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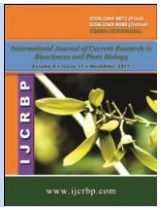

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Chlorinated Plant Steroids and their Biological Activities

Valery M. Dembitsky[1]*, Tatyana A. Gloriozova[2] and Vladimir V. Poroikov[2]

[1] *Biochemistry Laboratory, National Scientific Center of Marine Biology, 17 Palchevsky Str., Vladivostok, Russia 690041*
[2] *Institute of Biomedical Chemistry, Moscow, Russia 119121*

Corresponding author.

Abstract

The present review describes the biological activities of natural plant chlorinated steroids. About forty biologically active chlorinated steroids have shown confirmed cytostatic, antineoplastic, anti-eczematic, antidiabetic, antibacterial, and other activities. The structures and reported and predicted activities of chlorinated steroids are available. With the computer programme PASS and based on structure–activity relationships (SAR), some additional activities are also predicted, which point towards new possible applications of these lipids. This review emphasizes the role of chlorinated steroids as an important source and potential leads for drug discovery and they are of great interest to chemists, physicians, biologists, pharmacologists and the pharmaceutical industry.

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Introduction

Halogenated steroids represent a small group of natural lipid molecules and are found in plants, and marine invertebrates and seaweeds. Through the 1960s, halogenated natural products were thought to be infrequent and poisonous products that have since increased dramatically to nearly 5,000 (Gribble, 1996, 1998, 1999, 2010, 2015; Dembitsky and Tolstikov, 2003; Cabrita et al., 2010). Previously, we devoted two books (Dembitsky and Tolstikov, 2003, 2005) and several reviews to halogenated fatty acids (Dembitsky and Srebnik, 2002), alkanes and cycloalkanes (Dembitsky and Tolstikov, 2003a), alkaloids (Dembitsky, 2002; Dembitsky and Tolstikov, 2003b), terpenoids and steroids (Dembitsky and Tolstikov, 2002, 2003c,d), and other natural terrestrial and marine metabolites (Dembitsky, 2006; Dembitsky and Tolstikov, 2003e,f,g).

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 (Dembitsky et al., 20017a-d). 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; Lagunin et al., 2011; Levitsky et al., 2016).

This review is devoted to an interesting topic, i.e., natural chlorinated steroids, which are found in plants.

Chlorinated plant steroids

It is known that natural metabolites, including lipids, can contain halogen atoms, such as fluorine, chlorine, bromine and iodine, are introduced into marine organisms (Dembitsky and Tolstikov, 2003; Gribble, 2015; Dembitsky, 2002, 2006) but in plants, chlorine atoms are predominantly found (Gribble, 2010, 2015; Misico et al., 2011; Chen et al., 2011; Dembitsky and Tolstikov, 2003).

Fluorinated fatty acids have been found in Australian and South African plants, which belonging to families *Dichapetalum* and Phyllanthaceae. The Australian plants *Acacia georginae* growing in Queensland also accumulated fluoroacetate up to 250–400 mg (Ward et al., 1964; Dembitsky and Srebnik, 2002). Bromine containing metabolites have been found in lichens (Řezanka and Guschina, 1999; Rezanka and Dembitsky, 1998, 1999). This is rather an exception to the rules.

Only a chlorine containing steroids were found in plants. Thus, the first chlorine-containing steroids, jaborosalactone C (**1**) and jaborosalactone E (**2**), were isolated from the leaves of the *Jaborosa integrifolia* plant (family Solanaceae) (Tschesche et al., 1968). The *Acnistus breviflorus* plant also produced steroids (**2**) and (**3**), which possess cytostatic activity. Steroids with similar structure, such as cytotoxic withanolide (**3**), were isolated from *Withania frutescens* (family Solanaceae) (Chen et al., 2011) and physalolactone C (**4**), which was found in the fruits of *Physalis peruviana* (Cape gooseberry) (Ali et al., 1984). Physalolactone (**5**) from the roots and a minor steroid of the leaves, 4-deoxyphysalolactone (**6**), were obtained from extract of *P. peruviana* (Frolow et al., 1981). Physaguline B (**7**) was discovered in *Physalis angulata* (Shingu et al., 1992). Withanolide D chlorohydrin (**8**) and (**5**) and (**9**) were discovered in *Withania somnifera* and *Acnistus breviflorus* (Nittala et al., 1981; Bessalle and Lavie, 1992), respectively. Further research showed that *Withania somnifera* generates withanolide C (**9**), (**5**) and (**10**). Steroids (**6**, **9** and **10**) were also present in *Dunalia tubulosa* (family Solanaceae) and related to the mentioned family (Kirson and Glotter, 1981). Steroids of a new structural type, jaborochlorodiol (**11**) and jaborochlorotriol (**12**), were discovered in the extracts from a flowering plant *Jaborosa magellanica* of the family Solanaceae (Punta Arenas, Chile) (Fajardo et al., 1991).

