Microwave Assisted Synthesis and Antimicrobial Potential of Quinoline-Based 4-Hydrazide-Hydrazone Derivatives

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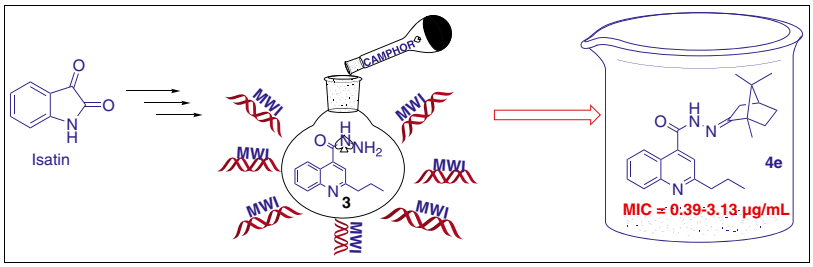

Quinoline is a benzo-fused pyridine which is a therapeutically important heterocycle in medicinal chemistry research and new drug development. A series of 12 new hydrazide-hydrazone motifs bearing quinoline core **4a–l** was successfully synthesized by microwave irradiation technique. The synthesis involved four steps strategies which was initiated by ring-opening synthetic modification of isatin to quinoline-4-carboxylic acid through Pfitzinger approach. The structure of the reactive intermediates **1, 2,** and **3** as well as the targeted quinoline **4a–l** were confirmed by the result of physicochemical parameters and spectroscopic means which include FTIR, UV, ^{1}H and ^{13}C NMR as well as DEPT 135 NMR. The *in vitro* antimicrobial screening of the targeted hydrazide-hydrazones **4a–l** alongside with gentamicin (clinical standard) against six microorganisms was determined using agar diffusion. The result from the MIC test showed that this series of hydrazide-hydrazones exhibited remarkable efficacy as antimicrobial agents with **4e** being the most active antibacterial agent with MIC value ranging from 3.13 to 0.39 µg/mL on the six organisms tested.

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INTRODUCTION

The structure of un-substituted quinoline was confirmed by the syntheses in which allylaniline was passed over glowing lead oxide or from *o*-nitrocinnamaldehyde [1]. Quinoline is characterized by a double ring structure composed of benzene and pyridine ring fused at two adjacent carbon atoms, while the pyridine ring contains five carbon atoms and a nitrogen heteroatom [2]. Due to wide application of quinoline core in many medicinal and industrial processes, various synthetic approaches have been used for the synthesis of this valuable heterocyclic system. These methods include the following: Pfitzinger approach which is reaction of isatin with ketones and aldehyde [3]; Doebner–Von Miller method, which is composed of reaction of an aniline with α,β-unsaturated carbonyl compounds [4]; Conrad–Limpach method which is based on the condensation of anilines with β-ketoesters [5]; Combe synthetic approach which involves the reaction of β-diketones, with primary aryl amines like aniline [6] and Friedlander synthetic approach which proceeded by the condensation of 2-aminoaryl ketones with α-methyleneketones [7]. Another method which has become one of the most efficient processes for the synthesis of quinolines is Povarov synthetic approach which is an inverse electron demand aza-Diels–Alder reaction of *N*-aryl imines, derived from aldehydes and anilines, with electron rich olefins [8] and Skraup method [9]. Quinoline skeletons are recurrently encountered heterocyclic compounds in medicinal chemistry literature with wide spread pharmacological diversity such as anticancer [10] antioxidant [11], antileishmanial [12], antibacterial [13], analgesic, anti-inflammatory [14], antifungal [15], antimalarial [16], antitumor [17], and DNA enzyme topoisomerase I inhibitory [18] among others.

Furthermore, in the recent time, the chemistry of carbon–nitrogen double bond of hydrazone is fast becoming the backbone of condensation reaction in benzo-fused *N*-heterocycles [19]. Hydrazone containing azomethine –NHN═CH protons constitute an important class of compounds for new drug development [19] which have been reported to possess, among others, antimicrobial [20], antitubercular [21], and antiplatelet [22]. Also, a recent review on pharmacological activities

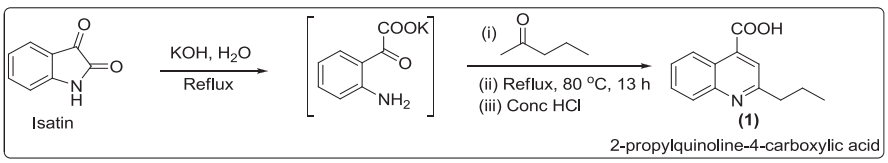
of hydrazone derivatives showed them to display anticonvulsant, anti-inflammatory, antimalarial, antioxidant, antidepressant, and antifungal [23]. In an earlier review, which dealt with exploring biological activities of hydrazone, it was unveiled that they exhibited analgesic, central nervous system (CSN), antiprotozoal, cardio-protective and anticancer activities [24]. Due to occurrence of microorganisms' drug resistance and emergence of new diseases which have contributed to the alarming rate of global health threat, there is a continuous need for the synthesis of new heterocyclic compounds as potential antimicrobial agents. Therefore, we have herein designed and synthesized 12 novel hydrazide-hydrazones of quinoline **4a–l** in order to investigate their antimicrobial potential for possible future drug discovery.

RESULTS AND DISCUSSION

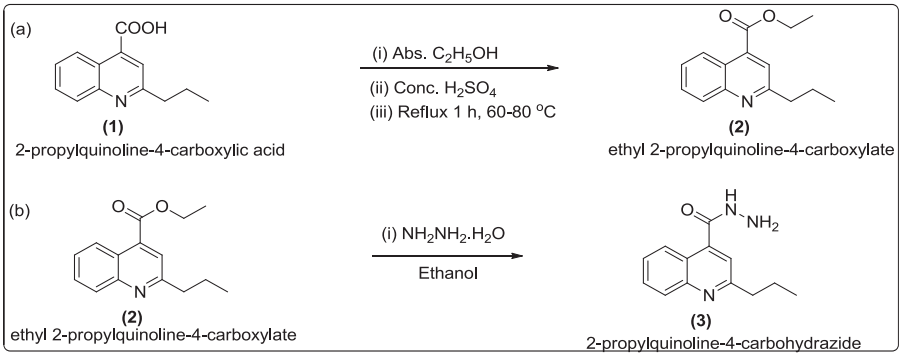
Chemistry. In the continuation of our research effort on the design and discovery of biologically active hydrazones [19,20], we have herein embarked upon the microwave-assisted synthesis of quinoline-based hydrazide-hydrazone through an eco-friendly synthetic approach in order to evaluate their antimicrobial potentials for possible future drug discovery. First and foremost, the reaction was initiated by the synthesis of 2-propylquinoline-4-carboxylic acid **(1)** according to the Pfitzinger synthetic procedure earlier reported [3]. This involved the ring-opening reaction of isatin under the influence of aqueous KOH by heating under reflux, followed by ketonization of the reactive intermediate with pentan-2-one at a reflux temperature of 80–90°C for 13 h to form the potassium salt of 2-propylquinoline-4-carboxylic acid. The choice of pentanone as the required ketone is to access 2-propyl substitution on the quinoline nucleus. The resulting solution was then worked-up by acidification with concentrated hydrochloric acid (Conc. HCl) to a pH of 2, after which colored solid was precipitated. It was cooled and the solid formed was filtered by suction and air-dried to afford 2-propylquinoline-4-carboxylic acid **1** as red colored crystalline compound (Scheme 1). Secondly, the compound **(1)** was esterified *via* reaction with absolute ethanol at temperature of 60°C by heating under reflux for 1 h in the presence of catalytic amount of concentrated sulphuric acid (Conc. H_2SO_4) to achieve a solution which was worked-up by adding water and extracted in two portions with diethyl ether. The organic layer was combined and dried over anhydrous Na_2SO_4 to trap any escaped moisture. The filtrate was evaporated to dryness in order to afford ethyl 2-propylquinoline-4-carboxylate, **2** (Scheme 2a). Subsequently, the hydrazinolysis of **2** was carried out by reacting it under reflux for 1 h with equimolar quantity of hydrazine hydrate in ethanolic environment to afford 2-propylquinoline-4-carbohydrazide, **3** in high yield (Scheme 2b). Finally, new 12 derivatives of hydrazide-hydrazone bearing quinoline core, **4a–l** were synthesized by microwave assisted condensation reaction of the NH_2 free end of hydrazide of intermediate **3** with sp^2 hybridized carbonyl center of various aliphatic and alicyclic ketones in the presence of ethanol (Scheme 3). The microwave assisted reaction was completed between 1 and 3 min. The thermodynamic justification for faster reaction rate under microwave was explained in our previous work [20].

