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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SOME NOVEL ASPARTIC ACID DERIVATIVES OF NUCLEOBASE

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ABSTRACT

A systematically planned organic synthesis of the compound was carried out in order to synthesize new compound which have significant anti-cancer and other anti-microbial properties. RNA & DNA are emergent hetrocycle. Highly emergent physiological activity have been shown by amino acid. The combination of these two reactants must give molecules with highly improved biological properties. With this aim and object , the synthesis of the compound had been carried out in solvent phase by microwave process. Structure of the synthesized compound was characterized by highly sensitive instrumental technic like Mass spectra, ^{13} C NMR, Infra-Red spectra, UV spectra etc. Structure of the compounds were further confirmed by different physicochemical methods.

Keywords

Nucleobase, Aspartic acid, Amino acid derivatives, Antimicrobial activity.

Introduction:

Amino acid and their derivatives of Nucleobase were very important class of heterocyclic compounds. These derivatives were show various biological activities like antifungal, antibacterial, anticancer, anti-inflamatory activities Generally nucleobases were also acts as a CNS stimulants and anti oxidants. 2 Amino butan 1,4 dioic acid which was non essential amino acid. It was act as a metabolite in the urea cycle and also taken part in gluconeogenesis.It was worked as a nitrogen donor in biosynthesis of inosine. It was act as a Hydrogen acceptor in ATP chain synthesis. Aspartic acid increased significantly the formation and release of alanine from muscles.

Because of these biological importance much at tension was provided for the synthesis of alanine derivatives of nucleobases. It was thought bto synthesis of new alanine derivatives and screen them for their biological activity

Materials and Method

The derivatives of amino acid had been carried out by reacted with various nucleobases. . This section deals with the preparation of alanine and aspartic acid derivatives of nucleobases.

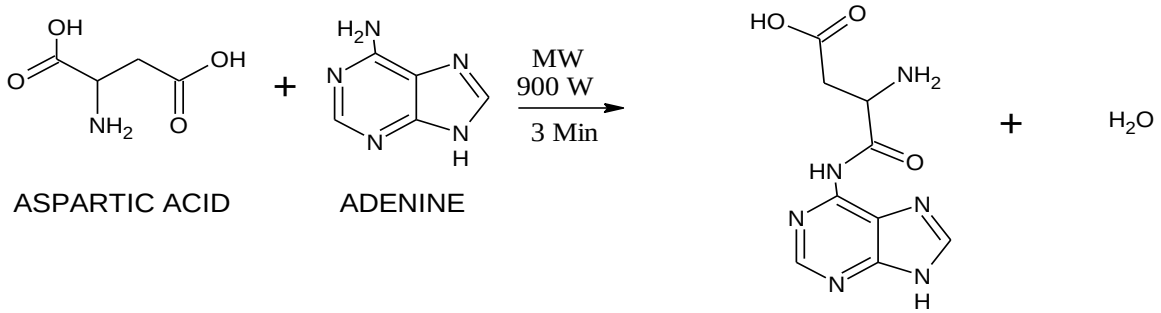
All the chemicals were used of analytical grade without further purification. , Aspartic acid, Adenine, Guanine, Thymine, Uracil, Ethanol, Distilled water, Acetone was used.

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

Aspartic acid and Nucleobase were taken equally in respect to the moles (0.02 : 0.02).The properly taken compounds were mixed with distilled water. The reaction mixture of the compound was transferred into a RBF (250 ml).Then it 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 sometime the RBF was taken from the oven. Then the reaction mixture was transferred into evaporating dish and evaporate

the mixture and the product was collected. Recrystallize from 20% aqueous acetone. When we were used guanine, the reaction was taken place in ethanol on behalf of water.

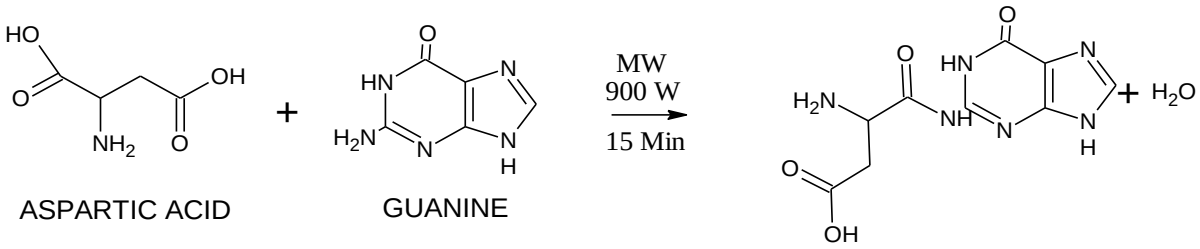
1. Product M_3A (Aspartic acid + Adenine)



