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Biological Activities of Organometalloid (As, At, B, Ge, Si, Se, Te) Steroids

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ABSTRACT

Organometallic steroids (OS) represent an interesting class of biologically active hormones including anabolic steroids. Currently, more than 1,000 OS have been synthesized, and many are widely used in medical practice, including sports medicine and pharmacology. In this review, we present structures of OS that contain (along with the composition of a molecule of metalloids) As, At, B, Ge, Si, Se, and Te. We also used an algorithm that works with a PASS programme containing approximately one million chemical structures and approximately 8,000 validated biological activities and allows you to calculate the predicted activity from the chemical structure of the steroidal molecule. From the huge variety of steroidal structures, we selected more than 100 OS that belong to seven groups, including boronic steroids, arsenosteroids, astatosteroids, germylated steroids, silasteroids, selena steroids and tellura steroids. The biological activity for these groups of OS is presented in this paper. Additionally, it is important to note that these selena and tellura steroids showed a high anticancer activity and they can be used as anti-parkinsonian, anti-Alzheimer's disease and anti-neurodegenerative agents.

INTRODUCTION

Bioorganometallic chemistry is an area at the intersection of many areas of science and the medicinal chemistry and pharmaceutical industry, and above all, medicine, pharmacology, organic and inorganic chemistry (Jaouen and Salmain, 2015). Steroids belong to the class of natural lipids, which are produced by microorganisms (Galán *et al*., 2017), plants (Valitova *et al*., 2016), animals (Guzman *et al*., 2017) and marine algae and invertebrates (Fiorucci *et al*., 2012; Zubair *et al*., 2016). Steroids and their derivatives have a huge number of diverse structures and have a wide range of biological activities (Xu *et al*., 2004). Currently, more than 70,000 natural and synthetic steroids and their derivatives are known. Organometalloid steroids (OS), or steroids containing semi-metals, are a unique class of chemical compounds that are not found in nature, and only synthesized molecules that have a huge variety of chemical structures are known (Chiusoli *et al*., 1979; Zeelen, 1994; Ehrenstein 1948; Omar *et al*., 2008). OS are widely used in research and the medical and pharmaceutical industries (Charney and Herzog, 1967).

Concept organometallic steroids were introduced in the mid-1950s by a few groups of scientists (Thackray *et al*., 1985). Presently, approximately 1,000 synthetic OS and their derivatives are known at present time (Coogan and Dyson, 2012; Parshall, 1987).

We selected more than 100 stable OS, including anabolic steroids, which are interesting from the point of view of medicine and pharmacology and for the pharmaceutical industry (Jaouen and Salmain, 2015). Many OS show anti-tumour, antiviral and antibacterial activity (Fuentes-Aguilar *et al*., 2017).

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All of the steroids were separated on seven groups of steroids that represent: group one, boronic steroids; group two, arsenosteroids; group three, astatosteroids; group four, germylated steroids; group five, silasteroids; group six, selena steroids, and group seven, tellura steroids. We used the PASS computer programme that use the structure-activity relationship (SAR) algorithm to determine the relationship between chemical structure steroids and determines the biological activity of OS. This is the first attempt to determine the biological activity of synthetic OS containing various metalloid(s) in their structures. This review emphasizes the role of OS as an important source of leads for drug discovery, and they are of great interest to chemists, physicians, biologists, pharmacologists and the pharmaceutical industry.

STRUCTURE ACTIVITY RELATIONSHIP FOR ORGANOMETALLOID STEROIDS

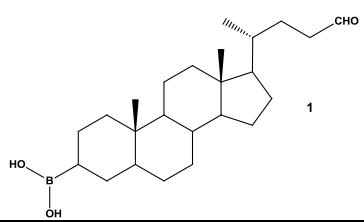
The acronym PASS stands for *Prediction of Activity Spectra for Substances* (www.pharmaexpert.ru).The PASS software product, which predicts more than 8,000 pharmacological effects and biochemical mechanisms on the basis of the structural formula of a substance, may be efficiently used to find new targets (mechanisms) for some ligands and, conversely, to reveal new ligands for some biological targets. Upon entering a structural formula of a chemical substance, the program returns the potential biological activities of this compound. PASS has been well accepted by the community, and is now actively used in the field of medicinal chemistry, by both academic organizations and pharma companies. The PASS program can be used in the fields of: SAR (qualitative structure-activity relationship), medicinal chemistry, computational chemistry, drug discovery, drug repositioning, chemical toxicity, natural and synthetic compound effects. 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 (Levitsky *et al*., 2016; Dembitsky *et al*., 2017; Sergeiko *et al*., 2008). 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 (Filz and Poroikov, 2012; Borodina *et al*., 2003; Lagunin *et al*., 2011). Synthetic OS were used to calculate their pharmacological activity. Using MOL or SD files as an input for PASS program, the user may get a list of probable biological activities for any drug-like molecule as an output. For each activity, P_a and P_i 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 263 types of biological activity are predicted with Pa>70% and 587 with Pa>50%. In a biological activity spectrum estimated by PASS, the activity predicted with the highest probability is called the focal activity. Although the majority of the known biological activities for respective OS are associated with antineoplastic action, their number is less than 60% among the predicted focal activities.Confirmed activity is the activity found for this steroid and confirmed by the PASS system. The criteria for choosing synthetic OS containing various metalloid atom(s) are presented in our article. The first requirement when choosing an OS for the study of their biological activity using the PASS system is the chemical stability of steroids. For a comprehensive determination of the activity of the individual steroid metalloid, we used a fixed position of the metalloid atoms in the position of the steroid skeleton. So, different metalloids were incorporated mainly in position 3, 4, 6, 7, 11 and 16. Other metalloids were to a lesser extent in position 1, 2, 5, 20 and 24. Rare representatives of steroids containing metalloid atom in position 10, 13, 19, and other positions (Tables 1, 2, 3, 4, 5, 6, and 7).

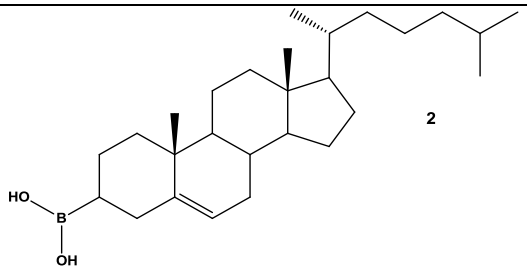
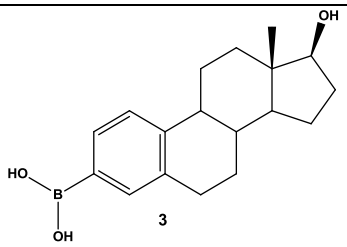
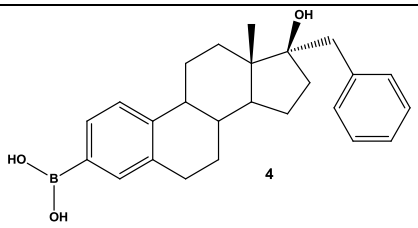
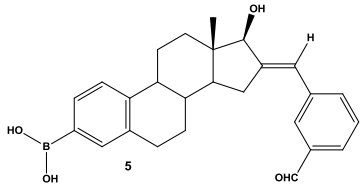
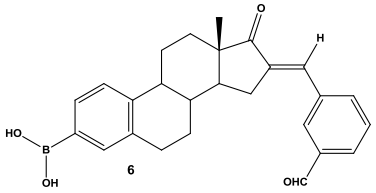
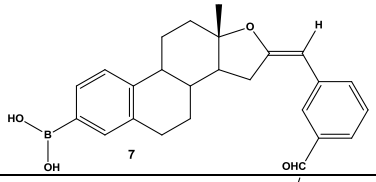
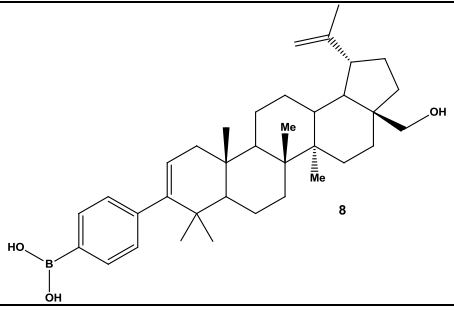
BORONIC STEROIDS

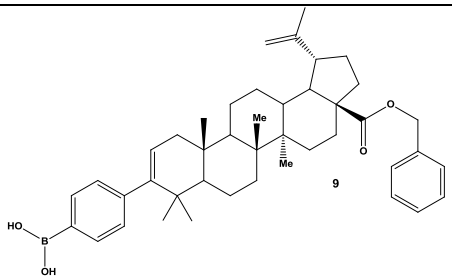
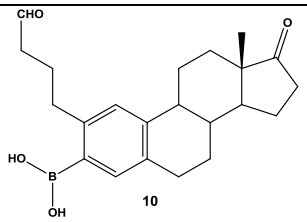
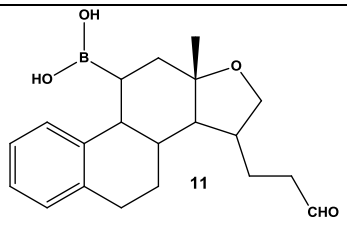
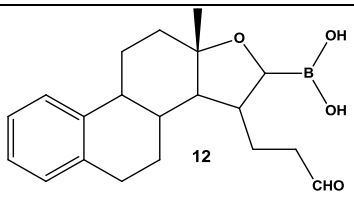
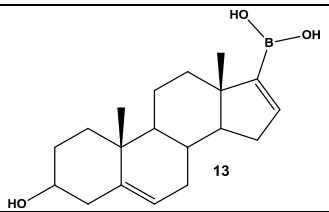
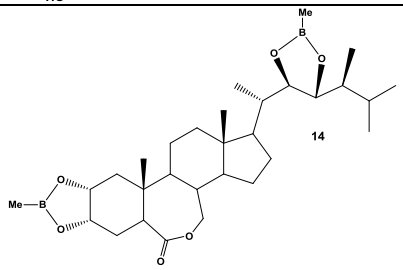
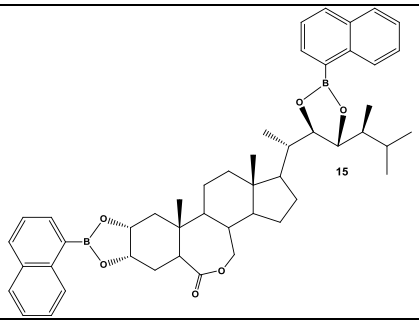
Organoboron chemistry is an area of organic and inorganic chemistry that studies the chemical compounds of boron and carbon (C-B or C-O-B). Organic compounds of boron, which are now include more than 100,000 compounds, have a wide spectrum of biological activities (Ali *et al*., 2005; Dembitsky *et al*., 2003, 2004). The medical chemistry of boron is an area of organic chemistry that studies the biological activity of organoboranes (Smoom *et al*., 2012; Dembitsky *et al*., 2011). Organic compounds of boron are devoted to a large number of excellent reviews and books.

They are also inhibitors of many enzymes and show antibacterial, anticancer and other activities (Smoom *et al*., 2012). We selected fifteen steroids that contain a boron atom. The main activities that are characteristic of boronic steroids are: antineoplastic, anti-eczematic, and anti-hypertensive properties and these steroids are apoptosis agonist agents. The other biological activity is shown in Table 1.