Characterization. Spectroscopic characterization of the newly synthesized hydrazide-hydrazones **4a–l** was carried out using UV–vis, IR spectral data, ^{1}H NMR, ^{13}C NMR and DEPT 135. According to the spectroscopic study, the electronic transition of UV–vis spectra for the hydrazide-hydrazones of quinoline, **4a–l** gave rise to wavelength (λ_{max}) ranging from 203 nm for **4a** to 428 nm for **4 l** with log ε_{max} of 4.04 for both (Experimental). The first set of wavelengths (λ_{max}) in all the synthesized compounds were found between 203 and 225 nm and they were as a result of л→л* transition indicating the presence of C═C peculiar to benzene nucleus. This indicated that all the hydrazide-hydrazones, **4a–l** possessed benzene ring as one of their core system. Considering **4a** as a representative of the targeted compounds, its first wavelength was 203 nm (log ε_{max} = 4.04) while some bathochromic shifts were experienced at 225 (log ε_{max} = 4.08), 251 (log ε_{max} = 4.10), 254 (log ε_{max} = 4.38), and 305 nm (log ε_{max} = 4.11). They were as a result of the combinatory effect of л→n transition of C═O and C═N as well as extensive conjugation of C═C moieties. The longest

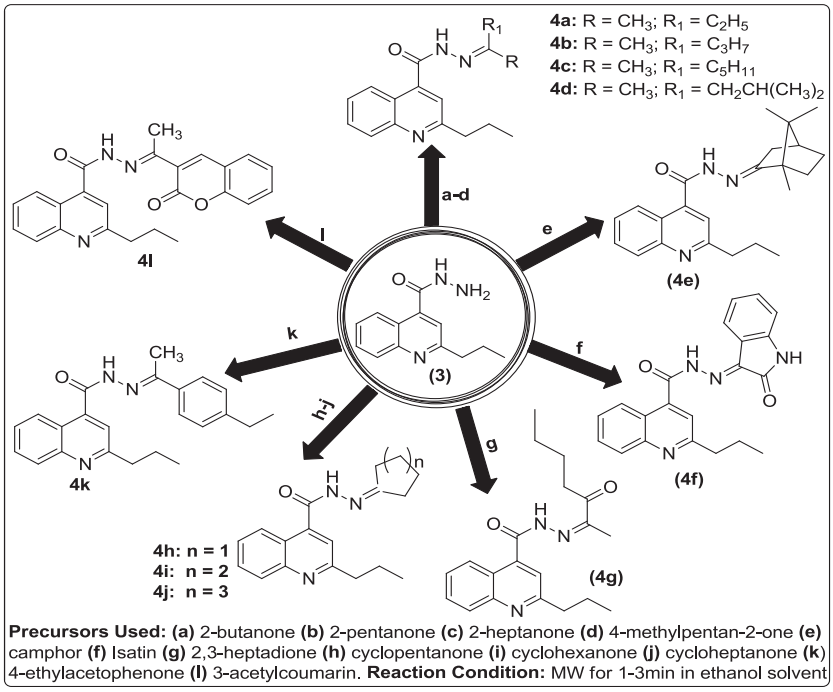
Scheme 1. Pathway for the synthesis of 2-propylquinoline-4-carboxylic acid, **1**.



Scheme 2. Pathways for the synthesis of (a) ethyl 2-propylquinoline-4-carboxylate, **2.** (b) and quinoline hydrazide, 2-propylquinoline-4-carbohydrazide, **3.**



Scheme 3. Hydrazide-hydrazones of quinoline core, **4a–l**.



wavelength of 428 nm (log ε_{max} = 4.04) was observed in compound **4 l**. This might be due to the presence of auxochromic character of C═N and additional C═C conjugation contributed by the benzene of the coumarin template. The infrared spectra of all the compounds, **4a–l** showed absorption bands because of the stretching vibration of N–H of hydrazide, C–H of aromatic, C–H of aliphatic, C═O of hydrazide and amide, C═C of aromatic and C═N of hydrazone, and imine at 3415–3244 cm^{-1}, 3151–3010 cm^{-1}, 2981–2804 cm^{-1}, 1715–1668 cm^{-1}, 1638–1603 cm^{-1} and 1589–1575 cm^{-1}, respectively. The absorption bands observed at bending vibrational frequencies of 1467–1360 cm^{-1}, 1254–1123 cm^{-1}, 987–965 cm^{-1}, and 774–722 cm^{-1} depicted the presence of aliphatic (CH_3, CH_2) deformation, C–N of hydrazide, ═C–H bending and aryl bonded hydrogen respectively. In addition, some bands were peculiar to some compounds alone and not for the entire targeted scaffolds. In terms of the ranges of the bands of each functional group, the highest N–H band was found in **4a, 4e, 4f,** and **4h** at 3415 cm^{-1} while the lowest N–H band was found in **4d** at 3244 cm^{-1}. The C–H band of aromatic ranged from 3151 cm^{-1} for **4b** to 3010 cm^{-1} for **4g** and **4h**. Carbonyl bands were available for all the compounds with carbonyl of amide in **4g** being the highest (1715 cm^{-1}) while the carbonyl of hydrazide of **4c** had the lowest carbonyl absorption frequency of 1668 cm^{-1}. In a similar manner, the stretching vibrational frequency of C═C varied

between 1638 cm^{-1} for compound **(4c)** to 1603 cm^{-1} for compound **4b** while the highest absorption frequency for C═N was 1589 cm^{-1} for **4b** and **4k** and lowest being 1575 cm^{-1} for **4i, 4j,** and **4k**. The deformed aliphatic groups attached to benzene were found between 1467 cm^{-1} for **4b–4k** and 1360 cm^{-1} for **4i**. The confirmatory evidence for the C–N of hydrazide was responsible for the bands ranging from 1254 cm^{-1} for **4f** to 1123 cm^{-1} for **4c** while the rest of the bands were at the finger print region.

