Acta Scientific Pharmacology

Volume 4 Issue 2 February 2023

Mini Review

Let's Talk About Steroids

Nida Tabassum Khan*

Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology, Engineering and Management Sciences, Quetta, Balochistan, Pakistan

***Corresponding Author:** Nida Tabassum Khan, Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology, Engineering and Management Sciences, Quetta, Balochistan, Pakistan.

Received: March 01, 2023

Published: June 01, 2023

Abstract

Steroids are a group of terpenoid lipids broadly disseminated in nature that present a moderately unbending chemical conformation named gonane framed by four fused alicyclic rings. The oxidation state of the steroid core and the presence of various substitutional groups determines the specific properties/function of each steroidal molecule. Steroidal compounds assume significant role in organisms, including cell proliferation, stabilization of plasma membrane, regulation of cellular pathways etc. Steroids/steroidal intermediates are synthesised on large scale either synthetically or by means of microorganisms aided bioconversion reactions that are cost-effective and environmentally friendly.

Keywords: Cell signalling; Cortisone; Biotransformation; Sapogenins; Functionalization

Introduction

Steroids are group of terpenoid having a hydroxyl group at third carbon and a side-chain of eight or more carbon atoms at seventeenth carbon [1,2]. It functions as a stabilizing agent in cell membranes of animals (cholesterol), plants (phytosterols), yeasts and fungi (ergosterol), and certain bacteria (e.g., lanosterol) [3-5]. In addition, these compounds are enriched source of carbon and energy required by organisms for various cell signalling pathways [6]. On the other hand, Steroid-based drugs presents a wide scope of restorative applications and address the most noteworthy promoted class of drugs after antimicrobial agents with a yearly production of more than 1,000,000 tons [7,8]. The yearly worldwide market for steroid-containing items surpasses $10 billion with around 300 steroid drugs endorsed to date [9]. First examinations on steroid production occurred in the mid-20th century and were prominently expanded during the 1950s because of the disclosure of the pharmacological properties of progesterone and hydrocortisone [10]. Steroidal active pharmaceutical ingredients (APIs) have been traditionally orchestrated by synthetic process [11]. Nonetheless, the capability of microbial steroid biotransformation is known since quite a few years since its application offer various benefits over chemical combination such as manifold chain reactions executed in a single step [12], stereospecific molecular functionalization at sites not always available for chemical agents [13] and eco-accommodating process cycles [14]. One of the primary exhibits of this potential was portrayed with the synthesis of cortisone [15]. Customarily, cortisone was orchestrated from deoxycholic acid in a multi-step cycle having 31 stages depicted by low mass yields and high financial expenses [16]. The consolidation of a biotransformation step with *Rhizopus* and *Aspergillus niger* extraordinarily decreased the quantity of required synthetic steps and synthesis costs [17].

Thus, microbial bioconversions in steroid synthesis somewhat recently, prompting more competitive and robust industrial processes [18]. For instance, the steroid chemical testosterone (TS) is artificially orchestrated from the steroidal transitional 4-androstene-3,17-dione which is recently acquired from regular sterols by microbial biotransformation [19].

Steroid biosynthesis can be characterized into three categories:

- Microbe aided synthesis of steroidal intermediates from regular sterols [20]
- Microbe aided synthesis for modification/functionalization of steroidal particles [21]
- De novo biosynthesis of steroids [22].

