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Review

Incorporation of functional feed ingredients to substitute antimicrobials in animal nutrition: Opportunities for livestock production in developing countries

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Livestock including cattle, goats, sheep, pigs and poultry are kept under traditional farming systems producing manure, supporting crop production, insurance and financing emergency cash needs, and improving social status. The livestock feed resource base is mostly natural graze and crop residues whose quality and supply are dependent upon unreliable rainfall patterns. Due to rising demand for cropland, overgrazing, bush encroachment and bush burning, grazing supplies are being depleted. Grazing is supplemented using commercial feeds heavily infused with antibiotics contributing to antimicrobial resistance. Feed constitutes the largest expenditure, thus incorporating functional feed ingredients is favored. The study serves to increase farmers' awareness to substituting antimicrobials with functional feed ingredients. A systematic review of literature was done and keywords related to animal nutrition, functional feeds and antimicrobial resistance were used to identify relevant articles. Results revealed that functional feeding of livestock offers a potential diversity to animal production systems and may increase profitability in animal husbandry ventures. Functional feed ingredients improve productivity and vigor by enhancing digestibility, preserving and stabilizing beneficial gut microflora, and having a favorable impact on the environment. Probiotics, plant phytogenic compounds, and prebiotics, have the potential to replace antimicrobials as environmentally-friendly therapeutics and growth promoters.

Key words: Animal nutrition, antimicrobial resistance, developing countries, functional feeds, livestock production.

INTRODUCTION

In the Southern African Region, livestock constitutes over 60% of the region's total land area suitable for livestock farming. This contributes significantly to food security across the Southern African Development Community

(SADC) region (Casey, 2021). Small scale variegated livestock farming, including ruminants and non-ruminants, has become popular in most developing countries (Ndlovu et al., 2020). The farm animal resources of Southern African Development Community (SADC) are rich and immensely diverse, with livestock populations in SADC estimated at 64 million cattle, 39 million sheep, 38 million goats, 7 million pigs, 1 million horses, and 380 million poultry (Molina-Flores et al., 2020; SADC, 2022). Livestock products contribute to livelihood in two ways: directly, via products for consumption; and indirectly, via sales to generate cash or exchanges for cereals or other crops (FAO, 2015).

Livestock production in smallholder areas of Zimbabwe is practiced for feeding the family and for sale. Furthermore, livestock produce manure which is used to support crop production, and provide insurance as well as financing emergency cash needs and social status (Mutami, 2015). They could be used as draught power to transport goods and people, to pull plows, carts, and sleds (Mota-Rojas et al., 2021). Milk could be added to the diet. When killed, the hides provide clothing and blankets. The commonest animals that have now become domestic are cattle, goats, sheep, pigs, donkeys, and poultry. Less common domestic animals include rabbits and horses (Nhangare et al., 2015). In the Zimbabwean culture, animals play other important roles. In the marriage process, for example, cattle are an essential part. Several cattle are required from the bridegroom by the bride's family. This forms part of the *lobola.* In addition, a special cow is required for the bride's mother (Parker, 2015).

Livestock species play very important economic and socio-cultural roles for the well-being of rural households in Africa (Ndlovu et al., 2020). These roles include amongst others food supply, source of income, asset saving, source of employment, soil fertility, livelihoods, transport, agricultural traction, agricultural diversification, and sustainable agricultural production (Casey, 2021). Most importantly livestock are greatly considered as living savings and can be converted into cash whenever the family needs it. It is a security asset influencing access to informal credits and loans and is also a source of collateral for loans (Taruvinga et al., 2022). In many rural regions, especially where financial markets are absent or non-existent, livestock stocks or herds are a source of asset accumulation and a measure of prosperity, a good example is in the rural remote areas of the Matabeleland region which is famously known for livestock production (Ndlovu et al, 2020). In Zimbabwe, this area is commonly referred to as the livestock country and falls under the Agro-ecological regions IV and V of the country characterised by low annual rainfall at 450-500 nm per annum (Taruvinga et al., 2022).

Traditional courts have long used animals as fines for offenses and crimes. The type of animal and the number will depend on the severity of the crime. Murder, for example, could call for as many as ten oxen as fine (Belay et al., 2022). Many clans keep special ox for their ancestors, and ceremonies centered on it are conducted regularly by members of the clan. Though, to a lesser extent, other animals like goats and fowl are involved in all these traditional practices. Until money was introduced to the local culture, the measure of a man's wealth was the number of domestic animals he had, in particular, cattle (Molina et al., 2020). Today, domestic animals, while still playing most of their traditional roles have become important commercial commodities. In the studies recently reviewed, the contribution of livestock to household income in pastoral systems ranges from 49.1 to 100% across sub-Saharan Africa with cattle contributing 70 to 90% (Oduniyi et al., 2020). Goats and sheep are valued as a source of meat, as well as a resource that can be sold for cash (Fekadu et al., 2018). In semi-arid Zimbabwe and Swaziland, goats are kept in mixed farming by 70% of farmers. The management of small ruminants is usually subordinate to the labor and energy needed for crop production (Ndlovu et al., 2020). Management systems for small ruminants in the humid zone of Cameroon depend on factors such as the time of year, the availability of labor, and the contribution of small ruminants to household income (Belay et al., 2022).

