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Review Article

Red osier dogwood and its use in animal nutrition: A review

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ABSTRACT

As the human population increases globally, the food animal industry has not been spared from the monumental demand for edible animal products, particularly meat. This has necessitated the simultaneous expansion of the productivity of the animal sector to meet the ever-growing human needs. Although antibiotics have been used in food animal production with commendable positive impacts on their growth performance, their sole contributive factor to the increasing incidence of antimicrobial resistance has ushered the strict restrictions placed on their use in the animal sector. This has handed a setback to both animals and farmers; thus, the intense push for a more sustainable antibiotic alternative for use in animal production. The use of plants with concentrated phytogenic compounds has gained much interest due to their beneficial bioactivities, including antioxidant and selective antimicrobial. While the reported beneficial activities of phytogenic additives on animals vary due to their varying total polyphenol concentrations (TPC), red osier dogwood (ROD) plant materials boast of high TPC with excellent antioxidant prowess and growth improvement capacities compared to some plant extracts commonly used in research. However, its adoption in research and commercial scale is still low. Thus, the present review aims to provide concise information on the dietary potential of ROD plant materials in animal feeding.

1. Introduction

The global demand and consumption of animal meat have increased due to the increasing human population. Among the animal meat produced annually, chicken, pork, and beef contribute a significant percentage of total animal protein consumed worldwide (Food and Agricultural Organization of United Nations, 2021), possibly due to their improved meat yield potentials. This could be attributed to antibiotic usage as growth-promoting agents in animal production (Castanon, 2007; Kumar et al., 2018). From the introduction of antibiotics in the first half of the 1900s, animal industries have witnessed an indiscriminate upsurge in the application of antibiotics, which without any ambiguity has contributed to improved feed conversion efficiency, curbed the incidence of diseases, and to some extent, maintained intestinal health of animals (Proctor and Phillips, 2019). Despite the positive impacts of antibiotics, weightier health concerns relating to antibiotic-resistant pathogens and residues in the food chain have been reported as one of the greatest threats to human health. The long-term use of antibiotics is predicted to cause the death of approximately 10 million people globally (World Health Organization, 2019), including 400,000 Canadians (Kane, 2019), from antibiotic-resistant diseases by 2050, if it is not adequately double-checked. Furthermore, Graham et al. (2007) mentioned that the disadvantages associated with antibiotics use outweigh their potential benefits.

It is no surprise that the famous era of antibiotic use as growth boosters in animal production is fast fading following restrictions

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handed by the European Union in 2006 (Wierup, 2001; Tokić et al., 2007), and many countries have followed suit. For example, in Canada, the preventative use of category I and II antibiotics has been eliminated in 2014 and 2018, respectively with readiness to discontinue the preventive use of category III antibiotics as soon as possible (Mehdi et al., 2018; Treena, 2018; Chicken Farmers of Canada, 2020). Although there are many benefits with these precautionary strategic restrictions, they have considerable consequential effects. At the farm level, the prohibition of antibiotics has favoured the proliferation of bacterial diseases that negatively impact the animal industries (Casewell et al., 2003; Attia et al., 2011). Thus, the increasing pressure to source for potent and sustainable alternatives to reduce or replace antibiotics not only for the public health interest but also to salvage animal health concerns.

For an immemorable time, medicinal plants have been used for fighting infectious diseases in both humans and animals as ethnoveterinary measures. The introduction of plants parts or their derived products into animal nutrition have been extensively researched and proven a worthy reduction or replacement strategy for antibiotic growth promoters (AGP) (Windisch et al., 2008; den Hartog et al., 2016). Remarkably, many research publications have consistently articulated that the direct application of plant extracts in animal nutrition plays a significant role in promoting growth performance (Murugesan et al., 2015; Ahsan et al., 2018; Akanmu, 2018; Saleh et al., 2018; Kholif et al., 2021), revamping gut health of animals (Spernakova et al., 2007; Stanaćev et al., 2010, 2011; Mountzouris et al., 2011; Puvača et al., 2013; Kholif et al., 2021) and improving physicochemical properties of animal meat (Rossi et al., 2013; Džinić et al., 2015). Medicinal plants are able to do what they do because of their phytochemical constituents, usually polyphenols (Hashemi and Davoodi, 2011; Máthé, 2015; Wenk, 2003), with concentrations varying from plant to plant. While other plants materials, including cinnamon (Ali et al., 2021), olive (Gorzynik-Debicka et al., 2018), rosemary (Petiwala et al., 2013), etc. have been reported to contain an excellent amount of polyphenols, red osier dogwood (ROD) could be comparably better in terms of its total phenolic content and oxygen reactive absorbance capacity.

Red osier dogwood (*Cornus sericea* L.), an ornamental flowering shrub naturally growing in all provincial areas of Canada and the boreal regions of the United States (Isaak et al., 2013; Scales, 2015), is an excellent medicinal plant commonly used by North American tribal people as traditional means to cure diarrhea, fever, and dermal diseases (Obomsawin, 2007; Scales, 2015). Plant parts of ROD, including leaves, stem, fruit, flowers, and root, contain very high concentrations of phenolic compounds (Isaak et al., 2013; Scales, 2015; Hassan et al., 2019), including quercetin, gallic acid, ellagic acid, tyrosol, catechin, epicatechin, rutin, kaempferol, cyanidin, caffeic acid, and anthocyanins (Balasundram et al., 2006; Isaak et al., 2013; Scales, 2015; Lee et al., 2018). These phenolic compounds are known for their strong redox buffering and antimicrobial bioactivities (Hagiwara et al., 2010; Isaak et al., 2013; Nair and Nair, 2013; Puvača et al., 2013; Abuelsaad et al., 2014; BenSaad et al., 2017). In the light of this, novel *in vivo* research findings on the antioxidant and antimicrobial potentials of ROD have been demonstrated in animals, including swine (Scales, 2015; Amarakoon, 2017; Koo et al., 2018, 2021; Lee et al., 2018; Jayaraman et al., 2018), broiler chickens (Mogire et al., 2021; Erinle et al., 2022a–c), rabbits (Scales, 2015), and ruminants (Scales, 2015; Gomaa et al., 2018, 2021; Wei et al., 2018, 2019). Notwithstanding the elaborate *in vitro* and *in vivo* studies that have investigated phytogenic constituents of ROD as influenced by several environmental factors and their nutraceutical potentials, the rate of its exploitation in animal feeding is still very low. Therefore, there is a need for a holistic insight that emphasizes the potential of ROD in animal production. To the best of our knowledge, this is the first review that aims to provide consolidatory information on the potential of ROD to improve growth performance, oxidative and immune-related stress, and intestinal health of monogastric and ruminant animals.

2. Red osier dogwood

Red osier dogwood belongs to the genus *Cornus* (Cornaceae family, usually shrubs) and has several attributable names because of its color, geographical location, or ethnical perceptions. Botanically, ROD is named *C. sericea, Cornus stolonifera*, *Swida sericea, Swida stolonifera* or *Thelycrania sericea*. However, some of its common names include red-stemmed dogwood, red osier dogwood, American dogwood, California dogwood, creek dogwood, western dogwood, poison dogwood, waxberry cornel, red twig dogwood, red-osier cornel, red willow, red brush, red rood, and Kinnikinic.

2.1. Ecology and hardiness of red osier dogwood

Red osier dogwood prevalently inhabits riparian, wet and boggy areas of the northern-temperate zone; however, it is by no means limited to the Canadian provinces and the United States. It produces white flowers, white to blue berries, and red stalk, sometimes referred to as winter dogwood and often attracts birds and other animals in their overall ecosystem (Gucker, 2012). Generally, plant species belonging to the genus *Cornus* are usually hardy, including ROD. They can withstand unfavourable cold temperatures, thrive in several soil conditions with varying nutrient levels and pH (Hardy, 1989; Pijut, 2004; Gucker, 2012). In addition, they can tolerate flooding because of their non-tap rooting system (Beaudry 1999), especially when fully established. Although it does well during the warm season, a laboratory study showed that ROD could even be acclimatized to temperatures lower than −90 °C (Gucker, 2012). Propagation of ROD is achieved by seeding or vegetatively by cutting and easily dispersed by animals. However, several methods of cultivating ROD are documented by Swanson (2019). Upon seeding, it takes about 60 days to germinate and attain heights of 15.24 and 60.96 cm in the first and second year, respectively. The optimum temperature for germination ranges from 10 to 25 °C (Acharya et al., 1992).

