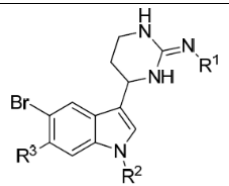
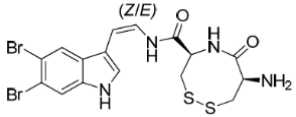
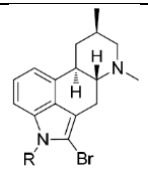
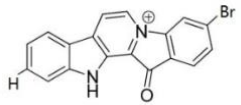
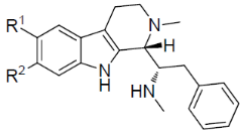
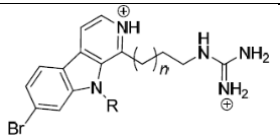
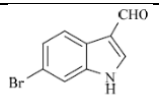
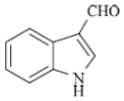
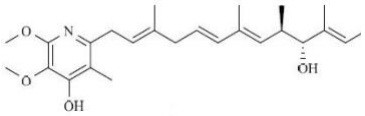
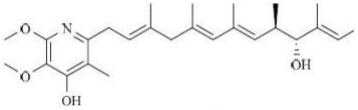
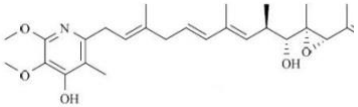
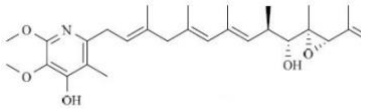
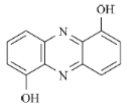
Tab.S1 Other alkaloids from the host ascidians

Compound	Structure	Host Ascidian	Activity	Ref.
Aplicyanin B Aplicyanin D Aplicyanin F	 R_1=Ac,$R_{2,3}$=H Aplicyanin B R_1=Ac,R_2=OMe, R_3=H Aplicyanin D R_1=Ac,R_2=OMe, R_3=Br Aplicyanin F	*Aplidium cyaneum*	1.Potent antimitotic; 2.Cytotoxic against HT29, A549 and MDA-MB-231 cells.	[1]
Tanjungide A		*Diazona* cf. *Formosa*	Cytotoxicity against A549, HT29 and MDA-MB-231 cells.	[2]
Pibocin A Pibocin B	 R=H Pibocin A R=OMe PibocinB	*Eudistoma* sp.	Antimicrobial and cytotoxic effects against mouse Ehrlich carcinoma cells	[3] [4]
3-bromofascaplysin		*Didemnum* sp.	Anticancer activity towards HL60, THP-1, HeLa, MDA-MB-231, DLD-1, SNU-C4 and SK-MEL-28 cells.	[5] [6]

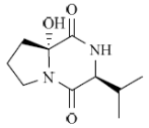
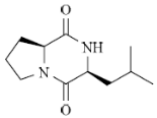
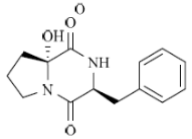
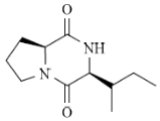
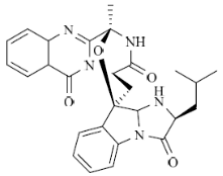
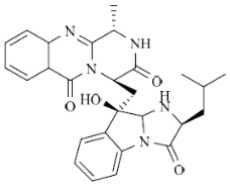
Tab.S1 *Cont.*

Eudistomidin B Eudistomidin G	 R_1 = Br, R_2 = H Eudistomidin B R_1 = H, R_2 = Br Eudistomidin G	*Eudistoma glaucus*	Cytotoxic activity towards L1210 cell	[7] [8]
Opacaline B Opacaline C	 R = OH, n = 2 Opacaline B R = H, n = 1 Opacaline C	*Pseudodistoma opacum*	Antimalarial activity against a chloroquine-resistant *Plasmodium falciparum*	[9]

