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# Insight on hormonal uses in fish farming and its impact on human health and the environment

Mohammad Elshahat Abd Al-Fatah

Biochemistry department, Veterinary Medicine Directorate, Kafrelshiekh, Egypt

Corresponding author: moh2009200@yahoo.com

**Abstract**

In the last decades, aquaculture is one of the most sectors of world food production and its production has been increased tremendously to overcome overpopulation. Therefore, several methods are used to rapid growth and increase production such as sex reversal, artificial production, and hybridization using 17α-methyltestosterone. From this point, this review is aimed in to use 17α-methyltestosterone in fish and its adverse effect on human health and the environment. It has been demonstrated that there are no hormonal residues in fish flesh after stopping treatment within a few days. However, it has an adverse effect on the environment after escaping these residues from fish hatcheries into nature water then accompanied after those dynamic consequences and the possible impacts of those on human health through endocrine system disrupting.

**Keywords**: fish culture, methyltestosterone, sex reversal, human health, environmental hazards.

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## 1. Introduction

Overpopulation with decreasing living demand among developing societies opens the tendency to go looking for a healthy food particularly fish. The shortage of animal protein sources is one of the reasons for raising fish production. Aquaculture has been growing robustly worldwide thanks to advances in the technical management in fish production to overcome increasing demand for fish with low cost and the least time. Therefore, the usage of growth promoters is one of the trials to obtain high production via improvement the daily body gain. However, these substances are illegal methods to an abnormal increase in fish production rates. These substances may include some chemicals and hormones like 17α-methyltestosterone and 17β-estradiol (Abu-Taleb, Osman, & Faisal, 2016). The 17α-methyltestosterone is a synthetic steroid hormone and male-specific mainly used in sex reversal in fish as well as improve muscle growth and male sexual character development. Thereby, the hazards of overuse of these hormones lie in the tissue residues for these substances and their metabolites that have a greater effect on human health causing liver tumors, carcinoma, and early embryonic death **(Ibrahim, 2009)**.

Hormones are substance signals responsible for communications between various sorts of cells that contain receptors are protein structures specialized in molecular recognition. Once hormone-receptor interaction happens a series of biochemical reactions resulting in specific biological responses **(Reis-Filho, de Araújo, & Vieira, 2006)**. These hormones are steroids produced from cholesterol that classified depending on their structure such as androgens, estrogens, progesterone, mineral corticoids, and glucocorticoids. Three of them are sex hormones, but androgens and estrogens are the main sex hormones utilized in fish development **(Guedes-Alonso,**

**Montesdeoca-Esponda, Sosa-Ferrera, & Santana-Rodríguez, 2014)**. In aquaculture, hormones are utilized in artificial reproduction and sex reversal. These mechanisms have allowed farmers the chance to propagate the species that do not naturally reproduce in captivity and control the timing of reproduction to suit production cycles **(Taranger et al., 2010)**. However, it should be taken into consideration many factors like the side effect of these hormones in farming fish and potential risks on human and environmental health, time and dosage of treatment due to improper time and /or the insufficient dose may ultimately to kill of fishes **(Mylonas, Fostier, & Zanuy, 2010)**.

Recently, the issue of food safety has been a terrible problem for different countries because of over usage of veterinary drugs and hormones in food-producing animal including aquaculture. In relevant to hormonal residues in fish, several studies have been applied to different species such as carp, silvery minnow, yellow croaker, and tilapia in different countries reported the presence of hormone residues in tissue samples of fish collected from fish farming or purchased from supermarkets **(Chen, Wang, Gwo, & Chen, 2012; Guedes-Alonso, Sosa-Ferrera, & Santana-Rodriguez, 2017; Liu et al., 2011; Wang et al., 2012)**. Thereby, ingestion of contaminated food with these residues may prompt endocrine issues and may ultimately to cancer **(Bergman, Heindel, Jobling, Kidd, & Zoeller, 2013)**. Some statistical reports in Puerto Rico reported that 3000 children had suffered from premature sexual development and ovarian cysts because of eating contaminated food with zeranol residues **(Duarte, da Silva, & Meirelles, 2002)**. In this manner, hormones use in food-producing animals meet distinctive legitimate guidelines in different countries. Most countries allowed using natural steroids such as testosterone, 17β-estradiol, and progesterone besides, the synthetic compounds such as zeranol and trenbolone

