Educational Administration: Theory and Practice
2024, 30(1), 1619-1628
ISSN: 2148-2403
https://kuey.net/

Research Article

"Synthesis, Characterization And In Silico Studies Of Novel Substituted Azetidinone, Substituted Thiazolidinone Containing Naphthalene Moiety, With Their Biological Activity"

Gaurav Kumar*[1], Indu Singh[1a] Sanjeev Kumar Bhatt[2], Nancy[3], Nitin[4], Deepak Kumar Gautam[5], Amrish Soam[6],

[1*,2,3,4,5,6] Research Scholar, Department of Chemistry, Meerut College, Meerut, Utter Pradesh

[1a]Associate Professor, Department of Chemistry, Meerut College, Meerut, Utter Pradesh

***Corresponding author: -Gaurav Kumar (gauravkumar1133@gmail.com)**

Citation: Gaurav Kumar, et.al (2024) "Synthesis, Characterization And In Silico Studies Of Novel Substituted Azetidinone, Substituted Thiazolidinone Containing Naphthalene Moiety, With Their Biological Activity", *Educational Administration: Theory and Practice, 30(1), 1619-1628*
Doi: 10.53555/kuey.v30i1.6467

ABSTRACT

A novel class of compounds (8-12) of azetidinone and (13-17) derivatives of drug, thiazolidinone were synthesis. Among of them, Synthesis of novel compound 9, N-(3-chloro-2-oxo-4-(p-tolyl)azetidin-1-yl)-2-(naphthalen-2-ylamino)acetamide) of series (8-12) , and compound 15 , N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-2-(naphthalen-2-ylamino)acetamide of series (13-17) were showed valuable characteristic and efficacy as antibacterial activity. Chloro and nitro(compound no-10,11,51,16) substituted thiazolidinone derivatives were showed better biological activity as compare to standard drugs ciprofloxacin, for regarding this observation and same result find in molecular docking using Auto dock Vina against two proteins 4uro (DNA Gyrase b),3v7r (biotin protein ligase), heterocyclic compounds of these derivative are very useful in the field of medicinal chemistry. These derivatives of thiazolidinone as well as azetidinone nucleus possesses were show remarkable, better clinically efficacy with low toxicity. Purity of these derivatives were checked with the help of TLC. The structure of new synthesised compounds was identified and confirmed by elemental analysis, IR, NMR, and activity of new synthesised these drugs were screened for their antibacterial activity.

Keywords: Azetidinone, Thiazolidinone, Naphthalene, Biological activity. Molecular docking

Introduction:

The domain of heterocyclic chemistry has ascended to paramount importance in both medical and industrial spheres, catalyzed by the burgeoning recognition of its prospective applications in antibacterial, antifungal, and anti-inflammatory contexts. Heterocyclic compounds, owing to their diverse structures and reactivities, have emerged as pivotal entities in the quest for novel therapeutic agents. Among these, thiazolidenone and azetidenone derivatives, notably those incorporating the naphthalene moiety, have exhibited remarkable antibacterial efficacy. The synthesis of thiazolidenone derivatives, characterized by a five-membered ring containing sulfur and nitrogen atoms, has proven particularly successful in yielding compounds with potent antibacterial properties. Similarly, azetidenone derivatives, comprising a four-membered ring, have showcased noteworthy antibacterial, antifungal, and anti-inflammatory effects. The incorporation of the naphthalene moiety into these structures has further enhanced their antibacterial activity, emphasizing the significance of structural modifications in tailoring biological effects. Recent research endeavors have illuminated the antibacterial potential inherent in thiazolidenone and azetidenone derivatives, underscoring the need for continued exploration in this fertile ground. Building upon these insights, the present study proposes the synthesis of novel substituted thiazolidenone and azetidenone derivatives, specifically integrating the naphthalene moiety. This strategic modification is rooted in the anticipation that the resultant compounds will manifest heightened antibacterial efficacy, surpassing the performance of their predecessors. The rationale behind this synthetic pursuit lies in the multifaceted nature of heterocyclic compounds, which affords a myriad of possibilities for structural variations to optimize pharmacological attributes. By introducing the naphthalene moiety, we aim to capitalize on its proven enhancing effects on antibacterial activity, thereby contributing to

the ongoing discourse on the design and synthesis of effective antibacterial drugs. This research aspires not only to expand the repertoire of antibacterial agents but also to deepen our understanding of the intricate interplay between chemical structure and biological function, propelling the field towards innovative therapeutic interventions. In the ensuing sections, we delve into the synthetic methodologies employed, elucidate the structural characteristics of the designed derivatives, and present a comprehensive evaluation of their antibacterial efficacy. The outcomes of this study, we posit, will furnish valuable insights for the advancement of antibacterial drug development, fostering a nuanced comprehension of the intricate relationship between chemical structure and pharmacological effects.

