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NATURALLY OCCURRING STEROIDS CONTAINING A TERTIARY BUTYL GROUP AND THEIR BIOLOGICAL ACTIVITIES

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ABSTRACT
The present review article describes distribution and biological activities of steroids containing a tertiary butyl group. More than 65 biological active steroids have shown confirmed antitumor, antiviral, or apoptosis, and other activities. The structures, reported and predicted activities of a selection of describes steroids are reported. With the computer program PASS based on structure–activity relationships (SAR) some additional activities are also predicted, which point toward new possible applications of these lipids. This article emphasizes the role of steroids containing a tertiary butyl group as an important source of leads for drug discovery.

KEYWORDS: Steroids, neo, tertiary butyl group, lipids, activities.

1. INTRODUCTION

Biologically active metabolites containing a tertiary butyl group(s) [or tert-butyl unit(s)] are rather rare compounds that have been found in nature.[1,2] These compounds were found in cyanobacteria, the leaves of plants, fungi and marine invertebrates and algae.[1,2]

A tertiary butyl group (tert-butyl, t-Bu, or -CMe_3) is commonly used in organic chemistry; [3,4,5,6,7] however, in lipid chemistry or as is currently called lipidomics, such a group (or unit) has a very specific name, a neo group (or neo unit), which occurs in the composition of hydrocarbons (alkanes and alkenes) and fatty (carboxylic) acids.[1,2,6,7] Interestingly, it is unclear if a tertiary butyl group occurs in natural compounds.[1,2] This group is voluminous in the skeleton of the molecule and it participates in the steric interactions between the molecules. If we use the term from lipidomics, [1] then it is quite realistic to name steroids containing a tertiary butyl group as neo steroids. We will use this term for *neo steroids* in this article.

As already proved by numerous works, there is a relationship between structure and activity, and this principle is called SAR (Structure-Activity-Relationship). We used the computer program PASS, containing about one million chemical compounds and more than 8,000 biological activities, and calculated the biological activity of different natural and/or synthetic compounds.[8,9] PASS predictions are based on SAR analysis of the training set consisting of more than one million drugs, drug candidates and lead compounds. The algorithm of PASS practical utilization is described in detail in several publications.[10-13] For each activity, Pa and Pi values are calculated, which can be interpreted either as the probabilities of a molecule belonging to the classes of active and inactive compounds, respectively, or as the probabilities of the first and second kind of errors in prediction. A computer analysis of the predicted biological activity spectra showed that 398 types of biological activity are predicted with Pa>70% and 167 with Pa>50%. In a biological activity spectrum estimated by PASS, the activity predicted with the highest probability is called the focal activity.

This review is a comprehensive survey on natural steroids containing a tertiary butyl group obtained from terrestrial and marine organisms. This is the first article to review natural steroids containing a tertiary butyl group (*neo steroids*).

2. NEO STEROIDS OF TERRESTRIAL ORIGIN

The first three neo steroids, which are called 3β-methoxy-24-methyl-lanost-9(11)-en-24-ol (1), 24ξ-methoxy-24,25-dimethyl-lanost-9(11)-en-3-one (2), and 3β,24ξ-dimethoxy-24,25-dimethyllanost-9(11)-ene (3), were isolated from *Neolitsea pulchella* (Lauraceae, Hong Kong) in the early 1970s.[14,15] The genus Shirodamo (Neolitsea) is an evergreen shrub tree of Camphoraceae with approximately 85 species, and the leaf, bark and fruit oils of some plant species showed antibacterial activity.[16]

Two triterpenoids, 24,25-dimethyl-9(11),23-lanostadienol (4) and 24,25-dimethyl-lanosta-9(11),23-dien-3-one (5), were obtained from the stems of *Quercus* spp. (*Q. bambusaefolia*, *Q. championi*, and *Q. myrsinaefolia*).[17] Wallenone (6), a C32 tirucallane-type triterpene, was isolated from the leaves of *Gyrinops wala* (Thymelaeaceae, which is a small tree grown on Ceylon).[18] More recently, the same compound was isolated from the ethyl acetate extract of the dried leaves of *Esenbeckia stephani* (Rutaceae).[19]

The 25-methyl-dolichosterone [7, (22*R*,23*R*)-2α,3α,22,23-tetra-hydroxy-25-methyl-24-methylene-5α-cholestan-6-one] was isolated from French bean seeds *Phaseolus vulgaris* (family Fabaceae).[20-24] Other scientists studying the seeds of this plant additionally found a series of neo-steroids (8-16).[20,23,25-27] In addition, the neo steroid (17) was isolated from the English ryegrass pollen of *Lolium perene* (family Poaceae).[28] Two neo steroids (10 and 11) belonging to the brassinosteroid family have also been extracted from *Arabidopsis thaliana*.[29,30] Structures and biological activities of neo steroids (1-17) are shown in Figure 1 and Table 1, respectively.

The 3,24-dimethoxy-24,25-dimethyl-5α-lanost-9(1)-ene (18) and 24-methoxy-24,25-dimethyl-5α-lanost-9-ene (19) tragopogonosides were obtained from the whole plants of *Tragopogon pratensis*, which is also called Goat's-beard.[31] The neo sterol 24-methylene-25-methyl-lathosterol (20) was isolated from the aerial parts of the herbaceous plant *Sicyos angulatus*.[32] The leaves and bark of *Schefflera octophylla* (family Araliaceae) from southwest areas of China (Qingyuan Mountain) contains 24,25-dimethyl-5-cholestene (21).[33]

The seeds of herbaceous plant *Lens culinaris* (family Fabaceae) contain 24-methylene-25-methylcholesterol (22).[34] This steroid has also been found in the seeds of a medicinal plant called horsegram *Dolichos biflorus* (family Fabaceae), [35] in the leaves and pods of *Wrightia tinctoria* (family Apocynaceae),[36] in the roots, leaves, stems, and flowers of *Kalanchoe daigremontiana* (family Crassulaceae),[37] in the Chinese yam (family Dioscoreaceae) *Dioscorea opposita*, and in the Chinese herbaceous perennial plant *Salvia przewalskii*.[38] The 24-methylene-25-methylcholesterol (22) was also found in a whisk fern *Psilotum nudum*.[39] Two neo steroids (22 and 23) were present in the leaves and stems and the pericarp of the fruit and roots of a plant from the family Cucurbitaceae.[40]

The tirucallane triterpenoid, aquilacallane B (24), was isolated from the leaves of *Aquilaria sinensis*. The obtained neo steroid exhibited weak cytotoxic activity against some cells.[41] The resin of this plant has been used as a traditional sedative, analgesic, and digestive Chinese traditional medicine.[42] A herbaceous plant, *Ocimum basilicum* (family Labiateae), from Pakistan is used for the aerial parts, leaves, seeds, flowers, and roots used as medicines and contains (22*E*)-24ξ-ethyl-25-methylcholesta-5,22-diene-3β-ol-3-O-D-glucopyranoside (25).[43] Essential oils from fresh leaves and flowers are used as aromatic additives in food, pharmaceutical and cosmetic preparations.[44] Traditionally, *O. basilicum* extracts have been used to treat headaches, cough, diarrhoea, and impaired renal function.[45]

The anticancer agent, t-Bu 7α,12α-dihydroxy-4,4,14α-trimethyl-3,11,15-trioxo-5α-chol-8-en-24-oate (26), which is called t-butyl lucidenate B, was isolated from the fruiting bodies of an oriental fungus *Ganoderma lucidum*.[46]

Cytotoxic 24,25-dimethyl-5-cholestene-2,3-oxide (27) was isolated from a wild fungus, *Boletus edulis*, which was collected from the Changbai Montain area.[47] Three neo steroids (28-30) have been isolated from auxotroph *Saccharomyces cerevisiae* strain GL7.[48] The sterol C24-methyl transferase from *Trypanasoma brucei* TbSMT1 produces 24-methyl sterols that serve as substrates for 24-dimethyl sterols that contain a Δ25(27)-bond, and neo steroids (31 and 32) were isolated from the extract.[49] Structures and biological activities of neo steroids (18-32) are shown in Figure 2 and Table 2, respectively.

3. NEO STEROIDS OF MARINE ORIGIN

Neo steroids that have been found in marine invertebrates and most of these compounds are produced by sponges. The 24-methylene-25-methylcholesterol (22) was isolated from the freshwater green alga *Hydrodictyon reticulatum*.[50] Epipolasterol (3β,22*E*,24ξ)-25,28-Dimethylstigmasta-5,28-dien-3-ol (33) was isolated from the sponges *Halichondria* sp. and *Epipolasis* sp, and their methanolic and aqueous extracts were found to increase the activities of Na^{+}-K^{+} ATP-ase and Mg^{++} ATP-ase.[51,52,53]

Topsentinols A (34), C (35), D (36), E (37), F (38), H (39), I (40) and J (41) contain a tertiary butyl group in care steroids. All of these neo steroids were obtained from the Okinawan marine sponge *Topsentia* sp. Topsentinol B showed antifungal activity against *Trichophyton mentagrophytes*.[54] This is a rare case for living organisms when a marine sponge contains eight neo steroids.

