Synthesis, Spectral Characterization, Insecticidal And Antibacterial Activities Of Some 5- {[-3-[(6-Chloropyridin-3-Yl) Methyl]-2-(Nitroimino) Imidazolidin-1-Yl] Methyl} 2, 3-Substituted Pyridine Derivatives

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ABSTRACT

In an effort to discover promising molecules with good insecticidal activities, a set of Substituted 2-(nitroimino)imidazolidin-1-yl]methyl} 2,3-substituted pyridine derivatives were synthesized, which were constructed by starting material imidacloprid and bio-assayed. The structures of the newly synthesized compounds were confirmed by FT-IR,^{1}H NMR,^{13}CNMR and Mass spectroscopic data. The bioassay tests showed that synthesized compounds Chloro (2&3) and Carboxyl(4&5) substitution showed higher bioactivities than against H.armigera(Hub) ,Mealybugs (Planococcuscitri) and Mango hoppers [Idioscopusclypealis (Lethierry)] ,as well as Tobacco bacterial wilt & . Tomato bacterial wilt.Compounds substituted with electron withdrawing group exhibited potential vector control agents towards Pest Management in Agriculture science.

Keywords: Neo-nicotinoid Analogue, Characterization, Insecticidal, Antibacterial ,Vector Cnotrol.

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INTRODUCTION

H.armigera (Hübner), *Mealybugs* (Planococcuscitri) and *Mango hoppers*(Idioscopusclypealis) are recognized as a insect pest andhas a high harmful potential for various commercially important crops around the Globe, includingcotton, corn,tobacco,soybeans andtomatoes[1]. Nicotine is one of the oldest known plant origin insecticides, which have the remarkable insecticidal Property. Nicotineterminate the insects quickly within an hour causing tremors, convulsions and subsequently paralysis. Before 1746, the insecticidal activities of crude extract of tobacco leaves were used to control the insects. Metcalf hasreported that 1.2 million pound of free nicotine was

used in Agriculture in USA during 1944[2].Some biological characteristics, such asmobility,polyphagy, and facultative diapauses, can increase the survival and populationupsurgeof the pest in agrosystem[3]. These pestilence, which attack more than 150 different hostspecies, are considered as the most commercially important insect pests in many countries, such asJapan, China,Indiaand Southeast Asia[4].Owing to their biological characteristics and more damage potential, successful prevention and control of these pests becomes atough work . The prevention and control of H. armigera is mainly dependent on chemical pesticides[5].However, total dependence on the application of synthetic insecticides to control H. armigera has notachieved the desired success, and has resulted in the unfolding of pesticide resistance, environmentalcontamination, disruption of ecological stability, and healthhazards[6]. Neonicotinoid insecticides are the latest class of synthetic insecticides in the past two decade sand the biggest selling insecticide class worldwide through compound such as imidacloprid[7].Thus, nemures attempts have been made to find replacement methods for its control. Recently,Pyridine moiety was found to be very notable in the discovery of novel insecticidesand several modifications around its structure have been reported. New insecticidal molecules are developed in the present work on the basis of the following: incorporation of the substructural unit of hydrazone into the backbone of imidacloprid. Based on this hypothesis, a imidacloprid derivative containing substituted pyridine structure are designed and synthesized (scheme). Biological assays reveal that the synthesized compound exhibitexcellent insecticidal activities against different insect species.

EXPERIMENTAL

Material &Methods:All the reagents and chemicals were purchased from Merck chemicals used without further purification. Melting points determination was taken in open capillary tubes and is uncorrected. Thin layer chromatography is performed with E. Merck pre-coated silica gel plates with iodine as spot developing chemical agent.FTIR spectra in KBr were recorded on Perkin-Elmer FTIR 783spectrometer. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded CDCl3 solvent containing tetra methyl silane (TMS) as internal references were recorded on Bruker Avance II (400 MHz) spectrometer; Elemental analyses were performed on a PerkinElmer 2400. Massspectra obtained by QP2010 (Shimadzu) spectrometer.

Synthetic procedure

1,3-bis[(6-chloropyridin-3-yl)methyl]-*N*-nitroimidazolidin-2-imine(2)

The solution of imidacloprid (1mole) in 10 ml methanol ,add 2-3 drops of acetic acid then add 2-chloro 3 chloro-methyl pyridine (1 mole) . The mixture was then refluxed for about 2 hrs. And the progress of reaction was monitored by TLC. After the completion of the reaction, the mixture was further working add 10 ml ethyl acetate & 20 ml of water ,then organic layer is washed with the help of braine solution the organic layer distilled by using Rotavapour to get white solid compound, yield 77%.Compound 3 to 5 are prepared according to the procedures above.

1,3-bis[(6-chloropyridin-3-yl)methyl]-*N*-nitroimidazolidin-2-imine (2) Yield (77%), m.p. 158°C; IR (KBr, ν cm1):2907(CH2 str),1614(C=N str), 1561(NO2),1444(CH=CH str), 758(C-Cl str), 1H NMR (DMSO-d6, ppm) δ 4.82-4.84 (s, 2H, CH2), 3.88 (t, J=7.5 HZ, CH2), 3.92 (t, J=7.5 HZ,CH2), 7.26-8.31 (M,Ar); 13C NMR (DMSO-d6, ppm) 153,151,146,145,140,139,133,124,50,47;MS ($C_{15}H_{14}Cl_2N_6O_2$), (m/z) :382,380,354,344,255,238,209,125,87,47(M+).