2.2. Phenolic and nutrient profiles of ROD

Phenolic compounds are diverse groups of phytochemicals produced in the chain of reactions involving three metabolic pathways, namely pentose phosphate, shikimic acid, and phenylpropanoid (Lin et al., 2010). They contain one or more hydroxyl constituents attached to an aromatic structure through which they elicit their strong antioxidant prowess by acting as free radical scavengers, oxygen singlet scavengers and/or metal ion chelator (Giannenas et al., 2013; Embuscado, 2015).

Polyphenols are prevalently found within plants, particularly medicinal plants. They confer a series of beneficial bioactivities on animals ingesting the plants depending on their metabolic processes. Low dietary total polyphenol content in foods has been negatively correlated with the incidence of poor glycemic index, mostly in diabetic individuals (Thompson et al., 1984; Williamson, 2013; Smeriglio et al., 2016). Although depending on the season when harvested, ROD could be recognized as one of the most potent phytogenic additives given its rich polyphenolic profile and high total polyphenol concentration. The extraction of polyphenol content in air-dried, spray-dried, or freeze-dried ROD has been demonstrated using methanol with 2% formic acid (Isaak et al., 2013; Scales, 2015) or hydrothermal method at 98 °C (Apea-Bah et al., 2020). While both methods are commercially used, proponents of the hydrothermal extraction method worry over the health, safety, and flammable concerns of the alcohol extraction model. Without prejudice to the foregoing, there are no comparative studies to determine the best optimized extraction methods in ROD.

Phytochemical analysis of ROD plant materials revealed that ellagic acid, quercetin, and gallic acid and their derivatives were the prominent phenolics (Vareed, 2005; Isaak et al., 2013; Scales, 2015), the combination of which has significant health importance in a living system (Mehrzadi et al., 2020; Patil and Killedar, 2021). Quercetin and kaempferol were specifically shown to reduce gastric inflammation in mice infected with *Helicobacter pylori* through the downregulation of *IL*-8 and p38 mitogen-activated protein kinase (Zhang et al., 2017; Yeon et al., 2019). The general molecular structure of quercetin, gallic acid, and anthocyanin are shown in Fig. 1.

Although, these compounds could be found in many other plants including olive (Serreli and Deiana, 2018), in the most recent comparative study conducted by Isaak et al. (2013), methanol-extract of air-dried ROD sourced in Manitoba contains a very high amount of total phenolic content (TPC) with the peak value at 220 mg gallic acid equivalence (GAE)/g dry weight (DW), higher than the 40.27 mg GAE/g DW reported by Makris et al. (2007) for olive extract. Another medicinally important plant is garlic which has been consistently noted for its powerful antioxidant capacity due to its phenolic and organosulfur compounds. Some garlic cultivars and extracts have been evaluated to contain TPC ranging from 21.27 to 33.96 mg GAE/g fresh weight (Chen et al., 2013) and 6.95 to 19.69 mg GAE/g fresh weight (Lu et al., 2011), respectively. Wei et al. (2019) also reported that the TPC of ROD was higher when compared to lemongrass, lavender, rosemary, and calendula. The peak TPC value in ROD may range from 220 to 265 mg GAE/g (Isaak et al., 2013; Wei et al., 2019; Yang et al., 2019; Erinle et al., 2022a). The amount of phenolic content in a plant material has been considered an important determinant of their redox buffering capacity (Isaak et al., 2013). This suggests that ROD is a better plant material that is yet to receive the necessary attention it deserves. The polyphenol profile, TPC, and total anthocyanins content in ROD are presented in Table 1.

In-feed polyphenols have been extensively reported to interfere with nutrient digestion due to their enzyme-inhibition tendency. Interestingly, such interference could be associated with the concentrations of polyphenols, the plant type from which they are derived, and the constituent food matrix in which they are incorporated. The complete understanding of the pharmacokinetics and pharmacodynamics of plant bioactive substances starting from their digestion in the mouth to metabolism at organ-specific sites is essential in determining their beneficial health effect in animal production. Unfortunately, both concepts are yet to be comprehensively unraveled in research. However, many research hypotheses have speculated the metabolic pathways of polyphenols in humans and animals using *in vitro* simulation methods (Tarko et al., 2013; Smeriglio et al., 2016). Polyphenols, including anthocyanins, are rapidly absorbed during digestive processes in the stomach and small intestine of rats which is characterized by the intense red coloration of the stomach and intestine (Talavéra et al., 2003; He et al., 2009; Mullen et al., 2010). In a study mimicking the absorption of ROD polyphenols in humans using an *in vitro* coculture model, a rapid absorption and transportation of quercetin-3-glucoside, quercetin-glucuronide, rutin, quercetin-3-*O*-malonylglucoside, and kaempferol-glucoside without any hindrance (Jiang et al., 2019). Furthermore, anthocyanins, including cyanidin-3-*O*-galatoside, pelargonidin-3-*O*-glucoside, and pelargonidin-3-*O*-rutinoside, which are predominantly found in some *Cornus,* were reported to be high when exposed to an acidic condition of the stomach (David et al., 2019). This suggests a possible high bioavailability of ROD polyphenols particularly in the gastrointestinal tract (GIT) sections with highly or slightly acidic pH. Such bioavailability could translate to a high concentration of ROD bioactive substances in the blood and eventually at specific target organs given its rapid absorption and transportation.

In addition to the polyphenolic profile, ROD plant, usually the shoot, has been shown to contain a considerable amount of nutrients, as shown in Table 2. These include 6.7% crude protein, 4.2% ether extract, 29.2% crude fibre, 56.8% nitrogen-free extract, 1.13% calcium, 0.33% phosphorus, and 3.497 IU/g carotene (Fashingbauer and Moyle, 1963). Meanwhile, Lee et al. (2018) reported 88.6% dry

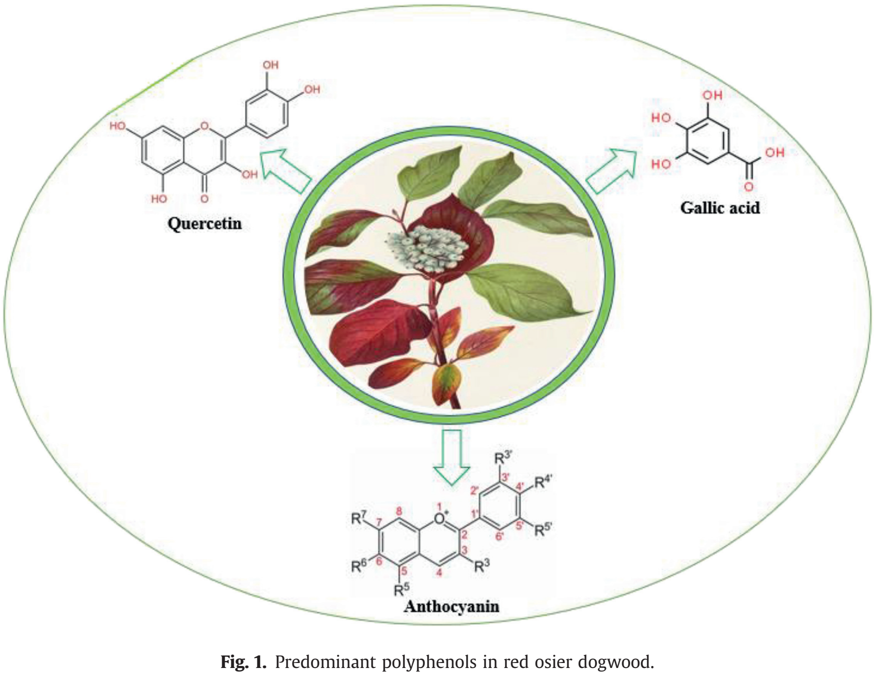

Fig. 1. Predominant polyphenols in red osier dogwood.

