RESEARCH ARTICLE Am. J. PharmTech Res. 2014; 4(4) ISSN: 2249-3387

AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Anthelmintic and Anti-Bacterial Studies of Synthesized Azetidinones Derivatives of Quinazolinones

Bhavna Kandpal[1*], Jyotsna Meshram[1], Ambareen Shaikh[1]

1. Department of chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur, Maharashtra, India.

ABSTRACT

The present work deals with the synthesis of azetidinone derivatives of quinazolinones and the structures of the compounds obtained have been established based on spectral (IR, ^{1}H NMR, ^{13}C NMR and Mass) data. The present study also involves in vitro anthelmintic and antibacterial activity of the synthesized derivatives a few strains (gram positive and gram negative) of bacteria. All the compounds showed against moderate to satisfactory activities.

Keywords: Azetidinones, Quinazolinones, Anthelmintic, Antibacterial.

*Corresponding Author Email: bhavnakandpal21@gmail.com

Received 14 April 2014, Accepted 10 May 2014

Please cite this article as: Kandpal B *et al.*, Anthelmintic and Anti-Bacterial Studies of Synthesized Azetidinones Derivatives of Quinazolinones. American Journal of PharmTech Research 2014.

INTRODUCTION

Azetidin -2 - one, a four-membered cyclic lactam also known as β-lactam skeleton has been recognized as a useful building block for synthesis of a large number of organic molecules by exploiting the strain energy associated with it [1]. A large number of 3-chloro monocyclic β –lactam having substitution at positions 1 and 4 possess powerful anti-bacterial [2], anti-microbial [3],anti-fungal [4] anti-tubercular [5] and anticonvulsant [6] activity. The β-lactam ring is the main feature of the most of the penicillin and other antibiotics.

Quinazolinones and their derivatives are versatile nitrogen containing heterocyclic compounds which have been known as a promising class of biologically active compounds and has broad spectrum medicinal values such as analgesic [7], anti-inflammatory [8], antibacterial [9], anti-fungal [10], anti-cancer [11] etc. The stability and pharmacological properties of Quinazolinones has inspired us to synthesize quinazolone substituted amide linkage containing azetidinone and their derivatives with the objective to enhance the biological activities. In our present work we have synthesized a **series N- (3- chloro- 2 - (substituted)- 4-oxoazetidin-1-yl -4-(4-oxo-2-phenylquinazolin-3 (4H) -yl)** benzamide in good yield.

The synthesized ethyl 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzoate **1** on reaction with hydrazine hydrate(2) gave 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzohydrazide **3**, on reaction with substituted benzaldehydes **4** in the presence of glacial acetic acid as a catalyst yielded (substituted benzylidene) - 4 - (4 – oxo – 2 – phenyl quinazoline – 3 (4H) -yl) benzohydrazide **5** which on further reaction with triethylamine and chloroacetyl chloride yielded N- (3- chloro- 2 -(substituted)- 4-oxoazetidin-1-yl -4-(4-oxo-2-phenylquinazolin-3 (4H) -yl) benzamide **(6a-6j)**.All the synthesized compounds were studied for their in vitro anthelmintic and antibacterial activities.

MATERIALS AND METHODS

All reagents and solvents are of analytical grade and used directly. All melting points were determined by open tube capillaries method and are uncorrected. IR spectra (υ_{max} in cm^{-1}) were recorded on Schimadzu-IR Prestige 21 spectrophotometer using KBr technique. ^1H NMR spectra were recorded on Bruker-Advance (400 MHz), spectrophotometer using DMSO-d_6 solvent and TMS as internal standard. Mass spectra were recorded on Waters Micromass Q-T of micro spectrometer. TLC was carried out using Silica gel G procured from Merck. Solvent used was petroleum ether and ethyl acetate (7:3).

Synthesis of 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzohydrazide [12]

A mixture of ethyl 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzoate (1 mol) and hydrazine hydrate (2mol) were refluxed for in absolute ethanol for 6 to 8 h. When the excess of alcohol was distilled off, the quinazolone hydrazides separated out as solid masses. These hydrazides were recrystallized from ethanol.