Small-scale animal farming helps farmers diversify their businesses, spreads farming risks, and opens doors for the use of waste materials like crop leftovers to join the human food chain using marginal resources (Mutami, 2015). Promoting livestock production helps communities with vulnerable and underprivileged individuals, such as women, people with HIV/AIDS, orphans, the elderly, and the poor in general, by reducing the danger of drought, especially in drought-prone areas (Ndlovu et al., 2020). Livestock is regarded as a typical way to demonstrate wealth in Botswana and offers its owners social status. It also confers economic status because it makes it easier for households to secure unofficial credits and loans. Additionally, livestock is employed in customary rituals, ceremonies, and celebrations as well as presented as a gift during worship (such as during the ancestor's including dual-purpose breeds; fancy or ornamental breeds; meat producers or hybrid broilers, and egg producers or hybrid layers (Sreenivasaiah, 2015).

Species that are raised by the small scale farmers installation, ceremonial slaughter, and bride wealth) (Archer et al., 2021).

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Poultry farming is another small-scale farmer's technique. There are four basic classifications for poultry include chickens or other fowl, turkeys, ducks, geese, guinea fowls, and pigeons (Mgaya, 2019). The data kept and the approaches taken, however, differ greatly. The majority of the chickens are raised in a free-range environment. They can be kept for a variety of functions, such as producing meat, breeding, and eggs. They can also occasionally be used as exhibits in agricultural fairs. In addition to being a cheap and superior source of protein for sheep feed, their droppings are one of the greatest types of manure on the farm (Belay et al., 2022). The feathers are used to fill beds, pillows, and cushions. They are also used pretty frequently in various traditional crafts and costumes. Poultry products are used in the production of some pet foods. Some fertilizers are made using the blood and feathers of chickens (Nadaraja, 2020).

Despite having several advantages, livestock still face a nutritional challenge that limits their productivity. The feed resource base for livestock production in developing countries is natural grazing and crop residues (Tavirimirwa et al., 2019). The quality and supply of these resources are seasonally variable. Grazing resources in many areas are diminishing due to increases in cropping land. Bush encroachment and overgrazing have reduced grazing resources in pastoral areas (Mutami, 2015). One of the most serious of these is the indiscriminate burning of the veld, resulting in critical shortages of grass during winter and early spring (Ndlovu et al., 2020). Population growth has forced farmers to move to mountainous areas, further away from grazing pastures and veterinary extension services, increasing transportation costs for inputs and services (FAO, 2017).

ANIMAL NUTRITION

Animal nutrition focuses on the dietary needs of animals. It studies the composition and characteristics of the material consumed by the animal, and how this material is metabolized in the digestive tract of monogastrics, ruminants, and lower digestive tract fermenters (McGrath et al., 2018). Knowledge of grazing preferences and adaptations amongst ruminant livestock species helps in planning grazing systems for each species and also for multiple species grazed together or on the same acreage (Guyomard et al., 2021). Animal feeds are classified as concentrates, roughages, and supplements (additives) (Kirkpinar and Acikgoz, 2018). Concentrates are low in fiber and high in digestible nutrients, including, maize, cottonseed, barley, and sorghum (Stein et al., 2016). Roughages are high in fiber and relatively low in digestible nutrients, such as pasture grasses, alfalfa, silage, hays, stover, straw, and root crops (Feruda et al., 2018). Supplements (additives) are materials that are administered to the animal to enhance the effectiveness of nutrients and exert their effects in the gut or on the gut walls, for example, antibiotics, minerals, and vitamins (Markowiak and Slizewska, 2018).

Feed additives

Blending of additives in feed is being practiced for various reasons including improving nutritional profile, enhancing therapeutic effect and digestibility. The most common additives are antibiotics which have a prophylactic function. Additives can also be infused to stabilize feed (Kyriakopoulou, 2021). It is known that feed degrades with time reducing its shelf life. Rancidity, for example, results from chemical reactions between reactive forms of oxygen and the production of aldehydes (-CHO-) and ketones (-C=O-) and degrades unsaturated fatty acids (Makała, 2021). Anti-oxidants such as selenium, vitamin E, and other additives can be infused into feed to reduce this effect (Xiao et al., 2021). Other additives in this category are pellet binders and mold inhibitors (Makała, 2021). Also, some additives have been used to aid the digestion of ingesta, to increase voluntary feed intake with the use of feed flavors such as molasses, or modify metabolism in animals (Kirkpinar and Acikgoz, 2018).

Challenges encountered in animal nutrition

Several challenges are encountered in animal nutrition. These include anti-nutritional factors, prohibitive costs of protein sources, droughts, competition with humans, and antibiotic resistance (FAO, 2022). Antibiotics are used at therapeutic levels, by injection or in food, or in water, to treat diseases caused by bacteria (Hassan et al., 2020). Additionally, sub-therapeutic levels are added to the food to enhance the rate of growth (Manyi-Loh et al., 2018). Antibiotics, used as feed additives with a growth promoting effect, have been used mainly in pig and poultry feeds, typically at levels of 20-40 mg/kg, which give improvements of 4-16% in growth rate and 2-7% in efficiency of food conversion (EFSA, 2015). Ruminants depend primarily on bacteria in the rumen for their nutrient supply thus the use of antibiotics in nutrient diets is considered disadvantageous (Hassan et al., 2020). The widespread use of antibiotics coupled with the ability of resistant bacterial strains to evolve over a short period and transfer resistance to other strains has resulted in populations of bacteria that are resistant to many antibiotics (Ventola, 2015). This has limited the effectiveness of antibiotic treatment against disease. Thus, the use of antibiotics as growth promoters has been curtailed by legislation in recent years (Manyi-Lo et al., 2018). The use of antibiotics as feed additives in Europe has been banned because antibiotics have the potential to be absorbed in livestock products.

