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Research Article

MOLECULAR PROPERTIES AND BIO-ACTIVITY SCORE OF 2-(2-METHYL-4-OXOQUINAZOLIN-3(4H)-yl)-N'-[(E)-(SUBSTITUTEDPHENYL) METHYLIDENE] ACETOHYDRAZIDE

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ABSTRACT

The molecular properties and the bio-activity score of 2-(2-methyl-4-oxoquinazolin-3(4*H*)-yl)-*N*'-[(*E*)-(substitutedphenyl)methylidene]acetohydrazidewere calculated by usingmolinspiration software. These compounds have miLogP values in the region of<5indicating that they have moderately permeability through cell membranes. TPSA between 76.36 to 122.18 (far below 160) and a molecular mass of less than <500. The number of violations is 0 and rotb<6, the total number of hydrogen bond donors is <5 (The sum of OHs and NHs), and the total number of hydrogen bond acceptors is <9 (The sum of Os and Ns). These findings revealed that the compounds can easily bind to receptors, and they were used to calculate the bioactivity score. The bioactivity score of GPCR ligands (This score between -5.0 to 0.0 the complex is moderately active), ion channel modulators, nuclear receptor ligands, and inhibitor bioactivity towards kinase, protease, and enzymes, on the other hand, demonstrated and molinspiration galaxy 3D structure generator that the compounds have a moderate score for all receptors.

INTRODUCTION

Quinazolines are heterocyclic fused ring compounds that are of great interest due to the wide range of pharmacological actions, they haveever-increasing resistance to antibiotics necessitates ongoing research for novel biologically useful chemicals, both natural and manufactured. Quinazoline derivatives are widely employed in the pharmaceutical sector, medicine, and agriculture due to their broad biological applications[1]. Quinazolinone analogues have been found to exhibit anti-inflammatory [2], antibacterial [3], antioxidant [4], anticancer[5], anticonvulsant[6], antiviral[7], and antihypertensive[8] properties. The formation of a new molecule in a drug discovery study is influenced by a number of factors, one of which is the 'rule of five,' which predicts absorption or penetration. H-bond donors, H-bond acceptors, molecular weight, and the computed Log P (CLogP) value are among the additional descriptors.

The goal of this study is to determine the molecular characteristics and bioactivity score of 2-(2-methyl-4-oxoquinazolin-3(4H)-yl)-N'-[(E)-(substitutedphenyl)methylidene]acetohydrazide.The molinspiration software was used to extract parameters such as MiLogP, TPSA, and drug similarity. Molecular hydrophobicity influences drug absorption, bioavailability, drug-receptor interactions, molecule metabolism, and toxicity. The Molecular Polar Surface Area (TPSA) is linked to a molecule's hydrogen bonding potential and is determined as the sum of fragment contributions from O- and N-centered polar fragments. TPSA is a good predictor of drug transport properties like gastrointestinal absorption, bioavailability, and blood-brain barrier penetration. A molecule's drug similarity data can be used to evaluate a drug's molecular properties and bioactivity.[9]Lipinski *et al*. [10] have made contributions to the creation of new medications by developing computational and experimental methods for estimating solubility and permeability of new drug candidates. According to Lipinski *et al*.[10], a candidate molecule with poor absorption and permeability should have the following properties, as predicted by rule five: MiLogP values below 5, while the chloro, bromo and methylanalogues showed higher values, indicating that these compounds had good permeability.

The TPSA of all the derivatives was determined to be between 76.36 and 122.18 (far below 160) and their molecular weights

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were less than 500. The number of hydrogen bond donors (<5) and acceptors (< 9) were determined to be less than 5 and 10 respectively, which is Lipinski's limit. This log-based rule's computational approach is extensively characterised, and as a result of this significant contribution, other similar methodologies have been established, allowing the construction of diverse programmes for the prediction of novel drug candidates, including ADME characteristics. Cheminformatics Molinspiration [11] is an example of a platform.

MATERIALS AND METHODS

The quinazolinone derivatives were predicted for their score of molecular properties and bioactivity are calculated by using the molinspiration online software. The molecular structure of 2-(2-methyl-4-oxoquinazolin-3(4H)-yl)-N'-[(E)-(substitutedphenyl)methylidene]acetohydrazide(5a-5m, Figure-2) was drawn using online molinspiration software (www.molinspiration.com) for calculation of molecular properties (Log P, Total polar surface area, number of hydrogen bond donors and acceptors, molecular weight)and calculation of bioactivities (GPCR ligands, kinase inhibitors, ion channel modulators, enzymesinhibitors, protease inhibitors and nuclear receptors).