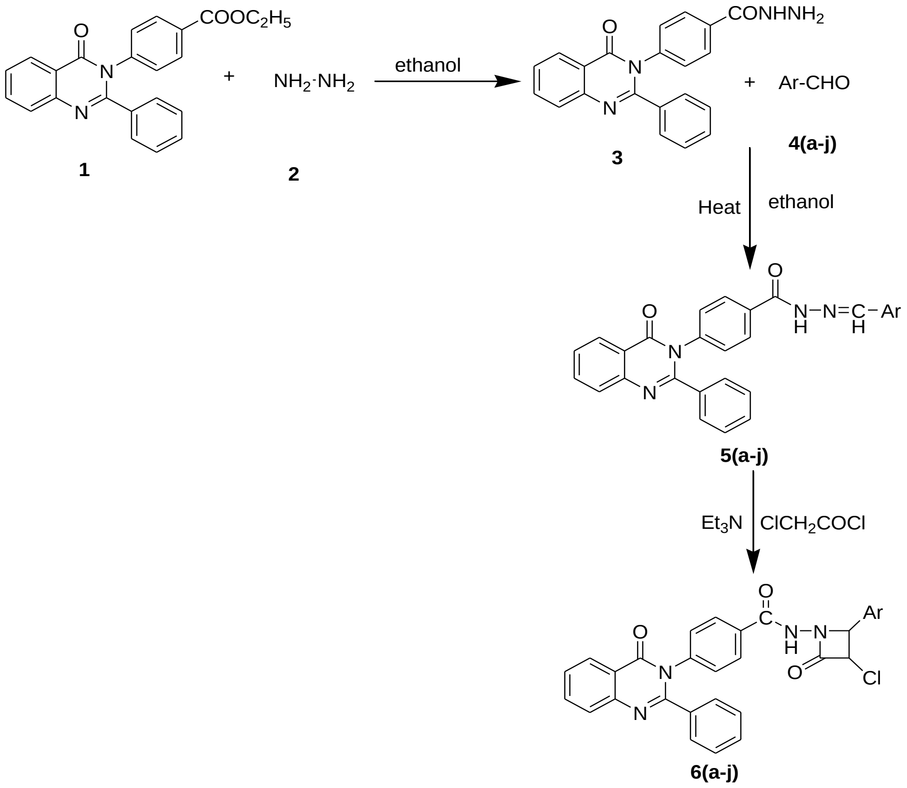
Synthesis of (Substituted benzylidene) -4- (4-oxo - 2 – phenyl quinazoline – 3 (4H) - yl benzohydrazide [13]

A mixture of 4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzohydrazide(0.01mol) and substituted benzaldehyde (0.01mol) was refluxed in methanol(60.0 mL) in the presence of a catalytic amount of glacial acetic acid for 10 h. After reaction completion, the reaction mass was cooled to room temperature, and poured onto ice-cold water with vigorous string. The separated solid was filtered, washed with 5% sodium bisulfite solution to remove excess aldehyde & recrystallized from chloroform.

Synthesis of N- (3- chloro- 2 - (substituted)- 4-oxoazetidin-1-yl -4-(4-oxo-2-phenylquinazolin-3 (4H) -yl) benzamide [14]

A mixture of compound (5a-5j) (0.01mol) chloroacetyl chloride (0.01mol) in dioxane and Triethylamine were stirred at 0-5^0 C for 3 h. The progress of reaction was monitored by TLC using hexane and methanol (8:2) mixture as eluent .The solid obtained after removal of 1, 4-dioxane was recrystallized from ethanol.