The aerial parts of *Tolpis proustii* and *T. lagopoda* (La Gomera, Canary Islands) led to the isolation of chlorinated sterols 30-chloro-3β-acetoxy-22α-hydroxyl-20(21)-taraxastene (**13**) and acetylated analogue (**14**). The *in vitro* antioxidant activities of the extracts were assessed by the DPPH and ABTS scavenging methods. The cytotoxicity of isolated compounds showed activity against the human myeloid leukaemia K-562 and K-562/ADR cell lines (Triana et al., 2012).

Withanolide Z (**15**) was isolated from *Withania somnifera* as inhibitor of topoisomerase I from parasite *Leishmania donovani* (Pramanick et al., 2008). Cytotoxic phyperunolides C (**16**) was found in leaves of *Physalis peruviana* (Lan et al., 2009; Dinan et al., 1997). Hsieh and co-authors (2007) isolated cytotoxic tubocapsenolide G (**17**) from *Tubocapsicum anomalum.* 14β-Hydroxywithanolide named physagulin I (**18**) has been isolated from *Physalis* species, and has an α-oxygenated function at position 15 (Nagafuji et al., 2004), and other 14β-hydroxywithanolide named jaborosalactol 23 (**19**) has been isolated from the flowering plant in the family Solanaceae, the nightshades, *Jaborosa bergii* (Nicotra et al., 2003).

Nicotra and co-authors (2006) reported the isomeric clorohydrin, jaborosalactone 37 (**20**) from *Jaborosa rotacea*, and jaborosalactone T (**21**) was isolated from *Jaborosa sativa* (synonym *Trechonaetes sativa*) collected in Argentina (Bonetto et al., 1995).

Anomanolide D (**22**) was identified as the 16α-hydroxy substituent from fruits of *Tubocapsicum anomalum* collected in Japan (Kiyota et al., 2007), and a 16,17-dihydroxylated withajardin, tubonolide A (**23**), was found in the same plant (Kiyota et al., 2008). Unusual 15,21-cyclowithanolides (norbornane type), jaborosalactols 21 (**24**) and 22 (**25**) were isolated from *Jaborosa bergii* (Glotter et al., 1977). An acid hydrolysate of a methanolic extract of *Tubocapsicum anomalum* contains TH-6 (**26**) (Shingu et al., 1990).

A group of spiranoid withanolides with a 17(20)-ene-22-keto system, jaborosalactones 3 (**28**) and 6 (**29**) were isolated from *Jaborosa runcinata* collected in Argentina (Cirigliano et al., 2002), and jaborosalactone 10 (**27**) was found in both *Jaborosa runcinata* and *Jaborosa odonelliana* (Cirigliano et al., 2005).

Two chlorinated 24,25-epoxy-γ-lactols (**30** and **31**) were

isolated from plants of *Jaborosa parviflora* (Garcia et al., 2009), and the clorohydrins jaborosalactone 42 (**32**) and jaborosalactone 49 (**33**) was isolated from *J. caulescens* var. *bipinnatifida* (Nicotra et al., 2007) and *J. laciniata* (Cirigliano et al., 2007).

A group of 13,14-seco-16,24-cycloergostane constituents named physalins (**34**, **35**, **36** and **37**) have been found in *Brachistus stramoniifolius, Margaranthus solanaceous* (sub nom. *Physalis solanaceous*), *Schraderanthus viscosus* (sub nom. *Saracha viscosa*) (Ripperger and Kamperdick, 1998; Makino et al., 1995; Kawai et al., 1996).

Two withanolides has a hemiketal bridge between what must have originally been ketone functions at C-12 and C-22, with six-membered ring with a β-oriented hydroxy group at C-12 and a spiroketal at C-22 upon formation of the D-lactone, both compounds (**38** and **39**) isolated from *Jaborosa rotacea* (Nicotra et al., 2006).

Structures of steroids are shown in Figs. 1 and 2, and the biological activities of plant chlorinated steroids are presented in Table 1.

Table 1. Biological activities of chlorinated plant steroids (**1**-**39**).

