**An efficient synthesis of some new 1,4-disubstituted phthalazine derivatives and their anticancer activity**

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**ABSTRACT**

A novel series of phthalazine derivatives bearing isoindol-1,3-dione moiety were synthesized by treating ethyl{4-[4- (1,3-dioxo-1,3-dihydroisoindole-2-yl)-phenyl] phthalazin-1-yloxy}acetate (**3**) and {4-[4-(1,3-Dioxo-1,3-dihydroisoindol-2-yl)phenyl]phthalazin-1-yloxy} acetic acid hydrazide (**7a**) with various chemical reagents.The newly synthesized compounds were characterized on the basis of their spectral (1H NMR, 13C NMR, Ms, IR) analyses. In vitro, most of the synthesized derivatives were screened for their antitumor activity against MCF-7 cells using MTT assay. Compounds **16b**, **18**, **13**, **15**, **17** showed the most potent cytotoxic effect concluded from their IC50 values 50, 70, 150, 180 and 100 μg/ml respectively.

**Keywords:** Phthalazin-1-(2H)-One; Acid hydrazide, Isoindol-1,3-dione; Antitumor activity.

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**INTRODUCTION**

Breast cancer is the most common form of cancer and the second most frequent cause of cancer death among women [1]. Regardless of the use of surgical treatment and irradiation, chemotherapy still remains an important option for the treatment of solid cancers. Chemotherapeutic drugs should preferentially target tumor cells without harming normal cells or tissues. However, although new cytotoxic agents with unique mechanisms of action have been developed continuously, many of them have not been therapeutically useful due to low tumor selectivity and harsh side effects [2]. These facts prompted us to design and develop novel potent and selective anti-breast cancer agents. 1,4-Disubstituted phthalazines have received a considerable attention as antitumor agents in the past few years [3,4]. A successful example is N-(4-chlorophenyl)-4-(pyridin-4-ylmethyl)phthalazin-1-amine also known as Vatalanib (PTK-787) which is VEGFR (vascular endothelial growth factor receptor) inhibitor and is currently in Phase III clinical trials for metastatic colorectal cancer [5]. [4-(3,4-difluoro-phenylsulfanylmethyl)-phthalazin-1-yl]-(3-fluoro-phenyl)-amine II displayed excellent selectivity against MDA-MB-231 cell line [6]. Furthermore, N-(4- fluoro-phenyl)-2-[4-(4-pyridin-4-ylmethyl-phthalazin-1-yl)-piperazin-1-yl]-acetamide III has shown more potent