

# EFFECTS OF DIFFERENT LEVELS OF BUCLIZINE HYDROCHLORIDE FOR PIGS DURING THE GROWTH AND FATTENING PHASE

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↳ Supporting Information

**ABSTRACT:** The Study aimed to determine the effect of Buclizine hydrochloride in the bristles diet at the growing and fattening stage and also determine the economic and cost-benefit output. The experimental design was a completely randomized block design (DBCA) with 4 treatments and 6 repetitions, a total of 24 experimental units, and Landrace bristles with a live weight of  $\pm 18$  kg at the beginning of the investigation. Based on the results, the T3 treatment (Buclizine 0.050 mg/kg/animal/week) was the best level of Buclizine supplementation for both growing and fattening stages for efficiency and food conversion in treated animals. T3 treatment has the final weight of  $53.83 \pm 5$  kg over T1 treatment which has the  $48.5 \pm 6$  Kg over T2 and T4 which get totaled 47 Kg of final weight. The Economic efficacy of treatment T3 (Buclizine 0.050 mg/kg/animal/week) was in the level of best benefit ratio between the treatments. Regarding hematological alterations, there was no type of alteration at the renal or hepatic level, since the analysis of the blood biochemistry revealed a correct functioning of these organs. It's concluded that using Buclizine hydrochloride in the level of 0.05 mg/kg/animal/week in pigs can be efficient in term of growing and fattening performance with economic efficacy.

**Keywords:** Appetite stimulant, Buclizine, Fattening animals, Food conversion, Pig.

## INTRODUCTION

In recent years, there has been an increase in the consumption of pork, for which it is predicted that meat production with the greatest increase in human consumption will continue to rise since pork is the most highly valued worldwide (FAO, 2017). The demand for this kind of meat is very high since producers are forced to produce in greater quantity with high efficiency and in the shortest possible time to supply the demand of the current market (Havliček et al., 2020; Soleimani and Gilbert, 2021).

Nowadays, using non-hormonal appetite stimulants in fattening animals is a new challenge for animal nutritionists (Orzuna-Orzuna et al., 2021; Trevisi et al., 2021). In this regard, various orexigenic chemicals and medications can be used in pig breeding (Prvulović et al., 2007; Carter, 2015; Li, 2017). The use of Buclizine Hydrochloride was planned to meet this proposed goal, which is a drug with antihistamine action of the varied function at the level of the central nervous system with a sedative effect, and anticholinergic and non-hormonal orexigenic effect on the neurovegetative system (Babu, 2011). Having these effects on the animal would induce an increase in appetite and subsequently an increase in body weight, which would be given by a stimulating effect on appetite (Brines et al, 2016; García Romero et al., 2020).

With attention to the properties of Buclizine, the aim of the study was to determine the effect of Buclizine Hydrochloride in the bristles diet at the growing and fattening stage and also determine the economic and cost-benefit output.

## MATERIALS AND METHODS

This study consisted of three descriptive, experimental, and investigative parts with a duration of 12 weeks, for the determination of the best inclusion level of Buclizine hydrochloride for pigs during the growth and fattening phase.

### Experimental material

24 Landrace breed pigs were used for the present investigation. Three levels of Buclizine (0.025 mg/kg, 0.05 mg/kg, and 0.1 mg/kg) were supplemented according to table 1.

**Table 1 - Description of the treatments in present experiment.**

Treatment	Description of provided diets	Time of use	No. of animals/ Treatment
T1	Witness (control)	3	6
T2	Buclizina 0.025 mg/kg/animal/week	3	6
T3	Buclizina 0.05 mg/kg/animal/week	3	6
T4	Buclizina 0.1 mg/kg/animal/week	3	6
Total			24

### Methods

Before the arrival of the pigs, the farm was cleaned and disinfected with Creolin (CREOLINA®, Italy) and with a portion of 100 ml in 20 Lt of water and then the different pigs were divided into 4 quartiles for each study, handling tables and metal bars. Pigs were preliminarily designated by general analysis (discard of animals in poor health due to veterinary inspections). The animals were given 2 weeks of adaptation to the environment and feeding condition. Identification of all pigs was developed and conducted to maintain a record for experimental phase and typify each pig under study. In addition to this, experimental posters were handled in each of the pigs showing the treatment and the block to which each one corresponds.

### Ethical approval

All procedures of experiment was in according to animal ethics and welfare with attention to international regulations for pig (Lara de la Casa, 2017).

### Treatments

Buclizine Hydrochloride was administered as a weekly application according to the dose previously established for Buclizine treatments (Table 1), with a total of 3 applications throughout the investigation.