In earlier and present time, our surrounding, we see different life treating infection cause by bacterial infection. Thiazolidinone naphthalene, azetidinone are useful structural requirement in the field of medicinal chemistry. Napthalene drug derivatives exhibit different biological activity like anti inflammatory[1,3] biological active receptor [2,4] antibacterial [5,8] as a effective enzyme [6] anti tublin agent [7] and thiazolidinone were show various activity ie. Various Biological activity [9,12,13,14]. And as a antifungal agent [10], antimicrobial agents, insecticidal properties [11]. And moiety of azetidinone also play a vital role in the field of meditational, these work as biological active agents [15,18,24,27,28].

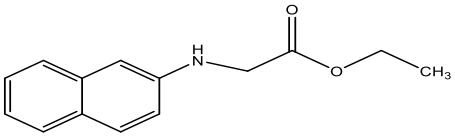
Thiazolidinone derivatives which contain small ring heterocyclic nitrogen, sulphur and oxygen electro negative active atom show better results due to their medicinal properties in biological system and it also affected by different rate, older drug show high frequency of renal toxicity and several adverse effect. However this research work, synthesised some novel drug derivatives 7-12, and 13-17 which shown the better to moderate antibacterial activity with less side effects.

Material and Method:

For synthesis work, different reagent were purchased commercially which are (AR) grade and purified standard procedure, a desire reagents dissolve in proper solvents at which reaction was completed at different condition. Melting points were recorded by ordinary glass capillary tube it may be incorrect. The homogeneity of all newly synthesized portion, purity and completion of reaction was confirmed by use of ordinary (TLC) plate coated with silica gel- G, spot were visualized after drying it and put it in iodine chamber, this plate comes with iodine vapor visualized the clear spot. IR spectra recorded with help Perkin Elmer spectrum and FTIR, and confirmed different portion of elemental parts. Beckman spectrometer check different value of UV, VIS (cm^{-1} max.) Brucker (300) DPX help to predict and recorded. ^1H NMR values and the value of chemical shift expressed in ppm (δ) scale using tetra methyl silane as an internal standard, it is use in $CDCl_3$ solvent.

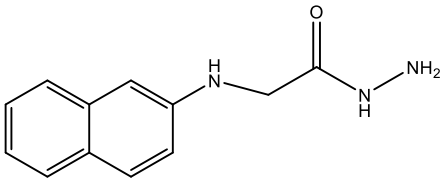
Experimental:

Formation of ethyl-2-(naphthalin-2-yl amino) acetate (1):



Organic compound naphthaline-2-amine (0.01mol) was transferred into 100 ml R B Flask and make a solution in acetone then add ethyl chloroacetate (0.01mol)and a pinch of potassium carbonate with continuously shaking it for 30 min o magnetic stirrer. then reflux on water bath. The reaction was monitored for desire form of molecules with help of TLC using silica gel. It was filtered, washed with cool H_2O. The final product was dried in vacuum desiccators to give white crystalline solid compound(1) yield 82% .IR (KBr) ν_{max} in cm^{-1}1604 C=C,1648 C-N, 3485 N-H, 1647 C=O, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ, 7.11-7.78 ,7×1H (m, =C-H naphthalene ,) , δ 6.28 ,1×1H (s, -$NHCH_2$) , δ 3.62 ,1×2H (d, -CH_2), δ 4.02 ,1×2H (d, -**CH_2**CH3) δ 1.21 ,1×3H (t, -CH_3), m/z: 227.13 (100.0%), 228.13 (16.2%),.

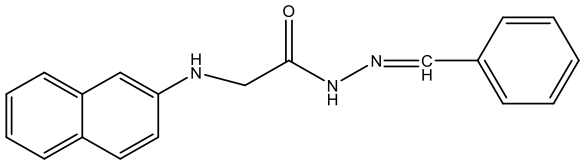
Formation of 2-(naphthalene-2-ylamino)acetohydrazide (2) :



Take the compound (1) and transferred into RB Flask of 250 ml and added 8 ml of ethyl alcohol then reaction mixture was shacked it for some time as 6 min at normal temperature then transferred hydrazine hydrate slowly with shaking.The reaction mixture reflux on water bath about 3h. Progress of reaction was recorded through (silica) TLC by using toluene and ethyl acetate solution as eluent in 4:1 ratio. It was visualize in iodine

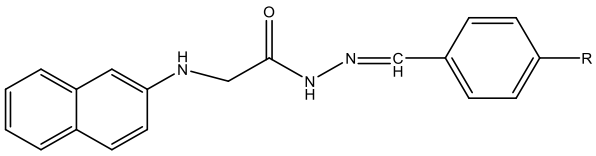
chamber. After completion, it put for some time to decrease the temp now it cooled, filtered & washed with distilled H_2O. It is dried and obtained compound 2.Yield 79%. IR (KBr) ν_{max} in cm^{-1} 1606 C=C,1650 C-N, 3480 N-H, 1645 C=O, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.10-7.79 ,7×1H (m, =C-H naphtha. ,) , δ 6.27 ,1×1H (t, -**NH**CH_2) , δ 3.62,1×2H (d, -**CH**$_2$NH), δ 3.41 ,1×2H (d, -NH_2), m/z: 215.11 (100.0%), 216.11 (13.0%),

3: N'-benzylidene-2-(naphthalen-2-ylamino)acetohydrazide (3):