SCHEME 1



	Ar		Ar
6a	2-HOC_6H_4	6f	4-ClC_6H_4
6b	4-HOC_6H_4	6g	4-$MeOC_6H_4$
6c	2-$NO_2C_6H_4$	6h	4-$N(Me)_2C_6H_4$
6d	3-$NO_2C_6H_4$	6i	C_4H_4O
6e	2-ClC_6H_4	6j	C_9H_7N

CHARACTERIZATION DATA OF COMPOUNDS 6(a-j)

N-(3-chloro-2-(2-hydroxyphenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6a)

IR KBr (cm^{-1}): 3118 (Ar C-H), 2973 (C-H), 1695 (-C=O), 766 (-C-Cl), 1610 (-C=N), 1357 (C–N stretch tertiary). MS: m/z 536 (M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 5.4 (s, 1H, -OH), 7.6(s, 1H, -NH), 4.3(d, 1H,-N-CH), 5.6 (d, 1H, Cl-CH), 7.4-7.9 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7(C-20), 164.9(C-21), 163.5(C-22), 64.4(C-23),52.4(C-25),130.9(C-26),154.1(C-27),115.7(C-28),128.2(C-29),121.2(C-30),128.4(C-31).Elemental analysis (Cald): C=67.10, H=3.94, N=10.43; Found: C=67.04, H=3.90, N=10.38%.

N-(3-chloro-2-(4-hydroxyphenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2- phenylquinazolin-3(4H)-yl) benzamide (6b)

IR KBr (cm^{-1}): 3005(Ar C-H), 2955 (C-H), 1695 (-C=O), 780(-C-Cl), 1610 (-C=N), 1355 (C–N stretch tertiary). MS: m/z 536 (M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 5 (s, 1H, -OH), 7.6(s, 1H, -NH), 4.14(d, 1H,-N-CH), 5.44 (d, 1H, Cl-CH), 7.18-7.34 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7(C-20),164.9(C-21),163.5(C-22),64.1(C-23),62.4(C-25),136.1(C-26),128.4(C-27),115.7(C-28), 156.5 (C-29),115.7(C-30),128.4(C-31).Elemental analysis (Cald): C=67.10, H=3.94, N=10.43; Found: C=67.06, H=3.89, N=10.39%.

N-(3-chloro-2-(2-nitrophenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6c)

IR KBr (cm^{-1}): 1550(-NO$_2$), 3076(Ar C-H), 2955 (C-H), 1695 (-C=O), 775(-C-Cl), 1610 (-C=N), 1337 (C–N stretch tertiary). MS: m/z 565 (M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 7.6(s, 1H, -NH), 4.11(d, 1H,-N-CH), 5.38 (d, 1H, Cl-CH), 7.18-7.34 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7(C-20),164.9(C-21),163.5(C-22),63.1(C-23),53.8(C-25),137.5(C-26),147(C-27),120.9 (C-28),127.7(C-29),134.7(C-30),127.9(C-31).Elemental analysis (Cald): C=63.67,H=3.56, N=12.37; Found: C=63.54, H=3.55, N=12.34%.

N-(3-chloro-2-(3-nitrophenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6d)

IR KBr (cm^{-1}): 1445(-NO_2), 3095(Ar C-H), 2955 (C-H), 1695 (-C=O), 775(-C-Cl), 1610 (-C=N), 1334 (C–N stretch tertiary). MS: m/z 565 (M^+, 100%).^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ/ppm: 7.5(s, 1H, -NH), 4.11(d, 1H,-N-CH), 5.88 (d, 1H, Cl-CH), 7.18-7.34 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7(C-20),164.9(C-21),163.5(C-22),64.1(C-23),61.4(C-25),144.4(C-26),122.2(C-27),148.2(C-28) ,119.1 (C-29), 129.5(C-30),133.1(C-31).Elemental analysis (Cald): C=63.67 ,H=3.56, N=12.37; Found: C=63.52, H=3.51, N=12.32%.

