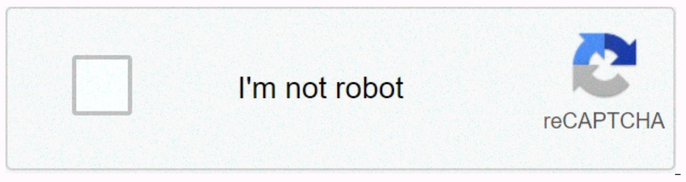

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Microbial biotransformation of steroids ppt

Open Access Peer Review Chapta By Arturo Cano Flores, Submitted by Javier Gomez and Rigoberto Ramos Submission: July 25th 2018 Review: March 14 2019 Published: May 10th 2019DOI: 10.5772/intechopen.85849 The introduction of the hydroxyl group biohydroxylation in the steroid skeleton is an important step in the synthesis of physiologically used steroids and an important step in the synthesis of new steroids used as hormones. Currently there are about 300 known steroid drugs that make up the second category in the pharmaceutical market after antibiotics. Several bio-transformations have been applied on an industrial scale, in the production of steroid hormones and drugs, with different types of raw materials functioning by chemical, regio, and stereoscopic reactions (hydroxylation, buyer-viriger oxidation, oxidation reaction, group carbonyl reduction, isotrification, and Michael addition, condensation reaction, etc.). In green chemistry, bio-transformation is an important chemical methodology for more sustainable industrial processes. Bio-transformed asteroid compounds Biologically converted bio-converting microbial steroids (stereo = solid) are alcohol-derived organic compounds widely distributed in animal and plant worlds. Its basal skeleton has 17 carbon atoms in a four-ring ring system known as cyclopentanoperhydrofenantrene (gonane and estran). This group of substances classifies life-important compounds such as cholesterol, bile acids, sex hormones, vitamin D, corticosteroids, cardiac aglycones, and antibiotics. Some of the most powerful toxins are steroid alkaloids. Steroids are responsible for important biological functions in cells. For example, steroids derived from androstan, pregnan, and Estran have hormonal activity [1,2,3,4,5]; bile acids are important for the digestion and absorption of fat. Aglycone in the electrocardiocardios are used to treat heart disease. Sterols are the building blocks of cell membranes and are essential for cell stability and development. Also, precursors of bile acids and steroid hormones.[6] a large number of steroids are used as anti-inflammatory agents,[6] immunosuppressants, progeste drugs, diuretics, anabolics, and contraceptives[7, 8, 9]. Some are used to treat prostate and breast cancer [10,11], as active ingredients used to treat adrenal insufficiency[12], heart disease prevention[13], antifungal agents[14], and obesity[15] and AIDS[16]. Recently, antiviral activity against herpes simplex virus type I in several steroid glycolysaccharides was determined. The therapeutic effects of some steroid hormones are associated with interactions with intracellular receptors and act as transcription factors in the regulation of gene expression. Steroids such as dehydroepiandrosterone (DHEA), progesterone, pregnenolone and its sulfated derivatives have been reported.20] similarly, 17β-ethralol, allopregnaron and its synthetic derivatives (aphoxolana and ganakicerone) are considered neurosteroids and are attributed to their action at the level of CNS[19]. The physiological activity of the steroid depends on its structure, type, number, spatial orientation, and the resynthesity of different functional types present in the quadrant core as well as the oxidation state of the ring. For example, the presence of oxygenation function in C-11β is extremely important for anti-inflammatory activity. The hydroxyl function of C-17β determines the androgen properties; Corticosteroids have 3-keto-4-ene and pregnan side chains in C-17. Currently, about 300 steroid drugs are known, and this number tends to increase. Their production represents the second category of the pharmaceutical market after antibiotics [24, 25]. Today, steroids represent one of the largest sectors in the pharmaceutical industry in the global market in the U.S. region with over 10 billion tons per year [23]. Steroid drug and hormone production is one of the best examples of applications bio transformation has on an industrial scale [3, [21]. Microbial conversion is an effective tool for the preparation of various compounds[26], which is difficult to obtain with conventional chemical methods and has been widely used for bio-conversion of steroids. In 1950, in addition to hydroxylation of the latter in C-11α using lysopas species, pharmacological effects of cortisol and progesterone were reported. This began a very important stage in the development of the synthesis of steroids with biological activity. Currently, a great diversity of microbial systems in the pharmaceutical industry for the commercial production of steroids and other drugs is recognized. Hundreds of microbiological conversions of steroids have been reported in the literature; also, many bioconversions are incorporated into numerous partial synthesis of new compounds for evaluation of hormones, drugs, etc. [21, 29, 30, 31, 32]. Chemical derivatives of some steroids are reported to have better therapeutic benefits than initiating materials. However, the main objective in research and development of the steroid pharmaceutical industry now consists of the detection and insolation of microbial strains with new activity or more efficient transformation ability, and genetic and metabolic engineering can play a prominent role in bacterial, fungal, and plant metabolism [33, 34, 35, 36]. The