Table 1: Predicted biological activities of boronic steroids (**1-15**).

Boronic steroids	Predicted activities (Pa)*
	Antieczematic (0.804 Antihypertensive (0.798)) Myocardial ischemia treatment (0.751) Antineoplastic (0.735) Dermatologic (0.716) Bone diseases treatment (0.703) Antiosteoporotic (0.681) Immunosuppressant (0.672) Antipsoriatic (0.665) Prostate disorders treatment (0.655)

	Antineoplastic (0.796) Antieczematic (0.796) Dermatologic (0.767) Antihypercholesterolemic (0.756) Bone diseases treatment (0.749) Immunosuppressant (0.729) Antiosteoporotic (0.717) Prostate disorders treatment (0.711) Antipruritic (0.708) Antipsoriatic (0.703) Myocardial ischemia treatment (0.692) Antihypertensive (0.675)
	Antineoplastic (0.910) Antiseborrheic (0.891) Alopecia treatment (0.877) Gynecological disorders treatment (0.866) Psychosexual dysfunction treatment (0.821) Radiosensitizer (0.767) Dermatologic (0.757) Chemosensitizer (0.743) Antipsoriatic (0.724) Prostatic (benign) hyperplasia treatment (0.713) Ovulation inhibitor (0.674)
	Antineoplastic (0.883) Antiseborrheic (0.877) Gynecological disorders treatment (0.849) Psychosexual dysfunction treatment (0.817) Radiosensitizer (0.758) Chemosensitizer (0.733) Dermatologic (0.730) Prostatic (benign) hyperplasia treatment (0.695) Antipsoriatic (0.691) Ovulation inhibitor (0.667)
	Antineoplastic (0.844) Psychosexual dysfunction treatment (0.756) Radiosensitizer (0.738) Antiosteoporotic (0.730) Bone diseases treatment (0.726) Gynecological disorders treatment (0.693) Chemosensitizer (0.684) Dermatologic (0.653) Prostatic (benign) hyperplasia treatment (0.631) Antipsoriatic (0.634)0.870
	Antineoplastic (0.870) Psychosexual dysfunction treatment (0.772) Radiosensitizer (0.740) Gynecological disorders treatment (0.714) Chemosensitizer (0.689) Dermatologic (0.659) Prostatic (benign) hyperplasia treatment (0.647) Antipsoriatic (0.634) Apoptosis agonist (0.597)
	Antineoplastic (0.866) Psychosexual dysfunction treatment (0.754) Radiosensitizer (0.732) Chemosensitizer (0.669) Gynecological disorders treatment (0.631) Antimetastatic (0.614) Antipsoriatic (0.603) Dermatologic (0.547)
	Antineoplastic (0.876) Apoptosis agonist (0.807) Radiosensitizer (0.718) Dermatologic (0.717) Severe acute respiratory syndrome treatment (0.690) Antipsoriatic (0.670) Chemosensitizer (0.668) Immunosuppressant (0.653) Psychosexual dysfunction treatment (0.648) Hepatic disorders treatment (0.638) Antiinflammatory (0.594) Antiviral (0.546)

	Antineoplastic (0.839) Severe acute respiratory syndrome treatment (0.775) Apoptosis agonist (0.768) Radiosensitizer (0.689) Dermatologic (0.685) Antipsoriatic (0.648) Chemosensitizer (0.634) Antiinflammatory (0.623) Immunosuppressant (0.622) Psychosexual dysfunction treatment (0.609) Hepatoprotectant (0.539) Antiacne (0.501)
	Antineoplastic (0.817) Psychosexual dysfunction treatment (0.759) Gynecological disorders treatment (0.707) Radiosensitizer (0.691) Ovulation inhibitor (0.678) Prostatic (benign) hyperplasia treatment (0.652) Dermatologic (0.650) Chemosensitizer (0.649) Male reproductive disfunction treatment (0.641) Antipsoriatic (0.583)
	Antineoplastic (0.682) Antineoplastic (lymphocytic leukemia) (0.526) Radiosensitizer (0.521)
	Antineoplastic (0.762) Antiseborrheic (0.625) Radiosensitizer (0.587) Antineoplastic (renal cancer) (0.574) Chemosensitizer (0.525) Antineoplastic (breast cancer) (0.524) Prostate cancer treatment (0.513) Antineoplastic (pancreatic cancer) (0.512)
	Antineoplastic (0.881), Neuroprotector (0.870) Ovulation inhibitor (0.863), Dermatologic (0.770), Antiseborrheic (0.770), Chemosensitizer (0.755) Radiosensitizer (0.738), Apoptosis agonist (0.742) Immunosuppressant (0.737), Antipsoriatic (0.728) Antiinflammatory (0.729), Respiratory analeptic (0.720) Prostate disorders treatment (0.712) Antihypercholesterolemic (0.671)
	Genital warts treatment (0.894) Antineoplastic (0.849) Hepatic disorders treatment (0.807) Antieczematic (0.707) Immunosuppressant (0.669) Rhinitis treatment (0.662) Dermatologic (0.653) Antipsoriatic (0.642) Apoptosis agonist (0.639) Macular degeneration treatment (0.597) Hepatoprotectant (0.589) Prostate disorders treatment (0.555)
	Genital warts treatment (0.879) Cardiotonic (0.802) Antineoplastic (0.783) Hepatic disorders treatment (0.759) Antipsoriatic (0.728) Dermatologic (0.688) Antieczematic (0.680) Antiarrhythmic (0.678) Rhinitis treatment (0.644) Antiinflammatory (0.634) Immunosuppressant (0.628) Apoptosis agonist (0.614) Antifungal (0.606) Macular degeneration treatment (0.525)

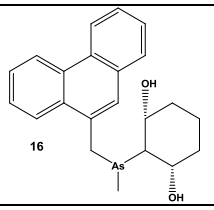
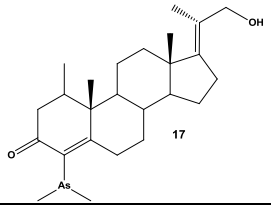
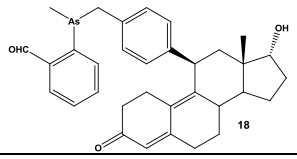
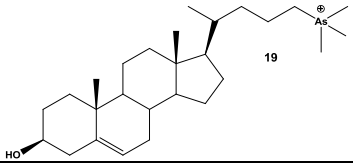
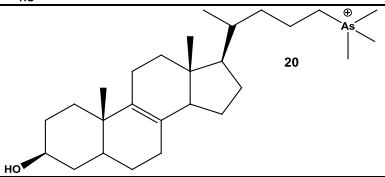
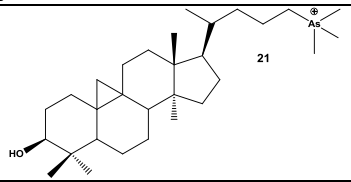
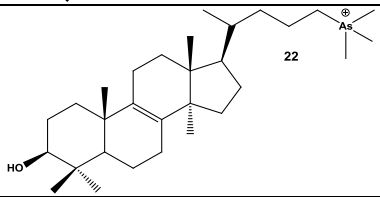
* Only activities with Pa > 0.5 are shown.

ARSENOSTEROIDS

Arsenic compounds, including hydrocarbons, lipids, phospholipids, fatty acids and sugars, are often found in nature (Dembitsky and Rezanka, 2003; Dembitsky and Levitsky, 2004). Arsenolipid analogues of phosphatidylcholine, sphingomyelin and fatty acids are found in fish, crustaceans, lichens, mollusks, sponges, and other species of marine and freshwater invertebrates as well as brown and green algae (Khan and Francesconi, 2016; Arroyo-Abad *et al*., 2016; Yu *et al*., 2018). Many studies have shown that arsenolipids are inhibitors of glycerin kinase, bovine carbonic anhydrase, promyelocytic leukaemia and inhibit the growth of certain types of cancer cells (Roggenbeck *et al*., 2016; Sele *et al*., 2012). Surprisingly, arsenosteroids are not found in nature.

Apparently, this is due to the problem of isolation and identification of these compounds. In the near future, these interesting and possibly biologically active compounds will be found in many species of marine organisms (Arroyo-Abad *et al*., 2016; Yu *et al*., 2018; Dembitsky and Levitsky, 2004). Synthetic arsenosteroids form a small group of compounds and their activity is shownin Table 2. Arsenosteroids have shown anticancer activity (Table 2).

Table 2: Predicted biological activities of arsenosteroids (**16**-**22**).

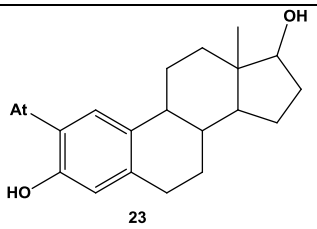
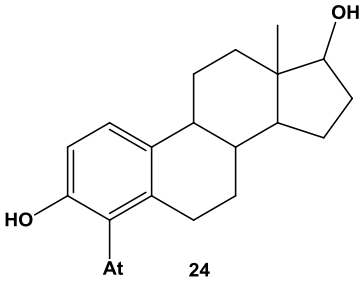
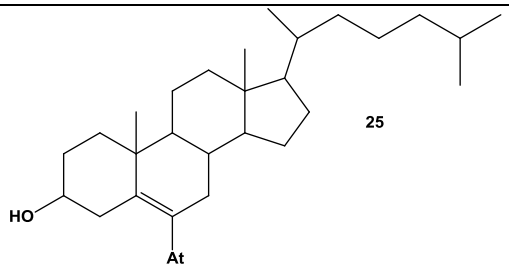
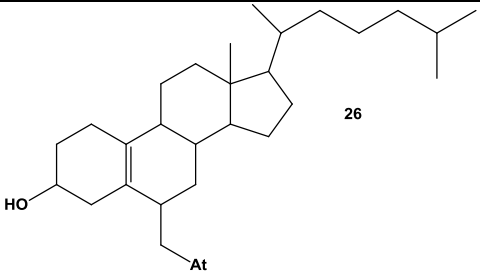
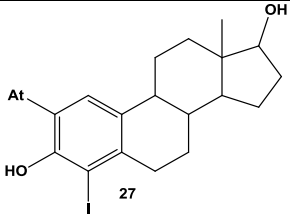
Arsenosteroids	Predicted activities (Pa)*
	Antineoplastic (0.781) Antieczematic (0.729) Alopecia treatment (0.715) Vasoprotector (0.614) Antiviral (Arbovirus) (0.575) Antinephrotoxic (0.552)
	Antineoplastic (0.870) Antiseborrheic (0.865) Dermatologic (0.818) Prostate disorders treatment (0.641) Bone diseases treatment (0.574) Ovulation inhibitor (0.565) Antiinflammatory (0.517)
	Antineoplastic (0.844) Alopecia treatment (0.628) Contraceptive (0.625) Gynecological disorders treatment (0.604) Apoptosis agonist (0.574)
	Antineoplastic (0.983) Antiprotozoal (0.941) Antiviral (0.866) Prostate disorders treatment (0.716) Bone diseases treatment (0.700) Hypolipemic (0.663) Cholesterol synthesis inhibitor (0.589)
	Antineoplastic (0.982) Antiprotozoal (0.947) Antiviral (0.882) Antipruritic (0.746) Dermatologic (0.740) Antiosteoporotic (0.720)
	Antineoplastic (0.985) Antiviral (0.939) Hypolipemic (0.788) Hepatic disorders treatment (0.775) Apoptosis agonist (0.755) Antiinflammatory (0.629)
	Antineoplastic (0.984) Antiprotozoal (0.946) Antiviral (0.927) Hypolipemic (0.741) Apoptosis agonist (0.716) Antiinflammatory (0.627) Prostate disorders treatment (0.584)

* Only activities with Pa > 0.5 are shown.