Table 1
Total phenolic content and polyphenol profile of some *Cornus* species extract.

Polyphenols	Polyphenol profile	*C. sericea*[1]	*C. stolonifera*[2]	*C. stolonifera*[3]	*C. stolonifera*[3]	*C. stolonifera*[4]	*C. stolonifera*[5]	*C. mas*[6]
1. Quercetin	Quercetin	0.47	8.06 − 12.58	–	826.0	0.72	–	–
	Quercetin-3-glucoside	1.72	–	–	–	–	–	5.10
	Quercetin-3-glucoronide	–	–	–	–	–	–	69.90
	Quercetin-3-galactoside	18.17	–	–	–	–	–	14.60
	Quercetin-3-rhamnoside (Quercitrin)	0.17	–	–	–	–	–	27.40
	Quercetin-3-rutinoside (Rutin)	0.70	7.46 − 18.77	2746	–	0.83	–	24.80
	Quercetin-3-xyloside	–	–	–	–	–	–	26.10
	Kaempferol-3-glucoside	0.09	–	–	–	–	–	–
	Kaempferol-3-galactoside	–	–	–	–	–	–	41.30
2. Gallic acid	Gallic acid	69.35	–	1670	64.00	0.54	5.96	–
	Ellagic acid	–	–	–	688.0	0.45	3.42	–
	4-Hydroxybenzoic acid	2.31	–	–	–	–	–	–
	Protocatechuic acid	3.71	–	–	–	–	–	–
	p-Coumaric acid	5.95	–	–	–	–	–	–
	Caffeic acid	8.40	–	–	–	–	–	–
	Ferulic acid	0.71	–	–	–	–	–	–
	Neochlorogenic acid	1.45	–	–	–	–	–	–
	Methyl gallate	–	–	–	557.0	0.92	–	–
	Ethyl gallate	–	–	–	–	–	36.54	–
	Chlorogenic acid	8.95	–	–	–	–	–	–
	Vanillic acid	0.30	–	–	–	–	–	–
3. Epicatechin	Catechin	–	–	–	–	0.15	–	–
	Epicatechin	–	–	–	–	0.80	–	–
4. Anthocyanins	Cyanidin 3-*O*-galactoside	–	–	–	–	–	–	2.80
	Pelargonidin 3-*O*-glucoside	–	–	–	–	–	–	8.70
	Pelargonidin 3-*O*-rutinoside	–	–	–	–	–	–	0.20
Total anthocyanin content		–	26 − 1,263[7]	–	–	–	–	–
Total phenolic content		238.81	43 − 220	26.51	–	12.3	–	–
References		Erinle et al. (2022a)	Isaak et al. (2013)	Yang et al. (2019)	Lee et al. (2018)	Wei et al. (2018); Gomaa et al. (2018)	Zheng et al. (2021)	Pawlowska et al. (2010)

[1] Milligrams standard equivalent per gram.
[2] Milligrams per gram air-dried sample.
[3] Milligrams per 100 g sample.
[4] Percentage (%).
[5] Milligrams per gram.
[6] Milligrams per 10 g.
[7] Cyanidin-3-glucoside equivalent (μg)/air-dried sample (g).

matter, 9.61% crude protein, 13.25% neutral detergent fibre (NDF), 10.10% acid detergent fibre (ADF), 4.40% ether extract, 4.93% total starch, and 3,881 kcal/kg gross energy. Fibre fractions of <40% and <50% NDF in legume and grass forages, respectively, and <35% ADF in all forage types have been considered of good quality (Van Saun, 2013). A lower NDF and ADF values suggest improved voluntary intake with better digestibility. Thus, ROD plant material could be considered a phytogenic/nutritional feed additive or feedstuff; however, its high phenolic concentration could deter its high inclusion level as a composite feed ingredient for poultry species.

Table 2
Nutrient profile of red osier dogwood.

Nutrient composition	Fashingbauer and Moyle (1963)	Lee et al. (2018)	Wei et al. (2018)	Gomaa et al. (2018)
Dry matter, %	–	88.6	93.3	–
Crude protein, %	6.70	9.61	10.8	8.8
Ether extract, %	4.20	4.40	–	–
Crude fibre, %	29.2	–	–	–
Nitrogen-free extract, %	56.8	–	–	–
Neutral detergent fibre, %	–	13.3	23.6	37.3
Acid detergent fibre, %	–	10.1	31.7	–
Total starch, %	–	4.93	–	–
Organic matter, %	–	–	92.1	92.1
Gross energy, kcal/kg	–	3881	–	–
Calcium, %	1.13	–	–	–
Phosphorus, %	0.33	–	–	–
Carotene, IU/g	3.50	–	–	–

Given the nature of the GIT of ruminants with high ruminal microbial populations that specialize in the fermentation of forages, high inclusion levels of ROD plant materials could be more tolerated. It has been estimated that approximately 90% of polyphenols are digested in the GIT sections with highly populated microbial communities (Tarko et al., 2013).

2.3. Seasonal variation of phenolic component of ROD

Red osier dogwood plant contains varying concentrations of total polyphenolic compounds depending on seasons (Isaak et al., 2013), as shown in Fig. 2. Seasonal variations have been reported to influence the phytochemical profile in medicinal plants due to varying duration of sunlight rather than temperature (Anesini et al., 2008; Isaak et al., 2013). According to Harbowy et al. (1997), sunlight plays a significant role in the biosynthesis of phenolic compounds in plants and usually, plants exposed to more sunlight contain more phenolics. For example, total polyphenol content amaranth cultivars exposed to more sunlight had higher TPC compared to shaded variety of the same plant (Khandaker et al., 2008). The concentration of total phenolics in ROD has been confirmed to be consistently highest during the summer (Isaak et al., 2013; Scales, 2015), while anthocyanin peaked at autumn and winter seasons (Isaak et al., 2013). The antioxidant bioactivity of ROD is not affected by the varying temperature. The plant protects itself from light-induced oxidative damage by increasing anthocyanin production in autumn (Feild et al., 2001). From the extrapolated and analyzed data from the Environment Canada's National Climate Data and Information Archive (2012), which showed normal ranged temperature during the summer and fall seasons, but low precipitation in summer of 2011, Isaak et al. (2013) concluded that precipitation could be one of the confounding factors contributing to the variation in phenolic compounds in *C. stolonifera*. In addition to this, Popović et al. (2018) advocated that geographical location may also be responsible for the variability in phenolic compounds in 2 species of Cornus, namely, *Cornus mas* and *Cornus sanguinea*. Besides possible interaction between phenolics and food matrix, integration of the aforementioned factors may be responsible for the inconsistent results obtained in many *in vivo* phytoadditive studies. While it cannot yet be affirmatively concluded that one factor is primely responsible for the variation, there could be a need for more environmental studies to validate these speculations.

