



Chemical Biodiversity and Bioactivities of Saponins in Echinodermata with an Emphasis on Sea Cucumbers (Holothuroidea)

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Abstract

Echinoderms are a source of a broad range of secondary metabolites with a large variety of bioactive properties. Although pigment and lipid derivatives are the major groups of bioactive compounds found in crinoids and ophiuroids, saponins represent the most abundant and diverse marine natural products (MNPs) in the phylum Echinodermata. This review is for researchers that are interested in MNPs derived from echinoderms, but with a particular focus on the structural diversity and biological function of saponins. Among the echinoderms, these steroidal compounds are mostly known for and structurally most diverse within sea cucumbers. Through compilation of extensive tables, this review provides a reference book, summarizing not only the major chemical classes of well-known secondary metabolites in the phylum Echinodermata but also further focusing on the presence of bioactive saponins in echinoderms in general and within different sea cucumber species in particular. The final compilation aims to correlate the vast structural diversity of saponins with known biological functions. The here presented data revealed that holothurians, holotoxins, cucumariosides, and echinosids are not only the most abundant saponin compounds in various genera of sea cucumbers but that these saponins can also be used as potential chemotaxonomic markers for different sea cucumber

species. By studying the structure-function relationships of triterpene glycosides in echinoderms in general, or in particular within holothurians, the vast structural diversity, taxonomic distribution, and bioactivity of the molecules can be deciphered, which provides an opportunity to focus future research efforts on target species that contain MNPs with novel pharmacological activities.

Keywords

Secondary metabolites · Chemical diversity · Taxonomic markers · Structure-function analysis · Saponins · Echinoderms · Sea cucumber

7.1 Marine Natural Products (MNPs)

Compared to synthesized organic compounds, natural products (NPs) have long been used as efficient and often less harmful sources of drug molecules (Molinski et al. 2009). NPs refer to both primary and secondary metabolites; however, in the past, research on secondary metabolites mostly described ecological interactions of organisms with their environment, the pronounced biological and pharmacological activities, their great chemical diversity, and their higher tendency to interact with other biologically relevant molecules (Croteau et al. 2000).

The marine environment came into the focus of NPs right after technologies for studying marine ecosystems improved. Since the early 1900s, the idea of utilizing marine ecosystems as the potentially largest source for marine natural products (hereafter MNPs) was shaped. Although research on MNPs dates back more than 50 years and more than 32,000 studies related to MNPs have been published (MarineLit; <http://pubs.rsc.org/marinlit/>), only a few marine-derived compounds resulted in clinical trials (Mayer et al. 2017). That is, from 52 marine invertebrate-derived compounds that reached clinical trials, only seven compounds, isolated from sponges, mollusks, tunicates, and their associated bacteria, have so far

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been approved. Unfortunately, 45 of the total 52 MNPs have been discontinued from clinical trials (Fig. 7.1) due to low production yields and/or high costs.

In this review, we provide an overview on the MNPs reported from echinoderms with an emphasis on MNPs (i.e., particularly triterpene glycosides) reported from shallow water sea cucumbers. While there is extensive literature on the chemistry of MNPs from sessile marine organisms such as sponges, ascidians, and corals, MNP data on slow-moving invertebrates such as echinoderms are much more limited. Up to now, more than 7,000 living echinoderms species, divided into three sub-phyla and five different classes, have been described (Fig. 7.2). The evolutionary divergence of echinoderms with chordates rather than invertebrates makes their biochemistry and physiology rather similar with vertebrates. They can synthesize vertebrate-type steroids, which regulate their reproductive, growth, and developmental processes (Schoenmakers 1979). Therefore, it can be hypothesized that echinoderms can be promising substitution candidates of the synthetic compounds for producing efficient secondary metabolites helpful for human health. Although several defense mechanisms such as presence of spine, cuvierian tubules (CTs), evisceration, toxic secretion, and unpalatability are generally described for echinoderms and particularly for holothurians, they do not have a significant escape behavior and therefore likely depend on chemical defense strategies, such as triterpene glycosides, to protect themselves against predators (Iyengar and Harvell 2001; Bahrami et al. 2016). Saponins represent a diverse group of

triterpene glycosides that have been mainly described from plants and are also one of the major secondary metabolite classes in Echinodermata including holothurians. Saponins are promising MNPs with the capacity to influence physiological and immunological processes and thus have been implicated as bioactive compounds in many ecological studies (Kalinin et al. 1996; Francis et al. 2002). In the following sections, we will discuss in more detail the role of saponins and other bioactive compounds in echinoderms in general, however, with a major focus on sea cucumbers.

7.2 MNPs in Echinoderms

From 28,609 MNPs that have been reported until 2016, more than 35% of the total compounds were isolated from echinoderms. However, the reported chemical diversity of MNPs from echinoderms, compared to other phyla, was not high (Blunt et al. 2018).

Typical reported MNPs derived from echinoderms are sulfated compounds that can be largely classified into two major groups: aromatics and saponins. Among the five classes of echinoderms (Fig. 7.2), aromatic sulfated compounds have only been reported in crinoids and ophiuroids as pigments derived from anthraquinones or naphthoquinones, whereas most of the saponins have been isolated from asteroids, echinoids, and holothuroids (Kornprobst et al. 1998) (Tables 7.1 and 7.2). Among various types of secondary metabolites that have been isolated

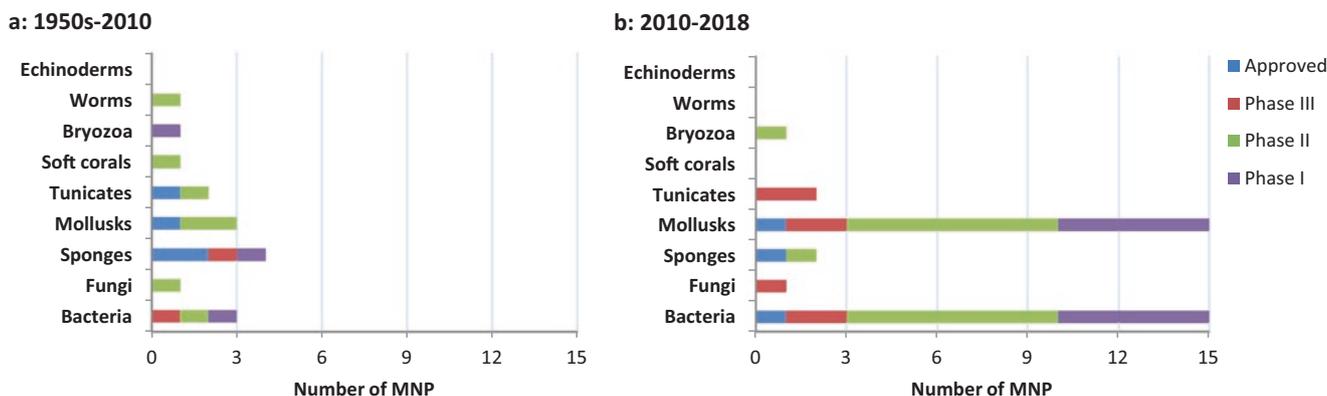


Fig. 7.1 Overview of marine organisms from which MNPs entered the pharmaceutical pipeline (a) from 1950s to 2010 and (b) from 2010 to 2018. (Compiled with data from Mayer and Hamann 2002; Mayer et al. 2017; <http://marinepharmacology.midwestern.edu>)

Fig. 7.2 Phylogenetic tree for the phylum Echinodermata (modified after Telford et al. 2014)

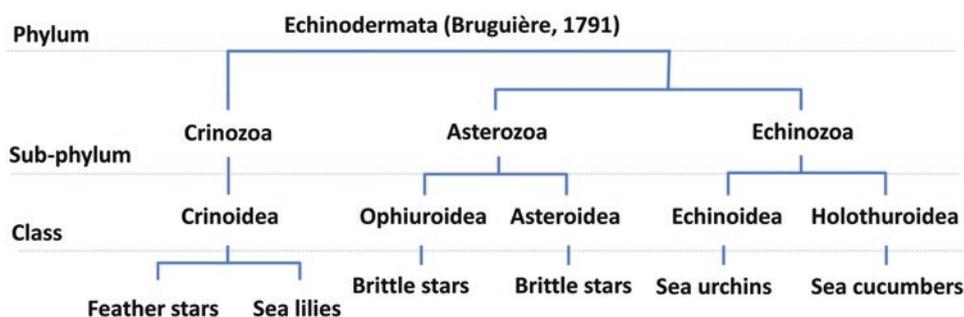


Table 7.1 Classes of echinoderms, major classes of secondary metabolites, examples of compounds, their bioactivity, and example species for which the compounds have been reported

	Major classes of secondary metabolites	Examples of bioactive compounds	Biological activity	Example of organisms	References
Crinoids: Lipids, pigments, polyketides	Polyketides	Rhodoptilometrins, crinemodin	Antipredatory	* <i>Comanthus bennetti</i>	Rideout et al. (1979)
	Lipids	Ganglioside, cerebrosides	n.d.	* <i>Comanthina schlegelii</i>	Inagaki et al. (2007)
	Naphthopyrones	Naphthopyrones comaparvin	Anti-inflammatory	<i>Comanthus parvicirrus</i>	Karin et al. (2004), Folmer et al. (2009), Chovolou et al. (2011), and Chen et al. (2014)
	Anthraquinoid pigments	Gymnochrome D	Antiviral	* <i>Gymnocrinus richeri</i>	Laille et al. (1998)
Asteroids: Steroidal derivatives of cholesterol, fatty acids, ceramides, and few alkaloids and proteins	Lipids	Hexadecanoic acid	Antifouling	<i>Linckia laevigata</i>	Guenther et al. (2009)
	Lipids	Sphingolipids	n.d.	<i>Ophidiaster ophidianus</i>	Jin et al. (1994)
	Asterosaponins	Thornasteroside A	Antitumor	<i>Asteropsis carinifera</i>	Malyarenko et al. (2012)
	Fatty acids	Eicosanoic acid	n.d.	<i>Culcita novaeguineae</i>	Bruno et al. (1992) and Inagaki (2008)
	Protein	Ciguatoxins	n.d.	<i>Marthasterias glacialis</i>	Silva et al. (2015)
	Polyhydroxysteroids	Laeviusculosides	Hemolytic, cytotoxic activity	<i>Henricia leviuscula</i>	Ivanchina et al. (2006) and Fedorov et al. (2008)
Ophiuroids: Carotenoids, gangliosides, brominated indoles, phenyl propanoids, terpenes, steroids	Steroidal glycosides	Steroidal glycosides	Antiviral	<i>Ophiarachna incrassata</i>	D'Auria et al. (1993)
	Steroidal compound	Polyhydroxysterols	Antiviral	<i>Astrotoma agassizii</i>	Comin et al. (1999)
	Terpene	2,3-Dimethyl butenolide	Antitumor	<i>Ophiomastix mixta</i>	Lee et al. (2007)
	Carotenoid	Ophioxanthin	Antioxidant	<i>Ophioderma longicauda</i>	D'Auria et al. (1985)
Echinoids: Protein, polysaccharides, lipid, pigments	Naphthoquinoid pigment	Echinochrome A	Antioxidant, antimicrobial, anti-inflammatory, antitoxic agents	* <i>Anthocidaris crassispira</i>	Berdyshev et al. (2007) and Jeong et al. (2014)
	Peptides	Strongylostatin	Anticancer	<i>Strongylocentrotus droebachiensis</i>	Pettit et al. (1981)
		Strongylocins	Antimicrobial	<i>Strongylocentrotus droebachiensis</i>	Li et al. (2008)
	Polysaccharide	Sulfated fucan	Anticoagulant	<i>Lytechinus variegatus</i>	Pereira et al. (1999)
	Steroidal compounds	n.d.	Anticancer	<i>Diadema savignyi</i>	Thao et al. (2015a)
Ganglioside	DSG-A	Neuritogenic	<i>Diadema setosum</i>	Yamada et al. (2008)	

(continued)

Table 7.1 (continued)

	Major classes of secondary metabolites	Examples of bioactive compounds	Biological activity	Example of organisms	References
Holothuroids: Triterpene glycosides, peptides, polysaccharides, lipids	Triterpene glycoside	Holothurins (A–B)	Antifungal, anticancer, ichthyotoxic	<i>Holothuria atra</i> , <i>Holothuria fuscocinerea</i>	Yamanouchi (1955), Kobayashi et al. (1991), Popov et al. (1994), and Zhang et al. (2006d)
	Triterpene glycoside	Echinoid A	Antifungal	<i>Actinopyga echinites</i>	Kitagawa et al. (1985)
	Triterpene glycoside	Holotoxin A–F	Anticancer, antifungal, antiprotozoa	<i>Apostichopus japonicus</i>	Kitagawa et al. (1976), Anisimov et al. (1983), Maltsev et al. (1985), and Wang et al. (2012)
	Triterpene glycosides	Holotoxin	Antifungal	<i>S. japonicus</i>	Yano et al. (2013)
	Polysaccharides	Glucosamine, Galactosamine	Antihyperlipidemic, antioxidant	<i>A. japonicus</i>	Liu et al. (2012)
	Sulfated polysaccharides	FucCS, GAGs	Anticoagulant, antithrombin, antiparasitic	<i>Ludwigothurea grisea</i>	Mourão et al. (1998), Borsig et al. (2007), and Marques et al. (2016)
	Sulfated polysaccharides	FucCS	Anticoagulant, antithrombin, antihyperglycemic, antiviral, insulin-sensitizing	<i>Thelethota ananas</i> , <i>Cucumaria frondosa</i>	Borsig et al. (2007), Huang et al. (2013), and Hu et al. (2014a)
	Sulfated polysaccharides	FucCS	Anticoagulant, antiparasitic	<i>Isostichopus badionotus</i>	Marques et al. (2016)
	Sulfated polysaccharides	GAGs	Antihyperlipidemic	* <i>Metriatyla scabra</i>	Liu et al. (2002)
	Fatty acid	EPA-enriched PL, 12-MTA, ODAs	Antioxidant, antihyperglycemic, anticancer, antihyperlipidemic	<i>C. frondosa</i> , <i>Stichopus japonicus</i>	Yang et al. (2003), Nguyen et al. (2011), Hu et al. (2014b), Wu et al. (2014), and Ku et al. (2015)
	Lipid	Cerebrosides, galactocerebrosides, AMC-2	Anticancer, antihyperlipidemic	* <i>Stichopus variegatus</i> , <i>Acaudina molpadioides</i> , <i>Bohadschia argus</i>	Sugawara et al. (2006), Ikeda et al. (2009), Zhang et al. (2012), and Du et al. (2015)
	Sphingolipid	Cerebroside	Antioxidant	<i>S. japonicus</i> , <i>Acaudina molpadioides</i>	Duan et al. (2016) and Xu et al. (2011)
	Lysophospholipid	LPC, L-PAF	Anti-inflammatory	<i>Holothuria atra</i>	Nishikawa et al. (2015)
	Peptide	Phenoloxidase, lysozyme	Antimicrobial	<i>C. frondosa</i>	Beauregard et al. (2001)
	Peptide	ACE inhibitory peptide	Antihypertension	<i>Acaudina molpadioides</i>	Zhao et al. (2009)
Peptide	T-antigen-binding lectin	Antibacterial	<i>Holothuria scabra</i>	Gowda et al. (2008)	
Phenolic compounds	n.d.	Anti-inflammatory	<i>S. japonicus</i>	Song et al. (2016)	

(continued)

Table 7.1 (continued)

	Major classes of secondary metabolites	Examples of bioactive compounds	Biological activity	Example of organisms	References
	Phenolic compounds	(Z)2,3-DPAN	Anticancer	<i>Holothuria parva</i>	Amidi et al. (2017)
	Pigments	Carotenoids	Antioxidant	<i>Holothuria atra</i>	Esmat et al. (2013)
	Pigments	β -carotene, echinenone, canthaxanthin, etc.	Antioxidant	<i>Plesiocolochirus minaeus</i>	Maoka et al. (2015)
	Sulfated alkene	2,6-DMHS, OS, DS	Antibacterial, antifungal	<i>A. japonicus</i>	La et al. (2012)
	Mucopolysaccharide	SJAMP	Antitumor, immunomodulatory effect	<i>S. japonicus</i>	Song et al. (2013)
	Glycolipid/Sphingolipid	2,6-DMHS, OS, DS	Anticancer	<i>A. japonicus</i>	La et al. (2012)
	Saponin	Frondanol A ₅	Anticancer	<i>C. frondosa</i>	Janakiram et al. (2010) and Jia et al. (2016)
	Saponin	n.d.	Antihyperlipidemic	<i>Pearsonothuria graeffei</i>	Hu et al. (2010) and Wu et al. (2015)
	Monosulfated triterpene glycosides	Cumaside	Radioprotective	<i>Cucumaria japonica</i>	Aminin et al. (2011)

n.d. not defined, *EPA-enriched PL* eicosapentaenoic acid-enriched phospholipids, *FucCS* fucosylated chondroitin sulfate, *GAGs* glycosaminoglycan, *2,6-DMHS* 2,6-dimethylheptyl sulfate, *OS* octyl sulfate, *DS* decyl sulfate, *ACE* angiotensin I-converting enzyme, *LPC* lysophosphatidylcholine, *L-PAF* lyso-platelet activating factor, *SCEA-F* ethyl acetate solvent fraction of sea cucumber, *EPA-enriched PC* eicosapentaenoic acid-enriched phosphatidylcholine lipids, *12-MTA* 12-methyltetradecanoic acid, *(Z)2,3-DPAN* (Z)-2,3-diphenylacrylonitrile, *SJAMP* *stichopus japonicus* acid mucopolysaccharide, *ODAs* 7(Z) octadecenoic acid, and 7(Z),10(Z)-octadecadienoic acid

*Based on WoRMS (2019), the accepted names changed from: *Metriatyla scabra* to *Holothuria scabra*; *Comanthus bennetti* to *Anneissia bennetti*; *Comanthina schlegelii* to *Comaster schlegelii*; *Gymnocrinus richeri* to *Neogymnocrinus richeri*; *Anthocidaris crassispina* to *Heliocidaris crassispina*; *Stichopus variegatus* to *Stichopus horrens*

from echinoderms, saponins are the most abundant. Compounds were derived from mainly two classes (i.e., Asteroidea and Holothuroidea) (Haug et al. 2002), which will be discussed in more detail in Sect. 7.3.

7.2.1 Crinoids (Feather Stars and Sea Lilies)

The most primitive form of current echinoderms are the crinoids (Karleskint et al. 2010). Sea lilies are, unlike feather stars, sessile and are found mainly in depths >100 m, whereas feather stars inhabit coral reefs from the intertidal to the deep-sea oceans. Moreover, feather stars are physically able to escape from predators by crawling, swimming, or hiding between corals or rocks (Ruppert et al. 2004; Karleskint et al. 2010). Furthermore, crinoids use other physical and chemical defense mechanisms to protect them against fish predators. For example, crinoids use spike-like pinnules as well as toxic chemical compounds such as polyketide derivatives and oxidized quinones that also give them their colorful appearance (Kenta et al. 2015; Feng et al. 2017). According to WoRMS¹

2017, although they consist of nearly 700 species worldwide, until now only a few studies examined their bioactive compounds. According to the MarinLit database (2018), only 25 marine species from 16 different genera of crinoids have so far been screened for novel MNPs (Feng et al. 2017) (Table 7.1).

7.2.2 Asteroids (Sea Stars)

This class of echinoderms is, with over 1500 species, widely distributed and thus plays important ecological roles. Asteroids are opportunistic feeders, and species such as the temperate Ochre sea star *Pisaster ochraceus* and the tropical coral-eating crown of thorn sea star *Acanthaster planci* are keystone species (Paine 1969). Asteroids are known to use both physical and chemical defense mechanisms. Autotomy (i.e., found in *Evasterias troschelii* and *Pycnopodia helianthoides*), spines, modified tube feet called “pedicellaria,” camouflage, quick locomotion, and shedding have been reported as physical defenses (Bryan et al. 1997; Candia Carnevali and Bonasoro 2001). However, some species such as the sea star *Pteraster tesselatus* rely to a great extent on their mucus as chemical defense (Nance and Braithwaite

¹World Register of Marine Species.

Table 7.2 Steroidal compounds reported from echinoderms, except Holothuroids, and (if reported) their biological activities (Holothuroids see Table 7.3)

Class	Family	Species	Isolated compounds	Biological activity	References	
Crinoids	Hemicrinidea	<i>Neogymnocrinus richeri</i>	Several steroids	n.d.	De Riccardis et al. (1991)	
Asterozoa	Asterozoa	<i>Asterias amurensis</i>	Thornasteroside A, versicosides A–C, and asteronylpentaglycoside sulfate, anasteroside B	n.d.	Hwang et al. (2011, 2014)	
			Crude saponin	Insecticide and repellent activity	Park et al. (2009)	
			Asterosides A–D, glycoside B, asterosaponins	n.d.	Riccio et al. (1988)	
			Asterosaponin-4	Cytotoxic	Okano et al. (1985)	
			Asterosaponin A, A ₄	Antitumor	Ikegami et al. (1973)	
		<i>Asterias vulgaris</i>		13 steroidal compounds	n.d.	Findlay and Agarwal (1983)
		<i>Asterias forbesi</i>		Forbeside D	n.d.	Findlay and He (1991)
				Forbesides A–B	Anti-inflammatory, Antiviral	Findlay et al. (1987)
				Forbesides C–E, E ₁ -E ₃ , F-H, L	n.d.	Findlay et al. (1989), Findlay and He (1991), D'Auria et al. (1993), and Jiang et al. (1993)
				Forbeside H	n.d.	Findlay et al. (1992)
		<i>Asterias rubens</i>		Ruberosides A–F	n.d.	Sandvoss et al. (2000, 2003)
		<i>Asterias rathbuni</i>		Rathbuniosides R ₁ -R ₂	Cytotoxic	Prokof'eva et al. (2003)
		<i>Anasterias minuta</i>		Minutosides A, B	Antifungal	Chludil et al. (2002b)
				Anasterosides A–B, versicoside A	Antifungal	Chludil et al. (2002b)
		<i>Asterias rollestoni</i>		Amurensoside, forbeside		Zhang et al. (2013)
		<i>Aphelasterias japonica</i>		Aphelasteroside F	Inhibition of cell proliferation	Popov et al. (2016)
				Ophidianoside F	n.d.	Ivanchina et al. (2005)
				Aphelasteroside C (1), cheliferoside L ₁ (2), 3-O-sulfoasterone (3), forbeside E ₃ (4), and 3-O-sulfothornasterol A (5) aphelaketotriol (6)	Hemolytic activity except compound (3)	Ivanchina et al. (2000)
		<i>Leptasterias hylodes</i>		Polyhydroxylated steroids	Antibacterial, hemolytic activity	Levina et al. (2010)
				Hylodoside A, novaeguinoside Y	Hemolytic activity	Levina et al. (2010)
		<i>Leptasterias ochotensis</i>		Leptasteriosides A–F	Anticancer	Malyarenko et al. (2014)
		<i>Diplasterias brucei</i>		Diplasteriosides A, B	Anticancer	Ivanchina et al. (2011)
<i>Coscinasterias tenuispina</i>		Tenuispinosides A–C, coscinasteroside A–F	n.d.	Riccio et al. (1986d)		
<i>Distolasterias nipon</i>		Nipoglycosides A–D, versicoside A, and thornasteroside A	n.d.	Minale et al. (1995)		
		Distolasterosides D ₁ –D ₃	Neurogenic and neuroprotective effect	Palyanova et al. (2013)		
<i>Distolasterias elegans</i>		Pycnopodioside C	n.d.	Andriyashchenko et al. (1996)		
<i>Lethasterias fusca</i>		Lethasterioside A	Anticancer	Ivanchina et al. (2012)		
<i>Lysastrosoma anthosticta</i>		Lysaketotriol and iysaketodiol	Immunomodulatory activities	Levina et al. (2009)		

(continued)

Table 7.2 (continued)

Class	Family	Species	Isolated compounds	Biological activity	References
			Luridosides A, marthasterone, marthasteroside, pyncopodioside C	n.d.	Levina et al. (2001)
		<i>Marthasterias glacialis</i>	Thornasteroside A, maculatoside A ₁ , A ₂ , B–C	n.d.	Bruno et al. (1984) and Minale et al. (1985)
	Oreasteridae	<i>Pentaceraster gracilis</i>	Pentacerosides A and B, maculatoside	Maculatoside: cytotoxic	Vien et al. (2017)
		^a <i>Anthenea chinensis</i>	Anthenoside A, E, G, H, I, J, K	Antitumor	Ma et al. (2009a, 2010)
		<i>Culcita novaeguineae</i>	Culcinosides A–D	Cytotoxic	Lu et al. (2018)
			Novaeguinosides I,II, A–E, regularoside B	Antitumor	Tang et al. (2005) and Ngoan et al. (2015)
			Sodium (20R,24S)-6 α -O-(4-O-sodiumsulfato- β -d-quinovopyranosyl)-5 α -cholest-9(11)-en-3 β ,24-diol 3-sulfate	Anticancer	Ma et al. (2009b)
			Sodium (20R,24S)-6 α -O-[3-O-methyl- β -d-quinovopyranosyl-(1 \rightarrow 2)- β -d-xylopyranosyl-(1 \rightarrow 3)- β -d-glucopyranosyl]-5 α -cholest-9(11)-en-3 β ,24-diol 3-sulfate	Anticancer	Ma et al. (2009b)
			Galactocerebroside	n.d.	Inagaki et al. (2006)
			Polyhydroxylated steroids	Antibacterial, hemolytic activity	Levina et al. (2010)
			Hylodoside A, novaeguinoside Y	Hemolytic activity	Levina et al. (2010)
			Culcitoside C ₂ –C ₃	Hemolytic activity, cytotoxic	Prokof'eva et al. (2003)
			Culcitoside C ₁ –C ₈	n.d.	Kicha et al. (1985, 1986) and Iorizzi et al. (1991)
			Regularosides A–B, thornasteroside A, marthasteroside A ₁	Cytotoxic	Tang et al. (2006)
			Asterosaponin 1, novaeguinosides I and II	Antitumor	Cheng et al. (2006) and Tang et al. (2009)
		<i>Protoreaster nodosus</i>	Nodososide	Anti-inflammatory, cytotoxic	Riccio et al. (1982b) and Thao et al. (2015b)
			Ganglioside, galactocerebroside, ganglioside PNG-2A	n.d.	Pan et al. (2010, 2012) and Kenta et al. (2015)
			Three steroids	n.d.	Riccio et al. (1982b) and Minale et al. (1984b)
			Protoreasteroside	n.d.	Riccio et al. (1985d)
		<i>Pentaceraster alveolatus</i>	Protoreasteroside	n.d.	Riccio et al. (1985d)
		<i>Halityle regularis</i>	Halityloside A–F, halityloside H	n.d.	Iorizzi et al. (1986)
			Regularosides A, B, thornasteroside A	n.d.	Riccio et al. (1986c)
		<i>Oreaster reticulatus</i>	Sulfated glycosides analog of nodososide	n.d.	De Correa et al. (1985)
			Reticulatosides A, B, ophidianoside F	n.d.	Iorizzi et al. (1995)
		<i>Choriaster granulatus</i>	Granulatosides A–E	D–E: Immunomodulatory effect	Pizza et al. (1985a) and Ivanchina et al. (2017, 2018)

