



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم

# بسم الله الرحمن الرحيم



**HANAA ALY**



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# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

### قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
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كلية العلوم – قسم الكيمياء



## Design and Synthesis of Some New Thiazole, Pyridine and Pyrimidine Derivatives for Biological Evaluation

Thesis Submitted by

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كلية العلوم – قسم الكيمياء



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## Contents

ABSTRACT.....	
SUMMARY.....	i-viii
1. INTRODUCTION .....	1
1.1 Thiazoles .....	2
SYNTHETIC METHODS OF 1,3-THIAZOLE DERIVATIVES:.....	3
1.1.1 From Thioamide .....	3
1.1.2 From Thiourea and Thiourea Derivatives.....	4
1.1.3 From Thiosemicarbazone .....	7
1.1.4 From miscellaneous reagents.....	12
1.2 Pyridines .....	14
Synthesis of theino[2,3-b]pyridine derivatives .....	15
1.2.1 From pyridine derivatives .....	15
1.2.2 From thiophene derivatives .....	19
1.3 Pyrimidines.....	21
Synthesis of pyrimidine-2-thione derivatives .....	22
1.3.1 From thiourea .....	22
1.3.2 From 6-aminothiouracil .....	24
1.4 The Biological importance of thiazoles, thienopyridenes, pyrimidines .....	26
1.4.1 Biological activities of thiazoles .....	26
1.4.2 Biological activities of pyridine and thienopyridine derivatives .....	29
1.4.3 Biological activities of pyrimidines .....	32

<b>۲. RESULTS AND DISCUSSION .....</b>	<b>۳۶</b>
<u>۲. ۱ Part ۱: Synthesis, characterization and investigation of antiproliferative activity of novel thiazole, pyridine and pyrimidine derivatives using Fluoroacetophenone .....</u>	<u>۳۶</u>
۲. ۱. ۱ Chemistry.....	۳۷
۲. ۱. ۲ Cytotoxicity activity.....	۴۷
<u>۲. ۲ Part ۲: Synthesis, Antiproliferative Activity and Molecular Docking Study of Novel Nicotinamides as Prospective Anticancer Agents .....</u>	<u>۵۱</u>
۲. ۲. ۱ Chemistry.....	۵۳
۲. ۲. ۲ Antiproliferative activity.....	۶۰
۲. ۲. ۳ Molecular docking .....	۶۳
<b>Spectral data</b>	
.....	۷۰
<b>۳. EXPERIMENTAL .....</b>	<b>۱۳۸</b>
<u>Part ۱: Synthesis, characterization and investigation of antiproliferative activity of novel thiazole, pyridine and pyrimidine derivatives using Fluoroacetophenone .....</u>	<u>۱۴۱</u>
<u>Part ۲: Design, Synthesis, and Molecular Docking Study of Novel Heterocycles Incorporating Nicotinamide or Thienopyridine as Potent Anticancer Agents .....</u>	<u>۱۵۸</u>
<b>۴. REFERENCES .....</b>	
۱۷۸	





**List of Figures**

Figure 1: Thiazoles containing Rhodanine moiety .....	1
Figure 2: Natural products contain pyridine nucleus .....	14
Figure 3: Resonance structures of theinopyridine .....	15
Figure 4: Pyrimidine nucleus present in DNA & RNA .....	21
Figure 5: Marketed drugs containing thiazole scaffold .....	26
Figure 6: Marketed drugs containing thienopyridine scaffold.....	29
Figure 7: Marketed drugs containing pyrimidine scaffold .....	33
Figure 8: % inhibition in Surviving fractions in different cancer cell lines after treatment with single dose (100 µg/ml) of pyridine and 1,3-thiazole compound derivatives . MCF-7 Human breast carcinoma cell line (A), HCT-116 Human colon carcinoma cell line (B), HEPG-2 Human Liver carcinoma cell line (C), Values are the means ± SD of three independent experiments performed in triplicates. ....	48
Figure 9: Cytotoxicity of Doxorubicin as reference standard and compound number 7c on MCF-7 Human Breast carcinoma cell line (A) and VERO African Green monkey kidney normal cell line (B). Values are the means ± SD of three independent experiments performed in triplicates.....	49
Figure 10: Natural products contain pyridine nucleus .....	51
Figure 11: Drugs with improved water solubility .....	52
Figure 12: Dose dependent antiproliferative data of the nineteen compounds against HCT-116 cancer cells according to the MTT assay after 48 h of exposure. 61	
Figure 13: Dose dependent antiproliferative data of the nineteen compounds against MCF-7 cancer cells according to the MTT assay after 48 h of exposure. ...	61
Figure 14: Dose dependent antiproliferative data of the nineteen compounds against HepG2 cancer cells according to the MTT assay after 48 h of exposure....	61
Figure 15: The 2D docked model of compound 2d and 26d into the active site of 4k9g and 4dkv.....	68