2.4. Antioxidant capacity of ROD

Oxygen radical absorbance capacity assay is one of the standard methods of evaluating total antioxidant activity of polyphenols. Given that plants, including ROD, contain varying phenolic concentrations, oxygen radical absorbance capacity (ORAC) would therefore be sufficient to compare the efficacy of ROD with some selected medicinal plants used in animal nutritional studies. Red osier dogwood was reported to have a peak ORAC value of 1,632 μmol trolox equivalents (TE)/g DW in the summer (Isaak et al., 2013) compared to the ORAC values of 627.14, 744.95, 524.76, and 1,280 μmol TE/g DW in methanol-extract of leaves of tea, parsley, basil, and olive plants, respectively as reported by Wojcikowski et al. (2007). The ORAC of these plants is graphically presented in Fig. 3. Comparing the red and green leaves of ROD, Scale (2015) reported that the ORAC was higher in dark green ROD leaves, which could be obtained during the summer. This is not surprising as a higher concentration of ellagic and gallic acids was recorded in the dark green leaves. Generally, red-colored leaves are rich in anthocyanins. Anthocyanins, including cyanidin 3-*O*-galactoside, pelargonidin 3-*O*-glucoside, and pelargonidin 3-*O*-rutinoside, are effective antioxidants, inhibitors of Gram-negative bacteria, anticancer, and anti-inflammatory agents (Bruce et al., 2000; Kang et al., 2003; Cooke et al., 2005; Smeriglio et al., 2016). The higher ORAC values reported in ROD suggested it could be more effective and efficient at abating oxidative stress caused by microbial

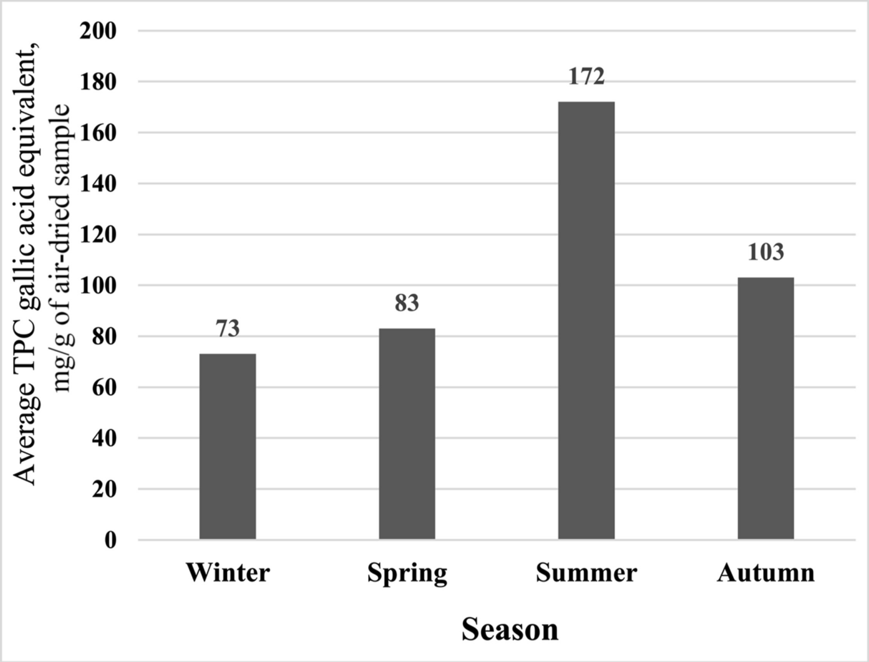

Fig. 2. A bar chart showing an approximate total phenolic concentration (TPC) gallic acid equivalent milligram dry weight per season. Adapted from Isaak et al. (2013) and was estimated by finding average of TPC per season in span of 3 years: 2010, 2011, and 2012.

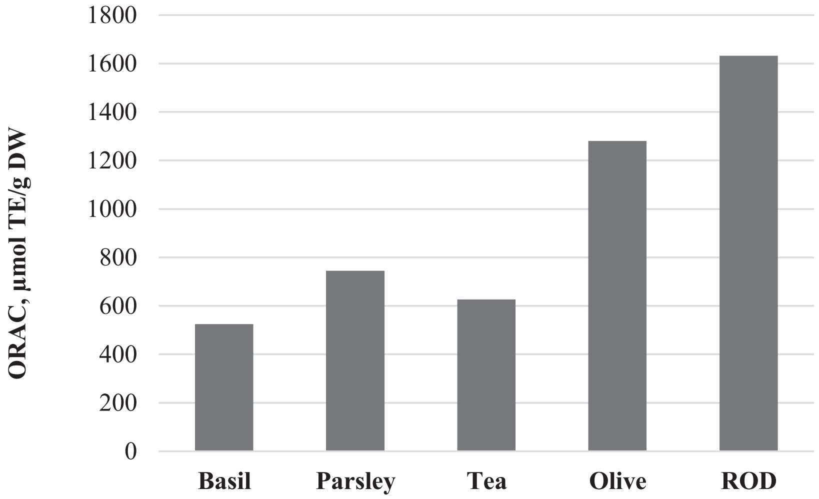

Fig. 3. Oxygen reactive absorbance capacity (ORAC) of red osier dogwood (ROD) and some plants. Adapted from Isaak et al. (2013). TE = trolox equivalents; DW = dry weight.

contamination and free radicals in the gut. Scales (2015) found that ellagic acid and gallic acid concentration levels in green leaves of ROD were higher during the summer months.

A strong antioxidative prowess of gallic acid has been demonstrated in mice (Palafox-Carlos et al., 2012; Nair and Nair, 2013). In the reports of Hagiwara et al. (2010) and BenSaad et al. (2017), ellagic acid has shown the capacity to prompt the occurrence of death of cancer cells and exert their antimicrobial and immunomodulatory activity. Both ellagic and gallic acids are predominantly present in ROD as shown in Fig. 4. The rutin present in ROD could be easily hydrolyzed to quercetin and rutinose in the presence of HCl at 100 °C. The antioxidant capacity of individual phenolic using ABTS$^{\cdot}$+ revealed that gallic acid and quercetin have higher antioxidative activity compared to catechin (Kopjar et al., 2016).

Anthocyanin is an important group of flavonoids, a sub-class of phenolic compounds characterizing the bright coloration (other than green) in response to stress conditions in plants (Steyn et al., 2002; Hatier and Gould, 2008). The concentration of anthocyanins in the ROD plant was highest during winter but had a correspondingly lower ORAC (Isaak et al., 2013). The complementary findings reported by Scales (2015) and Isaak et al. (2013) showed that ORAC value of ROD was higher when the leaves were dark green, which is obtainable in the summer compared to the red ROD leaves during the autumn and winter. During summer periods, there is high irradiance from the sun, which excites chlorophyll in plants, thus increasing the rate of biosynthesis of metabolites (Buttery and Buzzell, 1977). The increased rate of photosynthesis of primary metabolites could facilitate an increased synthesis of

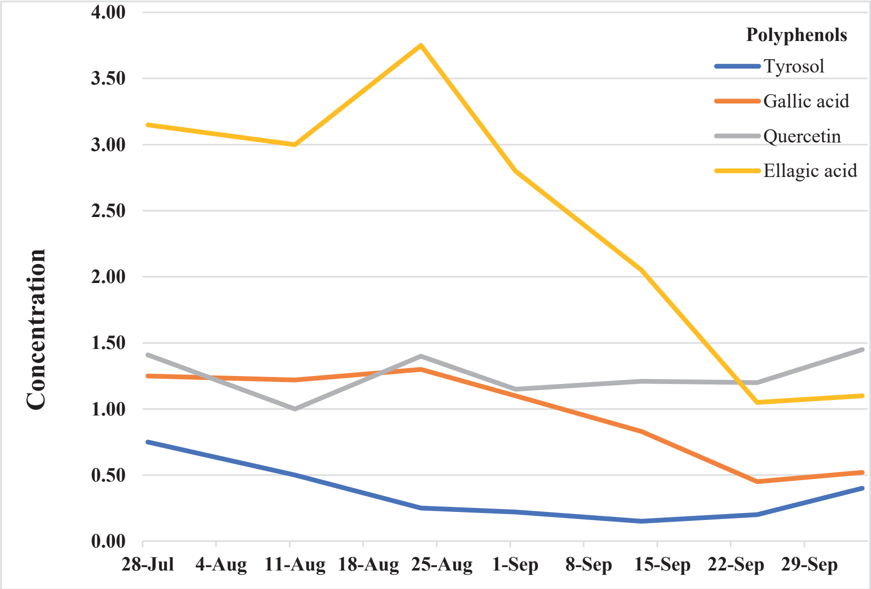

Fig. 4. A line chart showing varying composition of polyphenols (×10^6 trolox equivalents/100 g samples) in red osier dogwood at different months of summer and autumn seasons. Adapted from Scales (2015).

secondary metabolites; this might be explained by the higher antioxidative capacity in green ROD leaves obtainable during summer compared to during winter and autumn. We speculate that a blend of ROD's specific plant parts harvested in the summer (higher in ellagic acid, gallic acid, quercetin, etc.) and winter (higher in anthocyanins) could potentiate the antioxidative properties of ROD than when singly used. Possible synergistic effects from a combination of polyphenols have been reported (Palafox-Carlos et al., 2012; Kopjar et al., 2016). The beneficial health effects of *Cornus* polyphenols have been extensively reported by Vareed (2005).

