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Review Article
Direct-Fed Microbial: Beneficial Applications, Modes of Action and Prospects as a Safe Tool for Enhancing Ruminant Production and Safeguarding Health

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Abstract
Recently, animal food industry has shown an increasing interest in Direct-Fed Microbials (DFM) to keep the concept of safe food supply at the consumer level. In the absence of suitable growth stimulant after banning the use of antibiotics in animal feed, a positive manipulation of rumen microbes has become the field research for entrepreneurs and research scientists. Direct-fed microbials is a term reserved for naturally occurring live microbes that can be supplemented orally to produce a beneficial health response in the host animal. A number of genera of live microorganisms including; bacteria, yeast and fungi are frequently used in different combination feed as DFM for domestic ruminants. It has been documented that these live culture of microbes improve ruminant productivity, milk production, immunity, digestibility of feed, counter infectious pathogens and protect health. Possible attempts have also been undertaken to justify the mechanism of these microbes. This review tries to summarize the effect of supplementation of DFM on the production, immune response, fermentation pattern and safeguarding health. The discussed concepts and advances concerning to DFM implementation will be useful not only for the researchers, animal owners, feed manufacturers, pharmacists, pharmaceutical companies, stake holders but will also boost the economic gains and profits by promoting the ruminant health and production through feed modification.

Key words: Direct-fed microbials, ruminant, productivity, mode of action, immunity, health

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INTRODUCTION

The concept of microbial manipulation was first coined when the consumption of yoghurt by Bulgarian peasants was associated with their longevity (Metchnikoff, 1907). Now it is generally accepted that certain group of viable microbes are beneficial for livestock species. Rumen harbours variety of microbes actively involved in initial and very first step of digestion of green fodder and concentrate diet. Age of animal, feeding pattern and diet formulation influence and determines the microbial environment of rumen in four stomach animals (Dhanasekaran *et al*., 2008; Apas *et al*., 2015; Yadav and Shukla, 2015).

The concern over the use of intensive antibiotics has triggered to the newer sense of the importance of DFM in the livestock production. The word probiotics and DFM are used interchangeably but in fact they are not the same. The DFM has been defined by the US Food and Drug Administration Authority as the feed product containing the source of live naturally existing microbes (Brashears *et al*., 2005). The DFM has been used in livestock industry over the last 20 years to enhance milk production, weight gain and feed efficiency (LeJeune and Wetzel, 2007). They are provided to the animals in the form of bolus or sometime mixed with the feed.

The major cause of rumen microbial study is to improve feed utilization, animal health and production, as well as animal safety by improving immune status which is possible only by controlled fermentation and lowering ruminal diseases. In the past few decades, a number of feed additives have been used for example antibiotics, sodium bicarbonate, slow release urea, methane inhibitors and defaunting agents have been successfully utilized in ruminants nutrition in order to manipulate the microbial ecosystem (Seo *et al*., 2010). However, due to a number of toxic problems associated with these additives, researchers are looking for safer additives in ruminant nutrition (Barton, 2000). Further, these products have been criticized by the consumers from the safety point of view.

In view of the recent criticism, the use of probiotics has become a suitable alternative that can survive in the rumen of animals (Dhama *et al*., 2008; Fon and Nsahlai, 2013). When suitable DFM (selected bacteria, yeast or fungi) are supplemented to the ruminants through diet, they help in establishing healthy microflora in the gut by checking the dysbiosis and undesired alterations in the pH. In early stages of neonatal life, gut colonization with DFM microbes set up healthy microbiota in the gastrointestinal tract, which plays crucial role in protecting budding calves against various infections, bacterial diarrhea and pathogenic challenges (Dhama *et al*., 2008; Varankovich *et al*., 2015; Yuan *et al*., 2015). Administration of selected DFM strains in young and adult both types of ruminants augment the health and production performance, improves the immunological aura in the body and compete with the invading microbes without leaving any residual toxic effects in an eco-friendly manner (Ohashi and Ushida, 2009; Yeoman and White, 2014). These multitasking approaches of DFM support and strongly recommend their optimal usage in the livestock industry.

This review discusses the DFM with a focus on their multiple beneficial roles in ruminants such as effects on performance and productivity, mitigation of methane emission, immunomodulatory properties, countering infectious pathogens and protecting health. Information compiled with the concepts and recent advances would encourage more research and validation of practical prospects of DFM supplementation in ruminant feeding and health. It will be highly useful for researchers, animal owners, feed manufacturers, pharmacists, pharmaceutical companies, stakeholders and would help in gaining economic returns by promoting ruminant health and production through feed modification.

DIRECT-FED MICROBIALS

The word probiotic is composed of two words: pro means in favour and biotic means life. The term probiotic has been defined as "Those living organisms which are used as feed supplement and produced beneficial impact on the host animal through improving the intestinal microbial balance" (Fuller, 1989). The Food and Drug administration of USA has directed to use the term "direct-fed microbial" instead of probiotic (Miles and Bootwalla, 1991). The definition of DFM is broad in nature and includes variety of organisms like yeast, fungi, bacteria and cell fragments (Oetzel *et al*., 2007; Elghandour *et al*., 2014b). The DFM grow in the rumen has a beneficial effect on microbial ecosystem (Seo *et al*., 2010). Variety of DFM is being used in the ruminants around the world which can be classified into three major classes: bacterial, fungal or combination of both. The most common among them is the bacterial DFM which can further be classified as lactic acid producing bacteria (LAB), second is lactic acid utilizing bacteria (LUB) and other microorganisms (Elghandour *et al*., 2015). The most common genus used in DFM are Propionibacterium, Streptococcus, Lactobacillus,

Bacillus and some other important bacteria such as, *Prevotella bryantii* and *Megasphaera elsdenii* (Kung, 2006; Seo *et al*., 2010). The use of these bacteria allow the producers to decrease the time in adaptation to high concentrate diet and reduce the incidence of acidosis in lactating animals (Kung, 2006; Elghandour *et al*., 2015).

TYPES OF DFM

Rumen microbes: Generally the population of rumen microbes is composed of different kinds of bacteria, protozoa and fungi, only a small number of these communities qualify for their potential as DFM (Miron *et al*., 2001). Most of the studies have focused on using such a DFM targeting the metabolism of lactic acid such as, *Selenomonas ruminantium*, *Megasphaera elsdenii* and *Propionibacterium freudenreichii* (Wiryawan and Brooker, 1995; Klieve *et al*., 2003; Raeth-Knight *et al*., 2007). Other approach includes the utilization and reduction of lactic acid such as, *Prevotella bryantii* 25A which consume starch (Chiquette *et al*., 2008). Another group of DFM includes fibrolytic rumen bacteria namely *Ruminococcus albus* and *Ruminococcus flavefaciens* in an effort to enhance fiber digestion (Krause and Otzel, 2006; Chiquette *et al*., 2007). Logically DFM derived from the rumen may possibly be more capable to adjust into the microbial community since they are origined from the environment from which they have been extracted eliminating the need of daily administration (McAllister *et al*., 2011).

Lactic acid producing bacteria: Majority of DFM used in cattle production are lactic acid producing bacteria (LAB) including *Enterococcus* spp., *Streptococcus* spp., *Lactobacillus* spp. and *Pediococcus* spp. (McAllister *et al*., 2011). This class of DFM has been used in almost all types of livestock. In suckling calves, LAB are administered as bolus while in dairy and beef animals, they are mixed with diet. Furthermore, LAB are also inoculated into the forage before the process of ensiling in order to enhance the preservation, increasing feeding value and aerobic stability of silage (Schmidt *et al*., 2009).