Furthermore, the physicochemical parameters of the synthesized compounds **4a–l** evaluated and documented were molecular formula, molecular weight, percentage yields, melting points, color, and elemental composition values for carbon, hydrogen, and oxygen (Experimental). The molecular weight of the compounds, **4a–l** ranged from 283.87 for **4a** to 399.44 for **4l**. The weights were above 200 g/mol, which partially revealed the bicyclic nature of the compounds, **4a–l**, since a monocyclic aromatic has molecular weight <200 g/mol (e.g. benzene = 78 g/mol). The majority of the compounds have arbitrarily high melting point values and **4e, 4f,** and **4l** did not even melt at 300°C. It is a clear indication of the formation of hydrazide bond which has similar thermal behavior as amide bond with high tendency of hydrogen bonding character. This was in agreement with our earlier finding [19] wherein 3-hydrazinoquinoxalin-2(1*H*)-one was reported to have high melting point values (m.p.>360°C). The percentage yields of the synthesized hydrazide-hydrazones **4a–l** ranged from 70% for **4d** to 94% for **4l**. The good to excellent yields obtained showed that microwave irradiation technique was cost-effective and highly efficient in the complete conversion of the precursor to the quinoline-based hydrazide-hydrazones, **4a–l**. The visual observation of the compounds showed that the color varied in the order: red for **4f**; yellow for **4l;** white for **4e;** black for **4h** and **4k**, while the rest of the compounds were brown. The result of elemental analysis did not only correlate well with the molecular masses of the compounds but also showed a consistent minimum difference of not more than ±0.24 between % calculated and % found for the carbon, hydrogen and nitrogen of the prepared compounds, **4a–l** (Experimental).

Antimicrobial activity. Antimicrobial sensitivity testing of targeted hydrazide-hydrazones **4a–l** was carried out *in vitro* against six organisms using agar-well diffusion method [25]. The media were inoculated with test organisms and DMSO was used as negative control. The positive control on bacteria was gentamicin. The zones of inhibition (Z.O.I.) in millimeters were measured after 24 h of incubation and duly recorded as shown in Table 1. The choice of gentamicin as clinical standard is because, at low concentrations, gentamicin only inhibits growth of the bacteria through induction of prokaryotic ribosomes to misread mRNA [19]. Gentamicin also prevents initiation of protein synthesis and leads to death of microbial cells. Gentamicin inhibits bacterial growth by inhibiting protein biosynthesis just like Streptomycin and other aminoglycoside antibiotics. Interestingly, it was observed that majority of the compounds exhibited probable and highly promising significant activities based on the large zone of inhibition reported. In fact, many of these hydrazide-hydrazone of quinoline derivatives **4a–l** had larger zones of inhibition against all the six organisms when compared to gentamicin standard. Generally

Table 1

The sensitivity testing of hydrazide-hydrazones **4a–l** with zone of inhibition (mm).

Sample Code	Organisms used and Z.O.I. (mm)					
	S. aureus	*B. lichenformis*	*M. varians*	*E. coli*	*P. vulgaris*	*P. aeruginosa*
4a	39.00 ± 1.25	38.00 ± 1.25	33.00 ± 1.25	30.00 ± 1.15	*R*	29.00 ± 1.10
4b	28.00 ± 1.25	23.00 ± 1.04	23.00 ± 1.00	15.00 ± 1.01	13.00 ± 1.00	24.00 ± 1.11
4c	18.00 ± 1.11	31.00 ± 1.25	24.00 ± 1.08	25.00 ± 1.25	18.00 ± 1.08	26.00 ± 1.09
4d	38.00 ± 1.25	13.00 ± 1.00	14.00 ± 1.07	11.00 ± 1.01	13.00 ± 1.08	20.00 ± 1.14
4e	40.00 ± 1.25	33.00 ± 1.25	33.00 ± 1.25	30.00 ± 1.15	31.00 ± 1.25	38.00 ± 1.25
4f	25.00 ± 1.06	16.00 ± 1.00	11.00 ± 1.01	15.00 ± 1.08	14.00 ± 1.18	14.00 ± 1.14
4g	19.00 ± 1.20	8.00 ± 1.00	8.00 ± 1.00	3.00 ± 0.45	32.00 ± 1.25	4.00 ± 0.46
4h	42.00 ± 1.25	11.00 ± 1.00	14.00 ± 1.00	4.00 ± 0.39	17.00 ± 1.11	8.00 ± 0.39
4i	26.00 ± 1.19	13.00 ± 1.03	13.00 ± 1.01	13.00 ± 1.03	8.00 ± 0.44	8.00 ± 0.41
4j	31.00 ± 1.25	24.00 ± 1.21	14.00 ± 1.14	18.00 ± 1.22	18.00 ± 1.22	25.00 ± 1.25
4k	30.00 ± 1.25	16.00 ± 1.14	14.00 ± 1.09	19.00 ± 1.21	12.00 ± 1.03	22.00 ± 1.25
4l	32.00 ± 1.25	25.00 ± 1.24	20.00 ± 1.17	15.00 ± 1.07	18.00 ± 1.20	20.00 ± 1.25
Gent.	23.00 ± 1.25	15.00 ± 1.08	18.00 ± 1.21	25.00 ± 1.19	25.00 ± 1.20	*R*

S. aureus, *Staphylococcus aureus; B. lichenformi*, *Bacillus lichenformis; M. varians, Micrococcus varians; E. coli*, *Escherichia coli; P. vulgaris, Proteus vulgaris; P. aeruginosa, Pseudomonas aeruginosa;* Gent., Gentamicin (Clinical standard); Z.O.I., Zone of Inhibition. Values are mean ± SD of triplicate determination.

speaking, compound **4h** showed the largest zone of inhibition (42.00 ± 1.25 mm) against *Staphylococcus aureus* while **4g** had the least zone of inhibition of 3.00 ± 0.45 mm against *Escherichia coli* among all the screened compounds.

The compound **4a–l** inhibited the growth of *S. aureus* effectively with Z.O.I. ranging from 18.00 ± 1.11 mm for **4c** to 42.00 ± 1.25 mm for **4h** while Z.O.I. of gentamicin against the same organism was 23.00 ± 1.25 mm. Thus, compounds **4k** competed favorably with gentamicin while all other compounds showed better activity than gentamicin with larger zones of inhibition (i.e. Z.O.I. $>$ 23 mm) except compounds **4c** and **4g** with Z.O.I. of 18 ± 1.11 mm and 19 ± 1.20 mm, respectively against *S. aureus*. The antimicrobial activity against *Bacillus lichenformis* showed that **4a** had largest Z.O.I. of 38.00 ± 1.25 mm while the least growth inhibitor was **4g** with Z.O.I. of 8.00 ± 1.00 mm. The Z.O.I. of gentamicin against *B. lichenformis* was 15.00 ± 1.08 mm. This helped us to know that four compounds, **4d, 4g, 4h,** and **4i** had Z.O.I. values which were lower than that of gentamicin while the remaining eight compounds inhibited the growth of *B. lichenformis* at Z.O.I. value larger than that of gentamicin. With respect to *Micrococcus varians*, compounds **4a** and **4e** were the most probable growth inhibitors due to their large Z.O.I. values of 33.00 ± 1.25 mm while **4 g** was the least probable due to small Z.O.I. value of 8.00 ± 1.00 mm. The Z.O.I. of gentamicin against *M. varians* was 18.00 ± 1.21 mm. This assisted in identifying that there were five compounds having Z.O.I. values (from 20.00 ± 1.17 to 33.00 ± 1.25 mm) greater than that of clinical standard (gentamicin) while seven compounds were having Z.O.I. values (from 8.00 ± 1.00 to 14.00 ± 1.14 mm) less than that of gentamicin as far as growth inhibitory potential against *M. varians* was concerned.

