Efficient Synthesis, Spectral Characterization, Computational Studies and Antimicrobial Activities of Some Quinazolinone C-nucleosides Derivatives

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This paper is dedicated to the soul of my Prof. Dr Moustafa M. Habib.

Abstract

In this study, A series of triazolo quinazolinone bearing carbohydrate moieties were synthesized to investigate their possible antibacterial and antifungal activities. Some nucleosides ***3a-f*** *were prepared by treating an aqueous ethanolic solution of hydrazino quinazolinone derivative* ***2*** *with aldohexoses and aldo-pentoses in the presence of a catalytic amount of acetic acid. Acetylation of the sugar hydrazones with acetic anhydride in pyridine at room temperature gave the corresponding poly-O-acetyl derivatives* ***4a-f****. Attempted oxidative cyclization of the sugar hydrazones* ***3b,d,f*** *following intramolecular nucleophilic substitution protocol, using one pot conditions with bromine in acetic acid in the presence of anhydrous sodium acetate, followed by acetylation with acetic anhydride afford the corresponding triazolo acetate derivatives* ***5b, d, f .*** *Continuously, the reaction of the sugar hydrazones* ***3b, d, f*** *with bromine water gave the corresponding quinazolino triazole derivatives* ***6b, d, f****. On the other hand, deacetylation of triazolo per-O-acetylated derivatives* ***5b, d, f*** *with methanolic ammonia gave the triazolo derivatives* ***6b, d, f****. The structural elucidation of the products was confirmed by their elemental analyses and spectral data. To identify the experimentally observed results, quantum chemical calculations have been performed on the sugar hydrazone* ***3b*** *in both forms and its precursors using a Gaussian 09 program, applying density functional method, DFT/B3LYP exchange-correlation with the 6-311G (d, p) basis set. From the output file we can consider different reactivity descriptors from frontier molecular orbitals energies such* as *ionization potential (IP*), chemical potential (μ), *electron affinity (EA), hardness (η), softness(* σ*), electrophilicity and nucleophilicity, from this data we can conclude the active sites of the studied molecules and charge transfer was evidenced from quinazolin hydrazone* ***2*** *to glucose , this was in good agreement with Mulliken atomic charges calculated at DFT/B3LYP/6311. Also, optimization of the two forms of* ***3b*** *takes place using Ab initio Hartree-Fock at 6-311G (d, p) basis set and semi-empirical calculations PM3&PM6 were used for calculating the optimization energies and dipole moments to compare the nature of the molecule after optimization at different levels. On the other hand, some of the synthesized compounds were screened for their antimicrobial activities using the inhibition zone diameter test, some of these compounds showed promising antibacterial and antifungal activities.*

Keywords *quinazolinone, aldohexoses, aldopentoses, sugar hydrazones, triazolo-quinazolinone, antibacterial, antifungal, DFT, HOMO, LUMO, MEP.*

I. INTRODUCTION

Organic compounds with different heterogeneous rings, whether isolated or fused cyclic rings have recently been of great interest in both medicinal and industrial applications and offer a wide range of vital activities [1, 2]. In medical chemistry, quinazoline/ quinazolinone and its derivatives are an essential building block for many drugs [3-7] such as albaconazole, raltitrexed, methaqualone, proquazone. Methaqualone has calmative effects, proquazone is an anti-inflammatory drug, the albaconazole is antifungal drug **Fig.1**. In recent years, quinazoline is used as antitumor agents [8-11], a raltitrexed drug quinazoline uses to treat large intestine cancer. Much attention has been focused on the synthesis of derivatives of 1,2,4 triazole because of its role in a wide range of biological activities [12-14], the shipment of triazole by click chemistry is a relatively recent trend for the synthesis of new medications important molecules. Ouahrouch et al. benefited from this reaction and reacted alkylated propargyl quinazoline with azido-2',3',5'-tri-obenzoylribose to synthesize 1,2,3-triazoles, and the compounds were examined as *in vitro* anti-HIV agents in the laboratory and showed promising activity [15]. As a result, the synthesis of C nucleosides, as well as cyclic analogues containing 1,2,4 triazole, attracted many workers in the field in their attempts to enhance the biological activity of these compounds [16-21]. Since natural nucleosides and their analogues have

found many applications such as antibiotics, fungicides, antitumor and antiviral agents. Today, nucleoside chemistry represents an important area of research for the discovery of modern drugs [22, 23]**.** Therefore, the integration of various alternatives in a 1,2,4-triazole ring fused with various heterocycle ring systems give compounds with improved biological activities [24-27]. Nowadays, computational chemistry is a rapidly evolving branch of modern chemistry that studies the properties of molecules to get an idea about the properties of matter [28]. Ab initio and semi-empirical calculations are techniques for calculating atomic and molecular structures, effectively and understanding the nature of chemical bonding, where the HF method gives approximate solutions to effective bond lengths after optimization [29,30]. Recently, the Functional Density Theory (DFT) has been widely used to study chemical systems and widely applied in theoretical chemistry along with the closely related HF method, but DFT is a relatively more accurate method because it produces reliable results and accurately measures calculated structures [31-33]. In this regard and in continuation of my work [34,35], on the synthesis of new heterocyclic compounds from the quinazolinone hydrazone derivative **(2)** see results and discussion section), Some new derivatives were planned for triazolo quinazolinone C-nucleoside. Different types of strategies were used to discover the structural formula of the synthesized compounds and their biological activities. Also, in this study, the Gaussian 09 software package [36] was used to improve the structures of the two forms of the quinazolinone-nucleoside derivative and to calculate their molecular properties as an introduction to the synthesis of the target compounds.

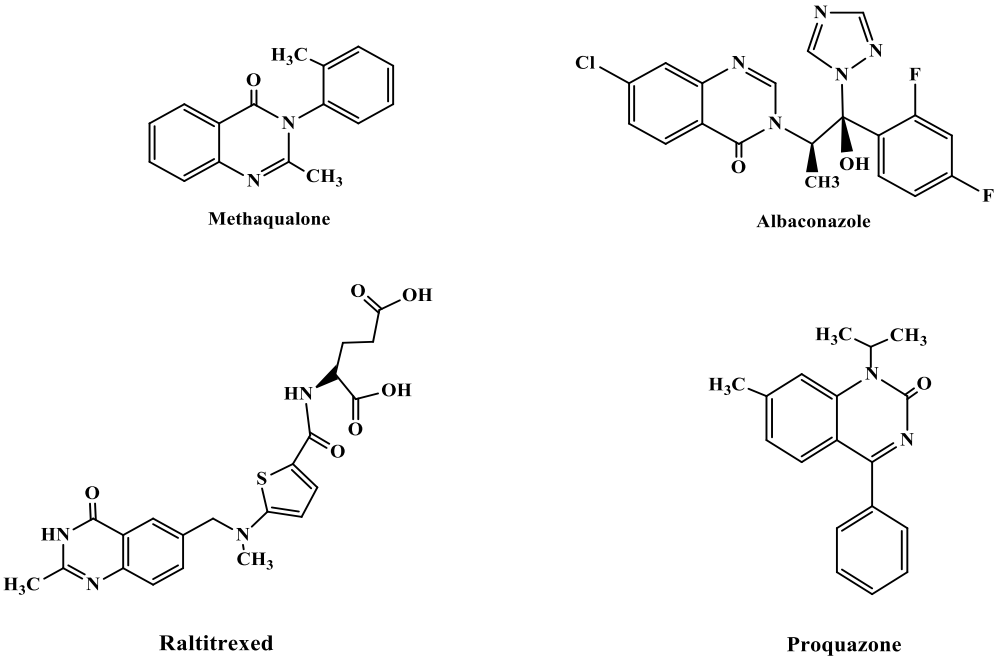


Fig. 1: Structures of some quinazolinone drugs.

