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Aloe Vera as potential emerging herbal feed additive: A boon for livestock rearing

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Abstract

Aloe vera (*Aloe vera* (L.) burm. f.) is a member of Asphodelaceae (Liliaceae) family and mainly grows in the tropical or subtropical part of Africa, Asia, Europe and America, whereas in India, found in Rajasthan, Andhra Pradesh, Gujarat, Maharashtra and Tamil Nadu. Aloe vera known for its medicinal value from ancient history of India, Egypt, Greece, Rome and China and have been mentioned throughout recorded history and given a high ranking as an all-purpose herbal plant. There are over 250 species of aloe grown around the world. However, only two species are grown today commercially, with *Aloe barbadensis* Miller and *Aloe aborescens* being the most popular. Presently, the use of aloe vera has gained great attention because of its use as herbal feed additive in livestock and poultry feeds. Animal nutritionist is trying to exploit the potential use of aloe vera as a growth promoter and in this connection they have done lots of studies related to nutrition.

Keywords: Aloe vera, feed additive, medicinal importance

1. Introduction

Recently the ban on the use of antibiotic as a growth promoters (AGP) in animal feeds, due to their residual effect in animal products as well as development of bacterial resistance in animals and human body, have make a way to look for alternatives of antibiotics in order to eliminate their impact on animals (Yang *et al.*, 2009) [95]. Many feed additives like prebiotics, probiotics, organic acids and plant extracts have beneficial effects on animal production. Medicinal herbs properties to improve digestibility, antimicrobial, anti-inflammatory, antioxidant and immune-stimulant activity must be exploited in feeding of animals as well as safe food product for human beings. Now a day's aloe vera popularly used by naturopaths, yoga gurus, alternative medicine promoters and feed additives. Given the significance of healthy animal food as well as human health, a broader range of research is dedicated to replace antibiotic growth promoter (AGP) with other additives, especially probiotics, prebiotics, enzymes, organic acids, and herbs (Verstegen and Williams, 2002) [94]. Many studies have been carried out on using additives, including medicinal herbs, as alternatives to antibiotics, with direct or indirect effects on animal growth and performance. Medicinal herbs, as a new class of additives to animal and poultry feeds have beneficial properties such as antioxidant, antimicrobial, and antifungal (Hardy, 2002) [42] as well as immunomodulatory and anticoccidial effects, which lead to increased use of herbs. Furthermore, many countries around the world, with plenty resources of different kinds of medicinal herbs, can use these herbs as natural feed additives for animals and poultry. The main emphasis is on those herbs that are used to supplement feeds, are helpful in achieving a larger number of objectives (improving nutrient utilization and growth performance, immunity response, intestinal microflora, and controlling particular diseases); in other words the focus is on multifunctional herbs.

The most important part of aloe vera is leaf which is composed of two main sections: latex and gel (Boudreau and Beland, 2006) [10]. The gel is composed of about 98.5-99.5% water (Femenia *et al.*, 1999) [32], and the remaining dry matter contains more than 75 biologically active ingredients (Boudreau and Beland, 2006) [10] which have medicinal effects that are useful in treating diseases. Major ingredients of aloe vera include anthraquinones, polysaccharides, vitamins, enzymes and low molecular weight compounds (Choi and Chung, 2003) [14] which gives aloe vera its antiinflammatory, immunomodulatory, wound healing, antiviral, antifungal, antitumor, antidiabetic and antioxidant effects (Christaki and Florou-

Paneri, 2010) [15]. Number of studies have suggest that many benefits of aloe vera are due to its polysaccharides contained in gel, which compose a large part of dry matter in this gel (Hamman, 2008) [40]. Almost 60% of dry matter of aloe vera gel is composed of polysaccharides (McAnalley, 1989) [65] and active compound is acemannan which has immunomodulatory, antimicrobial, and antitumour effects (Choi and Chung, 2003) [14], antioxidants, wound healing, immune-modulatory and antidiabetic activities (Pandey *et al.*, 2010) [77].