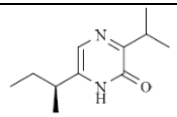
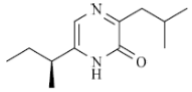
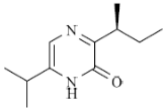
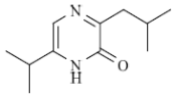
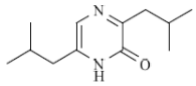
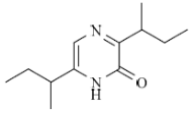
Tab.S2 Other alkaloids from the ascidian-associated microbes

Compound	Structure	Origin microbe	Host Ascidian	Activity	Ref.
6-bromoindole-3-carbaldehyde		*Acinetobacter* sp.	*Stomozoa murrayi*	1.Antimicrobial activities to *Bacillus marinus* and *Vibrio campbellii;* 2. Inhibited the adhesion of cyprid larvae of *Balanus amphitrite.*	[10] [11]
Indole-3-carbaldehyde					
Piericidin A1		*Streptomyces* sp.	Unidentified ascidian fromIwayama	Inhibited the growth of RG-E1A-7 and Neuro-2a cells.	[12] [13] [14]
Piericidin A2					
Piericidin C7					
Piericidin C8					
1,6-dihydroxyphenazine		*Nocardiopsis dassonvillei*	*Botryllus schlosseri*	1.Antimicrobial activities to *Vibrioanguillarum* and *Vibrio parahaemolyticus*; 2. Lethal activity to *Artemia salina*; 3.Inhibit activity of Alpha-glucosidase.	[15] [16]

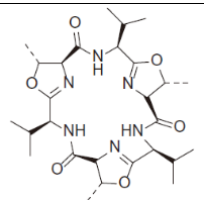
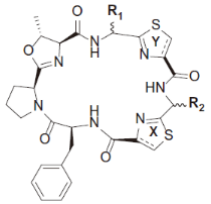
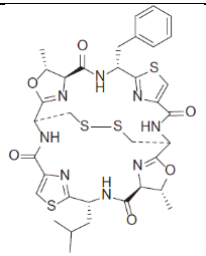
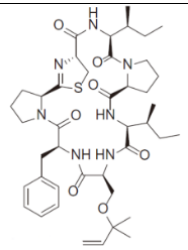
Tab.S2 *Cont.*

Bacillusamide B		*Streptomyces* sp.	*Didemnum* sp.	Cytotoxic against HCT116, HepG2 and MCF7 cells.	[17] [18] [19]
Cyclo (6-OH-D-Pro-L-Phe)					
Cyclo (L-Pro-L-Leu)					
Cyclo (L-Pro-L-Ile)					
Fumiquinazoline H		*Acremonium* sp.	*Ecteinascidia turbinate*	Antimicrobial activity against *Candida albicans.*	[20]
Fumiquinazoline I					

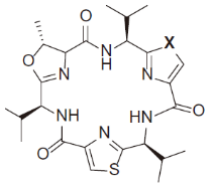
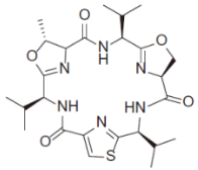
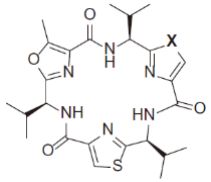
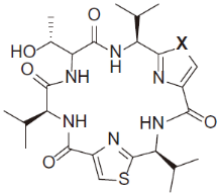
Tab.S2 *Cont.*

(S)-6-(sec-butyl)-3-isopropylpyrazin-2(1H)-one					
(S)-3-(sec-butyl)-6-isopropylpyrazin-2(1H)-one					
(S)-6-(sec-butyl)-3-isobutylpyrazin-2(1H)-one					
(1H)-pyrazinones analogues deoxymutaaspergillic		*Streptomyces* sp.	*Didemnum* sp.	Inhibited the growth of HCT116, HepG2 and MCF7 cells.	[21] [22]
Acid 3,6-diisobutyl-2(1H)-pyrazinone					
3,6-disec-butyl-2(1H)-pyrazinone					

