Cytotoxicity of quinonoid pigments from sea urchins

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Shells and spines of sea urchins are rich in bioactive compounds, which can be used for many biomedical applications. In traditional Chinese medicine, sea urchin shells were used for heart diseases treatment and for the resolution of phlegm (Shang et al., 2014). Korean researchers showed the anti-diabetic effect of powdered sea urchin shells on type 2 diabetic rats (Kim, Kim, Lim, Yoon, Kim, & Lee, 2011). Minerals from the shells can be used for replacing and reconstruction of damaged or defective hard tissue (Tămăşan, Ozyegin, Oktar, & Simon, 2013; Zhang, & Vecchio, 2013; Hou et al., 2016); polysaccharides from the shells possess an anti-inflammatory effect (Jiao et al., 2015); and proteins from the shells and spines demonstrate antitumour activity (Shang et al., 2014). Secondary metabolites specific to sea urchins – polyhydroxynaphthoquinones (PHNQs) – also exhibit a wide range of pharmacological activities. For example, the extract of *Strongylocentrotus droebachiensis* shells, which contain PHNQ pigments, demonstrated antiallergic effects (Pozharitskaya et al., 2013b). The most well-known sea urchin pigment, echinochrome A, also showed antiallergic activity (Itoh et al., 2016). Echinochrome A protected mitochondrial functions from cardiotoxic agents such as doxorubicin, sodium nitroprusside and *tert*-butyl hydroperoxide (Jeong et al., 2014a). Echinochrome A treatment enhanced the oxygen consumption rate and the mitochondrial ATP level in rat cardiomyoblast cells and up-regulated the biogenesis of transcription genes (Jeong et al., 2014b). Egyptian scientists demonstrated the potential of echinochrome A in the treatment of rats with experimental type 1 and type 2 diabetes (Mohamed, Soliman, & Marie, 2016). In addition, echinochrome A is the active substance in the cardioprotective and antioxidant drug histochrome, produced in Russia from the sand dollar *Scaphechinus mirabilis* (Mishchenko, Fedoreev, & Bagirova, 2003). At the same time, properties of other PHNQ pigments are not so detailed studied.



Figure 1. *Mesocentrotus nudus*

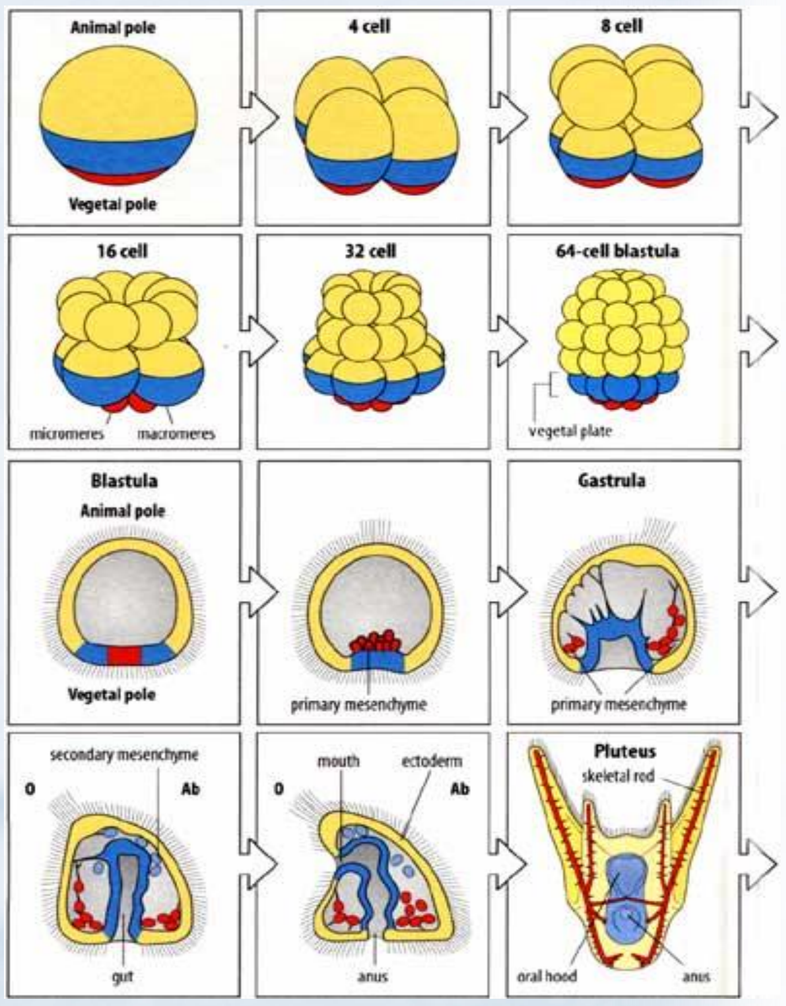
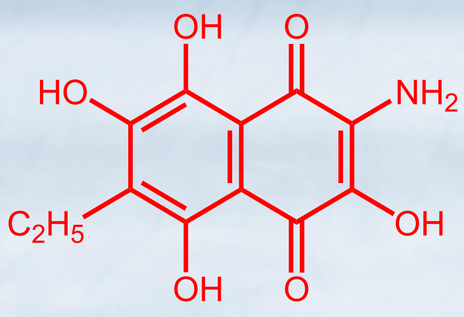