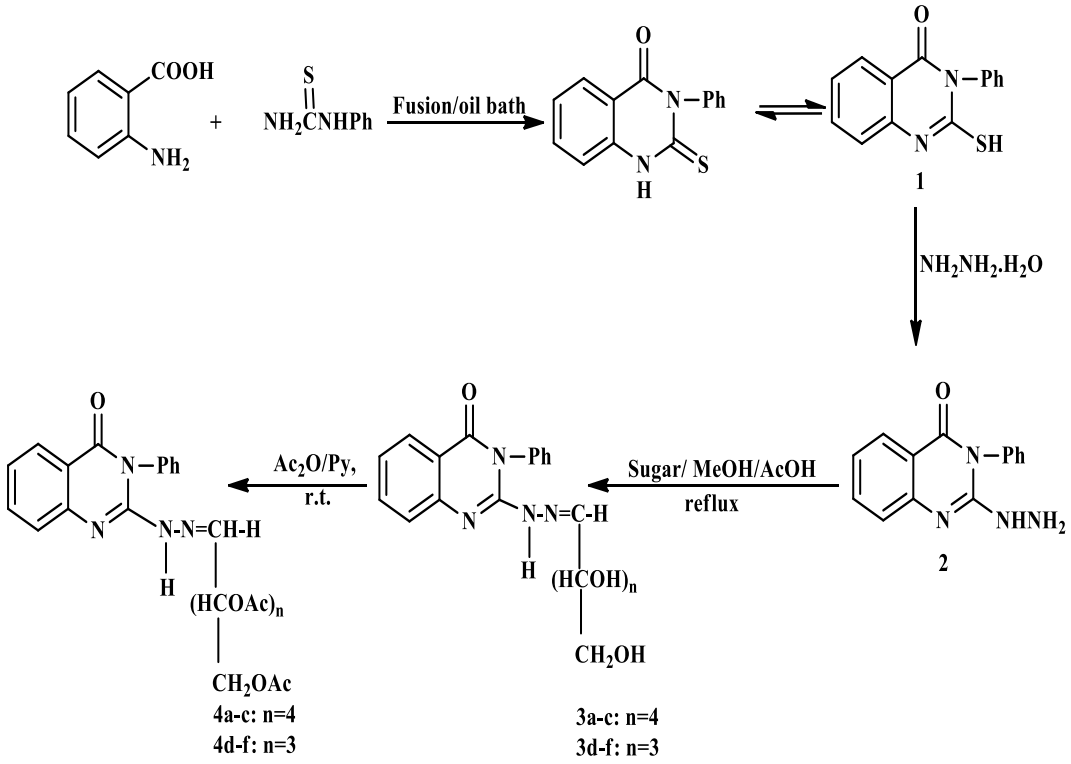
II. Results and discussion

A. Chemistry

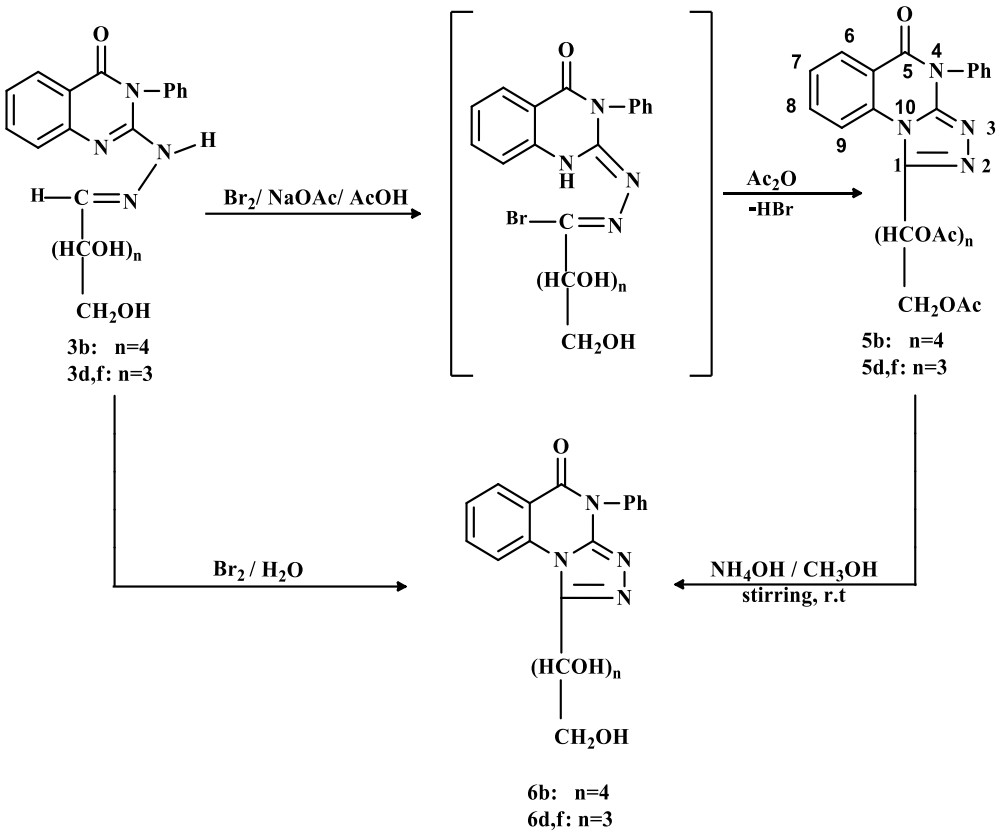
Different methods for the synthesis of C nucleosides have been reported [37-42] our designed pathways for the target compounds production were more efficient due to less reaction steps as shown in **Scheme 1** , the synthesis of C-nucleosides involving direct attachment of the preformed quinazolinone ring as an aglycon unit to a sugar unit, via nucleophilic addition to the aldehydic carbonyl of the open-chain
form of sugars. Condensation of 2-Hydrazino-3-phenyl-3H-quinazolin-4-one **2** with an equimolar amount of galactose, glucose, mannose, arabinose, ribose and xylose in the presence of catalytic amount of acetic acid gave the corresponding hydrazones **3a-f**, their structural formula were confirmed by IR spectra which showed bands at 3493-3436 cm^{-1} due to OH groups, at 3211-3062 cm^{-1} related to NH groups, at 1698-1690 cm^{-1} due to the C=O of quinazolinone and at 1665-1616 cm^{-1} due to C=N bands. The 1H NMR spectra of these hydrazones showed the (=NNH) at δ 10.93-10.64 ppm, NH group protons disappeared after addition of D_2O, the quinazolinone protons, and the phenyl ring at C-3 and azomethine proton appeared at δ 8.67-7.08 ppm besides the multiplet at 4.79-3.29 ppm for OH groups of the sugar moiety and another multiplet at δ 4.20-3.29 ppm for the hydrogen groups at sugar chain. The structure of compounds **3a-f** was also confirmed by ^{13}C NMR data (see Experimental section). The ^{13}C NMR spectrum of **3b** was characterized by a signal at

δ 165 ppm corresponding to alditol-1-ylidene C-1' atom of the glucose residue, signals at δ 73, 72., 71 and 69 ppm were assigned to its C-5',C-4', C-3'and C-2' atoms respectively, and signals at δ 161, 153, 146, 133, 127, 126 and 121 ppm were attributed to quinazolinone carbon atoms in positions 4, 2, 9, 7, 6, 5&8, and 10 respectively. Acetylation of the hydrazones **3a-f** with acetic anhydride in pyridine at room temperature for about 72 hours gave the corresponding per-O-acetyl derivatives **4a-f.** The IR spectra of **4a-f** showed unexpected band ranged from 3307-3042 cm^{-1} corresponding to NH group, also it showed the other characteristic bands for OAc at 1749-1743 cm^{-1}, (C=N) at 1645-1616 cm^{-1}, and (C=O) group showed characteristic band at 1695-1691 cm^{-1} , The ^{1}H NMR spectra of **4a-f** displayed a singlet at δ 10.93-10.64 ppm related to the NH group which exchangeable with D_2O , the five or six acetyl groups appeared at δ 3.65-2.80 ppm, beside the other signals which confirm the hydrazone acetate structures. Also, ^{13}C NMR spectra of **4a** confirmed the structures (see Experimental), which showed signals at δ 170.2 ppm of the carbonyl acetyl group, 161 ppm the carbonyl of the quinazolinone ring at C-4, 153.4 ppm the azomethine carbon.

one pot reaction of the hydrazones **3b, d, f** with stochiometric equivalent of bromine and excess of anhydrous sodium acetate in acetic acid, followed by treatment with acetic anhydride at room temperature, afforded the corresponding 1-(per-*O*-acetylalditol-1-yl)-4-phenyl-1,2,4-triazolo [4,3-*a*]quinazolin-5(4*H*)-ones **5b, d, f** due the oxidative cyclization [43] via the formation of the non-isolated bromo hydrazone intermediate, **Scheme 2**. Elemental analysis indicated that six and five acetyl groups were introduced in the corresponding hexose and pentose derivatives, respectively, besides the other spectral data which confirmed the structure. (see Experimental section).



Scheme 1. Synthesis of the hydrazone derivatives.



Scheme 2. Synthesis of the triazole derivatives

The triazole derivative **6 b,d,f** were obtained either via the reaction of the corresponding hydrazone derivatives **3b,d,f** with bromine water by the attack on the hardest basic site, followed by elimination of hydrogen bromide and electro-cyclization to give **6b,d**,**f**, or by the treatment of the triazole acetate derivatives **5b,d,f** with methanolic ammonia with stirring at room temperature to give the corresponding
de-*O*-acetylated derivatives **6b,d,f**. The ^{1}H NMR spectra of the triazole derivatives showed the loss of two protons from precursor **3b, d, f** and confirmed the assigned structure. Also, in ^{1}H NMR spectra of **6b, d, f,**
the aldose proton signals were observed and no azomethine signal could be detected, thus confirming that heterocyclization occurred. (see Experimental section).