### Feeding

Pig feeding was carried out starting with commercial diets 1.5 Kg/Animal/Day, which was increased according to the phase of the period in which the animals subject to the study were found and the nutritional requirements of the subjects, until ending at 3 Kg /Animal/Day after the investigation.

### Statistical analysis

Statgraphic (version 16) software and ANOVA method were used for statistical analysis.

## RESULTS AND DISCUSSION

### Statistical analysis

The variables that were evaluated at initial weight presented in table 2. The results obtained by Fisher's test, probability, and an average of treatments for the kg variables were not statistically significant. Similar results obtained by Kulkarni et al. (1972), which showed a statistical non-significance (NS) at the beginning of his assessment of the effect of Buclizine Hydrochloride in the Feeding of rats. It can be obviously seen a probability of  $P < 0.05$  for the first week through the analysis of variance carried out on the treatments under study in the following weeks, and they were significant obtaining discrepancies between the treatments. The weekly weight gain during the growth stage using a means comparison test (Tukey) could be observed throughout each of the weeks an increase in the weight of each treatment, in which it was determined that T3 was developed more in compared to the other treatments (during 3 months; 12 weeks), in which data obtained for the 8 weeks indicated a positive result (\*) for the T3 (Table 5).

### Weight gain in the growth stage

For the variable weight gain per week, it can be observed in table 5 according to the analysis of variance, carried out on the treatments under study throughout of the weeks, varied results are seen in which there is not a varied significance in the treatments, between weeks 2, 6, 7 and 8 there were significant results ( $p < 0.05$ ), which indicates that there were significant results between the proposed treatments. It can be seen that the coefficient of variation was low, resulting in the data obtained in the field being accepted.

### Monthly weight in the growth phase

The statistical inequality of the treatments in monthly weight gain at growth phase is ( $P < 0.05$ ) during the two months, which proves that there was significance statistics. Also T3 obtained a better performance with a weight gain of  $\pm 2$  kg in the first month of the growth phase and of +4 kg of weight gain in the second month.

### Feed conversion during the growth phase

According to the analysis of variance, the significant results are observed ( $P < 0.05$ ), which indicates that they presented significant inequality for the established treatments. It could be said that there was a positive effect in the

inclusion of Buclizine Hydrochloride as a stimulant of appetite in feed conversion of pigs in the growth phase. The treatments according to the food conversion in the growth phase observed inequality between the averages of the treatments during each of the weeks that make up the experiment (\*). In this case, the lowest average is what is sought, since in this variable we can deduce how many kilograms of feed may be needed to form a kilogram of live weight of the pig, in which it could be observed that T3 was the best in terms of feed conversion.

**Table 2 - Initial pig weights at 2 months of age.**

Sources	Degrees of freedom	Sum of squares	Mean squares	Fisher	Probablilty
Blocks	5	5.83	1.16		
Treatments	3	2.33	0.77	1.63 (NS)	0.22
Error	15	7.16	0.47		
Total	23	15.33			
CV %	3.8				

\*T: Treatments; NS: Non-significant statistical response; CV: Coefficient of variation.

**Table 3 - Weekly weight in the growth stage in treated pigs with Buclizine Hydrochloride.**

Weekly Weights	Sum of squares	Medlum squares	Fisher	Significance level	CV (%)
First week	4.8333	1.61111	2.79	*	3.95
Second week	12.8333	4.27778	6.02	*	4.13
Third week	16.1667	5.38889	5.64	*	4.53
Fourth week	22.3333	7.44444	8.82	*	4.05
Fifth week	32.3333	10.7778	10.32	*	4.26
Sixth week	46.1250	15.3750	12.06	*	4.46
Seventh week	60.7917	20.2639	15.62	*	4.22
Eighth week	106.833	35.6111	35.22	*	3.48

\* Significant statistical differences in P: 5%

**Table 4 - Growth stage weekly weights in treated pigs with Buclizine Hydrochloride.**

Weekly Weights	Treatments				Significance level
	T1	T2	T3	T4	
First week	18.83 <sup>b</sup>	19.000 <sup>a</sup>	20.000 <sup>a</sup>	19.167 <sup>a</sup>	*
Second week	19.833 <sup>b</sup>	20.000 <sup>b</sup>	21.667 <sup>a</sup>	20.167 <sup>b</sup>	*
Third week	21.000 <sup>b</sup>	21.167 <sup>b</sup>	23.000 <sup>a</sup>	21.167 <sup>b</sup>	*
Fourth week	22.000 <sup>b</sup>	22.167 <sup>b</sup>	24.333 <sup>a</sup>	22.167 <sup>b</sup>	*
Fifth week	23.500 <sup>b</sup>	23.333 <sup>b</sup>	26.000 <sup>a</sup>	23.167 <sup>b</sup>	*
Sixth week	24.667 <sup>b</sup>	24.667 <sup>b</sup>	27.667 <sup>a</sup>	24.167 <sup>b</sup>	*
Seventh week	26.500 <sup>b</sup>	26.000 <sup>b</sup>	29.667 <sup>a</sup>	25.667 <sup>b</sup>	*
Eighth week	28.333 <sup>b</sup>	27.667 <sup>b</sup>	32.500 <sup>a</sup>	27.167 <sup>b</sup>	*

