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Role of IGF-1 in goat semen freezing: A Review

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ABSTRACT

This review is based on the importance of Insulin-like Growth Factor-1 (IGF-1) in goat semen cryopreservation. Recent studies indicate that certain growth factors determine the seminal quality due to the interaction between seminal plasma and spermatozoa. Cryopreservation is the technique used to preserve semen at extremely low temperatures for extended periods, which is essential for artificial insemination (AI) and selective breeding programs. IGF-I promotes the proliferation and maturation of spermatozoa. IGF-I is involved in sperm motility, DNA fragmentation, membrane integrity and fertilizing capacity. There was a significant positive correlation between the weight of animals and IGF-1 genotype diversity. This review aims to investigate the effect of IGF-1 fortification in semen cryopreservation. Further, the review article also assesses the role of IGF-1 in improving the post-thaw quality and viability of goat semen, with the ultimate goal of enhancing the success rates of AI. The research gap this review aims to fill is the limited understanding of the role of IGF-1 fortification on goat semen cryopreservation.

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1 Introduction

Insulin-like growth factor I (IGF-I) regulates the cell cycle, promotes cell proliferation, or prevents apoptosis (Ziegler et al. 2015; Werner et al. 2016). In the context of goat semen cryopreservation, adding egg yolk to the semen extender before freezing is a common practice to protect the sperm membrane from the sudden drop in temperature. However, the presence of lecithin in egg yolks can interact with phospholipase enzymes from the bulbourethral goat gland, leading to the production of lysolecithin, which may have toxic effects on goat sperm, causing membrane damage and loss of motility (Sauerwein et al. 2000; Macpherson et al. 2002). IGF-I is found in seminal plasma and helps in testicular spermatogenesis and steroidogenesis, with dysregulation potentially contributing to male infertility (Sauerwein et al. 2000; Macpherson et al. 2002).

Milk and dairy products contain significant amounts of IGFs and IGF-binding proteins (IGFBPs). While research has primarily focused on IGFs, there have been reports of shortened IGFBPs and IGFBP glycosylation in milk, although IGFBPs have received less attention than IGFs (Meyer et al. 2017). High concentrations of IGF-1 in milk promote the proliferation of human colon cancer cell culture (Purup et al. 2007). This raises concerns about the potential health risks associated with consuming milk and other dairy products, highlighting the importance of considering IGF-1 levels when evaluating their safety.

IGF-I is structurally and functionally similar to insulin and act via endocrine, autocrine and paracrine processes to regulate the growth, development and differentiation of cells and tissues (Partridge et al. 2011; Kim 2014; Thornton et al. 2016). The level of this hormone can be influenced by various factors, including the duration of breastfeeding and individual traits (Rasouli et al. 2017). Studies have shown that IGF-1 levels in milk and dairy products can vary based on breed, lactation stage, and management practices (Meyer et al. 2017). Considering the potential risks associated with high IGF-1 levels, it is crucial to investigate further and understand the relationship between IGF-1 in dairy products and its potential impact on human health.

The coding gene of growth hormone (calpastatin, IGF-1, leptin, pituitary transcription factor-1) are the key genetic determinant influencing goat weight (Schenkel et al. 2005; Casas et al. 2006; Misrianti 2009; Arman et al. 2012).

2 Mechanism of action of IGF-1

The mechanism of action of IGF-1 involves promoting cell proliferation and differentiation and preventing apoptosis (Ziegler et al. 2015; Werner et al. 2016). It acts as a growth factor that regulates the cell cycle and plays a significant role in various physiological processes, including spermatogenesis and steroidogenesis (Sauerwein et al. 2000; Macpherson et al. 2002).

The regulation of IGF-1 and insulin levels in the blood is influenced by dietary factors, particularly protein and calorie intake. Studies have shown that food consumption, especially the amount of protein consumed, can affect the circulating levels of IGF-1 and insulin (Magistrelli et al. 2005). This highlights the importance of proper nutrition in modulating the levels of these growth factors.

In the context of milk and dairy products, it is worth mentioning that they contain significant amounts of IGF and IGFBP. While the focus has primarily been on IGFs, the role of IGFBPs in milk has received less attention (Meyer et al. 2017). High concentrations of IGF-1 in milk serum have been associated with the growth and development of human colon cancer cells (Purup et al. 2007). Therefore, the presence of IGFs in dairy products raises concerns regarding their potential impact on human health, particularly concerning cancer risk.

The IGF-1 gene is a key gene influencing goat weight; its genotype diversity has also been associated with this (Lestari et al. 2020). This phenomenon suggests that variations in the IGF-1 genotype contribute to goats' growth and weight differences. Identifying and characterizing genes associated with favourable phenotypes, including the IGF-1 gene, can provide valuable information for improving goat breeding programs and ensuring their sustainability.

Furthermore, climatic variables such as photoperiod, temperature, and the temperature-humidity index have been found to impact the level of IGF-1 in young goats. Increases in photoperiod and ambient temperature have been associated with higher IGF-1 output in goats (Pehlivan 2019). This highlights the influence of environmental factors on regulating IGF-1 levels and suggests the need to consider these factors when studying the role of IGF-1 in goat physiology.

