ISSN: 0067-2904

Quinoline-2-carboxlic acid derivatives bearing oxadiazole moiety: Synthesis, Skin Antitumor, Antibacterial, antifungal activities, and POM studies for the Identification of the Pharmacophore Sites

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Received: 31/3/2024 Accepted: 1/9/2024 Published: 30/9/2025

Abstract

A new series of chalcone derivatives featuring an oxadiazole-quinoline moiety were successfully synthesized through a multi-step reaction sequence, commencing with quinoline-2-carboxylic acid as the starting material. First, the carboxylic group was chlorinated to form an acid chloride, following reacted with hydrazine hydrate. The resulting product underwent cyclization with carbon disulfide in an alkaline solution to produce 5-(quinolin-2-yl)-1,3,4-oxadiazole-2-thiol, followed by alkylation using chloroacetone. In the final step, an aldol condensation reaction was carried out by grinding the acetone derivative with various aromatic aldehydes, yielding the desired chalcones. The synthesized compounds were characterized by R_f, FTIR, ^{1}HNMR, and ^{13}CNMR. The effects of compound S6 were evaluated using an MTT assay. This assay was performed on two cell lines - the skin cancer cell line A375 and the normal cell line HdFn (human dermal fibroblasts) which performed a significant inhibition rate. All synthesized compounds were evaluated against four different types of bacteria like *S. aureus, streptococcus epidermidis, E.coli, Klebsiella spp.* and one type of fungi *like Candida albicans*. Additionally, (Petra/Osiris/Molinspiration) POM analyses were utilized to identify pharmacophore sites for the newly synthesized compounds.

Keywords: Quinoline-2-carboxylic acid, Chalcones, skin anticancer, Antimicrobial, POM analyses (Petra/Osiris/Molinspiration).

مشتقات 2-كوينولين-حامض الكاربوكسيل تحوي على وحدة الاوكسادايازول :من ناحية التحضير وتقييمها كمضاد لسرطان الجلد، ومضاد للبكتريا، و مضاد للفطريات ،ودراسات نظرية البوم لتشخيص المواقع الدوائية

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الخلاصة

تم تخليق سلسلة جديدة من مشتقات الجالكون التي تحوي على وحدة كونيولين –اوكسادايزول. بنجاح حضرت هذه المركبات من خلال سلسلة من التفاعلات باستخدام 2–كوينولين–حامض الكاربوكسيليك كمادة اولية. حيث تم تحويل تلك المادة الاولية الى كلوريد الحامض المقابل عن طريق تفاعلها مع ثايونيل كلورايد ، ومن ثم تم ادخال مشتق الحامض الناتج بتفاعله مع الهيدرازين المائي *لينتج* مركب الكوينولين هيدرازايد المقابل ، –بعدها تم حولقة المركب الاخير بتفاعله مع ثنائي كبريتيد الكربون في محلول قلوي لينتج مركب 5– (كوينولين–2–يل)1،3،4–اوكسادايزول–2–ثايول ومن ثم اكلة المركب الاخير باستخدام كلوروأسيتون، وأخيرا تم إجراء تفاعل الدول من خلال تفاعل مشتق الأسيتون الناتج مع الألديهيدات الاروماتية المختلفة بطريقة الطحن لإنتاج الجالكونات .تم تشخيص المركبات المحضرة بواسطة قياس عامل الاحتجاز R_f والاشعة تحت الحمراء وبروتون الرنين النووي المغناطيسي والكاربون النووي المغناطيسي .تم تقييم النشاط المضاد للسرطان للمركب S6 باستخدام طريقة MTT على الخطوط الخلوية لسرطان الجلد A375 مقارنة مع خطوط الخلايا الطبيعية HdFn واظهر تثبيطا كبيرا. تم تقييم فعالية المركبات المحضرة من ناحية النشاط المضاد للبكتريا باستخدام اربع انـواع مختلفة منها مثل *S. aureus, streptococcus epidermidis, E.coli, Klebsiella spp* ونوع واحد من الفطريات *albicans* مثل *Candida* . اضافة الى استخدام تحليل POM كدراسة نظرية عبر دمج ثلاث برامج (Petra/Osiris/Molinspiration) لتحديد المواقع الدوائية المحتملة لتلك المركبات المخلقة الجديد.