Arylaldehyde and 2-3 drops of acetic acid was added to a 100 ml beaker which contained 2 in ethanol (20 ml) and heated and refluxed it about 6h. Product was filtered, washed with petroleum ether & recrystallized using suitable solvent to give compound (3).yield 72%. IR (KBr) ν_{max} in cm^{-1}1603 C=C,1652 C-N,1650 C=O , 3486 N-H, 1555 CH=N,3050 C-H, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.09-7.78 ,7×1H (m, =C-H naphtha. ,) , δ 6.25 ,1×1H (t, -**NH**CH_2) , δ 3.61,1×2H (d, -**CH**$_2$NH), δ 11.07 ,1×2H (d, -NHN), δ 8.47 ,1×1H (d, -CH=N), δ 7.55-7.76 ,5×1H (s, -CH = CHAr), m/z: 303.14 (100.0%), 304.14 (20.5%),

General process for formation of N-substitutedbenzylidene-2-(naphthalene-2-ylamino)acetohydrazide (4-7):



R =H, CH_3, Cl, NO_2, C_2H_5

Compound (2) and various substituted Arylaldehyde were taken similar pattern of step 3 are followed for synthesis Product obtained was filtered, washed with petroleum ether & recrystallized using suitable solvent to give compound (4-7).

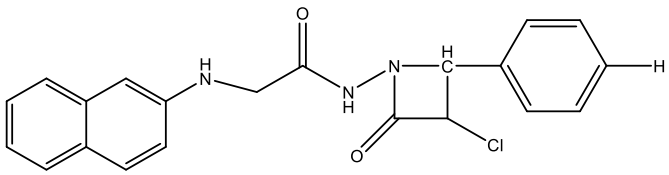
4: Yield 70% .IR (KBr) ν_{max} in cm^{-1}1605 C=C,1648 C-N, 1651 C=O ,3485 N-H, 1550 CH=N,3050 C-H. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.12-7.79 ,7×1H (m, =C-H naphtha. ,) , δ 6.28 ,1×1H (t, -**NH**CH_2) , δ 3.73,1×2H (d, -**CH**$_2$NH), δ 11.07 ,1×2H (d, -NHN), δ 8.46 ,1×1H (d, -CH=N), δ 7.23-7.76 ,4×1H (s, -CH = CHAr), δ 2.41,4×1H (s, p- CH_3), m/z: 317.15 (100.0%), 318.16 (21.6%).

5: Yield 65% .1602 C=C,1643 C-N, 1645 C=O ,3482 N-H, 1552 CH=N,3046 C-H.748 C-Cl. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.11-7.76 ,7×1H (m, =C-H naphtha. ,) , δ 6.26 ,1×1H (t, -**NH**CH_2) , δ 3.71,1×2H (d, -**CH**$_2$NH), δ 11.05 ,1×2H (d, -NHN), δ 8.47 ,1×1H (d, -CH=N), δ 7.24-7.76 ,4×1H (s, -CH = CHAr), m/z: 337.10 (100.0%), 339.10 (32.0%), 338.10 (20.5%), 340.10 (6.6%),

6: Yield 68%. IR (KBr) ν_{max} in cm^{-1}1604 C=C,1651 C-N, 1648 C=O ,3484 N-H, 1552 CH=N,3049 C-H.1570 C-NO_2. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm, δ ,7.11-7.79 ,7×1H (m, =C-H naphtha. ,) , δ 6.25 ,1×1H (t, -**NH**CH_2) , δ 3.73,1×2H (d, -**CH**$_2$NH), δ 11.06 ,1×2H (d, -NHN), δ 8.44 ,1×1H (d, -CH=N), δ 7.22-7.79 ,4×1H (s, -CH = CHAr), m/z: 348.12 (100.0%), 349.13 (20.5%),

7: Yield 69 % .IR (KBr) ν_{max} in cm^{-1}1605 C=C,1647 C-N, 1649 C=O ,3485 N-H, 1550 CH=N,3051 C-H. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm, δ ,7.09-7.78 ,7×1H (m, =C-H naphtha. ,) , δ 6.27 ,1×1H (t, -**NH**CH_2) , δ 3.75,1×2H (d, -**CH**$_2$NH), δ 11.07 ,1×2H (d, -NHN), δ 8.46 ,1×1H (d, -CH=N), δ 7.22-7.76 ,4×1H (s, -CH = CHAr), δ 2.72 ,1×2H (t, -CH_2) δ 1.18 ,1×3H (t, -CH_3) m/z: 331.17 (100.0%), 332.17 (22.7%),

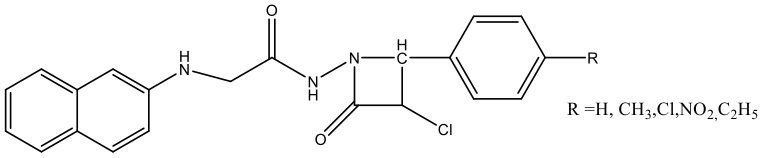
8 : N-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-2-(naphthalen-2-ylamino)acetamide :



