



Association of DGAT1 With Cattle, Buffalo, Goat, and Sheep Milk and Meat Production Traits

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Milk fatty acids are essential for many dairy product productions, while intramuscular fat (IMF) is associated with the quality of meat. The triacylglycerols (TAGs) are the major components of IMF and milk fat. Therefore, understanding the polymorphisms and genes linked to fat synthesis is important for animal production. Identifying quantitative trait loci (QTLs) and genes associated with milk and meat production traits has been the objective of various mapping studies in the last decade. Consistently, the QTLs on chromosomes 14, 15, and 9 have been found to be associated with milk and meat production traits in cattle, goat, and buffalo and sheep, respectively. Diacylglycerol O-acyltransferase 1 (DGAT1) gene has been reported on chromosomes 14, 15, and 9 in cattle, goat, and buffalo and sheep, respectively. Being a key role in fat metabolism and TAG synthesis, the DGAT1 has obtained considerable attention especially in animal milk production. In addition to milk production, DGAT1 has also been a subject of interest in animal meat production. Several polymorphisms have been documented in DGAT1 in various animal species including cattle, buffalo, goat, and sheep for their association with milk production traits. In addition, the DGAT1 has also been studied for their role in meat production traits in cattle, sheep, and goat. However, very limited studies have been conducted in cattle for association of DGAT1 with meat production traits in cattle. Moreover, not a single study reported the association of DGAT1 with meat production traits in buffalo; thus, further studies are warranted to fulfill this huge gap. Keeping in view the important role of DGAT1 in animal production, the current review article was designed to highlight the major development and new insights on DGAT1 effect on milk and meat production traits in cattle, buffalo, sheep, and goat. Moreover, we have also highlighted the possible future contributions of DGAT1 for the studied species.

Keywords: DGAT1, polymorphisms, milk production, meat production, genetic marker

INTRODUCTION

Milk production traits have fundamental importance in livestock production and the related economy (1, 2). The milk fatty acids have shown an essential role in cheese production, and it has been found that milk fat includes about 98% triglycerides (TGs) (3). In addition to milk production, scientists are also taking an interest in the quality of meat. The trends for meat quality instead of meat yield are gradually changing in many countries (4, 5). In order to improve productivity, the animal with better quality traits such as milk production, growth, meat, and carcass quality have been selected and used in the breeding program in the animal industry.

Genetic factors can influence milk fat composition, and its genetic variation has been reported in previous studies (6, 7). Consistently, it has been documented that the carcass and meat quality traits are under the control of several genes (4). Selection aimed at increasing the frequency of alleles with a positive effect on a given trait was initiated by geneticists (8). In general, identifying and validating genetic markers for milk production traits are the initial and crucial steps to establish a marker-assisted selection (MAS) system. Thus, the increasing productive performance through genetic selection is a common goal for many animal breeding programs worldwide (9–11).

Several studies have targeted the bovine quantitative trait loci (QTLs) on chromosome 14 for their association with milk production traits (12–20). Acyl CoA:diacylglycerol acyltransferase (DGAT1) gene at chromosome 14 has been documented as a candidate marker for the QTLs associated with milk production traits through cattle genome and linkage mapping studies (21, 22). Besides DGAT1 association with milk production traits, many studies have documented that the genes on bovine chromosome 14 regulate many economic traits including meat production in beef cattle (23–26). Urbinati et al. explored several genes on chromosome 14 that had significantly regulated metabolism, melanin biosynthesis (pigmentation), bone development, and meat production in dairy cattle. They have documented the pleiotropic ability of DGAT1 for both influencing meat and milk quality in dairy cattle (27). Later on, DGAT1 was reported as a production-associated gene in several animals including buffalo, sheep, and goat. Keeping in view the importance of DGAT1 gene in animal production, the current review was designed to highlight the possible research development on DGAT1 role in cattle, buffalo, sheep, and goat milk and meat production trait regulation.

SHORT DESCRIPTION OF DGAT1 IN CATTLE, BUFFALO, SHEEP, AND GOAT

Diacylglycerol *O*-acyltransferase 1 (DGAT1), Ensembl ID (Ensembl: ENSBTAG00000026356) was identified as one underlying QTL for milk production traits located on the centromeric region of the bovine chromosome 14 having 17 exons with 14,117 base pair (bp) (21, 22). *DGAT1* gene (Gene ID: 102390126) in buffalo located on chromosome 15 has a size of 10,733 bp distributed in 19 exons (28). The expression of DGAT1 has been documented in the small intestine, liver, adipose tissue,

and mammary gland (29, 30). In sheep, *DGAT1* (Gene ID: 100126245) is located on chromosome 9 and consisted of 17 exons (31), while in goat, *DGAT1* gene (Gene ID: 100861225) is located on chromosome 14 with 18 exons (<https://www.ncbi.nlm.nih.gov/gene/100861225>).

