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# SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDIES OF SOME NOVEL LYSINE DERIVATIVES OF NUCLEOBASES

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## ABSTRACT

*With an objective to synthesize compounds with anti-cancer and other anti-microbial properties, a systematically planned organic synthesis was carried out. The organic compounds were synthesized from reacting partner in solvent phase in microwave method. Nucleobase had been a very significant heterocyclic and also amino acids are having highly significant physiological activity. The synthesized compounds were characterized by sensitive instrumental method like. Mass spectra,$^{13}C$ NMR. Infra-Red spectra, Uv spectra etc. Their structures were thus confirmed by different physicochemical methods.*

**Keywords:** Nucleobase , Lysine , Amino acid , Antimicrobial activity , Antifungal activity , Antibacterial activity.

## 1. Introduction

Amino acid and their derivatives of RNA & DNA bases were very important class of heterocyclic compound. These derivatives were various biological activity like antibacterial, antifungal, anticanceranti-inflammatoryactivity. Nucleobase were energy rich compound that drive metabolic working in cells. Amino acid used to hypertension and diabetes. It was also absorption of calcium.

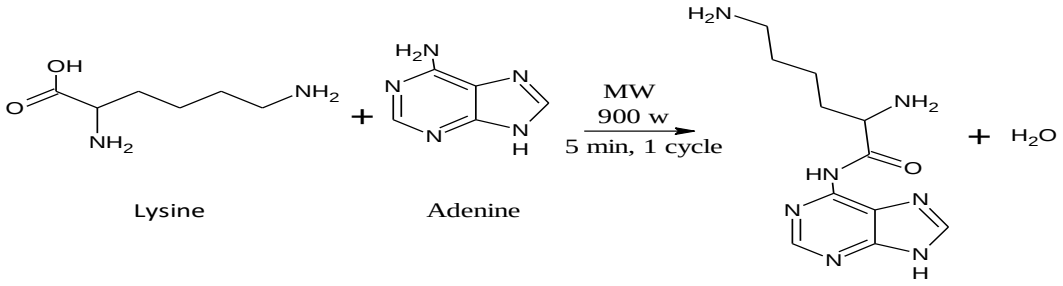
## 2. Materials and Method

All the chemicals of the analytical grade were used without further purification. Lysine, Adenine, Guanine, Thymine, Uracil, Ethanol, Distilled water. Amino acid derivatives was synthesized as per the procedure reported in with different nucleobase.

**General procedure for synthesis of various RNA & DNA base & amino acid derivative**

Lysine and RNA & DNA base were weighed equally in respect to the moles (0.02 : 0.02).The properly weighed compounds were thoroughly mixed using distilled water. The mixture of the compound was transferred into a RBF (250 ml).Then the RBF was place into microwave oven and set the microwave at full microwave radiation (900 W) as per reaction time and start the microwave oven. After the completion of reaction the RBF was taken from the oven very carefully. Then the reaction mixture was transferred into evaporating dish and evaporate the mixture and the product was collected. Recrystallize from hot water. When we were used guanine, the reaction was takenplace in ethanol on behalf of water.

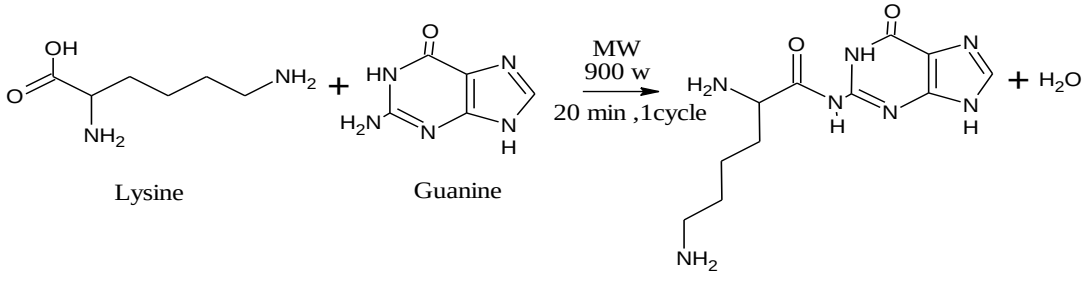
**(1)** Product $M_{15}A$ (Lysine+ Adenine )