In addition, consumers of the animal product will get antibiotics indirectly in low concentrations which can increase bacterial resistance and chemical residues and can cause allergic effects in humans (Arsène et al., 2022). The inclusion of antibiotics in livestock feed is associated with the emergence of several resistant pathogenic strains, including *Salmonella* species, *Campylobacter* species, and *Escherichia coli* (Markowiak and Śliżewska, 2018). To improve feed performance and disease resistance, thereby reducing the need for antimicrobial treatments, functional feed ingredients promoting disease resistance and acting as growth promoters may add positively to existing therapeutic strategies (Peng and Biao, 2021). With the banning of the use of antibiotics, natural ingredients are widely used as an alternative to feed additives. The functional feed ingredients include phytogenic bioactives, enzymes, probiotics, as well as prebiotics (Mandey and Sompie, 2021).

FUNCTIONAL FEED INGREDIENTS

Functional feed ingredients are a mixture of both organic and inorganic components which are varied according to the raw materials and their extraction process. Feed ingredients are added during feed formulation to improve the quality of the feed and health performance as well as the feeding efficiency of animals (Erickson and Kalscheur, 2020). Most of the feed ingredients are nutritious including proteins, vitamins, minerals, and fatty acids or non-nutritious such as polysaccharide fibers, antioxidants, immune stimulants, phytochemicals, prebiotics, and probiotics which are added in the culture system to improve growth (Bharathi et al., 2019). Feed formulations containing functional components are needed to increase livestock productivity, reduce mortality, and improve feed conversion ratios (Wanda et al., 2018). Furthermore, this feed can also affect the amount of methane, nitrogen, ammonia, phenol, indole, and biogenic amines produced from livestock feces which pollute the environment (Mahfuz and Piao, 2019).

Sources of alternative natural functional feed ingredients

These functional feed ingredients exist in three main forms which are of plant, animal, and microbial origin.

Functional feed ingredients of plant origin

Functional components include phytochemicals which are plant-derived, non-nutritive, and biologically active chemicals (Izydorczyk and Dexter, 2018). The most abundant sources of functional sources are grains, fruits, and vegetables. Broccoli and other cruciferous vegetables, grapes, tomato, soybean, oat, oranges, garlic, and tea are examples of plants that provide functional feed ingredients naturally and have played a functional role in both animals and humans (Kasapidou et al., 2015). Moreover, animal products like milk, fermented milk products, and freshwater fish contain antioxidants, covalently linked linolenic acid, long-chain omega-3, -6, and -9 polyunsaturated fatty acids, and organic acids (Arshad et al., 2021). The seeds of the family Fabaceae (Leguminosae) are the most important part of the legumes that are used as ingredients for animal feed manufacturing (Kasapidou et al., 2015). These include soybeans, groundnuts, sugar beans, and groundnuts. These contain proteins, vitamins, and antioxidants which are useful for body function (Arshad et al., 2021).

Fruit and vegetable processing by-products

Fruit and vegetable processing by-products are promising sources of valuable substances such as phytochemicals (carotenoids, phenolics, and flavonoids), antioxidants, antimicrobials, vitamins, and dietary fats that possess biological activities and nutritional factors (Zehiroglu et al., 2019). Examples of these by-products include orange peels, orange pulp, potato peels, tomato seeds, and sunflower seeds. The incorporation of these by-products into feed also solves environmental issues of disposal and prevents pollution (Kasapidou et al., 2015). The fruit and vegetable by-products remain underexploited as functional feed ingredients.

Plant extracts

Plant extracts are composed of hundreds of individual components that are secondary plant metabolites that can be naturally obtained from parts of plant materials or synthesized directly. Phytogenic bioactive agents are plant secondary metabolites that contain compounds of nutritional value, non-nutritive or anti-nutritive (Markowiak and Śliżewska, 2018). They are categorized as Generally Recognized As Safe (GRAS) (Steele et al., 2016). The phytogenic compounds used include herbal plants, spices, or extracts of the active components contained in plants. These active components exhibit antimicrobial, antifungal, and antioxidant activity (El-Zahar et al., 2022). Currently, many studies have been carried out using plants or their extracts as supplementary feed for ruminants or monogastrics. Compared to synthetic antibiotics, phytogenics have been proven to be more natural, free of residue, and have been used to offset animal growth (El-Zahar et al., 2022) Some of the active phytogenic components include essential oils, flavonoids, saponins, and tannins.

Essential oils

Most plant extracts are plant secondary metabolites in oil form, essential oils, which are mixed oil compounds such as carvacrol, cinnamaldehyde, and oregano (Polo, 2015). They are lipophilic, volatile, and responsible for the aroma and color of plants (Sharifi-Rad et al., 2017). Essential oils have been widely used as feed additives and exhibit many biological activities including antioxidant, antifungal, antiviral, antiprotozoal, antibacterial, and anti-inflammatory (El-Zahar et al., 2022). These activities increase livestock production, especially the efficiency of the feed conversion ratio. The important active components of essential oils are terpenoids (monoterpenoids and sesquiterpenoids) and phenylpropanoids (Hassan et al., 2020).

Antimicrobial activity mechanism is achieved by damaging and changing the conformation of the microbial cell wall thus affecting electron transport, ion gradients, and protein translocation, and causing loss of chemiosmotic control (Legros et al., 2021). This mechanism is more effective against Gram-positive bacteria because the cell membrane directly interacts with the hydrophobic components of the essential oil (Andrade-Ochoa et al., 2021). Furthermore, many essential oils are small enough to penetrate the cell walls of Gram-negative bacteria which are hydrophilic (Hassan et al., 2020). Their main disadvantage is that this activity affects the microbial population responsible for digestion and livestock metabolism (Simitzis, 2017). The use of essential oils at high dosages is toxic to chickens. The optimum dose of essential oil as supplementary feed for chickens is 20-200 ppm (Irawan et al., 2021). The application of essential oils is done by adding plants directly to the main component of the feed or as a result of extraction.