In conclusion, the mechanism of action of IGF-1 involves its regulation of cell proliferation, differentiation, and survival. Dietary factors influence its levels, and its presence in milk and dairy products raises concerns regarding its potential effects on human health. The IGF-1 gene plays a crucial role in goat weight, and environmental factors can impact the levels of IGF-1 in goats. Understanding the complex interactions and functions of IGF-1 in various biological processes can provide valuable insights for both animal breeding programs and human health considerations.

3 Types of IGF-1

IGF-I, IGF-II and IGFBP-2 have been found in goat milk (Prosser 1996). Studies in goats have demonstrated that these peptides can cross from circulation to breast secretions (Prosser and Schwander

Table 1 Different type of IGF and its role

Type of IGF	Location	Role	Reference
IGF-I	Seminal plasma (horse)	Presence confirmed after immunoprecipitation and Western ligand blotting	Macpherson et al. 2002
IGF-II	Human seminal plasma	Identified in human seminal plasma along with other IGFBPs and protease activity of IGFBP-3	Baxter et al. 1984; Ramasharma et al. 1986; Ovesen et al. 1995
IGFBP-1	Human seminal plasma	Found in human seminal plasma along with other IGFBPs and protease activity of IGFBP-3	Baxter et al. 1984; Ramasharma et al. 1986; Ovesen et al. 1995
IGFBP-2	Seminal plasma (horse, equine)	Quantified in equine seminal plasma; levels unaffected by sexual activity	Macpherson et al. 2002
IGFBP-4	Human seminal plasma	Identified in human seminal plasma along with other IGFBPs and protease activity of IGFBP-3	Baxter et al. 1984; Ramasharma et al. 1986; Ovesen et al. 1995
IGFBP-5	Equine seminal plasma	Present in equine seminal plasma	Macpherson et al. 2002
Fragments of IGFBP-3	Human seminal plasma	Identified in human seminal plasma along with other IGFBPs and protease activity of IGFBP-3	Baxter et al. 1984; Ramasharma et al. 1986; Ovesen et al. 1995

1996). Similarly, the most prevalent IGFBPs in pig milk include IGFBP-2, IGFBP-3, IGFBP-4 and an unidentified IGFBP with a molecular weight of 28 kDa (Monaco et al. 2005). IGFBP-5 was recently discovered using mass spectrometry in the milk of tammar wallabies (Modepalli et al. 2016). During parturition, the concentration of IGF-I, IGF-II and IGFBPs are typically higher compared to later stages of breastfeeding (Meyer et al. 2017). IGF-II has been investigated as a modulator of prolactin dependant morphogenesis, as its production restored alveologenesis in prolactin receptor-defective mammary epithelial cells (MEC).

In-vitro studies have shown that sodium butyrate, fortified as dose-dependent in milk, increases messenger RNA expression and IGFBP-3 secretion. This, in turn, leads to the enhancement of growth hormone and IGF-I concentrations in the blood of calves (Wang et al. 2017). Dairy processing techniques affect the amount of IGF 1 and its binding protein. The intact and fragmented IGF-I, IGFBP-2 and IGFBP-5 forms were found in milk samples (Meyer et al. 2017).

Furthermore, in cattle, GH and IGF-I play a vital role in regulating osteogenesis and muscle development (Curi et al. 2005). However, it is worth noting that the content provided does not directly address the role of IGF-I in semen freezing or its impact on sperm parameters. The information primarily focuses on the presence and effects of IGF-I, IGF-II, and IGFBPs in milk and their significance in various contexts.

Levels of IGF-I and IGFBP-2 were determined in seminal plasma using radioimmunoassay. IGFBPs were found in seminal horse plasma after immunoprecipitation, and Western ligand blotting techniques were used to confirm their presence. Equine seminal plasma included IGF-I, IGFBP-2, and IGFBP-5. IGF-I, IGF-I/protein, total IGF-I, IGFBP-2, IGFBP-2/protein, and total IGFBP-2 levels in seminal plasma were not markedly different ($P < 0.13$) (Macpherson et al. 2002). It has also been investigated how IGF proteins work as post-testicular regulators of reproductive function. Human seminal plasma has been shown to include IGF-I, IGF-II, IGFBP-1, IGFBP-2, IGFBP-4, fragments of IGFBP3 and IGFBP-3 protease ability (Baxter et al. 1984; Ramasharma et al. 1986; Ovesen et al. 1995). Equine seminal plasma samples were used to quantify IGF-I and IGFBP-2. Sexual activity did not alter IGF-I and IGFBP-2 levels.

The freezing of goat semen is a crucial technique in preserving genetic material for long-term storage and breeding programs. However, it is important to consider the potential implications of IGF-1 in both semen freezing and milk production. This comprehensive review aims to examine the role of IGF-1 in goat semen freezing while addressing its presence and effects in milk.

4 IGF-1 in Semen Freezing

Previous studies have highlighted a correlation between seminal plasma IGF-1 levels and sperm motility, appearance, and fertility rates. To further understand the impact of IGF-1, investigations have been conducted to assess DNA fragmentation, membrane integrity, and fertilizing capacity. These studies have shed light on the important aspect of IGF-1 in sperm function and its importance in maintaining the quality of frozen goat semen.