1-[(6-chloropyridin-3-yl)methyl]-3-[(2,6-dichloropyridin-3-yl)methyl]-*N*-nitroimidazolidin-2-imine(3)

Yield (73%), m.p. 157°C; IR (KBr, ν cm1):2907(CH2 str), 1614(C=N str), 1563(NO2), 1440(CH=CH str), 754(C-Cl str),1H NMR (CDCl3, ppm) δ 4.82-4.84 (s, 2H, CH2), 3.88 (t, J=7.5 HZ, CH2), 3.92 (t, J=7.5 HZ,CH2), 7.26-8.31 (M,Ar), ,(DMSOd6, ppm) 154,153,151,148,145,140,139,124,121,115,50,47,MS ($C_{15}H_{13}Cl_3N_6O_2$) , (m/z) : 416,414,386,378,342,289,255,254,159,125,121,87,47 (M+).

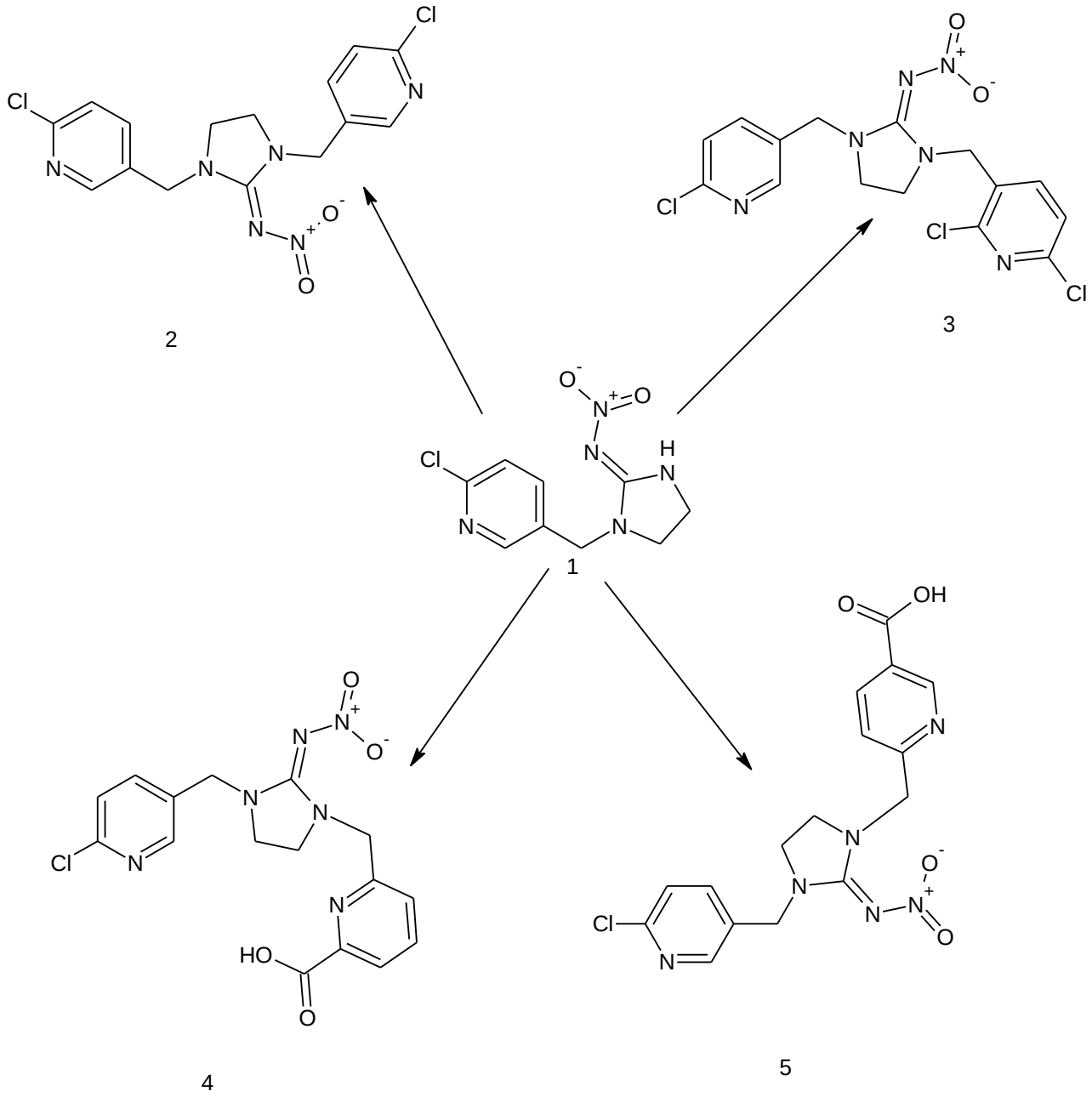
5-{[(2*Z*)-3-[(6-chloropyridin-3-yl)methyl]-2-(nitroimino)imidazolidin-1-yl]methyl}pyridine-3-carboxylic acid

(4) Yield (79%), m.p. 156°C; IR (KBr, ν cm1):2908(CH2 str),1704(COOH).1617(C=N str), 1563(NO2),1444(CH=CH str), 758(C-Cl str), 1H NMR (CDCl3, ppm) δ 4.82-4.84 (s, 2H, CH2), 3.88 (t, J=7.5 HZ, CH2), 3.92 (t, J=7.5 HZ,CH2), 7.36-8.30 (M,Ar), 11.06 (s, COOH), 13C NMR (DMSOd6, ppm) 167,165,163,153,151,145,139,136,133,127,124,123,56,49,48,; MS ($C_{16}H_{15}ClN_6O_4$), (m/z) : 390,372,354,363,255,135,125,96,87,47(M+).

