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Effect of Yeast Cell Wall on Gut Health, Immunity and Milk Production of Dairy Cattle in Normal and Heat Stress Conditions. Review

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ABSTRACT

This review focuses on the most recent literature to bring to light the major beneficial effects of the yeast cell wall (YCW) and its products on dairy cattle. These products include viable yeast, yeast culture, nutritional yeast, and fractionated yeast products. The yeast cell wall is one of these products and belongs to the fractionated yeast products used to promote production performance and health in dairy cows. The yeast and YCW were proven to have positive impacts on dairy cattle performance in terms of milk yield, milk components, and overall quality. As well, these products showed beneficial effects under heat stress conditions. The YCW is a natural fermentation derivative of yeast cells such as Saccharomyces cerevisiae species consists mainly of β-glucan (29% to 64%), mannan (31%), and some other compounds like protein (13%), lipids (9%), chitin (1–2%) with β-glucan and mannan being the main bioactive molecules. The mode of action through which YCW elicit their beneficial functions in dairy cow explain their effect on cows' metabolism and digestion, immunity, rumen and intestine health, and subsequent performance and well-being. These modes of action include improving gastrointestinal (GI) tract health, stimulating immune system components as it is considered an immunomodulator additive, mycotoxin binding ability, and improving antioxidant capacity. Therefore, yeast and YCW products are one of the promising areas of ruminant nutrition in dairy cows, not only because of their nutritional and health benefits to dairy cows but also due to their negligible residual effects on dairy cows' bodies and products.

Keywords: Yeast, Yeast cell wall, Dairy cow; Performance

INTRODUCTION

Yeasts are found everywhere in nature in colossal amounts. There are about 60 different genera of yeast, comprised of approximately 500 different species varying in their cellular morphology, metabolism of different substrates, and reproduction processes (Stone, 2006).

Only a few of these species are used commercially; most yeast species are neither harmful nor beneficial to humans and animals. Some yeast genera are pathogenic (Candida, Cryptococcus, Torulopsis, and Trichosporon), while some species like *Saccharomyces cerevisiae*, *Kluyveromyces marxianus, and Candida utilis* have beneficial effects (Øverland *et al.,* 2013). The *Saccharomyces cerevisiae* is the predominant species used in animal feed formulation (Broadway *et al*., 2005). Yeasts are single-cell, microscopic eukaryotic microorganisms with about 3–4 µm in size classified in the fungi kingdom and have a nuclear membrane and cell

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walls. The intracellular composition of yeast includes amino acids, peptides, carbohydrates, lipids, vitamins, minerals, salts, monosodium glutamate, nucleic acids (RNA), enzymes, and cofactors (Riba *et al.,* 2021). Yeast cell walls are glucans, glycoproteins, mannans, and chitin (Ingraham, 2010).

Dairy cows receiving supplementation of Yeast and Yeast Cell Wall product derived mainly from *Saccharomyces cerevisiae* species were found to consume more dry matter and produce more milk during the pre- and postpartum periods, that was positively influenced the lactation performance in dairy cows (Bruno *et al*., 2009; Lees *et al.,* 2021). Wafa *et al.,* (2020) found that milk yield increased in quantity terms (12.4%) as well in terms of quality, mainly total solids.

Different researchers also found that Yeast and Yeast Cell Wall product supplementation to dairy cattle improved mammary health, decreased somatic cell count, and decreased the incidence of clinical and subclinical mastitis (Nocek *et al*.,2011; Oltramari et al.,2014; Ryman *et al*., 2013).

During heat stress periods, feeding dairy cows with Yeast and Yeast Cell Wall product mitigates the negative impact of heat stress on cows' performance, improves milk yield with a significant increase in milk fat percentage, and maintains milk persistency (Dehghan-Banadaky *et al*., 2013; Liu *et al*., 2014; Zhu *et al*., 2016:2017).

The unique combination of bioactive compounds found in yeast and yeast cell walls makes yeast cells a good choice as nutritional supplements in animal feeds and functional nutritional and nutraceuticals for food-producing animals. Yeast contains a high concentration of nucleotides and proteins. The general matrix of the yeast cell contains hydrolytic enzymes (nucleases and proteases) that destroy these nucleotides and proteins by autolysis.(Tangüler *et al.,* 2009) Proteases degrade proteins into peptides and amino acid derivatives, while nucleases degrade nucleic acids, DNA, and RNA into nucleotides. Yeast and yeast-derived products are developing areas of research (Hassan, 2011).

There *is a* wide range of yeast and yeast-based feed additives that have been recently used for dairy cattle nutrition and are considered among the most common supplements added to dairy ration (Broadway *et al*., 2015). Yeast and yeast-based feed additive products enhance dry matter intake and overall animal performance (Shurson, 2017). These products include viable yeast products, yeast culture, nutritional yeast products, specialty yeast products (irradiated yeast, selenium yeast, chromium yeast, and Phaffia yeast), and Fractionated yeast products (AAFCO, 2017). Yeast cell wall (YCW) is one of these products and belongs to fractionated yeast products used to promote production performance and health in dairy cattle (AlZahal *et al*., 2014).

