

Perspective

Why Fish is a Natural Diabetic Animal?

Mohammad Ashraf Malik¹, Shubham Komarewar¹ and Showkat Ahmad Dar^{2*}

¹Central Institute of Fisheries Education, India

²Department of Aqualife Medicine, Chonnam National University, South Korea

Introduction

Glucose is one of the most physiologically important monosaccharides for the production of energy in most of the organisms. Glucose is considered as the central molecule in carbohydrate metabolism. It is the only monosaccharide which is utilized directly from blood hence it is most preferred monosaccharide in most of the organism. However, in contrast, fishes show very poor tolerance towards glucose utilization. Dietary glucose in fish results in prolonged hyperglycemic blood condition and it takes a long interval for its clearance (Thomas, 2001). This prolonged hyperglycemic condition triggers physiological stress in fishes and results in reduced growth and higher Feed Conversion Ratio (FCR). Several factors are responsible for prolonged hyperglycemia in fish which have to be considered while incorporating carbohydrate in fish diet. Although there is no specific dietary requirement of carbohydrates in fish. While it is widely used among aquaculturists for balancing the energy requirement and reducing the feed cost.

Glucose intolerance

Glucose intolerance is a term that refers to the inability of an organism to promptly react with glucose content. It is the inability of an animal to utilize glucose properly for the metabolic activities in the body which results in the accumulation of glucose in the blood and leads to the hyperglycemic condition. Glucose intolerance is reported in almost all teleosts. The glucose intolerance in fish is assessed by using the Glucose Tolerance Test (GTT). GTT involves administering a bolus of glucose either orally or intravenously, and if plasma glucose does not return to baseline within 1h to 2 h, the subject (human) is considered to have impaired glucose tolerance. The GTT has been used in many fish studies to test glucose tolerance and in most cases, hyperglycemia is persistent (Thomas, 2001) [1].

Insulin and glucagon responses in fish

The responses of insulin and glucagon have been analyzed in several fish species, principally *salmonids*. It is generally accepted that, in fish, insulin secretion in response to amino acids is stronger than to glucose (Navarro et al. [2]) although this information has been

obtained mainly from carnivorous species. Studies of other species demonstrate that the alimentary pattern affects hormonal secretion and should be taken into account when the effect of secretagogues is analyzed (Table 1).

Facts about fish prolonged hyperglycemia

The pre-prandial glucose level reported in fish blood is 25 mg/dl to 90 mg/dl while the post-prandial glucose level is 300 mg/100 ml. Clearance of the blood glucose is very slow in fishes, it takes up to 6 hrs to 7 hrs, while in human beings it takes only 30 min. However, exceptionally in some fishes it takes up to 24 hr for its clearance. Further Resting glucose turnover rates for fish species are in general 20 to 100 times lower than values reported in mammals of equivalent body mass, consistent with their lower body temperatures and metabolic rates. Such prolonged hyperglycemia results in adverse physiological conditions and induces stress on the animal. However, no such effect of stress was found in fishes compared to terrestrial animals [5,6].

What is the impact of hyperglycemia on fish physiological and growth?

Hyperglycemia in fish shows adverse effects on fish growth. It leads to reduced growth, high FCR, and low SGR. So, hyperglycemia is considered a stress indicator in fish. Prolonged high glucose level leads to the release of steroid hormone "cortisol". Stressed fish need more energy for stress mitigation and cortisol induces proteolysis and lipolysis for the production of energy. This results in over-utilization of proteins and lipids which finally leads to reduced growth [7,8].

Why glucose intolerance in fish?

Teleostei fishes show persistent hyperglycemia that is coincident with transient hyperinsulinemia. The fact that teleosts generally have high plasma insulin compared with mammals, implies insulin-deficiency is not a suitable explanation for persistent hyperglycemia. Insulin is the hormone that works in regulating the control over glucose level in *Teleostei*. It is seen that insulin level in starved fish is 1 ng/ml to 3 ng/ml and in well-fed fish; it is 5 ng/ml to 48 ng/ml. Thus, insulin secretion is not the limiting factor for the glucose intolerance, rather the long hyperglycemic condition which is maintained for a long time even up to 24 hrs may be due to the two main reasons:

- 1) Presence of insulin degradation enzymes.
- 2) Due to low-efficiency insulin-receptor binding or probably due to the presence of a low number of insulin receptors.

There are additional features that need to be reviewed with respect to glucose metabolism in fish including the effects of swimming, migration, maturation, reproduction, and environmental parameters such as temperature, salinity, PH and toxicants, all factors that

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***Corresponding author:** Showkat Ahmad Dar, Department of Aqualife Medicine, Chonnam National University, South Korea, E-mail: showkatdar53@gmail.com

Table 1: A partial list of teleost fish species where glucose tolerance tests have been performed.

Rainbow trout	O	B	ND	Hyperglycemia at least 7 hrs. Pre-spawning female mild hyperglycemia
Rainbow trout	IP	300	ND	Hyperglycemia at least 18 h
Blasco et al. [3] Brown trout	IV	500		Hyperglycemia corrected by 8h fastening Increased hyperglycemic response
Chinnok salmon	O	1670	(~2.5)	Hyperglycemia at least 36 h
Carp	O	167	(~3)	Hyperglycemia related to diet approx 5 h. longer for other species
Wright et al. [4]	IP	2000	ND	Hyperglycemia exceed for 6 h
Silver European eel	IV	500	ND	Hyperglycemia corrected by 9h
Channel catfish	O	1670	ND	Hyperglycemia corrected by 6h

are known to impact glucose metabolism fishes. As a whole, in the last 50 years fish researchers have tried to better understand how fish glucose metabolism works. Today, the interest in fish glucose metabolism is driven by forces that include the development of a sustainable aquaculture. New developing countries are emerging on the economical horizon that is demanding higher food quality at a time that commercial fish stocks are severely challenged. Studies of the possible role of gastrointestinal hormones in the secretion of pancreatic hormones, together with an understanding of the mechanisms of this secretion, would help us to understand the role of insulin and glucagon as metabolic regulators.

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