

Chemical Structure, Classification and Clinical Significance of Steroid Hormones: A Review Article

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ABSTRACT: Steroid hormones are extremely important in controlling a wide range of body functions. They start from controlling growth before birth and thinking ability and go on to relate to the beginning and development of many illnesses. These hormones act in many different organs both to keep a person healthy and sometimes to cause disease. Learning about how steroid hormone compounds are grouped and their chemical shapes is key for explaining their many effects in biology. Normally, people group steroid hormones into five types—glucocorticoids, mineralocorticoids, male hormones, female estrogens, and hormone progesterone's based on their shapes, chemical relation to each other, and what they do in the body. The current paper tries to review existing knowledge about how steroids are built structurally and how they have been classified while also pointing out where our understanding is lacking and needs more research. By improving our understanding of these compounds—especially their production, ways they work, and effects on health and illness—this study helps make clinical practices better and improve treatment plans. Also, the article points out upcoming paths for more studies to answer open questions and make health results better for different groups of people.

Keywords: Steroid hormones, Androgen, Testosteron, Estrogen, Cortisol, Glucocorticoids, Health



1. INTRODUCTION

Steroid hormones can influence varied physiological processes. From the very beginning of life, they affect fetal development; later, they continue cognitive functions and disease states. In that manner, health and disease in the body systems are conditioned by steroid hormones since these compounds perform numerous physiological actions [1],[2],[3]. Because the classification and chemical structure of steroid hormones have been largely resolved, little is left that ails our understanding of these aspects. More important, however, is the need to further elucidate how different steroid hormones interact within the context of combined effects on neurodevelopmental outcomes. Elevated fetal steroid levels are associated with autism; however, it is a relationship that demands more nuanced studies considering multiple hormonal interactions [4], [5].

Sex steroid hormones must be taken into account as a significant component in maintaining oral health, which is complicated and varies between individuals. Age, hormonal treatments, and medical conditions constitute a few of the factors that can cause changes in hormone levels. The particular mechanisms and clinical consequences of this topic are still being investigated [6]. Steroid hormones could potentially be environmental contaminants of major significance, according to laboratory investigations, which have been mostly confirmed by limited field research. Discovering the main pathways of steroid hormones affecting the aquatic environment requires more investigation [7].

The influence of phytoestrogens on human health, mainly related to hormonal therapies, is very little known. In the upcoming research work, emphasis should be laid on studying the long-term effects of these compounds and their interactions with endogenous steroid hormones [8], [9]. Furthermore, more in-depth study is needed regarding the implication of steroid hormones in pathological conditions like adrenocortical carcinoma and endometriosis to find out how hormonal classification could impact treatment outcomes [10], [11].

2. CHEMICAL STRUCTURE AND METABOLISM

The intracellular transport of cholesterol to the steroidogenic tissues marks the beginning of steroid hormone biosynthesis. In earlier studies, a focus was placed on the important steps that are actually involved in the biosynthesis of steroid hormones (figure 1). According to them, mutations in the genes encoding for the transport protein as well as StAR and CYP11A1 could result in congenital lipid adrenal hyperplasia and other disorders. This basically brings to an important realization concerning cholesterol metabolism and clinically relevant steroidogenic pathways; it allows one to gain some perception into deficiencies in steroid hormones along with proper management [12].

