

# Mitochondrial Pro-Apoptotic Properties of isolated compounds from two soft corals of Persian Gulf

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**Background:** Soft corals are an important source of cytotoxic organisms. Some locals use these marine organisms traditionally to treat cancer. Therefore, this study was designed to isolate the cytotoxic extracts and compounds of two species of *sinularia* soft corals along with their mechanisms against MCF-7 and MDA-MB231 cell lines through MTT assay, Annexin PI flow cytometry, generation of ROS, and also mitochondrial membrane potential.

**Methods:** The soft corals were phytochemically investigated through different partitioning and chromatography methods. Then cytotoxicity of extracts and isolated compounds of *S. compressa* and *S. variabilis* against MCF-7 and MDA-MB-231 and MCF-10A cell lines was tested. Flow cytometry method was used for apoptosis induction and the production of reactive oxygen species (ROS) and the mitochondrial transmembrane potential was determined by The DCFDA and JC-1 probes. Caspase-9, Bax, and Bcl-2 proteins were assessed with ELISA Kit, and by western blot analysis.

**Results:** A novel 16,17-epoxy-23-methylergostane derivative with four known steroid compounds were isolated from *S. variabilis*. One monoterpene, one sesquiterpene, five fatty acids, one phthalate, and two steroidal compounds were isolated from *S. compressa*. The novel compound showed cytotoxic activity against MCF-7 and MDA-MB-231 with IC50 values of  $31.44 \pm 1.17$  and  $25.67 \pm 1.05$  IM, respectively. It was revealed to diminish  $\Delta\Psi_m$  in a dose-dependent way in breast cancer cells. The chloroform extract showed cytotoxic activity with IC50 values of  $32.51 \pm 0.70$   $\mu\text{g/ml}$ , and  $8.53 \pm 0.97$   $\mu\text{g/ml}$  against MCF-7 and MDA-MB-231 cancer cells, respectively. The induction of the intrinsic apoptosis pathway was found by ROS generation, attenuation of Bcl-2 and induction of Bax proteins. It was supported by activation of caspase-9, increased apoptotic cells and also decrease of  $\Delta\Psi_m$ . There was no detectable sign of hepatic or renal toxicity in the SCE 100 mg/kg in the acute toxicity.

**Conclusions:** Phytochemical analysis of two *Sinularia* species identified bioactive and novel compounds for the first time. The present study demonstrates that chloroform extract and novel compounds of these soft corals showed antiproliferative activities on breast cancer cells by inducing an intrinsic pathway of apoptosis.