DGAT1 ROLE IN MAMMARY GLAND DEVELOPMENT AND SYNTHESIS OF TRIACYLGLYCEROL

The development of the mammary gland is a complex process that is necessary for normal lactation. The interactions between the mammary epithelium and surrounding stroma are crucial for normal mammary gland development. Furthermore, adipocytes are the most abundant cells in the stroma. Stromal adipocytes synthesize and store large amounts of TGs, which may serve as reservoirs of substrates for milk production by the mammary epithelium. During this process, adipocyte TGs must be hydrolyzed and the fatty acids transferred to the epithelial cells for re-esterification. TG synthesis is catalyzed by diacylglycerol *O*-acyltransferase 1 (DGAT1) enzymes, which covalently join diacylglycerol with fatty acyl CoA (**Figure 1**) (32). A study has identified genes encoding two mammalian DGAT enzymes, DGAT1 and DGAT2 (33). *DGAT1* gene is expressed in nearly all tissues, including the mammary glands (34). Mice lacking DGAT1 (*Dgat1*^{-/-}) have decreased TG content in tissues and cannot lactate (35). Furthermore, Cases et al. found that the mice lacking DGAT1 had faced impaired mammary gland with decreased epithelial proliferation and alveolar development. Similarly, it has been documented that the insufficient level of DGAT1 in both the stromal and epithelial tissues is associated with impaired mammary gland development (36). The knockdown of DGAT1 in bovine mammary epithelial was associated with a reduced level of TG synthesis in bovine mammary epithelial cells (BMECs) (37).

DGAT1 Role Association With Fat Metabolism and Milk Production Traits

The vital role of DGAT1 in fat metabolism makes them a best choice as a candidate marker in animal production. The mechanism of DGAT1 role in fat metabolism is shown in **Figure 2**.

Consequently, DGAT1 was documented to have a significant influence on milk production in cattle in Germany (38). Ardicli et al. documented the association of DGAT1 with milk production traits in dairy cattle and concluded that DGAT1 could be used as a genetic marker to improve the milk production traits (39, 40). Through the genome-wide association study (GWAS), it has been well established that DGAT1 is associated with milk production traits (41–43). Consistently, Jiang et al. documented through a GWAS that *DGAT1* gene is correlated with milk fat yield; however, a negative link of single-nucleotide polymorphism (SNP) (rs109421300) in DGAT1 with milk and protein yields was noticed in U.S. Holstein cattle (44). The SNP (rs109421300) has A and G alleles, while G allele was associated with antagonistic pleiotropy for positive fat yield and negative

