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RESEARCH PAPER

# IDENTIFICATION OF PARP-1 INHIBITORS AGAINST BREAST CANCER USING *IN SILICO* REPURPOSING OF FDA APPROVED DRUGS: DOCKING BASED APPROACH, MM/GBSA AND ADME ANALYSIS

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**Drug discovery approaches have been time consuming and require huge monetary investments. The repurposing of already existing drugs is a promising approach for the faster and cost-effective drug discovery against various diseases. Cancer, being a heterogenous disease, requires special attention and breast cancer becomes a medical emergency, as it is the most diagnosed cancer among women associated with higher chances of relapse and recurrence. Targeted therapies overcome the toxic effects of conventional cancer therapies, and the development of new targeted therapies are the need of the hour due to the problems of acquired resistance, and deteriorating cancer scenario. PARP-1 emerges an attractive target for drug discovery against breast cancer due to its vital role in DNA repair. Therefore, the aim of the present work was to repurpose existing FDA approved drugs targeting PARP-1 inhibitors as anti-breast cancer agents. A three-tier virtual screening followed by binding energy analysis, was performed to find the FDA approved drugs exhibiting good and stable binding characteristics with PARP-1. Further, a comparative analysis of the *in silico* ADME profile of the drugs was carried out. Combined results of the *in silico* analysis were used for selecting best hits against PARP-1. Two best hits, Candesartan and Mycophenolic acid, were selected and the structural features of both the compounds matched with PARP-1 selective inhibitor, Olaparib. Further, *in vitro* and *in vivo* validation of the *in silico* results is warranted for assessing the potential of these compounds as repurposed PARP-1 inhibitors.**

**Key words:** PARP-1 inhibitor, Breast cancer, *In silico* analysis, Virtual screening, Drug repurposing.

## INTRODUCTION

Drug repurposing encompasses techniques for deciphering the utility of existing drugs for a new medical condition, other than the one for which it is indicated [1]. The approach can be used for testing existing drugs in pre-clinical animal models directly, while considerably saving time as well as money. The repurposing initiatives are appealing due to the already tested safety, efficacy and toxicity profile of the drug. As compared to the new drug applications, which account for 10% of the market approvals, the repurposed drugs take an upper hand as approximately 30% of them make up to the market [2]. Various drugs have been successfully repurposed for newer clinical indications, such as, the antihypertensive Minoxidil repurposed