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Health Benefits of Conjugated Linoleic Acid (CLA) and Influencing Factors in Dairy Products: A Review

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ABSTRACT: Conjugated linoleic acid (CLA), has garnered significant interest for its potential health benefits and presence in dairy products. CLA is primarily formed in the rumen through microbial bio-hydrogenation of dietary unsaturated fatty acids and accumulates in milk fat. Various factors influence CLA concentrations in milk, including diet, seasonal variations, breed, and processing conditions. CLA's health benefits include reducing cancer risk, modulating immune responses, and supporting cardiovascular health. It may also aid in fat metabolism and demonstrate anti-inflammatory and antioxidant properties. However, CLA supplementation can have adverse effects, such as impaired insulin sensitivity and elevated lipid peroxidation. Despite these challenges, CLA-enriched dairy products hold promise as functional foods. Future research should focus on optimizing production strategies and evaluating CLA's long-term health impacts. This review highlights the potential of CLA in improving human health and its modulation through ruminant diet management and innovative dairy processing techniques.

Keywords: Conjugated linolenic acid (CLA), dairy products, health benefits, functional food.

INTRODUCTION

Conjugated linoleic acid (CLA) is a collective term describing a mixture of positional and geometrical isomers of linoleic acid (LA, C18:2), which involves a double bond at positions 8 and 10, 9 and 11, 10 and 12 or 11 and 13. Each of these positional conjugated diene isomers can occur in a cis-trans, trans-cis, cis-cis or trans-trans geometrical configuration. CLA is produced in the rumen as a result of incomplete bio-hydrogenation of LA (Lactic Acid). In the rumen, dietary lipids are rapidly hydrolyzed and the resulting unsaturated free fatty acids can undergo bio-hydrogenation via the rumen micro-organisms. As a result, ruminant animals absorb mainly saturated fatty acids and foods made from ruminants contain these same fatty acids, regardless of the fatty acid composition of the ruminant's diet. However, when bio-hydrogenation is incomplete, CLA can escape from the rumen and can be absorbed through the gastrointestinal tract, thereby providing the peripheral tissues with various isomers of CLA (Silva, 2014). Under natural conditions, most of the CLA is produced from the intermediates of the bio-hydrogenation of poly unsaturated fatty acids (PUFA) in the rumen. Two processes occur in the rumen metabolism of lipids, the first one is hydrolysis of the ester bonds by microbial lipases (Dawson *et al*., 1977) and followed by the bio-hydrogenation of PUFA. The major substrates for bio-hydrogenation are linoleic acid (cis-9, cis-12 18:2) and α-linolenic acid (cis-9, cis-12, cis-15 18:3), after that a sequence of isomerizations results in the formation and accumulation of vaccenic acid (VA) in the rumen, which is the common intermediate in the bio-hydrogenation of these two fatty acids and the main precursor for the endogenous synthesis of cis-9, trans-11 LA in the mammary gland (Griinari and Bauman 1999; Harfoot and Hazlewood 1988). All isomers of CLA, the cis-9, trans-11 comprises 75–90% of total CLA and are derived from linoleic acid and α-linolenic acid (Bauman *et al*., 2003).

Conjugated linoleic acid (CLA) in milk and dairy products has attracted significant interest due to its potential health benefits and varying concentrations based on production factors. CLA levels in milk fat can be influenced by several factors, including the animal's diet, seasonal variations, and bacterial cultures. Studies indicate that CLA concentrations in dairy products can vary between 0.06 to 2.96% of total fatty acids, with higher values during periods of green feed in summer months (Jahreis *et al.*, 1997; Zongo *et al*., 2021). Additionally, fermented dairy products, such as those using *Lactobacillus acidophilus*, have been shown to increase CLA content (Blasi and Cossignani 2019). CLA is known for its anti-carcinogenic, immune-boosting, and anti-inflammatory properties. These benefits make CLA-enriched dairy products particularly valuable, with studies highlighting the potential of CLA to reduce cancer risk when incorporated into regular milk consumption (Biglu *et al*., 2017). Additionally, CLA has been found to support cardiovascular health by reducing blood clotting (Badinga and Miles 2011). CLA in milk and dairy products offers multiple health benefits and is influenced by both natural factors and production methods. This article presents a review on potential health benefits of CLA and factors affecting its concentration in milk and milk products.