purpose of this paper is to emphasize the importance of bio-transformation using microorganisms, to obtain steroid compounds of pharmaceutical interest, as a chemical biological strategy to alternate with chemical synthesis, and to emphasize various types of chemical reactions.In the functionalization of steroid skeletons. In green chemistry, bio-transformation, an important methodology in organic chemistry, is important. Microbiological conversion of steroids is an essential chemical tool used in the preparation of many intermediaries and the generation of new drugs, and chemical functionalization - hydroxide, Baeyer-Villeger oxidation, reduction, isomerization, Michael addition, and condensation reactions can also be performed in very complex ways by chemotherapy, regio, stereo, and selective methods in different positions of the steroid skeleton. Currently, any stereogenic center of the steroid skeleton can be specifically stereo-selectively hydroxylized. Today, biohydroxylation of C-11α, 11β, 15α, and 16 α is performed industrially through microbial hydroxylation with good yield and enumiomer excess (ee). Below are some of the microbiological transformations performed on different natural and synthetic steroids[25]: In the literature, a well-documented regio and stereoscopic hydroxylation in C-14 with progesterone (1) and α adrogens in other steroids by a well-functioning fungus, Tam Nostilam Piliform (ATCC 8992), Mucor Glyceosianus (ATCC 1207a), Actinomcol Elegance (MMP 3132), and Zygodesmus sp. (ATCC 14716), etc. T. pyriform and 14α-hydroxyprogesterone (2, 32%) and 9α-hydroxyprogesterone (3,1.4%) were obtained from the incubation of 1. On the other hand, 1 incubation with M. glyceocyanus resulted in 2 (13.4%), 7α, 14α-dihydroxyprogesterone (4, 6.5%) and 6β, 14α-dihydroxyprogesterone (5,2.8%). A biological transformation of 1 using A. humigatus after 24 hours of incubation resulted in different mono and dihydroxylation products: 11α-hydroxyprogesterone (6, 33%, 11α 15β-dihydroxyprogesterone (7, 17%), 7β, 15β-dihydroxyprogesterone (8, 14%), 15β-hydroxyprogesterone (9), 7β-hydroxyprogesterone (10), 9 and 10 were detected in the smallest amounts. Finally, in 72 hours, the main product was 7 (48%) 8 (25%), which is more easily hydroxylized than position 7β at positions 11α and 15β at 1 [38,39]. Incubation of 1 resulted in low gins saprolognia, 4-androsten-3,17-dyon (11), testosterone (12), and test lactene (13). Compound 13 (98%) was also obtained from bio-conversion of 1 using A. sojae (PTCC 5196). The bioconvesting pathway for the presence of Beyer-Virigar monooxygenase (BVMO) can perform both oxygen esterification of 20 ketosteroids and oxygenation emulsification of 17 ketosteroids[41]. Compounds 15α-hydroxyprogesterone (14,47%) and 12β, 15α-dihydroxyprogesterone (15,25%) fusalium culmorum [42] were used to separate 1 by biological conversion. In the biocontestation of 1 using bacteria, thermophilic Bacillus stearozamophyllus, four products of monohydroxylation, 20α-hydroxyprogesterone (16,61%), 6β-hydroxyprogesterone (17,21%) and(18, 14%), and 9,10-Secoprenen-3,9,20-Trianne (19, 4%) were separated. Efficient regio and stereosotic selectivity were observed in one large biotransform by the system Mucor 881 (M881), resulting in hydroxylation derivatives 6, 6β, 11α-dihydroxyprogesterone (20), and 6β-hydroxyprene-4-ene-3,11,20-trione (21). In the literature, mucor and rhizome species can hydroxylize the described position, but are described with a lower yield. The fungal system M881 showed the ability to hydroxylation at 6β and 11α positions of 4-ene-3-1 steroids (1, 11, 12 and 211). In recent years, it has been reported that 11 days and androsta-1.4-jien-3,17-ione (22) were obtained in 1 bio transformation using penicylium orrancio glyceum for 10 days. These products were observed in 1 bio-transformation using Bacillus sphericus. Hydroxylation in C-17 was mainly observed. Bioreconnition of 1 using geovacs gargensis (DSM 15378) resulted in the production of seco derivatives generated by the rupture of 1 (Fig. 1) of seco derivatives (9,10-seco-4-pregnen-20α-hydroxy-3,9-dion) [Figure 1]. Secosteroids are an important group of various biological activities. Bio-transformation products of progesterone (1). In the biological conversion of 5β-dihydroprogesterone (24) using T. Pyrihormi, 14α-hydroxy-5β-pregnan-3,20-dion (25, 11.8%), 3β, 14α-dihydroxy-5β-pregnan-20-one (26,0.5%), 14α-dihydroxy-5β-5β-pregnan-3,20-dihydroxy-3,20-pregnadion (27.4%), 3β-hydroxy-5β-pregnan-20-1 (28) characterized during biological transformation of 26 (0.6%) and 3β, 9α, 14α-trihydroxy-5β-pregnan-20-1 (29, 16%) after being incubated for 96 hours. By 28 microbiological transformations using actinomcol elegance, compounds 25 and 28 were generated at a lower yield than T. pyriform, and a minor product identified as 3β, 9α-dihydroxy-5α-pregnan-20-1 (Fig. 2) was produced [Fig. 2]. Bio-transformed products of 5β-dihydroprogesterone (24). 16-dehydroprogesterone (4,16-pregnadien-3,20-dyon, 31) it has been reported to use machor pyriforma to give different hydroxylation products: 14α-hydroxyprenia-4 , 16-jien-3,20 dion (32, 1%), 7α, 14α-dihydroxyplegna-4,16-jien-3,20 dion (33,78%), 3β, 7α, 14α-trihydroxy-5α-pregna-16-en-20-one (34,3%) and 3α, 7α, 14α-trihydroxy-5α -Pregna-16-en-20-one (35,2%); As a result of 32 incubations and M. pyriformosis, 33-35 (Fig. 3) [50] was formed. Biodegenering products of 16-dehydroprogesterone (31). In contrast, bioconformation of 17α-hydroxyprogesterone (36) using M. pyriforma resulted in four compounds after 48 hours of incubation: 17α, 20α-dihydroxypregn-. 