Cyclophosphamide (CP) is one of the most widely used anticancer drugs for various malignancies. However, its long-term use leads to ALDH1A1-mediated inactivation and subsequent resistance which necessitates the development of potential ALDH1A1 inhibitors. Currently, ALDH1A1 inhibitors from different chemical classes have been reported, but these failed to reach the market due to safety and efficacy problems. Developing a new treatment from the ground requires a huge amount of time, effort, and money, therefore it is worthwhile to improve CP efficacy by proposing better adjuvants as ALDH1A1 inhibitors. Herein, the database constituting the FDA-approved drugs with well-established safety and toxicity profiles was screened through already reported machine learning models by our research group. This model is validated for discriminating the ALDH1A1 inhibitors and non-inhibitors. Virtual screening protocol (VS) from this model identified four FDA-approved drugs, raloxifene, bazedoxifene, avanafil, and betrixaban as selective ALDH1A1 inhibitors. The molecular docking, dynamics, and water swap analysis also suggested these drugs to be promising ALDH1A1 inhibitors which were further validated for their CP resistance reversal potential by *in-vitro* analysis. The *in-vitro* enzymatic assay results indicated that raloxifene and bazedoxifene selectively inhibited the ALDH1A1 enzyme with IC_{50} values of 2.35 and 4.41 μM respectively, whereas IC_{50} values of both the drugs against ALDH2 and ALDH3A1 was >100 μM. Additional *in-vitro* studies with well-reported ALDH1A1 overexpressing A549 and MIA paCa-2 cell lines suggested that CP sensitivity was further ameliorated by the combination of both raloxifene and bazedoxifene. Collectively, *in-silico* and *in-vitro* studies indicate raloxifene and bazedoxifene act as promising adjuvants with CP that may improve the quality of treatment for cancer patients with minimal toxicities.

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