± 67.5 g) and QC60 (821.6 ± 67.5 g), followed by NRC (785.0 ± 68.5 g), RC (649.1 ± 92.6 g), QC30 (639 ± 75.4 g), and Q30 (567 ± 57.8 g). The latter groups presented a statistically significant difference ($P = 0.7730$) compared to Q60 and QC60. The highest mean weight was recorded on day 7 for the QC60 group (1 053.3 ± 40.1 g). However, differences were not statistically significant ($P > 0.050$) when compared with groups Q60 (1 035 ± 57.6 g), QC30 (924 ± 63.9 g), and NRC (994 ± 53.4 g). Group Q30, with a mean weight of 864 ± 52 g resulted also in a non-significant difference ($P > 0.2290$) when compared with the RC group (900 ± 92 g). At the end of the treatment on day 14, the QC60 group registered the highest mean weight (1 421.6 ± 57.7 g) but was not statistically different ($P > 0.1100$) as compared with the Q60 group (1 371.6 ± 102 g). The same lack of statistically significant difference occurred when comparing the group QC30 (1 218 ± 79.2 g) with the Q60 group. In NRC group, which showed the highest mean weight on day 14 (1 139 ± 63.2 g) a statistically significant difference was observed ($P < 0.0010$) when compared to QC60 and Q60. Groups QC and RC did not show statistically significant differences ($P = 0.1390$) with CN (Table 1).

Daily weight gain

On day 1, the Q30 group registered a DWG with negative values compared to all other groups ($P < 0.0010$). But, on day 7 all groups showed a positive DWG and there was no statistically significant difference among groups ($P = 1$). At the end of treatment, on day 14, groups QC30 and Q60 presented the highest DWG.

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Table1. Mean and SD of body weight (g) during the treatment days

	Group[1]					
Day	**QC30**	**Q30**	**QC60**	**Q60**	**NRC**	**RC**
1	639 ± 75.4 ^{bc}	567 ± 57.8^{c}	821.6 ± 67.5^{a}	821.6 ± 67.5^{a}	649.192.6^{bc}	785.0 ± 68.5^{ab}
2	703 ± 60.8^{bc}	557 ± 56.4^{d}	901.6 ± 27.5^{a}	845 ± 50.7^{ab}	665 ± 90.8^{cd}	839 ± 55.3^{a}
3	765 ± 49.8^{bc}	675 ± 53.3^{c}	938.3 ± 45.3^{a}	881.6 ± 36.8^{ab}	711.6 ± 90.7^{c}	877 ± 53.3^{ab}
4	792 ± 44.9^{bc}	734 ± 51.6^{c}	975 ± 47.6^{a}	920 ± 18^{ab}	758.3 ± 95.7^{c}	907 ± 60^{ab}
5	850 ± 48.6^{bc}	788 ± 54.2^{c}	1 031.6 ± 16^{a}	968.3 ± 52.5^{ab}	805.8 ± 85.8^{c}	935 ± 66.4^{ab}
6	867 ± 60.8^{abc}	826 ± 55.1^{c}	1023.3 ± 32.5^{a}	1 011.6 ± 53.4^{ab}	869.1 ± 101.5^{bc}	975 ± 55.9^{ab}
7	924 ± 63.9^{abc}	864 ± 52^{c}	1 053.3 ± 40.1^{a}	1 035 ± 57.6^{ab}	900 ± 92^{bc}	994 ± 53.4^{abc}
8	974 ± 51.7^{a}	934 ± 73^{a}	1 096.6 ± 45.3^{a}	1 078.3 ± 71.1^{a}	940.8 ± 100.4^{a}	1 011 ± 71.8^{a}
9	1 009 ± 64.4^{bc}	944 ± 54.2^{c}	1 203.3 ± 54.8^{a}	1 133.3 ± 102.7^{ab}	987.5 ± 107^{bc}	1 036 ± 86.8^{abc}
10	1 044 ± 64.2^{bc}	981 ± 60.1^{c}	1 264.6 ± 52.9^{a}	1 170 ± 107.5^{ab}	1 019.6 ± 103^{bc}	1 046 ± 75.2^{bc}
11	1 081 ± 58.4^{b}	1 024 ± 70.5^{b}	1 283.2 ± 52.5^{a}	1 198.3 ± 102.7^{ab}	1 051.6 ± 110.2^{b}	1 075 ± 70^{b}
12	1 118 ± 59^{bc}	1 063 ± 55.5^{c}	1 301.6 ± 70.2^{a}	1 246.6 ± 85^{ab}	1 110 ± 96.4^{bc}	1 093 ± 67.7^{bc}
13	1 144 ± 65.5^{bc}	1 075 ± 44.7^{c}	1 383.3 ± 43.6^{a}	1 296.6 ± 95.1^{ab}	1 103 ± 95^{c}	1 113 ± 93.9^{c}
14	1 218 ± 79.2^{bc}	1 095 ± 84.1^{c}	1 421.6 ± 57.7^{a}	1 371.6 ± 102^{ab}	1 155.8 ± 90.4^{c}	1 139 ± 63.2^{c}