(continued)

Table 7.2 (continued)

Class	Family	Species	Isolated compounds	Biological activity	References	
	Ophidiasteridae	<i>Hacelia attenuata</i>	Nodososide, attenuatosides A-I, B-I, B-II, and C, polyhydroxysteroids	n.d.	Minale et al. (1983)	
			Attenuatosides S-I–S-III, S-D, thornasteroid	n.d.	Minale et al. (1984a)	
			Ophidianosides B, C, F	n.d.	Riccio et al. (1985c)	
		<i>Linckia laevigata</i>	Thornasteroside A, marthasteroside A ₁ , ophidianoside F, maculatoside, laevigatoside	n.d.	Riccio et al. (1985b)	
			Granulatoside A	Neuritogenic activity	Qi et al. (2006)	
			Nodososide	n.d.	Minale et al. (1984c)	
			Linckosides A–Q	Neuritogenic activity	Qi et al. (2002, 2004) and Han et al. (2006, 2007a)	
			Linckosides L ₁ –L ₇ , echinasteroside C	Neuritogenic activity, cytotoxic	Kicha et al. (2007a, b, c)	
			Ophidiaster ophidianus	Ophidianoside B–F	n.d.	Riccio et al. (1985c)
		<i>Certonardoa semiregularis</i>	Certonardoside A–J, halytoside D	Antiviral	Wang et al. (2002)	
			Certonardoside K–N, culcitoside C ₆	Cytotoxic, antibacterial	Wang et al. (2003)	
			Certonardosterol Q ₁ –Q ₇ , B ₂ –B ₄ , A ₂ –A ₄ , D ₂ –D ₅ , H ₃ , H ₄ , E ₂ , E ₃ , P ₁ , O ₁	Cytotoxic, antitumor	Wang et al. (2004a, b)	
			Certonardoside B ₂ , B ₃ , P ₁ , P ₂ , O ₁ , J ₂ , J ₃ , I ₂ , I ₃ , H ₂	Cytotoxic, antitumor	Wang et al. (2004a, 2005)	
		<i>Nardoa gomophia</i>	Halityloside A, B, D, E, H, I, marthasteroside A ₁ , thornasteroside A, and 2 polyhydroxysteroids	n.d.	Riccio et al. (1986b)	
		<i>Nardoa novaecaledonia</i>	Halityloside A, B, D	n.d.	Riccio et al. (1986b)	
		Asterinidae	<i>Patiria pectinifera</i>	Polyhydroxysteroids	Cytotoxic.	Peng et al. (2010)
				Cucumarioside F ₁ , F ₂	Indicative of trophic marker	Popov et al. (2014)
Asteroaponin P ₁ , P ₂ , polyhydroxysteroids	Asteroaponin P ₁ : neurogenic and neuroprotective effect			Kicha et al. (1983, 2000, 2004) and Palyanova et al. (2013)		
Pectinoside A	Immunological activity			Kawase et al. (2016)		
<i>Asterina pectinifera</i>	Pectinosides A–J, acanthaglycciside C		Cytotoxic	Dubois et al. (1988), Honda et al. (1990), Jiang and Schmidt (1992), and Li et al. (2013)		
<i>Asterina batheri</i>	Astebatheriosides A–D		Astebatheriosides B–D: anti-inflammatory	Thao et al. (2013)		
<i>Patiria miniata</i>	Patiriosides A–G		Antitumor	Dubois et al. (1988), and D'Auria et al. (1990)		

(continued)

Table 7.2 (continued)

Class	Family	Species	Isolated compounds	Biological activity	References	
	Asteropectinidae	<i>Astropecten polyacanthus</i>	Astropectenols A, C, D	Antiparasitic	Thao et al. (2013, 2014)	
		<i>Astropecten monacanthus</i>	Astrosteriosides A, D, C	Anti-inflammatory, anticancer	Thao et al. (2013, 2014) and Dai and Yu (2015)	
		<i>Craspidaster hesperus</i>	Asterosaponin	n.d.	Wen et al. (2004)	
		<i>Psilaster cassiope</i>	Psilasteroside	Cytotoxic	De Marino et al. (2003)	
		<i>Astropecten latespinosus</i>	Latespinosides A–D	Weak-cytotoxic	Higuchi et al. (1996)	
	Echinasteridae	<i>Henricia leviscula</i>		Laevisculoside, laevisculoside A–J, H ₂ sanguinosides A–B	Hemolytic activity	Kalinovskii et al. (2004), and Ivanchina et al. (2006)
				Laevisculoside G	Anticancer	Fedorov et al. (2008)
				Sanguinoside C	Cytotoxic	Levina et al. (2003)
		<i>Henricia sanguinolenta</i>		Laevisculoside, sanguinoside A–B	n.d.	Kalinovskii et al. (2004)
				Sanguinoside C	Cytotoxic	Levina et al. (2003)
		<i>Henricia derjugini</i>		Henricioside H ₁ –H ₃ , hexaol	n.d.	Ivanchina et al. (2004)
				Henricioside H ₁ , levisculoside G	Antifungal	Kaluzhskiy et al. (2017)
		<i>Henricia sp.</i>		Henriciosides H ₁ –H ₃	n.d.	Kicha et al. (1993)
		<i>Henricia downeyae</i>		Asterosaponins	Antibacterial, antifungal, feeding deterrent	Palagiano et al. (1996)
		<i>Echinaster brasiliensis</i>		Brasilienoside, desulfated dihydro-echinasteroside A, echinasteroside B–G, marthasteroside A ₁	n.d.	Iorizzi et al. (1993)
		<i>Echinaster sepositus</i>		22,23-epoxysteroidal (cyclic) glycosides	n.d.	Riccio et al. (1981), and Minale et al. (1997)
				Amurasterol, asterosterol	n.d.	De Simone et al. (1980)
				Sepositoside A	Cytotoxic	De Simone et al. (1981)
				Echinasterosides A, B ₁ , B ₂ , laevisculosides C, I	n.d.	Zollo et al. (1985), Levina et al. (1987), and Iorizzi et al. (1993)
		<i>Echinaster luzonicus</i>		Sepositoside A, luzonicosides A, D	Cytotoxic, anticancer	De Simone et al. (1981), Riccio et al. (1982a), and Malyarenko et al. (2017)
Stichasteridae	<i>Neosmilaster georgianus</i>		Santiagoside	n.d.	Vázquez et al. (1992)	
	<i>Cosmasterias lurida</i>		Cosmasterosides A–D, forbeside H	n.d.	Roccatagliata et al. (1994)	
			Luridosides A–B	n.d.	Maier et al. (1993)	
Asteropseidae	<i>Asteropsis carinifera</i>		Asteropsoside A, regularoside A, and thornasteroside A	Antitumor	Malyarenko et al. (2012)	
			Cariniferosides A–F	No cytotoxicity	Malyarenko et al. (2011)	
			Polyhydroxysteroids	n.d.	Malyarenko et al. (2010)	

(continued)

Table 7.2 (continued)

Class	Family	Species	Isolated compounds	Biological activity	References
Ophiuroidea	Archasteridae	<i>Archaster typicus</i>	Five steroids	Anticancer	Yang et al. (2011)
			Archasterosides A–C	Anticancer	Kicha et al. (2010a, b)
	Luidiidae	<i>Luidia maculata</i>	Thornasteroside A, maculatosides A–C, A ₂	Anticancer	Minale et al. (1985)
			Thornasterol	n.d.	Andriyashchenko et al. (1996)
			Luidiaquinoside, psilasteroside	Cytotoxic	De Marino et al. (2003)
	Acanthasteridae	<i>Acanthaster planci</i>	Thornasterols A and B	Cytotoxic	Kitagawa and Kobayashi (1977, 1978)
			Acanthaglycoside B–F, marthasteroside A ₁ , and versicoside A–B	n.d.	Itakura and Komori (1986)
			5-Deoxyisonodososide, isonodososide	Cytotoxic	Pizza et al. (1985b)
			Nodososide	n.d.	Minale et al. (1984c)
	Goniopectinidae	<i>Goniopecten demonstrans</i>	Goniopectenosides A–C	Antifouling	De Marino et al. (2000)
		<i>Hippasteria phrygiana</i>	Hippasteriosides A–D	Hippasterioside D: anticancer	Kicha et al. (2011)
	Phrygiasterol (1), phrygioside B (2), borealosite C (3)		(1,2): Anticancer	Levina et al. (2004, 2005)	
	Goniasteridae	<i>Mediaster murrayi</i>	Mediasteroside M ₁	Anticancer	Prokof'eva et al. 2003
		<i>Ceramaster patagonicus</i>	Ceramasterosides C ₁ –C ₃	Cytotoxic	Prokof'eva et al. (2003)
	Heliasteridae	<i>Heliaster helianthus</i>	Helianthoside	Cytotoxic	Vázquez et al. 1993
		<i>Labidiaster annulatus</i>	Labiasteroside A	n.d.	de Vivar et al. (1999)
	Solarestridae	^b <i>Solaster borealis</i>	Solasteroside A, borealositides A–D, amurenoside B	Cytotoxic	Iorizzi et al. (1992)
	Zoroasteridae	<i>Myxoderma platyacanthum</i>	Myxodermoside A and 9 polyhydroxysteroids	n.d.	Finamore et al. (1991)
	Brisingidae	<i>Novodinia antillensis</i>	steroidal saponins: Sch 725737 and Sch 725739	Cytotoxic	Yang et al. (2007)
Ophiuroids	Ophiocomidae	^c <i>Ophiocoma dentata</i>	Sulfated polyhydroxysterols	Antiviral	D'Auria et al. (1993)
		^d <i>Ophiarthrum elegans</i>	Sulfated polyhydroxysterols	Antiviral	D'Auria et al. (1987, 1993)
		<i>Ophiocoma erinaceus</i>	n.d.	Hemolytic activity	Amini et al. (2014)
	Ophiopholidae	<i>Ophiopholis aculeata</i>	Sulfated polyhydroxysterols	Cytotoxic and hemolytic activity	Aminin et al. (1995)
	Ophiomyxidae	<i>Ophiarachna incrassata</i>	Sulfated polyhydroxysterols	Antiviral	D'Auria et al. (1987, 1993)
	Hemieuryalidae	<i>Ophioplocus januarii</i>	Sulfated steroids	Antiviral	Roccatagliata et al. (1996)
	Gorgonocephalidae	<i>Astrotoma agassizii</i>	Polyhydroxysterols	Antiviral	Comin et al. (1999)
	Ophiodermatidae	<i>Ophioderma longicauda</i>	Longicaudosides A–B	n.d.	Riccio et al. (1985a, 1986a)
Echinoids	Diadematidae	<i>Diadema savignyi</i>	Steroidal compounds	Anticancer	Thao et al. (2015a)
	Toxopneustidae	<i>Tripneustes gratilla</i>	Epidioxysterol	Cytotoxic	Liu et al. (2011)

^aThe accepted name changed from “*Anthenea chinensis*” to “*Anthenea pentagonula*”^bThe accepted name changed from “*Solaster borealis*” to “*Crossaster borealis*”^cThe accepted name changed from “*Ophiocoma dentata*” to “*Breviturma dentata*”^dThe accepted name changed from “*Ophiarthrum elegans*” to “*Ophiomastix elegans*”

1979). Based on the hypothesis that saponins and saponin-like compounds produce various sugars upon hydrolysis (Fieser and Fieser 1956), Ward (1960) proposed that mucous-like compounds secreted from *Pteraster tessellates* have a saponin or saponin-like nature. Starfishes produce a wide range of MNPs (Table 7.2), which are largely described as lipid-like or lipid soluble molecules. Asteroids produce various steroidal derivatives, fatty acids, ceramides, and few alkaloids to either defend themselves or communicate (Table 7.1). Some of the latter compounds have been reported to possess pharmacological activities (Maier, 2008). After sea cucumbers, this group of echinoderms has also been reported to produce a large number of saponins, which have been isolated from different organs (i.e., stomach, arm, gonads, and digestive system) and possess various roles in digestion (Garneau et al. 1989; Demeyer et al. 2014), reproduction (Mackie et al. 1977) and the defense against potential predators (Harvey et al. 1987). Assessing the isolated steroidal glycosides from 1973 to 2016 revealed that most of the MNP studies on sea stars had focused on the families

Asteroidea (26%), Echinasteridae (17%), Oreasteridae (16%), and Ophiasteridae (13%; Table 7.2 and references therein).

The glycoside compounds of starfish are classified into three main groups of steroidal glycosides: asterosaponin, polyhydroxylated glycosides, and macrocyclic glycosides (Kicha et al. 2001; Maier 2008; Demeyer et al. 2014). Although steroidal glycosides are the characteristics of asteroids, triterpene glycosides have also been isolated from starfishes such as *Asterias rollestoni* (Zhan et al. 2006) and *Patiria pectinifera* (Popov et al. 2014). The isolated saponins from *A. rollestoni* (rollentosides A–B) have a similar aglycone and carbohydrate moiety than those observed in some sea cucumber species (Popov et al. 2014). Given the similar structures of rollentoside B (Zhan et al. 2006) and cucumarioside A₁₅ that have been extracted from the sea cucumber *Eupentacta fraudatrix* (Silchenko et al. 2012a), it has been argued that the starfish fed on the sea cucumber (Popov et al. 2014; Fig. 7.3). Furthermore, it seems that *A. rollestoni* is

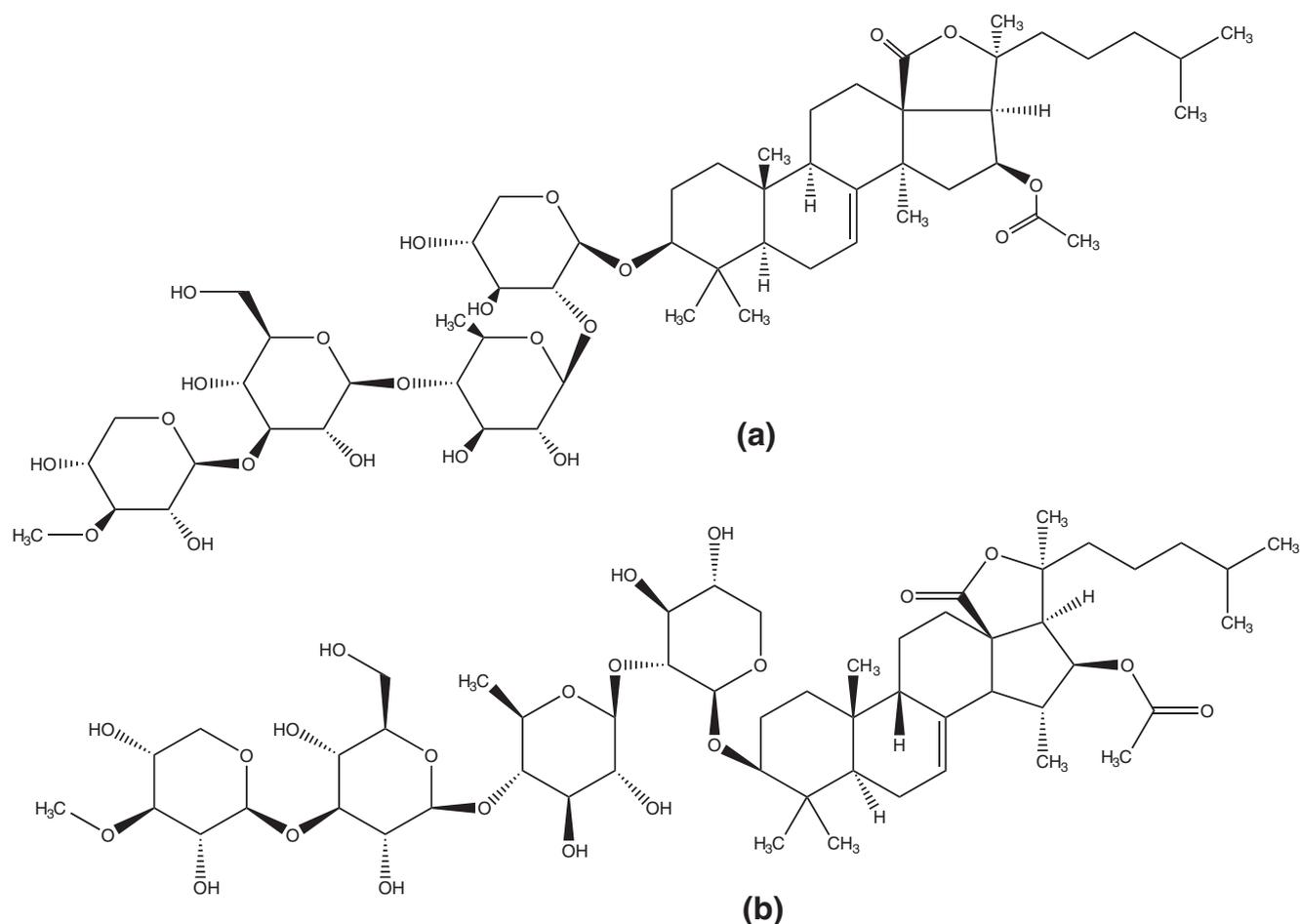


Fig. 7.3 (a) Rollentoside B isolated from *Asterias rollestoni* and (b) Cucumarioside A₁₅ isolated from *Eupentacta fraudatrix* with similar chemical formula of C₅₅H₈₈O₂₂ (produced with ChemDraw, version 16.0.1.4 (77))

able to digest and also to accumulate the toxic triterpene glycosides that were originally derived from sea cucumbers.

7.2.3 Ophiuroids (Brittle Stars)

With over 2000 species, brittle stars are the largest group of echinoderms (Hickman et al. 2001). These organisms are widely distributed, and their feeding behavior can be suspension feeding, deposit feeding, and/or predation (Stöhr et al. 2012). Although brittle stars have numerous physical defense mechanisms such as fast locomotion, a quick removal of their extremities, and the ability to hide under rocks and crevices, some species still rely on chemical defenses. However, based on the MarineLit database, to this day only a few studies focused on ophiuroids. Nuzzo et al. (2017) mentioned that several classes of secondary metabolites such as carotenoids, gangliosides, brominated indoles, phenylpropanoids, several groups of terpenes, and steroids have been isolated from brittle stars (Table 7.1). The presence of sulfated steroids in starfish (see Sect. 7.3) and brittle stars is an indicator of the phylogenetically close relation between these two classes of echinoderms (Levina et al. 1996, 2007).

7.2.4 Echinoids (Sea Urchins)

Sea urchins, the living representative of echinoids, are free-moving echinoderms (Clemente et al. 2013). They typically have physical defense mechanisms such as fused skeleton plates, spines, and pedicellaria for pinching or capturing prey (Jangoux 1984). Some families such as Diadematidae, Echinothuriidae, and Toxopneustidae contain venoms (Thiel and Watling 2015). The main MNPs of sea urchins are proteins, polysaccharides, and pigments, which are located in the spines, testes, gonads, and/or pedicellaria (Shang et al. 2014; Jiao et al. 2015). Studies on their MNPs have mainly focused on proteins derived from naphthoquinone pigments that showed antibacterial, antioxidant, and anti-inflammatory activities. Few studies focused on steroidal components of sea urchins (Table 7.2), with the exception of *Tripneustes gratilla* (Liu et al., 2011) and *Diadema savignyi* (Thao et al. 2015a), from which several steroidal constituents had been described.

7.2.5 Holothuroids (Sea Cucumbers)

Sea cucumbers have been recognized as an interesting source of MNPs, since they are already used as traditional food and medicine source in Asian countries (i.e., healing wounds, eczema, arthritis, impotence; Ridzwan 2007; Althunibat et al. 2013). The enriched nutrition profile of

sea cucumbers and their high protein, low sugar, and cholesterol-free content make holothurians a valuable food source, especially for people who suffer from hyperlipidemia (Wen et al. 2010; Bordbar et al. 2011). To date, antibacterial (Ghanbari et al. 2012; Soliman et al. 2016), antifungal (Ghannoum and Rice 1999; Soliman et al. 2016), antiviral (Mayer and Hamann 2002), antitumor and anticancer (Anisimov et al. 1973; Wu et al. 2007a; Janakiram et al. 2015; Fedorov et al. 2016), anti-schistosomal (Mona et al. 2012), and anti-inflammatory (Song et al. 2016) activities are the reported bioactive effects that were obtained from various classes of sea cucumber-derived secondary metabolites. Although a wide range of chemical classes from sea cucumbers such as peptides (Zhao et al. 2009; Song et al. 2016), polysaccharides (Liu et al. 2012; Marques et al. 2016), glycosphingolipids (Sugawara et al. 2006), polyunsaturated fatty acids (Yang et al. 2003; Hu et al. 2014b), and ceramides and gangliosides (Ikeda et al. 2009) were studied (Table 7.2), only a few products reached pre-clinical trials (Mayer et al. 2010).

7.3 Saponins in Echinoderms

The major group of bioactive compounds that are responsible for the biological activities of echinoderms are glycosides (Bhakuni and Rawat 2005; Dong et al. 2011). Saponins are common compounds that have been isolated from various terrestrial plants, but within the animal kingdom, they are reported only in few marine organism groups such as sponges (Kubanek et al. 2000), sea cucumbers (Yamanouchi 1955), and starfishes (Kitagawa and Kobayashi 1977). Echinoderms harbor in comparison to other marine invertebrates by far the most of the 350 reported saponin compounds.

Saponins are complex amphipathic glycosides composed of a steroid (largely found in sea stars) or triterpenoid aglycone (most commonly found in sea cucumbers) and a carbohydrate moiety (Minale et al. 1995). Saponins consist of hydrophilic (glycone) and hydrophobic (aglycone) components. The sugar moiety of saponins is mostly composed of glucose (Glc), xylose (Xyl), galactose (Gal), glucuronic acid (Glu), rhamnose (Rha), and/or methylpentose and is connected to the hydrophobic compartment (sapogenin) via glycosidic bonds. The nature of the side chains and the positions of various carbohydrate residues, or monosaccharide compositions, affect the membranotropic activities and functional properties of this chemical group.

Saponins show a broad range of bioactivities and ecological functions ranging from cytotoxic, hemolytic, antibacterial, antiviral, antifouling, antifungal, and anti-inflammatory activities, immunomodulatory effects, ichthyotoxicity, and deterrent/attractant properties for predators/symbionts (see Tables 7.2 and 7.3 for more details). Furthermore, the inter-

Table 7.3 Triterpene glycosides of different orders of holothurians and their bioactivity

Order	Family	Species	Saponin compounds	Biological activity	References
Apodida	Synaptidae	<i>Ophiodesoma grisea</i>	n.d.	Hemolytic activity	Kalimin et al. (2008)
		<i>Synapta maculata</i>	Synaptoside A	Cytotoxic	Avilov et al. (2008)
Elasipodida	Elpididae	<i>Kolga hyalina</i>	Kolgaosides A, B	Antitumor	Avilov et al. (2008)
		<i>Rhipidothuria racovitzai</i>	Achlioniceosides A ₁ -A ₃	Low cytotoxicity n.d.	Silchenko et al. (2014b) Antonov et al. (2009)
Holothuriida	Holothuriidae	<i>Holothuria atra</i>	n.d.	Antifouling and antibacterial activities	Soliman et al. (2016)
			Holothurin A-B, Echinocide A-B	Antifungal	Kobayashi et al. 1991
			Ethanolic extracts	Antifungal and antibacterial	Abraham et al. (2002)
		<i>Holothuria leucospilota</i>	Holothurin A-B	Antimicrobial	Kitagawa et al. (1979, 1981d)
			Holothurin	Ichthyotoxic	Yamanouchi (1955)
			Leucospilotoside A-C, holothurin B, B ₂	Leucospilotoside B: antitumor	Han et al. (2007b, 2008b, 2009a, 2010b)
			Holothurinoside E ₁ , holothurin A-B, B ₃ , desholothurin A, bivittoside D	Hemolytic activity	Van Dyck et al. (2010)
		n.d.	Holothurin A-B, A ₂ , holotoxin A ₁	Immunomodulatory activity	Popov et al. (1994)
		<i>Holothuria fuscocinerea</i>	Holothurin	Hemolytic activity	Pocsidio (1983)
			Fuscocinerosides A-C, pervicoside C, holothurin A	Antifungal, cytotoxic	Zhang et al. 2006d
			Holothurin	Hemolytic activity	Pocsidio (1983)
			Pervicosides A-C	Antifungal	Kitagawa et al. (1985, 1989)
			Holothurins A, B	Cytotoxic	Anisimov et al. (1980)
	Nobilisides A-D	Nobiliside A: antifungal, antitumor	Wu et al. (2006a, 2007a, 2009a), Zhang (2009), Guo and Xiong (2009) and Zhang and Zhu (2017)		
<i>Holothuria scabra</i>	Echinocide A	Anticancer	Li et al. (2010)		
	24-dehydroechinoside A, echinoside A, holothurin A	Antifungal	Kobayashi et al. (1991)		
	24-Dehydroechinoside A	Antitumor	Han et al. 2012		
	Fuscocineroside C, echinoside A, holothurin A ₁ , A ₄	Anticancer	Dang et al. (2007) and Han et al. (2012)		
	Scabraside A,B, echinoside A, holothurin A ₁	Antifungal	Han et al. (2008a, 2009b)		
	Scabrasides A-D, fuscocineroside C	Antitumor	Han et al. (2009b, 2012)		
	Holothurins A ₃ -A ₄	Cytotoxic	Dang et al. (2007)		
Echinocide A and holothurin A ₁ -A ₄	Cytotoxic	Han et al. (2009b)			

(continued)

Table 7.3 (continued)

