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Steroid Hormones in Reproduction and Roles of GnRH-a in Gonadal Maturation of Marine Fish: A Review

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Authors' contributions

This work was carried out in collaboration among all authors. All authors contributed to write the first draft of the review. Authors HMS, PXK and PMT revised the written manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Reproduction in teleosts is regulated by a series of hormones including gonadotropin-releasing hormones (GnRHs), gonadotropins (GTHs) and steroid hormones. To contribute better understanding of steroid hormones in reproduction and GnRH-a in gonadal maturation, this literature review is concerned with the changes of steroid hormone levels in relation with sex inversion, reproductive behavior and gonadal development as well as the application of GnRH-a for inducing maturation of marine fish. The results revealed that in many species of teleost, steroid hormones E_2, 11-11-KT and DHP are abundantly produced in gonadal tissues under the control of pituitary gonadotropins, and are essential for critical steps of gametogenesis. Plasma steroid levels have been used as indicators for both of the sex of the fish and its stage in the seasonal reproductive cycle, particularly with regard to induction of spawning. Determination of plasma steroid levels in relation with the sexual status of the gonads over several reproductive seasons might provide valuable information on the mechanisms of sex inversion in ambisexual fish species. In addition, changes of plasma steroid levels in correlation with gonadal development, number of

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spawning, fecundity, were described clearly in many marine species. The review also indicated that exogenous administration of GnRH-a triggered for final maturation of brood stock of some teleosts. In summary E_2, T, 11-KT and C21 steroids are in relation with sex inversion, reproductive processes and GnRH-a is successful for inducing gonadal maturation in some fish species.

Keywords: Steroid hormones; marine fish; GnRH-a; reproduction.

1. INTRODUCTION

In most female teleosts, a reproductive cycle includes the processes involving in ovarian development, ovulation, and spawning activity. During these processes, in addition to external factors, such as photoperiod and temperature, hormonal co-ordination is required to control the reproduction. Nowadays, it has been known that hormones, including gonadotropin- releasing hormone (GnRH), gonadotropin (GTH), and steroid hormones regulate reproduction in fish through the brain-pituitary-gonad axis. It is generally accepted that GnRH in the brain of teleosts is involved in the reproduction via stimulating GTH secretion in the pituitary through GnRH receptors. GTH is associated with gonadal maturation through the activation of steroid hormone synthesis in the gonad [1,2].

GnRH was first isolated from mammals [3], and later from other tetrapods [4] and teleosts [5]. To date, eight GnRH forms have been identified in teleosts and two or three GnRHs are coexisted in the same species. Recently, a large body of work has shown that two common forms are chicken GnRH-II (cGnRH-II) and salmon GnRH (sGnRH), and a third form is among seabream GnRH (sbGnRH), herring GnRH (hrGnRH), medaka GnRH (mdGnRH) (also called pejerrey GnRH (pjGnRH), and whitefish GnRH (wfGnRH) in fishes possessing three GnRH forms [6]. The GnRH forms were named following the species in which they were first isolated, except for the mammalian GnRH (mGnRH) [2,5,7,8,9,10]. It is generally accepted that GnRH in the brain of teleosts is involved in the reproduction via stimulating GTH secretion in the pituitary through GnRH receptors [6]. Two types of GTH, GTH-I (also called follicle-stimulating hormone, FSH) and GTH-II (luteinizing hormone, LH) had been confirmed in a variety of species. Similar to other vertebrates, GTH in teleosts is a heterodimeric glycoprotein containing a common α-subunit and a hormone specific β-subunit. GTH is associated with gonadal maturation through the activation of steroid hormone synthesis in the gonad in many teleosts [1,11,12,13,14,15,16,17]. Steroid hormones including 17β-estradiol (E_2), Testosterone (T), 11-ketotestosterone (11-KT) and 17α20β- dihydroxy-4-pregnen-3-one (DHP) play an important role in the regulation of the reproductive process in teleosts, such as oocyte growth, maturation, and ovulation in female or spermatogenesis and spermiation in male fish [18]. Some steroid hormones are involved in sexual and spawning behavior of fish. Both E_2 and T are produced in the ovary of female teleosts. The ovarian two-cell model synthesizes E_2 and T, where the theca cells synthesize T, which is subsequently aromatized by cytochrome P450 aromatase (CYP19) to E_2 by the granulosa cells [19]. E_2 is responsible for vitellogenesis in female fish through the activation of vitellogenin (Vtg) and eggshell Zr-protein formation in liver. From the liver, Vtg is secreted into blood, transported to the ovary and absorbed into maturing oocytes. In addition to a precursor for E_2 synthesis, T can enhance stimulatory effects of GTH *in vitro* [20] and may also be involved in oocyte development through the initiation of GVBD during final oocyte maturation [21]. In males, spermatogenesis is regulated by 11-KT. C-21 steroids or closely related C-21 steroids, such as DHP and 17α, 20β, 21-trihydroxy-4-pregnen-3-one (20β-S), regulate the final maturation of the oocytes and ovulation or spermiation [18]. Among them, DHP is a common maturation-inducing hormone (MIH) in the majority of teleosts investigated [1,22,23]. On the other hand, some fish, such as the bambooleaf wrasse *Pseudolabrus japonicus* [24] and kyusen wrasse *Halichoeres poecilopterus* [22] can have more than one MIH. In this paper, we review the understanding of steroid hormones in reproduction and GnRH-a in inducing gonadal maturation of marine fish.