Take the compound (3), (0.01mol) and it transfer into beaker then add 2-3 drops of triethyl amine, chloroacetyl chloride (0.01) was added drop by drop with constant stirring. After formation of compound, it was cheked with TLC on silica gel G the compound was washed with ether and dried. The compound (8) is obtained, Yield 50% .1603 C=C,1652 C-N, 1645 C=O , 1547 CH=N,3047 C-H, 3485 N-H,753 C-Cl, δ ,7.11-7.78 ,7×1H (m, =C-

H naphtha. ,) , δ 6.27 ,1×1H (t, -**NH**CH_2) , δ 3.65,1×2H (d, -**CH_2**NH), δ 11.08 ,1×2H (d, -NHN), δ 5.08 ,1×1H (d, four member ring-CH=N), δ 7.27-7.36 ,5×1H (s, -CH = CHAr), δ 5.44 ,1×2H (d, -CCl) .. m/z: 379.11 (100.0%), 381.11 (32.0%), 380.11 (22.7%), 382.11 (7.3%),

(9-12) : General process for formation of N-(3-chloro-2-oxo-4-substitutedphenylazetidin-1-yl)-2-(naphthalene-2-ylamino)acetamide (9-12)



(9-12)

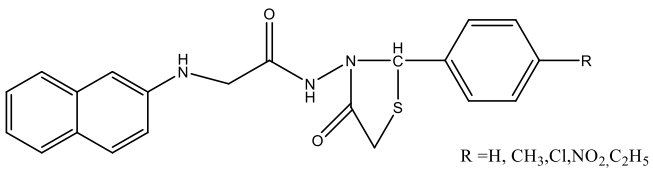
Take the reagent 4-7 in a separate beaker and make a Solution into ethanol (25 mil) in each then added 2-3 drops of triethyl amine & chloroacetyl chloride (0.01 mol) In the form of drop to drop, slowly with stirring then reflux it 2-3h. The resulting mixtures were cooled, filtered & recrystallised from appropriate solvent to give compound (9-12) respectively. Yield 63%. IR (KBr) ν_{max} in cm^{-1}1605 C=C,1651 C-N, 1647 C=O , 1549 CH=N,3050 C-H, 3484 N-H,750 C-Cl, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.09-7.76 ,7×1H (m, =C-H naphtha. ,) , δ 6.27 ,1×1H (t, -**NH**CH_2) , δ 3.62,1×2H (d, -**CH_2**NH), δ 11.07 ,1×2H (d, -NHN), δ 5.07 ,1×1H (d, four member ring-CH=N), δ 7.29-7.36 ,4×1H (s, -CH = CHAr), δ 5.43 ,1×2H (d, -CCl) . δ 2.19 ,1×3H (s, -CH_3). m/z: 393.12 (100.0%), 395.12 (32.0%), 394.13 (23.8%),

10: Yield 68 % .IR (KBr) ν_{max} in cm^{-1}1606 C=C,1653 C-N, 1649 C=O , 1544 CH=N,3046 C-H, 3481 N-H,752 C-Cl, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.10-7.78 ,7×1H (m, =C-H naphtha. ,) , δ 6.26 ,1×1H (t, -**NH**CH_2) , δ 3.60,1×2H (d, -**CH_2**NH), δ 11.04 ,1×2H (d, -NHN), δ 5.03 ,1×1H (d, four member ring-CH=N), δ 7.19-7.23 ,4×1H (s, -CH = CHAr), δ 5.42 ,1×2H (d, -CCl) . m/z: 413.07 (100.0%), 415.07 (63.9%), 414.07 (22.7%), 417.06 (10.2%),

11: Yield 67% .IR (KBr) ν_{max} in cm^{-1}1602 C=C,1650 C-N, 1650 C=O , 1546 CH=N,3048 C-H, 3482 N-H,753 C-Cl,1568 C-NO_2, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.11-7.75 ,7×1H (m, =C-H naphtha. ,) , δ 6.27 ,1×1H (t, -**NH**CH_2) , δ 3.61,1×2H (d, -**CH_2**NH), δ 11.05 ,1×2H (d, -NHN), δ 5.04 ,1×1H (d, four member ring-CH=N), δ 7.22-7.35 ,4×1H (s, -CH = CHAr), δ 5.40 ,1×2H (d, -CCl). m/z: 424.09 (100.0%), 426.09 (32.0%), 425.10 (22.7%), 427.09 (7.3%),

12: yield 65%. IR (KBr) ν_{max} in cm^{-}1603 C=C,1648 C-N, 1650 C=O , 1550 CH=N,3046 C-H, 3487 N-H,751 ,C-Cl. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.12-7.78 ,7×1H (m, =C-H naphtha. ,) , δ 6.25 ,1×1H (t, -**NH**CH_2) , δ 3.60,1×2H (d, -**CH_2**NH), δ 11.03 ,1×2H (d, -NHN), δ 5.06 ,1×1H (d, four member ring-CH=N), δ 7.24-7.36 ,4×1H (s, -CH = CHAr), δ 5.45 ,1×2H (d, -CCl) . δ 2.72 ,1×2H (q, -CH_2) . δ 1.18 ,1×3H (t, -CH_3) . m/z: 407.14 (100.0%), 409.14 (32.0%), 408.14 (24.9%), 410.14 (8.0%).