B. Computational analysis

a) Reactivity descriptors

Following our previous work [34, 35, 44], all computational studies were performed with the Gaussian 09 [45] with density functional methods at B3LYP calculations using 6-311G (d, p) basis set. Also, HF and semi-empirical methods (PM3& PM6) were used for some studies as implemented in the computational package. The computational studies of this work divided into two parts: The first part was the optimization of the starting hydrazone **2** [35], glucose and open chain & cyclic form of the sugar hydrazone derivatives **3b**, from DFT calculations [46-48] , based on the HOMO & LUMO energies of the studied compounds some reactivity parameters were calculated as shown in **Table I**. The energies of the frontier orbitals HOMO (highest occupied molecular orbitals and LUMO (lowest unoccupied molecular orbital) are principally used descriptors in QSAR analysis. A higher HOMO energy suggests higher affinity of a molecule to react as a nucleophile, a lower LUMO energy suggests stronger electrophilic nature of a molecule. In general, chemical potential (μ) is the link between structure and reactivity as the greater chemical potential of studied compounds the greater its reactivity. The electronegativity of glucose recorded high value confirming its high electron acceptor capability from the hydrazone moiety of compound **2**, this was also, confirmed by the chemical potential values which is a potential index indicates the direction of electron density through molecules, electron flow occurs from system with higher chemical potential to the one with small chemical potential. Consequently, the hydrazone **2** has high chemical potential (electron donor) and glucose has lower chemical potential (electron acceptor), the calculated electrophilicity index ($\omega = \mu^2/2\eta$) measures the total ability to attract electrons, shows the tendency of an electrophile to acquire an

extra amount of electron density, regarding electrophilicity, one observes from **Table II** the high electrophilicity of glucose compared with the hydrazone **2**. Hence, glucose is better electrophile than the quinazolinone hydrazone **2**. Furthermore , simple index was chosen for the nucleophilicity (N) which explain the maximum number of electrons that an electrophile can acquire, is defined as N = E_{HOMO} (ev) + 9.12 (ev), where -9.12 is the energy of the HOMO of tetracyano ethylene (TCE), this nucleophilicity scale is referred to TCE and taken as a reference because TCE exhibits the lowest HOMO energy (= -9.12 eV). The resistance of a molecule to exchange electron density with the environment given by the chemical hardness (η) & softness (σ**)** has shown to be a powerful tool.

TABLE III

Reactivity parameters of the studied compounds calculated by B3LYP/6-311G (d, p)

Parameter	**glucose**	**2**	**3b (open chain)**	**3b (cyclic form)**
Homo energy (eV)[a] (E_{HOMO})	-7.533	-6.100	-0.21026	-0.20882
Lumo energy (eV) (E_{LUMO})	-1.132	-1.410	-0.03932	-0.04084
Energy gap (eV) (E_{LUMO} -E_{HOMO})	**6.400**	**4.690**	**0.17094**	**0.16798**
Dipole moment (Debye)	6.562	2.213	5.2083	4.7102
Ionization potential IP(eV)= $-E_{HOMO}$	7.533	6.100	0.21026	0.20882
Electron affinity EA (eV) = $-E_{LUMO}$	1.132	1.410	0.03932	0.04084
Electronegativity χ (eV) = (IP +EA)/2	4.333	3.755	0.24958	0.12483
Chemical potential $\mu = -\chi$	-4.333	-3.755	- 0.24958	-0.12483
Hardness η = (IP-EA)/2	1.601	2.345	0.08547	0.08399
Softness $\sigma = 1/\eta$	0.625	0.426	11.700	11.906
Electrophilicity $\omega = \mu^2/2\ \eta$	5.864	3.006	0.36448	0.09277
Nucleophilicity = E_{HOMO} + 9.12	1.587	3.020	8.90994	8.91118

Moreover, according to energy gap, energy of the produced hydrazo glucosyl quinazolinone **3b** have the lowest energy gap in its two forms (0.17094 & 0.16798 eV the open chain and the cyclic form respectively) compared with this of the hydrazone **2** (4.690 eV) or glucose (6.400 eV) **Fig. 2** . On the other hand, the electronegativity of glucose recorded high value confirming its high electron acceptor capability from the hydrazone **2**. Meanwhile, the collected results in **Table IV** confirm that glucose is the electron acceptor while hydrazone **2** is the electron donor one and reflect the reactivity of the molecules. Charge transfer is usually occurred if the energy gap between the E_{HOMO} (-6.100 eV) of donor and the E_{LUMO} of acceptor (-1.132ev) is relatively small which equal (-4.968) in our system that supports the presence of charge transfer.

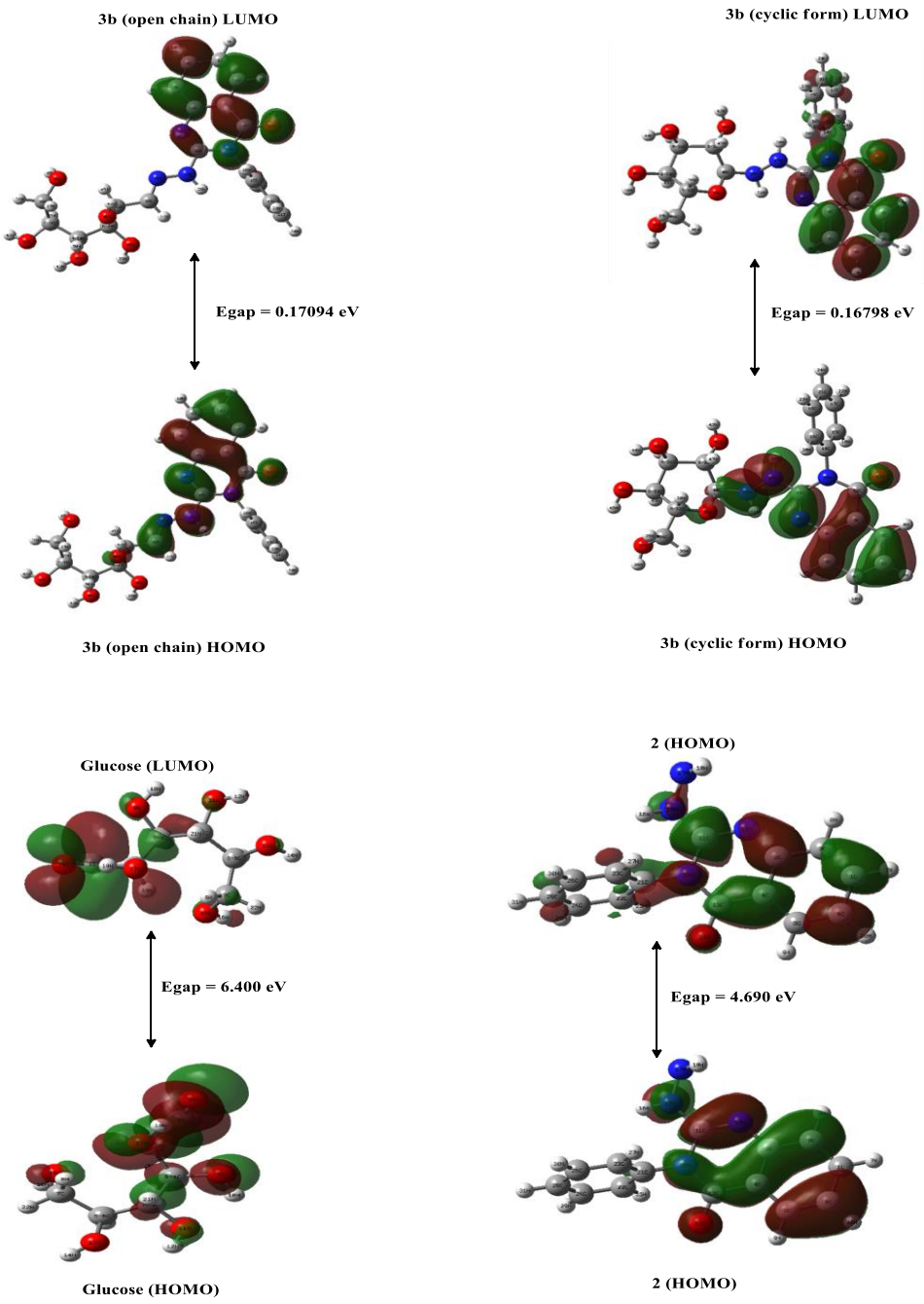


Fig.2: Frontier molecular orbital of the studied compounds calculated at the B3LYP/6-311G (d, p).

b) Mullikan atomic charges and molecular electrostatic potential (MEP):

Mulliken atomic charges for the reactants and product are computed at the same level of the theory at the same basis set and the results are presented in **Table II**. One can conclude that the computed charges are going in agreement with the values of the reactivity parameters in **Table I** & **Figure 3**. Consequently, the atomic charges on the most centers, especially the carbon atom of the aldehydic group, also the oxygen atoms of the hydroxyl groups in the glucose moiety of the product supporting its electron acceptor capability. Hence, C30, H37, O40, O42, O44 and O46 recorded 0.064, 0.135, -0.443, -0.426, -0.385 and -0.413º compared with 0.056, 0.118 , -0.361, -0.361, - 0.379 and – 0.292 º for free glucose. Consistence with the above-mentioned results, with respect to quinazolinone hydrazone **2**, a decrease in atomic charges were recorded which confirms its electron donating character, especially, C2, C3,C4, C5,C6 of quinazoline ring, O13, N26 and N29, they recorded -0.024, - 0.200, 0.086, -0.063, -0.078, -0.348, -0.383, -0.124 º for the product compared with that of the free quinazolinone hydrazone **(2)** which record -0.380, 1.507, -0.859, -0.171, -0.185, -0.403, -0.440 and -0.564º respectively. The decrease of charge on the carbon of quinazoline ring of the product compared with free quinazolinone hydrazone **(2)** confirms the presence of intramolecular charge transfer within the molecule from the π ring system towards the π* of the mentioned nitrogen centers.

