Review Article

Journal of Advanced Veterinary Research
(2024) Volume 14, Issue 2, 335-338

The use of ractopamine as a feed additive: A review

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ARTICLE INFO

Recieved: 18 August 2023

Accepted: 22 October 2023

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Keywords:

Ractopamine
Livestock production
Feed additive

ABSTRACT

Ractopamine hydrochloride is a β-adrenergic agonist that increases growth, feed efficiency, and fat deposition. Because of its ability to increase muscling, average daily gain, efficiency, and carcass weight, ractopamine hydrochloride has been used as a feed additive growth enhancer. Ractopamine is also a member of the phenylethanolamine class of chemicals, which is used as a feed supplement in meat-producing animals. This review threw the light on the use of ractopamine to improve weight gain and as a feed addition. Furthermore, the potential negative health effects of ractopamine were explored.

Introduction

β-agonists bind to β-adrenergic receptors and elicit cellular responses along the same pathway as naturally occurring hormones in the body such as dopamine, adrenaline, and norepinephrine (Bell *et al*., 1998). β-agonists are used to alleviate airway blockages in humans, as well as having an anabolic impact on skeletal muscle (Smith, 1998). β-adrenergic drugs boosted test animal weight gain, feed efficiency, carcass leanness, and dressing percentage (Ricke *et al*., 1999).

Ractopamine hydrochloride is a β-adrenergic agonist that promotes growth, feed efficiency, and fat deposition (Boler *et al*., 2012). Ractopamine hydrochloride, according to Scramlin *et al*. (2010), has been employed as a feed additive growth promoter due to its capacity to boost muscling, average daily gain, efficiency, and carcass weight. Furthermore, ractopamine belongs to the phenylethanolamine class of compounds, which is employed as a feed supplement in meat-producing animals (Lonare *et al*., 2018). According to Anna *et al*. (2021), ractopamine is approved to promote weight gain and feed efficiency in cattle. According to Phillip *et al*. (2021), ractopamine is used in pigs to enhance growth and body performance. Furthermore, ractopamine is allowed as a feed additive in many countries for increased growth and body performance in swine production, however it stimulates tumor growth by inducing asparagine synthetase expression (Fan, 2022).

This review threw the light on the use of ractopamine to increase the weight gain and its use as a feed additive. Besides, the potential adverse health effects of ractopamine were also discussed.

Ractopamine hydrochloride

Ractopamine's structure is comparable to those of catecholamine, epinephrine, and norepinephrine. Lipolysis and glycogenolysis are regulated by these hormones (Mersmann, 1989). Ractopamine is a -adrenergic agonist that is licenced for use as a growth regulator in pigs and other livestock (Ricke *et al*. 1999). Furthermore, Moody *et al*. (2000) said that ractopamine is the most important member of the 1-adrenergic receptor agonist family in clinical use. Ractopamine hydrochloride is a frequently used growth booster in beef cattle and is known as a repartitioning agent (Swaminath *et al*. 2002). Furthermore, Blanca *et al*. (2005) said that ractopamine is the most effective -agonist utilised as a growth-promoting drug in meat-producing animals. According to Johnson *et al*. (2014), supplementation of -adrenergic receptor agonists has been demonstrated to promote feed intake in ruminants, possibly by increasing γ-aminobutyric acid levels in the brain. According to Samuelson *et al*. (2016), ractopamine hydrochloride is the most commonly used -adrenergic receptor agonist for finishing beef cattle production. Ractopamine hydrochloride is a -adrenergic agonist that has been licensed by the FDA for use in feeding animals in the United States for the last 28 to 42 days of the finishing phase (Davis and Belk, 2018).

Mode of action of ractopamine hydrochloride

Ractopamine has been shown to promote lipolysis (Liu *et al*., 1994). Furthermore, Wellenreiter and Tonkinson (1990) discovered that feeding ractopamine to turkeys improved body performance through increased protein accretion and decreased fat deposition. In skeletal muscle, ractopamine stimulates protein synthesis and increases protein accretion (Helferich *et al*., 1990). Mills and Liu (1990) likely observed that ractopamine induces lipogenesis rather than lipolysis. Watkins *et al*. (1990) discovered that ractopamine plays a significant role in promoting muscle growth by increasing nitrogen retention and protein synthesis, as well as