1. Introduction

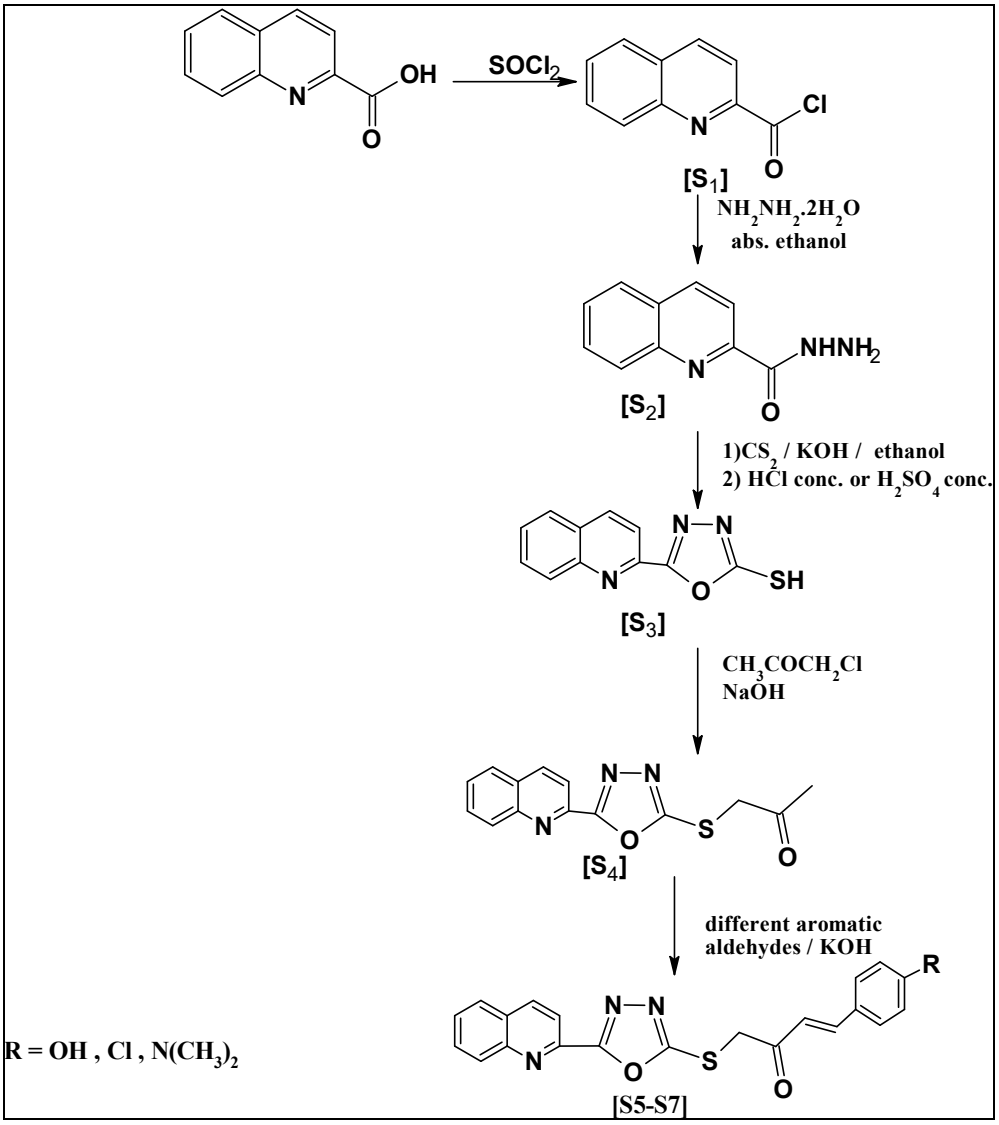
Heterocyclic compounds play a vital role in numerous fields due to their diverse and far-reaching applications [1-2]. Numerous studies been conducted on heterocycles within the fields of pharmacy [3], medicine [4], and industry [5]. Many researchers have extensively conducted a depth exploration of heterocycles, owing to their significance in these domains. Quinolones, a subclass of heterocycles characterized by containing nitrogen atom which can be produced by chemical synthesis in addition to biosynthesis [6-7]. Quinolones play very important group due to a wide range of biological activities [8], such as anticancer agents [9-10], antibacterial agents [11], antimalarial agents [12], anticonvulsant [13], Alzheimer agents [14] adenosine receptor antagonists [15], caspase-3 inhibitions anti-inflammatory agents [16].

The oxadiazole molecule contains a heterocyclic ring structure. Due to the varying positions of its heteroatoms, oxadiazole can exist in multiple isomeric forms [17-18]. The 1,3,4-oxidiazole is the most important among them which it shows a lots of therapeutic activities like antibacterial [19,20], anticonvulsant [21], anti-inflammatory [22], antitumor [23-25] like anti-proliferative agent targeting tubulin hypoglycemic [26], cytotoxic activities [27], insecticidal [28], anti-viral [29], anti-tubercular [30] antioxidant [31] anti-Alzheimer activity [32] anthelmintic activities [33], antidepressant [34], antihypertensive activities [35] anti-allergic **[36].** The 1,3,4-oxidiazole is present in many commercially available drugs such as furamizole, raltegravir, nesapidil, and drug Zibotentan [37]. Moreover, tetrazole derivatives have been utilized in numerous applications, including as corrosion inhibitors, polymers, drug candidates, and synthetic dyes [38].

Chalcones contain a ketoethylenic group with an α, β-unsaturated carbonyl moiety. They are an important class of compounds that have been extensively studied by research groups since the 1st century. These continued investigations are due to significant findings regarding the biological activities of many chalcones. Specifically, various chalcones have demonstrated

promising activities such as antimalarial [39], antileishmanial [40-41], anticancer [42-43], anti-inflammatory [44-45], antimicrobial [46], cytotoxic [47], and antihyperglycemic effects [48]. The Pharmacophore Optimization Method (POM) is utilized to identify and optimize the crucial structural features responsible for the biological activity of various types of drugs. The Principal Inventor of POM Theory is by prof. T. Ben Hadda, who collaborated with the National Cancer Institute (NCI) and the Tuberculosis Antimicrobial Acquisition Facility (TAACF) of the USA to develop the Concept and Applications of POM Theory using three programs (Petra/Osiris/Molinspiration) [49]. In the context of POM analysis, Pharmacokinetic predictions for synthesized compounds were leveraged to evaluate their distribution, absorption, toxic properties, metabolism, and drug-likeness predictions [50]

Due to this review, in the present study, various quinoline derivatives bearing oxadiazole moiety linked to different chalcones were synthesised, with the aim of evaluating their biological activity against skin cancer, bacteria, fungi using different assays. They also aimed to identify possible pharmacophore sites of the new compounds using POM studies to provide insights into their structure-activity relationships. All synthesized compounds are shown in the Scheme1.