The YCW is a natural fermentation derivative of yeast cells such as *Saccharomyces cerevisiae* species consists mainly of β-glucan (29% to 64%) and Mannan (31%), and some other molecules like protein (13%), lipid (9%), chitin (1–2%) with β-glucan and Mannan being the main bioactive molecules (Liu *et al*., 2021). Glucans are the primary polysaccharide component in the yeast cell wall, with β-glucans being predominant. β-glucans have functional biological activities making them one of the most helpful livestock animal feed supplements because of their potential beneficial effects on animal health and growth performance (Liu *et al*., 2021). Their ability to promote the desired response, for example, induces leukocyte activation and produces inflammatory mediators (Burdick Sanchez *et al*., 2021). They are well-known as toxins-, viruses- and pathogenic bacteria-binders (Vetvicka *et al*., 2014). White blood cells (Macrophages) have receptors for β-glucans, after binding to this receptor, β-glucans have the activity to trigger IL-1 production since IL-1 is produced only by macrophages, also increases the production of IL-6 and IL-8, which represent essential activators of other white blood cells increasing their division and count in the blood (Rop *et al.,* 2009).

Mannans are considered the second most crucial component of yeast cell walls. Mannan-oligosaccharides (MOS) serve as prebiotics or sources of nutrients for selected beneficial microbes in the gastrointestinal tract, leading to a probiotic effect (Spring *et al*., 2015). The results of feeding MOS to horses, rabbits, poultry, pigs, and calves were reviewed by Spring *et al.* (2015). They found a marked improvement in animal performance attributed to the biological activities of MOS and their capacity to prevent the colonization of pathogens in the gastrointestinal tract, improve the integrity of the intestinal mucosa, and modulate immune system activity. They may be involved in antioxidant and anti-mutagenic defense mechanisms (Spring *et al*., 2015).

Different yeast and yeast-based feed additives have been administered to food-producing livestock for more than 100 years (Stone, 2005). Elimination of growth-promoting antibiotics in animal feed in the European Union and the United States has led to a significant increase in interest in using alternative products (including yeast products) to improve animal health and growth performance (Shurson, 2017). In the case of dairy cattle, YCW is commonly used to enhance ruminal and intestinal microflora populations, the establishment of a healthy gastrointestinal tract environment as a primary step for enhancing dry matter intake and daily gain. This would improve animal performance and health, giving them conditions to enhance the synthesis of proteins and vitamins and improve milk production and quality (Nocek *et al*., 2011). Maintaining a healthy gut through supplementation of natural feed additives like YCW is crucial under the pressure of an antibiotic ban (Ma *et al*., 2020).

The mode of action through which YCW elicit their functions in dairy cattle explains their effect on metabolism and digestion, immunity, rumen and intestine health, and subsequent performance and well-being. These modes of action include improvement of gastrointestinal (GI) tract health, stimulating immune system components as it is considered an immunomodulator additive, mycotoxin binder, and improving antioxidant capacity (Liu *et al*., 2021). This review will focus on reviewing the most recent literature in order to highlight the major beneficial effects of yeast and yeast cell walls on dairy cattle performance, milk production, gut health, and immune responses under normal and heat-stress conditions.

The Different Yeast Species of Importance in Animal Feeding

Viable Yeast Product

A wide range of yeast and yeast-based products used as feed additives are produced for animal production applications. The most popular prebiotic supplement offered to dairy cows is yeast. Live yeast, YCW, purified cell wall components such as mannooligosaccharides (MOS), β-glucans, and yeast fermentation or culture products, which are by-products of yeast fermentation, are all examples of yeast supplements. The appearance, composition of biologically active components, and production system application of these products varied. (Burdick Sanchez *et al*., 2021).

Viable yeast products are generally added to animal feeds for their potential prebiotic and subsequent probiotic effects (Stone, 2006). Active dry yeast is comprised of 15–25 billion live yeast cells per gram. Processes for drying viable yeast include tunnel dried, fluid-bed dried, and roto louver dried. The pelleting process uses steam (moist heat) to condition the feed prior to force through a pellet die. Moist heat is considered one of the most effective methods for killing microorganisms because it inhibits enzyme systems and their metabolic activity within the organism. Yeast cell viability and cell vitality are important factors to consider when assessing the functionality of yeast cells in pelleted feeds (Tangüler *et al.,* 2009). Survival of unprotected yeast cells would be expected to be low after the typical pelleting process, and this must be taken into account when making decisions about whether to feed those (Stone, 2006).

Yeast Cultures

Yeast cultures are unique because they contain a combination of yeast biomass and fermentation metabolites produced during specific fermentation processes. To produce yeast cultures, a specific media is inoculated with live yeast cells and allowed to ferment under specific conditions (Riba *et al.,* 2021). The composition of the various metabolites produced depends on the media used and the fermentation conditions (Stone, 2006).

Nutritional Yeast Products

Nutritional yeast products include dried yeast, brewer's dried yeast, and whey yeast. Whey yeast is considered to be a nutritional yeast product because it consists of the yeast biomass of yeasts and is fed for its nutritional value. Brewer's yeast is commonly used in the animal feed industry as a specialty micronutrient supplement. Torula yeast (Candida utilis) also contains high concentrations of protein, minerals, and vitamins. Yeast products contain twice the amount of lipid (ether extract) compared with dehulled soybean meal (Øverland *et al.,* 2013). Nutritional yeast products could be produced from low-value, non-food lignocellulosic biomass for use in aquaculture feeds (Dubey *et al.,* 2010)

Specialty yeast products

Specialty yeast products include irradiated yeast, selenium yeast, chromium yeast, and Phaffia yeast. Irradiated yeast contains ergosterol which can be converted to vitamin D2 when irradiated with ultraviolet light (Stone, 2006). Selenium yeast is commercially produced and marketed as a highly bioavailable form of Se (selenomethionine). Phaffia yeast produces a red pigment or carotenoid (astaxanthin) and is used in trout and salmon feeds to enhance the red pigmentation in fillets (Stone, 2006).