$^{a-c}$ Different literals indicate statistically significant differences between columns.
[1]QC30 = Quinfamide/carbopol 30 mg/kg; Q30 = Quinfamide 30 mg/kg; QC60 = Quinfamide/carbopol 60 mg/kg; NRC = Non-random control; RC = Random control

However, comparisons with all other groups revealed no statistically significant differences ($P = 1$). As gathered from the data in Table 2, the DWG presented constant variations in all groups throughout the 14 days of this trial. Nevertheless, no variations in feed intake were recorded, and food waste was minimal, less than 10 percent.

Feed intake

On the first day, FI was highest in the NRC group (156.77 ± 13.67 g) compared to all groups ($P < 0.0010$), and no further differences were detected among groups, except the lowest FI recorded for the Q30 group (17.47 ± 2.14 g) ($P < 0.0010$). On day 7, the highest FI was in Q60 (89.99 ± 5.01 g), but lacking statistically significant difference ($P > 0.050$) compared with the NRC group (79.99 ± 4.30 g). FI for the Q30 group (73.99 ± 4.45 g) increased considerably, but again no statistically significant difference could be detected when compared with QC30 (75.99 ± 5.25 g), QC60 (71.75 ± 2.88 g), and NRC (79.99 ± 4.30 g). The lowest FI was recorded for the RC group (53.62 ± 5.34 g) ($P < 0.0010$) compared to all other groups. In contrast, on day 14, the group with the highest FI was RC (106.63 ± 8.39 g). Yet statistically significant differences were not obtained when compared with NRC (105.71 ± 5.49), QC60 (101.65 ± 4.12), Q30 (99.99 ± 7.68), and Q60 (96.09 ± 7.05 g) ($P = 1$ in all cases). Only the QC30 group (73.99 ± 4.81 g) presented a statistically significant difference ($P < 0.0010$) when compared to the rest (Table 3).

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Table2. Mean and SD of the daily weight gain (g) during the treatments

	Group[1]					
Day	QC30	Q30	QC60	Q60	NRC	RC
1	16 ± 27^{a}	-34 ± 9.6^{b}	28.3 ± 22.5^{a}	51.6 ± 55^{a}	52.5 ± 11.7^{a}	15 ± 12.2^{a}
2	64 ± 30.2^{a}	-10 ± 7.9^{c}	80 ± 60.8^{a}	23.3 ± 18.9^{abc}	5.8 ± 9.1^{bc}	54 ± 26^{ab}
3	62 ± 54.1^{ab}	118 ± 9^{a}	36.6 ± 20.8^{b}	36.6 ± 25.1^{b}	56.6 ± 19.1^{b}	35 ± 19^{b}
4	27.6 ± 21.5^{a}	59 ± 7.4^{a}	36.6 ± 20.8^{a}	38.3 ± 18.9^{a}	46.6 ± 14^{a}	30 ± 19^{a}
5	57.4 ± 31.5^{a}	45 ± 9.3^{a}	56.6 ± 61.7^{a}	48.3 ± 41.6^{a}	47.5 ± 14^{a}	28 ± 18.9^{a}
6	17 ± 89.6^{a}	38 ± 16^{a}	-8.3 ± 46.4^{a}	43.3 ± 11.5^{a}	63.3 ± 17.7^{a}	40 ± 25.7^{a}
7	57 ± 95.1^{a}	38 ± 7.5^{a}	30 ± 8.6^{a}	23.3 ± 7.6^{a}	30.8 ± 13.5^{a}	19 ± 20.4^{a}
8	50 ± 17.3^{a}	70 ± 44.5^{ab}	43.3 ± 18.9^{ab}	43.3 ± 24.6^{ab}	40.8 ± 17.1^{ab}	17 ± 22.5^{b}
9	35 ± 13.6^{b}	10 ± 41^{b}	106.6 ± 12.5^{a}	55 ± 43.3^{ab}	46.6 ± 12.1^{b}	25 ± 27.1^{b}
10	35 ± 10^{a}	37 ± 14.8^{a}	43.3 ± 20.8^{a}	36.6 ± 12.5^{a}	32.1 ± 8.4^{a}	10 ± 41.8^{a}
11	37 ± 13.9^{a}	41 ± 14.7^{a}	36.6 ± 5.7^{a}	28.3 ± 12.5^{a}	32 ± 14.5^{a}	29 ± 26^{a}
12	37 ± 86.2^{a}	39 ± 26.7^{a}	18.3 ± 18.9^{a}	48.3 ± 20.2^{a}	58.3 ± 14^{a}	18 ± 4.4^{a}
13	26 ± 84.2^{a}	12 ± 44.9^{a}	81.6 ± 31.7^{a}	50 ± 13.2^{a}	15.8 ± 14.9^{a}	20 ± 10^{a}
14	74 ± 16.3^{a}	20 ± 58.8^{a}	38.3 ± 20.2^{a}	75 ± 26.4^{a}	27.5 ± 32.2^{a}	26 ± 7.4^{a}