2. Chemistry of Aloe Vera

The chemistry of aloe vera is quite complex and it has more than 200 different types of bioactive molecules (Davis, 1997) [24] which is responsible for its medicinal and growth promoting properties. The aloe vera leaf gel contains about 98% water (Bozzi *et al.*, 2007) [11] whereas, total solid content of aloe vera gel is 0.66% and soluble solids are 0.56%. On DM basis aloe gel consists of polysaccharides (55%), sugars (17%), minerals (16%), proteins (7%), lipids (4%) and phenolic compounds (1%). The gel also contains number of vitamins including the important antioxidant, vitamins A, C and E. Vitamin B₁ (thiamine), niacin, Vitamin B₂ (riboflavin),

choline and folic acid (Lawless and Allen, 2000) [58]. Also contains many minerals like calcium (involved in teeth and bone formation, muscle contractions and heart health), magnesium (provides strength to teeth and bones, maintains healthy muscles and nervous system, activates enzymes), zinc (speeds up wound healing, mental quickness assists with healthy teeth, bones, skin, immune system, and digestive aid), manganese (activates enzymes, builds healthy bones, nerves and tissues), chromium (assists with protein metabolism and balancing of blood sugars), selenium which all influence our brain performance. Additional minerals found in aloe vera include copper, iron, potassium, phosphorus and sodium, aloe vera also contains the trace minerals of rhodium and iridium used in cancer and tumor research experiments. Many of the medicinal effects of aloe leaf extracts have been attributed to the polysaccharides found in the inner leaf parenchymatous tissues (Davis *et al.*, 1994) [25], but it is believed that these biological activities should be assigned to a synergistic action of the compounds contained therein rather than a single chemical substance (Domkat *et al.*, 2013) [29]. The chemical constituents of aloe vera leaves including the pulp and exudate are shown in Table 1.

Table 1: Chemical composition of Aloe vera (Ni and Tizard, 2004; Dagne *et al.*, 2000; Choi and Chung, 2003; Surjushe *et al.*, 2008) [14, 18, 73, 91]

Class	Compounds	Properties
Anthraquinones/anthrones	Aloe-emodin, aloetic-acid, anthranol, aloin A and B, isobarbaloin, emodin, ester of cinnamic acid	Aloin and emodin-analgesics, antibacterials and antivirals
Carbohydrates	Pure mannan, acetylated mannan, acetylated glucomannan, glucogalactomannan, galactan, galactogalacturan, arabinogalactan, pectic substance, xylan, cellulose	Alprogen- antiallergic, anti-inflammatory
Chromones	8-C-glucosyl-7-O-methylaloeol, 8-C-glucosyl-(S)- aloesol, 8-C-glucosyl-7-O-methyl-(S)-aloesol, 8-C-glucosyl-7-O-methylaloeol, 8-C-glucosyl-noreugenin, isoaloesin D, isorabaichromone, neoaloesin A	Anti-inflammatory
Enzymes	Alkaline phosphatase, amylase, carboxypeptidase, catalase, cyclooxygenase, cyclooxygenase, lipase, oxidase, phosphoenolpyruvate carboxylase, superoxide dismutase	Bradykinase- reduce excessive inflammation while others help in the breakdown of sugars and fats
Inorganic compounds	Calcium, chlorine, chromium, copper, iron, magnesium, manganese, potassium, phosphorous, sodium, zinc	Essential for proper functioning of various enzymes
Miscellaneous	Arachidonic acid, γ -linolenic acid, steroids (campesterol, cholesterol, β -sitosterol), triglycerides, triterpenoid, gibberillin, lignins, potassium sorbate, salicylic acid, uric acid	
Amino acids	Alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, hydroxyproline, isoleucine, leucine, lysine, methionine, phenylalanine, proline, threonine, tyrosine, valine	
Proteins	Lectins, lectin- like substance	Lignin- penetrative effect into skin Saponins- soapy substances, antiseptic properties
Saccharides	Mannose, glucose, L-rhamnose, aldopentose	
Vitamins	B ₁ , B ₂ , B ₆ , C, β -carotene, choline, folic acid, α -tocopherol	Vitamin A, C and E- antioxidant