5-{[(2*E*)-3-[(6-chloropyridin-3-yl)methyl]-2-(nitroimino)imidazolidin-1-yl]methyl}pyridine-2-carboxylic acid

(5) Yield (81%), m.p. 158°C; IR (KBr, ν cm1): 2908(CH2 str),1706(COOH) 1617(C=N str), 1563(NO2),1444(CH=CH str), 758(C-Cl str), 1H NMR (CDCl3, ppm) δ 4.82-4.84 (s, 2H, CH2), 3.88 (t, J=7.5 HZ, CH2), 3.92 (t, J=7.5 HZ,CH2), 7.36-9.07 (M,Ar), 11.07 (s, COOH) 13C NMR (DMSOd6, ppm) 166,162,153,148,145,140,139,134,127,123,122,54,50,48, (1C, s; MS ($C_{16}H_{15}ClN_6O_4$)(m/z) : 390,372,354,363,255,135,125,96,87,47 (M+).

SCHEME 2



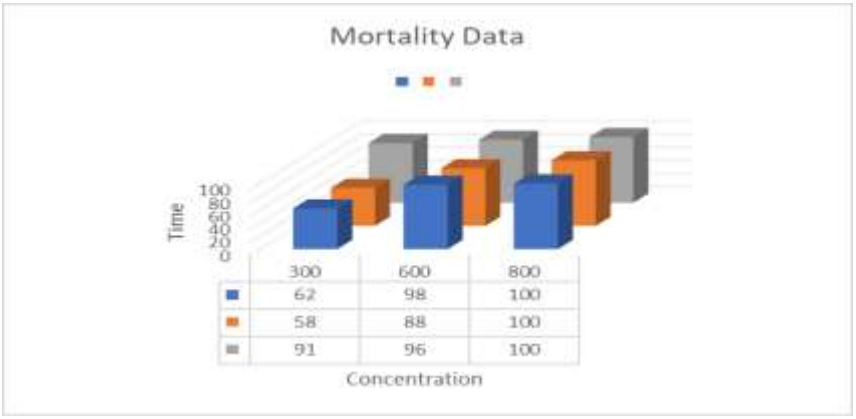
INSECTICIDAL ACTIVITY[8,9] :

The standard solutions of standard and synthesized compounds(2,3,4,&5) were prepared by dissolving them in 1% acetone and 1% DMF with 0.1% Tween-20 solution, to get 300, 600 and 800 mg litre-1 concentration. The treatments of these compounds were done through oral route, by dipping the fresh tobacco leaves in different concentrated solutions and then feed to Mealybugs. Simillarly, Mango hopper nymph &H.armigera(Hub) were feed with treated fresh inflorescence. The mortality data was collected, after 72 hrs. Of treatment and presented in**Table-1 to Table-3.**.

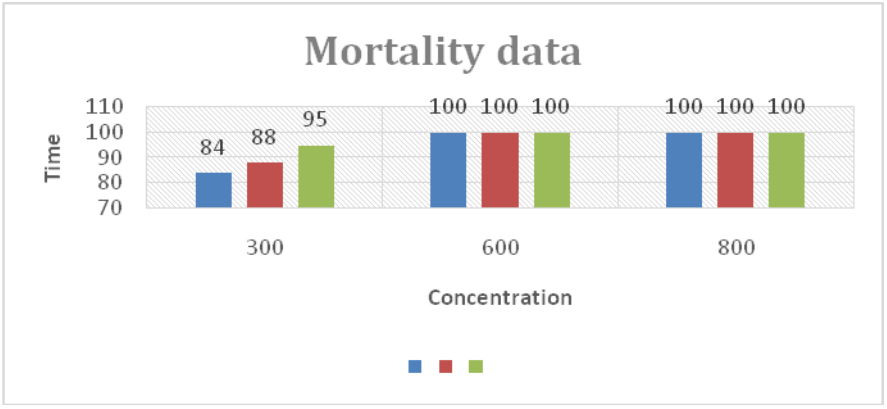
Table-1: Mortality data of treated compounds against sucking insect pests.

Compound Name	Concentrations mg. litre-1	Mortality after 24 hrs. of treatment		
		H.armigera(Hub)*	Mealybugs*	Mango hoppers*
2	300	62	58	91
	600	98	88	96
	800	100	100	100
3	300	84	88	95
	600	100	100	100
	800	100	100	100
4	300	76	87	94
	600	100	100	100
	800	100	100	100
5	300	82	89	96
	600	100	100	100
	800	100	100	100
Imidacloprid	300	52	46	90
	600	100	100	100
	800	100	100	100
Control (Solvent)	--	5	4	8