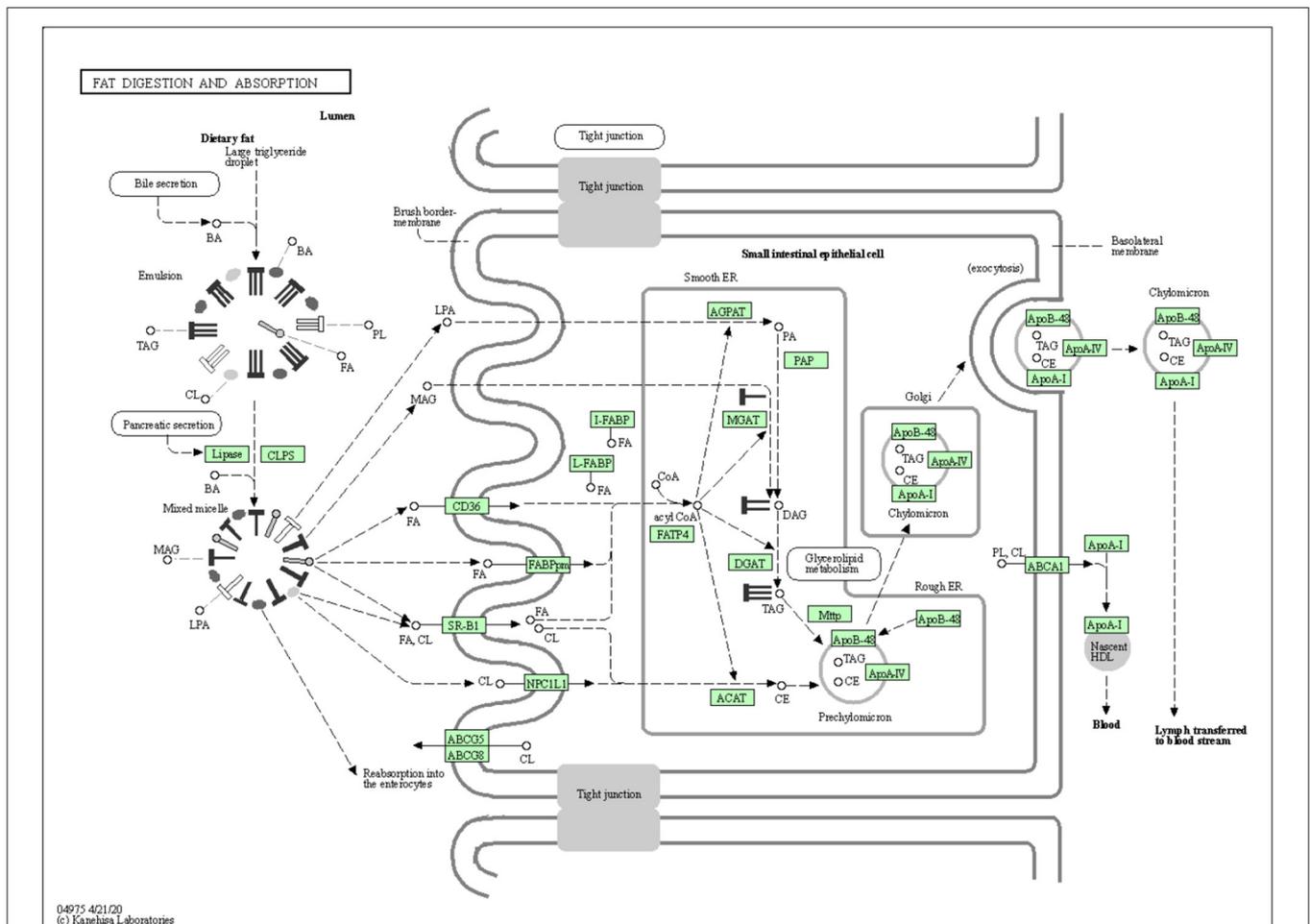


FIGURE 2 | The mechanism of DGAT1 role in fat digestion and metabolism (<https://david.ncicrf.gov/kegg.jsp?path=bta04975\protect\LY1\textdollarFat%20digestion%20and%20absorption&termId=550009625&source=kegg>).

was detected on exon 8 of *DGAT1* gene of *Bos taurus*: (Figure 3) (21, 22, 45). Later on, many studies documented the significant association of *DGAT1* K232A polymorphism with milk production traits in dairy cattle (45–49). The *DGAT1* region analysis in six Indian cattle (Sahiwal, Rathi, Deoni, Tharparkar, Red Kandhari, and Punganur) revealed fixed *DGAT1*^K allele (Figure 3) (45). Moreover, Tania et al. documented that the desired region sequence of control cows showed heterozygous situation for already detected mutation in three cows.

The allelic frequency and the influence of the *DGAT1* K232A polymorphism have been illustrated in dairy cattle populations in different countries including New Zealand (12, 19, 21, 50), Israel (13), the Netherlands (51, 52), Germany (53, 54), Poland (55, 56), China (57–59), France (60), India (45), and Sweden (47).

Furthermore, it has been well established that the *DGAT1* K allele is linked to a higher fat yield, fat content, and protein content and lower milk production protein and lactose yield (42, 46, 47, 54). Few reports also studied that the increase in milk fat and protein percentages was associated with the K variant in *DGAT1*, while the increase in milk yield was linked to the A

variant in dairy cattle (40, 47). Berry et al. documented that the K allele of *DGAT1* K232A is significantly associated with higher milk fat content, protein content, and milk fat yield and lower milk and protein yield in dairy cattle in Denmark (61). Bovenhuis et al. (42) found that the changes in milk production traits during early lactation might be due to *DGAT2* (33) in addition to *DGAT1*. Furthermore, Bovenhuis et al. showed that milk protein is directly associated with phosphate, calcium, and magnesium contents; thus, *DGAT1* K232A polymorphism may change the milk mineral composition (42). In a recent study, the lactation stage interaction with genotypes (*SNP* × *lact*) was evaluated for seven milk production traits (milk yield, lactose yield, lactose content, fat yield, fat content, protein yield, and somatic cell score) in 1,800 first-parity Dutch Holstein–Friesian (20). It has been reported that *DGAT1* K232A effect on milk production changes with lactation stage (20, 42). The influence of *DGAT1* K232A on milk yield tends to decrease in the early lactation stage when the cows experience negative energy balance (NEB) (42); however, the effect was constant for milk fat throughout the lactation but slightly lowered in early lactation (20). The

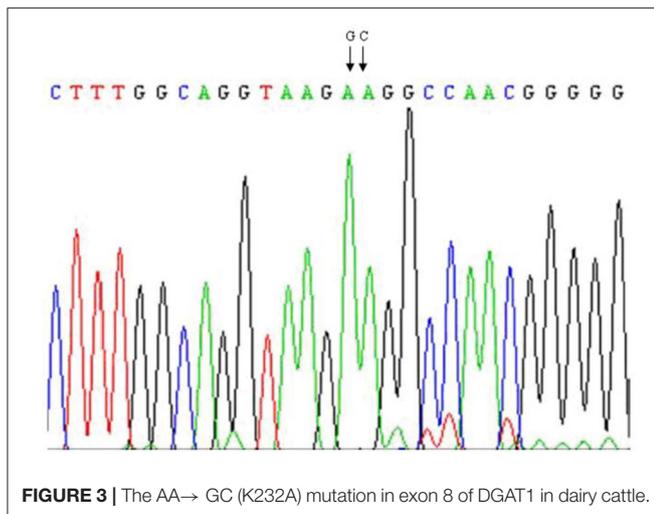


FIGURE 3 | The AA→ GC (K232A) mutation in exon 8 of DGAT1 in dairy cattle.

