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Aquaporins as Central Players in Thermoregulation and Mammary Gland Function

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Abstract

At the cellular level, Aquaporins (AQPs) are specialized transmembrane protein channels that facilitate rapid water movement across cell membranes, playing a crucial role in thermoregulation and sustainable milk production. These aquaporins play vital roles in maintaining body water homeostasis by regulating water permeability in organs such as the kidney, lung, and skin. In the mammary gland, AQPs contribute to gland development, epithelial cell differentiation and the regulation of water movement necessary for efficient milk secretion and composition. Beyond the mammary gland, aquaporins are critically involved in skin physiology, where they regulate hydration, barrier function, wound healing and cellular proliferation. Dysregulation of aquaporin expression has been associated with impaired lactation, skin disorders, and altered tissue homeostasis. Understanding the integrative roles of aquaporins provides valuable insights into mammalian biology and may support the development of therapeutic strategies for lactation and dermatological disorders. Therefore, the objective of this communication is to highlight key physiological responses to water balance with particular emphasis on aquaporin-mediated water transport, and to emphasize the importance of monitoring thermoregulatory markers.

Keywords: Aquaporins, Lactation, Mammary gland, Milk

1. Introduction

Aquaporins (AQPs) are trans-membrane protein involved in water transport and different cellular functions such as cell adhesion, signalling and proliferation (Kaushik et al., 2024) [32]. Aquaporins play fundamental roles in water and small solute transport across epithelial and endothelial barriers (Verkman and Mitra, 2000) [59]. To date, 13 members of the aquaporin gene family have been identified in humans: AQP0–AQP12 (Castle, 2005) [12]. The proteins encoded by aquaporin genes have been classified into two major groups based on their substrate permeabilities: [1] some aquaporins are permeated by water and include AQP0, AQP1, AQP2, AQP4, AQP5 and AQP8 (Agre et al., 2002) [1]; [2] others, the aquaglyceroporins exhibit permeability to water and small neutral solutes such as glycerol and urea and include AQP3, AQP7, AQP9 and AQP10 (Agre et al., 2002; Hibuse et al., 2006) [1, 25]. Aquaporins in cattle are involved in the renal regulation of water excretion and maintenance of proper acid-base balance (Michalek et al., 2019) [42]. Finally, AQP6, 11, and 12, sometimes referred to as unorthodox aquaporins, have specific or as yet unelucidated properties (Rojek et al. 2008). Recent immunohistochemical studies in the rat and mouse mammary gland have confirmed the presence of AQP1 and AQP3 proteins in both species (Matsuzaki et al., 2005) [40]. Human tissues have provided immunohistochemical evidence for AQP1 and AQP3 in human mammary glands (Mobasher and Marples, 2004; Mobasher et al., 2005) [43, 45]. AQP3 helps maintain skin hydration and also influences lipid metabolism, keratinocyte growth, and wound healing by supporting cell migration and proliferation (Boury-Jamot et al., 2009) [6]. There are nine aquaporins located in epithelial cells lining the individual sections of the nephron and collecting tubules (Michalek et al., 2019).