ASTATOSTEROIDS

Astatine (At) is natural radioelement that has short-lived isotopes, and synthetic organic astatine compounds are commonly used for radiotherapy (Kugler *et al*., 1985). Steroids containing astatine, which are called astatosteroids, were first synthesized approximately 40 years ago (Visser *et al*., 1981). Some astatosteroids (2- and 4-astatoestradiol and 6-At-cholesterol, **23**, **24**, **26** and **27**) have been synthesized in high radiochemical yields by the reaction of $^{211}At/I_2$ and the corresponding chloromercury compounds. The stability *in vitro* was determined under different conditions in comparison with the analogous iodo compounds (Kugler *et al*., 1985). More recently, 6-astatomethyl-19-norcholest-5(10)-en-3β-ol (**26**) was synthesized at a yield of 60-70% (Liu *et al.*, 1985). The biological activity of these compounds has not been determined. The predicted biological activity of astatosteroids is presented in Table 3. The most characteristic biological properties for these steroids were antineoplastic, anti-seborrheic, anti-secretoric and anti-hypercholesterolemic activities.

Table 3: Predicted biological activities of astatosteroids (**23**-**27**).

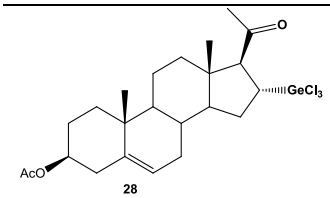
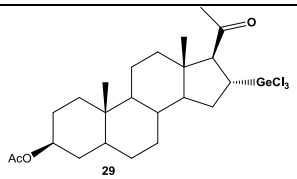
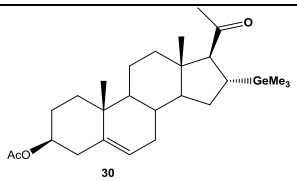
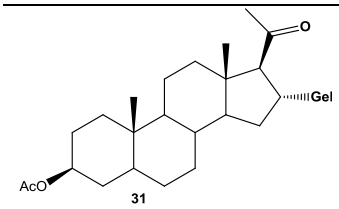
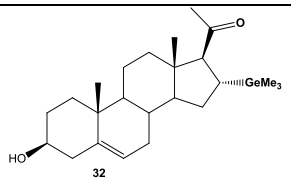
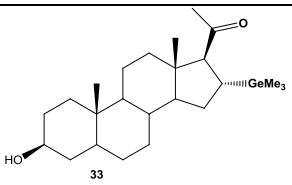
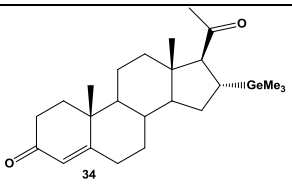
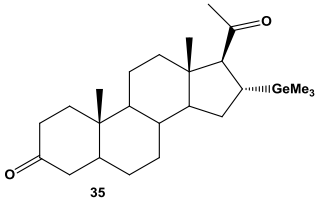
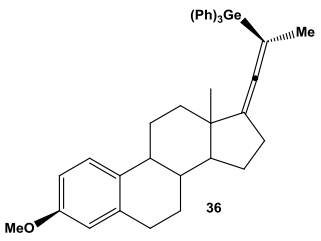
Astatosteroids	Predicted activities (Pa)*
 23	Antiseborrheic (0.936) Alopecia treatment (0.923) Antihypercholesterolemic (0.920) Antisecretoric (0.884) Antineoplastic (0.849) Growth stimulant (0.805) Respiratory analeptic (0.789) Ovulation inhibitor (0.776) Bone diseases treatment (0.743) Antiosteoporotic (0.741) Genital warts treatment (0.738) Neuroprotector (0.715) Menopausal disorders treatment (0.688)
 24	Antiseborrheic (0.934) Alopecia treatment (0.913) Antihypercholesterolemic (0.901) Antisecretoric (0.836) Antineoplastic (0.823) Ovulation inhibitor (0.738) Diuretic (0.731) Antiosteoporotic (0.724) Genital warts treatment (0.721)Bone diseases treatment (0.720) Growth stimulant (0.703) Neuroprotector (0.696) Respiratory analeptic (0.689) Prostate disorders treatment (0.673) Menopausal disorders treatment (0.657)
 25	Respiratory analeptic (0.976) Antihypercholesterolemic (0.967) Anesthetic general (0.924) Antineoplastic (0.824) Antipruritic (0.805) Bone diseases treatment (0.796) Antiosteoporotic (0.789) Hypolipemic (0.785) Dermatologic (0.779) Immunosuppressant (0.766) Hepatoprotectant (0.760) Neuroprotector (0.758) Antipsoriatic (0.739) Antiinflammatory (0.728) Apoptosis agonist (0.724) Prostate disorders treatment (0.719)
 26	Antihypercholesterolemic (0.927) Antineoplastic (0.834) Antieczematic (0.825) Dermatologic (0.805) Antiosteoporotic (0.787) Bone diseases treatment (0.784) Antipruritic (0.781) Hypolipemic (0.740) Prostate disorders treatment (0.704) Anesthetic general (0.703) Antipsoriatic (0.685)
 27	Antihypercholesterolemic (0.912) Antiseborrheic (0.911) Alopecia treatment (0.873) Antineoplastic (0.839) Antisecretoric (0.837) Bone diseases treatment (0.777) Diuretic (0.764) Male reproductive disfunction treatment (0.764) Antiosteoporotic (0.746) Antiinflammatory (0.745) Neuroprotector (0.735) Respiratory analeptic (0.692) Ovulation inhibitor (0.674) Menopausal disorders treatment (0.651)

* Only activities with Pa > 0.5 are shown.

GERMYLATED STEROIDS

In 2016, one hundred and thirty years have passed since the discovery of the element Germanium (Ge), and the synthesis of its first organic compounds. However, this area of element-organic chemistry began to develop most intensively only in the 1950s (Rappoport, 2003; Terent'ev *et al*., 2011). In those years,the chemistry of organogermanium compounds was so poorly studied that it was not even possible to determine the biological activity and mechanisms of action on a living organism. Organogermanium compounds show anti-tumour, antiviral, immunomodulating, neurotropic, cardiovascular, and radioprotective activities. According to the literature, organogermanium compounds have a wide spectrum of biological activity but unlike silicon compounds they are practically non-toxic (Menchikov and Ignatenko, 2013; Lukevics *et al*.,1990; Asai, 1977). Several germylated steroids in position 16 were synthesized by the addition of trichlorogermane to a conjugated Δ16-double bond. The 16α-trichlorogermyl-3β-acetoxy-pregnan-20-ones (**28** and **29**) and 16α-trimethylgermyl-progesterones (**30**-**35**) showed that it is very stable (Karpenko *et al.*, 1998, 1999, 2011). An unusual germylated steroid (**36**) has been obtained from a Δ16-allopregnene-20 one (Heusler *et al*., 1959). The biological activity of these compounds has not been reported, and the predicted biological activity of germylated steroids is presented in Table 4. The most characteristic biological properties for these steroids were antineoplastic, anti-seborrheic and dermatologic activities.

Table 4: Predicted biological activities of germylated steroids (**28**-**36**).

Germylated steroids	Additional predicted activities (Pa)*
 **28**	Respiratory analeptic (0.870) Antineoplastic (0.860) Antihypercholesterolemic (0.806) Neuroprotector (0.798) Antiseborrheic (0.782) Ovulation inhibitor (0.775) Anesthetic (0.738) Menopausal disorders treatment (0.732) Prostate disorders treatment (0.721) Antipruritic (0.718) Antiinflammatory (0.698) Dermatologic (0.688)
 **29**	Respiratory analeptic (0.874) Antiseborrheic (0.868) Anesthetic general (0.856) Antineoplastic (0.852) Erythropoiesis stimulant (0.827) Antipruritic (0.737) Neuroprotector (0.726) Cytoprotectant (0.714) Antieczematic (0.712) Prostate disorders treatment (0.702) Menopausal disorders treatment (0.674)
 **30**	Antineoplastic (0.957) Antiacne (0.939) Dermatologic (0.928) Respiratory analeptic (0.779) Neuroprotector (0.734) Ovulation inhibitor (0.724) Prostate disorders treatment (0.704) Antihypercholesterolemic (0.700) Menopausal disorders treatment (0.679)
 **31**	Antineoplastic (0.961) Antiacne (0.952) Dermatologic (0.935) Antiseborrheic (0.830) Erythropoiesis stimulant (0.793) Respiratory analeptic (0.785) Anesthetic general (0.735) Prostate disorders treatment (0.681) Antipruritic (0.679) Antieczematic (0.675)
 **32**	Antineoplastic (0.960) Antiacne (0.951) Dermatologic (0.940) Anesthetic general (0.841) Ovulation inhibitor (0.774) Erythropoiesis stimulant (0.770) Menopausal disorders treatment (0.741) Antihypercholesterolemic (0.738) Neuroprotector (0.729) Prostate disorders treatment (0.720) Respiratory analeptic (0.715) Antieczematic (0.695)
 **33**	Antineoplastic (0.964) Antiacne (0.960) Dermatologic (0.948) Anesthetic general (0.915) Erythropoiesis stimulant (0.896) Antiseborrheic (0.797) Antieczematic (0.735) Respiratory analeptic (0.722) Prostate disorders treatment (0.700) Menopausal disorders treatment (0.682) Antipruritic (0.681)
 **34**	Antiacne (0.970) Antineoplastic (0.969) Dermatologic (0.955) Anesthetic general (0.816) Ovulation inhibitor (0.745) Prostate disorders treatment (0.738) Antiseborrheic (0.691) Antipruritic (0.673) , Menopausal disorders treatment (0.665) Erythropoiesis stimulant (0.655) Prostatic (benign) hyperplasia treatment (0.649)
 **35**	Antiacne (0.980) Antineoplastic (0.974) Dermatologic (0.972) Antiseborrheic (0.831) Erythropoiesis stimulant (0.768) Prostate disorders treatment (0.743) Prostatic (benign) hyperplasia treatment (0.651) Anesthetic general (0.631) Menopausal disorders treatment (0.606)
 **36**	Antiseborrheic (0.918) Ovulation inhibitor (0.847) Antineoplastic (0.821) Dermatologic (0.776) Alopecia treatment (0.741) Prostate disorders treatment (0.714) Antiosteoporotic (0.622) Antiacne (0.613) Bone diseases treatment (0.607) Prostatic (benign) hyperplasia treatment (0.606) Menopausal disorders treatment (0.596) Dementia treatment (0.562)

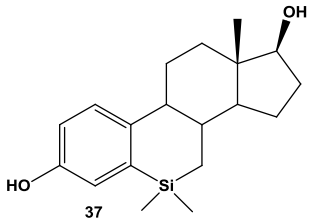
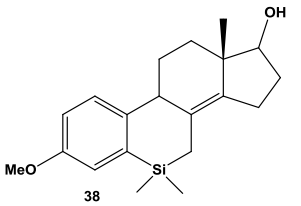
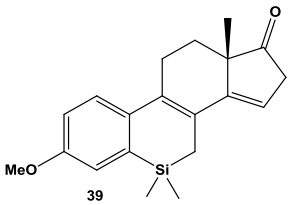
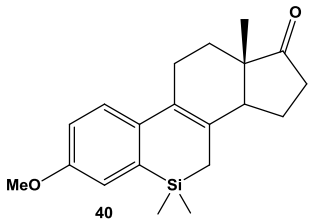
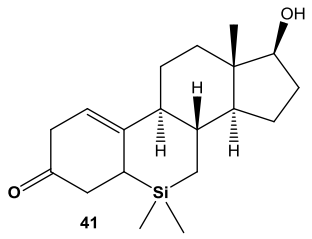
* Only activities with Pa > 0.5 are shown.