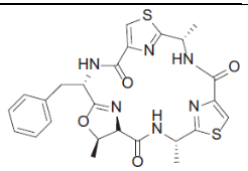
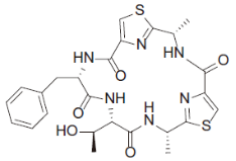
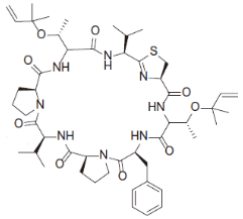
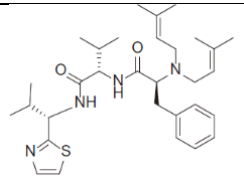
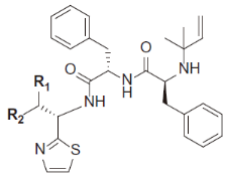
Tab.S3 Other polypeptides from the host ascidians

Compound	Structure	Host Ascidian	Activity	Ref.
Cycloxazoline		*Lissoclinum bistratum*	1. Inhibited HL60 cell accumulated in G2/M phase; 2. Cytotoxic against HL60, T24 and MRC5CV1 cells.	[23]
Lissoclinamide		*Lissoclinum patella*	Inhibited the growth of human bladder carcinoma and fibroblast cell.	[24]
Ulithiacyclamide B		*Lissoclinum patella*	1. Cytotoxic against KB cells; 2.Inhibitor of Macrophage Scavenger Receptor.	[25]
Mollamide		*Didemnum molle*	1.Cytotoxic against CV1, A549, HT29, and P388 cells; 2. RNA synthesis inhibitor.	[26]

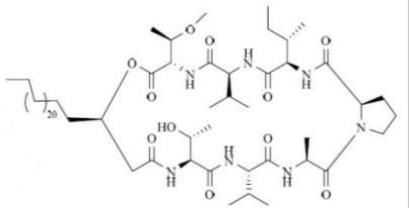
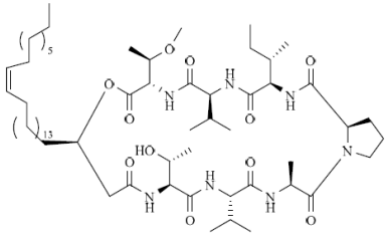
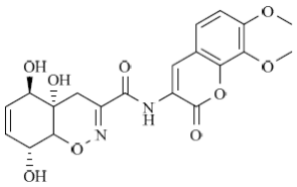
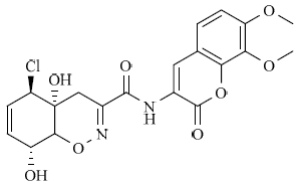
Tab.S3 *Cont.*

Bistratamide E Bistratamide F Bistratamide G Bistratamide H Bistratamide I Bistratamide J	 X= S Bistratamide E  Bistratamide F  X= O Bistratamide G X= S Bistratamide H  X = O Bistratamide I X = S Bistratamide J	*L. bistratum.*	Cytotoxic against HCT 116 cells	[27] [28]

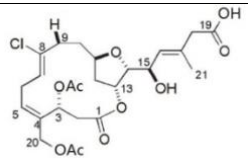
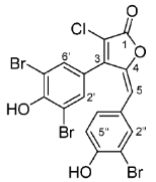
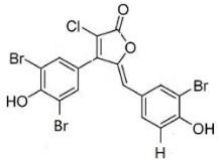
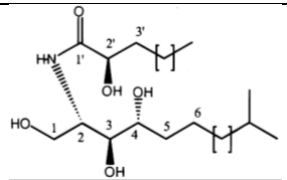
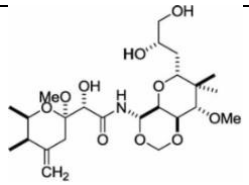
Tab.S3 *Cont.*