13: **2-(naphthalen-2-ylamino)-N-(4-oxo-2-phenylthiazolidin-3-yl)acetamide:** Take the solution of compound of Schiff base 3 **(o**.01mol) and thioglycollic acid (0.01 mol) in N, N dimethyl formamide (17 ml) with a pinch of anhydrous $ZnCl_2$ in RBF. This mixture content was mixed properly by stirring. Now it was refluxed for 4-5.Hour. The progress of the reaction was checked with the help of TLC using ethyl acetate: toluene 1:4 as an eluent. Excess solvent was separated through distilled off. Mixture was cool down, and then resulting portion was poured into crushed ice water and put it for formation of crystal at overnight. The crystal were obtained.Yield 70% . . IR (KBr) ν_{max} in cm^{-1}1605 C=C,1650 C-N, 1648 C=O , 1552 CH=N,3048 C-H, 3486 N-H,782, C-S. δ ,7.10-7.74 ,7×1H (m, =C-H naphtha. ,) , δ 6.28 ,1×1H (t, -**NH**CH_2) , δ 3.61,1×2H (d, -**CH_2**NH), δ 11.27 ,1×2H (d, -NHN), δ 5.92 ,1×1H (d, four member ring-CH-N), δ 7.23-7.36 ,4×1H (s, -CH = CHAr), δ 3.80-3.71 ,1×2H (q, C-CH_2S) . m/z: 377.12 (100.0%), 378.12 (22.7%),



(13-17)

(14-17): 2-(naphthalen-2-ylamino)-N-(2-(substituted phenyl)-4-oxothiazolidin-3-yl)acetamide :

Take the solution of compound of Schiff base 3 **(o**.01mol) and thioglycollic acid (0.01 mol) in N, N dimethyl formamide (17 ml) with a pinch of anhydrous $ZnCl_2$ in RBF. This mixture content was mixed properly by stirring. Now a similar procedure like 13 are applied. These crystals were recrystallised from ethanol, yield of the compound 14-17 observed. Yield product varied 65 -70%. Data and analytical value are given table-1

The following compounds (14-17) were prepared using a similar procedure described to compound 13. The physical, spectral data (values) of derivatives (14-17) was given in table 1&2 respectively.

14 : Yield 73%. . IR (KBr) ν_{max} in cm^{-1}1601 C=C,1646 C-N, 1642 C=O , 1550 CH=N,3048 C-H, 3486 N-H,782, C-S. ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.11-7.75 ,7×1H (m, =C-H naphtha. ,) , δ 6.26 ,1×1H (t, -**NH**CH_2) , δ 3.62,1×2H (d, -**CH**$_2$NH), δ 11.27 ,1×2H (d, -NHN), δ 5.92 ,1×1H (d, four member ring-CH-N), δ 7.21-7.37 ,4×1H (s, -CH = CHAr), δ 3.79-3.71 ,1×2H (q, C-CH_2S) . δ 2.18 ,1×3H (s, -CH_3) . m/z: 391.14 (100.0%), 392.14 (23.8%),

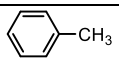
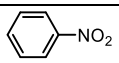
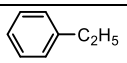
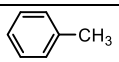
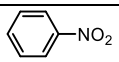
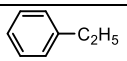
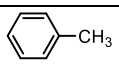
15: Yield 67% . IR (KBr) ν_{max} in cm^{-1}1602 C=C,1648 C-N, 1646 C=O , 1553 CH=N,3049 C-H, 3486 N-H,781, C-S.752 C-Cl, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.10-7.72 ,7×1H (m, =C-H naphtha. ,) , δ 6.24 ,1×1H (t, -**NH**CH_2) , δ 3.60,1×2H (d, -**CH**$_2$NH), δ 11.24 ,1×2H (d, -NHN), δ 5.90 ,1×1H (d, four member ring-CH-N), δ 7.19-7.35 ,4×1H (s, -CH = CHAr), δ 3.78-3.65 ,1×2H (q, C-CH_2S) . m/z: 411.08 (100.0%), 413.08 (32.0%), 412.08 (22.7

16 : Yield 65% .IR (KBr) ν_{max} in cm^{-1}1605 C=C,1652 C-N, 1647 C=O , 1554 CH=N,3048 C-H, 3486 N-H,776, C-S, 1567 C-NO_2, ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.11-7.75 ,7×1H (m, =C-H naphtha. ,) , δ 6.25 ,1×1H (t, -**NH**CH_2) , δ 3.64,1×2H (d, -**CH**$_2$NH), δ 11.25 ,1×2H (d, -NHN), δ 5.90 ,1×1H (d, four member ring-CH-N), δ 7.15-7.28 ,4×1H (s, -CH = CHAr), δ 3.81-3.70 ,1×2H (q, C-CH_2S) . m/z: 422.10 (100.0%), 423.11 (22.7%), 424.10 (4.5%),