In 1949, Bergmann and Feeney [55] discovered haliclonasterol (25-methyl-24ξ-ergosta 5,7,22- rien-3β-ol) (42) in marine sponges belonging to the genus Haliclona. They were studying the sterol composition of acetone extracts from the sponges *H. variabilis*, *H. permollis*, *H. coerulescens*, *H. viridis*, *H. rubens*, and *H. longleyi* and showed that haliclonasterol was present in all of the investigated species. Haliclonasterol was also detected in the marine green algae *Monostroma nitidum* and *Enteromorfa linza*[56] and other species belonging to the phylum Chlorophyta.[57,58] It was also found in other sponge species[59] and in three sea anemones including *Palythoa mammilosa*, *Zoanthus proteus*, and *Condylactis*

gigantean.[60] Li and Djerassi [61] identified an axinyssasterol (43) and (3β,24*E*)-25-methyl-stigmasta-5,24(28)-dien-3-ol (44) from a *Pseudoaxinyssa* species for the first time. In the Australian sponge *Trachyopsis* sp, 64% of the total sterols were axinyssasterol.[62] The (3β,22*E*,24ξ)-28,28-Dimethyl-stigmasta-5,22,25-trien-3-ol acetate (45) and (3β,22*E*)-25-methyl-stigmasta-5,22-dien-3-ol (46) were obtained from an EtOH extract of the sponge *Halichondria* sp.[63,64] and the compound (46) was also found in specimens of the sponge *Trachyopsis aplysinoides* from Sri Lanka inshore waters.[64] Structures and biological activities of neo steroids (33-46) are shown in Figure 3 and Table 3, respectively.

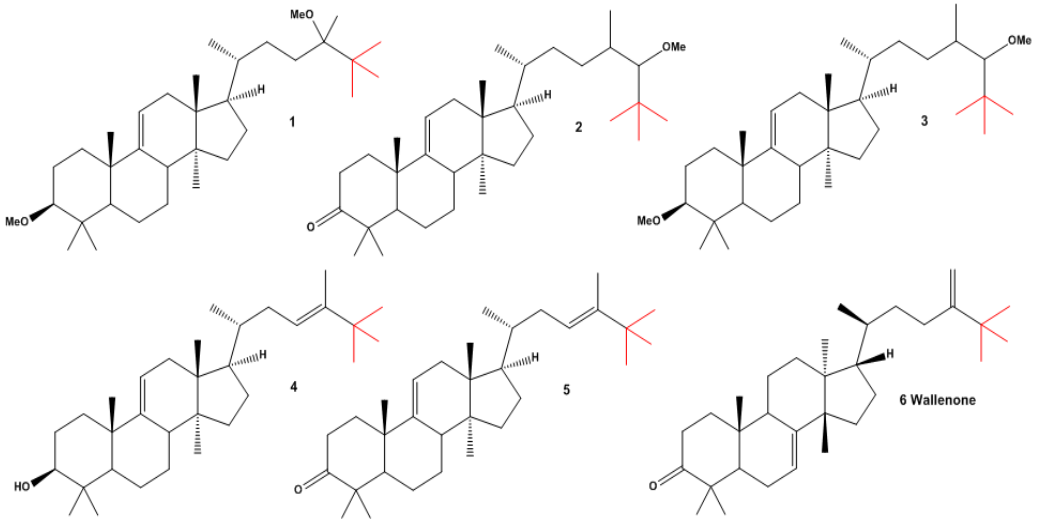
The antimicrobial halistanol (47) and its trisulfate (48) were isolated from the Okinawan sponge *Halichondria* cf. *moorei* more than 25 years ago.[65] More recently, halistanol trisulfate was found in different sponge species.[59,66-70] Halistanol trisulfate has a strong haemolytic potency. Halistanol sulfate E (49) was present in an extract of the marine sponge *Epipolasis* sp.[71] Halistanol trisulfate, sterol sulfate, and Sch 572423 (50) were detected in a marine sponge *Topsentia* sp.; both metabolites were identified as platelet P2Y12 inhibitors with an IC_{50} of 0.48 and 2.2 μM, respectively.[72] Some sponge steroids contain sulfate groups in positions 3α and 2β. This series of compounds includes a compound (51) as a possible biogenetic precursor of halistanol sulfate.[59,73]

Neo steroid, which is called halistanol sulfate F (52), is an anti-HIV agent that destroys or inhibits the replication of HIV-2 and was isolated from a marine sponge *Pseudoaxinissa digitate*.[74] The neo sulfated steroid, which is called ibisterol C (53), was extracted from sponges of the *Xestospongia* species collected off the Philippine coasts and also from sponges of the *Topsentia* species collected off the Bahamas Islands. This sterol is toxic to cancer cells and inhibited the integrase VIH infection.[75] Tri-sulfated neo sterol (54) was isolated from the sponge *Trachiopsis halichondroides*, which was collected in the North Pacific Ocean.[75]

A tri-sulfated steroid (55) was extracted from the sponge *Topsentia ophiraphidites* collected off of Colombia (Caribbean Sea). This neo sokotrasterol sulfate triggers angiogenesis *in vivo* and epithelial budding *in vitro*. These effects are associated with cyclooxygenase-2 and vascular endothelial cell growth factor functions.[76] Same saturated sulfated steroids (56) were isolated from the sponge *T. ophiraphidites*. This steroid showed antimicrobial, ichthyotoxic, and anti-HIV activities and included haemolytic, glucanase inhibiting and thrombin receptor interaction activities. Thus, this sterol inhibits the GTP/GDP exchange from G protein with the GTP hydrolysing RAS (P21) protein.[76] Triterpenoid saponins, erylosides C (57), D (58), E (59), I (60) and J (61), were isolated from the sponge *Erylus nobilis* (Jaeju Island, Korea) and sponges of the *Penares* species. These compounds exhibited moderate cytotoxicity against a human leukaemia cell line K 562.[77,78,79] Structures and biological activities of neo steroids (47-59) are shown in Figure 4 and Table 4, respectively.

The Atlantic tropical sponge *Erylus goffrilleri* contains unusual lanostane glycoside, eryloside E (58), [80] lanostane glycosides, erylosides R (62), T (63), U (64), F5 (65), V (66) and F7 (67) with β-D-galactopyranose and were isolated from the Caribbean sponge *Erylus goffrilleri*.[81] Anticancer agents, erylosides R (62), T (63), V (66), and F7 (67) exhibit cytotoxic activities against Ehrlich carcinoma tumour cells (IC_{50} of 20-40 μM).[80]

Triterpene glycoside, which is called holothurin A4 (68) was isolated from the sea cucumber, *Holothuria scabra*. This neo glycoside steroid (68) was found to be strongly cytotoxic to both cancer cell lines, KB and Hep-G2, with 50% inhibitory concentrations (IC_{50}) of 1.12 and 0.57 μg/mL.[82] Structures and biological activities of neo steroids (60-68) are shown in Figure 5 and Table 5, respectively.



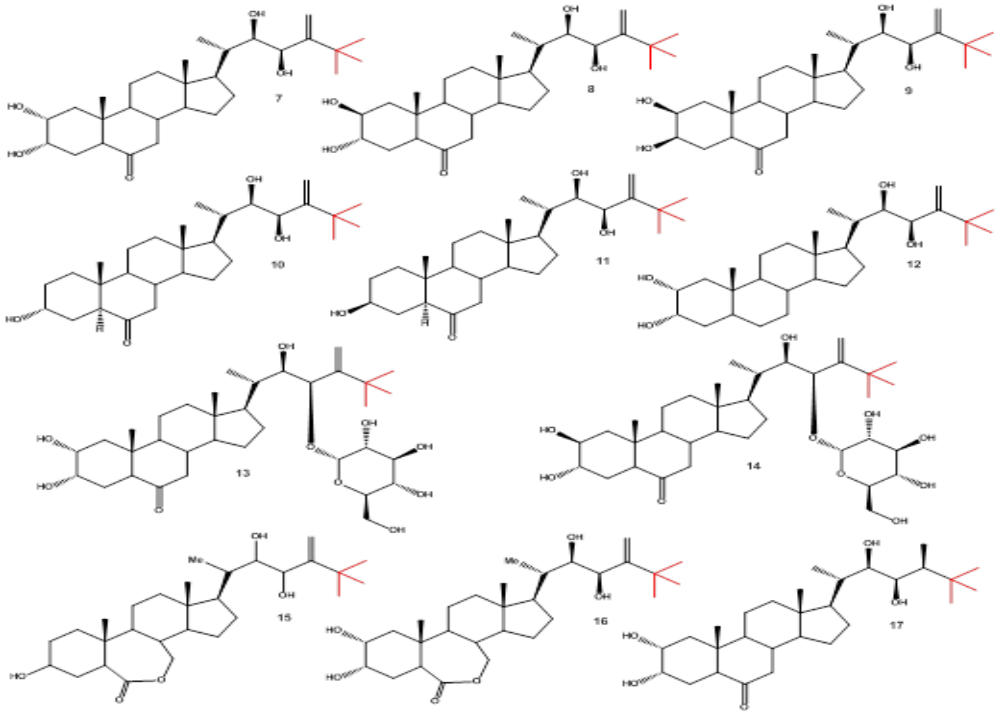


Fig 1: Neo steroids isolated from plants.