Fractionated Yeast Products

Yeast condensed soluble, hydrolysates, extracts, and cell walls comprise another category of ingredients produced and used in the food and feed industry. Yeast autolysates contain both intracellular and cell wall fractions and are made up of lysed entire yeast cells (using acids or enzymes or a high salt solution to rupture cells produced by increased osmotic pressure). Yeast extracts are made up entirely of intracellular components, whereas yeast cell wall products are made up entirely of carbohydrates found in the cell wall (Riba *et al*., 2021). The food sector generally uses yeast autolysates and extracts to enhance the flavor of foods (Hassan, 2011).

The carbohydrate content and composition of yeast vary depending on the growing conditions. Intracellular carbohydrates are primarily comprised of glycogen and trehalose. The cell wall represents about 15–20% of the dry weight of yeast cells, and the main carbohydrate fractions are β-glucans and mannans (Halasz and Lasztity, 1991).

Glucans are the primary polysaccharide component in *Saccharomyces cerevisiae* and are a highly insoluble part of the support structure of the cell wall. The inner layer of yeast cell walls is made up of insoluble β-glucan (30–35%), the middle layer is made up of soluble glucan (20–22%), and the outside layer is made up of glycoprotein (30 %). Glucans are made up of 1, 3 glucans with 1, 6 branch connections, and during yeast autolysis, both Endo and Exo-1, 3 glucanases are generated. Because of their potential favorable impacts on animal health and growth performance, β-glucans are becoming increasingly popular in the animal feed industry (Vetvicka *et al*., 2014) Mannans are the second most important component of yeast cell walls, and they are linked to a branch structure by -1, 6 bonds, with side chains made up of mannose units linked to the backbone by -1, 2 bonds (Halasz and Lasztity, 1991). Spring *et al.* (2015) found that mannan oligosaccharides (MOS) can operate as prebiotics, or sources of nourishment for certain microorganisms in the gastrointestinal tract, resulting in a probiotic effect (Spring *et al.,* 2015).

Yeast also contains a high concentration of nucleotides and proteins. The general matrix of the yeast cell contains hydrolytic enzymes (nucleases and proteases) that destroy these nucleotides and proteins by autolysis. Proteases degrade proteins into peptides and amino acid derivatives, while nucleases degrade nucleic acids, DNA, and RNA into nucleotides (Halasz and Lasztity, 1991).

The effect of yeast supplementation on dairy cows' performance is well documented. Yeast cell wall biological functions could modulate dairy cow's performance and well-being. This review will highlight the effect of yeast cell wall products on dairy cow gastrointestinal tract environment, immune system, udder health, milk quality, and quantity, and performance during heat stress.

Effect of Yeast and YCW on Dairy Cow

Effects on *Gastrointestinal Tract Environment*

Yeast and YCW have numerous positive effects on gastrointestinal tract function. They can alter permeability and enhance nutrient absorption through decreased mucus thickness (Liu *et al*., 2021). They can improve the peristalsis movement, increase villus height and crypt depth, and tighten the junction between epithelial cells enhancing intestinal integrity and barrier function (Ma *et al*., 2020). This barrier prevents the passage of pathogenic microorganisms and their harmful components from the intestine lumen to the body system, thus reducing the incidence of inflammation and disease (Ma *et al.,* 2020). B-glucan repairs the intestinal barrier damage and maintains the mucosal membrane's integrity by triggering the intestinal epithelial cell to secret neurotransmitters and cytokines in the mucosa (Chen *et al.,* 2019). These neurotransmitters and cytokines include acetylcholinesterase, substance P, serotonin, and the close-linked protein (Chen *et al*., 2019). This substance is responsible for the upregulation of tight junction protein expression (Ma *et al.,* 2020).

In a recent study on dietary supplementation of the YCW to weaned calves, Jian Ma and his colleagues (2020) found that calves fed YCW significantly increased the mRNA expression of Occludin, the tight junction protein in the mucosa of jejunum and ileum, which could enhance the intestinal epithelial cell wall structure and integrity, preventing pathogenic bacteria and toxic substances from entering submucosa through the intestinal epithelial space and enhance the control of tight junction permeability (Ma *et al*., 2020).

Yeast Cell Wall (YCW)

Supplementation can also modulate the rumen environment in dairy cattle to prevent rumen acidosis after feeding high concentrate ration and cereal grains (Lean *et al.,* 2000). Their metabolism end product is lactate, responsible for lowering rumen pH (Desnoyers *et al.,* 2009). Yeast cell wall supplementation is found to modulate the rumen microbial ecosystem and enhance microflora's diversity and richness, causing an increase in lactate fermentative bacteria, leading to lower lactate concentration in the rumen (lean *et al*.,2000). Ganan and his colleagues found that Mannan extract enhances the proliferation of beneficial lactic acid bacteria, improving their growth, gastrointestinal viability, and adherence to intestinal epithelial cells (Ganan *et al.,* 2012).

Xiao *et al*. (2019) studied the effects of *Saccharomyces cerevisiae* fermentation products on the microbial ecosystem in the rumen and large intestine of dairy calves. They found that the inclusion of *Saccharomyces cerevisiae* fermentation product (SCFP) at 0.5 % of the basal diet modulates the rumen microbial ecosystem, improves beneficial microorganism species in the large intestine, the bacterial community in the rumen, and later in rectum microbiota. Supplementation of SCFP stimulated colonization by fibrolytic bacteria (Lachnospiraceae) in the intestine and (Ruminococcaceae) in the rumen (Xiao *et al.,* 2019).