2. Relevance of Aquaporins to milk production

Milk is a secreted body fluid that consists of water plus lipids, electrolytes, vitamins, sugars and specific milk proteins. The delivery of water to the mammary gland by the circulatory system and the movement of water across endothelial and epithelial barriers are critical for milk synthesis and secretion in lactating (Blaug et al., 2001) [3]. However, the functional anatomy of the mammary gland has not been extensively studied in the context of water transport across endothelial and epithelial barriers and bulk fluid movement in lactating animals. Consequently, very little published information on; AQP1 and AQP3 proteins have shown their presence in the capillary and mammary epithelial cells, respectively (Matsuzaki et al., 2005) [40]. Similar observations suggest that AQP1 and AQP3 proteins are also present in nonlactating human mammary glands (Mobasher et al., 2004) [43]. Data recently published on aquaporins in the bovine mammary gland (Mobasher et al., 2011) [44] confirm some of the recent observations made by (Matsuzaki et al., 2005) [40] in rodent mammary glands and similar observations in human mammary glands (Mobasher et al., 2004) [43]. Bovine data also confirm the presence of these proteins in the bovine mammary gland, although in distinct cellular locations (Mobasher et al., 2011) [44]. Expression of AQP1, at high abundance, is also observable in myoepithelial cells underlying teat duct epithelia (Mobasher et al., 2011) [44]. The physiological reason for this is at present unknown, but high AQP1 levels in this location may contribute to increased permeability of teat duct epithelia in the lactating bovine mammary gland. The relative abundance of the protein also appears to represent a distinct aspect of differentiation of myoepithelial cells in this location, compared with those surrounding the acini. Wooding et al. (1977) [61] reported that Goats' milk is known to contain numerous cell fragments known as "christiesomes" which originate from secretory epithelial cells of the mammary gland. These cell fragments are known to contain intact and well-preserved endoplasmic reticulum, mitochondria and lipid droplets. Furthermore, they are capable of triglyceride synthesis. It has been found that although cows' milk contain very few cellular fragments, it does contain different and denser particles containing fewer vesicles and numerous microvillus-like protrusions on one side known as "sunbursts" (Wooding et al., 1977) [61]. It has been suggested that these particles are residues of dead cells, but these fragmented cytoplasm-containing entities may contain membrane proteins, which are targeted to the apical membranes of mammary secretory epithelial cells. Recent studies have provided evidence for urinary excretion of AQP2 water channel proteins during pregnancy (Buemi et al., 2001) [9]. Biochemical analysis of "christiesomes" and "sunbursts" should reveal if these cellular fragments contain membrane proteins of the apical membranes of alveolar epithelial cells. Comparing this data with published data from rodent studies clearly indicates that some of the aquaporins expressed in the lactating mammary tissues were found in expected anatomical

locations. Immunohistochemical labelling in the rat mammary gland revealed that AQP1 is localized to the capillaries and AQP3 is localized to the basolateral membranes of the alveolar secretory cells. These results confirm the presence of aquaporins in lactating mammary glands and its role in the control of milk water content by diluting the sugar, protein and lipid contents of milk to an isotonic solution (Mobasher et al., 2011) [44].

3. Role of AQP1, AQP3 & AQP5 in Mammary Gland

Matsuzaki et al. (2005) [40] reported presence of lower molecular weight band in the mammary gland. Which remained intact after glycosidase treatment. It was emphasized that lactating rat mammary gland expresses the water-channel proteins AQP1 and AQP3 (Table 1), as measured by RT-PCR, immunoblotting, and immunohistochemistry. AQP1 is present in endothelial cells of the capillaries and venules where it is located in both the apical and basolateral membranes. AQP1 is a water-selective channel and seems to play a role in the transcellular transfer of water from the blood to the interstitial space. In alveolar secretory epithelia, AQP3 is localized to the basolateral membrane. Labelling for AQP3 differs in intensity among alveoli, which might be caused by the different state of the alveolar secretory cells, namely, synthetic or secretory. AQP3 is absent in the epithelial duct of the virgin female rat, and a small amount of AQP3 is present in the pregnant rat. AQP3 seems to be expressed upon the differentiation of alveolar secretory cells of mammary gland. Some ducts expressed an abundance of AQP3 and others expressed little or no AQP3. There seems to be no relation between the expression level of AQP3 and the position of the duct, namely, whether the duct is intralobular, interlobular, or a main duct. The significance of this differential expression level remains unclear. Transfer of water and/or glycerol from the interstitial fluid into the secretory epithelial cells through the basolateral membrane. Since water and glycerol are essential for the synthesis and secretion of milk, AQP3 may serve as a channel for both. In the lactating rat, significant amounts of glycerol are required to produce milk triglycerides (Garton, 1963) [21].

Although the majority of the glycerol carbon of milk triglycerides seems to be derived from plasma glucose (Garton, 1963) [21], plasma glycerol may be taken up via AQP3 and incorporated directly into milk triglycerides. The presence of AQP3 in some intralobular and interlobular ducts have suggested that the duct cells also participate in the secretion of milk. In different studies, the expression of AQP3 in the main duct suggests additional roles for this protein. AQP3 is present in the basal and intermediate layers of the stratified epithelium, as seen in the epidermis. Matsuzaki et al. (2003) [41] predicted the presence of AQP5 in the apical membrane of the secretory cell, as is commonly seen in glands such as the salivary, lacrimal, and sweat glands (Matsuzaki et al., 2003) [41].