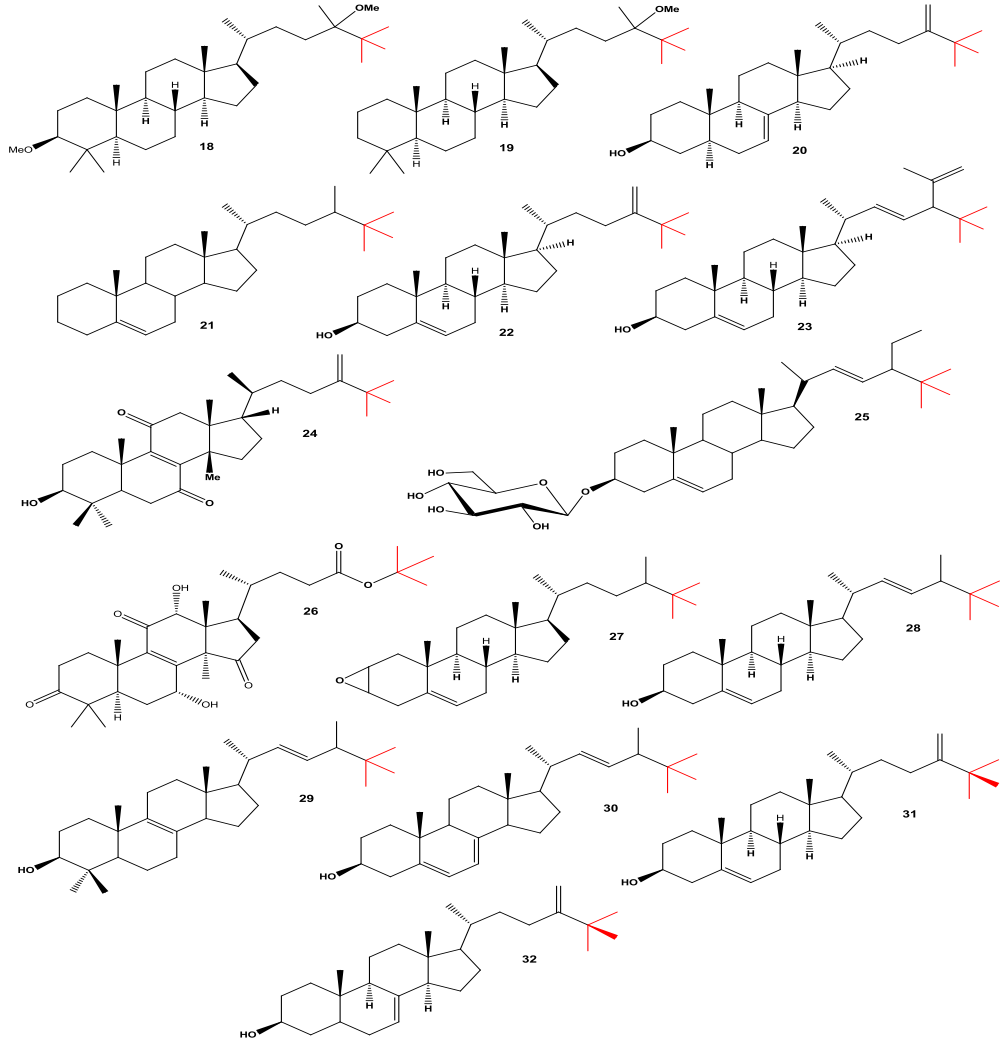


Fig 2: Neo steroids isolated from plant, fungi and yeast.

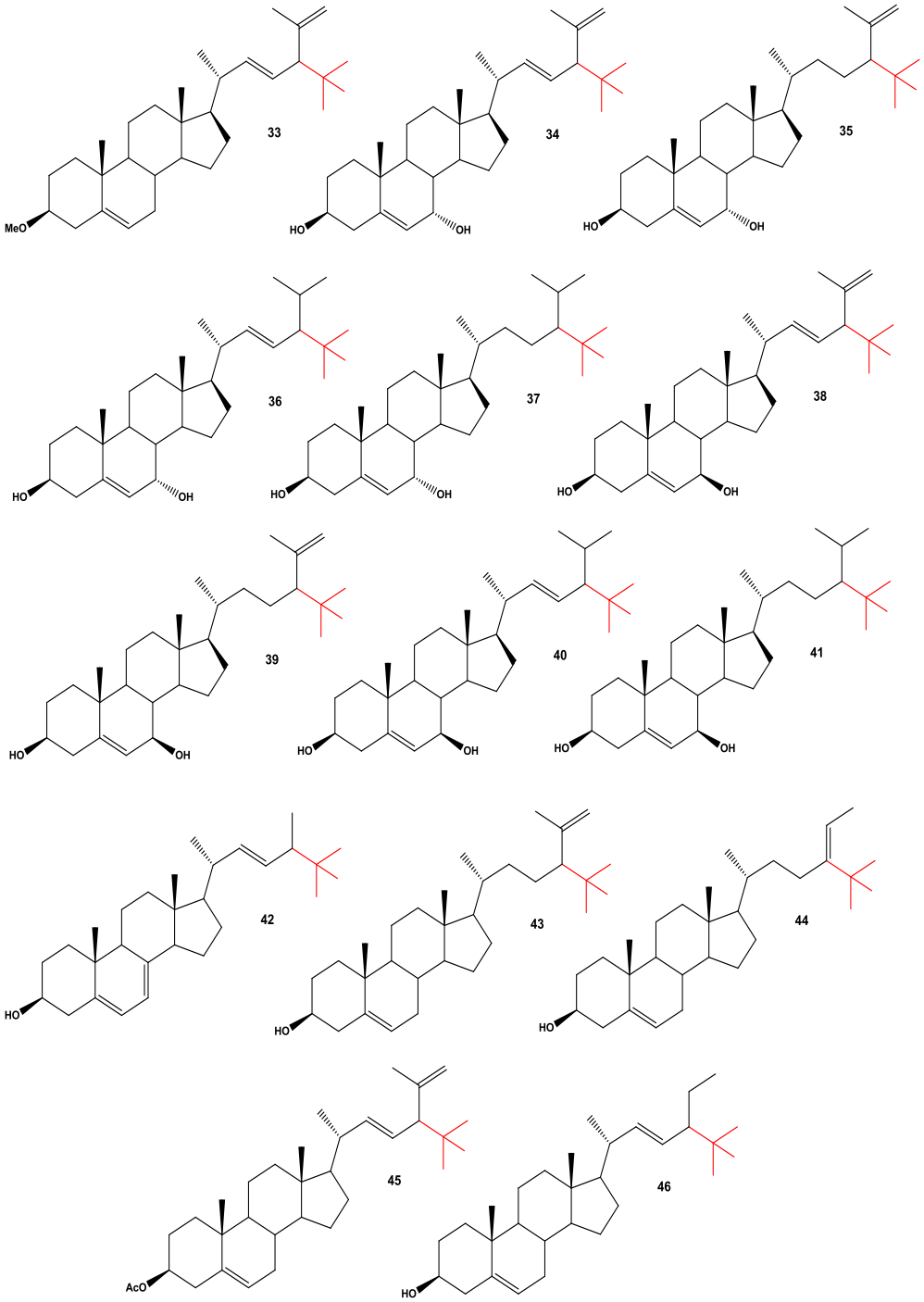


Fig 3: Neo steroids isolated from marine sponges, anemones and algae.

