Iranian Journal of Applied Animal Science

Generic Zilpaterol Sources Affect Similarly the Meat Quality of Hairy Lambs When Compared with Patent Zilpaterol

Short Communication

O. Carrillo-Muro[1], A. Rivera-Villegas[2], B.I. Castro-Pérez[2], J.D. Urías-Estrada[2], C. Angulo-Montoya[2], P. Hernández-Briano[1], A. Plascencia[3*], A. Barreras[4] and A. Estrada-Angulo[2]

[1] Unidad Académica de Medicina Veterinaria y Zootecnia, Universidad Autónoma de Zacatecas, Fresnillo 98500, Zacatecas, México
[2] Facultad de Medicina Veterinaria y Zootecnia, Universidad Autónoma de Sinaloa, Culiacán 80260, Sinaloa, México
[3] Departamento de Ciencias Naturales y Exactas, Universidad Autónoma de Occidente, Unidad Guasave, 81048, Sinaloa, México
[4] Instituto de Investigaciones en Ciencias Veterinarias, Universidad Autónoma de Baja California, Mexicali, Baja California, México

Received on: 15 Jul 2020
Revised on: 4 Oct 2020
Accepted on: 15 Oct 2020
Online Published on: Sep 2021

*Correspondence E-mail: aplas_99@yahoo.com

Online version is available on: www.ijas.ir

ABSTRACT

Twenty-four Pelibuey × Katahdin (46.7±2.4 kg initial shrunk weight) crossbred intact male lambs were used in a 33-d growth-performance experiment order to compared two sources of generic zilpaterol *vs.* patent zilpaterol on five variables of meat quality (water holding capacity, color, purge loss, cook loss, and shear force) shear force) of lambs finished with a high-energy diet. Dietary treatments consisted of a corn-based finishing diet (13.3% crude protein and 2.11 Mcal of net energy for maintenance/kg dry matter) supplemented with no zilpaterol (control) or supplemented with the label dosage (125 mg of product/kg diet, as-fed basis) with patent brand zilpaterol [Zilmax® (ZIL)] or with two generic ZH sources [Grofactor® (GRO) or Zipamix® (ZIPA)]. Weight at slaughter was 50.93, 54.55, 54.20, and 54.50 kg for control, ZIL, GRO, and ZIPA, respectively. The average intake of zilpaterol was 0.16 mg ZH/kg live weight. There were no differences between zilpaterol sources on meat quality variables evaluated. Compared to controls, zilpaterol supplementation did not appreciably affect color, water-holding capacity, and drip loss. However, supplemental zilpaterol averaged an increased 36% shear force (4.11 *vs.* 2.63). It is concluded that the generic zilpaterol sources tested in the present experiment affect similarly the meat quality of hairy lambs fed a high-energy diet than patent brand zilpaterol. Zilpaterol affected mainly the tenderness of the meat.

KEY WORDS generic, lambs, meat quality, zilpaterol.

INTRODUCTION

As of 2018, zilpaterol hydrochloride (ZH), a beta-adrenergic agonist, is an approved feed additive for beef cattle in 17 countries. It was originally patented and marketed under the trade name Zilmax (Hoechst Roussel Vet S.A, France). However, following patent expiration, additional "generic" forms of the compound have been approved for marketing in countries where the use of ZH as a feed additive is authorized. A generic drug is a pharmaceutical drug that contains the same chemical substance as a drug that was originally protected by chemical patents. Generic drugs are allowed for sale after the patents on the original drugs expire. Because the active chemical substance is the same, the medical profile of generics is believed to be equivalent in performance (Dunne *et al.* 2013). A generic drug has the same active pharmaceutical ingredient as the original, but it may differ in some characteristics such as the manufacturing process, formulation, excipients, color, taste, and packaging. Even still, generic ZH dosed from 0.10 to 0.20 mg/kg live has been shown a similar effects on growth performance and carcass characteristics than patent brand ZH when supplemented in finishing hairy lambs (Avendaño-Reyes *et al.* 2018). On the other hand, previous reports indicate that some generic ZH affects differently the meat quality in cattle (Avendaño-Reyes *et al.* 2016) and fat depot in lambs (Rivera-Villegas *et al.* 2019). However, information about the effects of generic ZH on lamb meat quality is scarce, and no information is available on the effects of different generic ZH sources on meat quality of lambs that have been tested in the same experiment. For this reason, the aim of this experiment was to compare two sources of generic ZH *vs.* patent brand ZH in meat quality of lambs finished with high-energy diet.