FACTORS AFFECTING CLA CONTENT IN MILK AND MILK PRODUCTS

A. Diet and season

The diet and seasonal changes affects the CLA content in milk and milk products (Zongo *et al*., 2021). Feeding fresh pasture and forage to cows increase the CLA content of milk (White *et al*., 2001; Acosta Balcazar *et al*., 2022). The higher proportions of herbage in the cows' diet shows positive effect on CLA Content (Bär *et al*., 2020). Adding peanut oil/ sunflower oil/ linseed oil which are rich in linolenic acid to the basal diet increases CLA upto 500% (Kelly *et al*., 1998). Thanh *et al*. (2023) reported that cow fed with blend of linseed oil and fish oil yield milk with higher CLA content. Fish oils and vegetable oils increase the CLA content from 0.61 to 1.34 g of CLA/100 g of fat (Siurana and Calsamiglia 2016). In a study it is found that linseed oil also increases CLA from 0.61 to 0.90 g (Siurana and Calsamiglia 2016). Another study showed that fish oils and vegetable oils when fed in combination, increases CLA content by 2.1 times (Whitlock *et al*., 2002). Linoleic acid rich diet increases the CLA content of milk more than the diet rich in oleic or linolenic acid (Kelly *et al*., 1998; Dhiman *et al*., 2000). According to Govari *et al*. (2020), there was a substantial ($p < 0.05$) increase in CLA content of ovine milk produced by Karagouniko sheep fed under grazing grassland in April as compared to December.

Chouinard *et al.* (2001) observed that supplementing extruded soyabean than ground soyabean increases CLA content. Extrusion process increases the bioavailability of oils in the rumen for bio-hydrogenation by rumen microflora (Stanton *et al*., 2003). CLA content is more in summer than in winter because of availability of green pasture (Ledoux *et al*., 2005; Lock and Granworthy 2003). In a study it was found that CLA is more in rainy season than in dry season (Nunes *et al*., 2017). Thus, the diet given to the dairy cows is the main factor affecting the content of CLA in milk. Therefore, changes in diets may allow enrichment of milk with CLA.

B. Breed and parity

The CLA content in the milk of Holstein Friesian cows was found to be higher than that of Brown Swiss cows, with values of 4.4 mg/g of fatty acids and 4.1 mg/g of fatty acids, respectively. Milk from HF had higher CLA than Gersey cows (White *et al.*, 2001). Kelsey *et al*. (2003) observed little or no effect due to parity and breed on CLA and CLA desaturase index. The CLA content was found independent of breed and parity (Kala *et al*., 2018). Tsiplakou *et al*. (2006) also reported the interspecies differences in the CLA content among sheeps. According to Prandini *et al*. (2011), sheep cheese has a higher CLA content than goat and cow cheese. Compared to milk from multiparous cows, the fraction of CLA isomers in the fatty acid from primiparous cows was greater (Lashkari *et al*., 2021). Wilms *et al*. (2022) reported that primaparous (PP) cows had 63% more conjugated linoleic acid (CLA, cis-9, trans-11) than multiparous (MP) cows. Agyare and Liang (2021) reported that yak butter has about four times higher CLA than cow, sheep and goat butter.

C. Processing conditions

CLA content of milk was found negligibly affected by pasteurization (Luna *et al*., 2007; Bisig *et al*., 2007). The content of c-9, t-11 CLAs in milk pasteurized was found more as compare to the milk which was micro-filtered and pasteurized. This could be attributed to greater volumetric average diameter and volume surface average diameter of globules in micro-filtered and pasteurized milk than in used pasteurized milk (Yue *et al*., 2016). This shows that the CLA content in milk and milk products depends on the initial CLA content of milk, processing and production conditions. Rodríguez-Alcalá *et al*. (2014) reported that the total CLA content of milk increase after HTST pasteurization. However, sigma tropic rearrangement of C18:2 *cis*-9, *trans*-11 to C18:2 *trans*-9, *trans*-11 after sterilization. They also found the reduction in CLA content of milk after microwave and UHT processing compared with untreated samples.