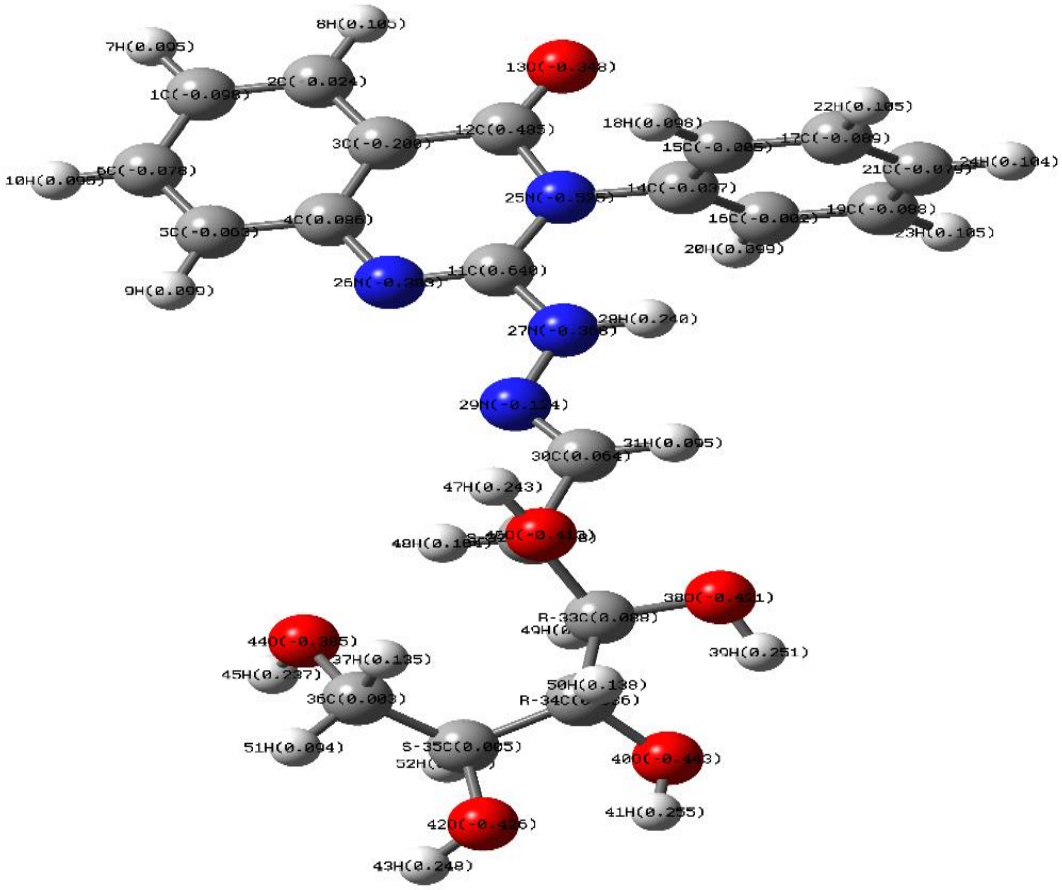


Fig. 3: **Optimized structure of (3b) with Mulliken charges calculated at B3LYP / 6-311G (d.p).**

TABLE II

Mulliken atomic charges in gas phase calculated by B3LYP/6–311 G (d, p) method.

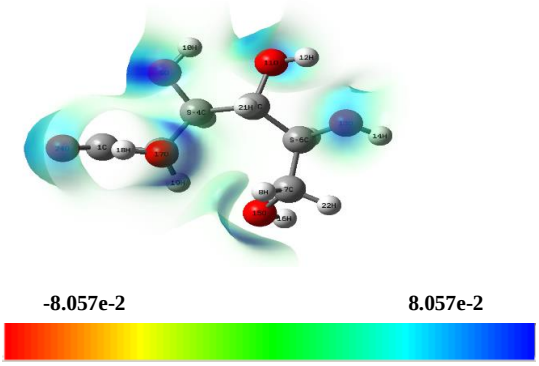
Atom	Product	Monomer	Atom	Product	Monomer
1C	-0.098	-0.096	28H	0.240	0.367
2C	-0.024	-0.380	29N	-0.124	-0.564
3C	-0.200	1.507	30C	0.064	0.055
4C	0.086	-0.859	31H	0.095	0.195
5C	-0.063	-0.171	32C	-0.008	-0.004
6C	-0.078	-0.185	33C	0.088	0.048
7H	0.095	0.112	34C	0.036	0.011
8H	0.105	0.152	35C	0.005	-0.003
9H	0.099	0.108	36C	0.003	-0.002
10H	0.095	0.149	37H	0.135	0.118
11C	0.640	0.186	38O	-0.421	-0.473
12C	0.485	-0.214	39H	0.251	0.250
13O	-0.348	-0.403	40O	-0.443	-0.361
14C	-0.037	-1.880	41H	0.255	0.262
15C	-0.005	0.494	42O	-0.426	-0.361
16C	-0.002	0.798	43H	0.248	0.269
17C	-0.089	-0.216	44O	-0.385	-0.379
18H	0.098	0.146	45H	0.237	0.244
19C	-0.088	-0.143	46O	-0.413	-0.292
20H	0.099	0.140	47H	0.243	0.198
21C	-0.079	0.010	48H	0.164	0.145
22H	0.105	0.135	49H	0.103	0.160
23H	0.105	0.137	50H	0.138	0.132
24H	0.104	0.110	51H	0.094	0.126
25N	-0.525	0.231	52H	0.097	-0.049
26N	-0.383	-0.440			
27N	-0.368	0.135			

On the other hand, electrostatic potential map (MEP) give a good idea about the reactivity in a molecule. The reactivity displayed depending on the color of the region for electrophilic or nucleophilic attacks [49]. The MEP maps of the hydrazo glucosyl quinazolone **3b**, glucose and quinazolinone hydrazone **2** calculated at B3LYP/6-31G (d, p) method/basis set are shown in **Fig.4** where the different values of electrostatic potential at MEP surface are represented by different colors increasing in the order red < orange < yellow< green< blue. The negative potential (red color) regions have electrophilic reactivity (nucleophilic attack regions) while the blue regions of the MEP surface represent nucleophilic reactivity (electrophilic attack regions), the green colored regions show the neutral part. For compound **(2)** the limit unit ranged from -6.300 to 6.300 unit in the order red < yellow < green < blue color. For glucose, the limit unit ranged from -7.229 to 7.229. Regarding the condensation product, the limit ranged from -7.046 to 7.046 one observes from the maps that the most negative regions are located on the carbonyl oxygen atom of the of the quinazoline ring and the positive regions are found on the hydrazone moiety and the hydrogen atoms. This confirms the charge transfer process from quinazolinone hydrazone **2** towards glucose and the donor centers are the π system of the quinazoline ring beside the hydrazide moiety, and the acceptor centers on glucose are mainly the five oxygen atoms of the hydroxyl groups.

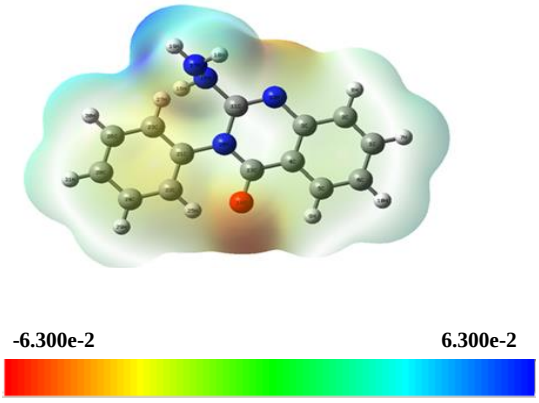
C. Calculation of dipole moments & optimization energies at different computational methods for 3b

The second part of the optimization was carried out using Hartree-Fock (HF) calculations with 6-311G (d,p) basis set , and semi-empirical (AM1, PM3, PM6) for both the open chain gluco-hydrazone derivative and its cyclic form in gas phase, to predict and confirm the more stable conformation depending on the results obtained and collected in **Table III& IV** , it was observed from the data that the dipole moment values (Debye) calculated in the gas phase for both forms of **3b**, affected by the method used for optimization as shown in **Figs. 5& 6**. Moreover, we can conclude that the optimization of both forms using Hartree-Fock (HF) at 6311basis set, systematically have higher value of dipole moments. Also , the calculations showed the wide range

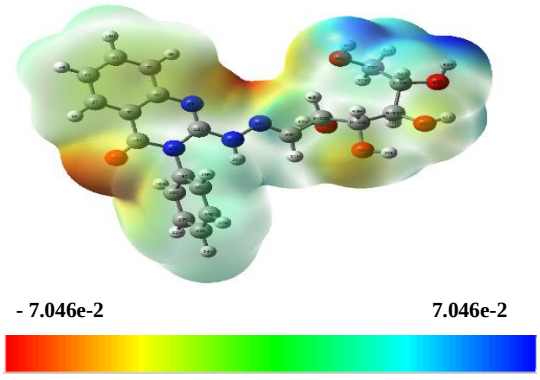
differences in the optimization total energies (Hartree) depending on the method used.



(A)



(B)



(C)

Fig. 4: Calculated MEP for glucose (A), quinazolinone hydrazone (B) and hydrazo glucosyl quinazolone (C) at B3LYP/6-311G (d, p).

TABLE III

Optimization results of the open chain form of (3b).