Table 1: Aquaporins in Mammary Gland: Localization and Functional Roles

Aquaporin	Cellular Localization	Primary Function
AQP1	Capillary endothelial cells (apical & basolateral membranes), myoepithelial cells	Water transport across endothelium
AQP3	Basolateral membrane of alveolar secretory epithelial cells; some ductal epithelium	Water and glycerol transport
AQP5	Apical membrane of secretory epithelial cells	Water secretion (as in salivary/sweat glands)

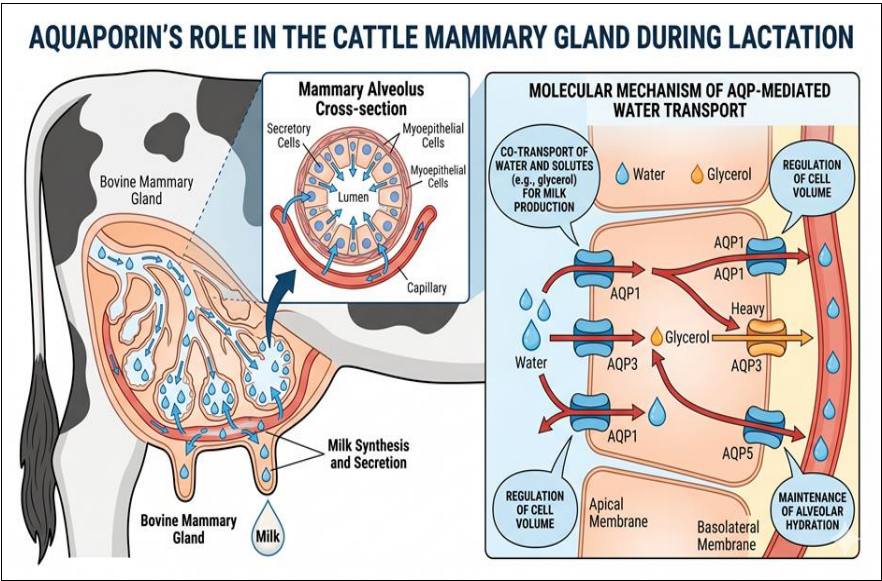


Fig 1: The Bovine Mammary Gland and Lactation Mechanics

Fig 1. A cross-sectional view of the alveolar epithelial network mapping specialized AQP sub-types: AQP1 heavily expressed in the vascular endothelium and supporting myoepithelial layers to accelerate fluid influx from blood plasma into the secretory tissue matrix. AQP3 localized primarily at the basolateral membrane of secretory epithelial cells, managing the directional trans-cellular transport of water and metabolic glycerol essential for milk lipid synthesis. AQP5 situated at the apical plasma membrane, directly regulating fluid secretion into the alveolar lumen to control milk volume, viscosity, and tonicity.

4. Structure and function of the skin

The skin, the body’s largest organ, is composed of three primary layers: the epidermis, dermis, and hypodermis (subcutaneous tissue) (Bollag et al., 2020 and Jiao et al., 2024) [5]. These layers function together to protect against environmental stress, regulate water loss, and support immune defence and sensation. The epidermis, the outermost layer, contains five sublayers, with the stratum corneum (SC) forming the main barrier against water loss and external agents (Nestle et al., 2009 and Mayer & Maibach, 2013) [48]. The predominant cells are keratinocytes, which produce keratin and form a protective barrier (Jiao et al., 2022) [28]. These cells originate in the basal layer, where epidermal stem cells (ESCs) reside. ESCs enable continuous renewal of the epidermis through proliferation and differentiation (Kammeyer et al., 2015) [30]. Beneath lies the dermis, composed of connective tissue rich in collagen, elastin, and extracellular matrix components like proteoglycans (PGs) and glycosaminoglycans (GAGs). These elements maintain skin strength, elasticity, and hydration. With aging, reduced collagen synthesis and increased degradation lead to diminished firmness and elasticity (Shin et al., 2019) [54]. The hypodermis, mainly made up of adipose tissue, provides insulation and cushioning. It also includes dermal white adipose tissue (dWAT), which surrounds hair follicles and supports adipose-derived stem cells (ASCs).

ASCs aid in skin regeneration, repair, and immune modulation. However, with age, this layer becomes thinner, ASC activity declines, and the skin’s healing ability decreases (Kubo et al., 2012 and Liu et al., 2024) [34].