Through the reduction of lactate, YCW supplementation aids in buffering rumen pH and rumen stability, rendering the rumen environment more suitable for beneficial bacteria to grow, such as cellulolytic bacteria Ruminococcus albus, which degrade cellulose (Terré *et al.,* 2015). Hence YCW supplementation to dairy cattle fed a highly concentrated diet helps in lowering the incidence of acidosis and avoiding acidosis complications like decreased dry matter intake and inflammation that have deleterious consequences on dairy cattle performance (Bradford *et al.,* 2015).

Thrune *et al.* (2009) studied the effects of yeast supplementation on rumen health and rumen acidosis for Holstein dairy cows in late lactation supplemented with 0.5 g/head/d of *Saccharomyces cerevisiae*, an active dry yeast. They found that the mean ruminal pH was more significant when the yeast was supplemented (6.53 ± 0.07) than the control (6.32 ± 0.07). Average maximum and minimum ruminal pH were also more significant when yeast was supplemented (7.01 ± 0.09 and 5.97 ± 0.08, respectively) compared with the control (6.80 ± 0.09 and 5.69 ± 0.09, respectively). Time spent under the subacute acidosis threshold, pH less than 5.6, was lower with yeast supplementation compared with control cows, and they concluded that yeast supplementation did tend to affect overall ruminal volatile fatty acid concentration lowering the incidence of rumen acidosis (Thrune *et al*., 2009).

The positive effect of YCW supplementation on dairy cattle is not limited to the growth and proliferation of beneficial bacteria but also to providing essential nutrients like organic acids and growth factors like mannose (Burdick *et al*., 2020). In addition, it includes the prevention of pathogenic bacteria of attachment to GIT wall, and the YCW components mannan, and β-Glucan bind to pathogenic bacteria directly (Liu *et al.,* 2021). These pathogenic bacteria include Salmonella, Escherichia coli, Clostridia, Listeria, and Fusobacteria (Posadas *et al*., 2017). Mannan structure is identical to the pathogenic bacteria structure receptor located on the intestinal wall (Liu *et al.*, 2021). It has a high affinity to bind to the pathogenic bacteria before attaching to the intestinal wall (competitive exclusion), preventing bacterial cell attachment and adhesion, the first step in the infection process (Liu *et al.,* 2021). B-glucan has an antibacterial capacity; it can damage the bacterial cell wall, alter the permeability of the bacterial cell wall membrane, enter inside the bacterial cell, and change its metabolism (Khan *et al.,* 2016).

Mannan, the other component of YCW when entering the GIT, is hydrolyzed by mannosidase into shorter-chain fatty acid (mannose), which is an essential element in the electron transport chain and adenosine triphosphate gene expression and synthesis, providing the beneficial bacteria with the energy needed to maintain the cell morphology and function (Abbott *et al.,* 2015). The bacteriostatic effect of YCW studied in vitro, Trevisi and his colleagues (2012) test the ability of a yeast cell wall (YCW) to inhibit the enterotoxigenic Escherichia coli (ETEC) adhesion on the brush border of porcine intestinal villi, and they found that the affinity between YCW receptors and (ETEC) is high. That yeast cell wall captured enterotoxigenic E. coli significantly and reduced the number of pathogens on the intestinal wall (Trevisi *et al.,* 2012). Table (1) summarizes a review of literature studies reporting an improvement in dairy cows' gastrointestinal environment and functions due to feeding yeast and yeast cell wall products.

Table 1: Effect of yeast and yeast cell wall product supplementation on gastrointestinal environment and functions of dairy cows.

Yeast Species/Type	**Period Fed Diets**	**Dosage (g/kg of Feed or % of Diet or CFU)**	**Improved Parameters**	**References**
Saccharomyces cerevisiae- active dry yeast	18 days	0.5 g/head/day	Decrease the incidence of acidosis	Thrune *et al*. (2009)
active dry *Saccharomyces cerevisiae* (ADSC)	Ten weeks	8×10^{10} CFU\head per day	Increase in cellulolytic microbes within the rumen.	Al-zahal *et al*. (2014)

Saccharomyces cerevisiae fermentation products (SCFP)	56 days	0.5% of the basal diet	Increased the microbial species richness in the large intestine.	Xiao et al. (2019)
live yeast (LY) *Saccharomyces cerevisiae*	17 weeks	5×10^{10} CFU/cow/day	Increase rumen pH Prevent acidosis.	Kumprechtová *et al*. (2019)
YCW: β-glucan ≥ 30%, mannan-oligosaccharide ≥ 35%),	60 days	0.16% of the basal diet	Improve the barrier function of the small intestine.	Ma *et al*. (2020).
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YCW: β-glucan ≥ 30%, mannan-oligosaccharide ≥ 35%),	60 days	0.16% of the basal diet	Improve the barrier function of the small intestine.	Ma *et al*. (2020).