17: Yield 62 % .IR (KBr) ν_{max} in cm^{-1}1601 C=C,1650 C-N, 1643 C=O , 1551 CH=N,3046 C-H, 3486 N-H,775 C-S, 1567 C-NO_2 . ^{1}HNMR($CDCl_3$ + DMSO-d_6) δ in ppm δ ,7.12-7.75 ,7×1H (m, =C-H naphtha. ,) , δ 6.26 ,1×1H (t, -**NH**CH_2) , δ 3.64,1×2H (d, -**CH**$_2$NH), δ 11.25 ,1×2H (d, -NHN), δ 5.91 ,1×1H (d, four member ring-CH-N), δ 7.12-7.28 ,4×1H (s, -CH = CHAr), δ 3.82-3.75 ,1×2H (q, -CH_2) .δ 2.72 ,1×2H (q, -CH_2) . δ 1.19 ,1×3H (t, -CH_3) . m/z: 405.15 (100.0%), 406.15 (24.9%), 407.15 (4.5%),

Observation Table:

Table 1 Physical & Analytical data of compounds (1-17):

Compound No.	R Group and their Position	Molecular Formula	Yield %	Recrystalised Solvent	Elemental Analysis					
					%C		%H		%N	
					Calctd.	Found.	Calcd.	Found	Calcd.	Found
1	-	$C_{15}H_{17}NO$	82	Ethyl alcohol	79.26	79.24	7.54	7.52	6.16	6.18
2	-	$C_{12}H_{13}N_3O$	79	Ethyl alcohol	66.96	66.96	6.09	6.08	19.52	19.51
3		$C_{19}H_{17}N_3O$	72	methyl alcohol	75.23	75.24	5.65	5.64	13.85	13.83
4		$C_{20}H_{19}N_3O$	70	Ethyl alcohol	75.69	75.6	6.03	6.05	13.24	13.23
5		$C_{19}H_{16}ClN_3O$	65	ether	67.56	67.55	4.77	4.76	12.44	12.45
6		$C_{19}H_{16}N_4O_3$	68	Ethyl alcohol	65.51	65.52	4.63	4.62	16.08	16.07
7		$C_{21}H_{21}N_3O$	69	Ethyl alcohol	76.11	76.10	6.39	6.38	12.68	12.66
8		$C_{21}H_{18}ClN_3O_2$	50	Ethyl alcohol	66.40	66.41	4.78	4.77	11.06	11.06
9		$C_{22}H_{20}ClN_3O_2$	63	Ethyl alcohol	67.09	67.07	5.12	5.13	10.67	10.68
10		$C_{21}H_{17}Cl_2N_3O_2$	68	ether	60.88	60.87	4.14	4.13	10.14	10.15
11		$C_{21}H_{17}ClN_4O_4$	67	ether	59.37	59.32	4.03	4.05	13.19	13.20
12		$C_{23}H_{22}ClN_3O_2$	65	Ethyl alcohol	67.73	67.71	5.44	5.43	10.30	10.31
13		$C_{21}H_{19}N_3O_2S$	70	Ethyl Alcohol	66.82	66.82	5.07	5.08	11.13	11.15
14		$C_{22}H_{21}N_3O_2S$	73	Ethyl Alcohol	67.50	67.52	5.41	5.42	10.73	10.75
15		$C_{21}H_{18}ClN_3O_2S$	67	methyl Alcohol	61.24	61.25	4.40	4.41	10.20	10.22

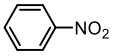
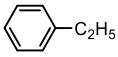
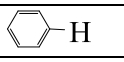
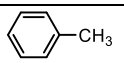
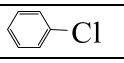
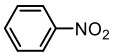
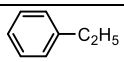
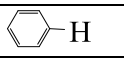
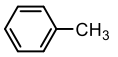
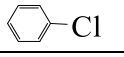
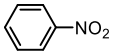
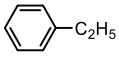
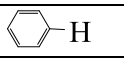
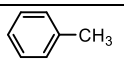
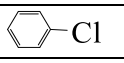
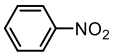
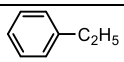
16		$C_{21}H_{18}N_4O_4S$	65	Ethyl Alcohol	59.71	59.73	4.29	4.31	13.26	13.28
17		$C_{23}H_{23}N_3O_2S$	62	Ethyl Alcohol	68.12	68.15	5.72	5.75	10.36	10.38

Table 2 Anti Bacterial activity of compounds (1-17):

Sno	**Substituent R Group**	**Compounds**	Antibacterial activity# **[Diameter of the inhibition zone (mm)]**	
			Escherichia coli Ess 2231	**Staphylococcus. Aureus 209p mm**
1	-	$C_{15}H_{17}NO$	-	9
2	-	$C_{12}H_{13}N_3O$	10	-
3		$C_{19}H_{17}N_3O$	12	1
4		$C_{20}H_{19}N_3O$	10	-
5		$C_{19}H_{16}ClN_3O$	14	13
6		$C_{19}H_{16}N_4O_3$	-	10
7		$C_{21}H_{21}N_3O$	13	11
8		$C_{21}H_{18}ClN_3O_2$	14	16
9		$C_{22}H_{20}ClN_3O_2$	-	15
10		$C_{21}H_{17}Cl_2N_3O_2$	17	18
11		$C_{21}H_{17}ClN_4O_4$	15	16
12		$C_{23}H_{22}ClN_3O_2$	17	15
13		$C_{21}H_{19}N_3O_2S$	16	14
14		$C_{22}H_{21}N_3O_2S$	14	15
15		$C_{21}H_{18}ClN_3O_2S$	16	17
16		$C_{21}H_{18}N_4O_4S$	14	16
17		$C_{23}H_{23}N_3O_2S$	**13**	14
18	-	Ciprofloxacin	14	15