Order	Family	Species	Saponin compounds	Biological activity	References
			Crude extract	Antioxidant	Suwanmala et al. (2016)
			Ethanolic extracts	Antifungal and antibacterial	Abraham et al. (2002)
	<i>Holothuria poli</i>		Holothurins B ₂ -B _n , Holothurins A-B	n.d.	Silchenko et al. (2005c)
			methanol and aqueous extracts	Antifungal	Ismail et al. (2008)
			Bivittoside	Cytotoxic	Omran and Khedr (2015)
	<i>Holothuria tubulosa</i>		Holothurinoside	Antifouling	Ozupek and Cavas (2017)
			Holothurins A-B	n.d.	Silchenko et al. (2005c)
			Holothurinoside	Antifouling	Ozupek and Cavas (2017)
			Methanol and dichloromethane extracts	Anti-inflammatory	Herencia et al. (1998)
	* <i>Holothuria fuscopunctata</i>		Impatienside B, arguside F, and pervicoside D	Antifungal	Yuan et al. (2009b)
			Axilogside A, holothurin B	Antifungal	Yuan et al. (2008)
			Desulfated glycosides	Antifungal	Kobayashi et al. (1991)
	<i>Holothuria forskali</i>		Holothurinosides A-D	Antitumor, antiviral	Rodriguez et al. (1991)
	<i>Holothuria floridana</i>		n.d.	hypothermic, and hemolytic activities	Kaul (1986)
			Holothurins A ₁ -A ₃ , B ₁	n.d.	Kuznetsova et al. (1982b), Oleinikova et al. (1982), and Oleinikova and Kuznetsova (1983)
			Holothurin A ₁	Few inhibition of Na ⁺ /K ⁺ -ATPase activity	Gorshkova et al. (1989)
	<i>Pearsonothuria graeffei</i>		Disulfated Holothurin A	Hemolytic activity	Van Dyck et al. (2010)
			Desholothurin A, holothurinoside C	Hemolytic activity	Van Dyck et al. (2010)
			Holothurinoside J ₁	Hemolytic activity	Van Dyck et al. (2010)
			Disulfated echinoside A	Stimulator of hepatic fatty acid β-oxidation and suppression of FA biosynthesis/anticancer	Zhao et al. (2011, 2012) and Wen et al. (2016)
			Disulfated echinoside A	Antimetastatic activity	Zhao et al. (2011)
			Echinoside A, disulfated echinoside A	Antitumor	Zhao et al. (2012)
			n.d.	Antihyperlipidemic activity	Hu et al. (2010)
	<i>Holothuria grisea</i>		Holothurin A ₁	n.d.	Oleinikova et al. (1982)
			Griseaside A, 17-dehydroxyholothurinoside A	Cytotoxic	Yi et al. (2008)
	<i>Holothuria edulis</i>		Holothurin A	Anti-fungal	Kobayashi et al. (1991)
			Ethyl acetate fraction	Anti-inflammatory	Wijesinghe et al. (2015)
	<i>Holothuria hilla</i>		Hillasides A-C	Antitumor, cytotoxic	Wu et al. (2006b, 2007b, 2009b)
	<i>Holothuria lessoni</i>		Holothurinoside A ₁ , E ₁	n.d.	Bahrami et al. (2014)
			Lessonioside A-D	Acetylated saponin	Bahrami et al. (2014) and Bahrami and Franco (2015)
			Lessonioside E-G, M	Nonacetylated saponin	Bahrami and Franco (2015)
			Holothurinoside X-Z	n.d.	Bahrami et al. (2014)

<i>Holothuria moebii</i>	Sulfated and desulfated saponins	Cytotoxic	Yu et al. (2015)
<i>Holothuria sp.</i>	n.d.	Antiviral	Farshadpour et al. (2014)
<i>Holothuria impatiens</i>	Impatienside A ^a , bivittoside D	Cytotoxic, Antitumor	Sun et al. (2007)
<i>Bohadschia argus</i>	Bivittoside types	Antitumor	Kuznetsova et al. (1982a)
	Argusides A–E	Cytotoxic	Liu et al. (2007, 2008a, b)
<i>Bohadschia bivittata</i>	Holothurin C	Inhibition of Na ⁺ /K ⁺ -ATPase activity	Gorshkov et al. (1982)
	Bivittosides A–D	Antifungal	Kitagawa et al. (1981c)
	Bivittosides A–B	Inhibition of Na ⁺ /K ⁺ -ATPase activity	Kitagawa et al. (1981c) and Gorshkova et al. (1989)
<i>Bohadschia vitensis</i>	Bivittoside D	Antiviral, anti-fungal, and spermicide	Lakshmi et al. (2008, 2012) and Maier (2008)
<i>Bohadschia marmorata</i>	Impatiensides A ^a –B, marmortosides A–B, 25-acetoxibivittoside D, bivittoside D	Antifungal	Yuan et al. (2009a)
<i>Bohadschia cousteaui</i>	Bivittosides	Antitumor	Kuznetsova et al. (1982a)
<i>Bohadschia graeffei</i>	Cousteasides A–J	Antifungal	Elbandy et al. (2014)
<i>Bohadschia subrubra</i>	Holothurin A, echinoside A	Antifungal	Kobayashi et al. (1991)
	Impatienside A ^a ; bivittoside C, D; araguside C; holothurinose F, H, H ₁ , I, I ₁ , K ₁	Hemolytic	Van Dyck et al. (2010)
<i>Actinopyga agassizi</i>	Holothurin A	Ichthyotoxic	Chanley et al. (1959)
	24-Dehydroechinoside A	Ichthyotoxic	Kalinin et al. (2008)
	Holothurin	Antitumor	Sullivan et al. (1955)
	Holothurin	Antiparasitic (against <i>Trypanosoma lewisi</i>)	Styles (1970)
	Holothurin	Mitogenic activity	Nigrelli and Jakowska (1960)
	n.d.	Antibacterial, immunomodulatory effect	Kalinin et al. (2008)
<i>Actinopyga lecanora</i>	n.d.	Hemolytic activity	Poscizio (1983)
	Holothurins A–B	Antifungal	Kumar et al. (2007)
	Holothurins A, A ₁ , B, lecanorosides A and B	Antitumor	Zhang et al. (2008)
	Holothurin A, holothurin B	Antiparasitic	Singh et al. (2008)
	n.d.	Antibacterial	Ghanbari et al. (2012)
<i>Actinopyga echinites</i>	Echinosides A–B	Antifungal, antischistosomal	Kitagawa et al. (1980) and Melek et al. (2012)
	Ethanollic extracts	Antifungal and antibacterial	Abraham et al. (2002)

(continued)

Table 7.3 (continued)

Order	Family	Species	Saponin compounds	Biological activity	References
		<i>Actinopyga mauritiana</i>	Echinoides A–B, 24- ehydroechinosides A–B	Antifungal	Kobayashi et al. (1991)
		<i>Actinopyga flammea</i>	n.d.	Antineoplastic and cytotoxic	Pettit et al. (1976)
		<i>Actinopyga miliaris</i>	Echinoides, Holothurinogenins	Antitumor, antifungal	Bhatnagar et al. (1985) and Mondol et al. (2017)
		<i>Cucumaria japonica</i>	Ethanolic extracts	Antifungal and antibacterial	Abraham et al. (2002)
			Cucumarioside	Immunomodulatory effect	Polikarpova et al. (1990)
			Cucumarioside	Antifungal	Barrakov et al. (1980)
			Cucumarioside	mitogenic Antiproliferative activity	Turischev et al. (1991)
			Cucumarioside A ₄₊₂	Hemolytic activity, immunomodulatory effect, antiviral	Aminin et al. (2001) and Kalinin et al. (2008)
			Cucumarioside A ₇₋₂	Hemolytic, cytotoxic, inhibition of Na ⁺ /K ⁺ -ATPase activity, immunomodulatory effect, antiviral, antitumor	Avilov et al. (1991b), Kalinin et al. (1996), Aminin et al. (2001), Agafonova et al. (2003), MENCHINSKAYA et al. (2014), and PISLYAGIN et al. (2017)
			Cucumariosides A ₁₋₂ , A ₂₋₃ , A ₂₋₄ , A ₄₋₂	n.d.	Avilov et al. (1991b)
			Cucumarioside A ₃	Hemolytic, immunomodulatory effect	Aminin et al. (2001)
			Cucumariosides A ₇₋₁ , A ₇₋₂ , A ₇₋₃	Hemolytic, cytotoxic, immunomodulatory effect	Drozdova et al. (1993), Kalinin et al. (1996), Aminin et al. (2001), and Agafonova et al. (2003)
			Cucumarioside A ₆₋₂	Antitumor, cytotoxic, hemolytic, immunomodulatory effect	Kalinin et al. (1996), Drozdova et al. (1997), and Aminin et al. (2001)
			Cucumariosides A ₀₋₁ , A ₀₋₂ , A ₀₋₃	n.d.	Drozdova et al. (1993)
			Cucumarioside A ₃	Antitumor, hemolytic	Kalinin et al. (1996) and Drozdova et al. (1997)
			Cucumarioside G ₁	Inhibition of Na ⁺ /K ⁺ -ATPase activity	Anisimov et al. (1983)
			Cumaside	Immunomodulatory and hemolytic effect	Aminin et al. (2006)
			Cucumarioside	Immunomodulatory effect, antibacterial, Antiviral	Sedov et al. (1984, 1990), Grishin et al. (1990), and Aminin (2016)
		<i>Cucumaria frondosa</i>	Frondoside A	Antiproliferative effects, Antitumor, anticancer, Immunomodulatory effect	Al Shemaili et al. (2014), Girard et al. (1990), Al Marzouqi et al. (2011), Attoub et al. (2013), Ma et al. (2012), and Aminin et al. (2008)
			Frondoside D	n.d.	Yayli and Findlay (1999)
			Frondoside C	Antitumor	Avilov et al. (1998)
			Frondosides B, A ₂₋₁ –A ₂₋₈	n.d.	Findlay et al. (1992) and Silchenko et al. (2005a, b)
			Frondoside A ₇₋₂ , A ₇₋₃ , A ₇₋₄ , isofrondoside C	n.d.	Silchenko et al. (2007a)

			* <i>Cucumaria echinata</i>	Cucumechinosides A–F	Antifungal, anticancer, antiprotozoal	Miyamoto et al. (1990b)
			Cucumechinol A–C	n.d.	Miyamoto et al. (1990a)	
			Disulfated Penaustrosides A–B	n.d.	Miyamoto et al. (1992)	
				CEL-I	Hemolytic activity	Hatakeyama et al. (1999)
			CEL-III	Hemolytic activity	Oda et al. (1999)	
			<i>Cucumaria fallax</i>	Fallaxosides B ₁ , C ₁ –C ₂ , D ₁ –D ₇	Cytotoxic, hemolytic	Silchenko et al. (2016a)
				Okhotosides B ₁ –B ₃	Antitumor, cytotoxic	Silchenko et al. (2008)
			<i>Cucumaria okhotensis</i>	Okhotosides A ₂₋₁₁ , A ₁₋₁₁ , B ₁ –B ₃	Immunomodulatory activity, cytotoxic	Silchenko et al. (2007b, 2008) and Aminin et al. (2010)
			<i>Cucumaria</i>	Froncosa A ₁	Immunomodulatory activity	Aminin et al. (2010)
				Cucumarioside A ₂₋₅₅ , A ₃₋₂ , A ₃₋₃ , Isokoreoside A, koreoside A	n.d.	Avilov et al. (2003)
			<i>Conicospermium</i>	Lefevreosides A ₁ , A ₂ , C, D	n.d.	Rodriguez and Riguera (1989)
			<i>Cucumaria koreaensis</i>	Koreoside A	n.d.	Avilov et al. (1997)
			<i>Cucumaria miniata</i>	Cucumarioside A ₇₋₃	n.d.	Drozhdova et al. (1997)
			<i>Mensamaria intercedens</i>	Intercedensides A–C, D–I	Antitumor, cytotoxic	Zou et al. (2003, 2005)
			<i>Hemioedema spectabilis</i>	Hemoiedemosides A–B	Cytotoxic, antifungal	Chludil et al. (2002a)
			* <i>Pentacta quadrangularis</i>	Phyllinopside E (PE)	Antitumor, Antiangiogenesis, cytotoxic	Tian et al. (2005, 2007)
			<i>Pentacta australis</i>	Phyllinopsides A, B, E, F	Cytotoxic	Yi et al. (2006) and Zhang et al. (2006a)
				Phyllinopsides A–B, pentactaside I, II, and III	Cytotoxic	Han et al. (2010a)
			<i>Actinocucumis typica</i>	Pentactaside B, C	Antitumor	Han et al. (2010c)
				Desulfated penaustrosides A–D	n.d.	Miyamoto et al. (1992)
<i>Colochirus robustus</i>	Typicosides A ₁ , A ₂ , B ₁	Immunomodulatory effect, cytotoxic	Pislyagin et al. (2014)			
	Typicosides A ₁ , A ₂ , B ₁ , C ₁ , C ₂ , intercedenside A, holothurin B ₃	Antifungal, cytotoxic	Silchenko et al. (2013b)			
** <i>Cercodemas anceps</i>	Colochiroside E	n.d.	Silchenko et al. (2016c)			
	Colochirosides D, A ₁ –A ₃ , B ₁ –B ₃	Cytotoxic, hemolytic activity	Silchenko et al. (2015a, 2016c, b)			
* <i>Pseudocnus dubiosus leoninus</i>	Colochiroside A	Antitumor	Cuong et al. (2015)			
	Cercodemasoides A–E	Cytotoxic	Cuong et al. (2015)			
	Pseudocnoside A	Anticancer, antiproliferative	Careaga et al. (2014)			

(continued)

Table 7.3 (continued)

Order	Family	Species	Saponin compounds	Biological activity	References
		<i>Staurocucumis liouvillei</i>	Liouvilloosides A–B	Cytotoxic, antiviral	Maier et al. (2001)
		** <i>Staurocucumis turqueti</i>	Liouvilloosides A ₁ –A ₅ , B, B ₂ Turquetoside A	n.d. n.d.	Antonov et al. (2008, 2011) Silchenko et al. (2013d)
		<i>Pseudocolochirus violaceus</i>	Violaceosides A, B, C, E, I–III	Cytotoxic	Zhang et al. (2006b, c) and Silchenko et al. (2014a)
		* <i>Duasmiodactyla kurilensis</i>	Violaceoside D, G Kurilloosides A, C	Cytotoxic n.d.	Silchenko et al. (2014a) Avilov et al. (1991a)
Sclerodactylidae		<i>Eupentacta fraudatrix</i>	Cucumarioside G ₁	Cytotoxic, hemolytic, inhibition of Na ⁺ /K ⁺ -ATPase activity	Gorshkov et al. (1982), Afiyatullof et al. (1985), and Kalinin et al. (2008)
			Cucumarioside G ₂	Hemolytic activity	Avilov et al. (1994)
			Cucumariosides H ₁ –H ₈	Hemolytic activity, cytotoxic	Silchenko et al. (2012c)
			Cucumarioside C	Cytotoxic	Anisimov et al. (1974)
			Cucumariosides A ₁ –A ₁₀ , A ₁₄ , A ₁₅ , A ₈	Antifungal, hemolytic activity	Melek et al. (2012) and Silchenko et al. (2012a, b)
			Cucumarioside B ₂	Antifungal	Melek et al. (2012) and Silchenko et al. (2012a, b, d)
			Cucumariosides G ₁ , G ₂ , G ₄ , G _{4-A}	Hemolytic activity	Kalinin et al. (1992a, b, 2008)
			Cucumariosides F ₁ , F ₂	n.d.	Popov et al. (2014)
			Cucumariosides I ₁ –I ₃	Cytotoxic and immunostimulatory activities	Silchenko et al. (2013a, b, c)
			Cucumarioside B ₁	Hemolytic activities, antifungal	Melek et al. (2012) and Silchenko et al. (2012a, b, d)
			Cucumariosides A ₁ –A ₁₅	Cytotoxic	Silchenko et al. (2012a)
		* <i>Cucumaria fraudatrix</i>	Cucumariosides G ₁ , G ₃ , G _{3-A}	Cytotoxic, hemolytic activity	Afiyatullof et al. (1985) and Popov (2002)
		<i>Cladolabes schmeltzii</i>	Cladolosides A ₁ –A ₆ , B ₁ –B ₂ , C, C ₁ –C ₄ , D, D ₂ , E ₁ , E ₂ , F ₁ , F ₂ , G, H ₁ , H ₂ , J ₁ , K ₁ , K ₂ , L ₁ , M, M ₁ , M ₂ , N, I ₂ , O, P, P ₁ , P ₃ , Q, R	Cytotoxic	Silchenko et al. (2013e, 2014c, 2015b, 2017a, 2018a, b)
Psolidae		<i>Psolus fabricii</i>	Psolososide A	Hemolytic activity	Kalinin et al. (1996)
			Psolososides A, B	Inhibition of Na ⁺ /K ⁺ -ATPase activity	Kalinin et al. (1989a) and Gorshkova et al. (1999)
		<i>Psolus eximius</i>	Eximioside A	n.d.	Kalinin et al. (1997)
		<i>Psolus patagonicus</i>	Patagonicosides A–C	Antifungal, cytotoxic	Murray et al. (2001), Muniain et al. (2008) and Careaga et al. (2011)
Phylloporidae		<i>Pentamera calcigera</i>	Calcigerosides B, C ₁ , C ₂	Cytotoxic	Avilov et al. (2000b)
			Cucumarioside G ₂	No cytotoxicity	Avilov et al. (2000b)
			Calcigerosides D ₁ –D ₂ , E	n.d.	Avilov et al. (2000a)
		<i>Neothyonidium magnum</i>	Magnumosides A ₁ –A ₄ , B ₁ –B ₄ , C ₁ –C ₄	Cytotoxic, hemolytic	Silchenko et al. (2017b)

Synallactida	Stichopodidae				Antifungal	Kitagawa et al. (1976) and Maltsev et al. (1984, 1985)
Synallactida	Stichopodidae	** <i>Apostichopus japonicus</i>	Holotoxin A, B, C		Antifungal	Kitagawa et al. (1976) and Maltsev et al. (1984, 1985)
			Holotoxin A ₁		Antiprotozoal, antitumor	Kitagawa et al. (1976) and Anisimov et al. (1983)
			Holotoxin A ₁ , cladoloside		Neurotoxic, cytotoxic	Yun et al. (2018)
			Holotoxin A ₁		Cytotoxic, antiproliferative activity	Ishida et al. 1993 and Popov et al. 1994
			Holotoxins A ₁ , B ₁		Inhibition of Na ⁺ /K ⁺ -ATPase activity	Maltsev et al. (1984) and Gorskova et al. (1989)
			Apostichoposide C		Inhibition of Na ⁺ /K ⁺ -ATPase activity	Gorskova et al. (1989)
			Holotoxin A ₁ , B ₁ and holothurin A		Contraceptive effect	Mats et al. (1990)
			Cladoloside B		Antifungal	Wang et al. (2012)
			Holotoxins A ₁ , B ₁ , D ₁ , A		Antifungal	Wang et al. (2012)
			25,26-Dihydroxy-holotoxin A ₁		Antifungal	Wang et al. (2012)
		Holotoxins D-G		Antifungal	Wang et al. (2012)	
		(Nortriterpene glycoside) 26-nor-25-oxo-holotoxin A ₁		Antifungal	Wang et al. (2012)	
		Holotoxins F, G, H		Antifungal	Liu et al. (2012) and Wang et al. (2012)	
		* <i>Stichopus japonicus</i>		Antifungal	Kitagawa et al. (1976)	
		<i>Stichopus chloronotus</i>		Antioxidant	Husni et al. (2009)	
				Antimicrobial, antifungal, cytotoxic, antitumor	Anisimov et al. (1983) and Maltsev et al. (1985)	
				Inhibition of Na/K ⁺ -ATPase activity	Gorskova et al. (1989)	
				Antifungal	Kitagawa et al. (1981a, b)	
				n.d.	Sharypov et al. (1981)	
				Antineoplastic and cytotoxic	Petit et al. (1976)	
<i>Stichopus horrens</i>		Cytotoxic	Cuong et al. (2017)			
		Cytotoxic	Vien et al. (2018)			
		Antifungal	Wang et al. (2014)			
* <i>Stichopus variegatus</i>		Antifungal	Kobayashi et al. (1991)			
<i>Stichopus hermanni</i>		Antifungal	De Moncerrat Iniguez-Martinez et al. (2005)			
* <i>Stichopus parvinensis</i>		n.d.				
* <i>Stichopus multifidus</i>		Inhibition of Na/K ⁺ -ATPase activity	Gorskov et al. (1982)			
<i>Thelenota ananas</i>		Antifungal	Stomik et al. (1982) and Maltsev et al. (1985)			
		Antitumor	Petit et al. (1976)			
		Immunomodulatory effect	Gorskova et al. (1989)			
		Antifungal	Kobayashi et al. (1991)			

(continued)

Table 7.3 (continued)

Order	Family	Species	Saponin compounds	Biological activity	References
			Telothurins A–B	Antitumor	Kuznetsova et al. (1982a)
			n.d.	Antineoplastic and cytotoxic	Pettit et al. (1976)
			n.d.	Antiviral	Hegde et al. (2002)
		<i>Thelenota anax</i>	Stichlorosides A ₁ , B ₁ , C ₁	Antifungal	Kobayashi et al. (1991)
			Telothurin	Antitumor	Kuznetsova et al. (1982a)
			Stichoposides C–D	Antitumor, anticancer	Yun et al. (2012) and Park et al. (2014)
		<i>Australostichopus mollis</i>	Neothyonidioside	Antifungal	Yibmantasiri et al. (2012)
			Mollisosides A, B ₁ –B ₂	n.d.	Moraes et al. (2005)
	Synallactida	<i>Synallactes nozawai</i>	Synallactosides A ₁ , A ₃ , B ₁ , B ₂ , C	n.d.	Silchenko et al. (2002)
Perciculida	Pseudostichopodidae	<i>Pseudostichopus trachus</i>	Pseudostichoposides A,B	n.d.	Kalinin et al. (1989b) and Silchenko et al. (2004)

^aMarmoratoside A = impatienside A (Van Dyck et al. 2010)

*Based on WoRMS (2019), the accepted names changed from: *Stichopus multifidus* to *Astichopus multifidus*; *Neothyonidium magnum* to *Massinium magnum*; *Pseudocnus dubiosus leoninus* to *Pentactella leonina*; *Cucumaria fraudatrix* to *Eupentacta fraudatrix*; *Holothuria axiologa* to *Holothuria fuscopunctata*; *Pentacta quadrangularis* to *Cholochirus quadrangularis*; *Stichopus variegatus* to *Stichopus horrens*; *Stichopus parvimensis* to *Apostichopus parvimensis*; *Duasmodycyla kurilensis* to *Thyonidium kurilensis*; *Pentacta quadrangularis* to *Colochirus quadrangularis*; *Bohadschia bivittata* to *Bohadschia vittensis*; *Cucumaria echinata* to *Pseudocnus echinatus*; *Stichopus japonicus* to *Apostichopus japonicus*

**Synonymised names: *Staurocucumis turqueti* = *Cucumaria turqueti*/*Cucumaria spatha*; *Cercodemus anceps* = *Colochirus anceps*

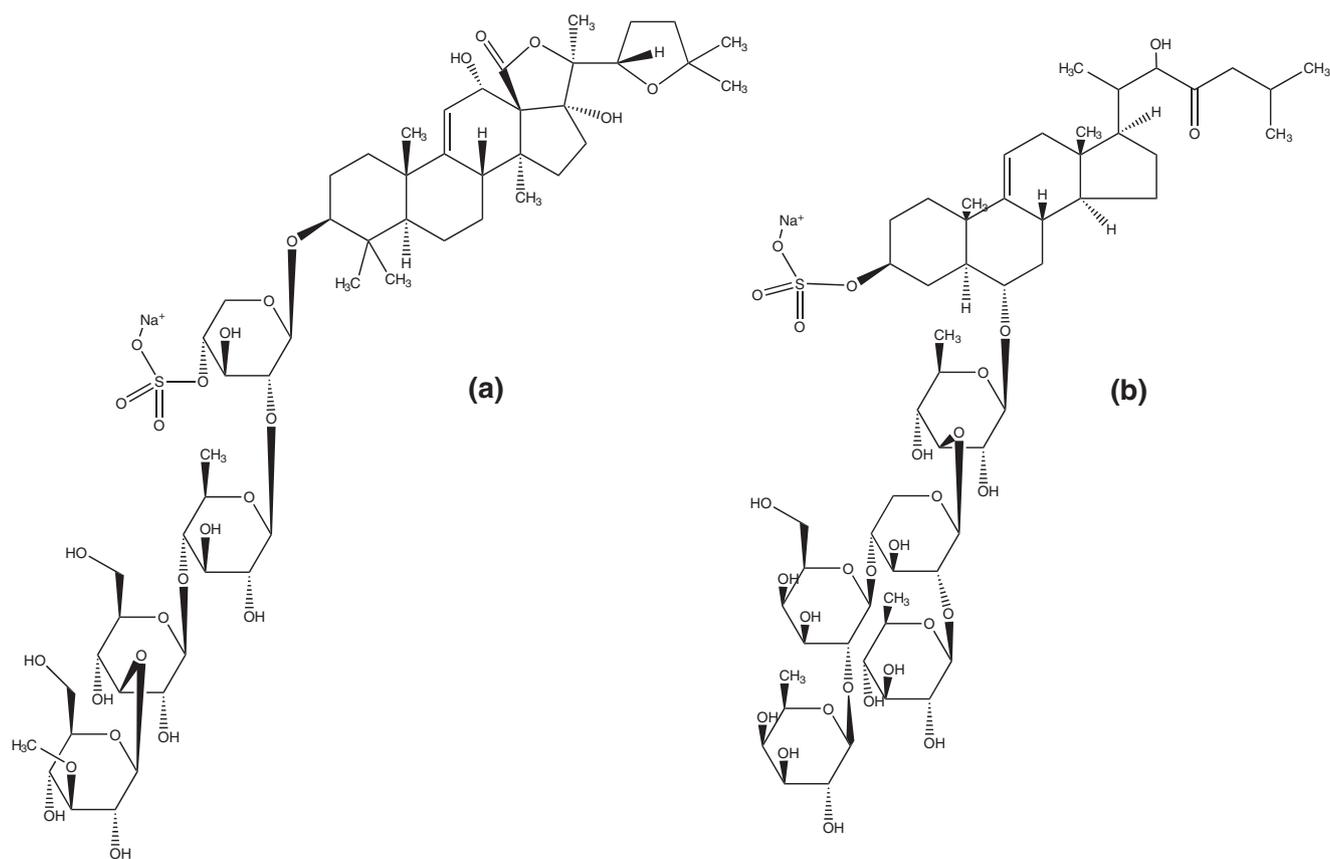


Fig. 7.4 Examples of (a) a triterpene glycoside structure: Holothurin A isolated from the sea cucumber *Holothuria leucospilota* (Kitagawa

et al. 1981d) and (b) a steroidal glycoside structure: Thornasteroside A isolated from the sea star *Acanthaster planci* (Kitagawa and Kobayashi 1978) (produced with ChemDraw, version 16.0.1.4 (77))

actions between aglycone components (i.e., sapogenin) and sterols of the cell membranes can result in a saponification process that may lead to cell lysis (Bahrami et al. 2016).

The sulfate group seems to be one of the most essential groups in most saponins derived from ophiuroids, asteroids (Table 7.2), and holothuroids (Table 7.3). However, there is a basic difference in the position of this functional group between echinoderms (Fig. 7.4). For both sea stars and brittle stars, the sulfate group is located in the hydrophobic part (aglycone) of the molecule, whereas in holothurians the sulfate group is placed within the hydrophilic moiety (glycone) (Kornprobst et al. 1998). The structural differences of asterosaponin and triterpene glycosides showed that not only the presence but also the position of the sulfate groups may be important, resulting in potentially different biological activities of saponins (Maier 2008; Malyarenko et al. 2015).

As the sea cucumbers contain the highest variety of saponin species, we will next (see Sect. 7.3.1) focus on the distribution and function of triterpene glycosides that have been reported exclusively from holothurians.

