The Pharma Innovation Journal 2020; SP-9(9): 175-178

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2020; SP-9(9): 175-178

www.thepharmajournal.com
Received: 27-07-2020
Accepted: 02-09-2020

Smriti Shukla
M.V.Sc, Animal Physiology Division, NDRI, Karnal, Haryana, India

Gaurav Kumar
PhD Scholar, Animal Physiology Division, NDRI, Karnal, Haryana, India

Amangeet Parashar
Veterinary Surgeon Faridabad, Haryana Government, Haryana, India

Sudha Saini
Senior Research Fellow, Animal Physiology Division, NDRI, Karnal, Haryana, India

Corresponding Author:
Smriti Shukla
M.V.Sc, Animal Physiology Division, NDRI, Karnal, Haryana, India

Role and distribution of aquaporins in renal system

Smriti Shukla, Gaurav Kumar, Amangeet Parashar and Sudha Saini

Abstract
Aquaporins plays a major role in water movement in kidney, especially in renal medulla where ADH acts to reabsorb water and it is positively correlated with ADH different environmental temperature. AQP2 are involves in long term regulations of urinary concentration because the collecting ducts are importantly involved in the regulation of body water balance by vasopressin-regulated water reabsorption. Upregulation of AQP2 and AQP3 expression in both ureteral and urinary bladder tissue. The fold change expression of AQP3 was found to be highest expressed in ureter and urinary bladder as compare to AQP1 & AQP2 in summer season. AQPs may play a regulatory role in urothelial cell volume and osmolality and in determining the composition of final urine.
In the goats significant rise in the physiological reactions occurred during summer showing a positive correlation with the temperature and physiological responses so as to overcome the environment stress during different seasons of animals. The variations in the haematological counts, circulatory electrolytes, blood biochemical components observed in the goats during summer seasons depicting its thermo tolerance. The significant increase in the ADH and cortisol concentrations was high during summer showing a direct relationship with efficient water balancing mechanism in the body.

Keywords: Aquaporins, kidney, water

Introduction
Aquaporins, also known as AQPs, were first reported in 1988 by Denker [5] *et al*., who purified a large amount of a 28-kDa protein from human erythrocyte membranes. Aquaporins (AQPs) are a class of membrane water channels whose primary function is to facilitate the passive transport of water across the plasma membrane of the cell in response to osmotic gradients that are created by the active transport of solutes. Aquaporins have a pair of highly conserved signature sequences, asparagine-proline-alanine (NPA) boxes, to form a pore. However, some have little conserved amino acid sequences around the NPA boxes unclassifiable to two previous AQP subfamilies, classical AQPs and aquaglyceroporins. Agre *et al*., 1998 [2] found that AQPs are widely expressed in the body, particularly in cell types that are involved in fluid transport, such as epithelial cells in several organs, as well as in some cell types that do not have an obvious role in fluid transport, such as adipocytes. AQPs belong to a family of intrinsic membrane proteins that act as selective channels for water and for solutes such as glycerol and urea. AQPs also have a diversity of functions: some related to water transport such as fluid secretion, fluid absorption, and cell volume regulation, and the others not directly related to water transport such as cell adhesion, cell migration, cell proliferation, and cell differentiation. Some AQPs even permeate nonionic small molecules, ions, metals, and possibly gasses. Ishibashi K. (1994) [11] reported that AQP gene disruption studies have revealed their physiological roles: water transport in the kidney and exocrine glands, glycerol transport in fat metabolism and in skin moisture, and nutrient uptakes in plants. Furthermore, AQPs are also present at intracellular organelles, including tonoplasts, mitochondria, and the endoplasmic reticulum. Hohmann *et al*., 2000 [10] foundthat Currently, at least 13 isoforms of AQPs (AQP0-12) have been identified in mammals. Based on their permeability, mammalian AQPs are divided into three groups:

a. Water-selective permeable aquaporins (AQP0, AQP1, AQP2, AQP4, AQP5, AQP6, and AQP8)
b. GLPs permeable to water, glycerol, urea, and other solutes (AQP3, AQP7, AQP9, and AQP10)
c. Subcellular aquaporins or super-aquaporins (AQP11 and AQP12), which have low homology with the other AQPs

And there are 2 families of Aquaporins are found in *E.coli*

a. glycerol uptake facilitator (GlpF)
b. aquaporin Z (AQPZ)

In plants are separated into five main homologous subfamilies

a. Plasma membrane Intrinsic Protein (PIP)
b. Tonoplast Intrinsic Protein (TIP)
c. Nodulin-26 like Intrinsic Protein (NIP)
d. Small basic Intrinsic Protein (SIP)
e. X Intrinsic Protein (XIP)

There are 2 family of Aquaporin i.e. Aquaporin (AQPs) and Aquaglyceroporins (AQGPs) which having permeability in different medium like water and glycerol respectively.