Lactic acid producing bacteria are more effective since they are environment friendly and can alter the environment through a number of mechanisms. The lactic acid produced by LAB is one of the key compounds that can change the pH of the competitor bacteria, in addition, to production of antimicrobial substance known as bacteriocin (Servin, 2004; McAllister *et al*., 2011). Other compounds such as mevalonolactone, benzoic acid, diacetyl, reuterin and methylhydantoin are also produced by some of the LAB (Brashears *et al*., 2005). It has also been suggested that LAB in combination of other bacteria and yeast showed synergistic activities in many of the commercial products (McAllister *et al*., 2011).

Other bacteria: Some other types of bacteria such as *Bifidobacterium* spp. and *Bacillus* spp. have been successfully used as DFM. The endospores produced by *Bacillus* spp. are environmentally stable and thermo-tolerant which make these bacteria competitively superior in ensuring their survival during storage or pelleting (McAllister *et al*., 2011). *Bacillus* spp. are present in rumen in low number and play a minor role in the degradation of cell wall. Strains of Bifidobacterium used as DFM do not originate from the rumen, however, they play key role in starch digestion (Stewart *et al*., 1997).

Yeast culture: The official definition of yeast culture is a dry product composed of yeast and the media on which it was grown dried in such a manner to preserve the fermenting capacity of the yeast (Yoon and Stern, 1995). The effect of yeast preparation on the rumen fermentation and performance has been well elucidated and has generated considerable scientific interest in the past few decades. It is now well accepted that yeast culture can beneficially modify rumen microflora, digestive and fermentative activities in the rumen.

First published report on the use of the yeast was made public in 1925 describing the use of yeast as a protein source in ruminant ration in lactating cows (Eckles and Williams, 1925). The use of live yeast has been associated with high production of ethanol toxicity; therefore, dead yeast is preferred to be used in animal diet (Yoon and Stern, 1995). The application of yeast increased during 1950's when, Renz and Koch (1956) reported that inclusion of 50 g day^{-1} yeast culture increased milk yield.

Saccharomyces cerevisiae is being extensively used as a DFM for the improved performance and milk yield in dairy cattle. Recent analysis has demonstrated that *S. cerevisiae* in dairy cows improved feed intake, rumen pH and volatile fatty acids, organic digestibility and decreased lactic acid in the rumen (Desnoyers *et al*., 2009). *Saccharomyces cerevisiae* are aerobic bacteria which can metabolize lactic acid, alter the population of rumen microbes due to its unique ability to utilize oxygen thereby producing an environment which is more suitable for the growth of anaerobic bacteria in the rumen and increase the fibrolytic bacteria (Jouany *et al*., 1999; McAllister *et al*., 2011). In addition to *Saccharomyces cerevisiae*, *Aspergillus oryzae* and *Aspergillus niger* have also been used in ruminant nutrition, however, their role is limited to crude enzyme extract instead of whole cell, primarily targeted to increase fibre digestion in the rumen (McAllister *et al*., 2011).

For ruminants, yeast culture has been considered as the most promising DFM for nutrient utilization. Previously it was suggested that yeast cannot survive and multiply in the anaerobic culture, however, later evidences suggest that *Saccharomyces cerevisiae* may multiply and grow in the rumen conferring beneficial impact on cellulysis and productive traits (Dawson and Newman, 1988; Harris and Lobo, 1988; Dutta *et al*., 2009).

MECHANISM OF ACTION OF DFM

Many factors are involved in understanding the mode of action of DFM such as dose, feeding time, duration and frequency and strains. Moreover, some DFM act via rumen while other influence the gastrointestinal tract (Puniya *et al*., 2015). Inside rumen the type of DFM such as LUB or LAB influence, the later mainly prevent the acidosis of the rumen in dairy animals through facilitating the rumen microbes which can survive in the presence of lactic acid in the rumen (Yoon and Stern, 1995; Nocek *et al*., 2002). The former type of bacteria mainly decreases the concentration of lactic acid and keeps the pH at normal level. One such example is *Megasphaera elsdenii* which utilize the lactic acid in the rumen (Yang *et al*., 2004; Kung, 2006). Furthermore, this bacteria utilize lactate, glucose and maltose in addition to competing with lactate producing organism (Russell and Baldwin, 1978). Propionibacteria is present in the rumen in high number in animals fed with medium concentrate diet which modify the rumen conditions through conversion of lactate into propionate resulting in the higher production of hepatic glucose (Stein *et al*., 2006).

The DFM has also been proposed to produce antibacterial compounds such as bacteriocin and hydrogen peroxide which competitively exclude the pathogenic bacteria. Hydogen peroxide can characteristically oxide the sulfhydryl group in hexokinase and glycerol aldehyde -3-phosphate dehydrogenase causing blockage of glycolysis (Carlsson *et al*., 1983; Dicks and Botes, 2010). The bacteriocin produced by LAB does not allow the binding of substrates to ribonucleotide reductase interfering with the DNA synthesis of target microbes (Dicks and Botes, 2010).

Recently, it has been proposed that DFM can modulate the host immune system through stimulating and activation of the dendritic cells, natural killer cells, macrophages, T and B lymphocytes and neutrophils of the intestines (Krehbiel *et al*., 2003). When the DFM is administered, they are absorbed by the intestinal wall and various immune players such as dendritic cells, macrophages and natural killer cells surround them which result in the stimulation of the immune response (Dicks and Botes, 2010). The LAB such as Lactobacillus casei Shirota and *Lactobacillus rhamnosus* Lr23 is also involved in the stimulation of macrophages to produce the cytokines (TNF-α) as reported by Matsuguchi *et al*. (2003).

Many theories have been forwarded in explaining the mechanism through which yeast exerts their beneficial impact on host. Yeast may have buffering effect through reduction of pH (Elghandour *et al*., 2014a, b). Yeast can also improve the oxygen availability on the surface of freshly ingested food to maintain metabolism (Newbold *et al*., 1996). Furthermore, DFM such as *S. cerevisiae* can compete with the starch utilizing bacteria thereby preventing the accumulation of lactate and provides organic acids and vitamins to the cellulytic bacteria and LUB (Chaucheyras *et al*., 1995; Lynch and Martin, 2002).

The rumen pH is mainly determined by the concentration of lactic acid (Williams *et al*., 1991). Fermentation of carbohydrate depresses pH leading to reduction in the number of cellulytic bacteria, impair degradation of forage and dry matter intake (Orskov *et al*., 1978; Thomas and Rook, 1981; Williams, 1989).

BENEFICIAL APPLICATIONS OF DFM

Various beneficial applications of DFM in ruminants viz., effect on ruminant performance, productivity, immunomodulatory activities, protecting from pathogens/ infections, safeguarding health and mitigation of methane emission are discussed in below sections. An overview of modes of actions and beneficial applications of DFM for enhancing ruminant production and protecting health is depicted in Fig. 1.

