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Problems in the use of chemical and functional nomenclatures for steroids in human physiology, biology and pharmacology

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Steroid compounds are important messengers in the human body that can be described using multiple nomenclature systems, each reflecting a different perspective on structure or function. Chemical nomenclature, based on IUPAC conventions, classifies steroids according to their ring structure and functional groups, whereas functional nomenclature reflects a compound's source, biological action, regulatory pathways, metabolism, or clinical application. These parallel systems are often applied inconsistently across disciplines, leading to ambiguity in interpretation and communication. This review outlines the foundations of chemical and functional naming, highlights circumstances in which nomenclature becomes inconsistent, and illustrates how physiology, molecular biology, receptor diversification, genetics, oncology, and the microbiome complicate terminology. Because clinicians, biochemists, pharmacologists, and researchers often apply different naming logics, coherent definitions and consistent usage are necessary for clear scientific discourse. This review proposes considerations to support more precise application of steroid nomenclature in academic publications.

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1. Introduction

Steroids are a large and diverse class of biologically active lipids that play fundamental roles in human biology and physiology. They function as structural components of cell membranes, signalling molecules, metabolic regulators, and hormones. Steroids can be designated by several nomenclature systems that reflect distinct scientific priorities. Some inconsistencies are the results of the historical evolution of steroid discovery and knowledge of their biological effects as well as the effects from multiple biochemical pathways. Steroids were first distinguished alphabetically in order of isolation[1,2] but this became inadequate as the number of steroids exceeded 26 in number. Chemical nomenclature follows rules of the International Union of Pure and Applied Chemicals (IUPAC) and identifies compounds according to the characteristic four-ring carbon skeleton and associated functional groups.[3] Functional nomenclatures, in contrast, emphasize the sources, physiological actions, regulatory mechanisms, metabolic pathways, and therapeutic indications. Because these systems capture different dimensions of a steroid's identity, a single compound may be described by multiple, correct, but potentially confusing names (Fig. 1). As interdisciplinary research involving endocrinology, neuroscience, pharmacology, oncology, molecular genetics, and microbiome science expands, inconsistent nomenclature complicates the interpretation of results and the comparison of findings across fields.

This review examines where problems arise between chemical and functional naming, identifies the scientific and clinical contexts in which terminology diverges, and outlines considerations for more accurate and uniform nomenclature in publications. The consequences of inconsistent nomenclature can lead to a breakdown in communication between disciplines or ambiguity in clinical interpretation. A discussion of the issues is timely with the increasing use of molecular biology, the continued development of new classes of steroid analogues and the rapid expansion of interdisciplinary research enriched with improved analysis of steroids and systems biology.

2. Chemical nomenclature

From a chemical perspective, steroids can be divided into several categories based on structural characteristics and modifications to the steroid nucleus.[3] Cholesterol is the most prominent sterol in humans and serves as a critical component of cell membranes as well as the precursor for steroid hormones, bile acids, and vitamin D. Sterols are one of the most important classes of steroids and are characterized by the presence of a hydroxyl group at the third carbon position and a side chain at carbon seventeen. Bile acids and bile salts represent another chemically distinct group of steroids derived from cholesterol in the liver. Bile acids are derivatives of the 24 carbon atom cholane and the 27 carbon atom cholestane mostly with a carboxyl group. Bile acids play an essential role in the

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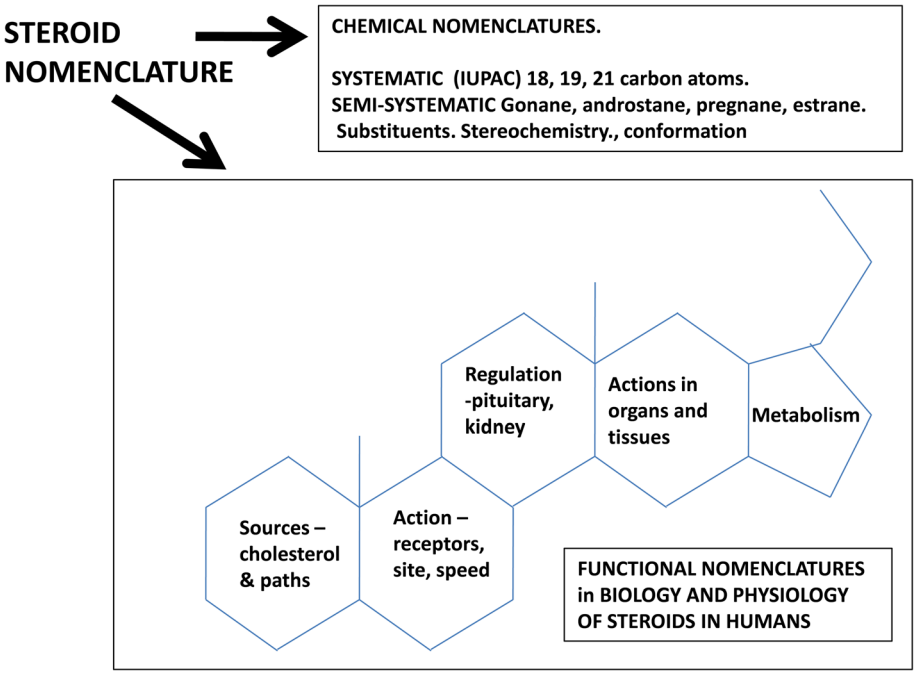


Fig. 1 Chemical and functional nomenclatures for steroids. Steroids can be defined by chemical structure according to clear rules. Functional nomenclatures depend on sources, actions at receptors, actions in organs and tissues, regulation and clearance.

digestion and absorption of dietary lipids by facilitating the emulsification of fats in the small intestine. A nomenclature for bile acids was proposed.[4] Another chemically distinct group is the secosteroids, in which one of the steroid rings is broken. Vitamin D is an example of secosteroids and is an important regulator of calcium and phosphate metabolism. Secosteroids and bile acids will not be discussed further in this review.[5]

Historically, steroids were assigned trivial names based on order of discovery[1,2,6] (Table 1) or origin (*e.g.*, estrone, progesterone from estrous and pregnancy respectively), many of which

Table 1 Chemical nomenclature of steroids by letters (Kendall, Reichstein, Wintersteiner)[a]