main reasons documented for these changes were NEB (42) and effects of pregnancy because repartitioning of nutrients is required between milk production and fetus development (18, 20). Furthermore, it is hypothesized that DGAT2 shows more critical role than DGAT1 in early lactation, which could be another contributory factor to the above-observed changes (42). In contrast, it was noticed by a study that DGAT1 effects increased in all the three stages of lactation day 5–95, from day 96 to 215, and from day 216 to 305 (62). Lu and Bovenhuis assumed that pregnancy in the late stage of lactation might be one reason for changes in milk production contents, especially lactose contents (18). Mao et al. evaluated the effects of the DGAT1 genotypes on milk production traits in dairy cattle; it was confirmed through an association study that dairy cows with KK genotype were significantly superior in milk fat and protein contents compared with AA and KA. In contrast, higher 305-day fat yield and 305-day protein yield were reported in cows with genotype KA compared with AA or KK genotypes (61). A recent study reported the interactions of DGAT1 K232A with milk fat and protein percentages. In addition, the lactation stage was the critical factor associated with the effect of DGAT1 polymorphism on milk fat and protein percentages. The AA genotype was linked to a reduction in milk fat percentage, while KK significantly increased milk protein percentage (49). Venbergue et al. selected 21 dairy cows and divided them into three groups based on the DGAT1 K232A genotype (eight cows each of KK and KA genotype; five cows of AA).

Furthermore, the KK genotype cows presented higher milk fat and protein contents, higher κ -casein percentage, and lower milk yield (63). Consequently, the DGAT1 AA genotype was associated with low milk fat and protein contents and higher milk yield and lactose yield than the DGAT1 KK genotype in dairy cattle (64). Consistently, it has been found that the K allele in DGAT1 is linked to higher milk fat and protein contents, while the A allele showed association with higher milk yield in dairy cattle (7, 42, 65). In contrast, Mach et al. did not find any significant effect of DGAT1 polymorphism

on milk production traits in dairy cattle (66). A study proved through a gene expression experiment that the enzyme activity level of the alanine variant was lesser than that of the lysine variant (51). Interestingly, Demeter et al. explored the effect of DGAT1 polymorphism on non-return rates for insemination. Furthermore, the findings of Demeter et al. provided a roadmap to determine the associated effects of breeding to improve the composition of milk fat on reproduction, thus enabling a better assessment of breeding programs prior to implementation (52).

Few studies have reported that the effect of DGAT1 K232A also depends on the breed (53, 67), lactation stage (68, 69), and parity (41, 60). Furthermore, it has been documented that milk fat contents were not constant throughout lactation in dairy cattle (68, 69). The genetic effect of DGAT1 on milk production traits showed interaction with the lactation stage (18, 20). The possible reasons for the decreasing effects of DGAT1 on milk production traits, especially on milk protein contents during the first and second lactation, might be due to the dilution effect and *de novo* fatty acid synthesis (42). Consistently, it has been reported that in early lactation, dairy cows experienced a NEB. The dairy cows mobilize body reserves to fulfill energy deficiency utilized to maintain milk yield (41). Bionaz et al. (70) provided evidence for differential expression of DGAT1 during lactation. They showed that significant changes in DGAT1 expression only occurred in early lactation (<15days), whereas in late lactation, no significant changes in DGAT1 expression were detected. Consistently, few studies also documented that DGAT1 expression in the bovine mammary gland alters with the initiation of lactation (70–73). However, these studies noticed that the changes in DGAT1 expression were not constant throughout lactation in dairy cattle.

In addition, Lu et al. studied the effect of DGAT1 K232A polymorphism on milk metabolome and proteome obtained from two groups of cows (AA and KK genotype cows). It was found that milk from cows with KK genotypes consisted of less uridine diphosphate (UDP)-linked sugar, citrate and creatine, and more stomatin, choline, carnitine, and sphingomyelin when compared with milk obtained from cows having AA genotypes. Thus, the cows different in DGAT1 polymorphism showed variations in milk metabolome and proteome, which helps us to understand the mechanism behind the effect of DGAT1 K232A polymorphism on milk production characteristics (37).

The genetic effect of DGAT1 polymorphism on milk production is also affected by the season. Recently, a study noticed the significant effect of winter and summer on the genetic effect of DGAT1 polymorphism on milk production traits; in winter, the DGAT K232A effect was negatively associated with milk fat (74). However, neither increasing nor decreasing effect of allele DGAT K232A was reported on milk content traits with change in temperature in the Polish Holstein–Friesian breed. However, some of the milk production traits (milk protein yield and milk yield) were not constant throughout the lactation and slightly decreased with change in environmental temperature (20–28°C). The more prominent effect of DGAT K232A in Polish Holstein–Friesian was not observed because the temperature was moderate (5°C–28°C) in this study (75). Shahzad et al. noticed the low hepatic expression of DGAT1 in periparturient dairy cattle during summer compared with spring (76). Consistently,

a study reported that the KK genotype of DGAT K232A polymorphism showed association with triacylglycerol (TAG) composition in milk fat in summer, while in winter, the effect among genotypes (AA cow and KK cow) was smaller for TAG composition in milk (77). Bovenhuis et al. documented the effect of DGAT1 polymorphism on milk, fat, protein yield, and fat and protein content. Furthermore, it was noticed that DGAT1 polymorphism also influenced lactose content and lactose yield (42). In addition to DGAT K232A, the DGAT1 variable number of tandem repeat (VNTR) was also found to be associated with milk fat percentage in dairy cattle. The promoter VNTR polymorphism has shown effect on specificity protein 1 (SP1) binding sites and regulate the expression of *DGAT1* gene as well (78). The research development on DGAT-K232A has also been summarized in **Table 1**.