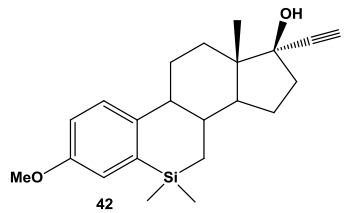
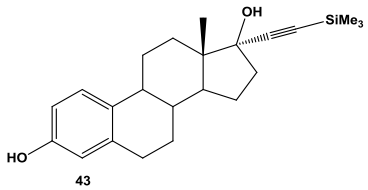
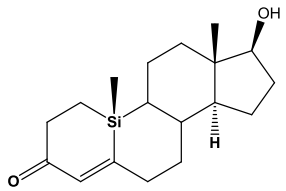
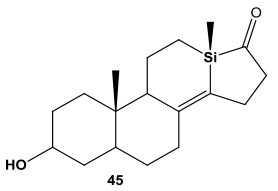
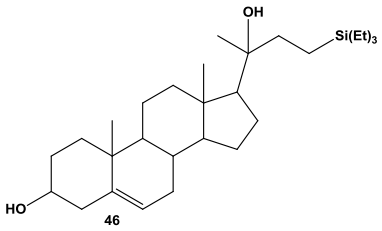
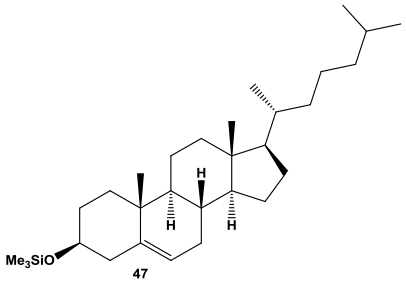
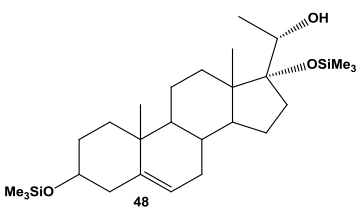
SILASTEROIDS

The element silicon (Si) and organosilicon compounds belong to a class of metalloids. Silicon derivatives, such as sugars and other organic compounds, are widely used in the pharmaceutical industry and medicine (Lee, 2017; Terent'ev *et al*., 2011). Silicon-containing steroids, which are usually called silasteroids, are synthesized as potential oestrogenic agents, anti-estrogenic, and antifertility agents (Lukevics *et al*., 1990; Garson and Kirchner, 1971; Simon, 2014). Silasteroids (**37**-**42**) containing the silicone atom in position 6 constitute the bulk of the known synthetic steroids (McPhail and Miller, 1975; Pitt *et al*., 1975). The main properties that are characteristic of these compounds are antineoplastic, psychotropic and anti-seborrheic activities (Table 5).

Steroids of 10- (**44**) and 13-silasteroids (**45**) containing silicone at position 10 and 13 were synthesized (Ouhabi, 2006; Díez-González *et al*., 2008; Blanco *et al*., 2005) but their activity was not studied. Both of these compounds show antineoplastic activity and have a Pa greater than 0.97. The biological activities of other silasteroids are shown in Table 5.

Table 5: Confirmed and predicted biological activities of silasteroids (**37**-**48**).

Silasteroids	Activity reviewed	Activities confirmed (Pa)*	Additional predicted activities (Pa)*
 37	Contraceptive Agent Garson and Kirchner, 1971 Pitt *et al*., 1975	Contraceptive (0.579) Ovulation inhibitor (0.572)	Antineoplastic (0.992) Psychotropic (0.879) Antiseborrheic (0.873) Alopecia treatment (0.831) Anxiolytic (0.762) Hypolipemic (0.626) Prostate disorders treatment (0.598) Bone diseases treatment (0.596) Antiosteoporotic (0.579) Neurodegenerative diseases treatment (0.587) Menopausal disorders treatment (0.554)
 38	Contraceptive Garson and Kirchner, 1971 Pitt *et al*., 1975	Contraceptive (0.541) Ovulation inhibitor (0.512)	Antineoplastic (0.985) Psychotropic (0.815) Anxiolytic (0.754) Neurodegenerative diseases treatment (0.725) Hypolipemic (0.597) Genital warts treatment (0.621) Antieczematic (0.563) Antiseborrheic (0.549) Alopecia treatment (0.513)
 39	Ovulation inhibitor Contraceptive Garson and Kirchner, 1971 Pitt *et al*., 1975	Ovulation inhibitor (0.473)	Antineoplastic (0.995) Psychotropic (0.827) Anxiolytic (0.806) 5 Hydroxytryptamine 2A antagonist (0.765) 5 Hydroxytryptamine 2 antagonist (0.588)
 40	Ovulation inhibitor Contraceptive Garson and Kirchner, 1971 Pitt *et al*., 1975	Ovulation inhibitor (0.584)	Antineoplastic (0.994) Psychotropic (0.834) Anxiolytic (0.823) 5 Hydroxytryptamine 2A antagonist (0.740) Prostate disorders treatment (0.508)
 41	Ovulation inhibitor Contraceptive Garson and Kirchner, 1971 Pitt *et al*., 1975	Ovulation inhibitor (0.649) Contraceptive (0.620)	Antineoplastic (0.973) Antiseborrheic (0.881) Alopecia treatment (0.822) Psychotropic (0.702) Apoptosis agonist (0.687) Skeletal muscle relaxant (0.661) Prostate disorders treatment (0.655) Erythropoiesis stimulant (0.618) Hypolipemic (0.618) Menopausal disorders treatment (0.606)

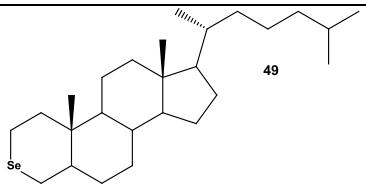
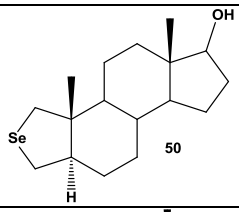
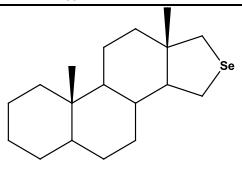
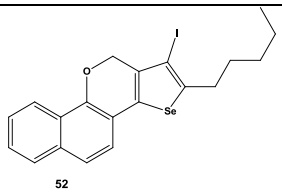
 42	Contraceptive Agent Garson and Kirchner, 1971 Pitt *et al*., 1975	Ovulation inhibitor (0.826) Contraceptive (0.680)	Antineoplastic (0.984) Psychotropic (0.846) Anxiolytic (0.742) Antiseborrheic (0.724) Antiosteoporotic (0.673) Prostate disorders treatment (0.634) Bone diseases treatment (0.630) Menopausal disorders treatment (0.601) Gynecological disorders treatment (0.571)
 43	Not studied		Antiseborrheic (0.940) Antineoplastic (0.871) Ovulation inhibitor (0.859) Hypolipemic (0.818) Contraceptive (0.799) Antiosteoporotic (0.748) Antipruritic (0.742) Alopecia treatment (0.728) Prostate disorders treatment (0.690) Antiarthritic (0.689) Antiinflammatory (0.687) Menopausal disorders treatment (0.686)
 44	Not studied		Antineoplastic (0.977) Antiarthritic (0.896) Antiseborrheic (0.805) Alopecia treatment (0.780) Hypolipemic (0.634) Antieczematic (0.627) Erythropoiesis stimulant (0.616) Apoptosis agonist (0.616) Prostate disorders treatment (0.613) Ovulation inhibitor (0.606) Contraceptive (0.575) Bone diseases treatment (0.553) Menopausal disorders treatment (0.546)
 45	Not studied		Antineoplastic (0.943) Antiarthritic (0.927) Hypolipemic (0.751) Erythropoiesis stimulant (0.728) Antiseborrheic (0.706) Atherosclerosis treatment (0.688) Skeletal muscle relaxant (0.673) Respiratory analeptic (0.629) Antipruritic (0.623) Alopecia treatment (0.606) Neurodegenerative diseases treatment (0.602) Prostate disorders treatment (0.585) Contraceptive (0.572)
 46	Not studied		Antineoplastic (0.905) Contraceptive (0.813) Dermatologic (0.773) Antiinflammatory (0. 755) Hypolipemic (0.752) Antifungal (0.748) Immunosuppressant (0.735) Prostate disorders treatment (0.705) Respiratory analeptic (0.704) Anxiolytic (0.699) Ovulation inhibitor (0.687) Psychotropic (0.683) Apoptosis agonist (0.670) Antiosteoporotic (0.647) Atherosclerosis treatment (0.636)
 47	Not studied		Antihypercholesterolemic (0.917) Antineoplastic (0.883) Antiprotozoal (Leishmania) (0.858) Respiratory analeptic (0.800) Antieczematic (0.799) Immunosuppressant (0.776) Antipruritic (0.771) Prostate disorders treatment (0.765) Dermatologic (0.765) Anesthetic general (0.729) Antiosteoporotic (0.713) Antiinflammatory (0.712) Apoptosis agonist (0.701) Antifungal (0.672)
 48	Not studied		Antineoplastic (0.899) Anabolic (0.878) Antihypercholesterolemic (0.796) Antiinflammatory (0.750) Prostate disorders treatment (0.745) Immunosuppressant (0.738) Respiratory analeptic (0.728) Ovulation inhibitor (0.693) Dermatologic (0.689) Contraceptive (0.648) Antipruritic (0.623) Prostatic (benign) hyperplasia treatment (0.605) Menopausal disorders treatment (0.603)

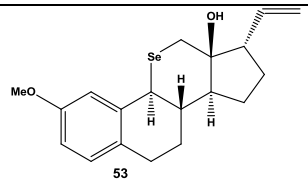
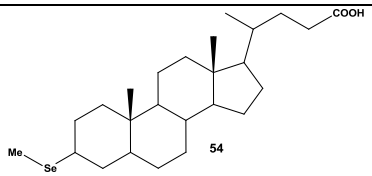
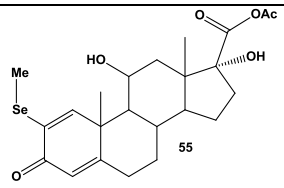
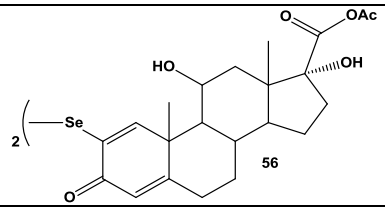
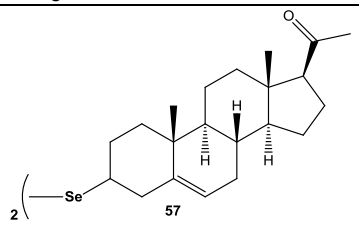
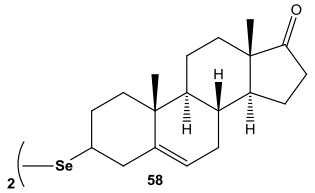
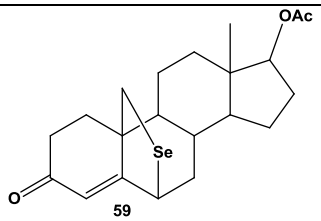
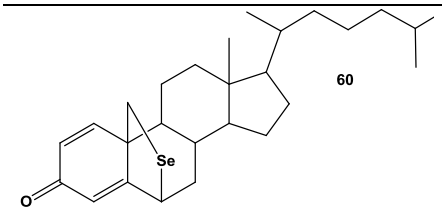
* Only activities with Pa > 0.5 are shown