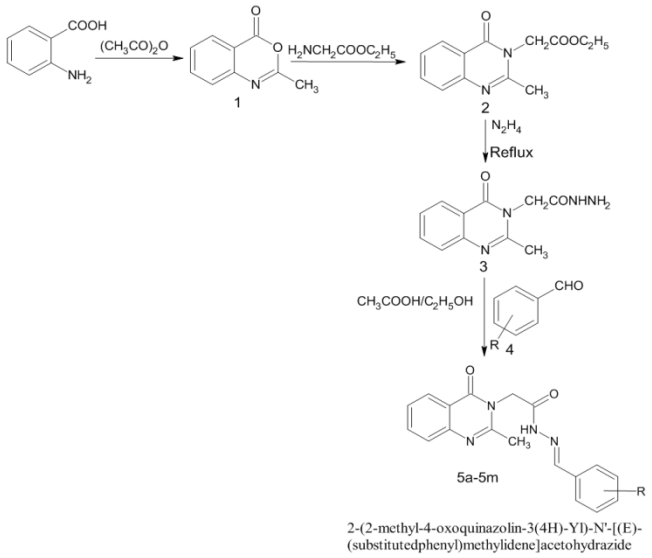


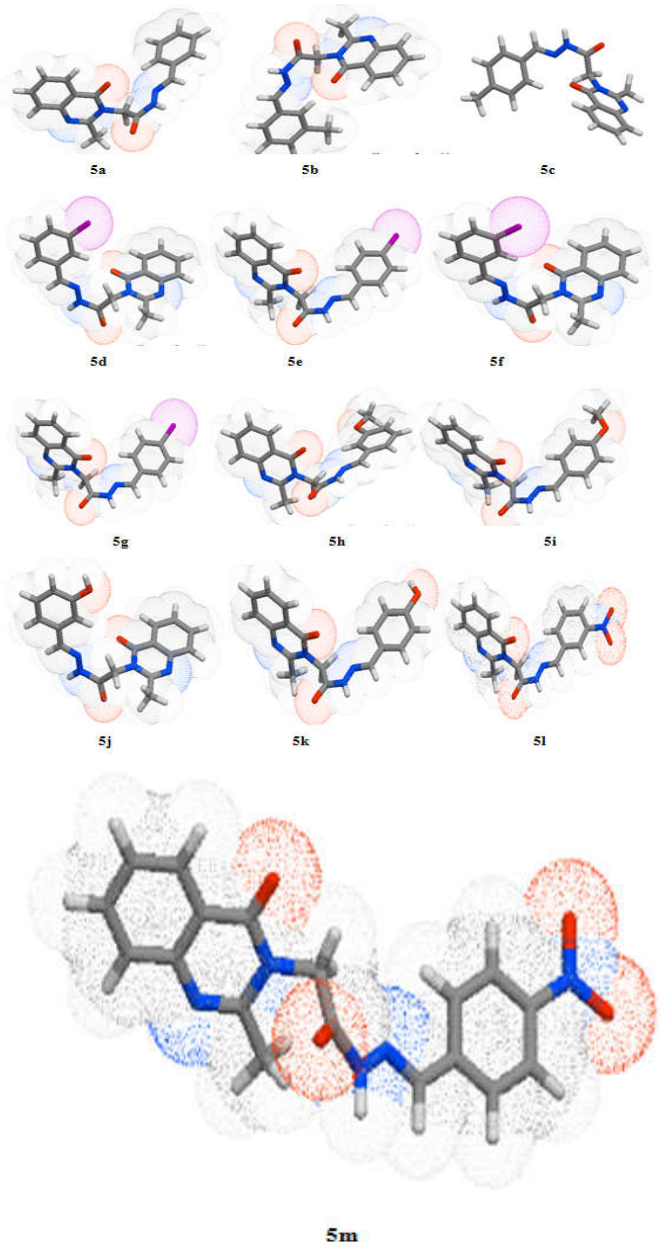
Fig 2 Scheme of synthesis

Molinspiration Software

Parameters like miLogP, TPSA, and drug similarity were obtained using the molinspiration software. Drug absorption, bioavailability, drug-receptor interactions, molecule metabolism, and toxicity are all affected by molecular hydrophobicity.

