ANNA WIECZOREK

ABSTRACT

In the present work I synthesized a series of ferrocenyl analogues and conjugates of activators of tubulin polymerization: paclitaxel and docetaxel, and an inhibitor of tubulin polymerization: plinabulin.

I found the replacement of the *N*-benzoyl group of the paclitaxel with the ferrocenoyl group and 4-ferrocenylbutyryl group increases the cytotoxicity of ferrocenyl analogues in comparision with paclitaxel and rises the ability to induce tubulin polymerization approx. 10-fold. The conjugates of taxanes with ferrocenyl group at position 2'-*O* exhibit similar or higher cytotoxicity in comparison with paclitaxel, but do not demonstrate any ability to activate tubulin polymerization.

In the second part of my research I synthesized a series of ferrocenyl conjugates of plinabulin. Durring the synthesis of these conjugates, I discovered a new unusual transformation of the piperazine-2,5-diones to oxazole-azlactones. The repleacement of a phenyl group in plinaulin with ferrocenyl moiety decreases ability of these compounds to inhibit tubulin polymerization. I also found that this modification leads to increasing cytotoxicity towards tumor cell lines of the multidrug resistant phenotype and causes that one of the compounds has an ability to inhibit activity of ABCB1 and ABCG2 proteins in contrast to plinabulin, which does not have such properties.