In vitro studies have demonstrated ROD's antioxidant capacity in the upregulation of hemeoxygenase-1, superoxide dismutase (SOD) and glutathione peroxidase (GPx) (Yang et al., 2019). In addition, both Jiang et al. (2019) and Yang et al. (2019) reported that polyphenols in ROD extracts also prevented pro-inflammatory responses in Caco-2 cells by repressing gene expression of inflammatory cytokines. This was obviously not surprising as ROD has shown to be a potent redox buffer due to its high ORAC values.

3. Potentials of ROD in animal production

3.1. Effects of ROD on the growth performance and gut morphology of animal

Determination of growth performance is one of the important parameters considered in assessing the efficacy of feed or feed additives in animal production. In recent times, the use of bioactive substances from plants has shown the potential to influence the growth and health of animals (Salobir et al., 2012). The effects of air-dried raw or extract of ROD reported in the literature is presented in Table 3. In studies using air-dried raw ROD, the ROD is usually a mixture of the plant parts, including 75% leaves and 25% bark (Koo et al., 2021), 75% leaves, 10% bark, and 15% stem (Gomaa et al., 2018; Wei et al., 2018, 2019) or 60% leaves and 40% bark (Amarakoon, 2017). It is not unexpected that animals would respond differently to the varying dietary supplements. This raises some knowledge-based questions about the growth response of animals fed different combinations of ROD plant parts.

3.1.1. Swine and poultry

The application of ROD in swine and poultry research is gaining momentum as their antibiotic-replacement potential is been currently investigated. Koo et al. (2018, 2021) and Jayaraman et al. (2018) reported that dietary supplementation of 4% air-dried raw ROD (containing 75% leaves and 25% bark) helped to maintain the growth performance of weaned piglets challenged with *Escherichia coli* in the same capacity as those receiving 0.025% in-feed bacitracin methylated disalicylate (BMD). In a study demonstrated by Lee et al. (2018), dietary inclusion of 0.2% and 0.4% ROD extract were reported to reduce average daily gain in weaned piglets; however, specifically at the 0.4% ROD extract inclusion level, the body weight of the piglets was observed to marginally improve body weight compared to antibiotic and control fed piglets. In another study where 0.5% ROD extract was applied in matured pigs, growth performance and volatile fatty acids (VFA) were not affected; however, the average daily gain was numerically higher among pigs fed dietary 0.5% ROD extract compared to control (Zheng et al., 2021). Given the above, it could be assumed that the best inclusion levels of either air-dried raw ROD or ROD extract are yet to be attained. Similarly, in broiler chickens, Mogire et al. (2021) established that incorporation of ROD extract did not influence growth performance, feed conversion ratio, and relative organ weight in broiler chickens; however, it favourably matched up the expectations when compared with broiler chickens fed avilamycin antibiotic. Regarding ROD-antibiotic comparison, Mogire et al. (2021) reported that ROD improved birds' livability by their mortality-reductive capacity. Furthermore, Erinle et al. (2022a) demonstrated that in broiler chickens challenged with *Salmonella Enteritidis* lipopolysaccharides (*SE*-LPS), feeding ROD extract at 0.3% and 0.5% was reported to maintain average feed intake, feed efficiency, and mortality compared to birds fed bacitracin diet. Interestingly, suitable antibiotic alternatives have been defined to include phytogenic extracts, beneficial microbial culture, special plant fibre, antimicrobials, or other metabolites which are usually naturally derived and could particularly improve growth and gut health either in a marginal, equivalent and/or better capacity compared to antibiotic effect when delivered under the same condition (Erinle et al., 2022a). This suggests the prospect that comes with the use of ROD, particularly in the pursuit of reducing antibiotic use in animal production. The inclusion of ROD into the diets of broiler chickens and rabbits have proven to reduce mortality (Scales, 2015; Mogire et al., 2021). The stepwise biochemical mechanism with which phytogenic compounds in ROD influences growth performance has not been fully unravelled; however, the selective antimicrobial action of ROD polyphenols could be related to the reduced mortality.

On gut morphology, there are significant impacts of ROD extract on the architecture of the small intestinal section. In studies comparing the efficacy of ROD with antibiotics, Mogire et al. (2021) and Erinle et al. (2022a) reported that ROD improved villus height to crypt depth ratio (VH:CD) in the jejunal and ileal section of the GIT of broiler chickens fed diets supplemented with ROD extract from 0.1% to 0.3%. Meanwhile, in chickens challenged with *SE*-LPS, a deeper crypt depth was reported in chickens fed ROD extract from 0.3% to 0.5%, which was perceived to be ROD's ameliorative mechanism in improving the gut (Erinle et al., 2022a). In weaned piglets, higher inclusion levels of air-dried raw ROD from 2% to 4% were demonstrated to enhance VH:CD in the jejunal and ileal section of the GIT (Jayaraman et al., 2018; Koo et al., 2021). In the small intestine, high VH:CD indicates more surface area for nutrient digestibility and absorption (da Silva et al., 2009). It could be perceived that ROD polyphenols do not in any way impede nutrient digestion and absorption in monogastric animals. According to Mogire et al. (2021), supplementation of ROD extract was observed to increase ileal digestibility of amino acids and crude fat in broiler chickens, while crude fat, protein, and dry matter digestibilities were not affected. Contrary to the existing belief that polyphenols may negatively impact nutrients, the polyphenol profiles of ROD extract were shown to upregulate amino acid transporter genes, including *B^0AT1* and *CAT1* (Mogire et al., 2021). Although, there are only a few existing studies that have applied ROD extract in broiler chickens and swine, however, the promising research outcome with ROD begs for more studies to reinforce the existing beneficial effects of ROD and determine the optimum inclusion levels which is yet to be reported in swine and poultry research.

3.1.2. Ruminants

The application rates of ROD into animal nutrition would be critical for the maximization of its potential. While the tolerable limit of ROD is dependent on the type of animal species, ruminants can utilize ROD at higher inclusion levels. Although ruminants, including cattle, sheep, and goats, possess complex stomach structures, there are specific variations in their digestive capabilities. The effects of dietary ROD on the growth performance of goats and sheep and pseudo-ruminant like rabbits are yet to be demonstrated in research. In cattle, application of ROD up to 10% − 12% to substitute barley silage and barley concentrate has been shown by Gomaa et al. (2018) and Wei et al. (2019). In farms where more grains or grain-forage combinations are being fed to cattle, there is a higher incidence of

Table 3
Summary on the potential application of red osier dogwood (ROD) both in *in vitro* and *in vivo*.

