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SYNTHETIC DEVELOPMENT IN NITROGEN CONATAINING STEROIDS AZA D HOMOANDROSTENE SYSTEMS

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Abstract- Steroids that contain nitrogen atoms are referred to as aza-steroids; this category of bioactive molecules is an important group with many therapeutic uses (anticancer and enzyme inhibitors). Of the many different types, aza-D-homo-androstene systems have been of particular interest due to the modification of the D-ring of the steroid by replacing carbon atoms in the ring with nitrogen atoms and/or expanding the D-ring and these modifications increased their biological activity and receptor selectivity. In this article, we will review methods developed to make aza-D-homoandrostene derivatives. The methods discussed include the transformation of 17-keto steroids, techniques for expanding the rings, cyclization methods, and including a heterocycle. We will also discuss some of the current synthetic techniques, including Nazarov-type cyclization, aza-diels-alder reactions, and functionalization at C-17. These aza-D-homoandrostene derivatives have demonstrated biological activity as 5 alpha-reductase inhibitors, antiandrogens, and anticancer agents. This article discusses their biological activity and summarizes recent advances and future directions for nitrogen-containing steroidal frameworks.

Keywords: Aza-steroids; D-homoandrostene; nitrogen-containing steroids; steroid synthesis; ring expansion; 17-aza steroids; heterocyclic steroids; medicinal chemistry

I. INTRODUCTION

One of the most important classes of both synthetic and natural organic compounds are called "steroids" (steroid compounds). Steroids are found throughout nature (in humans, and animals, in plants, and all types of microorganisms) and have a variety of unique functions, but they are all similar structurally because they all contain the same general chemical backbone - a cyclopentanoperhydrophenanthrene (also called "phenanthrene"), with A-B-C three fused 6 membered rings and D, 1 five membered ring. Steroids are chemically similar to each other because of the rigidity of their primary chemical structure (the very rigid primary steroids can serve as a platform for substituent groups to be added onto). Steroids are involved in multiple physiologic processes, such as metabolism; inflammation; the immune response; as well as stimulating or regulating reproduction. Examples of naturally occurring steroids, including cholesterol, steroid hormones (testosterone and estrogen), and bile acids, have received considerable research attention due to their physiologic importance and the therapeutic agents derived from them.[1]

In the past few decades, there have been considerable efforts directed toward modifying the steroid nucleus in order to increase biological activity, increase the pharmacokinetic properties of the drug, and decrease the number of side effects. One of the most productive methods that have been used in steroid chemistry to date is the incorporation of a heteroatom into the steroid core structure. A class of heteroatom-modified anabolic steroids, would be those containing one or more nitrogen heteroatoms in place of a number of carbon-derived steroidal nuclei and referred to as aza-steroids; these molecules are structurally similar (but not identical) to the parent steroids. Thus, aza-steroids provide medicinal chemists access to steroids with unique electronic characteristics and increased binding to targets within biological systems. The introduction of nitrogen into the steroid structure will frequently provide enhanced solubility, increased binding of drugs to enzymes/receptors, and provide an additional means for forming hydrogen bonds; therefore, resulting in pharmacological compounds with improved pharmacologic activities.

Steroid compounds with nitrogen atoms (azasteroids) can exert many biological activities such as: antiandrogenic,

anticancer, antimicrobial; anti-inflammatory; and inhibition of various enzymes. A considerable body of work has been done examining the potential of azasteroid compounds to be used as inhibitors of both 5α-reductase and aromatase, two critical enzymes in the regulation and biosynthesis of steroid hormones. Inhibition of these enzymes is a potential therapeutic strategy to treat benign prostatic hyperplasia (BPH), prostate cancer and hormone-dependent disorders. The success of currently available clinical agents containing nitrogen-based steroid scaffolds has further stimulated research on new azasteroids to develop additional therapeutic options.[2]

Steroids can undergo several types of modifications to alter their structure; one specific type of modification that alters their biological function are those which modify the structure of the D ring of the steroid (the smallest and most deformable ring in the steroid nucleus). The D ring is particularly susceptible to modification through ring expansion, ring contraction and heteroatom incorporation. An example of a class of steroids modified through this method are called D-homo steroids, where the five-membered D ring is modified to create a six-membered D ring. These modifications can radically change the conformation of a steroid and possibly lead to an increase in biological activity. When an Aza-D-homoandrostene system has nitrogen included in the six-member D-ring then these new structures are called Aza-D-homoandrostene systems.