Effects on Dairy Cattle Immunity

The YCW is well known as an immune-modulator and biological response modifier (Broadway *et al.,* 2015; Shurson, 2017; Burdick Sanchez *et al*., 2021). Using YCW as feed additives can alter innate and adaptive immune system components either directly or indirectly (Majtán *et al.,* 2005). The first response comes from the innate immune system after exposure to an immunogenic substance like a pathogen. These immediate non-specific responses include the cellular barriers, white blood cell activation (macrophages and neutrophils), and secretion of cytokines and complement factors to neutralize and kill the pathogen (Liu *et al.,* 2020). When the pathogen escapes the innate defense mechanism, the adaptive immune response plays its role by activating T-cell and B-cell lymphocytes. This process is well organized, helping the body return to a normal physiological state, but the immune response will deteriorate (Burdick Sanchez *et al.,* 2021).

Supplementation of YCW to dairy cattle induces pronounced responses in the immune system, β-glucan, and Mannan can activate macrophages and stimulate mitosis, improve oxidative burst and phagocytosis capacity of white blood cells, and increase the level of acute-phase protein during periods of stress (Fomenky *et al.,* 2018). Stimulation of macrophage and dendritic cell to secrete tumor necrosis factor and cytokines such as interleukins 1, 2, and 6, increase the lysis activity of macrophages by increasing their capacity to secrete lysozyme (Liu *et al*., 2020). The effect of YCW supplementation on adaptive immune response expressed activation of B-cell to produce immunoglobulin and increasing antibodies titer (IgG) in the serum of dairy cows and their calf supplemented with YCW during gestation periods compared to non-supplemented cows (Jang *et al.,*2013). In another study, Fröhdeová and his colleagues showed that there is an increase in IgG, IgA, and IgM antibodies titer in the serum of cows that received YCW supplementation through their gestation periods and in the serum of their calf immediately after birth (Fröhdeová *et al.,* 2014). Similarly, Wafa and her colleagues (2020) showed a significant increase in serum immunoglobulins (IgG, IgM, and IgA) concentrations in dairy cows and their calves supplemented with inactivated yeast strains of Saccharomyces cerevisiae (40g\head\day) three months before calving until three months post-calving, indicating that yeast supplementation improves the immune status for dairy cows and their calves through increase antibodies concentration and subsequent improvement in health status (Wafa *et al.,*2020). The transfer of passive immunity from dams to their calves was enhanced after adding yeast cell walls to dairy cows' diet . The addition of 10g \head \day of mannan oligosaccharide (MOS) yeast cell wall to dairy cows during the last three weeks of the dry period increases serum rotavirus neutralization titers at calving in cows supplemented with MOS indicating improvement in specific immunity response. Similarly, more extraordinary serum rotavirus neutralization titers were detected in calves born from cows supplemented with MOS during the gestation period compared with calves from cows fed the control diet. Also, significant increases in serum protein concentrations immediately after birth in calves born from dams supplemented with Mannan oligosaccharides compared with calves born from cows not supplemented with MOS (Franklin *et al*., 2005). This finding indicates that supplementation of dry cows during the gestation period with MOS enhanced their immune response to rotavirus and improved the passive immunity transfer from dams to their calves (Franklin *et al*., 2005).

β-glucan induces B cells to produce antibodies response by binding complement receptor type three (CR3), Dectin-1, or toll-like receptors on macrophages, neutrophils, dendritic cells, and natural killer cells. This binding initiates a cascade of steps that end with antibody production (Liu *et al.,* 2020). For example, Fröhdeová and his colleagues (2014) showed that supplementing pregnant cows with yeast culture resulted in higher blood IgG concentrations two days post-calving in both the cows and their calves (Fröhdeová *et al.,* 2014). Ryman *et al*. (2013) evaluate the effect of adding active dried Saccharomyces cerevisiae yeast and B-complex vitamins (OmniGen-AF) as an immuno-modulator feed supplement to dairy heifers in an attempt to prevent mastitis. They found that neutrophils from treated animals showed increased surface-binding of bacteria, phagocytic activity, and reactive oxygen species production compared with the control group, which means strengthening innate immunity response enhancing the innate immune response against pathogens and healthier animals and reducing disease incidence like mastitis and resulting in less antibiotic use (Ryman *et al.,* 2013).

The cumulative effect of YCW supplementation on immune system modulation appears on dairy cattle health by decreasing disease incidence and alleviating the negative consequences of stress. For example, during heat stress, the hypothalamic-pituitary-adrenal axis (HPA)is stimulated, and the addition of YCW to heat-stressed high lactating dairy cattle reduces the severity of the effect of activation of the (HPA)axis, and this is measured by decreased cattle rectal temperature (Sanchez *et al.,* 2015).

Alteration of the gastrointestinal environment in dairy cattle after the addition of YCW is a crucial step in modulating immune response and disease resistance, for example, increasing the abundance of fibrinolytic bacteria in the gastrointestinal tract of ruminants in contrast to cellulytic bacteria like Eubacterium rumination that leads to enhance nutrient uptake and simultaneously improving immune function (Chaucheyras-Durand *et al.,* 2001). Table (2) summarizes literature studies reporting an improvement in the immune responses of dairy cows as a result of feeding yeast and yeast cell wall products.

Table 2: Effect of yeast and yeast cell wall products supplementation immune responses of dairy cows.