5. Functional Significance of Aquaporins in Skin Physiology

5.1. Distribution and Localization of Aquaporins in the Skin

Aquaporins (AQPs) are expressed in various layers and cell types within the skin, highlighting their diverse functional roles (Boury-Jamot et al., 2006) [7]. AQP1 and AQP3 are broadly distributed in both the dermis and epidermis. AQP1 is primarily localized in dermal capillary endothelial cells, where it facilitates water transport and supports wound healing (Mobasheri et al., 2004 and Ishida et al., 2018) [43]. AQP3 is predominantly found in keratinocytes of the basal and spinous layers of the epidermis, contributing to skin hydration and barrier function (Hara et al., 2002) [22]. AQP5 is well-documented in eccrine sweat glands, where it plays a key role in sweat secretion by increasing water permeability in secretory cells (Tricarico et al., 2022) [58]. Although some studies suggest AQP5 may also be expressed in keratinocytes and involved in their proliferation, this role requires further confirmation (Tricarico et al., 2022) [58]. AQP7 and AQP11 are primarily expressed in the hypodermal adipose tissue. AQP7 is also found in dermal and epidermal dendritic cells, supporting immune cell functions (Liu et al., 2024) [38, 39]. It should be noted that while Badaut et al. (2014) [2] describe AQP7 and AQP11 in brain tissues, their expression in skin adipose and immune cells has been corroborated by more recent skin-focused studies (Liu et al., 2024) [38, 39]. AQP8 is localized in dermal fibroblasts and has been implicated in protecting these cells from oxidative stress (Liu et al., 2024) [38, 39]. Both AQP9 and AQP10 are expressed in the epidermis, suggesting specialized roles in skin hydration and lipid metabolism (Karimi and Ahmadi, 2024) [31]. Overall, the distinct but overlapping distribution of

aquaporins throughout skin layers reflects their critical involvement in hydration, immune response, and barrier integrity.

5.2. Functional Roles of AQP1 and AQP3: Hydration, Cell Migration and Barrier Homeostasis

AQP1 is primarily expressed in dermal capillary endothelial cells, where it plays a vital role in facilitating water transport across the endothelial barrier. This water permeability is essential for maintaining skin hydration and enabling efficient fluid exchange within the dermis. Moreover, AQP1 contributes to endothelial cell migration, a critical process during skin wound healing and angiogenesis (Mobasher et al., 2004, Ishida et al., 2018 and Osorio et al., 2019) ^[43]. Beyond its water channel function, AQP1 also acts as a cation channel, regulated by intracellular signaling pathways, which may influence cellular functions related to migration and proliferation (Boassa and Yool, 2002 and Tomita et al., 2017) ^[4].

AQP3, the most abundant aquaglyceroporin in the epidermis, is mainly located in keratinocytes of the basal and spinous layers. It facilitates the transport of water, glycerol, and hydrogen peroxide (H_2O_2), molecules essential for skin hydration, energy metabolism, and redox signaling (Hodeib et al., 2017) ^[26]. Studies on AQP3-deficient mice demonstrate that lack of this protein results in significantly reduced skin moisture and elasticity, as well as impaired barrier repair, emphasizing AQP3's role in maintaining skin hydration and integrity (Hara et al., 2002 and Qin et al., 2011) ^[22]. Supplementing these models with glycerol successfully restores hydration, confirming that glycerol transport via AQP3 is a key mechanism for skin moisture retention (Hara and Verkman, 2003 and Choudhary et al., 2015) ^[23].

In addition to hydration, AQP3 promotes keratinocyte proliferation and differentiation by enabling glycerol uptake, which supports phosphatidylglycerol synthesis through activation of the phospholipase D2 (PLD2) pathway. This signaling cascade is crucial for maintaining epidermal homeostasis and effective skin barrier function (Bollag et al., 2020 and Qin et al., 2011) ^[5]. Importantly, decreased AQP3 expression observed during aging and following UV exposure is associated with increased skin dryness and a reduced capacity for repair, highlighting its relevance in skin aging and photo-damage (Seleit et al., 2017, Li et al., 2010 and Cao et al., 2008) ^[53].

