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NOVEL HETEROCYCLIC SCHIFF BASE SYNTHESIS AND ANTIMICROBIAL STUDIES

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ABSTRACT

With the aim to synthesize the biologically active molecules a variety of novel **heterocyclic Schiff base** were synthesized via condensation of **heterocyclic** substituted aldehydes and amblodipine base. These newly synthesized compounds were characterized by physical, chemical and spectral analysis data and are further screened for their antimicrobial activity using different Antimicrobes.

KEY WORDS: Amblodipine base, **heterocyclic** Aldehydes, **Schiff base** Antimicrobial Activity.

INTRODUCTION

In medicinal and pharmaceutical field, Schiff bases as well as azo compounds are biologically important compounds.[1-3] It has been suggested that the azomethine linkage might be responsible for biological activities displayed by Schiff bases.

In addition to this, Schiff bases are precursors for the synthesis of some pharmacologically important compounds like thiazolidinone derivatives. Furthermore, they are reported to show a variety of interesting biological actions including antibacterial[4-8],antianxiety, antidepressant[9] antifungal, anti mouse hepatitis virus (MHV)[10], inhibition of herpes simple virus type 1 (HSV-1) and adenovirus type 5 (Ad 5)[11], anti-cancer[12-16], anti-mosquito larvae[17] and herbicidal activities.[18] In agricultural chemistry, it is known that the presence of a chloro and azo moiety in different types of azomethine compounds can exhibit pesticide activity.[19-20]

Over the past 25 years, the extensive research has been devoted to use of Schiff bases as the synthesis for the preparation of various hetrocycles like 2-azetdinones, thiazolidinones.

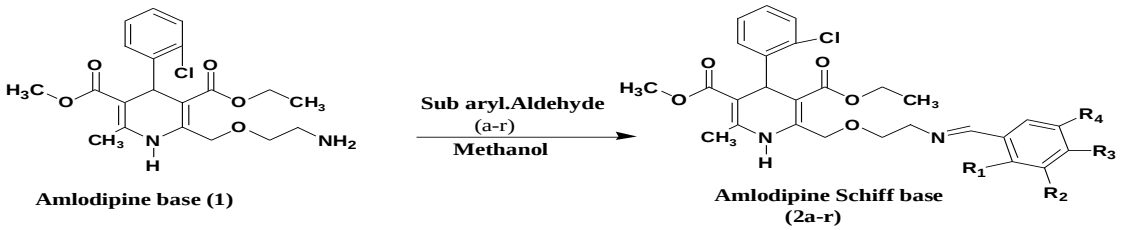
However, no reference is reported on the hetrocycles prepared from amlodipine Schiff bases. With this view we reported here the synthesis of some novel amlodipine Schiff bases via condensation of substituted aldehydes and amlodipine bases in presence of acetic acid at reflux temperature. This newly synthesized sc were Schiff bases Screened for their antimicrobial studies which show moderate to good activity.

MATERIALS AND METHODS

Experimental: Melting points were uncorrected and determined in open capillaries. The purity of the compound is checked by TLC. The IR spectra were recorded on FTIR Shimadzu spectrometer, and ^{1}HNMR spectra were recorded on a Varian 300 MHz spectrometer ($CDCl_3$) using TMS as an internal standard. Mass spectra were recorded on VG 70704 mass spectrometer at 70 ev.

Typical Procedure

Synthesis of 4-(2-chloro-phenyl-2-methyl-6-{2-[(thiophen-2-yl -methylene)-amino–ethoxymethyl}-1,4-dihydropyridine-3,5-dicarboxylic acid 5-ethylester3-methyl esters (5a): An equimolar mixture amlodipine base (1.0gm, 0.002mol) and thiophene 2-carboxyaldehyde (0.273 g, 0.002mol) in 10ml methanol catalytic amount of acetic acid was refluxed for 4-5 hrs. After completion of reaction (checked by TLC), the excess of solvent was removed on rotary evaporator to yield solid which was washed with petroleum ether followed by crystallization from methanol.



