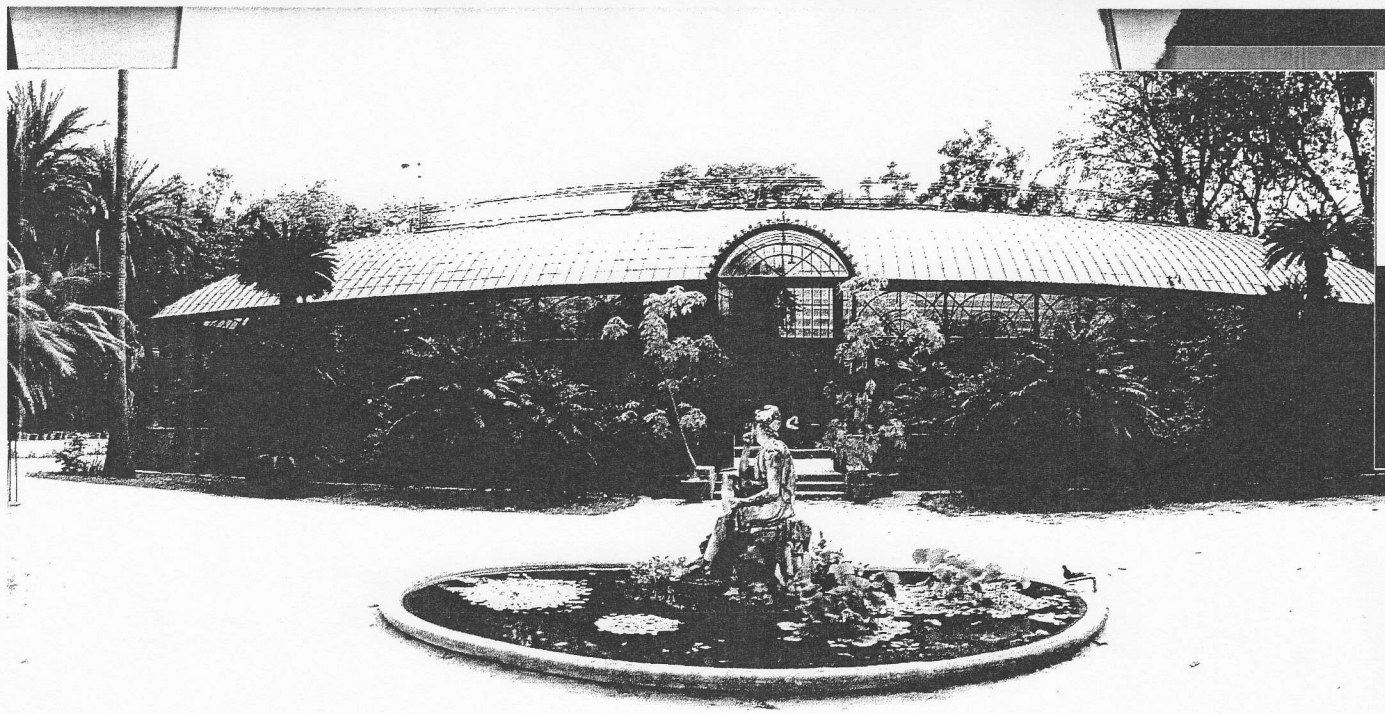

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P60 - JAHA, A NOVEL HISTONE DEACETYLASE INHIBITOR: CYTOTOXIC EFFECT ON TRIPLE-NEGATIVE BREAST CANCER CELLS

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Histone deacetylase inhibitors (HDACi) have emerged as effective anticancer agents in the clinical practice. Jay Amin hydroxamic acid (JAHA), is a metal-based analogue of the HDACi suberoylanilide hydroxamic acid SAHA [1] obtained by the formal replacement by a ferrocene bioisostere of the aryl *cap* in SAHA. In the present study, the effects of JAHA on MDA-MB231 cells, obtained from triple-negative human breast carcinoma, were evaluated. JAHA exhibits high cytotoxic activity on breast cancer cells, with an IC_{50} = 8.45 μM at 72 h. Following treatment with JAHA at this concentration, the viability of MDA-MB231 cells was analyzed using an MTT assay, and apoptosis onset, alteration of cell proliferative rate, intracellular reactive oxygen species (ROS) generation and mitochondrial membrane potential ($\Delta\Psi m$) alteration, if occurring, were evaluated by flow cytometry [2]. In addition, Western blot analysis was performed to examine the expression of autophagy-associated proteins. The results demonstrated that treatment with JAHA induced a non-apoptotic type of cell death, and an alteration of cell proliferation characterized by the accumulation of cells in the G_1 and subG_0 phases of the cycle. The most interesting results on JAHA mechanism of action regard its ability to induce early ROS production and subsequent dissipation of $\Delta\Psi m$ and autophagy inhibition, that were confirmed by the reversion of the cytotoxic effect obtained by co-treatment with either anti-oxidant (butylated hydroxytoluene) or autophagy-promoter compound (rapamycin). An in vitro "scratch assay" has also been performed to measure migration of cells treated for 24 h with 8.45 μM JAHA compared to control. Preliminary indications suggest that JAHA has no effect on the motile behaviour of MDA-MB231 breast cancer cells. In light of such results, it appears that JAHA may be a promising potential chemotherapeutic agent for triple-negative breast cancer.

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