$^{a-c}$ Different literals indicate statistically significant differences between columns.
1QC30 = Quinfamide/carbopol 30 mg/kg; Q30 = Quinfamide 30 mg/kg; QC60 = Quinfamide/carbopol 60 mg/kg; NRC = Non-random control; RC = Random control

Table 3. Mean and SD of feed intake (g) during the treatment

	Group[1]					
Day	QC30	Q30	QC60	Q60	NRC	RC
1	32.9 ± 3.8^{b}	17.4 ± 2.1^{c}	31.59 ± 2.5^{bc}	30.32 ± 2.9^{bc}	33.37 ± 4.81^{b}	156.77 ± 13.6^{a}
2	51.97 ± 4.49^{b}	21.99 ± 2.22^{c}	31.94 ± 0.56^{c}	34.93 ± 2.10^{c}	33.73 ± 4.67^{c}	137.18 ± 13.4^{a}
3	56.98 ± 3.74^{b}	35.99 ± 2.84^{b}	44.99 ± 2.17^{b}	36.43 ± 1.46^{b}	41.87 ± 24.67^{b}	145.99 ± 8.88^{a}
4	58.64 ± 3.99^{bc}	38.00 ± 2.66^{d}	66.56 ± 3.25^{b}	37.14 ± 0.72^{d}	53.32 ± 6.73^{c}	83.99 ± 5.56^{a}
5	63.39 ± 3.99^{c}	54.99 ± 3.78^{cd}	84.99 ± 1.32^{b}	79.99 ± 4.33^{b}	45.98 ± 4.58^{d}	139.99 ± 9.37^{a}
6	89.99 ± 6.32^{a}	81.99 ± 5.47^{a}	56.21 ± 1.78^{b}	83.29 ± 4.40^{a}	50.65 ± 5.91^{b}	87.84 ± 5.13^{a}
7	75.99 ± 5.25^{b}	73.99 ± 4.45^{b}	71.75 ± 2.88^{b}	89.99 ± 5.01^{a}	53.62 ± 5.34^{c}	79.99 ± 4.30^{ab}
8	72.99 ± 3.88^{c}	70.99 ± 5.55^{c}	83.32 ± 3.44^{c}	104.99 ± 6.92^{b}	73.92 ± 7.89^{c}	123.99 ± 8.81^{a}
9	94.99 ± 6.06^{ab}	89.99 ± 5.17^{b}	63.32 ± 2.88^{c}	108.32 ± 9.81^{ab}	105.47 ± 11.43^{ab}	106.99 ± 8.96^{a}
10	95.27 ± 6.21^{b}	111.99 ± 6.86^{a}	69.99 ± 2.97^{c}	104.99 ± 9.65^{ab}	95.48 ± 9.43^{b}	88.99 ± 6.40^{b}
11	68.91 ± 3.82^{c}	85.99 ± 5.92^{b}	76.59 ± 3.13^{bc}	89.97 ± 7.71^{b}	131.45 ± 12.89^{a}	131.99 ± 8.62^{a}
12	93.99 ± 4.96^{b}	94.92 ± 8.25^{b}	83.29 ± 4.49^{b}	94.99 ± 6.48^{b}	131.65 ± 11.68^{a}	91.99 ± 5.70^{b}
13	85.99 ± 4.92^{bc}	79.99 ± 3.32^{c}	106.59 ± 3.36^{a}	101.65 ± 7.45^{a}	99.65 ± 8.58^{a}	95.59 ± 8.00^{ab}
14	73.99 ± 4.81^{b}	99.99 ± 7.68^{a}	101.65 ± 4.12^{a}	96.09 ± 7.05^{a}	106.63 ± 8.39^{a}	105.71 ± 5.49^{a}