Yeast Species/Type	**Period Fed Diets**	**Dosage (g/kg of Feed or % of Diet or CFU)**	**Improved Parameters**	**References**
Mannan oligosaccharide (MOS) YCW	One month	10 g\head\day	Enhance the transfer of passive immunity to calves. Increase in the WBC count.	Franklin *et al.* (2005)
active dried *Saccharomyces cerevisiae* yeast and B-complex vitamins	16 months	4 g /100 lb of body weight daily	Increased neutrophil function: increased surface-binding of bacteria, phagocytic activity, and ROS production.	Ryman *et al.* (2013)
Saccharomyces cerevisiae yeast culture	105 days	50 g\head\day	Increase serum IgG antibodies.	Fröhdeová *et al.* (2014)
yeast culture inactivate strains of *Saccharomyces cerevisiae*.	Six months	40 g\head\day	Increase Serum immunoglobulins (IgG, IgM and IgA), increase RBCs and WBCs counts.	Wafa *et al.* (2020)
Saccharomyces cerevisiae fermentation products (SCFP)	11days	19 g\head\day	Increase WBC. Decrease cortisol. Improve innate immunity response.	Al-Qaisi *et al.* (2020)

Effects on Milk Production and Milk Quality

Yeast and yeast-based products have been reported to enhance immunity and health during stressful events by acting as immunomodulators and biological response modifiers, thereby mitigating some of the adverse effects of pathogenesis and morbidity in part by enhancing general gut health and modifying the microbiome's composition (Broadway *et al.,* 2015).

Studies implemented on YCW supplementations to dairy cattle diets revealed performance enhancement; improvement in dry matter intake, weight gain, nutrient digestibility, rumen health, health status, and well-being (Dann *et al.,* 2000). Supplementation of yeast product to early lactation dairy cows improved dry matter intake, milk yield, and fat-corrected milk yield also enhanced (Wohlt *et al.,* 1998). Crude protein and acid detergent fiber digestibility were significantly improved (Wohlt *et al*., 1998). Dann and his colleagues (2000) found that dairy cows reach the peak of milk production earlier after yeast product supplementation, even through stressful conditions.

Cows receiving a specific supplementation of yeast produced more milk and consumed more dry matter during the pre-and postpartum periods; ruminal digestion of forage also increased with elevation in blood glucose and milk lactose concentration (Nocek *et al.,* 2006; Rossow *et al.,* 2018). Robinson *et al.* (2016) evaluate the effects of *Saccharomyces cerevisiae* yeast-based feed additives on the effective response of high-producing early lactation dairy cows. They found an increase in milk yield response which included increases in yields of proper protein, lactose, and energy, as well as a tendency for a milk fat yield increase, energetic output increase suggesting an increase in efficiency of nutrient use, and post ruminal response occurred to improve gut health in the small intestine thereby leading to increased nutrient absorption efficiency (Robinson *et al*., 2016).

The dietary inclusion of YC at a level of 40 g/h/d for six months, three months before parturition, and three months after parturition had positive effects on milk production (milk yield and composition) (Wafa *et al.,* 2020). Daily actual milk yield was 12.4% higher than control. Daily 4% FCM was also higher (17.7%) milk fat and total solids contents were higher (Wafa *et al.,* 2020). Early lactating Holstein cows supplemented with 10g of yeast cell wall powder every day for ten weeks increased milk production and composition and improved blood energy metabolites that overcame negative energy balance cases (Aung *et al*., 2019).

Lactational performance in multiparous dairy cows was enhanced after yeast product supplementation, uncorrected daily milk, solids-corrected milk, and 4% fat-corrected milk production was 9–16% greater than control cows (Lehloenya *et al*., 2008). Similarly, feeding a yeast culture of *Saccharomyces cerevisiae* improved yields of milk and milk components in heat-stressed multiparous Holstein cows (Bruno *et al.,* 2009; Lees *et al.,* 2021).

Kumprechtová *et al*. (2019) reported 4% increase in daily milk yield when 5×1010 CFU/cow/day live *Saccharomyces cerevisiae* yeast (LY) was added to early lactating Holstein cows, mean rumen pH was higher in supplemented group blunted the acidosis onset, and blood glucose also increased suggest that live yeast slightly mitigated negative energy balance (Kumprechtová *et al*.,2019).

The impact of (YCW) supplementation to dairy cattle diet on production performance also includes mammary health improvement, somatic cell count, and the incidence of sub-clinical mastitis for YCW-supplemented cows was also reduced (Nocek *et al.,*2011).

The number of new clinical cases of mastitis supporting the bioactivity of yeast cell wall components as immunomodulating substances (Proudfoot *et al.,* 2009; Nocek *et al*., 2011; Kuczaj *et al.,* 2014). The immunomodulatory activities of the yeast cell wall act on local and systemic immune system components decreasing the milk SCC (Yuan *et al.,* 2015). Feeding a yeast culture of *Saccharomyces cerevisiae* fluid (SCCF) positively affects the performance of lactating dairy cows by improving feed intake, milk quality, and energy balance of dairy cows under heat stress. Adding SCCF (5 ml/head, 2.0×107 CFU/mL) for three weeks to daily cow's diet increases dry matter intake (DMI) and decreases milk somatic cell count, reflecting an improvement in milk quality and health status (Lim *et al*., 2021).

White blood cells, mainly neutrophils, are the first defense mechanism against pathogenic bacteria that infect the mammary gland causing mastitis (Ryman *et al.,* 2013). Neutrophil infiltration in the mammary gland initiates the phagocytosis process that engulfs pathogenic bacteria and induces degranulation processes that produce reactive oxygen species (ROS), preventing bacterial growth and colonization (Ryman *et al*., 2013).

Ryman *et al*. (2013) found that active dried *Saccharomyces cerevisiae* yeast and B-complex vitamins supplementation to pregnant dairy heifers stimulate the activity of neutrophils. Neutrophils from the supplemented group showed increased activity surface-binding of bacteria, phagocytic activity, and higher reactive oxygen species (ROS) production. This improvement in neutrophil functions will boost the innate immune system response and increase cows' bodies to get rid of pathogenic bacteria that cause mastitis (Ryman *et al.,* 2013).