Kendall	Kendall	Reichstein	Wintersteiner
A	11-Dehydrocorticosterone	5α-Pregnan-3β,11β,17α,20β,21-pentol	5α-Pregnan-3β,11β,17α,20β,21-pentol
B	Corticosterone	H	
C	Allo-THF	Allo-THF	D
D	Adrenosterone	5α-Pregnan-3β,17α,21-triol-11,20-dione	A 11-dehydrocorticosterone
E	Cortisone Epi E 20β-dihydrocortisol	4-Pregnene-11β,17α,20β,21-tetrol-3-one	FCortisol
F	Cortisol	M	
Fa		Cortisone	
G	5α-Pregnan-3β,17α,21-triol-11,20-dione	D Adrenosterone – androst-4-ene-3,11,17-trione	B corticosterone
H	5α-Pregnan-3β,21-diol-11, 20-dione	Corticosterone	
J	5α-Pregnan-3β,17α,20β-triol	J 5α-pregnan-3β,17β,20β-triol	
K	5α-Pregnan-3β,17β,20β,21-tetrol	K 5α-Pregnan-3β,17α,20β,21-tetrol	
L		5α-Pregnan-3β,17α-diol-20-one	5α-Pregnan-3β,17α,21-triol-11,20-dione
M		Cortisol	
O		5α-Pregnan-3β,17α,20α-triol	
P	P	5α-Pregnan-3β,17α,21-triol-20-one	
Q	Dihydro-DOC	21-Hydroxy-4-pregnene-3,20-dione (DOC)*	
R	R	5α-Pregnan-3β,11β,21-triol-20-one	
S	11-Deoxycortisol	11-Deoxycortisol	
T		20β Dihydro-11-dehydrocorticosterone	
U		20β-Dihydro cortisone	
V		5α-Pregnan-3β,11β,17α,21-tetrol-20-one	

[a] Cortexone is sometimes used for * DOC 11-deoxycorticosterone. Uro is used for tetrahydro-cortisol and cortisone metabolites in urine – urocortisol, urocortisone.

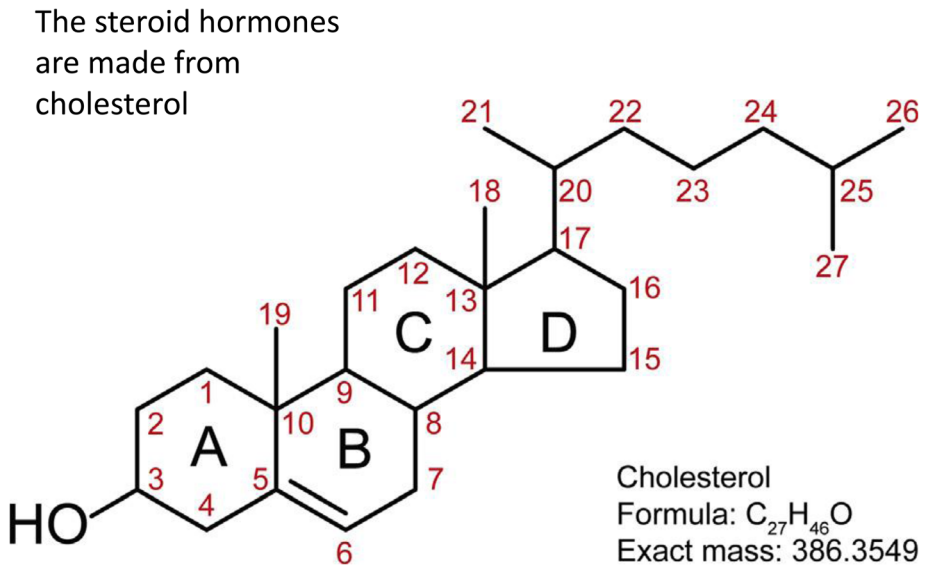


Fig. 2 Structure of cholesterol and numbering of carbon atoms. Single hydrogen atoms are placed at C3, 5, 6, 8, 9, 14, 17, 20 and 25. Two hydrogens atoms are placed at C1, 2, 4, 7, 11, 12, 15, 16, 22, 23, 24. Three carbon atoms are placed at C18, 19, 21, 26, 27.

persist in common use. Modern research often relies on abbreviations (*e.g.*, T for testosterone, E2 for estradiol, DHEA for dehydroepiandrosterone), which simplify communication but obscure structural relationships and can introduce ambiguity in interdisciplinary contexts. Chemical nomenclature defines steroids by their core cyclopentanoperhydrophenanthrene structure, with the carbon atoms numbered and rings (A–D) labelled systematically according to IUPAC rules (Fig. 2). Carbon

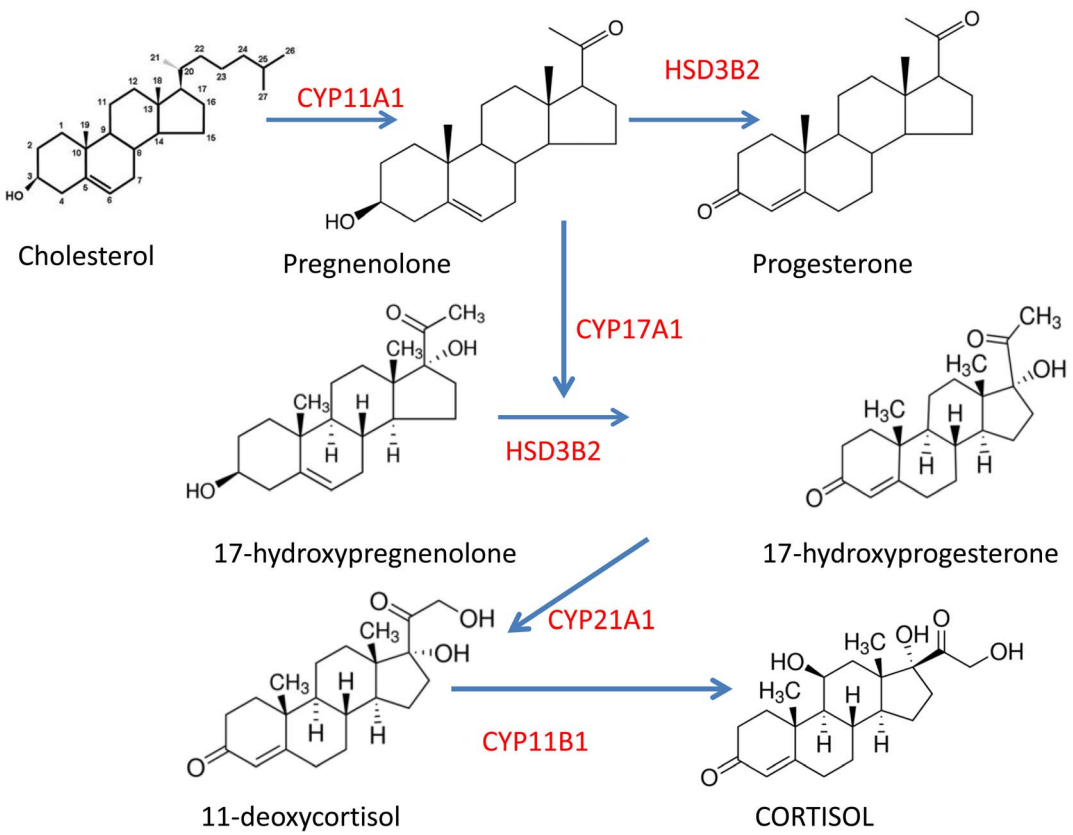


Fig. 3 Synthesis of cortisol. The actions of five enzymes convert cholesterol to cortisol in the adrenal cortex. Four enzymes are cytochrome P450 oxidoreductases (CYP). The C3β-hydroxyl group is oxidised by 3β-hydroxysteroid dehydrogenase type 2 (HSD3B2).