$^{a-d}$ Different literals indicate statistically significant differences between columns.
[1]Q30= Quinfamide/carbopol 30 mg/kg; Q30= Quinfamide 30 mg/kg; Q/C60= Quinfamide/carbopol 60 mg/kg; NRC= Non-random control; RC= Random control

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Table 4. Mean and SD of the feed conversion ratio (g) during the treatment period

	Group					
Day	QC30	Q30	QC60	Q60	NRC	RC
1	0.09 ± 1.09[a]	-0.55 ± 0.17[a]	2.51 ± 2.85[a]	-1.7 ± 3.69[a]	0.65 ± 0.11[a]	10.88 ± 12.88[a]
2	1.03 ± 0.65[ab]	-0.76 ± 1.47[b]	1.24 ± 1.66[ab]	2.25 ± 1.49[ab]	3.67 ± 4.20[a]	3.28 ± 2.19[a]
3	1.6 ± 1.19[ab]	0.30 ± 0.04[b]	1.48 ± 0.70[ab]	1.75 ± 1.75[ab]	0.82 ± 0.54[b]	6.17 ± 5.34[a]
4	-0.31 ± 4.65[a]	0.65 ± 0.09[a]	2.20 ± 1.02[a]	1.12 ± 0.46[a]	1.22 ± 0.37[a]	5.57 ± 6.38[a]
5	2.50 ± 3.46[a]	1.25 ± 0.22[a]	6.56 ± 8.97[a]	2.73 ± 2.11[a]	1.05 ± 0.34[a]	3.35 ± 2.32[a]
6	1.20 ± 3.06[a]	2.44 ± 0.86[a]	4.09 ± 6.36[a]	2.03 ± 0.62[a]	0.85 ± 0.23[a]	1.48 ± 0.94[a]
7	0.97 ± 1.43[a]	2.02 ± 0.48[a]	2.49 ± 0.54[a]	4.17 ± 1.48[a]	2.31 ± 1.69[a]	0.5 ± 10.08[a]
8	1.58 ± 0.47[a]	1.28 ± 0.60[a]	2.13 ± 0.72[a]	3.47 ± 2.78[a]	2.20 ± 1.31[a]	4.1 ± 7.41[a]
9	3.17 ± 1.57[a]	3.31 ± 4.05[a]	0.59 ± 0.04[a]	7.53 ± 10.60[a]	2.35 ± 0.46[a]	1.6 ± 14.15[a]
10	2.91 ± 0.90[a]	3.63 ± 1.96[a]	2.02 ± 1.29[a]	3.06 ± 0.86[a]	3.21 ± 1.17[a]	3.4 ± 4.01[a]
11	2.14 ± 0.97[b]	2.54 ± 1.55[b]	2.12 ± 0.37[b]	3.76 ± 1.99[ab]	4.72 ± 1.77[ab]	6.73 ± 3.33[a]
12	2.51 ± 3.87[a]	-2.30 ± 9.57[a]	8.76 ± 6.81[a]	2.37 ± 1.45[a]	2.38 ± 0.64[a]	5.36 ± 1.27[a]
13	-0.73 ± 4.34[a]	2.22 ± 2.32[a]	1.51 ± 0.79[a]	2.10 ± 0.42[a]	3.52 ± 6.48[a]	7.51 ± 7.42[a]
14	1.03 ± 0.21[a]	1.35 ± 5.02[a]	3.18 ± 1.56[a]	1.37 ± 0.40[a]	2.96 ± 5.06[a]	4.42 ± 1.69[a]

[a-b] Different literals indicate statistically significant differences between columns.
[1]QC30 = Quinfamide/carbopol 30 mg/kg; Q30 = Quinfamide 30 mg/kg; QC60 = Quinfamide/carbopol 60 mg/kg; NRC = Non-random control; RC = Random control