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
1	*Jaborosa integrifolia* (Tschesch et al., 1968) Not studied		Hepatic disorders treatment (0.940) Antieczematic (0.924) Macular degeneration treatment (0.921) Cytostatic (0.904) Antineoplastic (0.875) Immunosuppressant (0.810) Angiogenesis inhibitor (0.812) Antifungal (0.778) Apoptosis agonist (0.759) Antipruritic (0.709) Antiinflammatory (0.707) Antibacterial (0.694) Antipsoriatic (0.682) Alzheimer's disease treatment (0.659) Antihypercholesterolemic (0.621) Antioxidant (0.598)
2	*Jaborosa integrifolia* (Tschesche et al., 1968) *Acnistus breviflorus* (Chen et al., 2011) Cytostatic	Cytostatic (0.875)	Hepatic disorders treatment (0.933) Antieczematic (0.932) Macular degeneration treatment (0.926) Antineoplastic (0.869) Immunosuppressant (0.834) Antiasthmatic (0.819) Antifungal (0.811) Antipruritic (0.779) Antiallergic (0.776) Antiinflammatory (0.759) Alzheimer's disease treatment (0.744) Antipsoriatic (0.736) Apoptosis agonist (0.716) Antibacterial (0.681)
3	*Acnistus breviflorus* *Withania frutescens* (Chen et al., 2011) Cytostatic	Cytostatic (0.921)	Antieczematic (0.919) Macular degeneration treatment (0.912) Hepatic disorders treatment (0.908) Antineoplastic (0.850) Myocardial infarction treatment (0.843) Immunosuppressant (0.809) Antifungal (0.797) Alzheimer's disease treatment (0.736) Angiogenesis inhibitor (0.712) Antibacterial (0.681) Apoptosis agonist (0.672)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
4	*Physalis peruviana* (Ali et al., 1984) Not studied		Antidiabetic (0.938) Antieczematic (0.902) Myocardial infarction treatment (0.823) Lipoprotein disorders treatment (0.785) Antiinflammatory (0.778) Antineoplastic (0.779) Alzheimer's disease treatment (0.664) Antipruritic (0.651) Autoimmune disorders treatment (0.645) Immunosuppressant (0.644) Antifungal (0.603) Neurodegenerative diseases treatment (0.585) Apoptosis agonist (0.578)
5	*Physalis peruviana* (Frolow et al., 1981) *Withania somnifera* and *Acnistus breviflorus* (Nittala et al., 1981; Bessalle and Lavie, 1992) Not studied		Antidiabetic (0.981) Lipoprotein disorders treatment (0.938) Antieczematic (0.902) Myocardial infarction treatment (0.800) Antineoplastic (0.733) Antipruritic (0.697) Immunosuppressant (0.674) Alzheimer's disease treatment (0.666) Apoptosis agonist (0.633) Antifungal (0.599) Neurodegenerative diseases treatment (0.581) Antiinflammatory (0.557)
6	*Physalis peruviana* (Frolow et al., 1981) Not studied		Antidiabetic (0.980) Lipoprotein disorders treatment (0.939) Antieczematic (0.897) Myocardial infarction treatment (0.796) Alzheimer's disease treatment (0.696) Antineoplastic (0.698) Immunosuppressant (0.645) Antipruritic (0.640) Apoptosis agonist (0.605) Neurodegenerative diseases treatment (0.602) Antiinflammatory (0.539) Antiparkinsonian (0.510)
7	*Physalis angulata* (Shingu et al., 1992) Not studied		Antieczematic (0.910) Apoptosis agonist (0.888) Antineoplastic (0.860) Immunosuppressant (0.791) Antipruritic (0.769) Antiinflammatory (0.734) Antifungal (0.711) Cytostatic (0.643) Hepatoprotectant (0.626) Antibacterial (0.615) Antiasthmatic (0.594)
8	*Withania somnifera* *Acnistus breviflorus* (Nittala et al., 1981; Bessalle and Lavie, 1992) Not studied		Antieczematic (0.926) Neurodegenerative diseases treatment (0.883) Alzheimer's disease treatment (0.863) Myocardial infarction treatment (0.854) Antipruritic (0.758) Antiparkinsonian (0.756)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
			Antineoplastic (0.733) Antiinflammatory (0.722) Immunosuppressant (0.699) Antidiabetic (0.690) Antifungal (0.687) Antibacterial (0.658) Hepatoprotectant (0.642)
9	*Withania somnifera* *Acnistus breviflorus* (Nittala et al., 1981; Bessalle and Lavie, 1992) *Dunalia tubulosa* (Kirson and Glotter, 1981) Not studied		Lipoprotein disorders treatment (0.968) Antidiabetic (0.953) Antieczematic (0.912) Antipruritic (0.800) Antiinflammatory (0.770) Immunosuppressant (0.751) Antineoplastic (0.757) Apoptosis agonist (0.673) Alzheimer's disease treatment (0.670) Antifungal (0.654) Cardiotonic (0.634) Antiasthmatic (0.608)
10	*Dunalia tubulosa* (Kirson and Glotter, 1981) *Jaborosa magellanica* (Fajardo et al., 1991) Not studied		Antieczematic (0.930) Myocardial infarction treatment (0.872) Antineoplastic (0.866) Cytostatic (0.819) Hepatoprotectant (0.803) Immunosuppressant (0.789) Antipruritic (0.770) Antifungal (0.753) Macular degeneration treatment (0.711) Apoptosis agonist (0.709) Respiratory analeptic (0.643) Antipsoriatic (0.641) Antibacterial (0.633)
11	*Jaborosa magellanica* (Fajardo et al., 1991) Not studied		Antieczematic (0.823) Antineoplastic (0.785) Antiinflammatory (0.731) Allergic conjunctivitis treatment (0.629) Antipruritic (0.624) Immunosuppressant (0.592) Antifungal (0.555) Apoptosis agonist (0.503)