atoms are numbered according to a standardized system used in steroid chemistry, which facilitates comparison between different steroid molecules. Structural diversity among steroids arises from the chemical modifications. Structural features such as bond saturation, oxidation state, and the presence and orientation of substituents are defined by precise chemical terms. These include the addition or removal of functional groups such as hydroxyl or keto groups, variations in the position of double bonds within the rings, and differences in the length or composition of side chains attached to the nucleus. Stereochemistry also plays a crucial role, as the spatial orientation of substituent groups can significantly influence shape of the molecule and biological activity. Cortisol, for example, is chemically 11β,17α,21-trihydroxypregn-4-ene-3,20-dione, while aldosterone is 11β,21-dihydroxypregn-4-ene-18-al-3,20-dione. These designations capture structural detail but do not reflect physiological activity.

Steroid biosynthesis begins with cholesterol, which serves as the principal precursor for all steroid hormones in humans (Fig. 3). Through a sequence of enzymatic transformations involving hydroxylation, oxidation, and cleavage reactions, mainly in the mitochondria and smooth endoplasmic reticulum of steroidogenic cells, cholesterol is converted into various steroid intermediates and ultimately into different classes of biologically active steroids.

2.1 Limitations of chemical classification

Although chemical nomenclature is unambiguous, it is impractical for routine clinical or physiological communication. Semi-systematic chemical nomenclature includes the trivial names that are widely used for steroids. Most scientific writing therefore intermixes chemical names, trivial names, and abbreviations, creating opportunities for inconsistency unless each term is clearly defined. The chemical classification that organizes steroids based on structural features is nevertheless particularly useful for understanding biosynthetic relationships among steroid molecules. Chemical classification alone does not however adequately account for biological function. Cholesterol for example is structurally classified as a sterol but performs several distinct roles, including maintaining membrane fluidity, serving as a precursor for steroid hormones, and participating in cellular signalling pathways.[7] Another limitation of structural classification is that relatively small chemical modifications can significantly alter biological activity. Differences in hydroxylation patterns or stereochemical orientation may dramatically influence receptor binding and metabolic stability.[8] As a result, structurally similar molecules may exhibit substantially different physiological effects.

Recent advances in analytical techniques, particularly mass spectrometry-based steroid profiling, have also revealed numerous steroid metabolites that do not fit neatly into traditional chemical categories[9] These discoveries suggest that the diversity of steroid structures in biological systems is greater than previously recognized, highlighting the limitations of purely structural classification systems.

3. Functional nomenclatures of steroids in human biology and physiology

Functional nomenclature refers to steroids by where they originate, what they do, or how they act, how they are controlled, and how they are removed from the body. Unlike chemical nomenclature, which is fixed, functional nomenclature is context-dependent and can shift with advances in physiology or molecular biology.

3.1 Source-based nomenclature

Terms such as adrenal steroid, gonadal steroid, placental steroid, or neurosteroid arise from the tissue of origin. Cholesterol is the basis for all steroid synthesis but the complement of enzymes varies between and within the tissues. The enzymes in steroid biosynthesis are cytochrome P450 enzymes[10,11] and hydroxysteroid dehydrogenases[12] that need certain redox partners and co-factors.[13] Each organ can have more than one zone with different complements of enzymes. The steps in biosynthesis are linked in common pathways from cholesterol to cortisol (Fig. 3), to aldosterone (*via* progesterone, deoxycorticosterone and corticosterone) and to the sex steroids (from pregnenolone *via* dehydroepiandrosterone). The adrenal cortex has three layers of cells with different functions. The outer zona glomerulosa meets aldosterone synthesis, the intermediary zona fasciculata is for cortisol synthesis and inner zone reticularis secretes DHEAS. In the testes leydig cells produce testosterone and sertoli cells produce sperm. In the ovary androgens are produced in thecal cells and estrogens are produced in granulosa cells, through a paracrine route. In addition to classical endocrine routes between cell types and cellular compartments the mitochondria and endoplasmic reticulum, there are now recognised to be a backdoor route to dihydrotestosterone[14] (Fig. 4) and novel pathways to androgens in some disease states.[15] Molecular biology has refined the genetic basis of the enzymes,[8,16] studies have revealed additional sites of synthesis such as skin and adipose tissues.[17,18] A prominent example is the transition from "neurosteroid"[19] to "neuroactive steroid"[20] reflecting evidence that many such compounds active in the brain are not necessarily synthesized there.

Improvements in analytical chemistry have been fundamental to realising the concentrations of steroids in circulation[21] and the tissue content of steroids.[22] Multiple reference ranges are needed for the variations with sex, age, development, phase of life and period in the menstrual cycle when interpreting results from patients for example polycystic ovary syndrome.[15]

3.2 Action-based nomenclature

In addition to structural classification, steroids can also be categorized according to their physiological functions based on dominant biological actions each linked with receptors in target tissues (Fig. 5). Glucocorticoids are steroid hormones produced

