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Development of New Chemical Entities (NCEs) Hybridizing Phenolic Group of 7-Hydroxy,4-Methyl Coumarin for Possible Biological Activity.

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Abstract

Coumarin is a naturally occurring benzopyrone with diverse pharmacological properties, making it an attractive scaffold for the development of new therapeutic agents. The present study aimed to design, synthesize, characterize, and biologically evaluate novel O-substituted 7-hydroxy-4-methyl coumarin derivatives with potential antibacterial and anti-Parkinson activities. Initially, molecular docking studies were carried out against the monoamine oxidase-B (MAO-B) protein (PDB ID: 4FOF) to identify promising candidates for synthesis. The selected derivative (Molecule A) demonstrated a binding affinity of −7.2 kcal/mol, which was superior to the standard drug selegiline (−5.7 kcal/mol), suggesting favorable interactions with the target protein. The synthesized compounds were prepared through a three-step synthetic route involving Pechmann condensation, chloroacetylation, and amination. Structural confirmation was achieved using FTIR, Mass spectroscopy, and ^13C NMR spectral analyses, which verified the successful synthesis of the target molecule. The synthesized derivative exhibited satisfactory physicochemical properties, acceptable ADMET characteristics, and compliance with Lipinski's rule of five. Antibacterial activity was evaluated using the disk diffusion method against Staphylococcus aureus and Escherichia coli. Molecule A demonstrated moderate antibacterial activity, producing inhibition zones of 8.1 mm and 8.0 mm at 10 µg/mL against S. aureus and E. coli, respectively, compared with gentamycin. Overall, the findings indicate that the synthesized coumarin derivative possesses promising in-silico anti-Parkinson potential along with moderate antibacterial activity. These results support the potential of 7-hydroxy-4-methyl coumarin derivatives as lead molecules for further optimization and biological evaluation. Future studies should focus on synthesizing additional derivatives and validating their pharmacological efficacy through in-vitro and in-vivo investigations.

Keywords: Coumarin, 7-Hydroxy-4-methyl coumarin, Molecular docking, MAO-B inhibitor, Anti-Parkinson activity, Antibacterial activity, Synthesis, Spectral characterization.

1. INTRODUCTION:

Coumarin, the name is coming from the word ‘Coumarou’. Now, what is the Coumarou? Well, it is the French word for the tonka beans. The word tonka bean is taken from the Galibi (Carib) tongue spoken by natives of French Guiana (one source for the plant); it also appears in Old Tupi, another language of the same region, as the name of the tree. The old genus name Coumarouna, was formed from another Tupi name for tree, Kumaru.

Coumarins are the best-known aromatic lactones. The isolation of coumarin was first reported by Vogel in Munich in 1820. He associated the pleasant odor of the tonka bean from Guiana with that of clover, Melilotus officinal. The name coumarin originated from a Caribbean word 'Coumarou' for the tonka tree, which was known botanically at one time as Coumarouna odorat a Aubl. Coumarin is now well accepted trivial name.

Coumarin is a well-known naturally occurring organic compound. It is utilized in various fields like medicine, dyes, and fluorescence. Coumarins are abundantly expressed in nature and may be found as secondary metabolites in many plant sections involving the seeds, roots, leaves, peels, flowers, and fruits. Because the majority of recovered coumarins exhibit various biological activities.

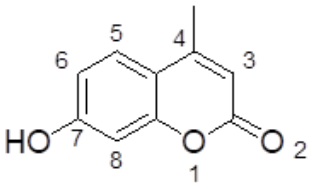


Fig.1.1 7-hydroxy,4-methyl coumarin

Numerous clinical disorders including excessive protein edema, chronic infections, cancer, blood coagulation, oxidative stress, Alzheimer's disease and inflammation may benefit from the usage of coumarins with varying structural properties. The vast family of substances known as coumarins (α-benzopyrones) comes from both natural and synthetic sources and current research has focused especially on how they block enzymes. Many plant species seeds, roots, and leaves naturally contain derivatives of coumarins as secondary metabolites.
Coumarin is a naturally occurring organic compound widely recognized for its distinct aromatic properties. With a molecular structure comprising a benzene ring fused to a lactone, it is found in various plant species, including tonka beans, sweet clover, and cinnamon. Due to its sweet, vanilla-like scent, coumarin has gained significant popularity in the fragrance and flavor industries. In addition to its sensory appeal, coumarin and its derivatives exhibit notable biological activities, including anticoagulant, anti-inflammatory, and potential anticancer effects. However, despite these promising properties, concerns over its toxicity at high doses, particularly its hepatotoxicity and possible carcinogenicity, have led to regulatory restrictions on its use in food and beverages. This review explores the chemical properties, biological effects, applications and safety concerns surrounding coumarin providing a comprehensive overview of its multifaceted role in both industry and medicine.

- ## Sources:

Coumarin is primarily found in various plant species, especially in the seeds and leaves of the tonka bean (*Dipteryx odorata*) and sweet clover (*Melilotus officinalis*). Other sources include cinnamon, lavender, and

vanilla, although in lower concentrations. The compound is part of a larger group of plant metabolites that play roles in plant defense mechanisms.

- **Coumarin Activities:**

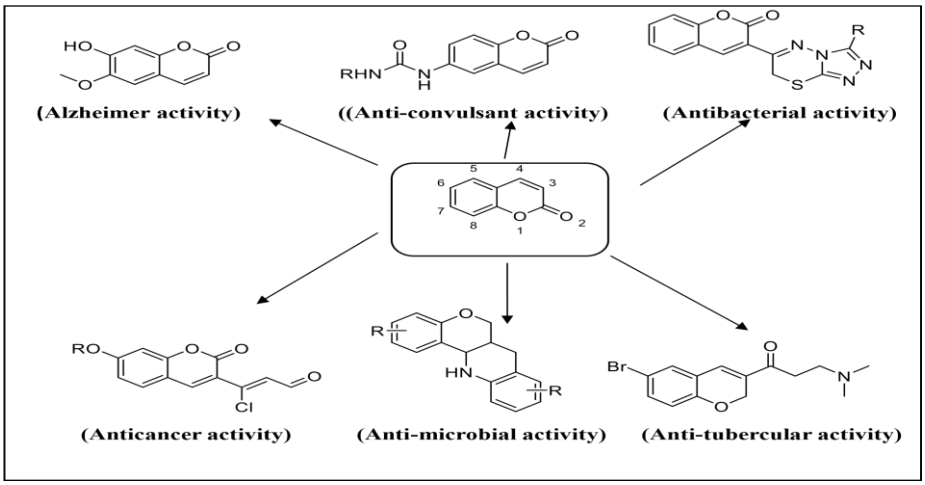


Fig 1.2. Pharmacological activities of coumarin

- **Uses:**

1. Fragrance Industry: Due to its sweet scent, it is widely used in perfumes, air fresheners, and other scented products.

2. Flavoring Agent: In some countries, it was used as a flavoring in foods and beverages, often as a substitute for vanilla or cinnamon.

3. Pharmaceutical Applications: As a precursor, coumarin is used to synthesize compounds like warfarin, an important anticoagulant drug.

2.AIM AND OBJECTIVES:

2.1 AIM: Development of new chemical entities (NCEs) hybridizing phenolic group of 7-hydroxy,4-methyl coumarin for possible biological activity.

2.2 OBJECTIVES:

i. Designing 7-hydroxy,4-methyl coumarin derivatives based on literature review and rational drug design techniques.

ii. Screening molecular docking investigations of developed 7-hydroxy,4-methyl coumarin derivatives. Screen out probable biological targets from *In-silico* theoretical research.

iii. Synthesizing O-substituted 7-hydroxy,4-methyl coumarin derivatives to offer a high yield in a short reaction time.

iv. Characterization of synthesized derivatives by spectrum analysis such IR, MS, NMR.

v. Screening the synthesized derivatives for possible biological activity.