N-(3-chloro-2-(2-chlorophenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6e)

IR KBr (cm^{-1}): 3008(Ar C-H), 2962 (C-H), 1738 (-C=O), 775(-C-Cl), 1613 (-C=N), 1336 (C–N stretch tertiary). MS: m/z 555(M^+, 100%).^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ/ppm: 7.6(s, 1H, -NH), 4.08(d, 1H,-N-CH), 5.12 (d, 1H, Cl-CH), 7.20-7.41 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15), 121.7 (C-16), 127.7 (C-17) ,129.8 (C-18),127.7 (C-19),121.7 (C-20),164.9 (C-21),163.5 (C-22),63.6 (C-23),53.3(C-25),143.5(C-26),132.3(C-27),128.7 (C-28),128.2(C-29), 126.7 (C-30),128.4(C-31).Elemental analysis (Cald): C=64.87 ,H=3.63, N=12.77; Found: C=64.78, H=3.60, N=12.75%.

N-(3-chloro-2-(4-chlorophenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide) (6f)

IR KBr (cm^{-1}): 3094(Ar C-H), 2989(C-H), 1679 (-C=O), 762(-C-Cl), 1619(-C=N), 1338 (C–N stretch tertiary). MS: m/z 555(M^+, 100%).^{1}H NMR (400 MHz, DMSO-*d*$_6$) δ/ppm: 7.6(s, 1H, -NH), 4.19(d, 1H,-N-CH), 5.23 (d, 1H, Cl-CH), 7.18-7.72 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8 (C-18),127.7 (C-19),121.7 (C-20),164.9 (C-21),163.5(C-22),64.1(C-23),62.4(C-25),141.6(C-26),128.4(C-27),128.7(C-28),132.3(C-29),128.7 (C-30),128.4(C-31).Elemental analysis (Cald): C=64.87 ,H=3.63, N=12.77; Found: C=64.78, H=3.59, N=12.73%.

N-(3-chloro-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6g)

IR KBr (cm^{-1}): 3093(Ar C-H), 2948 (C-H), 1695(-C=O), 768(-C-Cl), 1613 (-C=N), 1336 (C–N stretch tertiary). MS: m/z 537(M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 3.73 (s,3H,-OCH$_3$),7.4(s, 1H, -NH), 4.06(d, 1H,-N-CH), 5.32 (d, 1H, Cl-CH), 7.74-7.98 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7 (C-20),164.9 (C-21),163.5 (C-22), 64.1 (C-23),62.4 (C-25),135.8 (C-26), 128 (C-27), 114.1 (C-28),158.7 (C-29),114.1 (C-30),128.1 (C-31), 55.9 (C-32).Elemental analysis (Cald): C=66.98 ,H=4.12, N=10.41; Found: C=66.94, H=4.09, N=10.36%

N-(3-chloro-2-(4-(dimethyl amino) phenyl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenyl quinazo lin-3(4H)-yl) benzamide (6h)

IR KBr (cm^{-1}): 3077(Ar C-H), 2986 (C-H), 1690(-C=O), 763(-C-Cl), 1610(-C=N), 1335 (C–N stretch tertiary). MS: m/z 563(M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 2.85(s, 6H,-N(CH$_3$)$_3$),7.2(s, 1H, -NH), 4.16(d, 1H,-N-CH), 5.28 (d, 1H, Cl-CH), 7.74-7.93 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7 (C-20),164.9 (C-21),163.5 (C-22), 64.1 (C-23),62.4 (C-25),133 (C-26), 127.9 (C-27), 114.1 (C-28),147.6(C-29),114.1 (C-30),127.9(C-31),40.3(C-32), 40.3(C-33).Elemental analysis (Cald): C=68.14,H=4.65, N=12.42; Found: C=68.10, H=4.62, N=12.40%

N-(3-chloro-2-(furan-2-yl)-4-oxoazetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6i)

IR KBr (cm^{-1}): 3078(Ar C-H), 2988(C-H), 1685(-C=O), 765(-C-Cl), 1698(-C=N), 1335 (C–N stretch tertiary). MS: m/z 510(M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 7.4(s, 1H, -NH), 4.09(d, 1H,-N-CH), 5.44 (d, 1H, Cl-CH), 6.24-7.9 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSO-d6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7 (C-20),164.9 (C-21),163.5 (C-22), 62.3 (C-23),60.1(C-25),151.1 (C-26), 105.9(C-27), 110.0(C-28),141.5(C-29).Elemental analysis (Cald): C=65.82,H=3.75, N=10.97; Found: C=65.79, H=3.73, N=10.88%.