Flavonoids

Flavonoids are plant phenolic compounds that are useful as appetite enhancers, reducing feed intake, and increasing pigment in animal products (Lin et al., 2016). They are also useful therapeutic elements such as anti-inflammatory, anti-fungal, antioxidant, and wound-healing agents (Yacout, 2016). Flavonoid supplements increase calf growth, and calf performance during weaning, and increase humoral immunity (Lin et al., 2016). Various mechanisms of action of flavonoids in animal feed have been studied. Ullah et al. (2020) indicated a study whereby calves were given medium and high doses of flavonoids, at 7.3×10^{-4} and 3.6×10^{-3} g/kg body weight, respectively. There was an increase in humoral immune response at the age of 4-5 weeks of calves followed by an increase in body weight at weeks 5 and 6 at both flavonoid doses.

Saponins

Saponins are classified into two major groups including steroidal saponins (structural derivatives of spirostanes and furostan) and triterpenoid saponins (derivatives of oleanane) (El Aziz et al., 2019). The use of plants containing saponins or extracts of saponins in ruminants and non-ruminants (monogastric) was reported to increase the quality and production of livestock (Peng and Biao, 2021). In ruminants, the administration of saponins or saponin extracts as feed additives has been reported to reduce ammonia levels and odors in livestock manure (Tong et al., 2022). Saponins have anti-inflammatory activity and anti-protozoal effects thus they can suppress the number of protozoa in the rumen (Tedeschi et al., 2021). The anti-protozoal mechanism is facilitated by the formation of saponin complexes with sterol compounds on the protozoan cell membrane destroying the protozoal cell membrane and cell lysis occurs (Yacout, 2016). Including saponins in non-ruminant (monogastric) animal feed increased growth and feed efficiency, as well as improved the quality of livestock meat (Tufarelli et al., 2018). The addition of saponins and L-carnitine to chicken feed was also reported to improve the reproductive capacity of hens (Murali et al., 2015). The use of saponins has been reported to improve the immune system of livestock (Tedeschi et al., 2021).

Tannins

Tannins are complex polyphenolic compounds produced by plants. They are classified into hydrolyzable tannins (HT) and condensed tannins (CT) (Tong et al., 2022). Hydrolyzable tannins consist of a carbohydrate core group with a phenolic carboxylate bonded by an ester bond, while CT is composed of flavon-3-ols oligomers (Smeriglio et al., 2017). Tannins are anti-nutritional factors because of their ability to form complexes with proteins found in the feed so that these proteins cannot be digested, especially by non-ruminant livestock (Yacout, 2016). Their ability to bind protein is used to protect the protein concentrate of soybean meal in ruminant feed (Mukherjee et al., 2016). *In vitro* evaluation of protein digestibility of soybean meal mixed with tannin extracts of *Acacia* spp. showed a high decrease in soy protein degradation (protein protection) (Oladipupo et al., 2021). *In vivo* evaluation in sheep showed that the use of soy protein concentrate protected by banana stem extract increased the digestibility of feed nutrients (Riyanto and Sudibya, 2018). Evaluation studies of tannins as feed additives show that the tannins found in some plant extracts can prevent the colonization of parasites, bacteria, protozoa, and viruses in the digestive tract of livestock, thus they are widely used as traditional medicines for diarrhea and dysentery (Nyahangare et al., 2015). In ruminants, tannins inhibited the growth of *E. coli* O157:H7 in cow dung (Afzal et al., 2023). Furthermore, the use of small amounts of tannins was reported to reduce the number of proteolytic bacteria, *Butyrivibrio* *fibrisolvens* A58 and *Streptococcus bovis* 45S1, in the rumen (Devyatkin et al., 2021). The addition of pomegranate extract which is rich in polyphenols and antioxidants can potentially improve the immune system and health of ruminants (Akalin et al., 2018).

Tong et al. (2022) reported that the use of tannins as a ruminant feed additive has both beneficial and detrimental effects depending on the source and concentration of the tannins applied. Tannins at low concentrations can increase the efficiency of microbes in the rumen, have an antioxidant effect, and can protect healthy cells against toxic substances (Tong et al., 2022). However, at high concentrations tannins become anti-nutritional factors reducing the ability of livestock to digest protein and carbohydrates hence they become an anti-nutritional factor in ruminants (Huang et al., 2018). The application of high amounts of grape extract (3%) in non-ruminant (monogastric) feed reduced the growth performance of broilers, but in optimum amounts (up to 1%) could inhibit the growth of pathogenic bacteria. Additionally, the administration of chestnut wood tannins (0.20%) accelerated their growth and reduced broiler mortality (Buyse et al., 2021). The addition of chestnut wood tannin extract to rabbit feed by 0.5% was reported to increase rabbit body weight and reduce livestock mortality due to anti-microbial activity (Mancini et al., 2019). Tannin extract from chestnut wood is known to be rich in HT such as castalagin, this extract is reported to have an anti-microbial effect against several types of microbes such as *E. coli*, *Bacillus subtilis*, *Salmonella* Enteritica, *Clostridium perfringens*, and *Staphylococcus aureus* (Devyatkin et al., 2021).