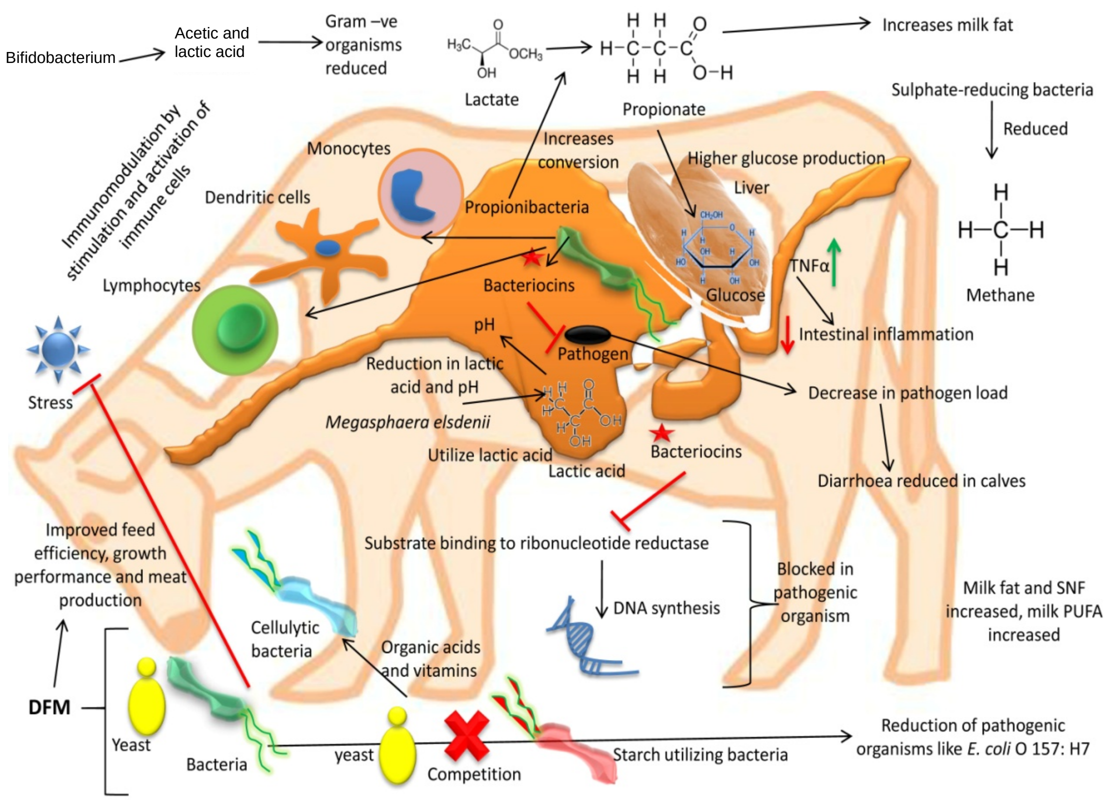

Fig. 1: An overview of modes of actions and beneficial applications of DFM for enhancing ruminant production and protecting health

EFFECT OF DFM ON RUMINANT PERFORMANCE

The purpose of feeding DFM prior to the start of rumination is to establish and maintain stable normal intestinal microbes rather than a production stimulant. In neonates, the microbes of the gastrointestinal tract are very unstable, abrupt dietary or environmental change may cause an alteration in the microbial population of the GIT which may result in diarrhea (Sandine, 1979). Most of the studies dealing with the use of DFM in ruminant production are related with neonatal dairy calves. In young calves, the rapid establishment to adapt to solid feed by stabilizing the rumen and intestinal microbes and the exclusion of enteric pathogen is the primary goal of the use of DFM (Dhama *et al*., 2008; Puniya *et al*., 2015).

Experimentally, there are several bacteria which can potentially act as DFM but they have not been commercialized. One such bacteria is *M. elsdenii* which is used in lactating animals, however, when cows are abruptly shifted from high forage diet to concentrate diet, *M. elsdenii* is often incapable to prevent lactic acidosis (Puniya *et al*., 2015). Similarly, *E. faecium* succeeded less likely in feedlot cattle adapted to high grain diet (Beauchemin *et al*., 2003).

The several conditions faced by newly produced calves such as weaning, traction and dehorning has effect on microbial environment (Elghandour *et al*., 2015). These conditions may change the microbiota in the negative directions thereby reducing the performance and weight gain. The administration of DFM is expected to change the microbial population in the positive direction (Krehbiel *et al*., 2003). Limited data is available on the administration of DFM in stressed calves, however, there is a general consensus that supplementation of DFM to the diet of such calves may improve the health and performance of stressed calves (Elghandour *et al*., 2015).

Commonly used DFM in young calves are *Streptococcus* and *Lactobacillus* species. In contrast to adult ruminants, young ruminants have the ability to digest a significant amount of ration which is associated with the risk of increased proliferation of microorganisms resulting in the increased chance for diarrhea and also weight loss (Elghandour *et al*., 2015). Here the role of DFM is very important which may obtain positive impact on the GIT function thereby modifying the bacterial concentration in the positive direction (Abu-Tarboush *et al*., 1996; Kung, 2001). It is the reason of using DFM that in an experiment conducted by Nakanishi *et al.* (1993) in which Holstein calves supplemented with *Lactobacillus acidophilus* showed rumination at 30 day compared to untreated calves, indicating the ability of this bacterium to promote ruminal development (Elghandour *et al.*, 2015). Recently, Dicks and Botes (2010) concluded that Bifidobacteria produce acetic and lactic acid at such a ratio (3:2) which may be beneficial for the control of Gram-negative bacteria in the GIT, probably the shift towards the more production of acetate is lethal for the survival of Gram-negative bacteria and other microbes such as moulds and yeast (Gilliland 1989; Elghandour *et al.*, 2015). Growth performance has also been shown to improve when LAB was supplemented in young calves (Adams *et al.*, 2008; Frizzo *et al.*, 2010). Increased reduction in the incidence of diarrhea has been reported by using DFM especially Lactbacillus (Abu-Tarboush *et al.*, 1996).

The DFM have been rarely used in high producing dairy cows, however, its use during early lactation may be the best candidate since cows are in negative energy balance with high fermentable carbohydrate which is associated with lactic acidosis (Kung, 2006). It has been shown that DFM improves performance in dairy cows through high intake of dry matter and enhance the milk yield and milk contents such as protein, blood sugar and insulin concentration (Nocek *et al.*, 2003; Nocek and Kautz, 2006; Oetzel *et al.*, 2007). In beef cattle, to prevent ruminant acidosis caused by high fermentable diet, DF is recommended. The DFM in beef cattle showed improved feed efficiency, growth performance and meat production (Ghorbani *et al.*, 2002; Krehbiel *et al.*, 2003). The supplementation of DFM in the diet of feedlot ruminants has caused improved feed efficiency and daily gain, carcass characteristics and dry matter intake (Huck *et al.*, 1999; Galyean *et al.*, 2000).

The most important role of DFM in feedlot cattle is the reduction of pathogenic bacteria such as, *Escherichia coli* in the GIT (Elghandour *et al.*, 2015). Studies have shown that different kinds of DFM have reduced the population of *E. coli* O 157: H7 in feedlot cattle (Ohya *et al.*, 2000).

Composition of diet and environmental conditions determines the growth response of animals in case of yeast supplementation, however, type of animals may not be affected since daily live weight were equally increased in dairy and beef calves (Hughes, 1988).

Williams *et al.* (1987) demonstrated higher daily weight gain in lambs fed a diet supplemented with yeast culture. In contrast, Quigley *et al.* (1992) found that yeast culture affected ruminal metabolites with no influence on dry matter intake and weight gain in calves. Similarly, Mir and Mir (1992) observed that supplemental live-yeast did not positively impact the feed utilization in steers.

MILK PRODUCTION AND COMPOSITION

Modern dairy farms are targeting high milk production utilizing feed composed of high concentrates to meet the metabolic demand of the higher milk production. Such feeding system is associated with metabolic dysfunction like rumen acidosis especially during poor feeding condition and composition.

