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Synthesis, Characterization and Biological Activity of Some Novel Phenylalanine Derivatives of Nucleobase

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ABSTRACT

With an objective to synthesize compounds with anti-cancer and other anti-microbial properties ,a systematically planned organic synthesis has been 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,13C NMR. Infra-Red spectra, Uv spectra etc. Their structures were thus confirmed by different physicochemical methods.

Keywords: Nucleobase , Phenylalanine, Amino acid , Antimicrobial activity , Antifungal activity , Antibacterial activity.

I. INTRODUCTION

Amino acid on reaction with RNA & DNA, gives heterocyclic derivatives. This derivatives are useful against several biological activities like anti-bacterial, anti-fungal, anti-cancer, anti-inflammatory activities. Nucleobases act as CNS stimulant and anti-oxidant. 2-Amino-3-phenylpropionic acid is an essential amino acid. It is also used at anti-depressant and in synthesis of dopamine. So it is interesting to form Phenylalanine derivatives using systematic synthesis method.

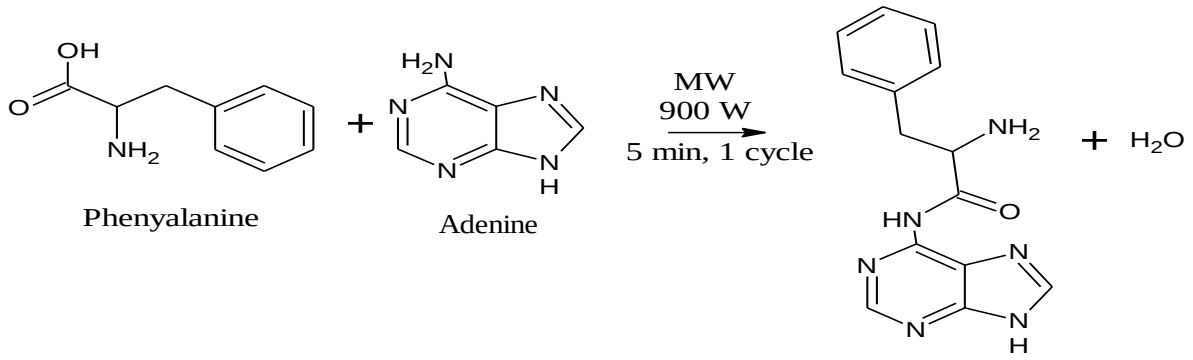
II. MATERIALS AND METHOD

All the chemicals of the analytical grade were used without further purification. Phenylalanine, 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

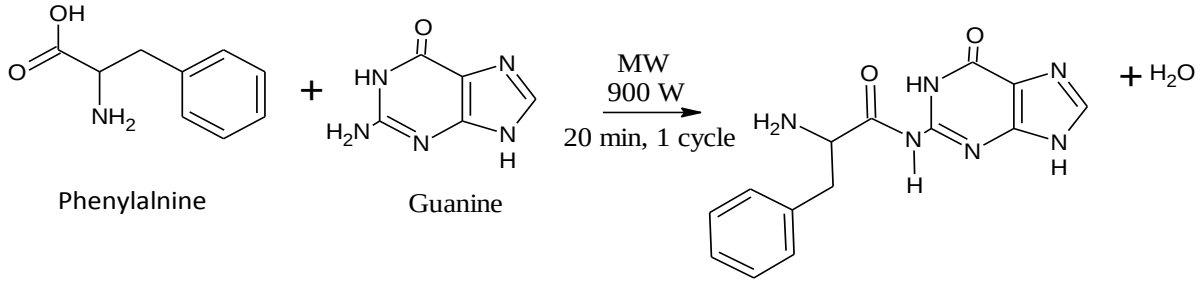
Phenylalanine and RNA & DNA base were weighed equally in respect to the moles (0.02 : 0.02).The properly weighed compounds were thoroughly mixed using distilled water. The mixture of the compound was transferred into a RBF (250 ml).Then the RBF was place into microwave oven and set the microwave at full 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 an the product was collected. Recrystallize from hot water. When we were used guanine, the reaction was taken place in ethanol on behalf of water.