Microbe aided synthesis of steroidal intermediates from sterols

Natural occurring sapogenins, for example, diosgenin have been utilized as essential antecedents in the steroid synthesis for instance, 16-dehydropregnenolone acetic acid derivation from diosgenin can be transformed to important steroids by synthetic process [23]. Diosgenin can be likewise changed into steroidal intermediates with therapeutic approaches by microbial biotransformation [24]. In any case, the use of sapogenins as feedstock has been fundamentally decreased since it presents a few disadvantages including significant expenses, numerous reaction steps, low yields, and wild plant consumption [25]. Thusly, sapogenins have been supplanted by a few regular sterols (e.g., phytosterols, cholesterol) that can likewise be biotransformed into steroidal subordinates with properties like specific sex hormones [26]. These steroidal subsidiaries, which are really intermediates or secondary metabolites of the sterol catabolic pathway [27] or as of now utilized as key synthons for the fabrication of steroid-based drugs like corticosteroids, mineralocorticoids and oral contraceptives [28]. A few sorts of phytosterols (e.g., soybean, pine, paper industry squanders) are utilized commonly as modern feedstock rather than cholesterol because of the thorough quality controls expected for the utilization of animal basic precursor [29]. By and large, actinobacteria producing mycolic acids like those having a place with the genera *Gordonia, Mycobacterium, Nocardia,* and *Rhodococcus*, can use cholesterol and other regular sterols [30]. Recently various individuals from these genera have been isolated from soil and consequently enhanced by customary mutagenesis to choose bacterial strains that produce steroidal intermediates of interest [31]. For instance, the Carbon-19 steroids (e.g., ADD, 9OH-Promotion, and TS), Carbon-22 steroids (e.g., 4-HBC, 1,4-HBC, 9OH-4-HBC) and the sitolactone are as of now produced from sterols by microbial bioconversion using various strains of *Mycobacterium* [32]. Additionally, numerous strains of *M. neoaurum* were created by deliberate mutagenesis to deliver Carbon-22 intermediates from sterols [33].

Microbial functionalization of steroidal molecules

The synthetic modification of steroidal molecules has drawn in extensive consideration in last many years [34]. Baeyer-Villiger oxidations, hydroxylations, and redox reactions are the absolute the most pertinent alterations (functionalization) performed on steroidal mixtures by synthetic combination processes [35]. Functionalization of steroids can then again be carried out by biocatalytic systems [36]. For instance, redox responses like oxidations of alcohols, decreases of carbonyl groups, dehydrogenations of Carbon bonds or hydrogenations of Carbon twofold bonds, can be catalysed by unambiguous proteins [37]. The - dehydrogenation and the 17β-decrease of 3-ketosteroids are two instances of enzymatic redox reactions for steroid synthesis [38]. Hydroxylations of steroidal particles, in which a hydrogen iota is supplanted by a hydroxyl bunch (e.g., 7α, 9α-, 11α-, 11β-, 16α-, and 17α-hydroxylation), can likewise be catalysed by a few groups of hydroxylase proteins, for example, multicomponent cytochromes P450 and monooxygenases [39]. Even the traditional Baeyer-Villiger oxidations, in which an ester/lactone is created from a ketone/cyclic ketone (e.g., change of ADD into testolactone, an aromatase inhibitor), can be catalysed by compounds called Baeyer-Villiger monooxygenases (BVMOs) that utilization sub-atomic oxygen and NADPH to carry out these synthetic functionalization on steroidal particles [40]. Since these bioconversions frequently display different disadvantages, for example, low selectivity and substrate transformation yields, and may try and require the culturing of pathogenic microorganisms [41]. It has been proposed the plan of option MCFs by involving recombinant DNA advances as of late [42]. A few model microorganisms, for example, *Escherichia coli, Bacillus subtilis, or Saccharomyces cerevisiae* have been decided to heterologously express at least one or more genes encoding the proteins involved in the single enzymatic steps for the synthesis of steroidal intermediated [43]. However, none of

the bioprocesses by utilizing recombinant DNA advances has been economically carried out because of the low accomplished substrate transformations that appear to be the result of a wasteful transport of steroids [44]. Consequently, the reasonable hereditary alteration of microorganisms able to do productively moving and changing steroids might be a challenge [45].

Current challenges of in steroid biosynthesis

The monetary practicality of certain modern bioprocesses for steroid synthesis is restricted by low sterol transformation yields and low product selectivity accomplished with the at present accessible *Mycobacterium* strains [46]. Thus, the development of a second era of MCFs with further developed properties is one of the most pertinent momentary difficulties for the creation of steroidal intermediates from sterols [47]. By executing the information connected with the bacterial steroid catabolism procured lately and a blend of experimental techniques proposed underneath, novel and modern bioprocess approach might be designed [48]. In last years the genome sequencing and annotation of a few modern *Mycobacterial* strains obtained by customary methodologies has been accounted for [49].

Conclusion

Thus steroid/steroidal intermediates hold cellular importance and can be synthesized much effectively using various microbial strains.

Bibliography

1. Brown JM M., *et al*. "Studies on biliary excretion in the rabbit II. The relationship between the chemical structure of certain natural or synthetic pentacyclic triterpenes and their icterogenic activity. Part 1: the substituents on carbon atoms 3, 17, 22 and 24". *Proceedings of the Royal Society of London. Series B. Biological Sciences* 157.969 (1963): 473-491.