5.3. AQP5 in Keratinocyte Regulation and Sweat Secretion

AQP5 plays a crucial role in sweat gland physiology by increasing membrane water permeability in the secretory cells of eccrine sweat glands. This function is essential for the production and secretion of sweat, which aids in thermoregulation and skin hydration (Liu et al., 2023) ^[37]. Beyond its role in sweat glands, AQP5 is also expressed in keratinocytes, where it promotes cell proliferation and dedifferentiation processes vital for epidermal renewal and repair. Notably, AQP5 expression decreases with age, which may impair epidermal stem cell activity and contribute to the decline in skin regeneration and function commonly observed in aging skin (Zhou et al., 2020) ^[64].

5.4. Immunomodulatory and Antioxidant Roles of AQP3, AQP5, AQP7, and AQP8

Aquaporins (AQPs) are integral membrane proteins that contribute significantly to immune homeostasis and defence mechanisms in the skin. Among these, AQP3 plays a critical role in immune cell function by facilitating the transport of hydrogen peroxide (H_2O_2) into CD8+T cells, a process essential for redox signalling and effective endocytosis. AQP3 also supports macrophage phagocytosis and the migration of both macrophages and T cells, thereby enhancing innate and adaptive immune responses. Additionally, AQP3 influences inflammatory signalling by promoting the transcription of pro-inflammatory cytokines such as IL-6 and TNF- α and is involved in activating the NLRP ^[3] inflammasome during innate immune responses (Nalle et al., 2020, Zhu et al., 2011 and De-Baey et al., 2000) ^[47].

AQP5 regulates the migration of neutrophils and promotes the activation and proliferation of dendritic cells, which are essential for effective immune surveillance and defence during skin inflammation or injury (Rump and Adamzik, 2018 and De-Santis et al., 2019) ^[52].

Predominantly expressed in dendritic cells, AQP7 facilitates antigen uptake and chemotactic migration, playing a vital role in allergic immune responses and skin immune surveillance (Tricarico et al., 2022, Wang et al., 2008 and Hara-Chikuma et al., 2017) ^[58]. In contrast, AQP8 is mainly found in dermal fibroblasts and contributes to antioxidant defence by controlling intracellular H_2O_2 levels. This protective role helps preserve skin integrity and delays damage related to oxidative stress and aging (Liu et al., 2024) ^[38, 39].

5.5. AQP9 in Differentiation and Immune Defence

AQP9 is associated with differentiated keratinocytes and immune cells like neutrophils and T cells. It regulates cell migration, tight junctions, and immune sensitization, particularly in allergic and infectious responses (Karimi and Ahamadi 2024) ^[31]. Its expression is influenced by differentiation agents like vitamin D3 and retinoic acid, reflecting a specialized role in skin immunity and barrier integrity.

5.6. AQP10 and AQP11 in Barrier Function and Lipid Metabolism

AQP10 is primarily localized in the stratum corneum, the outermost layer of the epidermis, where it is believed to support skin barrier function in a manner similar to AQP3 by facilitating the transport of water and small solutes (Tricarico et al., 2022) ^[58]. Both AQP10 and AQP11 are expressed in adipocytes within the hypodermis, the subcutaneous fat layer of the skin. Notably, AQP11 is found on the membranes of the endoplasmic reticulum (ER), situated near lipid droplets, indicating its role in intracellular glycerol transport and lipid metabolism. These functions are crucial for maintaining the lipid balance and homeostasis of the skin, which in turn supports overall skin health, hydration, and repair (Laforenza et al., 2013) ^[35].

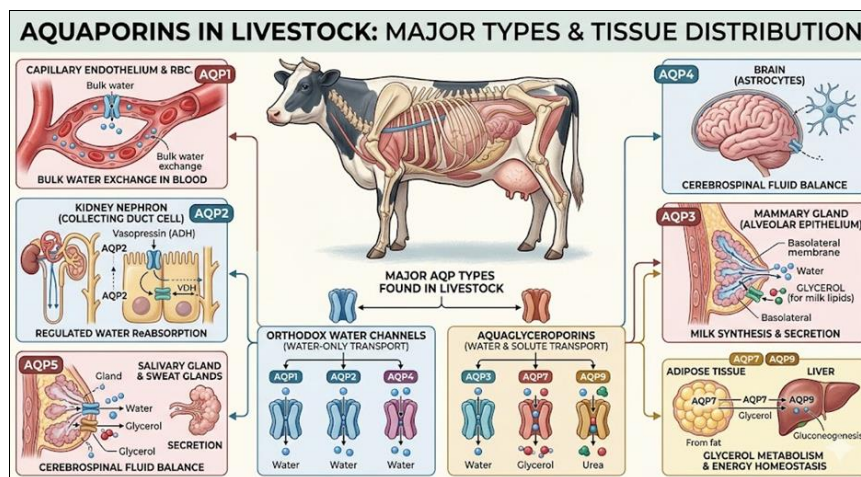


Fig 2: Molecular Transport of Aquaporins across specialized Bovine Tissues.

