

ABSTRACT

Breast cancer is the second highest cause of death worldwide. Metastasis is the leading concern in such patients, along with the non-responsiveness of chemotherapy. Plants in our surroundings could have high therapeutic potential but usually remain unnoticed in the present day in scientific investigations. It is well known that India is a rich repository of medicinal plants and that various herbal medicine practices are considered a living tradition in the country. Using medicinal plant parts for greater effectiveness without adverse effects is an emerging trend in today's therapeutic approach. Melatonin is considered to be one of the anti-cancer metabolite showing protective effect in breast cancer. So our study aims to understand what happens if we treat breast cancer cells with these two natural compound individually as well as a co-treatment. The present study focuses on screening important medicinal plants through preliminary and advanced phytochemical analysis for their ability to inhibit breast cancer progression. *Butea monosperma* (*Bm*), *Saraca asoca* (*Sa*), *Melia azedarach* (*Ma*) and *Solanum virginianum* (*Sv*) were taken for preliminary phytochemical analysis and anti-proliferative activity determination on breast cancer cells (MCF-7, MDA-MB 231). The study showed the potent activity of *Sv* leaves on both breast cancer cell lines. In combinational approach, melatonin and *Sv* leaf extracts were evaluated for dosage determination on MCF-7 and MDA-MB-231 cell lines. Further phyto-composition of *Sv* leaf extracts were analysed through GC-MS and HR-LC-MS/MS analyses which indicated the presence of various remarkable secondary metabolites, i.e. alivicine, solasodine, quercetin, solamargin, ritterazin, quinic acid etc. Out of the molecular interaction between target proteins and nine selected phytocompounds, Ritterazine A showed effective binding. Further, cytotoxicity studies on non-cancerous cells (HEK-293), cell migration inhibition assay, clonogenic assay, FACS analysis,

and gene expression study were performed. The gene expression study reveals the anti-breast cancer activity of *Sv* leaf extracts in combination with Melatonin. The relative upregulation of anti-apoptotic (*CASP3*, *CASP8*, *CASP9*, *BAX*), anti-inflammatory (*IL4*, *IL10*) and down-regulations of pro apoptotic (*BCL2*) and metastatic genes (*MMP2*, *MMP9*) indicate their therapeutic activity against breast cancer. It will be interesting to study the effect of *Sv* leaf extract *in vivo* as a crude form along with the action of its identified potent phyto-molecules. In conclusion, the present study explains the systematic analysis of the plant's potential as an anticancer agent along with melatonin. It is therefore alluded that it can pave the way towards a novel drug development that could specifically target metastatic breast cancer, a need of the hour.

Keywords: Phytochemistry, breast cancer, anti-proliferative activity, melatonin, combinational approach.