3. NEED OF WORK:

i. 7-hydroxy,4-methyl coumarin derivatives occupy great relevance in the domain of novel medication development due to their possible pharmacological actions.
ii. Extensive literature evaluations have repeatedly revealed that chemicals belonging to the class of coumarin demonstrate a varied spectrum of positive effects.
iii. These chemicals display selective action, which implies they have the capacity to target certain biological processes or molecules, boosting their therapeutic efficacy while decreasing potential negative effects.
iv. The synthesis of 7-hydroxy,4-methyl coumarin derivatives has been discovered to generate substantial amounts in a comparatively quick reaction time.
v. 7-hydroxy,4-methyl coumarin derivatives are proved to feature decreased toxicity profiles while demonstrating a wide variety of biological activity.
vi. Researchers are currently involved in the development of innovative ways to expand the molecular diversity of basic starting materials for the synthesis of these derivatives.
vii. There is a pressing need to quantify and develop efficient, yield-oriented processes for the preparation of 7-hydroxy,4-methyl coumarin derivatives optimizing the synthesis methods and supply of these derivatives for preclinical and clinical studies.

4. MATERIALS AND EQUIPMENTS:

The substance used during this recommended study was L.R. as well as AR grades that were purchased from Sigma Aldrich, Tokyo Chemical Industry (TCI), Merck, and Research Laboratory.

4.1 Materials:

a) List of chemicals:

Table No.4.1 List of chemicals

Sr. No	Chemical Name	Company Name
1.	Resorcinol	Loba Chemie
2.	Ethyl acetoacetate	Loba Chemie
3.	Conc. Sulphuric acid	Loba Chemie
4.	Chloroacetyl chloride	Loba Chemie
5.	Tri-ethyl amine	Loba Chemie
6.	Dichloromethane	Loba Chemie
7.	Acetone	Loba Chemie
8.	Dry Dichloromethane	Loba Chemie
9.	Sodium Sulphate	Loba Chemie
10.	Magnesium sulphate	Loba Chemie
11.	N, N-DMED	TCI
12.	N, N-DEED	TCI
13.	Chloroform	Loba Chemie
14.	Ethyl acetate	Loba Chemie
15.	Petroleum ether	Loba Chemie
16.	Conc. Nitric acid	Loba Chemie

17.	Ethanol	Loba Chemie
18.	Methanol	Loba Chemie
19.	Silica gel	Loba Chemie
20.	Acetonitrile	Research lab
21.	Dry Acetonitrile	Loba Chemie
22.	Di-ethyl ether	Loba Chemie

b) List of Instruments:

Table No. 4.2 List of instruments

Sr. No	Names of Instruments Used	Model/make
1	Digital Weighing Balance	Elder Instruments Pvt. Ltd.
2	Hot Air Oven	Nano lab. India.
3	Refrigerator	Blue Star Ltd. Mumbai.
4	Heating Mantle with Stirrer	Dan Logitech Ltd. Haryana.
5	Magnetic stirrer	Indosati.
6	Digital pH meter	Lab junction.

5. EXPERIMENTAL WORK:

5.1 Methodology:

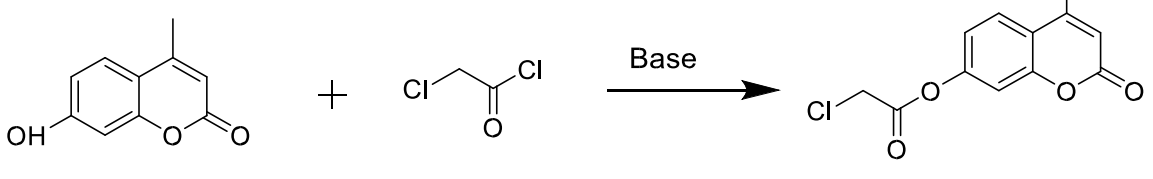
5.1.1 Proposed Scheme, Mechanism and Procedure for Synthesis:

- **Synthesis by conventional method:**

Scheme of Proposed Work:

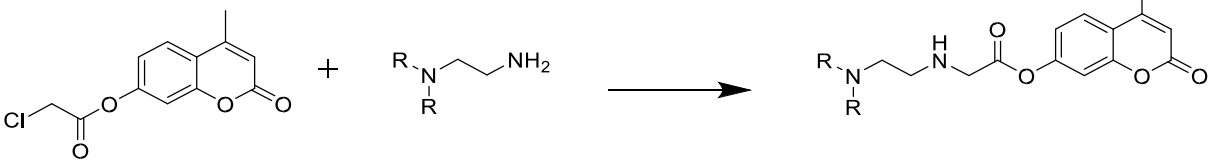
1. Synthesis of 7-hydroxy,4-methyl coumarin:

Synthesis of 4-methyl-2-oxo-2H-chromen-7-yl -2-chloroacetate:



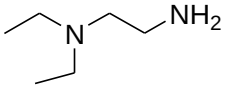
7-hydroxy,4-methyl coumarin **Chloroacetyl chloride** **4-methyl-2 oxo - 2H chromen- 7 yl- 2-chloroacetate**

2. Amination of O-substituted 7-hydroxy,4-methyl coumarin:



4-methyl-2oxo-2H-chromen-7-yl-2- chloroacetate **Amines** **O-substituted 4-Chromen-7yl-2-chloroacetate**

5.2 Structures of amine:

Sr. No	Structures of amines
1.	

5.3 Mechanism:

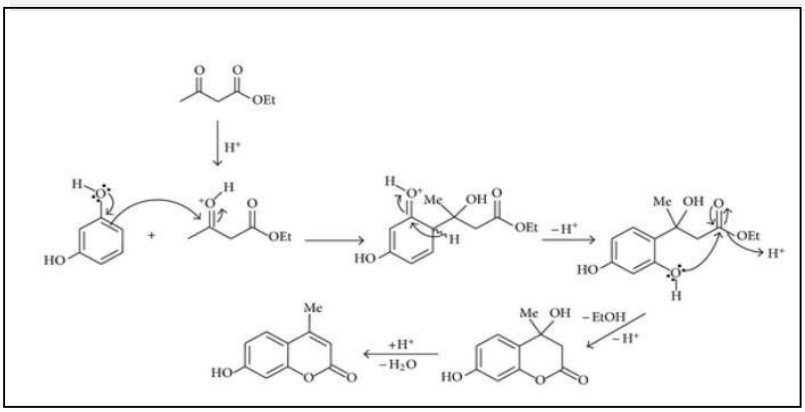


Fig.5.3.1 Mechanism of 7-hydroxy,4-methyl coumarin by Pechmann condensation

5.4 Procedure of synthesized compounds:

- **Step 1: Synthesis of 7-hydroxy,4-methyl coumarin:**

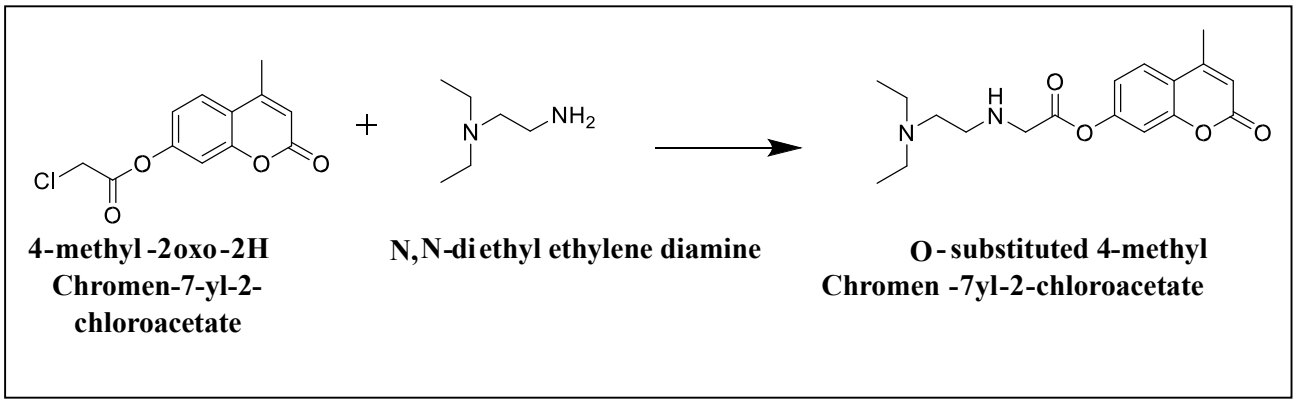
In Round bottom flask (RBF) transfer the concentrated sulfuric acid (15 ml) and flask fitted with a thermometer. Submerge the flask under ice bath. When the temperature drops below 10°C, add a solution of resorcinol (3.70 gm), ethyl acetoacetate (10 ml) drop wise with stirring. During the addition process, keep the ambient temp. below 10°C with use an ice-salt bath; roughly 2 hours. For about eighteen hours, let the reaction mixture sit at RT. Finally, transfer it, vigorously stirring, into a smashed ice. Collect the precipitate by suction filtering and wash with cold water, the yield is 90%. Recrystallize from 95 percent alcohols.

