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# Synthesis and biological evaluation of new quinazolinone derivatives

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ABSTRACT

New *N*-substituted-2-methyl quinazolin-4(3*H*)-ones derivatives comprising 1,3,4-thiadiazole, Schiff bases and 2-azetidinone moieties are reported. The structures of the newly prepared compounds were confirmed by FT-IR and $^{1}$H NMR spectra. The compounds were also evaluated for their antimicrobial, antioxidant and study of inhibition on some enzymes activities. The results suggest that the compounds possess broad spectrum of *in-vitro* antimicrobial activity. Antioxidant results obtained into the present study indicate that compound **5** show moderate better scavenging activity. Compound **5** demonstrated inhibitory effects on GOT, GPT, GGT and ALP activities, and these effects increase with increasing the concentration of the compound.

## 1. Introduction

Quinazolinone is an interesting and important aromatic heterocyclic system. Substituted 4(3*H*) quinazolinones possess a wide rang of pharmacological activities such as antimicrobial [1,2], anticancer [3], antiviral [4], anti-inflammatory [5], anti-tubercular [6], antitumor [7], antioxidant [8] and anticonvulsant [9].

1,3,4-Thiadiazole derivatives play role owing to their wide range of biological activity [10] and industrial applications [11]. It is also well established that varion derivatives of 1,3,4-thiadiazole exhibit broad spectrum of pharmacological properties such as anticonvulsant [12] and liver enzymes inhibition [13].

Furthermore, the 2-azetidionone skeleton, otherwise known as the β-lactam ring, has recognized as a useful building block in synthesis of biologically important compounds [14]. In recent years, significant attention has been drawn to 2-azetidinone derivatives due to their diversified therapeutic activites like antioxidant and cholesterol absorption inhibition [15].

### *1.1. Glutamate oxaloacetate transaminase (GOT) (EC 2.6.1.1)*

It's also called aspartate aminotransferase (AST), one of the most important of transaminases enzyme, and catalyzes the transfer of the amino group of aspartate to α-ketoglutrate. GOT is widely distributed in human tissues; heart, liver, skeletal muscle and kidney. The clinical usefulness of the enzyme is largely restricted to the diagnosis of heart and liver diseases. Large amount of GOT may be released into the blood. Very high levels are observed in acute liver disease while lesser elevation is seen in chronic liver disease [16-18].

### *1.2. Glutamate pyruvate transaminase (GPT) (EC 2.6.1.2)*

Also reffered to as alanine amino transferase (ALT), which is prevalent in mammalian tissue catalyzes the transfer of the amino group of alanine to α-ketoglutrate. GPT found in a highest concentration in liver in spite of its active occurrence in skeletal muscles, heart and kidney. The GPT activity in tissues is generally less than GOT. GPT level is found to increase in the following diseases; infection hepatitis, liver cirrhosis and biliary cirrhosis, obstructive jaundice, liver cancer [16,18,19].

### *1.3. Gama glutamate transferase (GGT) (EC 2.3.2.2)*

Also known as Gama Glutamate Transpeptidase (γ-GT) or (GGT) and is found in kidneys and liver and catalyzes the transfer of a gamma-glutamyl group from glutathione (GSH) to an amino acid. GGT levels are increased in most forms of liver disease, especially cholestasis, a plasma membrane-bound enzyme, provides the only activity capable to affect the hydrolysis of extracellular glutathione, thus favoring the cellular utilization of its constituent amino acids [16,20].


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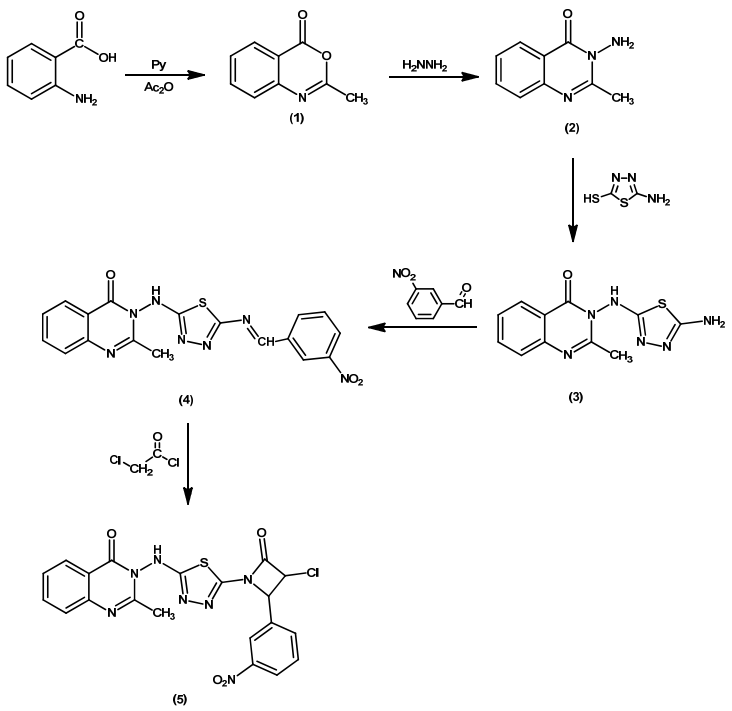

**Scheme 1**

### *1.4. Alkaline phosphatase (ALP) (EC 3.1.3.1)*

Alkaline phosphatase is present in high concentration in the liver, bone and intestinal epithelium. These tissues each contain specific isoenzymes of ALP. Phosphatase transfers a phosphate moiety from one group to another, forming an alcohol and a second phosphate compound at high pH. The activity of ALP has been elevated in the bone and liver disease such as malignant disease and carcinoma with osteoblastic metastasis [18,19].