Nevertheless, upon the screening against three Gram-negative organisms (*E. coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*), noticeable activities were observed, except screening of **4a** against *P. vulgaris* and gentamicin against *P. aeruginosa* where resistance was observed. According to screening against gram negative *E. coli*, the largest and smallest Z.O.I. were observed to be 30.00 ± 1.15 mm for **4a** and **4e** and 3.00 ± 0.45 mm for **4g**, respectively. The Z.O.I. of gentamicin against *E. coli* was 25.00 ± 1.19 mm, which implied that **4c** competed favorably with gentamicin while two compounds **4a, 4e,** inhibited *E. coli* growth at Z.O.I. larger than that of gentamicin. The antimicrobial activity against gram positive *P. vulgaris* depicted **4g** as the most effective with largest Z.O.I. of 32.00 ± 1.25 mm while **4i** was the least active with smallest Z.O.I. of 8.00 ± 0.44 mm. The *in vitro* screening of the samples **4a–l** against *P. aeruginosa* showed that all compounds were probably more active than gentamicin, because this organism (*P. aeruginosa*) developed resistance against gentamicin, but had broad spectrum of activity with Z.O.I. ranging from 4.00 ± 0.46 mm for **4g** to 38.00 ± 1.25 mm for **4e**. In the overall, hydrazide-hydrazone **4e** had the best activity across the strains of the Gram-negative and Gram-positive organisms used in this present study.

Both community-associated and hospital-acquired infections with *S. aureus* have increased in the past 20 years. Types and presentation of *S. aureus* infection include the following: skin and soft tissue (impetigo) infection, scalded skin syndrome (Ritter disease), folliculitis, furuncle, bone infections (osteomyelitis) in children [26], septic arthritis, toxic shock syndrome, thrombophlebitis, deep tissue abscess, and infection among other which in turn leads to high mortality rate [27]. Based on all the information aforementioned on *S. aureus*, the selectivity index (S.I.) of quinoline hydrazide-hydrazones **4a–l** against the *S. aureus* was evaluated (Fig. 1). The comparative study of activity potential of **4a–l** with gentamicin was considered because, in humans, gentamicin has structurally different ribosomes from bacteria, thereby allowing the selectivity of this antibiotic for bacteria. The selectivity index of gentamicin was unity, while any compounds with S.I. $>$ 1, have a better selectivity index as compared with gentamicin whereas those with the S.I. $<$ 1 possessed lesser selectivity index than gentamicin antibiotic. On this note, it is interesting to note that four compounds **4a, 4d, 4e,** and **4h** exhibited a better selectivity index when compared to gentamicin against *S. aureus*, while the rest of the compounds were less selective than gentamicin on *S. aureus*.

Based on the broad activity spectrum noticed during the antibacterial screening, MIC of the targeted compounds **4a–l** was carried out against the six organisms using serial dilution method [25], with varying concentration from 50 to 0.39 μg/mL as shown in Table 2. The most susceptible organism to the efficacy of **4a–l** was *S. aureus* because 13 compounds inhibited the growth of this organism at MIC value as low as 0.39 μg/mL except two compounds; **4j** which inhibited *S. aureus* growth at MIC value of 0.78 μg/mL and **4e** with MIC of 1.56 μg/mL against *S. aureus* growth. Thus, hydrazide-hydrazones, **4a–l** synthesized herein could pave way for new drug development for combating infectious diseases caused by *S. aureus*. Compound **4a** could not inhibit the growth of *P. vulgaris* at MIC value ≤50 μg/mL. The MIC of synthesized compounds **4a–l** ranged from 1.56 to 25.00 μg/mL against *B. lichenformis*; 1.56 to 12.50 μg/mL against *M. varians*; 0.78 to 25.00 μg/mL against *E. coli*; 0.39 to 25.00 μg/mL against *P. vulgaris*; and 0.78 to 50.00 μg/mL against *P. aeruginosa*. Based on

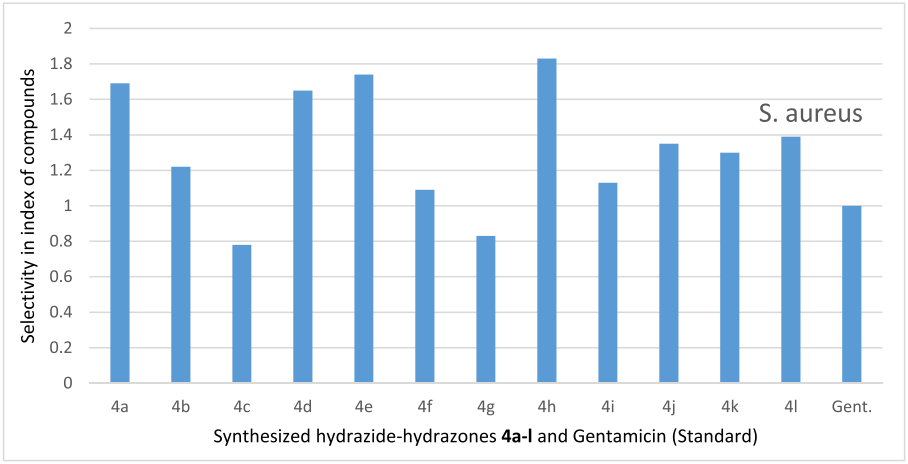


Figure 1. Result of the selectivity index of hydrazide-hydrazones **(4a–l)** against *S. aureus*. [Color figure can be viewed at wileyonlinelibrary.com]

Table 2

The minimum inhibitory concentration (MIC) test of hydrazide-hydrazones **4a–l** (μg/mL).

	Organism Used					
Code No	*S. aureus*	*B. lichenformis*	*M. varians*	*E. coli*	*P. vulgaris*	*P. aeruginosa*
4a	0.39	6.25	6.25	25.00	Nil	12.50
4b	0.39	25.00	1.56	12.50	6.25	25.00
4c	0.39	1.56	6.25	0.78	6.25	1.56
4d	0.39	6.25	3.13	3.13	1.56	6.25
4e	1.56	1.56	3.13	3.13	0.39	0.78
4f	0.39	1.56	3.13	6.25	12.50	1.56
4g	0.39	3.13	3.13	12.50	6.25	3.13
4h	0.39	12.50	12.50	25.00	25.00	50.00
4i	0.39	3.13	3.13	3.13	6.25	3.13
4j	0.78	12.50	3.13	6.25	3.13	12.50
4k	0.39	6.25	3.13	1.56	12.50	25.00
4l	0.39	1.56	3.13	25.00	6.25	3.13

the result of visual screening of MIC values across the gram positive and Gram-negative organisms used herein, compound **4e** emerged as the most potent antimicrobial agent with MIC from 0.39 to 3.13 μg/mL. Hence, it is a worthwhile adventure to explore these compounds further to investigate their cytotoxicity profile so as to further harness and identify their potential for possible novel drug discovery. This is needful, especially, in a time like this when drug resistance challenge has become a strong toolbox for global health threat and undesirable avenue for high mortality rate among mankind and livestock.

CONCLUSION

The quinoline group has been proven to have remarkable utilities in medicinal chemistry as one of the most widely used antibiotics and antimalarials in the world. The microwave irradiation method showed to be very effective, cheap, fast, and economical. It also promotes environmental friendly synthetic approach because the toxicity and hazardous discharges from chemical usage is not experienced and the synthesis was carried out successfully in a neat and green reaction medium. As envisaged, most of the novel hydrazide-hydrazones of quinoline were shown to have higher inhibitory potentials than the antibiotic standard, gentamicin used in most cases. 2-Propyl-(*N*′-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)quinoline-4-carbohydrazide, **4e** emerged as the most active antibacterial agent with MIC values ranging from 1.59 to 0.39 μg/mL on the six organisms tested.

