https://doi.org/ 10.33472/AFJBS.6.9.2024.1251-1264

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Synthesis and characterization of Newer Quinazoline Derivatives by using parallel synthesizer and evaluating their antimicrobial and sedative and hypnotic activities

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ARTICLE INFO

Volume 6,Issue 9, 2024

Received:22 Mar 2024

Accepted : 27 Apr 2024

doi: 10.33472/AFJBS.6.9.2024.1251-1264

ABSTRACT:

Designing a highly effective class of innovative antimicrobial agents poses a significant challenge in the field of pharmaceutical research and development. The ongoing research focuses on discovering a new series of quinazoline and its derivatives with various substitutions. The synthetic process involves a couple of steps to prepare the quinazoline compound by reacting an amphoteric aromatic acid like Anthranilic acid the desired chlorine compound Benzoyl chloride in presence of highly flammable, weakly alkaline, heterocyclic organic compound Pyridine, resulting in the formation of 2-phenyl-benzoxazine-4-one which is an intermediate compound which is further allowed to react with the hydrazine hydrate along with the pyridine and upon reflux for 3 hours will yield the desired quinazoline compound 3-Amino-2-phenyl-quinazoline-4-one. All the synthesized compounds undergo characterization use.

Techniques such as IR spectroscopy, Proton nuclear magnetic resonance (1HNMR), Carbon ^{13}C NMR , Mass spectral methods. Furthermore, these compounds are screened for their antimicrobial activity against bacterial strains such as E. coli, Pseudomonas aeruginosa, Bacillus subtilis, and fungal strains like Aspergillus, and candida albicans.

KEY WORDS:- Quinazoline derivatives, green synthesis, anti-bacterial activity, Zone of Inhibition

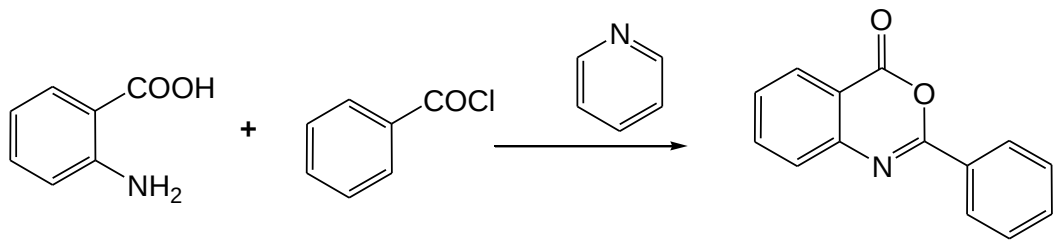
INRODUCTION:

Quinazoline derivatives are an important group of heterocyclic compounds that have a naphthalene ring with one or more carbon atoms substituted by nitrogen. Quinazoline is formed by combining benzene and pyrimidine rings, which is why it is sometimes called benzo pyrimidine. It is closely related to quinoline, naphthalene, and benzo thiophene. Quinazoline has a molecular weight of 130.15 and a molecular formula of $C_8H_6N_2$ [1], and it exists as a colorless powder. Its melting point is 48 °C (118 °F; 321 K) and boiling point is 241.8±9.0 °C. Quinazoline and its derivatives are soluble in organic nonpolar solvents such as dimethyl sulfoxide and dimethyl formamide. The demand for greener methods prompts the employment of a variety of ecologically friendly reaction conditions, including the reusable solid acids to replace polluting inorganic acids catalyst like sulfuric or hydrochloric acids and room temperature avoidance in media healing. Since solid acids offer several advantages, including ease of handling, less plant deterioration and ecologically acceptable waste disposal methods, they play a significant role in the transformation of organic matter. They have different biological activities like Anti-neoplastic[2], Anti-tubercular[3], Anti-anxiety[4], Anti-inflammatory[5], Anti-amoebic[6], Anti-depressant[7], Anti-fungal[8], Anti-bacterial[9], Anti-protozoal[10], Anti-diabetic[11], Analgesic[12], and used in other neurodegenerative disorders[13], and used as fluorescent dying agent, electroluminescent materials, chemical switches, and semi-conductors.

MATERIALS AND METHODS:

This experiment employed synthetic-grade chemicals and solvents that were acquired from National Scientific Products and Delta Scientific Company. The reaction progress was monitored via melting point and TLC. Melting point was carried out on Lab India melting point apparatus. Infrared (IR) spectra were obtained using a Bruker IR Affinity FTIR spectrophotometer employing the KBr pellet method. Proton Nuclear Magnetic Resonance (^{1}H NMR), Carbon Nuclear Magnetic Resonance (13C NMR) spectra were acquired on Bruker 500 MHz NMR Spectrometer (NIPER Hyderabad) employing appropriate deuterated solvents and reported in parts per million.

Experimental Procedures:



Anthranilic acid **benyol chloride** **2-phenyl-4H-benzo[1,3]oxazin-4-one**

Step:- 01

Step:- 01 Synthesis of 2-Phenyl- [3,1]-benzoxazine-4-one.