Research demonstrations	Application rates	Findings	References
In vitro			
Red dogwood extract (RDE) prevents inflammatory responses in Caco-2 Cells and Caco-2 BBe1/EA.hy926 Cell co-culture	100 μg/mL	i. ↑Rate of polyphenols absorption. ii. Prevention of IL-8 production. iii. ↓Gene expression of *IL-8*, *TNF-α*, *IL-6, ICAM-1*, *VCAM*-1, and *COX-2* in *TNF-α* inflamed *Caco-2* cell.	Jiang et al. (2019)
Effect of Manitoba-grown RDE on recovering Caco-2 cells from H_2O_2-induced oxidative damage.	100 μg/mL	i. ↑Cell viability. ii. Prevention of IL-8 and ROS production. iii. ↑Gene expression of *HO-1*, *SOD*, *GSH-Px*, and *Nrf-2*. iv. ↓Diffusion of fluorescein. v. ↑Transepithelial resistance. vi. ↑Relative mRNA concentration of tight junction claudin-1, claudin-3, and occludin. vii. Repaired structural integrity of ZO-1. viii. ↑ Protein expression of ZO-1 and claudin-3.	Yang et al. (2019)
Inclusion of red osier dogwood (ROD) in high-forage and high-grain diets affected *in vitro* fermentation.	0, 3%, 6%, or 12%	i. ↑ ROD levels ↓ total VFA concentration. ii. ↑ Acetate to propionate ratio. iii. ↓ DMD and fermentation pattern at lower pH. iv. ↓ Rumen acidosis caused by high-grain diets.	Wei et al. (2018)
Effect of dried distillers grains with solubles and RDE on fermentation pattern and microbial profiles of a high-grain diet in an artificial rumen system.	0 and 1%	i. ↑ Acetate to propionate ratio. ii. ↓Starch disappearance and possible reduce rumen acidosis. iii. Little variation in Shannon diversity index. iv. ↑ Rumen *Treponema*.	Gomaa et al. (2021)
***In vivo* (Ruminants)**			
In situ ruminal digestibility of ROD in finishing beef heifers.	0, 3%, 7%, and 10%	i. ↓ Effective degradability of protein similar to monensin. ii. ↑ROD levels ↓ soluble fraction and gradually ↑degradable fraction of barley grain diet. iii. ↓ Rumen acidosis caused by high-grain diets.	Gomaa et al. (2018)
Feeding ROD to beef heifers fed a high-drain diets affected feed intake and total tract digestibility.	0, 3%, 7%, and 10%	i. No effect on rumen pH and total VFA concentrations. ii. ↑ ROD levels ↓ ruminal NH_3—N concentration. iii. ↑ ROD levels ↑ DMD. iv. ↑ ROD increase feed intake better than antibiotics v. ↑ ROD levels ↑ plasma concentration of haptoglobin and serum amyloid. vi. ↑ Immune status and antioxidant activity in cattle.	Wei et al. (2019)
***In vivo* (Swine)**			
Dietary supplementation of ROD polyphenol extract changes the ileal microbiota structure and increases *Lactobacillus* in a pig model.	0 and 0.5%	i. ↑*Lactobacillus delbrueckii* and *Lactobacillus mucus* suggesting a prebiotic-effect of ROD polyphenol extract.	Zheng et al. (2021)
Effects of dietary ROD on growth performance, blood profile, ileal morphology, and oxidative status in weaned pigs challenged with *E. coli* K88$^+$.	2% and 4%	i. No effect on growth performance. ii. ↑ SOD and ↓ MDA concentrations in the serum in equal capacity of an antibiotics. iii. ↓ Ileal crypt depth and ↑ ileal VH:CD.	Koo et al. (2021)
Effects of dietary supplementation with ground ROD on oxidative status in weaned pigs challenged with *E. coli* K88$^+$.	2% and 4%	i. ↓ Serum and ileal MDA with 4% ROD supplementation which is comparable to antibiotics. ii. Both 4% ROD and antibiotics ↓ serum and ileal SOD. iii. Serum and ileal MDA and SOD were not affected by 2% ROD.	Koo et al. (2018)
Effects of dietary supplementation with ground ROD on growth performance, blood profile, and ileal histomorphology in weaned pigs challenged with *E. coli* K88$^+$.	2% and 4%	i. No effect on growth performance. ii. No effect on PUN and plasma glucose. iii. ↓ Ileal crypt depth and marginally ↑ ileal VH:CD.	Jayaraman et al. (2018)
Effects of ROD extract on nutrient digestibility and growth performance of weaned piglets.	0.2% and 0.4%	i. ↓ BW in 0.2% fed weaned piglets compared to those fed antibiotics diet. ii. ↓ADG in ROD treatments; however, the ADG was similar to weaned piglets fed basal diet. iii. No effect on fecal score, apparent total tract digestibility of dry matter and energy.	Lee et al. (2018)
Regulation of oxidative stress in weaned piglets challenged with *E. coli*.	2% and 4%	i. No effect on BW. ii. ↓TBARS among weaned pigs fed 4% ROD and antibiotics similar to the unchallenged pigs. iii. ↑ SOD activity in the serum and ileum.	Amarakoon (2017)
***In vivo* (Poultry)**			
	0.1% and 0.3%	i. No effect on growth performance. ii. ↑ Birds livability.	Mogire et al. (2021)

(*continued on next page*)

Table 3 (*continued*)

Research demonstrations	Application rates	Findings	References
Effects of ROD extracts on growth performance, intestinal digestive and absorptive functions, and meat quality of broiler chickens		iii. ↓ Jejunal crypt depth among chickens fed 0.1% and ↑ VH:CD in both 0.1% and 0.3% ROD treatments. iv. ↓ mRNA abundance for cationic amino acid transporter in ROD and antibiotic treatments. v. ↑ mRNA abundance for neutral amino acid transporter. vi. 4% ROD ↑ apparent ileal digestibility of crude fat. vii. All the ROD and PC treatments ↑ amino acid digestibility.	
Effect of ROD extract on growth performance, blood biochemical parameters, and gut functionality of broiler chickens challenged or unchallenged with *Salmonella* Enteritidis lipopolysaccharides.	0.3% and 0.5%	i. Both levels of ROD extract marginally improved average weight gain of broiler chickens compared to antibiotic-treated birds. ii. No effect on caecal SCFA, relative immune organs, and serum antioxidants. iii. ↑Relative abundance of caecal *Lactobacillus* and *Streptococcus* genera. iv. ↑Crypt depth and VH:CD in both unchallenged and challenged group of birds. v. ↑Plasma GLB and ↓A:GLB among birds receiving 0.3% ROD extract.	Erinle et al. (2022a)
***In vivo* (Rabbit, Cattle, and Horse)**			
Rabbit trial	–	↓ Incidence of mortality in rabbits diagnosed with a severe case of diarrhea.	Scales (2015)
Cattle trial	–	↑ Weight gain/animal per day in cattle.	
Horse trial	0.68 kg daily	Enhanced healing process of horses suffering from a severe leg infection.	

↑ = Increase; ↓ = Decrease; *IL-8* = interleukin-8; *TNF-α* = tumor necrosis factor-alpha; *IL-6* = interleukin-6; *ICAM-1* = intercellular adhesion molecule-1; *VCAM-1* = vascular cell adhesion molecule-1; *COX-2* = cyclooxygenase 2; ROS = reactive oxygen species; *HO-1* = hemeoxygenase-1, *Nrf-2* = nuclear factor (erythroid-derived 2); *ZO-1* = zonula occludens-1; SOD = superoxide dismutase; GSH-Px = glutathione peroxidase; MDA = malondialdehyde; VFA = volatile fatty acid; DMD = dry matter digestibility; VH:CD = villus height to crypt depth ratio; BW = body weight; ADG = average daily gain; SCFA = short chain fatty acid; GLB = globulin; A:GLB = albumin to globulin ratio.

