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Feed Additives in Animal Health

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Abstract

Animal feed additives are used all over the world for various livestock including poultry for more reasons than one like to provide essential nutrients, increase palatability of the feed, improve their growth performance, as well as optimize the utilization of the feed. Animals with high growth performance need to maintain a high health status, and the use of proper additives is a predominant argument in such cases. With increasing industry standards and consumer awareness as well as demand for healthy food products of animal origin, there is an increased pressure on the industry for more natural and non-residual alternatives than the conventional feed additives used till recently as animal feed products. Consumer and animal welfare are primary concerns dictating the valuable alternatives of animal feed additives. Some of the alternatives seen for use as animal feed additives are probiotics, prebiotics, enzymes, and herbs. Such choice of feed additives is backed by scientific and empirical research on these alternatives as herbs and their extracts (botanicals) have been found to have a wide range of activity which cannot only stimulate feed intake but also stimulate endogenous secretions or have antimicrobial, coccidiostat, or anthelmintic activity.

Ban of antibiotic use as growth promoters, costeffectiveness, and increased awareness about harmful residual effect cause herbal feed additive to gain importance in sustainable livestock production. Animal husbandry sector gets benefited by the use of number of feed additives such as ascorbic acid, prebiotic, probiotic, and herbal extracts. Medicinal properties of the herbs to improve antimicrobial, anti-inflammatory, antioxidant, digestibility, and immune-stimulant activity must be explored in the feeding of animals as well as safe food

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for human beings. Standardization of correct dosage regime of herbal feed additives for a particular function is the demand of situation so more research should be conducted in this direction.

Keywords

Feed additives \cdot Phytogenic product \cdot Probiotics \cdot Prebiotics \cdot Enzymes \cdot Herbs \cdot Plant extracts \cdot Quality control

1 Introduction

One of the greatest challenges faced by farm managers, livestock rearers, animal scientists, as well as nutritionists involved in animal feed industry or research domain is designing the balanced ration practices of high yielding animals along with maintaining the cost-benefit ratio. Also, to be taken in consideration is the fact that meat, dairy, and animal by-product costs are not stable and vary for various reasons, and one among them is the feed cost involved (Thornton 2010). Feed costs represent the largest input cost in animal husbandry practices (estimated to be 35-50%). In general there is an opinion that animals ate plants, or grass or some other "food" natural to their ilk, but in reality, in today's farms, feeding livestock and poultry is a complicated endeavor fraught with controversy and split opinions. Feed additives have been considered as a group or class of feed ingredients which in a non-nutrient role can cause the desired animal response. Such responses may include a shift in pH, growth, or modifying the metabolic response of the animal (Hutjens 1991). According to the European Commission, feed additives are products used in animal nutrition for purposes of improving the quality of feed and the quality of food from animal origin or to improve the animals' performance and health, e.g., providing enhanced digestibility of the feed materials. Several feed additives may contain various

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R. C. Gupta et al. (eds.), Nutraceuticals in Veterinary Medicine, https://doi.org/10.1007/978-3-030-04624-8_23

nutrients such as sodium and protein which are part of sodium bicarbonate or yeast culture, respectively. Technically, feed additives are neither considered a requirement nor do guarantee high animal productivity or economic profitability in animal husbandry practices (Animal Feed Additives 2018, web source). There has been a rapid increase in the demand to be met from dairy and meat industry owing to increasing population pressure. Food security which is the second in the list of Sustainable Development Goals in form of "zero hunger" and 12th sustainable development goal which is "responsible consumption and production" are both sought after in animal feed industry up to a greater extent.

The importance of feed additives is gaining popularity day by day owing to the benefits that they can ascertain like growth promotion in animals, control over infectious diseases as well as enhancement of feed digestibility (Specialty Feed Additives Report 2016). There is a steadfast growth graph of animal feed additives market which is projected to grow in the future due to the rapid increase in demand for meat, meat products as well as dairy products around the globe (Animal Feed Additives Report 2014). The consensus of meat and dairy farmers has increased towards feed quality and certifications associated with them owing to frequent occurrences of epidemics such as bird flu, other diseases such as foot-and mouth-disease, and environmental concerns have led to increase in concern over animal health around the globe.

The top consumers of feed additives in the world are North America and Asia-Pacific. They account for more than 60% of the consumption of animal feeds in the world (Animal Feed Additives Report 2014). Asia-Pacific is estimated to be the fastest growing region in terms of revenue. Growth is particularly high in emerging economies such as India, China, and Brazil because of gradual increase in the income levels of population owing to increased industrialization and boom in service sector, and in the process it has given an uplift to the feed industry as well due to rising per capita meat consumption (Ruminant Feed Market Report 2018). Species wise the largest market coverage is of poultry feed additives which are followed by market share for feed additives for swine (Animal Feed Additives Report 2014). The main driving factors of the global market of animal feed additives can be classified as:

- (a) Rise in global meat consumption
- (b) Increasing awareness toward meat quality and safety
- (c) Increasing mass production of meat
- (d) Recent disease outbreaks in livestock

(Kearney 2010; Henchion et al. 2017).

The restraints of the market are increasing raw material cost and regulatory structure. However, increasing cost of natural feed products is creating an opportunity for feed additives as a cheap alternative. Leading manufacturers are focusing on the expansion of businesses across regions and setting up new plants for increasing their production capacity.

Though there are various definitions of feed additives, a comprehensive definition put forward by the European Commission is: "Feed additives are products used in animal nutrition for purposes of improving the quality of feed and the quality of food from animal origin, or to improve the animals' performance and health, e.g. providing enhanced digestibility of the feed materials."

With the tightening of the noose of regulatory authorities and stronger social media, there is hardly any scope to flout the norms set for industries. For any animal feed additives to be marketed, the process of scientific evaluation and validation to ascertain presence or absence of any harmful effects on human and animal health or environment needs to be performed in stringently (European Commission 2018). So, various domains such as health, environmental sustainability, regulatory requirements, and even climate change are a part of production, marketing, and postutilization effects which are assimilated with the feed production industry.

Classification of Animal Feed Additives

Feed additives are classified into various categories according to different parameters. Feed additives can be of various types:

Based on European Commission regulations Based on holistic approach Based on their origin and function

2

Feed additives can be categorized as feed antioxidants, compound acidifiers, complex enzymes, mycotoxin adsorbent, mildew prevention, vitamins and electrolytes, L-carnitine hydrochloride, diluted chromium nicotinate, fattening agents, amino acids, antibiotics, binders, minerals, herbs, and premix. A widely recognized classification of animal feed additives based on European Commission regulations and guidelines is as below.

One additional class of feed additives used to include the technological interventions employed in feed additives is *Technological additives*.

2.1 Based on European Commission Regulations

2.1.1 Sensory Additives

This refers to a group of additives which improve the palatability (i.e., voluntary intake) of a diet by stimulating appetite, usually through the effect these products have on the flavor or color of the diet. For example, feed flavors or sweeteners such as vanilla extract may well encourage piglets to eat a ration.

