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Effect of newly synthesized progesterone derivatives on apoptotic and metastatic pathway in MCF-7 breast cancer cells

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Background: Breast cancer is the second leading cause of mortality among women worldwide. Anticancer agents consisting of hybrid molecules are used to improve efficacy and reduce drug resistance. Alteration of different genes is involved in the development of cancer. Consequently, novel anticancer drugs with increased selectivity and specificity are required to overcome limitation of current drugs. A variety of synthetic steroid derivatives have been contrived, most these derivatives can interact with the steroid receptors because of a similarity of shape. Also, the investigation of modified steroid derivatives condensed with various heterocyclic rings has a great attention. Impaired apoptosis and metastasis are critical in cancer development and is a major barrier to effective treatment.

Methods: Several progesterone derivatives were synthesized. The structure of the newly derivatives was elucidated and confirmed using the analytical and spectral data. The newly synthesized progesterone derivatives, compounds 1, 2, 3, 4, 5, 6 and 7 were tested for their cytotoxic effects against human breast cancer cells (MCF-7) using neutral red uptake assay. Using QRT-PCR (Quantitative Real Time-Polymerase Chain Reaction), the expression levels of *P53, P21, Cdc2, Bcl-2, Survivin, CCND1, VEGF, HIF-1α, FGF-1, MMP-2, MMP-9, Ang-1 and Ang-2* genes were investigated.

Results: All tested compounds showed low IC50 values that were comparable to that of tamoxifen. The most active compounds against MCF-7 cancer cell line was in the descending order of 5>1>2>6>4>7>3. The study revealed that all newly synthesized compounds down-regulated the expression levels of *BCL-2, surviving, VEGF, Ang-2* and *MMp-9*. Compound 2-7 down-regulated CCND1 gene expression, nevertheless, this was only significant in case of compounds 2, 3 and 6. However, *P53* were up-regulated by compounds 3. Moreover, compound 1 significantly down-regulated *MMP-2* and compound 3 and 7 significantly down-regulated *FGF-1*.

Conclusion: This study introduced promising pro-apoptotic and anti-metastatic anticancer agents acting through the regulation of key regulators of apoptosis, cell cycle and metastasis related genes.

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Biologics to enhance current orthopedic procedures

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In orthopaedic surgery a transition to improve current orthopedic procedures is underway. Surgical techniques, instruments and implants have been greatly refined and improvements in imaging accuracy, namely magnetic resonance (MR) can now clearly identify pathology. The final frontier is to improve biology and hopefully healing. The use of biological materials to foster improved outcomes has been highlighted by major scientific breakthroughs of which have defined the critical pathways of healing and regeneration. The list includes blood-derived preparations, growth factors, bone marrow preparations and expanded stem cells. These biologic adjuncts can provide effective treatments during surgery or during the postoperative period. It is likely that biologic treatments will actively enhance many areas of orthopedic surgery to improve the healing capabilities of currently performed surgical procedures today and in the future. This review will systematically assess the peer-reviewed evidence based literature highlighting advances in both pre-clinical studies and clinical trials involving biological substances in the treatment of meniscus, ligament and articular cartilage surgical repair.

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