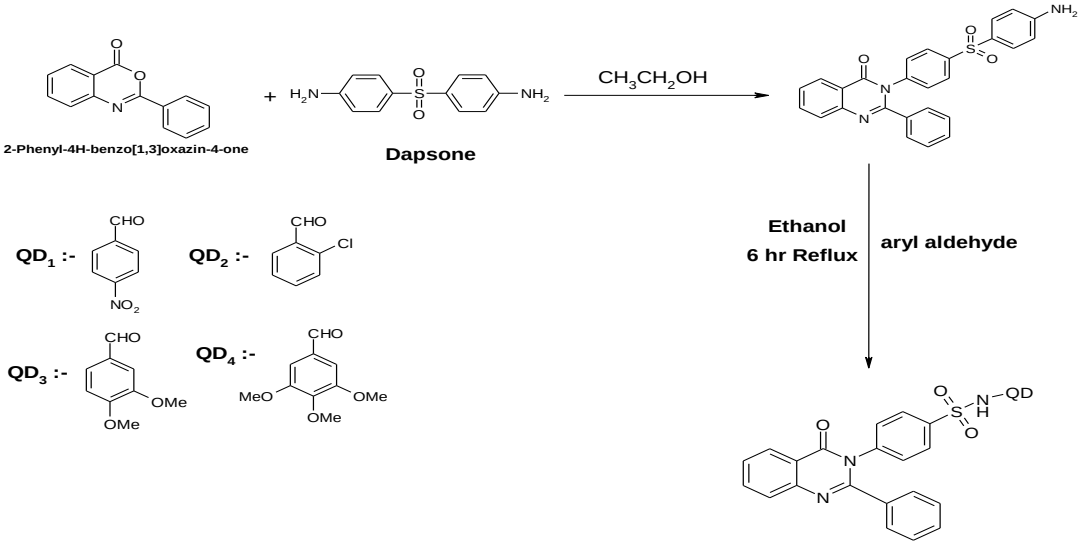
0.1 mol of Anthranilic acid was dissolved in 30 ml of dry pyridine by gentle shaking in a breaker. To this solution mixture add 0.2 mol benzoyl chloride dissolved in dry pyridine (30 ml) by constant stirring. This addition process is done about a half an hour. After adding the resultant solution, the mixture was subjected to vigorous stirring for one hour mechanically. It is left aside for an hour at room temperature and the solution mixture is treated with 10 % sodium bicarbonate. Addition of sodium bicarbonate is continued till the effervescence due to the evolution of carbon dioxide ceased. The separated solid is allowed to settle down at the bottom of the beaker and subjected for vacuum filtration to separate out the solid from the solution mixture. It is washed repeatedly with the cold water until there is no smell of pyridine and unreacted benzoyl chloride. The solid product was dried overnight and recrystallized from dilute ethanol to get pure sample (2-phenyl- [3,1] benzoxazine-4-one) as white crystalline powder. Yield 80 %; MP; 196-198 °C.

IR (KBr, Vmax, Cm -1): 3044 (C–H), 1760 (C=O), 1605 (C=N), 1466 (C=C), 1312 (C–N). ^{1}H NMR: - CH (1-benzene): 7.26; CH (benzylidenimin): 7.29-8.11; (C=O)-O): 0.21,0.34,0.87. ^{13}C NMR: - CH (1-benzene)- 122.2-135.3, C (1-benzene) – 116.4, 129.9, 154.1, C (1-imine)- 156.1,C (1-amide)- 159.5, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=O)-O – 0.1, 5.2, 1.6, 2.1.

Synthesis of 3-[4-(4-aminobenzenesulfonyl) phenyl]-2-phenylquinazolin-4(3H)-one

(0.01 moles, 3.34 gm) of 2-phenyl- [3,1] benzoxazine-4-one is dissolved in 25 ml of ethanol in an RBF to this add 0.03 moles dapsone (7.44 gm) to it. The mixture was refluxed for 4 hr. and after cooling pour the mixture in to ice-cold water and separate the solid by using vacuum filter. This solid is dried and recrystallized from ethanol. Yield 72 %, MP: - 144 °C.

IR (KBr, Vmax, Cm -1): 3052 aromatic, 2922 aliphatic (C-H), 1761 (C=O), 1594 (C=N), 1493 (C=C), 1443 (C–N), 1380 (O=S=O), 3349 (R-NH2).



Scheme :- 01

Synthesis of 3-[4-(4-amino-substituted benzene sulfonyl) phenyl]-2-phenylquinazolin-4(3H)-one derivatives.

A mixture of 3-[4-(4-aminobenzenesulfonyl) phenyl]-2-phenylquinazolin-4(3H)-one (4.55 g, 0.01 mol), 0.01 mol aryl aldehyde (4-Nitro benzaldehyde, 2-Chloro benzaldehyde) and 20ml ethanol was refluxed for 6 hr. The resultant mixture was poured into ice-water. The separated solid was filtered and washed with water. Recrystallization of the crude product from ethanol afforded colorless crystals of aryl aldehyde derivative of 3-[4-(4-aminobenzenesulfonyl) phenyl]-2-phenylquinazolin-4(3H)-one. Recrystallization of the crude product from ethanol to obtain colorless crystals of aryl aldehyde derivative of 3-[4-(4-aminobenzenesulfonyl) phenyl]-2-phenylquinazolin-4(3H)-one. The yield of the product is 65%.