Scheme 1 : Synthesis of Chalcones Derivatives [S5-S7]

2. Materials and Methods

2.1. Materials

The necessary initial compounds were obtained from Aldrich Company and utilized as received, without additional purification steps. TLC was conducted using Merck aluminium plates coated with 0.2 mm of silica gel 60 F-254 using hexane: ethyl acetate (7:3) mixture as mobile phase. FTIR spectra were recorded in the spectral range (500-4000) cm^{-1} using potassium bromide disks on Shimadzu FTIR-8400 infrared spectrometer" in college science for woman . ^{1}H-NMR spectra solvent DMSO-d6 was recorded on a 500 MHz spectrometer with TMS as an internal standard in, Iran**.**

Synthesis of quinoline-2-carbonyl chloride (S1) and Synthesis of quinoline-2-carbohydrazide (S2)

The compound S1 was synthesised according to literature [31] and without separation of the product, whereas, compound S2 was synthesized using a mixture of compound S1(1.9g, 0.01 mol) in ethanol (30mL) and hydrazine hydrate 80% (0.1mol, 6 mL), following the mixture was stirred at room temperature for 12hrs., concentrated, cooled and filtered to obtain quinoline-2-carbohydrazide S2.

R_f : 0.01 (7:3);organic colour; yield: 91% ; m.p: 76-77 ºC.

FTIR(KBr, ν_{max} ,cm^{-1}) : 3331- 3213 (NH) & NH_2, 1701 (C=O)

5-(quinolin-2-yl)-1,3,4-oxadiazole-2-thiol (S3)

A mixture of hydrazide compound S2 (3.7g, 0.02 mol), potassium hydroxide (0.64g , 0.012 mol) in water (3mL) and ethanol (30mL) was stirred for 10 min., then CS_2 (12mL) was added slowly while Stirring under cold condition (0-5 ºC) after that the mixture was refluxed for 7 hrs., the resulting solution was concentrated, and the solid product was filtered and recrystallized from ethanol. **R_f:** 0.54; yield: 65%; yellow needle; m.p:147-148 ºC.

FTIR (KBr, ν_{max} ,cm^{-1}): 3071 (C-H)armatic, 2430 (S-H), 1612 (C=N),

^{1}HNMR: 11.3 (s,1H, S-H), 7.3-8.8(m,6H,Ar-H);^{13}CNMR:162,161(2C=N), 147, 145, 134, 129, 125,124,123,122,120 (Ar-C)

1-{[5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl]sulfanyl}propan-2-one S4

A mixture of compound S3 (2.2g, 0.01mol), dimethylformamide (35 mL) and triethylamine (1.4 mL, 0.01mol) was stirred at room temperature for 10min. Chloroacetone (0.8mL, 0.01mol) was then added dropwise, and the reaction mixture was stirred for 1 hrs. then heated at 75ºC for 8 hrs. After complete the reaction, the solid product was filtered and recrystallized by ethanol R_f: 0.8 (7:3); gray color; yield:63%; m.p:81-83 ºC ; FTIR(KBr, ν_{max} ,cm^{-1}): 1737 (C=O),1660 (C=N) ; ^{1}HNMR: 2.3 (s,3H, CH_3), 3.6(s,2H,CH_2); 7.1-8.7 (m,6H,Ar-H); ^{13}CNMR: 201(C=O), 165, 161(2C=N),, 147, 146, 129, 136, 130, 129, 127, 126, 121(Ar-C), 39(CH_2-S), 27(CH_3)

(3*E*)-4-(4-hydroxyphenyl)-1-{[5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl]sulfanyl}but-3-en-2-one S5-S7

A mixture of compound S4 (7g, 0.025mol), the selected aldehyde (*p*-hydroxy benzaldehyde/ *p*-chlorobenzaldehyde/ *p*-(Dimethylamino)benzaldehyde) (0.025 mol) and sodium hydroxide (1g, 0.025mol.) was ground in a mortar at room temperature. After incubation the reaction mixture for the 30 min, during it had turned into a yellow solid, the solid was then treated with 70 mL of cold water. The mixture was neutralized by adding dilute hydrochloric acid. This caused a solid precipitate to form, which was collected by filtration. The spectral data of the all chalcone derivatives S5-S7 are given below.