## 2. Experimental

### *2.1. Materials and measurements*

All reagents were commercially available at (Aldrich Chemical Co.) and were used without further purification. Melting points were determined with an electrical thermal melting point apparatus and are uncorrected. Purity of the compounds was checked on silica coated Merck-TLC plates using water, chloroform benzene and acetone as mobile phase. FT-IR measurements were recorded on Shimadzu model FT-IR-8400S. $^1$H NMR spectra were obtained with a Bruker spectrophotometer model Ultra Shield at 300 MHz in DMSO-$d_6$ solution with the TMS as internal standard.

#### *2.1.1. Synthesis of 2-methyl-4H-benzo[d][1,3] oxazin-4-one (1)*

This compound has been synthesized by following the procedure mentioned in reference [21], by refluxing a mixture of anthranilic acid (0.01 mol) and 10 mL of acetic anhydride for 4 h, then the reaction mixture was cooled and the product obtained was recrystallized from water (Scheme 1). Yield: 92%. M.p.: 180-182 °C. FT-IR (KBr, ν, cm$^{-1}$): 1693 (C=O), 1651 (C=N). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.3-7.5 (m, 4H, Ar-H), 2.4 (s, 3H, $CH_3$).

#### *2.1.2. Synthesis of 3-amino-2-methyl quinazolin-4(3H)-one (2)*

A mixture of 2-methyl quinazoline-4(3*H*)-one (**1**) (0.01 mol) and hydrazine hydrate (99%) (10 mL) in absolute ethanol (25 mL) was refluxed for 7 h. The excess of solvent was distilled off then the product was left to cool, filtered and then recrystallized from ethanol (Scheme 1). Yield: 78%. M.p.: 150-151 °C. FT-IR (KBr, ν, cm$^{-1}$): 3370, 3300 ($NH_2$), 1686 (C=O). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.4-6.8 (4H, m, Ar-H), 5.6 (2H, s, $NH_2$), 2.4 (3H, s, $CH_3$).

#### *2.1.3. Synthesis of 3-[(5-amino-1,3,4-thiadiazol-2-yl) amino]-2-methyl quinazolin-4(3H)-one (3)*

A mixture of 3-amino-3-methyl-quinazoline-4(3*H*)-one (**2**) (0.02 mol) and 2-amino-5-mercapto-1,3,4-thiadiazole (0.02 mol) in absolute ethanol (30 mL) was refluxed for 14 h till the evolution of $H_2S$ finished. The excess solvent was distilled of and the product recrystallized for chloroform (Scheme 1). Yield: 60%. M.p.: 113-115 °C. FT-IR (KBr, ν, cm$^{-1}$): 3377, 3279 ($NH_2$), 1670 (C=O). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.61-7.56 (m, 4H, Ar-H), 6.1 (s, 2H, $NH_2$), 4.6 (s, 1H, NH), 2.4 (s, 3H, $CH_3$).

#### *2.1.4. Synthesis of (E)-2-methyl-3-((5-((3-nitrobenzylidene) amino)-1,3,4-thiadiazole-2-yl)amino)quinazolin-4(3H)-one (4)*

A mixture of compound **3** (0.02 mol) and 3-nitro benzaldehyde (0.02 mol)) was refluxed in absolute ethanol (25 mL) for 7 h. The reaction mixture was cooled and the product obtained recrystallized from ethanol (Scheme 1). Yield: 75%. M.p.: 156-157 °C. FT-IR (KBr, ν, cm$^{-1}$): 1690 (C=O), 1617, (C=N), 1539, 1324 ($NO_2$). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 8.5 (s, 1H, N=CH), 8.27-7.63 (m, 8H, Ar-H), 4.7 (s, 1H, NH), 2.3 (s, 3H, $CH_3$).

#### *2.1.5. Synthesis of 3-((5-(3-chloro-2-(3-nitrobenzyl)-4-oxo azetidin-1-yl)-1,3,4-thiadiazol-2-yl)amino)-2-methyl quinazolin-4(3H)-one (5)*

To a stirred solution of compound **M4** (0.01mol) and triethyl amine (0.02 mol) in dry dioxin (15 mL), chloroacetyl chloride (0.02 mol) was added dropwise at (0-5 °C), the reaction mixture was then stirred for 6 h, then poured into ice-water. The solid was filtered and recrystallized from benzene (Scheme 1). Yield: 66%. M.p.: 175-177 °C. FT-IR (KBr, ν, $cm^{-1}$): 1755 (C=O, β-Lactom), 1653 (C=O). $^1$H NMR (300 MHz, DMSO-$d_6$, δ, ppm): 7.37-6.81 (m, 8H, Ar-H), 4.6 (s, 1H, NH), 4.9 (d, 1H, N-CH), 5.0 (d, 1H, CH-Cl), 2.4 (s, 3H, $CH_3$).