Feed conversion ratio

Table 4 shows the mean ± 1 SD of FCR. The group with the highest mean values recorded on day 1 was NRC (10.88 ± 12.88), followed by QC60 (2.51 ± 2.85), RC (0.65 ± 0.11), QC30 (0.096 ± 1.09), Q30 (-0.55 ± 0.17) and Q60 (-1.7 ± 3.69). However, no statistically significant difference among groups could be detected (P = 1). On days 2, 3, and 11 there was a statistically significant difference (P = 1) among groups, and this trend persisted until day 14 when the highest FCR was recorded for NRC (4.42 ± 1.69), followed by QC 60 (3.18 ± 1.56), CA (2.96 ± 5.06), Q30 (1.35 ± 5.02) and QC30 (1.03 ± 0.21). However, comparisons of means were not statistically significant (P = 1).

Oocysts count per gram of feces

Two days after the initial treatment in all groups receiving quinfamide, no oocysts could be observed. On day 3, they were found only in the Q30 and NRC groups, but no statistically significant difference was observed when compared to groups (P = 0.1300). This pattern remained unaltered until day 14. However, it is worth stating that in the QC60 group, no oocysts were observed during the first 9 days after treatment, and only a few oocysts could be detected on days 10 to 14 (Table 5).

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Table 5. Oocysts count per gram of feces (10 × 3) during treatment

	Group[1]					
Day	QC30	Q30	QC60	Q60	NRC	RC
1	0[a]	0[a]	0[a]	0[a]	0[a]	0[a]
2	0[a]	0[a]	0[a]	0[a]	0[a]	0[a]
3	0[a]	31.6 ± 125.8[a]	0[a]	0[a]	0[a]	3.98 ± 19.9[a]
4	2.5 ± 6.3[a]	6.3 ± 79.4[a]	0[a]	19.9 ± 158.4[a]	12.5 ± 63[a]	6.3 ± 79.4[a]
5	0[a]	6.3 ± 63[a]	0[a]	15.8 ± 100[a]	12.5 ± 63[a]	0[a]
6	39.8 ± 158.4[a]	25.1 ± 79.4[a]	0[a]	5 ± 19.9[a]	251.1 ± 79.4[a]	3.1 ± 15.8[a]
7	36.8 ± 158.4[a]	15.8 ± 50.1[a]	0[a]	7.9 ± 39.8[a]	398.1 ± 100[a]	15.8 ± 12.5[a]
8	15.8 ± 158.4[a]	3.9 ± 19.9[a]	0[a]	251.1 ± 125.8[a]	2 511.8 ± 128.8[a]	31.6 ± 125.8[a]
9	25.1 ± 100[a]	25.11 ± 100[a]	0[a]	2 511.8 ± 15.8[a]	1 584.8 ± 39.8[a]	31.6 ± 125.8[a]
10	19.9 ± 63[a]	100 ± 100[a]	251.1 ± 158.4[a]	158.4 ± 79.4[a]	316.2 ± 79.4[a]	31.6 ± 125.8[a]
11	50.1 ± 50.1[a]	158.4 ± 100[a]	19.9 ± 199.5[a]	6.3 ± 25.1[a]	1995.2 ± 39.8[a]	6.3 ± 79.4[a]
12	1000 ± 50.1[a]	7.9 ± 15.8[a]	19.9 ± 199.5[a]	7.9 ± 31.6[a]	2 511.8 ± 50.1[a]	25.1 ± 25.1[a]
13	398.1 ± 31.6[a]	100 ± 100[a]	5 ± 15.8[a]	10 ± 63[a]	501.1 ± 31.6[a]	501.1 ± 6.3[a]
14	100 ± 63[a]	158.4 ± 19.9[a]	6.3 ± 25.11[a]	10 ± 50.1[a]	630.9 ± 39.8[a]	501.1 ± 5[a]

[a] Indicates a statistically significant difference between columns.
[1]QC30 = Quinfamide/carbopol 30 mg/kg; Q30 = Quinfamide 30 mg/kg; QC60 = Quinfamide/carbopol 60 mg/kg; NRC = Non-random control; RC = Random control

Discussion

Coccidiosis is a disease that affects different species and can cause serious economic losses in rabbits. Thus, treatment must be effective, and managed promptly, focusing on the particular conditions of the farm[16] to improve the therapeutic results and reduce the development of resistance.[17] In this study, the treatments with quinfamide were administered for three consecutive days after weaning in Q30, QC30, Q60, and QC60 groups, because at this age there is greater susceptibility to clinical coccidiosis.[6, 9] In Q60 and QC60 groups, the treatment was administered again on day 7.[8, 18] Two control groups were set; one was randomized to the animals from different litters and another control group was established including rabbits from a single litter without randomization. As each litter was weaned, this allowed for two management approaches to be considered.[6]