acetate but only residues of synthetic compounds have maximum residue levels because they are the most strong endocrine compounds **(Duarte, et al., 2002)**. Some substances are natural or synthetic used for therapeutic purposes. Hence, the Codex Alimentarius Commission (Codex) concludes that resides coming about utilization of these hormones in animal growth purposes according to good animal husbandry practice do not represent any hazards to human health. Consequently, the use of hormones for sexual purposes is not controlled by legal guideline of any country nor regional bodies' recommendations that manage sanitation. Consequently, the main objective of this article is to focus on the use of hormones in fish farming and the impact of hormonal residues on human health.

**Uses of hormones in fish cultivating**

**Sex reversal**

Sex reversal can be done during sex differentiation with hormonal treatment. This method began because of the overpopulation of stocked fish ponds and the stunted growth of fish in light of the crowdedness of fish in ponds. Commercially, mixed-sex fish got unwanted for producers because of changing fish sizes at harvest from little to enormous in view of the quick development of males than females. Subsequently, producers have been discovered difficulty in establishing the uniformity of fish. So the male fry is favored because of quick development and large size to get high yield within the rearing period. Production of mono-sex in fish can be accomplished by several techniques such as separation of male and female manually, hybridization, chromosomal manipulation, and hormonal treatment. The simple technique and more efficient is hormonal treatment (sex reversal) and it very well may be controlled by androgen and estrogen hormones **(Megbowon & Mojekwn, 2014)**. Practically, it is more productive through expanding weight gain and development

rate besides, accomplishing consistency and controlling the undesirable breeding **(Singh, 2013; Taranger, et al., 2010)**.

There are two methods for producing mono-sex fish populations. The first method is direct by treated with hormones to obtain the desired sex. Production of mono-sex males depends on the administration of 17α-methyltestosterone to sexually undifferentiated fry to develop into male with functioning reproductively. That has been widely employed and commonly used in tilapia **(Megbowon, Fashina-Bombata, Mojekwn, & Okuade, 2009)**. Production of mono-sex females has been induced by using different types of estrogens such as estrone, ethynylestradiol, stilbesterol, and 17β-estradiol. There is the convenience of using the17β-estradiol (natural estrogen) rather than the synthetic one. The second method is indirect by treatment of parents or breeders with hormones to neo male (XX) or neo female (XY and ZZ). Moreover, these protocols rely upon several factors including route of administration, duration, and time of treatment, dose, and type of used substance **(Piferrer, 2001)**. Notwithstanding the utilization of sex steroid hormones, there are other synthetic substances such as aromatase inhibitors that induce sex reversal techniques are accessible in fish. The aromatase inhibitors, for example, Fadrozole are normally applied in sex reversal in fish and mechanistically act through two ways:(i) irreversible deactivate the aromatase enzyme that changes androgens to estrogens or (ii) competitive exclusion of aromatase to estrogen producing cell receptors **(Budd, Banh, Domingos, & Jerry, 2015)**. It has been demonstrated effective in inducing the sex reversal in Nile Tilapia **(Kobayashi, Kajiura-Kobayashi, & Nagahama, 2003; Kwon, Haghpanah, Kogson-Hurtado, McAndrew, & Penman, 2000)** and olive flounder (*Paralichthys olivaceus*) **(Kitano, Takamune, Nagahama, & Abe, 2000)**. Furthermore, it has been found that administration of Fadrozole to fish