Processing condition and whey component play an important role in CLA formation in processed cheese. WPC along with its lower molecular weight fractions increased CLA formation while high molecular weight factions of WPC found no effect (Shantha *et al*., 1992). Processing of processed cheese at 80 and 90°C under atmospheric conditions increased the CLA content while no effect was observed when heated at 70 and 85°C under nitrogen. This increase could be explained by the fact that both processing temperature and the presence of air play a role in the formation of CLA. The presence of air during processing could result in the formation of oxygen radicals, which could increase the formation of the linoleic acid radical thereby increasing the concentration of CLA. Oxygen radicals, such as the hydroxyl radical, are known to initiate lipid oxidation by causing the formation of lipid free radicals. CLA was found at developed concentrations in all cheddar-based processed cheeses than in unprocessed cheddar, except for American cheese (Dhiman *et al.,* 1999).

Indeed Dhiman *et al.* (1999) described that the processing of milk into mozzarella cheese did not change the fatty acid composition of CLA and between all cheeses sampled, Blue, Edam and Swiss cheese had the highest CLA concentrations. Microwaving of cheese directly for 10 min. decreased the CLA content by 53% (Herzallah *et al.,* 2005). This may be partially attributed to acceleration of lipid oxidation by microwaves or production of pro-oxidants (Ha *et al*., 1989; Lin *et al.*, 1998). The tendency toward a decrease in CLA content upon heating could be attributed to fat oxidation resulting in formation of hydroperoxides, which might cause CLA conversion or degradation.

Butler *et al.* (2011) reported that the level of CLA in cream was not altered significantly when it was processed into butter while Domagala *et al.* (2009) reported significant increase in the CLA content of sour cream by fermentation. The effect of homogenization on CLA content was non-significant in milk (Van Hekken *et al.,* 2017). Clarification of ghee at 110°C to 120°C increased CLA from 30 to 280% (Garcia *et al*., 1994). Heating of milk and raw ingredients increased CLA as the anaerobic conditions created by isolated packets during heating led to its auto-oxidation (Garcia *et al.,* 1994). High pressure processing showed no significant change in the CLA content of cow milk up to 900 MPa (Rodríguez-Alcalá *et al*., 2014).

D. Effect of storage conditions on CLA content

Oxidation of CLA was found to occur faster than Trans-Vaccenic Acid (TVA) during storage irrespective of UHT and storage conditions (Martínez-Monteagudo *et al.,* 2015). It was observed that Heptanal was the major volatile compound released during the oxidation of CLA, so it can be used as a marker for heat treatment of milk enriched with CLA and TVA. CLA content decreased in cow yoghurt significantly when stored at 5°C while opposite results was observed for sheep yoghurt (Serafeimidou *et al*., 2013). Kim *et al.* (2009) reported that four month aged cheese contains a greater CLA concentration than seven month-aged cheese. Ioannidou *et al*. (2022) found the significant increase in CLA content of Graviera cheese during ripening particularly from day 90 to day 120. Moderate increase in the CLA content of ewe cheese was observed at the end of ripening due to microbial cultures (Buccioni *et al*., 2010). Paszczyk *et al.* (2016) demonstrated that the type of applied starter culture and storage time affected the content of CLA in fermented milk drinks. Specific culture caused a significant increase in CLA content in the stored fermented milk drinks.

Fermentation conditions, including temperature, pH, and duration, are another critical component that represents CLA production and affects LAB development (Dahiya and Puniya 2018). Sensory properties of CLA enhanced in milk, butter and cheese were found to be appreciable even after storage (Jones *et al*., 2005). It was observed that the content of cis-9, trans-11 CLAs non-significantly increased from day 0 to 4 of storage, and noticeably increased thereafter up to 7^{th} day. In white cheeses produced from whole milk with four different probiotic cultures, the cis-9, trans-11 CLAs contents increased during 90 days of ripening (*E faecium*, *Lb. paracasei*, *Bifidobacterium longum* and *Lb. acidophilus*) (Gursoy *et al*., 2012). The trans-10, cis-12 CLAs increased significantly with storage time in pasteurized milk and micro-filtered and pasteurized milk (Yue *et al*., 2016).