7.3.1 Structural Diversity of Saponins in Holothuroids

The first report of polar and low volatile triterpene glycosides within the animal kingdom was in 1952 and originated from a sea cucumber extract (Nigrelli and Zahl 1952). The initial studies on the bioactive properties of compounds derived from sea cucumbers explained the ichthyotoxic activities of saponins, which were extracted from the body wall and the CTs of *Holothuria leucospilota* and *Actinopyga agassizi* (Nigrelli and Jakowska 1960; Yamanouchi, 1955). Most of the subsequently identified saponins were mainly isolated from three families of sea cucumbers: Holothuriidae, Stichopodiidae, and Cucumariidae (see Table 7.3).

The chemical structure of saponins in holothurians can be very complex in terms of the presence/absence and position of different functional groups (e.g., hydroxyl groups), which may differentiate them from other echinoderms as well as from each other marine invertebrates (Bahrami et al. 2014). The generic name of holothurian-derived saponins is Holothurin, which are nearly all 3β -glycosylated saponins

(Kornprobst et al. 1998). In most sea cucumbers, triterpene glycosides contain the aglycone lanostane with an 18(20)-lactone (e.g., holostane 3 β -ol; Kalinin 2000; Caulier et al. 2011) and an oligosaccharide chain that consists of D-Xyl, D-Quinov, D-Glc, D-3-O-methyl-Glc, and D-3-O-methyl-Xyl (Caulier et al. 2011; Bahrami et al. 2016).

Triterpene glycosides exhibit different bioactivities, which might aid the likelihood of survival for its producing organisms. This is also highlighted by their broad bioactivities as well as their broad ecological functions (e.g., anti-predatory defense). Although the structure of each unit affects the bioactivity of the compound, linear oligosaccharide structures (i.e., tetraosides) have shown to be the optimum quantity of monosaccharide units in the glycoside (Minale et al. 1995; Kalinin et al. 2008). Furthermore, allelopathic properties of saponins, as well as the presence of various functional groups like amides, hydroxyl groups, acetyl groups, and sulfate groups in different species of sea cucumber, can inhibit larval attachment of macroorganisms and also affect the growth of different strains of gram-positive and gram-negative bacteria (Soliman et al. 2016). By changing the hydrophobic-hydrophilic balance of bacterial cells, extracted saponins may affect permeability and stability of the bacterial cell wall, which in turn can ultimately lead to cellular death (Lawrence et al., 1957; Soliman et al. 2016). Additionally, due to their hydrophilic properties, saponins regulate oocyte maturation and can thus affect the reproduction cycle of organism by synchronizing the maturation process (Kalinin et al. 2008).

The vast chemical diversity of saponin in sea cucumbers makes them effective models for studying their biochemical evolution and applying these compounds as potential holothurian chemotaxonomic markers (Kalinin et al. 1996, 2008; Kalinin 2000). Depending on the taxonomic group of sea cucumbers, the number, composition, and location of monosaccharide units, and position of functional groups in the holostane skeleton (i.e., hydroxyl, acetylate, sulfate, double bonds, etc.) may affect the bioactivity of the compounds (Stonik 1986; Kalinin 2000). For example, the presence of trisulfated glycosides in members of the family Cucumariidae is unique for this taxonomic group (Bahrami et al. 2016). Recent chemotaxonomic analysis supported the evolution of saponins in both glycone and aglycone moieties.

The general trend of glycone evolution in Holothuroidea is from non-sulfated to sulfated compounds. Bondoc et al. (2013) studied saponins from three species of Holothuroidea by using MALDI²-FTICR³ MS⁴ and nano-HPLC⁵-chip

Q-TOF⁶-MS, and by applying maximum likelihood analysis, molecular biology, and evolutionary software packages, they created mass chemical and genetic fingerprints of saponins. They concluded that evolution of saponins leads to glycone parts with higher membranolytic activities and hydrophilicity with lower metabolic cost (Kalinin and Stonik 1996; Bondoc et al. 2013; Kalinin et al. 2015). Therefore, the glycone evolution of Holothuroidea was likely in the following order (Kalinin et al. 2016):

1. Transition from non-sulfated to sulfated hexaoside or pentaosides
2. Changing from hexaoside and pentaosides to linear tetraosides and biosides:
 - (a) Carbohydrate contains sulfate group at C-4 of first xylose unit.
 - (b) Shifting sugars with C-6 Glc and 3-O-methyl-Glc to sulfated at C-4 of first xylose

Kalinin et al. (2015) mentioned that sulfated tetraosides are a common characteristic of Holothuria and Actinopyga; however, sea cucumbers of the genus *Bohadschia* contain both non-sulfated and sulfated carbohydrate units (i.e., hexaosides and tetraosides). Bivittoside D extracted from *Bohadschia vitiensis* is a hexaoside non-sulfated glycoside that evolved to a sulfated tetraoside (Holothurin A₂), which has been also found in *Holothuria scabra* (Dang et al. 2007) and *Pearsonothuria graeffei* (Zhao et al. 2011). Further structural modification leads to compounds with two monosaccharides (i.e., biosides such as echinoside B) from *Holothuria leucospilota* (Han et al. 2009a) and *Actinopyga echinites* (Kitagawa et al. 1985). The general direction of aglycone evolution is more complicated and depends on the presence or absence of lactone, keto, hydroxyl groups, as well as position of double bonds (Kalinin et al. 2015):

1. Presence/absence of lactone: It shifts from lanostane derivatives without lactone to lanostane with an 18(16)-lactone and holostane with an 18(20)-lactone.
2. Shifting the position of double bonds and the keto group. In general, transition of aglycones occurs from low oxidation to higher oxidized compounds.
 - (a) Transition of aglycone compounds having a 7(8) double bond, and a carbonyl group at C-16, to compounds oxidized at C-22 or C-23 without the oxygen at C-16
 - (b) Transition of aglycone molecule from 9(11) double bond and C-16 keto group to compounds having oxygen at C-16, and then to compounds without oxygen, but containing a 12 α -hydroxyl group

²Matrix-assisted laser desorption/ionization.

³Fourier transformation cyclotron resonance.

⁴Mass spectrometry.

⁵Nano-high-performance liquid chromatography.

⁶Quadrupole time-of-flight.

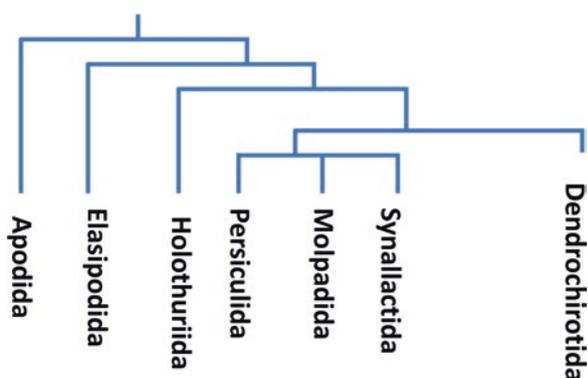


Fig. 7.5 Phylogeny of Holothuroidea. Produced based on Miller et al. (2017). Holothuriida is the new accepted name for the order of Aspidochirotida

Overall, based on morphological, molecular, and paleontological analysis, there has been a clear evolutionary distance between Apodida and other species of the orders Dendrochirotida and Holothuriida (Fig. 7.5; Avilov et al. 2008). Several studies reported that the presence of the 3-O-methyl group in the terminal monosaccharide units of holothurians (*Psolus fabricii*, *Cucumaria japonica*, *Hemoidema spectabilis*, etc.) increased the membranolytic activities of the compound. Kalinin et al. (2008) described that during evolution of the terminal monosaccharide unit from glucuronic acid (GlcA) to Glc, the 3-O-methyl group was conserved due to the protective properties against predatory fish.

A unique group of sea cucumbers are the Synallactida. They are mostly epibenthic and their remarkable defense behavior is shedding (Kropp 1982). Their typical chemical defenses are holotoxins, stichoposides, and stichlorosides (Table 7.3). The common characteristics of stichoposides and holotoxins are the presence of a double bond at C-25 (C-26), while the presence of α -acetoxy group at C-23 and a 3-O-methyl-D-Glc in their polysaccharide chain are another feature of stichoposides. The presence of a keto-group at C-16 is observed for most holotoxins. Interestingly, there is a sulfate group present in stichoposides (Mondol et al. 2017). Thus, the presence of a particular aglycone or glycone glycoside can be a taxonomic marker for certain genera such as the genera *Bohadschia*, *Pearsonothuria*, and *Actinopyga* (Kalinin et al. 2016). The presence, expellability, and stickiness of CTs of Holothuriidae (i.e., *Bohadschia argus*, *Holothuria forskali*) affect the chemical diversity of triterpene glycosides of the sea cucumbers (Honey-Escandón et al. 2015). Among Holothuriidae, the genus *Bohadschia* is considered a more primitive group since it contains well-developed CTs with expellability and stickiness and possesses non-sulfated and less-oxidized glycosides in both the CT and body wall (Kalinin et al. 1996, 2008; Honey-Escandón et al. 2015). In contrast, more sul-

fated and oxidized glycosides have been reported within species without CTs or with dysfunctional CTs such as *Holothuria hilla* and *Actinopyga echinites* (Honey-Escandón et al., 2015). However, members of Dendrochirotida and Apodida also showed different patterns. Species of the order Apodida such as *Synapta maculata* are considered the most primitive group of Holothurians. They contain 3-O-methyl Glc-A in a carbohydrate chain and an 8(9) double bond in the aglycone moiety, which affects their membranolytic activity and hydrophilicity of the glycosides (Avilov et al. 2008).

7.4 Discussion and Conclusions

Predation, the biological interaction where a predator eats its prey, is a main driving force for community structure and ecosystem organization (Duffy and Hay 2001). It has been suggested that before the development of physical defenses, echinoderms used initially maternally derived chemical defenses from early larval stages to protect themselves against predators (Iyengar and Harvell 2001). Therefore, secondary metabolites play an important role in chemical defense of marine sessile and slow moving organisms and thus may affect and shape the community structure and increase the level of biodiversity of the ecosystem (Paul et al. 2007). Unfortunately, there is still a lack of information with regard to the ecological function of many MNPs, especially from echinoderms, while various pharmacological activities (e.g., antiviral, antitumor) have been widely reported. This represents a research opportunity for chemical ecologists who want to investigate how small modifications in molecules can affect ecological functions and community structure.

As summarized in Table 7.2, echinoderms have proven to be a rich source of bioactive compounds with most reported compounds in Asteroids and Holothuroidea reported as saponins. Although various steroidal compounds of starfishes have been reported, only a few studies have investigated the biological activities of these compounds. Within ophiuroids, steroidal compounds, terpenes, and carotenoids have been isolated, and their mode of action has been summarized as antiviral and antitumor activities (Table 7.2).

The class Holothuria is a particularly rich source of MNPs with a multitude of reported activities. In the past decades, sea cucumbers have been increasingly harvested and consumed due to their nutritional values (high protein, low sugar, and no cholesterol (Liu et al. 2007, 2002; Wen et al. 2010) and their use in traditional medicine. Although a wide spectrum of bioactivities such as cytotoxic, hemolytic, antifungal, and immunomodulatory properties have been described for different sea cucumbers, in the extraction and compound purification process, often compounds with different chemical structures were combined, and thus the bio-

logical function of the individual compounds remain largely unknown. Therefore, their pharmaceutical potential has not yet been fully explored, which make them still promising candidates for the discovery of future MNPs with novel pharmaceutical applications. Furthermore, past studies focused largely on shallow-water holothurians, whereas deep-water specimens encounter particular harsh physico-chemical conditions. Such conditions include strong hydrostatic pressure, low temperature, and possibly oxygen shortage, which could affect formation, structure, gene regulation, and biosynthesis of secondary metabolites, thus making deep-water specimens a potential interesting target for future MNP screening campaigns.

Saponins are highly diverse, common, and abundant MNPs in echinoderms. Among this group of the secondary metabolites, holothurins, holotoxins, cucumariosides, and echinosids are the most abundant compounds in various genera of sea cucumbers (Table 7.3). Most of the reported triterpene glycosides in sea cucumbers showed cytotoxicity as well as antifouling, antifungal, and antibacterial effects of saponins (Miyamoto et al. 1990b; Aminin et al. 2015; Soliman et al. 2016), providing sea cucumbers with an effective chemical defense mechanism against microbial attacks, fouling organisms, and potentially predators.

The principal mechanisms for the bioactivities of triterpene glycosides are most likely changing membranolytic effects and increased hydrophilicity of the compounds, which may not only affect their bioactivities but also make them potential trophic and taxonomic markers. Depending on the marine habitat and the defensive responses of holothurians, each group contains their own special mixture of saponins, which are often unique chemical signatures and thus can be used in chemotaxonomy to differentiate most holothurians at the family level. Furthermore, by studying structure-activity relationships (SAR), taxonomists may be able to predict physiological differences and their ecological role within the organisms.

Defense responses of holothurians vary at order or family levels, which is to some extent reflected in the stereochemistry of the saponins. The general evolution of aglycone is based on the presence/absence or position of lactone, keto, hydroxyl groups, and double bonds, which leads from low oxidized to more oxidized compounds. The direction of glycone evolution depends on the presence/absence or number and position of sulfate and acetoxy groups, type of sugar units and their (non)linear structure, as well as position of methyl group. For example, Apodida are considered as the most primitive sea cucumbers due to the presence of 3-O-methyl Glc-A in the glycone and 8(9) double bond in the aglycone moiety. Among Holothuriida, *Bohadschia* is

the most primitive genus due to the presence of non-sulfated glycosides and functional CT.

In summary, studying the evolutionary pattern of structure-function relationships of holothurian's triterpene glycosides helps to understand their chemical-structural diversity, taxonomic distribution, ecological function, as well as bioactivity of the molecules, which can lead to a more targeted and efficient assessment of MNPs with novel pharmacological activities.

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Appendix

This article is related to the YOUMARES 9 conference session no. 9: "Biodiversity of Benthic Holobionts: Chemical Ecology and Natural Products Chemistry in the Spotlight." The original Call for Abstracts and the abstracts of the presentations within this session can be found in the Appendix "Conference Sessions and Abstracts", Chapter "7 Biodiversity of Benthic Holobionts: Chemical Ecology and Natural Products Chemistry in the Spotlight", of this book.

References

- Abraham TJ, Nagarajan J, Shanmugam SA (2002) Antimicrobial substances of potential biomedical importance from holothurian species. *Indian J Mar Sci* 31:161–164
- Afiyatullof SS, Tishchenko LY, Stonik VA et al (1985) Structure of cucumarioside G₁ - A new triterpene glycoside from the holothurian *Cucumaria fraudatrix*. *Chem Nat Compd* 21:228–232. <https://doi.org/10.1007/BF00714918>
- Agafonova IG, Aminin DL, Avilov SA et al (2003) Influence of Cucumariosides upon Intracellular [Ca²⁺]_i and Lysosomal Activity of Macrophages. *J Agric Food Chem* 51:6982–6986. <https://doi.org/10.1021/jf034439x>
- Al Marzouqi N, Iratni R, Nemmar A et al (2011) Frondoside A inhibits human breast cancer cell survival, migration, invasion and the growth of breast tumor xenografts. *Eur J Pharmacol* 668:25–34. <https://doi.org/10.1016/j.ejphar.2011.06.023>
- Al Shemali J, Mensah-Brown E, Parekh K et al (2014) Frondoside A enhances the antiproliferative effects of gemcitabine in pancreatic cancer. *Eur J Cancer* 50:1391–1398. <https://doi.org/10.1016/j.ejca.2014.01.002>
- Althunibat OY, Ridzwan BH, Taher M et al (2013) Antioxidant and cytotoxic properties of two sea cucumbers, *Holothuria edulis* Lesson and *Stichopus horrens* Selenka. *Acta Biol Hung* 64(1):10–20. <https://doi.org/10.1556/ABiol.64.2013.1.2>
- Amidi S, Hashemi Z, Motallebi A et al (2017) Identification of (Z)-2,3-diphenylacrylonitrile as anti-cancer molecule in Persian gulf sea cucumber *Holothuria parva*. *Mar Drugs* 15:1–14. <https://doi.org/10.3390/md15100314>

- Amini E, Nabiuni M, Baharara J et al (2014) Hemolytic and cytotoxic effects of saponin like compounds isolated from Persian Gulf brittle star (*Ophiocoma erinaceus*). *J Coast Life Med* 2:614–620. <https://doi.org/10.12980/JCLM.2.2014JCLM-2014-0056>
- Aminin DL (2016) Immunomodulatory properties of sea cucumber triterpene glycosides. In: Gopalakrishnakone P, Haddad V Jr, Tubaro A et al (eds) *Marine and Freshwater Toxins*. Springer, Dordrecht, pp 382–397
- Aminin DL, Agafonova IG, Fedorov SN (1995) Biological activity of disulphated polyhydroxysteroids from the pacific brittle star *Ophiopholis aculeata*. *Comp Biochem Physiol Part C Pharmacol Toxicol Endocrinol* 112C:201–204. [https://doi.org/10.1016/0742-8413\(95\)02012-8](https://doi.org/10.1016/0742-8413(95)02012-8)
- Aminin DL, Agafonova IG, Berdyshev EV et al (2001) Immunomodulatory properties of cucumariosides from the edible Far-Eastern holothurian *Cucumaria japonica*. *J Med Food* 4:127–135. <https://doi.org/10.1089/109662001753165701>
- Aminin DL, Pinegin BV, Pichugina LV et al (2006) Immunomodulatory properties of Cumaside. *Int Immunopharmacol* 6:1070–1082. <https://doi.org/10.1016/j.intimp.2006.01.017>
- Aminin DL, Agafonova IG, Kalinin VI et al (2008) Immunomodulatory properties of frondoside A, a major triterpene glycoside from the north Atlantic commercially harvested sea cucumber *Cucumaria frondosa*. *J Med Food* 11:443–453. <https://doi.org/10.1089/jmf.2007.0530>
- Aminin DL, Silchenko AS, Avilov SA et al (2010) Immunomodulatory action of monosulfated triterpene glycosides from the sea cucumber *Cucumaria okhotensis*: stimulation of activity of mouse peritoneal macrophages. *Nat Prod Commun* 5:1877–1880
- Aminin DL, Zaporozhets TA, Avilov S et al (2011) Radioprotective properties of cumaside, a complex of triterpene glycosides from the sea cucumber *Cucumaria japonica* and cholesterol. *Nat Prod Commun* 6:587–592
- Aminin DL, Menchinskaya ES, Pislugin EA et al (2015) Anticancer activity of sea cucumber triterpene glycosides. *Mar Drugs* 13:1202–1223. <https://doi.org/10.3390/md13031202>
- Andriyashchenko PV, Levina EV, Kalinovskii AI (1996) Steroid compounds from the Pacific starfishes *Luidia quinaria* and *Distolasterias elegans* CA125:86975. *Russ Chem Bull* 45:455–458. <https://doi.org/10.1007/BF01433994>
- Anisimov MM, Fronert EB, Kuznetsova TA et al (1973) The toxic effect of triterpene glycosides from *Stichopus japonicus* selenka on early embryogenesis of the sea urchin. *Toxicon* 11:109–111. [https://doi.org/10.1016/0041-0101\(73\)90163-3](https://doi.org/10.1016/0041-0101(73)90163-3)
- Anisimov MM, Shcheglov VV, Stonik VA et al (1974) The toxic effect of cucumarioside C from *Cucumaria fraudatrix* on early embryogenesis of the sea urchin. *Toxicon* 12:327–329
- Anisimov MM, Prokofieva NG, Korotkikh LY et al (1980) Comparative study of cytotoxic activity of triterpene glycosides from marine organisms. *Toxicon* 18:221–223
- Anisimov MM, Aminin DL, Rovin YG et al (1983) On the resistance of the cells of the sea cucumber *Stichopus japonicus* on the action of endotoxinstichoposide A. *Dokl AN SSSR* 270:991–993
- Antonov A, Avilov S, Kalinovskiy A (2008) Triterpene glycosides from Antarctic sea cucumbers. 1. Structure of Liouvillosides A₁, A₂, A₃, B₁, and B₂ from the sea cucumber *Staurocucumis liouvillei*: new procedure for separation of highly polar glycoside fractions and taxonomic revision. *J Nat* 71:1677–1685. <https://doi.org/10.1021/np800173c>
- Antonov AS, Avilov SA, Kalinovskiy AI et al (2009) Triterpene glycosides from antarctic sea cucumbers. 2. structure of Liouvillosides A₁, A₂, A₃ from the sea cucumber *Achlionice violaecuspidata* (= *Rhipidothuria racowitzai*). *J Nat Prod* 72:33–38
- Antonov AS, Avilov SA, Kalinovskiy AI et al (2011) Triterpene glycosides from Antarctic sea cucumbers III. Structures of liouvillosides A₄ and A₅, two minor disulphated tetraosides containing 3-O-methylquinovose as terminal monosaccharide units from the sea cucumber *Staurocucumis liouvillei* (Vaney). *Nat Prod Res* 25:1324–1333. <https://doi.org/10.1080/14786419.2010.531017>
- Attouf S, Arafat K, Gélaude A et al (2013) Frondoside A Suppressive Effects on Lung Cancer Survival, Tumor Growth, Angiogenesis, Invasion, and Metastasis. *PLoS One* 8:1–10. <https://doi.org/10.1371/journal.pone.0053087>
- Auria MVD, Riccio R, Minale L et al (1987) Novel marine steroid sulphates from Pacific Ophiuroids. *Org Chem* 52:3947–3952. <https://doi.org/10.1021/jo00227a001>
- Avilov SA, Kalinovskiy AI, Stonik VA (1991a) Two new triterpene glycosides from the holothurian *Duasmodyctyla kurilensis*. *Chem Nat Compd* 27:188–192
- Avilov SA, Stonik VA, Kalinovskii AI (1991b) Structures of four new triterpene glycosides from the holothurian *Cucumaria japonica*. *Chem Nat Compd* 26:670–675. <https://doi.org/10.1007/BF00630079>
- Avilov SA, Kalinin VI, Makarieva TN et al (1994) Structure of cucumarioside G₂, a novel nonholostane glycoside from the sea cucumber *Eupentacta fraudatrix*. *J Nat Prod* 57:1166–1171. <https://doi.org/10.1021/np50110a007>
- Avilov SA, Kalinovskiy AI, Kalinin VI et al (1997) Koreoside A, a new nonholostane triterpene glycoside from the sea cucumber *Cucumaria koraiensis*. *J Nat Prod* 60:808–810. <https://doi.org/10.1021/np970152g>
- Avilov SA, Drozdova OA, Kalinin VI et al (1998) Frondoside C, a new nonholostane triterpene glycoside from the sea cucumber *Cucumaria frondosa*: structure and cytotoxicity of its desulfated derivative. *Sect Title Carbohydrates* 76:137–141. <https://doi.org/10.1139/cjc-76-2-137>
- Avilov SA, Antonov AS, Drozdova OA et al (2000a) Triterpene glycosides from the far eastern sea cucumber *Pentamera calcigera* II: Disulfated glycosides. *J Nat Prod* 63:1349–1355. <https://doi.org/10.1021/np000002x>
- Avilov SA, Antonov AS, Drozdova OA et al (2000b) Triterpene glycosides from the Far-Eastern sea cucumber *Pentamera calcigera*. 1. Monosulphated glycosides and cytotoxicity of their unsulfated derivatives. *J Nat Prod* 63:65–71. <https://doi.org/10.1021/np9903447>
- Avilov SA, Antonov AS, Silchenko AS et al (2003) Triterpene glycosides from the Far Eastern sea cucumber *Cucumaria conicospermium*. *J Nat Prod* 66:910–916. <https://doi.org/10.1021/np030005k>
- Avilov SA, Silchenko AS, Antonov AS et al (2008) Synaptosides A and A1, triterpene glycosides from the sea cucumber *Synapta maculata* containing 3-O-methylglucuronic acid and their cytotoxic activity against tumor cells. *J Nat Prod* 71:525–531
- Bahrami Y, Franco C (2015) Structure Elucidation of New Acetylated Saponins, Lessoniosides A, B, C, D, and E, and Non-Acetylated Saponins, Lessoniosides F and G, from the Viscera of the Sea Cucumber *Holothuria lessoni*. *Mar Drugs* 13:597–617. <https://doi.org/10.3390/md13010597>
- Bahrami Y, Zhang W, Franco C (2014) Discovery of novel saponins from the viscera of the sea cucumber *Holothuria lessoni*. *Mar Drugs* 12:2633–2667. <https://doi.org/10.3390/md12052633>
- Bahrami Y, Franco CMM, Benkendorff K (2016) Acetylated triterpene glycosides and their biological activity from holothuroidea reported in the past six decades. *Mar Drugs* 14:1–38. <https://doi.org/10.3390/md14080147>
- Batrakov SG, Girshovich ES, Drozhzhina NS (1980) Triterpene glycosides with antifungal activity isolated from the sea cucumber, *Cucumaria japonica*. *Antibiotiki* 25:408–411
- Beauregard KA, Truong NT, Zhang H et al (2001) The Detection and Isolation of a Novel Antimicrobial Peptide from an Echinoderm, *Cucumaria frondosa*. *Adv Exp Med Biol* 484:55–62. <https://doi.org/10.1007/978-1-4615-1291-2>

