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SYNTHESIS AND STUDY OF ANTIMICROBIAL ACTIVITIES OF (E)-3-SUBSTITUTED PHENYL-1-PIPERIDINO-2-PROPEN-1-ONE CINNAMAMIDES.

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ABSTRACT:

Cinnamamides constitute an important class of compounds with a variety of biological properties, such as central nervous system depressant, anticonvulsant, muscle relaxant, antiallergic, antineoplastic, antitumor, anesthetic, analgesic and anti-infective activities and anti-infective activities, etc. In the agrochemical field, insecticidal, their avian repellent, herbicidal activities, and several excellent cinnamamide fungicides, for example dimethomorph, fluormorph and pyrimorph, have been successfully developed. Inspire of wide range of their applications and very less attention is paid towards the synthesis of Cinnamamides derivatives containing heterocyclic moiety. Literature survey and biological activities' of Cinnamamides have motivated to undertake the synthesized novel Cinnamamides entitled "(E)-3-Substituted phenyl-1-Piperidino-2-Propen-1-one Cinnamamide". Hence, to decide the use of newly synthesized chemical compound as a possible chemotherapeutic agent, it is very important to carry out its biological screening against the pathogenic microorganisms.

KEYWORDS:

Antimicrobial activity, Cinnamamides, heterocyclic moiety, Piperidine.

INTRODUCTION:

The man is well aware of the existence of many chemical agents which said to be effective in destroying microorganisms. The treatment of diseases with chemotherapeutic substances has

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been known since the 1500s. And since 1935 this therapy has been widely practiced. "Chemotherapeutic agents are chemical substances used for the treatment of infectious diseases or diseases caused by the proliferation of malignant cells." Most of the drugs belong to the class of heterogeneous compounds. Heterocyclic compounds played a vital role in the metabolism of all living cells; large numbers of them are five and six member heterocyclic compounds having one to three hetero atoms in their nucleus. Cinnamamides and their derivatives containing heterocyclic moiety were received much more attention due to variety of activities such as in medicinal field, insecticidal, herbicidal, CNS depressant, antitumor, bird repellent, anesthetic, analgesic etc.[1-6] Cinnamamides may be used as an intermediate or precursor in many organic syntheses and pharmaceutical formulations[7-9]. After going through the detail literature survey it was observed that there is no evidence for the use of simple Wittig reaction in the synthesis of Cinnamamides. H_2O is demonstrated to be an excellent medium for the Wittig reaction employing yields and aldehydes [10-13]. Solubility of the starting material will be increases by the addition of catalytic amount of sodium Lauryl Sulphate (SLS). Although the solubility in water appears to be an unimportant characteristic in achieving good chemical yields. The rate of Wittig reactions in water is unexpectedly accelerated [14]. Hence, Wittig reaction is a reliable method for the synthesis of a wide range Cinnamamides and can be applied with confidence. Due to wide range of such applications Cinnamamides and their derivatives acquires a great value in various fields. Hence, to decide the use of newly synthesized chemical compound as a possible chemotherapeutic agent, it is very important to carry out its biological screening against the pathogenic microorganisms.

EXPERIMENTAL:

MATERIALS AND METHODS

All reagents and solvents were procured from high quality chemicals. Progress of the reactions was monitored by Thin Layer Chromatography. The synthesized compounds were purified by using column chromatography and identity of compounds was confirmed by Melting Points, Elemental analysis, I.R., 1H NMR, 13C NMR and Mass spectral data.