- **Step 2: Synthesis of 4-methyl-2-oxo-2H-chromen-7-yl-2-chloroacetate:**

At 0°C, 01 ml of chloroacetyl chloride was dissolved in dry CH_2Cl_2. This solution was then progressively addition to a cooled mixture of 7-hydroxy,4-methyl coumarin and triethylamine (Et_3N) in 1:1 molar ratio CH_2Cl_2 under hourly N_2 use. After stirring the reaction mixture for a whole night at room temperature, distilled water and CH_2Cl_2 were used to extract it three times. Anhydrous Na_2SO_4 was used to dry the mixed organic layer, and it subsequently vaporized under low pressure. This approach generated a white solid result. The crude product was further refined by recrystallization from ethanol (methanol), with a 93% yield.

- **Step 3: Amination of O-substituted 7-hydroxy,4-methyl coumarin derivatives:**

In RBF, substituted 7-hydroxy,4-methyl coumarin and N, N- diethyl ethylene diamine in 1:1 molar ratio was dissolved in dry acetonitrile. After that, the resultant solution was left to reflux for five hours. Thin layer chromatography was employed to keep an eye on the reaction's progress. Finally yellow precipitate was produced. The resultant product was purified using thin layer chromatography.



4-methyl-2oxo-2H Chromen-7-yl-2-chloroacetate | **N,N-diethyl ethylene diamine** | **O-substituted 4-methyl Chromen-7yl-2-chloroacetate**

6. BIOLOGICAL EVALUATION:

6.1 Antibacterial activity:

i. Antibacterial research is conducted utilizing the disk plate method.

ii. It employs antibiotic discs to assess the degree to which antibiotics damage microorganism.

iii. The area surrounding the sample where the bacteria are still not visible due to their lack of evolution. One calls this a zone inhibition.

iv. Antimicrobial activity against *E. coli* and *S. aureus* was be evaluated.

6.2 The procedure of Staphylococcus aureus preparation:

i. First, dissolve 6 g of Vogel's Johnson agar flour in hundred milliliters of distilled water. Stir well.

ii. Warm with constant motion, and then boil for 1 minute to completely dissolve the powder.

iii. Set the autoclave to 121°C for 15 minutes. Cool to 45-50 °C.

iv. Pour 20ml of Vogel's Johnson agar medium into a petri plate and let it stand for 5 minutes.

v. Then, using a sterile inoculation loop, submerge bacteria horizontally and vertically in the Petri plate. The samples were then incubated for 24 hours to determine biochemical oxygen demand (BOD).

6.3 Disk diffusion method by using standard drug gentamycin:

i. MacConkey's agar medium was used. Bacteria were immersed in a typical saline solution. The dish's surfaces are then infected by applying an even coating of microbial inoculum to the agar.

ii. Next, a 6 to 8 mm hole is punched with a sterilized cork borer or tip. Next, add 20 µL of the gentamycin drug solution or antimicrobial agent at the required concentration 10µg/ml to the well.

iii. In a BOD incubator, agar plates are next incubated for 48 hours with *E. coli* and 24 hours with *S. aureus*. The antimicrobial medication diffuses throughout the agar medium, limiting the growth of the tested microbiological strain.

6.4 Disk-diffusion method by using synthesized derivatives:

i. MacConkey's agar medium was employed. Bacteria were submerged in a normal saline solution. The dish's surfaces are then infected by placing an even layer of microbial inoculum across the agar.

ii. Subsequently, a 6 to 8 mm hole is punched out with a sterilized cork borer or tip. Next, a volume of 20 µL of the synthetic drug solution or antimicrobial agent at the necessary concentration 10µg/ml, 05µg/ml, and 02µg/ml is added to the well.

iii. After that, agar plates are incubated for 48 hours for *E. coli* and 24 hours for *S. aureus* in a BOD incubator. The antimicrobial drug diffuses throughout the agar media, inhibiting the growth of the examined microbial strain.

iv. Zone of inhibition will be calculated.

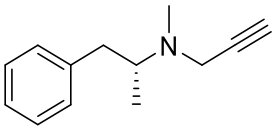
7. RESULTS AND DISCUSSION:

- **Molecular docking:**

Anti-Parkinson activity

Table. 7.1 Interaction of standard drug selegiline with MAO-B protein

Sr. No	Standard Drug Name and Structure	Protein code	Pose number	Dock score	Amino acid residues	Types of interaction

1	**Selegiline** 	**4FOF**	**1**	**-5.7**	**GLU581A** **LEU578A** **SER574A**	**Hydrogen bond**

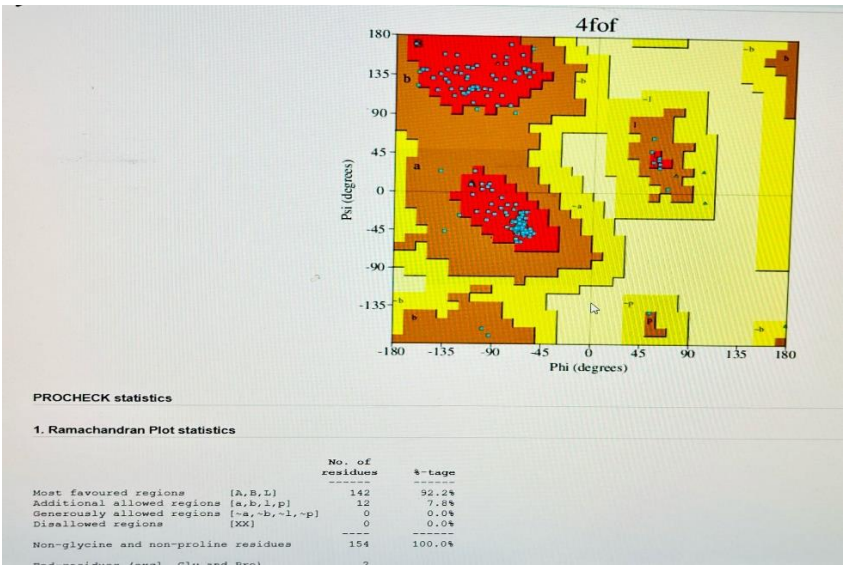
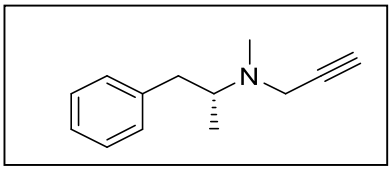


Fig No.7.1 Ramachandran plot



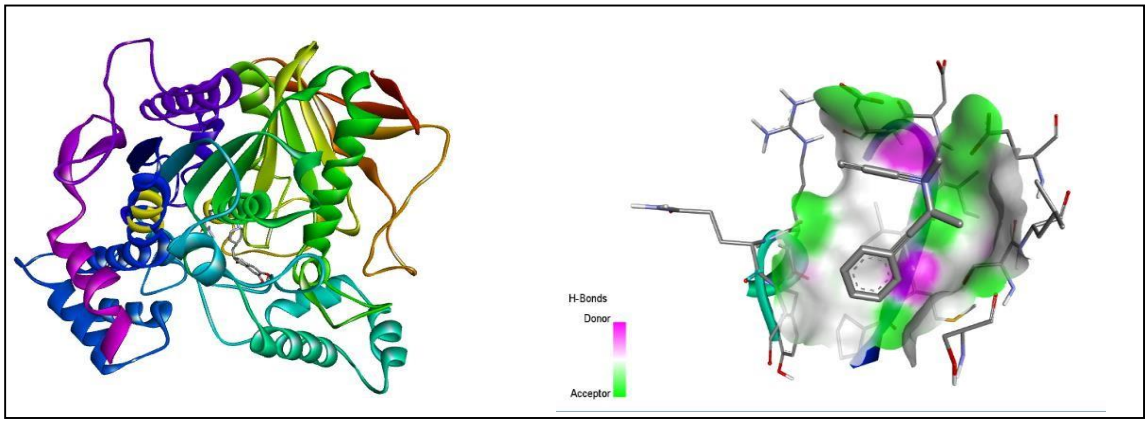


Fig. No. 7.2 3D visualization of binding interactions of standard drug selegiline