- Berdyshev DV, Glazunov VP, Novikov VL (2007) 7-Ethyl-2,3,5,6,8-pentahydroxy-1,4-naphthoquinone (echinochrome A): A DFT study of the antioxidant mechanism. 1. Interaction of echinochrome A with hydroperoxyl radical. *Russ Chem Bull* 56:413–429. <https://doi.org/10.1007/s11172-007-0067-3>
- Bhakuni DS, Rawat DS (2005) *Bioactive Marine Natural Products*. Springer, Dordrecht/Publishers, New Dehli
- Bhatnagar S, Dudouet B, Ahond A et al (1985) Invertébrés marins du lagon Neocaledonien IV. Saponines et sapogénines d'une holothurie, *Actinopyga flammea*. *Bull Soc Chim Fr*:124–129
- Blunt JW, Carroll AR, Copp BR et al (2018) Marine natural products. *Nat Prod Rep* 35:8–53
- Bondoc KGV, Lee H, Cruz LJ et al (2013) Chemical fingerprinting and phylogenetic mapping of saponin congeners from three tropical holothurian sea cucumbers. *Comp Biochem Physiol B Biochem Mol Biol* 166:182–193. <https://doi.org/10.1016/j.cbpb.2013.09.002>
- Bordbar S, Anwar F, Saari N (2011) High-value components and bioactives from sea cucumbers for functional foods - A review. *Mar Drugs* 9:1761–1805. <https://doi.org/10.3390/md9101761>
- Borsig L, Wang L, Cavalcante MCM et al (2007) Selectin blocking activity of a fucosylated chondroitin sulfate glycosaminoglycan from sea cucumber: Effect on tumor metastasis and neutrophil recruitment. *J Biol Chem* 282:14984–14991. <https://doi.org/10.1074/jbc.M610560200>
- Bruno I, Minale L, Pizza C et al (1984) Starfish saponins. Part 14. Structures of the steroidal glycoside sulphated from the starfish *Marthasterias glacialis*. *J Chem Soc Perkin Trans I* 0: 1875–1883
- Bruno I, D'Auria MV, Iorizzi M et al (1992) Marine eicosanoids: Occurrence of 8,11,12-trihydroxylated eicosanoic acids in starfishes. *Experientia* 48:114–115. <https://doi.org/10.1007/BF01923622>
- Bryan PJ, McClintock JB, Hopkins TS (1997) Structural and chemical defenses of echinoderms from the northern Gulf of Mexico. *Exp Mar Biol Ecol* 210:173–186
- Candia Carnevali MD, Bonasoro F (2001) Introduction to the biology of regeneration in echinoderms. *Microsc Res Tech* 55:365–368. <https://doi.org/10.1002/jemt.1184>
- Careaga VP, Muniain C, Maier MS (2011) Patagonicosides B and C, two antifungal sulphated triterpene glycosides from the sea cucumber *Psolus patagonicus*. *Chem Biodivers* 8:467–475
- Careaga VP, Bueno C, Muniain C et al (2014) Pseudocnoside A, a new cytotoxic and antiproliferative triterpene glycoside from the sea cucumber *Pseudocnus dubiosus leoninus*. *Nat Prod Res* 28:213–220. <https://doi.org/10.1080/14786419.2012.751596>
- Caulier G, Van Dyck S, Gerbaux P et al (2011) Review of saponin diversity in sea cucumbers belonging to the family Holothuriidae. *SPC Beche-de-mer Inf Bull* 31:48–54
- Chanley JD, Ledeen R, Wax J et al (1959) Holothurin. I. The Isolation, Properties and Sugar Components of Holothurin A. *Am Chem Soc* 81:5180–5183. <https://doi.org/10.1021/ja01528a040>
- Chen LC, Lin YY, Jean YH et al (2014) Anti-inflammatory and analgesic effects of the marine-derived compound comarparvin isolated from the crinoid: *Comanthus bennetti*. *Molecules* 19:14667–14686. <https://doi.org/10.3390/molecules190914667>
- Cheng G, Zhang X, Tang H-F et al (2006) Asterosaponin 1, a cytostatic compound from the starfish *Culcita novaeguineae*, functions by inducing apoptosis in human glioblastoma U87MG cells. *J Neurooncol* 79:235–241. <https://doi.org/10.1007/s11060-006-9136-y>
- Chludil HD, Muniain CC, Seldes AM et al (2002a) Cytotoxic and antifungal triterpene glycosides from the Patagonian sea cucumber *Hemoiedema spectabilis*. *J Nat Prod* 65:860–865. <https://doi.org/10.1021/np0106236>
- Chludil HD, Seldes AM, Maier MS (2002b) Antifungal steroidal glycosides from the Patagonian starfish *Anasterias minuta*: Structure - activity correlations. *J Nat Prod* 65:153–157. <https://doi.org/10.1021/np010332x>
- Chovolou Y, Ebada SS, Wätjen W et al (2011) Identification of angular naphthopyrones from the Philippine echinoderm *Comanthus* species as inhibitors of the NF- κ B signaling pathway. *Eur J Pharmacol* 657:26–34. <https://doi.org/10.1016/j.ejphar.2011.01.039>
- Clemente S, Hernández JC, Montañó-Moctezuma G et al (2013) Predators of juvenile sea urchins and the effect of habitat refuges. *Mar Biol* 160:579–590. <https://doi.org/10.1007/s00227-012-2114-3>
- Comin MJ, Maier MS, Roccatagliata AJ et al (1999) Evaluation of the antiviral activity of natural sulphated polyhydroxysteroids and their synthetic derivatives and analogs. *Steroids* 64:335–340. [https://doi.org/10.1016/S0039-128X\(99\)00016-1](https://doi.org/10.1016/S0039-128X(99)00016-1)
- Croteau R, Kutchan TM, Lewis NG (2000) Natural products (Secondary Metabolites). *Biochem Mol Biol Plants* 7:1250–1318. <https://doi.org/10.1016/j.phytochem.2011.10.011>
- Cuong NX, Vien LT, Hanh TTH et al (2015) Cytotoxic triterpene saponins from *Cercodemas anceps*. *Bioorg Med Chem Lett* 25:3151–3156. <https://doi.org/10.1016/j.bmcl.2015.06.005>
- Cuong NX, Vien LT, Hoang L et al (2017) Cytotoxic triterpene diglycosides from the sea cucumber *Stichopus horrens*. *Bioorg Med Chem Lett* 27:2939–2942. <https://doi.org/10.1016/j.bmcl.2017.05.003>
- D'Auria MV, Riccio R, Minale L (1985) Ophioxanthin, a new marine carotenoid sulphate from the Ophiuroid *Ophioderma longicaudum*. *Tetrahedron Lett* 26:1871–1872
- D'Auria MV, Riccio R, Minale L et al (1987) Novel marine steroid sulphates from pacific ophiuroids. *J Org Chem* 52(18):3947–3952. <https://doi.org/10.1021/jo00227a001>
- D'Auria MV, Maria I, Minale L et al (1990) Starfish saponins part 40. Structures of two new Asterosaponins from the starfish *Patritia miniata*: Patirioside A, and Patirioside B. *J Chem Soc Perkin Trans I* 1:1019–1023
- D'Auria MV, Minale L, Riccio R (1993) Polyoxygenated Steroids of Marine Origin. *Chem Rev* 93:1839–1895. <https://doi.org/10.1021/cr00021a010>
- Dai Y, Yu B (2015) Total synthesis of astrosteroside A, an anti-inflammatory asterosaponin. *Chem Commun* 51:13826–13829. <https://doi.org/10.1039/C5CC04734J>
- Dang NH, Van Thanh N, Van Kiem P et al (2007) Two New Triterpene Glycosides from the Vietnamese Sea Cucumber *Holothuria scabra*. *Arch Pharm Res* 30:1387–1391. <https://doi.org/10.1007/BF02977361>
- De Correa RS, Duque C, Riccio R et al (1985) Starfish saponins, Part 21. Steroidal glycosides from the starfish *Oreaster Reticulatus*. *J Nat Prod* 48:751–755. <https://doi.org/10.1021/np50041a006>
- De Marino S, Iorizzi M, Zollo F et al (2000) Three new asterosaponins from the starfish *Goniopecten demonstrans*. *European J Org Chem* 2000:4093–4098. [https://doi.org/10.1002/1099-0690\(200012\)2000:24<4093::AID-EJOC4093>3.0.CO;2-M](https://doi.org/10.1002/1099-0690(200012)2000:24<4093::AID-EJOC4093>3.0.CO;2-M)
- De Marino S, Borbone N, Iorizzi M et al (2003) Bioactive asterosaponins from the starfish *Luidia quinaria* and *Psilaster cassiope*. Isolation and structure characterization by two-dimensional NMR spectroscopy. *J Nat Prod* 66:515–519. <https://doi.org/10.1021/np0205046>
- De Moncerrat Iñiguez-Martinez AM, Guerra-Rivas G, Rios T et al (2005) Triterpenoid oligoglycosides from the sea cucumber *Stichopus parvimensis*. *J Nat Prod* 68:1669–1673. <https://doi.org/10.1021/np050196m>
- De Riccardis F, Giovannitti B, Iorizzi M, Minale L, Riccio R, Debitus C, De FBR (1991) Sterol Composition of the “ Living Fossil ” Crinoid *Gymnocrinus richeri*. *Comp Biochem Physiol B Comp Biochem* 100:647–651
- De Simone F, Dini A, Minale L et al (1980) The Sterols of the Asteroid *Echinaster sepositus*. *Comp Biochem Physiol B Biochem Mol Biol* 66:351–357
- De Simone F, Dini A, Finamore E et al (1981) Starfish saponins. Part 5. Structure of sepositoside A, a novel steroidal cyclic glycoside from the starfish *Echinaster sepositus*. *J Chem Soc Perkin Trans I* 1:1855–1862. <https://doi.org/10.1039/P19810001855>

- de Vivar M, Maier M, Seldes AM (1999) Polar metabolites from the Antarctic starfish *Labidiaster annulatus*. An des la Asoc Quim Argentina 87:247–253
- Demeyer M, De WJ, Caulier G et al (2014) Molecular diversity and body distribution of saponins in the sea star *Asterias rubens* by mass spectrometry. Comp Biochem Physiol B Biochem Mol Biol 168:1–11. <https://doi.org/10.1016/j.cbpb.2013.10.004>
- Dong G, Xu T, Yang B et al (2011) Chemical constituents and bioactivities of starfish. Chem Biodivers 8:740–791. <https://doi.org/10.1002/cbdv.200900344>
- Drozдова OA, Avilov SA, Kalinovskii AI et al (1993) New glycosides from the holothurian *Cucumaria japonica*. Chem Nat Compd 29:200–205
- Drozдова OA, Avilov SA, Kalinin VI et al (1997) Cytotoxic triterpene glycosides from far-eastern sea cucumbers belonging to the genus *Cucumaria*. Liebig's Ann 1997:2351–2356. <https://doi.org/10.1002/jlac.199719971125>
- Du L, Xu J, Xue Y et al (2015) Cerebrosides from sea cucumber ameliorates cancer-associated cachexia in mice by attenuating adipose atrophy. J Funct Foods 17:352–363. <https://doi.org/10.1016/j.jff.2015.05.040>
- Duan J, Ishida M, Aida K et al (2016) Dietary cerebroside from sea cucumber (*Stichopus japonicus*): absorption and effects on skin barrier and cecal short-chain fatty acids. J Agric Food Chem 64:7014–7021. <https://doi.org/10.1021/acs.jafc.6b02564>
- Dubois M-A, Noguchi Y, Higuchi R et al (1988) Structures of two new oligoglycoside sulfates: Pectinoside C and pectinoside D. Liebig's Ann 1988:495–500. <https://doi.org/10.1002/jlac.198819880603>
- Duffy JE, Hay ME (2001) The ecology and evolution of marine consumer-prey interactions. In: Bertness MD, Hay ME, Gaines SD (eds) Marine community ecology. Sinauer Associates, Sunderland, pp 131–157
- Elbandy M, Rho JR, Afifi R (2014) Analysis of saponins as bioactive zoochemicals from the marine functional food sea cucumber *Bohadschia cousteaui*. Eur Food Res Technol 238:937–955. <https://doi.org/10.1007/s00217-014-2171-6>
- Esmat AY, Said MM, Soliman AA et al (2013) Bioactive compounds, antioxidant potential, and hepatoprotective activity of sea cucumber (*Holothuria atra*) against thioacetamide intoxication in rats. Nutrition 29:258–267. <https://doi.org/10.1016/j.nut.2012.06.004>
- Farshadpour F, Gharibi S, Taherzadeh M et al (2014) Antiviral activity of *Holothuria* sp. a sea cucumber against herpes simplex virus type 1 (HSV-1). Eur Rev Med Pharmacol Sci 18:333–337
- Fedorov SN, Shubina LK, Kicha AA et al (2008) Proapoptotic and Anticarcinogenic Activities of Leviusculoside G from the Starfish *Henricia leviuscula* and Probable Molecular Mechanism. Nat Prod Commun 3:1575–1580
- Fedorov SN, Dyshlovoy SA, Kuzmich AS et al (2016) In vitro anticancer activities of some triterpene glycosides from holothurians of Cucumariidae, Stichopod, Psolidae, Holothuriidae, and Synaptidae families. Nat Prod Commun 11:1239–1242
- Feng Y, Khokhar S, Davis RA (2017) Crinoids: ancient organisms, modern chemistry. Nat Prod Rep 34:571–584. <https://doi.org/10.1039/C6NP00093B>
- Fieser LF, Fieser M (1956) Organic chemistry. Reinhold, New York
- Finamore E, Minale L, Riccio R et al (1991) Novel marine polyhydroxylated steroids from the starfish *Myxoderma platyacanthum*. J Org Chem 56:1146–1153. <https://doi.org/10.1021/jo00003a043>
- Findlay JA, Agarwal VK (1983) Aglycones from the saponin of the starfish *Asterias vulgaris*. J Nat Prod 46:876–880. <https://doi.org/10.1021/np50030a008>
- Findlay JA, He ZQ (1991) Polyhydroxylated steroidal glycosides from the starfish *Asterias forbesi*. J Nat Prod 54:428–435. <https://doi.org/10.1021/np50074a013>
- Findlay JA, Jaseja M, Burnell DJ (1987) Major saponins from the starfish *Asterias forbesi*. Complete structures by nuclear magnetic resonance methods. Can J Chem 65:1384–1391. <https://doi.org/10.1139/v87-234>
- Findlay JA, Findlay A, Findlay A et al (1989) Forbeside E: a novel sulphated sterol glycoside from *Asterias forbesi*. Can J Chem 67:2078–2080
- Findlay JA, He Z-Q, Blackwell B (1990) Minor saponins from the starfish *Asterias forbesi*. Can J Chem 68:1215–1217. <https://doi.org/10.1139/v90-188>
- Findlay JA, Yayli N, Radics L (1992) Novel sulfated oligosaccharides from the sea cucumber *cucumaria frondosa*. J Nat Prod 55:93–101. <https://doi.org/10.1021/np50079a014>
- Folmer F, Jaspars M, Solano G et al (2009) The inhibition of TNF- α -induced NF- κ B activation by marine natural products. Biochem Pharmacol 78:592–606. <https://doi.org/10.1016/j.bcp.2009.05.009>
- Francis G, Kerem Z, Makkar HPS et al (2002) The biological action of saponins in animal systems: a review. Br J Nutr 88:587. <https://doi.org/10.1079/BJN2002725>
- Garneau FX, Harvey C, Simard JL et al (1989) The distribution of asterosaponins in various body components of the starfish *Leptasterias polaris*. Comp Biochem Physiol B Biochem Mol Biol 92:411–416. [https://doi.org/10.1016/0305-0491\(89\)90302-7](https://doi.org/10.1016/0305-0491(89)90302-7)
- Ghanbari R, Ebrahimpour A, Abdul-Hamid A et al (2012) *Actinopyga lecanora* hydrolysates as natural antibacterial agents. Int J Mol Sci 13:16796–16811. <https://doi.org/10.3390/ijms131216796>
- Ghannouch MA, Rice LB (1999) Antifungal agents: Mode of action, mechanisms of resistance, and correlation of these mechanisms with bacterial resistance. Clin Microbiol Rev 12:501–517. doi:10.1128/9.2.501-517
- Girard M, Bélanger J, ApSimon JW et al (1990) Frondoside A. A novel triterpene glycoside from the holothurian *Cucumaria frondosa*. Can J Chem 68:11–18. <https://doi.org/10.1139/v90-003>
- Gorshkova BA, Gorshkova IA, Stonik VA et al (1982) Effect of marine glycosides on adenosinetriphosphatase activity. Toxicol 20:655–658. [https://doi.org/10.1016/0041-0101\(82\)90059-9](https://doi.org/10.1016/0041-0101(82)90059-9)
- Gorshkova IA, Gorshkov BA, Stonik VA (1989) Inhibition of rat brain Na⁺-K⁺-ATPase by triterpene glycosides from holothurians. Toxicol 27:927–936. [https://doi.org/10.1016/0041-0101\(89\)90104-9](https://doi.org/10.1016/0041-0101(89)90104-9)
- Gorshkova IA, Kalinin VI, Gorshkov BA et al (1999) Two different modes of inhibition of the rat brain Na⁺, K⁺-ATPase by triterpene glycosides, psolusosides A and B from the Holothurian *Psolus fabricii*. Comp Biochem Physiol C Pharmacol Toxicol Endocrinol 122:101–108. [https://doi.org/10.1016/S0742-8413\(98\)10085-3](https://doi.org/10.1016/S0742-8413(98)10085-3)
- Gowda NM, Goswami U, Khan MI (2008) T-antigen binding lectin with antibacterial activity from marine invertebrate, sea cucumber (*Holothuria scabra*): Possible involvement in differential recognition of bacteria. J Invertebr Pathol 99:141–145. <https://doi.org/10.1016/j.jip.2008.04.003>
- Grishin Y, Besednova NN, Stonik VA et al (1990) The regulation of hemopoiesis and immunogenesis by triterpene glycosides from holothurians. Radiobiologija 30:556
- Guenther J, Wright AD, Burns K et al (2009) Chemical antifouling defences of sea stars: Effects of the natural products hexadecanoic acid, cholesterol, lathosterol and sitosterol. Mar Ecol Prog Ser 385:137–149. <https://doi.org/10.3354/meps08034>
- Guo D, Xiong Y (2009) Preparation and characterization of *Holothuria nobilis* saponins nobilside A freeze-dried liposome CA152:19119. Dier Junyi Daxue Xuebao 30:202–207
- Han C, Qi J, Ojika M (2006) Structure–activity relationships of novel neurotogenic steroid glycosides from the Okinawan starfish *Linckia laevigata*. Bioorg Med Chem 14:4458–4465. <https://doi.org/10.1016/j.bmc.2006.02.032>
- Han C, Qi J, Ojika M (2007a) Linckosides M-Q: Neurotogenic steroid glycosides from the Okinawan starfish *Linckia laevigata*. J Nat Med 61:138–145. <https://doi.org/10.1007/s11418-006-0107-6>

- Han H, Yi YH, Li L et al (2007b) A new triterpene glycoside from sea cucumber *Holothuria leucospilota*. Chinese Chem Lett 18:161–164. <https://doi.org/10.1016/j.ccllet.2006.12.027>
- Han H, Yi Y, La M et al (2008a) Studies on antifungal and antitumor activities of scabraside A, B from *Holothuria scabra* Jaeger. Zhongguo Yaoxue Tongbao 24:1111–1112
- Han H, Yi YH, Liu BS et al (2008b) Leucospilotoside C, a new sulphated triterpene glycoside from sea cucumber *Holothuria leucospilota*. Chinese Chem Lett 19:1462–1464. <https://doi.org/10.1016/j.ccllet.2008.09.051>
- Han H, Yi Y-H, Li L et al (2009a) Triterpene Glycosides from Sea Cucumber *Holothuria leucospilota*. Chin J Nat Med 7:346–350. <https://doi.org/10.3724/SP.J.1009.2009.00346>
- Han H, Yi Y, Li L et al (2009b) Antifungal active triterpene glycosides from sea cucumber *Holothuria scabra*. Acta Pharmaceutica Sinica 44(6):620–624
- Han H, Xu Q-Z, Tang H-F et al (2010a) Cytotoxic Holostane-Type Triterpene Glycosides from the Sea Cucumber *Pentacta quadrangularis*. Planta Med 76:1900–1904. <https://doi.org/10.1055/s-0030-1249854>
- Han H, Zhang W, Yi YH et al (2010b) A novel sulphated holostane glycoside from sea cucumber *Holothuria leucospilota*. Chem Biodivers 7:1764–1769. <https://doi.org/10.1002/cbdv.200900094>
- Han H, Xu QZ, Yi YH et al (2010c) Two new cytotoxic disulphated holostane glycosides from the sea cucumber *Pentacta quadrangularis*. Chem Biodivers 7:158–167. <https://doi.org/10.1002/cbdv.200800324>
- Han H, Li L, Yi Y et al (2012) Triterpene Glycosides from Sea Cucumber *Holothuria scabra* with Cytotoxic Activity. Chinese Herb Med 4:183–188. <https://doi.org/10.3969/j.issn.1674-6384.2012.03.002>
- Harvey C, Garneau FX, Himmelman JH (1987) Chemodetection of the predatory seastar *Leptasterias polaris* by the whelk *Buccinum undatum*. Mar Ecol Prog Ser 40:79–86
- Hatakeyama T, Kamine T, Konishi Y et al (1999) Carbohydrate-dependent hemolytic activity of the conjugate composed of a C-type lectin, CEL-I, and an amphiphilic α -helical peptide, 43- β Ala₂. Biosci Biotechnol Biochem 63:1312–1314. <https://doi.org/10.1271/bbb.63.1312>
- Haug T, Kjuul AK, Styrvold OB et al (2002) Antibacterial activity in *Strongylocentrotus droebachiensis* (Echinoidea), *Cucumaria frondosa* (Holothuroidea), and *Asterias rubens* (Asteroidea). J Invertebr Pathol 81:94–102. [https://doi.org/10.1016/S0022-2011\(02\)00153-2](https://doi.org/10.1016/S0022-2011(02)00153-2)
- Hegde VR, Chan TM, Pu H et al (2002) Two selective novel triterpene glycosides from sea cucumber, *Thelecantha ananas*: inhibitors of chemokine receptor-5. Bioorganic Med Chem Lett 12:3203–3205
- Herencia F, Ubeda A, Ferrandiz ML et al (1998) Anti-inflammatory activity in mice of extracts from mediterranean marine invertebrates. Pharmacol Lett 62:115–120
- Hickman CP, Roberts L, Larson A (2001) Integrated principles of zoology. Mosby Publishers, St. Louis
- Higuchi R, Fujita M, Matsumoto S et al (1996) Isolation and structure of four new steroid glycoside Di-O-sulphates from the starfish *Asteropecten latespinosus*. Liebigs Ann 1996:837–840
- Honda M, Igarashi T, Komori T (1990) Structure of Pectinoside C: determination of the stereochemistry of the C-17 side chain of the steroidal aglycone. Liebigs Ann 1990:547–553
- Honey-Escandón M, Arreguín-Espinosa R, Solís-Marín FA et al (2015) Biological and taxonomic perspective of triterpenoid glycosides of sea cucumbers of the family Holothuriidae (Echinodermata, Holothuroidea). Comp Biochem Physiol Part B Biochem Mol Biol 180:16–39. <https://doi.org/10.1016/j.cbpb.2014.09.007>
- Hu X-Q, Wang YM, Wang JF et al (2010) Dietary saponins of sea cucumber alleviate orotic acid-induced fatty liver in rats via PPAR α and SREBP-1c signaling. Lipids Health Dis 9:25. <https://doi.org/10.1186/1476-511X-9-25>
- Hu S, Chang Y, He M et al (2014a) Fucosylated chondroitin sulfate from sea cucumber improves insulin sensitivity via activation of PI3K/PKB pathway. J Food Sci 79:H1424–H1427. <https://doi.org/10.1111/1750-3841.12465>
- Hu S, Xu L, Shi D et al (2014b) Eicosapentaenoic acid-enriched phosphatidylcholine isolated from *Cucumaria frondosa* exhibits anti-hyperglycemic effects via activating phosphoinositide 3-kinase/protein kinase B signal pathway. J Biosci Bioeng 117:457–463. <https://doi.org/10.1016/j.jbiosc.2013.09.005>
- Huang N, Wu MY, Zheng CB et al (2013) The depolymerized fucosylated chondroitin sulfate from sea cucumber potently inhibits HIV replication via interfering with virus entry. Carbohydr Res 380:64–69. <https://doi.org/10.1016/j.carres.2013.07.010>
- Husni A, Shin IS, You S et al (2009) Antioxidant Properties of Water and Aqueous Ethanol Extracts and Their Crude Saponin Fractions from a Far-eastern Sea Cucumber, *Stichopus japonicus*. Food Sci Technol 18:419–424
- Hwang IH, Kim WD, Kim SJ et al (2011) Asterosaponins Isolated from the Starfish *Asterias amurensis*. Chem Pharm Bull 59:78–83
- Hwang IH, Kulkarni R, Yang MH et al (2014) Complete NMR assignments of undegraded asterosaponins from *Asterias amurensis*. Arch Pharm Res 37:1252–1263. <https://doi.org/10.1007/s12272-014-0374-9>
- Ikedai Y, Inagaki M, Yamada K et al (2009) Isolation and structure of a galactocerebroside from the sea cucumber *Bohadschia argus*. Chem Pharm Bull (Tokyo) 57:315–317. <https://doi.org/10.1248/cpb.57.315>
- Ikegami S, Kamiya Y, Tamura S (1973) Studies on Asterosaponins-V: A novel steroid conjugate, 5 α -PREGN-9(11)-ENE-3 β ,6 α -DIOL-20-1-3-Sulfate, from a starfish saponin. Asterosaponin A. Tetrahedron 29:1807–1810
- Inagaki M (2008) Structure and biological activity of glycosphingolipids from starfish and feather stars. Yakugaku zasshi 128(8):1187–1194. <https://doi.org/10.1248/yakushi.128>
- Inagaki M, Nakata T, Higuchi R (2006) Isolation and structure of a galactocerebroside molecular species from the starfish *Calcita novaeguineae*. Chem Pharm Bull 54:260–261. <https://doi.org/10.1248/cpb.54.260>
- Inagaki M, Shiizaki M, Hiwataishi T et al (2007) Constituents of Crinoidea. 5. Isolation and structure of a new glycosyl inositolphosphoceramide-type ganglioside from the feather star *Comanthina schlegeli*. Chem Pharm Bull (Tokyo) 55:1649–1651. <https://doi.org/10.1248/cpb.55.1649>
- Iorizzi M, Minale L, Riccio R et al (1986) Starfish saponins, part 23. Steroidal glycosides from the starfish *Halityle regularis*. J Nat Prod 49:67–78. <https://doi.org/10.1021/np50043a007>
- Iorizzi M, Minale L, Riccio R et al (1991) Starfish Saponins, Part 46. Steroidal Glycosides and Polyhydroxysteroids from the Starfish *Calcita novaeguineae*. J Nat Prod 54:1254–1264. <https://doi.org/10.1021/np50077a003>
- Iorizzi M, Minale L, Riccio R et al (1992) Starfish saponins, 48. Isolation of fifteen sterol constituents (six glycosides and nine polyhydroxysteroids) from the starfish *Solaster borealis*. J Nat Prod 55:866–877. <https://doi.org/10.1021/np50085a005>
- Iorizzi M, De Riccardis F, Minale L et al (1993) Starfish saponins, 52. Chemical constituents from the starfish *Echinaster brasiliensis*. J Nat Prod 56:2149–2162. <https://doi.org/10.1021/np50102a018>
- Iorizzi M, Bifulco G, De Riccardis F et al (1995) Starfish saponins, part 53. A reinvestigation of the polar steroids from the starfish *Oreaster reticulatus*: Isolation of sixteen steroidal oligoglycosides and six polyhydroxysteroids. J Nat Prod 58:10–26. <https://doi.org/10.1021/np50115a002>
- Ishida H, Hirota Y, Nakazawa H (1993) Effect of sub-skinning concentrations of saponin on intracellular Ca²⁺ and plasma membrane fluidity in cultured cardiac cells. BBA - Biomembr 1145:58–62. [https://doi.org/10.1016/0005-2736\(93\)90381-9](https://doi.org/10.1016/0005-2736(93)90381-9)