2.1.2 Nutritional Additives

Additives provide specific nutrients for an animal for optimal growth. An example would be a vitamin, amino acid, or trace mineral. In most cases, such additives are simply concentrated forms of nutrients supplied in natural ingredients in the diet.

2.1.3 Zootechnical Additives

These additives improve the nutrient status and production of the livestock, not just by providing specific nutrients but also by assisting the more efficient use of the nutrients present in the diet. An example of such an additive would be an enzyme or direct-fed microbial product, both of which enhance the conditions of the intestinal tract, thus enabling more effective nutrient extraction from the diet. In this respect, they are often referred to as pro-nutrients, i.e., products which improve the nutritional value of a diet without necessarily providing nutrients directly. Other additives are used for environmental benefits that they provide to animal husbandry, and others are targeted for specific physiological functions.

2.1.4 Coccidiostats and Histomonostats

These additives control the health of poultry through direct effects. These compounds are used to control the intestinal health of poultry, and they directly act on the parasitic organisms inhabiting the intestines, and they are not classified as antibiotics (Feed additive classifications 2018).

2.1.5 Technological Additives

This classification refers to a group of additives which influences the technological aspects of the feed. These additives do not directly influence the nutritional value of the feed but may do so indirectly by improving its handling or hygiene characteristics. An example of such an additive would be an organic acid for the preservation of feed (Fig. 1).

2.2 Based on Holistic Approach

Apart from European classification, a more holistic classification provided by the Indian Council of Agricultural



Fig. 1 Classification of technological feed additives

Research, Ministry of Agriculture, Government of India, is shown in Fig. 2.

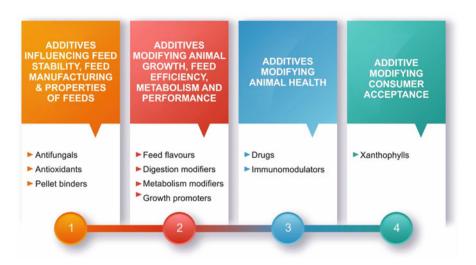
2.2.1 Additives That Influence Feed Stability, Feed Manufacturing, and Properties of Feeds

- (a) Antifungals
- (b) Antioxidants
- (c) Pellet binders

2.2.2 Additives That Modify Animal Growth, Feed Efficiency, Metabolism, and Performance

- (a) Feed flavors
- (b) Digestion modifiers
 - I. Enzymes
 - II. Prebiotics
 - III. Buffers
 - IV. Acidifiers
 - V. Ionophores
 - VI. Antibloat compound
 - VII. Isoacids
 - VIII. Salivation inducers
 - IX. Probiotics
 - X. Defaunating agents
- (c) Metabolism modifiers
 - I. Hormones
 - II. Beta-adrenergic agents (repartitioning agents)
- (d) Growth promotants
 - I. Antibiotics

Fig. 2 Indian Council of Agricultural Research (ICAR) classification of feed additives



- II. Chemotherapeutic agents
- III. Prebiotics and probiotics

2.2.3 Additives That Modify Animal Health

(e) Drugs

(f) Immunomodulators

2.2.4 Additives That Modify Consumer Acceptance

(a) Xanthophylls

Further to have a holistic classification to include all the types and subtypes of animal feed additives, including those included in the above classification based on the primary activity of function performed by a set class, we suggest the following detailed classification.

2.3 Based on Their Origin and Function (Fig. 3)

2.3.1 Additives That Enhance Feed Intake

Antioxidants

Antioxidants are compounds that prevent oxidative rancidity of polyunsaturated fats. Rancidity once develops may cause the destruction of vitamins A, D, and E and several of the B complex vitamins. Breakdown products of rancidity may react with lysine and thus affects the protein value of the ration. Ethoxyquin or BHT (butylated hydroxytoluene) can serve as an antioxidant in the feed.

Flavoring Agents

Flavoring agents are feed additives that are supposed to increase palatability and feed intake. There is a need for flavoring agents that will help to keep up feed intake. When highly unpalatable medicants are being mixed:

- During attacks of diseases
- When animals are under stress
- When less palatable feedstuffs are being fed either as such or being incorporated in the ration

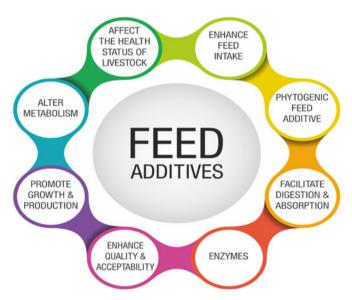


Fig. 3 Holistic classification of feed additives

Ruminants prefer sweet compounds. Additionally, cattle and goats respond positively to salts of volatile fatty acids. Horses will often refuse musty feed when there is so little mold that the owner fails to detect it.

2.3.2 Additives That Enhance the Quality and Acceptability of the Feed

Poultry owners will often enhance the yellow color by incorporating xanthophylls into broiler feed. Among various additives, arsanilic acid, sodium arsanilate, and roxarsone are added for the purpose.

Anticaking Agents

Anticaking agents are the anhydrous substance that can pick up moisture without themselves becoming wet. They are added to dry mixes to prevent the particles from clumping together and so keep the product free-flowing. They are either anhydrous salts or substance that hold water by surface adhesion yet themselves remain free-flowing:

- Salt or long chain fatty acids
- Calcium phosphate
- · Potassium and sodium ferrocyanide
- Magnesium oxide
- Salts silicic acid—Al, Mg, Ca, and salt
- Sodium aluminum silicate
- Sodium calcium aluminum silicate
- Calcium aluminum silicate

Humectants

These are the substance which is required to keep the product moist, for example, bread and cakes. Anticaking agents immobilize moisture that was picked up. Humectants are not of much use in poultry feed.

Firming and Crisping Agents

These are substances that preserve the texture or vegetable tissues and, by maintaining the water pressure inside them, keep them turgid. It prevents a loss of water from the tissues.

Sequestrants

Certain elements—copper and iron—can act as prooxidant catalytic and therefore need to the immobilized. Sequestrants are compounds added to do this. These compounds should have an affinity to metal ions and should prevent the metal in becoming engaged in oxidative action. Most effective sequestrants ethylenediaminetetraacetic acid (EDTA) is a calcium salt of EDTA which works satisfactorily as a sequestrant without interfering with trace mineral metabolism.

Sweeteners

It is the common constitution of food but yet used as an additive, e.g., sugar. Some are poorly digestible and may

cause digestive upsets. Saccharin is extensively used during World War I. It is a compound without any calorific value.

Additives such as humectants, firming and crisping agents, sweeteners, emulsifiers, stabilizers, acid, and buffers are not commonly used in poultry feeds.

2.3.3 Additives That Facilitate Digestion and Absorption

Grit

Poultry does not have teeth to grind any hard grain, most grinding takes place in the thick musculated gizzard. The more thoroughly feed is ground, the more surface area is created for digestion and subsequent absorption. Hence, when hard, coarse, or fibrous feeds are fed to poultry, grit is sometimes added to supply additional surface for grinding within gizzard. When mash or finely ground feeds are fed, the value of grit becomes less. Oyster shells, coquina shells, and limestone are used as grit.