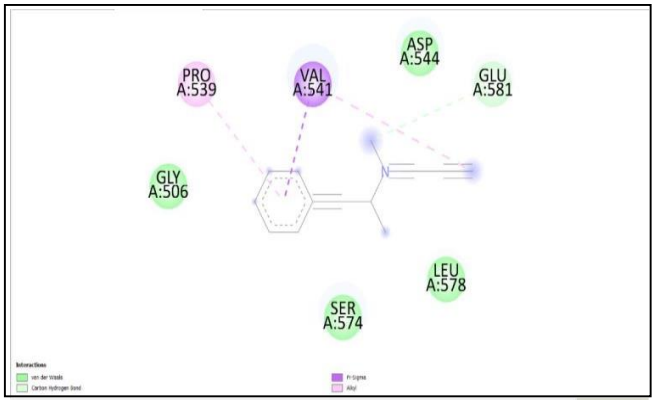


Fig. 7.3 2D interaction with standard drug selegiline

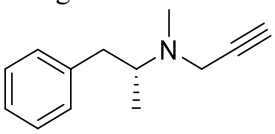
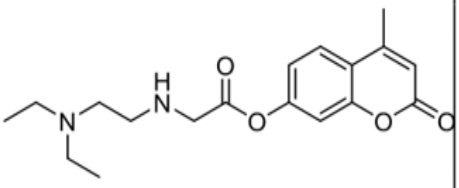
Sr. No	Standard Drug Name and Structure	Protein code	Pose number	Dock score	Amino acid residues	Types of interaction
1	Selegiline 	4FOF	1	-5.7	GLU581A LEU578A SER574A	Hydrogen bond

Table No.7.2 Interaction of synthesized derivatives with MAO-B protein

Molecule	Synthesized Derivatives	Protein code	Pose number	Amino acid residues	Types of interaction
A		4FOF	1	PHE547A ILE542A	Hydrophobic bond
				GLN545A ALA431A HIS584A ARG440A LEU546A TYR469A ASP466A PHE465A	H-bond

- **Docking images of Molecule A**

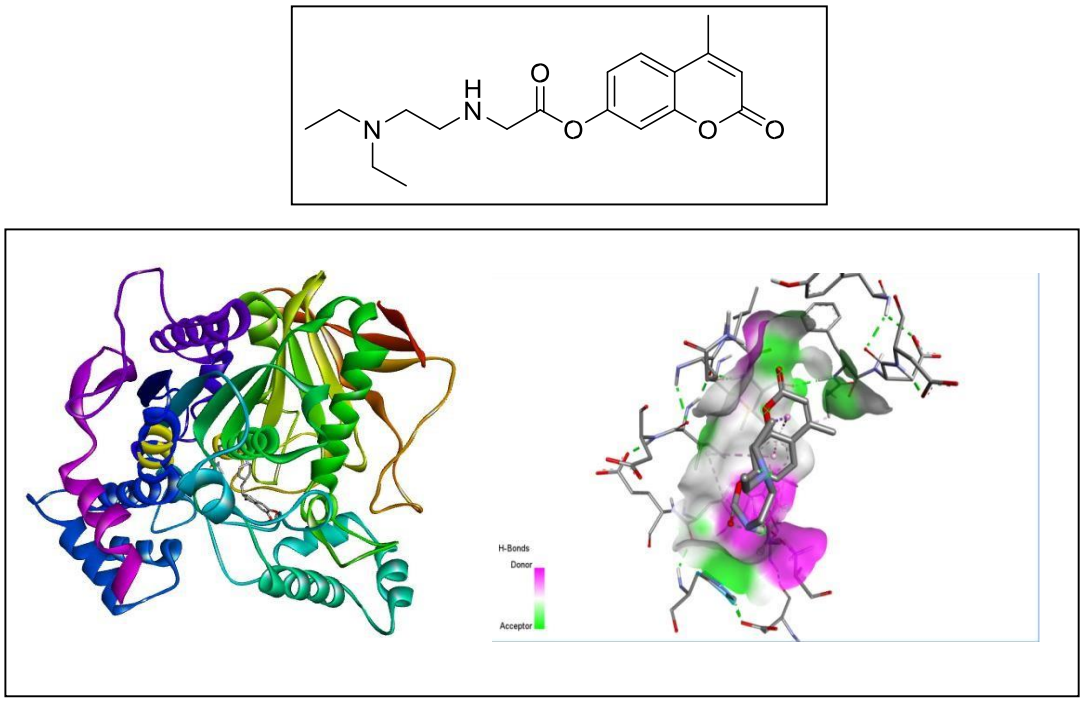


Fig. 7.4 3D visualization of molecule A with MAO B protein

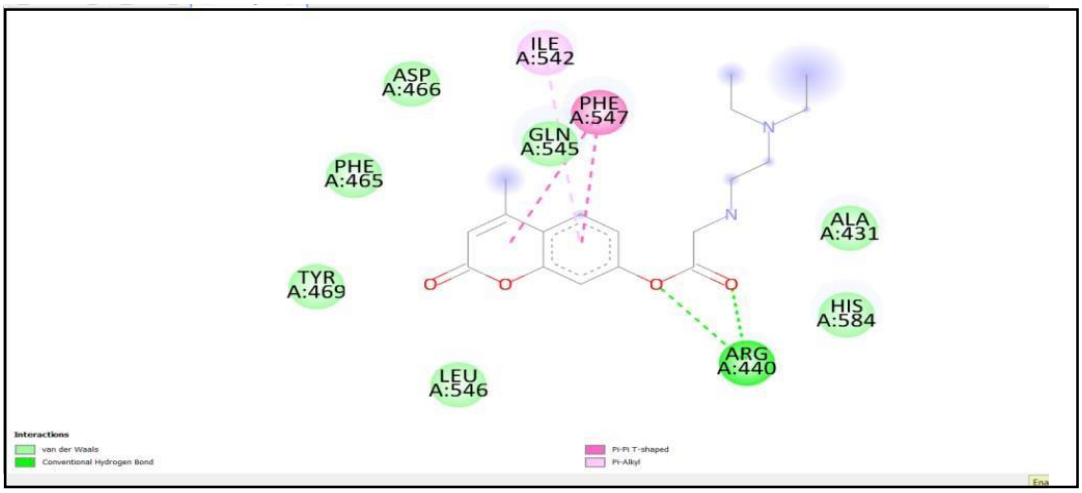


Fig.7.4 2D interaction of molecule A with MAO B protein

- **Binding affinities of synthesized drugs: Standard drug (selegiline):**

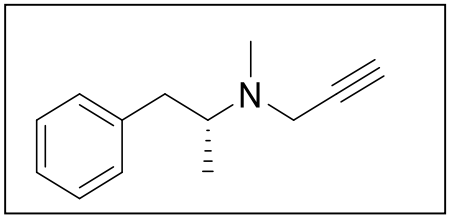


Table.7.3 Binding affinity of standard drug selegiline

Mode	Affinity (kcal/mol)	Dist. from rmsd l.b.	Best mode rmsd l.b.
1	-5.7	0.000	0.000
2	-5.6	2.054	6.882
3	-5.5	1.770	3.408
4	-5.4	1.240	3.703
5	-5.3	2.122	4.199
6	-5.3	23.430	24.972
7	-5.3	17.737	19.615
8	-5.2	18.853	19.114
9	-5.1	17.085	23.965

Molecule A:

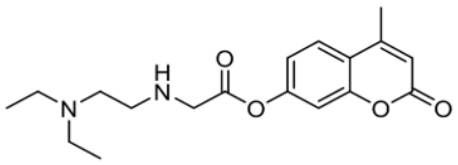


Table.7.4 Binding Affinity of Molecules

Mode	Affinity (kcal/mol) Molecule A
1	-7.2
2	-6.9
3	-6.4
4	-6.3
5	-6.1
6	-6.1
7	-6.1
8	-6.0
9	-5.9

Table.7.5 Lipinski rule of five

Synthesized compounds	Parameters with their limits				
	Mass (gm/mol)	H-bond Donor (<5)	H-bond Acceptor (<10)	Log p (<5)	Molar refractivity (40-130)
7-hydroxy,4-methyl coumarin	176.17	1	3	1.58	49.47

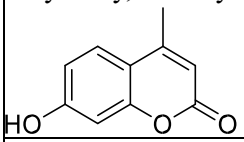
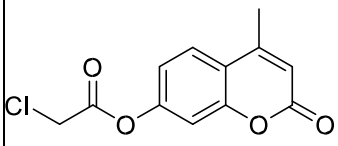
4-methyl 2-oxo 2H-chromen 7-yl-2-chloroacetate	252.65	0	4	2.16	63.75
N, N- diethyl ethylene diamine	332.39	1	6	3.45	93.49

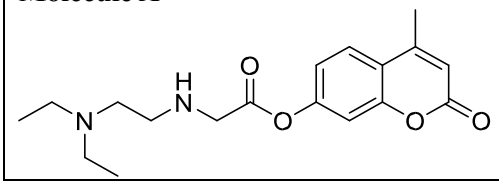
7.1 Physiochemical data:

Compounds were studied for physical properties like melting point, molecular weight, percentage yield, and R_f value. Melting point is the preliminary test used to confirm the synthesized compound in the early phase of research. The % yield of 7-hydroxy,4-methyl coumarin derivatives were in the range of 70-85%.

The synthesized compounds were established by the TLC method. The distance travelled by solute, starting material and solvent front were viewed in the UV chamber, marked and R_f value were calculated. The R_f value, % yield and melting point of each compound as shown in Table.

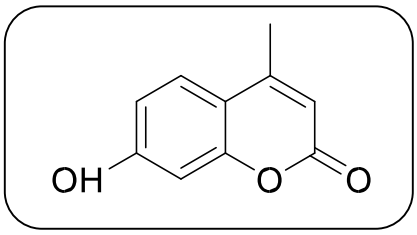
Table. 7.1.1 Physiochemical Data

Compounds	**Molecular formula**	**Molecular weight (gm/mol)**	**Melting point (°C)**	**% Yield (w/w)**	**Mobile phase**	**R_f value**
7-hydroxy,4-methyl coumarin 	$C_{10}H_8O_3$	176.17 gm/mol	185°C	90%	Chloroform: Ethyl acetate 05: 01	0.56
4-methyl-2oxo-2H chromen-7yl-2-chloroacetate 	$C_{12}H_9ClO_4$	252.65 gm/mol	180°C	85%	Dichloromethane: Ethyl acetate 05: 01	0.51

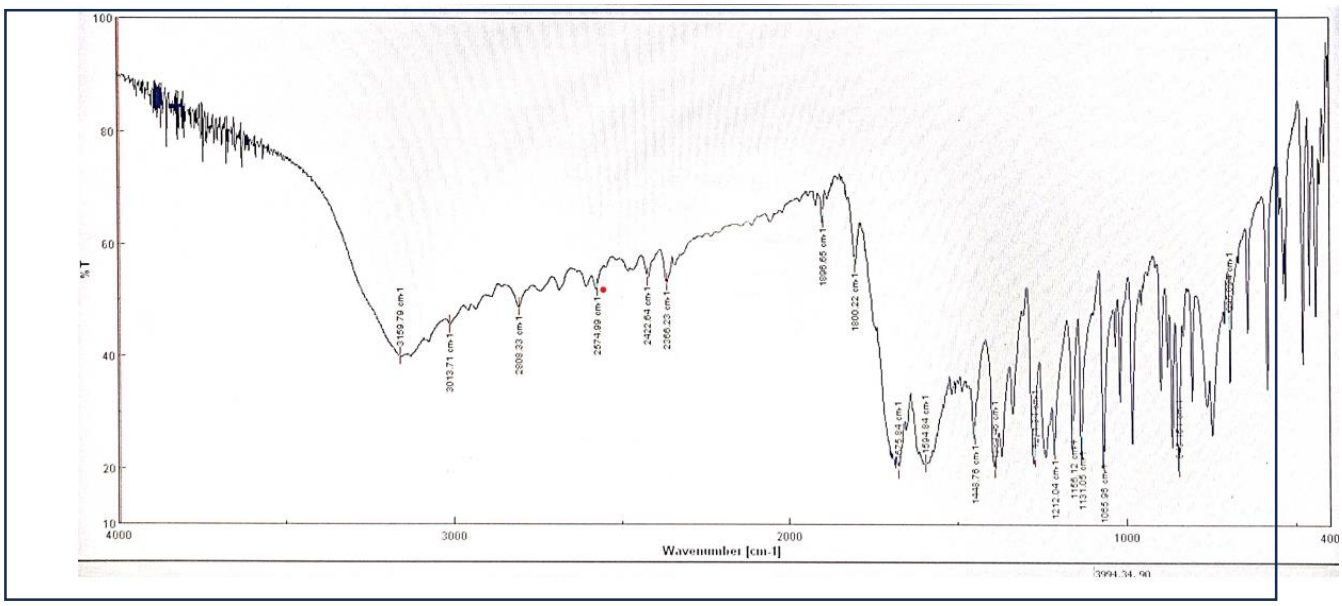
Molecule	**Molecular formula**	**Molecular weight (gm/mol)**	**Melting point (°C)**	**% Yield (w/w)**	**Mobile phase**	**R_f value**
Molecule A 	$C_{18}H_{24}N_2O_4$	331.17 gm/mol	180°C	75%	Chloroform: methanol 05: 0.2	0.52

7.2 Spectral Analysis of Compounds

Spectra 7.2.1: IR spectra of 7-hydroxy,4-methyl coumarin



The structure of **7**-hydroxy,4-methyl coumarin and 4-methyl-2-oxo-2Hchromen-7yl-2-chloroacetate were in good accord with FTIR spectra. The Jasco FTIR-4600 spectrophotometers were used to observe these spectra. The FTIR spectra of final compounds showed absorption bands for OH stretching at 3200 cm^{-1}, C=O stretching at 1650 cm^{-1}, CH_3 bend at 1448 cm^{-1}, C-Cl stretching 843.