Table 2: Proximate composition and biochemical activity of Aloe vera leaves (Ahmeda and Hussainb, 2013) [1]

Attributes	%	Biochemical activity in 1/10 i.e. 1 mL extract/10 mL distilled water	%
Ash	16.88	Superoxide dismutase (IU/mg)	2830.19
Crude fibre	73.35	Peroxidase (IU/mg)	3.72
Crude protein	6.86	Catalase (IU/mg)	2.80
Crude fat	2.91	Amylase (IU/mg)	24.02
Ascorbic acid	0.004	Reducing sugar (mg/ml)	123.33
		Total soluble sugars (mg/ml)	363.03

3. Biological activities of aloe vera in livestock and poultry

3.1 Effects of aloe vera supplementation on growth performance

Higher body weight gain, better feed conversion efficiency (FCE) and production of milk, meat and eggs are important economic goals in livestock and poultry farming. Earlier these goals are achieved by feed additive like antibiotics, but ban on application of antibiotic growth promoter (AGP) have affected these goals, resulting in poor growth performance

and production of animals. Many researchers have done to examine potential effects of feed additives, like prebiotics, probiotics, organic acids and herbs, on growth performance and production compared to those of antibiotics. An experiment conducted by Khan *et al.* (2014) [55] on birds fed diet supplemented with 1 % or 2 % aloe vera leaves had greater body weight gain, better feed intake and FCR than those fed diets without aloe vera leaves.

An experiment comparing the effects of aloe vera gel (mixed with feed) and AGP (virginiamycin) indicated that AGP resulted in better growth performance compared to the performance of groups that received aloe vera gel (at 1.5%, 2% and 2.5%), and the control group while no significant difference was observed between the antibiotic group and the 2% aloe vera gel group in terms of body weight gain and FCR (Darabighane *et al.*, 2011b) [22]. These results are agreed with findings of Mehala and Moorthy (2008) [66]. Similar to this finding, Mmereole (2011) [68] also observed that at 1 % dietary inclusion of aloe vera leaves powder in broiler diet, there was significant difference in body weight gains in birds fed aloe vera supplemented feed as compared to control group. However, Odo *et al.* (2010) [74], reported that, higher weight gain in birds fed 5 % level of inclusion aloe vera than those of 10 % and explained that aloe vera in large quantitative exerts a powerful purgative effect but in smaller quantity. In another study, Alemi *et al.* (2012) [5] reported a better growth performance in broilers treated with 0.75% and 1% aloe vera gel powder compared to the 0.5% aloe vera gel powder group and the control group. In support of this, Danhoff and McAnally (1988) [20] observed that the feeding of aloe vera accelerated the growth of new cells, thereby resulting to increase body weight. Contrary to above studies, Hassanbeigy Lakeh *et al.* (2012) [44] have observed that the supplementation of aloe vera gel (0.6, 1.2, 1.8, 2.4 and 3 mL) in broiler drinking water had no effect on feed intake over the total experiment period however, higher body weight gain and the smallest FCR was observed in the 1.8 mL aloe vera gel group. Das *et al.* (2011) [23] stated that the addition of 10 ml aqueous extract of aloe gel per litre of drinking water in broiler have beneficial effect on body weight gain and feed conversion efficiency that could be due to diversified antimicrobial activity of aloe vera gel. Actually, polysaccharides of aloe vera (mainly, acemannan) has prebiotic like effect which increase the number of lactobacillus colonies and reduce gram negative bacteria (Darabighane *et al.*, 2012) [21]. The fermentation product of lactobacillus is short chain fatty acid that will reduce the pH of lower intestine and create favorable environment for gram negative bacteria. Olupona *et al.* (2010) [75] have also observed that supplementation of aloe vera in drinking water had beneficial effect on final body weight, weekly body weight gain, and average feed intake. There are limited studies on aloe vera as herbal feed additives in pigs. However, in an experiment Qiao *et al.* (2013) [82] found that the 0.05 % aloe vera polysaccharide (AVP) shown better effect on growth of weaned piglets than 0.02 % AVP. They also found that, supplementation with higher concentrations of AVP not only increased ADG, but decreased the incidence of diarrhoea and weaning stress as well.