Higher milk yield with no change in milk composition has been reported due to the supplementation of *Lactobacillus acidophilus* (Jaquette *et al.*, 1988). Colenbrander *et al.* (1988) found that treatment of alfalfa with *L. acidophilus* improved milk production and composition in dairy cows with no effect on dry matter intake. Improved milk response has been reported in dairy cows and goats fed with yeast culture with increased milk fat, however the magnitude of response depends upon the stage of lactation (Williams *et al.*, 1991). Response of milk production may also depends upon production level for example, Hoyos *et al.* (1987) reported that dairy cows supplemented under high and low level of production with *Saccharomyece cerevisiae*, *S. faecium* and *L. acidophilus*. High production cows showed higher milk yield with no effect on the cows with low production, however, fat was similar in both the groups. Milk production in high producing cows was increased when *M. elsdenii* NCIMB 41125 was supplemented as compared to the control group (Erasmus *et al.*, 1992; Hagg and Henning, 2007; Aikman *et al.*, 2008). Gomez-Basauri *et al.* (2001) reported higher milk production (0.73 kg day^{-1}) with less feed consumption (0.42 kg day^{-1}) when cows were doses with lactic acid bacteria including *L. casei*, *L. acidophilus* and *E. faecium* in comparison to the control. On the same line, Boyd *et al.* (2011) found that using *L. acidophilus* NP51 and *Proponibacterium freudenreichii* NP24 may improve milk yield and digestibility in heat stressed cows. It is interesting that using a different strain (*L. acidophilus* LA747 and *P. freudenreichii* PF24) in the study of Raeth-Knight *et al.* (2007) found no effect on digestibility, performance and rumen characteristics. Other studies have shown higher milk yield when lactating cows were supplemented with a combination of fungal culture (*Saccharomyces cerevisae*) and lactic acid bacteria acidophilus and/or (*Lactobacillus plantarum*/*E. faecium*) (Komari *et al.*, 1999; Block *et al*., 2000). Propionibacteria converts lactic acid into propionic acid, are very important for the ruminants since the propionate represents a major source of energy of the animals and a DFM composed of such bacteria increased milk fat as well as milk yield in dairy cows (Nocek and Kautz, 2006; Oetzel *et al*., 2007).

In lactating cows, yeast culture significantly improved the dry matter intake and subsequent milk yield (Williams *et al*., 1991). Similarly, Wohlt *et al*. (1991) reported higher feed intake and milk yield when yeast culture was supplemented from 30 days pre-partum till week 18 of lactation. Pre-partum and post-partum dry matter intake and milk production have been reported by several authors in dairy animals (Wohlt *et al*., 1998; Dann *et al*., 2000; Nocek *et al*., 2003). Nikkhah *et al*. (2004) did not find any advantage on the intake of dry matter and milk production in dairy cows, however, milk fat and total solids were increased by the supplementation of live yeast culture.

IMMUNOMODULATION

A number of mechanisms are involved in improving the immune system of the host such as upregulating cell-mediated immune response, augmenting antibody production, enhancing dendritic cell-T interaction, reduction of epithelial cells apoptosis, production of Toll like receptor signaling etc. (McAllister *et al*., 2011). The DFM stimulates epithelial innate immunity which may suppress intestinal inflammation by increasing the production of TNF-α (Pagnini *et al*., 2010). The way the DFM affect the production of cytokines and chemokines in addition to T and B cell responses depends upon the types of DFM, the dose and duration of the experiment (McAllister *et al*., 2011). For example, a DFM consisting of *Bifidobacterium thermophilum*, *L. casei*, *E. faecium* and *L. acidophilus* heightened the expression of cytokines IL-6 but decreased cytokine IL-10 in chicken (Chichlowski *et al*., 2007). In another report LAB-based DFM depressed IFN- γ, IL-3 and IL-4 in chicks and also reduced the *Salmonella enterica* colonies in the intestines of chickens (Haghighi *et al*., 2008). Another study reported that in response to *L. acidophilus* DFM, IFN- γ, IFN- α, IL-18, STAT4, STAT2 and MyD88 were upregulated in the cecal tonsils of broilers (Brisbin *et al*., 2008).

It has also been proposed that DFM mediated immune response is more important in young ruminants since intestinal population is less established on one hand and on the other hand, intestinal tract is more susceptible to colonization of pathogenic microbes (McAllister *et al*., 2011). For example, *Lactococcus lactis* DPC 3147 was administered to adult lactating cows which successfully increased IL-1β and IL-8 gene expression but failed to show a response to control mastitis (Beecher *et al*., 2009).

PROTECTING FROM INFECTIOUS PATHOGENS

Probiotics such as, lactic acid bacteria have been reported to prevent and protect cattle from various pathogens, alleviate stress and boost immunity and have been suggested to be valuable alternative to antibiotics (Gupta and Gupta, 2007; Yasuda *et al*., 2007; Frizzo *et al*., 2010; Bayatkouhsar *et al*., 2013; Uyeno *et al*., 2015). The DFM Yeast as probiotic has been found effective in decreasing pathogenic effects of infectious bovine rhinotracheitis virus in calves (Cole *et al*., 1992). Probiotics strains were found to prevent and reduce mastitis and metritis in cattle by reducing adhesion of pathogenic bacteria, producing antimicrobial substances and with other modes of action (Otero *et al*., 2006; Gulbe *et al*., 2015). *Lactobacillus acidophilus* has been reported to provide protection from *E. coli* O157:H7 infection in cattle owing to their bacteriostatic/bacteriocidal effects (Schamberger *et al*., 2004; Poppi *et al*., 2015). *Lactobacillus plantarum* supplementation in feed reduced Clostridia load in faeces of goats (Maragkoudakis *et al*., 2010). A probiotic mixture of *Bacillus licheniformis* and *B. subtilis* supplementation in feed of sheep resulted in lesser lamb mortality (Kritas *et al*., 2006). A mixture of *L. acidophilus*, *L. helveticus*, *L. bulgaricus*, *L. lactis*, *Streptococcus thermophilus* and *Enterococcus faecium* given to sheep was found effective in checking faecal shedding of non-O157 Shiga toxin-producing *E. coli* (STEC) strain, an important food-borne pathogen of humans having public health concerns (Rigobelo *et al*., 2014). Probiotics could inhibit *Listeria monocytogenes* and their use has been suggested to prevent and control this important pathogen having public health concerns (Dhama *et al*., 2015).

MITIGATION OF METHANE EMISSION

Methane is a global concern and ruminants are though to contribute 12-15% to the total global methane emission. Lactating cows consuming 14.7% of gross energy from dry matter is estimated to produce 419 L of methane/day/cow (Holter and Young, 1992). It has been documented that cattle in developed countries are emitting 55 kg/day/animal methane gas compared to 35 kg/day/animal in developing countries. Methane is an important gas and its contribution towards the global warming is 25 times greater than carbon dioxide (Jeyanathan *et al*., 2014).