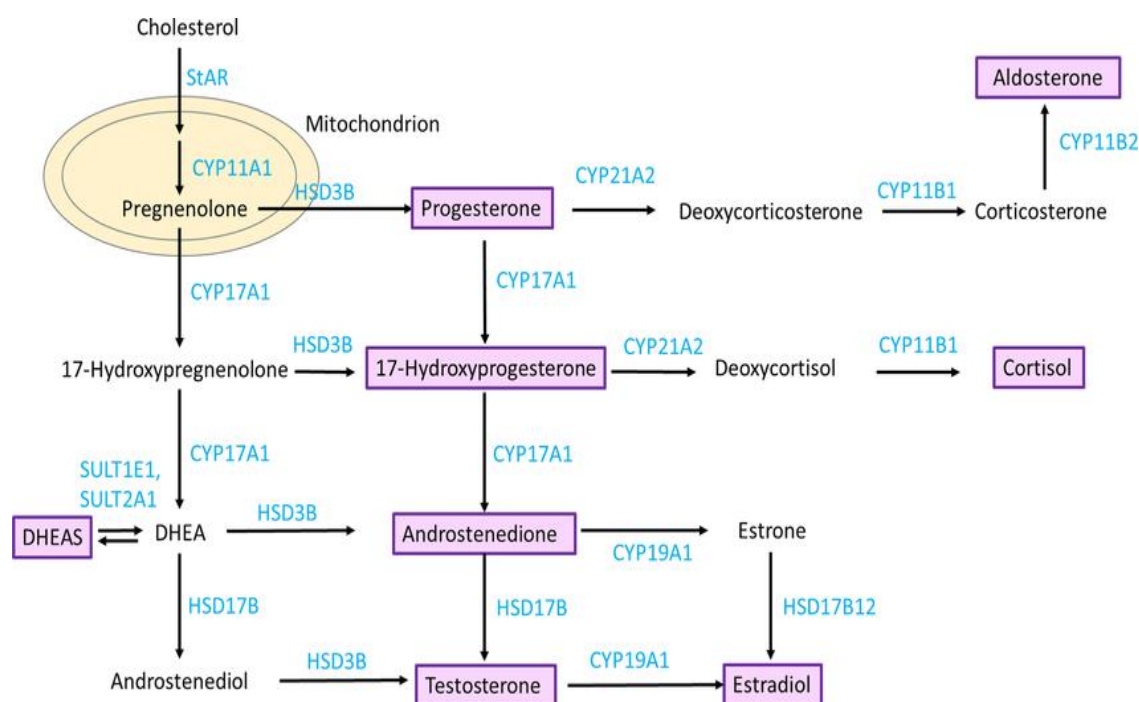


FIGURE 1. - Steroids hormone metabolism pathway [13]

All steroid hormones are related in terms of chemistry that ultimately derived from the 27 carbon (cholesterol). They have the basic structure of four fused carbon rings—three cyclohexane rings (A, B, and C) plus one cyclopentane ring (D), attached to form the cyclopentanoperhydrophenanthrene nucleus [14], (Figure 2), (Table1).

Based on the total number of carbon atoms and the chemical groups that are found at essential carbon residues, steroids are divided into five classes. These 21-carbon steroid hormones are referred to as "pregnenes" and are further separated into three distinct steroid families: mineralocorticoids (like aldosterone), glucocorticoids (like cortisol), and progestins (like progesterone). The ovary is the primary source of progestins, and the adrenal gland's cortex is the source of glucocorticoids and mineralocorticoids, which are all commonly referred to as corticosteroids. The most important structural distinction among each of the pregnene groups is that glucocorticoids and mineralocorticoids have a hydroxyl group (OH) at C21, whereas progestins have a methyl group (CH₃) at site C21. (Figure 2) 19 carbon steroids known as "androgens"—such as dehydroepiandrosterone (DHEA), androstenedione, and testosterone—can be produced by the metabolism of progestins and are released through the testis and the adrenal cortex. Typically, androgens undergo metabolism to produce estrogens, such as oestradiol-17 β , which have a distinctive 18-carbon structure[15]. (Figure 2)

Variation in functional groups attached to this core and the oxidation state of particular carbon atoms define the diversity of steroid hormones. They are generally non-polar molecules so that they can pass through cell membranes by simple diffusion and bind with intracellular receptors [14].