Parameter	**Cyclic Form**				
Method	**DFT/B3LYB**	**HF**	**AM1**	**PM3**	**PM6**
Energy (a.u)	-1445.41026638	-1436.20579363	-0.19615032	-0.21496679	-0.23946682
Dipole Moment (D)	4.7102	6.5957	2.1495	2.8753	3.50
RMSGradient Norm	0.00000354	0.03318434	0.00000229	0.00000586	0.00000229
Spin	doublet	doublet	doublet	doublet	doublet
Charge	zero	zero	zero	zero	zero

TABLE IV

Optimization results of the cyclic form (3b).

Parameter	**Open Chain Form**				
Method	**DFT/B3LYB**	**HF**	**AM1**	**PM3**	**PM6**
Energy (a.u)	-1446.05960046	-1436.81967061	-0.22572877	-0.23942263	-0.26377165
Dipole Moment (D)	5.2083	6.1628	2.9512	3.0570	3.9547
RMSGradient Norm	0.00000534	0.00000398	0.00000115	0.00000421	0.00000309
Spin	singlet	singlet	singlet	singlet	singlet
Charge	zero	zero	zero	zero	zero

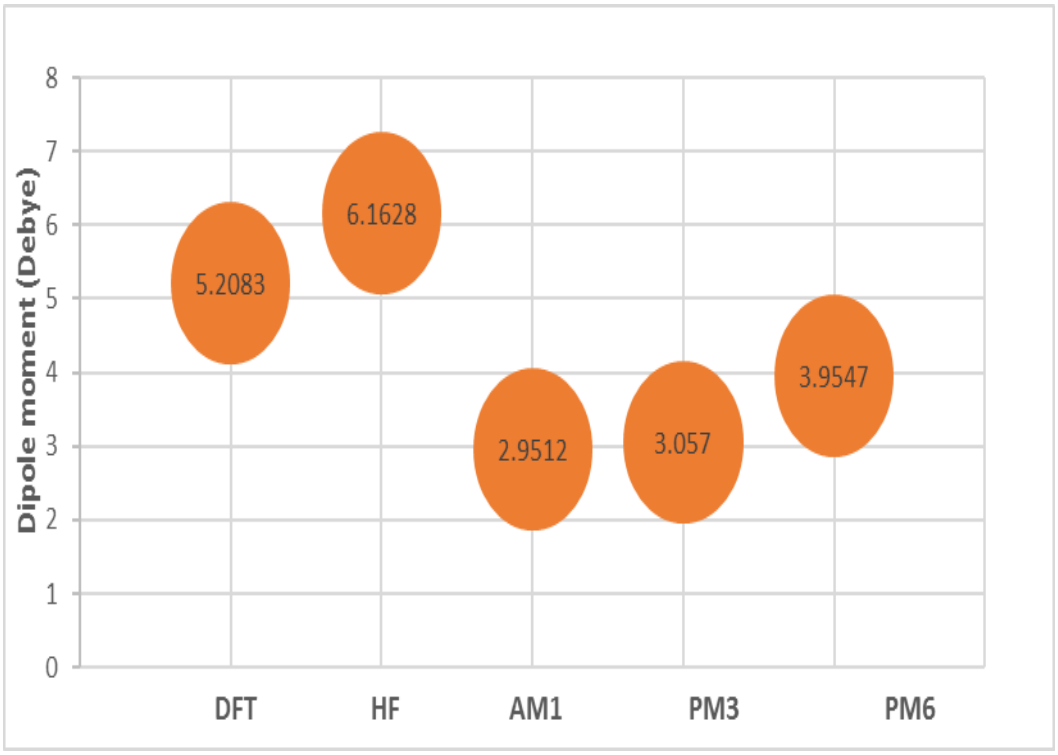


Fig. 5: Dipole moment of the open chain form of 3b optimized by different methods.

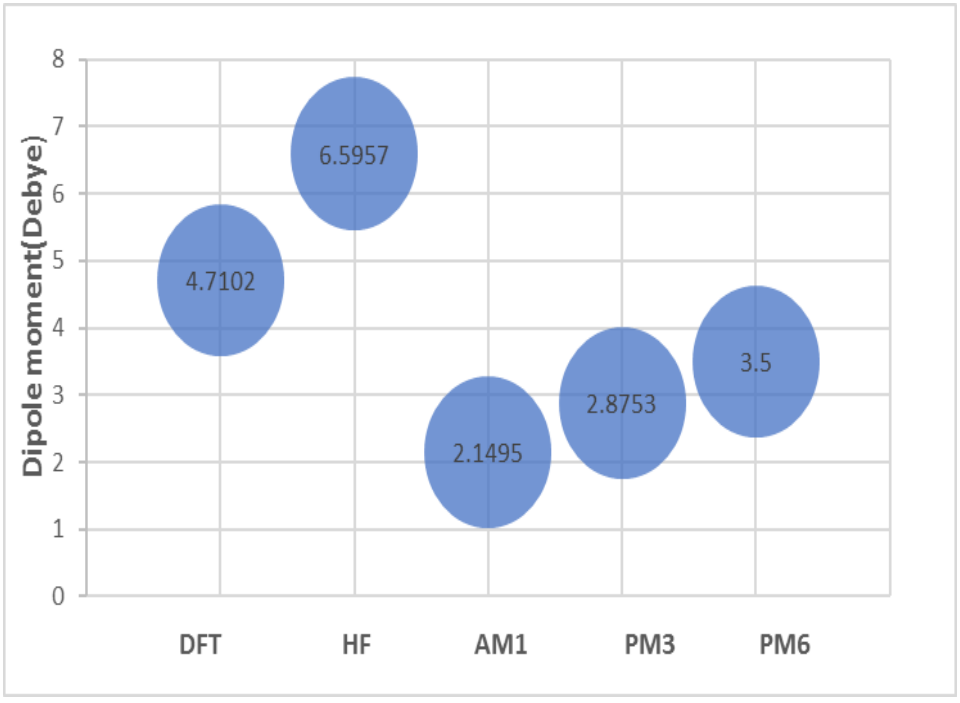


Fig. 6. Dipole moment of the cyclic form of 3b optimized by different methods.

a) Antimicrobial activities

The antimicrobial activities of some of the synthesized compounds **3a,c,d,f ; 4a,b,d,e,f; 5b** were tested against five different microorganisms Gram-negative and Gram-positive bacterial strains and fungi strain. Staphylococcus aureus ATCC6538P, Escherichia coli ATCC8739, Pseudomonas aeruginosa ATCC9027, Candida albicans ATCC2091 and Bacillus subtilis ATCC19659. using Ciprofloxacin (5 µg/disc) and Clotrimazole (10 µg/disc) as standard drugs. Firstly the zone of inhibition was measured for all the tested compounds using the agar well-diffusion method [50].The results recorded in **Table V** show that sugar hydrazone derivative with galactose and xylose **3a, f** showed a significant activity against Bacillus subtilis, while the acetate derivative **4e,f** ribose and xylose derivative showed a moderate activity against Staphylococcus aureus. The triazole acetate derivative of glucose showed an activity towards Pseudomonas aeruginosa.

TABLE V

Antimicrobial activities of the synthesized compounds 3a,c,d,f ; 4a,b, d,e,f; 5b.

Cpd	**S**		**E**		**Ps**		**B**		**C**	
	DMF	Cpd	DMF	Cpd	DMF	Cpd	DMF	Cpd	DMF	Cpd
3a	18	18	19	19	9	9	14	20	12	12
3c	17	17	20	20	9	9	14	14	12	12
3d	17	17	20	20	9	9	15	20	12	12
3f	9	9	20	20	9	9	9	9	12	12
4a	17	17	20	20	9	9	15	15	12	12
4b	9	9	20	20	9	9	9	9	12	12
4d	12	15	21	21	13	13	20	20	12	12
4e	9	9	20	20	9	9	9	9	12	12
4f	9	9	20	20	9	9	9	9	12	12
5b	17	17	20	20	9	15	15	15	12	12
Ciprofloxazine	9	30	9	30	9	30	9	30	-	-
Clotrimazole	-	-					-	-	17	10

III. Materials and methods

A. Chemistry

General

Melting points were determined on an Electrothermal apparatus 9100 (Rochford, UK), and they were uncorrected. Elemental analyses were performed at the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Nasr city, Cairo, Egypt, using FLASH 2000 CHNS/ O analyzer found values were within ±0.50% of the theoretical ones. IR spectra were recorded using potassium bromide disk on a Bruker FT-IR spectrometer Model: Tensor 37 and expressed in wave number (υ max) cm^{-1}. ^{1}H-NMR & ^{13}C-NMR was determined on a JEOL JNM ECA 500 MHz NMR (Faculty of Science, Alexandria University, Alexandria, Egypt) using tetramethyl silane (TMS) as internal standard, chemical shift values were recorded in ppm on δ scale. Some samples were performed at

the Regional Center for Mycology and Biotechnology (RCMB), Al-Azhar University, Nasr city, Cairo, Egypt on a Bruker 400 MHz NMR. All reactions were monitored by thin layer chromatography, carried out using flexible sheets 7.5x2.5 (Baker-flex) silica gel IB-F (J.T.BAKER CHEMICAL CO, WEST GERMANY). The spots were visualized using Vilber Lourmat ultraviolet lamp at 4w-365 and 4w-254 nm.