12	*Jaborosa magellanica* (Fajardo et al., 1991) Not studied		Myocardial infarction treatment (0.825) Antieczematic (0.815) Antineoplastic (0.707) Immunosuppressant (0.634) Allergic conjunctivitis treatment (0.618) Antipruritic (0.575) Antifungal (0.555) Antiinflammatory (0.551)
13	*Tolpis proustii* *T. lagopoda* (Triana et al., 2012) Antioxidant	Antineoplastic (0.918) Antineoplastic (myeloid leukemia) (0.520) Anticarcinogenic (0.515) Antineoplastic (pancreatic cancer) (0.503)	Antiseborrheic (0.799) Apoptosis agonist (0.793) Hepatoprotectant (0.780) Respiratory analeptic (0.757) Antisecretoric (0.755) Antiinflammatory (0.733)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
	Anticancer		Immunosuppressant (0.704) Lipid metabolism regulator (0.677) Atherosclerosis treatment (0.672) Antifungal (0.641) Antipruritic (0.640) Antiviral (Influenza) (0.606)
14	*Tolpis proustii* *T. lagopoda* (Triana et al., 2012)	Antineoplastic (0.892) Antimetastatic (0.551)	Apoptosis agonist (0.796) Antiseborrheic (0.770) Hepatoprotectant (0.739) Antiinflammatory (0.726) Antisecretoric (0.717)
	Antioxidant Anticancer		Immunosuppressant (0.713) Hepatic disorders treatment (0.701) Respiratory analeptic (0.663) Dermatologic (0.614) Lipid metabolism regulator (0.608)
15	*Withania somnifera* inhibitor of topoisomerase I (Pramanick et al., 2008)	Cytostatic (0.863) Antineoplastic (0.826)	Antieczematic (0.929) Cytostatic (0.863) Macular degeneration treatment (0.856) Hepatic disorders treatment (0.837) Antineoplastic (0.826) Immunosuppressant (0.816) Apoptosis agonist (0.797) Antipruritic (0.782) Alzheimer's disease treatment (0.729) Antifungal (0.716) Antipsoriatic (0.686) Antibacterial (0.613)
16	*Physalis peruviana* (Lan et al., 2009; Dinan et al., 1997)	Antineoplastic (0.765)	Lipoprotein disorders treatment (0.952) Antidiabetic (0.943) Antieczematic (0.904) Antineoplastic (0.765)
	Cytotoxic		Antipruritic (0.761) Antiinflammatory (0.746) Immunosuppressant (0.733) Antileukemic (0.651) Antifungal (0.643) Alzheimer’s disease treatment (0.619) Cardiotonic (0.598) Antiasthmatic (0.593) Apoptosis agonist (0.592) Spasmolytic. Urinary (0.578) Antiallergic (0.552)
17	*Tubocapsicum anomalum* (Hsieh et al., 2007)	Antineoplastic (0.833) Apoptosis agonist (0.768) Cytostatic (0.737)	Insulin promoter (0.986) Antieczematic (0.910) Myocardial infarction treatment (0.868)
	Cytotoxic		Antineoplastic (0.833) Apoptosis agonist (0.768) Cytostatic (0.737) Immunosuppressant (0.736) Antipruritic (0.681) Antifungal (0.670) Hepatoprotectant (0.664) Antiinflammatory (0.621)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
			Antipsoriatic (0.582) Antidiabetic (type 2) (0.569) Antileukemic (0.540) Antimetastatic (0.539) Antibacterial (0.535)
18	*Physalis angulata* (Nagafuji et al., 2004) Not studied		Antieczematic (0.914) Antineoplastic (0.854) Antiinflammatory (0.819) Immunosuppressant (0.817) Antifungal (0.795) Antipruritic (0.791) Apoptosis agonist (0.786) Antiparasitic (0.756) Cytostatic (0.722) Antiasthmatic (0.720) Antiallergic (0.657) Antibacterial (0.645) Antiprotozoal (0.632) Hepatoprotectant (0.620) Antipsoriatic (0.612)
19	*Jaborosa bergii* (Nicotra et al., 2003) Not studied		Antineoplastic (0.914) Antiasthmatic (0.834) Antiallergic (0.828) Apoptosis agonist (0.823) Immunosuppressant (0.782) Antiinflammatory (0.723) Antipruritic (0.710) Cardiotonic (0.686) Antifungal (0.656) Hepatoprotectant (0.550) Antipsoriatic (0.649) Respiratory analeptic (0.539) Antidiabetic (0.527)
20	*Jaborosa roracea* (Abe et al., 2006) Not studied		Apoptosis agonist (0.806) Antineoplastic (0.803) Immunosuppressant (0.786) Antiinflammatory (0.783) Antipruritic (0.759) Genital warts treatment (0.724) Antieczematic (0.718) Antiprotozoal (Plasmodium) (0.658) Antifungal (0.649) Cytostatic (0.534) Antiallergic (0.526) Antiasthmatic (0.525)
21	*Jaborosa sativa* (syn. *Trechonaetes sativa*) (Bonetto et al., 1995) Not studied		Insulin promoter (0.981) Myocardial infarction treatment (0.819) Antineoplastic (0.797) Antiprotozoal (Plasmodium) (0.786) Apoptosis agonist (0.695) Immunosuppressant (0.688) Genital warts treatment (0.630) Antiinflammatory (0.530)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
22	*Tubocapsicum anomalum* (Kiyota et al., 2007) Not studied		Insulin promoter (0.986) Myocardial infarction treatment (0.899) Antineoplastic (0.866) Apoptosis agonist (0.772) Cytostatic (0.743) Respiratory analeptic (0.712) Antiinflammatory (0.671) Antifungal (0.643) Immunosuppressant (0.597) Antidiabetic (type 2) (0.564) Antibacterial (0.519) Antimetastatic (0.506)