## *List of Figures*

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Figure 17: The electrostatic map of 2d into the active site of 3kg.....	68
<b>Figure 18:</b> The contact performance 2d into the active site of 3dk .....	69
<b>Figure 19:</b> The 2D docked model of compounds 2f and 2b into the active site of 3kg and 3p.o .....	69

**ABSTRACT**

**Name:** Manar ELsaied AbdElsatar Elasasy

**Title:** Design and Synthesis of Some New Thiazole, Pyridine and Pyrimidine Derivatives for Biological Evaluation

**Degree:** Philosophy of Doctor (Ph.D.)

Thiazoles, pyridine and pyrimidines, are few of the very important classes of heterocyclic compounds having great medicinal and pharmacological importance. In the present study, new series of biologically active compounds containing thiazole, pyridine and pyrimidine units have been synthesized and screened *in vitro* for their anticancer activities

The structures of all the new synthesized compounds were characterized by spectroscopic techniques such as, IR, NMR ( $^1\text{H}$  and  $^{13}\text{C}$ ), Mass spectroscopy and elemental analysis.

**Keywords:**

Thiosemicarbazone, thiazole, pyridine, pyrimidine, Nicotinamide, thienopyridine, and anticancer activity.

## Synthesis and Antiproliferative Activity of Novel Hydrazono Thiazolidene and Thiazole Derivatives Bearing Rhodanine Moiety

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**Abstract**—Some new fluoro-heterocyclic compounds containing thiazole and pyridine moieties have been synthesized and studied for their antiproliferative activity. Thiazole derivatives have been synthesized by the reaction of alpha-halo carbonyl compounds with thiosemicarbazones. Some pyridine derivatives have been synthesized by the reaction of chalcone with cyanothioacetamide and/or malononitrile. Spectroscopic methods have been used for elucidating molecular structures of the products. Cytotoxic activity of several derivatives has been tested against human breast cancer (MCF-7), human colon cancer (HCT-116) and human liver cancer (Hep-G2) by the SRB method. Most of compounds exhibit mild effect on the tested cell lines. One of thiazolidin-4-one derivatives has been characterized by moderate to strong effect on MCF-7 cell line.

**Keywords:** thiosemicarbazone, thiazole, pyridine, antitumor activity

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### INTRODUCTION

Rhodanines and their bioisostere thiazole derivatives [1–5] are considered as promising bioactive compounds (Fig. 1).

Molecules containing fluorine atoms exhibit a wide range of biological activities including anticancer activity [6, 7].

Thiosemicarbazides are widely used in medicinal chemistry as efficient intermediates in synthesis of biologically active compounds including antiviral [8], anticancer [9], antitumor [10], and some more. Thiosemicarbazone is one of the precursors in construction of novel class of thiazole containing rhodanine moiety (Fig. 1) characterized as anticancer [11], antioxidant [12], anti-inflammatory [13], antimicrobial [14], and anti-apoptotic [15] agents. Based on the above and

our prior experience in synthesis of new heterocyclic compounds [16–24], we have synthesized novel 2-[[1-(4-fluorophenyl)ethylidene]hydrazono]thiazole derivatives and tested their anti-proliferative activity.

### RESULTS AND DISCUSSION

In the current study, 4-fluoroacetophenone thiosemicarbazones **3a–3c** were synthesized by reacting 4-fluoroacetophenone **1** with thiosemicarbazides **2a–2c** in acidic media (Scheme 1). Analytical data of compounds **3a–3c** were similar to those reported earlier [25, 26].

Thiosemicarbazone derivatives were used as building blocks in the following synthesis of new fused thiazole rings [27, 28]. Hydrazine carbothioamide derivatives (**3a–3c**) were reacted with  $\alpha$ -halo acid or  $\alpha$ -halo esters (bromoethanoic acid, ethyl 2-bromoethanoate and ethyl 2-bromopropanoate) in the presence of  $\text{CH}_3\text{COONa}$ , the