4-en-3-one (37, 19%, 7α, 17α-dihydroxyprene-4-en-3,20-dyon (38, 25%), 6β, 17α, 20α-trihydroxyplexgun-4-en-3-one (39, 18%), 11α, 17α, 20α-trihydroplexygun-4-10 (15%) were observed.Pyriformasis can stereo-specifically hydroxylate the positions of C-6, C-7, C-11, and C-14, in addition to reducing the 4-en-3-1 system in the keto group of rings A and C-20 (Fig. 4) [50]. 36 biotransforms using tbathocal mormolm led to the formation of 14 (47%) and 15 (25%)[42].17α-hydroxyprogesterone biotransform products (36). Pregnenolone (3β-hydroxyprene-5-en-20-1, 41), a precursor to many steroid hormones, is bio-transformed by macorpiriforma and is converted into two metabolites, 3β, 7α-dihydroxy Preng-5-en-20-one (42) and 3β, 7α, 11α-trihydroxyprengu-5-en-20-one (43)[51], 43 (46.4) Here, 43 (46.4), two metabolites were obtained, and there were 41 biocontelligent products using mucorser cineloides var.lucitanics[52]. The two metabolites of pregnenolone (41) obtained from biological conversion of B. cinerea were characterized as 3β, 11α, 16β-trihydroxyprene-5-en-20-one (44,39%). 11α, 16β-dihydroxyprene-4-en-3,20-dyon (45, 6%). B. The formation of hydroxylation products in C-11 and C-16 by cinereae can be determined by the presence of acetyl groupes in C-20[53]. Forty-one metamorphosis using different microorganisms (Cunninghamella elegance, R. stronifer, and G. Fujikroy) were reported by Choudhary and others. 41 incubations using C. elegance are 3β, 7β, 11α-trihydroxyprene-5-en-20-one (46,28%), 3β, 6α, 11α, 12β 15β-pentahydroxyprengu-4-en-20-one (47, 4%), 3β, 6β, 11α-trihydroxypgun-4-en-20-one (48, 2%), While incubation with G. fujikroy, two products 3β, 7β-dihydroxyplegun-5-en-20-one (49, 3%) and 6β, 15β-dihydroxyprene-4-en-3,20-dion (50, 2%) were obtained. In 41 microbiological transformations using different Bacillus strains, 42 was the only product obtained using fusarium oxysporm var, which is the main product for which 42, 49, and 7-oxoprenenolone (51) were obtained. Bio-transformation of pregnenolone acetate (52) using C. elegance is 41, 22, 6β, 15β-dihydroxyandrosta-4-en-3 It was generated using 17-dion (53) and 11α, 15β-dihydroxyprengu-4-en-3, 20-dionron (54). 11α-hydroxyprene-4-en-3,20-dione (55) and 53 were obtained (Fig. 5). Biodegeneration products of pregnenolon (41) and acetyl derivatives (52). Microbiological metamorphosis of 13-ethyl-17β-hydroxy-18,19-diner-17α-pregn-4-en-20-yn-3-one (56) was tested at different fungal rhizome niglycans, R. Arichiz, Aspergillus Niger, Aoxeace, and Curara Kurula Lunala. Bioconversion of 53 rasemi mixtures by R. Arichs produces the only major product and (±)-13-ethyl-10β,17β-dihydroxy-18,19-diner-56-57% of R. Niglycan, A. Niger, and C. Lunata Biotranforms, compared to 17α-preg-4-en-20-yn-3-one (57,28.4%) More slowly inefficient[57]. The rasemi mixture (±)-13-ethyl-7β, 17β-dihydroxy-18, 19-dinah-17α-preg-4-en-20-yn-3-one (58, 4.3%) A. Obtained as a product to incubate 56 of the mixture with ocalaceus. None of the fungi tested could distinguish between 56 eangmiomar in the course of the hydrolysis reaction. InchesThe presence of hydroxylation derivatives in C-11 is due to the presence of ethyl group in C-13 or ethinyl group in C-17. Microbiological transformations of the rasemi mixture of compound 56 and dextroen anti-tee omer are described using a different cunningham lasera [58]. For example, the conversion of 56 rasemi mixtures by C. blakesrina (AS 3.910) is 57 (5.3%), 13-ethyl-6β, 17β-dihydroxy-18, 19-di Noah-17α-Pregun-4-en-20-yn-3-one (59, 3.6%, 13-ethyl-15α, 17β-dihydroxy-18,19- Dynoa-17α-Pregun-4-en-20-yn-3-one (60, 3.0%), and 13-ethyl-6β, 10β, 17β-trihydroxy-18,19-dinoa-17α-pre-pre g-4-en-20-yn-3-one (61,3 C. Etinurata (AS 3.1990), 61 (3.2%), 57 (1.2%), Elanchi Omadekistro 58 (2.9%) It was obtained while using. The conversion of 56 enantiomadextros using C. blakesleyana produced 57 (1.2%), 58 (2.9%), and 61 (3.2%), and using C. etinurata, the same compound was obtained, but at a lower yield. Thus, the microbial conversion of the rasemi mixture and 56 d-enantiomar using different caningamera species gave insufficient yield and low resolution, which was obtained for the hydrolytation reaction (FIG. 6) [58]. (+)-13-ethyl-17β-hydroxy-18, 19-dydoll-17α-preg-4-en-20-yn-3-ona (56). Danazole (17β-hydroxy-17α-pregna-2,4-diene-20-yno-[2,2,00] 3-d]-Biocontestation of isoxazole, 62), using fusarium lini, A. Niger, cephalosporium absidicola, 17β-hydroxy-2-(hydroxymethyl)- 17α-pregun-4-en-20-yn-3-one (63) and 17β-hydroxy-2-(hydroxymethyl)-17α-preg-1,4-diene-20-1-1-1). Bacillus Cereus gave 64, but only as a product. Microbial conversion of danazole (62) using C. blakesrina produced four compounds: 14β, 17β-dihydroxy-2-(hydroxymethyl)-17α-pregue-4-en-20-yn -3-one (65, 1.2%), 1α, 17β-dihydroxy-17α-pregna-2,4-diene-20-isoxazole (66,1.2%), 6β, 7β-dihydroxy-17α-pregnia-2,4-jiene-20-yno-oxox (2,3-d-d) is [67]. 64(1.2%)。 