DGAT1 Role in Buffalo Milk Production Traits

Buffalo milk is famous because of its high protein and fat content (82). Consistently, it has been shown that buffalo milk has higher milk fat content than cow milk (93). Thus, it is necessary to characterize DGAT1 in buffalo because of high milk fat yield production than that of cows (94). *DGAT1* gene has been characterized in previously reported studies in buffalo (94–97). Yuan et al. studied *DGAT1* gene and its polymorphisms in Chinese water buffalo. Furthermore, it has been revealed that SNP at exon 17 changes the amino acid sequence Ala residue to Val residue at position 484 in buffalo DGAT1 (95). Consequently, Mishra et al. characterized *DGAT1* gene in six different Indian water buffalo (Murrah, Bhadawari, Tarai, Pandharpuri, Marathwada, and Mehsana). The polymorphisms detected in DGAT1 reported by previous studies were significantly associated with milk production traits and could be a target as genetic markers for improvement of milk fat and milk yield production in water buffalo (95, 96).

Two SNPs (g.11,783 G>A and g.11,785 T>C) at exon 17 of DGAT1 in cattle were also identified in Murrah buffaloes (98). Furthermore, it was documented that SNP-g.11, 785 T>C is associated with milk fat and protein percentages in Brazilian Murrah buffaloes. The two SNPs g.8330T>C and g.9046T>C at exons 17 and 13 in *DGAT1* gene were identified in Riverine, Swamp, and crossbred buffalo. Furthermore, it was revealed that g.9046T>C had been associated with the change in amino acid sequence at position 484 arginine to histidine (99). The SNP g.9046T>C was associated with fat percentage, and buffalo with TT genotype showed a higher association for milk fat percentage than the CC genotype. Similarly, the SNP g.8330T>C of DGAT1 in Riverine buffalo was linked to peak milk yield, total milk yield, and protein percentage. The buffalo having a CC genotype showed a higher ability for milk yield and peak yield and less milk protein than the TT genotype (99). Compared with that of cattle, the high milk fat percentage in buffalo might be due to a fixed K allele (94). In contrast, Silva et al. did not find any effect of SNPs in DGAT1 on milk production traits in buffalo. The reason for this might be due to their distribution on the intron region, which is not essential for amino acid sequences on proteins (100).

A recently published study revealed that SNP-8426 C/T at exon 17 of DGAT1 changes the amino acid of Ala to Val in Iranian buffalo (101). Furthermore, the association of SNP-8426 C/T in DGAT1 with milk production traits might a good choice to consider as a genetic marker for enhancement of milk production in buffalo (101). The DGAT K allele was documented in Indian buffalo and cattle breeds (45). Consistently, the DGAT K232A polymorphism was documented by their association with higher milk fat yield, higher milk fat, and protein percent regulation in buffalo breeds (45, 102). Consistently, c.1053C>T polymorphism in the coding region of exon 17 in DGAT1 was found to be involved with milk production traits in the Italian Mediterranean and Romanian buffalo breeds (103). Furthermore, it was revealed that the T allele might be assumed to be *DGAT1* gene's ancestral state, being found in the majority of the sequenced species. Liu et al. through a GWAS reported the significant effect of DGAT family genes on milk production traits in buffalo (82). The published data show that the DGAT1 role in milk production traits in buffalo is lacking, and further validation is warranted. Besides, we did not find a single study regarding *DGAT1* gene importance in buffalo meat production. So still a huge gap is there to evaluate the association of DGAT1 with buffalo meat production.

DGAT1 Role in Goat and Sheep Milk Production

Due to the high content of short- and medium-chain fatty acids and smaller fat globules, goat milk is generally considered to have a high nutritional value (104). Goat milk in many countries around the world is of particular economic value and is attractive for many reasons, including its abundance in different nutrients and its health importance (105). Genetic selection programs for dairy goats are still rare in many developing countries, but breeding strategies for the commercial production of milk and meat from goats have been remarkably successful (106). In cheese production, milk fatty acids play an important technical function, while DGAT1 has an essential role in the biosynthesis of TGs exported to the milk. The important role of DGAT1 in the metabolism of milk fat makes *DGAT1* gene an interesting candidate for the genetic variation of milk characteristics in milk goats (107). DGAT1 also plays an essential function in physiological processes that include the synthesis of TAG, such as the absorption of intestinal fat (22, 36), the development of adipose tissue, and mammals' lactation (12, 19).

DGAT1 gene was characterized in goat by Angiolillo et al.; furthermore, an association study was suggested to explore the relationship of DGAT1 with TAG synthesis in the goat mammary gland (108). It has been documented that miR-145 regulates the fatty acids metabolism in goat mammary epithelial cells. MiR-145 acts on fatty acid regulating genes including DGAT1 in goat mammary epithelial cells. Furthermore, a significant change in fatty acid level was observed by knocking out the MiR-145, inhibiting the DGAT1 expression (109). Consequently, it has been reported that SP1 impairs the milk fatty acid synthesis by decreasing the expression of DGAT1 in goat mammary epithelial cells (110, 111).