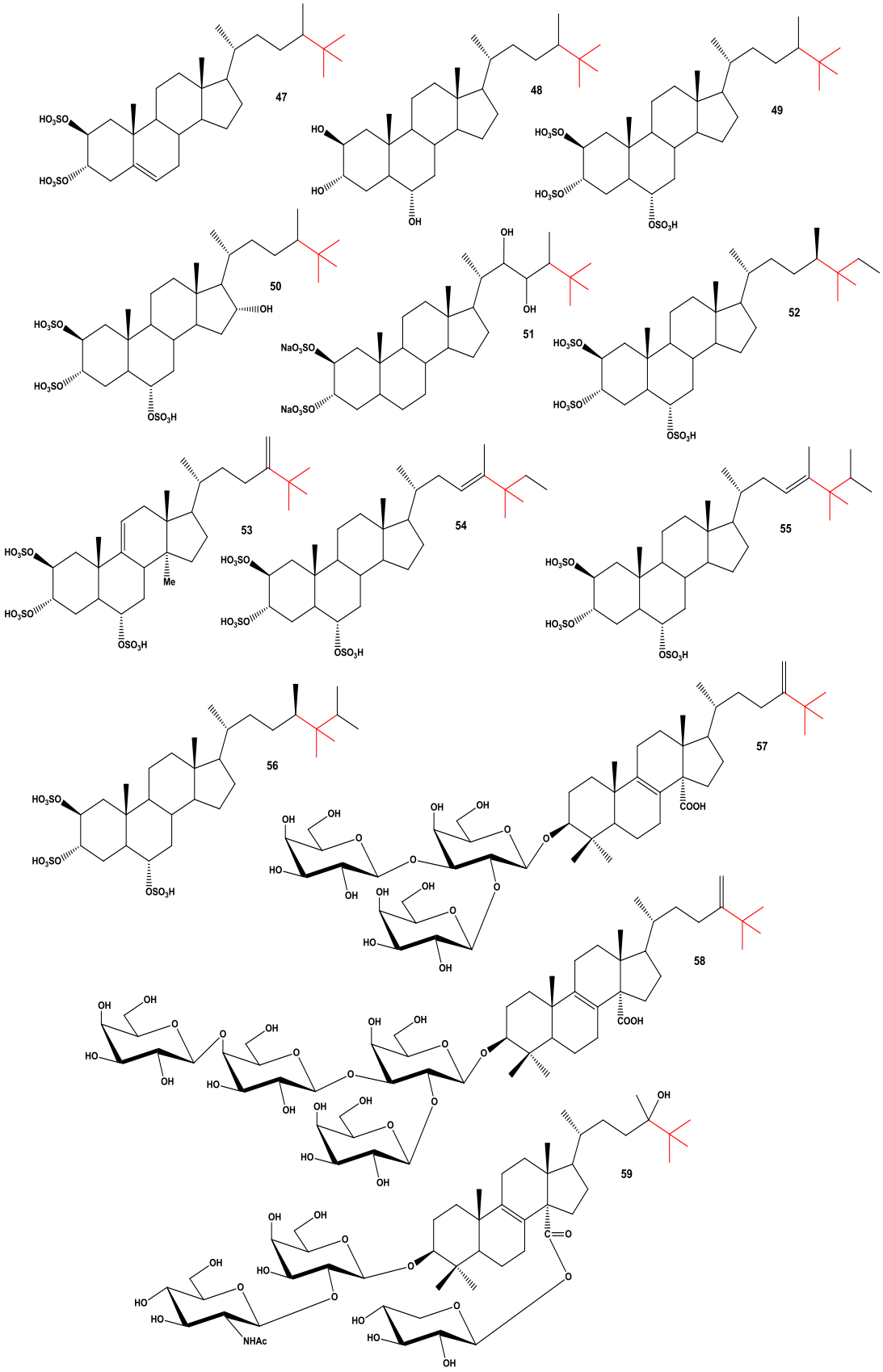


Fig 4: Neo steroids isolated from marine sponges.

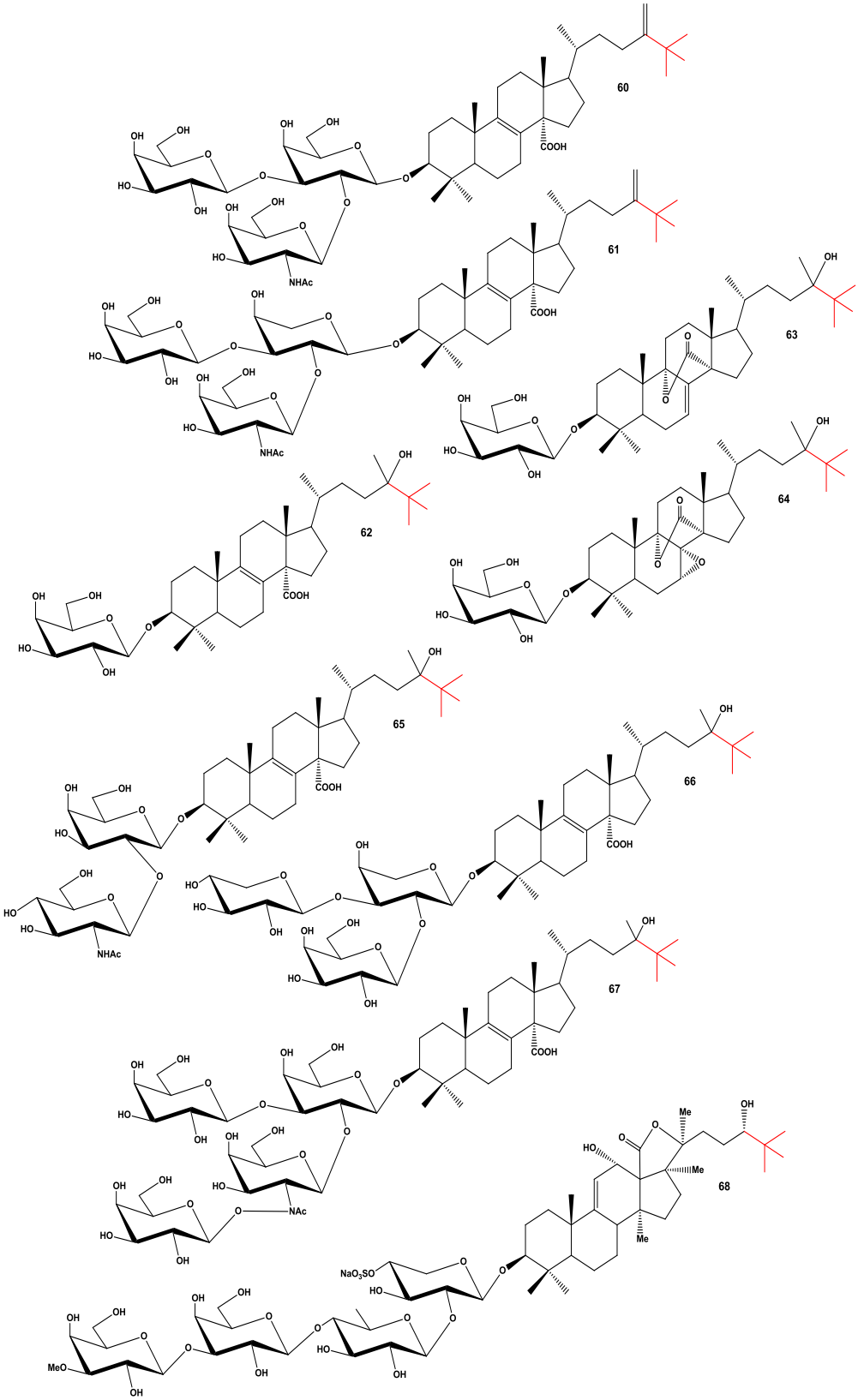


Fig 5: Glycosides of neo steroids isolated from marine sponge and holothurian species.

Table 1: Predicted pharmacological activities of neo steroids from plant, fungi and yeast (1-17)

No	Activity reviewed	Activities confirmed(Pa)	Predicted activities (Pa)*
1	Antiviral	Antiviral (Influenza) (0,686) Antiviral (0,505)	Chemopreventive (0,896) Hepatoprotectant (0,860) Apoptosis agonist (0,850) Antineoplastic (0,810) Hypolipemic (0,809) Antieczematic (0,808) Antiinflammatory (0,787) Antiulcerative (0,766) Immunosuppressant (0,751) Antipruritic (0,741) Antipsoriatic (0,734) Antifungal (0,712)
2	Antiviral	Antiviral (Influenza) (0,670)	Apoptosis agonist (0,817) Chemopreventive (0,799) Antineoplastic (0,806) Hepatoprotectant (0,775) Antifungal (0,775) Immunosuppressant (0,750) Antipruritic (0,715) Antiinflammatory (0,714) Antieczematic (0,700) Hypolipemic (0,694) Antipsoriatic (0,654) Antiosteoporotic (0,632) Prostate disorders treatment (0,625)
3	Antiviral	Antiviral (Influenza) (0,580)	Hepatoprotectant (0,873) Chemopreventive (0,825) Antineoplastic (0,823) Apoptosis agonist (0,817) Antifungal (0,799) Antieczematic (0,780) Hypolipemic (0,776) Immunosuppressant (0,767) Antipruritic (0,753) Antiinflammatory (0,718) Antipsoriatic (0,703) Lipid metabolism regulator (0,616) Prostate disorders treatment (0,608) Antiosteoporotic (0,606)
4	Not studied		Chemopreventive (0,911) Hepatoprotectant (0,895) Lipid metabolism regulator (0,891) Antineoplastic (0,888) Apoptosis agonist (0,867) Hypolipemic (0,852) Antieczematic (0,836) Antiinflammatory (0,830) Antipsoriatic (0,804) Antifungal (0,731) Atherosclerosis treatment (0,676) Antiosteoporotic (0,659) Prostate disorders treatment (0,654) Antiviral (Influenza) (0,615)
5	Not studied		Antineoplastic (0,874) Apoptosis agonist (0,872) Chemopreventive (0,842) Antiinflammatory (0,822) Antieczematic (0,795)