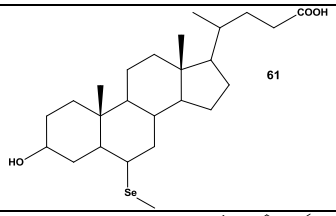
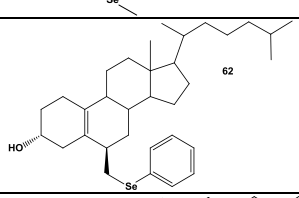
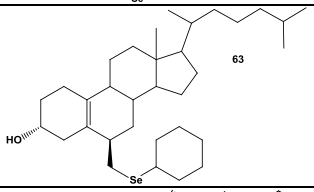
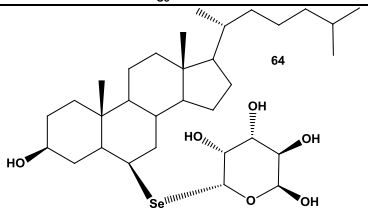
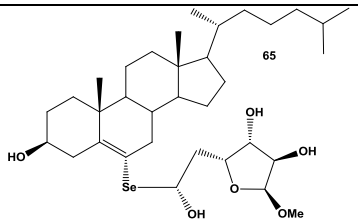
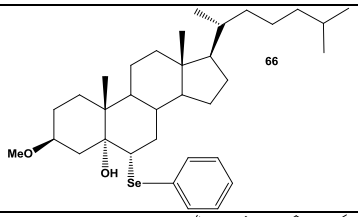
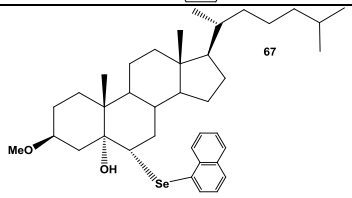
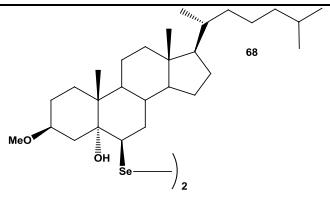
SELENA STEROIDS

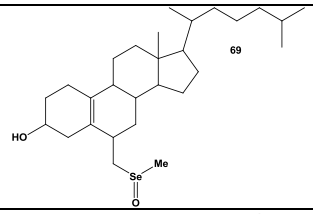
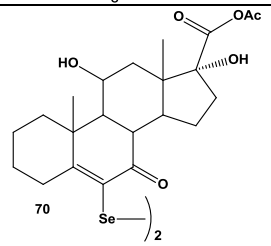
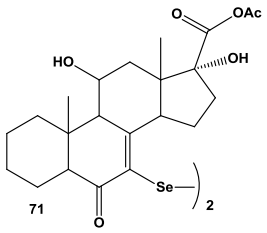
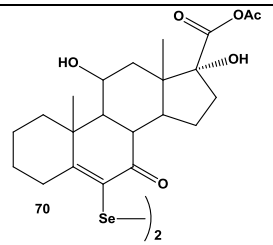
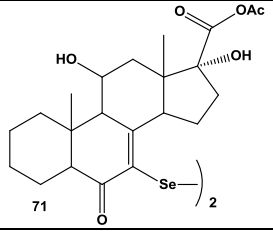
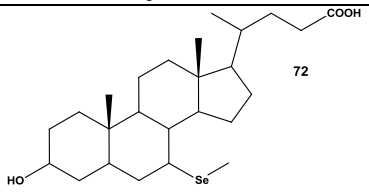
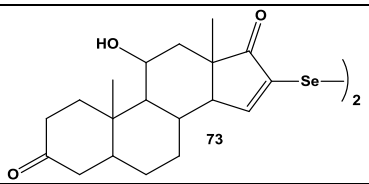
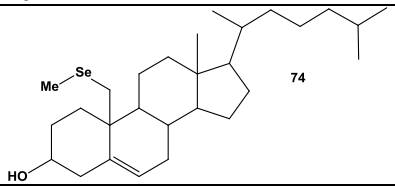
Selenium (Se) is a chemical element belonging to the 16th group of the periodic table and was discovered by Jöns Jacob Berzelius, a Swedish chemist, in 1817 (Rheinboldt, 1955). Selenium is an essential metalloid and it is one of the most necessary trace elements for humans (Conor, 2006). Selenium occupies an important place in the regulation of metabolism in humans and therefore it is necessary to monitor its presence in consumed foods (Terry *et al*., 2000). The Allium and Brassica families as well as Brazil nuts, mushrooms (shiitake and white mushrooms), beans, chia seeds, brown rice, sunflower, sesame and flax seeds, and cabbage and spinach contain high enough selenium and organoselenium concentrations (Pilon-Smits, 2015). Organoselenium compounds are chemical compounds containing bonds between carbon atoms and selenium (C-Se). These compounds are widely used in organic synthesis including the synthesis of pharmaceuticals. Organoselenium chemistry examines the properties and reactivity of selenium compounds. Recently, a large number of original books on the chemistry, biology, and medicine of organoselenium compounds have been published (Santi, 2014; Back, 1999). There are also many excellent reviews in the literature, which are devoted to the biological role and functions of organoselenium compounds (Li *et al*., 2013). Apparently, selena steroids are the main group of the essential metalloids that have been synthesized over the past 50 years and approximately 300 have been synthesized (Wirth, 2011; Ibrahim-Ouali *et al*., 2011; Ibrahim-Ouali, 2009). The selena steroids selected for this study are presented in Table 6. They can be contingently divided into four groups. The first group includes steroids in which the selenium atom is incorporated into the heterocycle of the core molecules (**49**, **50, 51** and **52**). For the selena steroids of this group, the main characteristics are antineoplastic and anti-seborrheic activities. Additionally, these Selena steroids of this group can be used to treat Alzheimer's disease (Table 6). The second group includes steroids where selenium is in the second and third positions of the steroid (**53-58**). For selena steroids of the second group, the main activities are antineoplastic, anti-hypercholesterolemia and anti-inflammatory. The third group includes steroids in which the selenium atom is in position six of the core molecules (**59-68, 70**). For selena steroids of the third group (**69**, **71-76**), respiratory analeptic, anaesthetic and anti-hypercholesterolemic are the main activities. In addition, they can be used as chemopreventive and hepatoprotectant agents. The fourth group includes steroids in which the selenium atom is in the hydrocarbon tail of the steroid (**77-84**). For the fifth group (**85-88**), the main activities are antiarthritic and antineoplastic. In addition, they can be used as for hypolipemic, anti-atherosclerosis, lipoprotein disorders and as antioxidant agents.

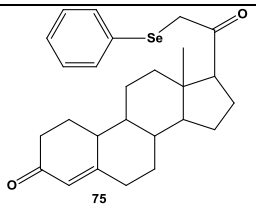
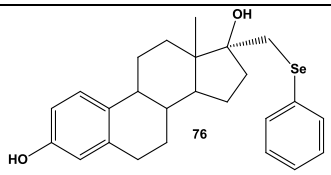
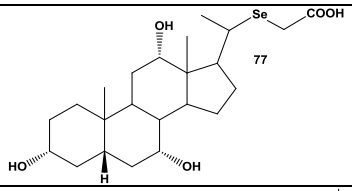
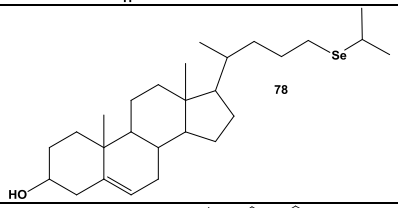
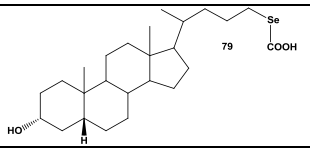
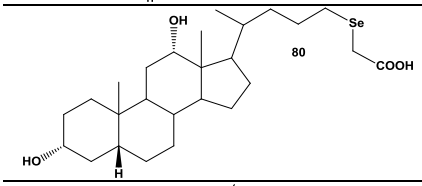
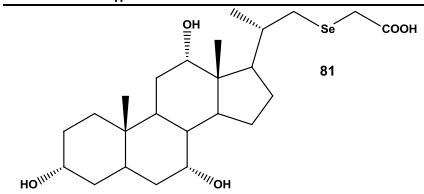
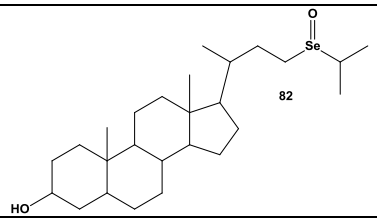
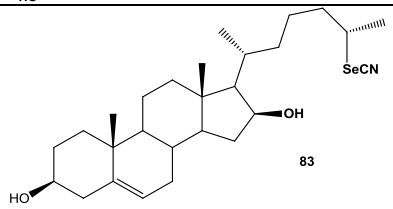
Table 6: Predicted biological activities of selena steroids (**49-85**).