4-(4-hydroxyphenyl)-1-{[5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl]sulfanyl}but-3-en-2-one S5 R_f**:** 0.58 (hexane: ethyl acetate ,7: 3) White color, yield 78% . m.p:107-109 ºC FTIR(KBr, ν_{max} ,cm^{-1}): 3327 (OH), 1650(C=O), 1620 (2C=N);^{1}HNMR ppm: 4-3.5(s, 1H, OH) and (s, 2H, CH_2), 6.9-9.3(m ,12H, Ar-H&vinyl-H,12H);^{13}CNMR ppm: 191(C=O), 165 , 161(2C=N),152,151,150,148,147,146,134,133,127,126,125,124,118,115,110 (Ar-C & 2C–olfinic), 39(C-S)

4-(4-chlorophenyl)-1-{[5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl]sulfanyl}but-3-en-2-one S6

R_f : 0.6 (hexane: ethyl acetate ,7: 3); pale yellow color; yield: 69 % . m.p: 102-105 ºC FTIR(KBr, ν_{max} ,cm^{-1}): 1668(C=O), 1650(C=N); ^{1}HNMR: 3.9(s, 2H,S CH_2),6.8-9.2 (m,12H, Ar-H&vinyl-H,12H);^{13}CNMR:190(C=O),155,152(2C=N), 150, 152, 144, 143,143, 136, 134, 132, 131,125,126,125, 124,123, 122(Ar-C & 2C–olfinic),39(C-S)

4-(4-(dimethylamino) phenyl)-1-{[5-(quinolin-2-yl)-1,3,4-oxadiazol-2-yl]sulfanyl}but-3-en-2-one S7

Rf : 0.6 (hexane: ethyl acetate ,7: 3); Orang color ; yield 58 % ; m.p 299-301 ºC ; FTIR(KBr, ν_{max} ,cm^{-1}): 1664(C=O),1600(C=N); ^{1}HNMR ppm:2.8(s,6H,CH_3),6.8-9.9(m,Ar-H&vinyl-H,12H); ^{13}CNMR:191(C=O),156 ,154(2C=N),153, 149, 147,146,146,145, 135, 133,131, 124,124, 122, 116, 122,111(Ar-C & 2C–olfinic),40(2N-C),39(C-S).

3. Results and dissection:

The chalcones were synthesized through a series of reactions outlined in Scheme 1. The synthesis commenced with the preparation of quinoline-2-carbonyl chloride S1, which was then converted to the corresponding hydrazide S2 without isolating the intermediate product. In this nucleophilic substitution reaction, the stronger nucleophile (-NHNH2) is displaced by the nucleophile ethoxy group. The FTIR spectrum showed an absorption bands at 3213 - 3331 cm^{-1} due to vNH and νNH_2 groups, band at 1701 cm^{-1} due to carbonyl of acid hydrazide group which showing lowering frequency than carbonyl of acid chloride Fig 1. Then, cyclization of hydrazide was carried out by its reaction with CS_2 in the presence of potassium hydroxide to produce 1,3,4-oxidazole-2-thiol derivative S3. The FTIR spectrum for the same compound showed the disappearance of carbonyl group and appearance of an absorption band at ν2400 cm^{-1} due to ν(SH) group which was appeared as singlet signal at δ11.3 ppm in ^{1}HNMR spectrum Fig 2. While, in ^{13}CNMR spectrum showed signals at 161 ppm and at 160 ppm for two carbons of oxadiazole ring.