ASPARTIC ACID ADENINE

M_3A

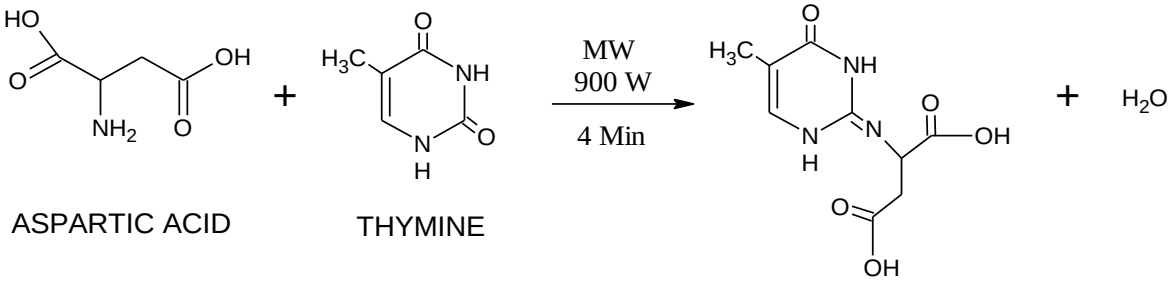
2. Product M_3C (Aspartic acid + Guanine)



ASPARTIC ACID GUANINE

M_3C

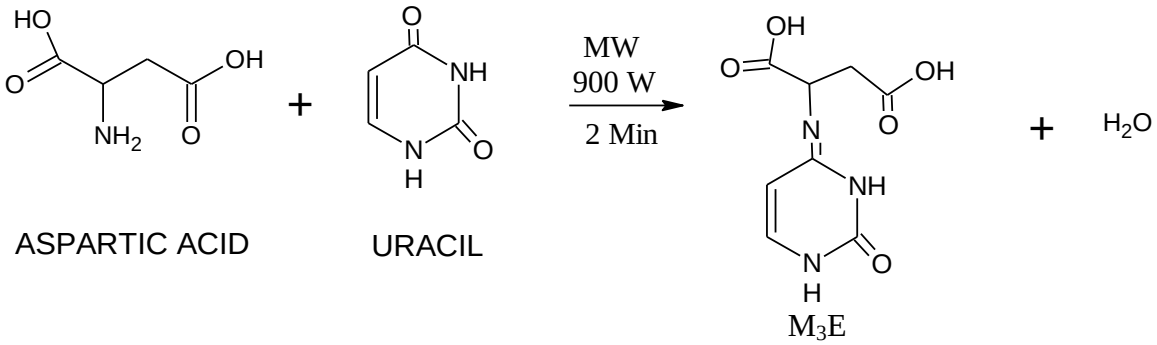
3. Product M_3D (Aspartic acid + Thymine)



ASPARTIC ACID THYMINE

M_3D

4. **Product M_3E (Aspartic acid + Uracil)**



Spectra Characterization:

(1) Compound M_3A

Infared Spectra Features (cm^{-1})

1649, 1520 -NH bend

1025, 1044, 1149,1336 -C-N Stretch

1746 -C=O Stretch

1671 -C=N Stretch

1574, 1490 -C=C Aromatic Stretch

809 -C-H Aromatic out of plane bend

1418 - CH_2 bend

3006 - CH_3 Stretch

2359 - 2889 -OH Stretch

1202, 1241-C-O Stretch

^{13}C spectral Features: (ppm)

11.75 R-CH_3

40.04 ,39.83, 39.62, 39.41,39.20, 39.99, 38.79 R_2-CH_2 , R_3-CH ,C-N

151.47, 164.89 R-COOH, C=O

107.64, 137.68 C=C

Mass spectral features :

240.1 Peak is observed due to $C_9H_{10}N_3O_5$.
224.2 Peak is observed due to $C_9H_9N_3O_4$.

184.1 Peak is observed due to $C_7H_8N_3O_3$. **Infared Spectra Features (cm^{-1})**

1650 : -NH, $-NH_2$ bend

1044, 1085,1115, 1336,1388 : -C-N Stretch

1748 : -C=O Stretch

1683 : -C=O (Amide)

1558, 141: -C=C Aromatic Stretch

658 : -C-H Aromatic out of plane bend

1506 : - CH_2 bend (Carboxylic acid)

2358 - 3010 : -OH Stretch (Carboxylic acid)

1151, 1245 : -C-O Steetch

^{13}C spectral Features: (ppm)

40.10 ,39.89, 39.68, 39.47,39.26, 39.05, 38.55: R_2-CH_2 , R_3-CH ,C-N

152.36 ,152.6 :R-CO-NH,C=O,R-COOH

138.82: C=C

Mass spectral features :

135.0: Base peak is observed due to
$C_5H_4N_5$ This is adnine peak.