Aza-D-homoandrostene derivatives that include a nitrogen atom in the expanded D-ring of the androstane steroid skeleton is an interesting subclass of nitrogen containing steroids. These compounds share characteristics from both the aza steroid series and the D-homo steroid series and thus have different physicochemical and biological properties. Nitrogen located within the D-ring can serve as a synthesizing agent to produce lactams or other heterocycles that may serve as critical pharmacophores within the context of drug discovery. Furthermore, modification to the D-ring can alter the orientation of the C-17 functional groups that could also influence how the compound interacts with biological targets including enzymes or receptors.[3]

The generation of Aza-D-homoandrostene systems is a research focus because of their diverse pharmacological potential. There have been many different methods to produce these very complex molecules

either via reactions involving expansion of rings, rearrangements, cyclizations and also via heterocyclic formation reactions. Traditional synthetic pathways to form the D-ring via expansion include the Beckmann rearrangement of steroidal oximes and Baeyer– Villiger oxidations, both of which have been used extensively. However, new synthetic techniques including aza-Diels–Alder reactions, intramolecular cyclisation and transition metal-catalysed reactions provide for greater efficiency and versatility when introducing nitrogen atoms into the steroid structure.[4]

The addition of nitrogen with the steroid nucleus substantially changes the chemical structure and influences biological activity of these types of compounds. For example, aza-D-homoandrostene derivatives have been shown to inhibit 5α-reductase, an enzyme that converts testosterone to its more active form dihydrotestosterone (DHT); therefore, this is a major mechanism for developing therapies for conditions related to excess testosterone levels such as benign prostatic hyperplasia and androgenic alopecia. In addition to their ability to inhibit 5α-reductase, other nitrogen-containing D-homo-steroids have been shown in pre-clinical cancer studies to have significant anti-cancer activity against a variety of tumor lines and these effects are likely a result of these compounds interfering with cell growth processes, triggering cell death and affecting hormone-receptor signaling pathways.[5]

Over the past few years, new methods of synthetic organic chemistry using computers have greatly increased the speed at which nitrogen-steroid compounds can be developed. Due to the availability of information from molecular modelling and structure-activity relationship (SAR) studies, we have learned a lot about how these compounds interact with bioligical receptors and we are able to accentuate the rational design of more potent or selective derivatives of nitrogen-steroid compounds. Lastly, the development of green and sustainable synthetic methods has become increasingly important for producing steroidal compounds, thereby reducing their environmental impact while increasing production efficiency.[6]

While great strides have been made on synthesizing Aza-D-homoandrostene systems, their challenging nature comes from the complex structure of steroids, and the need for regio- and stereoselective conversions. As such, improvements in synthetic methods and understanding of

the mechanisms involved in chemical reactions will allow for the rapid development of many new compounds that possess greater therapeutic value.[7]

II. STRUCTURAL FEATURES OF AZA-D-HOMOANDROSTENE SYSTEMS

The azasterone series of steroid molecules are chemically modified psychoactive pharmaceutical agents that fall into the nitrogen category of steroid compounds based on the presence of bonds formed from negative atoms. The most prevalent alteration done to the azasterone series occurs by adding a nitrogen atom to the A, B, or C rings, or extending and expanding the size of the D-ring occurs. All classes of azasterone are recognized as an example of classic steroid molecules that have been chemically altered and whose affinity for their biological targets has remained intact despite having undergone total modification.

2.1 Incorporation of Nitrogen Atom(s)

The presence of nitrogen atoms in the steroid skeleton is a defining feature in Aza-D-homoandrostene systems. The incorporation may occur in several ways:[9,8]

- Within the ring structure, nitrogen may be directly incorporated in the D-ring via ring expansion resulting in the formation of heterocycles such as imines, lactams and piperidines .
- Substitution of nitrogen as a substituent at the C-17 position may include its incorporation as an amino group (NH2), an amide group (C=O-NH2), a hydrazone group (N=NH2) or an imine group (C=N).
- With the use of advanced derivatives, multiple nitrogen atoms can be added to produce fused heterocycles or polyhalogenated steroids possessing multiple nitrogen substituents.

Effect of Nitrogen Incorporation

The presence of nitrogen significantly alters the electronic and chemical behavior of the molecule:[10]

- Increases basicity and protonation ability
- Enhances hydrogen bonding capacity (both donor and acceptor)
- Modifies dipole moment and polarity

- Improves aqueous solubility compared to non-aza steroids

2.2 Expansion of the D-Ring (D-Homo Modification)

A five-membered cyclopentane Ring is the D-ring in natural androstane steroids; the D-Ring in Aza-D-homoandrost-ene Systems is expanded to a six-membered ring by synthetic transformations. Typical synthetic Transformations used to Expand the D-Ring to a Six-Membered Ring are the Beckmann Rearrangement and Baeyer-Villiger Oxidation.[12,11]

Consequences of D-Ring Expansion[13]

- Formation of six-membered heterocycles (often lactams or amines)
- Increased conformational flexibility
- Alteration in stereochemistry at C-17
- Change in spatial orientation of substituents

2.3 Retention of Androgenic Steroid Backbone

Despite significant modifications in the D-ring, the A, B, and C rings of the steroid nucleus remain largely unchanged. This preservation is crucial because:[14]

- It maintains the rigid steroidal framework necessary for biological recognition
- Ensures compatibility with androgen receptors
- Preserves lipophilicity required for membrane permeability

Thus, Aza-D-homoandrostene systems combine structural novelty with biological familiarity, making them highly effective pharmacophores.