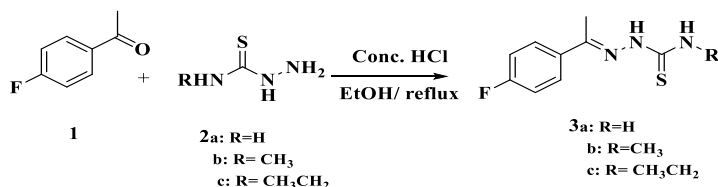
## SUMMARY

**Design and Synthesis of Some New Thiazole, Pyridine and Pyrimidine  
Derivatives for Biological Evaluation**

The purpose of this work is to synthesize novel biologically active compounds as drugs analogues through the following two parts:

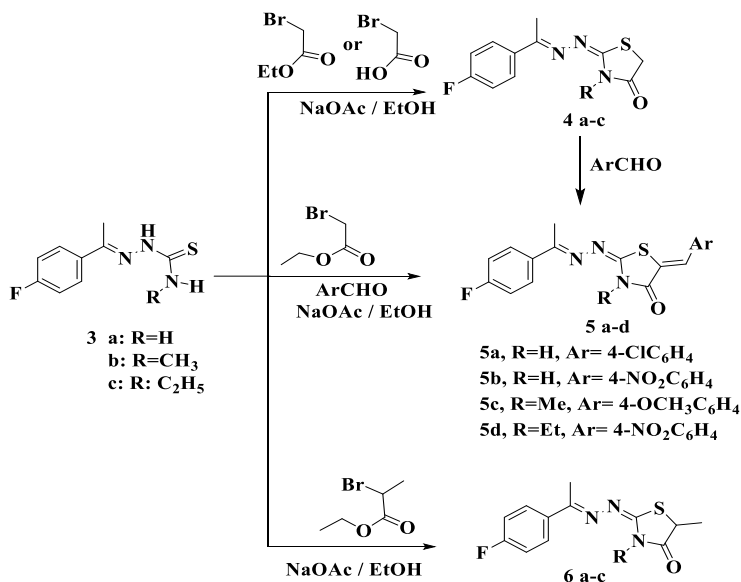
**Part 1: Synthesis, characterization and investigation of antiproliferative activity of novel thiazole, pyridine and pyrimidine derivatives using Fluoroacetophenone**

In this part of study,  $\alpha$ - fluoroacetophenonethiosemicarbazones **3a-c** were synthesized by reacting  $\alpha$ -flouroacetophenone **1** with the thiosemicarbazides **2a-c** in the presence of few drops of conc. HCl , in refluxing ethanol (**Scheme 1**).



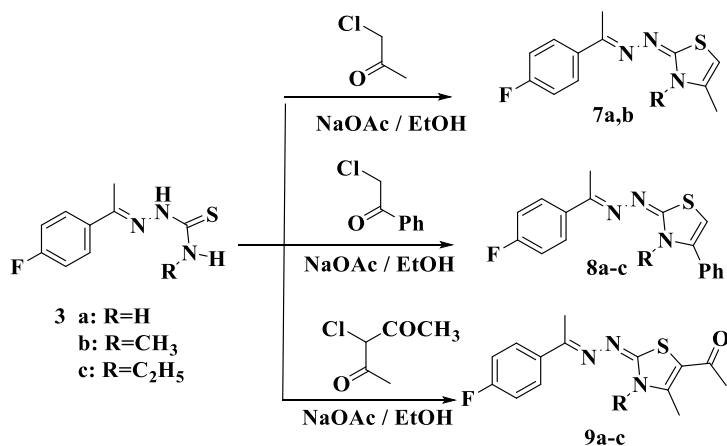
**Scheme 1: Synthesis of hydrazone carbothioamide derivatives 3a-c**

The thiosemicarbazones (**3a-c**) were reacted with  $\alpha$ -haloacid and/or  $\alpha$ -haloesters namely;  $\gamma$ -bromoacetic acid, ethyl  $\gamma$ -bromoacetate and ethyl  $\gamma$ -bromopropanoate, in the presence of anhydrous sodium acetate, the substituted thiazolidinones **4a-c**, **5a-d** and **6a-c** were obtained respectively (**Scheme 2**).



### Scheme 7: Synthesis of new thiazolidine-4-one derivatives

Different  $\alpha$ -halo substituted ketons namely, 1-chloropropane-2-one, 2-chloro-1-phenylethane-1-one and 2-chloropentane-2,3-dione were reacted with thiosemicarbazone derivatives (3a-c) under refluxing condition to afford the thiazole derivatives 7a,b, 8a-c and 9a-c respectively (Scheme 7).



### Scheme 8: Synthesis of new thiazole derivatives

Treatment of the thiosemicarbazones 3a-c with 2-oxo-N-arylpropanehydrazonoyl chloride 1a-c in the presence of a catalytic