Algae

The supplementation of algae as animal feed provides plentiful benefits, such as improved growth and body weight, reduced feed intake, enhanced immune response and durability towards illness, antibacterial and antiviral action as well as enrichment of livestock products with bioactive compounds (Saadaoui et al., 2021). Notable breakthroughs in algal biotechnology have made algae a powerful cell factory for food production and have led to rapid growth in use in the feed industry (Kusmayadi, 2021). There is a growing interest and evidence of the benefits of using macroalgae in livestock production systems, particularly for ruminants (Machado et al., 2015). The potential benefits of the macroalgae include improved carcass characteristics and meat quality, ruminal organic matter and total tract crude protein digestibility in cattle (Byeng et al., 2021), and color stability and extended beef shelf life of meat products. Macroalgae in pigs feed have been proposed to increase iodine concentration in pig meat which could be beneficial for its consumption by a deficient population (Saadaoui et al., 2021).

Algae has been evaluated for bioactive activity for decades. It possesses antibacterial, antioxidant, anti-inflammatory, anticoagulant, antiviral, and apoptotic activities (Afzal et al., 2023). Studies on seaweed revealed promising effects on feed utilization, growth performance, immune response, and disease resistance in several fish and shellfish species (Van Doan et al., 2019). Algae contain carotenoids which include carotenes and xanthophylls with relative abundance. These include β carotene, lutein, violaxanthin, zeanthanin, and fucoxanthin (Machado et al., 2015). These antioxidants have potential health benefits and are thus incorporated into livestock feed. They also contain phycobiliproteins including phycoerythrin, phycocyanin, and allophycocyanin which show multiple biological activities including antioxidant, anti-inflammatory, and anti-viral activities which could be used in the development of functional feed (Finamore et al., 2017).

The inclusion of *Ascophyllum nodosum* extract in feedlot cattle diets showed a reduction in *Escherichia coli* in fecal samples according to a study conducted by Zhou et al. (2018). Furthermore, the addition of *A. nodosum* extract at 2% in the diet of goats improved the anti-oxidant status of the animals exposed to simulated pre-slaughter stress (Zhou et al., 2018). Dietary inclusion of *A. nodosum* in dairy cows led to an improvement of the iodine content in milk, and a modification of its microbiota with a positive effect on milk hygiene and transformation (Chaves Lopez et al., 2016). The incorporation of macroalgal polysaccharides such as laminarin and fucoidan showed promising results when used as prebiotics in pig diets to modulate microbiota in the digestive tract and immunomodulating properties in pigs (Corino et al., 2021). Laminarin in the diet of pigs showed a downregulation of the expression of inflammatory cytokines in the colon and mucin gene expression in the ileum and colon (Rattigan et al., 2020). A reduction in Enterobacteriaceae counts was observed in pigs supplemented with fucoidan (Corino et al., 2021).

Functional feed ingredients of microbial origin

Probiotics

Probiotics are single or mixed microbial cultures that can provide indirect benefits to the host by improving the intestinal microflora. Probiotic organisms include lactic acid-producing bacteria such as *Lactobacillus*, *Enterococcus*, and *Streptococcus* species; spore formers such as *Bacillus* species and the single-cell yeast *Saccharomyces cerevisiae* (McGuffey et al., 2018). Fungal probiotics include *Aspergillus oryzae*, *Pleurotus* species, *Antrodia cinnamomea*, and *Codycerps militaris* (Chuang et al., 2020). The first role that they play in the digestive tract of animals is the stabilization of the gut microbiota (Kovacs, 2015). The potency of probiotics is influenced by the intestinal metabolism of the host animal, the genetic stability of microbial strains, and the capacity of bacterial colonization (Indira et al., 2019). Probiotic bacteria added to feed helps the animals by preventing colonization by pathogenic bacteria that contaminate feed (Markowiak and Śliżewska, 2018). *Lactobacillus* competes with pathogenic bacteria such as *E. coli* for attachment sites on the gut wall (van Zyle et al., 2020). Live probiotic bacteria can neutralize endotoxins produced by pathogenic bacteria that cause fluid loss (Polo, 2015). *Lactobacillus* ferment lactose to lactic acid thus reducing pH to an intolerable level for pathogenic bacteria (Nyazi et al., 2021). Hydrogen peroxide is also produced, which inhibits the growth of Gram-negative bacteria (Chaves Lopez et al., 2016).

Probiotics enhance immune competence. For example, oral inoculation of young pigs with *Lactobacillus* elevated serum proteins and white blood cell counts (Zhang et al., 2020). The provision of probiotic supplementary feed can have a positive effect on the immunity of livestock. This was explained by several researchers who reported that the administration of probiotics suppressed the number of enteropathogenic bacteria in livestock (Plaza-Diaz et al., 2019). Probiotics such as *Bacillus subtilis* and *Bacillus licheniformis* can be used as mycotoxin binders, especially in poultry with mycotoxin-contaminated diets (Riahi et al., 2021). The administration of *S. cerevisiae* and marine yeast can replace the function of growth-promoting antibiotics in broiler chicken and crayfish (Xu et al., 2021). Administration of prebiotics together with *Salmonella* Enteritidis-specific IgG antibodies can also be used to produce *Salmonella*-free eggs (Ricke, 2021). In *monogastrics*, *Lactobacillus, B. subtilis*, and *Streptococci* have been used as probiotics (Davyatkin et al., 2021).

The application of yeast, *S. cerevisiae*, in the form of live culture or dead cells (ghost probiotics), beneficially modifies rumen fermentation. The addition of yeast to beef cattle diets increased daily live weight and food conversion efficiency (Crossland et al., 2019). Yeast culture is a dried, fermented product containing small amounts of live yeast cells particularly *S. cerevisiae*, and metabolic by-products produced by the yeast during fermentation (Polo, 2015). Enzymes, vitamins, saccharides, and other metabolites produced from yeast fermentation have been used as functional feeds to benefit the growth, metabolism, and health of animals. Yeast culture and cell wall products containing manna oligosaccharides (MOS) and β-glucans are alternative functional feeds that have been used to benefit animals (Polo, 2015).

