Applied Clinical Pharmacology and Toxicology

Research Article

Kapila P, et al. App Clin Pharmacol Toxicol: ACPT-104.

Microwave Assisted Synthesis, Characterization and Antibacterial Studies of Some Biologically Potent Schiff Bases

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Citation: Kapila P, Pritam A, Chauhan K, Singh P, Sharma D, et al. (2017) Microwave Assisted Synthesis, Characterization and Antibacterial Studies of Some Biologically Potent Schiff Bases. App Clin Pharmacol Toxicol: ACPT-104.

Received date: 17 April, 2017; **Accepted date:** 18 July, 2017; **Published date:** 25 July, 2017

Abstract

A new series of biologically potent Schiff bases derived from para-chlorobenzaldehyde with some amino acids as 2-aminoethanoic acid, 2-amino-4-(methylthio) butanoic acid, 2-amino-3-sulfhydryl propanoic acid, 2-amino propanoic acid. These compounds were synthesized by microwave as well as thermal methods. Comparative studies have also been done by two synthetic methods. The structures of the Schiff bases were analyzed by using physical methods namely melting points, molecular weight determination and UV, IR and H1NMR spectroscopic means. The synthesized compounds have been screened for antimicrobial activity against gram negative (*Escherichia coli*) and Gram-positive (*Bacillus subtilis*) bacterial strain. All newly synthesized compounds showed significant antibacterial activity against microbial species.

Keywords: Amino Acids; Antimicrobial Activity; Microwave Synthesis; Para-chlorobenzaldehyde; Schiff Bases

Introduction

Increasing attention for environmental protection during the last decades has led both modern academic and industrial groups to develop chemical processes with maximum yield and minimum cost while using nontoxic reagents, solvents and catalysis. One of the tools used to combine economic aspects with the environmental ones is the green chemistry [1].

This process consists of microwave assisted synthesis [2] which has been carried out without isolation of any intermediate, resulting in reduction in time, saving money, energy and raw materials. In the last few years there has been an increased interest in the use of microwave in organic [3] and organ metallic compound synthesis [4-6] and it forms now the basis of a number of commercial systems [8]. Some interesting features of this method are the rapid reaction rates, simplicity, less consumption of solvent and the ease of work up after the reaction it has been observed that microwave irradiation generates rapid intense heating of polar substances, which results in the reduction of reaction time compared to conventional heating [7]. The compounds with the structure of –C=N- (azomethine group) are known as Schiff bases, which are usually synthesized from the condensation of primary amines and active carbonyl groups. Schiff bases derived from aromatic amines and aromatic aldehydes have a wide variety of applications in many fields, i.e., biological, inorganic and analytical chemistry [1-4]. In addition, Schiff bases and heterocyclic ring are important class of compounds in medicinal and pharmaceutical field [5-8]. Previous work on Schiff bases shows biological properties including antibacterial, antifungal antitumor, analgesic and anti-inflammatory activities [9-18]. In view of these observations the field of Schiff base complexes has been fast developing on account of the wide variety of possible structures for the ligands depending upon the aldehydes and amines. Schiff bases are considered as a very important class of organic compounds, which have wide applications in many biological aspects [1]. Transition metal complexes of Schiff bases are one of the most adaptable and thoroughly studied systems. These complexes have also applications in clinical, analytical and industrial in addition to their important roles in catalysis and organic synthesis [2]. Studies of a new kind of chemotherapeutic Schiff bases are now attracting the attention of biochemists [3,4]. Schiff base metal complexes can now be considered a widely studied subject due to their industrial and biological applications [5]. The discovery and development of antibiotics are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases. Antimicrobial agents reduce or completely block the growth and multiplication of bacteria and are helpful in the treatment of various infectious diseases like meningitis, malaria, tuberculosis, pneumonia, AIDS [24] and so forth. However, the increasing microbial resistance to antibiotics in use nowadays become necessitates for a search of new compounds with potential effects against pathogenic bacteria. Due to the great flexibility and diverse structural aspects of Schiff bases, a wide range of these compounds have been synthesized and reported to have antimicrobial and antitumor activities [7-13]. In the present work we are proposing the synthesis of biologically potent Schiff bases by microwave as well as conventional methods. Comparisons have also been drawn between these two synthetic methods. These compounds were analyzed by physic-chemical measurements and spectroscopic means. Antimicrobial activities have been checked against pathogenic bacteria.

Experimental

The compounds used for synthesis of Schiff bases are amino acids i.e., 2-amino ethanoic acid,2-amino-4-(methylthio)butanoic acid,2-amino-3-sulfhydryl propanoic acid and 2-amino propanoic acid (Qualikems) and an aldehyde, para chlorobenzyldehyde (S.D. Finechem.). The compounds were synthesized by microwave radiations as well as conventional heating methods.