Table 1: Content of CLA in milk and Milk Products.

Product	Content (mg/g of fat)
Cow milk	7.1-7.6
Buffalo milk	7.2-7.5
Goat milk	4.0
Cow ghee	8.2
Buffalo ghee	10.9
Condensed milk	7.0
Different Varieties of Cheese	3.6-8.0
Butter	4.2-4.5
Fermented milks	4.70
Yoghurt	0.30-0.50

HEALTH BENEFITS OF CLA

Earlier scientific interest in CLA was confined largely to rumen microbiologists who studied the cis-9, trans-11 CLA isomer. This changed when Ha *et al*. (1987) reported that CLA produced by base-catalyzed isomerization of LA was an effective inhibitor of benzopyrene initiated mouse epidermal neoplasia. Since then, CLA has gained considerable attention as a nutrient that exerts the following beneficial physiological effects in experimental animals and human beings. The CLA has following health benefits.

A. Anti-oncogenic effects of CLA

Based on the best data sources available in each country in 2022, the IARC estimates show how the cancer burden is rising, how underprivileged communities are disproportionately affected, and how vital it is to address cancer disparities globally. Most studies examining the anti-carcinogenic properties of CLA employed a blend of CLA isomers derived from vegetable oil, frequently comprising two or four primary isomers; the 2-isomer mix was nearly invariably employed (Bauman *et al*., 2020). Tumour promotion appears to be associated with the chronic formation of reactive nitrogen species (ROS) or changes in the redox state (Chaiswing and Oberley 2010). Antioxidants can counteract the promotion of tumors by reducing free radicals and oxidants (Frei, 1999). Ip *et al.* (1991) fed CLA to 37-day old rats for two weeks before the administration of the carcinogen 7, 12- dimethylbenz (a) anthracene (DMBA). A follow up study (Ip *et al*., 1994) showed that when the dose of DMBA was halved and tumors took longer to occur, dietary CLA concentrations between 0.05 and 0.5% produced dose-dependent inhibition of tumor incidence. Using a different model, Visonneau *et al*. (1997) fed severely combined immune-deficient mice with 1% CLA two weeks before subcutaneous injection of human breast adenocarcinoma (MDA-MBA 468) cells. The data obtained from a human study were consistent with reports of protective effects of dairy products against human breast cancer obtained from a recent perspective study although the number of cases (n = 88) involved were limited. One study involving the dose levels shown to produce 36% inhibition in animal models (0.04 $g.kg^{-1}$) would equate with human intakes in the region of 3 $g.d^{-1}$. Although earlier estimates supported the possibility of intakes in the region of 0.5–1.5 $g.d^{-1}$, more recent estimates provide much lower figures than this.

Table 2: Human dietary equivalents of CLA levels shown to produce protective effects in animals.

Action	Active dose levels in animals	Equivalent diet level in humans
Anti-carcinogen	0.04 $g.kg^{-1}$ body weight	3.0-3.5 $g.d^{-1}$
Anti-lipogenic	0.05% diet	12-20 $g.d^{-1}$
Anti-atherogenic (early lesions)	5 $g.kg^{-1}$	400 $g.d^{-1}$

An inverse relationship between milk consumption and breast cancer risk has been reported in women, suggesting an anti-carcinogenic effect of CLA in milk (Knekt & Jarvinen 1999). A CLA-rich diet, particularly through cheese intake, may have anti-carcinogenic effects in postmenopausal women, as observed in a 4-year study of 403 Finnish breast cancer patients (Aro *et al*., 2000).