This includes hydroxylation of al-C-1, C-6, and C-15, while oxidation at C-3 and N-O bond cleavage also occur (Fig. 7) [60]. The biotransform product of danzol (62) norlesisterone (17α-ethinyl-19-nortesterone, 68) is a powerful progestin used as a contraceptive. Its biotransformation with cephalosporium afphysicola (IMI 68689) resulted in the aromatization of ring A, which resulted in 17α-ethinylestriol (69), 69 biotransformed by Cunningham Elegance (NRRL 1392).) Compounds produced 19-nor-17α-pregna-1,3,5(10)-triene-20-yn-3,4,17β-triol (70), 19-nor-17α-pregnia-1,3,1 5 (10)-Trien-20-yn-3, 7α, 17β-triol (71), 19-nor-17α-pregna-1,3,5(10)-Trien-20-yn-3,11α, 17β-triol (72), 19-nor-17α-pregna-1,3,5(10)-trien-20-yn-3,6β,17β-triol (73), 19-nor-17α-pregna-1,3,5(10)-trien-20-yn-3,17β-diol-6β-methoxy (74) (Fig. 8)[61]. Biotransform products of noreciteron (68) and 17α-etinoylestridol(75) and 17β-methoxymestranol (76) are 69 mono and dial-quilted derivatives, respectively. When incubating 75 with C. elegance, two hydroxylation compounds were obtained: 6β-hydroxymestranol (77,2.8%) 6β, 12β-dihydroxymestra Nole (78, 3.6%) speculates that the presence of methoxyl in C-3 reduces the number of biodeformed products and introduces hydroxyl β in C-6 and C-12 in the β direction. 76 did not metastasize live due to the presence of methoxyl in C-17 [FIG. 9]. Bio-transformation of Mestranor products (75). Microbial conversion of 6-dehydroprogesterone (79) using Niger produced five metabolites: 6β-chloro-7α, 11α-dihydroxyplegna-4-en-3,20-dion (80, 1.0%), 7α-chloro-6β, 11α-dihydroxyplegna-4-en-3,20-dyon (81, 1.33%), 6α, 7α, - Epoxy-11α-hydroxyplegna-4-en-3,20-dyon (82, 1.33%, 6α, 7α, epoxypregna-4-en-d) 3,20-Dion (83, 2.0%), 11α-hydroxyplegna-4, 6-jien-3,20 dion (84, 2.33%). Compounds 11α-hydroxyadolosta-4,6-diene-3-1 (85, 15.4%) were obtained through 79 whole cell biorecontests by G. Fujikroy (ATCC 10704). The formation of 80 and 81 is an interesting discovery. This route provides an efficient way to slow chlorohydrin from the Alken function [63]. Compound 84 was obtained through 79 microbial transformations using R. niglycan [64], nigrosporasfaerica, mucorracemosus, and botriospha area obsa. 6-dehydroprogesterone (79) is a synthetic derivative of progesterone. Botriodiprodia theoblomer was used to synthesize 6-DPH from progesterone (Fig. 10). Biodegenering products of 6-dehydroprogesterone (79). Incubation of meleniberol acetate (86) using C. blakesleyana, which provides a pathway for monohydroxylation in C-11 (86), is 17α-acetoxy-11β hydro Xy-6-metylene pregna-4,6-jien-3,20-ione (figure)[11].66 Bio-transformation products of mele acetate (86). Biological conversion of 3β-hydroxy-17β-carvocycetyl-5β-androstenol (88) using T. pyriformi can be used to convert 3β, 14α-dihydroxy-17β-carboxethyl-3 5β-androstenol (89,9%) 9α, 14α-dihydroxy derivatives (90,12%) 2 minor products 14α, 15α-dihydroxy (91) and 15β-hydroxy (92)。。 Compound 92 was identified as a product of bio-transformation using A. elegance, M. glyceosiamus, and zygodesmus sp (FIG. 12)[38]. Biotransform product of 3β-17β-carboxyethyl-5β-androsteno (88). Androst-4-en-3,17-Dione (11), which plays an important role in drug metabolism, is biotransformed using M. pyriformosis, among many other functions, and one major The product is 6β-hydroxyandrost-4-en-3,17-dione (93, 13%, and 4 minor products, 14α-hydroxyandrost-4-en-3, 17-Dione (94, 2%), 7α-hydroxyadrost -4-en-3,17-Dion (95, 2%), testosterone (12, 3%), and 6β-hydroxytestosterone (96, 1%). In 11 bio transformations using M. glyceosiamus 94 (9%), 95 (4%), and 14α-hydroxytestosterone (97, 9%) major products were obtained. Similarly, 11 and 93 were identified in the mixtureProduct [67]. [38] From 11 incubations using M. pyriforma, 94-97 and 7α and 14α-dihydroxytestosterone (98) were obtained. Hydroxylation steroids of C-9 are an important intermediary in the synthesis of highly effective anti-inflammatory drugs. Microbiological transformations of 11-9α-hydroxyadrost-4-en-3,17-ione (99) were studied using rodococcus sp. in a low nutrient medium at a fixed pH [Fig. 13][68]. When 11 were incubated with bacillus strain HA-V6-3, metabolites 12, 93-97, 6β, 14α-dihydroxyandrost-4-en-3,17-dion (100), 11α-Hydroxyadochydrost-4-en-3,17-Theon (101), Androst -4-en-3, 6,17-Trione (102), and 5α-Androst-3,6,17- Trione (103) was manufactured as described by Scherf and Dettner[69]. Biode transformation products of Androst-4-en-3, 17-Diona (11). In 11 bioconvests using C. ablojicola, 93 and 94 were obtained[70], during 11 fermentations using Cruvura rialnata, product 101 (4%), 17β-hydroxyandrost-1,4-Jien-3-1 (104, 4.4%), Androsta-1,4-Jien-3,17-Theon (105, 3%), 11α, 17β-dihydroxyandros-4-en-3-one (106, 4%), 107 (15α-hydroxyandrost-1,4-jien-3,17-dion, 2.8%) were obtained (Fig. 13) [71]. [72] The 11 bio-transformations using beauberia basilana were studied in culture media at different pH (pH 6 and 7). At pH 6, two products were obtained: 106 and 6β, 11α-dihydroxyandrost-4-en-3,17-dyon (108), C-11α and C-6β with stereoscopic selective hydroxylation observed. At pH 7, compounds 12, 106, 3α, 11α, 17β-trihydroxy-5α-androstan (109), and 6β, 11α, 17β-trihydroxyandros-4-en-one (110) were obtained. 11 were separated from bio transformations of products 93 (14%) and 94 (75%) 11 (Figure 13). Obtaining hydroxylation derivatives at a specific location is one of the purposes of the steroid industry; for example, 14α-hydroxysteroids have been shown to have anti-inflammatory, contraceptive and antitumor effects. With 11 and 105 biocontests using different strains of fungus, C. lunata was allowed in the case of 11 and obtained major product production, 94; 105, 14α-hydroxyandrost-1,4-jien-3,17-dion (Fig. 111, 70%) (Fig. 13) [74]. Androsta-1,4-jien-3,17-dione (105) is a useful precursor in chemical or microbiological formulations of other steroid hormones and pharmaceuticals. Conversion of 105 by collet trichum lyni (As3.486) produced hydroxylation compounds at C-11α and C-15α: 15α-hydroxyandros-1,4-diene-3,17 -Theon (107), 11α 15α-dihydroxyandrost-1,4-diene-3,17-dyon (112), and 15α, 17β-dihydroxyandrot-1, 4-Jien-3-1 (113) [Fig. 14][75]. Biotransform products of Androsta-1,4-Jien-3, 17-Girone (105). Testosterone (12) was metabolized by M. glyceosaimas and T. pyriform. In 12 bio-transformations using M. glyceosiamus,