Feeding dairy cows with Saccharomyces cerevisiae yeast chelated with selenium as organic treatment positively affects milk components, milk somatic cell count, mammary gland health, and mastitis incidence (Oltramari *et al.,* 2014). Oltramari et al. (2014) investigated the effect of adding 278 mg. kg–1 DM selenium -yeast (*Saccharomyces cerevisiae*) for four months to lactating dairy cows. They found a significant increase in daily milk fat yield, somatic cell count (SCC) decreases, and considerable improvement in mammary gland health (Oltramari *et al*., 2014).

Table (3) summarizes literature studies reporting an improvement in milk yield and milk quality of dairy cows as a result of feeding yeast and yeast cell wall products.

Table 3: Effect of yeast and yeast cell wall product supplementation on milk quantity and quality of Dairy cow

Yeast Species/Type	Period Fed Diets	Dosage (g/kg of Feed or % of Diet or CFU)	Improved Parameters	References
YC plus enzymatically hydrolyzed yeast (YC+EHY)	14 weeks	28 g/cow per day.	Increase milk production, and increase milk protein.	Nocek *et al.* (2011)
active dry *Saccharomyces cerevisiae*	Ten weeks	8×10^{10} CFU\head\ day	4% fat-corrected milk yield increased.	AlZahal et al. (2014)
live yeast (LY) *Saccharomyces cerevisiae*	17weeks	5×10^{10} CFU/cow/d	Increased daily milk yield (+4%)	Kumprechtová *et al.* (2019)
the cell wall of yeast (*Saccharomyces cerevisiae*)	Ten weeks	10 g/cow/day	Improve milk production and composition. Improve blood energy metabolites	Aung *et al.* (2019)

yeast culture inactivate strains of *Saccharomyces cerevisiae.*	6 months	40 g\head\day	Increase 4% FCM milk yield, milk fat, total solids, and solids, not fat.	Wafa *et al.* (2020)

Table (4) summarizes literature studies reporting an improvement in the udder health of dairy cows as a result of providing yeast and yeast cell wall products.

Table 4. Effect of yeast and yeast cell wall products supplementation on udder health of Dairy cows

Yeast Species/Type	**Period Fed Diets**	**Dosage (g/kg of Feed or % of Diet or CFU)**	**Improved Parameters**	**References**
Saccharomyces cerevisiae cell+enzymatically hydrolyzed yeast (YC+EHY)	14 weeks	28 g\head\day	Decrease milk Somatic cell count Improve mammary gland health	Nocek *et al.* (2011)
active dried *Saccharomyces cerevisiae* yeast and B-complex vitamins	16 months	4 g\100 lb. of body weight daily	Enhancing the innate immune response against pathogens that cause mastitis.	Ryman *et al.* (2013)
selenium -yeast (*Saccharomyces cerevisiae*)	124 days	278 mg. kg–1 DM	Decrease somatic cell count, reduced the incidence of mastitis	Oltramari *et al* (2014), Weng et al (2018)
Saccharomyces cerevisiae culture fluid (SCCF)	Three weeks	(5 ml/head, 2.0×10^7 CFU/mL)	Improve milk quality, decrease somatic cell count	Lim *et al.* (2021)

Effects on Dairy Cattle Performance under Heat Stress Conditions

During heat stress periods, feeding dairy cows with yeast cell wall product mitigates the negative impact of heat stress on cows' performance, improves milk yield, and enhances immune status (Liu *et al*., 2014). On the other hand, YCW supplementation to endotoxin-challenged dairy cows was found to mount an immune response and decrease the physiological and acute-phase protein responses, enhancing health status (Sanchez *et al.,* 2013; 2014). Dehghan-Banadaky *et al.* (2013) investigate the effect of supplementation live yeast (LY) on mid-lactation dairy cows' performance during hot summer conditions, from July until August. Through five weeks of supplementation 4 g LY (S. Cerevisiae) they record a significant increase in milk fat percentage and blood glucose concentration (Dehghan-Banadaky *et al.,* 2013). Similarly, the effects of feeding a live saccharomyces cerevisiae yeast on the productive performance, blood metabolic profile, the immune function of transition dairy cows under the hot months of summer from 21 d pre-calving until 60 days after parturition were investigated by Nasiri and his colleagues (2019), they found that supplementation multiparous Holstein cows by (4g yeast/d/head) of live Saccharomyces cerevisiae yeast enhanced cellular immune function when plasma level of Hsp70 decreased, and stimulate lymphocytes activities in transition dairy cows indicating an immunomodulatory activity of yeast supplement(Nasiri *et al* ., 2019).

Saccharomyces cerevisiae fermentation product (SCFP) supplementation was effective in maintaining milk persistency of mid-lactation cows receiving diets containing low-quality forage even during hot periods. Lactation performance and rumen fermentation in mid-lactation Holstein dairy cows were improved when fed a diet containing low-quality forage supplemented with 180 g/d of SCFP per head every day for 10 weeks (Zhu *et al*., 2017).