B. Theories of cancer inhibition

Conjugated Linoleic Acid (CLA) is believed to influence various stages of carcinogenesis by modulating cell proliferation, inducing apoptosis, and regulating gene expression (Kalyankar *et al.,* 2022). Currently, two theories have been proposed to explain the possible biological effects of these isomers. In the first one, CLA isomers replace arachidonic acid in the membrane phospholipids, altering the synthesis of eicosanoids that are involved in cell signaling. This may be the reason behind the increment in the levels of IgA, IgM and 7 pro- (Tumor necrosis factor (TNF), cytokines and Interleukin (IL)-1E) and anti-inflammatory (IL-10) markers reported in both men (healthy) and women (healthy and overweight) assaying a dose of 1.1-3 g/day or in human hepatitis B antibodies in men with 1.7 g/day for 12 wk (Kwak *et al.,* 2009). In a recent study in mice, C18:2 c9, t11 (Rumenic Acid (RA)) reduced arthritis severity equivalently to celecoxib, through a reduction in IL-6 and IL-1β, thus suggesting that dietary RA may be an effective cyclooxygenase (COX2) inhibitor (Olson *et al.,* 2017). The second proposed mechanism places CLA as agonist of all PPAR isoforms, proteins involved in adipocyte proliferation, glucose uptake, mitochondrial function and inflammation. It also acts as an antioxidant; its antioxidant activity results from resonance enolization of the ß-hydroxyacrolein moiety of CLA which may chelate radicals.

C. Reduction of body fat accumulation

A meta-analysis of human studies found that CLA can reduce fat mass by 0.05–0.09 kg per week. The effects are most pronounced in the first six months, after which fat loss plateaus. CLA reduces the carcass fat content in mice (West *et al.,* 1998) and reduces the back fat thickness in pigs (Cook *et al*., 1993). Pigs fed CLA develop less body fat and show improved feed conversion efficiency (Dugan *et al*., 1997). When men with marked abdominal visceral obesity were given CLA supplementation for 4 weeks, it was seen that it may reduce abdominal fat as indicated by a significant reduction in SAD (Sagittal abdominal diameter) (Risérus *et al*., 2001). Two dosages of CLA were given *i.e*. 0.7 g and 1.4 g to two groups for 8 weeks consisting of male and female of age 19-24. The results obtained indicated that CLA supplementation may modulate body fat and serum lipids (Mougios *et al*., 2001).

(i) How CLA reduce the body fat?

The activity of carnitine-palmitoyl-transferase (CPT), the rate-limiting enzyme for fatty acid oxidation was increased by CLA. Furthermore, in a related in vitro experiment (Park *et al*., 1997), it was observed that adding CLA to the media of 3T3-L1 adipocytes (at levels found in the blood of rats fed 0.5% CLA) significantly reduces the activity of lipoprotein lipase (LPL), an enzyme involved in the uptake of fatty acids into adipose tissues from the blood, and reduces intracellular concentrations of triglyceride and glycerol. Dietary CLA supplementation increases lean tissues deposition and decreases fat deposition in pigs. Stimulation of fatty acid ß-oxidation leads to inhibition of adipose tissue triglycerides accumulation.

The reduction of body fat occurs not due to the reduction in the number of adipose cells directly rather by the reduction of their size. Considering that the size of the adipose cells is directly related to the triglyceride content inside the cells, its reduction results in a smaller cell size the increased ß-oxidation of mitochondrial fatty acids induced by CLA may be responsible for the reduction of triacylglycerol synthesis, not depositing them in the adipocyte, but reducing their size (Botelho *et al*., 2005). Stimulation of adipose tissue triglycerides breakdown also occurs; result was loss of appetite in human subjects. Satiety promoting hormone named as a "Leptin" was found increased in its activity in presence of CLA. A study by Norris *et al*. (2009) suggested that CLA may be beneficial for promoting weight loss but it has independently effect of satiety. Trans-10, cis-12 conjugated double bond in conjunction with a carboxyl group at C-1 is required for the inhibition of LPL activity.

D. Antiatherogenic effects of CLA

In one study it was observed that CLA fed at levels of 5 $g.kg^{-1}$ in rabbits and at varying levels of 0.06, 0.11 and 1.1% hamsters, the results were shown it protects against arterial accumulation of lipids in rabbits but the dose response was not influenced in the hamster. Natural isomer, cis-9, trans-11 CLA present in the dairy products and meat of ruminants, had little or no effect and also found no effect on lipid metabolism in the hamsters (De Deckere *et al*., 1999).