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results in producing viable sperm fit fertilization for two and a half months of treatment **(Bhandari, Higa, Nakamura, & Nakamura, 2004)**. Application of steroid hormones and aromatase inhibitors for sex control in fish can be done by many routes including systemic application (direct injection and silastic implantation), direct immersion, or dietary supplementation **(T. J. Pandian & Sheela, 1995)**. However, there are advantages and limitations for these methods of application on sex control in fish. Dietary supplementation and immersion are the most successful and commonly applied techniques at a commercial scale due to the simplicity of administration and application. The supplementation of hormones and chemicals to feed is a more powerful methodology on account of effectively control and allowing optimal dose to produce complete mono-sex populations **(B. Chatain, E. Saillant, & S. Peruzzi, 1999; Piferrer, 2001)**. However, there are some limitations for this method including degradation of the hormone during storage and variation in doses among individuals because of non-uniformity and concentration of hormone as well as the behavior of fish that affect the feeding rate and amount of hormone reaching fish in the feed. Likewise, there are other parameters, for example, water temperature and time exposure. While the systemic application is costly and requires the specialized capacity to be applied **(T. J. Pandian & Sheela, 1995; Piferrer, 2001)**. Regardless of the fruitful use of hormonal treatment in aquaculture, some challenges should be taken into consideration to forestall any adverse effects in produced fish, the environment, and purchasers. For instance, incorrect doses of hormones may induce deformities and becomes a stressful process leading to a decrease in survival rates and delay of sexual maturity. Furthermore, on large scale, it is considered a technique pollutes the environment with hormone due to presence of the high amount of hormone are metabolized and excreted in water within few

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days **(Beardmore, Mair, & Lewis, 2001; B. Chatain, E. Saillant, & S. Peruzzi, 1999)**. In Europe, hormonal uses are prohibited in commercial food fish, but some legislation related to consumer and environmental issues are investigated and indicated the presence of new chemicals are safer in sex reversal induction such as trenbolone acetate, 17α-methyldihydrotestosreone **(T.J. Pandian & Kirankumar, 2003)**.

Regardless of sex determination and differentiation mechanism in fish, there is no single technique that has demonstrated powerful in the control of sex in fish. Consequently, there are several methods of hormonal treatment, hybridization, chromosomal manipulation.

**Artificial reproduction**

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Artificial reproduction can occur through two strategies. The first strategy is to provide environmental parameters for natural reproduction through changes in temperature or photoperiod in the hatchery. The second strategy is to inject exogenous hormones to initiate or defer fish maturation or used in synchronization of spawning process to obtain fingerlings in the period, the profitability is higher **(Mylonas, et al., 2010)**. Therefore, the more period of multiplication progressed the greater the fish farmers' adaptability in the marketing of the larvae and young fish. Besides, the limitation of the spawning process for a certain period, this can permit for the higher throughput and turnover of nursery ponds.

Two methods have been emerged to induce reproduction where numerous hormones have been used. From these previous experiments, they found that injection of a GnRH analog with dopamine antagonist or gonadotropin offers the best results for success with fewer expenses as well as more stability and has a long

shelf life. Thus, these protocols are used for artificial reproduction in more than 30 species **(Almeida, 2013; Araújo et al., 2014; Zohar & Mylonas, 2001)**.

**An influence of hormones on human health**

Shortage of animal protein sources was one of the challenges to use the growth promoters for raising meat production with low cost and minimum time. Growth promoters are chemical or hormonal substances that are added to feed components to improve the daily body gain. These substances may be applied by illegal methods. These substances include synthetic steroids as 17α- methyltestosterone is a synthetically produced anabolic and androgenic steroid hormone is used to increase the muscle development and improvement of male sexual characters. Therefore, the potential hazards are arising from using anabolic steroids, the presence of substance residues, and their metabolites in tissues. These residues have a dangerous effect on a human because they can cause liver tumors, carcinoma, and increase embryo mortality **(Ibrahim, 2009)**.