ISSN: 2090-6277/2090-6269/

increasing lipolysis, which leads to lower fat accumulation and a favorable change in the lean/fat ratio of growing animals. Dietary ractopamine has been demonstrated to reduce lipolytic reactions as well as hyperinsulinemia (Anderson *et al*., 1990). Mills *et al*. (1990) proposed that ractopamine plays a crucial function in lipid biosynthesis decrease. In the pig, for example, ractopamine enhanced protein deposition while decreasing fat deposition (Adeola *et al*. 1992). Furthermore, Dunshea and King (1995) found that ractopamine lowers basal insulin concentrations while having no effect on plasma glucose or non-esterified fatty acids while increasing insulin's antilipolytic actions. Ractopamine increases lipolysis, protein synthesis, and lipogenesis inhibition in swine cattle and turkeys, resulting in fat loss, increased muscle mass, and enhanced feed efficiency (Smith 1998). When protein kinase A activated hormone sensitive lipase and inactivated acetyl CoA carboxylase, ractopamine promoted lipolysis and decreased lipogenesis via 1 and 2 receptors (Mills, 2002). Ractopamine likely enhanced both muscle and fat mass at the same time, probably due to the rapid metabolism of this β-agonists (Sumano *et al*., 2002). According to Mills *et al*. (2003), ractopamine hydrochloride binds to -adrenergic receptors on the adipocyte cell membrane and in skeletal muscle, as well as activating the Gs1 protein. According to Beerman and Dunshea (2005), ractopamine has an anabolic effect on protein metabolism, producing muscle fibre development and frequent changes in muscle fiber type. Beta-agonists cause muscle hypertrophy by increasing protein synthesis and/or lowering protein breakdown, whereas 1-agonists, such as ractopamine, decrease protein synthesis (Apple *et al*., 2007). Ractopamine is also utilized as a feed supplement in pigs, cattle, and turkeys to improve feed efficiency and carcass leanness by increasing lipolysis, protein synthesis, and decreasing lipogenesis and protein degradation (Strydom *et al*., 2009). According to Kriewald (2010), ractopamine has a steroid-like action, and adipolysis leading to stimulating lipolysis and protein synthesis. According to Farshid *et al*. (2011), ractopamine is employed as a lipolytic agent and growth enhancer in grill chickens. Ractopamine, according to De Almeida *et al*. (2012), modulates metabolism and redirects calories from adipose tissue to muscles, as well as increasing lipolysis and protein synthesis. According to Freire *et al*. (2013), ractopamine improved lean muscle accretion by shifting nutrients away from lipogenesis and towards muscular growth. According to Neumeier and Mitloehner (2013), ractopamine increased muscle growth via increasing protein synthesis and decreasing muscle protein breakdown. According to Arp *et al*. (2014), ractopamine improved body performance by increasing protein accretion and decreasing fat deposition. Ractopamine reduces fat storage in adipose tissue by increasing lipolysis and lowering lipogenesis (Mirhendi *et al*., 2018). β-adrenergic agonists are utilized in beef cattle to promote growth performance and carcass features by increasing protein synthesis and decreasing protein breakdown, according to Hergenreder *et al*. (2020). Ractopamine is a phenylethylamine-derived adrenergic agonist having pharmacological characteristics similar to endogenous catecholamines adrenaline and noradrenaline (Moshiur *et al*., 2022).

Pharmacokinetics of ractopamine

Within 7 days, Dalidowicz *et al*. (1986) discovered that around 9% of ractopamine was eliminated in the feces. According to Dalidowicz and Babbit (1986), approximately 88% of ractopamine was eliminated in urine within 7 days. Ractopamine was given orally rather than intravenously (Williams *et al*., 1987). Ractopamine is a β-agonist that is quickly and thoroughly absorbed from the gastrointestinal tract (Dalidowicz and Thomson, 1989). Ractopamine was readily absorbed following injection, with peak plasma concentrations occurring 0.5-2 hours after dosage. Ractopamine was found in urine and bile. The elimination half-life is around 6-7 hours (Smith *et al*., 1995). Elliot *et al*. (1998) discovered that ractopamine was excreted in the form of glucuronides. Maximum ractopamine residual concentrations were reported during administration, with residues remaining for several days after ractopamine was removed from the ration. Apart from these remnants, they were detectable for 2 weeks following withdrawal. Ractopamine can be found in sheep and bovine urine for at least 7 or 5 days after exposure (Smith and Shelver, 2002). Zhiyi *et al*. (2007) discovered residues in tissues (1 ng g-1), urine (0.5 ng g-1) and serum (0.5 ng g-1), liver (46.09 ng g-1) and kidney (169.27ng g-1), muscle (4.94ng g-1) and fat (3.28ng g-1) in pigs fed 18 mg kg-1ractopamine in ration twice daily for 28 days. Ractopamine hydrochloride serves as a repartitioning agent, redirecting nutrients and causing muscle growth by enhancing protein synthesis and lowering protein breakdown (Burnett *et al*., 2012). Cattle administered 0.67 mg/kg bwt ractopamine for 28 days had elevated plasma concentrations at 14 days (2.88 nh/ml) and high concentrations in urine at 7 day post treatment (4713.25 ng /mL), withdrawal ractopamine concentrations in plasma and urine at day 28 (Chaohua *et al*., 2016). Ractopamine recovery from plasma was 88-99% (Zhao *et al*., 2017). According to Carolina *et al*. (2019), low ractopamine concentrations were discovered in pig muscle (0.15 g kg1), kidney (0.5 g kg1), liver (0.5 g kg1), and lungs (1.0 g kg1), however ractopamine residue concentrations in urine remained below 1.35 g/L. The withdrawal times of ractopamine in goats were 1141.71 ± 255.85 h and in sheep were 989.741 ± 167.633 h. The safe time to slaughter after treatment with 1 mg of ractopamine was 3 months and 5 days, but the withdrawal times in sheep were 2 months and 22 days (Lazuardi *et al*., 2020).

