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Modulating Bone Marrow Microenvironment in Breast Cancer: Impact of Combined Chemotherapy and Herbal Extracts

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ABSTRACT

Despite advancements in diagnosis and therapy, breast cancer (BC) continues to be one of the most prevalent causes of cancer-related mortality worldwide. A critical challenge lies in the capacity of breast cancer cells (BCCs) to enter dormancy within the bone marrow (BM), a state that facilitates metastatic relapse and worsens prognosis. While conventional chemotherapeutic agents, such as 5-fluorouracil (5-FU), effective against proliferating tumor cells, often inflict collateral damage on healthy tissues. Recently, plant-derived extracts have garnered attention for their anti-inflammatory and immunomodulatory potential as complementary therapies. However, the combined effects of chemotherapy and herbal compounds on BM microenvironment and inflammation remain underexplored. This study used a DMBA-induced breast cancer rat model to investigate the effects of 5-FU, nitric oxide synthase inhibitors (L-NAME, nor-NOHA), and herbal extracts (*Inula helenium*, *Alchemilla smirnovii*, *Rumex obtusifolius*). Biomarkers such as IL-2, COX-2, TNF-α, VEGF-α, and MMP-2 were measured using ELISA, WB, and ICC/IF. BM histological changes were examined via H&E staining. The combination therapy reduced pro-inflammatory and metastatic markers while increasing IL-2, suggesting both anti-metastatic and immune-supportive effects. Herbal extracts also lessened 5-FU's damage to bone marrow tissue. These results indicate that combining herbal extracts with chemotherapy may improve immune function, reduce inflammation, and protect bone marrow,offering a promising strategy to enhance breast cancer treatment and limit side effects.

Keywords: breast cancer, bone marrow, herbal extracts, 5-FU; IL-2, pro-inflammatory markers

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