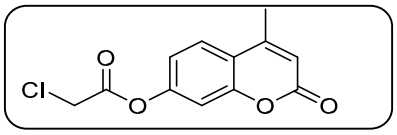
Graph No .01

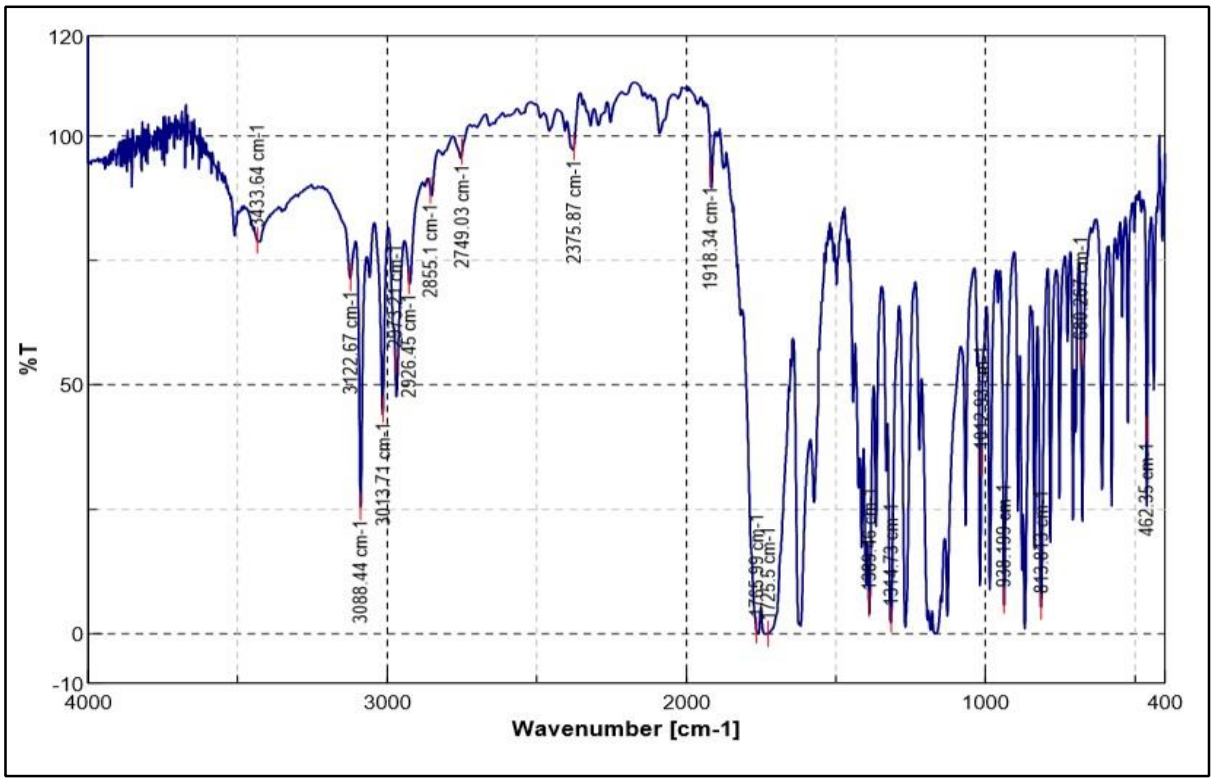
Table No.7.2.2: IR values of 7-hydroxy,4-methyl coumarin:

Functional Group	**Vibration**	**IR Absorption Range cm^{-1}**
Hydroxy (OH)	OH Stretching	3200
Aromatic H	C-H Stretching	3013
Aliphatic H	C-H Stretching	2800
C=O Bond	C=O Stretching	1650

C=C	C=C Stretching	1594
CH_3	CH_3 Bend	1448
C-O	C-O Stretching	1271

7.3: IR spectra of 4-methyl- 2-oxo-2H-chromen-7yl-2 chloroacetate



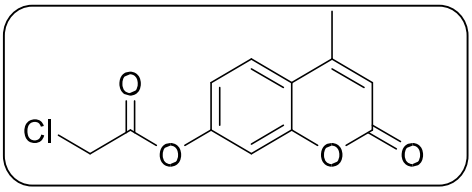


Graph No.02

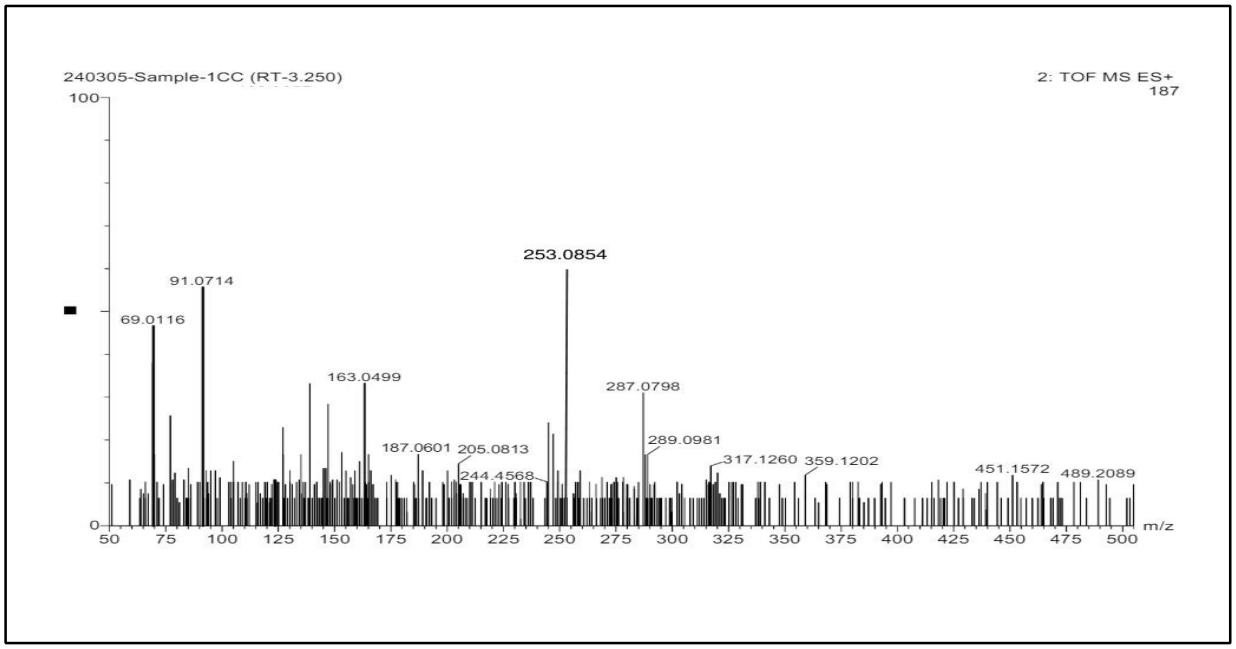
Table No.7.3.1: IR values of 4-methyl-2-oxo-2H-chromen -7yl-2chloroacetate

Functional Group	**Vibration**	**IR Absorption Range cm^{-1}**
C=O	C=O Stretching	1650
CH_3	CH_3 Bend	1365
C-O	C-O Stretching	1271
C-Cl	C-Cl Stretching	843

- **Mass spectra of 4-methyl- 2-oxo-2H-chromen-7-yl- 2chloroacetate:**



Mass spectra showed all M+ ion peaks matching to the molecular weight of synthesized compounds.

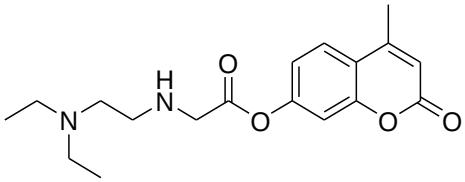


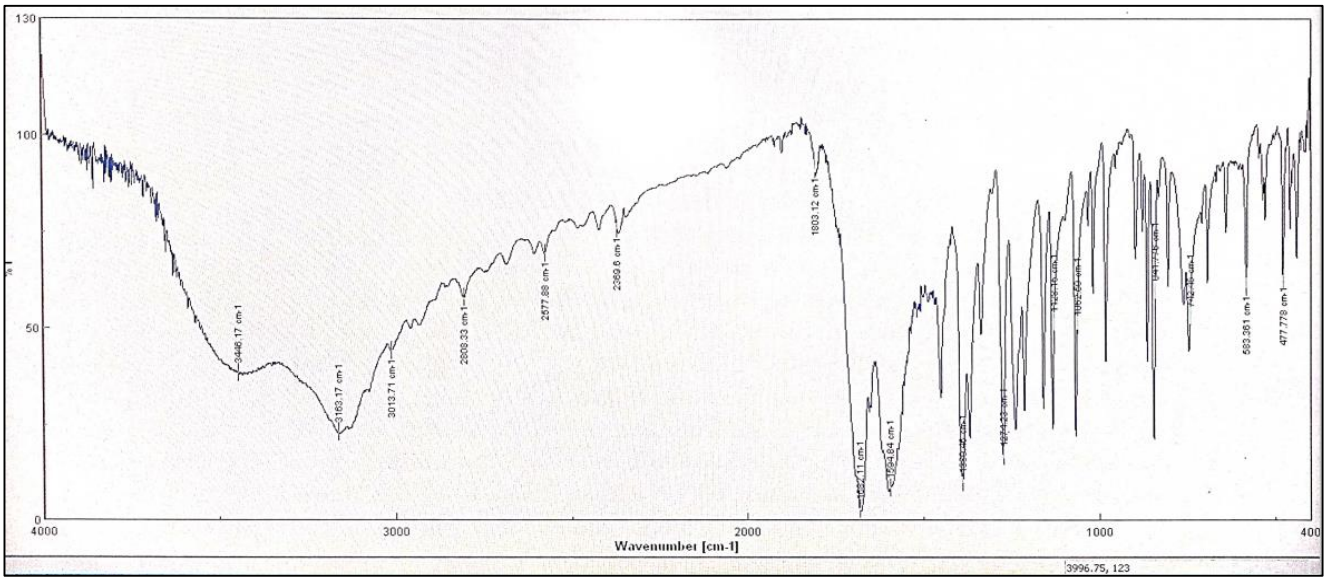
Graph No.03

Table No.7.3.2 Mass spectra values of 4-methyl-2-oxo-2H-chromen -7yl-2-chloroacetate