			Antipsoriatic (0,781) Hepatic disorders treatment (0,779) Hypolipemic (0,773) Antihypercholesterolemic (0,746) Immunosuppressant (0,731) Lipid metabolism regulator (0,725) Antiosteoporotic (0,681) Antiviral (Influenza) (0,564)
6	Antiviral	Antiviral (Influenza) (0,659)	Apoptosis agonist (0,869) Chemopreventive (0,857) Antineoplastic (0,841) Antieczematic (0,809) Hepatoprotectant (0,785) Antiinflammatory (0,784) Antipsoriatic (0,771) Hypolipemic (0,744) Immunosuppressant (0,735) Antiulcerative (0,714) Antifungal (0,709)
7	Not studied		Antineoplastic (0,908) Apoptosis agonist (0,906) Respiratory analeptic (0,903) Antieczematic (0,882) Anesthetic general (0,862) Antiinflammatory (0,853) Choleretic (0,798) Immunosuppressant (0,789) Hepatoprotectant (0,770) Antipsoriatic (0,763) Antipruritic (0,761) Erythropoiesis stimulant (0,740) Antiosteoporotic (0,657)
8	Antiviral	Membrane integrity antagonist (0,735) Transcription factor inhibitor (0,537) Membrane permeability enhancer (0,510)	Antineoplastic (0,908) Apoptosis agonist (0,906) Respiratory analeptic (0,903) Antieczematic (0,882) Anesthetic general (0,862) Antiinflammatory (0,853) Choleretic (0,798) Immunosuppressant (0,789) Hepatoprotectant (0,770) Antipsoriatic (0,763) Antipruritic (0,761) Erythropoiesis stimulant (0,740) Antiosteoporotic (0,657)
9	Antiviral	Membrane integrity antagonist (0,735) Transcription factor inhibitor (0,537) Membrane permeability enhancer (0,510)	Antineoplastic (0,908) Apoptosis agonist (0,906) Respiratory analeptic (0,903) Antieczematic (0,882) Anesthetic general (0,862) Antiinflammatory (0,853) Choleretic (0,798) Immunosuppressant (0,789) Hepatoprotectant (0,770) Antipsoriatic (0,763) Antipruritic (0,761) Erythropoiesis stimulant (0,740) Antiosteoporotic (0,657)
10	Not studied		Antineoplastic (0,907) Apoptosis agonist (0,902)

			Respiratory analeptic (0,895) Anesthetic general (0,862) Antieczematic (0,860) Choleretic (0,852) Antihypercholesterolemic (0,839) Erythropoiesis stimulant (0,812) Antiinflammatory (0,808) Immunosuppressant (0,785) Hepatoprotectant (0,776) Cytoprotectant (0,767) Antipsoriatic (0,765) Antipruritic (0,742) Antiosteoporotic (0,679) Prostate disorders treatment (0,678)
11	Antiviral	Antiviral (Influenza) (0,416) Membrane integrity antagonist (0,729) Lipoprotein lipase inhibitor (0,575) Membrane permeability enhancer (0,537)	Antineoplastic (0,907) Apoptosis agonist (0,902) Respiratory analeptic (0,895) Anesthetic general (0,862) Antieczematic (0,860) Choleretic (0,852) Antihypercholesterolemic (0,839) Erythropoiesis stimulant (0,812) Antiinflammatory (0,808) Immunosuppressant (0,785) Hepatoprotectant (0,776) Cytoprotectant (0,767) Antipsoriatic (0,765) Antipruritic (0,742) Antiosteoporotic (0,679) Prostate disorders treatment (0,678)
12	Antiviral	Antiviral (Influenza) (0,420) Membrane integrity antagonist (0,829) Lipoprotein lipase inhibitor (0,635) Membrane permeability enhancer (0,540) Immunostimulant (0,528)	Respiratory analeptic (0,934) Antineoplastic (0,914) Anesthetic general (0,912) Apoptosis agonist (0,907) Antieczematic (0,898) Antiinflammatory (0,873) Hepatoprotectant (0,794) Antipruritic (0,777) Antipsoriatic (0,775) Choleretic (0,773) Erythropoiesis stimulant (0,762) Prostate disorders treatment (0,704)
13	Antiviral	Antiviral (Influenza) (0,704)	Respiratory analeptic (0,985) Hepatoprotectant (0,966) Antihypercholesterolemic (0,917) Antineoplastic (0,910) Apoptosis agonist (0,896) Laxative (0,882) Choleretic (0,868) Chemopreventive (0,861) Antiinflammatory (0,860) Anesthetic general (0,855) Antieczematic (0,823) Antifungal (0,794) Anticarcinogenic (0,777) Antipruritic (0,749) Genital warts treatment (0,763) Antipsoriatic (0,734) Antibacterial (0,707)
14	Antiviral	Antiviral (Influenza)	Respiratory analeptic (0,985)

		(0,704)	Hepatoprotectant (0,966) Antihypercholesterolemic (0,917) Antineoplastic (0,910) Apoptosis agonist (0,896) Laxative (0,882) Choleretic (0,868) Chemopreventive (0,861) Antiinflammatory (0,860) Anesthetic general (0,855) Antieczematic (0,823) Antifungal (0,794) Anticarcinogenic (0,777) Antipruritic (0,749) Genital warts treatment (0,763) Antipsoriatic (0,734) Antibacterial (0,707)
15	Antiviral	Membrane integrity antagonist (0,629) Membrane permeability enhancer (0,517)	Antineoplastic (0,902) Apoptosis agonist (0,901) Genital warts treatment (0,895) Antieczematic (0,858) Hepatoprotectant (0,850) Antihypercholesterolemic (0,827) Antiinflammatory (0,827) Immunosuppressant (0,776) Antipsoriatic (0,722) Antipruritic (0,722) Respiratory analeptic (0,707) Anesthetic general (0,690) Erythropoiesis stimulant (0,625) Prostate disorders treatment (0,618)
16	Antiviral	Membrane integrity antagonist (0,640)	Apoptosis agonist (0,904) Antineoplastic (0,904) Genital warts treatment (0,895) Antieczematic (0,879) Antiinflammatory (0,863) Hepatoprotectant (0,843) Immunosuppressant (0,780) Antipruritic (0,745) Respiratory analeptic (0,727) Antipsoriatic (0,720) Anesthetic general (0,690) Antihypercholesterolemic(0,643) Prostate disorders treatment (0,624) Cholesterol synthesis inhibitor (0,596)
17	Antiviral	Antiviral (Influenza) (0,408) Membrane integrity antagonist (0,814) Lipoprotein lipase inhibitor (0,575) Membrane permeability enhancer (0,534)	Apoptosis agonist (0,922) Respiratory analeptic (0,887) Anesthetic general (0,885) Antiinflammatory (0,879) Antieczematic (0,869) Antineoplastic (0,865) Choleretic (0,806) Antipruritic (0,788) Hepatoprotectant (0,766) Antihypercholesterolemic (0,714) Antiseborrheic (0,712) Prostate disorders treatment (0,696) Antipsoriatic (0,681) Erythropoiesis stimulant (0,680) Antiosteoporotic (0,673)

* Only activities with Pa > 0.5 are shown

Table 2: Predicted pharmacological activities of neo steroids from plant, fungi and yeast.(18-32)

No	Activity reviewed	Activities confirmed(Pa)	Predicted activities (Pa)*
18	Antiviral	Antiviral (Influenza) (0,666)	Antieczematic (0,873) Antihypercholesterolemic (0,849) Hepatoprotectant (0,848) Respiratory analeptic (0,827) Hypolipemic (0,818) Antineoplastic (0,814) Chemopreventive (0,806) Cytoprotectant (0,798) Apoptosis agonist (0,794) Antipruritic (0,788) Antipsoriatic (0,775) Antiinflammatory (0,765) Antiosteoporotic (0,762)
19	Antiviral	Antiviral (Influenza) (0,597)	Antihypercholesterolemic (0,886) Antieczematic (0,848) Cytoprotectant (0,812) Hypolipemic (0,810) Choleretic (0,796) Antipsoriatic (0,781) Hepatoprotectant (0,780) Antineoplastic (0,784) Apoptosis agonist (0,777) Antiosteoporotic (0,768) Antipruritic (0,767) Respiratory analeptic (0,758) Antiinflammatory (0,749) Prostate disorders treatment (0,693)
20	Antiviral	Antiviral (Influenza) (0,502)	Respiratory analeptic (0,957) Antihypercholesterolemic (0,956) Anesthetic general (0,898) Hepatoprotectant (0,886) Antieczematic (0,872) Chemopreventive (0,857) Antineoplastic (0,847) Hypolipemic (0,836) Apoptosis agonist (0,826) Antipsoriatic (0,798) Antipruritic (0,773) Bone diseases treatment (0,760)
21	Not studied		Antihypercholesterolemic (0,915) Respiratory analeptic (0,902) Anesthetic general (0,862) Antieczematic (0,834) Antipruritic (0,800) Antiosteoporotic (0,770) Prostate disorders treatment (0,764) Antineoplastic (0,756) Hypolipemic (0,739) Immunosuppressant (0,720) Antiinflammatory (0,714) Antipsoriatic (0,709) Ovulation inhibitor (0,649)
22	Not studied		Respiratory analeptic (0,969) Antihypercholesterolemic (0,961) Anesthetic general (0,897) Antieczematic (0,872) Antineoplastic (0,869) Hypolipemic (0,827)