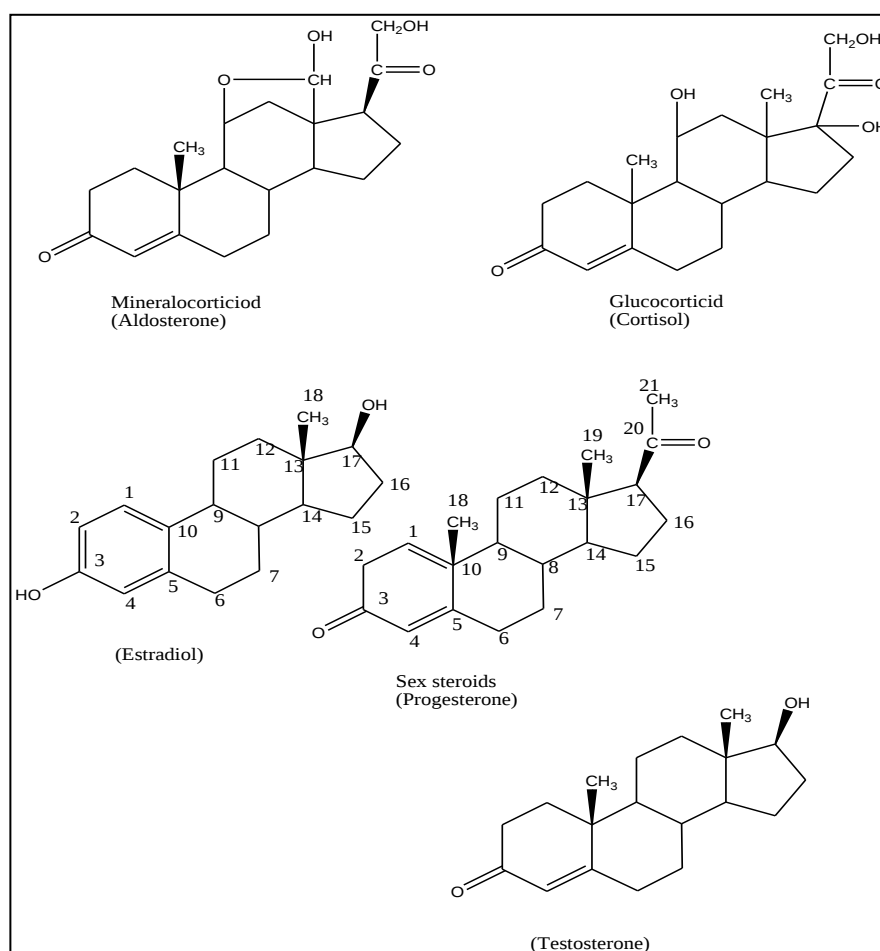


FIGURE 2. - Chemical structure of steroid hormones [7]

Table 1. - Structural classification of steroids with clinical relevance

Class	Carbon Atoms	Example	Clinical Relevance
Cholestanes	27	Cholesterol	Cell membrane component.[16]
Pregnanes	21	Progesterone	Pregnancy maintenace.[16]
Androstanes	19	Testosterone	Androgen therapy.[16]
Estranes	18	Estradiol	Menopausal hormone replacement.[16]

The hormone-receptor complex influences gene transcription once it is bound, leading to altered cellular activities. Because of their lipophilic nature, steroid hormones are actually transported in the blood by specific transport proteins. The chemical modifications of their structure determine specificity for the target, half-life, and potency; therefore, they are essential tools both within natural physiology and therapeutics [17].

Chemical steroid structures underline biologically related functions. For example, the structure of cholesterol shows how important it is to comprehend the synthesis of steroid hormones within the body. Enzymatic pathways responsible for cholesterol conversion into different types of steroid hormones could greatly influence hormonal equilibrium and general health [18]. Thus, enzyme classification and mechanisms are very important not only for hormone production but also for pharmacological intervention in regulating both cholesterol and, as a result, levels of steroid hormones [19].

Besides the role of cholesterol, the chemical structure of certain steroid hormones, like estrogen, has been proven to affect cognitive functions and memory, mostly in male rodents. This study underlines that sex differences must be matched to the effects of steroid hormones—an essential part of their classification [20]. Such evidence reflects the complex links between the chemical structure of steroid hormones and their biological effects that may vary dramatically depending on contexts and populations [19].

3. CLASSIFICATION

Steroids can be categorized by their structures and biological functions (as shown in Table.1) [16], [21].

3.1 FUNCTIONAL CLASSIFICATION

Steroid hormones refer to the lipophilic signaling molecules derived from cholesterol, the basic principle regulators of different physiological activities. They fall into the above-mentioned main five categories: glucocorticoids, mineralocorticoids, and steroid sex hormones (androgens, estrogens, and progestogens), which play different biological functions [21]. The metabolism and immune response regulation of glucocorticoids is one type of function. Mineralocorticoids participate in the regulation of blood pressure as well as electrolyte balance. Sex characteristics in males are formed by androgens; estrogens regulate female reproductive function. Progestogens are involved in pregnancy-specific applications as well as menstrual cycle applications [22]. (Table 1)