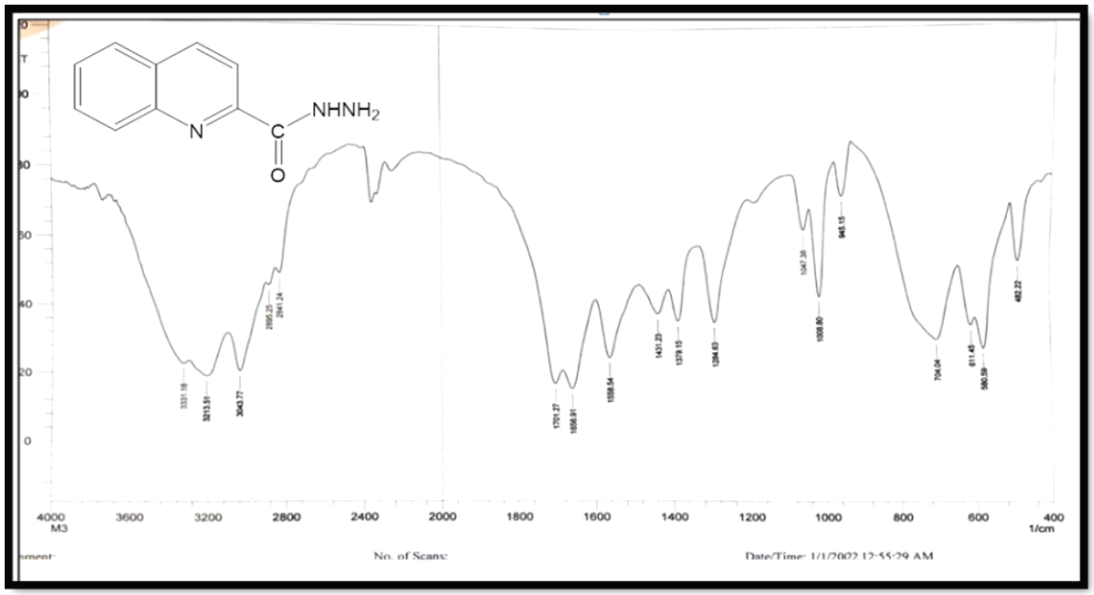


Figure 1: FTIR sepectrum for compound S2

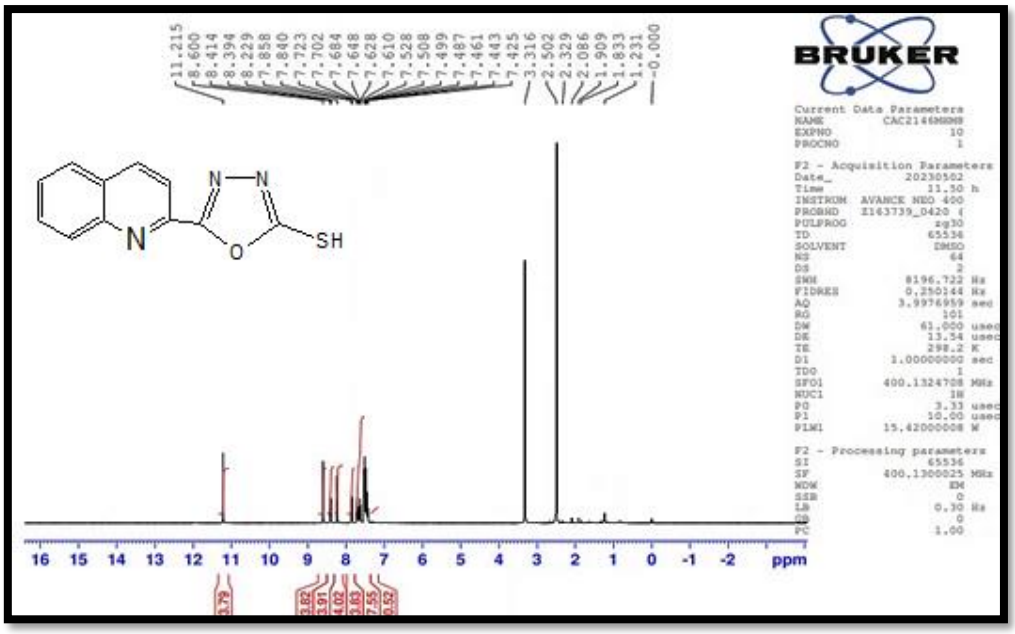


Figure2: [1]HNMR spectrum for compound S3

The sulfanylacetone derivatives S4 were synthesized by reacting compound S3 with chloroacetone via an alkylation process by an SN_2 mechanism. The FTIR spectrum of S4 showed absorption bands at 1738 cm^{-1} and at 1680 cm^{-1} corresponding to ν(C=O) and ν (C=N) respectively. Meanwhile, [1]HNMR spectrum for the same compound showed a new singlet signal at δ2.3 ppm due to three protons of methyl group and at δ3.6 ppm for two protons of methylene group, and showed a new signal at 201ppm for carbon of carbonyl acetone group in [13]CNMRsepectrum. Compound S4 was subjected to a base-catalysed condensation reaction with various aldehydes. The reaction was carried out in the presence of sodium hydroxide as the base. The new chalcone derivatives S5-S7 were synthesized via aldol condensation reactions between sulfanylacetone S4 and various aldehydes. The Aldol Condensation mechanism involved enolate ion from S4, which reacts with carbonyl of selected aldehyde to form β-hydroxy aldehyde, followed by dehydration. The FTIR of these compounds showed a shift to lower value absorption band of carbonyl group at 1650-1668 cm^{-1} than absorption frequency of carbonyl of compound S4 due to the conjugation of carbonyl group with a new olefinic carbon-carbon double bond (C=C) of the chalcone. The [13]CNMR spectrum for compound S7 shows signal at 191ppm for carbonyl group and other signals at 118ppm for vinilic carbon attached to the carbonyl group (CO<u>CH</u>=) as shown in Fig.4