3.2. Anti-coccidial activity

Coccidiosis is one of the dreaded diseases in poultry that affects mainly intestine that leads to impairs feed utilization, decreases broilers growth and egg production of laying hens and causes death of birds Lillehoj *et al.* (2004) [60]. Generally, *Eimeria* (*E.*) species responsible for coccidiosis in chickens include *E. tenella*, *E. necatrix*, *E. acervulina*, *E. maxima*, *E. brunetti* and *E. mitis* (Ayaz *et al.*, 2003; Shah *et al.*, 2009) [7, 87]. These species infect epithelial cells of the bird's intestine causing enteritis, bloody diarrhea and immune-suppression in chickens that paves the way to secondary disease conditions. Therefore, poultry disease management and maintenance of the immune functions for maximum consistent production

performance and growth in poultry industry are fundamental requirements for profitable farming. An excellent way to meet these requirements is to use anticoccidial drugs, chemotherapeutic and biological agents including vaccines (Lillehoj and Trout, 1996; Mehala and Moorthy, 2008) [61, 66]. Nevertheless, development of resistant pathogenic strains and drug residues in animal products used by the human beings are the major constraints in this regard (Delespoux and Koning, 2007; Reig and Toldra, 2008) [27, 83]. The increasing resistance to avian coccidiosis to anticoccidial drugs currently used by the poultry industry together with the requirement for drug and antibiotic free production systems has meant that it is now important to look for new ways to control the diseases. In this regard, aloe vera has been shown to have diverse biological activities. It has been used therapeutically for centuries and is of particular interest due to its historic reputation as a curative agent and dietary supplement (Mehala and Moorthy, 2008) [66].

In an experiment Akhtar *et al.* (2012) [2] observed that the orally administration of aloe vera extract (ethanol and aqueous extract) in the broiler chicken has significantly lowered the oocyst count in faeces with compared to control group. They also found that the broilers that received aqueous extract of aloe vera pulp had the lowest mean score lesion in caeca and intestine in comparison to the control group and the group that received ethanol extract of aloe vera pulp. Similar to this, Mwale *et al.* (2006) [71] also found that the increase in aloe vera and aloe spicata content significantly decreases coccidian oocyst count. A comparative study has done by Gadzirayi *et al.* (2005) [35] and reported that the anticoccidial effects of *A. excelsa* were comparable with sulphachlopyrazine sodium monohydrate in terms of improved live weight gains and reducing oocyst output in broiler chickens. Aloe vera treatments show tonic effects on the intestinal tract by benefiting microflora and reducing bowel putrefaction as well as reducing inflammation (Bland, 1985) [8].

In an *in vitro* trial done by Marizvikuru *et al.* (2006) [62] to know the effect of three concentrations (15%, 30% and 45%) of Aloe vera (*L.*) and *A. spicata* on the inhibition of the sporulation of avian coccidia oocysts. Both aloe extracts showed a concentration dependant anticoccidial effect though, *A. spicata* inhibited sporulation to a greater extent than aloe vera. Similar to this, Yim *et al.* (2011) [96] have also found that dietary supplementation of *A. vera* resulted in significantly lower gut lesion scores and reduced faecal oocyst shedding of *E. maxima* in broiler chickens. They also suggested that reduced faecal oocyst shedding; a protective role against eimeria infection in aloe-based chicken diets could be associated more with cell-mediated responses than antibody responses.

3.3. Antimethanogenic effect

Rumen is a diverse and unique microbial ecosystem composed of bacteria, protozoa, fungi and bacteriophage. In rumen hydrogen is produced during the anaerobic fermentation of nutrients. This hydrogen can be used during the synthesis of volatile fatty acids (VFAs) and microbial protein synthesis. The excess hydrogen from NADH is eliminated primarily by the formation of methane produced by methanogens. Methane is one of the greenhouse gases which have 21 times more global warming potential than carbon dioxide (IPCC, 2007). Methane produced in ruminants represents a substantial loss of 7-9% of gross energy intake which reduces the potential conversion of feed energy to metabolizable energy. Hence, the inhibition of

methanogenesis has long been considered from nutritional aspects and more recently from the perspectives on greenhouse gas emissions.