MATERIALS AND METHODS

All procedures were conducted within the guidelines of approved local official techniques specifications for the care and use of laboratory and farm animals (NOM-062-ZOO-1999) and humanitarian sacrifice (NOM-033-ZOO-2014).

Twenty-four Pelibuey × Katahdin (¼ Pelibuey and ¾ Katahdin, 46.7±2.4 kg initial shrunk weight) crossbred intact male lambs were used in a 33-d growth-performance experiment to evaluate the treatment effects on meat quality. Lambs were placed in individual pens (6 lambs/treatment). Description of diets and the management of experimental units prior and during the experiment were previously described by Rivera-Villegas *et al.* (2019). Dietary treatments (Table 1) consisted of a corn-based finishing diet (13.3% crude protein and 2.11 Mcal of net energy for maintenance/kg) supplemented with no zilpaterol (control), or the, same basal diet plus the label dosage (125 mg of product/kg diet, as-fed basis) of zilpaterol hydrochloride (ZH) as Zilmax® (ZIL, MSD Salud Animal Mexico, Santiago Tianguistenco, Mexico), Grofactor® (GRO, Laboratorios Virbac México, Guadalajara, Mexico), or Zipamix® (ZIPA, Pisa Agropecuaria, Guadalajara, Mexico). In such a way that treatments were configured by a 1 Control group, 1 group received a patent-brand ZH, and 2 groups received two different sources of generic ZH; then, treatments were: 1) controls, 2) brand ZH (ZIL), 3) generic ZH (GRO), and 4) generic ZH (ZIPA). According to the label, all products tested contained 4.8% ZH. Thus, the dosage of 125 mg of product/kg diet corresponds to a dietary ZH concentration of 6 mg/kg (as feed basis). Supplemental ZH was hand-weighed using a precision balance (Ohaus, mod AS612, Pine Brook, NJ), and premixed for 5 min with the other minor dietary ingredients (urea, limestone and trace mineral salt) before incorporation into a complete mixed basal diet using a 2.5 m^3 capacity paddle mixer (mod 30910-7, Coyoacán, México). To avoid contamination, the mixer was thoroughly cleaned between each treatment. Zilpaterol hydrochloride was supplemented for 30 d followed by a 3-d pre-harvest withdrawal when all lambs received the non-supplemented basal control diet. Zilpaterol treatments were withdrawn three days before harvest. All lambs were harvested on the same day. After humanitarian sacrifice, lambs were skinned, and the gastrointestinal organs were separated. After carcasses (with kidneys and internal fat included) were chilled in a cooler at -2 ˚C to 1 ˚C for 48 h. At 48-h of chilling, two longissimus muscle (LM) steaks (3-cm thick) from each carcass (6 per treatment) were removed between 12th and 13th rib interface, preserved immediately on dry ice, and shipped to the meat quality laboratory for storage at 4 ˚C until days postmortem. At 14 days postmortem, steaks were frozen at −20 ˚C vacuum packaged and stored for subsequent meat quality trait analysis. Variables measured included water holding capacity (WHC), color, purge loss (PL) at 24 and 48-h, cook loss (CL), and shear force (SF). The color values L* (lightness), *a** (redness), and *b** (yellowness) were determined using a Minolta CR-410 spectrophotometer (Konica Minolta Camera Co., Ltd, New Jersey, USA). The chroma (C*) and hue angle (h˚) were estimated as C*= [(*a**) 2 + (*b**) 2]½ , and *h*˚= tan − 1 (*b**/*a**). The 10-cm-thick steaks previously obtained from the rib were thawed and cooked at 21-d postmortem followed the procedures described by López-Carlos *et al.* (2014), previously cooked steaks were aged at 4 ˚C for 24 h. To obtain SF values, 1 × 1 × 3 cm cores were taken from each cooked steak parallel to the orientation of the muscle fibers. The SF measurements (kg/cm^2) were determined using a Lloyd texturometer (Lloyd Instruments, Fareham, Hampshire, UK) equipped with Warner-Bratzler shear blades with a crosshead speed of 50 mm/min. Water-holding capacity was determined using a modified compression technique from the method termed press-juice, in which 0.3 kg of a meat sample is positioned between 2 layers of filter paper and 2 plaques of acyclic Plexiglas, and compressed at a force of 5 N for 60 s using the Lloyd texturometer. The WHC was estimated as juice lost divided by the initial sample mass. Drip loss was measured using the technique described by López-Carlos *et al.* (2014). The zilpaterol hydrochloride concentrations for the various sources (blind samples) were assayed by MSD quality control laboratory (MSD Salud Animal Mexico, Santiago Tianguistenco, México). Data were analyzed using the 'mixed' procedure of SAS (2007). The results were analyzed according to a completely randomized design using each lamb as an experimental unit. The linear model for dependent variables included common effect, fixed component of treatment, initial weight as the covariate, and the variation between lambs within treatment as a random effect.