(2)Compound M_3C

Infared Spectra Features (cm^{-1})

1560 -NH, $-NH_2$ bend

1046, 1116,1148 1370 -C-N Stretch

1696 -C=O Stretch

1670 -C=O Stretch (Amide)

1473 -C=C Aromatic Stretch

778 -C-H Aromatic out of plane bend

1415 - CH_2 bend

2359 - 3114 -OH Stretch (carboxylic acid)

1213, 1257-C-O Stretch (carboxylic acid)

^{13}C spectral Features(ppm)

40.11 ,39.90, 39.69, 39.48,39.27, 39.06,
38.86 R_2-CH_2 , R_3-CH ,C-N

Mass spectral features :

149.1 Peak is observed due to

(3) Compound M_3D

$C_5H_5N_5O$. This is Guanine peak**.** 135.0 Base peak is observed due to $C_5H_3N_4O$.

135.1 Peak is observed due to $C_6H_7N_3O$

126.0 Base peak is observed due to

$C_5H_6N_3O$. This is Thymine peak.

112.1 Peak is observed due to $C_5H_6N_2O$.

(4) Compound M_3E

Infared Spectra Features (cm^{-1})

1558 -NH_2 bend

[1027, 1049, 1088, 1153,

1318] -C-N Stretch

1748 -C=O Stretch

1651 -C=N Stretch

A540, 1556 -C=C Aromatic Stretch

816 -C-H Aromatic out of plane bend

1417 - CH_2 bend

2361 - 2942 -OH Stretch (Carboxylic acid)

1183, 1220 -C-O Stretch

^{13}C spectral Features: (ppm)

40.07 ,39.86, 39.65, 39.44,39.23, R_2-CH_2 , R_3-CH

39.02, 38.82 C-N

151.49, 164.31 R-COOH, C=O

100.18, 142.16 C=C

Mass spectral features :

225.1 Peak is observed due to $C_8H_8N_3O_5$.

184.1 Peak is observed due to $C_7H_8N_3O_3$.

153.1 Peak is observed due to $C_6H_6N_3O_3$**.**

135.1 Peak is observed due to $C_6H_7N_3O$**.**

112.0 Base peak is observed due to $C_4H_4N_3O$. This is uracil peak.

Table 3.2 Various Derivatives of Amino Acid.

Sr . No	Compound Name	M.P	Nitrogen Rule [35]	Rule Of 13 [35]		Compund Formula	Base Formula C_nH_{n+r} [35]	Unsaturation Index (U) [35]
				N	r			
1	M_3A	>300°C	Yes	19	3	$C_9H_{10}N_6O_3$	$C_{19}H_{22}$	15
2	M_3C	>300°C	Yes	20	6	$C_9H_{10}N_6O_4$	$C_{20}H_{26}$	15
3	M_3D	>300°C	Yes	18	7	$C_9H_{11}N_3O_5$	$C_{18}H_{25}$	13
4	M_3E	>300°C	Yes	17	6	$C_8H_9N_3O_5$	$C_{17}H_{23}$	13

Antimicrobial Activity:

Man Is Closely Influenced By the Activities If Microorganisms. Microorganisms Are A Part Of Our Lives In More Ways Than Most Of Us Understand. They Have Shaped Our Present Environment And Their Activities Will Greatly Influence Our Future. Microorganisms Should Not Be Considered Separate From Human Beings, But Profound Beneficial Influence As A Part Of Our Life. They Are Employed In The Manufacture Of Dairy Products, Certain Foods, Min Processing Of Certain Medicines

And Therapeutic Agents, In Manufacture Of Certain Chemicals And In Numerous Other Ways.

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 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 durg

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 : Anti Bacterial Activity of Compounds

Bacteria	Zone inhibition in mm		
	M_3A	M_3D	M_3E
E coli	125	100	500
P.Areuginosa	250	250	250
S.Aureus	200	125	125
S.Pyogenus	200	200	125

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_3A	M_3D	M_3E
C.Albicans	500	500	1000
A.Niger	500	250	250
A.Clavatus	1000	250	250

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_3A,M_3D,M_3E 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_3A,M_3D,M_3E is 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_3A, M_3D, M_3E 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_3A, M_3D, M_3E is excellent as compare to the standard drug at same concentration.

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