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ANTIBACTERIAL ACTIVITES OF SOME NEW AMINO ACID-SCHIFF BASES

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ABSTRACT

Some new (N-indolidene-DL-glycine, N-indolidene-DL-alanine and N-indolidene-DL-valine) amino acid-Schiff bases were prepared by the condensation of indole-3-carboxaldehyde and DL-glycine, DL-alanine and DL-valine and characterized by elemental analysis, IR, UV-Vis, ^{1}H-NMR spectroscopy and ^{13}C-NMR spectroscopy. Antimicrobial activities of the amino acid-Schiff bases have been tested against four different microorganisms.

Key Words: Amino acid, schiff bases, antibacterial activity, microorganism

BAZI YENİ AMİNO ASİT-SCHİFF BAZLARININ ANTİMİKROBİYAL AKTİVİTELERİ

ÖZET

Indol-3-karboksaldehit ve DL-glycine, DL-alanine ve DL-valin'nin kondenzasyon yolu ile bazı yeni (N-indolidene-DL-glycine, N-indolidene-DL-alanine and N-indolidene-DL-valine) amino acid-Schiff bazları sentezlenerek yapıları element analizi, IR, UV-Vis, ^{1}H-NMR ve ^{13}C-NMR spektroskopi ile aydınlatıldı. Amino acid- Schiff bazlarının dört farklı mikroorganizmalara karşı antimikrobial aktiviteleri ölçüldü.

Anahtar Kelimeler: Amino asit, schiff bazları, antibakteriyal aktivite, mikroorganizma

1. INTRODUCTION

Chemists have reported on the chemical, structural and biological properties of Schiff bases. Schiff Bases are characterized by the -N=CH- (imine) group which imports in elucidating the

mechanism of transamination and rasemination reaction in biological system (1,2). Schiff bases are active against a wide range of organisms for example; Candida Albicans, Escherichia coli Staphylococcus aureus, Bacillus polymxa, Trychophyton gypseum, Mycobacteria, Erysiphe graminis and Plasmopora viticola.

Antibacterial activity has been studied more than antifungal activity. Because bacteriums can achieve resistance to antibiotics through biochemical and morphological modifications (3,4).

Bacteriums; Any of several types of microscopic or utra-microscobic single-celled organisms occurring in enormous numbers everywhere in nature, not only in land, sea and air, but also on or in many parts of the tissues of plants and animals, and forming one of the main biologically interdependent groups of organisms in virtue of the chemical changes which many of them bring about, e.g. all forms of decay and the building up of nitrogen compounds in the soil (5).

A literature survey reveals that although a few Amino acid- Schiff bases derived from amino acid have been prepared, their biological activity have scarcely been investigated.

In this study we report the synthesized and characterized some new Schiff Bases for pharmacologial studies.

2. MATERIALS and METHODS

All chemicals used in this investigation were reagent grade and were purified when necessary (6). Elemental analyses were carried out with a LECO-CHNS-9320 model. ^{1}H and ^{13}C-NMR spectra of ligands and their were recorded with a Bruker Spectrospin Avance DPX-400 using TMS as internal standard and DMSO as solvent. The electronic spectra were recorded on an Unicam-UV2-100 spectrofotometer in DMF. Infrared spectra of ligands and their complexes were recorded on a Mattson-4000 FT-IR in KBr pellets. The melting points of ligands and their complexes were determined with a Gallenkamp melting point apparatus.

2.1 Sythesis of Schiff Bases

A quantity of 5 mmol amino acid was dissolved in 10 mL of water and added with constant stirring to 20 mL MeOH solution containing 5 mmol KOH. The solution was stirred on a water bath at 300°C for two hours and then filtered. The filtrate was added drop wise to 10 mL of MeOH solution of indole-3-carboxaldehyde (5 mmol) with stirring on a water bath at 300°C for four hours, filtered and left to stand. On standing for a further 6 h, the yellow solid product that formed was collected by vacuum filtration, washed with a small volume of acetone and dried in vacuum.

2.2. Antibacterial Testing

The bacterial subcultures for B. subtilis, S. aureus, and E. coli were obtained from G. Ü. Gazi Hosbital, Microbiology Depertment. An antifungal susceptibility test was used C. albicans (ATCC 90028). The B. subtilis, S. aureus, E. coli and C. albicans liquid cultures were prepared in Brain Heart Infusion Broth (BHI). The bacterial and yeast cultures were incubated at 37°C for 18 h. The ligant and its complexes were stored dry at room temperature and dissolved 5000 g/cm^3 in dimethylsulfoxide (DMSO). Antibactericidal and Antifungicidal activities of each compound were evaluated by the well-diffusion method. 1 cm^3 of a 24 h broth culture containing 106 CFU/cm^3 was placed in sterile petri-dishes. Molten nutrient agar (15 cm^3) kept at ca. 45°C was then poured in the petri-dishes and allowed to solidify. Then holes of 6 mm diameter were punched carefully using a sterile cork borer and these were completely filled with the test solutions. The plates were incubated for 24 h at 37°C. The mean value obtained for the two holes was used to calculate the zone of growth inhibition of each sample.