Hypolipidaemic: The feeding of CLA lowered the plasma cholesterol and triglyceride levels in rabbits (Lee *et al*., 1994) and triacylglycerol levels in the mice

(Munday *et al*., 1999). It activates perixosome proliferatory activated receptor (PPAR) and increase sterol regulatory element binding protein. PPARα and PPARγ inhibit the development of atherosclerosis in the LDL receptor deficient mouse as well as platelets aggregation and thrombus formation in radicals.

Antioxidant: The study conducted by Ip *et al*. (1991) shown less peroxides percentage in rat mammary gland, but not in liver of CLA fed animals, and concluded that CLA acts as an antioxidant. Ha *et al*. (1990) observed that, upon long-term (15 days) incubation at 40°C, CLA was less prone to peroxide formation than LA (Lactic Acid), and that, upon addition to LA, CLA was more protective than ascorbic acid, α-tocopherol or butylated hydroxyl toluene (BHT). CLA isomers can donate H^+ ion and stop oxidation as CLA isomers showed the capacity to directly quench free radical as measured by photoemission and spectrophotometric methods.

E. Effect of CLA on metabolism

CLA prevents age-induced bone loss in mice by regulating both osteoblastogenesis and adipogenesis (Lin *et al.,* 2017). Studies from the University of Manitoba reported that CLA in their study, 52 weaning male Han: SPRD-cy rats were randomized to identical diets supplemented with or without CLA (1% of dietary fat) for eight weeks. In a results it was found that CLA did not affect bone mass, but it decreased the release of PGE2 (Prostaglandin E2) in kidney and attenuated parathyroid hormone levels by 60%.

(i) How CLA possibly effect bone growth and metabolism?

There has been limited information on effects of CLA on skeletal muscle. CLA increased the activity of CPT (Cryptotanshinone). CLA affects factors related to bone growth *i.e.* insulin-like growth factor (Insulin like Growth Factor-1), prostaglandin E2 (PGE2), cytokines, IL-1 and TNF (Tumor necrosis factor). This affects skeletal catabolism as well as immune function. It also leads to enhancement of lean body mass and immune function. PGE2 hormone which activity increases when there is any disorder related to bones. Some studies also shown that the collagen synthesis is in increased state after addition of CLA isomers. CLA also promote osteogenesis. CLA decrease the release of LTB4 a lipoxygenase product of arachidonic acid which is a strong bone resorption factor.

F. Effect of CLA on diabetes and insulin resistance

The CLA-fed rats had lower serum glucose and insulin concentrations during an oral glucose tolerance test, smaller adipocytes, smaller pancreatic cells, decreased liver weight and decreased fatty liver tissue than control rats. The consumption of CLA delayed the onset of hyperglycemia and diabetes in the diabetic fatty Zucker rat (Silva, 2014). A double-blinded, randomized trial in 25 obese men that measured insulin sensitivity directly showed that CLA decreased insulin sensitivity by 15% (Riserus *et al*., 2004). Another randomized, placebo-controlled trial in 32 subjects with type 2 diabetes illustrated that CLA increased fasting glucose and reduced postprandial insulin sensitivity (Moloney *et al*., 2004). In contrast, a decrease in plasma glucose concentrations was observed by Belury *et al*. (2018) in patients with type 2 diabetes.

(i) CLA and diabetes. Supplementing the diet with the fatty acid conjugated linolic acid (CLA) may lead to better weight control and disease management in diabetics. CLA added in diabetic patients' diets has lower body mass as well as lower blood sugar levels by the end of eight-week study. Binding of CLA to PPARγ and activate PPAR receptor which are involved in the insulin metabolism. It has similarity to thiazolidinedione drugs which are a class of insulin sensitizing agents that improve glucose utilization without stimulating insulin release. Further it acts as an anti-diabetic agent through enhancement of adipocyte differentiation. In some studies, it was also found that levels of this fatty acid in the blood stream led to lower levels of leptin, a hormone thought to regulate fat levels.