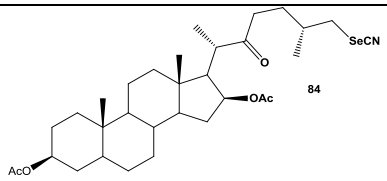
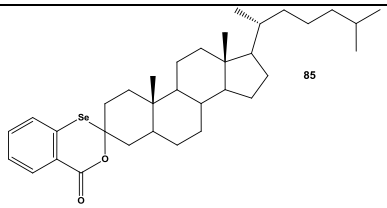
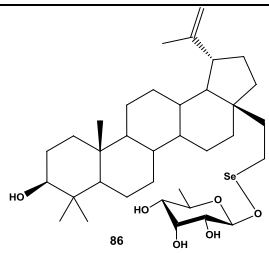
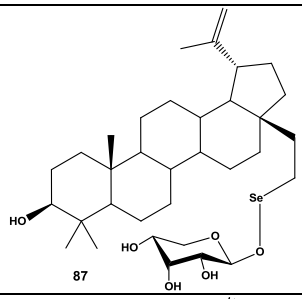
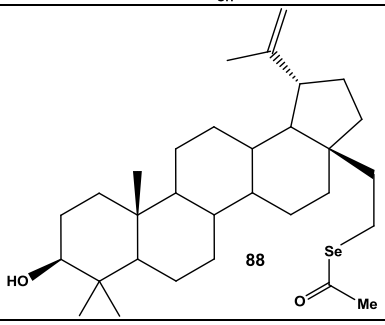
Selena steroids	Activity reviewed	Activities confirmed (Pa)*	Additional predicted activities (Pa)*
 49	Not studied		Antineoplastic (0.894) Antieczematic (0.862) Chemoprotective (0.775) Dermatologic (0.774) Anesthetic general (0.754) Antipruritic (0.747) Antiosteoporotic (0.732) Hypolipemic (0.730) Prostate disorders treatment (0.721) Alzheimer's disease treatment (0.702) Antipsoriatic (0.691) Apoptosis agonist (0.669) Hepatic disorders treatment (0.660)
 50	Not studied		Antiseborrheic (0.916) Antineoplastic (0.913) Alopecia treatment (0.889) Chemoprotective (0.816) Alzheimer's disease treatment (0.794) Erythropoiesis stimulant (0.780) Cerebrovascular disordes treatment (0.774) Antieczematic (0.769) Vascular (periferal) disease treatment (0.752) Antiosteoporotic (0.739) Prostate disorders treatment (0.723) Ovulation inhibitor (0.716) Antiinflammatory (0.711) Vasoprotector (0.695)
 51	Not studied		Antiseborrheic (0.878) Antineoplastic (0.874) Cerebrovascular disordes treatment (0.869) Alzheimer's disease treatment (0.833) Chemoprotective (0.831) Psychosexual dysfunction treatment (0.791) Neurodegenerative diseases treatment (0.775) Alopecia treatment (0.764) Prostate disorders treatment (0.753) Dermatologic (0.716) Ovulation inhibitor (0.692) Dementia treatment (0.635)
 52	Not studied		Ubiquinol-cytochrome-c reductase inhibitor (0.788) Antineoplastic (0.661) Hydroxylamine reductase (NADH) inhibitor (0.632)

 53	Not studied		Antineoplastic (0.938) Antiseborrheic (0.925) Chemoprotective (0.809) Alopecia treatment (0.788) Alzheimer's disease treatment (0.778) Erythropoiesis stimulant (0.756) Cerebrovascular disordes treatment (0.732) Antieczematic (0.711) Vascular (periferal) disease treatment (0.689) Antiosteoporotic (0.656) Antiinflammatory (0.633)
 54	Not studied		Antieczematic (0.902) Antineoplastic (0.846) Antihypercholesterolemic (0.841) Erythropoiesis stimulant (0.791) Chemoprotective (0.786) Anesthetic general (0.772) Antipruritic (0.760) Dermatologic (0.751) Antiseborrheic (0.719) Prostate disorders treatment (0.711) Bone diseases treatment (0.698) Hepatic disorders treatment (0.694)
 55	Not studied		Antiinflammatory (0.940) Antineoplastic (0.897) Antiseborrheic (0.831) Antiallergic (0.790) Anticarcinogenic (0.778) Antipruritic (0.778) Chemoprotective (0.750) Immunosuppressant (0.727) Dermatologic (0.697) Ovulation inhibitor (0.635)
 56	Not studied		Antiinflammatory (0.959) Antiseborrheic (0.898) Respiratory analeptic (0.870) Antiallergic (0.843) Antineoplastic (0.833) Antipruritic (0.816) Muscular dystrophy treatment (0.794) Immunosuppressant (0.777) Antiasthmatic (0.757) Inflammatory Bowel disease treatment (0.742) Cell adhesion molecule inhibitor (0.730) Ovulation inhibitor (0.723)
 57	Androgenic activity Li et al., 2013 Santi, 2014	Antiosteoporotic (0.575)	Anesthetic general (0.898) Prostate disorders treatment (0.814) Erythropoiesis stimulant (0.781) Antineoplastic (0.771) Dermatologic (0.762)) Antiinflammatory (0.750) Ovulation inhibitor (0.718) Neuroprotector (0.714) Prostatic (benign) hyperplasia treatment (0.710) Menopausal disorders treatment (0.700)
 58	Androgenic activity Li et al., 2013 Santi, 2014	Androgen agonist (0.404) Male reproductive disfunction treatment (0.851) Antiosteoporotic (0.620) Oxytocic (0.572) Psychosexual dysfunction treatment (0.404)	Ovulation inhibitor (0.918) Antineoplastic (0.876) Antiseborrheic (0.801)Prostate disorders treatment (0.793) Respiratory analeptic (0.772) Neuroprotector (0.754) Antiinflammatory (0.738) Antihypercholesterolemic (0.726) Dermatologic (0.720) Muscular dystrophy treatment (0.711) Prostatic (benign) hyperplasia treatment (0.705) Alopecia treatment (0.693)
 59	Fungicidalagent Li et al., 2013 Santi, 2014	Membrane permeability inhibitor (0.788) Cytochrome P450 inhibitor (0.559) Steroid synthesis inhibitor (0.530) Antifungal (0.476)	Antiseborrheic (0.926) Antineoplastic (0.899) Antisecretoric (0.796) Alzheimer's disease treatment (0.783) Ovulation inhibitor (0.757) Chemoprotective (0.740) Male reproductive disfunction treatment (0.730) Antiinflammatory (0.729) Alopecia treatment (0.720) Prostate disorders treatment (0.683) Bone diseases treatment (0.680)
 60	Fungicidalagent Li et al., 2013 Santi, 2014	Membrane permeability inhibitor (0.691) Mitochondrial electron transport inhibitor (0.554) Antifungal (0.477)	Antineoplastic (0.838) Antieczematic (0.823) Alzheimer's disease treatment (0.775) Antipruritic (0.758) Chemoprotective (0.731) Dermatologic (0.731) Antiosteoporotic (0.715) Antiinflammatory (0.701) Respiratory analeptic (0.675) Prostate disorders treatment (0.672) Vascular (periferal) disease treatment (0.656)

	Not studied		Antihypercholesterolemic (0.905) Anesthetic general (0.901) Antieczematic (0.899) Antineoplastic (0.858) Erythropoiesis stimulant (0.855) Hepatoprotectant (0.823) Antipruritic (0.798) Analeptic (0.796) Chemoprotective (0.774) Dermatologic (0.747) Anticarcinogenic (0.739) Biliary tract disorders treatment (0.736) Hepatic disorders treatment (0.732) Bone diseases treatment (0.721)
	Not studied		Antineoplastic (0.926) Antihypercholesterolemic (0.877) Antiinflammatory (0.865) Dermatologic (0.813) Antieczematic (0.799) Chemoprotective (0.780) Antipruritic (0.746) Antiosteoporotic (0.726) Antihypertensive (0.722) Hepatoprotectant (0.708) Prostate disorders treatment (0.676) Antipsoriatic (0.667)
	Not studied		Antihypercholesterolemic (0.908) Antineoplastic (0.882) Antieczematic (0.825) Dermatologic (0.799) Antipruritic (0.782) Antiosteoporotic (0.776) Bone diseases treatment (0.772) Hypolipemic (0.769) Respiratory analeptic (0.730) Chemoprotective (0.715) Antiinflammatory (0.713) Prostate disorders treatment (0.699)
	Cytotoxic activity therapeutic agents for Alzheimer's disease Li *et al*., 2013 Santi, 2014	Cytotoxic (0.630) Alzheimer's disease treatment (0.424)	Respiratory analeptic (0.963) Anesthetic general (0.946) Chemopreventive (0.916) Antihypercholesterolemic (0.912) Hepatoprotectant (0.901) Antineoplastic (0.884) Wound healing agent (0.880) Immunostimulant (0.830) Antieczematic (0.790) Antiinflammatory (0.780) Anticarcinogenic (0.753) Antifungal (0.735) Neuroprotector (0.729)
	Cytotoxic activity therapeutic agents for Alzheimer's disease Li et al., 2013 Santi, 2014	Cytotoxic (0.701) Alzheimer's disease treatment (0.428)	Respiratory analeptic (0.971) Antihypercholesterolemic (0.953) Chemopreventive (0.923) Hepatoprotectant (0.915) Anesthetic general (0.910) Antineoplastic (0.856) Immunostimulant (0.843) Neuroprotector (0.837) Antifungal (0.824) Wound healing agent (0.817) Antieczematic (0.815) Anticarcinogenic (0.804) Radioprotector (0.780) Antiinflammatory (0.773)
	Anticancer Li et al., 2013 Santi, 2014	Antineoplastic (0.828) Antineoplastic (sarcoma) (0.560) Antimetastatic (0.550) Antineoplastic (renal cancer) (0.513)	Antieczematic (0.828) Respiratory analeptic (0.769) Immunosuppressant (0.734) Antipruritic (0.728) Hepatoprotectant (0.715) Antifungal (0.702) Chemopreventive (0.677) Dermatologic (0.677) Antiinflammatory (0.655) Hepatic disorders treatment (0.627) Antipsoriatic (0.618)
	Anticancer Li et al., 2013 Santi, 2014	Antineoplastic (0.795) Antimetastatic (0.541) Antineoplastic (sarcoma) (0.540) Antineoplastic (renal cancer) (0.503)	Antieczematic (0.823) Antifungal (0.746) Immunosuppressant (0.733) Antipruritic (0.724) Respiratory analeptic (0.700) Hepatoprotectant (0.689) Dermatologic (0.672) Chemopreventive (0.665) Antiinflammatory (0.645) Antipsoriatic (0.608) Hepatic disorders treatment (0.604)
	Dimeric, Anticancer Li et al., 2013 Santi, 2014	Antineoplastic (0.809) Antineoplastic (sarcoma) (0.616) Antimetastatic (0.582) Prostatic (benign) hyperplasia treatment (0.560) Antineoplastic (renal cancer) 567 Antineoplastic (pancreatic cancer) (0.526)	Respiratory analeptic (0.921) Antieczematic (0.864) Analeptic (0.822) Antipruritic (0.794) Antihypercholesterolemic (0.776) Immunosuppressant (0.769) Anesthetic general (0.753) Choleretic (0.737) Hepatoprotectant (0.733) Proliferative diseases treatment (0.727) Chemopreventive (0.727)