2.4 Conformational and Stereochemical Considerations

The biological activity of steroidal compounds is highly dependent on their three-dimensional shape. In Aza-D-homoandrostene derivatives:[16,15]

- Ring expansion alters the overall molecular geometry
- Nitrogen incorporation affects bond angles and hybridization
- Substituents at C-17 may adopt different axial/equatorial orientations

2.5 Electronic and Physicochemical Modifications

The introduction of nitrogen and D-ring expansion leads to important changes in physicochemical properties:[18]

- **Lipophilicity (Log P):** Generally reduced due to nitrogen presence
- **pKa values:** Modified, affecting ionization at physiological pH
- **Molecular polarity:** Increased, improving interaction with polar binding sites
- **Metabolic stability:** Often enhanced due to resistance to enzymatic degradation

2.6 Structural Variations in Aza-D-Homoandrostene Systems

A wide variety of structural analogs can be generated based on the position and type of nitrogen incorporation:[19]

- **17-Aza steroids:** Nitrogen substituted at C-17
- **Lactam-containing D-homo steroids:** Nitrogen incorporated within expanded ring
- **Imino and hydrazone derivatives:** Featuring C=N linkages
- **Fused heterocyclic systems:** Additional rings attached to D-ring

2.7 Impact on Biological Target Interaction

The structural modifications in Aza-D-homoandrostene systems significantly influence their interaction with biological targets:[20]

- Enhanced binding to 5α-reductase enzyme, inhibiting conversion of testosterone to dihydrotestosterone
- Improved affinity for androgen receptors, enabling antiandrogenic activity
- Ability to interact with aromatase and other steroidogenic enzymes

2.8 Structure–Activity Relationship (SAR) Perspective [21]

From a SAR viewpoint:

- **Nitrogen at D-ring** → increased enzyme inhibition
- **Ring expansion** → better receptor accommodation
- **C-17 modification** → critical for potency and selectivity

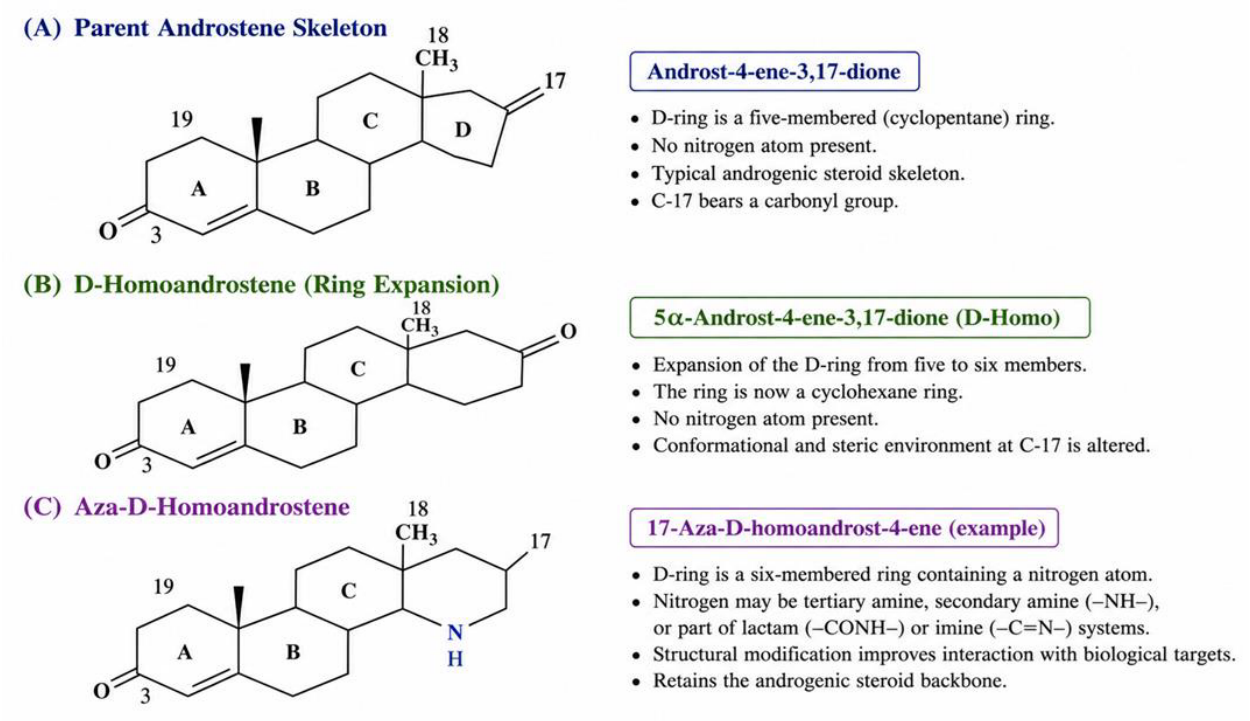

Figure 1: Structural Representation of Aza-D-Homoandrostene Systems Showing (A) Parent Androstene Skeleton, (B) D-Homoandrostene (Ring Expansion), and (C) Aza-D-Homoandrostene [24,23, 22]

III. SYNTHETIC APPROACHES

A significant amount of interest has focused on the preparation of Aza-D-homoandrostene analogues. This is due mainly to the potential for these compounds to serve as important drugs. As such, there have been numerous traditional and/or modern methods described in the literature that can be used to introduce nitrogen into the steroid framework and to expand the steroid D-ring system, several of which will be mentioned here.