G. CLA modulation of immune response

Tricon *et al*. (2004) studied that healthy human receiving 80:20 mixture of c9, t11-CLA: t10, c12-CLA for 8 weeks decreased T-cell lymphocyte activation and thus it positively influences the immune function. A newest human trial research by Penedo *et al.* (2013) showed that c9, t11 CLA in butter exerted immune-modulatory effects on healthy young adults, reducing the production of pro-inflammatory biomarkers associated with over-weight and obesity. Cook *et al*. (1993) hypothesized that this LA isomer may have an impact on the immune response in aging mammals. Chicks fed CLA and injected with the endotoxin lipopolysaccharide (LPS) continued to grow, whereas those not fed CLA either failed to grow or lost weight following LPS injection.

(i) How CLA modulate the immune response?

It enhances immune response while decreasing adverse effect of immune mediated catabolism (Cook *et al*., 1993) and it increases Ig production (Yamasaki *et al.*, 2001). CLA enhances the production of protective Ig, IgA, IgG and IgM while decreasing IgE (Martínez-Monteagudo *et al*., 2015) and decreases in proinflammatory substances like TNF-α and IgE. The potential of CLA to prevent catabolic losses without affecting the generation of adaptive immunity could improve growth and development.

ADVERSE EFFECT OF CLA

Oliveira *et al.* (2012) showed that the unprotected CLA supplementation decreases the milk production and secretion of milk components in grazing dairy ewes. In female FVB mice trial, Foote *et al*. (2010) showed that intake of 0.5% t10, c12-CLA resulted in hyper-insulinemia and hepatic lipid accumulation; in contrast, a low dose of t10, c12-CLA reduced adiposity in mice without negative effects on mammary development, inflammation, and metabolism, and suggest that previously reported detrimental effects relate to the use of excessive doses. T10, c12-CLA could stimulate mammary tumorigenesis activation of both proliferative and survival pathways in ErbB2 transgenic mice (Meng *et al.*, 2008). In a human study, supplementation with t10, c12-CLA in obese man induced hyperproinsulinemia, which could predict diabetes and cardiovascular disease (Riseru *et al.*, 2004).

Results from healthy postmenopausal women supplied with oil rich in CLA mixture (c9, t11-CLA and t10, c12CLA) or CLA enriched milk (c9, t11-CLA) indicated that both supplements increased the lipid oxidation while the effect from CLA enriched oil was more significant than those from CLA milk. Meanwhile, plasma triacylglycerol was significantly higher and HDL cholesterol was lower in women supplemented with the CLA mixture than with olive oil (Raff *et al*., 2008). Currently, most of the risks of CLA are attributable to the t10, c12-CLA isomer, while the c9, t11 CLA may be safe for human consumption, which needs to be further confirmed. CLA may also have side effects, including impaired insulin sensitivity, elevated lipid peroxidation, and changes in blood glucose and serum lipid concentrations.

CONCLUSIONS

From the above study it is clear that the CLA is very essential and useful fatty acid component. CLA is widely present in fermented milk products. CLA had lot of health benefits, from being anti-carcinogenic to modulating immune response, thus it is widely being used as a functional food. CLA has many nutritionally important biological properties so that an increasing intake of CLA is recommendable for humans. As one of the most accessible avenues, the CLA levels of milk and dairy products can be raised by manipulation of the diet of ruminants and, to a lesser extent, by manufacturing fermented dairy products or cheese with starter cultures selected for a high CLA-producing potential. The fatty acid profile in milk changed after CLA supplementation, but the amount of total CLA remained unaffected. Future research should investigate the carry over effects of feeding CLA on milk yield and extend these results on reproductive performance. As one of the most accessible avenues, the CLA levels of milk and dairy products can be raised by manipulation of the diet of ruminants and, to a lesser extent, by manufacturing fermented dairy products or cheese with starter cultures selected for a high CLA-producing potential.

FUTURE SCOPE

Future research on conjugated linoleic acid (CLA) should focus on optimizing production methods and understanding its broader applications. Innovative feeding strategies, including novel dietary supplements and forage combinations, can enhance CLA content in milk while maintaining animal health. Additionally, exploring advanced dairy processing techniques will help preserve or increase CLA levels during pasteurization, fermentation, and storage. Long-term human studies are essential to better understand CLA's health benefits and potential risks, particularly regarding insulin sensitivity, cardiovascular health, and inflammation. Finally, developing CLA-enriched functional foods tailored to specific health outcomes, such as cancer prevention or weight management, presents significant potential.

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