2. VARIATION OF STEROID HORMONES DURING REPRODUCTIVE CYCLE OF THE MARINE FISH AND THEIR ROLES

Steroid hormones play important roles in many physiological processes, particularly in the reproduction of vertebrates. In many species of teleost, steroid hormones E_2, 11-KT and DHP

are abundantly produced in gonadal tissues under the control of pituitary gonadotropins, and are essential for critical steps of gametogenesis (Table 1).

2.1 In Sex Inversion

Plasma steroid concentrations have been used as an indicator for both of the sex of the fish and its stage in the seasonal reproductive cycle, particularly with regard to induction of spawning. Determination of plasma steroid levels in relation with the sexual status of the gonads over several reproductive seasons might provide valuable information on the mechanisms of sex inversion in ambisexual species such as the sobaity *Sparidentex hasta* [25], red-spotted grouper *Epinephelus akaara* [26], seabass *Lates calcarifer* [27], anemone fish *Amphiprion melanopus* [28]. The study of [25] indicated that the seasonal pattern of plasma steroids correlated well with the changes of sexual status of the gonads during regression and recrudescence and that E_2 may be involved in the sex inversion of sobaity *Sparidentex hasta*. During the spawning season of this species, levels of the 11-oxygenated androgens in the males and E_2 in the females were highest, while maximum levels of T were found in the summer. Two peaks of testosterone glucuronide level were observed: one in the post-spawning period as E_2 and the 11-oxygenated androgens were falling and the other coincident with the peak of testosterone. 17,20β-P was detectable in only one male and one female fish in February. Plasma concentrations of 11-oxygenated androgens are more reliable than those of E_2 for determining the sex of sobaity, and may also be used as indicators of the occurrence of sex reversal. In the seabass *Lates calcarifer*, very low plasma levels of 11-KTwere found in premature females, E_2 and estrone in males remained stable during the reproductive cycle. Conversely, plasma level of T, estrone, and E_2 in females peaked during vitellogenesis and T and 11-KT peaked during spermiation in males. When sex type is compared over the whole cycle, levels of E_2 and estrone in females were higher than in males, while 11-KT and T levels in males were higher than in females. Transitional fish always exhibit low plasma levels for these four steroids (T 56.5 ± 12.5 pg/ml, 11-KT 59.0 ± 23.5 pg/ml, E_2 65.6 ± 36.0 pg/ml, and estrone 61.0 ± 47.5 pg/ml). Among gonadal androgens, 11β-hydroxyandrostenedione predominated in testes (3.95 ± 3.00 ng/g), except during spermiation (0.8 ± 0.5 ng/g), and remained low in ovaries (1.05 ± 1.4 ng/g). No differences were detected in gonads, for T and 11-KT whatever the sex type, but their concentrations were higher in vitellogenic and atretic ovaries. Androstenedione levels were slightly higher in testes (2.21 ± 2.00 ng/g) than in ovaries (1.53 ± 1.32 ng/g). Transitional gonads always showed low concentrations for these four androgens (T 0.66 ± 1.77 ng/g, 11-KT 0.14 ± 0.05 ng/g, androstenedione 0.30 ± 0.34 ng/g, and 11β-hydroxyandrostenedione 0.20 ± 0.23 ng/g). Gonadal E_2 was nearly undetectable in testes (0.06 ± 0.07 ng/g), low in ovaries (0.42 ± 0.46 ng/g), and strikingly high in transitional gonads (2.89 ± 1.64 ng/g) even at the very beginning of sex inversion. This estrogen plays an important role in the protandrous sex inversion process [27]. In the females of red-spotted grouper *Epinephelus akaara*, plasma E_2 and T levels reached peaks during vitellogenesis, and in males and natural sex-reversing fish, 11-KT, T and E_2levels were highest during spermatogenesis. High plasma levels of 11-KT were also observed in natural sex-reversing fish. In addition, in females, plasma 11-KT levels were very low and did not significantly fluctuate during the annual reproductive cycle. In breeding season, females displayed higher E_2 levels than males and sex-reversing fish, while males and sex-reversing fish showed higher 11-KT levels and, to a lesser extent, higher T levels than females. Furthermore, the changing pattern of sex steroids in males was similar to that in natural sex-reversing fish, and a second peak of plasma androgens 11-KT and T appeared in December both in male and natural sex-reversing fish; significantly higher plasma 11-KT levels were observed in natural sex-reversing fish than that in females from December to April. Changes of plasma sex steroids levels in red-spotted grouper were closely associated with sex inversion [26]. In addition, in a field population of the protandrous, sex-changing anemone fish *Amphiprion melanopus,* sex change was experimentally induced in males by removal of their dominant female pair mates. These sex-changing males were captured and sampled at 5, 10, or 20 days after female removal. Unmanipulated males and females were also sampled. In males, plasma levels of II-ketotestosterone (II-KT) were higher than, but levels of androstenedione (Ad), T, and E_2 were lower in females. Levels of Ad, T and E_2 in mature females continued to increase after 20-day after female removal. E_2 levels did not change from male levels until 20 days, when a significant increase over male levels was