3-(4-((E)-4-(4-nitrobenzylideneamino)phenylsulfonyl)phenyl)-2-phenylquinazolin-4(3H)-one (QD1):

IR (KBr, Vmax, Cm -1): 3075, aromatic, 2918, aliphatic (C-H), 1793 (C=O), 1593 (C=N), 1399 (C-N), 1299 (O=S=O), 1337 (O=N=O). 1H NMR: - CH (Benzene) :7.26; CH (benzylidenimin): 7.62 ,7.29, 8.11; (C=O)-N: 0.18, 0.69, 0.25 ; -NC(=O): 0.02,0.38 ; -S(=O)(=O): 0.64,0.17 ; N(=O)(=O): 0.26, 0.93. 13C NMR: CH (1-benzene)- 121.2-133.5, C (1-benzene) – 120.9-151.3, C (1-imine)- 164, C (1-amide)- 160.9, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, CH (1-Imine)- 160.1, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, 1-N(=O)=O – 0.9, 4.9,19.9, 6.1, 1-S(=O)(=O) – 2.0, 1.0, 5.0, 10.0.

3-(4-((E)-4-(2-chlorobenzylideneamino)phenylsulfonyl)phenyl)-2-phenylquinazolin-4(3H)-one (QD2):

IR (KBr, Vmax, Cm -1): 3060, aromatic, 2935, aliphatic (C-H), 1761 (C=O), 1587(C=N), 1452 (C-N), 767 (C-Cl), 1263 (O=S=O). 1H NMR: - CH (Benzene) :7.26; (C=O)-N: 0.18, 0.25, 0.69; -NC(=O): 0.38, 0.02; Cl (from 1-Benzene): 0.01-0.12, -S(=O)(=O); 0.64, 0.17; -O-C(benzene) 0.11, 0.49; CH(benzylidenimin): 7.62, 7.29, 8.11; CH_3 (methyl): 0.86.13C NMR: CH (1-benzene)- 114.4-133.5, C (1-benzene) – 120.9-163.0, C (1-imine)- 164, C (1-amide)- 160.9, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-O-C – 14.4, 1.0, 33.5, 7.7, CH (1-Imine)- 160.1, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, CH3 (Aliphatic)- 55.9, 1-S(=O)(=O) – 2.0, 1.0, 5.0, 10.0.

3-(4-((E)-4-(3,4,5-Trimethoxybenzylideneamino)phenylsulfonyl)phenyl)-2-phenylquinazolin-4(3H)-one (QD3):

IR (KBr, Vmax, Cm -1): 3066, aromatic, 2932, aliphatic (C-H), 1756(C=O), 1587 (C=N), 1459 (C-N), 1131 (O-CH_3), 1238 (O=S=O). 1H NMR: - CH (Benzene) :7.26; (C=O)-N: 0.18, 0.25, 0.69; -NC(=O): 0.38, 0.02; -S(=O)(=O); 0.64, 0.17; -O-C(benzene) 0.11, 0.49; CH(benzylidenimin): 7.62, 7.29, 8.11; CH_3 (methyl): 0.86.13C NMR: CH (1-benzene)- 114.4-133.5, C (1-benzene) – 120.9-163.0, C (1-imine)- 164, C (1-amide)- 160.9, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-O-C – 14.4, 1.0, 33.5, 7.7, CH (1-Imine)-

160.1, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, CH3 (Aliphatic)- 55.9, 1-S(=O)(=O) – 2.0, 1.0, 5.0, 10.0.

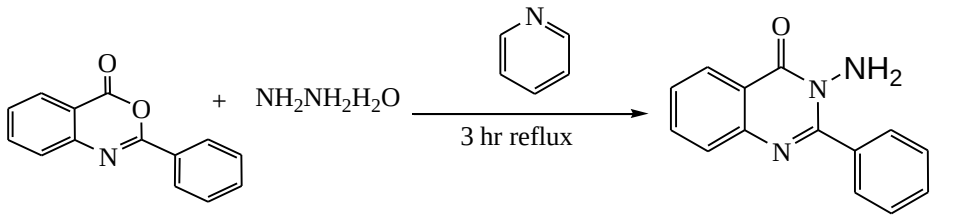
3-(4-((E)-4-(3,4,-Dimethoxybenzylideneamino)phenylsulfonyl)phenyl)-2-phenylquinazolin-4(3H)-one (QD4):

IR (KBr, Vmax, Cm -1): 3065, aromatic, 2944, aliphatic (C-H), 1754 (C=O), 1584 (C=N), 1457 (C-N), 1138 (O-CH_3), 1265 (O=S=O). 1H NMR: - CH (Benzene) :7.26; (C=O)-N: 0.18, 0.25, 0.69; -NC(=O): 0.38, 0.02; -S(=O)(=O); 0.64, 0.17; -O-C(benzene) 0.11, 0.49; CH(benzylidenimin): 7.62, 7.29, 8.11; CH_3 (methyl): 0.86.13C NMR: CH (1-benzene)- 114.4-133.5, C (1-benzene) – 120.9-163.0, C (1-imine)- 164, C (1-amide)- 160.9, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-O-C – 14.4, 1.0, 33.5, 7.7, CH (1-Imine)- 160.1, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, CH3 (Aliphatic)- 55.9, 1-S(=O)(=O) – 2.0, 1.0, 5.0, 10.0.

Step:- 02 Synthesis of 3-amino-2-phenyl-quinazoline-4(3H)-one

0.01 mol of 2-phenyl- [3,1]-benzoxazine-4-one and 0.01 mol hydrazine hydrate added in 50 ml of dry pyridine and refluxed for 3 hours. Later the reaction mixture was poured into the ice-cold water containing few drops of hydrochloric acid, keep that beaker aside for a period to settle down the solid and the separation of the solid is done by using vacuum filter and washed with water repeatedly. It was dried and recrystallized from ethanol. Yield 50 %; MP; 204 – 206 °C.