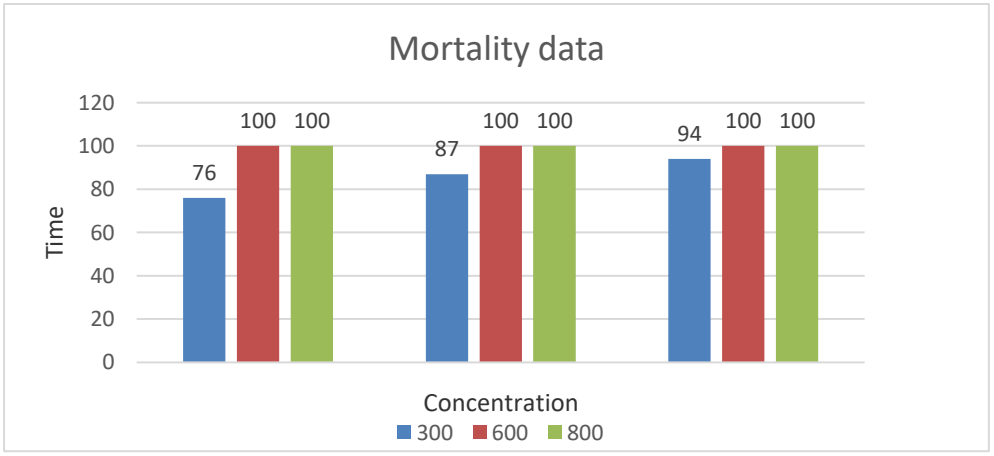
*Means of six replications



Mortality data of compound-2 after 24 hrs. of treatment

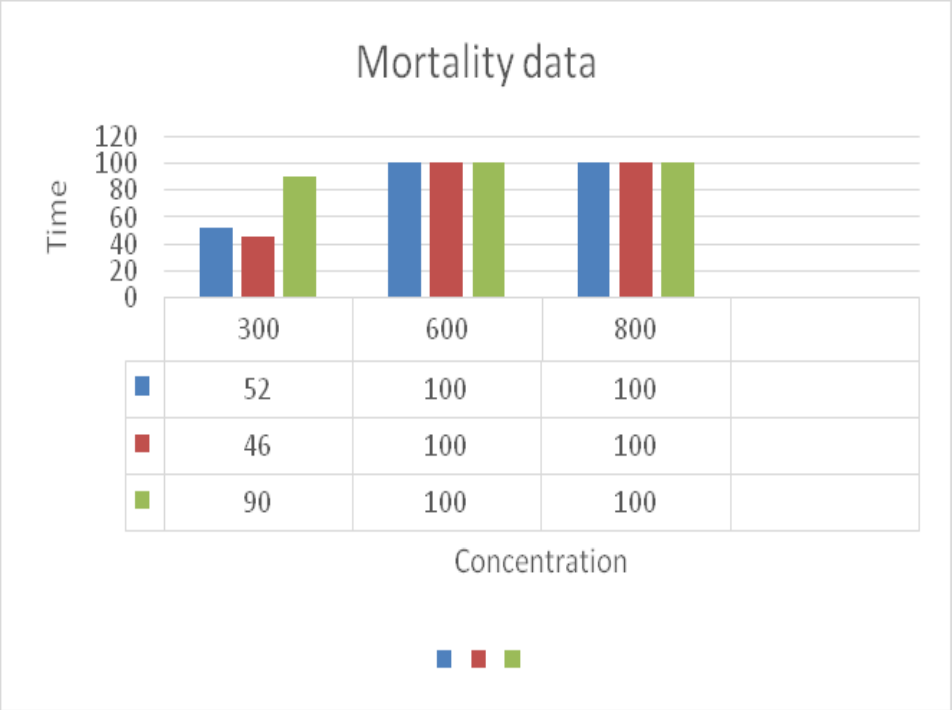


Mortality data of compound-3 after 24 hrs. of treatment



Mortality data compound-4 after 24 hrs. of treatment

Mortality data of compound -5 after 24 hrs. of treatment

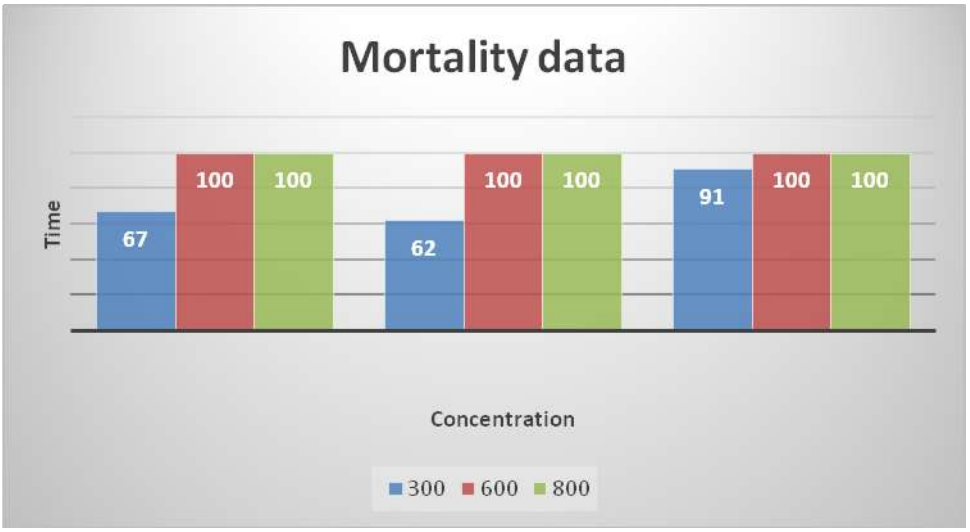


Mortality data of compound-Imidacloprid after 24 hrs. of treatment

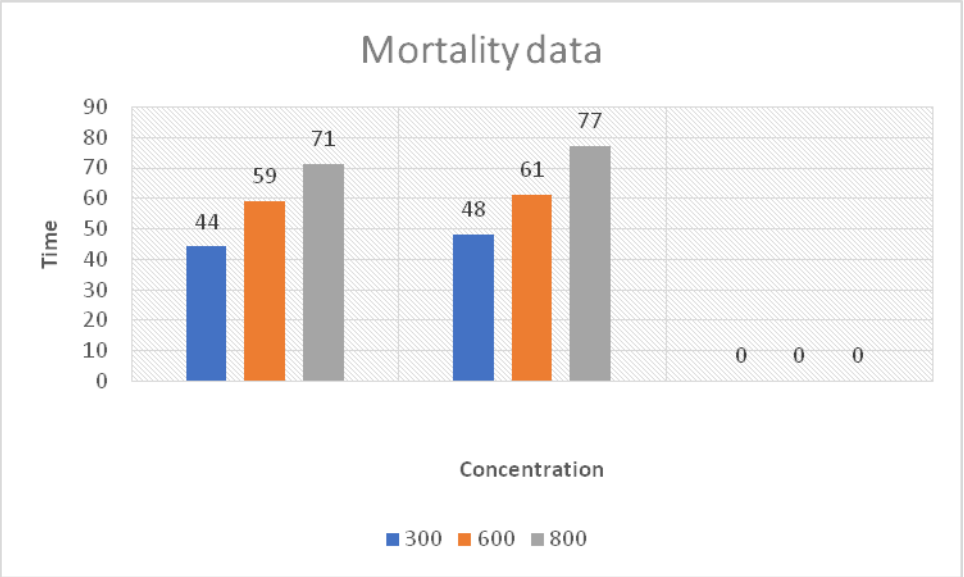
Table-2: Mortality data of treated compounds against sucking insect pests.