### *2.2. Biological activities*

#### *2.2.1. Antimicrobial activity*

The in vitro antimictrobial screening effects of the synthesized compounds evaluated against two Gram positive *Staphylococcus aureus* and *Streptococcus pyogenes* and two gram negative bacteria *Escherichia coli* and *Pseudomonass aeruginosa* and two fungal strains namely *Candida albicans* and *Aspergillus niger* using well diffusion method [22].

DMSO was run as a control and the test was performed at 10 mg/mL concentration using DMSO as solvent. The bacteria and fungi were sub-cultured in agar and potato dextrose agar medium and were incubated for 24 h for bacteria and 48 h for fungi at 37 °C.

#### *2.2.2. Antioxidant activity*

The free radical scavenging activity of compound **5** towards the radical (DPPH) 1,1-diphenyl-2-picryl hydrazyl was measured as described by reference [23]. The 2-azetidinone stock solution (1 mg/mL) was diluted to final concentration of 20-100 µg/mL. Methanolic DPPH solution (1 mL, 0.3 mmol) was added to sample solution in DMSO (3 mL) at different concentration.

The mixture was shaken vigorously and allowed to stand at room temperature for 30 min. the absorbance was then measured at 517 nm (As), using "Shimadzu175 spectrophotometer". The methanol solution of DPPH was used as control sample Ac. The ability of scavenge the DPPH radical was calculated using the following formula:

$$\% \text{ Radical scavenging activity} = 100 \times (Ac\text{-}As)/Ac \quad (1)$$

Methanol was used as the solvent and ascorbic acid as the standard.

#### *2.2.3. Effect of compound 5 on some enzymes activities*

##### *2.2.3.1. Effect of compound 5 on GOT and GPT activities*

Colorimetric determination of GOT or GPT activity according to the following reactions:

$$\text{L-Aspartate} + \alpha\text{-Ketoglutrate} \xrightarrow{\text{GOT}} \text{Oxaloacetic} + \text{Glutmate} \quad (2)$$

$$\text{Alanin} + \alpha\text{-Ketoglutrate} \xrightarrow{\text{GPT}} \text{Pyruvate} + \text{Glutmate} \quad (3)$$

The pyruvate or oxaloacetat formed was measured in its derivated form 2,4-dinitrophenylhydraone, which was absorbed at wave length 505 nm [16,24] .

##### *2.2.3.2. Effect of compound 5 on GGT activity*

Kinetic colorimetric method for the determination of GGT activity was assayed by Persijn and Van Der Slik [25]. The principle of the method was the measurement of the 5-amino-2-nitro-benzoate form from reaction, which was absorbed at wave length 405 nm [16].

$$\text{L-}\gamma\text{-gluamyl-3-carboxy-4-nitroanlide} + \text{Glycylglycine} \xrightarrow{\text{GGT}} \text{L-}\gamma\text{-glutamy-glycylglycine} + \text{5-Amino-2-nitrobenzoat} \quad (4)$$

##### *2.2.3.3. Effect of compound 5 on ALP activity*

Colorimetric determination of ALP activity according to the following reaction.

$$\text{Phenylphosphate} + H_2O \xrightarrow[\text{pH} = 10]{\text{ALP}} \text{Phenol} + \text{Phosphate} \quad (5)$$

The phenyl phosphate was hydrolyzed to phenol, which was measured in the presence of amino-4-antipyrine and potassium ferricyanide, which was yellow in alkaline solution, and absorbed at wave length 520 nm [26]. The enzymes GOT, GPT, GGT and ALP activities were measured in human serum using above methods with added 100 µL of DMSO to calculate the activities of these enzymes without inhibitors. A stock solution (0.1 M) of compound **5** were prepared and the following concentration of $1\times10^{-2}$, $1\times10^{-3}$, $1\times10^{-4}$, $1\times10^{-5}$, and $1\times10^{-6}$ M were prepared, diluting with dimethyl sulfoxide (DMSO). The enzymes GOT, GPT, GGT and ALP activities were measured in human serum using the same methods of these enzymes with replaces 100 µL of DMSO with 100 µL of compound **5** [16].

The inhibition percentages were calculated by comparing the activities with and without the compound and under the same conditions, according to the equation [16].

$$\% \text{ Inhibition} = \frac{(\text{Enzyme activity without inhibitor}) - (\text{Enzyme activity with inhibitor})}{\text{Enzyme activity withouth inhibitor}} \times 100 \quad (6)$$

A constant concentrations of compound **5** $1\times10^{-2}$ and $1\times10^{-4}$ M were used with different substrate concentrations of 40, 80, 120, 160 and 200 mmol/L for GOT, GPT 0.4, 0.8, 1.2, 1.6 and 2.0 mmol/L for γ-GT and 1, 2, 3, 4 and 5 mmol/L for ALP to study the types of inhibition. Buffers were used to prepare different substrates concentrations of these enzymes, GOT, GPT (phosphate buffer pH = 7.4, 100 mmol/L), γ-GT (TRIS buffer pH = 8.25, 100 mmol/L) and ALP (carbonate buffer pH = 10, 100 mmol/L).