Lysine Adenine

$M_{15}A$

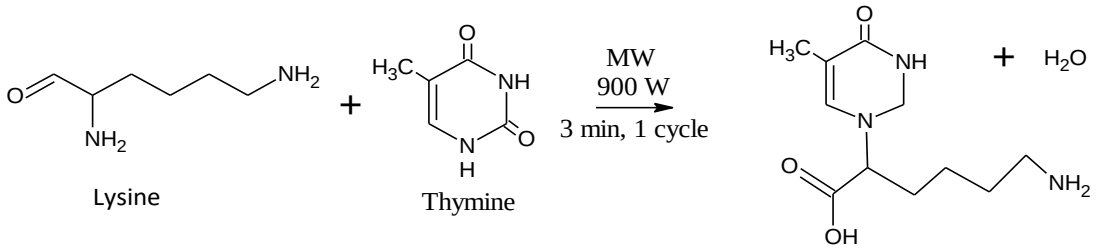
**(2)** Product $M_{15}C$ (Lysine + Guanine )




Lysine Guanine

$M_{15}C$

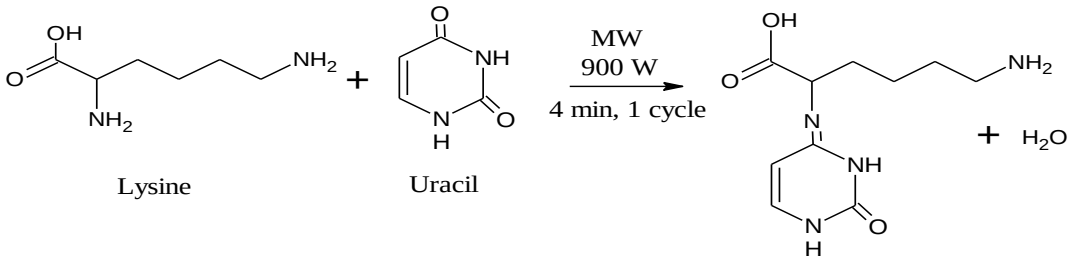
(3) Product $M_{15}D$ (Lysine + Thymine )




Lysine Thymine

$M_{15}D$

(4) Product $M_{15}E$ (Lysine + Uracil )




Lysine Uracil

$M_{15}E$

**3. Spectra Characterization:**

**(1) COMPOUND $M_{15}A$**

**IR spectral features($cm^{-1}$)**

1672:-C=O (Amide) Stretch

1597:-N−H, -$NH_2$ bend

1022,1050,1091,1153,1332:-C-N Stretch

1452 :-$CH_2$ bend

719:-CH(Ar)

1508,1507:-C=C(Ar)

**$^{13}$C spectral Features: (ppm)**

40.09 ,39.88, 39.67, 39.46,39.25,

39.04,38.83 : $R_2$-$CH_2$,$R_3$-CH,C-N

155.32,152.37 :R-CO-NH, C=O

139.28:C=C

**Mass spectral features**

135.01**:**Base peak is observed due to $C_5H_6N_5$. This is adenine peak.

**COMPOUND $M_{15}C$**

**IR spectral features**

**$cm^{-1}$**

1695:-C=O Stretch (Ketone)

1669:-C=O Stretch (Amaide)

1114, 1172, 1212, 1368:-C-N Stretch

1414:-$CH_2$ bend

777:-CH(Ar)

1473, 1559:-C=C(Ar)

**$^{13}C$ spectral Features: (ppm)**

40.11 ,39.90, 39.69, 39.48,

39.27:$R_2$-$CH_2$ , $R_3$-CH

39.07, 38.86:C-N

**Mass spectral features :**

135 .0 : Base peak is observed due to $C_5H_5N_4O$. This is Guanine peak.