\*Averages with the same letters do not differ statistically according to TUKEY test 0.05; \*Averages with different letters differ statistically according to TUKEY test 0.05.

**Table 5 - Variance analysis of weight gain for the growth stage in treated pigs with Buclizine Hydrochloride.**

Weight gain	Sum of squares	Mean squares	Fisher	Significance level	CV (%)
First week	0.50000	0.16667	2.50	NS	2.83
Second week	2.00000	0.66667	10.00	*	4.56
Third week	0.33333	0.11111	0.77	NS	5.39
Fourth week	0.50000	0.16667	2.50	NS	10.47
Fifth week	1.66667	0.55556	2.50	NS	11.56
Sixth week	1.45833	0.48611	4.07	*	8.96
Seventh week	1.66667	0.55556	2.94	NS	11.32
Eighth week	6.4583	2.15278	8.52	*	7.13

\*: Significant statistical differences; NS: Non-significant statistical response.

**Table 6 - Monthly weight in the growth phase in treated pigs with Buclizine Hydrochloride.**

Monthly weight gain	Treatments				Significance level	CV (%)
	T1	T2	T3	T4		
First month	22.000 B	22.167 B	24.333 A	22.167 B	*	4.05
Second month	28.333 B	27.667 B	32.500 A	27.167 B	*	3.48

Averages with the same letters do not differ statistically according to TUKEY 0.05; Averages with different letters differ statistically according to TUKEY 0.05; \*: Significant statistical differences.

**Table 7 - The analysis of variance for feed conversion during the growth phase in treated pigs with Buclizine Hydrochloride.**

Weight gain	Sum of squares	Mean squares	Fisher	Significance level	C.V (%)
First week	3.45	1.15	19.90	*	12.68
Second week	1.29	0.43	22.56	*	11.21
Third week	0.89	0.29	20.53	*	9.452
Fourth week	0.56	0.18	17.96	*	6.32
Fifth week	0.30	0.10	4.92	*	4.97
Sixth week	0.33	0.11	9.40	*	10.21
Seventh week	0.26	0.08	7.59	*	9.78
Eighth week	0.18	0.06	5.71	*	10.78

\*: Significant statistical differences

**Table 8 - Food conversion during the growth stage in treated pigs with Buclizine Hydrochloride.**

Growth feed conversion	Treatments				Significance level
	T1	T2	T3	T4	
First week	3.21	3.09	2.25	3.26	*
Second week	3.08	3.41	2.47	3.74	*
Third week	3.69	3.54	2.19	3.98	*
Fourth week	2.99	3.71	2.87	3.65	*
Fifth week	3.64	3.21	2.56	3.21	*
Sixth week	3.79	3.29	2.89	3.47	*
Seventh week	3.35	3.54	2.99	3.21	*
Eighth Week	3.33	3.65	2.87	3.65	*

\*: Significant statistical differences

### Weights per week in the fattening stage

The analysis of variance (ANOVA) was carried out to the treatments under study, for the ninth week that there was an inequality with a probability of ( $P < 0.05$ ), which means that the results obtained were significant during the subsequent weeks between the treatments, giving as a positive result the inclusion of Buclizine as an appetite stimulator in pigs in the fattening stage. The CV was low for each week, therefore the results obtained in the field were accepted. The treatments were based on the weekly weight variable during the mean comparison test (Tukey), showing an inequality between treatment averages, so it can be observed that the T3. It was the best treatment in the study, since the weight gain obtained was higher than the rest of the treatments as shown by the test in the fattening stage, and it could be observed using comparison of Tukey's means.

### Weight gain in the fattening stage

In table 11 according to the analysis of variance (ANOVA) performed on the treatments under study, it can be observed that varied results are seen over the weeks, which subsequently there is no marked significance in most weeks except for the eleventh week, which significant results were obtained ( $P < 0.05$ ). That is to say, there was a positive effect on the addition of Buclizine as a stimulator in pigs in the fattening phase. The behavior of the treatments for the weight gain variable within the growth stage can be seen in table 12; regarding the ninth week, it was observed that there was no significant difference; and from the eleventh week the differences between averages appear, since these were significant, thus showing the best and worst treatments for the fattening phase.