Competitive, noncompetitive and uncompetitive inhibition can be easily distinguished with the use of double reciprocal plot of the Lineweaver-Burk plot. Two sets of rate determination in which enzyme concentration was held constant, were carried out. In the first experiment the velocity of uninhibited enzyme was established, in the second experimental constant amount of inhibitor is included in each enzyme assay. Varieties of substances have the ability to reduce or eliminate the catalytic activity of specific enzyme.

When the enzymes activity is determined with and without compound **5**, it can be calculate the [$k$i, Apparent $v_{max}$ ($v_{mapp}$), Apparent $k_m$ ($k_{mapp}$), type of inhibition] by using Lineweaver-Burk equation and plotting $1/v$ against 1/[s] [19].

## 3. Results and discussion

### *3.1. Synthesis*

The new quinazolinone derivatives were prepared following the reaction sequences depicted in Scheme 1.

The 3-amino-2-methylquinazolin-4(3*H*)-one (**2**) was prepared by refluxing of compound **1** with hydrazine hydrate in absolute ethanol for 7 h.

**Table 1.** Antimicrobial evaluation of compounds **3-5**.

| Compound | Antibacterial Activity | | | | Antifungal Activity | |
|---|---|---|---|---|---|---|
| | Zone of inhibition in (mm) | | | | | |
| | Gram positive | | Gram negative | | Fungi | |
| | *S. aureus* | *S. pyogenes* | *P. aeragines* | *E. coli* | *C. albicans* | *A. niger* |
| 3 | 112 | 100 | 120 | 118 | 70 | 65 |
| 4 | 130 | 110 | 130 | 140 | 75 | 78 |
| 5 | 155 | 140 | 150 | 155 | 100 | 80 |
| Ampicillin | 100 | 100 | 100 | 100 | - | - |
| Fluconazole | - | - | - | - | 100 | 100 |

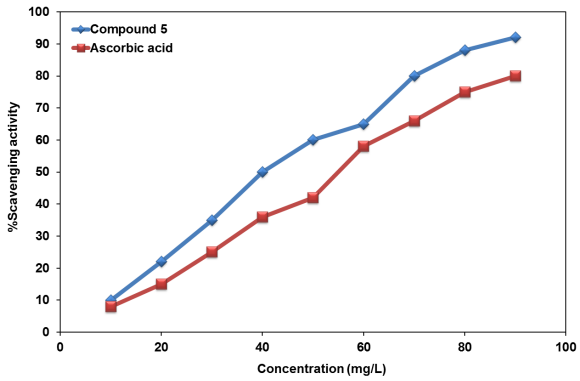


**Figure 1.** % Scavenging activity of the compound **5** using DPPH.

IR spectrum of compound **2** showed the appearance of new characteristic bands at 3370, 3300, 1686 and 1629 $cm^{-1}$, which belonged for $NH_2$, C=O, C=N, respectively. While the $^1H$ NMR showed singlet signal at 2.4 ppm due to methyl proton and a singlet at 6.1 ppm related to $NH_2$, while a multiplet signal at 7.61-8.05 ppm due to four aromatic protons.

Reaction of compound **2** with 2-amino-5-mercapto-1,3,4-thiadiazole afforded compound **3**. The reaction was followed using lead acetate paper till the end of liberation of $H_2S$. This reaction occurs via nucleophilic replacement of SH by amino group of compound **2**. The IR spectrum showed absorption bands due to $NH_2$ at 3336 and 3254 $cm^{-1}$ and NH band at 3134 $cm^{-1}$ for NH.

Condensation of compound **3** with 3-nitrobenzaldehyde in absolute ethanol gave Schiff base (**4**). The formation of Schiff base was indicated by the presence in their IR spectra of the azomethine (CH=N) stretching band at 1617 $cm^{-1}$, combined with the disappearance of $NH_2$ stretching band.

On the other hand, the cyclo addition of Schiff base (**4**) with chloroacetyl chloride in triethylamine and dioxane yielded azetidinyl derivative compound **5**. The IR spectrum of compound **5** showed the disappearance band of (CH=N) from azomethine at 1617 $cm^{-1}$, combined with the appearance of absorption band at 1755 $cm^{-1}$ (C=O) for β-lactam ring. The $^1H$ NMR spectrum of compound **5** showed singlet signal at 4.6 ppm due to NH and two doublets one at 4.9 ppm relate to N-CH another at 5.0 ppm due to CH-Cl, while amultiplet signal at 7.37-6.81 ppm due to aromatic protons.

### 3.2. *Biological activities*

#### *3.2.1. Antimicrobial activity*

Standard antibacterial drug (Ampicillin) and antifungal drug (Fluconazole) were used for comparison. The experiments were performed in triplicate in order to minimize errors.

Zone of inhibition produced by each compound was measured in mm and the results of antimicrobial studies are given in Table 1. Compound **3**, **4**, and **5** are potential antimicrobial. It seems that the compound **5** is very significant for activity against both bacterial and fungal species due to the presence of β-lactam ring.

#### *3.2.2. Antioxidant activity*

Hydrogen peroxide is generated in vivo by several oxidase enzymes and which product hydroxyl radical causes severe damage to biological systems. The antioxidant potential of compound **5** was determined on the basis of its scavenging of the stable (DPPH) free radical. Figure 1 showed that the compound **5** exhibit excellent antioxidant properties, the potential is comparable with antioxidant activity of ascorbic acid activity. This may be due to the presence of -NH group.