IR (KBr, Vmax, Cm -1): 3314 (s), 1596 (b) (NH2), 3061 (C-H), 1654 (C=O), 1596 (C=N), 1438 (C=C), 1312 (C–N). ^{1}H NMR: - CH (1- Benzene): 7.26; CH (benzylidenimin): 7.29-8.11; (C=O)-O): 0.18-0.69; NH_2 (amine): 2. ^{13}C NMR: CH (1-benzene)- 122.4-133.5C (1-benzene) – 120.9, 128.7, 151.3, C (1-imine)- 164, C (1-amide)- 160, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0.



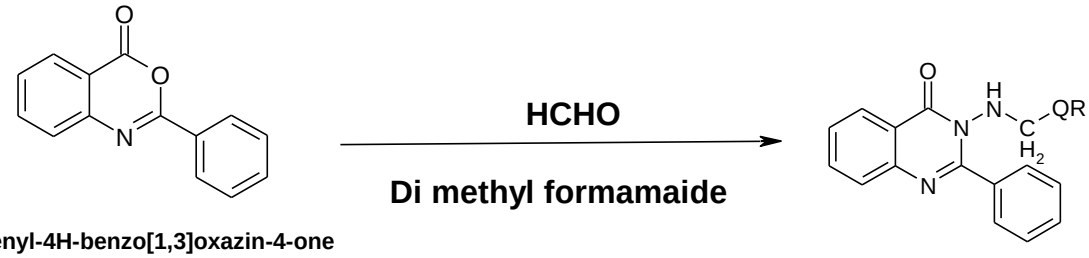
2-Phenyl-benza[1,3]-oxazin-4-one **3-amino-2-phenyl-quinazoline**

Step :- 02

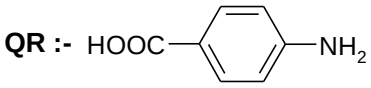
General procedures for Synthesis of 2-phenyl-3-(substituted methylamino) -(3H)-quinazoline-4-one.

Add 1ml of formaldehyde and 0.26ml, 0.005 mol(R:- para amino benzoic acid) drop by drop with stirring to form a slurry of 3-amino-2-phenyl-quinazoline-4-one (0.81 g, 0.005 mol) in

15 ml dimethylformamide. The reaction mixture was refluxed for about 30 min. Allow it to cool and pour this reaction mixture into ice-cold water, the solid obtained was filtered, washed with water, dried overnight, and recrystallized from ethanol.



2-Phenyl-4H-benzo[1,3]oxazin-4-one



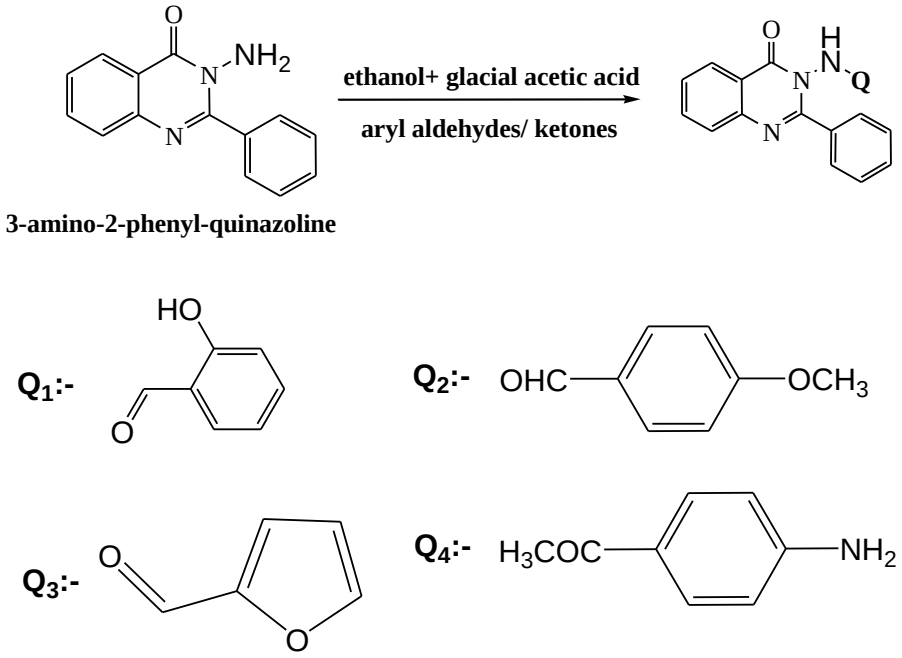
Scheme :- 02

3-((4-carboxy-phenylamino) methylamino)-2-phenylquinazolin-4(3H)-one:(QR_1)

IR (KBr, Vmax, Cm -1): 3117 (aromatic), 3059 (aliphatic), **(**C-H), 1671 (C=O), 1598 (C=N), 1521 (C=C), 1104 (C–N), 2863 (OH-COOH), 3342 (N-H),1778 (C-O), 1261 (N-N), 1104 (C-N). 1H NMR: - CH (Benzene) **:**7.26**;** (-C=O)-N:0.18,0.25,0.69; CH_2(methylene): 1.37; NH (amine):2.00, NH (aromatic): 4.00; CH (benzylidenimin): 7.62,7.29; 1-N-C: 0.22, 0.87; 1-C(=O) O: 0.21; OH(-COOH): 11.00. 13C NMR: CH(1-Benzene): 113-130,131.1. C(1-Benzene): 151.3,120.9,128.7,152.8,118.7; C(1-imine): 164.0; C(1-amide): 161.0; CH_2 (aliphatic): 67.3.