Didmolamide A DidmolamideB	 	*Didemnum molle*	Cytotoxic against HT29, MEL28, and A549 cells.	[29]
Patellin 6		*Lissoclinum* sp.	1.Cytotoxic against CV1, A549, HT29, and P388 cells; 2. Inhibited topoisomerase II activation.	[30]
Virenamide A Virenamides B Virenamides C	 Virenamide A  R_1= R_2= Me Virenamide B R_1= H; R_2= Ph Virenamide C	*Diplosoma virens*	1. Against CV1, A549, P388and HT29 cells; 2. Inhibited topoisomerase II.	[31]

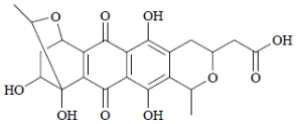
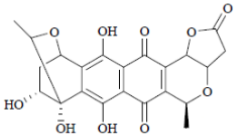
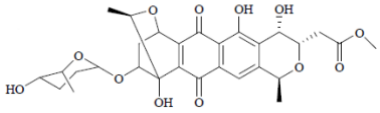
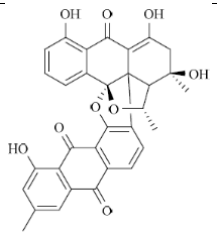
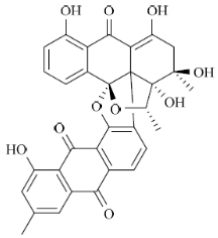
Tab.S4 Other Peptides from the ascidian-associated microbes

Compound	Structure	Origin microbe	Host Ascidian	Activity	Ref.
Peptidolipin B		*Nocardia* sp.	*Tridemnum orbiculatum*	Inhibited methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus*.	[32] [33]
Peptidolipin E					
Trichodermamide A		*Trichoderma virens*	*Didemnum molle*	1. Cytotoxic against HCT116 cell; 2.Antimicrobial activity against amphoterocin resistant *Candida albicans*, methacillin resistant *Staphylococcus aureus* and vancomycin resistant *Enterococcus faecium.*	[34] [35]
Trichodermamide B					

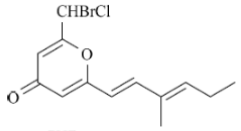
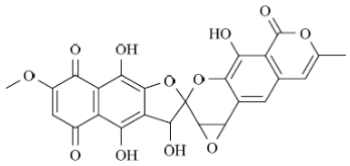
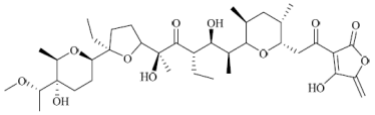
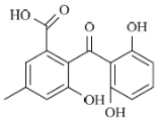
Tab.S5 Other polyketides from the host ascidians

Compound	Structure	Host Ascidian	Activity	Ref.
Biselide A		*Didemnidae* sp.	Inhibited the growth of MDA-MB-231 and NCI-H460 cells	[36]
Z-Rubrolide O		*Synoicumn* sp.	1. Inhibited superoxide production by human neutrophils; 2. Inhibited PMA-induced adhesion of neutrophils.	[37]
E-Rubrolide O				
Sphingosine 1a		*Cystodytescf dellechiajei*	Inhibited the activity of phospholipase A2.	[38]
Mycalamide A		*Polysincraton* sp.	1. Prevented EGF-induced transformation induced apoptosis of JB6 Cl41 P+ cells 2. Inhabited the growth of HeLa cell.	[39]