23	*Tubocapsicum anomalum* (Kiyota et al., 2008) Not studied		Insulin promoter (0.986) Myocardial infarction treatment (0.899) Antineoplastic (0.839) Antiinflammatory (0.714) Respiratory analeptic (0.712) Apoptosis agonist (0.696) Antifungal (0.645) Immunosuppressant (0.644) Cytostatic (0.581) Hepatoprotectant (0.568) Antidiabetic (type 2) (0.564) Stroke treatment (0.549) Prostate disorders treatment (0.548) Antihypercholesterolemic (0.536)
24	*Jaborosa bergii* (Glotter et al., 1977) Not studied		Antineoplastic (0.875) Antiasthmatic (0.816) Apoptosis agonist (0.795) Inflammatory Bowel disease treatment (0.790) Immunosuppressant (0.761) Antiinflammatory (0.694) Antieczematic atopic (0.667) Antipsoriatic (0.638(Rheumatoid arthritis treatment (0.552) Antiallergic (0.533)
25	*Jaborosa bergii* (Glotter et al., 1977) Not studied		Antineoplastic (0.885) Apoptosis agonist (0.824) Immunosuppressant (0.725) Cardiotonic (0.698) Antiinflammatory (0.685) Antifungal (0.599) Antipsoriatic (0.595) Spasmolytic. urinary (0.555) Antiallergic (0.539) Antiasthmatic (0.517) Antimetastatic (0.513)
26	*Tubocapsicum anomalum* (Shingu et al., 1990) Not studied		Antineoplastic (0.806) Myocardial infarction treatment (0.781) Antifungal (0.742) Apoptosis agonist (0.634) Immunosuppressant (0.630) Hypolipemic (0.599) Antiinfertility. female (0.570)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
			Antidiabetic (type 2) (0.561) Antibacterial (0.537) Antiprotozoal (0.528) Prostate disorders treatment (0.527)
27	*Jaborosa runcinata* *Jaborosa odonelliana* (Cirigliano et al., 2005) Not studied		Hepatic disorders treatment (0.934) Antiinflammatory (0.781) Antipruritic (0.749) Antineoplastic (0.708) Immunosuppressant (0.691) Antieczematic (0.636) Antiallergic (0.618) Antiasthmatic (0.571) Allergic conjunctivitis treatment (0.543) Antibacterial (0.538) Antiseborrheic (0.513) Menopausal disorders treatment (0.511) Antifungal (0.509)
28	*Jaborosa runcinata* (Cirigliano et al., 2002) Not studied		Hepatic disorders treatment (0.942) Antineoplastic (0.782) Antiinflammatory (0.768) Antiallergic (0.758) Antipruritic (0.755) Antiasthmatic (0.728) Immunosuppressant (0.704) Antieczematic (0.597) Antifungal (0.586) Antiseborrheic (0.570) Apoptosis agonist (0.544) Prostate disorders treatment (0.541) Menopausal disorders treatment (0.534) Hypolipemic (0.534)
29	*Jaborosa runcinata* (Cirigliano et al., 2002) Not studied		Hepatic disorders treatment (0.930) Antineoplastic (0.753) Antiinflammatory (0.727) Antiasthmatic (0.723) Immunosuppressant (0.717) Antiallergic (0.711) Antipruritic (0.689) Allergic conjunctivitis treatment (0.597) Antieczematic (0.591) Antifungal (0.559) Cytoprotectant (0.524) Prostate disorders treatment (0.519)
30	*Jaborosa parviflora* (Garcia et al., 2009) Not studied		Antineoplastic (0.888) Antiinflammatory (0.815) Immunosuppressant (0.788) Antieczematic (0.785) Apoptosis agonist (0.761) Antipruritic (0.681) Antifungal (0.629) Antiallergic (0.617) Antileukemic (0.609) Antiasthmatic (0.602) Antipsoriatic (0.536) Antibacterial (0.535)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
31	*Jaborosa parviflora* (Garcia et al., 2009) Not studied		Antineoplastic (0.907) Antiinflammatory (0.824) Antieczematic (0.786) Immunosuppressant (0.779) Antipruritic (0.722) Apoptosis agonist (0.673) Antifungal (0.597) Antileukemic (0.594) Antiallergic (0.578) Allergic conjunctivitis treatment (0.572) Antiasthmatic (0.564) Antipsoriatic (0.543)
32	*Jaborosa caulescens* var. *bipinnatifida* (Machin et al., 2010) *Jaborosa laciniata* (Cirigliano et al., 2007) Not studied		Antieczematic (0.850) Antipruritic (0.787) Antiinflammatory (0.778) Antineoplastic (0.765) Immunosuppressant (0.745) Antifungal (0.683) Allergic conjunctivitis treatment (0.649) Antiasthmatic (0.644) Antiallergic (0.641) Apoptosis agonist (0.570) Antibacterial (0.529)
33	*Jaborosa caulescens* var. *bipinnatifida* (Machin et al., 2010) *Jaborosa laciniata* (Cirigliano et al., 2007) Not studied		Antieczematic (0.850) Antipruritic (0.787) Antiinflammatory (0.778) Antineoplastic (0.765) Immunosuppressant (0.745) Antifungal (0.683) Allergic conjunctivitis treatment (0.649) Antiasthmatic (0.644) Antiallergic (0.641) Apoptosis agonist (0.570) Antibacterial (0.529)
34	*Margaranthus solanaceous* *Schraderanthus viscosus* (Makino et al., 1995; Kawai et al., 1996) Not studied		Antiprotozoal (0.956) Genital warts treatment (0.824) Antiinflammatory (0.801) Antineoplastic (0.761) Immunosuppressant (0.693) Antipruritic (0.579) Antiasthmatic (0.554) Antimetastatic (0.530) Apoptosis agonist (0.524) Antiallergic (0.507)
35	*Brachistus stramoniifolius* *Margaranthus solanaceous* *Schraderanthus viscosus* (Ripperger and Kamperdick, 1998) (Kawai et al., 1996) Not studied		Antiprotozoal (0.954) Genital warts treatment (0.805) Antineoplastic (0.759) Antiinflammatory (0.731) Immunosuppressant (0.677) Apoptosis agonist (0.540) Antibacterial (0.526) Antimetastatic (0.501)