Different strategies have been applied, among them the most important is the idea of DFM application. It was reported that addition of yeast culture reduced methane production in steers by 28% (Williams, 1989). Lynch and Martin (2002) reported a 20% methane reduction after a period of 48 h incubating mixed culture of rumen microorganisms in the presence of alfalfa. Chaucheyras-Durand *et al.* (2008) discussed three major effects of yeast on the rumen health through stabilizing rumen pH, feed degradation, establishing of microbes in the rumen. In addition to yeast, propionate production is the major biochemical pathway through bacterial DFM (Seo *et al.*, 2010). Propionate-producing bacteria utilize hydrogen and therefore reduce the methane production. It was reported that when a DFM based on *M. elsdenii* is used, the rumen pattern is shifted in favour of propionate production (Jeyanathan *et al.*, 2014). Other bacteria such as *Prevotella ruminicola* is also known for propionate formation through acrylate pathway (Wallnofer and Baldwin, 1967). Although propionate producing bacteria have been used to improve animal production. However, little attention has been given to methane production. An encouraging study of Berger *et al.* (2012) using a mixed culture of *Propionibacterium jensenii-Lactobacillus* spp. produced little methane production in lactating dairy cows showing the potential to mitigate rumen methane. Nitrate/nitrite-reducing bacteria can also play role in reducing rumen methane to act as H_2 sink to CO_2 in the rumen.

Sulphate Reducing Bacteria (SRB) have also been used to reduce the methane production in the rumen. The SRB competes with methane producing bacteria for common substrate such as H_2, format and acetate. The bacteria of SRB in the rumen consisted of genus *Desulfovibrio* and *Desulfotomaculum.* The introduction of sulphate is directly linked with the ability of SRB to compete with methanogenic bacteria. Paul *et al.* (2011) reported decreased methane production using the newly indentified, *Fusobacterium* sp., as a DFM.

CONCLUSION AND FUTURE PROSPECTS

Manipulation of gastrointestinal microbial ecosystem to augment animal performance and safeguarding health is one of the prime goals of animal scientists and veterinarians. In light of worldwide ban on the use of antibiotics and pressure to produce higher animal protein, the DFM offer an alternative option. This review has explored the production response with the supplementation of DFM on various aspects. In addition to positive impact of DFM on ruminant production, literature has also reported inconsistency in the response of animals which has been attributed to nature of microbial supplement, dose and duration, age of animal, environmental conditions and combination of these factors. In view of the increasing pressure to produce more and safe animal protein, future DFM research must be directed towards decreasing greenhouse gases and carbon footprint per unit of animal protein produced.

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REFERENCES

Abu-Tarboush, H.M., M.Y. Al-Saiady and A.H.K. El-Din, 1996. Evaluation of diet containing Lactobacilli on performance, Fecal Coliform and Lactobacilli of young dairy calves. Anim. Feed Sci. Technol., 57: 39-49.

Adams, M.C., J. Luo, D. Rayward, S. King, R. Gibson and G.H. Moghaddam, 2008. Selection of a novel direct-fed microbial to enhance weight gain in intensively reared calves. Anim. Feed Sci. Technol., 145: 41-52.

Aikman, P.C., P.H. Henning, A.K. Jones, S. Potteron and J. Siviter *et al.*, 2008. Effect of administration of *Megasphaera elsdenii* NCIMB 41125 lactate utilizing bacteria in early lactation on the production, health and rumen environment of highly productive dairy cows fed a high concentrate diet. KK Animal Nutrition Internal Report, KKAN, Umbogintwini, South Africa.

Apas, A.L., M.E. Arena, S. Colombo and S.N. Gonzalez, 2015. Probiotic administration modifies the milk fatty acid profile, intestinal morphology and intestinal fatty acid profile of goats. J. Dairy Sci., 98: 47-54.

Barton, M.D., 2000. Antibiotic use in animal feed and its impact on human health. Nutr. Res. Rev., 13: 279-299.

Bayatkouhsar, J., A.M. Tahmasebi, A.A. Naserian, R.R. Mokarram and R. Valizadeh, 2013. Effects of supplementation of lactic acid bacteria on growth performance, blood metabolites and fecal coliform and lactobacilli of young dairy calves. Anim. Feed Sci. Technol., 186: 1-11.

Beauchemin, K.A., W.Z. Yang, D.P. Morgavi, G.R. Ghorbani, W. Kautz and J.A. Leedle, 2003. Effects of bacterial direct-fed microbials and yeast on site and extent of digestion, blood chemistry and subclinical ruminal acidosis in feedlot cattle. J. Anim. Sci., 81: 1628-1640.

Beecher, C., M. Daly, D.P. Berry, K. Klostermann and J. Flynn *et al*., 2009. Administration of a live culture of *Lactococcus lactis* DPC 3147 into the bovine mammary gland stimulates the local host immune response, particularly IL-1β and IL-8 gene expression. J. Dairy Res., 76: 340-348.

Berger, C., A. Lettat, C. Martin and P. Noziere, 2012. Method for reducing methane production in a ruminant animal. WO 2012147044 A1, November 1, 2012. http://www.google.com/patents/WO2012147044A1?cl=en.

Block, E., J.E. Nocek, W.P. Kautz and J.A.Z. Leedle, 2000. Direct fed microbial and anionic salt supplementation to dairy cows fed 21 days pre- to 70 days postpartum. J. Anim. Sci., 78: 304-304.

Boyd, J., J.W. West and J.K. Bernard, 2011. Effects of the addition of direct-fed microbials and glycerol to the diet of lactating dairy cows on milk yield and apparent efficiency of yield. J. Dairy Sci., 94: 4616-4622.

Brashears, M.M., A. Amezquita and D. Jaroni, 2005. Lactic acid bacteria and their uses in animal feeding to improve food safety. Adv. Food Nutr. Res., 50: 1-31.

Brisbin, J.T., H. Zhou, J. Gong, P. Sabour and M.R. Akbari *et al*., 2008. Gene expression profiling of chicken lymphoid cells after treatment with *Lactobacillus acidophilus* cellular components. Dev. Comp. Immunol., 32: 563-574.

Carlsson, J., Y. Iwami and T. Yamada, 1983. Hydrogen peroxide excretion by oral streptococci and effect of lactoperoxidase-thiocyanate-hydrogen peroxide. Infect. Immunity, 40: 70-80.

Chaucheyras, F., G. Fonty, G. Bertin and P. Gouet, 1995. Effects of live *Saccharomyces cerevisiae* cells on zoospore germination, growth and cellulolytic activity of the rumen anaerobic fungus, *Neocallimastix frontalis* MCH3. Curr. Microbiol., 31: 201-205.

Chaucheyras-Durand, F., N.D. Walker and A. Bach, 2008. Effects of active dry yeasts on the rumen microbial ecosystem: Past, present and future. Anim. Feed Sci. Technol., 145: 5-26.

Chichlowski, M., J. Croom, B.W. McBride, L. Daniel, G. Davis and M.D. Koci, 2007. Direct-fed Microbial primalac and salinomycin modulate whole-body and intestinal oxygen consumption and intestinal mucosal cytokine production in the broiler chick. Poult. Sci., 86: 1100-1106.

Chiquette, J., G. Talbot, F. Markwell, N. Nili and R.J. Forster, 2007. Repeated ruminal dosing of *Ruminococcus flavefaciens* NJ along with a probiotic mixture in forage or concentrate-fed dairy cows: Effect on ruminal fermentation, cellulolytic populations and in sacco digestibility. Can. J. Anim. Sci., 87: 237-249.

Chiquette, J., M.J. Allison and M.A. Rasmussen, 2008. *Prevotella bryantii* 25A used as a probiotic in early-lactation dairy cows: Effect on ruminal fermentation characteristics, milk production and milk composition. J. Dairy Sci., 91: 3536-3543.

Cole, N.A., C.W. Purdy and D.P. Hutcheson, 1992. Influence of yeast culture on feeder calves and lambs. J. Anim. Sci., 70: 1682-1690.