3.1 Synthesis from 17-Keto Steroids

Naturally occurring 17-keto steroids such as androst-4-ene-3,17-dione have emerged as the most widely used and feasible means of synthesizing nitrogen-containing steroids using carbonyl (C) groups (C-17) as intermediates. The reactivity of the carbonyl group at C-17 makes it ideally suited for this application.[25]

The conversion of the 17-carbonyl group of steroid intermediates into nitrogen-containing intermediates (e.g., imines, oximes, amides, hydrazones, etc.), is the first step in synthesizing nitrogen-containing steroids. The conversion of the

carbonyl group is accomplished by means of condensation reactions.[26]

Upon preparation of nitrogen-containing intermediates, the intramolecular cyclization reactions are used to introduce nitrogen into the D-ring of the steroid. Among the transformations performed while carrying out the above pathway is the conversion of oximes to amides through Beckmann rearrangements.[27]

Artificial new methodologies for selectively functionalizing C17 and C20 sterols with nitrogen containing substituents have also recently improved this technique. With the use of modern catalysts and milder reaction conditions, these synthetic processes generate greater yields, selectivities, and scalability. [28]

3.2 Ring Expansion to D-Homo Steroids

The ring expansion process is one of the major stages in the synthesis of derivatives based on the 17-aza-D-homo-androstene ring expansion. In most organisms, the D-ring of steroid compounds contains a cyclopentane with five carbon atoms. There are several different chemical methods available for converting this cyclopentane into a cyclohexane containing six carbon atoms (i.e., from five to six carbons).[29]

The most commonly used methods include:

- **Baeyer–Villiger oxidation**, which introduces an oxygen atom and facilitates ring expansion via ester or lactone intermediates
- **Beckmann rearrangement of oximes**, leading to the formation of cyclic amides (lactams) containing nitrogen
- **Direct lactam formation**, where nitrogen is incorporated simultaneously with ring expansion

Formation of six-membered heterocyclic rings via these reactions occurs, most commonly in the form of a lactam, and results in D-homo-steroids containing nitrogen \(\text{N} \) within their structure. Steroid biological activity and physical conformation are greatly affected because of this modification of structure.[30]

3.3 Nazarov-Type Cyclization

Recent advancements in synthetic organic chemistry have introduced Nazarov-type cyclization as an efficient method for constructing nitrogen-containing D-homo steroid systems.[31]

This approach typically involves:

- Formation of allylic alcohol or dienone intermediates
- Activation under strong acidic conditions (e.g., triflic acid)
- Intramolecular cyclization leading to ring expansion and nitrogen incorporation

Nazarov-type cyclization offers several advantages, including:[32]

- High reaction efficiency and selectivity
- Ability to construct complex ring systems
- Formation of 6-azasteroid derivatives in good yields

This method is particularly useful for synthesizing structurally complex and highly functionalized steroidal frameworks.

3.4 Aza-Diels–Alder Reaction

The aza-Diels–Alder reaction is an important synthetic tool for the construction of nitrogen-containing heterocycles within steroid systems. This reaction involves a [4+2] cycloaddition between a diene and an imine (acting as the dienophile).[33]

Key features of this method include:

- Efficient incorporation of nitrogen atoms into cyclic structures
- Formation of six-membered heterocycles fused with the steroid nucleus
- High stereoselectivity and regioselectivity

3.5 Functionalization at C-17 Position

The C-17 position of the steroid nucleus is one of the most reactive and strategically important sites for chemical modification. Introduction of nitrogen at this position leads to the formation of various biologically active derivatives.[34]

Common modifications include:

- **17-aza steroids** (direct nitrogen substitution)
- **Amide and hydrazide derivatives**
- **Heterocyclic substitutions** involving nitrogen-containing rings

Substantial effects of these modifications on the compounds' biological activity and receptor binding affinity have been found. Modification by the C-17 functionalized nitrogen in steroid compounds results in the development of more active inhibitors of various enzymes, including 5α-reductase and aromatase.[35]