- Ismail H, Lemriss S, Ben Aoun Z et al (2008) Antifungal activity of aqueous and methanolic extracts from the Mediterranean sea cucumber, *Holothuria polii*. J Mycol Med 18:23–26. <https://doi.org/10.1016/j.mycmed.2008.01.002>
- Itakura Y, Komori T (1986) Biologically Active Glycosides from Asteroidea, X. Steroid Oligoglycosides from the Starfish *Acanthaster planci* L., 3. Structures of Four New Oligoglycoside Sulfates. Liebigs Ann 1986:499–508. <https://doi.org/10.1002/jlac.198619860308>
- Ivanchina NV, Kicha A, Kalinovskiy A et al (2000) Hemolytic polar steroidal constituents of the starfish *Aphelasterias japonica*. J Nat Prod 63(8):1178–1181. <https://doi.org/10.1021/np000030f>
- Ivanchina NV, Kicha AA, Kalinovskiy AI et al (2004) Absolute configuration of side chains of polyhydroxylated steroidal compounds from the starfish *Henricia derjugini*. Russ Chem Bull 53:2639–2642. <https://doi.org/10.1007/s11172-005-0166-y>
- Ivanchina NV, Malyarenko TV, Kicha AA et al (2005) Asterosaponin ophidianoside F from gonads of the Far-Eastern starfish *Aphelasterias japonica*. Chem Nat Compd 41:481–482. <https://doi.org/10.1007/s10600-005-0187-7>
- Ivanchina NV, Kicha AA, Kalinovskiy AI et al (2006) Polar steroidal compounds from the Far Eastern starfish *Henricia leviuscula*. J Nat Prod 69:224–228. <https://doi.org/10.1021/np050373j>
- Ivanchina NV, Malyarenko TV, Kicha AA et al (2011) Structures and cytotoxic activities of two new asterosaponins from the antarctic starfish *Diplasterias brucei*. Russ J Bioorganic Chem 37:499–506. <https://doi.org/10.1134/S1068162011030083>
- Ivanchina NV, Kalinovskiy AI, Kicha AA et al (2012) Two New Asterosaponins from the Far Eastern Starfish *Lethasterias fusca*. Nat Prod Commun 7(7):853–858
- Ivanchina NV, Malyarenko TV, Kicha AA et al (2017) A new steroidal glycoside granulatoside C from the starfish *Choriaster granulatus*, unexpectedly combining structural features of polar steroids from several different marine invertebrate phyla. Nat Prod Commun 12:1585–1588
- Ivanchina NV, Kicha AA, Malyarenko TV et al (2018) Granulatosides D, E and other polar steroid compounds from the starfish *Choriaster granulatus*. Their immunomodulatory activity and cytotoxicity. Nat Prod Res:1–8. <https://doi.org/10.1080/14786419.2018.1463223>
- Iyengar EV, Harvell CD (2001) Predator deterrence of early developmental stages of temperate lecithotrophic asteroids and holothuroids. J Exp Mar Bio Ecol 264:171–188. [https://doi.org/10.1016/S0022-0981\(01\)00314-8](https://doi.org/10.1016/S0022-0981(01)00314-8)
- Janakiram NB, Mohammed A, Zhang Y et al (2010) Chemopreventive effects of Frondanol A5, a *Cucumaria frondosa* extract, against rat colon carcinogenesis and inhibition of human colon cancer cell growth. Cancer Prev Res 3:82–91. <https://doi.org/10.1158/1940-6207.CAPR-09-0112>
- Janakiram NB, Mohammed A, Rao CV (2015) Sea cucumbers metabolites as potent anti-cancer agents. Mar Drugs 13:2909–2923. <https://doi.org/10.3390/md13052909>
- Jangoux M (1984) Diseases of echinoderms. Helgoländer Meeresunt 37:207–216. <https://doi.org/10.1007/BF01989305>
- Jeong SH, Kim HK, Song IS et al (2014) Echinochrome a protects mitochondrial function in cardiomyocytes against cardiotoxic drugs. Mar Drugs 12:2922–2936. <https://doi.org/10.3390/md12052922>
- Jia Z, Song Y, Tao S et al (2016) Structure of sphingolipids from sea cucumber *Cucumaria frondosa* and structure-specific cytotoxicity against human hepg2 cells. Lipids 51:321–334. <https://doi.org/10.1007/s11745-016-4128-y>
- Jiang Z-H, Schmidt RR (1992) The hexasaccharide moiety of pectininoside. Liebigs Ann 1992:75–982
- Jiang Z-H, Han X-B, Schmidt RR (1993) Synthesis of the sulfated steroidal glycosides Forbeside E3 and E1. Liebigs Ann 1993:1179–1184
- Jiao H, Shang X, Dong Q et al (2015) Polysaccharide constituents of three types of sea urchin shells and their anti-inflammatory activities. Mar Drugs 13:5882–5900. <https://doi.org/10.3390/md13095882>
- Jin W, Rinehart KL, Jares-Erijman EA (1994) Ophiadiacerebrosides: cytotoxic glycosphingolipids containing a novel sphingosine from a sea star. J Org Chem 59:144–147. <https://doi.org/10.1021/jo00080a023>
- Kalinin VI (2000) System-theoretical (Holistic) approach to the modeling of structural-functional relationships of biomolecules and their evolution: an example of triterpene glycosides from sea cucumbers (Echinodermata, Holothuroidea). J Theor Biol 206:151–168. <https://doi.org/10.1006/jtbi.2000.2110>
- Kalinin VI, Stonik VA (1996) Application of morphological trends of evolution to phylogenetic interpretation of chemotaxonomic data. J Theor Biol 180:1–10. <https://doi.org/10.1006/jtbi.1996.0073>
- Kalinin VI, Kalinovskii AI, Stonik VA et al (1989a) Structure of psolusoside B- A nonholostane triterpene glycoside of the holothurian genus *Psolus*. Chem Nat Compd 25:311–317
- Kalinin VI, Stonik VA, Kalinovskii AI et al (1989b) Structure of pseudostichoposide A- The main triterpene glycoside from the holothurian *Pseudostichopus trachus*. Chem Nat Compd 25:577–582
- Kalinin VI, Avilov SA, Kalinovskii AI et al (1992a) Cucumarioside G₃- A minor triterpene glycoside from the holothurian *Eupentacta fraudatrix*. Chem Nat Compd 28:635–636
- Kalinin VI, Avilov SA, Kalinovskii AI et al (1992b) Cucumarioside G₄ - A new triterpenglycoside from the holothurian *Eupentacta fraudatrix*. Chem Nat Compd 28:600–603
- Kalinin VI, Prokofieva NG, Likhatskaya GN et al (1996) Hemolytic activities of triterpene glycosides from the holothurian order Dendrochirotida: Some trends in the evolution of this group of toxins. Toxicon 34:475–483. [https://doi.org/10.1016/0041-0101\(95\)00142-5](https://doi.org/10.1016/0041-0101(95)00142-5)
- Kalinin VI, Avilov SA, Kalinina EY et al (1997) Structure of eximioside A, a novel triterpene glycoside from the Far-Eastern sea cucumber *Psolus eximius*. J Nat Prod 60:817–819. <https://doi.org/10.1021/np9701541>
- Kalinin VI, Aminin DL, Avilov SA et al (2008) Triterpene glycosides from sea cucumbers (Holothuroidea, Echinodermata). Biological activities and functions. In: Atta-Ur-Rahman (ed) Studies in natural products chemistry (Bioactive natural products) Elsevier Science Publisher 35:135–196
- Kalinin VI, Avilov SA, Silchenko AS et al (2015) Triterpene glycosides of sea cucumbers (Holothuroidea, Echinodermata) as taxonomic markers. Nat Prod Commun 10:21–26
- Kalinin VI, Silchenko AS, Avilov SA (2016) Taxonomic Significance and Ecological Role of Triterpene Glycosides from Holothurians. Biol Bull 43:616–624. <https://doi.org/10.1134/S1062359016060108>
- Kalinovskii AI, Levina EV, Stonik VA et al (2004) Steroid polyols from the far eastern starfish *Henricia sanguinolenta* and *H. leviuscula*. Russ J Bioorganic Chem 30:191–195. <https://doi.org/10.1023/B:RUBI.0000023107.90150.09>
- Kaluzhskiy LA, Shkel TV, Ivanchina NV et al (2017) Structural Analogues of Lanosterol from Marine Organisms of the Class Asteroidea as potential inhibitors of human and *Candida albicans* lanosterol 14 α -demethylases. Nat Prod Commun 12:1843–1846
- Karin M, Yamamoto Y, Wang QM (2004) The IKK NF- κ B system: A treasure trove for drug development. Nat Rev Drug Discov 3:17–26. <https://doi.org/10.1038/nrd1279>
- Karleskint G, Turner R, Small JW (2010) In: Brooks/Cole, Belmont (ed) Introduction to marine biology, 3rd edn
- Kaul P (1986) Marine pharmacology: bioactive molecules from the sea. Annu Rev Pharmacol Toxicol 26:117–142. <https://doi.org/10.1146/annurev.pharmtox.26.1.117>
- Kawase O, Ohno O, Suenaga K et al (2016) Immunological Adjuvant Activity of Pectininoside A, the Steroidal Saponin from the Starfish *Patiria pectinifera*. Nat Prod Commun 11:605–606

- Kenta G, Tatsuya S, Hideki T et al (2015) Total Synthesis and Neuritogenic Activity Evaluation of Ganglioside PNG-2A from the Starfish *Protoreaster nodosus*. *Asian J Org Chem* 4:1160–1171. <https://doi.org/10.1002/ajoc.201500282>
- Kicha AA, Kallnovsky AI, Levina E et al (1983) Asterosaponin P₁ from the starfish *Patria pectinifera*. *Tetrahedron Lett* 24:3893–3896
- Kicha AA, Kalinovsky AI, Levina EV et al (1985) Culcitoside C₁ from starfishes *Culcita novaeguineae* and *Linckia guildingi*. *Chem Nat Compd* 21:760–762
- Kicha AA, Kalinovskii AI, Andriushchenko PV (1986) Culcitosides C₂ and C₃ from the starfish *Culcita novaeguineae*. *Chem Nat Compd* 22:557–560. <https://doi.org/10.1007/BF00599260>
- Kicha AA, Kalinovsky AI, Gorbach NV et al (1993) New polyhydroxysteroids from the far-eastern starfish *Henricia* sp. *Chem Nat Compd* 29:206–210
- Kicha AA, Ivanchina NV, Kalinovsky AI et al (2000) Asterosaponin P₂ from the Far-Eastern starfish *Patiria (asterina) pectinifera*. *Russ Chem Bull* 49:1794–1795
- Kicha AA, Ivanchina NV, Kalinovsky AI et al (2001) Sulphated steroid compounds from the starfish *Aphelasterias japonica* of the Kuril population. *Russ Chem Bull* 50:724–727
- Kicha AA, Ivanchina NV, Stonik VA (2004) Seasonal variations in polyhydroxysteroids and related glycosides from digestive tissues of the starfish *Patiria (=Asterina) pectinifera*. *Comp Biochem Physiol Part B Biochem Mol Biol* 139:581–585. <https://doi.org/10.1016/j.cbpc.2004.06.011>
- Kicha AA, Ivanchina NV, Kalinovsky A et al (2007a) Sulfated steroid glycosides from the Viet Namese starfish *Linckia laevigata*. *Chem Nat Compd* 43:76–80. <https://doi.org/10.1007/s10600-007-0036-y>
- Kicha AA, Ivanchina NV, Kalinovsky A et al (2007b) New neuritogenic steroid glycosides from the Vietnamese starfish *Linckia laevigata*. *Nat Prod Commun* 2:41–46
- Kicha AA, Ivanchina NV, Kalinovsky AI et al (2007c) Four new steroid glycosides from the Vietnamese starfish *Linckia laevigata*. *Russ Chem Bull* 56:823–830. <https://doi.org/10.1007/s11172-007-0123-z>
- Kicha AA, Ivanchina NV, Huong TTT et al (2010a) Two new asterosaponins, archasterosides A and B, from the Vietnamese starfish *Archaster typicus* and their anticancer properties. *Bioorganic Med Chem Lett* 20:3826–3830. <https://doi.org/10.1016/j.bmcl.2010.04.005>
- Kicha AA, Ivanchina NV, Huong TTT et al (2010b) Minor asterosaponin archasteroside C from the starfish *Archaster typicus*. *Russ Chem Bull* 59:2133–2136. <https://doi.org/10.1007/s11172-010-0368-9>
- Kicha AA, Kalinovsky AI, Ivanchina NV et al (2011) Four new asterosaponins, hippasteriosides A - D, from the Far Eastern starfish *Hippasteria kurilensis*. *Chem Biodivers* 8:166–175. <https://doi.org/10.1002/cbdv.200900402>
- Kitagawa I, Kobayashi M (1977) On the structure of the major saponin from *Acanthaster planci*. *Tetrahedron Lett* 2:859–862
- Kitagawa I, Kobayashi M (1978) Saponin and Sapogenol. XXVI. Steroidal saponins from the starfish *Acanthaster planci* L. (Crown of Thorns). (2). Structure of the major saponin Thornasteroside A. *Chem Pharm Bull* 26:1864–1873. <https://doi.org/10.1248/cpb.37.3229>
- Kitagawa I, Sugawara T, Yosioka I et al (1976) Saponin and sapogenol. XIV. Antifungal glycosides from the sea cucumber *Stichopus japonicus* Selenka: 1. Structure of Stichopogenin A₄, the genuine aglycone of holotoxin A. *Chem Pharm Bull* 24:266–274. <https://doi.org/10.1248/cpb.37.3229>
- Kitagawa I, Nishino T, Kyogoku Y (1979) Structure of holothurin A a biologically active triterpene-oligoglycoside from the sea cucumber *Holothuria leucospilota* Brandt. *Tetrahedron Lett*:1419–1422. [https://doi.org/10.1016/S0040-4039\(01\)86166-9](https://doi.org/10.1016/S0040-4039(01)86166-9)
- Kitagawa I, Inamoto T, Fuchida M et al (1980) Structures of Echinostide A and B, two antifungal oligoglycosides from the sea cucumber *Actinopyga echinites* (JAEGER). *Chem Pharm Bull* 28:1651–1653. <https://doi.org/10.1248/cpb.37.3229>
- Kitagawa I, Kobayashi K, Inamoto T et al (1981a) The structure of six antifungal oligoglycosides, Stichlorosides A₁, A₂, B₁, B₂, C, and C₂, from the sea cucumber *Stichopus chloronotus* (Brandt). *Chem Pharm Bull* 29:2387–2391
- Kitagawa I, Kobayashi K, Inamoto T et al (1981b) Stichlorogenol and Dehydrostichlorogenol, Genuine Aglycones of Stichlorosides A₁, B₁, C₁ and A₂, B₂, C₂, from the Sea Cucumber *Stichopus Chloronotus* (BRANDT). *Biosci Biotechnol Biochem* 29:1189–1192. <https://doi.org/10.1248/cpb.37.3229>
- Kitagawa I, Kobayashi M, Hori M et al (1981c) Structures of four new triterpenoidal oligoglycosides, Bivittoside A, B, C, and D, from the sea cucumber *Bohadschia bivittata* MITSUKURI. *Chem Pharm Bull* 29:282–285. <https://doi.org/10.1093/jxb/erl177>
- Kitagawa I, Nishino T, Kobayashi M et al (1981d) Marine Natural Products. VIII. Bioactive triterpene- oligoglycosides from the sea cucumber *Holothuria leucospilota* (Brandt). Structure of holothurin A. *Chem Pharm Bull* 29:1951–1956. <https://doi.org/10.1248/cpb.37.3229>
- Kitagawa I, Kobayashi M, Inamoto T et al (1985) Marine Natural Products. XIV. Structures of echinosides A and B, antifungal lanostane oligosides from the sea cucumber *Actinopyga echinites* (Jaeger). *Chem Pharm Bull (Tokyo)* 33:5214–5224
- Kitagawa I, Kobayashi M, Hori M et al (1989) Marine Natural Products. XVIII. Four lanostane- type triterpene oligoglycosides, bivittosides A, B, C, and D from the Okinawan sea cucumber *Bohadschia bivittata* (Mitsukuri). *Chem Pharm Bull* 37:61–67
- Kobayashi M, Hori M, Kan K et al (1991) Marine Natural Products. XXVII Distribution of Lanostane-type triterpene oligoglycosides in ten kind of Okinawan sea cucumbers. *Chem Pharm Bull* 39:2282–2287. <https://doi.org/10.1248/cpb.37.3229>
- Kornprobst J-M, Sallenave C, Barnathan G (1998) Sulfated compounds from marine organisms. *Comp Biochem Physiol B Biochem Mol Biol* 119:1–51. [https://doi.org/10.1016/S0305-0491\(97\)00168-5](https://doi.org/10.1016/S0305-0491(97)00168-5)
- Kropp RK (1982) Responses of Five Holothurian Species to Attacks by a Predatory Gastropod *Tonna perdris*. *Pacific Sci* 36:445–452
- Kubaneck J, Pawlik JR, Eve TM et al (2000) Triterpene glycosides defend the Caribbean reef sponge *Erylus formosus* from predatory fishes. *Mar Ecol Prog Ser* 207:69–77. <https://doi.org/10.3354/meps207069>
- Kumar R, Chaturvedi AK, Shukla PK et al (2007) Antifungal activity in triterpene glycosides from the sea cucumber *Actinopyga lecanora*. *Bioorg Med Chem Lett* 17:4387–4391. <https://doi.org/10.1016/j.bmcl.2006.12.052>
- Kuznetsova TA, Anisimov MM, Popov AM et al (1982a) A comparative study in vitro of physiological activity of triterpene glycosides of marine invertebrates of echinoderm type. *Comp Biochem Physiol Part C Pharmacol Toxicol Endocrinol* 73:41–43. [https://doi.org/10.1016/0306-4492\(82\)90165-4](https://doi.org/10.1016/0306-4492(82)90165-4)
- Kuznetsova TA, Kalinovskaya NI, Kalinovskii AI et al (1982b) Glycosides of marine invertebrates. XIV. Structure of holothurin B₁ from the holothurian *Holothuria floridana*. *Chem Nat Compd* 18:449–451. <https://doi.org/10.1007/BF00579642>
- La M-P, Li C, Li L et al (2012) New bioactive sulfated alkenes from the sea cucumber *Apostichopus japonicus*. *Chem Biodivers* 9:1166–1171. <https://doi.org/10.1002/cbdv.201100324>
- Laille M, Gerald F, Debitus C (1998) In vitro antiviral activity on dengue virus of marine natural products. *C Cell Mol life Sci* 54:167–170. <https://doi.org/10.1007/s000180050138>
- Lakshmi V, Saxena A, Mishra SK et al (2008) Spermicidal Activity of Bivittoside D from *Bohadschia vitiensis*. *Arch Med Res* 39:631–638. <https://doi.org/10.1016/j.arcmed.2008.06.007>

- Lakshmi V, Srivastava S, Mishra SK, Shukla PK (2012) Antifungal activity of bivittoside-D 14 from *Bohadschia vitiensis* (Semper). *Nat Prod Res* 26(10):913–918
- Lawrence PG, Harold PL, Francis OG (1957) Antibiotics and Chemotherapy 4(1):1980–1989
- Lee J, Wang W, Hong J et al (2007) A new 2,3-dimethyl butenolide from the brittle star *Ophiomastix mixta*. *Chem Pharm Bull (Tokyo)* 55:459–461. <https://doi.org/10.1248/cpb.55.459>
- Levina EV, Kalinovskii AI, Andriyashchenko PV et al (1987) Steroid Glycosides from the starfish *Echinaster sepositus*. *Chem Nat Compd* 23:206–209
- Levina EV, Andriyashchenko PV, Stonik VA et al (1996) Ophiuroid-type steroids in starfish of the genus *Pteraster*. *Comp Biochem Physiol B Biochem Mol Biol* 114:49–52. [https://doi.org/10.1016/0305-0491\(95\)02121-3](https://doi.org/10.1016/0305-0491(95)02121-3)
- Levina EV, Andriyashchenko PV, Kalinovskii AI et al (2001) Steroid compounds from the Pacific starfish *Lysastrosoma anthosticta*. *Russ Chem Bull* 50:313–315. <https://doi.org/10.1023/A:1009503006894>
- Levina EV, Kalinovskii AI, Stonik VA et al (2003) Steroidal polyols from Far-Eastern starfishes *Henricia sanguinolenta* and *H. leviuscula leviuscula*. *Russ Chem Bull* 52:1623–1628. <https://doi.org/10.1023/A:1025613714119>
- Levina EV, Kalinovskii AI, Andriyashchenko PV et al (2004) A new steroidal glycoside phrygioside A and its aglycone from the starfish *Hippasteria phrygiana*. *Russ Chem Bull* 53:2634–2638. <https://doi.org/10.1007/s11172-005-0165z>
- Levina EV, Kalinovskii AI, Andriyashchenko PV et al (2005) Phrygiasterol, a cytotoxic cyclopropane-containing polyhydroxysteroid, and related compounds from the Pacific starfish *Hippasteria phrygiana*. *J Nat Prod* 68:1541–1544. <https://doi.org/10.1021/np049610t>
- Levina EV, Kalinovskii AI, Dmitrenok PS (2007) Steroid compounds from the Far East starfish *Pteraster obscurus* and the ophiura *Asteronyx loveni*. *Bioorg Khim* 33:365–370. <https://doi.org/10.1134/S1068162007030119>
- Levina EV, Kalinovskii AI, Dmitrenok PS (2009) Bioactive Steroidal Sulphates from the Ambulacrums of the Pacific Starfish *Lysastrosoma anthosticta*. *Nat Prod Commun* 4:1041–1046
- Levina EV, Kalinovskii AI, Dmitrenok PS et al (2010) Two new steroidal saponins, Hylodoside A and Novaeguinoside Y, from the starfish *Leptasterias hylodes reticulata* and *Culcita novaeguineae* (Juvenile). *Nat Prod Commun* 5:1737–1742
- Li C, Haug T, Styrvold OB et al (2008) Strongylocins, novel antimicrobial peptides from the green sea urchin, *Strongylocentrotus droebachiensis*. *Dev Comp Immunol* 32:1430–1440. <https://doi.org/10.1016/j.dci.2008.06.013>
- Li M, Miao ZH, Chen Z et al (2010) Echinoid A, a new marine-derived anticancer saponin, targets topoisomerase 2α by unique interference with its DNA binding and catalytic cycle. *Ann Oncol* 21:597–607. <https://doi.org/10.1093/annonc/mdp335>
- Li Z, Chen G, Lu X et al (2013) Three new steroid glycosides from the starfish *Asterina pectinifera*. *Nat Prod Res* 27:1816–1822. <https://doi.org/10.1080/14786419.2012.761621>
- Liu HH, Ko WC, Hu ML (2002) Hypolipidemic effect of glycosaminoglycans from the sea cucumber *Metriatyla scabra* in rats fed a cholesterol-supplemented diet. *J Agric Food Chem* 50:3602–3606. <https://doi.org/10.1021/jf020070k>
- Liu BS, Yi YH, Li L et al (2007) Arguside A: A new cytotoxic triterpene glycoside from the sea cucumber *Bohadschia argus* Jaeger. *Chem Biodivers* 4:2845–2851. <https://doi.org/10.1002/cbdv.200790234>
- Liu BS, Yi YH, Li L et al (2008a) Argusides D and E, two new cytotoxic triterpene glycosides from the sea cucumber *Bohadschia argus* Jaeger. *Chem Biodivers* 5:1425–1433. <https://doi.org/10.1002/cbdv.200890131>
- Liu BS, Yi YH, Li L et al (2008b) Argusides B and C, two new cytotoxic triterpene glycosides from the sea cucumber *Bohadschia argus* Jaeger. *Chem Biodivers* 5:1288–1297. <https://doi.org/10.1002/cbdv.200890115>
- Liu Y, Yan H, Wen K et al (2011) Identification of epidioxysterol from south China sea urchin *Tripneustes gratilla* Linnaeus and its cytotoxic activity. *J Food Biochem* 35:932–938. <https://doi.org/10.1111/j.1745-4514.2010.00426.x>
- Liu X, Sun Z, Zhang M et al (2012) Antioxidant and antihyperlipidemic activities of polysaccharides from sea cucumber *Apostichopus japonicus*. *Carbohydr Polym* 90:1664–1670. <https://doi.org/10.1016/j.carbpol.2012.07.047>
- Lu Y, Li H, Wang M et al (2018) Cytotoxic polyhydroxysteroidal glycosides from starfish *Culcita novaeguineae*. *Mar Drugs* 16:92. <https://doi.org/10.3390/md16030092>
- Ma N, Tang HF, Qiu F et al (2009a) A new polyhydroxysteroidal glycoside from the starfish *Anthenea chinensis*. *Chinese Chem Lett* 20:1231–1234. <https://doi.org/10.1016/j.ccllet.2009.05.012>
- Ma XG, Tang HF, Zhao CH et al (2009b) Two new 24-hydroxylated asterosaponins from *Culcita novaeguineae*. *Chinese Chem Lett* 20:1227–1230. <https://doi.org/10.1016/J.CCLET.2009.05.031>
- Ma N, Tang HF, Qiu F et al (2010) Polyhydroxysteroidal glycosides from the starfish *Anthenea chinensis*. *J Nat Prod* 73:590–597. <https://doi.org/10.1021/np9007188>
- Ma X, Kundu N, Collin PD et al (2012) Frondoside A inhibits breast cancer metastasis and antagonizes prostaglandin E receptors EP₄ and EP₂. *Breast Cancer Res Treat* 132:1001–1008. <https://doi.org/10.1007/s10549-011-1675-z>
- Mackie AM, Singh HT, Owen JM (1977) Studies on the distribution, biosynthesis and function of steroidal saponins in echinoderms. *Comp Biochem Physiol B Comp Biochem* 56:9–14. [https://doi.org/10.1016/0305-0491\(77\)90214-0](https://doi.org/10.1016/0305-0491(77)90214-0)
- Maier MS (2008) Biological activities of sulfated glycosides from echinoderms. In: Atta-Ur-Rahman (ed) *Studies in natural products Chemistry*. Elsevier Science Publisher 35:311–354
- Maier MS, Roccatagliata A, Seldes AM (1993) Two Novel Steroidal Glycoside Sulphates from the Starfish *Cosmasterias lurida*. *J Nat Prod* 56:939–942. <https://doi.org/10.1021/np50096a020>
- Maier MS, Roccatagliata AJ, Kuriss A et al (2001) Two new cytotoxic and virucidal trisulphated triterpene glycosides from the antarctic sea cucumber *Staurocucumis liouvillei*. *J Nat Prod* 64:732–736. <https://doi.org/10.1021/np000584i>
- Maltsev II, Stonik VA, Kalinovskii AI (1984) Triterpene glycosides from sea cucumber *Stichopus japonicus* Selenka. *Comp Biochem Physiol B Comp Biochem* 78:421–426
- Maltsev II, Stekhova SI, Schentsova EB et al (1985) Antimicrobial activities of glycosides from the sea cucumbers of family Stichopodidae. *Khim-Pharm Zhurn* 19:54–56
- Malyarenko TV, Kicha AA, Ivanchina NV et al (2010) Three new polyhydroxysteroids from the tropical starfish *Asteropsis carinifera*. *Russ J Bioorganic Chem* 36:755–761. <https://doi.org/10.1134/S1068162010060129>
- Malyarenko TV, Kicha AA, Ivanchina NV et al (2011) Cariniferosides A–F and other steroidal biglycosides from the starfish *Asteropsis carinifera*. *Steroids* 76:1280–1287. <https://doi.org/10.1016/J.STEROIDS.2011.06.006>
- Malyarenko TV, Kicha AA, Ivanchina NV (2012) Asteropsiside A and other asterosaponins from the starfish *Asteropsis carinifera*. *Russ Chem Bull* 61:1986–1991. <https://doi.org/10.1007/s11172-012-0275-3>
- Malyarenko TV, Kicha AA, Ivanchina NV et al (2014) Asterosaponins from the Far Eastern starfish *Leptasterias ochotensis* and their anticancer activity. *Steroids* 87:119–127. <https://doi.org/10.1016/j.steroids.2014.05.027>
- Malyarenko TV, Malyarenko OS, Ivanchina NV et al (2015) Four new sulfated polar steroids from the Far Eastern starfish *Leptasterias ochotensis*: Structures and activities. *Mar Drugs* 13:4418–4435. <https://doi.org/10.3390/md13074418>