Aquaporins in Kidney

At present, at least 7 aquaporins are expressed at distinct sites in the kidney and 4 members of this family (AQP1-4) have been demonstrated to play pivotal roles in physiology and pathophysiology for renal regulation of body water balance (Frokiaer *et al*., 2002) [23].

Aquaporins (AQPs) located in bovine kidneys and their potential role in the transport of water and other small molecules reported by Michałeka and Grabowskab in the year 2019 as shown in following table-

Table 1.

AQPs	Expressed cells/tissues	Localization	Function
AQP1	Epithelial cells of proximal tubules and thin descending loops of Henle	Apical (brush border) and basolateral membrane	Water transport
	Epithelial cells of glomerular Capillaries	Plasma membrane	
AQP2	Principal cells of collecting duct	Apical and basolateral membrane, intracellular vesicles	Water transport
AQP3	Principal cells of collecting duct	Basolateral membrane	Water/glycerol/ ammonia transport. Urea transport
AQP4	Epithelial cells of proximal tubules	Basolateral membrane	Water transport
AQP5	Epithelial cells of medullary tubules		Water transport
AQP6	Selected cells of collecting duct	Intracellular	Water/urea/glycerol/ anions transport
AQP7	Epithelial cells of proximal tubules	Apical plasma (brush border)	Water/urea/glycerol/ ammonia transport
AQP8	collecting duct Epithelial cells of proximal tubules	Intracellular	Water/ammonia transport
AQP11	Epithelial cells of proximal tubules	Intracellular	Water transport

Aquaporin 1(AQP1)

The higher expression of AQP1 gene in renal cortex in comparison to renal medulla in both the summer and winter seasons shows a possible involvement of AQP1 gene in Glomerular filtration. It also shows that AQP1 are involve in thermoregulation by highly expressing during summer. Agre *et al* 1993a [3] and Nielsen *et al*., 1995 [6] found that AQP1 is abundantly expressed in proximal tubule and descending thin limb of Loop of Henle but weak expression evident in the convoluted tubules role in the transcellular water movement across both surfaces of the cells thus, AQP1 may facilitate the water effectively in the proximal tubule.

AQP1 deficiency causes impairment in near isosmolar fluid absorption in proximal tubule, resulting in marked luminal fluid hypotonicity in end proximal tubule as a consequence of active solute absorption and reduced transepithelial water permeability. AQP1alsofacilitated transcellular water transport thus has an important role in kidney, as well as in various extrarenal epithelia such as choroid plexus and ciliary epithelium. Recently found thatAQP1 is facilitates the migration of epithelial cells in the proximal tubule cells possibly in response of the proximal tubule to injury. So that it may helpful in repairing of proximal tubule (Harachikuma *et al*., 2006) [9]. Some other use of aquaporin 1 in kidney which are investigate by Jeremiah *et al*, 2009 [12] that, urine AQP1 and ADFP (Adipophilin) concentrations appear to be sensitive and specific during cancers of proximal tubule origin in kidney. So that it may be useful as biomarkers for diagnosis purpose of kidney cancer. Some recent study also carried on the closing and opening of water channels in experimental conditions like cisplatin-induced polyuria is associated with a significant decrease in the expression of collecting duct water channels AQP2 and AQP3 and PCT water channel AQP1 in the inner medulla which may give their contribution during cure of oedema condition of animals (Kishore *et al*., 2000) [15].

Aquaporin 2 (AQP2)

AQP2 is located mainly in the apical plasma membrane and the intracellular vesicles (Kim *et al*., 2005, Noda and Sasaki 2005) [14]. AQP2 plays a major role in water movement in kidney, especially in renal medulla where ADH is positively correlated to water movement and helps in reabsorbing water. The increase in the Plasma Aldosterone, ADH and ANG-II concentrations is high during summer showing a direct relationship with efficient water balancing mechanism in the body (Gowda, 2018) [8]. The higher expression of AQP2 gene in renal medulla in comparison to renal cortex in both the seasons shows a possible involvement of AQP2 gene in Tubular reabsorption. It also shows that AQP2 are involve in thermoregulation by highly expressing during summer. Kim *et al*., 2005 [14] observed that AQP2 plays a major role in urine concentration in response to increased plasma arginine vasopressin levels. In relation to this we observed a positive co-relation between plasma ADH, Aldosterone and AQP2 gene expression in both winter and summer.