Molecular Formula	**$C_{12}H_9ClO_4$**
M^+	252.02
[M+1]	253.08

7.4 IR spectra of Molecule A:



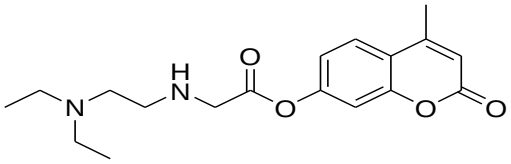


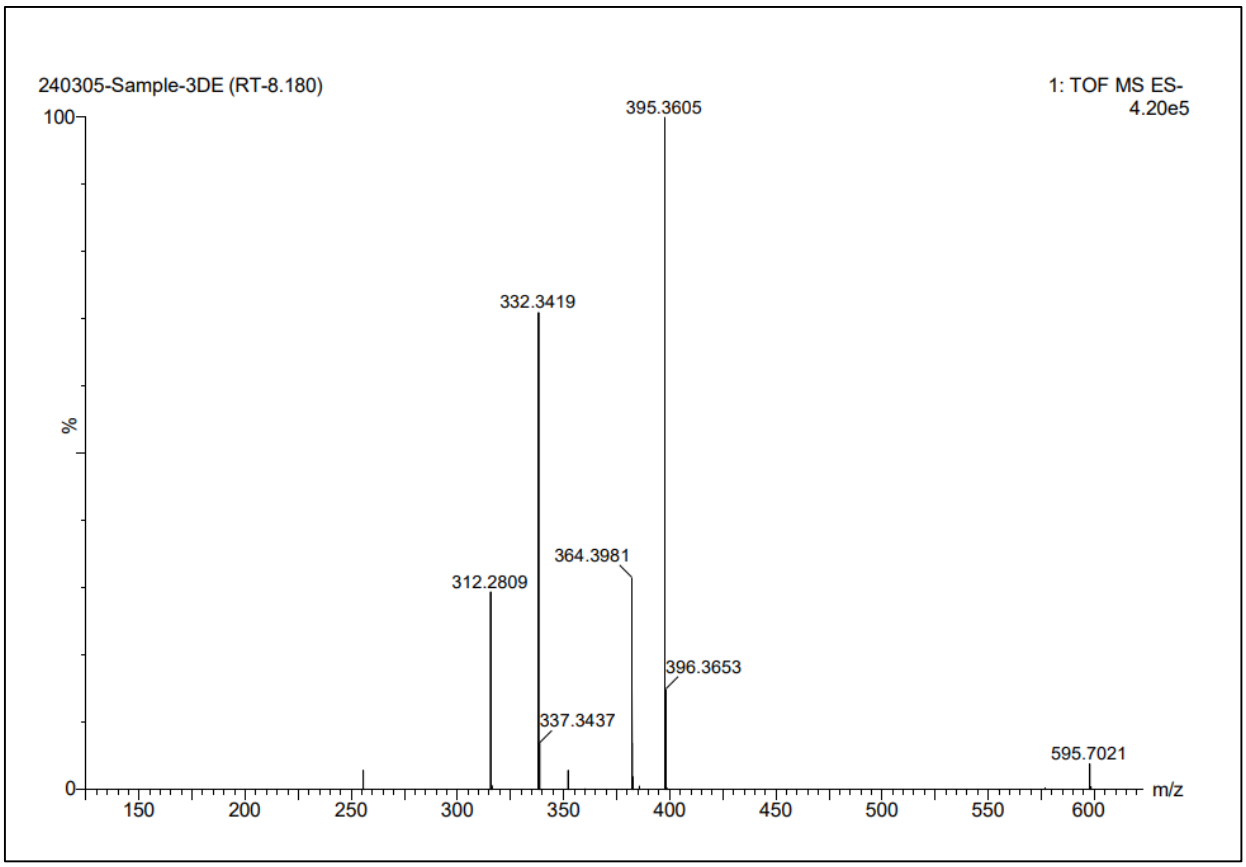
Graph No. 04

Table No.7.4.1 IR values of Molecule A

Functional Group	Vibration	IR Absorption Range cm^{-1}
N-H	N-H Stretching	3163
C-H	C-H Stretching	2808
C=O	C=O Stretching	1662
CH_3	CH_3 Bend	1389
C-N	C-N Stretching	1369
C-O	C-O Stretching	1274

- **Mass spectra of Molecule A:**



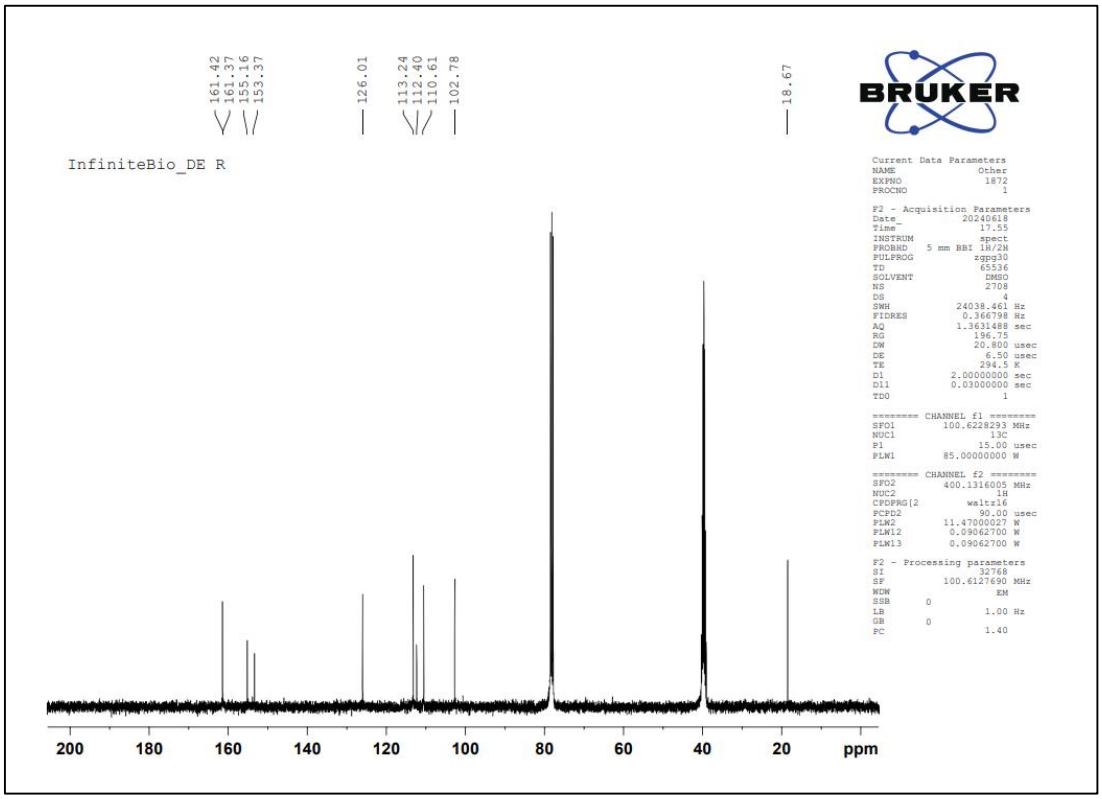


Graph No.05

Table No.7.4.2 Mass spectra values of Molecule A

Molecular Formula	**$C_{18}H_{24}N_2O_4$**
M^+	331.17
[M+1]	332.03

- **^{13}CNMR spectra of Molecule A**



Graph no. 06

Table No.9.4.3 NMR values of Molecule A

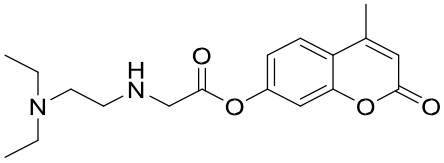
NMR Signal	Chemical shift
CH	160.1 ppm
C=O	150.4 ppm
N-H	101 ppm
C-O	80.0 ppm
C-C	50.0 ppm
N-C_2H_5	40.0 ppm

Above spectra data of Molecule, A (IR, NMR, Mass spectra) showed expected peaks, which indicates that molecule A was successfully synthesized.