Compound Name	Concentrations mg. litre-1	Mortality after 48 hrs. of treatment		
		H.armigera(Hub)*	Mealybugs*	Mango hoppers*
2	300	67	62	91
	600	100	100	100
	800	100	100	100
3	300	79	71	94
	600	100	100	100
	800	100	100	100
4	300	86	87	97
	600	100	100	100
	800	100	100	100
5	300	87	90	98
	600	100	100	100
	800	100	100	100
Imidacloprid	300	52	46	90
	600	100	100	100
	800	100	100	100
Control (Solvent)	--	5	4	8

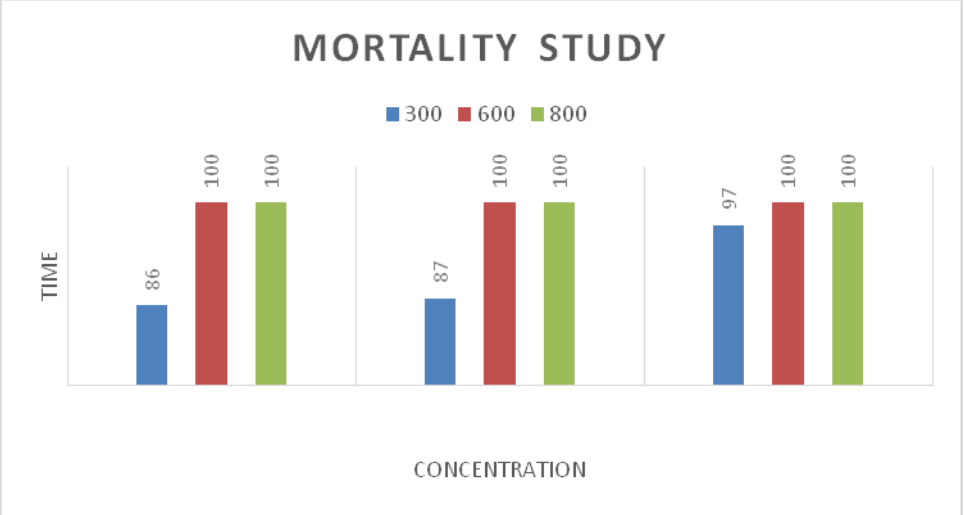
*Means of six replications



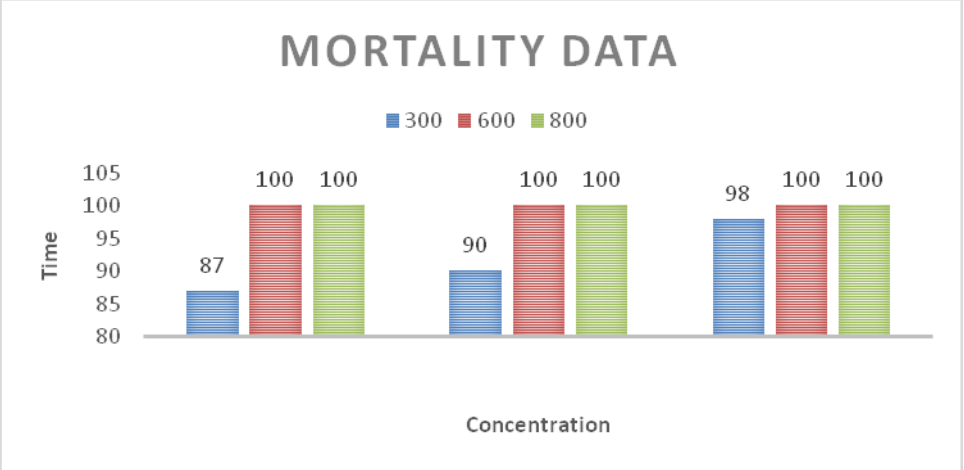
Mortality data of compound-2 after 48 hrs. of treatment



Mortality data of compound-3 after 48 hrs. of treatment



Mortality data of compound-4 after 48 hrs. of treatment



Mortality data of compound-5 after 48 hrs. of treatment

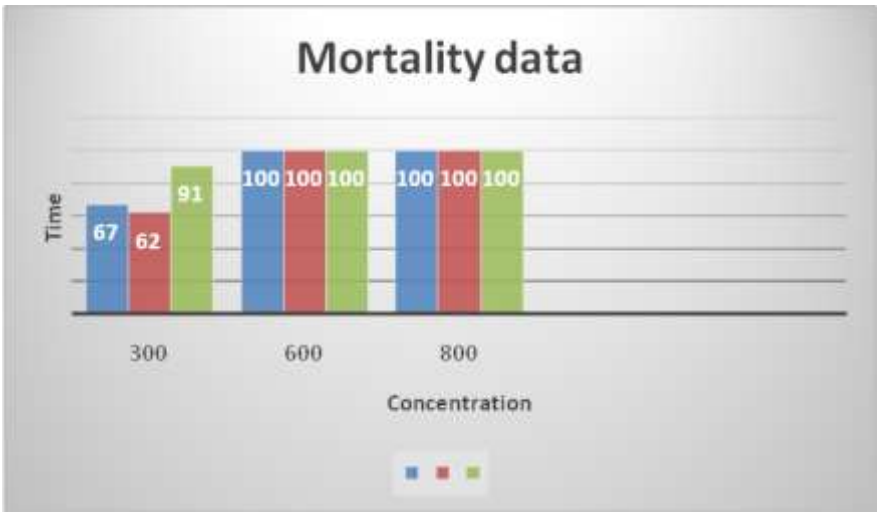
Mortality data of compound-Imidacloprid after 48 hrs. of treatment

Table-3: Mortality data of treated compounds against sucking insect pests.