AQP2 plays a key role in urine concentration in response to increased plasma arginine vasopressin levels. Binding of vasopressin to the basolateral V2 receptor causes increased intracellular cAMP production, protein kinase A (PKA) activation, phosphorylation of AQP2, and transport and fusion of AQPs with the apical plasma membrane, which results in increased water permeability of the connecting tubules and collecting ducts (Kim *et al*., 2005, Noda and Sasaki 2005) [14]. The collecting duct is the major site for vasopressin mediated regulation of body water homeostasis. AQP2 is the predominant vasopressin-regulated aquaporin. Nielsen *et al*., 2002 [23] showed in experiment that after fusion of AQP2 to apical plasma membrane either they will under goes endocytosis or is excreted into the urine. That's why approximately 3-6% of the total amount of AQP2 is excreted into urine (Nielsen *et al*., 2002) [23].

AQP2 are involves in longer term regulations of urinary concentration that modulate adaptational changes for acute response. Although the evidence for long-term regulation of AQP2 expression is now compelling, there is good evidence that expression of AQP3, the major basolateral water channel in the cortical and outer medullary collecting duct, is regulated by vasopressin Ecelbarger C A *et al*., 1995 [6].

Some pathological conditions are found when mice expressing an AQP2 gene with a mutation that causes nephrogenic diabetes insipidus (NDI) in humans have a severe urine concentrating defect. And animal was died by 6 days of age unless supplemental fluids are given (Yang *et al*., 2001) [25]. That's why it is very necessary to maintain the homeostasis of body any mutation in the gene of aquaporin 2 causes death of animals. Some ions may useful to treat nephrogenic diabetes insipidus (NDI) like lithium. The effect of chronic lithium therapy on the expression of the vasopressin-regulated water channel Aquaporin-2 (AQP2) in rat kidney was examined by Marples in year 1995 [6].

Aquaporin 3 (AQP3)

AQP3 relative expression in kidney is positively co-related with AQP2 expression in kidney. AQP3 expression was weaker in the cortical cells compared with the medullary cells this raises the possibility that the water transport activity by AQP3 may be higher in the distal CD than in the proximal CD. Basal AQP3 location on CD cells this indicates that they may play a role in water transport into and out of the cell (Maeda, 2008). It also helps in regulations of glycerol, urea as well as water. Because AQP3 is belongs to an aquaglyceroporins family and expressed at the basolateral membranes of principal cells in the collecting duct. A role in renal water reabsorption is expected AQP3 appears to be regulated at a biosynthetic level similar to AQP2 reported by Agre P., 2003 [1]. AQP3 is belongs to aquaglyceroporins family. Aquaglyceroporins seem to function primarily as a glycerol channel rather than a water channel. But the water transport through aquaglyceroporins is still important as revealed by polyuria in AQP3 null mice.

Some other recently reported aquaporins; plays major role in water balance in different organs

Elkjaer and his coworkers in 2001 found that in kidney, AQP8 is distributed in intracellular vesicles throughout cytoplasm in proximal tubule and collecting duct cells and also found that AQP8 is speculated to play a role in osmoequilibration between cytoplasmic and vesicular compartments, but functional studies regarding renal AQP8 expression have not been published.

Arrighi *et al*., 2016 [4] reported that, the epithelium lining of the buffalo excurrent ducts is implicated in diversified local processes of absorption and that, moreover, the manipulation of the luminal fluids likely undergoes seasonal- and aging-dependent changes. In particular, the reduced expression of AQP9 in the epithelium lining the corpus and cauda epididymis as well as the scrotal vas deferens during the non-mating period might lead to an altered reabsorption of luminal fluid, which, in turn, could be one of the factors responsible for the poorer semen quality compared to the mating period.