Amlodipine base (1)

Amlodipine Schiff base (2a-r)

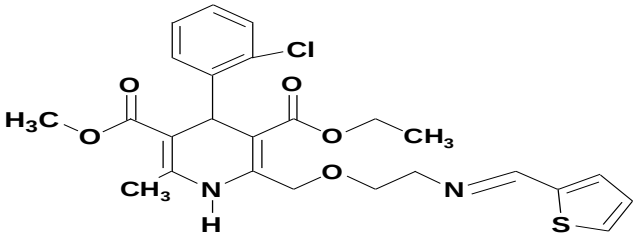
R = Thiophene, pyrrole, N-methyl Indol, N-benzyl-4-formyl piperidine, 4-(1H-1, 2, 4-trizol-1-yl), pyridine-2-carboxaldehyde.

The compounds (**5a-e)** were prepared by following the above procedure and their percentage yields and physical constants were recorded in Table IV. Their structures have been confirmed by Mass, IR and ^{1}HNMR spectra.

Table IV: Physical data of the compounds (5a-e)

Comp. No.	Yield (%)	M. P. (°C)
5a Thiophene 2-Carboxaldehyde	80	141-143
5b N-Methyl -3- Carboxaldehyde Indol 81	70	151-153
5c 4-(1H-1, 2, 4 –trizol-1-yl) benzaldehyde	64	126-128
5d N-Benzyl -4-formyl piperidine	70	153-155
5e 2-pyridine carboxaldehyde	82	149-151

Spectral analysis



(5a)

^{1}HNMR: ^{1}HNMR spectra were recorded in DMSO- d_6 on a Varian AS instrument at 400 MHz using TMS as an internal standard.

(5a):δppm1.1 (t, 3H, CH_3);2.17(s, 3H, CH_3); 3.47(s, 3H, OCH_3);3.85(d, 4H, CH_2); 3.95(m, 2H, CH_2); 4.5(dd, 2H, CH_2); 5.26(s, 1H, CH);7.0-8.0 (m, 7H, aromatic proton); 8.41(s, 1H, imine proton); 8.48 (s, 1H, N-H).

I.R.: I.R. spectra were recorded in KBr disc on Shimadzu FT-IR 8300 spectrophotometer.

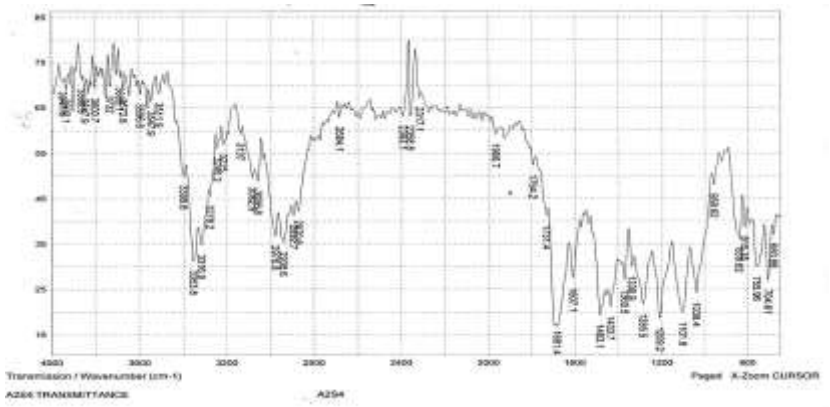
(5a): cm^{-1}3353 (NH), 1731, 1681 (C=O), 1607 (C=N)

Mass: Mass spectra were recorded on Water-Macromass Quattro-II mass spectrometer.