It is a challenging task for the animal nutritionist and rumen microbiologist to make livestock industry economical and eco-friendly by controlling heat production and methane emissions from the ruminants. To combat this problem, many attempts like concentrate supplementation, use of lipid supplementation (Nevel and Demeyer, 1996) [72] antibiotic growth promoters such as monensin and lasalocid, different categories of feed additives like halogenated methane analogues, bacteriocins, propionate enhancers, acetogens, fats, ionophores, defaunating agents, formate etc. (Asanuma *et al.*, 1999; Boadi *et al.*, 2004) [6, 9] had been tried, but the goal could not be successfully achieved either due to some harmful effects on animal itself or due to the presence of their residues in the animal products. Contrary to this, plants containing secondary metabolites are being used in the ethno-veterinary medical practices since long back and have yielded good effects on the animal health. One of the most promising known therapeutic plants is surely aloe. The middle part of leaves containing gel, made up of carbohydrates (acemannan), anthraquinones, enzymes, inorganic compounds, amino acids, vitamins and a miscellaneous (including salicylic acid). These potentially active chemical constituents give aloe well known therapeutic properties like wound healing, anti-inflammatory, immune-stimulating etc.

Calabro *et al.* (2013) [12] observed that a significant effect of *Aloe arborescens* supplementation on the *in vitro* fermentation characteristics of feedstuffs. The supplementation of 120 mg aloe higher than that advised for *in vivo*, has beneficial effect on gas production compared to the lowest dosage. The close association between SCFA and gas production *in vitro* is an indicator of energy availability to the animal (Getachew *et al.*, 2002) [36]. Hence, the increased volatile fatty acids production due to the aloe supplementation probably means higher milk yield and quality, especially in terms of fat. *A. arborescens* has interesting effect on the rumen microbial *in vitro* activity, stimulating microbial metabolism thereby increasing the volatile fatty acids production in the rumen. These effects may be attributed to the plant extracts rich in some active chemical compounds (flavonoid) that increase degradation of cell wall constituents, yield and efficiency of microbial protein synthesis (Sirohi *et al.*, 2009) [90]. Similar to this, Sachan *et al.* (2014) [85], had supplement five herbs namely *Trigonella foenum-graecum* (Methi), *Acacia concina* (Shikakai), *Trachyspermum ammi* (Ajwain), *Cinnamomum tamala* (Tejpatta) and *Aloe barbadensis* (Aloe vera) at the rate of 1.5%, 2.5% and 4.0% of ration and found that the addition of these herbs had no any adverse effect on rumen pH. There was significant ($P < 0.05$) improvement in IVDMD and IVOMD (%) of feed after addition of *Trigonella foenum-graecum* (66.22, 69.63) as compared to control (56.33, 61.37) respectively. Similarly, addition of aloe vera also tended to improve the IVDMD and IVOMD of feed in respect to control. Addition of other herbs *Acacia concina* (Shikakai), *Trachyspermum ammi* (Ajwain), *Cinnamomum tamala* (Tejpatta) did not show any improvement in the feed digestibility. Authours, concluded that *Trigonella foenum-graecum*, and *Aloe barbadensis* are the potential fermentation modifier. In agreement of this, Sirohi *et al.* (2009) [90] also reported that among the different extracts tested, IVDMD (%) increased by 15.42% after addition of *Aloe-barbadensis*.