No.	Plant name, Reference activity reviewed	Activities confirmed (Pa)	Predicted activities (Pa)*
36	*Brachistus stramoniifolius* (Ripperger and Kamperdick, 1998) Not studied		Antiprotozoal (0.958) Antiprotozoal (Plasmodium) (0.953) Genital warts treatment (0.798) Antineoplastic (0.766) Antiinflammatory (0.688) Immunosuppressant (0.593)
37	*Brachistus stramoniifolius* *Margaranthus solanaceous* *Schraderanthus viscosus* (Ripperger and Kamperdick, 1998) (Kawai et al., 1996) Not studied		Insulin promoter (0.984) Cytostatic (0.907) Antieczematic (0.907) Hepatoprotectant (0.875) Myocardial infarction treatment (0.861) Antineoplastic (0.848) Immunosuppressant (0.803) Respiratory analeptic (0.796) Antipruritic (0.756) Antifungal (0.752) Apoptosis agonist (0.729) Antihypercholesterolemic (0.725) Antiinflammatory (0.707) Antibacterial (0.630) Antiparasitic (0.626) Alzheimer's disease treatment (0.580) Antidiabetic (type 2) (0.570)
38	*Jaborosa rotacea* (Nicotra et al., 2006) Not studied		Insulin promoter (0.982) Cytostatic (0.921) Antieczematic (0.919) Macular degeneration treatment (0.912) Hepatic disorders treatment (0.908) Antineoplastic (0.850) Myocardial infarction treatment (0.843) Immunosuppressant (0.809) Antifungal (0.797) Alzheimer's disease treatment (0.736) Angiogenesis inhibitor (0.712) Antibacterial (0.681) Apoptosis agonist (0.672) Antipruritic (0.664) Antipsoriatic (0.663)
39	*Jaborosa rotacea* (Nicotra et al., 2006) Not studied		Antieczematic (0.922) Macular degeneration treatment (0.913) Hepatoprotectant (0.903) Antineoplastic (0.868) Cytostatic (0.866) Immunosuppressant (0.855) Antifungal (0.829) Antiasthmatic (0.799) Antipruritic (0.794) Antiinflammatory (0.776) Antiallergic (0.770) Apoptosis agonist (0.740) Antipsoriatic (0.720) Antibacterial (0.716) Alzheimer's disease treatment (0.687) Antioxidant (0.620)