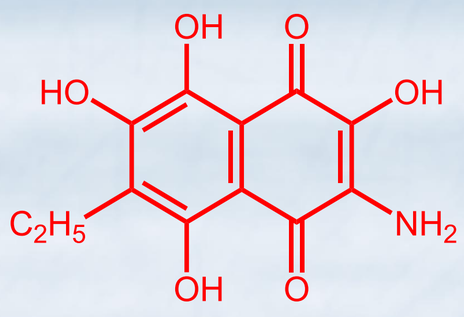
Figure 2. Sea Urchin development diagram
http://sunny.moorparkcollege.edu/~econnolly/F11development.htm



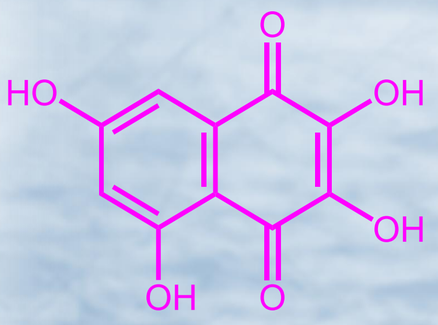
Echinochrome A (**1**)



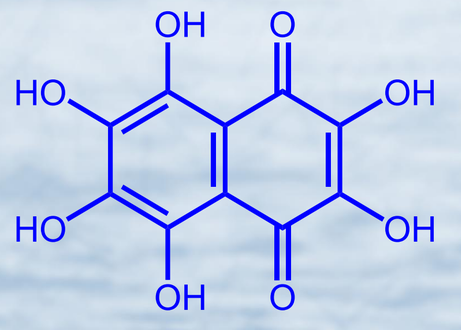
Echinamine A (**2**)



Echinamine B (**3**)



Spinochrome B (**4**)



Spinochrome E (**5**)

For this investigation echinochrome A (**1**) and echinamines A (**2**) and B (**3**) were isolated from sand dollar *Scaphechinus mirabilis*; spinochromes B (**4**) and E (**5**) were isolated from *Mesocentrotus nudus*.

Table 1. Cytotoxicity of compounds **1-5**

Compound	IC*
1	10
2	25
3	25
4	>100
5	>100

*The concentration (μg/ml) that inhibits cleavage of the eggs 20 h after the beginning of cell division in the control.

In this study we determined the cytotoxic effects of PHNQs **1-5** on embryos (Fig. 2) of the sea urchin *M. nudus*. Sea urchin gamete is an attractive bioassay object since it is easy to obtain synchronous samples of dividing cells, and the cell cycle duration lasts only 1 hour. This model, rapidly and at low cost, provides information on the disruption of the cell proliferation. The cytotoxic action of steroid glycosides from starfish, synthetic naphthoquinones and sesquiterpenoid quinones have been successfully studied using sea urchin eggs. In the present work we have shown that quinones **1-5** exhibited slight activities on the first cell cleavage of eggs with IC values ranging between 50.0 and 100.0 μg/ml. The cytostatic action of **1, 2** and **3** was increased on the stage of eight blastomers. On gastrula stage quinones **1, 2** and **3** displayed a moderate cytotoxic effect (MIC 10.0, 25.0 and 25.0 μg/ml, respectively) (Table 1). When the insemination was performed with eggs previously incubated with **1, 2** and **3** at the concentration of 2.0 μg/ml for 30 min, the fertilization was blocked completely, while the other compounds showed no significant inhibited effect. Thus, the cytotoxic activity of quinones 1-5 varied in the following sequence: **1** > **2**, **3** > **4**, **5**.

This study was supported by Russian Foundation for Basic Research, Grant No. 16-33-00297 mol_a.