Table 1 Composition of basal diet supplemented with different sources of zilpaterol hydrochloride

Item	Zilpaterol sources			
	None	Zilmax	Grofactor	Zipamix
Ingredient composition (%)				
Dry-rolled corn	64.50	64.50	64.50	64.50
Sudan grass hay	12.00	12.00	12.00	12.00
Soybean meal	10.00	10.00	10.00	10.00
Zilpaterol hydrocholride[1]				
Zilmax	----	+++	----	----
Grofactor	----	----	+++	----
Zipamix	----	----	----	+++
Molasses cane	8.00	8.00	8.00	8.00
Urea	0.43	0.43	0.43	0.43
Tallow	3.00	3.00	3.00	3.00
Trace mineral salt[2]	2.07	2.07	2.07	2.07
Dry matter (DM)	87.55	87.55	87.55	87.55
Chemical composition, (DM basis)				
Total crude protein (%)	13.23	13.23	13.23	13.23
Ether extract (%)	5.57	5.57	5.57	5.57
Neutral detergent fiber (%)	16.65	16.65	16.65	16.65
Calculated net energy[3] (Mcal/kg)				
Maintenance	2.11	2.11	2.11	2.11
Gain	1.44	1.44	1.44	1.44

[1] Sources of zilpaterol hydrochloride [Zilmax (ZIL, MSD Salud Animal Mexico, Estado de Mexico, Mexico); Grofactor (GRO, Laboratorios Virbac México, Guadalajara, Mexico), and Zipamix (ZIPA, Pisa Agropecuaria, Guadalajara, Mexico)] were supplemented to provide 6 mg zilpaterol hydrochloride/kg diet (as-fed basis).
[2] Mineral premix contained: Calcium: 28%; Phosphorous: 0.55%; Magnesium: 0.58%; Potassium: 0.65%; NaCl: 15%; vitamin A: 1100 IU/kg and vitamin E: 11 UI/kg.
[3] Based on tabular net energy (NE) values for individual feed ingredients (NRC, 2007).

As covariate was nonsignificant (P>0.05), then it was eliminated from the analysis. Contrasts performed were: 1) controls *vs*. ZH, analyzed as controls response *vs*. the average of the response of all ZH sources (ZIL+GRO+ZIPA/3), and 2) patent (ZIL) *vs*. generics (GRO and ZIPA), analyzed as ZIL response *vs*. the average of the response of generic ZH sources (GRO+ZIPA/2). Additionally, the treatment means were separated using the least significant difference test (Tukey´s test). Treatment effects were considered significant when the value of P ≤ 0.05, and were identified as trends when the value of P > 0.05 and ≤ 0.10.

RESULTS AND DISCUSSION

Assayed zilpaterol hydrochloride concentrations averaging 47.8, 47.3 and 51.2 g ZH/kg of product for ZIL, GRO, and ZIPA, respectively. Thus, based on average as-fed intake, ZH intake averaged 7.92, 7.73, and 8.1 mg/d, corresponding to 0.157, 0.153, and 0.162 mg ZH/kg LW for lambs fed ZIL, GRO, and ZIPA, respectively. Thus the average intake of ZH was 0.157 mg ZH/kg LW. Recommended doses for ZH are from 0.10 to 0.20 mg ZH/kg LW (Estrada- Angulo *et al*. 2008; Avendaño-Reyes *et al*. 2018).