### Monthly weight in the fattening stage

The table has shown the statistical difference in terms of the monthly weight gain which was developed in the fattening stage and the significant differences for all treatments, which indicated the inclusion of Buclizine an appetite stimulator that had a positive effect on the monthly weight gain of the selected animals in the growth and fattening phases.

### Feed conversion during the fattening stage

According to the analysis of variance (ANOVA) executed to the treatments under study, it can be observed that throughout the weeks of the fattening stage significant results are seen ( $P < 0.05$ ), that is, there was a positive result in the addition Buclizine as an appetite stimulant in the feed conversion of pigs in the fattening phase. The treatments based on feed conversion, a difference between averages can be observed during each of the weeks except for week 12 with the lowest average being, in this case, it can be seen T3 was the ideal treatment as it needed less food to form a kilogram of weight.

**Table 9 - ADEVA for weights of the weeks in the fattening stage in treated pigs with Buclizine Hydrochloride.**

Weight weeks	Sum of squares	Medium squares	Fisher	Significance level	CV (%)
First week	97.000	32.3333	31.29	*	3.05
Second week	129.125	43.0417	32.08	*	3.05
Third week	176.833	58.9444	38.17	*	2.87
Fourth week	178.125	59.3750	37.70	*	2.55

\*: Significant statistical differences ( $P < 0.05$ ). NS: Non-significant statistical response.

**Table 10 - Weights of the weeks in the fattening stage in treated pigs with Buclizine Hydrochloride.**

Weight Weeks	Treatments				Significance level
	T1	T2	T3	T4	
Ninth Week	33.167	31.833	36.667	31.667	NS
Tenth week	37.667	37.830	41.833	36.167	NS
Eleventh Week	42.667	41.500	47.833	41.000	NS
Twelfth Week	48.500	47.500	53.500	47.000	NS

NS: Non-significant statistical response.

**Table 11 - ADEVA for weight gain for the fattening stage in treated pigs with Buclizine Hydrochloride.**

Weight weeks	Sum of squares	Medium squares	Fisher	Significance level	Cv (%)
Ninth week	1.83333	0.61111	3.44	NS	9.55
Tenth week	2.45833	0.81944	2.86	NS	11.57
11 <sup>th</sup> week	4.79167	1.59722	12.23	*	6.83
Twelfth week	0.12500	0.04167	1.00	NS	3.43

\*: Significant statistical differences ( $P < 0.05$ ). NS: Non-significant statistical response.

**Table 12 - Weight gain for the fattening stage in treated pigs with Buclizine Hydrochloride.**

Weight gain	Treatments				Significance level
	T1	T2	T3	T4	
Ninth Week	4.833	4.166	4.166	4.500	NS
Tenth week	4.500	4.000	4.333	4.500	NS
Eleventh Week	5.000 <sup>b</sup>	5.333 <sup>b</sup>	6.000 <sup>a</sup>	4.833 <sup>b</sup>	*
Twelfth Week	5.833	6.000	6.000	6.000	NS

\*: Significant statistical differences ( $P < 0.05$ ). NS: Non-significant statistical response.

**Table 13 - Monthly weight gain in the fattening stage in treated pigs with Buclizine Hydrochloride.**

Monthly weight	Treatments				Significance level
	T1	T2	T3	T4	
Third month	48.50 <sup>b</sup>	47.50 <sup>b</sup>	53.85 <sup>a</sup>	47.00 <sup>b</sup>	*

\*: Significant statistical differences ( $P < 0.05$ ).

**Table 14 - Food conversion of treated pigs with Buclizine Hydrochloride.**

Weight gain	Sum of squares	Mean squares	Fisher	Significance level
Ninth week	0.15	0.05	9.92	*
Tenth week	0.09	0.03	9.87	*
11th week	0.14	0.04	8.74	*
Twelfth week	0.15	0.05	11.92	NS

\*: Significant statistical differences ( $P < 0.05$ ). NS: Non-significant statistical response.