N-(3-chloro-2-oxo-4-(quinolin-2-yl)azetidin-1-yl)-4-(4-oxo-2-phenylquinazolin-3(4H)-yl) benzamide (6j)

IR KBr (cm^{-1}): 3078(Ar C-H), 2988(C-H), 1685(-C=O), 765(-C-Cl), 1698(-C=N), 1335 (C–N stretch tertiary). MS: m/z 572(M$^+$, 100%).^{1}H NMR (400 MHz, DMSO-d_6) δ/ppm: 7.4(s, 1H, -NH), 4.11(d, 1H,-N-CH), 5.44 (d, 1H, Cl-CH), 6.24-7.9 (m, 16H, Ar-H). ^{13}C NMR (400 MHz, DMSOd6, δ / ppm) :164 (C-1),160.9 (C-2) ,120.9 (C-3), 128.8 (C-4),127.4 (C-5) ,133.5 (C-6), 122.4 (C-7), 151.3 (C-8), 128.7 (C-9), 126.1 (C-10), 128.9 (C-11),130.2 (C-12),128.9 (C-13),126.1 (C-14), 136.5 (C-15),121.7 (C-16),127.7 (C-17),129.8(C-18),127.7(C-19),121.7 (C-20),164.9 (C-21),163.5 (C-22), 64.1 (C-23),62.8(C-25),159.3(C-26), 122.1(C-27), 135.6(C-28),126.5(C-29), 127.8(C-30), 125.9(C-31), 129.7(C-32), 128.4(C-33), 146.8(C-34).Elemental analysis (Cald): C=69.29,H=3.88, N=12.24; Found: C=69.15, H=3.78, N=12.33%.

PHARMACOLOGICAL ACTIVITIES

Anthelmintic activity of synthesized derivatives (6a-6j)

Adult earthworm was collected from moist soil and washed with normal saline to remove all the faecal matter and waste surrounding their body. The earthworms of 3-5 cm in length were used in present investigations. The worms were divided into the respective groups containing six-earth worms in each group. All the prototypes were dissolved in minimum quantity of anthelmintic activity of 1-substituted imidazoles on 2%v/v Tween80 and the volume was adjusted to 10 ml with normal saline for making the concentration of 5, 10 and 20mg/ml. All the prototypes and the standard drug solutions were freshly prepared before commencement of the experiments. All the earthworms were washed in normal saline solution before they were released into 10 ml of respective formulation as follows, vehicle (2% v/v Tween 80 in normal saline), Albendazole(ALB) and Piperazine Citrate (PZC) were used at 20 mg/ml and prototypes (5, 10 and 20 mg/ml).The anthelmintic activity was determined in six observations. Six worms of about the same size per petridish were used. 5mg/ml. They were observed for their spontaneous motility and evoked responses. Observations were made for the time taken to paralysis and death of individual worms. Paralysis was said to occur when the worms do not revive even in normal saline. Death was concluded when worms lost their motility followed with fading away of their body colour.All the results were expressed as mean ± S.E.M and compared with *student't' test*. The data were statistically analyzed by one –way analysis of variance and $P<0.05$ were considered as significant.

Antibacterial activity of synthesized derivatives (6a-6j)

The synthesized derivatives **(6a-6j)** were screened for antibacterial activities in vitro against S. aureus, B. subtilis, E. coli and K. pneumonia using well diffusion method .The Ampicillin and Streptomycin were used as standard drugs and ethanol was used as negative control. In this technique Petri dishes of agar medium plate were prepared by pouring melted agar inoculated with above mentioned strains of bacteria. After the Agar settled, wells were made in the agar Petri dishes. Solutions of standard (1mg/ml) and test samples (500 µg /ml) were prepared using ethanol as a solvent in sterile cotton plugged tubes. Sample size for the entire compound and standard was fixed at 0.1 ml. The wells of agar Petri dishes were impregnated with standard and test compounds in the sterile condition. All the nutrient agar plates were incubated at 37°C for 24 to 48 hrs after which the plates were observed for zone of inhibition.