Buffers and Neutralizers

During the maximum production stage ruminants are given high doses of concentrate feeds for meeting demands for extra energy and protein requirement of the animal. The condition, on the other hand, lowers the pH of the rumen. Since many of the rumen microbes cannot tolerate low pH environment, the normally heterogeneous balanced population of microbes become skewed, favoring the acidophilic (acid-loving) bacteria. The condition often leads to acidosis and thereby upsets normal digestion. The addition of feed buffers and neutralizers, such as carbonates, bicarbonates, hydroxides, oxides, salts of VFA, phosphate salts, ammonium chloride, and sodium sulfate, has been shown to have beneficial effects. Recently the use of baking soda (NaHCO₃) has been shown to increase average daily gain by about 10%, feed efficiency by 5-10%, and milk production by about 0.5 L per head per day.

Chelates

The word "chelates" is derived from the Greek word "chele" meaning "claw" which is a good descriptive term for the manner in which polyvalent cations are held by the metalbinding agents. Prior to union with the metal, these organic substances are termed as "ligands." Ligand + mineral = chelate element.

Organic chelates of mineral elements, which are cyclic compounds, are the most important factors controlling absorption of a number of mineral elements. A particular element in chelated form may be released in ionic form at the intestinal wall or might be readily absorbed as the intact chelate. Chelates may be of naturally occurring substances such as chlorophyll, cytochromes, hemoglobin, vitamin B_{12} , some amino acids, etc. or may be of synthetic substances like ethylenediaminetetraacetic acid (EDTA).

Chelates as Feed Additives

Type I: Chelates that aid in transport and to store metal ions

Chelates of this group behave as a carrier for proper absorption, transportation in the circulatory system, and passing across cell membranes to deposit the metal ion at the site where needed. Among amino acids, cysteine and histidine are particularly effective metal-binding agents and may be of primary importance in the transport and storage of mineral elements throughout the animal body. Ethylenediaminetetraacetic acid (EDTA) and other similar synthetic ligands also may improve the availability of zinc and other minerals.

Type II: Chelates essential in metabolism

Many chelates of the animal body are holding metal ions in such a cyclic fashion which are absolutely necessary to be in that form to perform metabolic function. Vitamin B_{12} , cyto-chrome enzymes, and hemoglobin are some of the examples of this type. Hemoglobin molecule without its content of ferrous form of iron will be of no use in transporting oxygen.

Type III: Chelates which interfere with utilization of essential cations

There are some chelates found in the body which might have accidentally formed and are of no use to the subject. Rather, those chelates may be detrimental for the proper utilization of the element. Phytic acid-Zn chelate and oxalic acid calcium chelate are examples of this type.

2.3.4 Enzymes

Enzymes are the protein which has the property of catalyzing specific biochemical reactions. They are found in all plants and animals and are responsible for growth and the maintenance of health. Microorganisms also produce enzymes, and in recent years it has been possible to produce enzymes using microorganism on an industrial scale and extract and use these enzymes in a wide range of processes for the production of feed and natural products.

Poultry feeds are largely composed of plant and vegetable materials, and there are enzymes developed to degrade, modify, or extract the plant polymers found in some of the cereals and their by-products. The enzymes can be used to improve the feeding of poultry in the following ways:

- By improving the efficiency of the utilization of the feed
- By upgrading cereals by-products or feed components that are poorly digested
- By providing additional digestive enzymes to help poultry to withstand stress conditions, e.g., hot climates

Some of the cereals are compounds of polymers either of glucose (beta-glucan) or arabinose and xylose (pentosan or hemicellulose). These polymers are not well digested by poultry, and this can result in loss of energy in two ways. Energy may be lost because these polymers hinder the digestion of starch by coating starch granules and preventing the action of starch digesting enzymes in the intestine.

Energy may be lost because the animals own enzymes are not capable of degrading the polymers, and therefore they pass through the digestive system untouched. By adding microbial enzymes to the feed, these polymers can be degraded, and their energy value made available to the bird. The dual role of enzymes has been demonstrated in trials with barley-based feed supplemented with beta-glucanase, where the apparent increase in available energy was far in excess of that available in the beta-glucan of the barley. In this case not only was the problem of sticky dropping completely eliminated but the chicken's rate of growth was equivalent to that observed normally with feeds containing a higher energy density (e.g., wheat based).

Choice of Enzyme

- Because feed is normally composed of a single raw material of constant quality, it is important that the correct choice of enzyme product be made.
- Even in the case of a relatively well-defined problem such as that in barley, the use of multienzyme activity products has an advantage.
- The enzymes should fulfill the following criteria for practical application:
 - The enzymes must be active at the pH of the animals' digestive system and capable of surviving transit through the stomach.
 - They must be in a physical form in which they can be safely and easily mixed into all forms of animal feed.
 - The products should be of a high standardized activity that will remain stable both before and after incorporation into the feed or premix.

- The enzymes must be capable of surviving normal pelleting conditions.

2.3.5 Additives That Promote Growth and Production

Antibiotics

These are substances which are produced by living organisms (mold, bacteria, or green plants) and which in small concentration have bacteriostatic or bactericidal properties. They were originally developed for medical and veterinary purposes to control specific pathogenic organisms. Later, it was discovered that certain antibiotics could increase the rate of growth of young pigs and chicks when included in their diet in small amounts. Soon after this report, a wide range of antibiotics have been tested, and the following have been shown to have growth-promoting properties: penicillin, oxytetracycline (Terramycin), chlortetracycline, bacitracin, streptomycin, tyrothricin, gramicidin, neomycin, erythromycin, and flavomycin.

Increased weight gain is most evident during the period of rapid growth and then decreases. Differences between control and treated animals are greater when the diet is slightly deficient or marginal in protein, B vitamins, or certain mineral elements.

Mode of Action of Antibiotics

- Antibiotics "spare" protein, amino acids, and vitamin on diets containing 1-3% less protein, but balance experiments have often failed to show increased nitrogen retention. Growth stimulation has been greatest when the antibiotic penicillin supplement has been added to a ration containing no protein supplements of animal origin or to a ration low in vitamin B₁₂. Under hygienic conditions, growth increases are small.
- Intestinal wall of animals fed antibiotics is thinner than that of untreated animals which might explain the enhanced absorption of calcium shown for chicks.
- Reduce or eliminate the activity of pathogens causing "subclinical infection."
- Reduce the growth of microorganisms that compete with the host for supplies of nutrients.
- Antibiotics alter intestinal bacteria so that less urease is produced and thus less ammonia is formed. Ammonia is highly toxic and suppresses growth in nonruminants.
- Stimulate the growth of microorganisms that synthesize known or unidentified nutrients.

The following points should be kept in mind while using antibiotics for animal feeding:

- Antibiotics should be used only for:
 - Growing and fattening pigs for slaughter as pork or bacon
 - Growing chicks and turkey poults for killing as table poultry
- Antibiotics should not be used in the feed of ruminant animals (cattle, sheep, and goats), breeding pigs, and breeding and laying poultry stock.
- While adding antibiotics at the recommended level, care should be taken that they are thoroughly and evenly mixed with the feed.
- For best results, antibiotics should be used with properly balanced feeds. Also, the feeds containing antibiotics should be fed only to the type of stock for which they are intended.
- Antibiotics are not a substitute for good management and healthy living conditions or for properly balanced rations.