Preparation of the starting compounds:

3-Phenyl-2-mercapto/thioxo-2,3-dihydro-1H-quinazolin-4-one (1) [34]

A mixture of equimolar amounts of phenyl thiourea (15.2 g, 10 mmol) and anthranilic acid (13.7g,10 mmol) were fused together for 4 hours in a round bottomed flask provided with an air condenser in an oil bath at 175-180 °C, then cooled and added to cold water (40 mL). The solid product obtained was collected and recrystallized from ethanol to give **(1)**. Yield, 70%; m.p. > 300℃ ; IR (KBr): ν =3245 (NH), 2924(SH), 1661(C=O quinazolinone), 1621(CN), 1531(C=C), 1268 cm^{-1}(CS);^{1}H NMR (DMSO-d6): δ (ppm) 9.98 (s,1H, NH, exchangeable), 6.64-7.70 (m, 9H, ArH),5.45 (s,1H, SH, exchangeable) ^{13}C NMR (DMSO-d6): δ =179 (C-2, CS) , 165 (C-4, CO), 138 (C-9, C-11), 132(C-7), 130 (C-10), 128 (C-13, C-15), 127 (C-5), 125 (C-8), 124 (C-6, C-14), 120 (C-12, C-16); Anal. Calcd for $C_{14}H_{10}N_2OS$ (254.31): C, 66.12; H, 3.96; N, 11.02; S, 12.61%. Found: C, 67.56; H, 3.16; N, 10.20; S, 12.91%.

2-Hydrazino-3-phenyl- 3H-quinazolin-4-one (2)**[**35**]**

A mixture of **1** (4 g, 15.7 mmol) and hydrazine hydrate (1g, 20 mmol) was heated under reflux in 30 mL of 95% ethanol for 5 h, then the reaction mixture was concentrated and poured onto crushed ice. The separated crude solid was filtered off, washed successively with water, dried and recrystallized from ethanol to give **2** as colorless needles. The yield of **2** was 77%, m.p. 200–202°C and IR as reported previously in literature IR (KBr) : ν = 3583-3172 (multiple bands, NH_2, NH), 1650 (C=O quinazolinone), 1610 cm^{-1} (CN); ^{1}H NMR (CDCl3): δ (ppm) = 9.33 (s, H, NH, exchangeable), 7.19-7.89 (m, 9H, ArH), 4.55 (br s, 2H, NH_2); ^{13}C NMR: δ (ppm) = 161 (C-4,CO), 153(C-2), 149 (C-9), 134 (C-7), 128 (C-4'),133(C-1'),127(C-6),126 (C-5,C-8), 121 (C-10); Anal. Calcd for $C_{14}H_{12}N_4O$ (252.10): C, 66.65; H, 4.79; N, 22.21%. Found: C, 67.88; H, 5.40; N, 22.28%.

General procedures for the synthesis of sugar (3-Phenyl-4-quinazolones)-2-hydrazones (3a-f) [40] .

To a solution of 2-hydrazino-3-phenylquinazolinone **2** (1.25 g, 5.0 mmol) in pyridine (15 ml) acetic anhydride was added (2.50 mmol). The mixture was left overnight for two days. The solid that separated on cooling was filtered, washed with EtOH, and dried.

2-hydrazo-D-galactosyl-3-phenyl-4-quinazolone

(3a)**:** This compound was obtained as pale-yellow crystals, (0.87 g, and 70%), m.p.220–222°C; IR(KBr) ν 3477 (OH), 3073 (NH), 1694 (C=O quinazolinone),and 1616 cm^{-1} (C=N); ^{1}H NMR (DMSO-d6,500MHz): δ (ppm) 10.93 (s,1H,NH group, exchangeable with D_2O), 8.67-7.14 (m, 10H, ArH, H-1' of the sugar moiety), 3.81 (dd, 1H, H-6'a), 3.65-3.58 (m, 5H, OH-6', OH-3', OH-4',OH-5' exchangeable with D_2O, H-6'b), 3.40-3.29 (m,4H, H-2', H-3', H-4', H-5'), 2.80 (s, 1H,OH-2'), ^{13}C NMR (DMSO-d6,500MHz): δ (ppm) =164 (C-1', sugar moiety), 162 (C-4,CO), 153(C-2), 146 (C-9), 133 (C-7), 127(C-6), 126 (C-5,C-8), 121 (C-10), 72 (C-5', sugar moiety), 71 (C-4', sugar moiety), 70 (C-3', sugar moiety), 69 (C-2', sugar moiety); Anal. Calcd for $C_{20}H_{22}N_4O_6$ (414): C, 57.97; H, 5.31; N, 13.53; %. Found: C, 57.72; H, 5.63; N, 13.30%.

2-hydrazo-D-glucosyl-3-phenyl-4-quinazolone **(*3b*):**

This compound was obtained as pale-yellow crystals, (0.72 g, and 58%), m.p.223-225°C; IR(KBr) ν 3436(OH), 3211 (NH), 1691 (C=O quinazolinone), and 1616 cm^{-1}(C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.81 (s,1H,NH group, exchangeable with D_2O), 7.85-7.08 (m, 10H, ArH, H-1' of the sugar moiety), 4.48 (dd, 1H, H-6'a), 4.43 -4.27 (m, 5H, OH-6', OH-3', OH-4',OH-5' exchangeable with D_2O, H-6'b), 4.20-3.38 (m,4H, H-2', H-3', H-4', H-5'), 3.30 (s, 1H,OH-2' exchangeable with D_2O), ^{13}C NMR (DMSO-d6,500MHz): δ (ppm) =165 (C-1', sugar moiety), 161 (C-4,CO), 153(C-2), 146 (C-9), 133 (C-7), 127(C-6),126 (C-5,C-8), 121 (C-10), 73 (C-5', sugar moiety), 72(C-4', sugar moiety), 71(C-3', sugar moiety), 69 (C-2', sugar moiety); Anal. Calcd for $C_{20}H_{22}N_4O_6$ (414): C, 57.97; H, 5.31; N, 13.53; %. Found: C, 57.80; H, 5.50; N, 13.40%.

2-hydrazo-D-mannosyl-3-phenyl-4-quinazolone (3c)**:**

This compound was obtained as pale-yellow crystals, (0.85 g, and 68%), m.p. 215-217°C; IR(KBr) ν 3393(OH), 3075(NH), 1698 (C=O quinazolinone), and 1660 cm^{-1} (C=N); ^{1}H NMR (DMSO-d6,500MHz): δ 10.87 (s,1H,NH group, exchangeable with D_2O), 7.85-7.08 (m, 10H, ArH, H-1' of the sugar moiety), 4.48 (dd, 1H, H-6'a), 4.79 -4.43 (m, 5H, OH-6', OH-3', OH-4',OH-5' exchangeable with D_2O, H-6'b), 4.20-3.38 (m,4H, H-2', H-3', H-4', H-5'), 3.30 (s, 1H,OH-2' exchangeable with D_2O), ^{13}C NMR (DMSO-d6,500MHz): δ (ppm) =163 (C-1',

sugar moiety), 160 (C-4,CO), 153(C-2), 146 (C-9), 133 (C-7), 127(C-6),126 (C-5,C-8), 121 (C-10), 73 (C-5', sugar moiety), 72(C-4', sugar moiety), 71(C-3', sugar moiety), 69 (C-2', sugar moiety) 64 (C-6',sugar moiety); Anal. Calcd for $C_{20}H_{22}N_4O_6$ (414): C, 57.97; H, 5.31; N, 13.53; %; Found: C, 57.60; H, 5.52; N, 13.41%.

***2-hydrazo-D-arabinosyl-3-phenyl-4-quinazolone (3d)*:**

This compound was obtained as pale-yellow crystals, (0.95g, and 76%), m.p.143-145°C; IR (KBr) ν 3393(OH), 3062 (NH), 1695 (C=O quinazolinone), and 1665cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6, 500MHz): δ 10.65 (s,1H,NH group, exchangeable with D_2O), 8.03-7.19 (m, 10H, ArH, H-1' of the sugar moiety), 3.81 (dd, 1H, H-5'a), 3.65 (d, 1H, OH-5', exchangeable with D_2O), 3.58 (m, 2H,OH-3',OH-4' exchangeable with D_2O), 3.56-3.29 (m,4H, H-2', H-3', H-4', H-5'b), 2.80 (s, 1H,OH-2' exchangeable with D_2O), ^{13}C NMR (DMSO-d6,500 MHz): δ (ppm) =161 (C-4,CO), 153.5(C-1', sugar moiety), 153(C-2), 147 (C-9), 133 (C-7), 127(C-6),126 (C-5,C-8), 121 (C-10), 74 (C-3', sugar moiety), 72(C-4', sugar moiety), 71(C-3', sugar moiety), 64 (C-5', sugar moiety), 61 (C-2', sugar moiety); Anal. Calcd for $C_{19}H_{20}N_4O_5$ (384): C, 59.37; H, 5.24; N, 14.58 %; Found: C, 59.66; H, 5.07; N, 14.89 %.