RESULTS AND DISCUSSION

The target compounds *N- (3- chloro- 2 - (substituted)- 4-oxoazetidin-1-yl -4-(4-oxo-2-phenylquinazolin-3 (4H) -yl) benzamide* derivatives (6a-6j) were synthesized by three step synthetic protocol highlighted in Scheme1. Reaction progress was duly monitored by TLC and the products were isolated by simple and usual work up with 66 to 88% of yield economy. The yields, melting points and micro analytical data of the synthesized compounds are listed in Table 1. The structures of the compounds (6a-6j) were deduced from their elemental analyses and their IR, ^{1}H, ^{13}C NMR and mass spectral data. The solid state IR spectra of these compounds reveal a characteristic aromatic stretching at around 3038-3074 cm^{-1}. Sharp carbonyl stretching vibration was also recorded around1600-1900 cm^{-1}. The stretching vibrations for amide group (CONH) are recorded at around 1665-1680cm^{-1}. Spectra also cleared the information regarding the frequency ranging between 1525-1650 cm^{-1} and 1335-1350 cm^{-1} which corresponds to the presence of (-C=N) and (C–N stretch tertiary) respectively. The 1H NMR spectra were recorded in DMSO-d6 at room temperature using TMS as internal standard. The NMR data of all compounds reveal multiplets peak between 6.24 and 9.24 owing to the presence of aromatic protons. The spectra showed characteristic singlet at around 7.8 ppm for -CONH in the compounds. All other peaks in the IR and NMR spectra are in well agreement with the contents of functionalities in the synthesized molecules. The mass spectra of these compounds displayed a molecular ion peak at appropriate m/z values, which were corresponding well with the respected molecular formulas. All the compounds have given the satisfactory elemental analysis.

Table 1: Physical Data of Compounds (6a-6j)

Compounds	**Ar**	**M P (^{0}C)**	**Yield (%)**	**Mol. formula**	**Mol.wt**
6a	2-HOC$_6$H$_4$	158	73	$C_{30}H_{21}ClN_4O_4$	536
6b	4-HOC$_6$H$_4$	163	71	$C_{30}H_{21}ClN_4O_4$	536
6c	2-NO$_2$C$_6$H$_4$	116	66	$C_{30}H_{20}ClN_5O_5$	565
6d	3-NO$_2$C$_6$H$_4$	118	69	$C_{30}H_{20}ClN_5O_5$	565
6e	2-ClC$_6$H$_4$	167	88	$C_{30}H_{20}Cl_2N_4O_3$	555
6f	4-ClC$_6$H$_4$	164	81	$C_{30}H_{20}Cl_2N_4O_3$	555
6g	4-MeOC$_6$H$_4$	129	74	$C_{31}H_{23}ClN_5O_3$	537
6h	4-N(Me)$_2$C$_6$H$_4$	141	69	$C_{32}H_{26}ClN_5O_3$	563
6i	C_4H_4O	197	65	$C_{28}H_{19}ClN_4O$	510
6j	C_9H_7N	165	78	$C_{33}H_{22}ClN_5O_3$	572

In-vitro anthelmintic activity

All the synthesized compounds (**6a-6j**) acquired the anthelmintic activity at minimal dose of 5mg/ml. Compound **6e**, **6i** and **6j** had shown its significant activity at 5mg/ml for time taken to paralysis and death compared to the standard drugs Albendazole and Piperazine citrate used at

20mg/ml respectively. The interpreted results were given in **Table 2.** At the concentration of 10mg/ml compounds **6a**, **6e**, **6i** and **6j** exhibited their significant action for time taken to paralysis and death. While increasing the concentration (20mg/ml), compounds **6i** and **6j** significantly reduced the paralysis and death time as well.