TABLE 1 | Research development on DGAT1 K232A polymorphism association with milk production traits in dairy cattle.

Polymorphism	Production traits	Country	Breeds	References
DGAT1 K232A	Milk production traits	Belgium	Holstein–Friesian	Grisart et al. (51)
DGAT1 (K232A)	Milk fatty acid traits	Benin	Borgou and White Fulani	Houaga et al. (79)
DGAT1 K232A	Milk production traits	Brazil	Nellore, Guzerat, Red Sindhi, Gyr, Holstein, and Gyr × Holstein	Lacorte et al. (80)
DGAT1 K232A	Milk fatty acids	Chile	Holstein–Friesian, Jersey, Frisón Negro, Montbeliarde, and Overo Colorado	Carvajal et al. (81)
DGAT1 K232A	Milk production traits	China	Chinese local breed	Li et al. (82)
DGAT1 K232A	Milk production traits	Czech Republic	Holstein–Friesian	Kadlecova et al. (83)
DGAT1 K232A	Milk production traits	France	French Holstein, Normande, and Montbéliarde	Gautier et al. (60)
DGAT1 K232A	Milk production traits	France	Holstein × Normande crossbred	Vanbergue et al. (63)
DGAT1 K232A	Milk production traits	Germany	Holstein–Friesian, Fleckvieh and Braunvieh	Winter et al. (22)
DGAT1 K232A	Milk fat	Germany	German Holstein	Kuhn et al. (84)
DGAT1 K232A	Milk production traits	Germany	German Holstein	Kuhn et al. (85)
DGAT1 K232A	Milk production traits	India	Sahiwal, Rathi, Deoni, Tharparkar, Red Kandhari and Punganur	Tantia et al. (45)
DGAT1 (K232A)	Milk production traits	Ireland	Holstein–Friesian	Berry et al. (61)
DGAT1 K232A	Milk fat	Israel	Dutch Holstein–Friesian	Argov-Argaman et al. (86)
DGAT1 K232A	Milk production traits+ milk coagulation properties	Italy	Italian Holstein–Friesian	Bobbo et al. (87)
DGAT1 K232A	Milk production traits	Netherlands	Holstein–Friesian	Schennink et al. (7)
DGAT1 K232A	Milk production traits	Netherlands	Holstein–Friesian	Schennink et al. (88)
DGAT1 K232A	Milk production traits	Netherlands	Holstein–Friesian	Duchemin et al. (74)
DGAT1 K232A	Milk fat	Netherlands	Holstein–Friesian	Tzompa-Sosa et al. (65)
DGAT1 K232A	Milk metabolome and proteome	Netherlands	Holstein–Friesian	Lu et al. (37)
DGAT1 K232A	Milk production traits and lactose contents	Netherlands	Holstein–Friesian	Bovenhuis et al. (41)
DGAT1 K232A	Higher milk fat, protein and milk fatty acid	Netherlands	Holstein–Friesian	Bovenhuis et al. (42)
DGAT1 K232A	Higher milk fat, protein and lower milk yield	Netherlands	Holstein–Friesian	van Gastelen et al. (64)
DGAT1 K232A	Milk fatty acids	Netherlands	Holstein–Friesian	van Gastelen et al. (89)
DGAT1 (K232A)	Triacylglycerol in milk fat	Netherlands	Holstein–Friesian	Pacheco-Pappenheim et al. (77)
DGAT1 K232A	Milk production traits	New Zealand	Holstein–Friesian	Grisart et al. (21)
DGAT1 K232A	Milk production traits	Poland	Polish Holstein–Friesian	Vanbergue et al. (63)
DGAT1 K232A	Milk production traits	Poland	Polish Holstein–Friesian	Nowacka-Woszuik et al. (90)
DGAT1 K232A	Milk production traits	Poland	Polish Holstein–Friesian	Szyda et al. (69)
DGAT1 K232A	Milk production traits	Poland	Polish Holstein–Friesian	Komisarek J, Kolenda (75)
DGAT1 K232A	Milk fatty acids	Poland	Polish Holstein–Friesian	Kesek-Wozniak et al. (49)
DGAT1 K232A	Milk fat percentage and fatty acid	Romania	Romanian Holstein	Tăbăran et al. (91)
DGAT1 K232A	Milk production traits	Scotland	Holstein–Friesian	Banos et al. (46)
DGAT1 K232A	Milk production traits	Sweden	Swedish Red and Swedish Holstein	Näslund et al. (47)
DGAT1 K232A	Milk production traits	USA	Holstein–Friesian	Barbosa et al. (92)

Polymorphism in Caprine DGAT1 and Their Association With Milk Production

An et al. discovered different polymorphisms (g.407–408insC (in intron 14), g.6852C→ T, and g.6798C→ T (in exon 7) of *DGAT1* gene in Xinong Saanen (SN) and Guanzhong (GZ) goat breeds. Furthermore, a significant association of DGAT1 in-del (g.407_408insC) with milk yield and fat percentage were observed in Chinese dairy SN and GZ goats. Interestingly, the