Milk production was increased, rumen population was shifted towards beneficial fungi and certain cellulolytic bacteria (Ruminococcus albus, R. flavefaciens, and Fibrobacter succinogenes). This improvement in rumen function enhances microbial protein synthesis in the rumen and ensures a more excellent supply of energy (Zhu *et al.,* 2017). Similarly, supplementation of SCFP at 240g\head daily to heat-stressed lactating Holstein dairy cows succeeded in alleviating the negative consequences of heat stress during summer months when the average daily temperature humidity index was above 68. This supplementation sustains the persistency of high milk production, improves feed utilization and prevent negative energy balance (Zhu *et al*., 2016).

In another study, Al-Qaisi (2020) and his colleagues investigated the effect of adding 19g Saccharomyces cerevisiae fermentation product (SCFP) on multiparous lactating Holstein cow's diet during artificially induced heat stress conditions. Immune response parameters were improved in supplemented groups and the adverse effects of heat stress were ameliorated when cortisol and serum amyloid A protein concentration was reduced, and white blood cell count was improved with neutrophil being predominant (Al-Qaisi *et al*.,2020).

Table (5) summarizes literature studies reporting an improvement in dairy cow performance under heat stress conditions due to feeding yeast and yeast cell wall products

Table 5. Effect of yeast and yeast cell wall product supplementation on dairy cow performance under heat stress conditions

Yeast Species/Type	Period Fed Diets	Dosage	Improved Parameter	References
Saccharomyces cerevisiae yeast culture	June-November	30 g\head\day	Improve milk production and composition.	Bruno *et al.* (2009)
Live yeast LY (*Saccharomyces cerevisiae*)	July-August	4 g of LY ($15x10^9$ CFU/g)	Greater milk fat and blood glucose	Dehghan-Banadaky *et al* (2013)
Saccharomyces cerevisiae	60 days	33 g\head\d	Improve milk production and composition.	Liu *et al.* (2014)
Saccharomyces cerevisiae fermentation products (SCFP)	Nine weeks July - September THI >68	240 g\head\d	Decrease rectal temperature, sustain higher milk, feed efficiency, and energy balance.	Zhu *et al.* (2016)

Saccharomyces cerevisiae fermentation products SCFP	Ten weeks	180 g/head/d	Maintain milk persistency, and improve rumen function.	Zhu *et al.* (2017)
Live *saccharomyces cerevisiae*	80 days	4 g/head/d	Increased milk production and milk composition, lower plasma level of Hsp70.	Nasiri *et al.* (2019)
Saccharomyces cerevisiae fermentation products	11days	19 g\d	Increase white blood cell count. Decrease cortisol and serum amyloid A.	Al-Qaisi *et al.* (2020)
Saccharomyces cerevisiae	July-August	2.0×10^{7} CFU/d	Increased DMI, decrease SCC	Lim *et al.* (2021)

Conclusion

Yeast and yeast cell wall dietary supplementation to dairy cows can improve milk production and its components. Intestinal environment and health are enhanced as well. This beneficial effect could help lessen the negative impact of stress on dairy cattle production and improve their well-being. Yeast and YCW products are one of the promising areas in ruminant nutrition in general particularly dairy cows, not only because of their nutritional and health benefits to dairy cows but also due to their negligible residual effects on dairy cows' bodies and products. These positive impacts are highly considerable to improve sustainable dairy cattle farming.

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Conflict of interest

The authors declare that they have no conflict of interest.

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تأثير جدار خلية الخميرة على صحة القناة الهضمية والمناعة وإنتاج الحليب في أبقار الحليب في الظروف الطبيعية وتحت ظروف الاجهاد الحراري

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ملخص

هدفت هذه المراجعة العلمية الى تركيز الضوء على أحدث الأوراق العلمية المنشورة حديثا والتي تناولت الآثار الإيجابية لاستخدام جدار خلية الخميرة والمنتجات التي تعتمد عليها في تغذية الابقار الحلوب. تشمل هذه المنتجات الخميرة الحية, مستنبت الخميرة ,الخميرة الغذائية ,والمستحضرات المستخلصة من الخميرة. جدار خلية الخميرة يندرج تحت قائمة المستحضرات المستخلصة من الخميرة والتي تستخدم لتحسين اداء وانتاجية الابقار الحلوب وتحسين الوضع الصحي للأبقار. جدار خلية الخميرة هو مشتق تخمر طبيعي لخلايا الخميرة مثل نوع Saccharomyces Cerevisiae ويتكون من29%-64% بيتا جلوكان ,31%منان,13%بروتين,9% دهون و1-2% كيتين. الجزيئات الفعالة بيولوجياً هي البيتاجلوكان والمنان وتقوم هذه الجزيئات النشطة بالتأثير على عمليات الايض ,الجهاز المناعي ,الجهاز الهضمي وصحة الكرش والامعاء مما يؤدي الى تحسن اداء الابقار الحلوب ومستوى الرفاهية لديها. ان فعالية البيتاجلوكان والمنان داخل جسم الابقار الحلوب تشمل تحسين صحة الجهاز الهضمي ,تحفيز مكونات الجهاز المناعي باعتبار هذه الجزيئات محفزات للجهاز المناعي ولها القدرة على الارتباط بالسموم الفطرية كما اثبتت الدراسات قدرتها على تحسين مستوى مضادات الأكسدة. لذا تشكل الخميرة ومستحضرات جدار خلية الخميرة مجالا واعدا في تغذية المجترات ليس فقط بسبب تأثيرها على صحة الابقار وتغذيتها بل ايضا بسبب قلة وجود متبقيات غير امنه في جسم الابقار ومنتجاتها.

الكلمات الدالة: خميرة، جدار خلية الخميرة، بقرة حلوب، أداء.

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