EXPERIMENTAL

All chemical compounds were pure and of analytical grade. They were purchased from Sigma Aldrich, USA and except for cyclopentanone and isatin which were purchased BDH Chemicals, UK, but were made

available by Department of Chemistry, Covenant University. Melting points were determined in open capillary tubes on Stuart melting point apparatus and were uncorrected. The Infrared spectra were run using the Perkin Elmer FTIR Spectrophotometer (KBr pellet, 4000 to 400 cm^{-1}). The Ultraviolet–visible (UV–vis.) spectrophotometric analyses of all the samples were run in either dichloromethane (CH_2Cl_2), or Dimethyl sulphoxide (DMSO) solvents using UV-Genesys 10s v1.200 Spectrophotometer. The absorbance was plotted against the wavelength λ_{max} (nm) and the obtained molar absorptivity was used to calculate Log ε_{max}. The progress of the reaction and the level of purity of the compounds were routinely checked by Thin Layer Chromatography (TLC) on silica gel plates using different eluting solvent (solvent system) and the developed plates were visualized under UV light and in the iodine tank. Furthermore, the ^{1}H NMR and ^{13}C NMR spectra were recorded on NMR Bruker DPX 500 Spectrometer, manufactured by Bruker BioSpin Corporation, California, USA, operating at the machine frequencies of 500 and 125 MHz, respectively using either $CDCl_3$ or DMSO-d_6, as solvent for sample preparation prior to analyses. In addition, DEPT-135 NMR analysis was also evaluated for all the synthesized compounds. Tetramethylsilane (TMS) was used as internal standard with the deuterium signal of the solvent as the lock and chemical shifts δ were recorded in ppm and the coupling constants (*J*) were reported in Hertz (Hz) where distinct multiplicities were observed. Standard abbreviation was used for the multiplicity which include singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). The microwave assisted syntheses were carried out with the aid of CEM Discover Monomode oven operating at frequency of 2450 MHz monitored by a PC computer and temperature control was fixed at 140°C within the power modulation of 500 W. The reactions were performed in sealed tube within ramp time of 1 to 3 min while stirring was provided by an *in situ* magnetic stirrer. In addition, pH was monitored and confirmed during acidification using pH meter model PHB4. All drying was conducted at reduced pressure with DHG-9023A Vacuum Oven which was manufactured by Protech Holding Limited, Zhengzhou, China. The elemental analysis (C, H, and N) of the synthesized compounds were performed using a Flash EA 1112 elemental analyzer which was manufactured by Eltra GmbH, Haan, Germany. Results were found to be in good agreement with the calculated values (Table 1).

General procedure for microwave-assisted synthesis of hydrazide-hydrazone (4a–l). 2-Propylquinoline-4-carbohydrazide, **3** (3.0 g, 13 mmol) was dissolved in about 10 mL of ethanol in a 100 mL beaker covered with watch glass. The corresponding ketone (13 mmol) was added and the beaker was swirled thoroughly for proper homogeneity. The resulting mixture was then irradiated in microwave oven for a period of 1 to 3 min as the case may be, based on the result obtained from the monitored progress of reaction using TLC spotting in dichloromethane (DCM) as eluting solvent. The heated solution was allowed to cool to ambient temperature and filtered to afford the corresponding hydrazide-hydrazone of quinoline **(4a–l)** in good to excellent yields after column chromatograph.

N′–(Butan-2-ylidene)-2-propylquinoline-4-carbohydrazide (4a). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with butan-2-one (1.16 mL, 13 mmol) for 2 min afforded *N′*-(butan-2-ylidene)-2-propylquinoline-4-carbohydrazide, **4a** as brown solid**.** Yield 3.25 g (82%); m.p. 258°C; $C_{17}H_{21}N_3O$ (283.87): Anal. Found: C, 72.06; H, 7.47; N, 14.83% Calc.: C, 72.11; H, 7.52, N, 14.92%. ^{1}H NMR (δ, ppm in dmso-d_6): 7.75–7.73 (d, *J* = 10.0 Hz, 2H, Ar–H), 7.52 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 10.0 Hz, J_2 = 12.5 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.73–3.72 (m, 2H, CH_2), 3.31–3.25 (q, *J* = 8.0 Hz, 2H, **CH$_2$**CH_3), 3.17–3.11 (q, *J* = 8.20 *Hz*, 2H, **CH$_2$**CH_3), 2.40 (s, 3H, **CH$_3$**–C═N), 1.12–1.08 (t, *J* = 8.0 Hz, 3H, **CH$_3$**CH_2), 1.02–0.99 (t, *J* = 8.0 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 173.2 (C═O), 158.4, 151.2, 141.9, 135.0, 132.3, 127.4, 120.8, 117.0, 116.8, 110.0, 41.3, 29.3, 25.3, 20.2, 15.1, 10.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 141.9 (CH), 135.0 (CH), 132.3 (CH), 117.0 (CH), 116.8(CH), 20.2 (CH_3), 15.1 (CH_3), 10.1 (CH_3). Negative signals are 41.3, 29.3, and 25.3 (CH_2). UV–vis.: λ_{max} (nm)/ log ε_{max} (mol^{-1} cm^{-1}): 203 (4.04), 225 (4.08), 251 (4.10), 254 (4.38), and 305 (4.11). IR (cm^{-1}): νN-H 3415, νC–H aliph. 2981, νC═C 1633, νC–N 1140, ν = C–H bending 982.

N′-(Pentan-2-ylidene)-2-propylquinoline-4-carbohydrazide (4b). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with pentan-2-one (1.38 mL, 13 mmol) for 2 min afforded *N′*-(pentan-2-ylidene)-2-propylquinoline-4-carbohydrazide, **4b** as brown solid**.** Yield 3.16 g (76%); m.p. 261–262°C; $C_{18}H_{23}N_3O$ (297.39): Anal. Found: C, 72.70; H, 7.80, N, 14.13% Calc.: C, 72.65; H, 7.74; N, 14.09%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.77–7.75 (d, *J* = 10.0 Hz, 2H, Ar–H), 7.75 (s, 1H, Ar–H), 7.28–7.26 (dd, J_1 = 10.0 Hz, J_2 = 12.5 Hz, 2H, Ar–H), 4.76 (s, 1H, NH), 3.53–3.48 (q, *J* = 8.5 Hz, 2H, **CH$_2$**CH_3), 3.34–3.29 (q, *J* = 8.9 Hz, 2H, **CH$_2$**CH_3), 2.40 (s, 3H, **CH$_3$**–C═N), 2.08 (m, 2H, CH_2), 1.86 (m, 2H, CH_2), 1.27–1.24 (t, *J* = 8.90 Hz, 3H, **CH$_3$**CH_2), 1.10–1.06 (t, *J* = 8.50 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 173.1 (C═O), 158.8, 151.3, 141.9, 135.0, 132.3, 127.4, 120.8, 117.0, 116.8, 110.0, 41.3, 33.3, 29.3, 25.3, 20.2, 15.1, 10.1 (CH_3) ppm. DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 141.9 (CH), 135.0 (CH), 132.3 (CH), 117.0 (CH), 116.8(CH), 20.2 (CH_3), 15.1 (CH_3), 10.1 (CH_3). Negative signals are 41.3, 33.3, 29.3, and 25.3 (CH_2).

UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 225 (4.10), 250 (4.31), 265 (4.45), 275 (4.75), 317 (4.61). IR (cm^{-1}): νN–H 3358, νC–H arom. 3151, νC–H aliph. 2925, νC–H aliph. 2805, νC═O 1683, νC═C 1603, νC═N 1589, νCH_3 deformation 1467, νC–N 1248, ν = C–H bending 982, νAr–H 749.