The Δ^4 sex steroids are ones classified by a double bond between the 4 and 5 carbon atoms in the A-ring of the steroid nucleus. This class defines biological activity for these compounds. They are synthesized from cholesterol through a series of enzymatic reactions that include very important compounds such as testosterone, androstenedione, and progesterone (Figure 1). Testosterone and androstenedione are actually strong androgens responsible for male secondary sexual characteristics, while progesterone is more related to females in terms of function, where it plays an important role in menstrual regulation as well as in maintaining pregnancy [23]. The Δ^4 configuration increases their binding affinity to particular steroid receptors; hence, their physiologically potent effects. Generally, these hormones are synthesized in the gonads and adrenal glands; however, estrogen synthesis utilizes them as precursors. A type of Δ^4 steroid, thus differentiating them from pregnenolone and other Δ^5 steroids due to their bonding arrangement. High levels of these hormones in the development of the fetal brain may also be associated with neurodevelopmental disorders like autism; hence, a detailed classification based on hormonal profiles is critically needed. It brings forward that subtle differences by which various steroid hormones contribute to health outcomes should be better understood, mostly when such exposure happens in vulnerable populations-fetuses [4].

Phytoestrogens are plant compounds that resemble steroid hormones in structure and mimic their action. They are classified according to molecular structure and biological activity. Isoflavones, as phytoestrogens, where classification is necessary also for therapeutic usages along with potential risks [8]. This gives an idea about the wider implications of hormonal classification besides endogenous steroid hormones; it includes the plant compounds that can have effects on human health [24].

Steroid hormone classification relates significantly to a disease profile of cancers and endometriosis. For instance, breast cancer subtypes are mainly associated with hormonal profiles basally related to the absence of steroid hormone receptors for treating basal-like breast cancer, and this also defines the treatment options available [25]. Better treatment strategies will evolve from an understanding of the hormonal profiles and chemical structures involved. Endometriosis is an estrogen-dependent disease; therefore, molecular classification in the pathology of endometrial tissue highlights the importance of steroid hormones. These give an indication that detailed systems of classification that incorporate both aspects of hormonal activity and structure are necessary for better diagnostics and therapeutics [11].

4. CLINICAL SIGNIFICANCE OF STEROID HORMONES

Steroid hormones have transformed medicine with their use in anti-inflammatory treatments, endocrine disease management, reproductive health, cancer therapy, and synthetic derivatives [26].

4.1 CLINICAL SIGNIFICANCE OF GLUCOCORTICOIDS

Production of glucocorticoids belongs primarily to the steroid hormones synthesized by the adrenal cortex. Regulation of metabolisms, immune reactions, and stress-related processes is therefore controlled by these. They ensure that glucose levels are catered for in the body, suppress inflammatory reactions to insult, and also regulate protein as well as fat metabolism. In humans, the primary glucocorticoid is cortisol; it is accompanied by corticosterone in some other species. The hypothalamic-pituitary-adrenal (HPA) axis controls their release [27]. Glucocorticoids are steroid hormones involved in the regulation of various physiological aspects concerning primarily inflammation and immune responses. Clinically significant because treatment with them has been generalized for several conditions such as autoimmune diseases, inflammatory diseases, and malignancies. However, with careful use, adverse effects are often more pronounced than beneficial effects; hence, a balance required application [28].

Glucocorticoids are key drugs in autoimmune disease management. They are probably the most responsible for successful treatment of Graves' orbitopathy and sarcoidosis. In moderate-to-severe Graves' orbitopathy, intravenous glucocorticoids are preferred because they are more effective and better tolerated than oral treatment in achieving control of inflammation and related complications [29]. The same applies to symptomatic sarcoidosis since treatment must be individualized to maximize benefit while minimizing long-term toxicity. This, again, proves how important glucocorticoids are in the treatment of autoimmune diseases [30].

The very duality of nature it displays by modulating so many immune responses puts it across. In other words, treatment with steroids or, more specifically, glucocorticoids is associated with improvement in quality of life for inflammatory diseases but, on the other hand, can lead to several adverse effects [31]. This means that research has shown that glucocorticoid treatment for inflammatory diseases changes the landscape of immune cell populations [32]. The use of glucocorticoids was also uncovered to be more handy in acute management, such as in ulcerative colitis, where they help relieve symptoms rather quickly [33]. However, a word for very vigilant monitoring and consideration of alternative therapies to long-term side effects sums the role glucocorticoids play in clinical practice right up [34]. Even though these drugs have immense therapeutic value, quite a number of metabolic adverse effects result from their administration, particularly hyperglycemia and weight gain. Hence the management and prevalence of steroid-induced hyperglycemia becomes critical, as those metabolic derangements can have grave outcomes on patients [35],[36]. The pathophysiological mechanisms of these side effects make it necessary to monitor and manage patients who are on glucocorticoid therapy [33]. Long-term use of glucocorticoids can cause neuropsychiatric disturbances; therefore, psychological side effects should also be monitored with increased attention [37]. Case examples have shown the devastating cognitive and behavioral effects of treatment with glucocorticoids, stressing that even in this context therapeutic benefits have to be balanced against potential adverse outcomes [38]. In patients with ANCA-associated vasculitides, long-term treatment with glucocorticoids is also associated with significant problems, particularly an increased risk of infection and metabolic derangements. Therefore, treatment strategies should evolve, considering not only the effectiveness but also the risk of using glucocorticoids in such vulnerable populations [39].