3.4. Antifungal activity

There are many studies showing that resistance to infections enhanced by aloe either in animals, whether the infective agent is a bacterium, virus or fungus (Plaskett *et al.*, 1997; Fujita *et al.*, 1976) [33, 80]. The aloe extract showed the significant antifungal activity against numbers of fungi like, *Aspergillus niger*, *Cryptococcus neoformans*, *Penicillium maneffei*, *F. oxysporum*, *Phythium* sp. and *R. solani* (Khaing, 2011) [54]. Candidiasis infections are mainly caused by *Candida* (fungus) in a variety of places like a sore (thrush), vaginal and gastrointestinal tract. These are normally treated with the help of antifungal drugs, but aloe vera can remove candidiasis infections with its natural antifungal properties. Aloe vera shows its antifungal activities against other fungi such as *Candida parapsilosis*, *Candida krusei* and *Candida albicans* (Das *et al.*, 2011) [23]. Saks and Golan (1995) [86] reported that, the gel extract from leaves of aloe vera possesses inhibitory action on spore germination and mycelial growth of four common post harvest fungi, *P. digitatum*, *A. alternata*, *B. cinerea*, and *P. expansum*. The present study is in agreement with Fujita *et al.* (1978) [34] in which they confirmed the antifungal properties of aloe species, *Aloe arborescens* Miller spp. *Natulensis* Berger, active against the human fungal pathogen *Trichophyton mentugrophytes*.

3.5. Antiparasitic activity

Endo and ecto-parasites are very common in domestic animals especially in grazing animals, and they cause large economic losses. Alagesan *et al.* (2002) [3] made comparison between the following four sets of ingestible *i.e.* albendazole, neem oil, extract of neem seed with bittergourd, garlic, edible banana stem and aloe vera and reported that the aloe vera has strong antiparasitic activity. Similar to this, (Fajimi *et al.*, 2002b) [31] have also observed the beneficial effect of *Aloe variegata*, spread over mange lesions.

3.6. Effects on intestinal microflora

Maintenance of intestinal microflora is an important factor contributing to improved growth performance and immune response in animals. Extract of herbs play a significant role in balancing and improving intestinal microflora in animals. Pogribna *et al.* (2008) [81] reported that dietary supplement of aloe vera, may alter the production of short chain fatty acids and number of intestinal microflora. Many studies have been carried out on using additives, including herbs, as alternatives to antibiotics, with direct or indirect effects on intestinal microflora. Many studies have shown antimicrobial properties of herb extracts (Cowan, 1999; Hammer *et al.*, 1999) [17, 41] which can improve intestinal microflora population and enhance health of digestive systems through reduction in number of disease making bacteria (Mitsch *et al.*, 2004) [67]. Number of studies have reported antibacterial effects of *Aloe veragel* (Kwon *et al.*, 2011; Pandey and Mishra, 2010; Mbangi *et al.*, 2010; Alemdar and Agaoglu, 2009) [4, 57, 64, 77]. These studies, indicates that aloe vera supplementation in broilers' have beneficial effect on improving intestinal microflora, its ecosystem and gut morphology; increase in aloe vera gel in broiler feeds (1.5%, 2%, and 2.5%) leads to increased *Lactobacillus* count and decreased *E. coli* count (Darabighane *et al.*, 2012) [21]. In addition, Jiang *et al.* (2005) [50] also have reported an increase in *Lactobacillus* and *Bifidobacteria* count as well as a reduction in *E. coli* when acemannan (0.1% and 0.05%), polysaccharide (0.1%) and aloe vera gel (0.1%) were added to broiler feed. In another study, Dai *et al.* (2007) [19] found that herbs and

polysaccharide contained in aloe vera can reduce *E. coli* count while increasing the number of *Lactobacillus* and *Bifidobacteria*.

Although the exact mechanism by which aloe vera affects intestinal microflora in broilers is unknown, it is likely that this effect is similar to the antibacterial effects of some herbs, or likely that the polysaccharide contained in aloe vera (acemannan) has mechanism like that of prebiotics (Guo *et al.*, 2003, 2004 b) ^[37, 38], where as some researchers believed that the antibacterial effects of aloe vera to its fumaric acid content (He *et al.*, 2011) ^[45].

3.7. Antioxidant effect

Reactive oxygen species (ROS) is continuously produced during normal physiological events and they can easily initiate the per-oxidation of membrane lipids, leading to the accumulation of lipid peroxides. Under pathological conditions, ROS is overproduced and results in oxidative stress. Antioxidants are substances that delay or prevent the oxidation of cellular oxidizable substrates. They exert their effect by scavenging reactive oxygen species, activating a battery of detoxifying proteins or preventing the generation of reactive oxygen species (Halliwell *et al.*, 1992) ^[39]. In recent years, there has been an increasing trend in finding natural antioxidants, which can protect the body from free radicals and retard the progress of many chronic diseases (Kaur *et al.*, 2001; Kinsella *et al.*, 1993) ^[53, 56].