MOLECULAR DOCKING STUDY

The docking study utilised the DNA gyrase B PDB ID: 4uro and biotin protein ligase PDB ID: 3v7r to investigate the mechanism by which the small-molecule compounds function as antibacterial agents. The ligand-protein interaction behaviours were assessed using the docking score function, which was developed in Auto Dock Vina. Which is represent in fig-1and fig-2 Bacterial DNA gyrase is crucial in the study of antibacterial drugs because it facilitates the breaking of double-stranded DNA through the process of catalysing negative supercoiling. This activity is required for DNA replication, transcription, and recombination. The co-crystallised DNA-gyrase cleavage complex, a potent antibacterial agent, was analyzed. This complex cleaves DNA by inhibiting the ATPase binding site, which includes the essential exposed peptidoglycan of the cell wall. These chemicals, specifically 10, 11, 15, and 16, were determined to possess favourable biological activities.

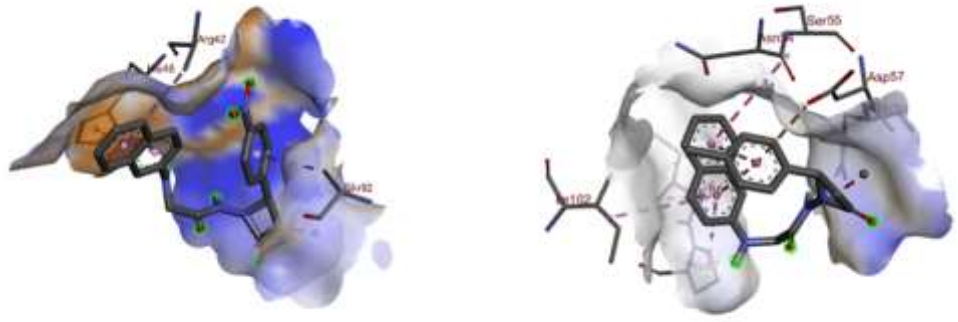


Fig.1- 3D structure protein ligand interaction of compound 10 and 11.

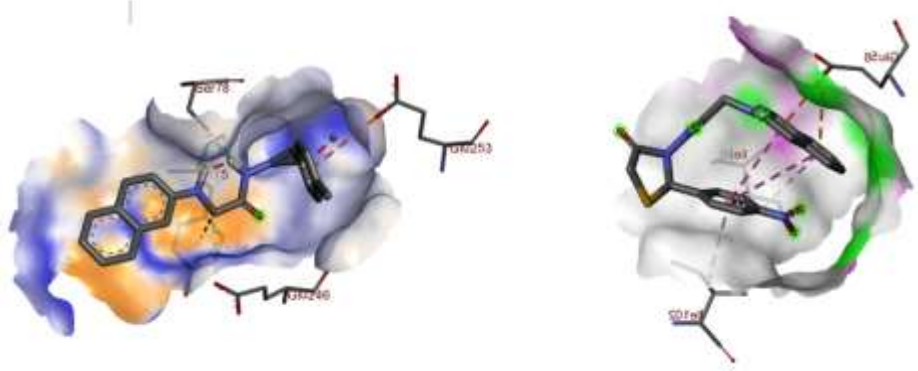


Fig.2- 3D structure protein ligand interaction of compound 15 and 16.

Result and Discussion:

All the new compound (3-7), (8-12) and (13-17) were tested their pharmacological activity ie. Anti-bacterial were recorded I table II. Docking studies also shows that compound 10, 11, 15 and 16 represent -9.2,k/cal -9.4 k/cal, -9.0 k/cal and -9.7 k/cal binding affinity respectively.

The antibacterial activity of compound (8-12) and (13-17) were performed on filter paper disc method (Gould and Bowie 1952)[30] against staphylococcus aureus 209p Escherichia coli ESS 2231,at a concentration of 250mg /ml. Media with 10% DMSO in methanol was set up in a control condition . The presence of methanol causes no visible change in the bacterial growth. The filter paper disc method was used to evaluate the anti bacterial activity of the synthesis derivatives. The observation and results of the bacterial study of the synthesis compound were recorded in table II From the bacterial study of the synthesis compound (8-12) and (13-17) were show the moderate to better activity. The Zone of inhibition (ZOI) Value obtained were indicate that the compound 10,11,15,16 show better activity , the value of the derivative also veriate with substituent, the cyclization of arylidine derivatives(3-7) into their corresponding azetidinone 8 -12 has increase the antibacterial activity however compound 15,16 are associated with good antibacterial activity. In addition to this, the screening data of anti-bacterial activity indicated that some compounds exhibited antibacterial activity against one or more bacterial test. Compound –(10) of azetidinone and compound of-(15) thiazolidinone were representing better antibacterial activity with low toxicity.