Colenbrander, V.F., R.J. Grant and G. Schaaf, 1988. Milk production and feed intake of dairy cows fed *Lactobacillus inoculated* alfalfa silage. Applied Agric. Res., 3: 55-59.

Dann, H.M., J.K. Drackley, G.C. McCoy, M.F. Hutjens and J.E. Garrett, 2000. Effects of yeast culture (*Saccharomyces cerevisiae*) on prepartum intake and postpartum intake and milk production of jersey cows. J. Dairy Sci., 83: 123-127.

Dawson, K.A. and K.E. Newman, 1988. Fermentations in rumen-simulating continuous cultures receiving probiotic supplements. J. Anim. Sci., 66: 500-500.

Desnoyers, M., S. Giger-Reverdin, G. Bertin, C. Duvaux-Ponter and D. Sauvant, 2009. Meta-analysis of the influence of *Saccharomyces cerevisiae* supplementation on ruminal parameters and milk production of ruminants. J. Dairy Sci., 92: 1620-1632.

Dhama, K., M. Mahendran, S. Tomar and R.S. Chauhan, 2008. Beneficial effects of probiotics and prebiotics in livestock and poultry: The current perspectives. Intas Polivet, 9: 1-12.

Dhama, K., K. Karthik, R. Tiwari, M.Z. Shabbir, S. Barbuddhe, S.V.S. Malik and R.K. Singh, 2015. Listeriosis in animals, its public health significance (food-borne zoonosis) and advances in diagnosis and control: A comprehensive review. Vet. Q., 35: 211-235.

Dhanasekaran, D., S. Saha, N. Thajuddin and A. Panneerselvam, 2008. Probiotic effect of *Lactobacillus* isolates against bacterial pathogens in *Claris orientalis*. Facta Univ.: Med. Biol., 15: 97-102.

Dicks, L. and M. Botes, 2010. Probiotic lactic acid bacteria in the gastro-intestinal tract: Health benefits, safety and mode of action. Beneficial Microbes, 1: 11-29.

Dutta, T.K., S.S. Kundu and M. Kumar, 2009. Potential of direct-fed-microbials on lactation performance in ruminants-a critical review. Livestock Res. Rural Dev., Vol. 21.

Eckles, C.H. and V.M. Williams, 1925. Yeast as a supplementary feed for lactating cows. J. Dairy Sci., 8: 89-93.

Elghandour, M.M.Y., J.C. Vazquez Chagoyan, A.Z.M. Salem, A.E. Kholif, J.S. Martinez Castaneda, L.M. Camacho and M.A. Cerrillo-Soto, 2014a. Effects of *Saccharomyces cerevisiae* at direct addition or pre-incubation on *in vitro* gas production kinetics and degradability of four fibrous feeds. Ital. J. Anim. Sci., 13: 295-301.

Elghandour, M.M.Y., J.C.V. Chagoyan, A.Z.M. Salem, A.E. Kholif, J.S.M. Castaneda, L.M. Camacho and G. Buendia, 2014b. *In vitro* fermentative capacity of equine fecal inocula of 9 fibrous forages in the presence of different doses of *Saccharomyces cerevisiae*. J. Equine Vet. Sci., 34: 619-625.

Elghandour, M.M.Y., A.Z.M. Salem, J.S.M. Castaneda, L.M. Camacho, A.E. Kholif and J.C.V. Chagoya, 2015. Direct-fed microbes: A tool for improving the utilization of low quality roughages in ruminants. J. Integr. Agric., 14: 526-533.

Erasmus, L.J., P.M. Botha and A. Kistner, 1992. Effect of yeast culture supplement on production, rumen fermentation and duodenal nitrogen flow in dairy cows. J. Dairy Sci., 75: 3056-3065.

Fon, F.N. and I.V. Nsahlai, 2013. Effect of direct-fed microbial consortia on ruminal fermentation of maize stover in sheep. Small Rumin. Res., 111: 71-75.

Frizzo, L.S., L.P. Sotto, M.V. Zbrun, E. Bertozzi, G. Sequeira, R.R. Armesto and M.R. Rosmini, 2010. Lactic acid bacteria to improve growth performance in young calves fed milk replacer and spray-dried whey powder. Anim. Feed Sci. Technol., 157: 159-167.

Fuller, R., 1989. Probiotics in man and animals. J. Applied Bacteriol., 66: 365-378.

Galyean, M.L., G.A. Nunnery, P.J. Defoor, G.B. Salyer and C.H. Parsons, 2000. Effects of live cultures of *Lactobacillus acidophilus* (strains 45 and 51) and *Propionibacterium freudenreichii* PF-24 on performance and carcass characteristics of finishing beef steers. Burnett Center Progress Report No. 8, November, 2000, Lubbock, Texas, USA.

Ghorbani, G.R., D.P. Morgavi, K.A. Beauchemin and J.A.Z. Leedle, 2002. Effects of bacterial direct-fed microbials on ruminal fermentation, blood variables and the microbial populations of feedlot cattle. J. Anim. Sci., 80: 1977-1985.

Gilliland, S.E., 1989. Acidophilus milk products: A review of potential benefits to consumers. J. Diary Sci., 72: 2483-2494.

Gomez-Basauri, J., M.B. de Ondarza and J. Siciliano-Jones, 2001. Intake and milk production of dairy cows fed lactic acid bacteria and mannanoligosaccharide. J. Dairy Sci., 84: 283-283.

Gulbe, G., A. Valdovska, V. Saulite and J. Jermolajevs, 2015. *In vitro* assessment for antimicrobial activity of *Lactobacillus helveticus* and its natural glycopeptides against mastitis causing pathogens in dairy cattle. Open Biotechnol. J., 9: 61-66.

Gupta, S. and R.K. Gupta, 2007. Therapeutic efficacy of probiotics during indigestion in cattle. Intas Polivet, 8: 205-207.

Hagg, F.M. and P.H. Henning, 2007. Evaluation of supplementation with *Megasphaera elsdenii* NCIMB 41125, a lactate utilizing rumen microorganism, on performance in Holstein dairy cows. KK Animal Nutrition Internal Report, Holstein Association USA, Inc., Brattleboro, VT.

Haghighi, H.R., M.F. Abdul-Careem, R.A. Dara, J.R. Chambers and S. Shariff, 2008. Cytokine gene expression in chicken cecal tonsils following treatment with probiotics and Salmonella infection. Vet. Microbiol., 126: 225-233.

Harris, Jr. B. and R. Lobo, 1988. Feeding yeast culture to lactating dairy cows. J. Dairy Sci., 71: 276-276.

Holter, J.B. and A.J. Young, 1992. Methane prediction in dry and lactating Holstein cows. J. Dairy Sci., 75: 2165-2175.

Hoyos, G., L. Garcia and F. Medina, 1987. Effects of feeding viable microbial feed additives on performance of lactating cows in a large dairy herd. J. Dairy Sci., 70: 217-217.

Huck, G.L., K.K. Kreikemeier and K.K. Bolsen, 1999. Effect of reconstituting field-dried and early-harvested sorghum grain on the ensiling characteristics of the grain and on growth performance and carcass merit of feedlot heifers. J. Anim. Sci., 77: 1074-1081.

Hughes, J., 1988. The effect of a high-strength yeast culture in the diet of early-weaned calves. Anim. Prod., 46: 526-526.

Jaquette, R.D., R.J. Dennis, J.A. Coalson, D.R. Ware, E.T. Manfredi and P.L. Read, 1988. Effect of feeding viable *Lactobacillus acidophilus* (BT1386) on the performance of lactating dairy cows. J. Dairy Sci., 71: 219-219.