4.2 CLINICAL SIGNIFICANCE OF MINERALOCORTICOIDS

Mineralocorticoids are a class of steroid hormones important in the control of electrolyte and water balance in the body. They mainly act on the kidney to promote sodium retention and potassium excretion, whereby blood pressure as well as fluid homeostasis is maintained. These hormones arise from the adrenal cortex; aldosterone is the most important mineralocorticoid in humans. The secretion of aldosterone is mainly governed by the renin-angiotensin-aldosterone system (RAAS). In essence, aldosterone proves to be an electrolyte balancer, an agent for blood pressure regulation, and a supporter of normal fluid balance. Their clinical relevance has attracted more attention recently, particularly their effects on chronic kidney disease (CKD), diabetes, and related cardiovascular events [40]. Recent work also highlights how mineralocorticoids harm cardiovascular health. Pivotal work by Pitt et al. It was shown that finerenone, a nonsteroidal selective mineralocorticoid receptor antagonist, significantly reduced cardiovascular events and renal failure in patients with type 2 diabetes and chronic kidney disease. The above study shows that mineralocorticoid receptors are a potential target for improving clinical outcomes in these high-risk populations; therefore, it enhances the clinical significance of mineralocorticoids concerning diseases of the heart [41]. A pooled Fidelity analysis from several trials further confirms the above by showing that finerenone decreased cardiovascular plus renal events versus placebo. The analysis gives an albuminuria screening recommendation to bring about intervention based on need, which could unmask benefit; hence, proactive management of mineralocorticoid levels could improve patient outcomes in cardiovascular as well as renal health [42].

Chronic kidney disease (CKD) is very potentiated with mineralocorticoid activity; therefore, several studies were implicated in it. Funder (2017) reviewed aldosterone effects on the kidney and cardiovascular system, stating that mineralocorticoid excess conditions are associated with fibrosis and progressive damage of the kidneys. This relation justifies the management strategies demanded to address mineralocorticoid receptor related-issues [43]. Currie et al. carried out a systematic review and meta-analysis of the impact of mineralocorticoid receptor antagonists on proteinuria as well as CKD progression; results showed that antagonists are not only more effective in lowering blood pressure but also in reducing urinary protein/albumin excretion, which is the key marker for CKD progression [44]. The hazards of hyperkalemia raised by this therapy should be considered in an emphasis that calls for individualized patient care [45].

The role of TGF β -1 is very relevant when discussing the clinical significance of mineralocorticoids in diabetic nephropathy. Chang et al. described how TGF- β 1 promotes renal fibrosis and allows mineralocorticoid excess to further aggravate the process. This places fibrogenic effects as a higher priority that could be reduced by mineralocorticoid receptor antagonism, therefore giving a new drug path for diabetic nephropathy management [46], [47].

4.3 CLINICAL SIGNIFICANCE OF SEX STEROID

Sex steroids are steroid hormones that regulate reproductive functions and sexual characteristics. They are produced mainly in the gonads (ovaries and testes) and adrenals. Steroid hormones affect puberty, fertility, and sexual behavior. The principal sex steroids comprise testosterone, estradiol, and progesterone, the levels and actions of which differ quite dramatically in males and females. Sex steroids have an absolutely central role in a host of different physiological processes and clinical conditions so that their action extends well beyond issues related to sexual development to general health-related endpoints in populations [48]. Hence, Hembree et al., 2017, indicates sex steroids as an essential component of endocrine treatment for gender dysphoria through a guideline that recommends hormone levels within the physiological range of the affirmed gender for mental as well as physical health. The

suggested multidisciplinary approach shows the need for endocrinologists to know about the benefits and risks of sex steroid therapy, including watching for bad effects and cancer dangers. This basic knowledge helps make protocols that improve the quality of life for patients with gender dysphoria [49].