Weight at slaughter was 50.93, 54.55, 54.20, and 54.50 kg for control, ZIL, GRO, and ZIPA, respectively. The carcass responses to the treatments were previously reported by Rivera-Villegas *et al*. (2019) in which zilpaterol (ZH) supplementation, regardless of ZH source, increased hot carcass weight (6.4%), dressing percentage (3.2%), LM area (15.6%), and shoulder muscle: fat ratio (28.7%), but decreased kidney-pelvic-heart fat, and fat thickness. However, compared with non-supplemented controls, only patent ZH appreciably decreased carcass fat distribution, including fat thickness, percentage kidney pelvic and heart fat, shoulder fat, and visceral fat.

There were no differences between zilpaterol source (patent *vs*. generics) on meat quality variables evaluated (Table 2). In previous reports, zilpaterol source (patent and generics) have been similar effects on growth performance and carcass characteristics in feedlot lambs (Rivera-Villegas *et al*. 2019) and in feedlot cattle (Avendaño-Reyes *et al*. 2016). With regard to the effects on meat quality between generic and patent brand zilpaterol, to our knowledge only one study are available (Avendaño-Reyes *et al*. 2016). These researchers comparing GRO vs ZIL (dosed at 0.15 mg/kg LW) in young bulls that were fed with a high energy diet (2.12 Mcal NE_m/kg diet DM). Chroma value (*C**) was lower to GRO reading at 48-h after slaughter, but this effect has vanished at the reading obtained at 14-d after slaughter in which no differences in meat color were detected between generic and patent brand zilpaterol. Our results, as well as previous findings could be indicative that the differences regard to quality control during manufacturing and marketing, uniformity, purity, drug particle size, and carrier used between generics and patent brand are minimal. Confirming the bioequivalence between patent brands and generic products.

Table 2 Effect of treatments on meat quality of hairy lambs finished with a high-energy diet

Item	Treatments[1]				SEM	P-value	
	Control	ZIL	GRO	ZIPA		Control *vs.* ZH[2]	Patent *vs.* generics[3]
Water holding capacity,%	24.84	21.20	23.14	23.25	1.35	0.15	0.24
Purge loss, %							
24-h	5.24	5.16	4.93	3.99	0.73	0.53	0.46
48-h	6.53	5.65	5.64	5.19	0.72	0.21	0.79
Color[4]							
L	41.10	40.66	40.45	39.07	1.00	0.43	0.55
*a**	21.23	21.07	21.64	20.80	0.55	0.91	0.83
*b**	6.01	5.05	5.86	5.05	0.41	0.16	0.44
Cook loss, %	23.72	19.56	21.92	21.04	1.83	0.19	0.41
Shear force, kg/cm^2	2.63	3.82	4.27	4.24	0.29	< 0.01	0.25

[1] Dietary treatments: Control: with no zilpaterol; ZIL: zilpaterol hydrochloride as patent brand Zilmax® (MSD Salud Animal Mexico, Santiago Tianguistenco, Mexico); GRO: Grofactor® as generic (Laboratorios Virbac México, Guadalajara, Mexico) and ZIPA: Zipamix® as generic (Pisa Agropecuaria, Guadalajara, Mexico).
[2] Contrast performed was control (with no zilpaterol) *vs.* the average of response ZH sources tested (ZIL+GRO+ZIPA/3).
[3] Contrast performed was patent ZH (ZIL) *vs.* the average of the response of generic ZH sources (GRO+ZIPA/2).
[4] The color values are interpreted as L* (lightness), a* (redness), and b* (yellowness).
SEM: standard error of the means.