3. RESULT AND DISCUSSION

Three new Schiff bases have been synthesized from the condensation of indole-3-carboxaldehyde with DL-glycine, DL- alanine and DL-valine (Fig.2). The analytical and physical data are listed in Table 1.

Table 1. Analytical and Physical data for the Schiff bases

Compound	Empirical Formula (Formula Weight)	*Yield %	m.p. (°C)	Analysis Found (Cald) %		
				C	H	N
Ind-gly	$C_{11}H_8N_2O_2$ (200)	62	162-164	65.49 (66.00)	3.59 (4.00)	13.56 (14.00)
Ind-ala	$C_{13}H_{11}N_2O_2$ (227)	67	176-177	68.40 (68.72)	4.85 (4.40)	12.63 (12.33)
Ind-val	$C_{15}H_{16}N_2O_2$ (256)	61	174-176	69.98 (70.31)	5.85 (5.60)	10.78 (10.93)

* The compounds are yellow.

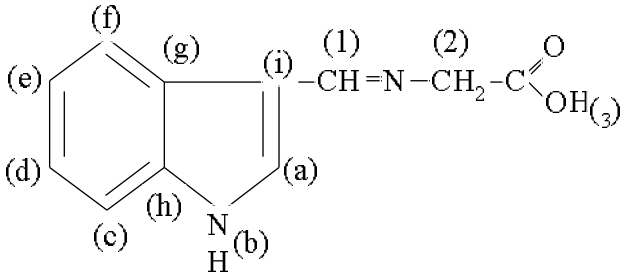
3.1. FTIR and UV-Vısıble Spectral Studies of amino acid-Schiff Bases

Schiff bases are soluble in methanol, ethanol, other polar solvents and n-hegzan. Analytical, physical electronic and characteristic i.r. spectral data of the Schiff bases are given in Table 2. The strong absorptions at 1532-1552 cm^{-1} and 1446-1423 cm^{-1} are attributed to the ring C=C stretching and $\equiv C$ -O-H in plane bending bands (7). The azomethine stretching bands are observed in the range 1632- 1612 cm^{-1}. The observation of bands in the range 2992-2981 cm^{-1} may be attributed to the $\nu_{vinilic}$ stretching vibration (8,9).

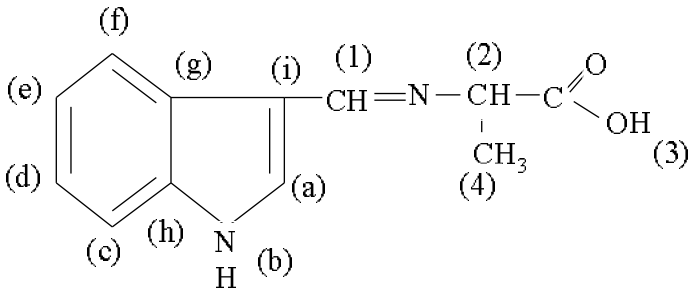
The electronic spectra of the Schiff bases in hegzan show three bands at 221-224, 261-264, 335-346 nm. The band in the 221-224 nm region is ascribed to a $\pi - \pi^*$ transition due to molecular orbitals originating in the -N-C- moiety (7). In the ligands, the band appearing in the 335-346 nm range is assigned to the azomethine chromophore $\pi - \pi^*$ transition. Bands at higher energies (261-264 nm and 221-224 nm) are attributed to the indole-ring $\pi - \pi^*$ and n-π^* transition (6).