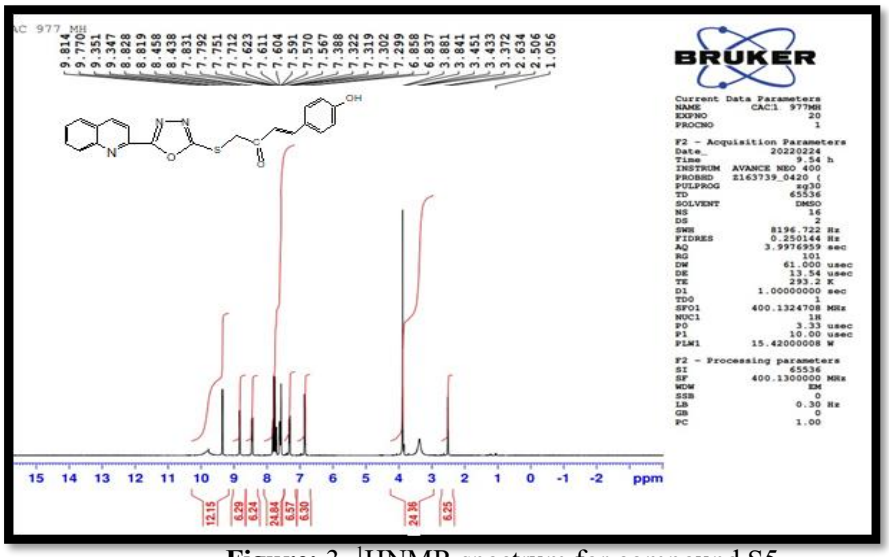


Figure: 3 [1]HNMR spectrum for compound S5

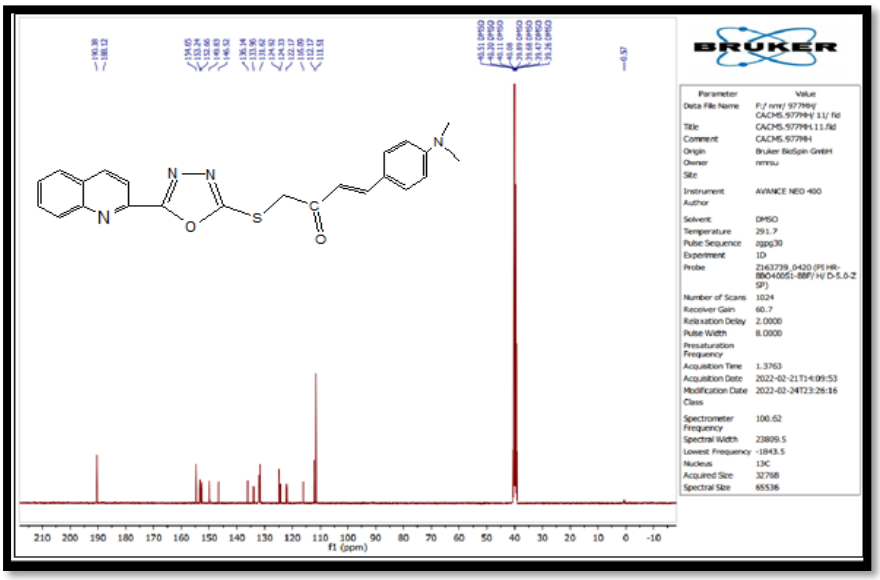


Figure 4: [13]C-NMR spectrum for compound S7

The newly synthesized compounds underwent POM analysis to identify their key pharmacophore sites, with the results presented in Tables 1 and 2.

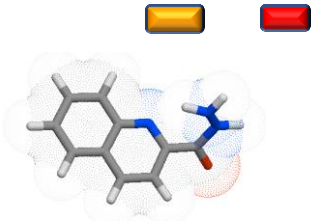
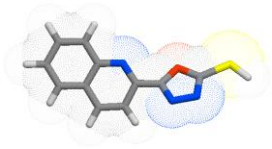
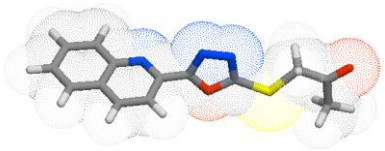
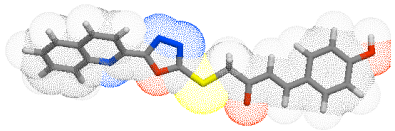
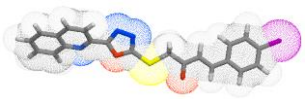
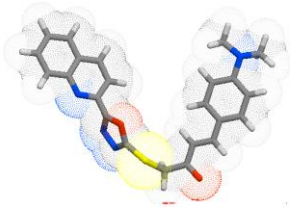
Table 1: Osiris calculations of Drug-score of compounds **S1-S7**

Compd.	**MW**	Toxicity risck [a]				Drug Score [b]			
		MUT	TUMO	IRRI	REP	CLP	S	D-L	D-S
S1	191					1.95	-3.69	-10.4	0.12
S2	187					0.35	-2.71	-5.84	0.28
S3	229					2.07	-4.62	-2.17	0.42
S4	285					2.51	-4.51	0.88	0.64
S5	389					3.94	-5.76	2.59	0.5
S6	407					4.89	-6.79	3.2	0.38
S7	416					4.18	-6.09	-1.75	0.09

[a] Not toxic ( ), Slightly toxic: ( ), Highly toxic: ( ). REP: Reproductive effective, IRRIT: Irritant, TUM: Tumorigenic, MUT: Mutagenic. [b] DS: Drug-Score, DL: Drug Likeness, Sol: Solubility. **SD1**:.

The pharmacokinetics properties of synthesized compounds [S_1-S_7] were shown in Table 2.

Table 2: pharmacokinetics properties of synthesized compounds **[S_2-S_7]**

Compounds. No.	3D optimized Structure	Molecular properties	Drug score
S2		miLogP 0.40 TPSA 68.01 natoms 14 MW 187.20 nON 4 nOHNH 3 nviolations 0 nrotb 1 volume 166.55	GPCR ligand -0.60 Ion channel modulator -0.91 Kinase inhibitor -0.50 Nuclear receptor ligand -1.55 Protease inhibitor -0.66 Enzyme inhibitor -0.18
S3		miLogP 3.51 TPSA 38.92 natoms 16 MW 228.28 nON 3 nOHNH 0 nviolations 0 nrotb 1 volume 190.36	GPCR ligand -1.05 Ion channel modulator -1.06 Kinase inhibitor -0.32 Nuclear receptor ligand -1.18 Protease inhibitor -0.68 Enzyme inhibitor -0.25
S4		miLogP 2.17 TPSA 68.89 natoms 20 MW 285.33 nON 5 nOHNH 0 nviolations 0 nrotb 4 volume 239.02	GPCR ligand -0.87 Ion channel modulator -1.19 Kinase inhibitor -0.51 Nuclear receptor ligand -1.25 Protease inhibitor -0.65 Enzyme inhibitor -0.22
S5		miLogP 3.67 TPSA 89.11 natoms 28 MW 389.44 nON 6 nOHNH 1 nviolations 0 nrotb 6 volume 329.30	GPCR ligand -0.51 Ion channel modulator -0.86 Kinase inhibitor -0.23 Nuclear receptor ligand -0.69 Protease inhibitor -0.33 Enzyme inhibitor -0.10
S6		miLogP 4.83 TPSA 68.89 natoms 28 MW 407.88 nON 5 nOHNH 0 nviolations 0 nrotb 6 volume 334.82	GPCR ligand -0.55 Ion channel modulator -0.90 Kinase inhibitor -0.28 Nuclear receptor ligand -0.84 Protease inhibitor -0.38 Enzyme inhibitor -0.18
S7		miLogP 4.25 TPSA 72.12 natoms 30 MW 416.51 nON 6 nOHNH 0 nviolations 0 nrotb 7 volume 367.19	GPCR ligand -0.51 Ion channel modulator -0.87 Kinase inhibitor 0.22 Nuclear receptor ligand -0.76 Protease inhibitor -0.35 Enzyme inhibitor -0.16