There was no effect of ZH on meat color. It is well known the importance of meat color for consumers, rejection of acceptance is highly associated with excessively darken color of meat. Even when there is limited information on the effect of ZH on the meat quality of lambs, previous reports indicate that ZH supplementation reduces, or tended to reduce, a* (redness) value in meat of lambs (patent brand ZH; Partida *et al.* 2015, and generic ZH; Cayetano-De-Jesús *et al.* 2020), and goats (patent brand ZH; López-Carlos *et al.* 2014). The main argument for explain the reduction in *a** value have been the "dilution effect" on myoglobin concentration resulting by an increase of sarcomere size by ZH supplementation (Carr *et al.* 2005) or by reduction of marbling (intramuscular fat depot) by ZH, considering that body fat becomes white when ruminants are feeding high-grain diets (Dunne *et al.* 2009). However, in feedlot cattle, consistent with the present study, the influence of supplemental ZH on color has been negligible (Elam *et al.* 2009; Montgomery *et al.* 2009; Walter *et al.* 2018). It has been reported that dietary energy concentration it's an important factor in myoglobin concentration (Daly *et al.* 1999). In the experiments performed with lambs and goats (López-Carlos *et al.* 2014; Partida *et al.* 2015; Cayetano-De-Jesús *et al.* 2020), dietary energy was below 2.03 Mcal of net energy for maintenance/kg DM (average of all experiments= 1.85 Mcal NE_m/kg), while in this experiment, the net energy value was 12% greater (2.11 Mcal NEm/kg). This energy concentration is similar to the dietary NE concentration in the studies with feedlot cattle in which no effect of ZH in meat color was observed (over of 2.10 Mcal NEm/kg, Elam *et al.* 2009; Montgomery *et al.* 2009; Walter *et al.* 2018). More research is needed to evaluate the effects of ZH on meat quality when supplemented on moderated energy diets (i.e.<2.0 Mcal NE_m/kg diet DM).

Compared to controls, ZH supplementation averaged an increased 36% shear force (4.11 *vs.* 2.63, P<0.05). There is scarce information about of ZH supplementation effect on SF values in the meat of lambs, However, the value determined here is very similar to the average increase of 38% reading at 5 and 10-d postmortem reported by Cayetano-De-Jesús *et al.* (2020) for lambs received 0.20 mg ZH/kg LW. Increases on SF of meat to ZH supplementation is a common response in feedlot cattle. Hilton *et al.* (2009) observed that, compared to the control group, meat of steers that were supplemented with ZH showed a higher SF recorded at 7, 14, and at 21 days postmortem. This becomes more evident with aging because it has been observed that SF not decreases with aging for the ZH treated steers, whereas the controls become more tender with aging. The lack of tenderization in ZH supplemented cattle has been attributed, in part, to increased levels of calpastatin, which interacts with the calpains that contribute significantly to postmortem tenderization of meat (Geesink and Koohmaraie, 1999).

CONCLUSION

It is concluded that the generic zilpaterol sources tested in the present experiment affect similarly the meat quality of hairy lambs finished with high-energy diet (>2.10 Mcal NE_m/kg) when compared with patent zilpaterol. Zilpaterol supplementation mainly affected tenderness of meat increasing shear force.

ACKNOWLEDGEMENT

Appreciation is expressed to CONACYT, Mexico, for fellowship support (CVU 714481) to Ph D student Alejandro Rivera Villegas.

REFERENCES

Avendaño-Reyes L., Meraz-Murillo F.J., Pérez-Linares C., Figueroa-Saavedra F., Correa A., Alvarez-Valenzuela F.D., Guerra-Liera J.E., López-Rincón G. and Macías-Cruz U. (2016). Evaluation of efficacy of Grofactor, a beta-adrenergic agonist base don zilpaterol hydrochloride, using feedlot finishing bulls. *J. Anim. Sci*. **94,** 2954-2961.

Avendaño-Reyes L., Torrentera N., Correa-Calderón A., López-Rincón G., Soto-Navarro S.A., Rojo-Rubio R., Guerra-Liera J.E. and Macías-Cruz U. (2018). Daily optimal level of a generic beta-agonist base don zilpaterol hydrochloride for feedlot hair lambs. *Small Rumin. Res*. **165,** 48-53.

Carr S.N., Ivers D.J., Anderson D.B., Jones D.J., Mowrey D.H., England M.B., Killefer J., Rincker P.J. and McKeith F.K. (2005). The effects of ractopamine hydrochloride on lean carcass yields and pork quality characteristics. *J. Anim. Sci*. **83,** 2886-2893.

Cayetano-De-Jesus J.A., Rojo-Rubio R., Grajales-Lagunes A., Avendaño-Reyes L., Macias-Cruz U., Gonzalez-del-Prado V., Olmedo-Juárez A., Chay-Canul A., Roque-Jiménez J.A. and Lee-Rangel H.A. (2020). Effect of zilpaterol hydrochloride on performance and meat quality in finishing lambs. *Agriculture*. **10,** 241-252.