The two-way link of sex steroids to health results is shown well in the work by Guo (2017), which points out how sex steroid treatment affects heart health. Male transgender individuals receiving hormone treatment may develop bad changes in lipid levels, while female transgender individuals might have better bone mineral density results. These data hint at a jumbled play where sex steroids both lower health risks and cause certain good effects for the state of being healthy. A note that there is little proof in these works calls for more study on the long-term health effects of sex steroid treatment in transgender people; it hints at the need for a form of care that varies per individual and their health profile [50]. The heart-protecting effect of estrogen is seen before menopause, and the increased risks are seen after menopause [51]. To know this is very important in making plans that target gender-specific differences to help stop heart-related illnesses. Likewise, other works argue for finding gender-based differences during heart checks to make care better [52],[53].

Bone health relates to the very fact that sex steroids are prominent in osteoporosis. Estrogen and testosterone are described by Kautzky-Willer et al. (2021) as essential for the maintenance of bone density in both sexes. That relationship between sex steroids and a disease like osteoporosis would mean these hormone levels would need to be tracked by clinicians, especially in aging populations, to preempt complications with bones [54]. That is also revealed in data on the effect of sex steroids on postmenopausal women and pathogenesis of non-alcoholic fatty liver disease, which again underlines specific prevention needs in that demographic [53]. Yılmaz et al. (2019) went on to explain the role of sex hormones concerning lung diseases, though he didn't make an explicit statement about asking us to learn about differences related to sex when it comes to lung function and susceptibility. The ability to detect markers for lung illnesses via the signaling processes of sex hormones might greatly better treatment plans and health results. This field shows a large gap in present study methods, emphasizing the need for customized therapy approaches that take these variations into account [55].

Another important area is the influence of sex steroids on neurological and psychiatric diseases. As Martin et al. (2021) put it, "We argue for the inclusion of sex as a variable in clinical studies to better understand the implications of sex differences on treatment outcomes". This knowledge is required to move further towards individualized treatments, taking into account hormonal effects on neurologic conditions, hence improving patient care [56]. On another note, Khosla and Monroe (2018) discussed potential effects of sex hormones on Alzheimer's disease, and, by extension, hormonal factors could direct future research and clinical strategies towards early detection and intervention. That existing literature has addressed these issues informed us that there are several knowledge gaps regarding the clinical significance of sex steroids [57]. For example, health outcomes associated with long-term use of sex steroid therapy in transgender populations need further investigation [50]. Also, the reasons behind differences in lung health and disease chances between sexes are not well looked into, showing a need for focused study in this area [58]. In addition, the effect of sex steroids on neurodegenerative diseases, mainly Alzheimer's, needs more focused studies to get a clearer picture of how these hormones affect disease progress and risk [57].

Androgens are a group of steroid hormones that mostly control the growth and expression of male traits and sexual functions but play important roles in females as well. In males, they are mainly produced by the testicles, while in females their production takes place in the adrenal glands and ovaries. Androgens have critical importance; first, they enable male genitalia to form. Later on, hormones like these create facial hair along with other secondary sex traits and voice deepening. They additionally help muscles grow and work bones into keeping their mass [58]. For example, they assist with sex drive and even mood regulation. The most powerful androgen is testosterone; others include dihydrotestosterone (DHT), androstenedione, and dehydroepiandrosterone (DHEA). Hormones affect cells by binding to receptor proteins located within cell nuclei from a variety of tissues [59].

Steroid hormones, mainly androgens are very essential in the onset and progression of Polycystic Ovary Syndrome (PCOS). The primary cause of the emergence of this disorder's symptoms is thought to be an excess of androgen [60]. The cause of hyperandrogenism is the overproduction of androgen by the adrenal glands and ovaries. The initial effect of excess androgen is poor folliculogenesis. In the first gonadotropin-independent stage, higher levels of androgens promote the development of primordial follicles and raise the quantity of tiny antral follicles. This could contribute to infertility by causing irregular or missing ovulation. Clinical manifestations of female hyperandrogenism include androgenic alopecia, hirsutism, acne, and/or elevated testosterone values [60],[61].