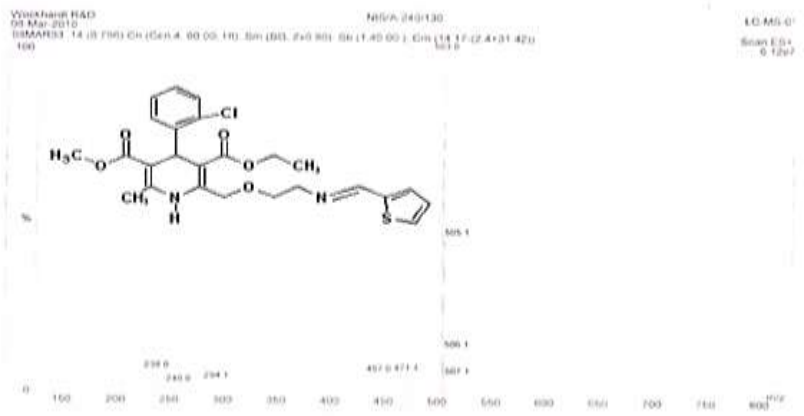
(5a): Mass (m/z) 503 [M+1]

Spectra

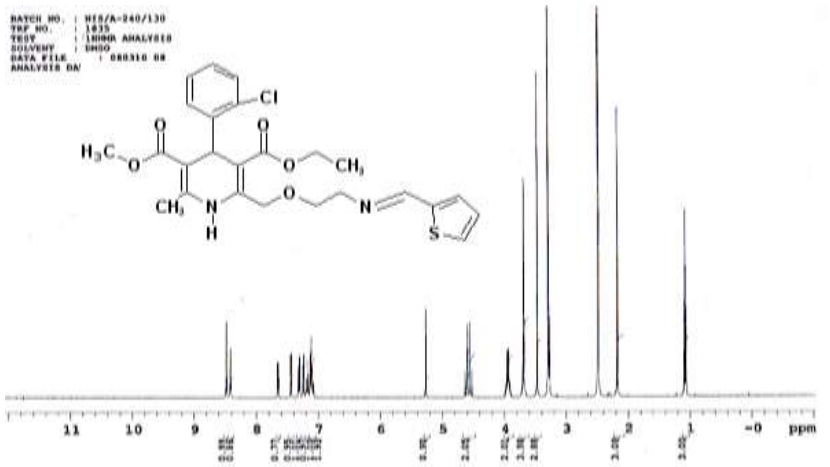
IR



MASS



NMR



Antimicrobial activity: Antimicrobial screening was done by using cup plate method[21-22] at a concentration of 100µg/ml. The compounds were evaluated for antibacterial activity against Bacillus subtilis gr +ve, Pseudomonas aeruginosa gr –ve , Staphylococcus aureus gr +ve, Escherichia coli gr –ve and antifungal activity against Aspergillus niger, Aspergillus Flavus, Curvularia, Alternaria. DMSO was used as solvent control . The results of antimicrobial data are summarized in **table 2.** All compounds show the moderate to good activity against bacteria and fungi.

RESULTS AND DISCUSSION

Table 2: Antimicrobial activity of synthesized compounds (I-V)

Products	Bacteria (Zone of Inhibition in mm)				Fungi (Zone of Inhibition in mm)			
	A	B	C	D	E	F	G	H
I	12	---	23	19	---	---	---	---
II	13	13	11	---	---	---	---	---

III	---	17	21	---	---	---	---	---
IV	14	---	11	---	---	---	---	---
V	---	---	12	---	---	---	---	---

A= *Bacillus subtilis gr +ve,* B= *Pseudomonas aeruginosa gr –ve,*

C= *Staphylococcus aureus gr +ve,* D= *Escherichia coli gr –ve,*

E= *Aspergillus niger*, F= *Aspergillus Flavus,* G= *Curvularia*

H= *Alternaria*.

A variety of novel **heterocyclic** schiff base were synthesized via condensation of substituted aldehydes and amlodipine bases in presence of acetic acid at reflux temperature. Work up procedure is simple and yield of the product is excellent.

All the newly synthesized **heterocyclic** schiff base were characterized by their chemical, physical and spectral analysis data and are further subjected to antimicrobial studies which exhibits moderate to good activity.

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