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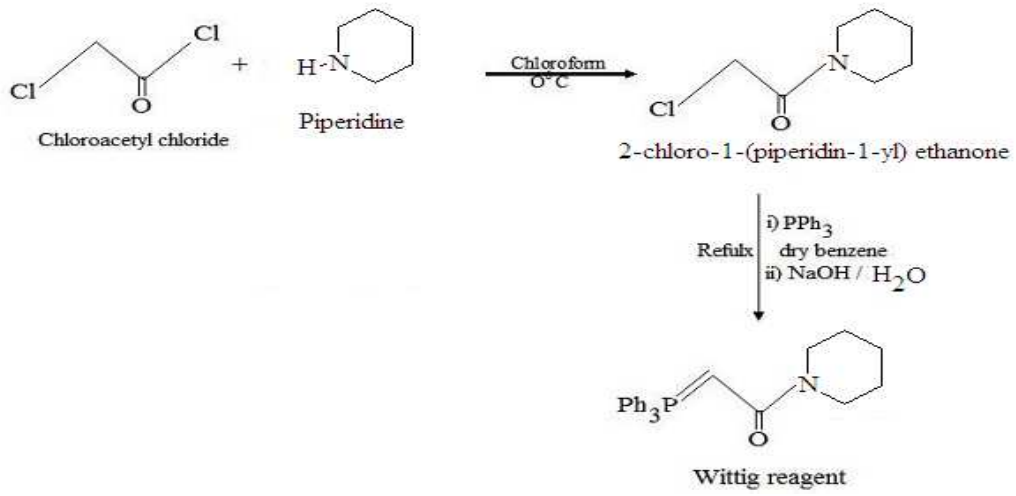
General Procedure

Preparation of Wittig Reagent: (Scheme 1):

Chloroacetyl chloride (0.1M) was added to the (0.1M) solution of piperidine in Chloroform at 0°C with constant stirring for 30 minutes. The reaction mixture was stirred at room temperature for 20 minutes and then washed with 10% Na_2CO_3 solution, the organic layer was separated and dried over Na_2SO_4, then evaporated to about 1/3rd volume and chloracetamide was collected as yellowish liquid. This liquid was added to the stirred solution of triphenyl phosphine in dry benzene and refluxed for 03 hours. White crystalline solid was obtained; it was dissolved in dry benzene (90ml) and water (10ml) solution. To this solution 1-2 drops of phenolphthalein indicator were added followed by the addition of 10% NaOH, till the pink color persist. Organic layer was separated, washed with water and evaporated to about 1/3rd volume. Finally, the liquid was scratched with hexane to obtain Wittig reagent.



Synthesis of (E)-3-Substituted phenyl-1-Piperidino-2-Propen-1-one Cinnamamide (Scheme 2):

In a 100 ml round bottom flask, 10 ml H_2O and a pinch of Sodium Lauryl Sulphate (SLS) were taken and flask was equipped with stir bar. To this solution aromatic aldehyde was added and the reaction mixture was stirred for 10 minutes at the room temperature. Then 01 g of Wittig reagent was added with constant stirring and the reaction mixture was refluxed for 3-4 hours. The

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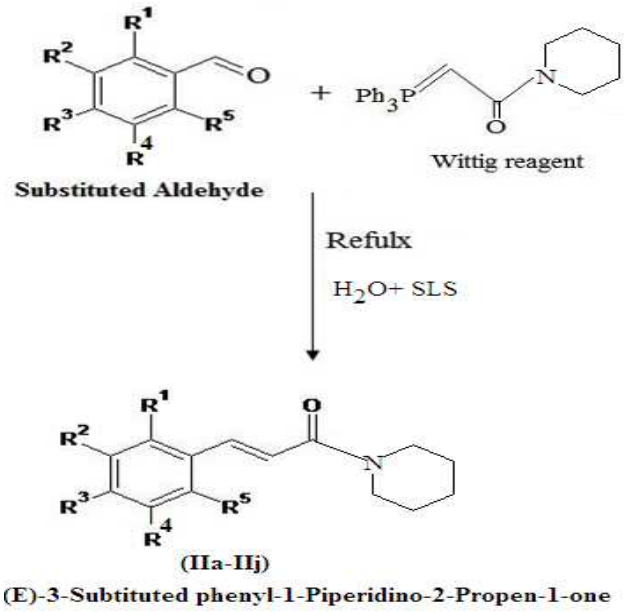
progress of reaction was monitored by thin layer chromatography. After completion of reaction, crude product was filtered off and purified by column chromatography by using silica (mesh 160) to obtained piperidino Cinnamamides (IIa-IIj).