Probiotic and Prebiotic

The animal gut is composed of nearly a thousand different types of microorganisms, some of them are beneficial some are not. The gut microflora plays a very important role in health and disease condition of the living being. The healthy condition is due to the presence of beneficial bacteria which is also termed as probiotic or due to the intake of nutrients that stimulate the endogenous beneficial microbes (prebiotics).

A probiotic is defined classically as a viable microbial dietary supplement that beneficially affects the host through its effects in the intestinal tract (Sanchez and Rivas-Estilla 2006). Probiotics are live microbial feed supplements which are beneficial to the host animals and help to improve their intestinal microbial balance.

A prebiotic is defined as a nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon (Gibson and Roberfroid 1995). Use of prebiotic causes change in the colonic microflora composition with dominance of a few of the potentially health-promoting bacteria, especially, but not exclusively, *Lactobacilli* and *Bifidobacterium* (Gibson and Roberfroid 1995). Prebiotics target animal-associated microbiota with the goal of improving health, whereas probiotics use live microorganisms.

Probiotics

The genera of bacteria which are most frequently used as prebiotics are *Lactobacilli* and *Bifidobacterium*, *Enterococcus faecium*, and spore-forming *Bacillus* spp., while some yeasts are also used such as *Saccharomyces*. There are several new uses of probiotics that were previously unthinkable. But the efficacy of these is not misunderstood and consider for the cure of everything. Probiotics are very specific and They benefit the host by:

- Having a direct antagonistic effect against specific group of undesirable or harmful organism through production of antibacterial compounds, elementary, or minimizing their competition of nutrients
- Altering the pattern of microbial metabolism in the gastrointestinal tract
- Stimulation of immunity
- Neutralization of enterotoxins formed by pathogenic organism

Prebiotics

Prebiotics were recognized for their ability to manipulate host microbiota to the benefit of the host (Gibson and Roberfroid 1995). Prebiotics provide nutrients to favorable microorganisms raise by the host, including administered probiotic strains and indigenous (resident) microorganisms. Therefore, prebiotics are differing from most of the dietary fibers such as cellulose, xylans, and pectins which inspire the growth of a wide range of gut microorganisms. Currently, two main groups dominate the prebiotic category with their effects acting through enrichment of *Lactobacillus* and/or *Bifidobacterium* spp. thus resulting in increased growth rate and improved feed efficiency:

I. Fructans (fructooligosaccharides (FOS) and inulin)

II. Galactans (galactooligosaccharides or GOS)

2.3.6 Additives That Alter Metabolism

Hormones

These are chemicals released by a specific area of the body (ductless glands) and are transported to another region within the animal where they elicit a physiological response. Extensive use is being made of synthetic and purified estrogens, androgens, progestogens, growth hormones, and thyroxine or thyroprotein (iodinated casein) to stimulate the growth and fattening of meat-producing animals. There is concern, however, about possible harmful effects of any residues of these materials in the meat or milk for the consumers.

The whole question whether hormones should be used as growth promoters is still debatable, but it seems logical that with any feeding system, the economic advantages, however great, should never take precedence over any potential risk to human health. These substances may induce cancer in human beings if taken over a prolonged period through products of the treated animals. The use of such substances in poultry rearing has been prohibited by law in the USA.

Implant

Implants are hormone or hormone-like products that are designed to release slowly, but constantly, the active chemicals for absorption into the bloodstream. These are implanted subcutaneously in the ear [e.g., diethylstilbestrol (DES)].

2.3.7 Additives That Affect the Health Status of Livestock

Antibloat Compounds

Surfactants such as poloxalene are used as a preventive for pasture bloat, and several other products which have been shown to be highly effective to prevent bloat are also available in the market.

Antifungal Additives

Mold inhibitors are added to feed liable to be contaminated with various types of fungi such as *Aspergillus flavus*, *Penicillium cyclopium*, etc.

Before adding commercial inhibitors, all feedstuff should be dried below 10% moisture. Propionic, acetic acid, and sodium propionate are added in high-moisture grain to inhibit mold growth. Antifungals such as nystatin and copper sulfate preparations are also in use to concentrate feeds to prevent molds.

Anticoccidials

Various brands of anticoccidials are now available in the country to prevent the growth of coccidia which are protozoa and live inside the cells of the intestinal lining of livestock.

Anthelmintics

Under some practical feeding conditions, anthelmintics have also been used. The compounds act by reducing parasitic infections.

2.3.8 Phytogenic Feed Additive

Phytogenic feed additives are the products which are derived from plants to be used in animal feeding to improve the quality of feed, performance, and health of agricultural livestock and quality of food from animal origin. Since the last two decades, this group of feed additive gets immense interest among the farmers, especially for use in poultry and swine farming. This increase in popularity is due to the increase in number of scientific publication in this field since 2000 which is also supported by the ban on the most of the antibiotic feed additives within the European Union (complete ban enforced in 2006), voluntarily withdrawal of the use of antibiotics as growth promoters by the USA, and growing discussion to restrict their use outside European Union. This ban and discussion is driven by the speculated risk for generating antibiotic resistance in pathogenic microorganisms.

Awareness among the people regarding the potential health hazards and environmental harm caused by the excessive use of synthetic pharmaceuticals including in-feed antibiotics as growth promoters and growth hormones and also public demand for organic foods have gradually changed the attitude toward these synthetic antibiotics (Greathead 2003; Rochfort et al. 2008).

Restrictions on the use of antibiotics as growth promoters have significantly increased the incidence of infection by pathogens, consequently having an inimical effect on the performance of livestock. This also intensifies the search for an alternative to the antibiotics as growth promoters and popularizes the phytogenic feed additive. Phytobiotics as a feed additive is a new member in the list of non-antibiotic growth promoters, such as probiotics, prebiotics, and organic acids, which are already well known in the field of livestock nutrition. The knowledge about their mode of action and aspect of the application is still rather limited, and it has a lot of potential in the coming time.

Phytogenic feed additive is a wide range of plant-derived products such as herbs, essential/aromatic oils, and oleoresins. They can be added to the diet of commercial animals to improve their productivity through enhancing feed properties, promoting animal's production performance, and improving the quality of products derived from these animals (Windisch et al. 2008).

Windisch et al. (2008) has also recommended some commonly used terms to classify different phytogenic compounds based on their origin and processing, including herbs (flowering, non-woody, and nonpersistent plants), spices (herbs with an intensive smell or taste commonly added to human food), essential oils (volatile lipophilic compounds), and oleoresins (extracts derived by nonaqueous solvents). The content of active substances and the chemical composition of phytogenic substance in the final products may vary widely depending on the plant parts used (seeds, leaves, etc.), geographical origins, and harvesting season (Burt 2004; Bakkali et al. 2008; Wendisch et al. 2008). Selection of particular part of a plant of particular species of a very particular geographical region is very important to get a specific needed effect. The active constituents of the same species of plant may vary depending on the different geographical region and climatic condition. These variations are the results of genetic and environmental interaction and a manifestation of biodiversity within the same plant species (Zhang et al. 2011).

