# Synthesis, characterization, anticancer activity, and molecular docking of novel maleimide–succinimide derivatives

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**Background and objective**
A wide range of maleimide heterobifunctional reagents are used for the preparation of targeted therapeutics. Succinimide derivatives are important compounds found in a variety of natural products that exhibit remarkable biological and pharmaceutical activity. The creation of new maleimide–succinimide derivatives will increase the importance and medicinal applications of these groups.
**Materials and methods**
The reaction of bismaleimide (**1–2**) with phenylhydrazide and 4-methylbenzohydrazide resulted in the formation of N'-[1-(4-[2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl] phenyl)-2,5-dioxopyrrolidin-3-yl] benzohydrazide (**3**), N'-[1-(4-[2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl] phenyl)-2,5-dioxopyrrolidin-3-yl]-4-methylbenzohydrazide (**4**), N'-[1-(4-(2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)-[1,1'-biphenyl]-4-yl)-2,5-dioxopyrrolidin-3-yl] benzohydrazide (**5**), and N'-[1-(4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-[1,1'- biphenyl]-4-yl)-2,5-dioxopyrrolidin-3-yl]-4-methylbenzohydrazide (**6**). The interaction of potential compounds with AKT1 and CDK2 proteins was performed using molecular docking to target the hydrogen bond and amino acid residues.
**Results**
The new compounds were characterized using Fourier-transform infrared spectroscopy, $^{1}$H-NMR, $^{13}$C-NMR spectroscopy, and mass spectrometry. The MTT assay was used to test cell viability against breast cancer cells (MCF-7). The cytotoxicity results revealed that compounds 3 and 5 were more toxic than compounds 4 and 6. Molecular docking of compounds that interacted with AKT1 and CDK2 showed affinity energy of –16.112 and –21.342 kcal/mol for compound 3, while –22.398 and –19.940 kcal/mol for compound 5. The root-mean-square deviation values for CDK2 and AKT1 were 2.27 and 1.61 for compound 3, respectively, and 1.93 and 1.90 for compound 5.
**Conclusion**
Toxicity and molecular docking studies revealed that compounds 3 and 5 could be developed as anticancer agents against breast cancer, indicating that further research is warranted.

**Keywords:**
bismaleimide, breast cancer, cell viability, docking studies, maleimide–succinimide derivatives

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## Introduction

Maleimides are a kind of heterocyclic molecule that may be found in natural goods [1] and are employed in chemical and pharmaceutical chemistry. These uses are mostly based on two common maleimide reactions: (a) Michael addition with amines [2,3], alcohols [4], or thiols [5,6]; (b) addition of the cyclopentadiene [7] or furan [8,9] moiety to the Diels–Alder reaction. Michael donors (aliphatic or aromatic amines, amides, carbamates, or azides) interact with electron-deficient alkene molecules (Michael acceptors) such as α, β-unsaturated esters, vinyl ketones, vinyl sulfones, acrylamides, acrylonitrile, and vinylphosphonates [10,11]. Hence, bismaleimides are a class of compounds connected to two groups of maleimides by nitrogen atoms via a bonder [12,13]. Maleimides have been extensively studied in such reactions because, due to the presence of an activated double bond, they can be easily converted to substituted succinimides [14]. In addition, the compounds from the corresponding saturated model bis-succinimides were synthesized. Many medically significant medicines, such as phensuximide, ethosuximide, methsuximide, and andrimias, utilize the succinimide molecule as a precursor [15,16]. Some derivatives had interesting biological activities, such as analgesic [17], anticancer [18], antisplasmodic