#### *3.2.3. Effect of compound 5 on some enzymes activities*

The biochemical tests revealed that compound **5** caused inhibitory effects on all enzymes activity. Figure 2 showed that the different concentration of compound **5** caused inhibitory effects on GOT, GPT, GGT and ALP enzyme, the value of the GOT, GPT, GGT and ALP enzymes activities without compound **5** were 18, 16, 6.545 and 30 U/L, respectively. The relationship between compound **5** concentration versus and the activities of enzyme as shown in Figure 3, these results observed that any increase in compound concentrations caused increase in percentage of inhibition of enzymes. The greater inhibition of compound **5** was demonstrated at concentration, $1\times10^{-2}$ M [16].

Figure 4 showed that the inhibitory effect by compound **5** was higher inhibitory on the ALP enzyme (%33.3) and the lower inhibitory effect was on the GOT enzyme (%25.5).

By using double reciprocal plot of the Lineweaver-Burk plot can be easily distinguished type of inhibition of enzyme activity, when was established the velocity of enzyme with and without inhibitor.

Table 2 and Figure 5 showed that the type of enzyme inhibitin using Lineweaver-Burk plot for compound **5** on serum GOT, GPT, GGT and ALP activities. A liquate $10^{-2}$ and $10^{-4}$ M of compound **5** were non-competitive inhibition for all enzymes activities. Non-competitive inhibition changed the $V_{max}$ of the enzyme but not the $K_m$. $K_m$ with $10^{-2}$ and $10^{-4}$ M of compound **5** on GOT, GPT, GGT and ALP enzymes were 200, 500, 1, 5 M, respectively.