Plenty of research studies have indicated the multiple roles of phytobiotics as a feed additive like growth promotion effects, antimicrobial activity, antioxidant activity, antiinflammatory activity, etc. Based on the investigations, it seems that modulation of the gut environment and intestinal morphology in swine and poultry is the hypothesized mode of action of phytogenic feed additives (Stein and Kil 2006; Li et al. 2012) (Table 1).

Plant Secondary Metabolites (PSM)

The biological and therapeutic property of a medicinal plant is closely related to the phytochemicals in it. An extensive summary is required for a comprehensive overview of chemistry, biochemistry, and bioactivity of plant secondary metabolites because they are a very large group of compounds. Out of the more than 100,000 different compounds of natural origin that have been described, more than 80,000 are derived from plants (Hashemi and Davoodi 2010). These phytochemicals can further be classified into major groups such as alkaloids, tannins, saponins, steroids, essential oils, acids, etc.

Different classifications had been put forward to classify this broad range of phytogenic substances based on their source of origin, chemical composition, usage, mode of action, etc. Regarding classification of the phytogenic substances/phytobiotics with respect to biological origin, chemical composition, formulation, and purity, phytogenic substances comprise a very wide range and can further be classified into four groups as herbs (products from flowering, non-woody, and nonpersistent plants), botanicals (entire or processed part of a plant, e.g., root, leaves, and bark), essential oils (hydrodistilled extracts of volatile plant compound), and oleoresins (extracts based on nonaqueous solvents) (Windish and Kroismayr 2006) (Fig. 4).

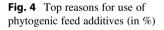
Classification of Phytogenic Based on Their Properties

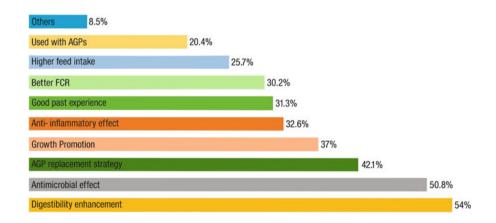
Antimicrobial, antioxidants and anti-inflammatory, growth promoters, palpability and gut function modulators, and immunomodulators

(I) Antibacterial Activity of Phytogenic Solutions

Herbs and spices are well known to exert antimicrobial actions in vitro against important pathogens including fungi (Windisch et al. 2008). A common feature of phytogenic compounds is that they are the very multifaceted mixture if bioactive component. Phytochemicals in phytogenic compounds are well known to have antimicrobial activity (Cowan 1999). Investigations on phytochemicals indicated that phenolic contents like carvacrol, thymol, phenylpropane, limonene, geraniol, and citronellal are the important active

Botanical name	Parts used	Important active constituents	Common uses	Reference
Asparagus racemosus	Root	Shatavarins I–IV, asparagamine	Galactogogue, antistress, immunostimulant	Ananthanarayana et al. (2002), Dahouda et al. (2009)
Acacia catechu	Stem wood extract, fruit	Catechin, quercetin, epicatechin	Antidiarrheal, anti-inflammatory, antioxidant	J.A. Duke (1992), Rastogi and Mehrotra (2005)
Allium sativum	Bulb	Allicin, allin, methyl allyl disulfide	Hypolipidemic, carminative, antiprotozoal, anti-inflammatory	Hussain et al. (1992), Sharma et al. (2000–2005)
Aloe barbadensis	Leaf	Aloin, barbaloin, emodin	Emmenagogue, anti-inflammatory, antibacterial	Blumenthal et al. (1998), Rastogi and Mehrotra (2005)
Balanites roxburghii	Fruit, seed, seed oil	Balanitisins A-E, marmesin, bergapten	Purgative, spasmolytic, anti-colic, anthelmintic	Bilore et al. (2004–2005), Hussain et al. (1992)
Cissus quadrangularis	Steam, root, leaves	Quadrangularins, piceatannol, pallidol	Fracture healing, useful in dyspepsia	Ananthanarayana et al. (2002), Rastogi and Mehrotra (2005)
Curcuma longa	Rhizome	Curcumin, turmerone, desmethoxycurcumin	Anti-inflammatory, carminative, spasmolytic, antioxidant, hepatoprotective	Blumenthal et al. (1998), J.A. Duke (1992), Hussain et al. (1992)
Eucalyptus globulus	Leaves, oils	Cineole, pinene, limonene, eucaglobulin	Anti-inflammatory, carminative, digestive, expectorant, antibacterial	Rastogi and Mehrotra (2005), Blumenthal et al. (1998), Hussain et al. (1992)
Glycyrrhiza glabra	Root	Glycyrrhizin, liquiritin, glabranins	Antihistaminic, expectorant, anti- inflammatory	J.A. Duke (1992), Blumenthal et al. (1998)
Leptadenia reticulata	Root	Hentriacontanol, stigmasterol, rutin	Galactogogue, stimulant, uterine cleanser	F. Mirzaei (2011), Hussain et al. (1992)
Ocimum sanctum	Whole plant, leave, oil	Eugenol, ursolic acid, carvacrol, luteolin, methylchavicol	Immunomodulator, anti- inflammatory, antitussive, antiprotozoal	Sharma et al. (2000–2005), D. Brown (1996), Rastogi and Mehrotra (2005)
Phyllanthus emblica	Fruit, leaves	Ascorbic acid, gallic acid, emblicanins A and B	Antioxidant, hepatoprotective, immunomodulator	Ananthanarayana et al. (2002), Rastogi and Mehrotra (2005)
Solanum nigrum	Whole plant	Solasodine, solasonine, solanine, solamargine	Hepatoprotective, antioxidant, mycotoxin inhibitor, diuretic	J.A. Duke (1992), Hussain et al. (1992)
Swertia chirata	Whole plant	Swertiamarin, swerchirin, gentianine	Hepatoprotective, anti-inflammatory, anthelmintic	Bilore et al. (2004–2005), Hussain et al. (1992)
Withania somnifera	Root	Withaferin-A, withanine, somniferin	Immunomodulator, antistress, antioxidant, adaptogenic	D. Brown (1996), J.A. Duke (1992)





compounds that have the antimicrobial function (Gheisar and Kim 2018). Limonene and compounds from Sanguinaria canadensis which are non-phenolic also show high antibacterial activity (Newton et al. 2002; Burt 2004). Yang

et al. (2015) suggested that the antimicrobial action of PFAs varies by the location of their functional hydroxyl or alkyl groups. Investigations show that the presence of delocalized electrons and the hydroxyl group of phenolic terpenoids are important elements for antimicrobial action of phytochemicals. Phytochemicals exert their antimicrobials activity through different mechanisms; tannins, for example, act by iron deprivation, hydrogen bonding, or non-specific interactions with vital proteins such as enzymes (Scalbert 1991). Tannic acid inhibits the growth of important intestinal bacteria such as Bacteroides fragilis, Clostridium perfringens, E. coli, and Enterobacter cloacae (Chung et al. 1993). Alkaloid is known to be a DNA intercalator and an inhibitor of DNA synthesis through topoisomerase inhibition (Karou et al. 2006). The main mechanism by which saponins display an antimicrobial activity is based on their ability to form a complex with sterols present in the membrane of microorganisms.