The possibility of risks associated with using the steroid hormones in fish consumers. **(Piferrer, 2001)** reported that residues of 17α- methyltestosterone is quickly metabolized and excreted after the withdrawal of a hormonally treated diet. Several previous studies have emphasized that administrated 17α- methyl testosterone doesn't find in fish meat. Some of them estimated the hormonal level in fish tissue fall to a normal level within a week after stopping administration **(Guerrero, 2008; Mlalila, Mahika, Kalombo, Swai, & Hilonga, 2015; Straus et al., 2013)**. Based on the scientific results of the previous literature about methyl testosterone, there is no possibility of persistence in adult fish as a marketable size.

Thereby there are absolutely no risks to consumers when MT treated fry for short time with recommended dosages. On contrary, there are potential hazards to fish consumers if MT-treated feed is applied at high levels than recommended dosages or for long periods. Additionally, researchers reported that MT might cause hepatotoxicity and fetotoxicity **(Vick & Hayton, 2001)** and increase human reproductive problems **(Moreno-Perez & Esteva De Antonio, 2012; T.J. Pandian & Kirankumar, 2003)**. These anecdotes have been unclear in many cases because the appearance of human health risks depends largely on dosing history and pharmacokinetics characteristics of many steroids **(Homklin, Ong, & Limpiyakorn, 2011; Vick & Hayton, 2001)**.

Continuously introduction of steroids into the environment at low concentrations by human excretion has a negative effect on human health which cause disrupting the normal endocrine systems **(Reis-Filho, et al., 2006)**. The contamination also has been originated by wastewater discharge from fish hatcheries that are no properly depurated. In this manner it has been accounted for that MT accumulates in sediments of ponds and stay recognizable in the soil for almost three months after stopping treatment **(Megbowon & Fashina-Bombatta, 2010)**. Approximately 99% of hormonally treated feed during the sex reversal is metabolized and released into the water by bile and urine excretion within a few days after treatment. These hormones are excreted mainly as inactive forms and don't have a direct biological activity where are conjugated with sulfuric and glucuronic acids. These conjugates act as a precursor which can be reconverted to free steroids with estrogenic activities by bacteria in the environment, such as the microorganisms in raw sewage and sewage treatment plants **(Yin, Kookana, & Ru, 2002).**

**Effect of steroid hormones genetically on human health**

Steroid hormones play important role in the regulation of physiological processes in humans and are under genetic control. In the case of the hormonal system, the disturbance may be accompanied by genetic related problems and complications on human health. Some studies reported that steroid metabolism participates in coronary artery disease **(Kaushik, Sontineni, & Hunter, 2010; Villablanca, Jayachandran, & Banka, 2010)**. **(Pott et al., 2019)** detected that there are genetic association links between steroid metabolism and coronary artery disease development. Furthermore, abnormal blood hormone levels have been accounted for to be related with methyltestosterone. Exogenous testosterone suppresses the production of both luteinizing hormone and follicle-stimulating hormone via a negative feedback mechanism and prompts decreased testicular sperm production followed by diminished testicular volume. Additionally, androgens play a permissive role in the development of prostate cancer and benign prostate hyperplasia **(Rolf & Nieschlag, 1998)**. On the other hand, it is recommended with long term treatment with testosterone for HIV-related weight loss and sarcopenia **(Seal, 2009)**.

**Conclusion**

The use of hormones in the production of male fish is very effective. It becomes relatively easily predictable that fish sex reversal has been a significant role in fast development and increasing production with low cost and effort. Although varieties of hormones have been utilized in sex reversal, the 17α-methyltestosterone is the most common and used with different treatments according to environmental factors. It has been illustrated that used hormones in sex reversal of fish fry don't have any side effect on fish meat after the withdrawal of hormonally treated feed and on human health. It should be taken into consideration that the hormones

escapes from hatchery bonds into wastewater drainage and may alter the dynamics environment. Therefore, continuous bioaccumulation of hormones in the environment has an adverse effect on human health through disturbances in the endocrine system and on genetic control occasionally.

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