N′-(Hepta-2-ylidene)-2-propylquinoline-4-carbohydrazide (4c). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with heptan-2-one (1.86 mL, 13 mmol) for 1½ min afforded *N′*-(hepta-2-ylidene)-2-propylquinoline-4-carbohydrazide, **4c** as brown solid. Yield 3.87 g (85%); m.p. 263–265°C; $C_{20}H_{27}N_3O$ (325.46): Anal. Found: C, 73.81; H, 8.36; N, 12.91% Calc.: C, 73.71; H, 8.27; N, 13.04%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.58–7.56 (d, J = 10.30 Hz, 2H, Ar–H), 7.21–7.19 (dd, J_1 = 10.5 Hz, J_2 = 10.9 Hz, 2H, Ar–H), 4.86 (s, 1H, NH), 3.73–3.70 (q, J = 9.1 Hz, 2H, **CH_2**CH_3), 3.31–3.26 (q, J = 8.9 Hz, 2H, **CH_2**CH_3), 3.15–3.04 (m, 2H, CH_2), 2.36 (s, 3H, **CH_3**C═N), 1.79–1.47 (m, 6H, 3 × CH_2), 1.26–1.23 (t, J = 8.9 Hz, 3H, **CH_3**CH_2), 0.96–0.93 (t, J = 8.5 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 173.1 (C═O), 158.8, 151.3, 141.9, 135.0, 132.3, 127.4, 120.8, 117.0, 116.8, 110.0, 41.3, 33.3, 29.3, 28.5 (2 × CH_2), 25.3, 20.2, 15.1, 10.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 141.9 (CH), 135.0 (CH), 132.3 (CH), 117.0 (CH), 116.8(CH), 20.2 (CH_3), 15.1 (CH_3), and 10.1 (CH_3). Negative signals are 41.3, 33.3, 29.3, 28.5 (2 × CH_2), and 25.3 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 208 (3.85), 215 (3.90), 224 (3.98), 230 (4.11), 257 (4.46). IR (cm^{-1}): νN–H 3411, νC–H aliph. 2957, νC–H aliph. 2931, νC–H aliph. 2861, νC═O 1668, νC═C 1638, νCH_3 deformation 1460, νC–N 1123, ν = C–H bending 982, νAr–H 725.

N′-(4-Methylpentan-2-ylidene)-2-propyl quinoline-4-carbohydrazide (4d). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with 4-methylpentan-2-one (1.62 mL, 13 mmol) for 2 min afforded *N′*-(4-methylpentan-2-ylidene)-2-propylquinoline-4-carbohydrazide, **4d** as brown solid. Yield 3.05 g (70.00%); m.p. 268°C; $C_{19}H_{25}N_3O$ (311.42): Anal. Found: C, 73.28; H, 8.09; N, 13.49% Calc.: C, 73.12; H, 8.15; N, 13.58%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.74–7.72 (d, J = 10.0 Hz, 2H, Ar–H), 7.51 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 10.0 Hz, J_2 = 12.5 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.73–3.72 (d, J = 7.2 Hz, 2H, **CH_2**CH), 3.15–3.11 (t, J = 8.5 Hz, 2H, **CH_2**CH_2), 2.40 (s, 3H, **CH_3**–C═N), 1.82–1.79 (m, 1H, CH), 1.71–1.67 (m, 2H, CH_2), 1.10–1.08 (d, J = 8.2 Hz, 6H, 2 × (**CH_3**)$_2$–CH), 0.99–0.97 (t, J = 8.0 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 173.2 (C═O), 158.4, 151.2, 141.9, 138.1, 128.7, 125.7, 120.8, 117.2, 115.3, 106.1, 44.2, 41.3, 29.3, 25.3, 21.3, 14.6 (2 × CH_3), 10.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 141.9 (CH), 138.1 (CH), 128.7 (CH), 117.2 (CH), 115.3 (CH), 44.2 (CH), 21.3 (CH_3), 14.6 (2 × CH_3), and 10.1 (CH_3). Negative signals are 41.3, 29.3, and 25.3 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 217 (4.24), 224 (4.05), 239 (4.26), 275 (4.62), 320 (4.45). IR (cm^{-1}): νN–H 3374, 3244, νC–H arom. 3036, νC–H aliph. 2980, νC–H aliph. 2889, νC═C 1688, νC═C 1605, νC═N 1587, νCH_3 deformation 1464, νC═N 1243, ν = C–H bending 965, νAr–H 774.

2-Propyl-(N′-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene) quinoline-4-carbohydraz ide (4e). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with camphor (1.99 g, 13 mmol) for 3 min afforded 2-propyl-(*N′*-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)quinoline-4-carbohydr azide**, 4e** as white solid**.** Yield 3.92 g, (77%); m.p. > 300°C; $C_{23}H_{29}N_3O$ (363.50): Anal. Found: C, 76.00; H, 8.04; N, 11.56% Calc.: C, 75.88; H, 8.16; N, 11.66%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.74–7.72 (d, J = 10.0 Hz, 2H, Ar–H), 7.51 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 10.0 Hz, J_2 = 12.5 Hz, 2H, Ar–H), 5.84 (s, 1H, NH), 3.78–3.77 (d, J = 4.8 Hz, 2H, **CH_2**CH), 3.31–3.25 (q, J = 7.4 Hz, 2H, CH_2**CH_2**CH), 2.40 (s, 3H, **CH_3**–C═N), 2.12 (m, 1H), 1.80 (m, 2H), 1.67 (m, 2H, CH_2), 1.48 (t, J = 5.8 Hz, 2H, **CH_2**CH_2), 1.25 (s, 6H, (**CH_3**)$_2$–C), 0.99 (t, J = 6.2 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 172.7 (C═O), 159.6, 151.0, 142.7, 134.9, 132.3, 127.4, 120.8, 117.0, 116.8, 110.4, 62.2, 44.0, 41.1, 29.8, 29.3, 25.3, 21.1, 15.1 (2 × CH_3), 11.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 142.7 (CH), 134.9 (CH), 132.3 (CH), 117.0 (CH), 116.8 (CH), 44.0 (CH), 21.1 (CH_3), 15.1 (2 × CH_3), and 11.1 (CH_3). Negative signals are 62.1, 41.1, 29.8, 29.3, and 25.3 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 215 (3.34), 236 (3.11), 431 (3.00), 437 (3.00). IR (cm^{-1}): νN–H 3415, νC–H aliph. 2949, νC–H aliph. 2935, νC–H aliph. 2883, νC═O 1688, νC═C 1620, νCH_3 deformation 1461, νC–N 1245, ν = C–H bending 966, νAr–H 728.

N′-(2-Oxoindolin-3-ylidene)-2-propylquinoline-4-carbohydrazide (4f). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with isatin (1.91 g, 13 mmol) for 3 min afforded *N′*-(2-oxoindolin-3-ylidene)-2-propylquinoline-4-carbohydrazide**, 4f** as red solid**.** Yield 4.72 g, (94%); m. p. > 300°C; $C_{21}H_{18}N_4O$ (358.39): Anal. Found: C, 70.21; H, 4.94; N, 15.48% Calc.: C, 70.38; H, 5.06; N, 15.63%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.98–7.96 (d, J = 8.2 Hz, 1H, Ar–H), 7.83–7.81 (d, J = 8.4 Hz, 1H, Ar–H), 7.74–7.72 (d, J = 10.0 Hz, 2H, Ar–H), 7.51 (s, 1H, Ar–H), 7.44–7.40 (m, 2H, Ar–H), 7.29–7.26 (dd, J_1 = 10.0 Hz, J_2 = 12.50 Hz, 2H, Ar–H), 6.01 (s, 1H, NH), 5.80 (s, 1H, NH), 3.15–3.13 (t, J = 8.5 Hz, 2H, **CH_2**CH_2), 1.71–1.67 (m, 2H, CH_2), 0.99 (t, J = 8.0 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 180.0 (C═O), 173.2 (C═O), 158.4, 151.2, 146.9, 141.9, 135.9, 135.3, 132.8, 131.9, 127.4, 126.6, 121.7, 120.4, 117.3,

116.7, 110.2, 109.1, 29.7, 25.5, 10.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 141.9 (CH), 135.9 (CH), 135.3 (CH), 132.8 (CH), 131.9 (CH), 121.7 (CH), 120.4 (CH), 117.3 (CH), 116.7 (CH), and 10.5 (CH_3). Negative signals are 29.7 (CH_2) and 25.5 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 212 (4.08), 225 (4.09), 236 (4.25), 257 (4.73), 314 (4.50). IR (cm^{-1}): νN–H 3415, νN–H 3281, νC–H arom. 3053, νC–H arom. 3020, νC–H aliph. 2854, νC═O 1723, νC═O 1688, νC═C 1614, νCH_3 deformation 1463, νC–N 1254, ν = C–H bending 985, νAr–H 752.