Product $M_{16}A$ (Phenylalanine + Adenine)



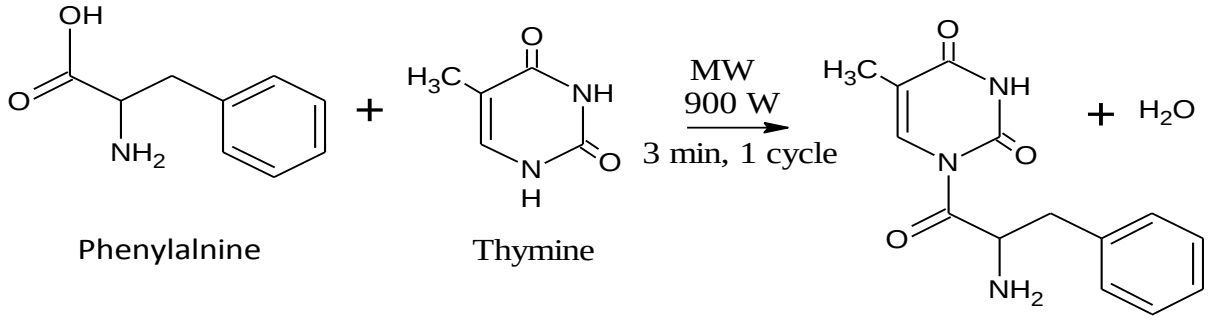
$M_{16}A$

Product $M_{16}C$ (Phenylalanine + Guanine)



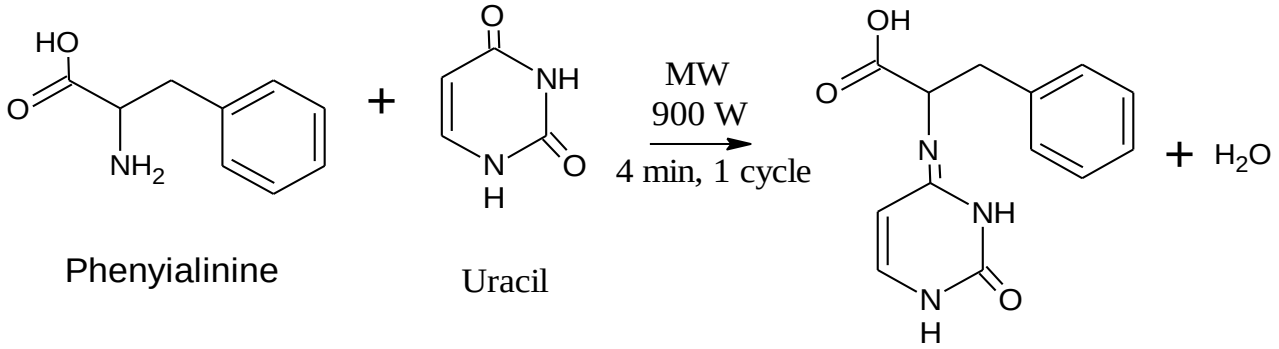
$M_{16}C$

Product $M_{16}D$ (Phenylalanine + Thymine)



$M_{16}D$

Product $M_{16}E$ (Phenylalanine + Uracil)



$M_{16}E$

Spectra Characterization:

COMPOUND $M_{16}A$

IR spectral features (cm^{-1})	**Assignment**
1671	-C=O Stretch (Amide)
1559	-N–H, $-NH_2$ bend
1021, 1051, 1091, 1220, 1305	-C-N Stretch
1452	$-CH_2$ bend
718	-CH(Ar)
1450, 15	-C=C(Ar)
^{13}C spectral Features: (ppm)	**Assignment**
40.08 ,39.87, 39.67, 39.46,39.2	R_2-CH_2 , R_3-CH
39.04, 38.83	C-N
155.76 ,152.37	R-CO-NH,C=O
138.89	C=C
Mass spectral features :	**Assignment**
284.2	(M+2)Molecular peak is observed due to $C_{14}H_{14}N_6O_1$.
178.1	Base peak is observed due to $C_7H_6N_5O_1$. This is adenine peak.