Synthesis of Schiff base

Conventional method: The Schiff bases were synthesized by thermal as well as microwave methods. The mixture of p-chlorobenzaldehyde (1.5 g) and calculated amount of amino acid were mixed in 5-6ml of ethanol were boiled for 9-10 min on heating mental at temperature 40-45˚C. The progress of the reaction was monitored by TLC (Thin Layer Chromatography). The melting point and solubility was checked and the purity of compounds was checked in different intervals. On completion of reaction the product was filtered off, dried and recrystallized from methanol.

Microwave method: In microwave-assisted synthesis foresaid amount of compounds were mixed with minimum amount of methanol and paste was form. This mixture was taken in an open borosil beaker and then irradiated (750 Watt) for 3-5 minutes. The drastic reduction in the reaction time was observed due to the rapid heating capability of microwaves. The progress of reaction was checked by TLC. After the completion of reaction, solid products obtained which were filtered off and recrystallised from methanol. It was observed that in microwave method less amount of solvent was consumed, reaction completion time was reduced as well as the yield was high as compare to conventional heating method.

Physical measurements and analytical methods: The molecular weights were determined by the Rast Camphor Method [18]. Sulphur and nitrogen were estimated gravimetrically (Messenger's method) as BaSO4 and by the Kjeldahl's method [17] respectively. The compounds were characterized by spectral techniques UV, IR and 1HNMR.

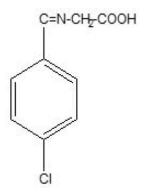
Antibacterial screening: Antibacterial activity was evaluated against Bacillus subtilis and Escherichia coli by the zone of inhibition test (Kirby-Bauer Test). The Nutrient agar medium in distilled water was autoclaved for 20 min at 15 psi before inoculation. Flat bottom Petri discs were used and nutrient agar solution was taken in them. The test compounds were dissolved in methanol to give 1000 ppm final concentrations. A microbial suspension is spread by a sterile swab, evenly, over the face of a sterile agar plate. The antimicrobial agent is applied to the center of the agar plate (in a fashion such that the microbial strains doesn't spread out from the center) and incubated. If substantial antimicrobial activity is present, then a zone of inhibition appears around the test products. The zone of inhibition is simply the area on the agar plate that remains free from the microbial growth. These Petri discs were incubated for 24 h at 25±2˚C and zone of inhibition was measured in mm.

Results and discussions

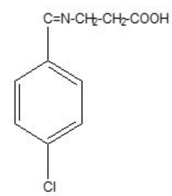
Various Schiff bases were synthesized by conventional as well as microwave methods using ethanol as solvent. The elemental analysis and spectral data are consistent with the formulation of compounds. (Table 1) shows the synthetic and analytical data of synthesized compounds.

Compounds	Empirical formula	Colour and state	M.P.	Elemental Analysis		Molecular weight
			(˚C)	N	S	Obs(cal)
				Obs.(cal.)	Obs.(cal.)	
p-chlorobenzal-diene glycine	C_8H_6O2NCl	white, solid	60	7.84 (7.61)	-	188.57(183.53)
($C_1C_6H_4$CHO)						
p-chlorobenzal-diene methionine						
($C_1C_6H_4$CHO)	$C_{12}H_{14}O_2$NSCl	creamish, solid	96	5.29 (5.16)	11.58(11.83)	267.97(271)
p-chlorobenzal-diene alanine						

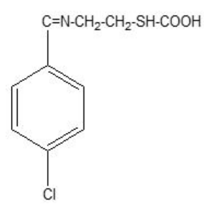
$(C_1C_6H_4CHO)$						
p-chlorobenzal-diene cystiene	$C_{10}H_9O_2NCl$	creamish, solid	42	6.46 (6.61)	-	208.42 (211.56)
$(C_1C_6H_4CHO)$						213.38 (208.16)
	$C_7H_7O_2NSCl$	white, solid	100	6.66 (6.72)	14.91 (15.40)	
(* cal-calculated, *obs-observed)						



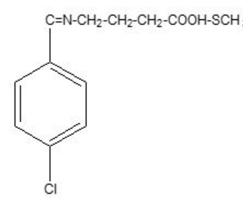
(A) p-chlorobenzaldienel glycine



(B) p-chlorobenzaldiene alanine



(C) p-chlorobenzaldiene cystiene



(D) p-chlororbenzaldiene methionine

High percentage yield, less amount of solvent and few minutes were consumed in completion of overall reactions by using microwave method as compared to conventional method.

Compounds	% Yield		Solvent (ml)		Time(min)	
	Thermal	Microwave	Thermal	Microwave	Thermal	Microwave,
p-chlorobenzal-diene glycine	43	86	5	3	9	3
p-chlorobenzal-diene methionine	50	83	6	4	10	4
p-chlorobenzal-diene alanine	41	79	5	3	8	2.5
p-clorobenzaldiene cystiene	55	74	5	3	9	3

Table 2: The comparison between thermal and microwave methods.