			Hepatoprotectant (0,826) Antipsoriatic (0,802) Antipruritic (0,792) Ovulation inhibitor (0,791) Antiosteoporotic (0,777) Antiinflammatory (0,776) Apoptosis agonist (0,759)
23	Not studied		Antihypercholesterolemic (0,964) Chemopreventive (0,911) Apoptosis agonist (0,905) Respiratory analeptic (0,900) Antineoplastic (0,882) Antieczematic (0,859) Hypolipemic (0,835) Antiinflammatory (0,817) Antipsoriatic (0,814) Antiosteoporotic (0,804) Radioprotector (0,787) Antipruritic (0,765) Prostate disorders treatment (0,741) Ovulation inhibitor (0,734) Atherosclerosis treatment (0,717)
24	Anticancer	Antineoplastic (0,870) Antineoplastic (melanoma) (0,540) Antineoplastic (pancreatic cancer) (0,537) Antineoplastic (sarcoma) (0,502)	Hepatoprotectant (0,847) Antieczematic (0,841) Chemopreventive (0,826) Apoptosis agonist (0,826) Hypolipemic (0,799) Antifungal (0,780) Antipsoriatic (0,764) Antiinflammatory (0,754) Antipruritic (0,740) Antihypercholesterolemic (0,733) Cholesterol synthesis inhibitor (0,674) Atherosclerosis treatment (0,651) Antiviral (Influenza) (0,605)
25	Anticancer	Antineoplastic (0,891) Anticarcinogenic (0,858) Antineoplastic (liver cancer) (0,843) Antineoplastic (sarcoma) (0,672) Antineoplastic, alkylator (0,622) Antimetastatic (0,551) Prostate cancer treatment (0,510)	Antihypercholesterolemic (0,989) Respiratory analeptic (0,988) Antitoxic (0,987) Chemopreventive (0,972) Neuroprotector (0,921) Anesthetic general (0,914) Hepatoprotectant (0,897) Radioprotector (0,889) Hemostatic (0,875) Apoptosis agonist (0,830) Antiinflammatory (0,821) Hypolipemic (0,800)
26	Anticancer	Antineoplastic (0,830) Antineoplastic (pancreatic cancer) (0,588) Antimetastatic (0,534)	Antieczematic (0,785) Apoptosis agonist (0,777) Chemopreventive (0,776) Choleretic (0,762) Immunosuppressant (0,731) Analeptic (0,716) Antihypercholesterolemic (0,691) Antipruritic (0,678) Antiinflammatory(0,668) Hepatoprotectant (0,658) Antipsoriatic (0,575) Atherosclerosis treatment (0,573) Cholesterol synthesis inhibitor (0,565)

			Antipruritic, allergic (0,554) Antiosteoporotic (0,538) Antiviral (Influenza) (0,519)
27	Not studied		Respiratory analeptic (0,921) Antihypercholesterolemic (0,852) Antieczematic (0,808) Antineoplastic (0,799) Antipruritic (0,780) Apoptosis agonist (0,737) Immunosuppressant (0,720) Hypolipemic (0,681) Antiinflammatory (0,675) Antipsoriatic (0,671) Antiosteoporotic (0,667) Prostatic (benign) hyperplasia treatment (0,660)
28	Not studied		Antihypercholesterolemic (0,969) Respiratory analeptic (0,907) Antineoplastic (0,877) Antieczematic (0,859) Apoptosis agonist (0,854) Anesthetic general (0,853) Hypolipemic (0,846) Antipsoriatic (0,827) Antiosteoporotic (0,826) Antiinflammatory (0,800) Radioprotector (0,796) Antipruritic (0,795) Immunosuppressant (0,793) Prostate disorders treatment (0,765) Neuroprotector (0,745) Ovulation inhibitor (0,738) Antiparkinsonian, rigidity relieving (0,725) Hepatoprotectant (0,704)
29	Not studied		Antihypercholesterolemic (0,920) Apoptosis agonist (0,898) Antineoplastic (0,872) Antieczematic (0,870) Hypolipemic (0,857) Antipsoriatic (0,845) Antiosteoporotic (0,821) Antiinflammatory (0,806) Antipruritic (0,787) Immunosuppressant (0,774) Prostate disorders treatment (0,737) Atherosclerosis treatment (0,729) Contraceptive (0,705) Lipid metabolism regulator (0,696) Antifungal (0,674)
30	Not studied		Antihypercholesterolemic (0,960) Apoptosis agonist (0,886) Antieczematic (0,870) Antineoplastic (0,863) Hypolipemic (0,851) Respiratory analeptic (0,846) Antipsoriatic (0,825) Antiosteoporotic (0,825) Immunosuppressant (0,776) Antipruritic (0,767)

			Anesthetic general (0,755) Hemostatic (0,753) Antiinflammatory (0,753) Prostate disorders treatment (0,734) Atherosclerosis treatment (0,683)
31	Not studied		Respiratory analeptic (0,969) Antihypercholesterolemic (0,961) Anesthetic general (0,897) Antieczematic (0,872) Antineoplastic (0,869) Hepatoprotectant (0,826) Hypolipemic (0,827) Proliferative diseases treatment (0,802) Antipsoriatic (0,802) Antipruritic (0,792) Ovulation inhibitor (0,791) Immunosuppressant (0,787) Antiosteoporotic (0,777) Antiinflammatory (0,776) Apoptosis agonist (0,759) Cholesterol synthesis inhibitor (0,745) Prostate disorders treatment (0,737)
32	Not studied		Respiratory analeptic (0,957) Antihypercholesterolemic (0,956) Anesthetic general (0,898) Hepatoprotectant (0,886) Antieczematic (0,872) Antineoplastic (0,847) Hypolipemic (0,836) Apoptosis agonist (0,826) Antipsoriatic (0,798) Antipruritic (0,773) Antiosteoporotic (0,759) Immunosuppressant (0,758) Cholesterol synthesis inhibitor (0,747) Erythropoiesis stimulant (0,746) Antifungal (0,736)

* Only activities with Pa > 0.5 are shown

Table 3: Confirmed and new pharmacological activities of neo steroids from marine invertebrates.(33-46)

No	Activity reviewed	Activities confirmed(Pa)	Additional predicted activities (Pa)*
33	Not studied		Antihypercholesterolemic (0,938) Apoptosis agonist (0,895) Chemopreventive (0,873) Antineoplastic (0,871) Respiratory analeptic (0,866) Antieczematic (0,863) Antiinflammatory (0,794) Antipsoriatic (0,789) Antiosteoporotic (0,764) Antipruritic (0,739) Prostate disorders treatment (0,726) Radioprotector (0,693) Atherosclerosis treatment (0,687) Ovulation inhibitor (0,640)
34	Antifungal	Antifungal (0,625)	Antihypercholesterolemic (0,952) Apoptosis agonist (0,916) Antineoplastic (0,892) Antieczematic (0,859) Chemopreventive (0,805)

			Antipsoriatic (0, 829) Antiosteoporotic (0,787) Antiinflammatory (0,779) Neuroprotector (0,740) Respiratory analeptic (0,731) Antipruritic (0,729) Atherosclerosis treatment (0,710) Prostate disorders treatment (0,683) Hepatoprotectant (0,645)
35	Antifungal	Antifungal (0,705)	Antihypercholesterolemic (0,944) Respiratory analeptic (0,907) Apoptosis agonist (0,863) Antieczematic (0,852) Antineoplastic (0,843) Chemopreventive (0,810) Antipruritic (0,782) Hepatoprotectant (0,778) Neuroprotector (0,780) Antiinflammatory (0,741) Cholesterol synthesis inhibitor (0,728) Anesthetic general (0,729) Antiosteoporotic (0,721) Antipsoriatic (0,718) Antiinfertility, female (0,712)
36	Antifungal	Antifungal (0,605)	Antihypercholesterolemic (0,965) Antineoplastic (0,886) Apoptosis agonist (0,885) Hypolipemic (0,872) Antieczematic (0,852) Antipsoriatic (0,813) Antiosteoporotic (0,809) Neuroprotector (0,769) Antipruritic (0,755) Antiinflammatory (0,752) Chemopreventive (0,747) Proliferative diseases treatment (0,705) Prostate disorders treatment (0,698) Antiparkinsonian, rigidity relieving (0,678) Atherosclerosis treatment (0,677)
37	Antifungal	Antifungal (0,687)	Antihypercholesterolemic (0,959) Respiratory analeptic (0,888) Antieczematic (0,845) Hypolipemic (0,841) Antineoplastic (0,828) Neuroprotector (0,824) Anesthetic general (0,816) Antipruritic (0,796) Hepatoprotectant (0,795) Apoptosis agonist (0,790) Antiosteoporotic (0,755) Chemopreventive (0,731) Cholesterol synthesis inhibitor (0,729) Antipsoriatic (0,724) Cytoprotectant (0,710) Biliary tract disorders treatment (0,703)
38	Antifungal	Antifungal (0,625)	Antihypercholesterolemic (0,952) Apoptosis agonist (0,916) Antineoplastic (0,892) Hypolipemic (0,861)