COMPOUND $M_{16}C$

IR spectral features(cm^{-1})	**Assignment**
1696	-C=O Stretch(Ketone)
1670	-C=O Stretch(Amide)
1116, 1149, 1172, 1257	-C-N Stretch
1413	$-CH_2$ bend
778	-CH(Ar)
1474, 1635	-C=C(Ar)
^{13}C spectral Features: (ppm)	**Assignment**
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 :	**Assignment**
148.1	(M-2)Molecular peak is observed due to $C_5H_5N_5O_1$.

135.0 Base peak is observed due to $C_5H_4N_4O$.
This is Guanine peak.

COMPOUND $M_{16}D$

IR spectral features (cm^{-1})	**Assignment**
1747	-C=O Stretch(Ketone)
1450	-CH_2 bend
1202	-C-O Stretch
2359- 2944	-OH Stretch(carboxylic acid)
1487, 1554	-C=C Aromatic stretch
808	-C-H Aromatic out of plane bend
1589	-NH, -NH_2 bend
1671	-C=N Stretch
^{13}C spectral Features: (ppm)	**Assignment**
11.75	R-CH_3
40.03 ,39.83, 39.62, 39.41,39.20,	R_2-CH_2 , R_3-CH
39.99, 38.78	C-N
151.47, 164.90	R-CO-NH, C=O
107.64, 137.69	C=C

Mass spectral features :	**Assignment**
197.1	Peak is observed due to $C_8H_{10}N_3O_3$.
166.1	Peak is observed due to $C_7H_6N_2O_3$.
126.0	Peak is observed due to $C_5H_6N_2O_2$.

This is Thymine peak.

Table 1. Various derivatives of phenylalanine:

Sr.No	Compound Name	M.P	Nitrogen Rule	Rules of 13[n]	Rules of 13[r]	Compound Formula	Base Formula C_nH_{n+r}	Unsaturation Index
5	$M_{16}A$	>300°C	YES	21	9	$C_{19}H_{17}N_3O$	$C_{21}H_{30}$	11
6	$M_{16}C$	>300°C	YES	22	12	$C_{14}H_{14}N_6O_2$	$C_{22}H_{34}$	11
7	$M_{16}D$	>300°C	YES	21	0	$C_{14}H_{15}N_3O_3$	$C_{21}H_{21}$	16
8	$M_{16}E$	>300°C	YES	19	12	$C_{13}H_{13}N_3O_3$	$C_{19}H_{31}$	9

Antimicrobial Activity:

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 loopful evenly over a quarter of p[late 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. Activity Bacterial of Compounds

Bacteria	Zone inhibition in mm		
	$M_{16}A$	$M_{16}D$	$M_{16}E$
E coli	120	90	490
P.Areuginosa	255	255	255
S.Aureus	190	120	120
S.Pyogenus	190	180	120

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 $M_{16}A$ extract is observed between. 125 mm to 250 mm. against respective strain. At each strain lowest MIC activity observed at 12.5mm 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 compound $M_{16}A$ is excellent as compare to the standard drug at same concentration.

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		
	$M_{16}A$	$M_{16}D$	$M_{16}E$
C.Albicans	450	450	900
A.Niger	450	225	225
A.Clavatus	900	225	225

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 $M_{16}A$, $M_{16}D$, $M_{16}E$ extract is observed between. 125 mm to 250 mm. against respective strain. At each strain lowest MIC activity observed at 12.5mm and maximum 250 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.

Antfungal activity of compound $M_{16}A$ is excellent as compare to the standard drug at same concentration.

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