97 (35%) and 94 were identified as the main products, other products were obtained. Conversely, 12 microbiological transformations using T. pyriform produced mainly 97 (10%).in 24 hours. After 72 hours of bio-transformation, we got four products: 93 (13%), 96 (7%), 97 (13%) and 111 (5%). It was found that T. pyriform produced a small amount of 14α-hydroxy derivatives (Fig. 15). In 12 biotransmations using testosterone biodemotion products (12). Nektria hematococca, four substances were separated and their performance depended on incubation time. The majority of the products were produced in 72 hours. Hydroxylation derivatives of C-11 produced the following compounds due to the α-azirode and dehydrogenation in C1-C2: 11α-hydroxyandrost-1,4-diene-3,17-dione (114, 8.) 0%, 11α, 17β-dihydroxyandrost-1,4-jien-3-one (115, 4.3%), 101 (1.9%), 104 (2.3%)[76] Products containing hydroxylation derivatives of 96 (32%) C-6β with 12 incubations produced at fusarium calum, 15α, 17β-di Includes hydroxyandros-4-en-3-one (116, 22%) 15α-hydroxyadrost-4-en-3,17-theon (117). Selective hydroxylation of 103 in C-6 with β adrogens and ally positions in the unsaturated 3-keto system is supported by the presence of π and hydroxylation in c-17, and hydroxylation in C-15 is a very frequent process performed by fungi of the genus Fusarium. Metabolites 11, 85, 105, and 115 were obtained as 12 oxidation and hydroxylation products using the fungus F. oxysporum var.cubense. Fungus, cephalosporiusa apfidicola, was hydroxylized at 12 to give the product 96 (47%), respectively [70] has hydroxylation derivatives at C-6β and C-14α. The 12 incubations between C. Lunata and Prerotas Osttoritus were 115 (13%) and [77], respectively, which each d'etre 11 (17%). Botrytis cinerea, a plant pathogenic fungus, produced 7β, 17β-dihydroxyandrost-3-1 (118,73%) as the only 12 bio-transformation products. The presence of hydroxyl group in C-17 in the androstan skeleton seems to have directed hydroxylation in the β direction at c-7 (Fig. 15) [53]. In 12 bio-conversions using thermosynoses, the main product obtained was 11 (90.2%), produced by oxidation of C-17, and 11 hydroxylation derivatives were produced at C-6 (93, C-6β, 1.1%). and (119, C-6α, 0.9%) 12,96 (C-6β, 3.9%), containing 120 (C-6α, 3.9%). This indicates that hydroxylation by α orientation in C-6 can be a common action of some thermosid bacteria [78]. 11 bio metamorphosiss using B. stea rosamophyllus in the presence of hydrolyzed enzymes - salicylic acid, chloramphenicol, cyclodekistrin, dexamethasone, riboflavin, lifinpicin-9,10-seco -4-Andros-3,9,17-Trione resulted in higher concentrations of compounds: (121), 5α-androst-3,6,17-trione (103)), 17β-hydroxy-androsted-3,6-dion (122), 3β, 17β-dihydroxyaderos-4-en-6-one (123), 17β-hydroxyandrost-4,6-die 14 (121). For example, the presence of glucose and cycloheximid favors the acquisition of 123, while the production of 124In the presence of rifapicin[79]. Products separated from 12 ecological transformations were 93 (21%), 94 (39%) and 99 (19%), and after 24 hours of incubation, 11 presences were detected. Janeczko and others[73] concluded that stereoscopic factors associated with the quality determine the position and direction of hydrochloric acids. For example, the carbonyl group of 11 C-17 directs the inroads of the hydroxyl group in C-14 having a α direction, and hydroxylation in C-6β is preferred by the presence of hydroxyl group in C-17 as in 12. In the case of progesterone (1) having an asyl group, dihydroxylation derivatives were observed in C-6 and C-14 [FIG. 15][73]. 11 and 12 incubations with C. lyni ST-1 showed different catalytic properties. 11 biode transformations gave two products: 15α-hydroxyadoxidrost-4-en-3,17-ione (117, 5%) 11α,15α-dihydroxyandrost-4-en-3,17-theon (125,64%), 12 obtained 15α-hydroxyandrost-4-en-3,17-theon (117,60%). Incubation of 1 resulted in 14 separations. [80] It was concluded that different hydroxylation sites between 11 and 12 suggest that C-17 affects the position of the hydroxyl group or carbonyl group introduced on the substrate (FIG. 15). Dehydroepiandrosterone (3β-hydroxyadoxyandrost-5-en-17-1,126) Endogenous prodomors secreted by the adrenal glands are precursors of androgens and estrogens. Incubation in M. Pyriholmi allowed the insocition of five compounds: 3β, 17β-dihydroxyandrost-5-5-ene (127), 3β,7α-dihydroxyandrost-5 -en-17-one (128), 3β-hydroxyandrot-3β-hydroxyandrost-5-en-7,17-dione (129), 3β, 17β-dihydroxyandrost-5-en-7-one (130), And 3β, 7α, 17β-trihydroxyandrost-5-ene (131). The action of the fungus was a three-dimensional specific hydroxylation product in C-7α (128 and 131) and a decrease in carbonyl group in C-17[51]. From 126 microbiological transformations using rhizome stronifers, six potducts were separated: 127 (20%), 128 (12%), 129 (20%), 3β, 17 β-dihydroxyandrost-4-4-ene (132, 12%), 17β-hydroxyadolos-4-en-3-one (133, 34%), and 3β, 11β-dihydroxyandros-4-en-17-11 (134, 171001001001000, 135%) [81] Biotransformed fusarium oxysporum to 126 in a mixture of four hydroxylation derivatives (127-129 and 130) was characterized as an acetylation derivative. Hydroxylation was good with 3β-hydroxy-Δ5-steroids in C-7 stereo-specific (α-aposom), but choletrikum musae reduced carbonyl group with C-17 and biocontectioned it to 126-127 (Fig. 16). Biodegenering products of dehydroepiandrortheron (126). 