	Not studied	Antineoplastic (0.904) Antihypercholesterolemic (0.875) Antieczematic (0.809) Chemoprotective (0.793) Dermatologic (0.776) Antipruritic (0.748) Antiosteoporotic (0.747) Bone diseases treatment (0.745) Hypolipemic (0.714) Prostate cancer treatment (0.638)
	Not studied	Antiinflammatory (0.950) Respiratory analeptic (0.893) Antiseborrheic (0.876) Antineoplastic (0.818) Antipruritic (0.793) Antiallergic (0.793) Immunosuppressant (0.757) Dermatologic (0.745) Cell adhesion molecule inhibitor (0.745) Hepatoprotectant (0.740) Ovulation inhibitor (0.712) Antiasthmatic (0.683)
	Not studied	Antiinflammatory (0.936) Respiratory analeptic (0.900) Antiseborrheic (0.831) Antineoplastic (0.813) Analeptic (0.797) Hepatic disorders treatment (0.771) Hepatoprotectant (0.766) Cell adhesion molecule inhibitor (0.752) Immunosuppressant (0.757) Antipruritic (0.745) Antiallergic (0.682)
	Not studied	Antiinflammatory (0.950) Respiratory analeptic (0.893) Antiseborrheic (0.876) Antineoplastic (0.818) Antipruritic (0.793) Antiallergic (0.793) Immunosuppressant (0.757) Dermatologic (0.745) Cell adhesion molecule inhibitor (0.745) Hepatoprotectant (0.740) Ovulation inhibitor (0.712) Antiasthmatic (0.683)
	Not studied	Antiinflammatory (0.936) Respiratory analeptic (0.900) Antiseborrheic (0.831) Antineoplastic (0.813) Analeptic (0.797) Hepatic disorders treatment (0.771) Hepatoprotectant (0.766) Cell adhesion molecule inhibitor (0.752) Immunosuppressant (0.757) Antipruritic (0.745) Antiallergic (0.682)
	Not studied	Choleretic (0.909) Antihypercholesterolemic (0.905) Anesthetic general (0.903) Antieczematic (0.899)Erythropoiesis stimulant (0.856) Antineoplastic (0.849) Hepatoprotectant (0.829) Analeptic (0.808) Antipruritic (0.793) Biliary tract disorders treatment (0.780) Chemoprotective (0.771) Dermatologic (0.731) Anticarcinogenic (0.725) Laxative (0.716)
	Not studied	Antiinflammatory (0.907) Antiseborrheic (0.870) Respiratory analeptic (0.861) Antineoplastic (0.855) Hepatic disorders treatment (0.792) Inflammatory Bowel disease treatment (0.750) Dermatologic (0.729) Antipruritic (0.729) Diuretic (0.728) Immunosuppressant (0.702)) Prostate disorders treatment (0.700) Antiallergic (0.698)
	Not studied	Chemopreventive (0.936) Antineoplastic (0.918) Antihypercholesterolemic (0.905) Antieczematic (0.821) Respiratory analeptic (0.817) Anticarcinogenic (0.815) Immunostimulant (0.813) Prostate cancer treatment (0.795) Anesthetic general (0.758) Antipruritic (0.756) Dermatologic (0.733) Antiinflammatory (0.730) Hepatoprotectant (0.718)

 75	Not studied		Antineoplastic (0.951) Chemoprotective (0.844) Dermatologic (0.775) Prostate disorders treatment (0.757) Antiseborrheic (0.717) Ovulation inhibitor (0.704) Antiinflammatory (0.704) Prostatic (benign) hyperplasia treatment (0.661) Antihypertensive (0.649) Menopausal disorders treatment (0.624) Antiosteoporotic (0.623)
 76	Not studied		Antiseborrheic (0.958) Antineoplastic (0.935) Antiinflammatory (0.918) Ovulation inhibitor (0.826) Chemoprotective (0.804) Alopecia treatment (0.798) Antihypertensive (0.789) Cognition disorders treatment (0.724) Dermatologic (0.705) Menopausal disorders treatment (0.658) Prostate disorders treatment (0.654) Anticarcinogenic (0.652) Antiosteoporotic (0.637)
 77	Not studied		Hypolipemic (0.995) Atherosclerosis treatment (0.991) Lipoprotein disorders treatment (0.982) Antiarthritic (0.981) Antioxidant (0.973) Antineoplastic (0.852) Erythropoiesis stimulant (0.823) Biliary tract disorders treatment (0.808) Antiseborrheic (0.783) Chemoprotective (0.748) Antieczematic (0.747) Hepatic disorders treatment (0.743) Hepatoprotectant (0.733) Laxative (0.709)
 78	Not studied		Antineoplastic (0.922) Chemopreventive (0.914) Antihypercholesterolemic (0.902) Hypolipemic (0.899) Respiratory analeptic (0.870) Antieczematic (0.845) Anticarcinogenic (0.822) Chemoprotective (0.812) Atherosclerosis treatment (0.791) Apoptosis agonist (0.770) Dermatologic (0.766) Antipruritic (0.757) Anesthetic general (0.753) Hepatoprotectant (0.742)
 79	Not studied		Antineoplastic (0.918) Anesthetic general (0.914) Hypolipemic (0.913) Respiratory analeptic (0.910) Chemopreventive (0.894) Antihypercholesterolemic (0.884) Antieczematic (0.875) Atherosclerosis treatment (0.822) Anticarcinogenic (0.801) Hepatoprotectant (0.794)
 80	Not studied		Hypolipemic (0.996) Atherosclerosis treatment (0.995) Lipoprotein disorders treatment (0.991) Antiarthritic (0.979) Antioxidant (0.978) Antineoplastic (0.904) Antieczematic (0.825) Chemoprotective (0.823) Anticarcinogenic (0.795) Anesthetic general (0.768) Erythropoiesis stimulant (0.756)
 81	not studied		Hypolipemic (0.995) Atherosclerosis treatment (0.989) Lipoprotein disorders treatment (0.980) Antiarthritic (0.971) Antioxidant (0.970) Antineoplastic (0.850) Antieczematic (0.833) Biliary tract disorders treatment (0.808) Chemoprotective (0.785) Hepatoprotectant (0.731) Erythropoiesis stimulant (0.730) Laxative (0.683)
 82	Not studied		Antieczematic (0.868) Antineoplastic (0.859) Respiratory analeptic (0.812) Erythropoiesis stimulant (0.795) Anesthetic general (0.789) Antipruritic (0.740) Antihypercholesterolemic (0.739) Hypolipemic (0.723) Dermatologic (0.722) Biliary tract disorders treatment (0.710) Prostate disorders treatment (0.700)
 83	Anticancer Li et al., 2013 Santi, 2014	Antineoplastic (0.894) Anticarcinogenic (0.784) Prostatic (benign) hyperplasia treatment (0.620) Antimetastatic (0.563)	Respiratory analeptic (0.875) Antiprotozoal (0.857) Antihypercholesterolemic (0.839) Chemopreventive (0.831) Anesthetic general (0.815) Antieczematic (0.815) Antipruritic (0.773) Hepatoprotectant (0.756) Apoptosis agonist (0.759) Dermatologic (0.743) Antiinflammatory (0.739) Antiosteoporotic (0.725)

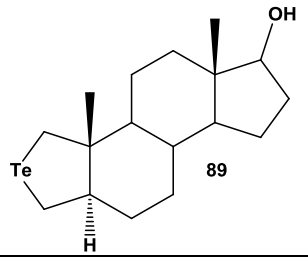
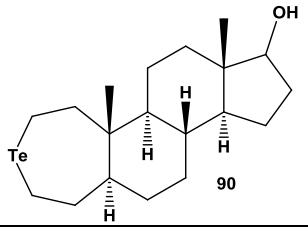
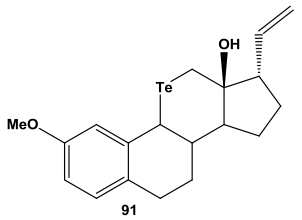
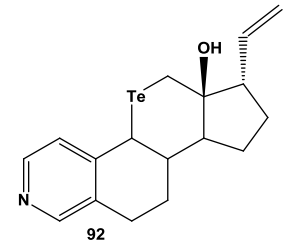
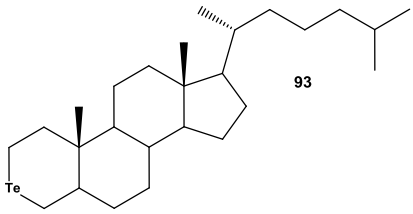
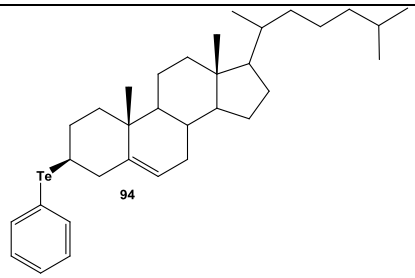
	Anticancer Li *et al*., 2013 Santi, 2014	Antineoplastic (0.895) Antimetastatic (0.638)	Antiprotozoal (0.881) Chemopreventive (0.791) Apoptosis agonist (0.675) Immunosuppressant (0.663) Antioxidant (0.625) Antieczematic (0.599) Dermatologic (0.598) Prostate disorders treatment (0.594) Hepatoprotectant (0.576) Hypolipemic (0.546)
	Not studied		Antihypercholesterolemic (0.879) Respiratory analeptic (0.857) Antieczematic (0.846) Anesthetic general (0.840) Hepatic disorders treatment (0.802) Antineoplastic (0.808) Antiinflammatory (0.779) Antipruritic (0.771) Dermatologic (0.760) Immunosuppressant (0.744) Anticonvulsant (0.718) Antipsoriatic (0.704)
	Anticancer Li *et al*., 2013 Santi, 2014	Antineoplastic (0.932) Anticarcinogenic (0.839) Antineoplastic (pancreatic cancer) (0.591) Antineoplastic (melanoma) (0.580) Antineoplastic (sarcoma) (0.548) Antineoplastic (lymphocytic leukemia) (0.524)	Chemopreventive (0.916) Hepatoprotectant (0.912) Antiviral (Influenza) (0.881) Respiratory analeptic (0.869) Apoptosis agonist (0.858) Antiprotozoal (Leishmania) (0.823) Antiinflammatory (0.795) Immunosuppressant (0.769) Dementia treatment (0.734) Antieczematic (0.746) Antifungal (0.687)
	Anticancer Li et al., 2013 Santi, 2014	Antineoplastic (0.915) Anticarcinogenic (0.819) Antineoplastic (melanoma) (0.601) Antineoplastic (pancreatic cancer) (0.569)	Hepatoprotectant (0.905) Chemopreventive (0.899) Antiprotozoal (Leishmania) (0.842) Apoptosis agonist (0.838) Antiinflammatory (0.796) Immunosuppressant (0.758) Antiviral (Influenza) (0.724) Antieczematic (0.732) Antipruritic (0.696) Hypolipemic (0.642) Antifungal (0.639) Dementia treatment (0.623) Antiviral (HIV) (0.561)
	Anticancer Li *et al*., 2013 Santi, 2014	Antineoplastic (0.873) Antineoplastic (pancreatic cancer) (0.556) Antineoplastic (melanoma)(0.556) Antimetastatic (0.587)	Apoptosis agonist (0.927) Antieczematic (0.771) Chemoprotective (0.741) Hepatoprotectant (0.741) Antiinflammatory (0.625) Erythropoiesis stimulant (0.595) Antiviral (Influenza) (0.593) Antiprotozoal (Leishmania) (0.565) Prostate disorders treatment (0.545) Immunosuppressant (0.549) Hypolipemic (0.536)