***2-hydrazo-D-ribonosyl-3-phenyl-4-quinazolone (3e)*:** This compound was obtained as pale-yellow crystals, (0.72g, and 58%), m.p.226-229 °C; IR(KBr) ν 3393(OH), 3065 (NH), 1707 (C=O quinazolinone) and 1665cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6, 500MHz): δ 10.64 (s,1H,NH group, exchangeable with D_2O), 7.85-7.08 (m, 10H, ArH, H-1' of the sugar moiety), 3.75 (dd, 1H, H-5'a), 3.65 (d, 1H, OH-5', exchangeable with D_2O), 3.58 (m, 2H,OH-3',OH-4' exchangeable with D_2O), 3.56-3.29 (m,4H, H-2', H-3', H-4', H-5b'), 2.80 (s, 1H,OH-2' exchangeable with D_2O). Anal. Calcd for $C_{19}H_{20}N_4O_5$ (384): C, 59.37; H, 5.24; N, 14.58 %; Found: C, 59.60; H, 5.05; N, 14.80 %.

***2-hydrazo-D-xylosyl-3-phenyl-4-quinazolone* (*3f*):** This compound was obtained as pale-yellow crystals, (0.90g, and 72%), m.p.210-212°C; IR(KBr) ν 3393(OH), 3074 (NH), 1690 (C=O quinazolinone) and 1665cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.89 (s,1H, NH group, exchangeable with D_2O),7.88-8.80 (m, 10H, ArH, H-1' of the sugar moiety), 3.80 (dd, 1H, H-5'a), 3.60(d, 1H, OH-5', exchangeable with D_2O), 3.58-3.29 (m,6H, H-2', H-3', H-4', H-5'b, OH-3',OH-4'), 2.80 (s, 1H,OH-2'). MS: m/z 236 (100), 221(5.45), 192(1.43), 146 (9.58), 120(27), 105(8.4), 91(29.46), 78(58.27), 64(19.15), 51(47.01). Anal. Calcd for $C_{19}H_{20}N_4O_5$ (384): C, 59.37; H, 5.24; N, 14.58 %; Found: C, 59.46; H, 5.00; N, 14.69 %.

General procedure for the synthesis of per-O-acetyl-sugar hydrazones derivatives (4a-f). To a cold solution of the sugar hydrazones **3a-f** (0.5g) in dry pyridine, acetic anhydride (5 mL) was added gradually with stirring at 0 ºC until the appearance of turbidity. The reaction mixture was left overnight for about 72 hours, then poured into crushed ice, the solution was extracted with chloroform, and the extract was washed well with water, dried over anhydrous sodium sulfate, and then evaporated under reduced pressure. The resulting syrup was crystallized from absolute ethanol to give **4a-f**. The solid that separated on cooling was filtered, washed with EtOH, and dried.

2-hydrazo-(penta-O-acetyl-D-galactosyl)-3-phenyl-4-quinazolone (4a): This compound was obtained as pale-yellow crystals (60 %) m.p. 143-145ºC; IR (KBr) ν 3242(NH), 1749 (OAc), 1695 (C=O quinazolinone) and 1636 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.93 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-6'a), 3.65 (s, 3H, OAc at C-6'), 3.58 (s, 9H, OAc at C-3',C-4', C-5'), 3.56 (m, 1H, H-6'b), 3.40-3.29 (m, 4H, H-2', H-3', H-4', H-5'), 2.80 (s, 3H, OAc at C-2'); ^{13}C NMR (DMSO-d6,500MHz): δ (ppm) =153(C-2), 147 (C-9), 133 (C-7), 127(C-6),126 (C-5,C-8), 121 (C-10), 74 (C-3', sugar moiety), 72(170 (CO Acetyl groups), 161 (C-4,CO), 153.5(C-1', sugar moiety), C-4', sugar moiety), 71(C-3', sugar moiety), 64 (C-5', sugar moiety), 61 (C-2', sugar moiety) 21 (CH_3 of the acetyl) ; Anal. Calcd for $C_{30}H_{32}N_4O_{11}$ (624) C, 57.69; H, 5.16; N, 8.97%; Found: C, 57.73; H, 5.29; N, 8.05 %.

2-hydrazo-(penta-O-acetyl-D-glucosyl)-3-phenyl-4-quinazolone (4b):This compound was obtained as pale-yellow crystals (65 %) m.p. 175-177 ºC;IR (KBr)ν 3284 (NH), 1743(OAc), 1691 (C=O quinazolinone), and 1616 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.81 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-6'a), 3.65 (s, 3H, OAc at C-6'), 3.58 (s, 9H, OAc at C-3',C-4', C-5'), 3.56 (m, 1H, H-6'b), 3.40-3.29 (m, 4H, H-2', H-3', H-4', H-5'), 2.80 (s, 3H, OAc at C-2'); Anal. Calcd for $C_{30}H_{32}N_4O_{11}$ (624) C, 57.69; H, 5.16; N, 8.97%; Found: C, 57.53; H, 5.21; N, 8.66 %.

2-hydrazo-(penta-O-acetyl-D-mannosyl)-3-phenyl-4-quinazolone (4c): This compound was obtained as pale-yellow crystals (60 %) m.p. 135-137ºC; IR(KBr) ν 3307(NH), 1745(OAc), 1695 (C=O quinazolinone) and 1645 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.87 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-6'a), 3.65 (s, 3H, OAc at C-6'), 3.58 (s, 9H, OAc at C-3',C-4', C-5'), 3.56 (m, 1H, H-6'b), 3.40-3.29 (m, 4H, H-2',

H-3', H-4', H-5'), 2.80 (s, 3H, OAc at C-2'). Anal. Calcd for $C_{30}H_{32}N_4O_{11}$ (624) C, 57.69; H, 5.16; N, 8.97%; Found: C, 57.07; H, 5.98; N, 8.72 %.

2-hydrazo-(tetra-O-acetyl-D-arabinosyl)-3-phenyl-4-quinazolone (4d): This compound was obtained as pale-yellow crystals (50 %) m.p. 140-143 ºC; IR (KBr) ν3290 (NH), 1749 (OAc), 1685 (C=O quinazolinone) and 1645 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.65 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-5'a), 3.65 (s, 3H, OAc at C-5'), 3.58 (s, 6H, OAc at C-3',C-4'), 3.56 (m, 1H, H-5'b), 3.40-3.29 (m, 3H, H-2', H-3', H-4',), 2.80 (s, 3H, OAc at C-2'). Anal. Calcd for $C_{27}H_{28}N_4O_9$ (552) C, 58.69; H, 5.07; N, 10.14 %; Found: C, 58.73; H, 5.21; N, 10.05 %.

2-hydrazo-(tetra-O-acetyl-D-ribosyl)-3-phenyl-4-quinazolone (4e): This compound was obtained as pale-yellow crystals (60 %) m.p. 155-157ºC; IR (KBr) ν 3246(NH), 1745 (OAc), 1695 (C=O quinazolinone),and 1645 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.64 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-5'a), 3.65 (s, 3H, OAc at C-5'), 3.58 (s, 6H, OAc at C-3',C-4'), 3.50 (m, 1H, H-5'b), 3.40-3.29 (m, 3H, H-2', H-3', H-4',), 2.80 (s, 3H, OAc at C-2'). Anal. Calcd for $C_{27}H_{28}N_4O_9$ (552) C, 58.69; H, 5.07; N, 10.14 %; Found: C, 58.73; H, 5.21; N, 10.22 %.

2-hydrazo-(tetra-O-acetyl-D-xylosyl)-3-phenyl-4-quinazolone (4f): This compound was obtained as pale-yellow crystals (60 %) m.p. 135-137ºC; IR(KBr) ν 3042(NH), 1745 (OAc), 1695 (C=O quinazolinone), and 1635 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 10.89 (s,1H,NH group, exchangeable with D_2O), 8.80 -7.88 (m, 10H, ArH, H-1' of the sugar moiety), 3.81(dd, 1H, H-5'a), 3.65 (s, 3H, OAc at C-5'), 3.58 (s, 6H, OAc at C-3',C-4'), 3.56 (m, 1H, H-5'b), 3.40-3.29 (m, 3H, H-2', H-3', H-4'), 2.80 (s, 3H, OAc at C-2'). Anal. Calcd for $C_{27}H_{28}N_4O_9$ (552) C, 58.69; H, 5.07; N, 10.14 %; Found: C, 58.70; H, 5.10; N, 10.12 %.

General Procedure for the Preparation of 1-(Per-*O*-acetyl-alditol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-*a*]quinazolin-5(4*H*)-ones (5b, d, f): To a mixture of **3b,d,f** (1.0 g, 2mmol) and anhydrous sodium acetate (0.60 g, 2mmol) in glacial acetic acid (10mL), a solution of bromine (0.5 g, 2.80 mmol) in glacial acetic acid (5 mL) was added and stirred for 2 h at room temperature. The mixture was treated with acetic anhydride (20 mL) and kept for 48 h at room temperature and then poured into crushed ice , extracted with chloroform, evaporated under reduced pressure yielded a residue which crystallized from methanol.