DGAT1 in-del (g.407_408insC) was not in the coding region but still has a positive effect on milk production traits (2), which might be due to its regulatory effect on the mechanism of mRNA deadenylation and degradation (112). Consistently, four polymorphisms (T21153G, C21154G, A21172C, and A21194T) were identified in DGAT1 of the Iranian Khalkhali goat (113). The variants T21153G and C21154G cause the transformation of serine to glycine amino acids, while A21172C was associated with

the change in aspartic acid to alanine amino acid. Furthermore, Evrigh et al. found that four mutations (T21153G, C21154G, A21172C, and A21194T) of DGAT1 in Iranian Khalkhali goat were significantly associated with milk yield and milk protein percentage (113). Martin et al. explored the two SNPs R251L and R396W in goat DGAT1. The SNPs were genotyped in two goat breeds (Saanen and Alpine breeds). The frequencies noted for R251L and R396W mutations in Saanen goat were 3.5 and 13%; however, only R396W was found with a frequency of 7% in the Alpine breed. Moreover, it was found that both the mutations in DGAT1 were associated with a decrease in milk fat; however, the association was not strongly significant for both the SNPs (114). As the two types of mutation lead to substitution in protein sequence (114), further experimental trials are highly warranted for these two SNPs R251L and R396W in DGAT1 with a higher goat population because the sample size was too low in a study by Martine et al. Similarly, Tabaran et al. did not find the significant influence of *DGAT1* gene on milk production traits in sheep and goat. Again, we found the same issue of less number of samples in the experiments of Tabaran et al. (115). For an association study, usually, a large size of population is needed (116). Recently, two important mutations (T703C and T713C) in DGAT1 of the Egyptian Zaraibi goat were identified (117). The polymorphism T713C was found at the coding region associated with the substitution of amino acid isoleucine to threonine. Furthermore, the polymorphism T713C significantly regulated the total solid content of milk, milk yield, and contents in Egyptian Zaraibi goat (117).

DGAT1 Role in Sheep Milk Production

The polymorphisms in DGAT1 have been studied for their association with milk production traits in sheep (118–120). Dervishi et al. identified four polymorphisms: two in exon 17 (g.8522C>T and g.8539C>T), one in exon 1 (g.358C>A), and one in intron 10 (g.7457C>A) of DGAT1 in the Spanish Assaf goat breed (121). Furthermore, it was detected that the SNP (g.358C>A) and (g.8522C>T) leads to a change in amino acid sequence at points p.Asp53Glu and p.Arg482Cys. The association study revealed that the sheep having genotype CC showed greater performance in milk fats than the CT genotype. Overall, the four detected SNPs in DGAT1 were associated with milk production traits in the Spanish Assaf goat breed (121). Consistently, in sheep, Scata et al. documented five new mutations in *DGAT1* gene, distributed on exon 17 (g.8539C>T), 5'_UTR (g.127C>A), intron 1 (g.1655C>T), intron 2 (g.5553C>T), and intron 10 (g.7492C>T). Additionally, a negative association of polymorphism g.5553C>T with milk fat content in Sarda, Altamurana, and Gentile di Puglia Italian sheep breeds was documented. Consequently, in the Sarda sheep breed, the variant g.127C>A was negatively associated with milk fat content (122).

DGAT1 ROLE IN MEAT PRODUCTION

DGAT1 is considered a key enzyme that controls the major pathway of TAG synthesis in the adipose tissue (123, 124). In animals, TAG can be found in the liver, small intestine, muscle, and adipose tissue and is considered the main component of

intramuscular fat (IMF) and a key role in energy metabolism (125). TAG also facilitates the cell membrane composition and transportation of lipoprotein (126). Furthermore, significant changes in lipid metabolism in several tissues of DGAT1 lacking mice have been documented (127). Consistently, it was validated that overexpression of DGAT1 is associated with raised TG biosynthesis, enhanced fatty acid oxidation, and preserved insulin sensitivity (128). In addition, Ying et al. experimentally proved the influence of DGAT1 TAG synthesis, resistance to insulin, and IMF deposition (129). Furthermore, it was found that DGAT1 overexpression regulated the glucose and lipid metabolism and catalyzed the TAG synthesis reaction, which is responsible for enhancing muscle insulin sensitivity and raising the content of the IMF (129). Furthermore, it was documented that DGAT1 mediates the TAG synthesis and IMF formation, possibly due to its effect on unsaturated fatty acid, insulin, and MAPK signaling (130). Altogether, it was observed that DGAT1 overexpression is associated with lipid and glucose metabolism, thereby facilitating the TAG biosynthesis (130).