Conclusion:

The study examined the pharmacological effects of newly developed compounds (3-7), (8-12), and (13-17) on staphylococcus aureus 209p and Escherichia coli ESS 2231 utilizing the filter paper disc technique. The findings indicated that compounds 10-12 and 13-17 exhibited moderate to superior activity. The Zone of Inhibition (ZOI) values revealed that compounds 10, 11, 15, and 16 had superior action. The arylidine derivatives (3-7) underwent cyclization to form the corresponding azetidinone compounds (8-12), resulting in an enhancement of their antibacterial activity. Compound 15,16 exhibited significant antibacterial activity. The screening data revealed that certain compounds had antibacterial activity against one or more bacterial tests. The combination of azetidinone compound -10 and thiazolidinone compound -15 exhibited enhanced antibacterial efficacy while maintaining

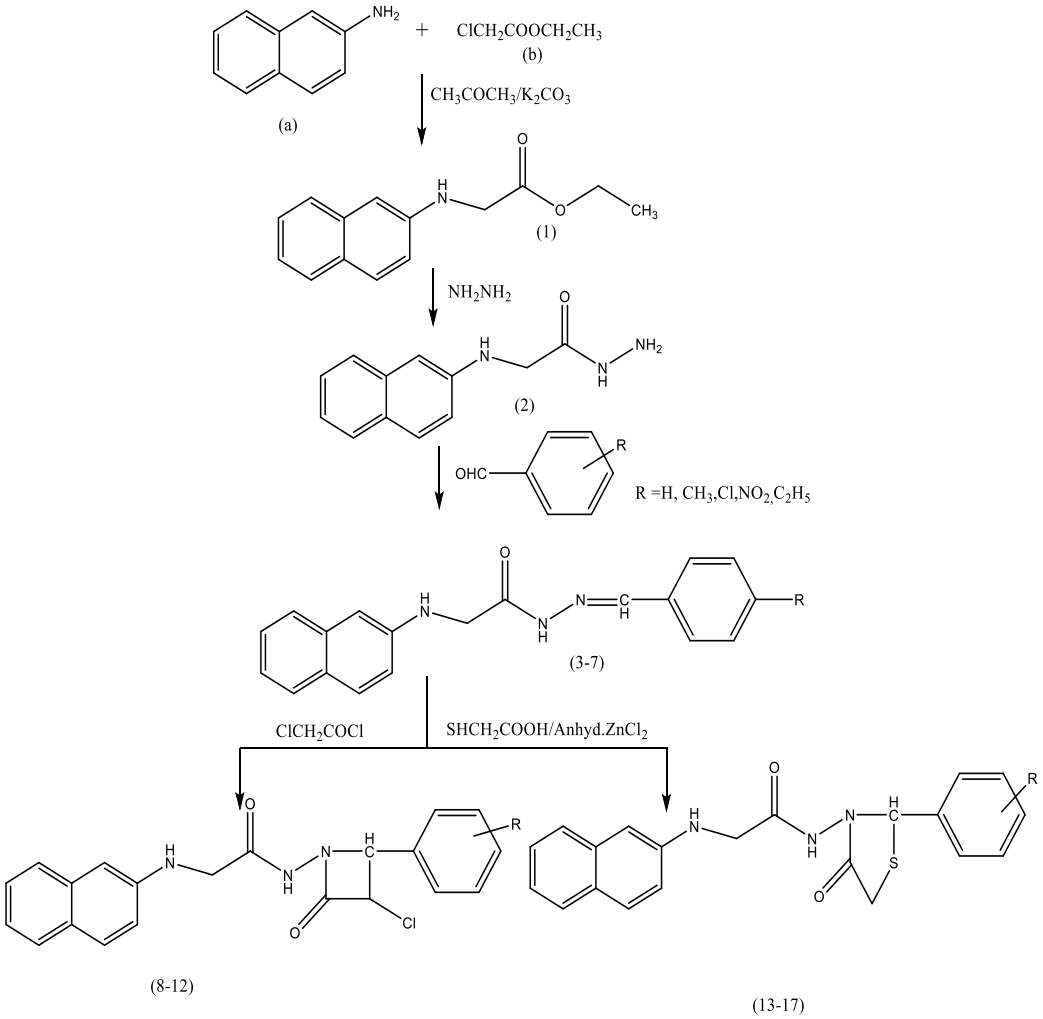
low toxicity. Naphthalene also enhanced the efficacy of azetidinone and thiazolidinone derivatives. Ultimately, the azetidinone molecule -10 and the thiazolidinone compound -15 exhibited superior antibacterial efficacy while maintaining low levels of toxicity. In this case it is also observed that naphthalene also influences towards the better activity of azetidinone ring and thiazolidinone rind derivatives.

Conflict of interest:

There is no conflict of interest

Acknowledgment:

This work is a part of PhD Research Programmed of Gaurav Kumar. We are thankful to the management staff of Meerut College Meerut, for providing the facility for conducting the research work and support.



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