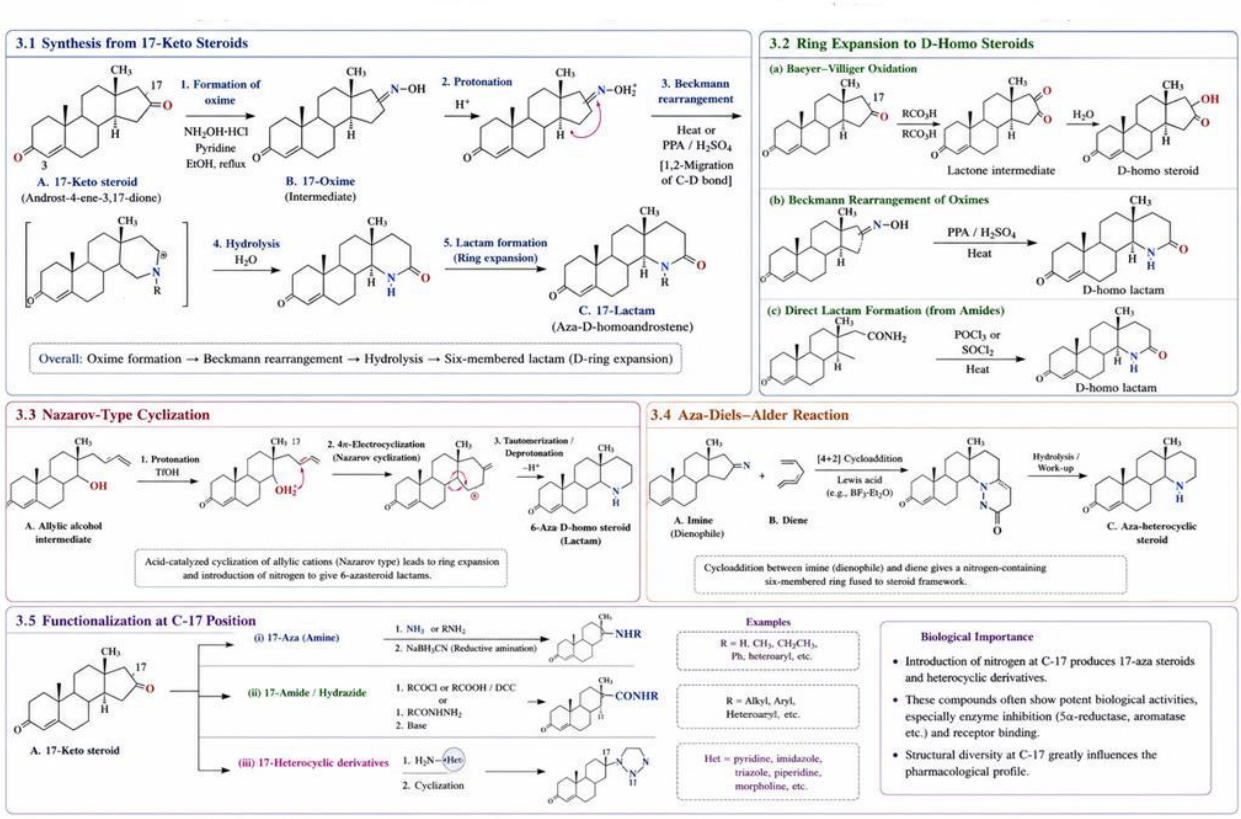

Figure 2: Reaction Mechanisms for the Synthesis of Aza-D-Homoandrostene Systems via 17-Keto Steroids, Ring Expansion, Nazarov Cyclization, Aza-Diels–Alder Reaction, and C-17 Functionalization [38,37, 36]

IV. BIOLOGICAL SIGNIFICANCE

Aza-D-homoandrogens derivatives have many pharmacological effects resulting from both their nitrogen content within their chemical structure and potential modification in the D-ring of the steroid. Improving their capacity to bind to the enzymes and receptors that participate in the metabolism of steroids makes these compounds good candidates for future therapeutic use for a number of reasons. Below is a summary of the major actions/activities of these compounds.[39]

Table 1: Biological Activities of Aza-D-Homoandrostene Derivatives [40,41]

S. No.	Biological Activity	Mechanism of Action	Pharmacological Significance
1	**5α-Reductase Inhibition**	Inhibits the enzyme 5α-reductase, preventing the	Useful in the treatment of benign prostatic hyperplasia

		conversion of testosterone into dihydrotestosterone (DHT)	(BPH), androgenic alopecia, and prostate disorders
2	**Anticancer Activity**	Induces apoptosis, inhibits cell proliferation, and interferes with cancer cell signaling pathways	Potential use in the treatment of hormone-dependent and non-hormone-dependent cancers
3	**Antiandrogenic Activity**	Binds to androgen receptors and blocks androgen-mediated biological responses	Effective in treating androgen-dependent diseases such as prostate cancer and hirsutism
4	**Antimicrobial Activity**	Disrupts microbial cell membranes or inhibits essential microbial enzymes	Useful against bacterial and fungal infections
5	**Anti-inflammatory Activity**	Inhibits inflammatory mediators and cytokine production	Helps in reducing inflammation in chronic diseases
6	**Antioxidant Activity**	Scavenges free radicals and reduces oxidative stress	Protects cells from oxidative damage and related disorders