Effect of ractopamine on body weight

Ractopamine boosted weight gain, carcass weight, and the area of the longissimus muscle, but had negative effects on fat tissue (Mersmann, 1998). According to Mersmann (2002), ractopamine at various dosages increased daily body weight gain, feed intake, and feed conversion ratio. Ractopamine hydrochloride is fed to animals to promote feed efficiency and weight gain (Mills *et al*., 2003). Cattle given 30 mg/kg ractopamine in their ration improved their feed efficiency, weight gain, and carcass leanness (Mills *et al*., 2003). According to Gruber *et al*. (2007), ractopamine supplementation increased feedlot steer growth performance and carcass traits. According to Kootstra *et al*. (2005), β-adrenergic agonists are efficient in promoting growth performance and improving feed conversion rate. According to Gruber *et al*. (2007), ractopamine treatment increased growth performance and carcass features of feedlot steers. According to Scramlin *et al*. (2010), ractopamine hydrochloride is a -adrenergic agonist that improves growth performance and weight gain. According to Yousefi *et al*. (2011), beta-adrenergic agonists improve the bodily performance of meat-producing animals and poultry. According to Alemanno and Capodieci (2012), ractopamine is utilized in animal production to reduce fat deposition, enhance feed conversion rate, and raise average daily weight gain. According to Kriewald *et al*. (2010), ractopamine is a synthetic-adrenergic agonist that is extensively utilized in ration for increased feed effectiveness, growth, body performance, and muscle leanness. Moslemipur *et al*. (2012) mentioned that β-adrenergic antagonist in grill meals improved performance and carcass composition. According to Nasroallah *et al*. (2013), ractopamine in ration at a dosage of 12 mg/kg ration induces improved growth performance of broiler chickens. Besides, Bohrer *et al*. (2013) mentioned that ractopamine is rationed to improve feed efficiency and carcass leanness. Mirhendi *et al*. (2014) reported that -adrenergic agonists increased poultry growth performance. According to Tang *et al*. (2016), ractopamine hydrochloride is used in the livestock industry to promote body weight gain, feed conversion rate, feed efficiency, and productivity. Ractopamine is utilized as a feed supplement to promote feed effectiveness, growth, and muscle leanness (Hakk *et al*., 2016). According to Jul *et al*. (2018), ractopamine is extensively used in the cattle business to boost feed efficiency and production. Furthermore, Ronald *et al*. (2019) reported that ractopamine could improve feed efficiency, body weight, average daily gain, and feed conversion rate. According to Harris *et al*. (2020), ractopamine hydrochloride increases lean muscle deposition in cattle. Similarly, Gabriel *et al*. (2021), pointed out that ractopamine

boosted beef cattle growth performance. Likely, pigs given ractopamine at a dose of 20 ppm for 28 days had residues in muscle and fat 24 hours after the final injection, with residues in kidney remaining greater than in liver (Phillip *et al*., 2021).

Adverse effect of Ractopamine

According to Wellenreiter and Tonkinson (1990), ractopamine dramatically boosted blood serum cholesterol and albumin levels while decreasing triglyceride, blood urea nitrogen, and globulin levels. Strydom *et al*. (2009) found that dogs given ractopamine had excessive pathological lesions in the heart, such as cardiac myofiber fragmentation with fibrosis near the hepatic artery, which was disrupted by fibrin and free red blood cells. Dogs given 1 mg/kg ractopamine for 9 days had elevated troponin levels, indicating myocardial injury, as well as necrosis and fibrosis. Yaeger *et al*. (2012). According to Nasroallah *et al*. (2013), ractopamine raised serum glucose, cholesterol, triglyceride, and lipolysis while simulating protein synthesis and decreasing uric acid. According to Asadi *et al*. (2013), hemoglobin content, red blood cell counts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and white blood cell counts did not differ between grill chickens fed different amounts of ractopamine. Giannetti *et al*. (2016) found that beta-agonists reduced lipids or lipolysis in sheep, which is caused by lipases that hydrolyze triacylglycerols to glycerol and free fatty acids-facilitates glycolysis, oxidation, and the tricarboxylic acid cycle, all of which can contribute to protein synthesis. According to Pane *et al*. (2020), ractopamine reduces extremely low density lipoprotein and increases Hematocrit and mean corpuscular hemoglobin concentrations while improving physical performance. Rivera *et al*. (2022) found that ractopamine increased daily weight gain by 30% while decreasing food conversion rate.

Conclusion

This review highlighted the important role of ractopamine as a feed additive to increase body weight gain, body mass, and feed conversion ratio in the livestock animals and poultry. However, the use of ractopamine in livestock production should be monitored regularly because of its potential adverse effects on the animal health, particularly on the cardiac muscle.

Conflict of interest

The authors declare that they have no conflict of interest.

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