Jeyanathan, J., C. Martin and D.P. Morgavi, 2014. The use of direct-fed microbials for mitigation of ruminant methane emissions: A review. Animal, 8: 250-261.

Jouany, J.P., F. Mathieu, J. Senaud, J. Bohatier, G. Bertin and M. Mercier, 1999. Influence of protozoa and fungal additives on ruminal pH and redox potential. S. Afr. J. Anim. Sci., 29: 65-66.

Klieve, A.V., D. Hennessy, D. Ouwerkerk, R.J. Forster, R.I. Mackie and G.T. Attwood, 2003. Establishing populations of *Megasphaera elsdenii* YE 34 and *Butyrivibrio fibrisolvens* YE 44 in the rumen of cattle fed high grain diets. J. Applied Microbiol., 95: 621-630.

Komari, R.K., Y.K.L. Reddy, J. Suresh and D.N. Raj, 1999. Effect of feeding yeast culture (*Saccharomyces cerevisae*) and *Lactobacillus acidophilus* on production performance of crossbred dairy cows. J. Dairy Sci., 82: 128-128.

Krause, M.K. and G.R. Otzel, 2006. Understanding and preventing subacute ruminal acidosis in dairy herds: A review. Anim. Feed Sci. Technol., 126: 215-236.

Krehbiel, C.R., S.R. Rust, G. Zhang and S.E. Gilliland, 2003. Bacterial direct-fed Microbials in ruminant diets: Performance response and mode of action. J. Anim. Sci., 81: E120-E132.

Kritas, S.K., A. Govaris, G. Christodoulopoulos and A.R. Burriel, 2006. Effect of *Bacillus licheniformis* and *Bacillus subtilis* supplementation of ewe's feed on sheep milk production and young lamb mortality. J. Vet. Med. Ser. A, 53: 170-173.

Kung, Jr. L., 2006. Direct-Fed Microbial and Enzyme Feed Additives. In: Direct-Fed Microbial, Enzyme and Forage Additive Compendium, Lundeen, T. (Ed.). Miller Publishing, Minnetonka, MN., USA.

Kung, L. Jr., 2001. Direct-fed microbials for dairy cows and enzymes for lactating dairy cows: New theories and applications. Proceeding of the Pennsylvania State Dairy Cattle Nutrition Workshop, (DCN`01), Grantville, PA., pp: 86-102.

LeJeune, J.T. and A.N. Wetzel, 2007. Preharvest control of *Escherichia coli* O157 in cattle. J. Anim. Sci., 85: E73-E80.

Lynch, H.A. and S.A. Martin, 2002. Effects of *Saccharomyces cerevisiae* culture and *Saccharomyces cerevisiae* live cells on *in vitro* mixed ruminal microorganism fermentation. J. Dairy Sci., 85: 2603-2608.

Maragkoudakis, P.A., K.C. Mountzouris, C. Rosu, G. Zoumpopoulou and K. Papadimitriou *et al*., 2010. Feed supplementation of *Lactobacillus plantarum* PCA 236 modulates gut microbiota and milk fatty acid composition in dairy goats-a preliminary study. Int. J. Food Microbiol., 141: S109-S116.

Matsuguchi, T., A. Takagi, T. Matsuzaki, M. Nagaoka, K. Ishikawa, T. Yokokura and Y. Yoshikai, 2003. Lipoteichoic acids from Lactobacillus strains elicit strong tumor necrosis factor alpha-inducing activities in macrophages through toll-like receptor 2. Clin. Diagn. Lab. Immunol., 10: 259-266.

McAllister, T.A., K.A. Beauchemin, A.Y. Alazzeh, J. Baah, R.M. Teather and K. Stanford, 2011. Review: The use of direct fed microbials to mitigate pathogens and enhance production in cattle. Can. J. Anim. Sci., 91: 193-211.

Metchnikoff, E., 1907. The Prolongation of Life; Optimistic Studies. Heinemann, London.

Miles, R.D. and S.M. Bootwalla, 1991. Direct Fed Microbials in Animal Production. In: Direct-Fed Microbials in Animal Production: A Review of Literature, Hutcheson, D.P. (Ed.). National Feed Ingredients Association, West Des Moines, IA., pp: 117-132.

Mir, P.S. and Z. Mir, 1992. Effect of addition of live yeast cultures (*Saccharomyces cerevisiae*) on feed digestibility in the rumen and performance of streers. J. Anim. Sci., 70: 309-309.

Miron, J., D. Ben-Ghedalia and M. Morrison, 2001. Invited review: Adhesion mechanisms of rumen cellulolytic bacteria. J. Dairy Sci., 84: 1294-1309.

Nakanishi, Y., C.W. Arave and P.H. Stewart, 1993. Effects of feeding Lactobacillus acidophilus yogurt on performance and behavior of dairy calves. J. Dairy Sci., 76: 244-244.

Newbold, C.J., R.J. Wallace and F.M. McIntosh, 1996. Mode of action of the yeast *Saccharomyces cerevisiae* as a feed additive for ruminants. Br. J. Nutr., 76: 249-261.

Nikkhah, A., M.D. Bonadaki and A. Zali, 2004. Effect of feeding yeast (*Saccharomyces cerevisiae*) on productive performance of lactating Holstein dairy cow. Iran. J. Agric. Sci., 35: 53-60.

Nocek, J.E., W.P. Kautz, J.A.Z. Leedle and J.G. Allman, 2002. Ruminal supplementation of direct-fed microbials on diurnal pH variation and *in situ* digestion in dairy cattle. J. Dairy Sci., 85: 429-433.

Nocek, J.E., W.P. Kautz, J.A.Z. Leedle and E. Block, 2003. Direct-fed microbial supplementation on the performance of dairy cattle during the transition period. J. Dairy Sci., 86: 331-335.

Nocek, J.E. and W.P. Kautz, 2006. Direct-fed microbial supplementation on ruminal digestion, health and performance of pre- and postpartum dairy cattle. J. Dairy Sci., 89: 260-266.

Oetzel, G.R., K.M. Emery, W.P. Kautz and J.E. Nocek, 2007. Direct-fed microbial supplementation and health and performance of pre- and postpartum dairy cattle: A field trial. J. Dairy Sci., 90: 2058-2068.

Ohashi, Y. and U. Ushida, 2009. Health-beneficial effects of probiotics: Its mode of action. Anim. Sci. J., 80: 361-371.

Ohya, T., T. Marubashi and H. Ito, 2000. Significance of fecal volatile fatty acids in shedding of *Escherichia coli* O157 from calves: Experimental infection and preliminary use of a probiotic product. J. Vet. Med. Sci., 62: 1151-1155.

Orskov, E.R., H.S. Soliman and A. MacDearmid, 1978. Intake of hay by cattle given supplements of barley subjected to various forms of physical treatment or treatment with alkali. J. Agric. Sci., 90: 611-615.

Otero, M.C., L. Morelli and M.E. Nader-Macias, 2006. Probiotic properties of vaginal lactic acid bacteria to prevent metritis in cattle. Lett. Applied Microbiol., 43: 91-97.

Pagnini, C., R. Saeed, G. Bamias, K.O. Arseneau, T.T. Pizarro and F. Cominelli, 2010. Probiotics promote gut health through stimulation of epithelial innate immunity. Proc. Natl. Acad. Sci. USA., 107: 454-459.