1-(1',2',3',4',5'-penta-O-acetyl-D-gluco-pentitol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-one (5b).This compound was obtained as reddish brown crystals in a 77% yield m.p. 145-147 °C, IR (KBr) ν 1775 (OAc), 1690 (C=O quinazolinone), 1610 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 7.85-7.08 (m, 9H, ArH), 6.58 (d, 1H, H-1'), 6.26 (dd, 1H, H-2'), 5.27 (dd, 1H, H-3'), 5.17 (m, 1H, H-4'), 4.18 (m, 1H, H-5a'), 4.05 (dd,1H,H-5'b), 2.19, 2.10, 2.00,1.98 and 1.96 (5s, 15H, 5-OAc). Anal. Calcd for $C_{30}H_{30}N_4O_{11}$ (622) C, 57.88; H, 4.82; N, 9.00 %; Found: C, 57.70; H, 5.10; N, 9.14 %.

1-(1',2',3',4',5'-penta-O-acetyl-D-arabinosyl-tetritol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)- one (5d). This compound was obtained as orange needles in a 77% yield, m.p. 175-177 °C, IR (KBr) ν 1775 (OAc), 1698 (C=O quinazolinone), 1630 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 7.85-7.08 (m, 9H, ArH), 6.58 (d, 1H, H-1'), 6.26 (dd, 1H, H-2'), 5.27 (dd, 1H, H-3'), 4.18 (m, 2H, H-4'a,b), 2.19, 2.10, 2.00, and 1.96 (4s, 12H, 4-OAc). Anal. Calcd for $C_{27}H_{26}N_4O_9$ (550) C, 58.91; H, 4.72; N, 10.18 %; Found: C, 58.70; H, 4.10; N, 10.14 %.

1-(1',2',3',4',5'-penta-O-acetyl-D-xylosyl- tetritol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-one (5f). This compound was obtained as orange needles in a 77% yield, m.p. 175-177 °C, IR (KBr) ν 1760 (OAc), 1698 (C=O quinazolinone), 1630 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ 7.85-7.08 (m, 9H, ArH), 6.58 (d, 1H, H-1'), 6.26 (dd, 1H, H-2'), 5.27 (dd, 1H, H-3'), 4.18 (m, 2H, H-4'a,b), 2.19, 2.10, 2.00, and 1.96 (4s, 12H, 4-OAc). Anal. Calcd for $C_{27}H_{26}N_4O_9$ (550) C, 58.91; H, 4.72; N, 10.18 %; Found: C, 58.80; H, 4.50; N, 10.12 %.

General Procedure for the Preparation of 1-(Alditol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-*a*]quinazolin-5(4*H*)-ones 6b,d,f.

Method (A)

A solution of **5 b, d, f** (1.0 g) in methanol (15 mL) was refluxed with 20% ammonia solution (20 mL) and for 4 hours. The resulting solution was evaporated under reduced pressure and the product was recrystallized from water and methanol to give **6b, d, f.**

Method (B)

A solution of bromine in ethanol/water (10 ml) was added dropwise to a solution of the appropriate hydrazone **3b, d, f** in ethanol (150 ml) and the reaction was stirred at room temperature, then kept overnight at room temperature. The solution was concentrated under reduced pressure, water was added, and the precipitated material was collected by filtration, washed with water, dried and recrystallized from methanol to give **6b, d, f.**

1-(D-gluco-pentitol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-one (6b). This compound was obtained as pale-yellow needles in

67% yield, m.p. 198-200 ºC; IR (KBr) ν 3436(OH), 1691 (C=O quinazolinone), and 1616 cm^{-1}(C=N); ^{1}H-NMR (DMSO-d6,500MHz): 7.85-7.08 (m, 9H,ArH), 4.48 (dd, 1H, H-5'a), 4.43-4.27 (m, 4H, OH-3', OH-4',OH-5' exchangeable with D_2O, H-5'b), 4.20-3.38 (m,4H, H-2', H-3', H-4', H-5'), 3.30 (s, 1H,OH-2' exchangeable with D_2O), Anal. Calcd for $C_{20}H_{20}N_4O_6$ (412): C, 58.25; H, 5.61; N, 13.59; %. Found: C, 58.80; H, 5.50; N, 13.40%.

1-(D-arabino-tetritol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-one (6d). This compound was obtained as yellow crystals in 76%; m.p.183-185°C; IR(KBr) ν 3393(OH), 1695 (C=O quinazolinone), and 1665 cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6, 500MHz): δ 8.03-7.19 (m, 9H, ArH), 5.05 - 4.42 (m, 4H, exchangeable with D2O, 4OH). 5.37–3.66 (m, 5H, arabinosyl protons), Anal. Calcd for $C_{19}H_{18}N_4O_5$ (382): C, 59.68; H, 4. 71; N, 14.65 %; Found: C, 59.66; H, 4.55; N, 14.60 %.

1-(D-xyloso-tetritol-1-yl)-4-phenyl-1,2,4-triazolo[4,3-a]quinazolin-5(4H)-one (6f). This compound was obtained as yellow crystals, (75%), m.p.170-172°C; IR(KBr) ν 3393(OH), 1690 (C=O quinazolinone) and 1665cm^{-1} (C=N); ^{1}H-NMR (DMSO-d6,500MHz): δ,7.88-8.80 (m, 9H), 4.55 - 4.82 (m, 4H, exchangeable with D2O, 4OH). 5.37–3.66 (m, 5H, xylosyl protons), Anal. Calcd for $C_{19}H_{18}N_4O_5$ (382): C, 59.68; H, 4. 71; N, 14.65 %; Found: C, 59.60; H, 4.50; N, 14.80 %.

B. Computational studies

The reactants (glucose and quinazoline hydrazone derivative **2**) and the product (glucosyl hydrazone **3a**) were calculated using B3LYP at 6-311G (d, p) as basis set [48]. The optimization processing was carried out by the aid of Gaussian 09 W package [36]. No imaginary frequency has been recorded during the optimization process and we have not applied any constrains during the optimization. GaussView 5.0 and program [36] has been used to extract the computation results and to visualize the optimization structures as well as to draw the frontier molecular orbital (FMOs), molecular electrostatic potential (MEP) maps [51].

C. Antimicrobial Activities

The tested compounds were screened against five different microorganisms Pseudomonas aeruginosa ATCC9027, Staphylococcus aureus ATCC6538P, Escherichia coli ATCC8739, Candida albicans ATCC2091, Bacillus subtilis .The agar well-diffusion method was applied for the determination of the inhibition zone.

Preparation of the agar plate:

The sterile nutrient agar was poured aseptically as 40 ml portions into sterile Petri dishes (15 cm in diameter) onto a level surface to obtain a layer of about 4 mm thickness and the plates were then left to solidify. After solidification, the plates were incubated in an inverted position at 37° C for 18 h to be over dried before use.

Preparation of the inoculum:

Each tested organism was subcultured in 3 ml sterile nutrient broth and the resultant microbial growth was firstly compared with 0.5 'McFarland Opacity Standard' which was equivalent to approximately 10^8 CFU/ml and properly diluted; if necessary, to achieve the same turbidity of the standard. The turbidity standard " 0.5 McFarland Opacity Standard" was prepared by transferring 0.5 ml of 1.175 % solution of barium chloride to 100 ml-graduated cylinder and completing to 100 ml with 1% sulfuric acid. This standard was placed in a tube identical to the one used for both cultures, sealed then kept in the dark at room temperature and used within one month.

Procedure of the test:

Sterile cotton swabs were separately dipped into each of the adjusted organism cultures and excess inoculum was removed by pressing and rotating the swab firmly several times against the wall of the tube above the level of the liquid. The swab was streaked all over the surface of the nutrient agar in three dimensions at an angle of 60° to obtain an even distribution of the inoculum. The plates were then left to dry at room temperature for few minutes. A sterile cork porer (8 mm in diameter) is used to make wells in the solid nutrient agar plates, so that the distance between the edges of each two wells is not less than 24 mm. Fill each well with 75 µl of the test compound and another well with same volume of DMF as a vehicle control. Allow a period of free diffusion for 2 h , then incubate at 37° C for 18-24 h.

Reading and interpretation of Results:

After incubation, the diameters of inhibition zones around the wells were measured, to the nearest mm, in three different directions using a ruler and the average diameter was recorded and compared to that of the control.

IV. CONCLUSIONS

In this study, some of sugar (3-Phenyl-4-quinazolones)-2-hydrazones (**3a-f**) were synthesized from the reaction of hexoses or pentoses with quinazoline hydrazone derivative **2**, their acetate derivatives were obtained **4a-f,** also the triazole acetate derivatives and their unacetylated one **5b, d, f**, **6b, d, f** respectively were obtained. All the structure of the synthesized compounds was conformed using different spectral tools as elemental analysis, Infrared and NMR spectra. The computational studies of the starting compounds, and the product **3b** were performed as an identification of the reactivity and stability of the studied compounds the HOMO-LUMO analysis of the molecules were performed by using DFT(B3LYP) method with 6-311G basis set. The dipole moments where found different with different methods used and the order of the dipole moment HF/6311> DFT/B3LYP/6311> PM6> PM3> AM1 for both open chain form and cyclic one of **3b** . In general, dipole moment differences and the HOMO-LUMO analysis of the organic compound using Gaussian 09w by PCM method. Density functional theory (DFT) at the level 6-311G (d, p) confirmed the high stability of the new compound based on the presence of strong hydrogen bonding beside charge transfer interaction. Optimization energy, energy gap (E_{LUMO} - E_{HOMO}), reactivity parameters, molecular electrostatic potential and Mulliken atomic charges asserted the high stability of the synthesized compound based on the presence of charge transfer interactions.

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