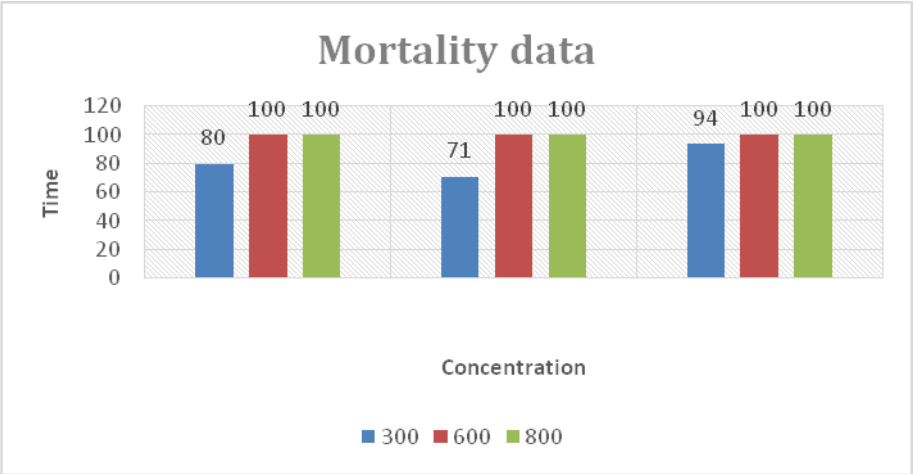
Compound Name	Concentrations mg. litre-1	Mortality after 72 hrs. of treatment		
		H.armigera(Hub)*	Mealybugs*	Mango hoppers*
2	300	67	62	91
	600	100	100	100
	800	100	100	100
3	300	80	71	94
	600	100	100	100
	800	100	100	100
4	300	87	87	97
	600	100	100	100
	800	100	100	100

5	300	90	90	98
	600	100	100	100
	800	100	100	100
Imidacloprid	300	52	46	90
	600	100	100	100
	800	100	100	100
Control (Solvent)	--	5	4	8

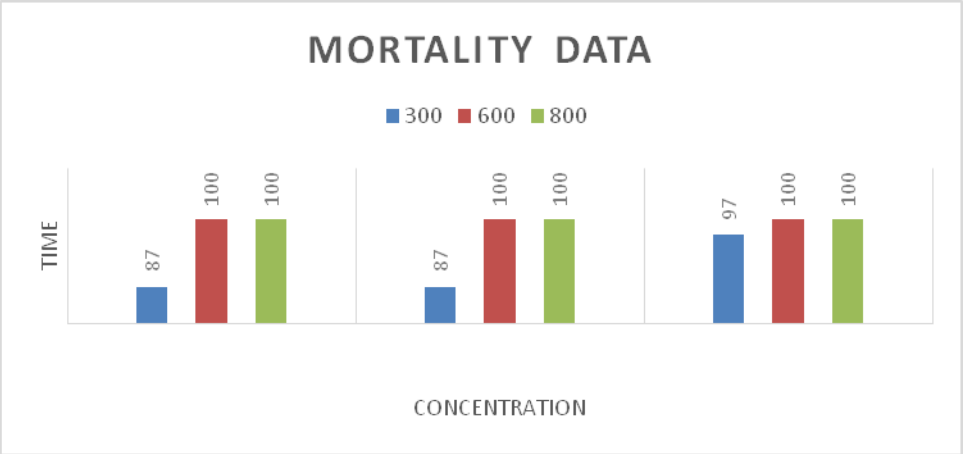
*Means of six replications



Mortality data of compound -2 after 72 hrs. of treatment



Mortality data of compound -3 after 72 hrs. of treatment



Mortality data of compound-4 after 72 hrs. of treatment

Mortality data of compound-5 after 72 hrs. of treatment

Mortality data of compound-Imidacloprid after 72 hrs. of treatment

ANTIBACTERIAL ASSAY

The antibacterial activities of all of the title compounds (2,3,4,&5)against tobacco bacterial wilt and tomato bacterial wilt were evaluated by a turbidimeter test [10]. Kocide® 3000 (Cu(OH)) was used as the positive control(200mg/L). The compounds were dissolved in 150 μL of DMSO, diluted with water containing Tween-20 (0.1%, Tween-20: water, v/v) to a final concentration of 300,600 & 800 mg/L, and then added to nutrient broth (NB) liquid medium in 5 mL tubes. About 40 μL of NB liquid medium containing the solanacearum pathogen was individually added to these tubes. Shaking at 30°C and 180 rpm for 48 h followed. The relative inhibition rate of the circle mycelium compared with the blank assay was calculated using the following equation.

Relative inhibitory rate (%) = $[(A_0 – A_1)/A_0] \times 100\%$

A_0 :Corrected OD values of the control medium of bacilli.

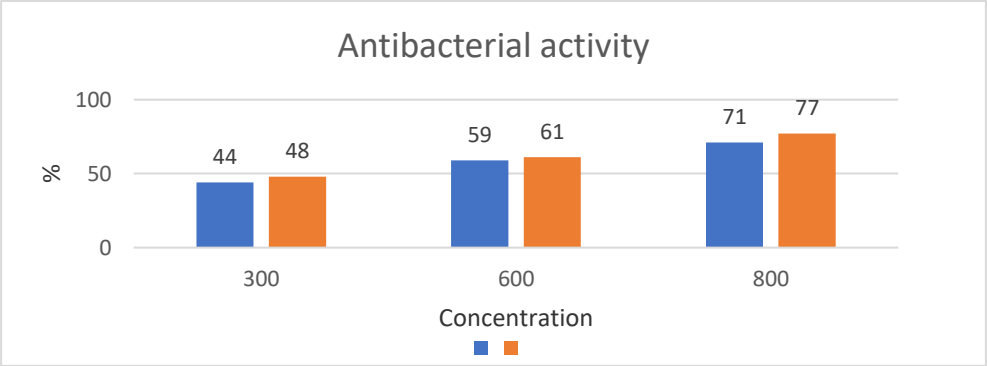
A_1 :Corrected OD values of the medium of toxic.