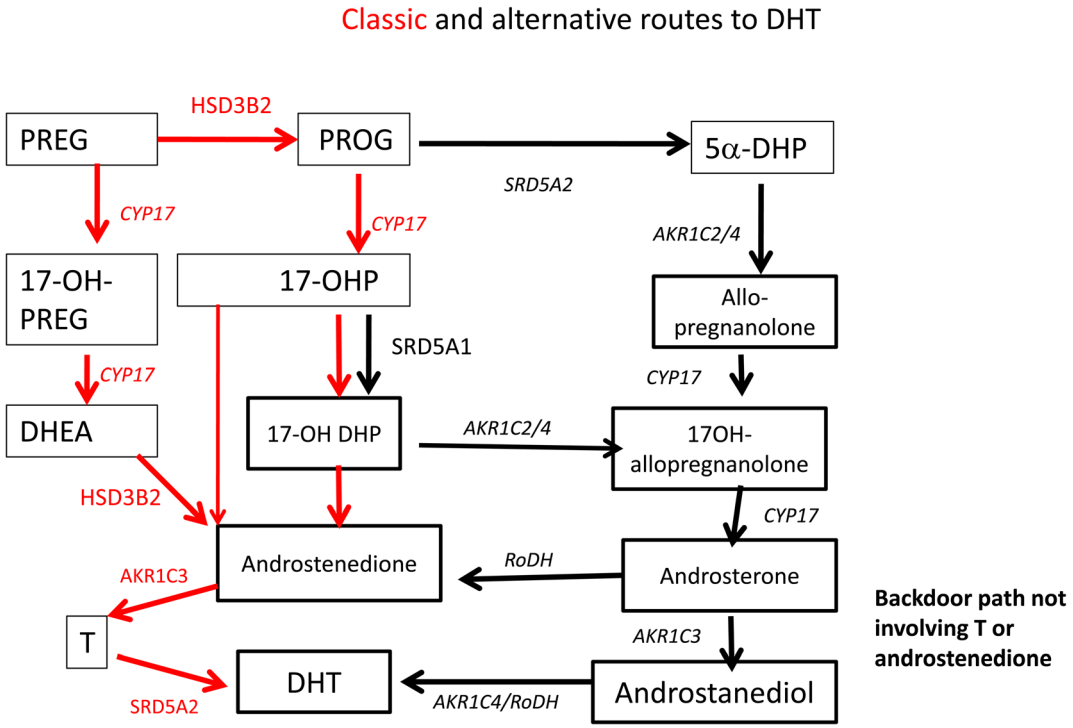


Fig. 4 Classic and alternative paths to DHT. Classic pathway of steroidogenesis. Pregnenolone is formed by action of P450scc on cholesterol. HSD3B2 mediates the conversion of Δ5 steroids present in the left-hand column to Δ4 steroids in middle column. The 17, 20 lyase activity of P450c17 transforms 17OH-pregnenolone into DHEA in the zona reticularis and testicular leydig cells; only tiny amounts of 17OH-progesterone are transformed to androstenedione in humans. Testicular 3β-hydroxysteroid dehydrogenase type 2 (HSD3B2) transforms DHEA to androstenediol; low concentrations of adrenal 17βHSD5 (AKR1C3) in the zona reticularis yield small amounts of testosterone. In genital skin, 5α-reductase type 2 (SRD5A2) further activates testosterone to dihydrotestosterone (DHT). 17OH-Preg, 17OH-pregnenolone; DHEA, dehydroepiandrosterone. Backdoor pathway of androgen biosynthesis. The backdoor route is similar to the classic route but with sequential 5α- and 3α-reduction of 17OH-progesterone, first by SRD5A1 to 17OH-dihydroprogesterone, and then 3α-reduction by AKR1C2 or AKR1C4 to produce 17OH-allopregnanolone. P450c17 can catalyze 17, 20 lyase activity using 17OH-allopregnanolone as the substrate; this reaction produces androsterone, which can be catalyzed by testicular 17β-hydroxysteroid dehydrogenase type 3 (17βHSD3) or adrenal 17βHSD5 (AKR1C3) to produce androstanediol. Androstanediol may then undergo 3α-oxidization, probably mediated by AKR1C4 (also called retinol dehydrogenase, RoDH), to produce the most active androgen, DHT. DHEA, dehydroepiandrosterone; DHT, dihydrotestosterone; AKR, aldo-ketoreductase.

primarily in the adrenal cortex. The most well-known glucocorticoid in humans is cortisol. These hormones regulate carbohydrate, protein, and lipid metabolism and play a central role in the body's response to stress. They also possess powerful anti-inflammatory and immunosuppressive properties.

Mineralocorticoids are another class of adrenal steroids that regulate electrolyte and fluid balance. Aldosterone is the principal mineralocorticoid in humans and acts primarily on the kidneys to promote sodium retention and potassium excretion, thereby maintaining blood pressure and extracellular fluid volume.

Androgens are steroid hormones responsible for the development and maintenance of male reproductive tissues and secondary sexual characteristics. Testosterone is the primary androgen produced by the testes, although smaller amounts are also produced by the adrenal glands. Androgens also contribute to muscle growth, bone density, and overall anabolic processes. Estrogens represent the major class of female sex hormones and are primarily produced by the ovaries. Key estrogens include estradiol, estrone, and estriol. These hormones regulate the menstrual cycle, promote the development of female secondary sexual characteristics, and play important roles in bone metabolism and cardiovascular health. Progesterone is important for the maintenance of pregnancy.

3.2.1. Receptor biology and the complexity of steroid action. Traditional models of steroid hormone action emphasize genomic mechanisms involving intracellular nuclear receptors. In this model, steroid hormones diffuse across the cell membrane, bind to specific receptors, and regulate gene transcription by interacting with hormone response elements in DNA[23] (Fig. 6). However, increasing evidence indicates that steroids can also exert rapid non-genomic effects through membrane-associated receptors and intracellular signalling pathways.[24] These mechanisms allow steroid hormones to influence cellular processes within seconds or minutes, suggesting that steroid signalling operates through multiple parallel pathways.

Another complicating factor is receptor promiscuity. Receptors have a similar arrangement of domains labelled A to F (Fig. 7.) but overall structures unique for binding of androgens (AR), estrogens (ER), glucocorticoids (GCR) and mineralocorticoids (MR). Many steroid receptors are capable of binding more