Table 2. Major IR absorption band (cm^{-1}) and electronic spectral data

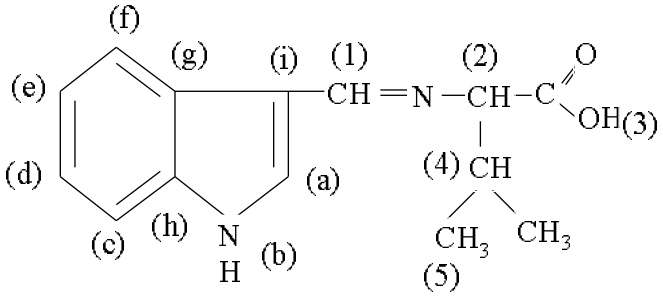
Compound	$\nu_{(OH)}$	$\nu_{(NH)}$	$\nu_{(CH=N-)}$	$\nu_{(CH)vinilic.}$	$\nu_{(-C=O)}$	$\nu_{(C=C)ring}$ $\nu_{(C-O-H)bending}$	$\lambda_{(nm)}$; [ε_{max}(L.cm^2 mol^{-1})]
Ind-gly	3256	3147	1632	2987	1718	1552 1446	223, [13300] 264, [4800] 335, [8820]
Ind-ala	3263	3148	1633	2992	1725	1555 1445	221, [21300] 261, [9200] 339, [9700]
Ind-val	3261	3146	1632	2989	1723	1532 1423	224, [12310] 267, [4730] 346, [8520]



Indole-3-carboxylidene-DL-glycine



Indole-3-carboxylidene-DL-alanine



Indole-3-carboxylidene-DL-valine

Figure 2. Structure of amino acid-Schiff baes

3.2. ^{1}H and ^{13}C NMR Spectral of amino acid-Schiff Bases

^{1}H-NMR and ^{13}C-NMR of amino acid-Schiff bases are given in Table 3. The ^{1}H-NMR spectra of the Schiff bases in DMSO exhibits signals at 8.27, 8.26 ppm and 7.85,7.82 ppm, attributed to CH=N- and -NH(ring) protons, respectively (6,8,9). The multisignals within the 7.58, 7.38 ppm range are assigned to the aromatic protons of both rings. The three signals at 2.57, 2.30 ppm and 2.12 ppm are assigned to the -CH_3, -CH_2-, and -CH, groups, respectively (7) The ^{13}C-NMR spectral data of the Schiff bases are in accord with the proposed structures (Table 3).

Table 3. ^{1}H and ^{13}C NMR Spectral Data (δ ppm) of Schiff Bases

Labelling number	Ind-gly		Ind-ala		Ind-val	
	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR
1	8.26, 1H	138.70	8.27, 1H	139.19	8.19	139.04
2	2.57, 2H	28.00	2.30, 1H	27.98	2.38	22.13
3	11.29, 1H	198.28	11.87, 1H	198.41	11.80, 1H	198.32
4	-	-	2.12, 3H	21.56	2.30, 3H	21.61
5	-	-	-	-	2.20, 6H	20.18
a	6.71, 1H	112.72	6.83, 1H	138.58	6.79, 1H	139.58
b	7.82, 1H	-	7.85, 1H	-	7.75, 1H	-
c	7.37, 1H	125.91	7.40, 1H	125.91	7.43, 1H	124.91
d	7.15, 1H	123.40	7.10, 1H	123.41	7.15, 1H	123.44
e	7.00, 1H	122.54	7.00, 1H	122.47	7.12, 1H	123.40
f	7.53, 1H	132.77	7.55, 1H	132.92	7.50, 1H	132.97
g	-	120.84	-	120.19	-	122.11
h	-	138.34	-	138.32	-	138.67
ı	-	113.26	-	113.28	-	113.80

Antibacterial affect of amino acid-Schiff Bases

The results of the antibacterial screening of the Schiff bases ind-gly, ind-ala and ind-val at a concentration of 5000 $\mu g/cm^3$ against all bacteria as have been found (Fig. 3). The inhibition zones were measured in mm and results are shown in Table 4. The results of antimicrobial screening, indicate that amino acid Schiff bases shows more activity against Staphylococcus aureus, Escherichia coli and Bacillus polymyxa than Candida albicans.

Ind-gly was found to be active against both strains of S. aureus and its inhibition zones was equal to 11 mm. Escherichia coli and Bacillus polymyxa were inhibited by ind-gly; inhibition zones were 12 and 6 mm, respectively.

Table 4. Biological Results of Synthesized Compounds (Inhibition Zones in mm)

Compound	*Staphylococcus aureus*	*Escherichia coli*	*Bacillus polymyxa*	*Candida albicans:*
Control (DMSO)	-	-	-	-
Ind-gly	11	11	6	2
Ind-ala	12	12	10	3
Ind-val	14	15	12	5

Ind-val was found to be the most active of them all. E. coli was the most sensitive and its inhibition zone was 18 mm. This compound showed to be active also against. Staphylococcus aureus, Bacillus polymyxa and Candida albicans The inhibition zones were 14, 12, and 5 mm, respectively

The results of antimicrobial screening, indicate that amino acid-Schiff bases shows activity against microorganisms. The activity of these substance may be due to carboxyl group (10).

The high activity of Ind-val may be due to the presence of electron donating effect (11). The alteration in the activity of different molecules against different organisms depends either on the impermeability of the cells of the microbes or differences in ribosomes of microbial cells (12).

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