Table-4: The antibacterial activity of synthesized compounds & Imidacloprid against Tobacco bacterial wilt and Tomato bacterial wilt at 300,600 ,800 mg/L.

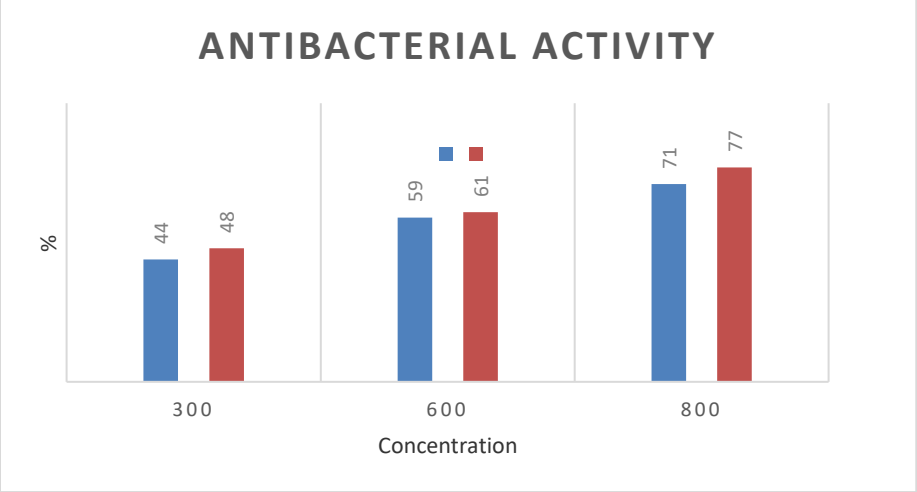
Compound Name	Concentrations mg. litre-1	**Tobacco bacterial wilt (%) ***	**Tomato bacterial wilt (%)***
1	300	44	48
	600	59	61
	800	71	77
3	300	47	49
	600	60	62

	800	77	81
4	300	43	47
	600	54	57
	800	70	72
5	300	44	48
	600	57	60
	800	70	72
Imidacloprid	300	42	40
	600	54	56
	800	69	66
Kocide® 3000 (Cu(OH))	200	100	100