UV Spectra

The UV spectra of Schiff bases have two bands at different wavelengths (λ nm) with their molar extinction coefficient values. The lower wavelength bands for all Schiff bases have a range between 246-255 nm. They are assigned to the aromatic nature of all Schiff bases. These bands have a molar extinction coefficient greater than 1000 and are attributed to the π-π* (benzenoid) transitions of the aromatic system [8]. The longer wavelength bands for Schiff bases have a range of values between 282-328 nm and are assigned to C=N linkages. This is due to n-π* transitions [6].

IR Spectra

The IR spectral data of the synthesized compounds are represented in the (Table 3). The sharp and strong bands appear in the region 1600-1695 cm-1 in the spectrum indicates the presence of imine group [18]. Sharp bands appear in this region assigned to the stretching mode of >C=N group. In the spectra bands appears in the range of 2800-3000 cm-1 assigned to CH2 groups attributed to the symmetric and asymmetric vibrations. A broad stretching band in the range between 2500-3000 cm-1 confirms the presence of carboxyl group. A strong to medium intensity bands are assigned to carbonyl groups in Schiff bases. They have a stretching frequency ranged between (1633.20-1745.51) cm-1. All stretching frequency lower than 1700 cm-1 can be explained by the fact of carboxylic acids can exists in dimeric trimeric and polymeric [16] species by the aid of intermolecular hydrogen bonding and the condition of IR measurement i.e. whether if it is in solid or solution state. Hence these strong hydrogen bonding states are accompanied by weaken the double bond of carbonyl group in carboxylic acid. The last results are expected and will shift the frequency of C=O group to lower value of wave number. Another sharp band was observed in two compounds at 2580 cm-1 and 2595 cm-1 indicates the presence of (SH) group.

IR Spectral data (cm^{-1})							^{1}HNMR Spectral data(δ,ppm)	
S,NO	Compounds	C=N	OH		CH_2	SH	CH_2	Aromatic
			(Str.)	(Ben.)			(s)	Proton(m)
1	p-Chlorobenzaldiene glycine	1694	2596	1483	2858	-	0.1	7.5-7.8
2	p-chlorobenzaldiene methionine	1694	2580	1447	2858	2580	0.12	7.1-8.1
3	p-chloro benzaldiene cystiene	2090	2554	1436	2950	2595	1	7.0-8.0
4	p-chloro benzaldiene alanine	1620	2506	1412	2936	-	1.2	7.6-7.9
*m-multiplet or complex,*s-singlet, *Str-stretching,* Ben-bending								

Table 3: Shows the Spectral data of newly synthesized compound.

^{1}HNMR

The above bonding patterns are further supported by the 1HNMR studies of synthesized Schiff bases. The 1HNMR spectral data are represented in (Table 4). Aromatic proton signals appear in the range of δ 7.0-8.1 ppm.CH2 proton signals appear in the range of δ 0.10-1.2 ppm. The absence of NH2 proton signals at δ 4-5 ppm clearly suggests the formation of azomethine bond in the synthesis [25].

Antimicrobial studies

The compounds have been screened in vitro for their antibacterial activity. The results are indicative of the fact that these compounds exhibit the antimicrobial properties. The results recorded from the biological activity were also further compared with the standard Amoxicillin. Antimicrobials can attack various targets in microorganisms, as a consequence of which the organisms are either destroyed or have their growth inhibited [5]. Since the complexes inhibit the growth of microorganism, it is assumed that the production of the enzyme is being affected and hence the microorganisms are unable to utilize the food for themselves, or the intake of ion decreases and consequently the growth ceases. The toxicity of antibacterial compounds against different species of bacteria depends either on the difference in ribosomes, or the impermeability of the cell to the antimicrobial agent. Bacterial screening data shows that under identical experimental conditions the compounds possess antimicrobial activities.

S.NO	Compounds	Antibacterial screening Diameter of inhibition zone, mm (after 24 h, concentration in ppm)	
		Bacillus subtilis	***Escherichia coli***
		1000	1000
1	p-Chlorobenzaldiene glycine	13	7
2	p-chlorobenzaldiene methionine	5	9
3	p-chloro benzaldiene cystiene	14	12
4	p-chloro benzaldiene alanine	11	10
5	Standard (Amoxicillin)	14	15

Table 4: The antimicrobial activities of Schiff bases.

P-Chlorobenzaldiene glycine, p-chlorobenzaldiene cystiene, p-chlorobenzaldiene alanine, shows better activity against gram +ve bacteria (*Bacillus subtilis*) whereas p-chlorobenzaldiene methionine shows effective results against gram-ve bacteria (*Escherichia coli*). P-chloro benzaldiene cystiene shows same result as that of standard Amoxicillin against gram+ve bacteria (*Bacillus subtilis*).

Acknowledgement

Authors are thankful to Punjab University, Chandigarh, India to provide the facilities H1NMR, IR spectra of synthesized compounds.

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