Mushrooms

By-products from the agricultural industry, including oyster mushroom waste *Pleurotus ostreatus*, monkeyhead mushroom (*Hericium erinaceus*), shiitake mushroom (*Lentinula edodes*), and *Agaricus bisporus* have valuable biological activities (Altop et al., 2022). These include antimicrobial, antioxidant, antifungal, and prebiotic properties (Yagi et al., 2019). They are a useful alternative to antibiotic growth stimulators in livestock, especially in poultry. *P. ostreatus* stems have medicinal and nutritive value. The stem waste is used as a phytogenic feed additive. A study was carried out by Hassan et al. (2020) to determine the effectiveness of *P. ostreatus* waste in broiler chickens on growth output, serum cholesterol, immune status, and antibody response. In the study, it was observed that the inclusion of 1% oyster mushroom waste in broiler diets enhanced growth and immunity as well as delayed poultry meat lipid oxidative rancidity.

Functional food ingredients of animal origin

Spray dried plasma

Spray-dried plasma (SDP) is a ready supply, easily accessible source of highly digestible amino acids. It is made from blood collected from slaughterhouses and is rapidly dried to preserve protein function (Campbell et al., 2019). SDP contains a high protein content comprised of albumins, globins, and globulins including immunoglobulins. The amino acid pattern is high in lysine, tryptophan, and threonine (Zampiga et al., 2021). It is however low in methionine and isoleucine (Lopez and Mohiuddin, 2022). The inclusion of SDP in feed improves food intake and food conversion efficiency and it is particularly effective in situations where there is a high level of pathogens (Chuchird et al., 2021). The growth-promotant and beneficial health effects of SDP are attributed to immunoglobulins (Van Dijk et al., 2018). The immunoglobulins act within the gut by preventing bacteria and viruses from damaging the gut wall. In this manner, intestinal function is maintained, that is, increased villi surface, increased enzyme production, and reduced diarrhea (Jandhyala et al., 2015). Numerous studies involving challenge or natural infection with pathogenic bacteria, viruses, or protozoa have reported reduced mortality and improved health indices in animals fed diets containing animal plasma as an alternative functional feed (Kasadipou et al., 2015).

Other sources of functional feed ingredients

Prebiotics

Prebiotics (oligosaccharides) are feed ingredients that cannot be digested, but have a good effect on the intestines and improve animal health (Tona et al., 2018). They are compounds, other than dietary nutrients, that modify the balance of the microbial population by promoting the growth of beneficial gut bacteria hence providing a healthier intestinal environment (Carballo et al., 2019). Health improvement occurs because prebiotics can increase the population of probiotics (Markowiak and Śliżewska, 2018). They naturally occur in foods. Examples include fructooligosaccharides (FOS) found in cereals; mano-oligosaccharides (MOS) found in yeast cell walls; galactooligosaccharides (GOS) found in soya bean meal, rapeseed meal, and legumes; and trans-galactooligosaccharides (TOS) from milk products (EFSA et al., 2022). The advantage of giving prebiotics to animal feed is that it can increase feed efficiency and stimulate livestock endurance. This functional feeding has been demonstrated in dogs, pigs, poultry, and young cattle (Markowiak and Śliżewska, 2018). Several studies have also shown that prebiotics are not degraded in the gastrointestinal tract, thus these functional carbohydrates can reach the large intestine and still have a positive effect on livestock (Campbell, 2019). Functional prebiotic and probiotic feed for laying fowls produce enteropathogen-free eggs (*Salmonella* spp.) that are healthy for humans. The administration of FOS to chickens reduces the formation of *S.* Enteritidis colonies by increasing the population of probiotic bacteria (Krysiak et al., 2021). Application of FOS at a level of 4.0 g/kg improved the growth of male chickens, food conversion rate, increased populations of *Lactobacterium* and *Brevibacterium* bacteria, suppressed *E. coli* bacteria, and increased amylase and protease activity (Cui et al., 2017).

BIOTECHNOLOGY IN ANIMAL NUTRITION

Biotechnology is a broad subject that focuses on the potential use of natural and modified organisms and systems in agriculture, medicine, the environment, and many other disciplines (Gupta et al., 2016). The subject can range from relatively simple breeding to highly sophisticate molecular and cellular manipulations to produce desired characteristics in plants and animals (Ahmer et al., 2020). It has been applied in both animal and human nutrition to improve the quality of food/ feed through the integration of some micro-ingredients and functional feeds (Ku and Sun-Hwa, 2020). Through the use of genome editing tools, the development of functional feeds can be made easy and possible, consequently improving the quality of the feed (Getabalew and Alemneh, 2019). Biotechnology has been used to improve animal nutrition through the protection of protein, amino acids, and fat; the use of enzymes to improve the release of nutrients from feed and to reduce the wastage of feed and fodder; prebiotics and probiotics or immune supplements to reduce gastro-intestinal pathogenic bacteria; production of feed and fodder with high nutritive values and genetic manipulation of rumen micro-flora to enhance animal health (Cammack et al., 2018).

Genetic manipulation of rumen microbes

Ruminal microbes can be altered genetically to increase their cellulolytic ability and reduce methanogenesis to improve the overall utilization of feed and fodder. This can be done to eliminate the anti-nutritional factors in feed and increase the essential amino acids, specifically limiting amino acid synthesis by rumen microbes. Research is being done to introduce the lignin breakdown property into ruminal microbes (Hassan et al., 2020). Depolarization of lignin by the ligninase enzyme, which is produced by the soft-rot fungus *Phanerochaete chrysosporium* (Junne, 2020), can be useful for animals.

