**Introduction**

Microtubule targeting agents (MTAs) that interfere with the dynamic state of the mitotic spindle are well-known and effective chemotherapeutic agents. These agents interrupt the microtubule network via polymerization or depolymerization, halting the cell cycle progression and leading to apoptosis. In our efforts to discover novel tubulin inhibitors, we developed novel pyrrole-based analogs targeting the colchicine binding site on tubulin and thereby interfering with tubulin polymerization.

**Results**

We report here 2 novel pyrrole-based carboxamides exhibit potent cytotoxic activities against epithelial cancer cell lines via targeting tubulin polymerization.

**Methods and Materials**

To identify the potential binding sites of CAs on the tubulin, the molecular docking procedure was performed by using Schrödinger molecular modeling software (Schrödinger, Inc., New York, NY, 2021). The impact of the CAs on the tubulin polymerization dynamic state was assessed by using the Tubulin Polymerization kit (Cytoskeleton Inc., Denver, Colorado, USA). Primary antibodies raised against the following proteins were used for western blotting: Cell Cycle and Apoptosis WB Cocktail (pHH3(Ser10)/Actin/ Cleaved PARP and caspase 3) for immunofluorescence staining – α-tubulin. The distribution of cell phases in HCC1806 cells was analyzed by Guava Muse Cell Analyzer using Cell Cycle Kit. Subcutaneous human tumor xenografts were generated in Balb/c mice with 100 µl of 5 × 106 HCC1806 breast cancer cells/mL suspensions in Dulbecco’s phosphate-buffered saline. The animal experimental protocols were approved by the Committee for Ethics of Animal Experimentation.

**Conclusion**

Collectively, we identified the novel CAs as the potent MTAs, inhibiting tubulin polymerization via binding to the colchicine-binding site, disrupting the microtubule network, and exhibiting anti-proliferative activities against the epithelial cancer cell lines both in vitro and in vivo.