Patel *et al.* (2012) ^[78] observed that both the plants (somniafer and aloe vera) possess excellent antioxidant and free radical scavenging activity. Screening of both the plant at different doses (100, 150 and 200 µg/ml) help to reveal the potential of individual plants. Both the plant possess almost equivalent hydrogen peroxide scavenging activity while the total antioxidant capacity was found much better in *Withania somnifera* as compare to aloe vera. The antioxidant activity of both the plant might be attributed to its polyphenolic content and other phytochemicals constituents.

3.8. Hypocholesterolemic effect

High blood cholesterol is a major risk factor for heart disease and stroke in human being. Daily supplementation with aloe vera stimulates immune system and improves wound healing. Iji *et al.* (2010) ^[47] has divided 40 male wistar rats into four groups of ten rats per group. Group I which served as the control received 0.9% physiological saline while those in groups II, III and IV received aloe vera gel (100, 250 and 500 mg/kg) respectively, for four weeks. There was significant ($P < 0.001$) reduction in plasma total cholesterol, triglycerides and LDL-cholesterol ratio compared with the control. In a similar manner, those animals that were administered with 500 mg/kg gel had significantly higher ($P < 0.001$) HDL-cholesterol ratio than those of the control. This study showed that, chronic administration of aloe vera gel extract showed cholesterol lowering action. Similar to this Chandrakar *et al.* (2008) ^[13] also observed cholesterol lowering action when animals fed to different doses (3, 4, 5 and 6 mg/kg/day) of raw extracts of aloe vera leaves along with cholesterol, there was significant decrease in serum cholesterol levels.

3.9. Immunostimulation/Immunosuppression

The immunomodulating effects of aloe-based carbohydrates are thought to function via activation of macrophage cells and stimulation of the antigen processing. Activated macrophage cells generate NO, secrete cytokines such as TNF- α and IL-6 and present cell surface markers. In a study, aqueous and

ethanolic extracts from the aloe vera pulp exerted stimulatory effects on humoral and cellular immune responses in chickens. The higher cellular immune responses in aloe vera administered chickens may be due to the aloe polysaccharides, especially acemannan (ACM), which activated the macrophages to produce inflammatory cytokines such as IL-1, IL-6 and TNF (Zhang and Tizard, 1996) ^[97]. The ability of aloe vera to stimulate the immune system is attributed to polysaccharides present in the aloe vera gel (Davis *et al.*, 1991) ^[26]. Acemannan was found to have immunomodulatory activity. It activates macrophages, enhance cytokine release, stimulate interactions between macrophages, T-lymphocytes and B-lymphocytes and enhance the generation of cytotoxic T-lymphocytes.

An important property of aloe vera that has been the subject of many *in vivo* and *in vitro* experiments is improvement in immune response, probably due to the acemannan contained in aloe vera (Harlev *et al.*, 2012; Djeraba and Quere, 2000; Zhang and Tizard, 1996; Karaca *et al.*, 1995) ^[28, 43, 52, 97]. Acemannan is a β (1-4)-linked acetylated mannan having mannose that can attach to mannose receptors in macrophages (Karaca *et al.*, 1995) ^[52] and activate these macrophages. Acemannan is potentiating antibody production against coxsackie virus and reduce radiation induced skin reactions in C₃H mice. Acemannan is also responsible for enhancing the alloresponsiveness of human lymphocytes (Helderman, 1988) ^[46] as well as induced the phenotypic and functional maturation of immature dendrite cells 60 and also stimulate the phagocytosis and the candidicidal activity of macrophages (Lee *et al.*, 2001) ^[59]. Alprogen inhibit calcium influx into mast cells, thereby inhibiting the antigen-antibody-mediated release of histamine and leukotriene from mast cells. Ro *et al.* (2000) ^[84] in a study on mice that had previously been implanted with murine sarcoma cells, acemannan stimulates the synthesis and release of interleukin-1 (IL-1) and tumor necrosis factor from macrophages in mice, which in turn initiated an immune attack that resulted in necrosis and regression of the cancerous cells. In an experiment on aloe vera effects on immunity of broilers, Valle-Paraso *et al.* (2005) ^[93] reported that, broilers treated with 2% aloe vera gel (with their drinking water) showed significant increase in antibody titer against newcastle disease virus (NDV) on days 37 and 52, compared to the control groups. Similar to this study Darabighane *et al.* (2012) ^[22] also reported an increase in antibody titer against NDV on days 24 and 38 by adding aloe vera gel to broiler feeds (at 1.5, 2 and 2.5%). In another study, Alemi *et al.* (2012) ^[5] added aloe vera gel powder (at 0.5, 0.75 and 1%) to broiler feeds and reported an increase in antibody titer against NDV.