Previous research has reported the impact of androgens on the hypothalamic-pituitary-adrenal stress system, which is very important in controlling both responses to stress and mental functions. In addition, Boehm et al. (2015) report that androgens may augment HPA activity; therefore, this enhancement may lead to sex differences in disorders related to stress, such as anxiety and depression [62]. Such findings place a rather central role for hormonal equilibrium with healthy states of mind and perhaps dysregulation of hormones like androgens with intensified expressions of mood disorders. Besides that, results were based on testosterone treatment of transgender males, which showed substantial optimizations toward healthier mental outcomes by lowering anxieties/depression. In short, it can formulate the premise that androgens do not play a lesser role in providing healthiness - mentally apart from their primary reproduction-associated function [63].

The progesterone-related mechanism has also been highlighted in several studies dealing with mental health during pregnancy. A study by Tilahun et al. (2021) proved that abnormal variations of progesterone levels in pregnancy are related to such increased risks in mental health issues as anxiety, depression, etc. Therefore, the authors recommend strong social support systems to offset the risks, which brings forth an explicit requirement for interventions targeted at improving mental well-being during such critical periods. This can further enable another future study investigating the interaction between hormonal changes and social elements relating to mental states among pregnant populations [64]. Moreover, Okoth et al. (2020) revealed that raises it to the level that combined oral contraceptives may be associated with cardiovascular risk, which brings forth an implication of hormonal treatments on women's health. That has also been a relationship justifying more extended explorations toward the long-term effects of hormonal contraceptives on reproductive and mental health outcomes [65].

Since the usage of androgens has spread beyond sports to a much larger segment of the population, it has developed into a serious public health problem. The steroidal androgens known as anabolic-androgenic steroids (AAS) can be manufactured to imitate the effects of the endogenous male hormone or natural androgens like testosterone, the male sex hormone [66],[67],[68]. Oral or injectable anabolic steroids are administered by doctors to deal with hormonal imbalances in hypogonadism, male impotence, and delayed puberty in teenage males; in women, they may be employed to treat endometriosis, osteoporosis, tumors in the breast, and decline in muscle in HIV/AIDS or cancer patients. Athletes frequently abuse it to improve performance and increase endurance [66]. AAS are abused by non-athletes to gain weight and build up muscle without gaining additional fat on the body. The detrimental consequences of AAS affect every organ, tissue, and function in the body, but they are particularly harmful over the long run and can include myocardial dysfunction, coronary atherosclerosis, arrhythmia, hypertension, hypogonadism, and sudden death. Acne, hirsutism, and voice deepening are among the long-term side effects for women; some females may develop breast atrophy along with oligomenorrhea or even menorrhea [66],[67].

5. ENVIRONMENTAL STEROIDS EFFECT ON HUMAN

Steroid hormones can have negative health impacts, in particular through endocrine-disrupting-chemicals (EDCs), as they interact with the body's hormonal systems, such as bisphenol A (BPA), which is a chemical substance with a significant manufacturing volume that is utilized to make a variety of different products like thermal paper receipts, epoxy resins, and polycarbonate plastics [69],[70]. Predominantly, BPA exposure in humans occurs via the diet after consuming BPA-contaminated food or drink, but it can also happen through dust inhalation or cutaneous contact by touching thermal receipts. Since it can function as a xenoestrogen, BPA is categorized as an endocrine-disrupting-chemical (EDC). Due to EDCs may serve as hormone mimics or interact with natural hormones' ability (like estrogen and androgen) to connect to their receptors; they amplify the effects of endogenous hormones. Additionally, researchers have demonstrated that contact with BPA is linked to a higher risk of diabetes type 2, insulin resistance, a disruption of the normal immunological response, obesity, cancer, and detrimental consequences on reproduction [69], [71], [72].

6. CONCLUSIONS

Steroid hormones are essentially diversified molecules of very powerful biological activity, derived in structure from cholesterol and involved in the control of very important and diverse physiological functions across systems. The classification of these hormones based on chemical structures and physiological roles provides not only a guide to normal biological activities but also an improved ability to understand pathologies that manifest in a multitude of disorders. Glucocorticoids for regulation of metabolism and immune responses, mineralocorticoids for regulation of fluid balance, complicated reproductive plus systemic actions of sex steroids, and clinical importance are obvious. New information relating to their structural analogs, Δ^4 steroids and phytoestrogens, shows complex interactions with health effects, particularly concerning vulnerable groups. Treatment using steroid hormones has associated complications that need management. A sophisticated and elaborated classificatory scheme that couples biochemical, clinical, and therapeutic aspects is essential for progress in personalized medicine. Further studies should keep on filling the gaps in knowledge, chiefly regarding sex differences, neurological involvement, and long-term impacts of steroid treatments.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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