- Malyarenko OS, Dyshlovoy SA, Kicha AA et al (2017) The inhibitory activity of Luzonicosides from the starfish *Echinaster luzonicus* against human melanoma cells. *Mar Drugs* 15:1–11. <https://doi.org/10.3390/md15070227>
- Maoka T, Nakachi S, Kobayashi R et al (2015) A new carotenoid, 9Z,9'Z-tetrahydroastaxanthin, from the sea cucumber *Plesiocolochirus minutus*. *Tetrahedron Lett* 56:5954–5955. <https://doi.org/10.1016/j.tetlet.2015.09.060>
- Marques J, Vilanova E, Mourão PAS et al (2016) Marine organism sulphated polysaccharides exhibiting significant antimalarial activity and inhibition of red blood cell invasion by *Plasmodium*. *Sci Rep* 6:1–14. <https://doi.org/10.1038/srep24368>
- Mats MN, Korkhov VV, Stepanov VR et al (1990) The contraceptive activity of triterpene glycosides—the total sum of holotoxins A1 and B1 and holothurin A in an experiment. *Farmakol Toksikol* 53:45–47
- Mayer AMS, Hamann MT (2002) Marine pharmacology in 1999: compounds with antibacterial, anticoagulant, antifungal, anthelmintic, anti-inflammatory, antiplatelet, antiprotozoal and antiviral activities affecting the cardiovascular, endocrine, immune and nervous systems, and other misc. *Comp Biochem Physiol* 132:315–339. <https://doi.org/10.1007/s10126-003-0007-7>
- Mayer AMS, Glaser KB, Cuevas C et al (2010) The odyssey of marine pharmaceuticals: a current pipeline perspective. *Trends Pharmacol Sci* 31:255–265. <https://doi.org/10.1016/j.tips.2010.02.005>
- Mayer AMS, Rodr AD, Tagliatalata-Scafati O et al (2017) Marine pharmacology in 2012–2013: marine the immune and nervous systems, and other miscellaneous mechanisms of action. *Mar Drugs* 15:1–61. <https://doi.org/10.3390/md15090273>
- Melek FR, Tadros MM, Yousif F et al (2012) Screening of marine extracts for schistosomicidal activity in vitro. Isolation of the triterpene glycosides echinosides A and B with potential activity from the Sea Cucumbers *Actinopyga echinites* and *Holothuria polii*. *Pharm Biol* 50:490–496. <https://doi.org/10.3109/13880209.2011.615842>
- Menchinskaya ES, Pisyagin EA, Kovalchik SN et al (2014) Antitumor activity of cucumarioside A2-2. *Chemotherapy* 59:181–191. <https://doi.org/10.1159/000354156>
- Miller A, Kerr A, Paulay G et al (2017) Molecular phylogeny of extant Holothuroidea (Echinodermata). *Mol Phylogenetics Evol* 111:110–131. <https://doi.org/10.1016/j.ympev.2017.02.014>
- Minale L, Pizza C, Zollo F (1983) Starfish saponins. Part 9. A novel 24-O-glycosidated steroid from the starfish *Hacelia attenuata*. *Experientia* 39:567–569
- Minale L, Pizza C, Plomitallo A et al (1984a) Starfish saponins. XII. Sulphated steroid glycosides from the starfish *Hacelia attenuata*. *Gazz Chim Ital* 114:151–158
- Minale L, Pizza C, Riccio R et al (1984b) Minor Polyhydroxylated Sterols from the Starfish *Protoreaster nodosus*. *J Nat Prod* 47:790–795. <https://doi.org/10.1021/np50035a006>
- Minale L, Pizza C, Riccio R et al (1984c) Starfish Saponins, XIII. Occurrence of Nodososide in the Starfish *Acanthaster Planci* and *Linckia Laevigata*. *J Nat Prod* 47:558. <https://doi.org/10.1021/np50033a037>
- Minale L, Riccio R, Squillace Greco O et al (1985) Starfish saponins—XVI. Composition of the steroidal glycoside sulphates from the starfish *Luidia maculata*. *Comp Biochem Physiol B Biochem* 80:113–118. [https://doi.org/10.1016/0305-0491\(85\)90431-6](https://doi.org/10.1016/0305-0491(85)90431-6)
- Minale L, Riccio R, Zollo F (1995) Structural Studies on Chemical Constituents of Echinoderms. *Stud Nat Prod Chem* 15:43–110
- Minale L, Riccio R, De Simone F et al (1997) Starfish saponin II: 22,23-Epoxysteroids, minor genins from the starfish *Echinaster sepositus*. *Tetrahedron Lett* 20:645–648. <https://doi.org/10.1038/sj.onc.1209954>
- Miyamoto T, Togawa K, Higuchi R et al (1990a) Constituents of holothuroidea, Isolation and structures of three triterpenoid aglycones, cucumechinol A, B, and C, from the sea cucumber *Cucumaria echinata*. *Liebigs Ann* 1990:39–42. <https://doi.org/10.1002/jlac.199019900106>
- Miyamoto T, Togawa K, Higuchi R et al (1990b) Six newly identified biologically active triterpenoid glycoside sulfates from the sea cucumber *Cucumaria echinata*. *Liebigs Ann* 1990:453–460
- Miyamoto T, Togawa K, Higuchi R (1992) Structures of four new triterpenoid oligoglycosides: DS-penaustrosides A, B, C, and D from the sea cucumber *Pentacta australis*. *J Nat Prod* 55:940–946. <https://doi.org/10.1021/np50085a014>
- Molinski TF, Dalisay DS, Lievens SL et al (2009) Drug development from marine natural products. *Nat Rev Drug Discov* 8:69–85. <https://doi.org/10.1038/nrd2487>
- Mona MH, Omran NEE, Mansoor MA (2012) Antischistosomal effect of holothurin extracted from some Egyptian sea cucumbers. *Pharm Biol* 50:1144–1150. <https://doi.org/10.3109/13880209.2012.661741>
- Mondol MAM, Shin HJ, Rahman MA et al (2017) Sea cucumber glycosides: Chemical structures, producing species and important biological properties. *Mar Drugs* 15:317. <https://doi.org/10.3390/md15100317>
- Moraes G, Northcote PT, Silchenko AS et al (2005) Mollisosides A, B₁, and B₂: Minor triterpene glycosides from the New Zealand and south Australian sea cucumber *Australostichopus mollis*. *J Nat Prod* 68:842–847. <https://doi.org/10.1021/np050049o>
- Mourão PAS, Guimarães MAM, Mulloy B (1998) Antithrombotic activity of a fucosylated chondroitin sulphate from echinoderm: Sulphated fucose branches on the polysaccharide account for its antithrombotic action. *Br J Haematol* 101:647–652. <https://doi.org/10.1046/j.1365-2141.1998.00769.x>
- Muniai C, Centurion R, Careaga C et al (2008) Chemical ecology and bioactivity of triterpene glycosides from the sea cucumber *Psolus patagonicus* (*Dendrochirotida: Psolidae*). *J Mar Biol Assoc UK* 88(4):817–823
- Murray AP, Muniaín C, Seldes AM et al (2001) Patagonicoside A: A novel antifungal disulfated triterpene glycoside from the sea cucumber *Psolus patagonicus*. *Tetrahedron* 57:9563–9568. [https://doi.org/10.1016/S0040-4020\(01\)00970-X](https://doi.org/10.1016/S0040-4020(01)00970-X)
- Nance JM, Braithwaite LF (1979) The function of mucous secretions in the cushion star *Pteraster tessellatus* Ives. *J Exp Mar Biol Ecol* 40:259–266. [https://doi.org/10.1016/0022-0981\(79\)90055-8](https://doi.org/10.1016/0022-0981(79)90055-8)
- Ngoan BT, Hanh TTH, Vien LT et al (2015) Asterosaponins and glycosylated polyhydroxysteroids from the starfish *Culcita novaeguineae* and their cytotoxic activities. *J Asian Nat Prod Res* 17:1010–1017. <https://doi.org/10.1080/10286020.2015.1041930>
- Nguyen TH, Um BH, Kim SM (2011) Two unsaturated fatty acids with Potent α -Glucosidase inhibitory Activity purified from the body wall of sea cucumber (*Stichopus japonicus*). *J Food Sci* 76:208–214. <https://doi.org/10.1111/j.1750-3841.2011.02391.x>
- Nigrelli RF, Jakowska S (1960) Effects of Holothurin, a steroid saponin from the Bahamian sea cucumber (*Actinopyga Agassizi*), on various biological systems. *Ann NY Acad Sci* 17:884–892. <https://doi.org/10.1111/j.1749-6632.1960.tb26431.x>
- Nigrelli R, Zahl P (1952) Some biological characteristics of Holothurin. *Exp Biol Med* 81(2):379–380. <https://doi.org/10.3181/00379727-81-19882>
- Nishikawa Y, Furukawa A, Shiga I et al (2015) Cytoprotective effects of lysophospholipids from sea cucumber *Holothuria atra*. *PLoS One* 10:1–14. <https://doi.org/10.1371/journal.pone.0135701>
- Nuzzo G, Gomes BA, Amodeo P et al (2017) Isolation of chemigrene sesquiterpenes and absolute configuration of isobutadiene from the brittle star *Ophionereis reticulata*. *J Nat Prod* 80:3049–3053
- Oda T, Shinmura N, Nishioka Y et al (1999) Effect of the Hemolytic Lectin CEL-III from Holothuroidea *Cucumaria echinata* on the ANS Fluorescence Responses in Sensitive MDCK and Resistant CHO Cells. *J Biochem* 125:713–720
- Okano K, Ohkawa N, Ikegami S (1985) Structure of ovarian Asterosaponin-4, an inhibitor of spontaneous oocyte maturation.

- tion from the Starfish *Asterias amurensis*. *Agri Biol Chemi* 49:2823–2826
- Oleinikova GK, Kuznetsova TA (1983) Two-stage smith degradation of holothurin B₁ from the holothurian *Holothuria floridana*. *Chem Nat Compd* 19:508–509. <https://doi.org/10.1007/BF00575731>
- Oleinikova GK, Kuznetsova TA, Rovnykh NV et al (1982) Glycosides of marine invertebrates. XVIII. Holothurin A₂ from the Caribbean holothurian *Holothuria floridana*. *Chem Nat Compd* 18:501–502
- Omran NE, Khedr AM (2015) Structure elucidation, protein profile and the antitumor effect of the biological active substance extracted from sea cucumber *Holothuria polii*. *Toxicol Ind Health* 31:1–8. <https://doi.org/10.1177/0748233712466135>
- Ozuppek NM, Cavas L (2017) Triterpene glycosides associated antifouling activity from *Holothuria tubulosa* and *H. polii*. *Reg Stud Mar Sci* 13:32–41. <https://doi.org/10.1016/j.rsma.2017.04.003>
- Paine RT (1969) A Note on Trophic Complexity and Community Stability. *Am Nat* 103:91–93
- Palagiano E, Zollo F, Minale L et al (1996) Isolation of 20 glycosides from the starfish *Henricia downeyae*, collected in the Gulf of Mexico. *J Nat Prod* 59:348–354. <https://doi.org/10.1021/np9601014>
- Palyanova NV, Pankova TM, Starostina MV et al (2013) Neuritogenic and neuroprotective effects of polar steroids from the far east starfishes *Patiria pectinifera* and *Distolasterias nipon*. *Mar Drugs* 11:1440–1455. <https://doi.org/10.3390/md11051440>
- Pan K, Inagaki M, Ohno N et al (2010) Identification of sixteen new galactocerebrosides from the starfish *Protoreaster nodosus*. *Chem Pharm Bull (Tokyo)* 58:470–474. <https://doi.org/10.1248/cpb.58.470>
- Pan K, Tanaka C, Inagaki M et al (2012) Isolation and structure elucidation of GM4-type gangliosides from the Okinawan starfish *Protoreaster nodosus*. *Mar Drugs* 10:2467–2480. <https://doi.org/10.3390/md10112467>
- Park HY, Kim JY, Kim HJ et al (2009) Insecticidal and repelenet activities of crude saponin from the starfish *Asterias amurensis*. *Fish Sci Technol* 12:1–5
- Park J-I, Bae H-R, Kim CG et al (2014) Relationships between chemical structures and functions of triterpene glycosides isolated from sea cucumbers. *Front Chem* 2:1–14. <https://doi.org/10.3389/fchem.2014.00077>
- Paul VJ, Arthur KE, Ritson-Williams R et al (2007) Chemical Defenses: From Compounds to Communities Linked. *Biol Bull* 213:226–251
- Peng Y, Zheng J, Huang R et al (2010) Polyhydroxy steroids and saponins from China sea starfish *Asterina pectinifera*. *Chem Pharm Bull* 58:856–858. <https://doi.org/10.1248/cpb.58.856>
- Pereira MS, Mulloy B, Moura PAS (1999) Structure and Anticoagulant Activity of Sulphated Fucans. *J Biol Chem* 274:7656–7667. <https://doi.org/10.1074/jbc.M002422200>
- Pettit GR, Herald CL, Herald DL (1976) Antineoplastic agents XLV: Sea cucumber cytotoxic saponins. *J Pharm Sci* 65:1975–1976
- Pettit GR, Hasler JA, Paull KD et al (1981) Antineoplastic Agents. 76. The Sea Urchin *Strongylocentrotus droebachiensis*. *J Nat Prod* 44:701–704. <https://doi.org/10.1021/np50018a015>
- Pislyagin EA, Aminin DL, Silchenko AS et al (2014) Immunomodulatory action of triterpene glycosides isolated from the sea cucumber *Actinocucumis typica*. Structure-activity relationships. *Nat Prod Commun Immunomodul* 9:771–772
- Pislyagin EA, Manzhulo IV, Gorpenchenko TY et al (2017) Cucumarioside A_{2,2} causes macrophage activation in mouse spleen. *Mar Drugs* 15:1–15. <https://doi.org/10.3390/md15110341>
- Pizza C, Minale L, Laurent D (1985a) Starfish saponins: XXVII. Steroidal glycosides from the starfish *Choriaster granulatus*. *Gazz Chim Ital* 115:585–589
- Pizza C, Pezzullo P, Minale L et al (1985b) Starfish saponins. Part 20. Two novel steroidal glycosides from the starfish *Acanthaster planci* (L). *J Chem Res Synop* 1985:76–77
- Pocsidio GN (1983) The Mutagenicity Potential of Holothurin of Some Philippine Holothurin. *Philipp J Sci* 112:1–12
- Polikarpova SI, Volkova ON, Sedov AM et al (1990) Cytogenetic study of the mutagenicity of cucumarioside. *Genetika* 26:1682–1685
- Popov AM (2002) A comparative study of the hemolytic and cytotoxic activities of triterpenoids isolated from ginseng and sea cucumbers. *Biol Bull* 29:120–128. <https://doi.org/10.1023/A:1014398714718>
- Popov A, Atopkina L, Samoshina NF et al (1994) Immunomodulating activity of tetracyclic triterpene glycosides of the dammarane and holostane series. *Antibiot Khimioter* 39:19–25
- Popov RS, Avilov SA, Silchenko AS et al (2014) Cucumariosides F₁ and F₂, two new triterpene glycosides from the sea cucumber *Eupentacta fraudatrix* and their LC-ESI MS / MS identification in the star fish *Patiria pectinifera*, a predator of the sea cucumber. *Biochem Syst Ecol* 57:191–197. doi:<https://doi.org/10.1016/j.bse.2014.08.009>
- Popov R, Ivanchina N, Kalinovsky A et al (2016) Aphelasteroside F, a new asterosaponin from the far eastern starfish *Aphelasterias japonica*. *Nat Prod Commun* 11:1247–1250
- Prokof'eva NG, Chaikina EL, Kicha AA et al (2003) Biological activities of steroid glycosides from starfish. *Comp Biochem Physiol Part B Biochem Mol Biol* 134:695–701. [https://doi.org/10.1016/S1096-4959\(03\)00029-0](https://doi.org/10.1016/S1096-4959(03)00029-0)
- Qi J, Ojika M, Sakagami Y (2002) linckosides A and B, two new neuritogenic steroid glycosides from the okinawan starfish *Linckia laevigata*. *Bioorg Med Chem* 10:1961–1966. [https://doi.org/10.1016/S0968-0896\(02\)00006-8](https://doi.org/10.1016/S0968-0896(02)00006-8)
- Qi J, Ojika M, Sakagami Y (2004) Linckosides C–E, three new neuritogenic steroid glycosides from the Okinawan starfish *Linckia laevigata*. *Bioorg Med Chem* 12:4259–4265. <https://doi.org/10.1016/j.bmc.2004.04.049>
- Qi J, Han C, Sasayama Y et al (2006) Granuloside A, a starfish steroid glycoside, enhances PC12 cell neuritogenesis induced by nerve growth factor through an activation of MAP kinase. *ChemMedChem* 1:1351–1354. <https://doi.org/10.1002/cmdc.200600190>
- Riccio R, De Simone E, Dini A et al (1981) Starfish saponins VI - unique 22,23-epoxysteroidal cyclic glycosides, minor constituents from *Echinaster sepositus*. *Tetrahedron Lett* 22:1557–1560. [https://doi.org/10.1016/S0040-4039\(01\)90377-6](https://doi.org/10.1016/S0040-4039(01)90377-6)
- Riccio R, Dini A, Minale L et al (1982a) Starfish saponins VII. Structure of Luzoncoside, a further steroidal cyclic glycoside from the pacific starfish *Echinaster luzonicus*. *Experientia* 38:68–70
- Riccio R, Minale L, Pagonis S et al (1982b) A novel group of highly hydroxylated steroids from the starfish *Protoreaster nodosus*. *Tetrahedron* 38:3615–3622. [https://doi.org/10.1016/0040-4020\(82\)80069-0](https://doi.org/10.1016/0040-4020(82)80069-0)
- Riccio R, D'Auria MV, Minale L (1985a) Unusual sulfated marine steroids from the ophiuroid *Ophioderma longicaudum*. *Tetrahedron* 41:6041–6046. [https://doi.org/10.1016/S0040-4020\(01\)91445-0](https://doi.org/10.1016/S0040-4020(01)91445-0)
- Riccio R, Greco OS, Minale L et al (1985b) Starfish saponins, part 18. steroidal glycoside sulfates from the starfish *Linckia laevigata*. *J Nat Prod* 48:97–101. <https://doi.org/10.1021/np50037a017>
- Riccio R, Pizza C, Squillace-Greco O et al (1985c) Starfish saponins. Part 17. steroidal glycoside sulfates from the starfish *Ophiaster ophidianus* (Lamarck), and *Hacelia attenuata* (Gray). *J Chem Soc Perkin Trans I* 1:655–660
- Riccio R, Zollo F, Finamore E et al (1985d) Starfish saponins, 19. A novel steroidal glycoside sulphate from the starfishes *Protoreaster nodosus* and *Pentacaster alveolatus*. *J Nat Prod* 48:266–272. <https://doi.org/10.1021/np50038a011>
- Riccio R, D'Auria MV, Minale L (1986a) Two New Steroidal Glycoside Sulphates, Longicaudoside-A and -B, from the Mediterranean Ophiuroid *Ophioderma longicaudum*. *J Org Chem* 51:533–536. <https://doi.org/10.1021/jo00354a025>

- Riccio R, Greco OS, Minale L et al (1986b) Starfish saponins, part 28. steroidal glycosides from pacific starfishes of the genus *Nardoa*. J Nat Prod 49:1141–1143. <https://doi.org/10.1021/np50048a036>
- Riccio R, Iorizzi M, Greco OS et al (1986c) Starfish Saponins, Part 22. Asterosaponins from the Starfish *Halityle Regularis*: A Novel 22,23-Epoxysteroidal Glycoside Sulfate. J Nat Prod 48:756–765. <https://doi.org/10.1021/np50041a007>
- Riccio R, Iorizzi M, Minale L (1986d) Starfish Saponins. Isolation of Sixteen Steroidal Glycosides and Three Polyhydroxysteroids from the Mediterranean Starfish *Coscinasterias Tenuispina*. Bull des Sociétés Chim Belges 95:869–893. <https://doi.org/10.1002/bseb.19860950912>
- Riccio R, Iorizzi M, Minale L et al (1988) Starfish saponins. Part 34. Novel steroidal glycoside sulphates from the starfish *Asterias amurensis*. J Chem Soc Perkin Trans 1:1337–1347. <https://doi.org/10.1039/P19880001337>
- Rideout JA, Smith NB, Sutherland MD (1979) Chemical defense of ctenoids by polyketide sulphates. Experientia 35:1273–1274. <https://doi.org/10.1007/BF01963951>
- Ridzwan BH (2007) Sea cucumber: the Malaysian heritage. Research Centre, IULM, Kuala Lumpur
- Roccatagliata AJ, Maier MS, Seldes AM (1994) Starfish saponins, part 2. Steroidal oligoglycosides from the starfish *Cosmasterias lurida*. J Nat Prod 57:747–754. <https://doi.org/10.1021/np50108a010>
- Roccatagliata AJ, Maier MS, Seldes AM et al (1996) Antiviral sulphated steroids from the ophiuroid *Ophioplocus januarii*. J Nat Prod 59:887–889. <https://doi.org/10.1021/np960171a>
- Rodriguez J, Riguera R (1989) Lefevreiosides: four novel triterpenoid glycosides from the sea cucumber *Cucumaria lefevrei*. ChemInform 21:2620–2636. <https://doi.org/10.1002/chin.199014299>
- Rodriguez J, Castro R, Riguera R (1991) Holothurinosides: new anti-tumor non sulphated triterpenoid glycosides from the sea cucumber *Holothuria forskali*. Tetrahedron 47:4753–4762
- Ruppert EE, Fox RS, Barnes RD (2004) Invertebrate zoology: a functional evolutionary approach. Thomson Brook/Cole, Belmont
- Sullivan TD, Ladue KT, Nigrelli RF (1955) The effect of holothurin, a steroid saponin of animal origin, on Krebs-2 ascites tumors in Swiss mice. Zoologica 40:49–52
- Sandvoss M, Pham H, Levsen K et al (2000) Isolation and structural elucidation of Steroid Oligoglycosides from the starfish *Asterias rubens* by means of direct online LC-NMR-MS hyphenation and One- and two-dimensional NMR investigations. Eur J Org Chem 2000:1253–1262
- Sandvoss M, Preiss A, Levsen K et al (2003) Two new asterosaponins from the starfish *Asterias rubens*: Application of a cryogenic NMR probe head. Magn Reson Chem 41:949–954
- Schoenmakers HJN (1979) In vitro biosynthesis of steroids from cholesterol by the ovaries and pyloric caeca of the starfish *Asterias rubens*. Comp Biochem Physiol B 63:179–184
- Sedov AM, Shepeleva IB, Zakharova NS et al (1984) Effect of cucumarioside (a triterpene glycoside from the holothurian *Cucumaria japonica*) on the development of an immune response in mice to corpuscular pertussis vaccine. Zhurnal mikrobiologii, epidemiologii, i immunobiologii 9:100–104
- Sedov AM, Apollonin AV, Sevast'ianova EK et al (1990) Stimulation of nonspecific antibacterial resistance of mice to opportunistic gram-negative microorganisms with triterpene glycosides from Holothuroidea. Antibiot Khimioter 35:23–26
- Shang X, Liu X, Zhang J et al (2014) Traditional chinese medicine -Sea urchin. Mini-Rev Med Chem 14:537–542
- Sharypov VF, Chumak AD, Stonik VA et al (1981) Glycosides of marine invertebrates. X. The structure of stichoposides A and B from the holothurians *Stichopus cloronotus*. Chem Nat Compd 17:139–142
- Silchenko AS, Avilov SA, Antonov AA et al (2002) Triterpene glycosides from the deep-water North-Pacific sea cucumber *Synallactes nozawai* Mitsukuri. J Nat Prod 65:1802–1808. <https://doi.org/10.1021/np0202881>
- Silchenko AS, Avilov SA, Kalinin VI et al (2004) Pseudostichoposide B – new triterpene glycoside with unprecedented type of sulfatation from the deep-water North-Pacific sea cucumber *pseudostichopus trachus*. Nat Prod Res 18:565–570. <https://doi.org/10.1080/14786410310001630591>
- Silchenko AS, Avilov SA, Antonov AS et al (2005a) Glycosides from the sea cucumber *Cucumaria frondosa*. III. Structure of frondosides A₂₋₁, A₂₋₂, A₂₋₃, and A₂₋₆, four new minor monosulphated triterpene glycosides. Can J Chem 83:21–27. <https://doi.org/10.1139/v05-243>
- Silchenko AS, Avilov SA, Antonov AS et al (2005b) Glycosides from the sea cucumber *Cucumaria frondosa*. IV. Structure of frondosides A₂₋₄, A₂₋₇, and A₂₋₈, three new minor monosulphated triterpene glycosides. Can J Chem 83:2120–2126. <https://doi.org/10.1139/v05-243>
- Silchenko AS, Stonik VA, Avilov SA et al (2005c) Holothurins B₂, B₃, and B₄, new triterpene glycosides from Mediterranean sea cucumbers of the genus *Holothuria*. J Nat Prod 68:564–567. <https://doi.org/10.1021/np049631n>
- Silchenko AS, Avilov SA, Antonov AS et al (2007a) Glycosides from the North Atlantic sea cucumber *Cucumaria frondosa* — Structures of five new minor trisulfated triterpene oligoglycosides, frondosides A₇₋₁, A₇₋₂, A₇₋₃, A₇₋₄, and isofrondoside C. Can J Chem 85:626–636. <https://doi.org/10.1139/v04-163>
- Silchenko AS, Avilov SA, Kalinin VI et al (2007b) Monosulfated triterpene glycosides from *Cucumaria okhotensis* Levin et Stepanov, a new species of sea cucumbers from Sea of Okhotsk. Bioorg Khim 33:81–90. <https://doi.org/10.1134/S1068162007010098>
- Silchenko AS, Avilov SA, Kalinin VI et al (2008) Constituents of the sea cucumber *Cucumaria okhotensis*. Structures of okhotsides B₁-B₃ and cytotoxic activities of some glycosides from this species. Nat Prod 71:351–356. <https://doi.org/10.1021/np0705413>
- Silchenko AS, Kalinovskiy AI, Avilov SA et al (2012a) Triterpene glycosides from the sea cucumber *Eupentacta fraudatrix*. Structure and biological action of Cucumariosides A₁, A₃, A₄, A₅, A₆, A₁₂ and A₁₅, seven new minor non-sulfated tetraosides and unprecedented 25-keto, 27-norholostane aglycone. Nat Prod Commun 7:517–525
- Silchenko AS, Kalinovskiy AI, Avilov SA et al (2012b) Triterpene Glycosides from the Sea Cucumber *Eupentacta fraudatrix*. Structure and Cytotoxic Action of Cucumariosides A₂, A₇, A₉, A₁₀, A₁₁, A₁₃ and A₁₄, Seven New Minor Non-Sulfated Tetraosides and an Aglycone with an Uncommon 18-Hydroxy Group. Nat Prod Commun Triterpene 7:845–852
- Silchenko AS, Kalinovskiy AL, Avilov SA et al (2012c) Structures and cytotoxic properties of cucumariosides H₂, H₃ and H₄ from the sea cucumber *Eupentacta fraudatrix*. Nat Prod Res 26(19):1765–1774. <https://doi.org/10.1080/14786419.2011.602637>
- Silchenko AS, Kalinovskiy AL, Avilov SA et al (2012d) Triterpene glycosides from the sea cucumber *Eupentacta fraudatrix*. Structure and biological action of Cucumariosides B₁, and B₂, two new minor non-sulfated tetraosides and unprecedented 25-keto, 27-norholostane aglycone. Nat Prod Commun 7:517–525
- Silchenko AS, Kalinovskiy AI, Avilov SA et al (2013a) Triterpene glycosides from the sea cucumber *Eupentacta fraudatrix*. Structure and biological action of cucumariosides I₁, I₃, I₄, three new minor disulfated pentaosides. Nat Prod Commun 8:1053–1058
- Silchenko AS, Kalinovskiy AI, Avilov SA et al (2013b) Structures and biological activities of typicosides A₁, A₂, B₁, C₁ and C₂, triterpene glycosides from the sea cucumber *Actinocucumis typica*. Nat Prod Commun 8:301–310
- Silchenko AS, Kalinovskiy AI, Avilov SA et al (2013c) Structure of cucumarioside I₂ from the sea cucumber *Eupentacta fraudatrix* (Djakonov et Baranova) and cytotoxic and immunostimulatory activities of this saponin and relative compounds. Nat Prod Res 27:1776–1783. <https://doi.org/10.1080/14786419.2013.778851>