Table 2 Anthelmintic Activity of Compounds (6a-6j)

S. No.	Comp.	Paralysis time(min)			Death time(min)		
		5mg/ml	10mg/ml	20mg/ml	5mg/ml	10mg/ml	20mg/ml
1	6a	17.1±0.001	11.8±0.02	10.5±0.008	24.7±0.05	18.7±0.005	13.9±0.009
2	6b	38.63±0.05	33.5±0.09	32.01±0.03*	41.7 ±0.07	26.9±0.01*	23±0.001*
3	6c	26.56±0.06	24.8±0.01*	20.9±0.008	35.8±0.009	28.6±0.001	21.7±0.09
4	6d	41.0±0.08	37.9±0.003	33.86±0.08	49.23±0.07	40.6 ±0.08*	36.8±0.01*
5	6e	19.1±0.05*	13.89±0.09	11.9±0.001	23.4±0.003	19.76±0.07*	12.8±0.03*
6	6f	18.8±0.004	15.78±0.07	12.9±0.008	24.8±0.009	21.7±0.08	17.5±0.01
7	6g	13.6±0.001	10.8±0.007	8.47±0.003	16.3±0.001	14.5±0.006*	11.8±0.004*
8	6h	45.7±0.003	41.1±0.009	39.7±0.001*	48.9±0.001	43.1±0.002	40.3±0.001
9	6i	11.1±0.005	8.67±0.003	6.9±0.006	12.9±0.01	11.1±0.06*	10.67±0.01*
10	6j	12.8±0.009	10.4±0.005*	7.6±0.008	15.9±0.007	12.3±0.008*	11.2±0.007*
11	PZC			5.06±0.26			9.39±0.02
12	ALB			4.32±0.28			8.35±0.05

$*$ $P<0.05$ against control at fourth hour. Results were expressed as mean ± S.E.M for n=6 rats in each group. The data were statistically analyzed by one way analysis of variance (ANOVA) and compared with student's' test

In-vitro antibacterial activity

The antibacterial activities of compounds **(6a-6j)** have been carried out using some strains of bacteria using well diffusion method. Ampicillin and streptomycin were taken as a standard drug. The compounds were tested against two strains of each of gram positive and gram negative bacteria. The interpreted results were given in **Table 3**. The screening results of antibacterial activity suggested that the compounds **(6a-6j)** showed moderate to excellent antibacterial activity at the concentration of 500μg/ml. Compounds **6e, 6g**, **6i** and **6j** were found to be potent antibacterial agents against all the tested strains of bacteria **6a**, **6b** and **6d** were moderately active, **6f** is slightly active only against S. aureus while **6h** is inactive against all strains of bacteria.

Table 3 Antibacterial Activity of Compounds (6a-6j)

Compounds	Gram Positive Bacteria		Gram Negative Bacteria	
	S.aureus	*B.subtilis*	*E.coli*	*K.pneumonia*
6a	++	++	+++	++
6b	++	-	+	+
6c	-	+	-	-
6d	-	+	+	+
6e	++	+++	++	+++
6f		+	-	+

6g	+++	+++	+++	++
6h	-	-	-	-
6i	+++	++	+++	+
6j	+++	+++	+++	++
Ampicillin	+++	++	+++	++
Streptomycin	+++	+++	+++	+++

Key to symbols: inactive = - (inhibition zone < 5 mm); slightly active = + (inhibition zone 5-10 mm); moderately active = + + (inhibition zone 10-15 mm); Highly active = + + + (inhibition zone > 15 mm).

CONCLUSION

Synthesis of N- (3- chloro- 2 - (substituted) - 4-oxoazetidin-1-yl – 4 - (4 – oxo – 2 - phenylquinazolin-3 (4H) -yl) benzamide derivatives were synthesized in good yield. All the compounds were characterized on the basis of elemental and spectral data. These compounds showed poor to excellent anthelmintic activity in comparison to reference drug Albendazole and pyrazole citrate at a dose of 20mg. These compounds were also found to be potent antibacterial agents at a concentration of 500 µg /ml against gram positive and gram negative strains of bacteria in comparison to reference drug (Ampicillin and Streptomycin). Thus, the target compound and its derivatives can be used as potent drugs helmintic and bacterial infection.