observed. The results suggest roles for androgens in male function and E_2 in female function in *A. melanopus*. However, E_2 increases lagged behind oogonial proliferation, arguing against an influence of this steroid in the initiation of female function [28]. In the protandrous hermaphrodite *Sparus aurata L.* displaying two reproductive cycles (RCs), during the first RC (RC1), level of 11-KT and T peaked at different stages of RC1 and they play specific roles in the testicular physiology. T is not essential in the testicular regression process in second RC (RC2) but E_2 is related to the initiation of ovarian development [29].

2.2 In Reproductive Behavior

Gonadal steroid hormones can have profound influences on the central nervous system and behavior of vertebrates either through organizational effects during early development or through activational effects in adults. A number of studies revealed the seasonal cycle of plasma levels of the gonadal steroids in relation to reproductive behavior in marine fish [30,31]. 11-KT plays the role in the induction of secondary sex characteristics that are involved in behaviors by courting male midshipman fish *Porichthys notatus* [31]. The plainfin midshipman is a deep-water teleost that seasonally migrates into the shallow intertidal zone where type I, or "singing," males build nests, acoustically court and spawn with females. The gonadosomatic index (GSI) and plasma steroid levels were measured from adult type I males and females collected over four time periods (non-reproductive, pre-nesting, nesting, and post-nesting) that corresponded to seasonal fluctuations in midshipman reproductive biology and behavior. Among type I males, plasma levels of T and 11-KT were low during the winter non-reproductive period, gradually increased during seasonal recrudescence of the testes in the spring pre-nesting period, and then peaked at the beginning of the summer nesting period. In the latter half of the nesting period and during the fall post-nesting period, plasma levels of T and 11-KT were low or non-detectable. Low, detectable levels of E_2 were also found in the plasma of 50% or more type I males during every seasonal period except the winter non-reproductive period. Among females, plasma levels of T and E_2 were low throughout the year but briefly peaked in April during the spring pre-nesting period when ovaries underwent seasonal recrudescence. The sex-specific peaks of steroid hormone levels in male and female midshipman may serve differential functions related to the physiology, reproductive behavior, and vocal communication of this species. Like in the plainfin midshipman, Modesto & Canario [30] propose a role for 11-KT in the development of structures important for reproductive behavior of the Lusitanian toadfish *Halobatrachus didactylus.* This species has group synchronous oocytes, which grow from November until June-July when they are released probably as a single batch. Plasma levels of E_2 and T in females increased during vitellogenesis and dropped rapidly during final maturation and ovulation, when 17,20β, 21-trihydroxy-4-pregnen-3-one (17,20β, 21-P) levels increased. The male reproductive apparatus is composed of paired testes and multichambered accessory glands, which secrete mucosubstances and are connected to the spermatic duct. Changes in the GSI of males paralleled the females but started to drop slightly earlier. The swimbladder and accessory glands also underwent important seasonal changes in weight reaching a maximum at spawning. T, 11-KT and 17,20α-dihydroxy-4-pregnen-3-one (17,20α-P) were generally low except for a sharp peak in June. 17,20β,21-P also peaked in June and then declined slowly. 17,20α-P was undetectable in males and females. As with other species of the family two types of males were identified: type I males with smaller testes (ca. 7-fold) and larger accessory glands (ca. 3-fold) and swimbladders than type II. Type I males also had significantly higher (ca. 6-fold) 11-KT levels than type II males [30].