Development of functional feeds using genome editing tools

Genome-editing tools, including meganucleases, zinc finger nucleases (ZNFs), transcription activator-like effector nucleases (TALENS), and clustered regularly interspaced short palindromic repeats (CRISPR) systems, have been applied to improve the quality of staple, oilseed, and horticultural crops which are components of feed with great accuracy and efficiency compared to conventional breeding (Hu and Hwa, 2018). Moreover, genetic knockouts applied to agriculturally relevant plants and animals using genome engineering methodologies are poised to revolutionize the nutrition content and the availability of food and feed crops (Sedeek et al., 2019). Thus, genome editing has been used to improve nutritional, neutraceutical and digestibility of feed.

Functional feed crops that have been produced using genome editing

Maize (Zea mays)

Maize, which constitutes a greater proportion of the feed part in animal feed, contains phosphate, also called inositol 1, 2, 3, 4, 5, and 6-hexakisphosphate, an anti-nutritional factor that affects protein absorption. The IPK1 gene encoding inositol-1, 3, 4, 5, 6-pentakisphosphate 2-kinase in maize was blocked using ZFNs by Shukla et al. (2019). Knockout of IPK1A, IPK, and MRP4, which encode two inositol phosphate kinases and multidrug resistance-associated protein 4 in the metabolism of phytates, has also been attempted using CRISPR/Cas9 and TALENs (Jiang et al., 2020).

Maize has low zein content for protein storage. To overcome the problem of reduced zein protein content, RNA interference (RNAi) and CRISPR/Cas9 targeted the gene ZmMADS47 encoding a MADS-box protein, which is an interacting partner of O2 to activate the zein gene promoter (Qi et al., 2016). Another intervention in maize was in its starch. Its metabolism was manipulated using

CRISPR/Cas9 to disrupt the waxy gene (W×1), which encodes a granule-bound starch synthase (GBSS) responsible for synthesizing amylose in maize. Several versions of waxy mutants have been exclusively developed to contain only branched amylopectin, which is a commodity in processed foods, adhesives, and high-gloss paper.

Wheat

The wheat storage protein gluten can trigger some health issues in some individual animals, such as celiac disease (Gil-Humanes et al., 2018). To reduce the contents of α-gliadin in the gluten protein, knockouts of α-gliadin genes were generated using CRISPR/Cas9, and their immunoreactivity was reduced by 85%. This resulted in CRISPR hypo-immunogenic wheat with low gluten content and possible suitability for the production of low-gluten wheat (Sánchez-León et al., 2018).

Rice

As in other cereal crops, rice starch has a large influence on glutinosity for feed quality (Zhang et al., 2018). By knocking out the starch branching enzyme gene SBEIIb using CRISPR/Cas9, a high-amylose and low-viscosity rice variety was produced (Sun et al., 2018). Conversely, low-amylose and glutinous rice was produced by knocking out the GBSS gene Waxy using CRISPR/Cas9 (Zhang et al., 2018).

Oilseed crops

To obtain edible or industrial oils, humans and animals have relied on oilseed crops such as soybean, rapeseed, sunflower, cotton, and nuts, which are grown as sources of protein in animals and for oil extraction purposes. Biotechnologists have tried to modify the fatty acid profiles of their seeds to improve oil quality according to the desired purpose (Ku and Sun-Hwa, 2020). At present, the target of genome editing has been the production of monounsaturated fatty acids, such as oleic acid (18:1), which is generally considered healthier and oxidatively more stable and hence is associated with a longer shelf life than products containing polyunsaturated fatty acids (PUFAs), such as linoleic acid (18:2) (Mariamenatu and Abdu, 2021). As such, the fatty acid desaturase 2 gene (FAD2) encoding delta-12 desaturase, which converts oleic acid to linoleic acid, was targeted and disrupted to alter the fatty acid profile by increasing the oleic to linoleic acid ratio in soybean and other oil seeds.

Soybean oil quality was first improved using TALENs to carry targeted mutations in two FAD2 genes (FAD2-1A and FAD2-1B), resulting in increased oleic acid levels (from 20 to 80%) and decreased linoleic acid levels (from 50 to 4.7%) (Wu et al., 2020). To further decrease the levels of linoleic acid Calyxt Inc., fatty acid desaturase 3 gene (FAD3) encoding delta-15 desaturase was knocked out by directly delivering TALENs into previous fad2-1a fad2-1b soybean plants (Demorest et al., 2016).

Biotechnology has the potential to improve the quality of food for both animals and humans. Many products have been developed through this intervention; some are sold as individual products, while others constitute some parts of a product. Therefore, gene editing has the potential to solve problems associated with nutrient availability in plants and reduce unwanted nutrient availability, thereby improving the quality of feed. CRISPR/Cas9 is the most currently favoured gene editing tool because of its accuracy and ease of use (Sánchez-Leon et al., 2018). Although these might prove to work and be beneficial, the long-term effects of these edited genes on humans and the environment should be monitored, as these might prove to be almost foreign to the current environment (Ayanoglu et al., 2020).

BENEFITS, CHALLENGES, AND RISKS ASSOCIATED WITH THE USE OF FUNCTIONAL FEED INGREDIENTS

The use of functional feeds has improved immunity as well as a growth promoter in fish and shrimp without compromising their health and is also sustainable for the environment (Mohan et al., 2019). Probiotics are important feed supplements in aquaculture due to their capacity to enhance health and prevent disease (Carballo et al., 2019). Functional feeds empower the fish to withstand stressful events and pathogenic pressure (Khattaby, 2022). This becomes evident through increased growth and survival rates.