DGAT1 Association With Meat Production Traits in Cattle

Many studies have investigated the effect of *DGAT1* gene on meat production traits in beef cattle (4, 5, 48, 131). The role of *DGAT1* gene for production traits has also been reported in seven cattle breeds (Angus, Belgian Blue, Charolais, Hereford, Holstein-Friesian, Limousin, and Simmental cattle) (132). Consequently, it was documented that *DGAT1* gene may affect the color (48) fat contents of meat in beef cattle (25). Yuan et al. studied the association of two SNPs (c.572A/G and c.1416T/G) in the exon region of *DGAT1* gene with meat production traits in beef cattle. It was documented that SNPs (c.572A/G and c.1416T/G) in DGAT1 have significantly influenced the backfat thickness, longissimus muscle area, marbling score, and fat color in beef cattle (133). The polymorphism DGAT1 K232A is the key variant associated with production including meat production traits. Few reports have illustrated the role of DGAT1 K232A in the regulation of IMF in beef cattle semitendinosus muscle (53, 134–136); however, Ardici et al. did not find any association of this polymorphism with meat production traits (40). Similarly, a study reported the nonsignificant effect of DGAT1 K232A on various meat traits (percentage of muscle, percentage of fat, and percentage of bones and drip loss) (137). Moreover, Cases et al. did not find any link of DGAT1 K232A polymorphism with meat production traits in Brahman Breed. The frequency of A genotype in DGAT1 in most beef cattle breeds including Charolais (16), Angus (138), Simmental (48), and Russian beef cattle (139) was higher than K genotype. Rump height (RH) in beef cattle has been significantly influenced by DGAT1 K232A polymorphism (140). Consequently, it was explored that DGAT1 K232A is strongly associated with meat fat and tenderness in three Spanish Cattle breeds (Berrenda en Colorado, Berrenda en Negro, and Cardena Andaluza). In addition, higher frequencies of the K allele were documented in all three breeds compared with the A allele (141). The IMF is an important parameter in practice for the evaluation of the nutritional quality of beef;

consistently, Wu et al. documented a noteworthy relationship of DGAT1-(10,433 and 10,434)-GC/GC genotype with marbling score and IMF in Chinese Simmental cattle (142). Importantly, the DGAT1 overexpression caused the significant alteration metabolism of fat metabolism, elevated TG synthesis, regulated fatty acid oxidation synthesis, enhanced fatty acid oxidation, and conserved the sensitivity of insulin (128, 143). Based on published literature, we concluded that although DGAT1 has an important role, very limited research studies explored the DGAT1 function of meat production in cattle.

DGAT1 Role in Sheep and Goat Meat Production

Xu et al. recorded a silent mutation of GCT (Ala487) to GCC (Ala487) on exon 17 of DDAT1 in the Chinese sheep breed. Furthermore, a significant association of the genotypes TT was confirmed with a higher muscle marbling score ($p < 0.05$) and IMF content and lower shear force and drip loss rate (144). An SNP (c.69 G>A) on exon 10 of DGAT1 was documented through sequence analysis in Barki, Najdi, and Harri sheep breeds, which causes the substitution of the amino acid (p.Lysine>Arginine). Furthermore, it was revealed that the detected SNP (c.69 G>A) was associated with meat production traits in Barki, Najdi, and Harri breeds (145). Consistently, Armstrong et al. also identified some novel SNPs of DGAT1 in Texel sheep, which were involved in the development of shoulder weight, fat thickness, rib-eye area, and live weights (146). A study detected SNPs on exons 16 and 17 of DGAT1 in the Lohari sheep breed and suggested that these variants might be considered in association research for meat production traits (31). Consequently, Mohammadi et al. reported a significant effect of SNPs on exons 16 and 17 of DGAT1 on fat-tail weight ($p < 0.05$) and backfat thickness in the two Iranian sheep breeds (Lori Bakhtiari and Zel). Furthermore, it was illustrated that the CC genotypes of sheep were associated significantly with fat-tail weight and backfat thickness (147). Ala Noshahr and Rafat documented the significant association of polymorphism T487C on exon 17 of the DGAT1 with carcass weight and dressing percentage in Moghani sheep. In addition CC genotypes Moghani breed showed a higher correlation with carcass weight and dressing percentage than TT genotypes (148). The DGAT1 role in goat meat is still not explored. Recently, a copy number variation (CNV) distribution was studied in the goat. It has been documented that the CNV reported in many genes including DGAT1 was associated with muscle development and metabolic processes in the goat (116).

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CONCLUSIONS

Based on our review, it has been concluded that DGAT1 can be used as a genetic marker for the improvement of milk production in dairy cattle. In addition, the DGAT1 showed some positive role in the enhancement of meat and carcass fatness quality in beef cattle. However, further studies are warranted to explore the role of DGAT1 in meat production quality improvement in different breeds of cattle. The DGAT1 also regulates the milk production traits in sheep, goat, and buffalo. However, very limited studies are available on DGAT1 association with milk production traits in buffalo, sheep, and goat. *DGAT1* gene showed some influence on meat production variables in sheep and goat, but not a single study reported the association of DGAT1 for meat production in buffalo. Overall, our review documented that DGAT1 has been studied extensively for milk production in milch animals. However, further validation of DGAT1 for their association with milk and meat production improvement is suggested in these animals to fill the gap with further research in this area.

AUTHOR CONTRIBUTIONS

MK and ZC: conceptualization and writing—original draft preparation. IK, AK, YL, JM, YM, SL, JX, and ZC: editing and technical review. ZC: visualization and supervision. All authors have read and agreed to the published version of the manuscript.

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