2.3 In Gonadal Development

Plasma steroid concentrations change and correlations exist among these changing levels with gonadal development, number of spawning, fecundity, was described clearly in many marine species such as sea bass *Dicentrarchus labrax,* winter flounder *Pleuronectes americanus,* black bream *Acanthopagrus butcheri,* Atlantic cod *Gadus morhua,* gilthead seabream *Sparus aurata.* A study showed that levels of 17α,20β-DiOH-P were low throughout the year. Plasma T and E_2 levels significantly increased in advanced gametogenesis period and then showed further increases in first half of the spawning period in parallel with the growth of the vitellogenic oocytesin the female seabass-*Dicentrarchuslabrax* [36]. Multiple spawning of individual females was also observed during the spawning period affecting the relative fecundity of the eggs. A possible role of E_2 on this behavior is discussed. In males, both plasma T and 11-KT

Table 1. Levels of testosterone, 11-ketotestosterone and estradiol in some fish species

Steroid level / Species	T (ng/ml)		11-KT (ng/ml)		E2 (ng/ml)		References
	Min	**Max**	**Min**	**Max**	**Min**	**Max**	
Pink salmon *Oncorhynchus gorbuscha*	88 (F)	300 (F)			1 (F)	10 (F)	[32]
Striped bass *Morone saxatilis*	<0.1 (F)	3.0 ±0.3 (F)			<0.1 (F)	2.0±0.5 (F)	[33]
Tilapia *Oreochromis mossambicus*	1.22±0.26 (F)	12.3±2.27 (F)			0.26±0.04 (F)	0.68±0.04 (F)	[34]
Sea bass *Lates calcarifer*		0.18±0.12 (F) 0.19 ±0.09 (M) 0.06 ±0.0 1 (TF)	<0.075 (M)	0.22±0.09 (M) 0.06 ±0.02 (TF)		0.60±0.37 (F) 0.07 ±0.04 (TF)	[27]
Winter flounder *Pleuronectes americanus*	Low (F) 0.8 (M)	>30(F) >25	ND (M)	300 (M)	15 (F)	>40	[35]
Red-spotted grouper *Epinephelus akaara*	0.92±0.35 (F) 1.64±0.19 (M) 1.63±0.39 (TF)		0.32± 0.03 (F) 6.23±0.99 (M) 5.92±1.21 (TF)			0.05±0.01 (F) 0.03±0.01 (M) 0.02 ±0.005 (TF)	[26]
Lusitanian toadfish *Halobatrachus didactylus*	<1(F)	1 (F) 1.88 ±0.2 (M)		3.06 ±0.5 (M)		4 ±0.52(F)	[30]