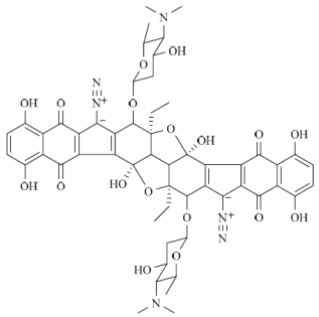
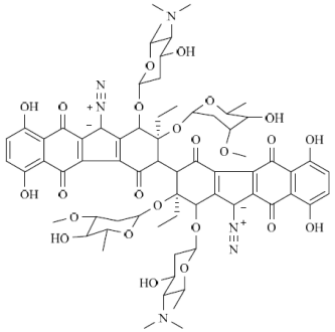
Tab.S6 Other polyketides from the ascidian-associated microbes

Compound	Structure	Origin microbe	Host Ascidian	Activity	Ref.
Granaticin		*Streptomyces* sp.	*Molgula manhattensis*	Against pathogens *Bacillus subtilis*, methicillin-sensitive *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, and *Pseudomonas aeruginosa.*	[40] [41] [42]
Granatomycin D					
Dihydrogranaticin B					
Bisanthraquinone 1		*Streptomyces* sp.	*Ecteinascidia turbinata*	1. Cytotoxic against HCT116 cell; 2. Antimicrobial activity against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus faecalis*.	[43] [44]
Bisanthraquinone 2					

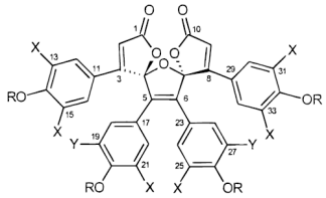
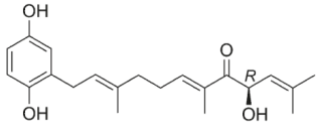
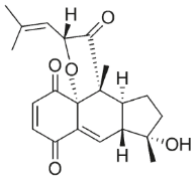
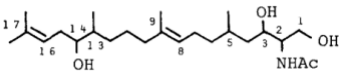
Tab.S6 *Cont.*

Halomadurone C Halomadurone D		*Actinomadura* sp.	*Ecteinascidia turbinata*	Activated nuclear factor E2-related factor antioxidant response element (Nrf2-ARE).	[45]
Griseorhodin A		*Streptomyces* sp.	*Aplidium lenticulum*	Inhibited human telomerase and retroviral reverse transcriptase.	[46]
Ecteinamycin		*Actinomadura* sp.	*Ecteinascidia turbinata*	Against microbial *Clostridium difficile* NAP1/B1/027.	[47]
Monodictyphenone		*Penicillium albobiverticillium*	Unidentified ascidian from Manado	Inhibited protein tyrosine phosphatase (PTP) 1B, T cell PTP (TCPTP), CD45 tyrosine phosphatase (CD45), and vaccinia H-1-related phosphatase (VHR).	[48]

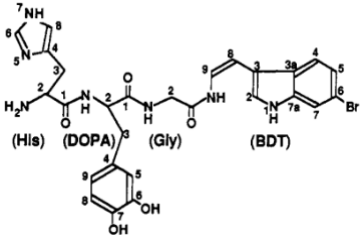
Tab.S6 *Cont.*

Lomaiviticin A		*Salinispora pacifica*	*Polysyncraton lithostrotum*	1. Potented DNA damaging; 2.Antimicrobial activities against *Staphylococcus aureus* and *Enterococcus faecium*; 3. Inhibited the growth of K562 cell.	[49]
Lomaiviticin B					

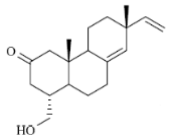
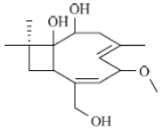
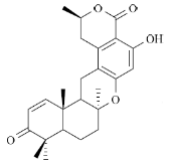
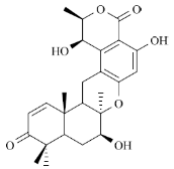
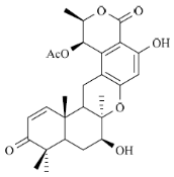
Tab.S7 Other kinds of compounds from the host ascidians