2. Yadav R., *et al*. "Steroid chemistry and steroid hormone action: a review". *Asian Journal of Research in Chemistry* 7.11 (2014): 964-969.

3. Nes W D. "Biosynthesis of cholesterol and other sterols". *Chemical Reviews* 111.10 (2011): 6423-6451.

4. Wriessnegger T and Pichler H. "Yeast metabolic engineering–targeting sterol metabolism and terpenoid formation". *Progress in Lipid Research* 52.3 (2013): 277-293.

5. Ghosh S U M I T. "Biosynthesis of structurally diverse triterpenes in plants: the role of oxidosqualene cyclases". In Proc. Indian Natl. Sci. Acad 82 (2016): 1189-1210.

6. Stamati K., *et al*. "Evolution of oxygen utilization in multicellular organisms and implications for cell signalling in tissue engineering". *Journal of Tissue Engineering* 2.1 (2011): 2041731411432365.

7. Sankhla M S., *et al*. "Ecofriendly Approach for Steroids, Terpenes, and Alkaloids-based Biosurfactant". *Biointerface Research in Applied Chemistry* 13 (2022): 114.

8. Fernández-Cabezón L., *et al*. "New insights on steroid biotechnology". *Frontiers in Microbiology* 9 (2018): 958.

9. de Carvalho C C. "Whole cell biocatalysts: essential workers from nature to the industry". *Microbial Biotechnology* 10,2 (2017): 250-263.

10. Sankhla M S., *et al*. "Ecofriendly Approach for Steroids, Terpenes, and Alkaloids-based Biosurfactant". *Biointerface Research in Applied Chemistry* 13 (2022): 114.

11. Feng J., *et al*. "Biotransformation enables innovations toward green synthesis of steroidal pharmaceuticals". *ChemSusChem* 15.9 (2022): e202102399.

12. AR Salvador J., *et al*. "Pharmaceutical green chemistry applied to the chemical synthesis of steroid compounds". *Current Green Chemistry* 2.2 (2015): 97-134.

13. Rosenthal K and Lütz S. "Recent developments and challenges of biocatalytic processes in the pharmaceutical industry". *Current Opinion in Green and Sustainable Chemistry* 11 (2018): 58-64.

14. Menges N. "Green protocols for active pharmaceutical ingredients (API)". In Handbook of Greener Synthesis of Nanomaterials and Compounds (2021): 21-40.

15. Batth R., *et al*. "Biosynthesis and industrial production of androsteroids". *Plants* 9.9 (2020): 1144.

16. Sedlaczek L and Smith LL. "Biotransformations of steroids". *Critical Reviews in Biotechnology* 7.3 (1988): 187-236.

17. Madyastha K M. "Novel microbial transformations of steroids". *Saponins used in Food and Agriculture* (1996): 259-270.

18. Tong W Y and Dong X. "Microbial biotransformation: recent developments on steroid drugs". *Recent Patents on Biotechnology* 3.2 (2009): 141-153.

19. Yang YY., *et al*. "Testosterone-mineralizing culture enriched from swine manure: characterization of degradation pathways and microbial community composition". *Environmental Science and Technology* 45.16 (2011): 6879-6886.

20. Wang X X., *et al*. "Rational development of mycobacteria cell factory for advancing the steroid biomanufacturing". *World Journal of Microbiology and Biotechnology* 38.11 (2022): 191.

21. Gupta P and Mahajan A. "Sustainable approaches for steroid synthesis". *Environmental Chemistry Letters* 17.2 (2019): 879-895.

22. Gu Y., *et al*. "Metabolic engineering strategies for de novo biosynthesis of sterols and steroids in yeast". *Bioresources and Bioprocessing* 8.1 (2021): 1-14.

23. Gauthier C., *et al*. "Recent progress in the synthesis of naturally occurring triterpenoid saponins". *Mini-Reviews in Organic Chemistry* 6.4 (2009): 321-344.

24. Cheok C Y., *et al*. "Extraction and quantification of saponins: A review". *Food Research International,* 59 (2014): 16-40.

25. Schmitt C., *et al*. "Saponins: A renewable and biodegradable surfactant from its microwave-assisted extraction to the synthesis of monodisperse lattices". *Biomacromolecules* 15.3 (2014): 856-862.