Note: min (lowest level in fish at immature gonad), max (highest level in fish at maturing gonad), F: Female, M: Male, TF: Transitional fish

initially increased in November and then showed further increasing during the rest of the period of gametogenesis to reach their peaks in the first half of the spawning period. These increased and sustained higher levels of plasma steroids coincided with the presence of spermiating males. A second peak of plasma T appeared at the end of the postspawning period-beginning of the pregametogenesis period both in males and females and their possible role with the preparation of the gonad for the next reproductive cycle is discussed. In another study, the pattern of seasonal gonadal development and variations in plasma sex steroids were investigated in adult male and female winter flounder *Pleuronectes americanus* [35]. The winter flounder reproductive cycle can be divided into five consecutive phases of relative reproductive activity including: (1) rapid gonadal recrudescence in the fall; (2) continued slow gonadal growth in females, or maintenance of the well- developed gonads in males, during the winter; (3) a prespawning phase of gonadal maintenance in the spring; (4) spawning early in the summer after the female gonads reach peak weight; and (5) the summer postspawning period when the gonads remain regressed. Female gonadal recrudescence in August is characterized by small increases in plasma estrogen levels and recruitment of small oocytes (≥150 μm) into yolk accumulation. Small increases in plasma estrogen levels were observed in gonadal recrudescence in the females. This hormone and T increased to peak just prior to spawning together with GSI and oocyte diameter. Levels of these steroids fall to very low values in post-spawned fish. In males, plasma levels of the androgenic steroid increases during spermiating and fell to lowest value after spawning. A study provided as complete an understanding as possible on changes in GSI, hepatosomatic index (HSI), gonadal stage and plasma concentrations of sex steroids were studied over one year in black bream *Acanthopagrus butcheri*. Black bream has an annual reproductive cycle with a 3-month spawning season in spring-early summer. GSI and HSI values were highest in October and May, respectively. Plasma levels of E2, T and 17,20βP were highest in ovulated females alongside GSI value. Higher levels of 17,20βP were observed in fish where final oocyte maturation (FOM) was undergoing than in fish with regressed gonads. In males, plasma levels of T and 11-KT increased spermiating fish, but levels of 17,20βP did not change with season. However, 17,20βP levels in spermiated fish were higher than in non-spermiated males. Daily changes in gonad condition indicated that females undergo daily cycles of ovarian maturation with ovulation occurring after midday. Plasma T and 17,20βP concentrations of females were elevated at midday in association with FOM, but E_2 showed no dial change. In males, partially spermiated fish were dominant in the early morning and fully spermiated fish at midday. Plasma T, 11-KT and 17,20βP concentrations were low at midnight and reached maximum levels at 06:00 hours [37]. In Atlantic cod *Gadus morhua,* the reproductive cycles of both female and male are characterized by distinct annual variations in gonadal size and developmental stage and these are associated with changes in sex steroids and liver size [38]. Plasma E_2 levels were highest and correlated to GSI in spawning females and lowest in spent females. Plasma T levels maintained at low values throughout ovarian development and lowest in spent females. Plasma level of 11-KT in males increased rapidly, while T increased at earlier testicular stages and reached peak during spermiation. High plasma levels of steroids in male and female during spawning serve to promote further development and growth of less advanced stages of germ cells.

During the migration of wild female pink salmon *Oncorhynchus gorbuscha,* E_2 level decreased dramatically at spawning, whereas the 17α,20β-P level increased rapidly, reaching highest level at arrival on the spawning grounds. Both T and 11-KT levels decreased steadily during migration but were still relatively high at spawning, whereas 17α, 20β-P levels increased rapidly as migration progress [32]. Berlinsky & Specker [33] demonstrated that levels of plasma steroids in the striped bass, *Morones axatilis* were low in primary and pre-vitellogenic females. Plasma levels of E_2 and T increased significantly together with GSI in vitellogenic fish. DHP levels were significantly elevated in females induced to spawn with human chorionic gonadotropin (HCG), suggesting that DHP may serve as the maturation-inducing steroid in this species [33]. The female Bonnet head shark *Sphyrna tiburo* showed high levels of plasma E_2 and T during mating and preovulatory stages. Progesterone levels are significantly elevated during preovulatory, ovulatory, and postovulatory stages, while dihydrotestosterone levels increase significantly during the preovulatory stage. This study suggests a regulatory role for this hormone during the period prior to implantation of the