126 bio-transformations using penicilium glyceopur purum and P. grabram produced: Hydroxylation derivatives are C-7α (95), C-14α (94) and C-15α (117), and 11 are the main products. In addition, P. glyceopurum produced a product for Bayer biliger oxidation to give lactone D-rings (tesporactone, 13) and their hydroxylation derivatives at C-15αP. grabram, on the other hand, produces compounds and 3β-hydroxy-17α-oxa D-homoandrost-5-en-17-one (136) and 3β-hydroxy-17α-oxa-D-homo 5α androstan-17-1 (Fig. 137)[82]. Bio transformation of 17α-ethinyl-17β-hydroxyandrost-4-en-3-one (ethisterone, 138) and 17α-ethyl-17β-hydroxyadrost-4-en-3-one (139) was described using the fungi kefalosporium abufidjicola and cannegueraelaegan. 138 bioconversions using C. ablojicola resulted in C. elegance, 17α-ethinyl-11α, 17β-dihydroxyandrost-4-en-3-1 (17α-ethinyl-17β-hydroxyandrost-4-1). It was obtained. 138 biocontests using C. abifidicola produced 17α-ethyl-17β-hydroxyandrost-1,4-jien-3-1 (142,2.2%). In contrast, incubating 139 with C. elegance resulted in two new products: 17α-ethyl-11α and 17β-dihydroxyandroto-4-en-3-one (143, 2.8%). and 17α-ethyl-6α, 17β-dihydroxy-5α-androstan-3-1 (144, 1.6% (Fig. 17) [83].17α-ethinyl-17β-hydroxyandrost-4-en-3-one (138) and 17α-ethyl-17β-hydroxyandrost-4-en-3-one (139). Adrenosterone (145) is an inhibitor of the enzyme estrogen synthase responsible for the formation of estrogen and has excellent clinical application. 145 bio-transformation absicolola using C are Androst-1,4-Jien-3,11,17-Trione (146, 3%), 17β-hydroxyandrone-4-en-3,11-ione (147, 2%), 17β-hydroxyandrot-1,4-jien-3,11-theonyon (14%) were produced. And 145 bio-transformations using fusarium lini (8.1%), while 147 (36.8%) were obtained from 145 biocontellites using tricothesium roseum (Fig. 18). Androsterone bio-transformation products (145). Biocontestation of mesterolone (1α-methyl-17β-hydroxy-5α-androst-3-1,149) was performed using synthetic androgenic steroids, different fungi described by Choudhary et al. Compounds 1α-methyl-5α-androst-3,17-dyon (150), 1α-methyl-andros-3,17-diol (151), and 1α-methyl-15α-hydroxy-5α-andros-3,17-dilon were obtained from 149 biological transformations using C. ablojicola. The incubation of 149 together with fusarium lini produced compound 152 and produced 1-methyl-5α-androst-1-en-3,17-dyon (153), 1α-methyl-6α, 17β-di Hydroxy-5α-andros-3-1 (154), 1α-methyl-1 5α, 17β-dihydroxy-5α-androst-3-1 (155), and 1-methyl-15α, 17β-dihydroxy-5α-andros-1-en-3-1 (156). Products obtained from 149 bioconvests using R. stronifers include 150, 154, 156, 1α-methyl-7α, and 17β-dihydroxy-17β They were 5α-androst-3-1 (157), and 1α-methyl-11α, 17β-dihydroxy-5α-andros-one (155). 149 bio-transformations using C. Blakesrina produced seven bio-transformation products, such as 154, 158, 1α-methyl-1β, 11β, 17β-trihydroxy-5α-plus androst-3-one (159), 1α-methyl-7α, 11β, 17β-trihydroxy-5α-androst-3-1 (160), 1α-methyl-1β-1β, 6α, 17 β-trihydroxy-5α-androst-3-1 (161), and 1α-methyl-1β, 11α, 17β-trihydroxy-5α-andros-3-ona (162). Get Macrophomina Feshonolina Biotransform 149(155) [86]. Furthermore, 141 biological transformations using C. Blakesleyana (ATCC 8688A) resulted in 1α-methyl-11β, 14α, 17β-trihydroxy-5α-androstan-3-1 (163, 0.4%), 1α-methyl-7β, 17β-dihydroxy-5α-androstan-3-1 (164,0.47%), 1α-methyl-17β-hydroxy-5α-androstan-3,7-dion (165,0.67%). C. Blakesleyana catalyzed β hydroxylation in C-11 and dihydroxylation and oxidation at various locations in the steroid skeleton (FIG. 19). Bio-transformation products of mestelerone (149). Fusarium oxysporm var in microbiological conversion of 3-hydroxystra-1, 3, 5-(10)-trien-17-17-1 (166). C-17 (3,17-dihydroxystra-1,3,5-(10)-triene, 167) reduced hydroxide (3,15α-dihydroxystra-1,3,5-(10)-trien, 168) reduced substance covense (FIG. 26) was separated [FIG. 26]. Bio-transformation products of 3-hydroxy-1,3,5-(10)-Trien-17-17-1 (166). Prednisone (169) is a synthetic corticosteroid (prodrug) used to treat autoimmune, inflammatory and kidney disease. 169 biological transformations using C. elegance generated by hydrogenation of Δ4 (5) and reduction of C-20 produce compounds 17α, 21-dihydroxy-5α-preg-1-en-3, 11,20-trione (170,15.6%). 17α, (20S), 21-trihydroxy-5α-preg-1-en-3, 11-dione (171,6.5%); Tronifer (5.5%) C. Lunata (6.2%) was 1,4-Pregnadiene-17α, (20S), 21-Trihydroxy-3, 11-Dione (172) (Figure 21) [88]。 Prednisone bio-transformation products (169). The main chemical transformations performed by different Acremonium species of various steroid compounds were oxidation, reduction, hydroxylation at different locations, isotrification, and hydrolysis of chains in C-17. Hydrocortisone (173) is an important anabolic material clinically used as an anti-inflammatory and antiallergic drug, in addition to being a raw material for the synthesis of many steroid hormones. 