7.5 Biological evaluation:

Antibacterial activity: The antibacterial activity of the newly synthesized molecule A as minimum inhibitory concentration (MIC) at the concentration range, 10µg/ml, 05µg/ml, 02µg/ml against *S. aureus* (gram-positive bacteria) and *E. coli* (gram-negative bacteria). Gentamycin as standard and the results are summarized. Molecule A showed comparatively good activity against *E. coli* and *S. aureus.*

Table no.7.5.1 Zone of inhibition of synthesized molecules

Molecules	**Concentrations µg /ml**	**Minimum Inhibitor Concentration (MIC) in µg/ml**	
		S. aureus	***E. coli***
Gentamycin	10 µg /ml	10mm	11mm
Molecule A 	10 µg /ml	8.1mm	8mm
	05 µg /ml	4mm	4.1mm
	02 µg /ml	2.2mm	2.1mm

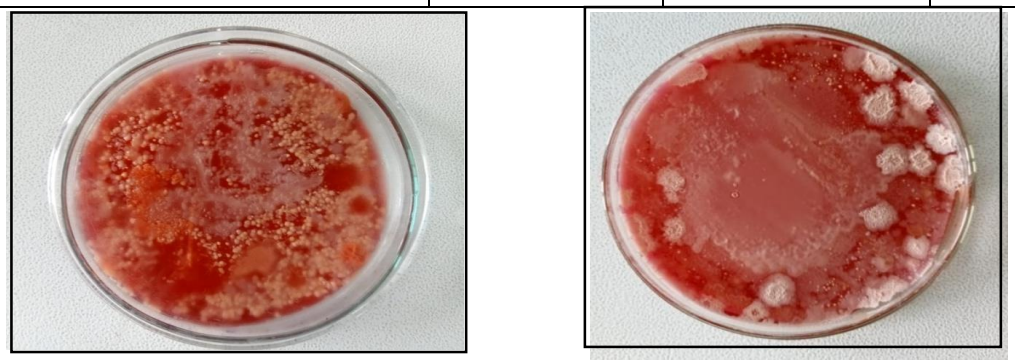
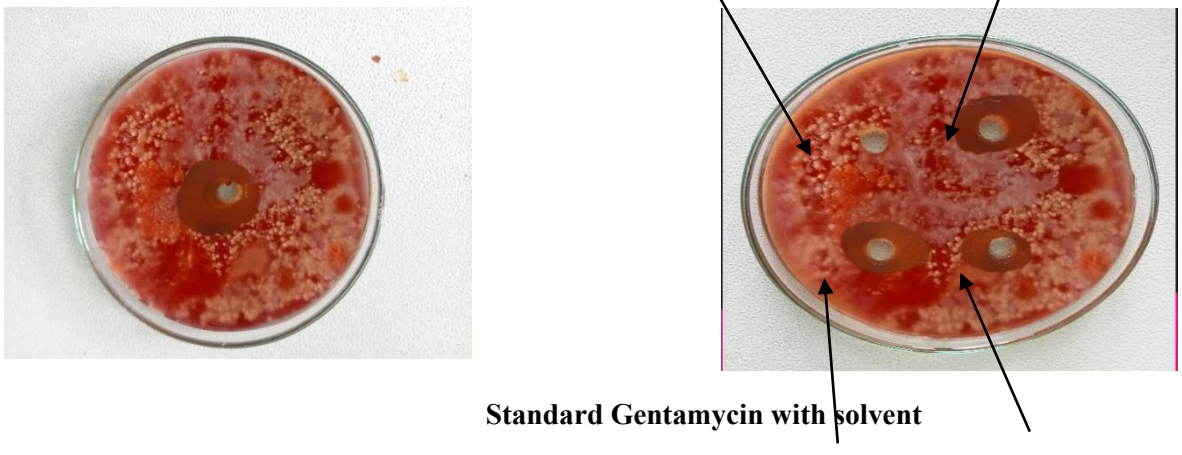


Fig.no 7.5.1 Staphylococcus aureus and Escherichia coli



Standard Gentamycin with solvent

1) Solvent **3** **4**

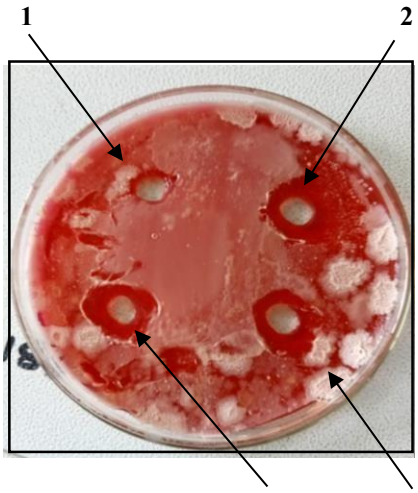
2) Molecule A with solvent 10 µg /ml

3) 05 µg /ml

4) 02 µg /ml

Fig.7.5.2 Zone of inhibition with gram positive bacteria using Molecule A

Standard Gentamycin with solvent



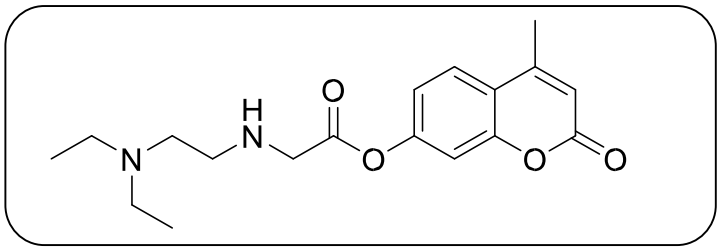
1) Solvent **3** **4**

2) Molecule A with solvent 10 µg /ml

3) 05 µg /ml

4) 02 µg /ml

Fig.7.5.3 Zone of inhibition with gram negative bacteria using Molecule A



To validate the artificially produced 7-hydroxy,4-methyl coumarin derivatives, spectral analysis was performed. All of the compounds FTIR, NMR, and mass data match the predicted structures.
The antibacterial activity of every produced derivative was evaluated.

8. CONCLUSION:

Molecular docking investigations were conducted to assess the derivatives. All derivatives adhered to the ADME-Tox properties. The binding energies of the synthesized molecules toward the target protein ranged from -7.2 to -6.6 kcal/mol. Analysis of derivatives interactions revealed engagements with the target proteins 4FOF through hydrogen bonds, hydrophobic bonds, and multiple van der Waals forces. Our synthesized molecule shows significant activity than that of standard drug selegiline. Staphylococcus aureus (Gram positive bacteria) and Escherichia coli (Gram negative bacteria) was used to assess the synthetic 7-hydroxy,4-methyl coumarin derivatives' biological activities.

The synthesized derivatives 4-methyl-2-oxo-2H-chromen-7yl-(2-(diethylamino)ethyl) glycinate were found to have good antibacterial activity, excellent docking results, and the ability to cross the Blood Brain Barrier (BBB) with a higher docking score, based on the investigation's overall findings. Especially, our synthesized molecules show theoretically significant In-silico Anti-Parkinson activity. So, our future aspects are to check In-vitro Anti Parkinson activities. Due to time constraints, we were unable to synthesize the greatest number of derivatives. However, in the future, we will enhance the number of derivatives with evaluating wide range of biological activities.

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