General procedures for the synthesis of 3-(substituted benzylidene amino)-2-phenyl quinazoline-4-(3H) one.

Take equal moles (0.01 moles) of 3-amino-2-phenyl-quinazoline-4(3H)-one and aryl aldehyde or ketone in 20 ml ethanol in a Round bottom flask. To this add glacial acetic acid and adjust pH to 4-4.5 and then reflux for 60 min. The reaction mixture was poured into ice water to allow the solid to settle. The solid is filtered by using a vacuum filter.



Scheme :- 03

3-(2-hydroxybenzylideneamino)-2-phenylquinazolin-4(3H)-one (Q1):

IR (KBr, Vmax, Cm -1): 3059, aromatic, 2925, aliphatic (C-H), 1657 (C=O), 1601 (C=N), 1161 (C-N), 1037 (C-C), 1037 (N-N), 3236 (OH). 1H NMR: - CH (Benzene) :7.26; CH (benzylidenimin): 7.29-8.11; OH (aromatic): 5; (C=O)-N: 0.18-0.69; -O from (1-Benzene) 0.17-0.53. 13C NMR: 166.75- C=O. 151.07- C=N, 159.79- C (Imine), 138.70- Ar C

3-(4-methoxy-benzylideneamino)-2-phenylquinazolin-4(3H)-one (Q2):

IR (KBr, Vmax, Cm -1): 3063, aromatic, 2946, aliphatic (C-H), 1819 (C=O), 1653 (C=N), 1241 (C-N), 1438 (C-O), 1522 (C=C), 3508 (N-H). 1H NMR: - CH (Benzene) :7.26; (C=O)-N: 0.18-0.69; -O-C from 1-Benzene: 0.11-0.49; CH_3 (methyl): 0.86.13C NMR: 77.02:- C-OH ,127.83:- CH (Benzene), 134.29:- C (Benzene), 165.13:- C=O

3-((furan-2-yl)methyleneamino)-2-phenylquinazolin-4(3H)-one (Q3):

IR (KBr, Vmax, Cm -1): 3054, aromatic, 2881, aliphatic (C-H), 1793 (C=O), 1671 (C=N), 1147 (C-N), 1131 (N-N), 1561 (C=C), 1329 (C-O). 1H NMR: - CH (Benzene) :7.26; CH (benzylidenimin): 7.29-8.11; (C=O)-N: 0.18-0.69, CH (2-furan) : 6.30. 13C NMR: CH (1-benzene)- 122.4-133.5, C (1-benzene) – 120.9-151.3, C (1-imine)- 164, C (1-amide)- 160, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, CH (2-Furan) – 109.5, 109.9, 143.9, C (2-Furan) – 149.1.

3-(4-amino-phenyl-methyl-imino)-2-phenylquinazolin-4(3H)-one (Q4):

IR (KBr, Vmax, Cm -1): 1340 , 2987 (C-H), 1743 (C=O), 1552 (C=N), 1473 (C=C). 1H NMR: - CH (Benzene) :7.26; CH (benzylidenimin): 7.29-8.11; (C=O)-N: 0.18-0.69;

CH_3(methyl): 0.86; NH_2 (aromatic C-NH) : 4.00. 13C NMR: CH (1-benzene)- 116.4-133.5, C (1-benzene) – 120.9-151.3, C (1-imine)- 164, 168.7, C (1-amide)- 160, 1-C=N – 0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-N – 0.8, 13.4, 18.2, CH3 (Aliphatic)- 19.5, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0.

2-(4-oxo-2-phenylquinazolin-3(4H)-yl)benzoic acid :

IR (KBr, Vmax, Cm -1): 3050, aromatic, 2929, aliphatic (C-H), 1619 (C=N), 1291 (C-N), 1133 (N-N), 1496 (C=C).). 1H NMR: - CH (Benzene) :7.26; CH (benzylidenimin): 7.29-8.11; (C=O)-N: 0.18-0.69; -N-C=O : 0.02-0.38; (C=O)-O : 0.21-0.87; OH(COOH): 11. 13C NMR: CH (1-benzene)- 121.5-134.2, C (1-benzene) – 115.6-151.3, C (1-imine)- 164, C (1-amide)- 160.9, 1-C=N – 2.7,0.5,0.1,2.3, 1-C(=N)-N – 4.4, 2.6,0.1,1.4, 1-N-C=O – 9.7, 8.1, 0.2, 4.4, C (1-Carboxyl) – 169.4, 1-C(=O)-N – 0.1, 3.4, 1.2, 5.0, 1-C(=O)-O – 2.1, 1.7, 0.1, 5.2, 1.6.

***In Vitro* anti-bacterial activity:**

Complete procedures are performed in sterile area. The antibacterial activity of naphthalene substituted sulphonamide derivatives was performed by the Disc diffusion method with respect to the cultured organisms. Three organisms used in the study are Bacillus subtills, pseudomonas aeruginosa, E.coli. The nutrient agar medium is used for disc diffusion method. For Disc diffusion method, 20 ml of agar medium was transferred into the Petri plate and kept aside until the medium gets solidify. Discs were dipped in different test solution having concentrations of 25µg/mL, 50µg/mL, 75µg/mL, 100µg/mL, and standard drug (ciprofloxacin) of concentration 50 µg/mL. After that Petri plates are placed in the BOD incubator for 24 hours at a temperature of 37°C. The zones are measured by using zone diameter reader.