* Only activities with Pa > 0.5 are shown.

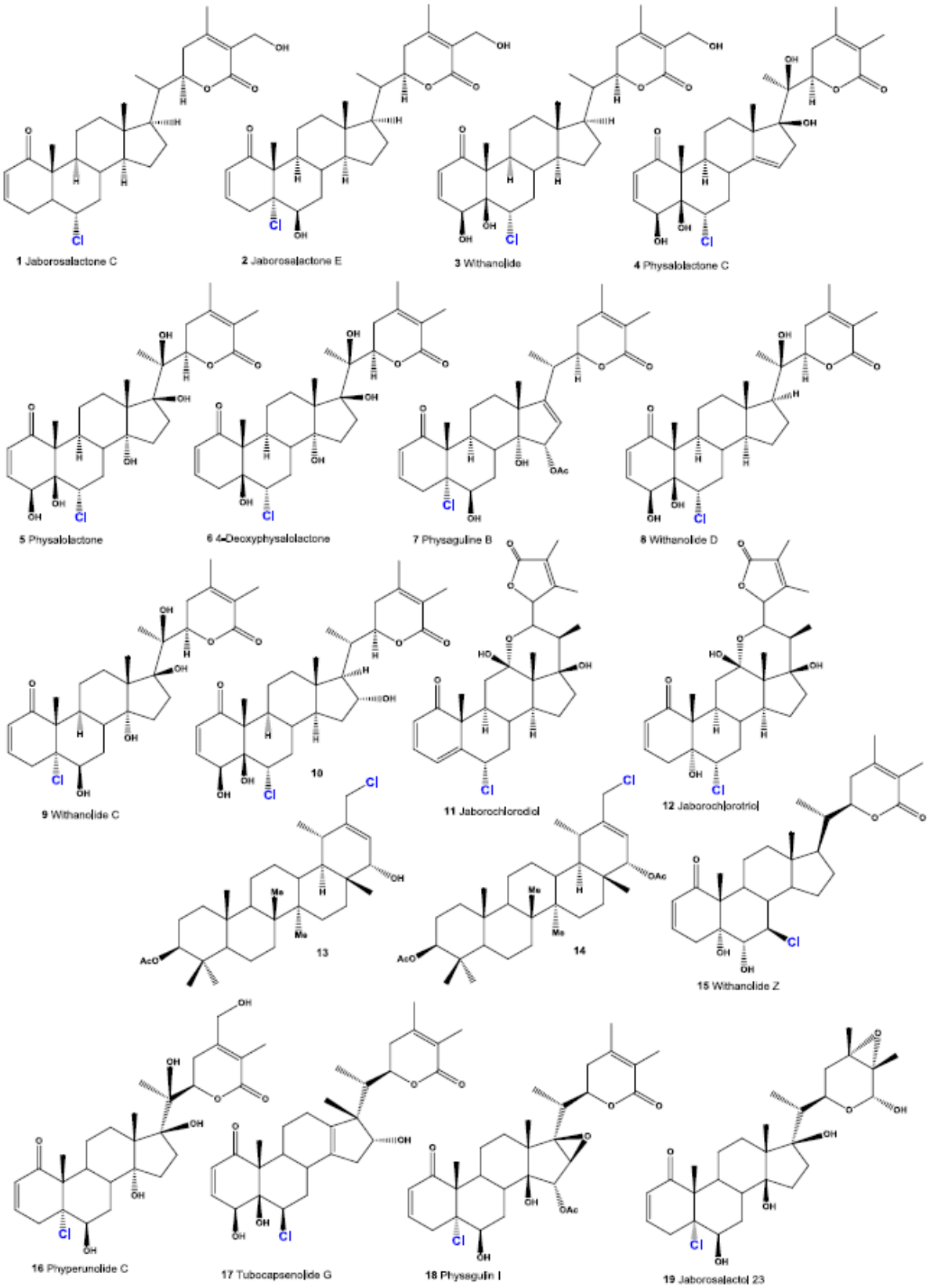

Fig. 1: Bioactive chlorinated plant steroids (**1-19**).