The molecular polar surface area (TPSA) is calculated as the total of fragment contributions from O- and N-centered polar fragments and is connected to a molecule's hydrogen bonding potential. TPSA is an excellent predictor of drug transport qualities such as gastrointestinal absorption, bioavailability, and blood-brain barrier penetration, among others. Drug similarity data of a molecule can be used to assess a drug's molecular characteristics and structure aspects[11]. The drug similarity score and different parameters of all acetohydrazide derivatives were determined Table 1 and the bioactivity scores presented in the following Table 2.

Molinspiration Galaxy 3D Structure Generator (5a-5m) (Fig. 3)



RESULTS AND DISCUSSION

2-(2-methyl-4-oxoquinazolin-3(4H)-Yl)-N'-[(E)-(substitutedphenyl)methylidene]acetohydrazide is a kind of acetohydrazide that is (5a-m) obeyed Lipinski's criterion or rule and showed good drug molecular properties score (Table-1). Most of the compounds showed miLogP values below 5, while the chloro, bromo and methyl analogues showed higher values, indicating that these compounds had good permeability. The TPSA of all the derivatives was determined to be between 76.36 and 122.18 (far below 160) and their molecular weights were less than 500.

The number of hydrogen bond donors (< 5) and acceptors (< 9) were determined to be less than 5 and 10 respectively, which is Lipinski's limit. All of the following compounds were found to have n violations = 0 and were flexible (with less than 9 rotatable bonds).

Bioactivity score of the compounds

Table 2 shows the bioactivity scores of the thirteen acetohydrazide derivatives chosen for calculation on the basis of GPCR ligand, ion channel modulator, nuclear receptor ligand, kinase inhibitor, protease inhibitor, and enzyme inhibitor as per the rule.

These scores can be regarded as active (Bioactivity score > 0), moderately active (Bioactivity score: -5.0-0.0), and inactive (Bioactivity score <-5.0) for organic compounds. All of the 2-(2-methyl-4-oxoquinazolin-3(4H)-Yl)-N'-[(E)-(substitutedphenyl)methylidene]acetohydrazide derivatives were moderately active (< 0.0) towards all of the compounds studied.

Table 1 Molecular properties score of compounds by using molinspiration. (5a-5m)

Comp Code	Physicochemical Properties						Lipinski's Rule	%Abs[d]	N viol[e]	N rot[f]	V[g] (Volume)
	R	MW[a]	TPSA[b]	milogP[c]	H_A	H_D					
5a	H	320.25	76.36	2.21	6	1	Yes	82.65	0	4	287.65
5b	3-CH_3	334.38	76.36	2.64	6	1	Yes	82.65	0	4	304.21
5c	4-CH_3	334.38	76.36	2.66	6	1	Yes	82.65	0	4	304.21
5d	3-Cl	354.80	76.36	2.87	6	1	Yes	82.65	0	4	301.18
5e	4-Cl	354.80	76.36	2.89	6	1	Yes	82.65	0	4	301.18
5f	3-Br	399.25	76.36	3.00	6	1	Yes	82.65	0	4	305.53
5g	4-Br	399.25	76.36	3.02	6	1	Yes	82.65	0	4	305.53
5h	3OCH_3	350.38	85.59	2.25	7	1	Yes	79.47	0	5	313.19
5i	4OCH_3	350.38	85.59	2.27	7	1	Yes	79.47	0	5	313.19
5j	3-OH	336.35	96.59	1.71	7	2	Yes	75.67	0	4	295.67
5k	4-OH	336.35	96.59	1.74	7	2	Yes	75.67	0	4	295.67
5l	3-NO_2	365.35	122.18	2.15	9	1	Yes	66.84	0	5	310.98
5m	4-NO_2	365.35	122.18	2.17	9	1	Yes	66.84	0	5	310.98

[a]**MW:** molecular weight, [b]**TPSA:** total polar surface area, [c]**miLogP:** molinspiration partition coefficient, [d]**%Abs:**%Abs = 109 − (0.345 × TPSA),[e]**nviol:** number of violations,[f]**nrotb:** number of rotatable bonds, H_A**:** number of hydrogen bond acceptors, H_D**:** number of hydrogen bond donors and [g]**V**: volume[g]

Table 2 Bioactivity score of compounds by using molinspiration. (5a-5m)