There was no mortality in any of the evaluated groups and no rabbit presented GI tract signs including diarrhea, emaciation, anorexia, weakness, weight loss, or growth retardation, even though high morbidity and mortality due to coccidiosis have been reported in this species.[8] At the beginning of this study, there were significant differences in the parameters assessed i.e., BW, DWG, FI, and FCR values. These differences were maintained throughout the study whether they were treated. This tendency has also been reported, for infected rabbits, and evaluating other anticoccidial drugs such as diclazuril.[19] At the end of the treatment in the QC60 and Q60 groups, the highest BW, DWG, and FCR were recorded as compared to the initial values. In the QC30 and Q30 groups, the lowest BW values were recorded at the beginning of the trial, while at the end of the treatment, the QC30 group

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showed the highest BW recorded, and a considerable increase in DWG and FCR, was observed. In contrast, the Q30 group shows one of the lowest mean BW, the lowest FI, and negative FCR values at the beginning of weaning. A lower BW was recorded in the RC group compared to the NRC group. However, the BW recorded in both groups was lower than in the QC60, Q60, and QC30 groups. The FI registered in the RC group was the highest at the beginning of the treatment and it decreased until it became similar to the values registered in the rest of the groups.

In this study, animals with natural coccidia infection were used in the Q30 and RC groups, coccidia was observed in feces from the third day of treatment, so it could not be considered that the administration of the treatment of the Q30 group presents an advantage as compared to the control groups. On the contrary, coccidia was observed up to day 9 of treatment in the QC60 group, and the lowest OPG at the end of the treatment, similar results in the oocyst elimination time have been reported for sulfachloropyridazine, amprolium, diclazuril, and trimethoprim.[20] In the QC30 and Q30 groups, the treatment was administered only once following how quinfamide has been evaluated against coccidia.[21] However, considering that the phase in which quinfamide could act as anticoccidial is not known, the treatment was administered again after seven days in the QC60 and Q60 groups, thus ensuring that it may interfere with coccidia during the susceptible phases of the life cycle, as it has been recommended for other anticoccidial drugs such as sulfonamides, whose dosing is indicated at intervals of 7 days through the drinking water.[20]

The absence or decrease of coccidia in feces, as well as the increase in the productive parameters of the treated animals compared to what was recorded in the control groups, suggest a therapeutic efficacy of quinfamide as has been reported for sulfonamide, diclazuril, and toltrazuril.[4, 22] In chicken broilers treated with quinfamide, there was also an increase in BW and a decrease in OPG of the treated animals compared to the infected control group.[12]

Administering the treatment mixed in water or food reduces handling and facilitates administration in large populations, however, when administering a drug in water, its potency could decrease if it does not have adequate quality or if it interacts with the material of drinking fountains, as is the case with toltrazuril,[22, 23] on the other hand, it could also modify the taste of the water and reduce its consumption.[24] In this study, no decrease in FI could be associated with a change in the taste of the food, as has been mentioned in other cases in which some flavoring agent has to be used to avoid rejection of the medicated food.[23] To consider quinfamide as a therapeutic option, it is important to evaluate residuality in tissues and establish an optimal withdrawal time. However, this may not be a problem because it is possible that the drug is not absorbed, as occurs in humans. Hence the withdrawal time would not be a problem for production, as is the case with diclazuril and robenidine.[25]

Conclusions

The administration of quinfamide as an in-feed anticoccidial drug in rabbits at weaning seems possible. Treatment with quinfamide improved productive parameters assessed i.e., BW, DWG, FI, FCR, and in particular, rabbits that received quinfamide

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plus carbopol at a dose of 60 mg/kg at weaning for 3 consecutive days with a re-dosing on day 7, for three consecutive days showed the best improvements in BW, DWG, FCR, without significantly increasing FI. In these rabbits, the time for coccidia to be undetected in their feces was longer and presented a lower egg count as compared with other dose schemes of quinfamide, and as compared with untreated control rabbits.

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Data availability

The original datasets used in this research and if applicable, supporting information files, are deposited and available for download at the SciELO Dataverse repository doi: 1048331/scielodata.IDZP30.

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Conflicts of interest

The authors have no conflict of interest to declare regarding this publication.

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