- Silchenko AS, Kalinovsky AI, Avilov SA et al (2013d) Triterpene glycosides from Antarctic sea cucumbers IV. Turquetoside A, a 3-O-methylquinovose containing disulfated tetraoside from the sea cucumber *Staurocucumis turqueti* (Vaney, 1906) (= *Cucumaria spatha*). *Biochem Syst Ecol* 51:45–49. <https://doi.org/10.1016/j.bse.2013.08.012>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2013e) Structure and biological action of Cladolosides B₁, B₂, C, C₁, C₂ and D, six new triterpene glycosides from the sea cucumber *Cladolabes schmeltzii*. *Nat Prod Commun* 8:1527–1534
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2014a) Structures of Violaceosides C, D, E and G, Sulfated Triterpene Glycosides from the Sea Cucumber *Pseudocolochirus violaceus* (Cucumariidae, Dendrochirotida). *Nat Prod Rep* 9:391–399
- Silchenko AS, Kalinovsky AI, Avilov SI et al (2014b) Kolgaosides A and B, Two New Triterpene Glycosides from the Arctic Deep Water Sea Cucumber *Kolga hyalina* (Elasipodida: Elpidiidae). *Nat Prod Commun* 9:1259–1264
- Silchenko AS, Kalinovsky AI, Avilov et al (2014c) Triterpene glycosides from the sea cucumber *Cladolabes schmeltzii*. II. Structure and biological action of cladolosides A1–A6. *Nat Prod Commun* 9:1421–1429
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2015a) Colochirosides B₁, B₂, B₃ and C, novel sulfated triterpene glycosides from the sea cucumber *Colochirus robustus* (Cucumariidae, Dendrochirotida). *NPC. Nat Prod Commun* 10:1687–1694. <https://doi.org/10.1080/13531040802284544>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2015b) Structures and biological activities of cladolosides C₃, E₁, E₂, F₁, F₂, G, H₁ and H₂, eight triterpene glycosides from the sea cucumber *Cladolabes schmeltzii* with one known and four new carbohydrate chains. *Carbohydr Res* 414:22–31. <https://doi.org/10.1016/j.carres.2015.06.005>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2016a) Structures and biogenesis of fallaxosides D₄, D₅, D₆ and D₇, trisulfated non-holostane triterpene glycosides from the sea cucumber *Cucumaria fallax*. *Molecules* 21:2–13. <https://doi.org/10.3390/molecules21070939>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2016b) Colochirosides A₁, A₂, A₃, and D, Four Novel Sulfated Triterpene Glycosides from the Sea Cucumber *Colochirus robustus* (Cucumariidae, Dendrochirotida). *Nat Prod Commun* 11:381–387
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2016c) Colochiroside E, an unusual non-holostane triterpene sulfated trioside from the sea cucumber *Colochirus robustus* and evidence of the impossibility of a 7(8)-double bond Migration in lanostane derivatives having an 18(16)-lactone. *Nat Prod Commun* 11:741–746
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2017a) Cladolosides I₁, I₂, J₁, K₁, K₂ and L₁, monosulfated triterpene glycosides with new carbohydrate chains from the sea cucumber *Cladolabes schmeltzii*. *Carbohydr Res* 445:80–87. <https://doi.org/10.1016/j.carres.2017.04.016>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2017b) Nine new triterpene glycosides, magnumosides A₁–A₄, B₁, B₂, C₁, C₂ and C₄, from the Vietnamese sea cucumber *Neothyonidium* (= *Massinium*) *magnum*: Structures and activities against tumor cells independently and in synergy with radioactive irradiation. *Mar Drugs* 15:1–22. <https://doi.org/10.3390/md15080256>
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2018a) Cladolosides O, P, P₁-P₃ and R, triterpene glycosides with two novel types of carbohydrate chains from the sea cucumber *Cladolabes schmeltzii*. *Carbohydr Res* 468:73–79
- Silchenko AS, Kalinovsky AI, Avilov SA et al (2018b) Cladolosides C₄, D₁, D₂, M, M₁, M², N, and Q, new triterpene glycosides with diverse carbohydrate chains from the sea cucumber *Cladolabes schmeltzii*. *An uncommon* 20,21,22,23,24,25,26,27-okta-nor-lanostane aglycone. The synergism of inhibitory action of non-toxic dose of the glycosides and radioactive irradiation on colony formation of HT-29 cancer cells. *Carbohydr Res* 468:36–44
- Silva M, Rodriguez I, Barreiro A et al (2015) First report of ciguatoxins in two starfish species: *Ophidiaster ophidianus* and *Marthasterias glacialis*. *Toxins (Basel)* 7:3740–3757. <https://doi.org/10.3390/toxins7093740>
- Singh N, Kumar R, Gupta S et al (2008) Antileishmanial activity in vitro and in vivo of constituents of sea cucumber *Actinopyga lecanora*. *Parasitol Res* 103:351–354. <https://doi.org/10.1007/s00436-008-0979-3>
- Soliman YA, Ibrahim AM, Tadros HRZ et al (2016) Antifouling and Antibacterial Activities of Marine Bioactive Compounds Extracted from some Red Sea Cucumber. *Contemp Appl Sci* 3:83–103
- Song Y, Jin SJ, Cui LH et al (2013) Immunomodulatory effect of *Stichopus japonicus* acid mucopolysaccharide on experimental hepatocellular carcinoma in rats. *Molecules* 18:7179–7193. <https://doi.org/10.3390/molecules18067179>
- Song J, Li T, Cheng X et al (2016) Sea cucumber peptides exert anti-inflammatory activity through suppressing NF-κB and MAPK and inducing HO-1 in RAW264.7 macrophages. *Food Funct* 7:2773–2779. <https://doi.org/10.1039/c5fo01622c>
- Stöhr S, O'Hara TD, Thuy B (2012) Global diversity of brittle stars (Echinodermata: Ophiuroidea). *PLoS One* 7:e31940. <https://doi.org/10.1371/journal.pone.0031940>
- Stonik VA (1986) Some terpenoid and steroid derivatives from echinoderms and sponges. *Pure Appl Chem* 58:423–436. <https://doi.org/10.1351/pac198658030423>
- Stonik VA, Mal'tsev II, Elyakov GB (1982) The structure of Thelenosides A and B from the Holothurian *Theleonata ananas*. *Chem Nat Compd* 18:590–593
- Styles TJ (1970) Effect of Holothurin on *Trypanosoma zewisi* Infections in Rats. *J Protozool* 17:196–198
- Sugawara T, Zaima N, Yamamoto A et al (2006) Isolation of Sphingoid Bases of Sea Cucumber Cerebrosides and Their Cytotoxicity against Human Colon Cancer Cells. *Biosci Biotechnol Biochem* 70:2906–2912. <https://doi.org/10.1271/bbb.60318>
- Sun P, Liu BS, Yi YH et al (2007) A new cytotoxic lanostane-type triterpene glycoside from the sea cucumber *Holothuria impatiens*. *Chem Biodivers* 4:450–457. <https://doi.org/10.1002/cbdv.200790037>
- Suwanmala J, Lu S, Tang Q et al (2016) Comparison of Antifatigue Activity of Five Sea Cucumber Species in a Mouse Model of Intense Exercise. *J Food Nutr Res* 4:12–19. <https://doi.org/10.12691/jfnr-4-1-3>
- Tang HF, Yi Y, Li L et al (2005) Three new asterosaponins from the starfish *Calcita novaeguineae* and their bioactivity. *Planta Med* 71(5):458–463. <https://doi.org/10.1055/s-2005-871215>
- Tang HF, Yi YH, Li L et al (2006) Asterosaponins from the starfish *Calcita novaeguineae* and their bioactivities. *Fitoterapia* 77:28–34. <https://doi.org/10.1016/j.fitote.2005.07.009>
- Tang HF, Yi YH, Li L et al (2009) Bioactive Asterosaponins from the Starfish *Calcita novaeguineae*. *J Nat Prod* 68:337–341. <https://doi.org/10.1021/np0401617>
- Telford MJ, Lowe CJ, Cameron CB et al (2014) Phylogenomic analysis of echinoderm class relationships supports Asterozoa. *Proc R Soc B Biol Sci* 281:20140479–20140479. <https://doi.org/10.1098/rspb.2014.0479>
- Thao NP, Cuong NX, Luyen BTT et al (2013) Anti-inflammatory asterosaponins from the starfish *Astropecten monacanthus*. *J Nat Prod* 76:1764–1770. <https://doi.org/10.1021/np400492a>
- Thao NP, No JH, Luyen BTT et al (2014) Secondary metabolites from Vietnamese marine invertebrates with activity against *Trypanosoma brucei* and *T. cruzi*. *Molecules* 19:7869–7880. <https://doi.org/10.3390/molecules19067869>
- Thao NP, Luyen BTT, Kim EJ et al (2015a) Steroidal constituents from the edible sea urchin *Diadema savignyi* Michelin induce

- apoptosis in human cancer cells. *J Med Food* 18:45–53. <https://doi.org/10.1089/jmf.2013.3105>
- Thao NP, Luyen BTT, Koo JE et al (2015b) Anti-inflammatory components of the Vietnamese starfish *Protoreaster nodosus*. *Biol Res* 48:12. <https://doi.org/10.1186/s40659-015-0002-2>
- Thiel M, Watling L (2015) Lifestyles and feeding biology. the natural history of the Crustacea, vol 2. Oxford University Press, Oxford
- Tian F, Zhang X, Tong Y et al (2005) PE, a new sulphated saponin from sea cucumber, exhibits anti-angiogenic and anti-tumor activities in vitro and in vivo. *Cancer Biol Ther* 4:874–882. <https://doi.org/10.4161/cbt.4.8.1917>
- Tian F, Zhu C, Zhang X et al (2007) Philinopside E, a new sulfated saponin from sea cucumber, blocks the interaction between kinase insert domain-containing receptor (KDR) and avb3 integrin via binding to the extracellular domain of KDR. *Mol Pharmacol* 72:545–552. <https://doi.org/10.1124/mol.107.036350.receptor>
- Turischev SN, Bolshakova GB, Sakandelidze OG et al (1991) Influence of complexes of holothurian triterpene glycosides on liver generation. *Izv Akad Nauk SSSR, Ser Biol* 2:306–310
- Van Dyck S, Gerbaux P, Flammang P (2010) Qualitative and quantitative saponin contents in five sea cucumbers from the Indian ocean. *Mar Drugs* 8:173–189. <https://doi.org/10.3390/md8010173>
- Vázquez MJ, Quiñóá E, Riguera R et al (1992) Santiagoside, the first asterosaponin from an antarctic starfish (*Neosmilaster georgianus*). *Tetrahedron* 48:6739–6746. [https://doi.org/10.1016/S0040-4020\(01\)80019-3](https://doi.org/10.1016/S0040-4020(01)80019-3)
- Vázquez MJ, Quindo E, Riguera R (1993) Helianthoside from *Heliaster helianthus*, an asterosaponin with a C3'-sulfated pyranose. *Can J Chem* 71:1174–1151
- Vien LT, Ngoan BT, Hanh TTH et al (2017) Steroid glycosides from the starfish *Pentacaster gracilis*. *J Asian Nat Prod Res* 19:474–480. <https://doi.org/10.1080/10286020.2016.1235038>
- Vien LT, Hoang L, Hanh TTH et al (2018) Triterpene tetraglycosides from the sea cucumber *Stichopus horrens*. *Nat Prod Res* 32:1039–1043. <https://doi.org/10.1080/14786419.2017.1378206>
- Wang W, Li F, Alam N et al (2002) New saponins from the starfish *Certanaroda semiregularis*. *J Nat Prod* 65:1649–1656. <https://doi.org/10.1021/np020234r>
- Wang W, Li F, Hong J et al (2003) Four New Saponins from the Starfish *Certanaroda semiregularis*. *Chem Pharm Bull* 51:435–439. <https://doi.org/10.1248/cpb.51.435>
- Wang W, Hong J, Lee C-O et al (2004a) Cytotoxic Sterols and Saponins from the Starfish *Certanaroda semiregularis*. *J Nat Prod* 67:584–591. <https://doi.org/10.1021/np030427u>
- Wang W, Jang H, Hong J et al (2004b) Additional cytotoxic sterols and saponins from the starfish *Certanaroda semiregularis*. *J Nat Prod* 67:1654–1660. <https://doi.org/10.1021/np049869b>
- Wang W, Jang H, Hong J et al (2005) New Cytotoxic Sulphated Saponins from the Starfish *Certanaroda semiregularis*. *Arch Pharmacol Res* 28:285–289
- Wang Z, Zhang H, Yuan W et al (2012) Antifungal nortriterpene and triterpene glycosides from the sea cucumber *Apostichopus japonicus* Selenka. *Food Chem* 132:295–300. <https://doi.org/10.1016/j.foodchem.2011.10.080>
- Wang XH, Zou ZR, Yi YH et al (2014) Variegatusides: New non-sulphated triterpene glycosides from the sea cucumber *Stichopus variegatus* Semper. *Mar Drugs* 12:2004–2018. <https://doi.org/10.3390/md12042004>
- Ward JA (1960) A further investigation on the swimming reaction of *Stomphia coccinea*. Master thesis. University of Washington
- Wen Z, Zhu Z, Shen D et al (2004) Determination of asterosaponins in *Asterias amurensis* and *Crepidaster hesperus* with ultraviolet spectrophotometry. *Fenxi Kexue Xuebao* 20:592–594
- Wen J, Hu C, Fan S (2010) Chemical composition and nutritional quality of sea cucumbers. *J Sci Food Agric* 90:2469–2474. <https://doi.org/10.1002/jsfa.4108>
- Wen M, Fu X, Han X et al (2016) Sea cucumber saponin echinoside A (EA) stimulates hepatic fatty acid β -oxidation and suppresses fatty acid biosynthesis coupling in a diurnal pattern. *J Nutr Sci Vitaminol (Tokyo)* 62:170–177. <https://doi.org/10.3177/jnsv.62.170>
- Wijesinghe WAJP, Vairappan CS, Jeo YJ (2015) Exploitation of Health Promoting Potentials of Edible Sea Cucumber (*Holothuria edulis*): Search of New Bioactive Components as Functional Ingredients. *Int Proc Chem Biol Environ Eng* 86:36–41. <https://doi.org/10.7763/IPCBEE>
- Wu J, Yi Y-H, Tang H-F et al (2006a) Nobilisides A - C, Three New Triterpene Glycosides from the Sea Cucumber *Holothuria nobilis*. *Planta Med* 72:932–935. <https://doi.org/10.1055/s-2006-931603>
- Wu J, Yi Y, Tang H et al (2006b) Structure and Cytotoxicity of a New Lanostane-Type Triterpene Glycoside from the Sea Cucumber *Holothuria hilla* holothurians. *Chem Biodivers* 3:1249–1254
- Wu J, Yi Y, Wu H et al (2007a) Studies on the in vitro antifungal and antitumor activities of nobiliside A from the sea cucumber *Holothuria nobilis* Selenka. *Zhongguo Yaolixue Tongbao* 23:139–140
- Wu J, Yi YH, Tang HF et al (2007b) Hillasides A and B, two new cytotoxic triterpene glycosides from the sea cucumber *Holothuria hilla* Lesson. *J Asian Nat Prod Res* 9:609–615. <https://doi.org/10.1080/10286020600882676>
- Wu J, Zhang J, Ding P et al (2009a) Nobiliside C purified from *Holothuria nobilis* for use as antitumor agent. *marinlit ID: A21616 (21787)*. Faming Zhuanli Shenqing Gongkai Shuomin
- Wu J, Zhang J, Ding P et al (2009b) Anti-tumor compound hillaside a separated from *Holothuria hilla* CA151:181594. *Marinlit ID: A22103 (22279)* Faming Zhuanli Shenqing Gongkai Shuomin
- Wu FJ, Xue Y, Liu XF et al (2014) The protective effect of eicosapentaenoic acid-enriched phospholipids from sea cucumber *Cucumaria frondosa* on oxidative stress in PC12 cells and SAMP8 mice. *Neurochem Int* 64:9–17. <https://doi.org/10.1016/j.neuint.2013.10.015>
- Wu M, Xu L, Zhao L et al (2015) Structural analysis and anticoagulant activities of the novel sulphated fucan possessing a regular well-defined repeating unit from sea cucumber. *Mar Drugs* 13:2063–2084. <https://doi.org/10.3390/md13042063>
- Xu J, Wang Y-M, Feng T-Y et al (2011) Isolation and anti-fatty liver activity of a novel cerebroside from the sea cucumber *Acaudina molpadioides*. *Biosci Biotechnol Biochem* 75:1466–1471. <https://doi.org/10.1271/bbb.110126>
- Yamada K, Tanabe K, Miyamoto T et al (2008) Isolation and Structure of a Monomethylated Ganglioside Possessing Neuritogenic Activity from the Ovary of the Sea Urchin *Diadema setosum*. *Chem Pharm Bull* 56:734–737. <https://doi.org/10.1248/cpb.56.734>
- Yamanouchi T (1955) On the poisonous substance contained in Holothurians. *Mar Biol Lab* 4:183–203
- Yang P, Collin P, Madden T et al (2003) Inhibition of proliferation of PC3 cells by the branched-chain fatty acid, 12-methyltetradecanoic acid, is associated with inhibition of 5-lipoxygenase. *Prostate* 55:281–291. <https://doi.org/10.1002/pros.10243>
- Yang S-W, Chan T-M, Buevich A et al (2007) Novel steroidal saponins, Sch 725737 and Sch 725739, from a marine starfish, *Novodinia antillensis*. *Bioorg Med Chem Lett* 17:5543–5547. <https://doi.org/10.1016/j.bmcl.2007.08.025>
- Yang X-W, Chen X-Q, Dong G et al (2011) Isolation and structural characterisation of five new and 14 known metabolites from the commercial starfish *Archaster typicus*. *Food Chem* 124:1634–1638. <https://doi.org/10.1016/j.foodchem.2010.08.033>
- Yano A, Abe A, Aizawa F et al (2013) The effect of eating sea cucumber jelly on Candida load in the oral cavity of elderly individuals in a

- nursing home. *Mar Drugs* 11:4993–5007. <https://doi.org/10.3390/md11124993>
- Yayli N, Findlay JA (1999) A triterpenoid saponin from *Cucumaria frondosa*. *Phytochemistry* 50:135–138. [https://doi.org/10.1016/S0031-9422\(98\)00463-4](https://doi.org/10.1016/S0031-9422(98)00463-4)
- Yi Y, Xu Q, Li L et al (2006) Philinopsides A and B, two new sulfated triterpene glycosides from the sea cucumber *Pentacta quadrangularis*. *Helv Acta* 89:54–63
- Yi Y, Sun G, Li L et al (2008) Purification of triterpene saponin compound griseaside A from *Holothuria grisea* Selenka for cancer therapy and antitumor agent development. *MarinLit ID: A20342* (20506). Faming Zhuanli Shenqing Gongkai Shuomin
- Yibmantasiri P, Leahy DC, Busby BP et al (2012) Molecular basis for fungicidal action of neothyonidioside, a triterpene glycoside from the sea cucumber, *Australostichopus mollis*. *Mol Biosyst* 8:902. <https://doi.org/10.1039/c2mb05426d>
- Yu S, Ye X, Huang H et al (2015) Bioactive Sulfated Saponins from Sea Cucumber *Holothuria moebii*. *Planta Med* 81:152–159. <https://doi.org/10.1055/s-0034-1383404>
- Yuan W-H, Yi Y-H, Xue M et al (2008) Two Antifungal Active Triterpene Glycosides from Sea Cucumber *Holothuria (Microthele) axiloga*. *Chin J Nat Med* 6:105–108. [https://doi.org/10.1016/S1875-5364\(09\)60010-8](https://doi.org/10.1016/S1875-5364(09)60010-8)
- Yuan W-H, Yi Y, Tang H-F et al (2009a) Antifungal Triterpene Glycosides from the Sea Cucumber *Bohadschia marmorata*. *Planta Med* 75:168–173. <https://doi.org/10.1055/s-0028-1088348>
- Yuan WH, Yi YH, Tan RX et al (2009b) Antifungal triterpene glycosides from the sea cucumber *Holothuria (Microthele) axiloga*. *Planta Med* 75:647–653. <https://doi.org/10.1055/s-0029-1185381>
- Yun SH, Park ES, Shin SW et al (2012) Stichoposide C induces apoptosis through the generation of ceramide in leukemia and colorectal cancer cells and shows in vivo antitumor activity. *Clin Cancer Res* 18:5934–5948. <https://doi.org/10.1158/1078-0432.CCR-12-0655>
- Yun SH, Sim EH, Han SH et al (2018) Holotoxin A1 induces apoptosis by activating acid sphingomyelinase and neutral sphingomyelinase in K562 and human primary leukemia cells. *Mar Drugs* 16:123
- Zhan Y-C, Sun Y, Li W et al (2006) A new triterpene glycoside from *Asterias rollentoni*. *J Asian Nat Prod Res* 8:631–636. <https://doi.org/10.1080/10286020500208626>
- Zhang J (2009) Antitumor effects of nobilside B from sea cucumber *Holothuria nobilis* and its acetoxy compounds CA151:279085. *Zhongguo Haiyang Yaowu* 28:41–43
- Zhang J-J, Zhu K-Q (2017) A novel antitumor compound nobilside D isolated from sea cucumber (*Holothuria nobilis* Selenka). *Exp Ther Med* 14:1653–1658. <https://doi.org/10.3892/etm.2017.4656>
- Zhang S-L, Li L, Yi Y-H et al (2006a) Philinopsides E and F, two new sulfated triterpene glycosides from the sea cucumber *Pentacta quadrangularis*. *Nat Prod Res* 20:399–407. <https://doi.org/10.1080/14786410500185584>
- Zhang S-Y, Yi Y-H, Tang H-F (2006b) Cytotoxic sulfated triterpene glycosides from the sea cucumber *Pseudocolochirus violaceus*. *Chem Biodivers* 3:807–817. <https://doi.org/10.1002/cbdv.200690083>
- Zhang S-Y, Yi Y-H, Tang H-F et al (2006c) Two new bioactive triterpene glycosides from the sea cucumber *Pseudocolochirus violaceus*. *J Asian Nat Prod Res* 8:1–8. <https://doi.org/10.1080/10286020500034972>
- Zhang SY, Yi YH, Tang HF (2006d) Bioactive triterpene glycosides from the sea cucumber *Holothuria fuscocinerea*. *J Nat Prod* 69:1492–1495. <https://doi.org/10.1021/np060106t>
- Zhang S-L, Li L, Sun P et al (2008) Lecanorosides A and B, two new triterpene glycosides from the sea cucumber *Actinopyga lecanora*. *J Asian Nat Prod Res* 10:1097–1103. doi:<https://doi.org/10.1080/10286020701604813>
- Zhang B, Xue C, Hu X et al (2012) Dietary sea cucumber cerebroside alleviates orotic acid-induced excess hepatic adipogenesis in rats. *Lipids Health Dis* 11(1). <https://doi.org/10.1186/1476-511X-11-48>
- Zhang G, Ren H-H, Zhang Y-B et al (2013) Chemical constituents of the starfish *Asterias rollestoni* Bell. *Biochem Syst Ecol* 51:203–206. <https://doi.org/10.1016/j.bse.2013.08.031>
- Zhao Y, Li B, Dong S et al (2009) A novel ACE inhibitory peptide isolated from *Acaudina molpadioidea* hydrolysate. *Peptides* 30:1028–1033. <https://doi.org/10.1016/j.peptides.2009.03.002>
- Zhao Q, Liu Z, Xue Y et al (2011) Ds-echinoside A, a new triterpene glycoside derived from sea cucumber, exhibits antimetastatic activity via the inhibition of NF-κB-dependent MMP-9 and VEGF expressions. *J Zhejiang Univ Sci B* 12:534–544. <https://doi.org/10.1631/jzus.B1000217>
- Zhao Q, Xue Y, Wang J et al (2012) In vitro and in vivo anti-tumour activities of echinoside A and ds-echinoside A from *Pearsonothuria graefei*. *J Sci Food Agric* 92:965–974. <https://doi.org/10.1002/jsfa.4678>
- Zollo F, Finamore E, Minale L (1985) Starfish saponins XXIV. Two novel steroidal glycoside sulphates from the starfish *Echinaster sepositus*. *Gazz Chim Ital* 115:303–306
- Zou Z-R, Yi Y-H, Wu H-M et al (2003) Intercedensides A–C, three new cytotoxic triterpene glycosides from the sea cucumber *Mensamaria intercedens* (Lampert). *J Nat Prod* 66:1055–1060. <https://doi.org/10.1021/np030064y>
- Zou Z, Yi Y, Wu H et al (2005) Intercedensides D-I, cytotoxic triterpene glycosides from the sea cucumber *Mensamaria intercedens* Lampert. *J Nat Prod* 68:540–546. <https://doi.org/10.1021/np040205b>

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