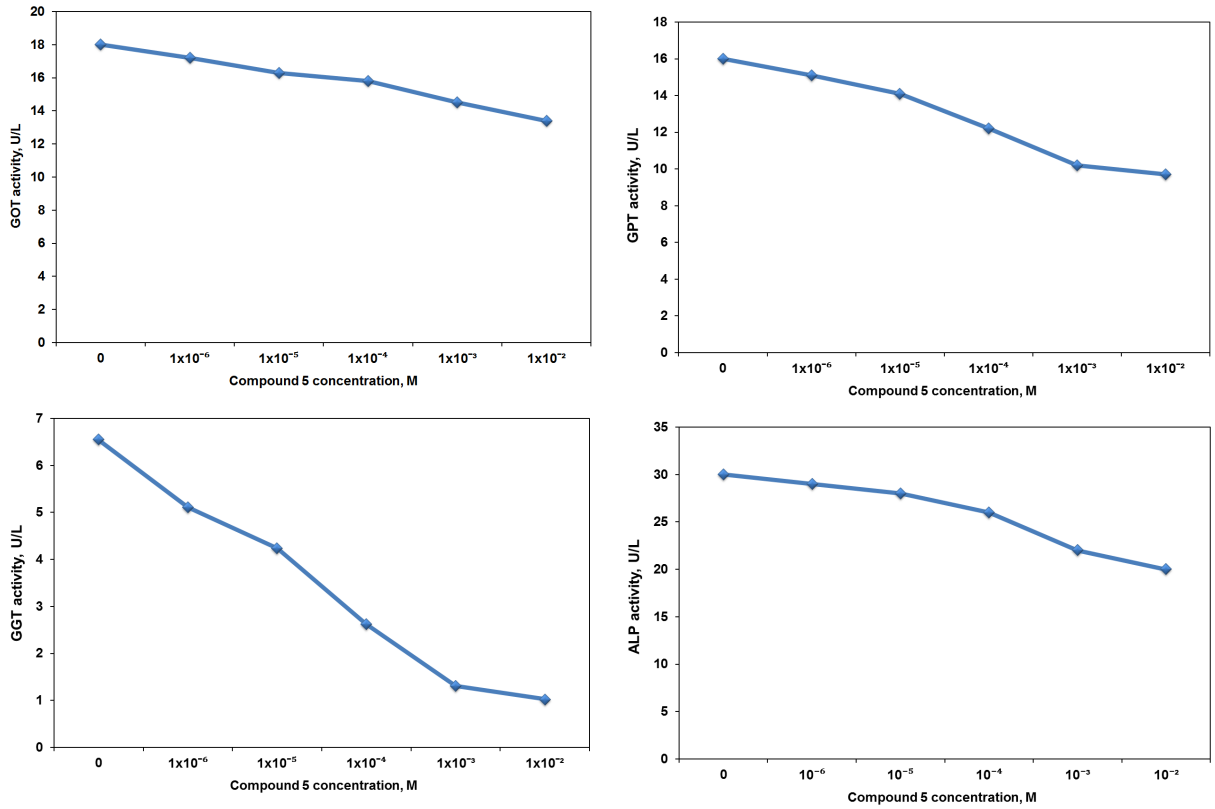


**Figure 2.** The relationship between concentration of compound **5** and GOT, GPT, GGT and ALP enzymes activities.

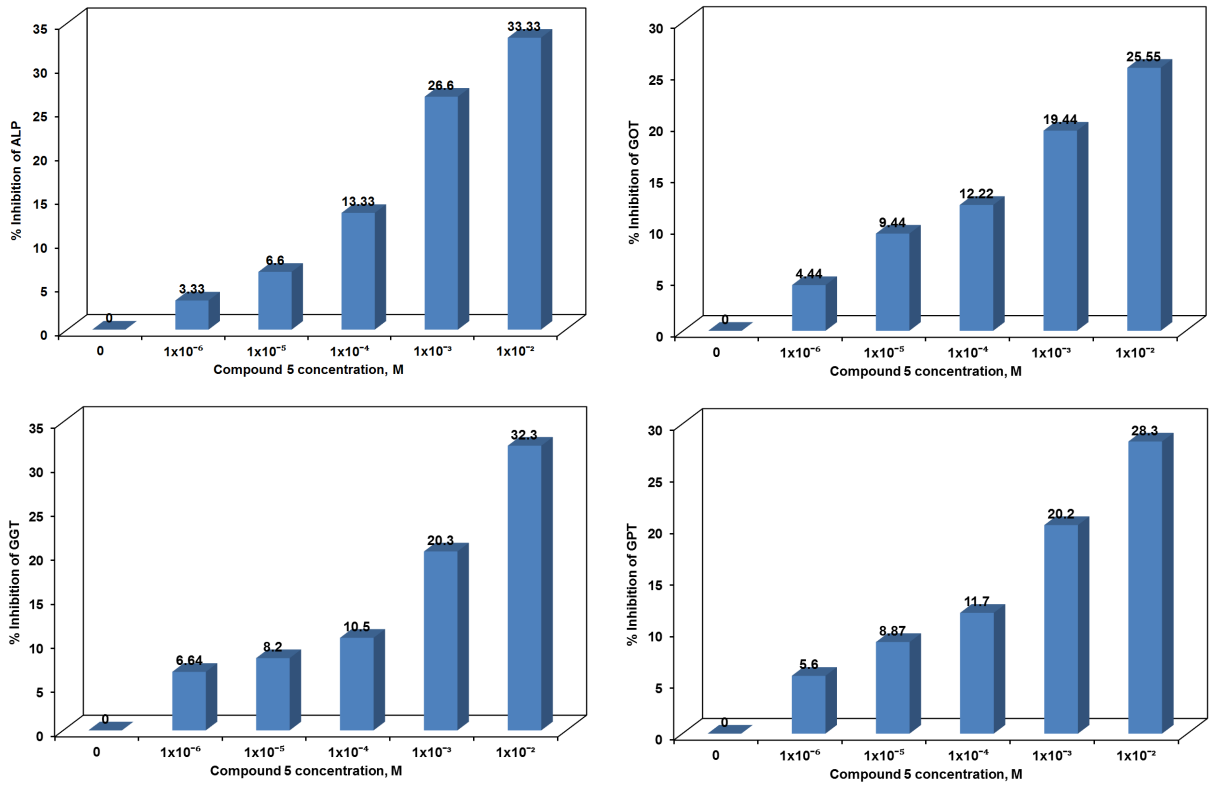


**Figure 3.** The percentages of inhibition of GOT, GPT, GGT and ALP enzymes and compound **5** concentration.

**Table 2.** The kinetic properties of GOT, GPT, GGT and ALP with compound **5**.

| Enzymes | Concentration of compound 5 | $k_{map}$, $k_m$ (M) | $v_{map}$ U/L | $k_i$ (M) | Type of inhibition |
|---|---|---|---|---|---|
| GOT | $10^{-2}$ | 200 | 20 | $25x10^{-4}$ | Non-competitive |
| | $10^{-4}$ | 200 | 11.12 | $125 x10^{-7}$ | |
| GPT | $10^{-2}$ | 500 | 10 | $25x10^{-4}$ | Non-competitive |
| | $10^{-4}$ | 500 | 20 | $66x10^{-6}$ | |
| GGT | $10^{-2}$ | 1 | 0.4 | $25x10^{-4}$ | Non-competitive |
| | $10^{-4}$ | 1 | 0.72 | $55x10^{-6}$ | |
| ALP | $10^{-2}$ | 5.00 | 20 | $66x10^{-4}$ | Non-competitive |
| | $10^{-4}$ | 5.00 | 33.3 | $2x10^{-4}$ | |