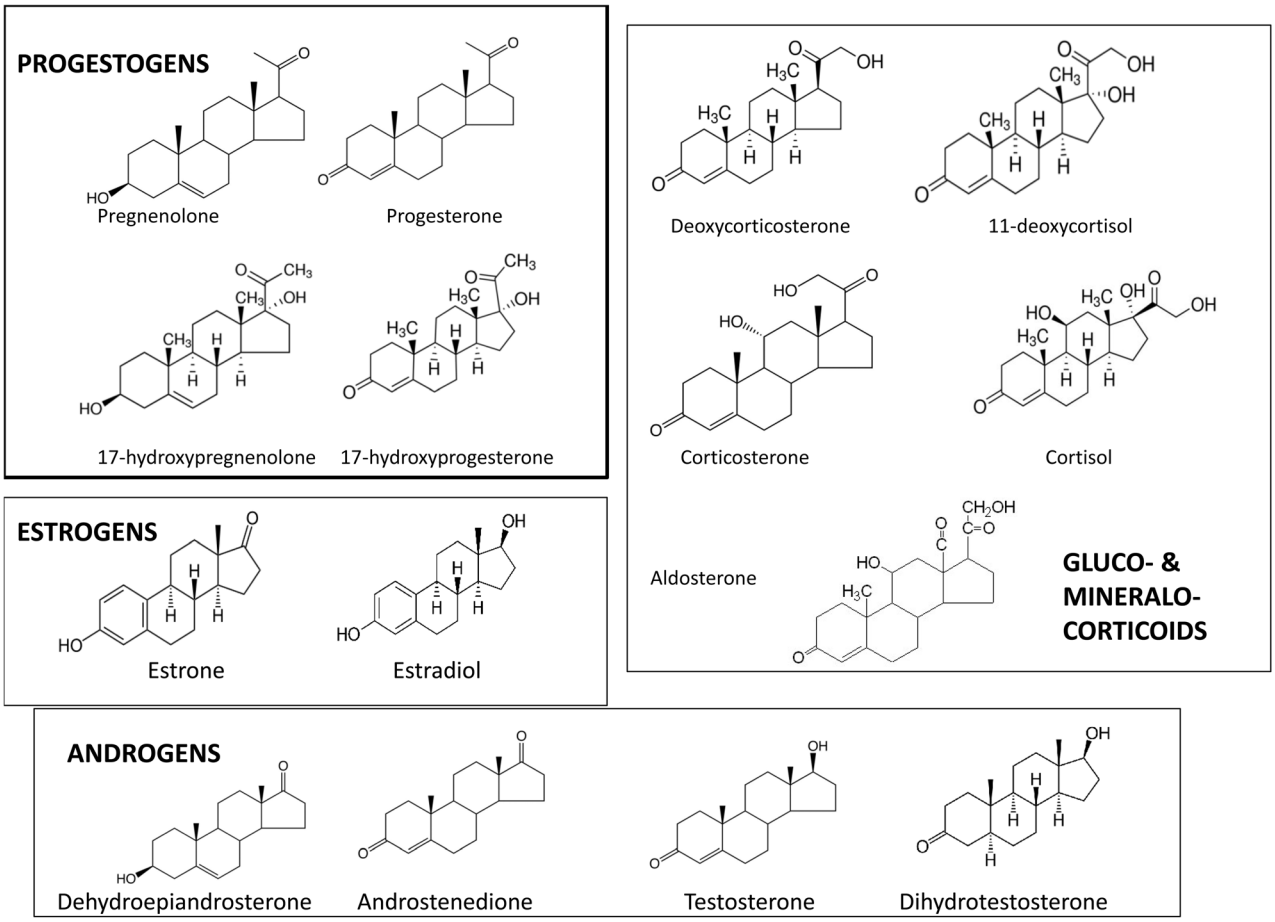


Fig. 5 Classes of steroids based on source and actions. Adrenal cortex synthesises glucocorticoid and mineralocorticoids that affect glucose and electrolyte homeostasis. Oestradiol and progesterone are female hormones produced in the early and late stages of the menstrual cycle. Progesterone then supports pregnancy. Androgens are produced by the adrenal cortex and gonads. Androgens influence male secondary sex characteristics.

than one ligand with varying affinity, and some steroids can activate multiple receptor types.[25] This cross-reactivity challenges the idea that individual steroids can be assigned to strictly defined functional categories. Cortisol binds to the mineralocorticoid receptor (MR) as well as the glucocorticoid receptor (GCR), however in most sites rich in MR, cortisol is inactivated to cortisone through the action of 11β-hydroxysteroid dehydrogenase type 2 (HSD11B2).[26]

The steroid receptors are part of a family of receptors that includes thyroid hormones and vitamin D. Steroids bind to intracellular receptors that act as transcription factors for enzymes, transporters, channels.[27] Steroid binds to the receptor, causing a conformational change that allows it to act as a transcription factor or trigger signaling cascades, resulting in effects on reproduction, the nervous system, and immune modulation. Activation of a steroid receptor (R) leads to physiological responses through genomic signaling (slow, nuclear-mediated gene transcription) and non-genomic signaling (rapid, membrane-associated, and cytoplasmic signaling).

3.2.2. Genomic mechanism (classical pathway). This is the primary mechanism acting over hours or days by modifying gene transcription in 4 stages.

3.2.2.1. Ligand binding and activation. Steroid diffuses through the cell membrane and binds to receptors located in the cytoplasm or nucleus. The steroid receptor is a member of the steroid receptor superfamily, the ER and PR existing primarily in two forms: -A (often acts as a repressor) and R–B (usually a stronger activator).

3.2.2.2. Dimerization and nuclear translocation. Upon steroid binding, the receptor dissociates from chaperone proteins (like heat shock protein [Hsp] 90), undergoes a conformational change, and forms dimers AA, AB, BB.

3.2.2.3. Gene regulation. The dimerized complex translocates to the nucleus, binding to specific DNA sequences known as steroid-responsive elements (REs) in the promoter regions of target genes.

3.2.2.4. Physiological response. This interaction initiates the transcription of target genes, leading to protein formation that causes cellular changes. Gene expression can be regulated indirectly by co-activators and co-repressors that act as accelerators and brakes to gene transcription.

3.2.3. Non-genomic mechanism (rapid signaling). Steroids also have rapid, non-genomic effects through signalling cascades at the cell membranes to affect ion channels, gamma

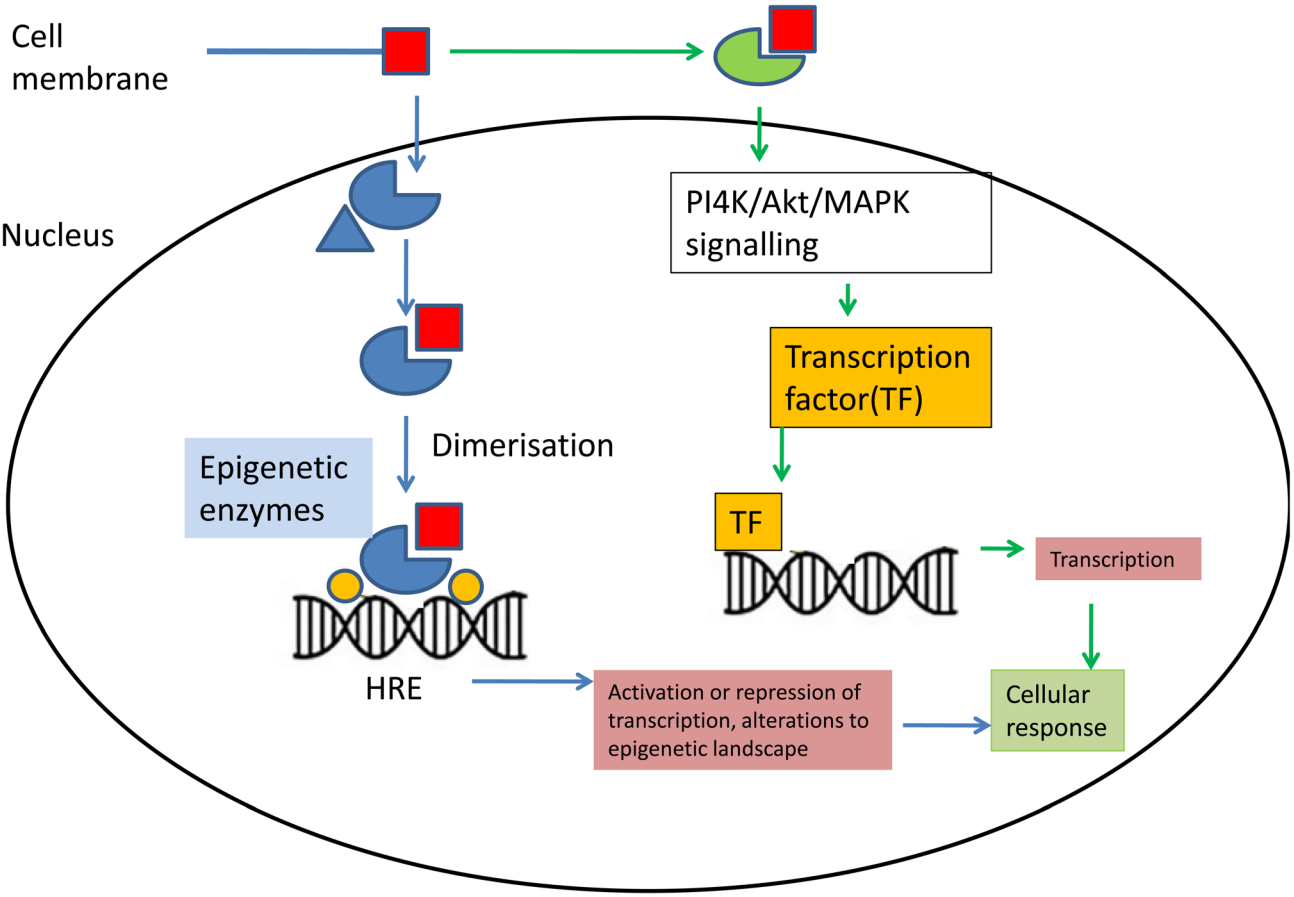
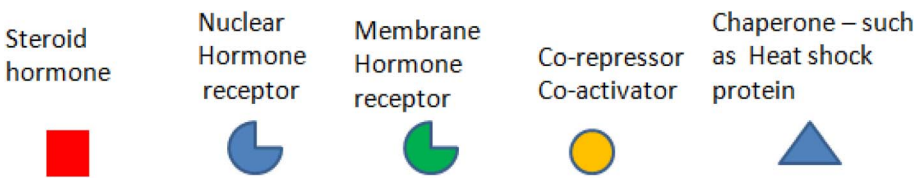