**Table 15 - Feed conversion during the fattening stage in treated pigs with Buclizine Hydrochloride.**

Fattening feed conversion	Treatments				Significance level
	T1	T2	T3	T4	
Ninth Week	3.89 <sup>b</sup>	3.21 <sup>b</sup>	2.86 <sup>a</sup>	3.87 <sup>b</sup>	*
Tenth week	3.69 <sup>b</sup>	3.33 <sup>b</sup>	2.98 <sup>a</sup>	4.1 <sup>b</sup>	*
Week 11	3.79 <sup>b</sup>	3.45 <sup>b</sup>	3.16 <sup>a</sup>	3.97 <sup>b</sup>	*
Twelfth Week	3.64	3.64	3.41	3.97	NS

\*: Significant statistical differences (P<0.05). NS: Non-significant statistical response..

**Table 16 - Initial hematological analysis in treated pigs with Buclizine Hydrochloride.**

Treatments	Blood Biochemistry							Significance level
	Glucose	Urea	Total bilirubin	Direct bilirubin	ALT	AST	ALP	
Reference	4.7-8.3	3.0-8.5	0.0-17.1	0.0-5.3	32 - 84	9 - 113	26 - 362	
T0	6.00	7.53	2.17	1.37	40.33	33.00	344.00	NS
T1	4.97	8.03	4.17	2.70	38.67	47.00	351.33	NS
T2	5.50	5.53	2.37	1.30	43.33	36.00	280.33	NS
T3	6.10	7.57	3.33	2.37	45.33	51.33	288.00	NS

ALT: Alanine aminotransferase; AST: Aspartate transaminase; ALP: Alkaline phosphatase; NS: Non-significant statistical response.

**Table 17 - Final hematological analysis.**

Treatments	Blood Biochemistry							Significance level
	Glucose	Urea	Total bilirubin	Direct bilirubin	ALT	AST	ALP	
Reference	4.7-8.3	3.0-8.5	0.0-17.1	0.0-5.1	32-84	9-113	26-362	
T0	6.76	6.37	3.72	2.30	59.63	51.65	113.47	NS
T1	7.15	7.28	3.90	1.90	48.48	48.67	99.22	NS
T2	6.34	5.57	2.93	2.83	48.62	50.45	100.85	NS
T3	6.61	5.62	3.95	2.72	57.72	49.92	111.18	NS

TB: Total bilirubin; Db: Direct bilirubin; ALT: Alanine aminotransferase; AST: Aspartate transaminase; ALP: Alkaline phosphatase; NS: Non-significant statistical response.

### Hematological assay

The hematological assay was performed at the beginning and at the end of the investigation. The values did not present a statistically significant difference, however numerically they are different, aspiring also no value was outside the indicated reference range, so we can affirm that, regarding the physiology, liver, kidney and pancreas of the animals under study, he was in a healthy and optimal physiological state for his performance. From the research of [Samaniego \(2014\)](#), it indicates that Buclizine, once introduced orally, reaches its maximum concentrations around two hours; its output is mainly through the kidneys and a tiny percentage in the feces, undergoes a liver transformation, noting a greater benefit in young individuals than in adults. Regarding urea, we observed that all the values for the different treatments did not vary, which indicates that the functionality of the pig's kidneys is in good condition. In detail, there are no documented pathological effects on the kidney in MEDLINE bulletins ([National Center for Biotechnology Information, 2021](#)).

### Economic analysis in the benefit/cost ratio

In cost-benefit analysis, both discharges and admissions were made during the best result of the T3 treatment take into account, which corresponded to the (Buclizine mixture 0.050 mg/kg/animal/week) with a cost-benefit index of \$ 1.98, which reveals that for every dollar invested during the research project, an investigation was achieved, determining that, he obtained a net profit of \$ 0.88, in addition to this it was found that the treatment T1 that belonged to the control treatment, that is, without the addition of Buclizine, it ended with an index of \$ 1.72, while those correspondingly ranked as the least profitable treatments with a cost-benefit index of \$ 1.60 for T2 and T4 treatments, respectively.

### CONCLUSION

Treatment T3 (Buclizine 0.05 mg / kg/animal/week) was the best level of inclusion of Buclizine, both for the growth stage and for the fattening stage, T3 obtained a final weight of 53.83 Kg, + 5 Kg above treatment T1, which was the one that had the closest results (48.5 Kg) to T3, and +6 Kg above T2 and T4, which had a total of 47 Kg of final weight. Regarding hematological alterations, it concluded that there was no type of alteration at the renal or hepatic level since the analysis of the blood biochemistry revealed a correct functioning of these organs. Regarding the cost-benefit relation, the T3 treatment (Buclizine 0.05 mg/kg/animal/week) was the one that presented the best cost-benefit relation among the treatments with an index of \$ 1.98.

## DECLARATIONS

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### Authors' contribution

All authors contributed to conduction, analyzing and writing of research manuscript, equally.

### Conflict of interests

The authors declare that there is no conflict of interests in this work.

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