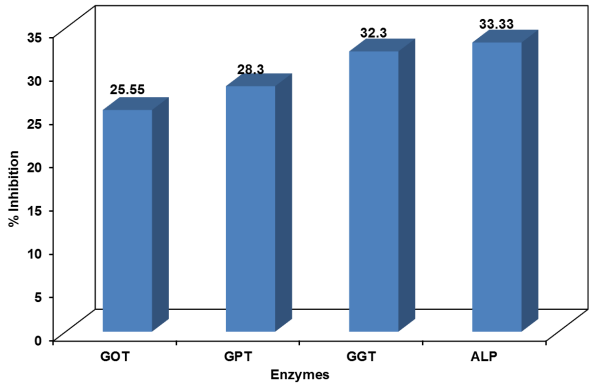


**Figure 4.** % Inhibition of GOT, GPT, GGT and ALP enzymes activities with $1\times10^{-2}$ M of compound **5**.

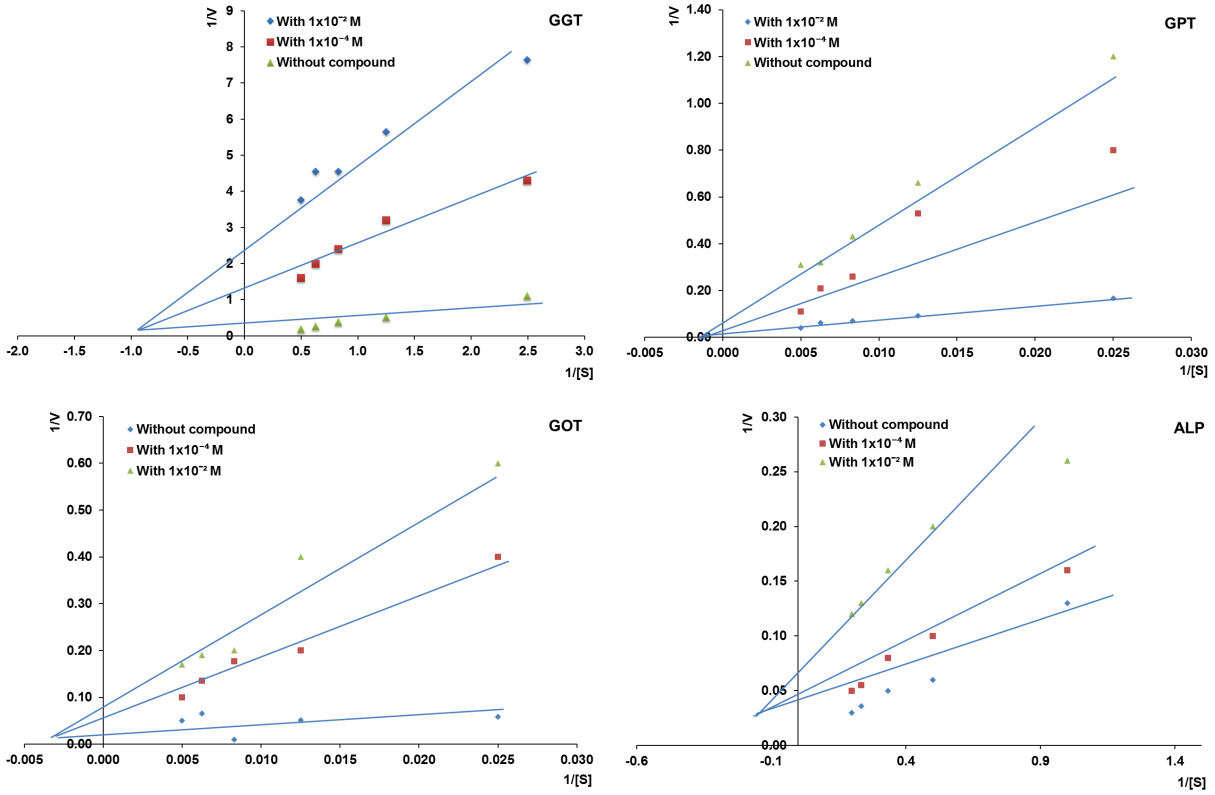


**Figure 5.** Lineweaver-Burk plots for compound **5** effects on GOT, GPT, GGT and ALP.

$V_{max}$ and $V_{mapp}$ with $10^{-2}$ and $10^{-4}$ M of compound **5** on GOT, GPT, GGT and ALP enzymes were (100, 20, 11.12), (50, 10, 20), (2, 0.4, 0.72), (50, 20, 33.3), respectively. By using Lineweaver-Burk equation was calculated the $K_i$ values of enzymes for compound which was studied in different concentration. The $K_i$ of compound **5** in $10^{-2}$ and $10^{-4}$ M on GOT, GPT, GGT and ALP enzymes were ($25\times10^{-4}$, $125\times10^{-7}$), ($25\times10^{-4}$, $66\times10^{-6}$), ($25\times10^{-4}$, $55\times10^{-6}$), ($66\times10^{-4}$, $2\times10^{-4}$) M, respectively.

The enzymes play important role in amino acid metabolism and in the urea and tricarboxylic acid cycles. We suggested that compound **5** molecule has (N-, O=, Cl, S and $NO_2$) groups by which, molecular of compound **5** interaction between the

groups with GOT, GPT, GGT and ALP enzymes, it inhibite the active sides enzymes by decreasing affinity of active sides of enzymes to react with the substrates. The results of our study are in agreement with before studies of same enzyme [17-19,23].

The tripeptide glutathione (GSH) is used by cells to detoxify hydroperoxides, produced during oxidative stress, and is consumed in the process. Previous studies have indicated that cells can be protected against oxidative stress by extracellular GSH through its degradation catalyzed by the exoenzyme gamma-glutamyl transpeptidase (GGT) and its de novo synthesis within the cytosol [24]. Because of this, induction of GSH depletion has been proposed as a good strategy for sensitizing tumor cells to anti-tumor agents [25]. We hypothesized that (GGT) would be increased as part of the adaptation of cells to oxidative stress.