## References

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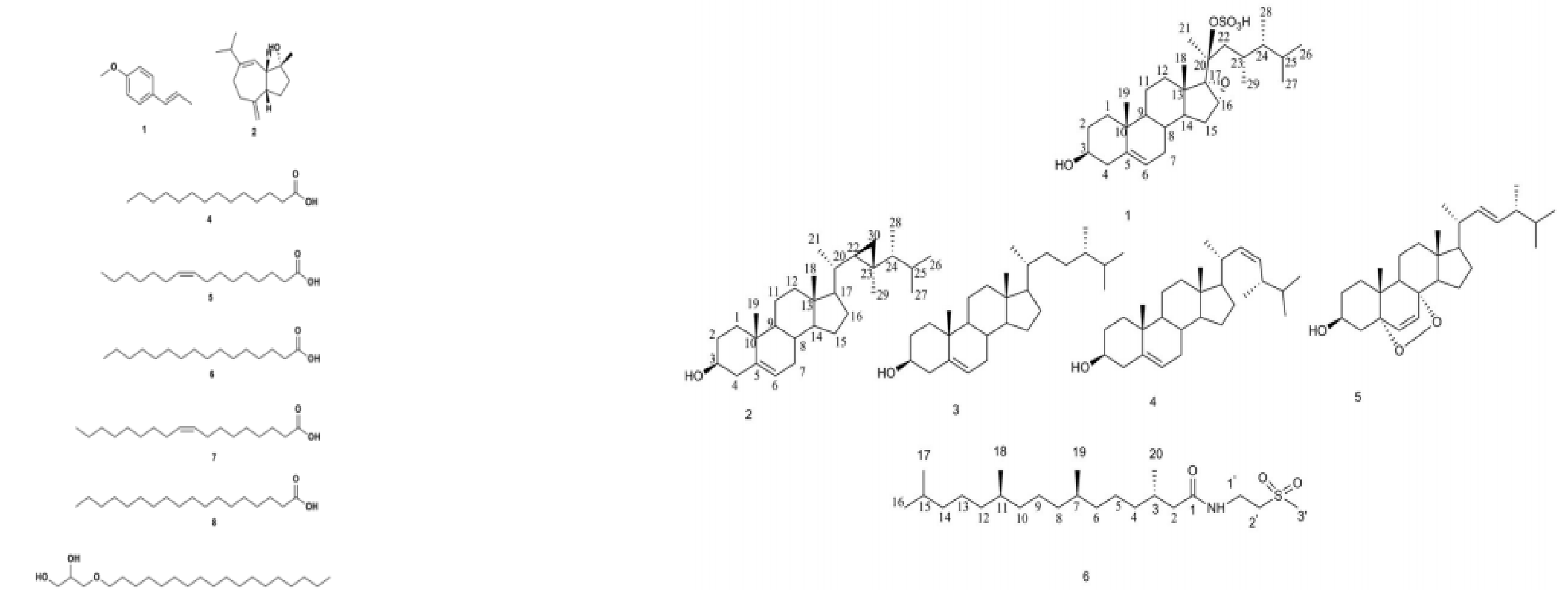
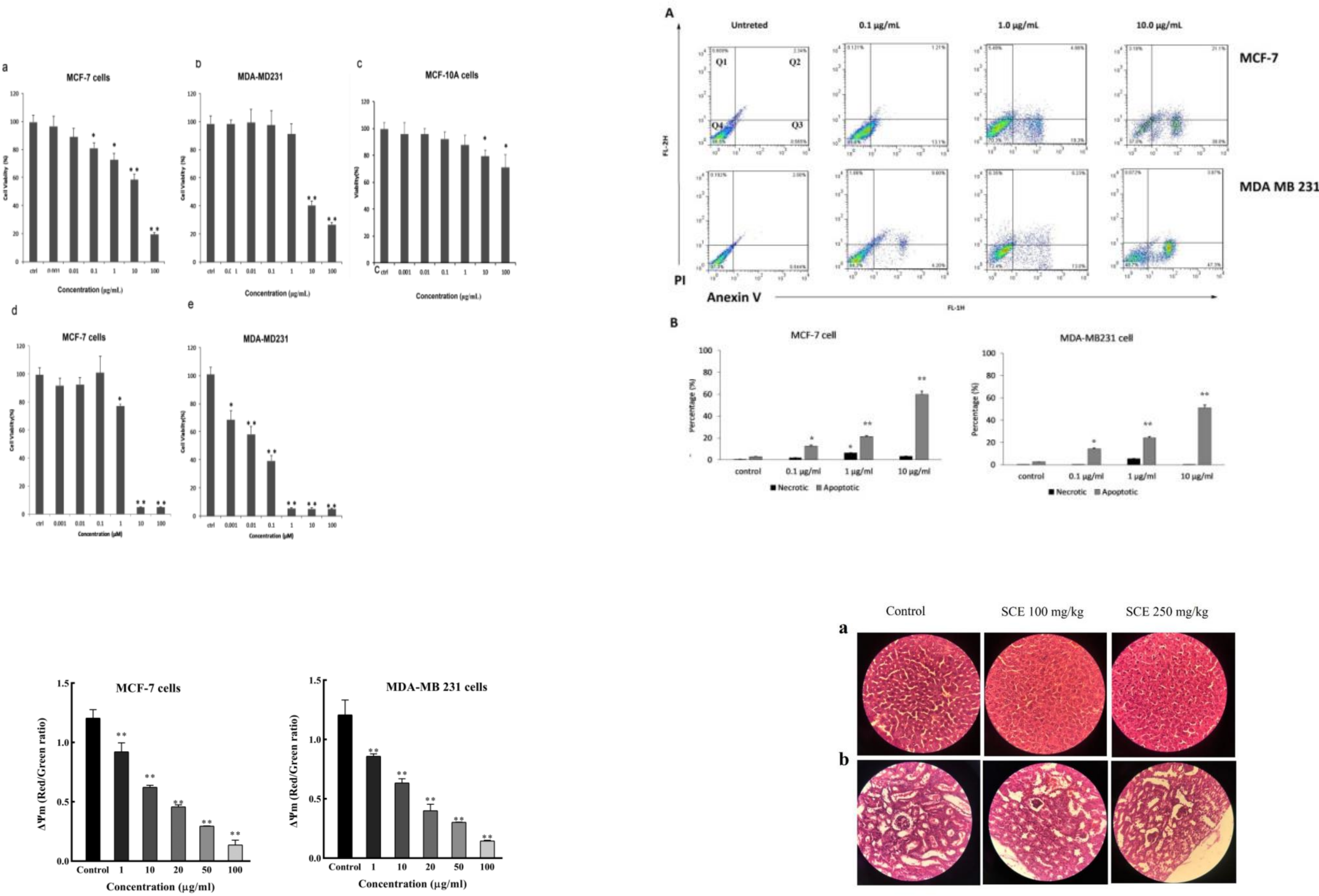