***In Vitro* anti-fungal activity**:

Complete procedures are performed in sterile area. The antifungal activity of dapsone derivatives was performed by the Disc diffusion method with respect to the cultured organisms. In this czapek dox agar medium is used as nutrient medium for growth of fungi such as Candida albicans and Aspergillus niger. 20 ml of nutrient agar medium was transferred into the Petri plate and kept aside until the medium gets solidify. After solidification, discs were dipped in different test solution having concentrations of 20mg/ml, 50mg/ml,80mg/ml,100mg/ml, and standard drug of concentration50mg/ml. Petri plates are then kept in the BOD incubator for 24 hrs. at 37ºc temperature. The zones were measured using the zone diameter reader.

***In-vivo* sedative and hypnotic activity**:

Experimental design:
Wistar rats were divided into 4 groups of each group containing Six animals.
Group – I Control (0.9% Saline)
Group – II Standard (Diazepam 2mg/kg)

Group – III Test - I (10 mg/Kg)

Group – IV Test - II (10 mg/Kg)

IR actiphotometer
An IR (Infrared) actophotometer is a device used to measure the activity of organisms, typically animals, by detecting their movement in response to infrared light. The mechanism of an IR actophotometer involves several key components:

- ***Infrared Light Source:*** The actophotometer emits infrared light into the testing chamber. This light is typically not visible to the human eye but can be detected by sensors.
- ***Testing Chamber:*** This is the space where the organisms are placed for observation. It is usually enclosed to prevent external light interference and to create a controlled environment for the experiment.
- ***Detection Sensors:*** These sensors are sensitive to infrared light and are positioned strategically around the testing chamber to capture the movement of organisms. When an organism moves within the chamber, it interrupts the infrared light beams, which is detected by the sensors.
- ***Data Acquisition System:*** The signals from the detection sensors are sent to a data acquisition system, which records the interruptions in the infrared light beams. This data is then processed to quantify the activity of the organisms over time.

Procedure
Carefully introduce the rats into the testing chamber. Be gentle to minimize stress, which could affect their behavior. Allow the organisms to acclimate to the testing chamber for a predetermined period, typically ranging from 15 minutes to an hour. This allows them to habituate to the new environment. Start the data acquisition system to begin recording the activity of the organisms. Depending on the experimental design, this may involve continuous monitoring over a specific time period or capturing activity in response to specific stimuli. 5 minutes observation time is kept as standard time for evaluation and the locomotor activity of the animal is assessed.

Results & Discussion:

Initially the starting compound, **2-Phenyl-[3,1]-benzoxazine-4-one** required for further synthesis was synthesized by reacting anthranilic acid with benzoyl chloride both dissolved in

pyridine and pour these solutions into a beaker and stir continuously for about half an hour and left aside for about an hour. The resultant mixture is treated with 10% sodium bicarbonate until the effervescence due carbon dioxide is ceased. This 2-Phenyl- [3,1]-benzoxazine-4-one along with 0.03moles dapsone were dissolving in ethanol and refluxed for 4hrs to obtain**3-[4-(4-aminobenzenesulfonyl)phenyl]-2-phenylquinazolin-4(3H)-one**which is further utilized to synthesize derivatives by treating with aryl aldehydes such as salicylaldehyde and anisaldehyde.

3-Amino-2-phenyl-quinazoline-4(3H)-one was synthesized in next step by treating 2-phenyl- [3,1]-benzoxazine-4-one and hydrazine hydrate by dissolving in pyridine refluxed for 3 hrs.For synthesis of quinazoline derivatives, 3-amino-2-phenyl-quinazoline-4-one was treated separately with formaldehyde, aniline, sulphanilamide, and diethyl amine and later cooled to obtain the **2-Phenyl-3-(substituted methylamino)-(3H)-quinazoline-4-one** derivatives. For the synthesis of **3-(substituted benzylidene amino)-2-phenyl quinazoline-4-(3H) one derivative,** 3-amino-2-phenyl-quinazoline-4(3H)-one which was synthesized earlier was treated with aryl aldehydes and ketones such as salicylaldehyde, anisaldehyde, furfuraldehyde, 4-aminoacetophneone, 4-nitobenaldehyde, 2-chlorobenzaldehyde.

Quinazoline and dapsone derivatives were synthesized and analyzed for their antibacterial, antifungal and antidiabetic activity. Melting points were recorded by using Thiel's tube. All reactions were monitored by thin layer chromatography on pre-coated silica gel and spots were visualized under UV light. The synthesized derivatives were confirmed by using infrared spectroscopy and 13CNMR.

The synthesized derivatives were tested against both gram positive bacterial strain such as *Bacillus subtilis* and gram-negative strains of bacteria such as *Pseudomonas aeruginosa & E.coli.* The concentrations of test were 25µg/mL, 50µg/mL, 75µg/mL, and standard concentration is 50µg/mL were prepared by dissolving in Dimethylsulphoxide (DMSO). Ciprofloxacin was used as standard for antibacterial activity. In case of antibacterial activity, the zone of inhibition ranged from 10.5-16.5 for gram positive strains and 13.4-18.5 for gram negative strains of bacteria.