Fig. 6 Steroid hormone signalling. (1) Genomic signalling (blue arrows) – ligand bound hormone receptors bind to hormone response elements (HRE) in the promoters of target genes. Co-activators and co-repressors and epigenetic regulatory enzymes interact with ligand bound nuclear receptors regulating their effect on transcription. (2) Non-genomic signalling (green arrows) – steroid hormones act rapidly with membrane hormone receptors that activate PI3, ASkt and MAPK pathways and downstream transcription factor (TF) signalling pathways.



amino butyric acid (GABA) and *N*-methyl-D-aspartate (NMDA) receptors, kinases, G-protein coupled receptors.[28] These effects occur within seconds to minutes and are often independent of gene transcription.

3.2.3.1. Membrane-bound receptor signaling (mRs). Steroid binds to membrane receptors (mRsα, β, γ), which are G-protein coupled receptors.

3.2.3.2. Cytoplasmic kinase activation. Activated receptors stimulate second messenger signaling pathways, including the activation of the mitogen-activated protein kinases (MAPKs), originally called extracellular signal-regulated kinases (ERKs) or MAPK/ERK pathway, cyclic AMP cyclic adenosine monophosphate/protein kinase A (cAMP/PKA), and phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) pathways.

3.2.3.3. Src kinase interaction. The R can also interact directly with Src kinases (family of protein tyrosine kinases) at the cell membrane, activating signaling cascades that influence cell survival, migration, and rapid tissue responses.

Animal models have proved useful in the studies but are not ubiquitous. Many steroids exhibit pleiotropic and context-dependent effects. Deoxycorticosterone (DOC), for instance, demonstrates both mineralocorticoid and glucocorticoid properties, challenging single-label classifications.[29] Receptor promiscuity, differential gene regulation, and sex-specific responses further complicate action-based naming.

3.3 Regulation-based nomenclature

Steroids are not stored in the endocrine glands but secreted on demand through peptide stimulation and second messengers (Fig. 8). Adrenocorticotrophic hormone ACTH directs synthesis of cortisol. Stress is an important drive to endocrine function.

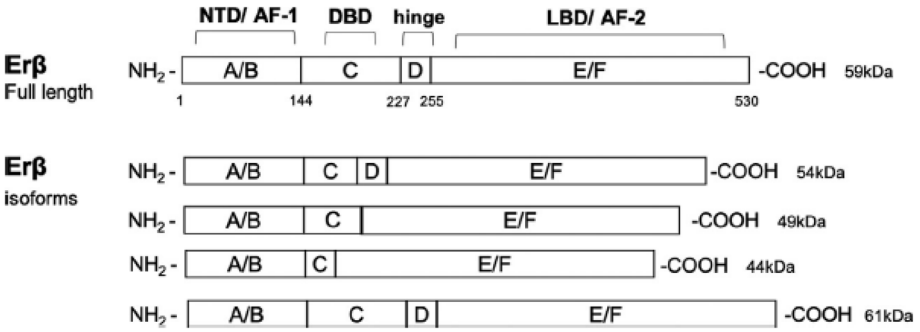


Fig. 7 Schematic for estrogen receptor beta (Erb) isoforms. As in all steroid receptors there are distinct functional domains labelled A to F. A/B N-terminal domain NTD; DBD/C NA binding domain; D hinge and E/F C-terminal region for ligand binding. Composition is unique to each receptor type. The full length Erb is 530 amino acids (59 kDa), truncated shorter forms are 54, 49 and 44 kDa, and an elongated isoform is 61 kDa due to alternative splicing and or alternate translation start sites.

Luteinising and follicle stimulating hormones (LH and FSH respectively, gonadotrophins) determine functions of the testes and ovaries. Nomenclature based on hypothalamic-pituitary regulation (*e.g.*, "gonadotropin-dependent steroids") can shift across developmental stages or disease states. For example, sex steroids produced during minipuberty, puberty, adulthood, pregnancy, and menopause differ substantially in regulatory control, leading to changing functional descriptions.

Aldosterone synthesis is driven by a cascade of peptides from renin release by the juxtaglomerular apparatus of the kidney that in turn releases angiotensin I (Ang 1) from angiotensinogen. The action of angiotensin converting enzyme (ACE) on Ang1 releases angiotensin II to act on the adrenal cortex to release aldosterone thus completing the renin–angiotensin–aldosterone system.

3.4 Metabolic-based nomenclature

Steroids need to be cleared from the body to limit further activity. The liver is the principal organ for inactivation of the steroids and the metabolites are removed in urine, bile and faeces.[30] Reduction of the double bond at C4,5 is known to reduce activity of steroids but overall two phases of steroid metabolism are recognised. The first phase involves reduction, oxidation and hydroxylation whilst the second phase involves conjugation of steroid metabolites with sulphate or glucuronide to reduce hydrophobicity. Steroid metabolites may however retain biological activity or acquire new functions, raising questions about appropriate naming.[9] Pathway-based terms (*e.g.*, 5α-reduced steroids, 11-oxygenated androgens)[14,31] are chemically descriptive but can blur functional categorization when metabolites exert actions distinct from their precursors.