rumen acidosis due to the high soluble fraction in grain-based diets. Interestingly, increasing levels of supplemental ROD from 3% to 10% in both barley grain diets was demonstrated to decrease effective degradability of protein, the disappearance of NDF, and soluble fraction in the rumen of beef heifers (Gomaa et al., 2018). A similar result, including a reduced dry matter digestibility and VFA was reported by Wei et al. (2018) in an *in vitro* rumen fermentation system. A decreased effective degradability of crude protein would imply an increase in the amount of ruminal by-pass protein, thus, increasing the availability of protein to the animal and reducing starch digestion and rumen acidosis. In a high-forage diet, Wei et al. (2018) reported that ROD decreases the nitrogen content of ammonia in the rumen model, which could be attributed to the protein-binding propensity of the polyphenol-rich plant. The effect of dietary ROD could be compared to monensin as the latter have also been reported to inhibit ruminal degradation of protein. Monensin—an ionophoric antibiotic, is reported to selectively alter ruminal bacteria population, which resultantly decreased and increased the concentration of acetate and propionate, respectively, in the rumen (Russell and Strobel, 1989; Wei et al., 2018), suggesting a lower acetate to propionate ratio (A:P). In contrast to monensin, increasing inclusion levels of ROD from 3% to 12% in high-grain diet was speculated to improve fibre digestion in the rumen by changing the fermentation pattern that would favour a higher A:P at low pH (Wei et al., 2018). In the same study, at a higher pH of 6.5, increasing ROD inclusion levels were reportedly shown to increase the concentrations of ruminal VFA, mainly acetate and butyrate. Propionate produced in the rumen is an important starting material for glucose synthesis in the liver; thus, catering for approximately 73% of glucose requirement in the body (Aiello et al., 1989; Seal and Reynolds, 1993). However, Allen (2000) reported that VFA produced in the rumen influences dry matter intake, with propionate conferring a substantial reduction in the amount of feed intake compared to acetate and butyrate. The effect of ROD on the dynamics of rumen VFA suggests their tendency to stimulate appetite in cattle. Wei et al. (2019) revealed that incremental substitution of ROD for silage affected neither total nor individual VFA; however, the total VFA was greater with ROD compared to antibiotic-treated heifers. Similarly, in an artificial rumen system, supplementation of 1% of ROD extract into wheat DDGS and basal diets resulted in no effect on VFA, nutrient disappearance and gas production, and total microbial nitrogen (Gomaa et al., 2021). In addition, Gomaa et al. (2021) reported that ROD extract was shown to reduce starch fermentability and increase NDF; thus, it could mitigate the occurrence of rumen acidosis.

This could imply that regardless of the type of diet fed, the supplementation of either air-dried raw ROD or ROD extract would consistently increase NDF disappearance and efficient fibre utilization and reduce the incidence of rumen acidosis in cattle. Optimum maximization of ROD in ruminants is largely dependent on the ruminal pH. If pH is kept at not less than 6.5, ROD has beneficial rumen modulatory effects.

3.2. *Effects of ROD on oxidative and immune-related stress in animal*

Oxidation is a common metabolic chemical process involved in the release of energy in living systems; however, it may also produce free radicals which are unstable, capable of independent existence and highly reactive due to the presence of their unpaired electrons. Drawing on the pool of bodily-produced antioxidants, free radicals cause their downregulation, thus, distorting the oxidative and immune status of animals.

3.2.1. *Swine and poultry*

In swine farming, piglets are reported to be highly susceptible to oxidative stress at weaning age, especially when infected with *E. coli* (Amarakoon, 2017). This is ascribable to the piglets' immature immune system during their early life. The newly developing immune system in newborns and infants has been related to their increased susceptibility to virulent pathogens (Russell et al., 2012). In most monogastric animals, particularly pigs, the weaning phase has been dubbed critical and stress-inciting phase due to the increased susceptibility to pathogenic microbes and endotoxins, and gastrointestinal disorders (Pié et al., 2007) in the young ones. In *E. coli*-challenged weaned piglets, Koo et al. (2021) and Amarakoon (2017) demonstrated that 4% inclusion level of ROD in weaners' diet did not only depress levels of thiobarbituric acid reactive substances (TBARS) and malondialdehyde but also caused upregulation of SOD when compared to both unchallenged and antibiotic-treated pigs thereby neutralizing the oxidative stress induced by endotoxigenic bacteria. The antioxidant potential of polyphenol-rich plant materials cannot be overemphasized. Polyphenols of grape pomace, apple, leaves of green teas and olive were reported to increase the levels of plasma GPx and total antioxidant capacity in weaned piglets (Jiang et al., 2014). In broiler chickens, body antioxidant enzyme-system and immune organs do not seem to have benefited from the antioxidant capacity of ROD extract. Erinle et al. (2022a) reported that supplementation of 0.3% and 0.5% ROD extract did not improve serum SOD and total antioxidant power in broiler chickens challenged or unchallenged with *SE*-LPS. Both Mogire et al. (2021) and Erinle et al. (2022a) reported that the incorporation of dietary ROD extract from 0.1% to 0.5% did not have an effect on the weights of immune-related organs, particularly the liver and spleen.

3.2.2. Ruminants

There are not many studies that have investigated the impact of ROD on oxidative and immune-related stress in ruminants. Overpopulation of GIT with pathogenic microbes contributes to a high production of oxidants and prooxidants, which would in turn increase the susceptibility of animals to pathogenic infection. In a study conducted by Wei et al. (2019), ROD was confirmed *in vivo* to increase the blood concentrations of SOD, antioxidant, haptoglobin, serum amyloid; a trend that increases with increasing supplementation levels of ROD from 3% to 10% as a replacement for barley silage. Haptoglobin, SOD, and blood antioxidant are components of the body antioxidant system. In reality, ROD should not only be considered as an “antioxidant” but also a “pro-antioxidant” due to their stimulatory effect on the body antioxidant enzyme system. It is incredible that ROD polyphenols do not only improve body antioxidant enzymes but also increase blood parameters, including white blood cells, lymphocytes, monocytes, and granulocytes which is an indication of improved lymphocyte function and cell-mediated immunity following the attainment of active immunization in beef heifers (Wei et al., 2019). Like in ruminants, our previous study on Salmonella-infected broiler chickens demonstrated that 0.3% ROD extract improved leukocytes, monocytes, and immunoglobulin M (Erinle et al., 2022b). In addition to the above, a decrease in faecal immunoglobulin A (IgA) concentration was reported when beef heifers were fed increasing levels of ROD up to 10% (Wei et al., 2019). Although IgA plays a significant immune-protective role by bathing mucosal surfaces, thereby preventing pathogen adherence and immune-related stress in the animal, its production is energy-consuming (Woof and Ken, 2006).

3.3. Effect of ROD on gut and rumen microbiota

Microbial community in the gut of animals, including bacteria, fungi, archaea, protozoans and viruses, impact nutrient utilization (Stanley et al., 2012; Park et al., 2017), immune system (Schokker et al., 2017; Lazar et al., 2018; Akinyemi et al., 2020), hormonal action (Zhenping et al., 2013), maturation of the gastrointestinal tract (Kelly and Conway, 2005) and general well-being of the animal. Bacteria species are the most reckoned microbe in the GIT, with approximately 10^{11} to 10^{12}/g organism of bacteria species colonizing the caecum compared to the 10^8 to 10^9/g organisms in the ileum of chickens (Witzig et al., 2015; Thomas et al., 2019). The 5 most abundant bacteria phyla reported in the literature are the Bacteroidetes, Firmicutes, Proteobacteria, Actinobacteria, and Spirochaetes (Thomas et al., 2019; Akinyemi et al., 2020; Mogire et al., 2021).