173 biocontracises using accremonium strict products 11β, 17β-dihydroxyandrost-4-en-3-one (174,8%), 11β, 17α, 20β, 21-tetra Hydroplegun-4-en-3-one (175, 11.2%, and 21-acetoxy-17β, 17α, 20-trihydroxyplegun-4-en-3-one (176, 7.6%)β β α; 173 bioconvertings using jiberella fujikroi resulted in 11β-hydroxyandrost-4-en-3,17-dion (177,41%), while B. sbris and R. stronifers resulted in 175 (15%). Products 173 (45%) and 3β, 11β, 17α, 21-tetrahydroxy-5α-pregnan-20-1 (178, 31%) obtained from 173 biocontractions using Bacillus cereus (Fig. 22) [90]. Hydrocortisone bio-transformation products (173). Incubation of 17β-methoxy-5α-androst-3-1 (179) and cephalosporium abscidricola (180) and 6β-methoxy-5α-and Lost-3β-all (180) and 6β-11α-dihydroxy-17β-methoxy-5α-androst-3-1;181; Biological transformation of 17β-metoxyestra-4-en-3-one (182) using C. absicolaMajor metabolites 6β-hydroxy-17β-methoxyestra-4-en-3-one (183). Similarly, microbiological conversion of 3β-metoxyados-5-en-17-one (184) gave a mixture of products: 7α-hydroxy-3β-metoxyados-184 5-en-17-one (185) and 7β-hydroxy-3β-methoxyandros-5-en-17-1 (Figure) 1611 (Figure 18). Biodeforming products of 17β-methoxy-5α-androst-3-1 (179). The literature describes that various steroids can be hydroxylized with several species of fungi belonging to the genus Aspergillus, fusarium, mortiella, and penicyllium and C-15. For example, Jekkel et al. [92] described more than 3000 fungal hydroxyls at C-15 positions as 13β-ethyl-4-gonnes-3,17-dione (187), who who who who who who who who is F. Nibert. Fungi α orientation at C-15 (15α-hydroxy-13β-ethyl-4-gonnen-3,17-dione, 188,77%) C-7β (7β, 15α-dihydroxy-13β-ethyl-4-gonene-3, 17-Diona, 189). On the other hand, 187 biocontests using Mortiera Psila were 188, 190 (10β-hydroxy-13β-ethyl-4-gonene-3,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,000,0 17-ione) and 191 (6β-hydroxy-13β-ethyl-4-gone-3,17-ione) (Fig. 24). Bio-transformed product of 13β-ethyl-4-gonenu-3, 17-Dione (187). Etinoviol diacetate (192) is a synthetic derivative 1 and is used as an oral contraceptive because it inhibits the ovulation process. 192 microbiological transformations using Cunninghamella elegance include 17α-etinoylestol-4-en-3β, 17β-diacetoxy-6α-ol (193,0.0 5%), producing four hydroxylation compounds characterized as 17α-etynylestr-4-en-3β, 17β-17β-6β-ol (1944). 1.0%), 17α-etiniretol-4-en-3β, 17β-diacetoxy-10β-ol (195, 0.5%), 17α-ethinyl -17β-acexycestol-4-en-3-one (196,1.4%) (Figure 25)[93].Biorecondited products of etinodiordiate (192). Desogestrel (13-ethyl-17-metylene-18,19-diner-17α-preg-4-en-20-yn-17-ol, 197) is an oralally active third-generation contraceptive. 197 conversions by C. Black secretions (ATCC 8688 A) resulted in four metabolites: 13-ethyl-11-metylene-18,19-dinoa-17α-preg-4-en-20-yn-6β,1 5β,17β -Triol (198), 13-ethyl-11-metylene-18,19-dinoa-17α-pregue-4-en-20-yn-3β, 6β, 17β-17β-17β-18 Triol (199), 13-ethyl-11-thylene-18,19-diner-17α-preg-4-en-20-yn-3α, 5α, 6β, 17β-tetraol (17β-tetraol) 2) and 13-ethyl-11-metylene-18,19-diner-17α-preggn-4-en-20-yn-6β,17β-dihydroxy-3-1 (201). Compounds 197 and 198 showed strong growth inhibition for drug-resistant strains of S. aureus (FIG. 26)[94]. Desoquestrell's Biode transformation products (197). Powerful antagonists of the drugs Mexerone (202) and Canlenone (203) and C-17 spironolactone and steroids and mineral corticoids [95]. 20 using a wide variety of microorganisms Biological transformations of 2 and 203 produced monohydroxylized products at different locations, and Beauberia Basiana produced 11α-hydroxymextlenone (204,67%) As a major product, it was obtained using 12β-hydroxymexlenone (205,50%) 6β-hydroxymexlenone (206,33%) mortiera isaberina. Dehydrogedration(Δ1(2)-mekuflenone, 207, 15%) not only cyclooxydoxic acid, but also rodococcus equi, nocardia aurentia, and comamorus testeroni were preferred. [96] 9α-hydroxycanlenone (208,30%) was obtained from 203 biode transformations using Corinespora Casicola. Conversion of canlenone (203) by choletrikum lyni ST-1 gave two hydroxyl compounds, 15α-hydroxycanlenone (209, 22%) and 11 α, 15α-dihydroxicanlenone (210,47%) (Fig. 27) [80]. Biodecontiting products of MexLenon (202) and Canlenone (203). One of the steroids used to treat breast cancer is exemestan (211), an inhibitor of steroid aromatase. From 211 conversions using macrophomina phasenelina, 16β, 17β-dihydroxy-6-metylene-androsta-1,4-diene-3-1 (212), 17β-hydroxy-6 -Metylene androsta-1,4-dieon-3,16-dyon (213), and 17β-hydroxy-6-metylene-androsta-1,4-death-1,4-die-1 (212). Using fusarium lini, the only product obtained was 11α-hydroxy-6-metylene androsta-1,4-jien-3,17-dion (Fig. 28][97]. The biodeformation product of Exemestan (211) (211) 4-hydroxandrost-4-ene-3,17-zeon (forfestane, 216) is an irreversible aromatase inhibitor used for breast cancer treatment in postmenopausal women and is used therapeutically. 