Figure 1. Structures of isolated metabolites from *Sinularia variabilis* a soft coral from Persian Gulf.



SCE Cytotoxicity Mediated through ROS Overproduction

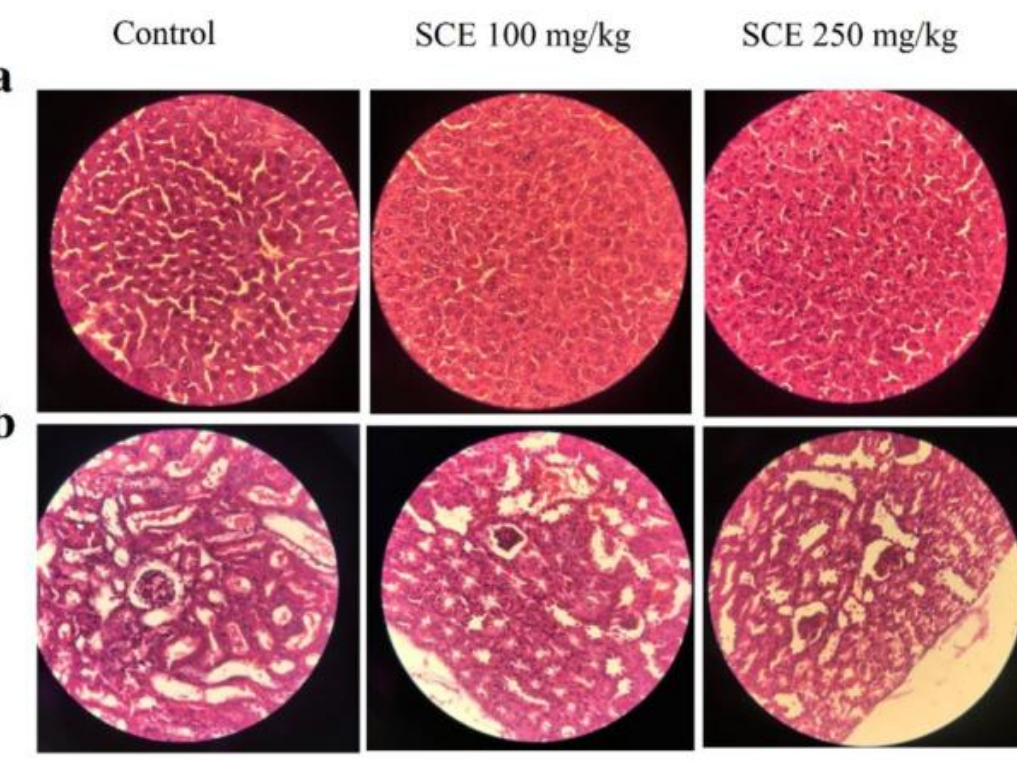


Table 1. Effects of SCE (0, 100, and 250 mg/kg) on kidney function test.