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## Synthesis and investigation of anti-cancer activity of new sulfamates of steroid estrogens

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Breast cancer (BC) is one of the most wide spread oncological diseases, and very often is estrogen-sensitive. Aromatase,  $17\beta$ -hydroxysteroid dehydrogenase (HSD) and estrone sulfatase (ES) are considered as suitable targets for the treatment of hormone-sensitive oncological diseases. New inhibitors of these enzymes based on estrogen sulfamates are of special interest, not least of all due to possibility for development of dual inhibitors of ES and aromatase or ES and  $17\beta$ -HSD. Such inhibitors also may play important role in the regulation of metabolic processes in prostate cancer. Almost all known steroid sulfamates have natural skeleton, despite the fact that products of their hydrolysis should not have hormonal activity. We synthesized sulfamates of  $8\alpha$ -steroid estrogen analogues and investigated perspectives of their use as inhibitors of BC cell growth, since their metabolism is different from metabolism of natural steroids. Additionally, some modifications in  $8\alpha$ -steroid skeleton may be introduced easier. We showed that  $7\beta$ -methyl-6-oxa-D-homo- $8\alpha$ -estrone sulfamate (**1**) is perspective ES inhibitor, and the product of its hydrolysis,  $7\beta$ -methyl-6-oxa-D-homo- $8\alpha$ -estrone (**2**) has no hormonal activity. Docking of steroid **2** into  $\alpha$ -ERLBD showed that crucial role in dramatic decreasing of uterotrophic activity belongs to  $\beta$ -methyl group at C-7, that became the reason for preparation of various  $7\beta$ -methyl-steroids. Synthesized steroids **3** and **4** fully block the growth of BC MCF-7 cell lines at the concentration 20  $\mu$ /ml, and do not affect the normal human skin fibroblast cell line growth. Finally, we found 5 steroids with activity against BC cells as has clinical standard tamoxifen. This important finding opens the new strategy for investigation of anti-cancer activity of such analogues in combination with medications having another mechanism of action.

### Biography

Alexander Shavva was Head of unique Department of Natural Chemistry Department at Saint-Petersburg State University during 25 years (1988-2014). He is Founder of steroid scientific direction in 1975. He has published more than 45+ patents and 120+articles. He was member of International Scientific Commissions and Head of Projects with big Pharmaceutical Firms.

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