According to the POM analysis, the atomic charges for compounds S5-S7 showed two groups from the same charge ($S^{\delta-}$, $O^{\delta-}$) makes these compounds possess a good biological activity against fungi as shown in Fig 6

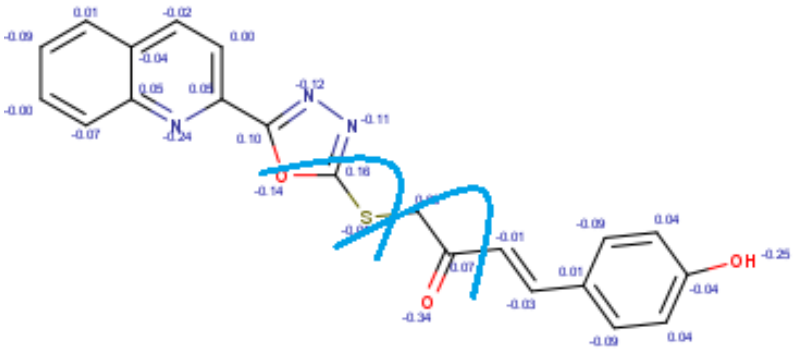


Figure 5 : Atomic charges for compound S5

Biological activities

1-Skin Anticancer: [51]

The anticancer activity of compound S6 was evaluated against the skin cancer cell line A573 and compared to the normal cell line HdFn at various concentrations, using the MTT assay. The results showed that the viability of the A537 cell was found to be greatest at50 µg/mL (73.1±0.7) and lowest at 400 µg/ml (41.7±1.91). The IC50 value for the skin cancer cell line A573 was 88.12, while 105.9 for a normal cell IC50. The results also showed that the most suitable concentration of compound S6 is 200 µg/mL, at which an approximately half of the cancer cells were destroyed compared to normal cells, as shown in Table 3 and Fig 7.

Table 3: the anticancer activity at different concentrations of compound (S6) on HdFn and A573 cell line

S	HdFn		A573	
Conc.(µg/mL)	**mean**	**SD**	**mean**	**SD**
400	68.86567	4.625051	41.705	1.91
200	82.87033	1.632872	47.56933	5.30
100	86.92167	1.819043	60.87967	6.02
50	93.094	2.383667	73.14833	1.45
25	94.32867	1.408324	82.48467	4.54

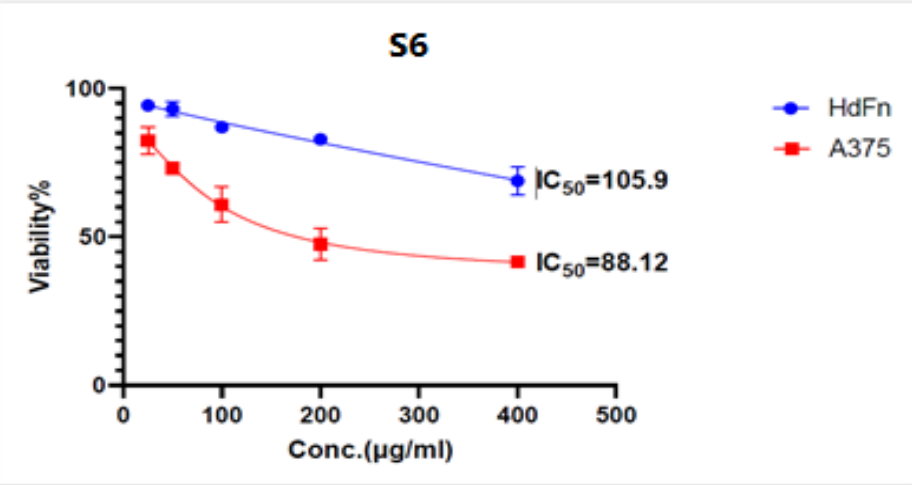


Figure 7: The viability of cell against different concertation of compound S6

The cytotoxic and antiproliferative properties of Compound S6 were investigated using human squamous cell carcinoma cell lines as the model system. The study elevated Compound S6's ability to inhibit the proliferation of these cancer cells. The results revealed a cytotoxic effect on skin cancer cell lines, as well as clear morphological changes in squamous cell lines human skin after treatment as shown in Table 4.