V. RECENT ADVANCES

In recent times, researchers have focused their attention on developing new compounds that utilize various functional groups on the nitrogen-based steroid skeleton (including Aza-D- and D-homoandrostene systems). These compounds represent a novel class of steroid-like substances and will increase the number of possible applications for these molecules within medicinal chemistry.[42] The introduction of additional nitrogen heterocycles fused or added to the nitrogen base steroid skeleton will lead to a greater range of structurally diverse compounds, as well as provide for increased pharmacological activity due to enhanced binding affinity and selectivity.[43]

The design of target-specific drugs such as the CYP17 inhibitors, which are used to block the production of enzymes needed to produce the male hormones (androgens), is an important area of development. By modifying the Aza-steroid structure, researchers have improved the effect of these drugs by accurately targeting the

active site on Enzymes and reducing their side effects. There have been positive results with this approach in treating men's hormone-dependent cancer (prostate cancer). [44]

Furthermore the new Synthetic Chemistry Processes have resulted in an increase in efficiency and selectivity for the Synthetic Chemical Pathway from Natural Products to Synthetic Products as Primary Sources.[45] These Techniques Include: Catalytic Reactions, Microwave-Assisted Synthesis and Green Chemistry Techniques; all of which are responsible for facilitating the Production of a range of Steroidal Derivatives that exhibit considerably larger Yields; reduced Timescales for Completion of Synthesis and greater Regio- and Stereoselectivity when Compared with their Predicted Value.

Furthermore, computational methods such as molecular docking and structure-activity relationships (SAR) have transformed how we develop and optimize chemical compounds through logically designing more biologically active compounds based on useful information provided about the interactions of drugs to their targets. In summary, these latest advancements have made it faster than ever to identify and synthesize new aza-D-homoandrostene derivatives with greater therapeutic potential than previously available.[46]

VI. FUTURE PERSPECTIVES

In the future, research on nitrogen steroids, specifically Aza-D-homoandrostene systems, will focus on developing more effective, more selective, and greener synthetic methods. As an example, greener synthetic methods would include such strategies as solventless reactions; using green reagents; energy-efficient synthetic methods (microwave- or ultrasound-assisted) to produce steroids with high yields and selectivity while limiting their resulting environmental effects.[47]

The production method for hybrid/better drugs continues to develop as new technology emerges for creating improved multifunctional steroidal agents. Innovative scientists create drugs that both improve and multiply their therapeutic targets through combining several different active ingredients along with combining different types of cyclic structure (i.e., 5- & 6-membered rings). These innovative drugs will reduce or prevent resistance patterns seen with traditional drugs and simultaneously improve overall outcomes through the use of new delivery systems.[48]

In addition, new drug delivery methods, such as transdermal systems, liposomal formulations and nanoparticle-based methods will provide significant improvements to the potential therapeutic benefits of aza-steroids by increasing effectiveness (site-specific), reducing systemic toxicity, and improving bioavailability.[49, 50]

VII. CONCLUSION

Aza-D-homoandrostene compound systems are an emerging class of steroid-like nitrogen-containing compounds that have a lot of potential in drug design. They can be produced via several large-scale synthetic approaches including ring-expansion and cyclization processes, as well as by attaching functional groups to the 17-position of the steroid backbone. Due to their diverse pharmacological properties, many of which relate to enzyme inhibition and anti-cancer activity, they are highly suitable as therapeutic agents. Continued advancements in both synthesis and structure-based drug development should continue to broaden the contribution of aza-D-homoandrostene compounds to the development of new and effective steroid-based drugs.

REFERENCES

[1] Abdelhalim, M. M., Kamel, E. M., Rabie, S. T., & Mohamed, N. R. (2011). Synthesis and biological evaluation of some nitrogen containing steroidal heterocycles. Steroids, 76(1-2), 78-84.

[2] ZDERIC, J. A., CARPIO, H., & LIMÓN, D. C. (1962). Steroids. CLXXXI. 1 11a-Aza-and 11a-Oxa-C-homo Steroidal Hormone Analogs. The Journal of Organic Chemistry, 27(4), 1125-1129.

[3] Zderic, J. A., & Iriarte, J. (1962). Steroids. CLXXVIII. 1 9a-Aza-C-homo Steroids. The Journal of Organic Chemistry, 27(5), 1756-1760.

[4] Thomas, C. (1992). Synthetic approaches to anti-hormonal steroids (Doctoral dissertation, City, University of London).

[5] Ajduković, J. J., Gaši, K. M. P., Jakimov, D. S., Klisurić, O. R., Jovanović-Šanta, S. S., Sakač, M. N., ... & Djurendić, E. A. (2015). Synthesis, structural analysis and antitumor activity of novel 17α-picolyl and 17 (E)-picolinylidene A-modified androstane derivatives. Bioorganic & Medicinal Chemistry, 23(7), 1557-1568.