			Antieczematic (0,859) Chemopreventive (0,829) Antipsoriatic (0,805) Antiosteoporotic (0,787) Antiinflammatory (0,779) Neuroprotector (0,740) Respiratory analeptic (0,731) Antipruritic (0,729) Atherosclerosis treatment (0,710) Prostate disorders treatment (0,683) Cytoprotectant (0,648) Hepatoprotectant (0,645)
39	Antifungal	Antifungal (0,705)	Antihypercholesterolemic (0,944) Respiratory analeptic (0,907) Apoptosis agonist (0,863) Antieczematic (0,852) Antineoplastic (0,843) Hypolipemic (0,826) Chemopreventive (0,810) Antipruritic (0,782) Neuroprotector (0,780) Hepatoprotectant (0,778) Antiinflammatory (0,741) Anesthetic general (0,729) Cholesterol synthesis inhibitor (0,728) Antiosteoporotic (0,721) Antipsoriatic (0,718) Antiinfertility, female (0,712) Cytoprotectant (0,705)
40	Antifungal	Antifungal (0,605)	Antihypercholesterolemic (0,965) Antineoplastic (0,886) Apoptosis agonist (0,885) Hypolipemic (0,872) Antieczematic (0,852) Antipsoriatic (0,813) Antiosteoporotic (0,809) Neuroprotector (0,769) Antipruritic (0,755) Antiinflammatory (0,752) Chemopreventive (0,747) Proliferative diseases treatment (0,705) Prostate disorders treatment (0,698) Antiparkinsonian, rigidity relieving (0,678) Atherosclerosis treatment (0,677)
41	Antifungal	Antifungal (0,687)	Antihypercholesterolemic (0,959) Respiratory analeptic (0,888) Antieczematic (0,845) Hypolipemic (0,841) Antineoplastic (0,828) Neuroprotector (0,824) Anesthetic general (0,816) Antipruritic (0,796) Hepatoprotectant (0,795) Apoptosis agonist (0,790) Antiosteoporotic (0,755) Chemopreventive (0,731) Cholesterol synthesis inhibitor (0,729) Antipsoriatic (0,724) Cytoprotectant (0,710)

			Biliary tract disorders treatment (0,703)
42	Not studied		Antihypercholesterolemic (0,965) Apoptosis agonist (0,892) Antieczematic (0,863) Antineoplastic (0,859) Hypolipemic (0,853) Antiosteoporotic (0,823) Antipsoriatic (0,821) Hemostatic (0,815) Chemopreventive (0,810) Respiratory analeptic (0,800) Immunosuppressant (0,773) Antipruritic (0,749) Antiinflammatory (0,748) Prostate disorders treatment (0,726) Atherosclerosis treatment (0,700) Antiparkinsonian, rigidity relieving (0,697)
43	Not studied		Respiratory analeptic (0,973) Antihypercholesterolemic (0,959) Anesthetic general (0,895) Chemopreventive (0,894) Antieczematic (0,852) Apoptosis agonist (0,842) Antineoplastic (0,827) Hepatoprotectant (0,806) Antipruritic (0,802) Hypolipemic (0,789) Antiinflammatory (0,785) Antiosteoporotic (0,750) Antiinfertility, female (0,741) Antipsoriatic (0,735) Wound healing agent (0,732) Prostate disorders treatment (0,726) Ovulation inhibitor (0,714)
44	Not studied		Antihypercholesterolemic (0,969) Respiratory analeptic (0,955) Antineoplastic (0,899) Antieczematic (0,852) Hepatoprotectant (0,848) Chemopreventive (0,817) Hypolipemic (0,807) Antipruritic (0,798) Antipsoriatic (0,784) Anesthetic general (0,769) Antiinflammatory (0,769) Apoptosis agonist (0,753) Antiosteoporotic (0,745) Cytoprotectant (0,723) Prostate disorders treatment (0,717) Ovulation inhibitor (0,712) Antifungal (0,689)
45	Not studied		Antihypercholesterolemic (0,962) Respiratory analeptic (0,928) Chemopreventive (0,906) Apoptosis agonist (0,897) Antineoplastic (0,875) Antieczematic (0,837) Hypolipemic (0,817) Antiinflammatory (0,814)

			Antipsoriatic (0,790) Proliferative diseases treatment (0,779) Antipruritic (0,765) Antiosteoporotic (0,763) Prostate disorders treatment (0,725) Atherosclerosis treatment (0,704) Lipid metabolism regulator (0,702)
46	Not studied		Antihypercholesterolemic (0,974) Respiratory analeptic (0,924) Anesthetic general (0,880) Antineoplastic (0,870) Antieczematic (0,861) Hypolipemic (0,848) Apoptosis agonist (0,847) Chemopreventive (0,827) Antipsoriatic (0,819) Antiosteoporotic (0,817) Antiinflammatory (0,794) Antipruritic (0,789) Prostate disorders treatment (0,755) Ovulation inhibitor (0,740) Hepatoprotectant (0,713)

* Only activities with Pa > 0.5 are shown

Table 4. Confirmed and new pharmacological activities of neo steroids from marine invertebrates.(47-59)

No	Activity reviewed	Activities confirmed(Pa)	Additional predicted activities (Pa)*
47	Antimicrobial	Antibacterial (0,497)	Wound healing agent (0,943) Hepatoprotectant (0,850) Antihypercholesterolemic (0,832) Antiinflammatory (0,786) Antineoplastic (0,765) Cholesterol synthesis inhibitor (0,759) Chemopreventive (0,743) Antieczematic (0,719) Biliary tract disorders treatment (0,718) Diuretic (0,696) Prostate disorders treatment (0,691) Antiosteoporotic (0,690) Antifungal (0,669) Atherosclerosis treatment (0,651)
48	Stronghemolytic	Biliary tract disorders treatment (0,754)	Respiratory analeptic (0,960) Anesthetic general (0,913) Antieczematic (0,885) Antihypercholesterolemic (0,873) Hepatoprotectant (0,829) Antipruritic (0,823) Hypolipemic (0,793) Antineoplastic (0,778) Antiinflammatory (0,773) Cytoprotectant (0,757) Biliary tract disorders treatment (0,754) Antiosteoporotic (0,748) Antipsoriatic (0,735) Prostate disorders treatment (0,720) Wound healing agent (0,706)
49	Not studied		Biliary tract disorders treatment (0,963) Hepatic disorders treatment (0,934) Wound healing agent (0,789) Antieczematic (0,737) Immunosuppressant (0,731)

			Antineoplastic (0,711) Cholesterol synthesis inhibitor (0,696) Antiinflammatory (0,689) Antiosteoporotic (0,668) Hypolipemic (0,667) Atherosclerosis treatment (0,665) Prostate disorders treatment (0,637) Cytoprotectant (0,637) Antipsoriatic (0,632)
50	PlateletP2Y12 inhibitor	Cholesterol synthesis inhibitor (0,692) Cytoprotectant (0,640)	Biliary tract disorders treatment (0,941) Hepatic disorders treatment (0,923) Wound healing agent (0,799) Antineoplastic (0,767) Immunosuppressant (0,762) Antiinflammatory (0,732) Antieczematic (0,703) Cholesterol synthesis inhibitor (0,692) Antiosteoporotic (0,675) Antifungal (0,644) Cytoprotectant (0,640) Hypolipemic (0,622) Atherosclerosis treatment (0,620) Prostate disorders treatment (0,599) Antibacterial (0,597) Antipsoriatic (0,579)
51	Not studied		Antiinflammatory (0,883) Hepatoprotectant (0,866) Apoptosis agonist (0,864) Antineoplastic (0,833) Biliary tract disorders treatment (0,791) Immunosuppressant (0,749) Antieczematic (0,749) Wound healing agent (0,666) Antifungal (0,664) Cytoprotectant (0,658) Prostate disorders treatment (0,645) Diuretic (0,638) Antisecretoric (0,636) Atherosclerosis treatment (0,633) Antipsoriatic (0,617) Antiosteoporotic (0,584)
52	Anti-HIV agent	Membrane permeability inhibitor (0,668)	Biliary tract disorders treatment (0,958) Hepatic disorders treatment (0,925) Wound healing agent (0,738) Antieczematic (0,733) Immunosuppressant (0,718) Cholesterol synthesis inhibitor (0,717) Hypolipemic (0,714) Antineoplastic (0,694) Antiinflammatory (0,677) Atherosclerosis treatment (0,658) Antiosteoporotic (0,637) Antifungal (0,630) Prostate disorders treatment (0,623) Cytoprotectant (0,619) Antipsoriatic (0,618) Antihypercholesterolemic (0,599) Hair growth stimulant (0,587)
53	Anticancer	Antineoplastic (0,806)	Hepatic disorders treatment (0,934) Biliary tract disorders treatment (0,885)

			Chemopreventive (0,780) Antiinflammatory (0,761) Antifungal (0,751) Immunosuppressant (0,739) Hypolipemic (0,736) Diuretic (0,695) Antipsoriatic (0,689) Cholesterol synthesis inhibitor (0,686) Antieczematic (0,672) Apoptosis agonist (0,671) Atherosclerosis treatment (0,663) Wound healing agent (0,613)
54	Anticancer	Antineoplastic (0,761) Prostatic (benign) hyperplasia treatment (0,526) Anticarcinogenic (0,514) Antimetastatic (0,504)	Biliary tract disorders treatment (0,945) Hepatic disorders treatment (0,936) Hypolipemic (0,778) Antiarthritic (0,778) Antieczematic (0,770) Antiinflammatory (0,753) Antihypercholesterolemic (0,728) Cholesterol synthesis inhibitor (0,702) Wound healing agent (0,691) Atherosclerosis treatment (0,684) Chemopreventive (0,677) Antipsoriatic (0,665) Antiosteoporotic (0,657)
55	Not studied		Biliary tract disorders treatment (0,943) Hepatic disorders treatment (0,934) Antineoplastic (0,748) Antieczematic (0,741) Antiinflammatory (0,731) Hypolipemic (0,713) Wound healing agent (0,709) Chemopreventive (0,692) Cholesterol synthesis inhibitor (0,688) Atherosclerosis treatment (0,664) Antipsoriatic (0,659) Antiosteoporotic (0,653) Prostate disorders treatment (0,645) Antifungal (0,612) Cytoprotectant (0,577)
56	Glucanaseinhibitor	Glucan endo-1,3-beta-D-glucosidase inhibitor (0,914)	Biliary tract disorders treatment (0,963) Hepatic disorders treatment (0,934) Wound healing agent (0,789) Antieczematic (0,737) Immunosuppressant (0,731) Antineoplastic (0,711) Cholesterol synthesis inhibitor (0,696) Antiinflammatory (0,689) Antiosteoporotic (0,668) Hypolipemic (0,667) Atherosclerosis treatment (0,665) Prostate disorders treatment (0,637) Cytoprotectant (0,637) Antipsoriatic (0,632) Antifungal (0,626)
57	Glucanaseinhibitor	Glucan endo-1,3-beta-D-glucosidase inhibitor (0,948)	Hepatoprotectant (0,987) Chemopreventive (0,980) Respiratory analeptic (0,961) Antihypercholesterolemic (0,929) Antineoplastic (0,897)