Essential oils have long been recognized for their antimicrobial activity (Lee et al. 2004), and they have gained much attention for their potential as an alternative to antibiotics in broiler chickens. Some studies with broiler demonstrated in vitro antimicrobial efficacy of essential oils against E. coli and Clostridium perfringens (Jamroz et al. 2003; Mistsch et al. 2004). Essential oils act on pathogenic bacteria by blocking quorum sensing (anti-quorum sensing) activity of the pathogenic bacteria. Extracts of plants of different species like Chamaesyce hypericifolia, Conocarpus erectus, and Quercus virginiana show quorum sensing inhibiting property and guard the growth of pathogenic bacteria (Adonizio et al. 2006). Moreover, structural properties such as the presence of functional groups (Farag et al. 1989) and aromaticity (Bowels and Miller 1993) are also responsible for the antibacterial activity of essential oils. It was postulated terpenoids regarding the that terpenoids and phenylpropanoids can penetrate the membrane of the bacteria and reach the inner part of the cell because of their lipophilicity (Helander et al. 1998). The important benefits of antimicrobial action of phytogenic products are that they can improve the microbial hygiene of carcasses. Aksit et al. (2006) illustrate that the addition of essential oil reduces the load of total viable bacteria or pathogens (e.g., Salmonella) on broiler carcasses.

(II) Antioxidant and Anti-inflammatory Action

Antioxidant activity is one of the important properties of phytogenic products which contribute to the reason for use as feed additives in humans as well as animals. Their ability to scavenge free radicals may play an important role in preventing some diseases caused by free radicals, such as cancer and heart diseases (Miguel 2010). The previous investigation has suggested that the antioxidant activity is due to their ability to donate hydrogen or an electron to free radicals and also delocalize the unpaired electron within the aromatic structure which are the main mechanisms of protecting other biological molecules against oxidation (Fernandez-Panchon et al. 2008; Giannenas et al. 2013). Brenes and Roura (2010) have reported that a wide range of herbs and their extracts have potential antioxidant functions, especially those products derived from the plant family Labiatae such as rosemary, oregano, and thyme. Blending of the phytogenic products like thyme in the feed of the ducks causes the reduction in thiobarbituric acid reactive substances (TBARS) value of breast meat significantly (Mohammadi et al. 2015a). Cherian et al. (2013) reported that feeding broiler chickens with PFA (Artemisia annua) resulted in a significant reduction in TBARS value in breast and thigh meat. The reduction in TBARS value might be due to an individual or shared antioxidant properties of polyphenolic compounds or vitamin E in Artemisia annua. The antioxidant activity of the phytogenic products is due to both phenolic and non-phenolic content (Cuppett and Hall 1998). Placha et al. (2014) have demonstrated that supplementing the diet of broiler chickens with thymol can reduce the oxidation of fatty acids indicated by the lower malondialdehyde level in duodenal mucosa. Franz et al. (2010) have advocated that phytobiotics can beneficially affect some antioxidant enzymes such as glutathione peroxidase and superoxide dismutase, consequently affecting lipid metabolism in animals. Other plant species such as coriander, curcuma, ginger, anise, and plants that are rich in flavonoids or anthocyanins also have antioxidant activities (Nakatani 2000; Wei and Shibamoto 2007). The active compounds of phytogenic compounds may have protective roles for feed lipids against oxidative damage, similar to antioxidants such as a-tocopheryl acetate or butylated hydroxytoluene that is usually added to diets (Gheisar and Kim 2018).

Inflammation is the normal protective phenomenon induced due to injury to the tissue or infection to counter invaders in the body (pathogens) and to remove dead or damaged host cells (Stevenson and Hurst 2007). Miguel (2010) stated that some essential oils have the ability to scavenge free radicals. In addition, they can also act as antiinflammatory agents because one of the inflammatory responses is oxidative burst in diverse cells. Essential oils (eucalyptus, rosemary, lavender, millefolia) and other plants (pine, clove, and myrth) are also used in mixed formulations as anti-inflammatory agents.

(III) Growth-Promoting Property

Regarding the growth-promoting activity of the phytogenic compounds, lots of investigations have been conducted during the last two decades. The growth-promoting activity of the herbal feed additive has been reported in swine (Wenk 2003; Kim et al. 2010; Mohammadi et al. 2015b). Li et al. (2012) compared the performance of pigs fed with the diets supplemented with essential oils and reported weight gain and digestibility of dry matter, and

crude protein were improved by 10.3%, 2.9%, and 5.9%, respectively. They suggested that improved performance of pigs was the result of improvement of the intestinal morphology and consequently improvement of nutrients digestibility. Yan et al. (2011) have reported that adding an herb extract blend (containing buckwheat, thyme, curcuma, black pepper, and ginger) to the diet of growing pigs resulted in increases in average daily feed intake (ADFI) and final body weight (BW). Feeding broiler chickens with the diet containing 0.075% of a phytogenic blend led to 3.9% and 3.4% improvement in BWG and FCR, respectively (Mohammadi et al. 2015a). According to the researcher proposal, phytogenic compounds act differently to elicit its growthpromoting activity. Improving palatability and flavor of feed, increasing feed intake, stimulating the secretion of digestive enzymes, and increasing antimicrobial activity are some of the main modes of action that might have led to the improved growth performance of animals (Jang et al. 2004; Czech et al. 2009). Different investigations have suggested that removal of in-feed antibiotics has resulted in the significantly negative effect on the performance of pig and poultry. This negative effect can be alleviated by incorporation of phytogenic product as growth promoters in the feed of pig and poultry (Yakhkeshi et al. 2011).

(IV) Influence on Palatability and Gut Function

It is claimed that phytogenic products are positively effective on the palatability and flavor of feed, thus promoting feed utilization and enhancing the production performance (Windisch et al. 2008). Some investigators had found a decrease in the feed intake due to incorporation of phytogenic products as growth promoters in feed (Maass et al. 2005; Roth-Maier et al. 2005), while some are claiming phytogenic solutions cause increase in the feed intake and palatability of feed (Kyriakis et al. 1998; Kroismayr et al. 2008). Chrubasik et al. (2005) have reported that a wide range of phytobiotics (including herbal plants and their extracts) are known to have beneficial impacts on the digestive tract (such as laxative and spasmolytic effects). In addition, they can prevent flatulence. Furthermore, Patel and Srinivasan (2004) have suggested that phytogenic substances can stimulate digestive secretions such as saliva and bile. They reported that improving enzyme activity is the main mode of nutritional action of phytogenic feed additive (PFA). Rao et al. (2003) have reported that the in vitro activities of rat pancreatic lipase and amylase are significantly enhanced when they were in contact with various spices and spice extracts. There is increase in enzymatic activities in pancreatic homogenate and pronounced bile acid flow in rats fed with phytogenic feed additive (Patel and Srinivasan 2000). Similar reports of enhancing the activities of digestive enzymes such as pancreatic amylase, trypsin, and maltase by essential oils in the diets of broiler chicken were given by researchers (Lee et al. 2003; Jang et al. 2004, 2007). Jamroz et al. (2006) suggested that feeding broilers with a diet supplemented with PFA resulted in stimulating the secretion of mucus in the intestine of broilers. This effect was assumed to reduce the adhesion of pathogens, thus stabilizing microbial eubiosis in the gut of animals.