Table 4: the toxicity of S_6 against skin cancer cell

Concentration	Average	Inhibition Rate%
0.0	1.70	0.0
0.75	1.65	4.90
1.50	1.50	10.45
3.125	1.50	11.85
6.20	1.45	15.90
12.5	1.35	18.95
25	1.39	23.65
50	1.105	34.75
100	0.85	50.85
200	0.545	66.60
400	0.35	79.85
800	0.205	87.95

Anticancer activity of compound (S6) was evaluated on human squamous skin cancer cell lines for (S6) using MTT assay. Fig 4 shows the morphological changes in (A) the untreated cell, (B) the treated cell

Examination of the untreated human skin squamous carcinoma cell line revealed several characteristics (Fig 8), including rapid proliferation, uniform staining, typical cell dimensions, and a normal nucleus-to-cytoplasm ratio. The culture also exhibited giant proliferative cells and instances of binucleated cells. While, treated human skin squamous carcinoma cell line showed homogenized stain, cellular malformation with clear shrinkage of chromatin and small size of the nucleus, and the ratio of the nucleus to the cytoplasm is small, as shown in Fig 9.

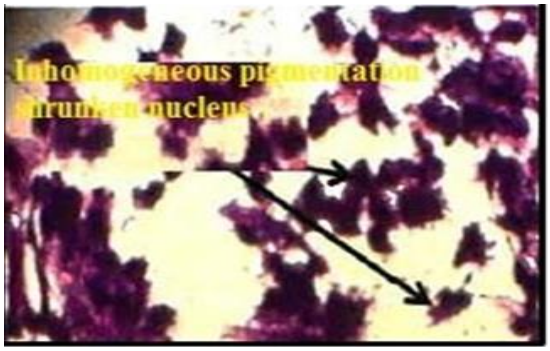


Figure 8: (A) Untreated cell,

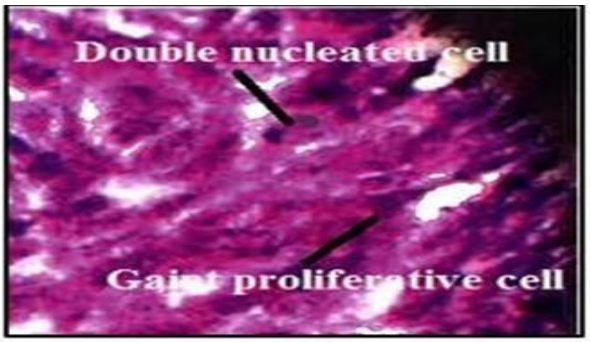


Figure 9: (B) Treated cell.

2- Antibacterial and Antifungal Activities:

All compounds S1-S7 were screened for antibacterial activity against *S. aureus,* and *Streptococcus epidermidi,* as Gram positive bacteria. They were also screened against *E. coli* and *Klebsiella sp.* as Gram negative bacteria. Additionally, they were screened for antifungal activity against *Candida albicans* for by well diffusion method and comparing the results using Ampicillin and ketoconazole as standard drugs. The compounds S1-S2 showed different antimicrobial activity when compared with standard drug ranged from weak to strong activity. These compounds showed weak activity on gram positive bacteria while, strong activity on gram negative bacteria, especially compound S5 which has a good activity against ***Klebsiella sp.*** as gram negative bacteria and against ***Candida albicans*** as antifungal in addition to compound S7 which has also a good activity against the same species of fungal. All the results were recorded in Table 5.

Table 5: The inhibition zone (mm) represents the antimicrobial activity synthesized compounds [S1- S7].

Comp. No.	Gram positive		Gram negative		Candida albicans
	S. aureus	*Streptococcus epidermidis*	*E. coli*	*Klebsiella sp.*	
	1 µg/mL	1 µg/mL	1 µg/mL	1 µg/mL	1 µg/mL
S1	10	-	10	-	-
S2	12	10	-	14	12
S3	10	12	15	-	-
S4	-	-	10	-	18
S5	10	10	-	14	23
S6	12	10	10	10	20
S7	12	10	10	12	22
Ampicillin	30	40	16	11	-
ketoconazole	-	-	-	-	20
Control (DMSO)	-	-	-	-	-

Conclusion

The chemical structures of new synthesized chalcones were characterized by physical properties, R_f, and different spectral methods FTIR, ^{1}HNMR, and ^{13}CNMR. The Compound S6 was evaluated by using MTT against A375 (skin cancer) comparing with HdFn as normal cell line. The all synthesized compounds were evaluated also against four different types of bacteria like *S. aureus, streptococcus epidermidis, E.coli, Klebsiella spp*. and one type of fungi like *Candida albicans*. Compounds S1-S2 exhibited a spectrum of antimicrobial activity,

ranging from weak to strong, when benchmarked against the standard drug. These compounds showed weak antimicrobial activity against gram-positive bacteria but strong antimicrobial activity against gram-negative bacteria and fungi. Furthermore, to identify promising new compounds with potential antimicrobial properties, the researchers employed POM analyses. The results showed the possibility of synthetic compounds being more effective against fungi than other types as result of the presence of two groups from the same charge ($S^{\delta-}$, $O^{\delta-}$) makes these compounds possess a good biological activity against fungi in addition to their a good physical properties.

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