3.10. Effects on reproductive performance

Estakhr and Javdan, (2011) ^[30] was carried an experiment to access the effect of aloe vera on reproduction, for that he administered aloe vera leaf pulp extract, gel extract and a mixture of both to three groups of 10 week old male wistar rats for 56 consecutive days and found that in all groups except control group the weights of the testes have increased. Epididymal sperm counts and sperm motility have been significantly increased compared to control groups. The testosterone level has remarkably increased in treated groups. As per these results, aloe vera has strong spermatogenic activity by increasing sperm parameters. This study strongly proposes that aloe vera specially its gel fortifies spermatogenesis and can be a good candidate for manufacturing fertility drugs. Contrary to this study,

Oyewopo *et al.* (2011)^[76] suggest that aloe vera has potential antifertility effects in the male rat.

3.11. Antitumor Effects

Polysaccharides isolated from aloe vera have been reported to have antitumor activity and the antitumor activity of acemannan has been examined in several animal species. A modified aloe vera polysaccharide, G2E1DS2 isolated from cellulose treated aloe vera gel was shown to activate macrophages and exhibit potent antitumor activity when injected into the peritoneum of mice implanted with sarcoma cells (Im *et al.*, 2005)^[48]. Similarly, intra peritoneal administration of both enriched and commercial forms acemannan to mice implanted with murine sarcoma cells significantly reduced the tumor burden and increased the survival rate (Peng *et al.*, 1991)^[79]. Supplementation of the cancer induced rats with vitamin C or aloe vera gel extract significantly inhibited the development and severity of carcinogenesis as reflected in the reduction of the percentage surface area of enzyme positive foci (Shamaan *et al.*, 1998)^[88].

3.12. Adverse or Toxic Effects

Consumption of aloe vera latex is also associated with watery diarrhoea leading to electrolyte imbalance and hypokalemia (Cooke *et al.*, 1981)^[16]. Other side effects include weight loss, central nervous system disturbances and abnormalities and kidney dysfunction. Compounds in aloe vera latex are also considered genotoxic and may be mutagenic (Mueller *et al.*, 1996)^[69]. The abuse of aloe vera latex containing laxatives is associated with melanosis coli, which may play a role in the development of colorectal cancer (Siegers *et al.*, 1993)^[89]. Intestinal tumours were induced in rats that consumed a diet containing chrysazin, a synthetic anthraquinone with dihydroxy groups like other natural anthraquinones (Mori *et al.*, 1985)^[69]. In addition, compounds in aloe vera latex are suspected to interact with certain oral conventional drugs in particular corticosteroids and cardiac glycosides (Mascolo *et al.* 2004)^[63].

4. Conclusion

Aloe vera, as an additive to livestock and poultry feed, has great potentials for improving nutrient utilization, intestinal health, immune response and growth performance. It has potential benefits as antimicrobial agents and used for controlling coccidiosis in poultry. Advantages of aloe vera added to feeds depend on several factors like form of use [powder, gel, extract (ethanolic or aqueous), polysaccharide extracted from gel], dosage, genetics of animals, ingredients of diet and farm management. Therefore, more studies are required to determine effective dosage and form of use as feed additives in livestock.

5. References

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