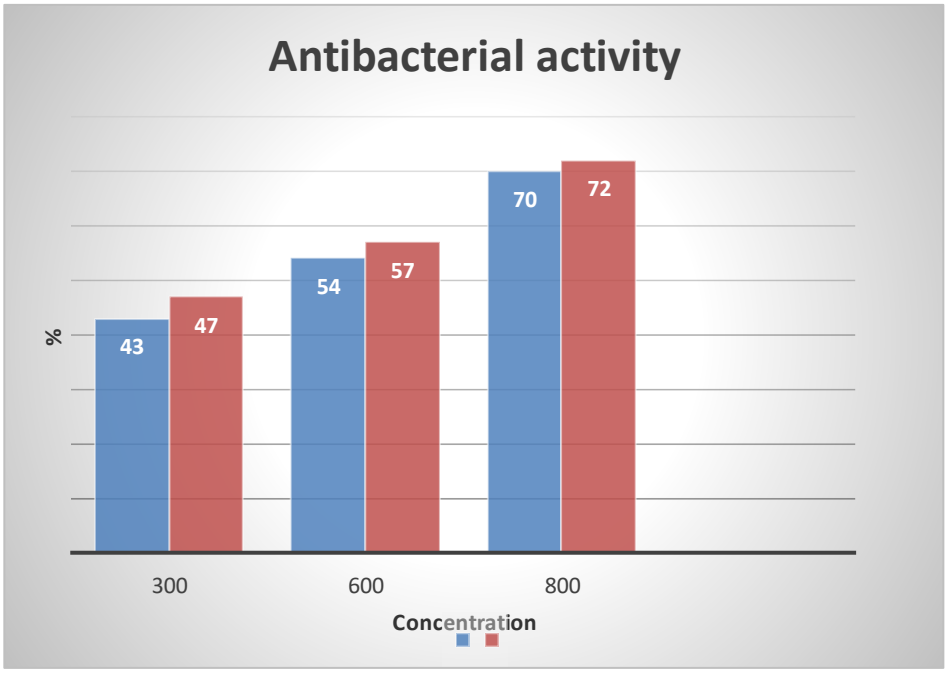
*Means of six replications



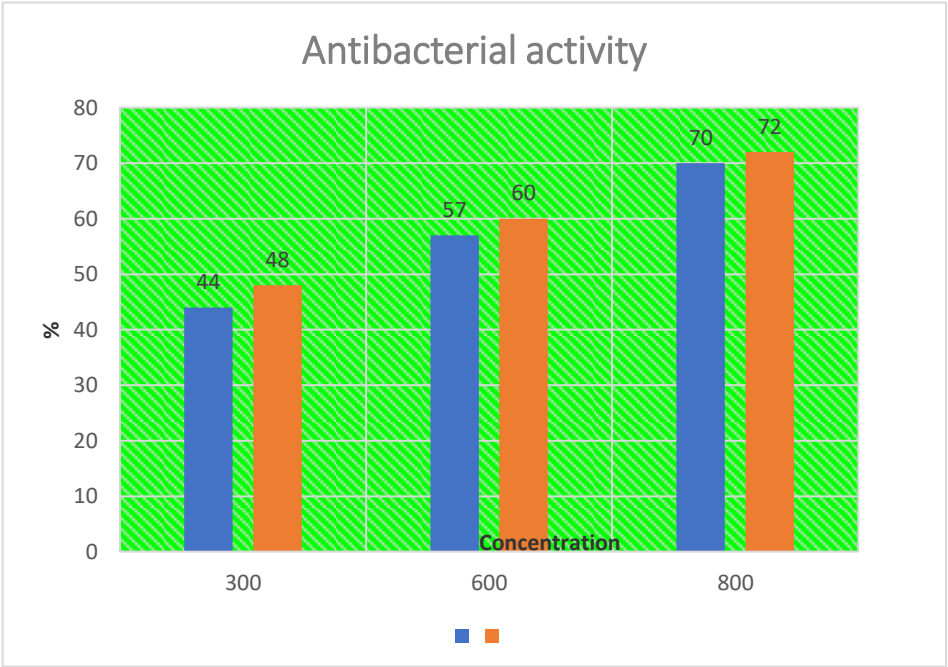
Antibacterial activity of compound-1



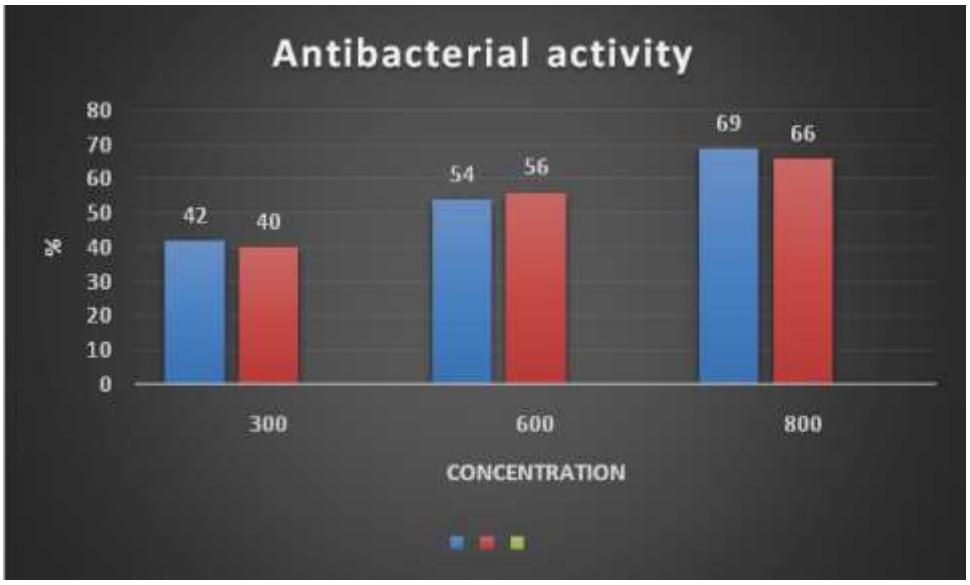
Antibacterial activity of compound-3



Antibacterial activity of compound-4



Antibacterial activity of compound-5



Antibacterial activity of compound-imidacloprid

RESULTS AND DISCUSSION

Chemistry: In the scheme, the 2-chloro-5-{[-2-hydrazinylideneimidazolidin-1-yl] methyl} pyridine (2) was obtained by Reduction of Imidacloprid, then The pH of solution was made alkaline by 5% NaOH & then extracted with ethyl acetate. The organic phase is thoroughly washed with Braine solution and dried over sodium sulphate to get yellowish brown colour compound, yield 79%.The IR spectrum of compound 2 displayed the characteristic sharp absorption bands of Cl and CH_2 at 758, 2907 cm-1, C=N 1614 cm-1 respectively. The ^{1}H-NMR spectrum) δ 4.82-4.84 (s, 2H, CH_2), 3.88 (t, J=7.5 HZ, CH_2), 3.92 (t, J=7.5 HZ,CH_2), 7.26-8.31 (M,Ar) ppm with Carbon NMR spectrums 153,151,146,145,140,139,133,124,50,47 other synthesized compounds also characterized through IR, Proton NMR & Carbon NMR respectively. The Mass spectral fragmentation pattern confirmed the all structure of the synthesized compounds in addition to other spectral data.

Biological Activity: **Insecticidal Activity,** The mortality rate of H.armigera(Hub) ,Mealybugs (Planococcuscitri) and Mango hoppers [Idioscopusclypealis]by synthesized novel neonicotinoid derivatives are shown in Table-1 to Table-3. The death rate of all insects at 600 &800mg litre-1 concentration solution was altogether higher than the death rate at all other concentrations synthesized compound. Biological assays reveal that most of the synthesized compounds exhibit excellent insecticidal activities against different insect species.

Antibacterial Activity: The synthesized molecule was evaluated for their antimicrobial activity against tobacco bacterial wilt and tomato bacterial wilt was evaluated by a Turbidimeter test. Kocide®3000 was used as a standard for antibacterial activity. All synthesized compounds showed Better activity than Imidacloprid.

CONCLUSION

A novel Neonicotinoid derivatives (2-chloro-5-{[-2-hydrazinylideneimidazolidin-1-yl]methyl}pyridine) synthesized by the reduction reaction from 1-[(6-chloropyridin-3-yl)methyl]-N-nitroimidazolidin-2-imine (Imidacloprid).All compound structures were characterized by FTIR, ^{1}H NMR, ^{13}C NMR,Mass and elemental analysis and their insecticidal and antibacterial activities were assessed. Initial biological activity tests showed that the title compound shows better insecticidal activities against Mealybugs. Simillarly, Mango hopper nymph &H.armigera(Hub) also screened at 300,600,800 mg/L .All synthesized compound shows than marketed Imidacloprid,Inintibacterial study synthesized molecule also showed promising antibacterial activities against Pseudomonas solanacearum (e.g., Tobacco bacterial wilt and Tomato bacterial wilt) at a dose of 800 mg/L.The obtained results are promising, which reviled that this work beneficial for further research on the development of new and effective bactericides and pesticides which might facilitate with being applied in management techniques to vector control.

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