References

1. Agre P, Kozono D. Aquaporin water channels: molecular mechanisms for human diseases. FEBS Lett. 2003; 555:72-78.
2. Agre P, Bonhivers M, Borgnia MJ. The aquaporins, blueprints for cellular plumbing systems. J Biological Chem. 1998; 273:14659-14462.
3. Agre P, Preston GM, Smith BL, Jung JS, Raina S, Moon C *et al*. Aquaporin CHIP: the archetypal molecular water channel. Americal J of Physio. 1993a; 265:F463-76.
4. Arrighi S, Bosi G, Accogli G, Desantis S. Aquaporins in the male buffalo genital tract. Reprod Dom Anim, 2016. doi: 10.1111/rda.12713 ISSN 0936–6768
5. Denker BM, Smith BL, Kuhajda FP, Agre P. Identification, purification, and partial characterization of a novel Mr 28,000 integral membrane protein from erythrocytes and renal tubules. Journal Biological Chemistry. 1988; 263:15634-n, 42.
6. Ecelbarger CA, Terris J, Frindt G, Echevarria M, Marples D, Nielsen S *et al*., Aquaporin-3 water channel localization and regulation in rat kidney. American Physiological society Journal. 269 (Renal Fluid Electrolyte Physiology. 1995; 38:F663-F672.
7. Elkjaer ML, Nejsum LN, Gresz V, Kwon TW, Jensen UB, Frøkiær J *et al*. Immunolocalization of aquaporin-8 in rat kidney, gastrointestinal tract, testis, and airways. American Journal of Renal Physiology. 2001; 281:F1047-F1057.
8. Gowda S. Relative expression analysis of aquaporins AQP1, AQP2 and AQP3 in digestive and renal system of buffaloes during different seasons. M.V.Sc, Animal physiology, NDRI, Karnal, 2018.
9. Hara-Chikuma M, Verkman AS. Departments of Medicine and Physiology, Cardiovascular Research Institute, University of California, San Francisco, San Francisco, California. Journal American Society Nephrology. 2006; 17:39-45.
10. Hohmann S, Laize AV, Tacnet F, Ripoche P. Polymorphism of Saccharomyces cerevisiae aquaporins. Yeast. 2000; 16:897-903.
11. Ishibashi K, Sasaki S, Fushimi K, Uchida S, Kuwahara M, Saito H *et al*. Molecular cloning and expression of a member of the aquaporin family with permeability to glycerol and urea in addition to water expressed at the basolateral membrane of kidney collecting duct cells. Proc Natl Acad Sci USA. 1994; 91:6269-6273.
12. Jeremiah ZA, Buseri FI. Sero-epidemiology of transfusion-transmissible infectious diseases among blood donors in Osogbo, south-west Nigeria Blood Transfusion. 2009; 7(4):293-299.
13. Khanna A. Acquired nephrogenic diabetes insipidus. Seminars in Nephrology. 2006; 26(3):244-8.
14. Kim S, Gresz V, Rojek A, Wang W, Verkman AS, Frøkiær J *et al*. Decreased expression of AQP2 and AQP4 water channels and Na, K-ATPase in kidney collecting duct in AQP3 null mice. Biology of the Cell. 2005; 97(10):765-778.
15. Kishore BK, Krane CM, Di Iulio D, Menon AG, Cacini W. Expression of renal aquaporins 1, 2, and 3 in a rat model of cisplatin-induced polyuria. Kidney International. 2000; 58(2):701-711.
16. Laforenza U, Gastaldi G, Grazioli M, Cova E, Tritto S, Faelli A *et al*. Expression and immunolocalization of aquaporin-7 in rat gastrointestinal tract. Biol. Cell. 2005; 97:605-613.
17. Madsen SS, Bujak J, Tipsmark CK. Aquaporin expression in the Japanese medaka (*Oryzias latipes*) in freshwater and seawater: challenging the paradigm of

intestinal water transport? The Journal of Experimental Biology. 2014; 217:3108-3121. doi:10.1242/jeb.105098
18. Maeda Y, Smith BL, Agre P, Knepper MA. Quantification of aquaporin- CHIP water channel protein in micro dissected renal tubules by fluorescence-based ELISA. J Clin. Invest. 2008; 95:422-428.
19. Marples D, Christensen S, Christensen EI, Ottosen PD, Nielsen S. Lithium-induced downregulation of aquaporin-2 water channel expression in rat kidney medulla. Journal of Clinical Investigation. 1995; 95(4):1838-1845.
20. Michałeka K, Grabowskaba M. Investigating cellular location of aquaporins in the bovine kidney. A new view on renal physiology in cattle. Research in Veterinary Science. 2019; 125:162-169.
21. Morishita Y, Matsuzaki K, Hara-chikuma M, Andoo A, Shimono M, Matsuki A *et al*., Disruption of Aquaporin-11 Produces Polycystic Kidneys following Vacuolization of the Proximal Tubule. Molecular and Cellular Biology. 2005; 25(17):7770-7779.
22. Nielsen S, Chou CL, Marples D, Christensen EI, Kishore BK, Knepper MA. Vasopressin increases water permeability of kidney collecting duct by inducing translocation of aquaporin-CD water channels to plasma membrane. Proceedings of the National Academy of Sciences. 1995; 92(4):1013-1017.
23. Nielsen S, Frokiaer J, Marples D, Kwon TH, Agre P, Knepper MA. Aquaporins in the Kidney: From Molecules to Medicine. Physiolog. Rev. 2002; 82(1):205-244.
24. Tingaud-Sequeira A, Calusinska M, Finn RN, Chauvigné F, Lozano J, Cerda J. The zebrafish genome encodes the largest vertebrate repertoire of functional aquaporins with dual paralogy and substrate specificities similar to mammals. BMC Evol. Biol. 2010; 10:38. Doi: 10.1186/1471-2148-10-38.
25. Yang Judith M, Yu Ming-Jiun, Stoedkilde Lene, Miller Lance R, Hoffert Jason D, Jorgen Pisitkun Trairak *et al*. Aquaporin-2 Regulation in Health and Disease. Veterinary Clinical Pathology/American Society for Veterinary Clinical Pathology. 2001; 41(4):455-470.