Compound	Structure	Classification	Host Ascidian	Activity	Ref.
Prunolide A Prunolide B Prunolide C	 R=H, X=Br, Y=Br Prunolide A R=H, X=Br, Y=H Prunolide B R=H, X=H,Y=H Prunolide C	spiroketal	*Synoicum prunum*	Inhibited the growth of HeLa cell.	[50]
Rossinone A Rossinone B	 	meroterpene	*Aplidium* sp.	1.Inhibited superoxide production; 2. Selective antiviral activity toward the DNA virus HSV-1 and the RNAvirusPV-1; 3. Antimicrobial activity against *Bacillus subtilis* and *Trichophyton mentagrophytes*; 4. Antiproliferative activity to P388 cells.	[51] [52]
Aplidiasphingosine		terpenoid	*Aplidium* sp.	Inhibited the growth of KB and L1210 cells	[53]

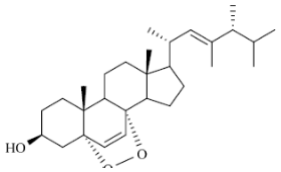
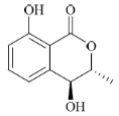
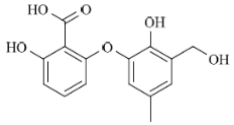
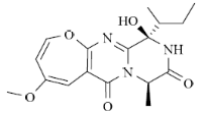
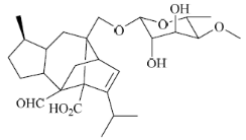
Tab.S7 *Cont.*

Halocyamines A		terpenoid	*Halocynthiaro retzi*	1.Inhibitory effects on the growth of *B. subtilis*, *B. megaterium*, *B.cereus* and the *Cryptococus neoformans*; 2. Cytotoxic against HepG2 and N18 cells.	[54] [55]

Tab.S8 Other kinds of compounds from the ascidian-associated microbes

Compound	Structure	classification	Origin microbe	Host Ascidian	Activity	Ref.
Gifhornenolone A		terpenoid	*Verrucosispora gifhornensis*	Unidentified ascidian from Hiroshima	Inhibited activity of androgen receptor.	[56]
Fuscoatrol A		caryophyllene	*Humicola fuscoatra*	Kuril colonial ascidium	1. Against microbial *Staphylococcus aureus* and *Bacillus subtilis*; 2. Cytotoxic on the eggs development of *Strongylocentrotus intermedius.*	[57]
Verruculide A		merosesquiterpenes	*Talaromyces verruculosus*	*Polycarpaaurata*	Inhibited the activity of protein tyrosine phosphatase 1B.	[58] [59] [60]
Chrodrimanin A						
Chrodrimanin H						

Tab.S8 *Cont.*

5,8-epidioxy-23-methyl-(22E,24 R)-ergosta-6,22-dien-3-ol		sterol	*Penicillium stoloniferum*	Unidentified ascidian from Qingdao	Inhibited the growth of P388 cells.	[61]
Penicillic acid		Furanones	*Aspergillus* sp.	*Eudistoma vannamei*	Cytotoxic against MDA-MB-435 and HCT8 cell lines.	[62]
2-hydroxy-6-(2O-hydroxy-3 O-hydroxymethyl-5-methylp henoxy)-benzoic acid		biphenyl ether	*Talaromyces albobiverticillius*	Unidentified ascidian from Manado	Inhibitory activities against protein tyrosine phosphatase 1B, T cell PTP and CD45 tyrosine phosphatase.	[63]
Oxepinamide A		isocoumarin	*Acremonium* sp.	*Ectcinascidia turbinata*	Anti-inflammatory activity on ear edema of mouse.	[64]
Diterpene glycoside sordarin		glycoside	*Talaromyces* sp.	Unidentified ascidian from Tweed Heads	Antifungal activity.	[65]

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