Figure 2. The functional landscape of bovine aquaporins is strictly dictated by pore selectivity and strategic tissue distribution. AQP1 manages trans-endothelial bulk water exchange in capillaries; AQP2 acts as the primary renal target for vasopressin (ADH) to regulate adaptive water reabsorption in the collecting duct; and AQP4 maintains strict cerebrospinal fluid balance within cerebral astrocytes. Secretory and metabolic pathways depend heavily on specialized AQP distribution. Apical AQP5 coordinates fluid output in exocrine and sweat glands to aid thermoregulation. Within the mammary gland, basolateral AQP3 funnels water and vital glycerol directly into the alveolar epithelium to support milk synthesis and lipid droplet formation. Systemically, the AQP7/AQP9 axis bridges adipose tissue and the liver, controlling glycerol mobilization from fat reserves and its subsequent hepatic uptake for gluconeogenesis during states of high metabolic demand.

6. Aquaporins in Skin Repair Mechanisms

Aquaporins (AQPs), particularly AQP3 and AQP8, are integral to several biological processes that promote skin regeneration and repair. They contribute to oxidative stress regulation, hydration, autophagy, and the maintenance of barrier integrity, making them potential therapeutic targets in aging and damaged skin.

6.1. Regulation of Oxidative Stress and Cell Survival

Aquaporins AQP3 and AQP8 play a crucial role in regulating oxidative stress by facilitating the transport of hydrogen peroxide (H_2O_2), a key reactive oxygen species (ROS) involved in intracellular signalling pathways. By controlling intracellular H_2O_2 levels, these aquaporins help modulate oxidative stress responses, which are vital for maintaining cell viability, promoting tissue repair, and preventing premature cellular aging (Karimi and Ahamadi 2024) [31]. Overexpression of AQP3 has been shown to enhance the survival and function of both young and senescent human dermal fibroblasts (HDFs) by reducing oxidative stress levels, thereby delaying the onset of cellular senescence and supporting skin regeneration (Tang et al., 2023) [55]. Similarly, AQP8 contributes to protecting dermal fibroblasts from oxidative damage by tightly regulating intracellular ROS concentrations. This regulation helps preserve key structural proteins such as collagen type I alpha 1 chain (COL1A1) and keratin 19 (KRT19), which are essential components for maintaining the skin's structural integrity and promoting effective regeneration (Liu et al., 2024) [38, 39].

6.2. Promotion of Autophagy

Autophagy is a vital cellular process that helps maintain skin health by removing damaged organelles and proteins, especially during skin injury and aging. This self-cleaning mechanism protects cells from accumulating harmful debris, thus preserving cellular function and preventing premature aging. AQP3 plays a significant role in regulating autophagy in skin cells. Its expression is upregulated in response to short-term UVA (Ultraviolet A) exposure, which activates JUN-mediated signalling pathways involving key autophagy-related proteins such as Beclin [1] and DEDD. This induction of autophagy promotes cell recovery, mitigates damage, and helps reduce cellular senescence, thereby supporting skin resilience against environmental stress (Xie et al., 2022) [63]. However, prolonged or chronic UVA exposure leads to a reduction in AQP3 levels, resulting in impaired autophagy. This suppression of the autophagic process contributes to the accumulation of cellular damage, accelerating skin aging and decreasing the skin's ability to repair itself. These findings underscore the time-sensitive regulatory role of AQP3 in managing cellular cleanup and maintaining skin homeostasis under UV stress (Xie et al., 2022 and Karimi and Ahamadi 2024) [63].