N′-(3-Oxoheptan-2-ylidene)-2-propylquinoline-4-carbohydrazide (4g). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with heptane-2,3-dione (1.79 mL, 13 mmol) for 3 min afforded *N′*-(3-oxoheptan-2-ylidene)-2-propylquinoline-4-carbohydrazide**, 4g** as brown solid**.** Yield 3.85 g, (81%); m.p. 290–291°C; $C_{20}H_{25}N_3O_3$ (339.43): Anal. Found: C, 71.01; H, 7.59; N, 12.55% Calc.: C, 70.77; H, 7.42; N, 12.38%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.75–7.73 (d, *J* = 10.2 Hz, 2H, Ar–H), 7.55 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 6.4 Hz, J_2 = 10.2 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.73–3.70 (t, *J* = 6.1 Hz, 2H, **CH$_2$**CH_2), 3.31–3.25 (q, *J* = 6.9 Hz, 2H, CH_2), 3.15–3.04 (m, 2H, CH_2), 2.36 (s, 3H, **CH$_3$**–C═N), 1.80–1.75 (m, 4H, 2 × CH_2), 1.12–1.08 (t, *J* = 6.1 Hz, 3H, **CH$_3$**CH_2), 1.02–0.99 (t, *J* = 6.4 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 173.3 (C═O), 172.5 (C═O), 159.6, 151.0, 142.7, 134.9, 132.3, 127.4, 120.8, 117.0, 116.8, 110.4, 62.2, 41.1, 29.8, 29.3, 25.3, 20.2 (CH_3), 15.1 (CH_3), 11.1 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 142.7 (CH), 134.9 (CH), 132.3 (CH), 117.0 (CH), 116.8 (CH), 20.2 (CH_3), 15.1 (CH_3), and 11.1 (CH_3). Negative signals are 62.2, 41.1, 29.8, 29.3, and 25.3 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 215 (4.33), 224 (4.43), 240 (4.33), 253 (4.49), 257 (5.14). IR (cm^{-1}): νN–H 3411, νC–H arom.3010, νC–H aliph. 2929, νC–H aliph. 2891, νC═O 1715, νC═O 1688, νC═C 1620, νCH_3 deformation 1461, νC–N 1244, ν = C–H bending 967, νAr–H 725.

N′-Cyclopentylidene-2-propylquinoline-4-carbohydrazide (4h). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with cyclopentanone (1.15 ml, 13 mmol) for 1½ min afforded *N′*-cyclopentylidene-2-propylquinoline-4-carbohydrazide**, 4h** as black solid**.** Yield 3.68g, (89%); m.p. 255°C; $C_{18}H_{21}N_3O$ (295.38): Anal. Found: C, 72.99; H, 6.97; N, 14.39% Calc.: C, 73.19; H, 7.17; N, 14.23%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.75–7.73 (d, *J* = 10.2 *Hz*, 2H, Ar–H), 7.55 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.76–3.72 (t, *J* = 7.4 Hz, 4H, 2 × **CH$_2$**CH_2), 3.31–3.27 (t, *J* = 5.6 Hz, 2H, CH_2), 3.17–3.13 (m, 2H, CH_2), 1.80–1.75 (m, 4H, 2 × CH_2), 1.02–0.99 (t, *J* = 6.2 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 172.5 (C═O), 159.6, 151.0, 142.7, 134.9, 132.3, 127.4, 120.8, 117.0, 116.8, 110.4, 61.9, 41.2, 35.8 (2 × CH_2), 29.6, 24.7, and 13.4 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 142.7 (CH), 134.9 (CH), 132.3 (CH), 117.0 (CH), 116.8 (CH), and 13.4 (CH_3). Negative signals are 61.9, 41.2, 35.8 (2 × CH_2), 29.6, and 24.7 (2 × CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 207 (3.79), 213 (3.79), 227 (4.13), 254 (4.39), 308 (4.11). IR (cm^{-1}): νN–H 3415, νC–H arom. 3030, νC–H aliph. 2930, νC–H aliph. 2865, νC═O 1688, νC═C 1605, νCN 1575, νCH_3 deformation 1467, νCH_2 deformation 1355, νC–N 1248, ν = C–H 965, νAr–H 725.

N′-Cyclohexylidene-2-propylquinoline-4-carbohydrazide (4i). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with cyclohexanone (1.35 mL, 13 mmol) for 2½ min afforded *N′*-cyclohexylidene-2-propylquinoline-4-carbohydrazide**, 4i** as brown solid**.** Yield 3.54 g (88%); m.p. 257–258°C; $C_{19}H_{23}N_3O$ (309.39): Anal. Found: C, 73.59; H, 7.31; N, 13.77% Calc.: C, 73.76; H, 7.49; N, 13.58%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.75–7.73 (d, *J* = 10.2 Hz, 2H, Ar–H), 7.55 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.76–3.72 (t, *J* = 7.4 Hz, 4H, 2 × **CH$_2$**CH_2), 3.31–3.27 (t, *J* = 5.6 Hz, 2H, CH_2), 3.17–3.13 (m, 2H, CH_2), 1.80–1.75 (m, 4H, 2 × CH_2), 1.25–1.22 (m, 2H, CH_2), 1.02–0.99 (t, *J* = 6.2 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 172.4 (C═O), 159.5, 151.0, 142.6, 135.0, 132.4, 127.4, 120.8, 117.2, 116.8, 110.4, 61.9, 41.2, 35.8 (2 × CH_2), 29.6, 24.7, 20.7, 13.9 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 142.6 (CH), 135.0 (CH), 132.4 (CH), 117.2 (CH), 116.8 (CH), and 13.9 (CH_3). Negative signals are 61.9, 41.2, 35.8 (2 × CH_2), 29.6, 24.7, and 20.7. UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 209 (4.57), 272 (5.42), 323 (5.25). IR (cm^{-1}): νN–H 3411, νC–H arom. 3025, νC–H aliph. 2929, νC–H aliph. 2875, νC═O 1688, νC═C 1607, νC═N 1575, νCH_3 deformation 1465, $\nu CH_2$1360, νC–N 1245, ν = C–H bending 987, νAr–H 722.