[6] Akhrem, A. A., & Titov, Y. A. (1970). Total Syntheses from CD Fragments. In Total Steroid Synthesis (pp. 243-307). Boston, MA: Springer US.

[7] Tremblay, M. R., Lescarbeau, A., Grogan, M. J., Tan, E., Lin, G., Austad, B. C., ... & Castro, A. C. (2009). Discovery of a potent and orally active hedgehog pathway

antagonist (IPI-926). Journal of medicinal chemistry, 52(14), 4400-4418.

[8] Casy, A. F., & Dewar, G. H. (1993). Ligands of Nicotinic Cholinergic Receptors (nAChR) Including Neuromuscular Blocking Agents. In The Steric Factor in Medicinal Chemistry: Dissymmetric Probes of Pharmacological Receptors (pp. 327-365). Boston, MA: Springer US.

[9] JAWAD, F. H. (1969). Synthesis and Evaluation of Some 4-AZA-20 Alpha-aminopregnanes as Antimicrobial Agents. The University of Mississippi.

[10] Tsuda, K., & Hayatsu, R. (1956). Cholesterol and related compounds. V. Synthesis of aza-D-homosteroids. Journal of the American Chemical Society, 78(16), 4107-4111.

[11] Huisman, H. O. (1971). Approaches to total synthesis of heterocyclic steroidal systems. Angewandte Chemie International Edition in English, 10(7), 450-459.

[12] Lovett, J. A., Darby, M. V., & Counsell, R. E. (1984). Synthesis and evaluation of 19-aza-and 19-aminoandrostenedione analogs as potential aromatase inhibitors. Journal of medicinal chemistry, 27(6), 734-740.

[13] Krojer, M., Keller, M., & Bracher, F. (2013). 7-Aza-des-A-steroids with antimicrobial and cytotoxic activity. Scientia Pharmaceutica, 81(2), 329.

[14] Biellmann, J. F. (2003). Enantiomeric steroids: synthesis, physical, and biological properties. Chemical reviews, 103(5), 2019-2034.

[15] Xie, W., Peng, H., Kim, D. I., Kunkel, M., Powis, G., & Zalkow, L. H. (2001). Structure–activity relationship of Aza-steroids as PI-PLC inhibitors. Bioorganic & medicinal chemistry, 9(5), 1073-1083.

[16] Bansal, R., & Suryan, A. (2022). A comprehensive review on steroidal bioconjugates as promising leads in drug discovery. ACS bio & med Chem Au, 2(4), 340-369.

[17] Hasserodt, J., Janda, K. D., & Lerner, R. A. (2000). A class of 4-aza-lithocholic acid-derived haptens for the generation of catalytic antibodies with steroid synthase capabilities. Bioorganic & medicinal chemistry, 8(5), 995-1003.

[18] Mesa, D., Augusto, Y. E., Hernández, G., Figueroa-Macías, J. P., Coll, F., Olea, A. F., ... & Espinoza, L. (2023). The Synthesis of Novel aza-Steroids and α, β-Unsaturated-Cyanoketone from Diosgenin. Molecules, 28(21), 7283.

[19] Lawrence, A. K., & Gademann, K. (2008). Aza-annulation strategies in alkaloid total synthesis. Synthesis, 2008(03), 331-351.

[20] Lourdusamy, M., Côté, J., Laplante, S., Labrie, F., & Singh, S. M. (1997). Synthesis and in vitro study of 17β-[N-ureylene-N, N′-disubstituted]-4-methyl-4-aza-5α-androstan-3-ones as selective inhibitors of type I 5α-

reductase. Bioorganic & Medicinal Chemistry, 5(2), 305-310.

[21] Tanimoto, H., & Kakiuchi, K. (2013). Recent applications and developments of organic azides in total synthesis of natural products. Natural product communications, 8(7), 1934578X1300800730.

[22] Uhle, F. C. (1961). The Synthesis of Azaoxaspirane Steroid Alkaloids1. Journal of the American Chemical Society, 83(6), 1460-1472.

[23] Vlattas, I. (1966). Studies in steroids and alkaloids (Doctoral dissertation, University of British Columbia).

[24] Huang, L. H., Wang, Y. G., Xu, G., Zhang, X. H., Zheng, Y. F., He, H. L., ... & Liu, H. M. (2011). Novel 4-azasteroidal N-glycoside analogues bearing sugar-like D ring: synthesis and anticancer activities. Bioorganic & medicinal chemistry letters, 21(20), 6203-6205.

[25] Varricchio, F., Doorenbos, N. J., & Stevens, A. (1967). Effect of azasteroids on gram-positive bacteria. Journal of bacteriology, 93(2), 627-635.