6.3. Skin Hydration and Barrier Repair

AQP3 plays a pivotal role in maintaining skin hydration and ensuring the integrity of the skin's barrier function. It facilitates the transport of both water and glycerol across keratinocyte membranes, essential for retaining moisture within the skin layers. Glycerol, in particular, acts as a natural humectant, helping to attract and hold water in the epidermis, thereby promoting skin softness and elasticity. Beyond its role in water transport, AQP3 also supports the expression of critical barrier-related proteins such as claudin-1, filaggrin, and CD44. Claudin-1 is a tight junction protein crucial for maintaining the skin's selective permeability. Filaggrin contributes to the formation of the skin's natural moisturizing factor, and CD44 is involved in cell adhesion and migration, all of which collectively uphold the structural and functional integrity of the skin barrier (Dumas et al., 2007) [17]. Various bioactive compounds have been found to enhance AQP3 expression, thereby improving skin hydration and barrier repair. Notably, all-trans retinoic acid, glycolic acid, and chrysin significantly upregulate AQP3 levels, leading to enhanced hydration of the stratum corneum and strengthening of the skin's protective barrier (Cao et al., 2008, Wu et al., 2009 and Tang et al., 2019) [11]. Additionally, natural extracts

such as Aloe vera and substances like trimethylglycine have demonstrated the ability to increase AQP3 expression. These natural agents contribute to the skin's repair mechanisms following environmental insults like UV radiation and pollution, supporting faster recovery and maintenance of healthy skin (Filatov et al., 2024) ^[19].

6. 4. Microbiome Modulation and AQP3 Expression

The gut-skin axis, a complex communication network between the gastrointestinal tract and skin, plays a crucial role in skin health and repair. Dysbiosis, or imbalance, in the gut microbiota can negatively affect skin repair mechanisms by disrupting immune responses and barrier function. Recent research highlights the promising role of probiotics in restoring this balance and modulating the expression of key proteins such as aquaporins, especially AQP3, which is essential for skin hydration and regeneration. Probiotics such as *Lactobacillus reuteri* DSM17938 have been shown to upregulate AQP3 expression, thereby enhancing skin barrier function. This modulation helps improve hydration and reduces inflammation, making such probiotics effective in managing conditions characterized by dry or inflamed skin (Khmaladze et al., 2019) ^[33]. Similarly, *Bifidobacterium animalis* CGMCC25262 not only increases AQP3 levels but also suppresses inflammatory pathways by inhibiting the ERK signaling cascade. This dual action contributes significantly to skin health by promoting repair and reducing inflammatory damage, further underscoring the therapeutic potential of probiotics in skin care (Zhu et al., 2024).

6. 5. Molecular and Therapeutic Regulation of Aquaporins

Targeting AQP3 through genetic and molecular pathways presents promising therapeutic opportunities for skin health and anti-aging interventions:

Suppression of miR-551b-3p via lncRNA PVT1 has been shown to upregulate AQP3 expression, leading to the inactivation of the ERK/p38 MAPK signaling pathway. This molecular interaction reduces fibroblast senescence, thereby offering a novel approach to counteract skin aging and promote tissue regeneration (Tang et al., 2023) ^[55]. Activation of PPAR γ (peroxisome proliferator-activated receptor gamma) enhances AQP3 transcription in keratinocytes. Studies have demonstrated that topical application of PPAR γ agonists, such as ciglitazone, can increase AQP3 levels in the skin. This upregulation supports improved skin hydration, barrier repair, and overall dermal homeostasis, highlighting its potential in dermatological therapies (Yang et al., 2020).

Conclusion

Aquaporins (AQPs) have emerged as crucial regulators of water and small solute transport in mammalian systems, with significant implications for mammary gland biology, lactation, and skin physiology. This review highlights the diverse expression patterns and functional roles of different aquaporin isoforms in maintaining cellular and tissue homeostasis. In the mammary gland, AQPs contribute to mammary development, epithelial cell function and efficient milk synthesis and secretion by facilitating osmotic water movement and supporting metabolic processes associated with lactation. Similarly, in the skin, aquaporins play indispensable roles in epidermal hydration, barrier maintenance, glycerol transport, wound healing, and skin elasticity. Among them, AQP3 has been extensively studied due to its direct involvement in maintaining skin moisture and

cellular proliferation. Future investigations integrating molecular, physiological and omics-based approaches may further clarify their mechanisms of action and reveal new opportunities for improving dairy productivity, mammary health, and dermatological therapies. Overall, aquaporins represent a promising and evolving field of research with broad relevance in mammalian physiology and translational biomedical sciences.

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