3.5 Application-based nomenclature

In pharmacology and clinical medicine, steroids are named according to therapeutic use (*e.g.*, "corticosteroids," "estrogen therapy," "androgen deprivation therapy"). Here, physiological function and chemical structure may be secondary to clinical context, again generating inconsistencies when compared with biochemical or molecular biological terminology. Steroids were first recognised to be anaesthetics[32] then the benefits of steroids to patients with rheumatoid arthritis started the age of anti-inflammatory actions[33] followed by the use of contraceptives[34] and anti-cancer agents.[35,36]

3.6 Microbial metabolism and the microbiome

The drive to the pharmaceutical industry to produce vast amounts of steroids led to the use of microorganisms to improve on chemical modifications of plant sterols.[37] The identification of steroids in bile and faeces enabled characterisation of steroid modifications by intestinal bacteria.[38–43] The activities were ablated in antibiotic treated animals[44] and spontaneously hypertensive rats.[45] Early work stalled because many of the microorganisms were anaerobic and difficult to culture and classify by chemical tests. This was decades before the microbiome could be identified with genetic techniques[46] and was recognised to have the power greater than the enzymes of the body to influence homeostasis. The microbiome introduces an additional layer of complexity by transforming host steroids into metabolites that may be absorbed and exert systemic effects. Bacterial enzymes—hydroxysteroid dehydrogenases, ketosteroid isomerases, sulfatases, and reductases—generate a diverse array of compounds with variable hormonal activity (Table 2).[47–49] Historically, such metabolites were presumed to lack function.[9] Modern sequencing and metabolomics reveal that many microbial derivatives exhibit endocrine, neuroactive, or immune-modulating actions. As microbiome research expands, clearer conventions are needed to integrate microbial metabolites into steroid nomenclature frameworks.

3.7 Life events and context-dependent nomenclature

Steroid profiles differ markedly across developmental stages and physiological states. Minipuberty, adrenarche, pregnancy, lactation, menopause, and aging each involve distinct regulatory patterns and steroidogenic pathways. Functional nomenclature often shifts with these contexts; a compound termed "androgenic" in one setting may have metabolic or neuroactive relevance in another. Such temporal variability reinforces the need for explicit definition of terms used in publications.

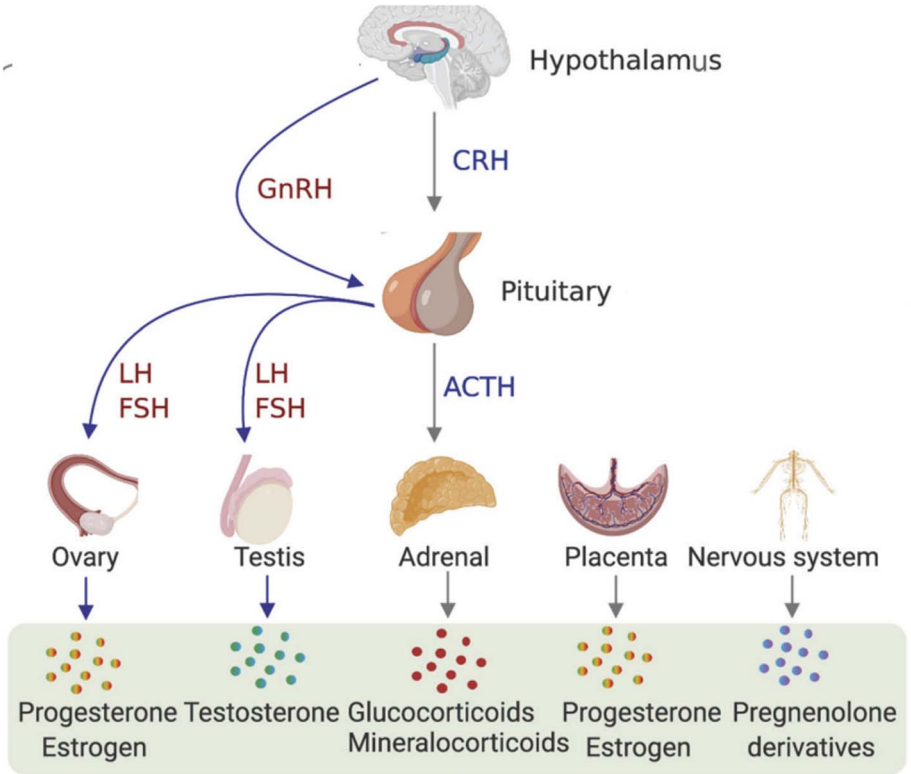


Fig. 8 Regulation of steroid hormone production. The hypothalamus secretes gonadotrophin releasing hormone (GnRH) and corticotrophin releasing hormone (CRH) in response to low concentrations of sex hormones and cortisol respectively. The pituitary gland responds to GnRH to secrete luteinising hormone (H) and follicle stimulating hormone (FSH) that acts on the ovaries or testes. The pituitary responds to CRH with adrenocorticotrophic hormone (ACTH) release that stimulates the adrenal cortex production of cortisol. Aldosterone synthesis is mainly controlled through the release of renin from the kidney and angiotensin production in the circulation.

3.8 Pathological effects and clinical practice

Abnormalities in steroid production can lead to diseases such as Addison's disease, which results from insufficient adrenal hormone production, and Cushing's syndrome, which is caused by excessive glucocorticoid levels. Congenital adrenal hyperplasia (CAH) is another important disorder characterized by defects in steroid biosynthesis enzymes. Clinical nomenclature frequently diverges from biochemical terminology. Terms such as "Cushingoid," "Addisonian," "androgen excess," "disorder of sexual development" and "estrogen deficiency" summarize complex hormonal patterns but do not specify chemical identities. Disorders of steroidogenesis, including CAH through enzyme deficiencies[50,51] and steroid action disorders expressed as androgen insensitivity for instance,[52] introduce additional layers of naming based on pathway disruption rather than chemical structure for estrogens[53,54] and adrenal steroids.[55] Diagnostic conventions often rely on shorthand labels, for example CAH, that must be interpreted within a clinical context. Nomenclature becomes particularly complicated when genetic variants modify enzyme activity or receptor function, generating phenotypes that do not correspond cleanly to established functional categories. CAH due to 21-hydroxylase deficiency can lead to adrenal insufficiency, loss of mineralocorticoid and androgen excess.

The microbiome is beginning to reveal many links with disease processes such as mental health and immunity needing greater clarification.[56–61] The increased power of analytical chemistry with machine learning to process the data in autonomous cortisol seretion,[62] primary aldosteronism,[63] preeclampsia,[64] adrenal tumours,[65] intrahepatic cholestasis,[66] diagnosis CAH,[67] polycystic ovary syndrome[68,69] for example and artificial intelligence to recognise the significance of bone health,[70] skin problems,[71] changes in paediatric growth,[72] infertility,[73] IVF treatment[74] and there will be further important studies in the next few years.