(V) Immunomodulators

Phytogenic additives are having potential effect on the immune system of living organisms. β -glucans (oligosaccharide) is found in plant components mainly in aleuronic layer of barley and oat bran is an important immunomodulator. Bamboo leaf extract appears a new and promising source of β -glucans. Ohtsuka et al. (2014) evaluated the effect of an extract of β -glucans obtained from bamboo leaves (*Sasa sensanensis*) in cattle and report the increase in the activity of CD8⁺T lymphocytes.

3 Quality Standards for Animal Feed Additive Industry

Faced with the problem of increasing nutritive value of the feed with limited resources of land and capital, soon it was discovered that unwanted chemicals and adulterants were being used in animal feeds and it helped to have a high analytical grading for the feed. So, came in place quality standards which laid down guidelines for the manufacturing to marketing of the animal feed and set up regulations which made it mandatory for feed manufacturers to abide by the set standards.

One of the premier authorities in the world with respect to animal feed industry—the American Feed Industry Association (AFIA)—has defined feed quality-control programs as: "All actions directed towards ensuring the product meets the specifications established by the manufacturer." AFIA is one of the most premier organizations (Maurya 2017). Any standard feed quality-control program must contain four necessary components (Pal and McSpadden Gardener 2006):

- Ingredient quality
- · Process control
- Finished feed quality
- Control of toxic substances, including pathogenic microorganisms

3.1 The Importance of Quality Assurance

Quality assurance is one of the most important criteria in maintaining the industry standards and also to apply for various certifications related to product manufacturing practices and standards. It creates a market value for the product and greater consumer acceptability. It needs to be understood that feed safety is not the only element that determines the safety of food of animal origin but that the use of other products, such as drugs and growth promoters (hormones and beta-agonists), also has an impact.

3.2 Quality Control of Feed

The process of conversion of high-quality ingredients into high-quality feeds involves three important components within the feed mill: personnel, machinery, and procedures. In event of any compromise in any of these three components, the consistent production of high-quality feeds is unlikely.

However, it is equally important to ensure the blending of personnel, machinery, and procedures together toward the common goal of efficient production of high-quality feeds (Jones 2006). Quality control in feed plant is of utmost importance for overall success and profitability of animal enterprises. The most critical factors affecting nutrition and high performance of animals are feed quality control and ration consistency. The degree of quality is the consistency in which feed is formulated, processed, produced, and delivered as compared to what is expected.

Quality has been defined as "Degree to which a set of inherent characteristics fulfills requirements" (Garg et al. 2013). This clearly indicates that achieving quality means fulfilling requirements. The requirements may come from customers and in some cases from regulatory authorities. Usually quality is verified by comparison with a known standard. However, a relative value of quality over time is extremely valuable and useful in many situations.

Animal performance is directly affected by feed quality, and this relationship is important as it not only encompasses the quantitative amounts of all feed components but also the digestibility and metabolism of those components. Thus, the main challenge that lies for animal science researchers as well as for nutritionists and other stakeholders involved in feed production is the consistent monitoring of all the aspects of feed production system and measurement of those variables that are good indicators of quality control.

In some cases, post-marketing quality checks are done to keep a tab on shelf life as well as customer satisfaction as it can have an enormous impact on quality as perceived by them. In view of this, monitoring of quality control at different points has been classified as under:

- · Quality control of raw materials and finished products
- Quality control during storage
- Quality control during production

3.3 Necessity for Quality Control

The objective of quality control of animal feed and feed additives is to ensure that consumer obtains feeds that are unadulterated and true to their nature and produce desired results. Quality control is, therefore, defined as the maintenance of quality at levels and tolerances acceptable to the buyer while minimizing the cost of processing.

The Bureau of Indian Standards is the nodal organization responsible for laying down the quality control specifications of various feed ingredients and compound feeds to ensure maintenance of the minimum contract specifications, suitable for inclusion in the compounded feeds, and indicating the maximum proportions of inclusion of feedstuffs (Uppal et al. 2004).

3.4 Evaluation of Feed for Quality

The feeds are usually subject to the following three types of tests: physical, chemical, and biological.

3.4.1 Physical Evaluation

Physical evaluation must be carried out by highly trained personnel to identify the changes in the nature of the raw material/ feeds. The main attributes checked in a physical evaluation are color, size, homogeneity, smell, taste, touch, and sound.

Physical Methods to Detect Adulteration or Contamination

The common contaminant or adulterant is husk or sand. The best method to detect husk in the feedstuff is winnowing while sieving is performed for differentiating contaminants based on particle size. Sand is detected in feed using a traditional yet effective method where a weighed quantity of the grain is soaked in water and then by sieving with hand the grains can be separated. The remaining water is decanted, and the settled sand is weighed to assess the level of contamination.

3.4.2 Chemical Evaluation

For chemical evaluation of animal feed, the first and foremost requirement is that of an analytical laboratory for precise estimation of nutrient contents and contaminants. Proximate principles of feed are analyzed using chemical evaluation.

3.4.3 Ingredient Specifications

Ingredient specifications of animal feeds and feed additives are crucial in a feed quality assurance program. Ingredient specifications serve as the basis on which agreements are written, feed/rations are formulated, and ingredient inspections are performed. Description of feed ingredients and general nutritional specifications may be found in BIS specifications for feeds and feed ingredients in India. It is done both for quantitative and qualitative specifications and standards.

3.5 Quality Control Legislations in Indian Feed Industry

In the organized sector, animal feed production is a competitive domain, and feed producers therefore attempt to produce feed of the highest possible quality (Dhobi and Malla 2015). Regular analysis of proximate principles is done for keep a check on the quality of feed. The animal feeds and feed additives are analyzed for amino acids, aflatoxin, ochratoxin, castor, tannins, and urease activity compulsorily among others. Raw materials employed in manufacturing of animal feed and finished products are subjected to microbial examinations such as microbial counts. Salmonella and Escherichia coli testing and mold count as well. Industry also employs latest technologies and modern equipment such as High-Performance Liquid Chromatography (HPLC) and near-infrared (NIR) analyzers for spectroscopic examination. Current analytical techniques are engaged to estimate vitamins, minerals, and other feed additives. Most of industries are promoting HACCP-Hazard Analysis and Critical Control Points- measures to guarantee safe feeds. Now, India is also following international standards of animal feed industry to upgrade its manufacturing standards and compete with the world market by indigenous manufacturing of animal feed and feed additives to reduce the cost as well.