5 Source of IGF-1

IGF-1 and its binding proteins in colostrum are more compared to the serum of Holstein neonates (Gale et al. 2004). Leydig and Sertoli cells release IGF-I, present in seminal plasma from the testes. IGF-I is crucial in spermatozoa movement, germ cell differentiation, and development (Roser and Hess 2001; Henricks et al. 1998). Photoperiod significantly affects the levels IGF-1 in goats (Flores et al. 2018).

6 Role of IGF-1 in semen diluents

The IGF system impacts the physiology and operation of sperm in several animals (Selvaraju et al. 2012). The differences in IGF-I concentration in seminal plasma affected the signal for germ cell growth, maturation, and spermatozoa viability (Selvaraju et al. 2012). The IGF-I complex from seminal plasma affected goat spermatozoa membrane intactness, capacitation, and DNA integrity. Skim milk-egg yolk extender formulations included diluted buck semen. IGF-I supplementation enhances the quality of semen in various species, including goats and bulls (Kumar et al. 2019). The sustainability of semen samples and their ability to maintain optimal quality may be attributed to the presence of antioxidant activities. However, these antioxidant activities can be depleted or lost during the handling of seminal plasma, especially when dilution is required, leading to a decrease in their levels and potentially placing strain on the cells. When discussing the importance of antioxidants in maintaining sperm quality and protecting against oxidative stress, the concept of glutathione (GSH) and its role in seminal dilution can be introduced. GSH, as an essential antioxidant, serves as a vital function in protein synthesis that may be lost during oxidative stress. Additionally, it forms a protective shield over sperm membranes to prevent lipid peroxidation and the generation of harmful free radicals (Almeida et al. 2021).

In seminal dilution, the loss of GSH can occur due to various factors, such as dilution during sample processing or exposure to reactive oxygen species. This reduction in GSH levels may have implications for sperm health and viability, compromising the ability to repair oxidative damage and maintain optimal cellular function.

7 Status of IGF-1 in semen diluents

This topic concerns numerous national and international research projects, works, and conferences. The effects of IGF-I on sperm capacitation, membrane intactness, and DNA integrity in goat spermatozoa have been reported by Susilowati et al. (2015). Gauthier et al. (2006) explored the physiological importance of IGFs and IGFBPs in milk. IGFBP ranking was proposed in bovine mammary secretions (Blum and Baumrucker 2002; 2008). Work has been done on stallions at the international level; 51 light-breeds, 3 to 20-year-old stallions were sampled for ejaculates from January through August 2000 in Florida, Maryland, and Texas.

8 Future Prospects

IGF-1 fortification could be a valuable tool for improving goats' artificial insemination and selective breeding programs. However, the effects of IGF-1 supplementation on the cryopreservation of goat semen is still needed more study. Specifically, future research should focus on the (i) optimal dose of IGF-1 for supplementation, (ii) timing of IGF-1 supplementation, (iii) duration of IGF-1 supplementation and (iv) the effects of IGF-1 supplementation on other aspects of semen quality, such as DNA fragmentation and capacitation. With further research, IGF-1 supplementation could become a standard practice for improving the cryopreservation of goat semen. This would significantly impact the goat industry, enhancing the artificial insemination per cent and selective breeding programs.

Conclusion

In conclusion, this review has shed light on the role of IGF-1 in goat semen cryopreservation and its implications for seminal quality. Various growth factors influence the interaction between seminal fluid and sperm cells, with IGF-I being recognized as one of the most significant factors due to its promotion of germ cell proliferation and sperm maturation. The freezing aspect of goat semen cryopreservation is a crucial factor to consider when examining the role of IGF-1 in seminal quality. Cryopreservation, which involves storing semen samples at extremely low temperatures, is essential for long-term storage and transportation. The review has aimed to highlight the potential involvement of IGF-I in sperm function by exploring the correlation between IGF-I and important attributes such as spermatozoa motility, appearance, and fertility rates.

Additionally, identifying genes associated with favourable phenotypes has been a focus, as it holds promise for enhancing goat breeding programs and ensuring their sustainability. Considering the safety of dairy products, the review suggests that IGF-I should be considered when assessing their safety profile. High levels of this hormone have been associated with potential cancer risk in individuals consuming milk and other dairy products. Thus, more study is required on the implications and potential health risks associated with IGF-I in dairy products.

Furthermore, the review has revealed a significant correlation between goat weight and the genetic diversity of IGF-1. This finding underscores the importance of genetic factors in influencing IGF-1 levels and highlights the potential for using IGF-1 as a marker for desirable traits in goat breeding programs.

Overall, this review serves as a roadmap for future studies in the field, providing valuable insights into the role of IGF-1 in goat semen cryopreservation and its broader implications for reproductive processes and dairy product safety. Continued research in this area will contribute to further advancements in goat breeding and the development safe and sustainable dairy products.

Conflict of Interest

I hereby declare that there is no conflict of interest for publication of this manuscript on behalf of all authors.

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