[26] Huo, H., Li, G., Shi, B., & Li, J. (2022). Recent advances on synthesis and biological activities of C-17 aza-heterocycle derived steroids. *Bioorganic & Medicinal Chemistry, 69*, 116882. https://doi.org/10.1016/j.bmc.2022.116882

[27] Sharma, K., Kumar, H., & Priyanka. (2023). Formation of nitrogen-containing six-membered heterocycles on steroidal ring system: A review. *Steroids, 191*, 109171. https://doi.org/10.1016/j.steroids.2022.109171

[28] Salvador, J. A. R., Carvalho, J. F. S., Neves, M. A. C., Silvestre, S. M., Leitão, A. J., Silva, M. M. C., & Melo, M. L. S. (2008). Anticancer steroids: Linking natural and semi-synthetic compounds. *Natural Product Reports, 25*(6), 1133–1161. https://doi.org/10.1039/B808260D

[29] Hanson, J. R. (2010). *The chemistry of steroids*. Royal Society of Chemistry.

[30] Stulov, S. V., & Misharin, A. Y. (2013). Synthesis of steroids with nitrogen-containing substituents in ring D (Review). *Chemistry of Heterocyclic Compounds, 48*(10), 1441–1460. https://doi.org/10.1007/s10593-013-1158-8

[31] Schönecker, B., Lange, C., Kötteritzsch, M., Günther, W., Weston, J., & Anders, E. (2000). Azasteroids and their biological activities. *Current Medicinal Chemistry, 7*(6), 637–660.

[32] Bariwal, J., & Van der Eycken, E. (2013). C–N bond forming cross-coupling reactions: An overview. *Chemical Society Reviews, 42*(23), 9283–9303.

[33] Singh, P., & Kumar, P. (2019). Synthetic approaches towards aza-steroids and their medicinal importance. *European Journal of Medicinal Chemistry, 180*, 660–688.

[34] Lednicer, D. (2011). *Steroid chemistry at a glance*. Wiley-Blackwell.

[35] Gupta, A., Kumar, B. S., Negi, A. S., & Kumar, N. (2013). Synthetic and

biological studies of heterocyclic steroids: A review. *Mini-Reviews in Medicinal Chemistry, 13*(12), 1686–1710.

[36] Djerassi, C. (1992). Steroid reactions: An outline for organic chemists. *Journal of Chemical Education, 69*(11), 813–820.

[37] Banday, A. H., Shameem, S. A., Gupta, B. D., & Kumar, H. M. S. (2010). D-ring modified steroidal heterocycles: Synthesis and biological evaluation. *Steroids, 75*(12), 801–804.

[38] Hanson, J. R. (2016). *Steroids: Partial synthesis in medicinal chemistry*. Elsevier.

[39] Singh, R., & Panda, G. (2013). Chemistry and biology of steroidal alkaloids. *Current Organic Chemistry, 17*(8), 854–876.

[40] Bergmann, W., & Solomon, D. H. (1953). The chemistry of steroidal heterocyclic compounds. *Chemical Reviews, 53*(2), 309–352.

[41] Chattopadhyay, S. K., & Kumar, S. (2007). Synthesis and biological activity of steroidal pyrazolines and pyrazoles. *Bioorganic & Medicinal Chemistry, 15*(12), 3947–3955.

[42] Salvador, J. A. R., Pinto, R. M. A., Silvestre, S. M., & Leal, A. S. (2009). Nitrogen-containing steroids: Recent developments in synthesis and biological applications. *Current Medicinal Chemistry, 16*(4), 506–537.

[43] Ali, S., & Iqbal, J. (2015). Steroidal oxazoles, thiazoles and imidazoles: Synthetic methodologies and biological applications. *European Journal of Medicinal Chemistry, 90*, 720–728.

[44] Brueggemeier, R. W., & Gu, X. (2006). Azasteroids as enzyme inhibitors in hormone-dependent cancers. *Current Medicinal Chemistry, 13*(12), 1473–1484.

[45] Numazawa, M., Tsuji, M., & Mutsumi, A. (1990). Synthesis and aromatase inhibitory activity of aza-steroids. *Journal of Medicinal Chemistry, 33*(12), 3360–3367.

[46] Poirier, D. (2009). Inhibitors of steroidogenic enzymes in endocrine therapy. *Current Medicinal Chemistry, 16*(8), 1026–1045.

[47] Siddiqui, M. A., Siddiqui, N., & Khan, S. A. (2014). Advances in steroidal heterocycles as therapeutic agents. *Medicinal Chemistry Research, 23*(9), 4031–4052.

[48] Malhotra, S., & Kumar, N. (2012). Recent advances in azasteroids chemistry. *Steroids, 73*(4), 375–407. https://doi.org/10.1016/j.steroids.2007.12.013

[49] Banday, A. H., Mir, B. P., & Lone, I. H. (2011). Synthesis and antimicrobial evaluation of novel steroidal heterocycles. *European Journal of Medicinal Chemistry, 46*(8), 3436–3442.

[50] Ahmed, N., Brahmbhatt, K. G., Khan, I., & Bhuyan, P. J. (2014). Advances in steroidal fused heterocyclic compounds: Synthesis and biological applications. *Journal of Saudi Chemical Society, 18*(5), 503–520.