ACKNOWLEDGEMENT

The authors thank Head, Department of Chemistry, Rashtrasant Tukadoji Maharaj Nagpur University, Nagpur for providing laboratory facilities and Director, SAIF, Chandigarh for providing necessary spectral data. Special thanks are due to the Head, Department of Biotechnology, Sindhu Mahavidyalaya Nagpur, India for providing antimicrobial screening.

REFERENCES

1. Rajasekaran. A, Periasamy. M, Venkatesan. S. Synthesis. Characterization and biological activity of some novel azetidinones. J. Dev. Biol. Tissue Engg. 2010; 2(1):5-13.
2. Sathe Bhushankumar. S, Saner. S.S, Md.Rageeb and Md.Usman. Synthesis and biological screening of various different derivatives of fluorobenzothiazole incorporated azetidinones. J. Pharma. Sci. Innov. 2012; 1(2):43-46.
3. Bhat.K I, Chaithanya. S K, Satyanarayana.P D and Kalluraya.B. The synthesis and antimicrobial study of some azetidinone derivatives with the Para- anisidine moiety. J. Serb. Chem. Soc. 2007; 72(5): 437-442.
4. Mehta.P, Davadra. P, Pandya. JR, Joshi. HS. Synthesis, characterization and antimicrobial activity of 2-azetidinone derivatives of benzimidazoles. Inter. Lett. Chem. Phy .Astro. 2014; 11(2):81-88.

5. Sharma.R, Samadhiya.P, Srivastava.SD and Srivastava.SK. Synthesis and pharmaceutical importance of 2-azetidinone derivatives of phenothiazine.J.Chem.Sci 2012; 124(3):633-637.
6. Kumar.V, M.M.J, Yogananda.R, Snehalatha, Shameer. H, Jayachandran. E, Sreenivasa. GM. Synthesis and characterization of novel n-substituted-3-chloro-2-azetidinones as potential anticonvulsant agents. J Bio Med Sci. and Res. 2009; 1(1):1-10.
7. Rajveer.CH, Kumaraswamy, Sudharshini and Rathinaraj.SB. Synthesis of some 6-bromo quinazolinone derivatives for their pharmacological activities. Int J Pharma and biosciences 2010; 1(3):1-10
8. Chandrika.MP, Yakaiah.T, Rao.ARR, Narsaiah.B, Reddy.NC, Shridar.J and Rao.V. Synthesis of novel 4, 6-disubstituted quinazoline derivatives, their anti-inflammatory and anti-cancer activity (cytotoxic) against U 937 leukemia cell lines .Euro J Med Chem 2008 ;43:846-852.
9. Tiwari.AK, Singh. VK, Bajpai.A, Shukla.G, Singh.S and Mishra.AK. Synthesis and biological properties of 4-(3H)-quinazolone derivatives. Euro J Med Chem 2009; 42:1234-1238.
10. Grover G and Kini SG. Synthesis and evaluation of new quinazolone derivatives of nalidixic acid as potential antibacterial and antifungal agents. Euro J Med Chem 2007; 41:256-26.
11. Tiwari.AK Mishra.AK, Bajpai.A, Mishra.P, Sharma.RK, Pandey.VK and Kumar.VK. Synthesis and pharmacological study of novel pyrido-quinazolone analogues as anti-fungal, antibacterial, and anticancer agents. Bioorg Med Chem Lett. 2007; 16: 4581-4585.
12. Parmar. SS and Arora. RC: Synthesis of quinazolone hydrazides as monoamine oxidase inhibitors. Canadian Journal of chemistry 1966; 44: 2100-2102.
13. Shah.TJ and. Desai.VA: Synthesis of some novel fluorinated 4-thiazolidinones containing amide linkages and their antimicrobial screening. Arkivoc 2007; 14:218-228.
14. Taj. T, Kamble. RR, Gireesh. T and Badami.BV. An expeditious green synthesis of Schiff bases and azetidinones derivative with 1, 2, 4-triazoles. J.Chem.Sci. 2011; 123(5):657-666.