embryos in the uterus [39]. In the cichlid fish *Oreochromis niloticus*, plasma levels of E_2 and T changed with ovarian stages with the peaks in the vitellogenic fish, and plasma levels of 17,20β-P were noticeable in pre-spawning fish [40]. In the Gudgeon *Gobio gobio*, plasma levels of E_2, T, and 17,20β-dihydroxy-4-pregnen-3-one were low in prematured fish and increased during spawning with presence of vitellogenic and final maturation oocytes [41]. In rainbow trout *Salmo gairdneri*, plasma E_2 levels in the females reached a peak in maturing ovarian fish, and declined to lower levels just prior to spawning. A peak of 17α-hydroxy-20β-dihydroprogesterone level was found several days prior to ovulation and decreased gradually over a month. E_2 fell prior to ovulation to basal levels prior to ovulation, and remained low. T levels decreased slowly from a peak prior to ovulation to basal levels at postovulation. However, the level of 17α-hydroxyprogesterone rose more slowly and stayed at a fairly constant level for 16-20 days [42]. In the white sucker *Catostomus commersoni*, 17-P, and 17,20-P levels were low in fish before spawning of both sexes, reached the peaks in ovulated females and spawning males, and then dropped to low levels in spent fish [43]. In females, E_2, T, levels were high in prespawning fish and declined significantly at ovulation and dropped to low values in spent fish. In female yellow tail kingfish *Seriolalalandi lalandi*, plasma levels of T and E_2 peaked during vitellogenesis, and plasma levels of 17,20βP were significantly elevated in fish with ovaries undergoing final oocyte maturation. Plasma levels of 17,20βP did not change with gonadal development in males but plasma levels of 11-KT and T were significantly elevated in spermiated males [44].

3. THE USE OF REPRODUCTIVE HORMONE INDUCING THE MATURATION OF BROODSTOCK OF FISHES

Exogenous hormones such as pituitary homogenate, HCG and semi-purified fish gonadotropins and synthetic GnRH- analogue (GnRH-a) have been used to induce maturation in many commercial fish. These preparations are often administered in two doses and interval between the first and second injections may vary depending on the species. Variable doses are used even for the same species and may be due to variable potencies of the gonadotropin preparations [45].

GnRH analogue has different types such as luteinizing hormone-releasing hormone analogues Gly10 (D-Ala6) LHRH- Ethylamide (LHRH-a), follicle-stimulating hormone–releasing hormone (*FSH*-RH) which are little bit different in active mechanism. GnRH in LHRH-a type has been successfully used to induce final maturation and synchronize ovulation in many commercially cultured teleosts [46,47,48]. They cause maturation and ovulation by inducing GTH secretion and then steroids in fish, for example the grouper [49], yellowtail flounder *Pleuronectes ferrugineus* [50], and starry flounder *Platichthys stellatus* [51]. Treatment of fish with exogenous hormones by injection typically results in the short-term induction of ovulation and changes in plasma T, E_2, DHP levels in several fish such as wild black bream *Acanthopagrus butcheri* [37], Waigieusea perch *Psammoperca waigiensis* [52] and *Kutumrutilus frisiikutum* [53].

A single LHRH-a injection or pellet implant appears to be effective or marine species such as milkfish, mullet, sea bass, and rabbitfish. Standardized methods using LHRH-a in combination with the dopamine antagonists pimozide, domperidone and reserpine have been developed for various species of carps and for marine teleosts that may not respond to LHRH-a alone or where a high dose of the peptide is required [54]. The LHRH-a acts by stimulating the release of gonadotropin from the pituitary, and the pimozide by suppressing the action of a natural hypothalamic gonadotropin release-inhibiting factor (GRIF) which has been identified as dopamine (DA) [55,56]. In many teleost species, maturation and ovulation have been induced by combined injections of luteinizing hormone-releasing hormone analogue (LHRH-a; Des-Gly" [D-Ala'] LHRH ethylamide) and pimozide (PIM) [57,58]. For example, LHRH-a acute release implantation induced oocyte maturation in *Dicentrarchus labrax* [59], final maturation and lead to high fertilization in Persian sturgeon *Acipenser persicus* [60].