Daly C.C., Young O.A., Graafhuis A.E., Moorhead S.M. and Easton H.S. (1999). Some effects of diet on beef meat and fat attributes. *New Zealand J. Agric. Res.* **42,** 278-287.

Dunne P.G., Monahan F.J., O'Mara F.P. and Moloney A.P. (2009). Colour of bovine subcutaneous adipose tissue: A review of contributory factors, associations with carcass and meat quality and its potential utility in authentication of dietary history. *Meat Sci*. **81,** 28-45.

Dunne S., Shannon B., Dunn C. and Cullen W. (2013). A review of the differences and similarities between generic drugs and their originator counterparts, including economic benefits associated with usage of generic medicines, using Ireland as a case study. *Pharmacol. Toxicol*. **14,** 1-10.

Elam N.A., Vasconcelos J.T., Hilton G., VanOverbeke D.L., Lawrence T.E., Montgomery T.H., Nichols W.T., Streeter M.N., Hutcheson J.P., Yates D.A. and Galyean M.L. (2009). Effect of zilpaterol hydrochloride duration of feeding on performance and carcass characteristics of feedlot cattle. *J. Anim. Sci.* **87,** 2133-2141.

Estrada-Angulo A., Barreras-Serrano A., Contreras G., Obregón J.F., Robles-Estrada J.C., Plascencia A. and Zinn R.A. (2008). Influence of level of zilpaterol chlorhydrate supplementation on growth performance and carcass characteristics of feedlot lambs. *Small Rumin. Res.* **80,** 107-110.

Geesink G.H. and Koohmaraie M. (1999). Postmortem proteolysis and calpain/calpastatin activity in callipyge and normal lamb bicep femoris during extended postmortmen storage. *J. Anim. Sci*. **77,** 1490-1501.

Hilton G.G., Montgomery J.L., Krehbiel C.R., Yates D.A., Hutcheson J.P., Nichols W.T., Streeter M.N., Blanton J.R. Jr. and Miller M.F. (2009). Effects of feeding zilpaterol hydrochloride with and without monensin and tylosin on carcass cutability and meat palatability of beef steers. *J. Anim. Sci.* **87,** 1394-1406.

López-Carlos M.A., Aguilera-Soto J.I., Ramírez R.G., Rodríguez H., Carrillo-Muro O. and Méndez-Llorente F. (2014). Effect of zilpaterol hydrochloride on growth performance and carcass characteristics of wether goats. *Small Rumin. Res.* **117,** 142-150.

Montgomery J.L., Krehbiel C.R., Cranston J.J., Yates D.A., Hutcheson J.P., Nichols W.T., Streeter M.N., Bechtol D.T., Johnson E., TerHune T. and Montgomery T.H. (2009). Dietary zilpaterol hydrochloride. I. Feedlot performance and carcass traits of steers and heifers. *J. Anim. Sci*. **87,** 1374-1383.

NRC. (2007). Nutrient Requirements of Small Ruminants, Sheep, Goats, Cervids, and New World Camelids. National Academy Press, Washington, D.C., USA.

Partida J.A., Casaya T.A., Rubio M.S. and Medina R.D. (2015). Effect of zilpaterol hydrochloride on the carcass characteristics of Katahdin Lamb terminal crosses. *Vet. Mexico OA*. **2,** 346-357.

Rivera-Villegas A., Estrada-Angulo A., Castro-Pérez B.I., Urías-Estrada J.D., Ríos-Rincón F.G., Rodríguez-Cordero D., Barreras A., Plascencia A., González-Vizcarra V.M., Sosa-Gordillo J.F. and Zinn R.A. (2019). Comparative evaluation of supplemental zilpaterol hydrochloride sources on growth performance, dietary energetics and carcass characteristics of finishing lambs. *Asian-Australasian J. Anim. Sci*. **32,** 209-216.

SAS Institute. (2007). SAS®/STAT Software, Release 9.3. SAS Institute, Inc., Cary, NC. USA.

Walter L.A.J., Schmitz A.N., Nichols W.T., Hutcheson J.P. and Lawrence T.E. (2018). Live growth performance, carcass grading characteristics, and harvest yields of beef steers supplemented zilpaterol hydrochloride and offered *ad libitum* or maintenance energy intake. *J. Anim. Sci*. **96,** 1688-1703.