Diosgenin prevents breast cancer metastasis via the inhibition of epithelial-mesenchymal transition.

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Background: Globally, breast cancer (BrCa) is the primary cause of cancer-related morbidity and death in women. Despite significant changes in healthcare activities like screening and early detection over the past few decades, African Americans (AA) continue to experience cancer health disparities. Many studies have been done on BrCa treatments, but AA patients have had less success than other racial or ethnic groups. Therefore, novel strategies are required to improve survival rates, lower BrCa mortality, and ultimately enhance the health of racial/ethnic minorities. Current treatment regimens, such as chemotherapeutic agents, are showing less effectiveness since they are linked to drug resistance, side effects, and the recurrence of the disease. Thus, the need for more potent therapeutic agents for BrCa is rising; these agents could be natural compounds that have been shown to have several targets, are less toxic and have fewer side effects. In this study, we investigated the effect of Diosgenin (DG), a natural compound derived from the plant *Dioscorea villosa*, on the BrCa cells metastasis using the disparity cell lines MDA-MB-468 (AA) and MDA-MB-231 (Caucasian American, CA). **Methods:** Cell viability and cytotoxicity of DG were estimated by live/ dead cell assay; scratch assay and clonogenic assays were carried out following treatment with DG with various concentrations (5uM to 40uM) for different time intervals. RT-qPCR and western blots were used to assess the expressions of EMT (epithelial to mesenchymal transition) and apoptotic markers. **Results:** Our results show DG considerably and dose-dependently reduced the number of colonies and the cell migration in both BrCa cell lines. Immunoblots and RT-PCR analysis showed a noticeable decrease in anti-apoptotic (BCL-xL) and increases in pro- (BAK, BAX) and -apoptotic (PARP) markers. Furthermore, high doses of DG increased EMT markers expression, such as E-Cadherin, which, in turn, decreased ZEB-1 expression. Therefore, it stops BrCa cells from undergoing EMT. In addition, the effects of DG on blocking EMT pathways were verified using Nanostring technology. **Conclusions:** Altogether, DG dramatically raised cytotoxicity and apoptosis and inhibited metastasis in both cell lines compared to control cells. These findings suggest that DG might be a therapeutic agent to treat BrCa metastases.