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ORIGINAL ARTICLE

Synthesis, spectral studies, *in vitro* and molecular docking studies of novel hydrazinyl carbothioamide derivatives

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Abstract Five novel compounds possessing hydrazinyl carbothioamide moiety were designed and synthesized. All the compounds were tested for *in vitro* biological activities. Most of the tested compounds displayed strong antibacterial and antifungal activities. Molecular docking studies suggested that the hydrazinyl carbothioamide moiety of compounds (**6**–**10**) can in general be accommodated the binding pocket of the breast cancer protein (1JNX) and are responsible for the activity of the whole of the molecule. The docking results provide a new insight into the design of hydrazinyl carbothioamide derivatives as breast cancer drug.

1. Introduction

Bacterial and fungal infections are growing problem in contemporary medicine, as a result of the increasing use of antibacterial agents for all kinds of infectious diseases on mankind, many drug-resistant pathogens have appeared on recent years besides that of various human diseases, cancer has proved to be one of the most intractable diseases to which human beings are subjected, and as yet no practical and generally effective drugs or methods of control are available. Therefore, identification of novel potent, selective and less toxic anticancer agents remains one of the most pressing health problems [1]. Hetero cycles possessing nitrogen and sulfur hetero atoms are found to exhibit a wide spectrum of biological activities including antibacterial [2] and antifungal [3], activities. Many hydrazinyl carbothioamide containing compounds are reported as herbicidal [4], fungicidal [5], anti-tubercular [6], anti allergic [7], anti anaphylactic [8], antiarthritic [9], antibiotic [10], antiviral [11], anti-inflammatory [12], analgesic [13] and psychotropic agents [14]. A series of hydrazine carbothioamide derivatives were synthesized possessing excellent antibacterial and antifungal activities [15–17], they have also been shown to possess antimalarial [18–20], antibiotic [21], anticancer [22], antiinflammatory [23], antihypertensive [24], tyrokinase PDGF–RTK inhibition [25] and anti-HIV [26,27] properties. The molecular docking technique [28,29], plays an important role in the drug design and discovery to predict the conformations of each ligand molecule at the active site. So it was planned to synthesize new hydrazinyl

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carbothioamide derivatives with 1, 4-disubstitution using a green route that is microwave organic reaction enhancement method (MORE) and test them for *in vitro* antifungal and antibacterial activities. The rigid molecular docking studies of newly synthesized hydrazinyl carbothioamide derivatives were carried out to predict the antibacterial activity and molecular docking are reported.