For milkfish *Chanos chanos*, implantation of T or T in combination with luteinizing hormone-releasing hormone analogue (LHRH-A) enhanced vitellogenesis and maintained the integrity of vitellogenic oocytes and caused some fish spawn [61]. For Nassau grouper *Epinephelus striatus*, females with average oocyte diameters ranging from 517-544 were spawned three times and one female two times by hormone induction. A primary injection of HCG (1,000 IU/kg body weight) was followed by

a second injection (500 IU/kg body weight) after 24h [62]. HCG, LHRH-a, and carp pituitary homogenate (CPH), used alone or in various combinations, were tested as spawning agents in captive brood stock using a two-injection sequence in which a priming dose (PD) was followed 24h later by a resolving dose (RD). As an alternative to hormone injection, intramuscular implantation of a cholesterol pellet containing LHRH-a (200-250 µg) increased oocyte diameter and make successful spawning in the females. Use of different hormones in combination showed no advantage over a single-hormone strategy. As HCG appeared to cause an immune response, LHRH-a is recommended for repeated application [63]. For grouper, *Epinephelus merra*, combination of artificial photothermal conditions with GnRH-a implantation seems to be effective to induce sexual maturation in immature fish. The results demonstrate a superior strategy for successful breeding of sexually immature marine teleost fish during non-breeding season by modulating environmental variables with GnRHa implantation [64]. For Shirbut fish LHRHA2+CPE combination can be recommended for ovulation of *Barbus grypus* in comparison CPE or alone other hormones [65]. For the mangrove red snapper, *Lutjanus argentimaculatus* (Forsskal 1775), using standardized indices of female maturity (based on mean oocyte diameter of ≥0.40 mm), time of injection (1000–1130) and sex ratio (one female to two males), a single injection of 100µg kg^{-1}LHRHa, successfully induced egg (62.5% success rate) and larval (43.8%) production. HCG at 1000 kg^{-1} and 1500 IU kg^{-1} induce spawning (77.3% and 80.0% respectively) and hatching success rates (72.7% and 60.0%, respectively) that were not significantly different from those of 100µg kg^{-1} LHRHa [66]. For the seabass *Lates calcarifer*, some captive females brood stock implanted with cholesterol-based pellets of the LHRH-a D-Trp6-desGly10-LHRH ethylamide or D-hArg(Et2)6,Pro9-NHet-LHRH at doses between 9.0 and 23.5 µg/kg body weight spawned. None of the sham-operated control fish spawned in any of the experiments. Other study used two GnRHa, [D-Ala6, Pro9-ethylamide] mammalian GnRH and [D-Arg6, Pro9-ethylamide] salmon GnRH, to induce spawning in sea bass. Injection of GnRHaor implantation of GnRHa in pellets with a cholesterol-cellulose matrix induced spawning. The results showed that pellets, pumps and repeated injections produced multiple spawnings, but the pellets were more reliable, cheaper, and less stressful to the fish [49]. Captive *Siganus guttatus* brood stock implanted with silastic-based pellets of the LHRH-a D-Nal (2)6 LHRH spawned 1-2 days earlier than sham-operated controls [67]. For southern flounder, *Paralichthys lethostigma*, induced spawning wild adults using only photothermal control has not occurred, but GnRHa implants have been successfully used to induce ovulation and allow strip-spawning. The spawning success achieved using the combination of photothermal conditioning and GnRH-a implants resulted in less stress to the fish, higher egg production and an extended spawning period [68]. For Atlantic salmon, *Salmo salar*, treatment with LHRH-a (25µg kg−1 body weight) by injection or in a cholesterol pellet advanced ovulation in fish held at both 6 and 11ºC, associated with high 17,20βP levels (>60 ng ml−1). In contrast, there was little production of 17,20βP in fish held at 16ºC irrespective of treatment (<25 ng ml−1). In controls, prior maintenance at 16ºC was associated with significant reductions in the fertility and survival of ova (84.0% and 17.3%, respectively) relative to 6ºC (97.9% and 75.6%, respectively) and 11ºC (95.3% and 44.4%, respectively). The fertility and survival of ova from LHRH-a treated fish held at 6 and 11ºC did not differ significantly from that of controls but LHRH-a treated fish held at 16°C either produced nonviable ova or died prior to ovulation. These observations indicate endocrine dysfunction and confirm a lack of maturational competence in Atlantic salmon maintained at elevated temperatures, and suggest that both impaired pituitary responsiveness and limited 20β-HSD activity may contribute to the observed lack of 17,20βP production in fish held at 16ºC [46].

4. CONCLUSION

The results of numerous studies revealed the important roles of some steroid hormones such as E_2, T, 11-KT and C21 steroids in reproductive process of teleosts. In addition, GnRH-a is effective for inducing maturation of some fish species.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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