Compound cod	R-Derivatives	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
5a	H	-0.42	-0.86	-0.65	-0.99	-0.59	-0.52
5b	3-CH_3	-0.43	-0.88	-0.65	-0.96	-0.59	-0.54
5c	4-CH_3	-0.44	-0.87	-0.65	-0.98	-0.60	-0.54
5d	3-Cl	-0.40	-0.82	-0.66	-0.98	-0.60	-0.53
5e	4-Cl	-0.41	-0.83	-0.64	-0.97	-0.60	-0.53
5f	3-Br	-0.52	-0.91	-0.70	-1.09	-0.69	-0.58
5g	4-Br	-0.51	-0.90	-0.67	-1.06	-0.67	-0.57
5h	3-OCH_3	-0.44	-0.87	-0.65	-0.92	-0.60	-0.53
5i	4-OCH_3	-0.43	-0.86	-0.64	-0.93	-0.59	-0.52
5j	3-OH	-0.37	-0.79	-0.60	-0.81	-0.56	-0.45
5k	4-OH	-0.36	-0.78	-0.58	-0.81	-0.54	-0.45
5l	3-NO_2	-0.54	-0.83	-0.71	-0.98	-0.67	-0.58
5m	4-NO_2	-0.53	-0.82	-0.71	-0.98	-0.66	-0.57

Table 3 Predicted biological activities by PASS Software.(5a-5m)

Comp Code	R-Derivatives	Anticonvulsant Activity		Antiviral (Picornavirus)		Anti-neoplastic (multiplemyeloma)		Antimycobacterial Activity	
		pa	pi	pa	pi	pa	pi	pa	pi
5a	H	0.576	0.022	0.510	0.046	0.230	0.079	0.190	0.127
5b	3-CH_3	0.484	0.039	0.397	0.112	0.330	0.056	0.162	0.153
5c	4-CH_3	0.531	0.029	0.434	0.085	0.335	0.052	0.183	0.134
5d	3-Cl	0.650	0.013	0.438	0.083	0.352	0.043	0.632	0.008
5e	4-Cl	0.647	0.013	0.476	0.062	0.357	0.040	0.637	0.008
5f	3-Br	0.626	0.016	0.299	0.230	0.297	0.081	0.729	0.005
5g	4-Br	0.615	0.017	0.329	0.184	0.299	0.079	0.713	0.005
5h	3-OCH_3	0.391	0.068	0.377	0.130	0.178	0.073	0.651	0.007
5i	4-OCH_3	0.420	0.057	0.241	0.104	0.320	0.063	0.648	0.007
5j	3-OH	0.370	0.077	0.394	0.115	0.332	0.054	0.660	0.007
5k	4-OH	0.398	0.065	0.431	0.087	0.336	0.052	0.657	0.007
5l	3-NO_2	0.502	0.035	0.572	0.026	0.313	0.068	0.743	0.004
5m	4-NO_2	0.552	0.026	0.562	0.029	0.312	0.068	0.744	0.004

Pa: Probability to be active; **Pi:** Probability to be inactive

However, when compared to other enzymes, all of the compounds had improved activity against kinase inhibitors. and the compounds were discovered to have moderate activity against all of the enzymes studied, implying that the parameters tested in this study will produce an intriguing result for the design of novel quinazolinone molecules as enzyme inhibitors.

PASS

On the basis of the computer programme PASS, new pharmacological activities for title compounds can be discovered. It compares the structure of a new chemical to that of other compounds. Structures of a physiologically active chemical that is well-known as a result, it is possible to estimate if a new this technique may have a specific effect on the chemical, can be employed at any time during the inquiry [12]. It betrays all of the predictions based on the facts. Synthetic compounds have a good chance of being active. antimycobacterial, antiviral and antineoplastic therapy of the condition as a result, we pursued in-vitro testing. Bioactivity score to determine the drug's effectiveness assemblages (Table 3).

CONCLUSION

In the present investigationthirteen novel molecules2-(2-methyl-4-oxoquinazolin-3(4H)-yl)-N'-[(E)-(substitutedphenyl)methylidene]acetohydrazidederivatives were only a few compoundsshowed higher miLogP value, all of the others followed the Lipinski rule, and the compounds were found to have moderate activity against all of the enzymes studied.

As a result, the parameters evaluated in this study will be useful in the development of novel quinazolinone molecules as enzyme inhibitors.

Conflict of Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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