216 bioconversions using lysopas orizae (ATCC 1145) were 4β, 5α-dihydroxyadrosoltol -3,17-theon (217,8.6%) Production resulted in 3,5α-dihydroxyandrost-2-ene-4,17-ione (218) [98], 217 biotransforms using Beauberia Basilana were 4, 17β-dihydroxyandrost-4-en-3-one (219, 5.3%, 3α, 17β-dihydroxy-5β-androstan-4-1 (220, 0.1) 9%), 4,11α, 17β-trihydroxyandrost-4-en-3-one (221, 2.4%) (Fig. 29)[99].Formestan biodeforming products (216). Methyltestosterone (222), anabolic steroids, were converted by Mucor's lasemosus in five days to produce two monohydroxylation products in C-7 (7α-hydroxymethyltestosterone, 223, 35%) and C-15 (15α-hydroxymethyltestosterone, 224, 21%) position, dihydroxylate (12,15α-dihydroxymethyltestosterone, 225, 22%) [100] Three additional products were recently identified: 11α-hydroxy-17α-methyltestosterone (226), 6β-hydroxy-17α-methyltestosterone (227), and 6β,11α-dihydroxy-17α-methyltestosterone (228). The ionization of hydroxylation products is a different carbon than 222 with different orientations, and has been reported in C-6β, C-7β, C-9α, C-11α, C-12β, and C-15α (FIG. 30). Bioregeneration products of methyltestosterone (222).Dianabol (methandrostenolone, 17α-methyl-17β-hydroxyl andros-1,4-diene-3 on, 229) oral anabolic steroids that promote protein synthesis (increasing muscle tissue). Five bioconversion products were obtained: 6β-hydroxydiadiabol (230), 15α-hydroxydiarpon (231), 11α-hydroxydiarpon (232), 6β, 12β-dihydroxydiar pombol (233), and 6β-dihydroxydiapon (234). Product 17β-Hydroxy-17α-Methyl-5α-Androst-1,4-Diene-3,6-Dyon (235), 7β-Hydroxydiarpon (236)(237), 17β-hydroxy-17α-methyl-5α-androst-1,4-dien-3,11-dyon (238), and 11β-hydroxydianabol (239) were obtained from 229 biocontests using macrophominafesthonolina. 229 biocontacts using several microorganisms have been reported, for example, penicilium notatum [102] converted 229 to 230 and 231, and Tricoderma Hamatam produced 232 [103]. Similarly, B. Bassiana, A. Ocraceus, Choletrixragenarium, and Sporotrikum sulfur reduction gave biotransformed products 232[104]. Absidia Grauca metabolizes 229 with compound 230, 236-237[105], whereas 229 biopolymers using A. coerula are 7α-hydro 239 was generated with Xydia pombol (240) [106], while 237 was obtained as the only product using B cinerea (Fig. 31) [107]. Dianabol Bio-Transformation Products (229). Metastarne (241) is a synthetic anabolic steroid, known for gaining muscle mass. 241 microbial conversions using M-phasenolina obtained 17β-hydroxy-17α (hydroxymethyl) -2α-methyl-5α-androstan-3,6-dion (242), C. Blakesley ana uses 7α-hydroxymetasterone (243, 2.0%), 7α, 16β-dihydroxymethasterone (244, 0.7%), 5α, 12β-dihydroxymetasterone (245, 1.0%), 7α, 7α, 12β-dihydroxymetasterone (246, 1.5%), 7α, and 9α-dihydroxymethastern (24.5%) were obtained. 241 incubations using fusarium lini produced different metabolites with dehydrogenation of ring A and D: 6β, 17β-dihydroxy-2,17α-dimethyl-5α andros-1,4-diene-3-1 (248, 1.0%, 15α, 17β-dihydroxy-2α, 17α-dimethyl-5α-andros-1,4-diene-3-1 (249, 0.6%) 6β, 17β-dihydroxy-2,17α-dimethylandros-1,4-diein-3-one (250,0.4%), 150, 0.4%). 14α, 15α-dihydroxy-2, 17-dimethyl-5α-andros-1,4,16-trien-3-one (251,0.3%), 17β-hydroxy-2,17α-dimethyl-5α Andros -5α-1,4-Jien-3,6-Dyon (252, 0.3%), 17β-hydroxy-2,17α-dimethyl-5α andros-1,4-jiene-3-one (253,1.0% (Fig. 32)[108].Bio-transformation products of masthastane (241). The bio-conversion process of different steroid compounds described in this review is not exhaustive, but aims to emphasize the importance of bio-conversion through different microorganisms as a useful chemical biological tool for obtaining new derivatives for research purposes and industrial applications. Examples include obtaining steroid compounds for the pharmaceutical industry. Bio-transformation of steroids is implemented in an important way in the partial synthesis of new steroids, for evaluation as hormones and drugs.Currently, there is a wide variety of steroids used as diuretics, anabolic, anti-inflammatory drugs, anti-anti-anti-irritant, anti contraceptives, antitumors, among other applications. Chemical functionalization of the sternum skeleton in different carbon atoms It is related to the biological activity of molecules. This is why microbial transformation plays an important role in obtaining these compounds through chemical conversion, such as oxidation of hydrochloric acid group in C-3 and C-17, isodymization of double bonds Δ5 (6) to Δ4 (5), and hydrogenation.Double bonds Δ1 (2) and Δ4 (5), and carbonyl in c-17 and C-20 β direction. Using fungi of different species of biohydroxylation-C-11α, C-11β, C-15β, and C-16α-genus roots performed at different locations in the steroid skeleton, Streptmyces with aspergillus, carbraria, cunningham, and high yields is an important chemical transformation in many synthesis schemes of new steroids. Hydroxylation of steroids - presents progesterone, testosterone, 17α-methyltestosterone, and 4-androsten-3,17-dion-4-en-3-11 systems, advancing high stereoscopic and re-formed properties at C-6 and C-11 positions, with β directions in the α direction of C-6 and c-11. The presence of methyl groups in C-10 is necessary for hydroxylation in C-11, as seen in derivatives of 19-nortecerone. Interest in bio-transformation of steroid compounds has increased in recent years, due to the acquisition of new useful pharmacologically active compounds. In addition to the development of new genetically modified strains, there is an increase in the availability of im im im im immatized enzymes and the manipulation of culture media. Steroid bio-transformation generally proceeds at a low to moderate yield. One of the main causes is when the solubility in water is low. Currently, methodologies are being developed that incorporate chemicals such as surfactants, ionic liquids, cyclodestolin, liposomes, etc., to increase yields and enable environmentally friendly processes in each biodekindic process. La Carrera de Biologia, Fes Zaragoza, UNAM. Fabiola Cano appreciates her suggestions and comments on improving the manuscript, built by scientists, for scientists. 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