

## *Abstract*

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Quinazoline derivatives constitute an important class of heterocyclic compounds, many of them possessed a wide range of biological activities as anti-inflammatory, analgesic, antifungal, antibacterial, anticancer and anticonvulsant activities.

The presence of natural bioactive products of quinazolines encourage researchers to take quinazoline nucleus as a core for the synthesis of multitude derivatives.

Looking at the biological significance of quinazoline nucleus, we aimed to design and synthesize new quinazoline derivatives and screen them for their cytotoxic activity. Moreover, other quinazolines and substituted quinazolinone derivatives are hybridized with different moieties in order to produce compounds with synergistic antitumor activity.

On the light of these findings, a new series of 2-substituted quinazolinone, 2,3-disubstituted quinazolinones and 2,4-disubstituted quinazoline derivatives were prepared.

**This thesis consists of the following parts:**

### **1. Introduction:**

In this section, literature review presents the various biological and pharmacological activities of quinazolines with a focus on their anticancer activities. Moreover, it displays different methods for their preparation.

### **2. Aim of the work:**

It includes the rationale upon which the newly synthesized compounds were designed.

### **3. Discussion:**

It deals with the discussion of the various experimental methods, mechanisms and conditions of reactions adopted for the synthesis of the prepared compounds and the confirmation of their structures by brief data of infrared, mass, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectra.

### **4. Experimental:**

This part presents the practical procedures used for the synthesis of reported and new intermediates, as well as new final compounds. Also, it includes their microanalytical, physical and spectral data.

In order to obtain the new compounds, the following compounds were prepared:

#### **\* Reported intermediates (7 compounds):**

- 2-Methylquinazolin-4(3*H*)-one **II**.
- 4-Chloro-2-methylquinazoline **III**.
- 2-(Bromomethyl)quinazolin-4(3*H*)-one **VI**.
- Methyl 2-acetamidobenzoate **XIII**.
- 2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)acetic acid **XIV**.
- 2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)acetyl chloride **XV**.
- 2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)acetohydrazide **XVI**.

#### **\* New intermediates (3 compounds):**

- 4-((4-Chloroquinazolin-2-yl)methylamino)benzenesulfonamide **VIII**.
- *N'*-(2-(Bromomethyl)quinazolin-4-yl)benzohydrazide **XI**.
- *N'*-Formyl-2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)acetohydrazide **XX**.

\* **New final compounds (25 compounds):**

- 2-((2-Methylquinazolin-4-yl)amino)propanoic acid **IVa**.
- 2-((2-Methylquinazolin-4-yl)amino)succinic acid **IVb**.
- 2-((2-Methylquinazolin-4-yl)amino)pentanedioic acid **IVc**.
- 2-((2-Methylquinazolin-4-yl)amino)-3-phenylpropanoic acid **IVd**.
- 3,5-Dimethoxy-*N'*-(2-methylquinazolin-4-yl)benzohydrazide **Va**.
- 3,4,5-Trimethoxy-*N'*-(2-methylquinazolin-4-yl)benzohydrazide **Vb**.
- *N'*-(2-Methylquinazolin-4-yl)benzohydrazide **Vc**.
- 4-((4-Oxo-3,4-dihydroquinazolin-2-yl)methylamino)benzenesulfonamide **VIIa**.
- *N*-(4-((4-Oxo-3,4-dihydroquinazolin-2-yl)methylamino)phenylsulfonyl)acetamide **VIIb**.
- 1-(4-((4-Oxo-3,4-dihydroquinazolin-2-yl)methylamino)phenylsulfonyl)guanidine **VIIc**.
- *N*-(Isoxazol-3-yl)-4-((4-oxo-3,4-dihydroquinazolin-2-yl)methylamino)benzenesulfonamide **VIIId**.
- 4-((4-Oxo-3,4-dihydroquinazolin-2-yl)methylamino)-*N*-(pyrimidin-2-yl)benzenesulfonamide **VIIe**.
- *N*-(4,6-Dimethylpyrimidin-2-yl)-4-((4-oxo-3,4-dihydroquinazolin-2-yl)methylamino)benzenesulfonamide **VIIIf**.
- 2-((2-(((4-Sulfamoylphenyl)amino)methyl)quinazolin-4-yl)amino)propanoic acid **IXa**.
- 2-((2-(((4-Sulfamoylphenyl)amino)methyl)quinazolin-4-yl)amino)succinic acid **IXb**.
- 2-((2-(((4-Sulfamoylphenyl)amino)methyl)quinazolin-4-yl)amino)pentanedioic acid **IXc**.

- 3-Phenyl-2-((2-(((4-sulfamoylphenyl)amino)methyl)quinazolin-4-yl)amino)propanoic acid **IXd**.
- 4-((4-(2-Isonicotinoylhydrazinyl)quinazolin-2-yl)methylamino)benzenesulfonamide **Xa**.
- 4-((4-(2-Benzoylhydrazinyl)quinazolin-2-yl)methylamino)benzenesulfonamide **Xb**.
- 4-((4-(2-(3,5-Dimethoxybenzoyl)hydrazinyl)quinazolin-2-yl)methylamino)benzenesulfonamide **Xc**.
- 4-((4-(2-(3,4,5-Trimethoxybenzoyl)hydrazinyl)quinazolin-2-yl)methylamino)benzenesulfonamide **Xd**.
- 1-(2-(2-Methyl-4-oxoquinazolin-3(4*H*)-yl)acetyl)pyrazolidine-3,5-dione **XVII**.
- 3-(2-(3,5-Dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl)-2-methylquinazolin-4(3*H*)-one **XVIII**.
- 2-Methyl-3-(2-(3-methyl-5-oxo-4,5-dihydro-1*H*-pyrazol-1-yl)-2-oxoethyl)quinazolin-4(3*H*)-one **XIX**.
- 3-((1,3,4-Oxadiazol-2-yl)methyl)-2-methylquinazolin-4(3*H*)-one **XXI**.

### **5. Pharmacological Screening:**

#### **Antitumor Screening:**

Fourteen compounds were chosen by U. S. National Cancer Institute for antitumor screening. The results revealed that all tested compounds showed moderate activity against panel of cell line especially CNS and renal cancer, while five compounds **Vb**, **VIIb**, **IXd**, **XIX** and **XXI** displayed a significant activity against one cell line.

**6. References:**

This part includes 148 references ranging from 1887 to 2015.

**7. Arabic Summary.**