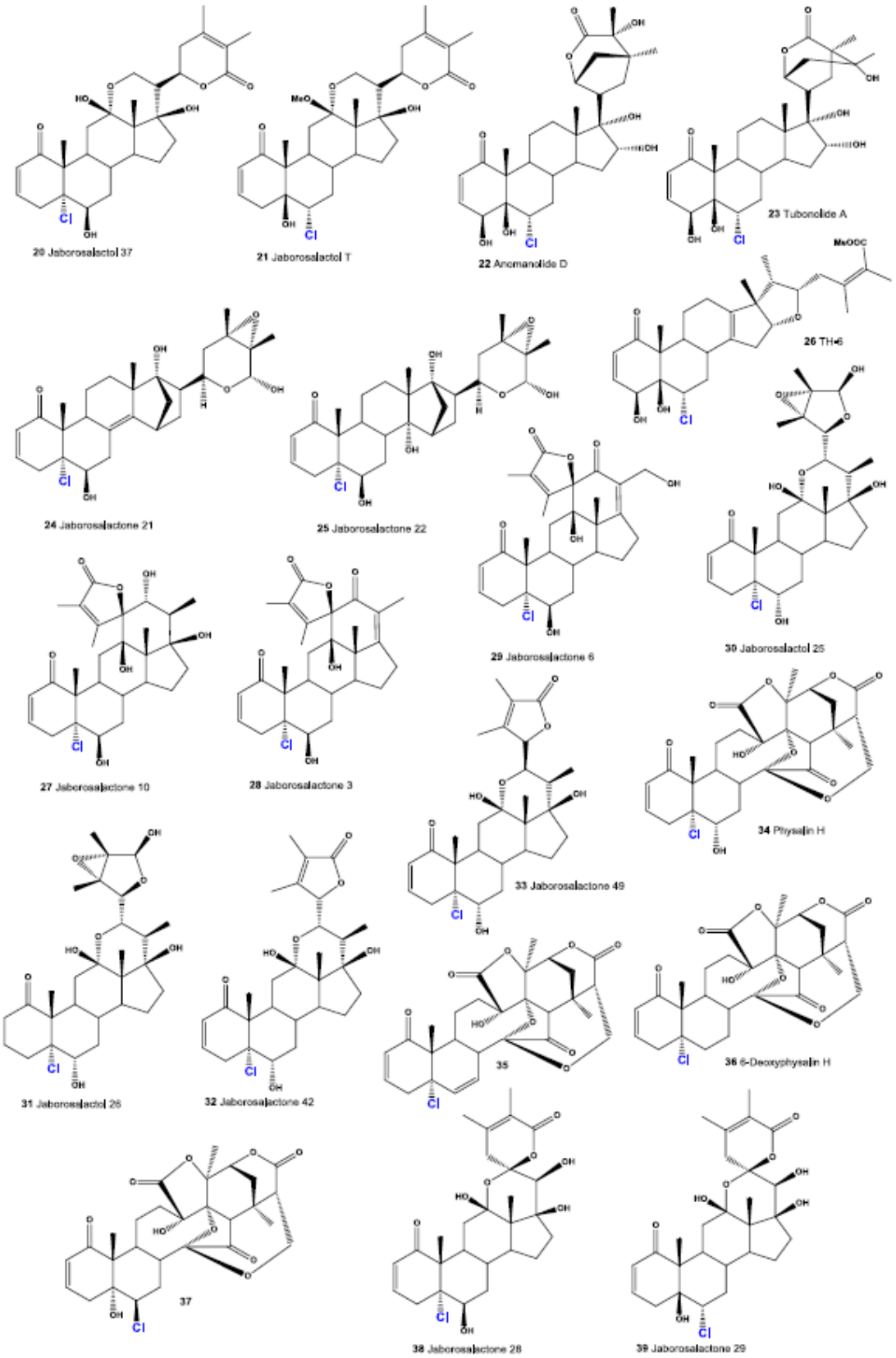

Fig. 2: Bioactive chlorinated plant steroids (**20**-**39**).

Conclusion

In this review, we present structures and distribution in plant kingdom of chlorinated steroids. Biological activity for these steroids is presented in this paper. The most characteristic biological activities for chlorinated steroids were cytostatic, antineoplastic, anti-eczematic, antidiabetic, antibacterial, and other activities.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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