ANTIMICROBIAL ACTIVITIES:

Antimicrobial activities of newly synthesized Cinnamamides containing heterocyclic moiety were carried out by using cup plate agar diffusion method at 1.0 mg / ml, 0.5 mg/ml, and 0.25 mg/ml in DMSO against using antibiotics ciprofloxacin. Plates were incubated 24hrs at 37^0C and zone of inhibition were measured in mm. Result have been incorporated in table, all synthesized compound were found to be moderately active against *S. aureus*, *Bacillus pumilus, and E.coli* bacteria at a different concentration.

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Table-1:-Substituted aromatic aldehydes used in the synthesis of Cinnamamides

Entries	R1	R2	R3	R4	R5
IIa	H	H	H	H	H
IIb	H	H	OMe	H	H
IIc	H	OMe	OMe	H	H
IId	H	OMe	OMe	OMe	H
IIe	H	-O-CH_2-O-		H	H
IIf	NO_2	H	H	H	H
IIg	H	H	Cl	H	H
IIh	H	H	NO_2	H	H
IIi	H	H	$N(Me)_2$	H	H
IIj	H	H	OH	H	H

Table-2:- Characteristics data for synthesized Cinnamamides

Entries	Molecular Formula	Molecular weight	Yield %	M.P. ^{0}C
IIa	$C_{14}H_{17}ON$	215	62	162
IIb	$C_{15}H_{19}O_2N$	245	64	174
IIc	$C_{16}H_{21}O_3N$	275	70	186
IId	$C_{17}H_{23}O_4N$	305	64	202
IIe	$C_{15}H_{17}O_3N$	259	68	192
IIf	$C_{14}H_{16}O_3N_2$	260	72	160
IIg	$C_{14}H_{16}ONCl$	249	52	180
IIh	$C_{14}H_{16}O_3N_2$	260	66	212
IIi	$C_{16}H_{22}ON_2$	258	60	188
IIj	$C_{14}H_{17}O_2N$	231	62	184

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Table-3:-Elemental analysis of synthesized compounds-

Entries	Molecular Formula	Mol. Wt.	% C	% H	% O	% N	% Cl
IIa	$C_{14}H_{17}ON$	215	78.10 (78.14)	7.96 (7.91)	7.43 (7.44)	6.51 (6.51)	--
IIb	$C_{15}H_{19}O_2N$	245	73.44 (73.47)	7.81 (7.76)	13.04 (13.06)	5.71 (5.71)	--
IIc	$C_{16}H_{21}O_3N$	275	69.79 (69.82)	7.69 (7.64)	17.43 (17.45)	5.09 (5.09)	--
IId	$C_{17}H_{23}O_4N$	305	66.86 (66.89)	7.59 (7.54)	20.96 (20.98)	4.59 (4.59)	--
IIe	$C_{15}H_{17}O_3N$	259	69.48 (69.50)	6.61 (6.56)	18.51 (18.53)	5.40 (5.41)	--
IIf	$C_{14}H_{16}O_3N_2$	260	64.60 (64.62)	6.20 (6.15)	18.44 (18.46)	10.76 (10.77)	--
IIg	$C_{14}H_{16}ONCl$	249	67.33 (67.33)	6.46 (6.41)	6.41 (6.41)	5.61 (5.61)	14.20 (14.23)
IIh	$C_{14}H_{16}O_3N_2$	260	64.60 (64.62)	6.20 (6.15)	18.44 (18.46)	10.76 (10.77)	--
IIi	$C_{16}H_{22}ON_2$	258	74.38 (74.42)	8.58 (8.53)	6.19 (6.20)	10.84 (10.85)	--
IIj	$C_{14}H_{17}O_2N$	231	72.70 (72.73)	7.41 (7.36)	13.83 (13.85)	6.06 (6.06)	--

In bracket calculated percentages of element.