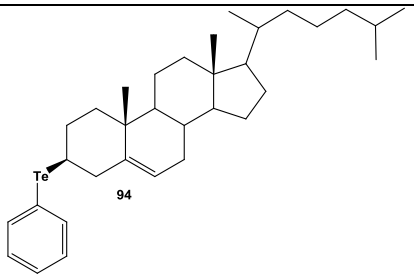
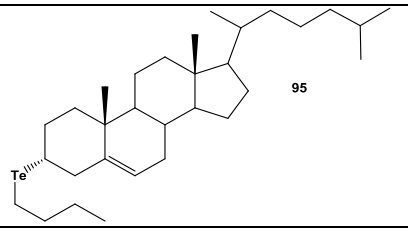
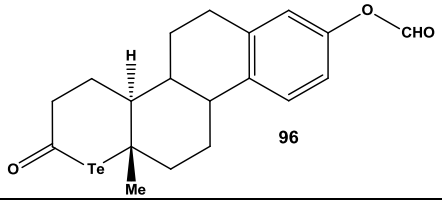
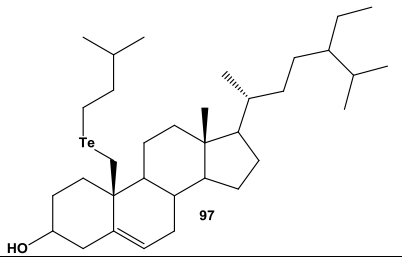
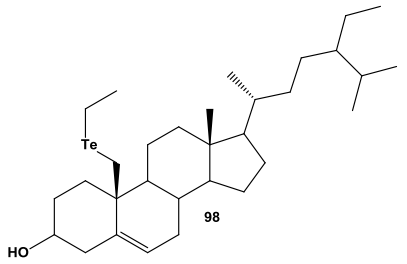
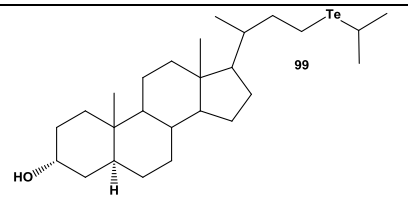
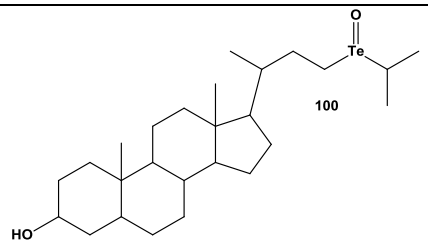
* Only activities with Pa > 0.5 are shown

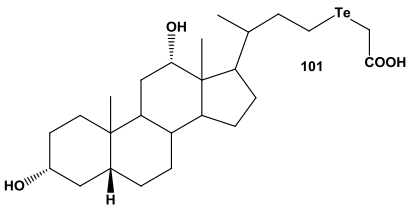
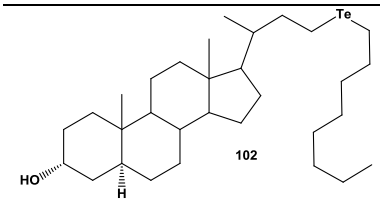
TELLURA STEROIDS

Tellurium (Te) is a toxic metalloid that was discovered by Franz-Joseph Müller von Reichenstein in 1782 (Divers and Shimosé, 1883). Organotellurium chemistry addresses the synthesis and properties of chemical compounds containing a carbon bond with tellurium. A large number of publications have been devoted to this topic but it is not a topic for our research (Sadekov et al., 1987). Tellura steroids are a rare group of organic synthetic compounds whose biological activity is of great interest for medicine, pharmacology, and the pharmaceutical industry (Ibrahim-Ouali, 2010, 2015; Knapp, 1980). For tellura steroids (**89**-**93**,**96**), whose tellurium is incorporated into the steroid skeleton, the following basic properties are characteristics: antioxidant, anti-inflammatory, antineoplastic, antiseborrheic, and antiprotozoal activities, and they can be used as anti-parkinsonian, anti-Alzheimer's disease and anti-neurodegenerative agents (Table 7). For tellura steroids (**97** and **98**), anti-inflammatory, antioxidant and anticancer properties are characteristics. The biological activities of other tellura steroids (**94**, **95**, **99**-**102**) are presented in Table 7.

Table 7: Predicted biological activities of tellura steroids (**89-105**).

Tellura-steroids	Activity reviewed	Activities confirmed (Pa)*	Additional predicted activities (Pa)*
	Not studied		Antioxidant (0.956) Antiinflammatory (0.936) Antineoplastic (0.935) Antiseborrheic (0.933) Alopecia treatment (0.912) Neurodegenerative diseases treatment (0.897) Alzheimer's disease treatment (0.877) Atherosclerosis treatment (0.873) Antiparkinsonian (0.868) Erythropoiesis stimulant (0.815) Antieczematic (0.807) Antiosteoporotic (0.800) Anesthetic general (0.799) Vasoprotector (0.785)
	Not studied		Antioxidant (0.946) Antiseborrheic (0.933) Antiinflammatory (0.930) Antineoplastic (0.930) Alopecia treatment (0.889) Anesthetic general (0.879) Neurodegenerative diseases treatment (0.871) Alzheimer's disease treatment (0.863) Atherosclerosis treatment (0.861) Respiratory analeptic (0.850) Erythropoiesis stimulant (0.846) Antiparkinsonian (0.833) Antiosteoporotic (0.783) Antihypercholesterolemic (0.769)
	Not studied		Antiprotozoal (Plasmodium) (0.818) Antiprotozoal (0.801) Antiinflammatory (0.779) Antioxidant (0.774) Alzheimer's disease treatment (0.757) Neurodegenerative diseases treatment (0.735) Antiparkinsonian (0.730) Antineoplastic (0.725) Atherosclerosis treatment (0.670) Ovulation inhibitor (0.625)
	Not studied		Neurodegenerative diseases treatment (0.825) Antiprotozoal (Plasmodium) (0.823) Antiparkinsonian (0.817) Antiprotozoal (0.810) Alzheimer's disease treatment (0.799) Antiinflammatory (0.789) Antineoplastic (0.759) Antioxidant (0.736) Atherosclerosis treatment (0.649)
	Not studied		Antiinflammatory (0.908) Anesthetic general (0.898) Atherosclerosis treatment (0.896) Antieczematic (0.887) Antineoplastic (0.872) Respiratory analeptic (0.872) Antihypercholesterolemic (0.864) Antioxidant (0.849) Alzheimer's disease treatment (0.843) Neurodegenerative diseases treatment (0.819) Antiosteoporotic (0.802) Prostate disorders treatment (0.754) Antiparkinsonian (0.744)
	Anticancer Knapp, 1980	Antineoplastic (0.828) Prostatic (benign) hyperplasia treatment (0.678) Antineoplastic (pancreatic cancer) (0.522) Prostate cancer treatment (0.501)	Antiarthritic (0.969) Antioxidant (0.967) Antihypercholesterolemic (0.889) Anesthetic general (0.845) Antieczematic (0.828) Respiratory analeptic (0.826) Antiinflammatory (0.794) Antipruritic (0.780) Dermatologic (0.772) Prostate disorders treatment (0.744) Antiosteoporotic (0.717) Atherosclerosis treatment (0.703) Alzheimer's disease 0.966 treatment (0.526)

	Anticancer	Antineoplastic (0.828) Prostatic (benign) hyperplasia treatment (0.678) Antineoplastic (pancreatic cancer) (0.522) Prostate cancer treatment (0.501)	Antiarthritic (0.969) Antioxidant (0.967) Antihypercholesterolemic (0.889) Anesthetic general (0.845) Antieczematic (0.828) Respiratory analeptic (0.826) Antiinflammatory (0.794) Antipruritic (0.780) Dermatologic (0.772) Prostate disorders treatment (0.744) Antiosteoporotic (0.717) Atherosclerosis treatment (0.703) Alzheimer's disease 0.966 treatment (0.526)
	Anticancer	Antineoplastic (0.927) Prostatic (benign) hyperplasia treatment (0.663) Antineoplastic (pancreatic cancer) (0.508)	Antioxidant (0.966) Atherosclerosis treatment (0.964) Antiinflammatory (0.955) Antiparkinsonian (0.946) Neurodegenerative diseases treatment (0.945) Alzheimer's disease treatment (0.928) Antihypercholesterolemic (0.886) Anesthetic general (0.845) Antieczematic (0.836) Respiratory analeptic (0.791) Antipruritic (0.781) Dermatologic (0.760) Prostate disorders treatment (0.730) Antiosteoporotic (0.683)
	Not studied		Antiinflammatory (0.908) Anesthetic general (0.898) Atherosclerosis treatment (0.896) Antieczematic (0.887) Antineoplastic (0.872) Respiratory analeptic (0.872) Antihypercholesterolemic (0.864) Antioxidant (0.849) Alzheimer's disease treatment (0.843) Antiosteoporotic (0.802) Antipruritic (0.792) Prostate disorders treatment (0.754)
	Not studied		Antihypercholesterolemic (0.958) Antiinflammatory (0.913) Atherosclerosis treatment (0.890) Respiratory analeptic (0.885) Antineoplastic (0.871) Anesthetic general (0.848) Alzheimer's disease treatment (0.838) Antieczematic (0.815) Antioxidant (0.807) Neurodegenerative diseases treatment (0.801) Antiosteoporotic (0.737)
	Not studied		Atherosclerosis treatment (0.977) Antioxidant (0.963) Antiinflammatory (0.962) Antihypercholesterolemic (0.956) Antiparkinsonian (0.955) Neurodegenerative diseases treatment (0.954) Alzheimer's disease treatment (0.940) Antineoplastic (0.932) Respiratory analeptic (0.877) Anesthetic general (0.830) Antieczematic (0.823) Antihyperlipoproteinemic (0.811) Antiosteoporotic (0.738)
	Not studied		Antiinflammatory (0.926) Antioxidant (0.922) Respiratory analeptic (0.916) Anesthetic general (0.910) Atherosclerosis treatment (0.908) Antineoplastic (0.895) Antieczematic (0.888) Neurodegenerative diseases treatment (0.877) Antihypercholesterolemic (0.869) Alzheimer's disease treatment (0.868) Antiparkinsonian (0.848)
	Not studied		Respiratory analeptic (0.959) Anesthetic general (0.937) Antiinflammatory (0.910) Antihypercholesterolemic (0.909) Antieczematic (0.901) Antineoplastic (0.892) Atherosclerosis treatment (0.876) Alzheimer's disease treatment (0.828) Neurodegenerative diseases treatment (0.808) Antipruritic (0.807) Biliary tract disorders treatment (0.807) Antiosteoporotic (0.788)

	Not studied	Antiinflammatory (0.911) Antihypercholesterolemic (0.886) Atherosclerosis treatment (0.883) Antioxidant (0.878) Anesthetic general (0.863) Antineoplastic (0.862) Antieczematic (0.856) Respiratory analeptic (0.850) Alzheimer's disease treatment (0.832) Erythropoiesis stimulant (0.828) Neurodegenerative diseases treatment (0.799) Hepatoprotectant (0.752)
	Not studied	Antiinflammatory (0.928) Antioxidant (0.926) Atherosclerosis treatment (0.910) Anesthetic general (0.894) Neurodegenerative diseases treatment (0.888) Antieczematic (0.885) Antineoplastic (0.884) Alzheimer's disease treatment (0.877) Antiparkinsonian (0.872) Respiratory analeptic (0.859) Antihypercholesterolemic (0.844) Hepatoprotectant (0.731)

* Only activities with Pa > 0.5 are shown

CONCLUSION

In this review, we present the structures of OS that contain (with the composition of a molecule of metals or metalloids) As, At, B, Ge, Si, Se, and Te that belong to seven groups that include boronic steroids, arsenosteroids, astatosteroids, germylated steroids, silasteroids, selena steroids and tellura steroids. The biological activity for these groups of steroids is presented in this paper. The most characteristic biological activities for astatosteroid steroids were antineoplastic, anti-seborrheic, anti-hypercholesterolemic, anti-secretoric and anti-hypercholesterolemic activities. The most characteristic biological activities for germylated steroids were antineoplastic, antiseborrheic and dermatologic activities. The main activities that are characteristic of silasteroids are antineoplastic, psychotropic and anti-seborrheic activities. Additionally, these selena and tellura steroids showed a high anticancer activity, and they can be used as anti-parkinsonian, anti-Alzheimer's disease and antineuro-degenerative agents.

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