Phytobiotics include a wide range of plant-derived products such as essential oils, herbs, and oleoresins (Mohsen and In, 2018). They can be added to the diet of commercial animals to improve their productivity by enhancing feed properties, promoting animals' production performance, and improving the quality of products derived from these animals (El-Zahar et al., 2022). Prebiotics stimulate metabolic activity in the intestines of broilers. Organic acids improve nutrient digestibility, cell proliferation, and epithelial and villi height while, amino acids and enzymes improve the growth performance and body weight of the broilers (Makala, 2021). The use of feed additives to improve the efficiency of growth and/or egg production, prevent disease and improve feed utilization is a strategy to improve the efficiency of the poultry industry (Zampinga et al., 2021).

Functional feeds play an important role in the production performance and physiological functions of animals; however, they have some disadvantages. The other concern with feeding functional feeds to livestock could be the contamination of the human food supply due to inadequate removal of feed additives in animals' tissues (Godde et al., 2021). Probiotics, prebiotics, and organic acids have possible side effects on the health of livestock (Uyeno et al., 2015). Increased animal productivity due to the use of functional feeds has led to an increase in the price of animal products (meat, milk) in the markets. This is because even as good and effective functional feeds are, they are very costly and have high manufacturing costs (Ruiz-Salmón et al., 2020).

James (2019), states that to use functional feeds, farmers must read the feed label to assure the additive is being fed at approved concentrations and indications. Medicated feeds should be used only as approved by FDA (label directions). Livestock producers should comply with the published withdrawal times to avoid residues in products for human consumption (Rana et al., 2019). Farmers should maintain mixing and distribution records to demonstrate that appropriate actions to avoid cross-contamination and product abuse are taken, including identification of the responsible party when feed ingredients are used (Matthews et al., 2019). Livestock producers should ensure that medicated feeds are stored properly and expiration dates and withdrawal times are strictly adhered to. All feed ingredients should be accompanied by label instructions for feeding and associated warnings (Junne, 2020). When used properly, feed ingredients offer tremendous benefits to stocker cattle producers. It is then concluded that the use of functional feeds in animals has a hugely beneficial impact.

SOCIAL, ETHICAL AND ENVIRONMENTAL ISSUES

The use of biotechnology in foods specifically to enhance their nutritional and health properties has enormous promise (Cabrera-Barjas et al., 2022). It is also possible to increase the security of human foods by increasing the digestibility of animal feed by lowering phytic acid, gossypol, and glycoalkaloids (Jiang et al., 2020). The use of gene editing techniques raises ethical concerns about the predictability of its positive and negative effects and how to balance anticipated impacts with the likelihood of unexpected impacts because the functional feeds might contain gene-edited ingredients (Lassoued et al., 2019). Biosafety issues will arise since the gene-edited organisms will be released into the environment. Non-target creatures, such as beneficial insects, other animals, and plants, could be adversely affected by poisonous substances and other factors (EC-ETHICS-GROUP, 2021). The discharge of the gene-edited organisms may have detrimental effects on biodiversity preservation and ecological instability due to vertical gene transfer and introgression of genetic material into wild populations (Waqar et al., 2021). Functional feed is not subject to any regulatory framework, whereas functional food items are. Some of the nations in the region, including Zimbabwe, Zambia, and Botswana, have put in place regulatory frameworks for feeds and foods developed from contemporary biotechnology, including genetically modified organisms (GMOs) and gene-edited (GE) goods (Cabrera-Barjas et al., 2022).

The majority of African nations have ratified the Cartagena Protocol on Biosafety, but given how quickly contemporary biotechnology is being applied to the production of feed and food, it is crucial that each nation in the region establish its own biosafety policy. Due to the trans-regional nature of GMOs and GEs, such policies must be coordinated at the sub-regional level to ensure effectiveness (Cabrera-Barjas et al., 2022).

CONCLUSION AND FUTURE PERSPECTIVES

Most developing countries, especially in Africa, have abundant crop-based products and by products which can be used as feed supplements with functional feed capabilities. This may shift the misconception that important feed ingredients should be added at commercial feed level only. Instead, it should be advanced to identify such products and their nutritional and antimicrobial properties for use in resource challenged communities in developing countries. In the future, the incorporation of functional ingredients to form functional feed can be a viable alternative in developing countries. Natural products which are easily accessible and locally available have the potential to substitute the use of antibiotics as feed ingredients that can improve livestock performance and health. These natural products are safe for livestock, humans, and the environment; can be used continuously, and have a variety of mechanisms. The use of natural ingredients as feed additives is expected to affect the performance and health of livestock, but with time, it should meet consumer demands for livestock products that do not contain synthetic chemicals and can maintain the stability of the product. Today, consumers are interested in improving their healthy life such as nutritional value in food, rich in protein, and low in cholesterol. It is hoped that the functional feed supplement will not only affect livestock but also be able to produce livestock products that have health value for consumers. Feeding grass with supplements of linseed oil and clover leaf can increase polyunsaturated fatty acids (PUFA) in beef which becomes a functional food. The provision of flavonoids, hesperetin, and naringenin extracted from orange peel, as a supplementary feed, has antioxidant properties and improves the performance of laying hens while producing eggs with the lower cholesterol content. Eggs with low cholesterol levels will improve human health or correlate with functional foods. In the future, the provision of supplementary feed as a functional feed can turn into a functional food source for developing country populations.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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