3.3.1. Swine and poultry

In broiler chickens, dietary supplementation of 0.1% and 0.3% ROD extract were reported to have no influence on the community diversity of both ileal and caecal microbiota; however, an increase in the population of Firmicutes and a decrease in Bacteroidetes phyla were observed (Mogire, 2020). This suggests an increased Firmicutes to Bacteroidetes ratio (FBR). Increased FBR has been positively correlated with increased body weight and energy utilization efficiency in broiler chickens (Singh et al., 2008). On the contrary, Erinle et al. (2022a;c) reported that Firmicutes, Actinobacteria, and Proteobacteria were the only phyla found in the caecal microbiota of broiler chickens fed dietary 0.3% and 0.5% ROD extract; however, the relative abundance of genera *Lactobacillus* and *Streptococcus* were greater than what was obtained among the antibiotic-fed birds. In matured pigs, dietary supplementation of 0.5% ROD polyphenol extract was reported to increase alpha diversity of the ileal microbiota and commensal bacteria counts, which are mostly Firmicutes and Proteobacteria phyla (Zheng et al., 2021). Remarkably, ROD polyphenol exhibited prebiotic effects on the gut microbiota by tremendously increasing the microbial population of *Lactobacilli*, particularly *Lactobacillus delbrueckii* and *Lactobacillus mucosae*, *Sharpea* and *Dialister*, and *Lachnospiraceae _bacterium_DJF_LS97k1* (Zheng et al., 2021). Many strains of *Lactobacillus species* are gut-friendly and have been shown to be capable of maintaining intestinal barrier function, especially in a diseased-condition, by modulating the expression of heat shock protein or tight junction proteins or by restricting adhesion of pathogens (Yu et al., 2012; Liu et al., 2015a; Sun et al., 2015; Zheng et al., 2021). Although there is no sufficient research evidence on the selective antimicrobial action of air-dried raw or extract of ROD on the dynamics of gut microbiota, their capacity to consistently improve the population of gut-friendly *Lactobacillus* is noteworthy.

3.3.2. Ruminants

The rumen is a typical anaerobic fermentation compartment harbouring diverse microbes, including bacteria, ciliate protozoa, anaerobic fungi, bacteriophages and methanogens (Zeineldin et al., 2018). Ruminal microbiota plays a significant role in the digestion and metabolism of plant fibres. As a result, modulation of ruminal microbiota would be a clear approach to maximizing the performance of ruminant species. Unfortunately, the impact of either raw air-dried ROD or its extract in *in vivo* rumen microbiota is still scant in literature and the mechanism through which it influences rumen microbial community is not clear. In a study involving the use of ROD in an artificial rumen system, Gomaa et al. (2021) reported that Firmicute and Bacteroidetes were the most abundant phyla in the ruminal microbiota; however, their relative abundance was not affected by the ROD supplementation. In the same study by Gomaa et al. (2021), supplementation of 1% ROD extract was seen to switch the relative abundance of *Prevotella* and *Fibrobacter* in high-grain treatment to *Treponema* in the ROD high-grain treatment combination while switching the dominance of *Acidaminococcus, Megashaera, Shuttleworthia*, and *Lactobacillus* in the dried distillers' grains solubles (DDGS) treatment to *Selenomonas* and *Schwartzia* in the ROD-DDGS treatment combination. The introduction of 1% ROD extract increases the acid detergent fibre fraction in a high-grain diet, and as a result, promotes the population of *Treponema.* The pectinolytic ability of *Treponema* and *Selenomonas* to efficiently degrade and utilize some partially indigestible fibre feedstuff has been reported by Sawanon et al. (2011) and Liu et al. (2015b). A decrease in *Treponema* abundance was associated with the occurrence of sub-ruminal acidosis (Zeineldin et al., 2018). Wei et al. (2019) revealed that incremental substitution of ROD for silage linearly crescendoed ruminal protozoa counts. While complete inhibition of ruminal protozoan is assumed to be desirable cattle as protozoan have been implicated in the incidence of methanogenesis, higher protozoan population have been correlated with increased total tract fibre digestion (Dai and Faciola, 2019). Incorporation of ROD into hay may be beneficial for the enhancement of fibre digestion in ruminants, particularly during forage-dearth seasons.

3.4. Potential of ROD on chicken meat quality

Genetic improvement of broiler strains for increased growth rate and big breast meat has contributed to the incidence of myopathy in their *Pectoralis major* (Maharjan et al., 2019). The incidence of white striping and woody breast is one of the most recent trends in accessing meat quality. Broiler chickens contribute immensely to the total amount of meat consumed among the human population; however, the incidence of myopathies can negatively affect consumer preferences. Although, the potential of ROD in reducing such incidence has not been adequately investigated, the study conducted by Mogire et al. (2021) is the first and only study that demonstrated the effect of ROD extract on the breast meat quality of broiler chicken. The author reported that 0.1% and 0.3% of ROD extract had no influence on white striping and wooden breast scores; however, it reduced red coloration of the breast muscle of broiler chickens. Red meat contains a high concentration of biogenic amines which are used for assessing health hazards, and its detection in meat has been associated with incipient spoilage (Vinci and Antonelli, 2002).

4. Improving the efficiency of ROD for animal

Some plant extracts have been reported to have no effect on the growth performance and health of animal, particularly poultry species (Hernández et al., 2004; Aydin et al., 2008; Al-Kassie et al., 2011) with an implication on their polyphenol content. The impact of polyphenols on digestive enzymes is controversial in literature, with many studies suggesting polyphenols reduce enzymatic activities. Considerable research shreds of evidence have also been presented that polyphenol derived from some plants, including green tea and chameleon plants, increased pepsin activity (Tagliazucchi et al., 2005; Garg et al., 2019). Ironically, the enzyme-inhibition tendency of ROD polyphenols could be of interest in ruminant production, given its capacity to improve protein efficiency and reduce rumen acidosis. In fact, ROD extract polyphenols were shown to improve digestibility and absorption of amino acids and crude fat, while other nutrient digestibilities remain unaffected in chickens (Mogire et al., 2021). Therefore, enhancing ROD for animal use should be targeted toward further enrichment of their polyphenol profile rather than the polyphenol-enzyme inhibition concerns.

Based on the available reports, ROD used in most current studies is made up of a varying proportion of plant parts, including 75% leaves, 10% bark, and 15% stem (Gomaa et al., 2018; Wei et al., 2018, 2019), 60% leaves and 40% bark (Amarakoon, 2017) or 75% leaves and 25% bark (Koo et al., 2021) obtained from immature ROD plant. Improving the use of ROD for animal use could be through the inclusion of their flowers/fruits/seeds in the preparation protocol prior to its incorporation in the animal feed. Biosynthesis of plant polyphenols is a systematic and dynamic process that is dependent on the plant, plant parts, and seasonal variation. According to Feduraev et al. (2019), there is a significant spike in the phenolic compounds and antioxidant activity in flowers/seeds compared to the roots, stems, and leaves. In fact, the authors reported a decreasing antioxidant activity in the following order: flowers/seed > leaves > root > stem. Although, this ordering pattern is not static and would greatly depend on the specific storage organ of the resident plant. In little bur-clover, leaf and seed extracts were reported to accumulate more phenolic and flavonoid compounds; thus, the 2 structures contain the highest TPC compared to the root and stem (Kabtni et al., 2020). Vareed (2005) highlighted that the flower/fruit of most *Cornus* species harbours arrays of phytochemicals compared to their leaf, stem, and root. Given the above information, we suspect that TPC could be higher in ROD flowers/fruits/seeds compared to other plant parts. Thus, the inclusion of ROD flowers/fruits/seeds in either raw or extract of ROD would afford a broader spectrum of polyphenol profiles and possibly a more comprehensive range of beneficial bioactivities. However, future *in vitro* and *in vivo* studies would be needed to confirm this speculation.

5. Conclusions

Air-dried raw ROD or its extract has shown to have an excellent polyphenolic profile and has shown the potential to improve growth performance, gut morphology, and intestinal microbiota of poultry and swine without negatively impacting nutrient digestibility. In ruminants, ROD consistently showed the capacity to influence rumen microbiota and nutrient metabolism that would afford the reduction of rumen acidosis. This review demonstrates the potential of ROD as a phytogenic feed additive in the animal industry for a safe and organic agriculture.

Author contributions

Taiwo Erinle: Writing - Original draft preparation, Writing - Reviewing and Editing. **Martine Boulianne:** Supervision, Writing - Reviewing and Editing. **Younes Miar:** Supervision, Writing - Reviewing and Editing. **Robert Scales:** Supervision, Writing - Reviewing and Editing. **Deborah Adewole:** Conceptualization, Writing - Reviewing and Editing, Funding acquisition, Supervision.

Declaration of competing interest

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, and there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the content of this paper.

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