In India the national quality control standards for manufacture and storage conditions of animal feeds and feed additives are regulated by a statuary body, the Bureau of Indian Standards (BIS). It was established under BIS Act, 1986. Before 1986, Indian standards Institute was regulating the quality control of several feed commodities. The objectives of BIS are as follows:

- I. Harmonious development of the activities for standardization of various commodities
- II. Marking
- III. Quality certification of goods
- IV. Attending to the connected methods

The Bureau has set up subcommittees for the standardization of different types of commodities. A subcommittee on animal feeds called Animal Feeds Sectional Committee has been specifically set up to check the quality of animal feeds and feed additives ingredients. The members of Animal Feeds Sectional Committee are a panel of eminent nutritionists and comprise of expert members from the following bodies:

- I. Indian Council of Agricultural Research (ICAR) institutes
- II. State agricultural universities
- III. Feed industry
- IV. Government departments having specialization in animal nutrition
- V. Feed technologist concerned with animal husbandry activities

The Government of India is empowered with registration act on the Agricultural produce (Grading and Marketing), known as 'AGMARK' standards to fix quality standards and prescribe terms and conditions for using the seal, 'AGMARK'.

Government is also bound to ensure following of control measures by legislation to ensure quality and safe feeds and feed additives at controlled cost. Many regulations have been put forward:

- I. The Prevention of Black Marketing and Maintenance of Supplies of Essential Commodities Act, 1980
- II. The Standards of Weights and Measures (Packaged Commodities) Rules, 1977
- III. The Consumer Protection Act, 1986
- IV. Schedule of Tariff Values of the Articles Liable to Cess for 2006–2007
- V. Agricultural Produce Cess Act, 1940
- VI. Edible Oils Packaging (Regulation) Order, 1998
- VII. The Prevention of Food Adulteration Rules, 1955

The latest legislation in this respect is Cattle Feed (Regulation of Manufacture and Sale) Order, 2009. However, in spite of all legal presence of these measures and legislations, feed quality checks in India leaves much to be desired. All said and done, not enough is done to keep a cap on feed quality in this country. This is very much factual for smallscale feed manufacturer, where adulteration is barricade.

The nodal organization involved in India toward developing interlinkages between industry academia and other sectors toward feed manufacturing practices and setting quality norms is the Compound Livestock Feed Manufacturers' Association (CLFMA).

3.6 Latest Developments in Feed Quality Assurance Sector in the World

Safe animal feeds can only be produced with safe ingredients. In order to combine the experience of existing feed ingredient assurance programs into one program that can operate across the world with one set of standards, the International Feed Safety Alliance (IFSA) as a joint project is initiated by the standard owners (IFSA Feed Ingredients Standard 2007). To comply with the standards of IFSA, the participant countries need to apply the principles of Hazard Analysis and Critical Control Points (HACCP) and Good Manufacturing Practice (GMP). Participants certified will have to demonstrate that there are controls at each step of the supply chain that guarantee the safety of the feed constituents supplied.

3.6.1 GMP: Good Manufacturing/Managing Practice

A key point for attention in the quality control programs for animal husbandry is the safety of animal feed. GMP standard is one of the main elements for any animal feed quality program (Coelho and de Toledo 2017).

3.6.2 Risk Management

Risk assessment forms the basis for determining control measures. Risk assessment is a component of risk management, resulting in:

- Determination of control measures for eliminating or reducing these risks and controlling them at an acceptable level, including tracking and tracing of products
- Determination of product standards and action values for undesirable contaminants in feeds
- Implementation of a measuring strategy (monitoring and verification) for checking whether or not the control measures are effective

In an HACCP methodology, a well-considered and sensible balance has to be established between preventive procedures and monitoring of feed constituents for the presence of risks. Nevertheless, where there are uncertainties about the ability to get a hold on the risks, precautionary measures such as eluding use of a specific product must be taken. Several control measures and product standards have already been combined in legislation, but they are moderately fragmented with many limitations. To address this shortcoming, the GMP+ standard for animal feed offers a coherent framework.

The GMP+ standard currently comprises the following elements:

- General requirements for a company's quality system, comparable with and based on the ISO 9002 standard, in order to render quality assurance demonstrable.
- Criteria for risk assessment based on HACCP principles.
- Several additional sub-codes including generic control measures in the production process allied to the use of additives, drugs, undesirable substances, and hygiene (*Salmonella*). These additional control measures have been specified for the production and supply of compound feedstuffs, premixes, straight feedingstuffs and feed

• Minimum requirements for in-company inspections, such as quality assurance for laboratory analyses, sampling frequency, etc.

A set of product standards, comprising of European Union legal standards, additional national legal standards, and several supra-legal standards settled with the partners in the chain.

3.6.3 Early Warning System

An early warning system (EWS) is intended to be a safety net, as a supplement to quality management systems like GMP, ISO 9002, and HACCP. The goal is to identify, communicate, and eliminate possible or potential hazards which may occur despite all preventive measures taken (Stark and Jones Frank 2009).

No quality system is able to avoid totally all problems which may be caused by incidental factors (human error, natural events) or criminal acts. A proactive approach must be adopted to prevent potential hazards manifesting themselves. Key elements in such a system include speed, care, confidentiality, accountability, and responsibility.

3.6.4 International Legislations Associated with Feed Safety

Food hazards associated with feeds form an important part of public health importance. Hazard is defined as "A biological, chemical or physical agent in, or condition of, food/feed with the potential to cause adverse health effect" (Sareen 2010).

Under WTO, SPS Article 3 which deals with harmonization encourages use of international standards for food safety and animal and plant health, i.e., Codex. Important Codex work on feed safety includes:

- Classification of foods and animal feeds (CAC/Misc 4-93)
- Codex General Standard for Contaminants and Toxins in Foods and Feeds (CODEX STAN 193-1995)
- MRLs for pesticides (CAC/MRL 1-2009), veterinary drug (2-2009), extraneous MRLs (CAC/MRL 3-2001)
- Code of Practice for the Reduction of Dioxin and Dioxinlike PCB Contamination in Foods and Feeds (CAC/RCP 62-2006)
- Code of Practice for the Reduction of Aflatoxin B1 in Raw Materials and Supplemental Feedingstuffs for Milk-Producing Animals (CAC/RCP 45-1997)
- Code of Practice on Good Animal Feeding (CAC/RCP 54-2004)

Other Codex Standards: Applicable to Feeds

Traceability: Principles for traceability/product tracing as a tool within a food inspection and certification system (CAC/GL 60-2006)

Risk Analysis:

- Working principles for risk analysis for application in framework of Codex Alimentarius
- Principles and GL for the conduct of microbiological risk management
- GL for conduct of food safety assessments of foods derived from recombinant-DNA animals
- Principles for the risk analysis of foods derived from modern biotechnology

HACCP: Recommended International Code of Practice—general principles of food hygiene (4 rev 2003) and Annex on HACCP systems and GL for its application

- Emergency situation—principles and guidelines for exchange of information in food safety emergency situations (CAC/GL 19-2004)
- Inspection & certification—principles (CAC/GL 20-1995); GL for design, operation, assessment & accreditation of food import & export inspection & certification systems (CAC/GL 26-1997)

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