**COMPOUND $M_{15}D$**

**IR spectral features**

**$cm^{-1}$**

1748:-C=O Stretch (Ketone)

1448:-$CH_2$ bend

1198:-C-O Stretch

2359- 2945:-OHStretch(carboxylic acid)

1588, 1478:-C=C Aromatic stretch

807 :-C-H Aromatic out of plane bend

1588:-NH, -$NH_2$ bend

1669:-C=N Stretch

**$^{13}C$ spectral Features: (ppm)**

11.75 :R-$CH_3$

40.03 ,39.82, 39.61, 39.40,

39.19: $R_2$-$CH_2$ , $R_3$-CH

38.98 ,38.77:C-N

151.47,164.90:R-CO-NH, C=O

107.64 ,137.69:C=C

**Mass spectral features :**

182.1**:**Base peak is observed due to $C_9H_{14}N_2O_2$

126.0:Base peak is observed due to $C_5H_6N_2O_2$.

This is Thymine peak.

**COMPOUND $M_{15}E$**

**IR spectral features**

**$cm^{-1}$**

1748:-C=O Stretch (Ketone)

1635, 1474:-C=C(Ar)

1413 :-$CH_2$Stretch

2359-2990 :-OH Stretch (carboxylic acid)

1370:-C-O Stretch

3113:-$CH_3$ Stretch

1670:-NH, -$NH_2$ bend

1696:-C=N Stretch

778:-CH(Ar)

40.06 ,39.86, 39.65, 39.44, 39.23:$R_2$-$CH_2$ , $R_3$-CH

39.02 ,38.91 : C-N

151.50, 164.32 : R-CO-NH,C=O

100.10,142.18 : C=C

**Mass spectral features :**

153.1: Peak is observed

due to$C_6H_{10}N_3O_1$.

126.1: (M-2) Molecular peak observed

due to $C_5H_6N_3O_1$.

112.0: Base peak is observed

due to $C_4H_6N_3O_1$.This is Uracil peak

**$^{13}$C spectral Features: (ppm)**

**Table 1 <u>Various derivatives of Lysine</u>:**

| Sr.No | Compound Name | M.P | Nitrogen Rule | Rules of 13[n] | Rules of 13[r] | Compound Formula | Base Formula | Unsaturation |
|---|---|---|---|---|---|---|---|---|
| 1 | $M_{15}A$ | >300°C | YES | 20 | 3 | $C_{11}H_{17}N_7O$ | $C_{13}H_{16}$ | 14 |
| 2 | $M_{15}C$ | >300°C | YES | 21 | 6 | $C_{11}H_{17}N_7O_2$ | $C_{21}H_{27}$ | 14 |
| 3 | $M_{15}D$ | >300°C | YES | 19 | 11 | $C_{11}H_8N_6O_3$ | $C_{19}H$ | 11 |

| | | | | | | | 30 | |
|---|---|---|---|---|---|---|---|---|
| 4 | $M_{15}E$ | >300°C | YES | 18 | 6 | $C_{10}H_{16}N_4O_3$ | $C_{18}H_{24}$ | 12 |

**4. Antimicrobial Activity**:

Antimicrobial agent kill microorganism and stop their growth **.**In 1928 Alexandar Fleming discovered a natural antimicrobial fungus.Peniciliumnotatum this discovery evolutinise the medicine world.Antimicrobial chemotherapy defined as the use of antimicrobial medicines for treatment of infection. Chemotherapy term used by Paul Ehrlich. Antimicrobial agent may inhibit;

- Cell wall synthesis
- Protein synthesis
- Damage cytoplasmic membrane
- Enzymatic activity
- Nucleic acid synthesis

Antimicrobial medication must be arranged by the sorts of organism to there were dynamic like Antibacterial drugs,Anti protozoal drugs, Antiviral drugs, Antifungal drugs and Anthelmintic drugs.

Anti-bacterial: - To treat the bacterial infection reduced by discovery and development and also clinical use of antibacterial in 20$^{th}$ century.