Paul, S.S., S.M. Deb and D. Singh, 2011. Isolation and characterization of novel sulphate-reducing *Fusobacterium* sp. and their effects on *in vitro* methane emission and digestion of wheat straw by rumen fluid from Indian riverine buffaloes. Anim. Feed Sci. Technol., 166-167: 132-140.

Poppi, L.B., J.D. Rivaldi, T.S. Coutinho, C.S. Astolfi-Ferreira, A.J.P. Ferreira and I.M. Mancilha, 2015. Effect of *Lactobacillus* sp. isolates supernatant on *Escherichia coli* O157:H7 enhances the role of organic acids production as a factor for pathogen control. Pesquisa Veterinaria Brasileira, 35: 353-359.

Puniya, A.K., A.Z.M. Salem, S. Kumar, S.S. Dagar and G.W. Griffith *et al*., 2015. Role of live microbial feed supplements with reference to anaerobic fungi in ruminant productivity: A review. J. Integr. Agric., 14: 550-560.

Quigley, III J.D., L.B. Wallis, H.H. Dowlen and R.N. Heitmann, 1992. Sodium bicarbonate and yeast culture effects on ruminal fermentation, growth and intake in dairy calves. J. Dairy Sci., 75: 3531-3538.

Raeth-Knight, M.L., J.G. Linn and H.G. Jung, 2007. Effect of direct-fed microbials on performance, diet digestibility and rumen characteristics of holstein dairy cows. J. Dairy Sci., 90: 1802-1809.

Renz, F. and A. Koch, 1956. Milk production with the active yeast concentrate Astoral. Zuchtungskunde, 28: 298-301.

Rigobelo, E.E.C., N. Karapetkov, S.A. Maesta, F.A. Avila and D. McIntosh, 2014. Use of probiotics to reduce faecal shedding of Shiga toxin-producing *Escherichia coli* in sheep. Beneficial Microbes, 6: 53-60.

Russell, J.B. and R.L. Baldwin, 1978. Substrate preferences in rumen bacteria: Evidence of catabolite regulatory mechanisms. Applied Environ. Microbiol., 36: 319-329.

Sandine, W.E., 1979. Roles of Lactobacillus in the intestinal tract. J. Food Protect., 42: 259-262.

Schamberger, G.P., R.L. Phillips, J.L. Jacobs and F. Diez-Gonzalez, 2004. Reduction of *Escherichia coli* O157:H7 populations in cattle by addition of colicin E7-producing *E. coli* to feed. Applied Environ. Microbiol., 70: 6053-6060.

Schmidt, R.J., W. Hu, J.A. Mills and L. Kung, Jr., 2009. The development of lactic acid bacteria and *Lactobacillus buchneri* and their effects on the fermentation of alfalfa silage. J. Dairy Sci., 92: 5005-5010.

Seo, J.K., S.W. Kim, M.H. Kim, S.D. Upadhaya, D.K. Kam and J.K. Ha, 2010. Direct-fed microbials for ruminant animals. Asian-Australasian J. Anim. Sci., 23: 1657-1667.

Servin, A.L., 2004. Antagonistic activities of lactobacilli and bifidobacteria against microbial pathogens. FEMS Microbiol. Rev., 28: 405-440.

Stein, D.R., D.T. Allen, E.B. Perry, J.C. Bruner and K.W. Gates *et al*., 2006. Effects of feeding propionibacteria to dairy cows on milk yield, milk components and reproduction. J. Dairy Sci., 89: 111-125.

Stewart, C.S., H.J. Flint and M.P. Bryant, 1997. The Rumen Bacteria. In: The Rumen Microbial Ecosystem, Hobson, P.N. and C.S. Stewart (Eds.). Chapter 2, Blackie Academic and Professional, London, UK., ISBN: 978-94-010-7149-9, pp: 10-72.

Thomas, P.C. and A.F. Rook, 1981. Recent Developments in Animal Nutrition. In: Recent Advances in Animal Nutrition, Haresign, W. and D.J.A. Cole (Eds.). Butterworths, London, UK., pp: 157-183.

Uyeno, Y., S. Shigemori and T. Shimosato, 2015. Effect of probiotics/prebiotics on cattle health and productivity. Microbes Environ., 30: 126-132.

Varankovich, N.V., M.T. Nickerson and D.R. Korber, 2015. Probiotic-based strategies for therapeutic and prophylactic use against multiple gastrointestinal diseases. Front Microbiol., Vol. 6. 10.3389/fmicb.2015.00685

Wallnofer, P. and R.L. Baldwin, 1967. Pathway of propionate formation in *Bacteroides ruminicola*. J. Bacteriol., 93: 504-505.

Williams, J.E., S. Grebing, S.J. Miller and L. Gieseke, 1987. The influence of supplemental yeast culture and sodium bicarbonate on performance and blood acid-base status in wether lambs exposed to elevated ambient temperature. J. Anim. Sci., 65: 156-156.

Williams, P.E., C.A. Tait, G.M. Innes and C.J. Newbold, 1991. Effects of the inclusion of yeast culture (*Saccharomyces cerevisiae* plus growth medium) in the diet of dairy cows on milk yield and forage degradation and fermentation patterns in the rumen of steers. J. Anim. Sci., 69: 3016-3026.

Williams, P.E.V., 1989. The Mode of Action of Yeast Culture in Ruminant Diets: A Review of the Effect on Rumen Fermentation Patterns. In: Biotechnology in the Feed Industry: Proceedings of Alltech's Fourth Annual Symposium, Lyons, T.P. (Ed.). Alltech Technical Publications, Nicholasville, USA., pp: 65-84.

Wiryawan, K.G. and J.D. Brooker, 1995. Probiotic control of lactate accumulation in acutely grain-fed sheep. Aust. J. Agric. Res., 46: 1555-1568.

Wohlt, J.E., A.D. Finkelstein and C.H. Chung, 1991. Yeast culture to improve intake, nutrient digestibility and performance by dairy cattle during early lactation. J. Dairy Sci., 74: 1395-1400.

Wohlt, J.E., T.T. Corcione and P.K. Zajac, 1998. Effect of yeast on feed intake and performance of cows fed diets based on corn silage during early lactation. J. Dairy Sci., 81: 1345-1352.

Yadav, R. and P. Shukla, 2015. An overview of advanced technologies for selection of probiotics and their expediency: A review. Crit. Rev. Food Sci. Nutr., (In Press). 10.1080/10408398.2015.1108957

Yang, W.Z., K.A. Beauchemin, D.D. Vedres, G.R. Ghorbani, D. Colombatto and D.P. Morgavi, 2004. Effects of direct-fed microbial supplementation on ruminal acidosis, digestibility and bacterial protein synthesis in continuous culture. Anim. Feed Sci. Technol., 114: 179-193.

Yasuda, K., S. Hashikawa, H. Sakamoto, Y. Tomita, S. Shibata and T. Fukata, 2007. A new synbiotic consisting of *Lactobacillus casei* subsp. casei and dextran improves milk production in Holstein dairy cows. J. Vet. Med. Sci., 69: 205-208.

Yeoman, C.J. and B.A. White, 2014. Gastrointestinal tract microbiota and probiotics in production animals. Annu. Rev. Anim. Biosci., 2: 469-486.

Yoon, I.K. and M.D. Stern, 1995. Influence of direct-fed microbials on ruminal microbial fermentation and performance of ruminants-A review. Asian-Australasian J. Anim. Sci., 8: 533-555.

Yuan, C.L., Z.Y. Yu, Y.T. Lin and L.H. Wang, 2015. Effects of probiotics on the calves and its affecting factors. China Dairy Cattle, 8: 9-12.