Table 2 Actions on steroids by bacteria in the intestine. The reactions were found to be catalysed by microbial enzymes in the intestinal tract of conventional rats

16α-dehydroxylation, saturation 16,17 double bond
21-dehydroxylation
Hydrolysis of glucuronides
Hydrolysis of sulphates
Saturation of 5,6 double bond
3α and 3β-hydroxysteroid oxidoreduction
11α and 11β-hydroxysteroid oxidoreduction
17β-hydroxysteroid oxidoreduction
20α and 20β hydroxysteroid oxidoreduction

Human-associated bacteria interact with host-produced steroids, but the physiological impact of such interactions remain unclear. Human gut bacteria were shown to convert corticoids into progestins through 21-dehydroxylation, thereby transforming a class of immuno- and metabo-regulatory steroids into a class of sex hormones and neurosteroids.[75] Levels of certain bacterial progestins, including allopregnanolone, are substantially increased in feces from pregnant humans. Allo-pregnanolone is better known as brexanolone, an FDA-approved drug for postpartum depression, the conclusion was that bacterial conversion of corticoids into progestins may affect host physiology, particularly in the context of pregnancy and women's health. The caveat is that cortisol is not excreted in bile.

3.9 Steroids and cancers

Hormone-dependent malignancies—including those affecting the prostate,[76] breast,[77] and ovary[78] highlight the interplay between chemical structure, receptor action, and therapeutic application. Oncology frequently employs nomenclature based on receptor modulation (*e.g.*, selective estrogen receptor modulators, androgen receptor inhibitors),[79–81] which does not necessarily reflect chemical class. The emergence of receptor-modifying drugs, enzyme inhibitors, and novel steroid analogues often yields naming practices that prioritize mechanism of action over structural features. As precision oncology advances, harmonizing chemical and functional terminology becomes increasingly important for accurate reporting and interpretation of clinical studies.

3.10 Pharmacological relevance

Steroids have extensive clinical applications due to their potent biological effects. Synthetic corticosteroids are widely used as anti-inflammatory and immunosuppressive agents in the treatment of conditions such as asthma, autoimmune diseases, and allergic reactions. Hormone replacement therapies involving estrogens, progesterone, or testosterone are used to treat hormonal deficiencies and certain endocrine disorders.

Synthetic anabolic steroids, which mimic the effects of androgens, have legitimate medical uses in certain conditions but are also widely abused to enhance athletic performance and physical appearance. Such misuse can lead to serious health consequences, including cardiovascular disease, liver damage, and hormonal imbalance.

The complexity of steroid biology has significant implications for pharmacology. Synthetic steroids are widely used in medicine, particularly as anti-inflammatory and immunosuppressive agents.[82] However, the structural similarity between different steroid hormones often leads to unintended receptor interactions and adverse side effects. For example, synthetic glucocorticoids may produce mineralocorticoid-related effects such as sodium retention and hypertension if they interact with mineralocorticoid receptors.[83] Conversely, attempts to design receptor-specific steroid analogues have demonstrated that achieving complete selectivity is challenging due to overlapping receptor binding properties.

Modern pharmacological approaches increasingly focus on selective receptor modulators and tissue-specific steroid analogues in order to minimize systemic side effects while maintaining therapeutic efficacy.[25] These strategies highlight the importance of understanding steroid function within complex biological networks rather than relying solely on traditional classification systems.

4. Emerging perspectives in steroid research

Advances in steroidomics and systems biology are transforming the understanding of steroid metabolism and signalling. High-resolution analytical techniques now allow researchers to identify large numbers of steroid metabolites and map their interactions within metabolic networks.[55] These findings suggest that steroids should be viewed as components of dynamic biochemical systems rather than isolated hormone classes. Furthermore, the growing recognition of intracrine and paracrine steroid signalling challenges the traditional view that steroid hormones act primarily through endocrine mechanisms.[84] Future classification systems may therefore need to incorporate metabolic pathways, receptor interactions, and tissue-specific regulation in order to provide a more comprehensive framework for understanding steroid biology.[85]

5. Conclusions

Steroids represent a structurally diverse and biologically important class of molecules derived from cholesterol. Their classification can be understood from both chemical and functional perspectives, reflecting differences in molecular structure and physiological activity. Chemically, steroids include sterols, bile acids, steroid hormones, and secosteroids, each distinguished by specific structural modifications. Functionally, the steroid hormones encompass glucocorticoids, mineralocorticoids, and sex hormones, as well as neurosteroids with specialized roles in the nervous system.

A comprehensive understanding of steroid classification provides important insights into their physiological functions and clinical applications. Continued research in steroid biochemistry and endocrinology is likely to reveal new mechanisms of action and therapeutic opportunities for steroid-based treatments. Chemical and functional classifications of steroids have historically provided valuable frameworks for understanding the structural diversity and physiological roles of these molecules. Chemical classification highlights structural relationships and biosynthetic pathways, whereas functional classification emphasizes endocrine activity and physiological effects. However, growing evidence from molecular endocrinology, receptor biology, and metabolomics indicates that steroid signalling is more complex than these traditional categories suggest. Many steroids exhibit overlapping functions, and tissue-specific metabolism can significantly alter their biological effects.

As research continues to reveal the complexity of steroid networks, more integrative classification approaches that incorporate metabolic pathways, receptor interactions, and tissue-specific regulation will likely become increasingly important for advancing both basic research and clinical applications.

Steroid nomenclature spans chemical, functional, regulatory, metabolic, and clinical systems, each valid within its own domain but potentially confusing when used inconsistently. Advances in molecular biology, receptor characterization, microbiome science, and clinical therapeutics have broadened the range of contexts in which steroids are studied, revealing numerous situations in which traditional nomenclature is ambiguous or inadequate. A comprehensive understanding of steroid classification provides important insights into their physiological functions and clinical applications. Continued research in steroid biochemistry and endocrinology is likely to reveal new mechanisms of action and therapeutic opportunities for steroid-based treatments.

To promote clarity in scientific communication, authors should explicitly define all nomenclature systems used, especially when combining chemical and functional terms. Authors should state the context in which functional names are applied (physiological, developmental, pathological, or microbial). Clinical or historical terms should be avoided when precise chemical naming is essential. Metabolites and analogues should be clearly identified, specifying whether nomenclature reflects structure, origin, or action. Steroids should be acknowledged to exhibit overlapping or divergent activities, particularly when a single term may be misleading.

In conclusion, consistent and well-defined nomenclature enhances interdisciplinary communication, supports reproducibility, and ensures accurate interpretation of findings across the diverse fields that study steroid biology.

Author contributions

The author is responsible for conceptualization, reviewing, writing and editing of the review. A draft was refined with the help of ChatGP.

Conflicts of interest

The author declares no conflict of interest.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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