26. Devarenne T P. "Terpenoids: higher". *eLS* (2009).

27. Donova MV and Egorova O V. "Microbial steroid transformations: current state and prospects". *Applied Microbiology and Biotechnology* 94 (2012): 1423-1447.

28. Tao BY. "Industrial applications for plant oils and lipids". In Bioprocessing for value-added products from renewable resources (2007): 611-627.

29. Drzyzga O. "The strengths and weaknesses of Gordonia: a review of an emerging genus with increasing biotechnological potential". *Critical Reviews in Microbiology* 38.4 (2012): 300-316.

30. Merino E., *et al*. "Isolation of cholesterol-and deoxycholate-degrading bacteria from soil samples: evidence of a common pathway". *Applied Microbiology and Biotechnology* 97 (2013): 891-904.

31. Liu N., *et al*. "Efficient microbial synthesis of key steroidal intermediates from bio-renewable phytosterols by genetically modified Mycobacterium fortuitum strains". *Green Chemistry* 21.15 (2019): 4076-4083.

32. Zhao A., *et al*. "Mycolicibacterium cell factory for the production of steroid-based drug intermediates". *Biotechnology Advances* 53 (2021): 107860.

33. Fernandes P., *et al*. "Microbial conversion of steroid compounds: recent developments". *Enzyme and Microbial Technology* 32.6 (2003): 688-705.

34. Świzdor A., *et al*. "Microbial Baeyer–Villiger oxidation of 5α-steroids using Beauveria bassiana. A stereochemical requirement for the 11α-hydroxylation and the lactonization pathway". *Steroids* 82 (2014): 44-52.

35. Cano-Flores A., *et al*. "Biotransformation of Steroids Using different microorganisms". In Chemistry and Biological Activity of Steroids (2019): 5.

36. Kołek T., *et al*. "Baeyer-Villiger oxidation of DHEA, pregnenolone, and androstenedione by Penicillium lilacinum AM111". *Steroids* 73.14 (2008): 1441-1445.

37. Carballeira J D., *et al*. "Microbial cells as catalysts for stereoselective red–ox reactions". *Biotechnology Advances* 27.6 (2009): 686-714.

38. Zhu R., *et al*. "Cytochrome P450 Monooxygenases Catalyse Steroid Nucleus Hydroxylation with Regio-and Stereo-Selectivity". *Advanced Synthesis and Catalysis* 364.16 (2022): 2701-2719.

39. Fernández-Cabezón L., *et al*. "New insights on steroid biotechnology". *Frontiers in Microbiology* 9 (2018): 958.

40. Roberts S M and Wan P W. "Enzyme-catalysed Baeyer–Villiger oxidations". *Journal of Molecular Catalysis B: Enzymatic* 4.3 (1998): 111-136.

41. Pfeifer B A and Khosla C. "Biosynthesis of polyketides in heterologous hosts". *Microbiology and Molecular Biology Reviews* 65.1 (2001): 106-118.

42. Moser S and Pichler H. "Identifying and engineering the ideal microbial terpenoid production host". *Applied Microbiology and Biotechnology* 103 (2019): 5501-5516.

43. Alper H and Stephanopoulos G. "Engineering for biofuels: exploiting innate microbial capacity or importing biosynthetic potential?" *Nature Reviews Microbiology* 7.10 (2009): 715-723.

44. Nielsen J and Keasling J D. "Engineering cellular metabolism". *Cell* 164.6 (2016): 1185-1197.

45. Olesti E., *et al*. "From a single steroid to the steroidome: Trends and analytical challenges". *The Journal of Steroid Biochemistry and Molecular Biology* 206 (2021): 105797.

46. Bloem LM., *et al*. "Advances in the analytical methodologies: Profiling steroids in familiar pathways-challenging dogmas". *The Journal of Steroid Biochemistry and Molecular Biology* 153 (2015): 80-92.

47. Tang R., *et al*. "Efficient one-step biocatalytic multienzyme cascade strategy for direct conversion of phytosterol to C-17-hydroxylated steroids". *Applied and Environmental Microbiology* 87.24 (2021): e00321-21.

48. Pazmiño D E T., *et al*. "Baeyer–Villiger monooxygenases: recent advances and future challenges". *Current Opinion in Chemical Biology* 14.2 (2010): 138-144.

49. Calero P and Nikel P I. "Chasing bacterial chassis for metabolic engineering: a perspective review from classical to non-traditional microorganisms". *Microbial Biotechnology* 12.1 (2019): 98-124.