N′-Cycloheptylidene-2-propylquinoline-4-carbohydrazide (4j). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with cycloheptanone (1.54 mL, 13 mmol) for 2½ min afforded *N′*-cycloheptylidene-2-propylquinoline-4-carbohydrazide**, 4j** as brown solid**.** Yield 3.74 g (89%); m.p. 261–263°C; $C_{20}H_{25}N_3O$ (323.43): Anal. Found: C, 74.19; H, 7.95; N, 13.08% Calc.: C, 74.27; H, 7.79; N, 12.99%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.75–7.73 (d, *J* = 10.2 Hz, 2H, Ar–H), 7.55 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 6.6 Hz, J_2 = 10.2 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.73 (t, *J* = 7.8 Hz, 4H, 2 × **CH$_2$**CH_2), 3.31–3.27 (t, *J* = 5.6 Hz, 2H, CH_2), 3.17–3.13 (m, 2H, CH_2), 1.80–1.75 (m, 4H, 2 × CH_2), 1.40 (m, 2H, CH_2), 1.25–1.22 (m, 2H, CH_2), 1.02–0.99 (t, *J* = 6.2 Hz, 3H, **CH$_3$**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 172.4 (C═O), 159.4, 151.0, 142.5, 135.0, 132.2, 127.5, 120.8,

117.2, 116.7, 110.6, 61.5, 41.2, 35.8 (2 × CH_2), 29.6 (2 × CH_2), 24.7, 20.7, 13.9 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 142.6 (CH), 135.0 (CH), 132.4 (CH), 117.2 (CH), 116.8 (CH), and 13.9 (CH_3). Negative signals are 61.9, 41.2, 35.8 (2 × CH_2), 29.6 (2 × CH_2), 27.7, 24.5, and 20.9. UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 209 (4.55), 251 (4.45), 296 (4.28), 314 (4.07). IR (cm^{-1}): νN–H 3412, νC–H arom. 3020, νC–H aliph. 2925, νC–H aliph. 2877, νC═O 1685, νC═C 1607, νC═N 1575, νCH_3 deformation 1465, νCH_2 1362, νC–N 1245, ν = C–H bending 985, νAr–H 722.

N′-(1-(4-ethylphenyl)ethylidene)-2-propylquinoline-4-carbohydrazide (4k). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with 4-ethylacetophenone (1.94 mL, 13 mmol) for 2 min afforded *N′*-(1-(4-ethylphenyl) ethylidene)-2-propylquinoline-4-carbohydrazide**, 4k** as black solid**.** Yield 4.25 g, (91%); m.p. 241–243°C; $C_{23}H_{25}N_3O$ (359.46): Anal. Found: C, 76.78; H, 6.88; N, 11.81% Calc.: C, 76.85; H, 7.01; N, 11.69%. ^{1}H NMR (δ, ppm in DMSO-d_6): 7.98–7.96 (d, *J* = 8.0 Hz, 2H, Ar–H), 7.75–7.72 (d, *J* = 10.2 Hz, 2H, Ar–H), 7.61–7.59 (d, *J* = 8.2 Hz, 2H, Ar–H), 7.52 (s, 1H, Ar–H), 7.29–7.26 (m, 2H, Ar–H), 5.80 (s, 1H, NH), 3.31–3.25 (q, *J* = 7.6 Hz, 2H, **CH_2**CH_3), 3.17–3.11 (q, *J* = 6.8 Hz, 2H, **CH_2**CH_2), 2.40 (s, 3H, **CH_3**–C═N), 1.80–1.74 (m, 2H, CH_2), 1.12–1.08 (t, *J* = 7.6 Hz, 3H, **CH_3**CH_2), 1.02–0.99 (t, *J* = 6.5 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 172.5 (C═O), 159.6, 151.0, 146.6 (2 × CH), 142.7, 134.9, 132.3, 127.4, 124.1 (2 × CH), 120.8, 117.0, 116.8, 110.4, 54.1, 29.7, 25.4, 20.1 (CH_3), 15.3 (CH_3), 13.4 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 146.6 (2 × CH), 142.7 (CH), 134.9 (CH), 132.3 (CH), 124.1 (2 × CH), 117.0 (CH), 116.8 (CH), 20.1 (CH_3), 15.3 (CH_3), and 13.4 (CH_3). Negative signals are 54.1 (CH_2), 29.7 (CH_2), and 25.4 (CH_2). UV–vis.: λ_{max} (nm)/ log ε_{max} (mol^{-1} cm^{-1}): 209 (4.55), 236 (4.45), 269 (4.28), 314 (4.07). IR (cm^{-1}): νN-H 3356, νC–H arom.3050, νC–H aliph. 2925, νC–H aliph. 2804, νC═O 1684, νC═C 1620, νC═C 1605, νC═N 1589, νCH_3 deformation 1461, νC–N 1248, ν = C–H bending 984, νAr–H 745.

N′-(1-(2-oxo-2H-chromen-3-yl)ethylidene)-2-propylquinoline-4-carbohydrazide (4l). Microwave assisted reaction of **3** (3.0 g, 13 mmol) with 3-acetylcoumarin (2.44 g, 13 mmol) for 3 min afforded *N′*-(1-(2-oxo-2*H*-chromen-3-yl)ethylidene)-2-propylquinoline-4-carbohydrazide**, 4l** as yellow solid. Yield 4.41 g, (85%); m.p. > 300°C; $C_{24}H_{21}N_3O_3$ (399.44): Anal. Found: C, 72.22; H, 5.19; N, 10.71% Calc.: C, 72.16; H, 5.30; N, 10.52%. ^{1}H NMR (δ, ppm in DMSO-d_6): 8.64 (s, 1H, Het–H), 7.96–7.94 (d, *J* = 8.0 Hz, 1H, Ar–H), 7.75–7.72 (d, *J* = 10.2 Hz, 2H, Ar–H), 7.70–7.66 (m, 2H, Ar–H), 7.52 (s, 1H, Ar–H), 7.29–7.26 (dd, J_1 = 10.20 Hz, J_2 = 12.50 Hz, 2H, Ar–H), 5.80 (s, 1H, NH), 3.31–3.27 (t, *J* = 6.8 Hz, 2H, **CH_2**CH_2), 2.40 (s, 3H, **CH_3**–C═N), 1.80–1.74 (m, 2H, CH_2), 1.02–0.99 (t, *J* = 6.8 Hz, 3H, **CH_3**CH_2). ^{13}C NMR (δ, ppm in DMSO-d_6): 177.2 (C═O), 172.5 (C═O), 161.5, 159.6, 155.2, 151.0, 142.7, 139.1, 135.2, 134.9, 132.3, 129.2, 127.4, 120.8, 117.0, 116.8, 114.0 (2 × CH), 111.9, 110.4, 54.1, 29.7, 20.1 (CH_3), 13.4 (CH_3). DEPT 135 (δ, ppm in DMSO-d_6): Positive signals are 161.5, 155.2, 142.7 (CH), 134.9 (CH), 132.3 (CH), 129.2 117.0 (CH), 116.8 (CH), 114.0 (2 × CH), 20.1 (CH_3), and 13.4 (CH_3). Negative signals are 54.1 (CH_2) and 29.7 (CH_2). UV–vis.: λ_{max} (nm)/log ε_{max} (mol^{-1} cm^{-1}): 215 (4.06), 221 (4.44), 251 (4.68), 317 (4.09), 428 (4.04). IR (cm^{-1}): νN–H 3410, νC–H arom. 3010, νC–H aliph. 2925, νC–H aliph. 2890, νC═O ester 1745, νC═O 1685, νC═C 1620, νC═N 1575, νCH_3 deformation 1460, νC–N 1243, ν = C–H 968, νAr–H 725.

Antimicrobial activity assay. The antimicrobial assay of the compounds **4a–l** was investigated against six organisms, namely *S. aureus*, *B. lichenformis*, *M. varians*, *E. coli*, *P. vulgaris*, and *P. aeruginosa*. Antibacterial sensitivity testing was carried out on using agar diffusion method while MIC test was determined by serial dilution method as described by a standard method [25] as shown in the supplementary information.

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DECLARATION OF INTEREST

The authors confirm that this article content has no conflict of interest.

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SUPPORTING INFORMATION

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