Anti-fungal activity was performed for the synthesized derivatives against candida albicanas and Aspergillus niger by using czepac dox agar medium. These derivatives showed good activity against fungi in comparison with standard drug ketoconazole. The concentrations of test were 25µg/mL, 50µg/mL, 75µg/mL, and standard concentration is 50µg/mL were prepared by dissolving in Dimethylsulphoxide (DMSO). The zone of inhibition for test compounds ranged from 14.6-18.2.

In addition to antibacterial and antifungal, Sedative & hypnotic activity was performed to analyze the locomotor activity of the synthesized derivatives. The locomotor counts of treatment groups visualized the sedative or hypnotic activity that resembles the anti-anxiety of animal. QD1 treatment group shows more potent sedative activity similar to that of standard drug when compared with control and QD2.

Table-1: Anti-bacterial activity by Zone of inhibition(mm)

Derivatives	Concentration	Bacillus subtilis	E. coli	Pseudomonas aeruginosa
Q_2	**25 µg/ml**	10.5	13.4	12.7
	50 µg/ml	12.3	15.3	15.4
	75 µg/ml	15.5	18.5	18.4
Q_3	**25 µg/ml**	10.7	14.6	13.4
	50 µg/ml	12.5	15.7	14.5
	75 µg/ml	14.6	17.3	17.9
QD_1	**25 µg/ml**	12.4	16.1	16.1
	50 µg/ml	14.7	18.4	17.5
	75 µg/ml	16.8	20,7	19.6
Ciprofloxacin (standard)	**50 µg/ml**	14.5	18.4	16.7

Table 2 :Anti-fungal activity by Zone of inhibition (mm)

Derivatives	Concentration	Candida albicanas	Aspergillus niger
Q_1	**20 µg/ml**	15.1	14.6
	50 µg/ml	16.3	15.5
	80 µg/ml	17.1	16.1
	100 µg/ml	18.5	17.8
QD_2	**20 µg/ml**	14.2	15.1
	50 µg/ml	16.3	16.3
	80 µg/ml	16.9	17.6
	100 µg/ml	18.1	18.2
Ketoconazole	**50 µg/ml**	16.8	17.9

Table 3 :

Observations of locomotor count in rats using IR actimeter

Group	Compound	Dose	Locomotor activity (IR movements)			
			0 Min	15 Min	30 Min	60 Min
I	Control	0.9% Saline	86	94	91	87
II	Standard (Diazepam)	2mg/kg	84	63	41	36
III	QD1	10mg/kg	81	74	51	58
IV	QD2	10mg/kg	78	65	62	64

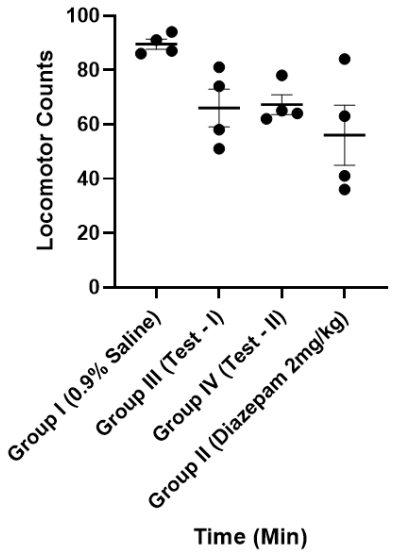


Fig 1: Comparison graph indicating the IR counts of locomotor activity in rats

Conclusion:

A series of quinazoline and dapsone substituted derivatives were synthesized using green synthetic techniques such as parallel synthesizer. Subsequent antimicrobial testing against gram-positive organism, *Bacillus subtilis* and gram-negative organism, *Pseudomonas aeruginosa*, *Escherichia coli* using the disc diffusion method revealed significant activity of

Q2, Q3 and QD1 against gram +ve bacteria in comparison with gram -ve bacteria Q1 and QD2 showed effective Antifungal activity against Candida albicans and Aspergillus niger. The locomotor counts of treatment groups visualized the sedative or hypnotic activity that resembles the anti-anxiety of animal. QD1 treatment group shows more potent sedative activity similar to that of standard drug when compared with control and QD2.

Acknowledgment:

The authors are thankful to management, principal, and staff members of Chalapathi Institute of Pharmaceutical Sciences (Guntur) for their continuous support and encouragement to carry out this research work.

Conflict of Interest:

The authors declare that there is no conflict of interests regarding the publication of this article.

References:

1. Karan, R.; Agarwal, P. Sinha, M.; Mahato, N. Recent Advances on Quinazoline Derivatives: A Potential Bioactive Scaffold in Medicinal Chemistry. ChemEngineering 2021, 5, 73. https://doi.org/10.3390/chemengineering5040073
2. Niu, Z.; Ma, S.; Zhang, L.;Liu, Q.; Zhang, S. Discovery of Novel Quinazoline Derivatives as Potent Antitumor Agents. Molecules 2022, 27, 3906. https://doi.org/10.3390/molecules27123906
3. KK Rajasekhar, ND Nizamuddin, Abdrrahman Shemsu Surur & Yenus Tadesse Mekonnen (2016) Synthesis, characterization, antitubercular and antibacterial activity, and molecular docking of 2,3-disubstituted quinazolinone derivatives, Research and Reports in Medicinal Chemistry, , 15-26, DOI: 10.2147/RRMC.S91474
4. Biswajit Dash (2019), SYNTHESIS AND ANTI-ANXIETY ACTIVITY OF SOME 7-CHLORO-3-[SUBSTITUTED (AMINO/PHENYL AMINO)] - 2 – PHENYL QUINAZOLIN-4 (3H)-ONE/THIONE DERIVATIVES. Universal journal of pharmaceutical sciences and research 5 (1), 18-28. DOI: 10.21276/UJPSR.2019.05.01.512
5. Mohamed F. Zayed, Memy H. Hassan (2013), Synthesis and biological evaluation studies of novel quinazolinone derivatives as antibacterial and anti-inflammatory agents. Saudi Pharmaceutical Journal (2014) 22, 157–162, http://dx.doi.org/10.1016/j.jsps.2013.03.004
6. Saba Tariq, Fernando Avecilla, Guru Prasad Sharma, Neelima Mondal, Amir Azam,Design, synthesis, and biological evaluation of quinazolin-4(3H)-one Schiff base conjugates as potential antiamoebic agents,Journal of Saudi Chemical Society, Volume 22, Issue 3,2018, Pages 306-315, ISSN 1319-6103, https://doi.org/10.1016/j.jscs.2016.05.006.
7. Wang HJ, Wei CX, Deng XQ, Li FL, Quan ZS. Synthesis and evaluation on anticonvulsant and antidepressant activities of 5-Alkoxy-tetrazolo[1,5-a]quinazolines.

Arch Pharm (Weinheim). 2009 Nov;342(11):671-5. doi: 10.1002/ardp.200900119. PMID: 19856330.

8. Chavan B. B., Bhalawane P.P., Kolsure A. K.1, Chabukswar A. R. Synthesis and Evaluation of Some New 4, 6- Disubstituted Quinazoline Derivatives for Antimicrobial and Antifungal Activities. Asian Journal of Biomedical and Pharmaceutical Sciences; 04 (33); 2014; 43-46.
9. F.A.; Alshammari, M.B.; Noreldein, S.G.; Darwesh, O.M. Discovery of Quinazoline-2,4(1H,3H)-Dione Derivatives as Potential Antibacterial Agent: Design, Synthesis, and Their Antibacterial Activity. Molecules 2022, 27, 3853. https://doi.org/10.3390/molecules27123853
10. Mendoza-Martínez C, Correa-Basurto J, Nieto-Meneses R, Márquez-Navarro A, Aguilar-Suárez R, Montero-Cortes MD, Nogueda-Torres B, Suárez-Contreras E, Galindo-Sevilla N, Rojas-Rojas Á, Rodriguez-Lezama A, Hernández-Luis F. Design, synthesis, and biological evaluation of quinazoline derivatives as anti-trypanosomatid and anti-plasmodial agents. Eur J Med Chem. 2015;96:296-307. doi: 10.1016/j.ejmech.2015.04.028.
11. Barmak A, Niknam K, Mohebbi G. Synthesis, Structural Studies, and α-Glucosidase Inhibitory, Antidiabetic, and Antioxidant Activities of 2,3-Dihydroquinazolin-4(1H)-ones Derived from Pyrazol-4-carbaldehyde and Anilines. ACS Omega. 2019 Oct 25;4(19):18087-18099. doi: 10.1021/acsomega.9b01906.
12. Alafeefy AM, Kadi AA, Al-Deeb OA, El-Tahir KE, Al-Jaber NA. Synthesis, analgesic, and anti-inflammatory evaluation of some novel quinazoline derivatives. Eur J Med Chem. 2010 Nov;45(11):4947-52. doi: 10.1016/j.ejmech.2010.07.067.
13. Haghighijoo Z, Zamani L, Moosavi F, Emami S. Therapeutic potential of quinazoline derivatives for Alzheimer's disease: A comprehensive review. Eur J Med Chem. 2022 Jan 5;227:113949. doi: 10.1016/j.ejmech.2021.113949. Epub 2021 Oct 27. PMID: 34742016.
14. Noolvi, Malleshappa & Patel, Harun. (2013). Synthesis, method optimization, anticancer activity of 2,3,7-trisubstituted Quinazoline derivatives and targeting EGFR-tyrosine kinase by rational approach 1st Cancer Update. Arabian Journal of Chemistry. 6. -. 10.1016/j.arabjc.2010.12.031.
15. Kumar KS, Ganguly S, Veerasamy R, De Clercq E. Synthesis, antiviral activity and cytotoxicity evaluation of Schiff bases of some 2-phenyl quinazoline-4(3)H-ones. Eur J Med Chem. 2010 Nov;45(11):5474-9. doi: 10.1016/j.ejmech.2010.07.058. Epub 2010 Aug 6. PMID: 20724039; PMCID: PMC7115544.
16. Alagarsamy, Veerchamy & Sankaranarayanan, Murugesan & Kumarasamy, Dhanabal & Murugan, M & E, De. (2007). Antihiv, antibacterial and antifungal activities of some novel 2-methyl-3-(substituted methylamino)-(3H)-quinazolin-4-ones. Indian Journal of Pharmaceutical Sciences. 69. 10.4103/0250-474X.33167.
17. Thilagavathi, R.; Kavitha, H.P.; Arulmozhi, R.; Babu, S.M. Synthesis of 3-{4-[4-(Benzylideneamino)benzenesulfonyl]- phenyl}-2-phenylquinazolin-4(3H)-one. Molbank 2009, 2009, M589. https://doi.org/10.3390/M589