We have used the **Broth Dilution Method** to evaluate the antibacterial activity.

The main advantage of the **'Broth Dilution Method'** for MIC determination lies in the fact that it can readily be converted to determine the MIC as well.

1. Serial dilutions were prepared in primary and secondary screening.
2. The control tube containing no antibiotic is immediately sub cultured [before inoculation] by spreading a lapful evenly over a quarter of plate of medium suitable for the growth of the test organism and put for incubation at 37 $^0$C OVERNIGHT. The tubes are then incubated overnight.
3. The MIC of the control organism is read to check the accuracy of the drug concentrations.
4. The lowest concentration inhibiting growth of the organism is recorded as the MIC.
5. The amount of growth from the control tube before incubation[which represents the original Inoculum] is compared.

**Table 2: Antibacterial Activity of Standard drug**

| Bacteria | Zone inhibition in mm | | | | |
|---|---|---|---|---|---|
| | **Gentamycin** | **Ampicillin** | **Chloramphenicol** | **Ciprofloxacin** | **Norfloxacin** |
| *E coli* | 0.05 | 100 | 50 | 25 | 10 |
| *P.Areuginosa* | 1 | 0 | 50 | 25 | 10 |
| *S.Aureus* | 0.25 | 250 | 50 | 50 | 10 |
| *S.Pyogenus* | 0.5 | 100 | 50 | 50 | 10 |

**Table 3 :Antibacterial Activity of Compounds**

| Bacteria | Zone inhibition in mm | | |
|---|---|---|---|
| | **$M_{15}A$** | **$M_{15}D$** | **$M_{15}E$** |
| *E coli* | 125 | 200 | 250 |
| *P.Areuginosa* | 200 | 250 | 125 |
| *S.Aureus* | 250 | 100 | 500 |
| *S.Pyogenus* | 250 | 50 | 500 |

**Table 4: Antifungal Activity of Standard durg**

| Fungi | Zone inhibition in mm | |
|---|---|---|
| | Nystatin | Greseofulvin |
| *C.Albicans* | 100 | 500 |
| *A.Niger* | 100 | 100 |
| *A.Clavatus* | 100 | 100 |

**Table 5: Antifungal Activity of Compounds**

| Fungi | Zone inhibition in mm | | |
|---|---|---|---|
| | $M_{15}A$ | $M_{15}D$ | $M_{15}E$ |
| *C.Albicans* | 500 | 1000 | 1000 |
| *A.Niger* | >1000 | >1000 | >1000 |
| *A.Clavatus* | >1000 | >1000 | >1000 |

**Result and Discussion**

According to observation table.3 Sample contain MIC range 0.001 ml to 0.005 ml constitute 0.01 mg in 10 ml solvent. The activity of $M_{15}A$, $M_{15}D$, $M_{15}E$ extract is observed between. 125 mm to 500 mm. against respective strain. At each strain lowest MIC activity observed in standard drugs minimum 0.05mm and maximum 250 mm. This activity indicate zone of inhibition against various bacterial strain such as *E.coli, p.areusinasa ,s.aureus and s.pyagenls* of same dilution. The activity of standard drug was given in table 2.

Antibacterial activity of compounds$M_{15}A$, $M_{15}D$, $M_{15}E$ are excellent as compare to the standard drug at same concentration.

According to observation table.5 Sample contain MIC range 0.001 ml to 0.005 ml constitute 0.01 mg in 10 ml solvent. The activity of $M_{15}A$, $M_{15}D$, $M_{15}E$ extract is observed between.500 mm to >1000 mm. against respective strain. At each strain lowest MIC activity observed in standard drugs minimum 100 mm and maximum 500 mm. This activity indicate zone of inhibition against various fungal strain such as *C.Albicans, A.Niger, A.Clavatus* of same dilution. The activity of standard drug was given in table.4.

Antifungal activity of compounds$M_{15}A$, $M_{15}D$, $M_{15}E$ are excellent as compare to the standard drug at same concentration.

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