			Antifungal (0,883) Anticarcinogenic (0,839) Apoptosis agonist (0,829) Antiprotozoal (Leishmania) (0,817) Antiulcerative (0,817) Antiinflammatory (0,808) Antithrombotic (0,799) Antipruritic (0,783) Antibacterial (0,779) Antieczematic (0,783) Antidiabetic (0,744)
58	Anticancer	Antineoplastic (0,901) Anticarcinogenic (0,852) Antimetastatic (0,587) Antineoplastic (sarcoma) (0,568) Antineoplastic (lymphocytic leukemia) (0,546) Antineoplastic (pancreatic cancer) (0,511)	Hepatoprotectant (0,983) Chemopreventive (0,974) Respiratory analeptic (0,945) Antihypercholesterolemic (0,919) Immunostimulant (0,902) Antifungal (0,888) Antiprotozoal (Leishmania) (0,843) Antiulcerative (0,839) Apoptosis agonist (0,834) Antiinflammatory (0,814) Hypolipemic (0,802) Antibacterial (0,790) Antieczematic (0,776 Antipruritic (0,769) Antithrombotic (0,769) Antidiabetic (0,742)
59	Anticancer	Antineoplastic (0,853) Anticarcinogenic (0,752) Antimetastatic (0,568) Antineoplastic (pancreatic cancer) (0,520) Antineoplastic (sarcoma) (0,512)	Hepatoprotectant (0,972) Immunostimulant (0,949) Wound healing agent (0,921) Respiratory analeptic (0,899) Chemopreventive (0,894) Antihypercholesterolemic (0,891) Antiulcerative (0,866) Antifungal (0,845) Antibacterial (0,804) Antiinflammatory (0,760) Antithrombotic (0,741) Antidiabetic (0,732) Apoptosis agonist (0,729) Hypolipemic (0,686) Atherosclerosis treatment (0,665)

* Only activities with Pa > 0.5 are shown

Table 5: Confirmed and new pharmacological activities of neo steroids from marine invertebrates.(60-68)

No	Activity reviewed	Activities confirmed(Pa)	Additional predicted activities (Pa)*
60	Anticancer	Antineoplastic (0,874) Anticarcinogenic (0,651) Antimetastatic (0,576) Antineoplastic (sarcoma) (0,553) Antineoplastic (pancreatic cancer) (0,530)	Respiratory analeptic (0,969) Immunostimulant (0,942) Hepatoprotectant (0,935) Chemopreventive (0,901) Antifungal (0,879) Antibacterial (0,827) Antiulcerative (0,815) Apoptosis agonist (0,767) Antihypercholesterolemic (0,748) Antiinflammatory (0,738) Hypolipemic (0,698) Antipruritic (0,686) Antidiabetic (0,682) Antiviral (Influenza) (0,673)

61	Anticancer	Antineoplastic (0,875) Anticarcinogenic (0,750) Antimetastatic (0,564) Antineoplastic (sarcoma) (0,528) Antineoplastic (pancreatic cancer) (0,513)	Hepatoprotectant (0,961) Immunostimulant (0,954) Chemopreventive (0,943) Respiratory analeptic (0,918) Antifungal (0,892) Antibacterial (0,839) Antihypercholesterolemic (0,825) Antiulcerative (0,822) Wound healing agent (0,808) Apoptosis agonist (0,759) Antiinflammatory (0,752) Antipruritic (0,747) Antithrombotic (0,706) Hypolipemic (0,688) Antidiabetic (0,678) Atherosclerosis treatment (0,663)
62	Anticancer	Antineoplastic (0,863) Anticarcinogenic (0,828) Antimetastatic (0,590) Antineoplastic (pancreatic cancer) (0,541) Antineoplastic (myeloid leukemia) (0,535)	Hepatoprotectant (0,981) Chemopreventive (0,961) Antihypercholesterolemic (0,961) Respiratory analeptic (0,936) Antifungal (0,846) Immunostimulant (0,846) Antiulcerative (0,809) Antidiabetic (0,804) Antipruritic (0,803) Hypolipemic (0,789) Wound healing agent (0,782) Antiviral (Influenza) (0,781) Antiinflammatory (0,785) Apoptosis agonist (0,778) Antithrombotic (0,755) Lipid metabolism regulator (0,747)
63	Anticancer	Antineoplastic (0,870) Anticarcinogenic (0,807) Antimetastatic (0,598) Antineoplastic (sarcoma) (0,535) Antineoplastic (pancreatic cancer) (0,517)	Chemopreventive (0,961) Respiratory analeptic (0,958) Hepatoprotectant (0,953) Antihypercholesterolemic (0,936) Antiulcerative (0,820) Antifungal (0,817) Antithrombotic (0,779) Non-steroidal antiinflammatory agent (0,774) Genital warts treatment (0,772) Antipruritic (0,770) Apoptosis agonist (0,761) Hypolipemic (0,758) Antidiabetic (0,755) Antibacterial (0,704) Antiviral (Influenza) (0,702)
64	Not studied		Respiratory analeptic (0,978) Chemopreventive (0,963) Hepatoprotectant (0,961) Antineoplastic (0,900) Antithrombotic (0,857) Antihypercholesterolemic (0,839) Antifungal (0,826) Apoptosis agonist (0,822) Non-steroidal antiinflammatory agent (0,762) Antiulcerative (0,762) Hypolipemic (0,760) Antipruritic (0,748)

			Anticarcinogenic (0,743) Antibacterial (0,737) Antidiabetic (0,726) Antiviral (Influenza) (0,713)
65	Not studied		Respiratory analeptic (0,953) Hepatoprotectant (0,915) Antineoplastic (0,843) Antifungal (0,840) Antihypercholesterolemic (0,833) Chemopreventive (0,817) Antiulcerative (0,816) Antibacterial (0,771) Antiviral (Influenza) (0,733) Antidiabetic (0,728) Apoptosis agonist (0,722) Antipruritic (0,712) Antiinflammatory (0,711) Hypolipemic (0,682) Atherosclerosis treatment (0,674)
66	Anticancer	Antineoplastic (0,872) Anticarcinogenic (0,865) Antimetastatic (0,568) Antineoplastic (sarcoma) (0,537) Antineoplastic (pancreatic cancer) (0,511)	Hepatoprotectant (0,992) Chemopreventive (0,984) Antihypercholesterolemic (0,959) Antifungal (0,884) Antipruritic (0,819) Wound healing agent (0,813) Antiinflammatory (0,813) Antithrombotic (0,808) Antidiabetic (0,804) Antiulcerative (0,800) Apoptosis agonist (0,797) Hypolipemic (0,773) Antibacterial (0,754) Atherosclerosis treatment (0,741)
67	Anticancer	Antineoplastic (0,839) Antimetastatic (0,569) Anticarcinogenic (0,559)	Hepatoprotectant (0,944) Chemopreventive (0,851) Antihypercholesterolemic (0,851) Antibacterial (0,742) Respiratory analeptic (0,839) Antifungal (0,836) Antiinflammatory (0,732) Antidiabetic (0,725) Apoptosis agonist (0,723) Antipruritic (0,707) Antiulcerative (0,688) Hypolipemic (0,686) Atherosclerosis treatment (0,662)
68	Strong anticancer	Anticarcinogenic (0,925) Antineoplastic (0,882) Antimetastatic (0,517) Antineoplastic (sarcoma) (0,509)	Chemopreventive (0,988) Hepatoprotectant (0,973) Antifungal (0,901) Wound healing agent (0,854) Antibacterial (0,836) Antiinflammatory (0,814) Apoptosis agonist (0,717) Genital warts treatment (0,695) Antiulcerative (0,671) Antipsoriatic (0,639) Antioxidant (0,636) Hypolipemic (0,629) Antidiabetic (0,589)

* Only activities with Pa > 0.5 are shown

CONCLUSION

In this review, we present structures and distribution in nature of neo steroids. Biological activity for these neo steroids is presented in this paper. The most characteristic biological activities for neo steroids were antineoplastic, anti-seborrheic, antiviral, and antifungal activities.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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