## 4. Conclusions

New derivatives of 2-methyl quinazolin-4(3*H*)-one were synthesized and characterized using spectroscopic techniques. We studied the antimicrobial activities of these derivitives against some gram positive and negative species as well as fungal species. It seems that the compound **5** is very significant for activity against both bacterial and fungal species and it is excellent antioxidant properties when comparable with antioxidant activityof ascorbic acid. Compound **5** is weakly inhibition on GOT, GPT, GGT and ALP enzymes activities. So, compound **5** can be used as easily accessible source of antioxidant and in pharmaceutical industry.

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## References

[1]. Hassanzadeh, F.; Jafari, E.; Hakimelahi, G. H.; Rahmani Khajouei, M.; Jalali, M.; Khodarahmi, G. A. *Res. Pharm. Sci.* **2012**, *7(2)*, 87-94.
[2]. Hong, Z.; Hai, Y. H.; Yuan, Y, H.; Xin, G.; Lin, H.; Qiag, R.; Ying, L.; Yang, L. I. *Molecules* **2010**, *15*, 9473-9485.
[3]. Suresha, K. G. P.; Prakasha, C.; Kapfo, W.; Channe, G. D. *E-Journal Chem.* **2010**, *7(2)*, 449-456.
[4]. Xingwen, G.; Xuejian, C.; Kia, Y.; Baoan, S.; Liu, G.; Zhuo, C. *Molecules* **2007**, *12*, 2621-2642.
[5]. Mosaad, S.; Mohsen, M.; Emad, M.; Nageh, A.; Salwa, M.; Marwa, F. *Acta. Pol. Pharm.* **2009**, *66(5)*, 487-500.
[6]. Kunes, J.; Bazant, J.; Pour, M.; Waisserk, K.; Slosarek, M.; Janota, J. *Farmaco* **2000**, *55*, 725-729.
[7]. Adel, S.; Mohamed, A.; Alaa, A.; Naglaa, I.; Magda, A.; Abdulaziz, M.; Mohamed, M.; Sami, G. *Eur. J. Med. Chem.* **2010**, *45*, 4188-4198.
[8]. Sakere, H.; Revanasiddappa, D.; Shiva Prasad, K.; Shiva Kumar, L.; Jayalakshmi, B. *Chem. Tech.* **2010**, *2(2)*, 1344-1349.
[9]. Rajasekaran, A.; Rajamanickam, V.; Darlinquine, S. *Eur. Rev. Med. Pharm.* **2013**, *17*, 95-104.
[10]. Sabir, H. Jyoti, S.; Mohd, A. *E-Journal Chem.* **2008**, *5(4)*, 963-968.
[11]. Heakal, F.; Fouda, A. S.; Radwan, M. S. *Int. J. Electrochem. Sci.* **2011**, *6*, 3140-3163.
[12]. Deng, X. Q.; Dong, Z. Q.; Song, M. X.; Shu, B.; Wang, S. B.; Quan, Z. S. *Arch. Pharm.* **2012**, *345(7)*, 565-573.
[13]. Firas, H. *Int. J. Res. Pharm. Chem.* **2012**, *2(1)*, 2231-2781.
[14]. Oana Maria, D.; Florentina, L.; Cornelia, V.; Mihai, M.; Valentin, N.; Romona, F.; Dragos, P.; Lenuta, P. *Molecules* **2013**, *18*, 4140-4157.
[15]. Nikalje G.; Ghodke S.; Mirza S. *World J. Pharm. Pharmaceut. Sci.* **2014**, *3(2)*, 2589-2625.
[16]. Al-Qaisi, Z. H. J.; Abbass, S. A. R.; Abdullah, A. H. *Int. J. Chem.* **2011**, *3(2)*, 140-148.
[17]. Stryer, L. Biochemistry, 3rd Edition, W. H. Freeman and Company, New York, 2005.
[18]. Thommas, M.; Devlin J. Text of Biochemistry with Clinical Correlations, 7th Edition, Medical Publication, New York, 2011.
[19]. Harry, R.; Mathews, A.; Preed, L. Biochemistry a short course, 5th Edition, Wiley-Liss, U.S.A, 2012.
[20]. Aldo, P.; Roberto, T.; Patrizia, T.; Mario, C.; Alfonso, P. *Free Radical Bio. Med.* **1997**, *22(5)*, 853-860.
[21]. Cyril, P.; Duran, S. *J. Heterocyclic Chem.* **2000**, *37(4)*, 725-729.
[22]. Greenwood, D.; Snack, R.; Peurtherer, J. Medical Microbiology: A Guid to Microbial Infections: Pathogensis, Immunity, Laboratory Diagnosis and Control, 15th Edition, Churchill Livingstne, Edinburgh, United Kingdom, 1997, p 690.
[23]. Osorio, M.; Aravena, J.; Vergara, A.; Taborga, L.; Baeza, E.; Catalan, K.; Gonzalez, C.; Carvajal, M.; Carrasco, H.; Espinoza, L. *Molecules* **2012**, *17*, 556-570.
[24]. Britman, S.; Frankel, S. *Am. J. Clin. Path*. **1957**, *28(1)*, 56-63.
[25]. Persijn, J. P.; Van Der, S. W. *J. Clin. Chem. Clin. Biochem*. **1976**, *14(9)*, 421-427.
[26]. Pesce, A. J.; Kaplan, L. A. Methods in clinical chemistry, 3rd Edition, Mosby Company, New Delhi, 1987.