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Table-4:-Antimicrobial Activities of the compounds (in mm)

Compounds	*Staphylococcus aureus*			*Bacillus pumilus*			*Escherichia coli*		
	1Mg/ml	0.5Mg/ml	0.25Mg/ml	1Mg/ml	0.5Mg/ml	0.25Mg/ml	1Mg/ml	0.5Mg/ml	0.25Mg/ml
IIa	16	14	10	14	12	--	18	11	10
IIb	13	12	10	16	13	12	22	17	15
IIc	19	16	13	15	13	10	26	13	10
IId	15	13	11	22	18	15	18	11	09
IIe	14	12	11	19	16	14	16	11	10
If	20	16	14	28	22	18	18	14	12
IIg	25	20	18	18	16	16	21	14	10
IIh	22	16	14	18	14	12	16	15	11
IIi	20	14	10	21	16	11	28	18	14
IIj	21	16	12	22	11	08	29	22	20

SPECTROSCOPIC DATA OF REPRESENTATIVE COMPOUNDS:

The IR spectra were recorded on Perkin Elmer spectrometer and 1HNMR spectra were recorded on Varian; USA makes Mercury plus 400 MHz, NMR Spectrometer by using CDCl3 with TMS as internal standard. H NMR Spectrometer by using CDCl3 with TMS as internal standard. The mass spectrum was recorded on Jeol make Accu TOF, Mass Spectrometer.

IIa=(E)-3- phenyl-1-piperidino-2-propen-1-one Cinnamamides-

IR spectra : (KBr) λmax (cm^{-1})1607cm^{-1}(-C=C-, olefinic), 1595; H NMR-(400 MHz, CDCl3, δ ppm) 1.2(m),(2H), CH_2; 1.4(m), (4H) CH_2; 3.4(t), (4H), $2CH_2$-N; 6.8(d), (1H), (CH=CHCO), J=15.94 HZ; 7.2(d), (1H), (CH=CH-Ar) J=15.94 HZ; 7.2-7.5(m), (5H), (Ar-H). Mass: m/z (%): 215.13 (100) (M)+, 216.0 (15.50).

IIb- =(E)-3-(p-methoxyphenyl)-1-piperidino-2-propen-1-one Cinnamamides- IR spectra : (KBr) λmax (cm^{-1}) 1685, 1600; 1H NMR-(400 MHz, CDCl3, δ ppm))- 1.2(m),(2H), CH_2; 1.4(m), (4H)

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CH_2; 3.4(t), (4H), $2CH_2$-N; 6.8(d), (1H), (CH=CHCO), J=15.94 HZ; 7.0(d), (1H), (CH=CH-Ar) J=15.94 HZ; 7.2-7.5(m), (4H), (Ar-H); 3.2(s), (3H), (-O-CH_3). Mass: m/z (%): 245.15 (100) (M)+, 246.14 (16.59).

RESULTS AND DISCUSSION:

All synthesized novel cinnamamides compounds contained heterocyclic moiety in the form of Piperidine. By using Witting reaction method novel cinnamamides containing heterocyclic moiety entitled "(E)-3-Substituted phenyl-1-Piperidino-2-Propen-1-one Cinnamamide" are synthesized from different aromatic aldehydes and Witting reagents having good yields. The yields of synthesized compounds were ranging from 52 to 72%. All synthesized compounds were characterized on the basis of melting point, elemental analysis, Rf value, IR spectra and 1HNMR spectral analysis. Preliminary results showed that all the synthesized compounds had certain antimicrobial activities against *S. aureus, Bacillus pumilus,* and *E.coli* at a different concentration.

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