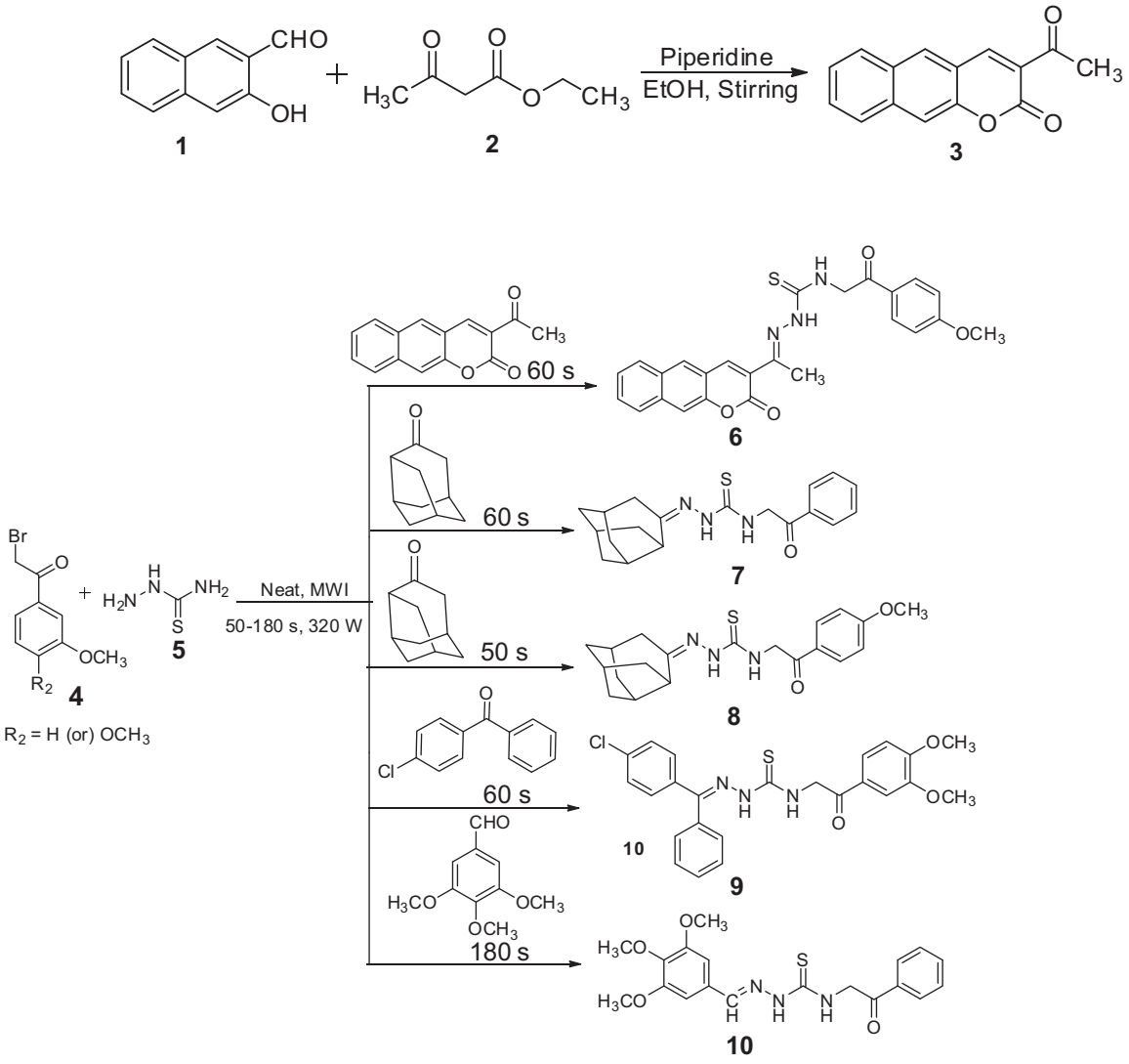
2. Results and discussion

2.1. Chemistry

In view of the large amount of literature that addresses organic-TSCs and their applications as potential antineoplastic and antibacterial agent, it is surprising that aryl ethanone incorporated analogs with these biological targets have not been extensively studied. So we determined to design and synthesize a series of N-14, N-17-disubstituted hydrazine carbothioamide derivatives (**6**–**10**) by the reaction of 2-bromo-1-aryl ethanone either with substituted ketone/aldehyde or with thiosemicarbazide Scheme 1. The synthesized compounds were characterized by (Preparation of 3-acetyl-2H-benzo[g]chromen-2-one), ^{1}H NMR Spectrum of compound **3** (Preparation of 3-acetyl-2H-benzo[g]chromen-2-one) (Fig. S1), IR, ^{1}H NMR, ^{13}C NMR, 2D NMR spectrum of ^{1}H–^{13}C COSY, HR-Mass spectrometry and Elemental analysis. In the IR spectrum of compound **6** the peaks at 1656, 1601, 1315 and 3429 cm^{-1} are due to carbonyl and C═O, C═N C═S and NH stretching frequencies.

2.2. NMR spectral analysis

In the ^{1}H NMR spectrum (Fig. S2) of compound **6** (Fig. 1) there is a singlet observed at 9.30 ppm that should be due to the coumarinyl benzylic proton (H-4). The (H-17a/b) protons of (H-17) appeared as singlet at 4.71 ppm. The two singlets appeared at 2.78 (methyl) and 3.89 (methoxy) each with three protons integral value must be due to the methyl and methoxy protons. The aromatic protons pertaining to the coumarinyl



Scheme 1 Synthesis of hydrazinyl carbothioamide derivatives (**6**–**10**).