Original Article

DESIGN, MICROWAVE ASSISTED SYNTHESIS AND CHARACTERIZATION OF BIOLOGICALLY ACTIVE SCAFFOLDS FOR ANALGESIC AND *IN-VITRO* GLUCOSIDASE INHIBITORY ACTIVITY

Annasaheb B.Jagnar[1]*,Rakesh Kumar Jat[1],Nachiket S.Dighe[2]

[1] Shri JJT University, Jhunjhunu, Rajasthan 333 001.
[2] Mrs. SWCOP, Ganegaon, Rahuri, Dist- A. Nagar, Maharashtra.
E-mail: annajagnar1111@gmail.com[1]

DOI: 10.47750/pnr.2022.13.S01.282

Abstract

Heterocyclic compounds comprise the major family of organic compounds. These are enormously essential with wide range of synthetic, pharmaceutical and industrial applications and are famous for their biological activities. There is an extensive spectrum of biological activities shown by many compounds containing five membered heterocyclic rings in their structure. A series of some new imidazole-azetidine and indole derivatives were synthesized by using microwave assisted technique. All these compounds were characterized by means of their IR, 1H-NMR and mass spectra, TLC, physical constants and elemental analysis.Imidazole-azetidine derivatives screened for their analgesic activity by eddy's hot plate, tail clip method, writhing method. Imidazole-azetidine have proven to be effective analgesic compounds. Indole is a bicyclic aromatic heterocyclic organic compound comprising of a six membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. A vast research has occurred on indole and its derivatives which resulted in many approved indole containing drugs in the world market as well as many are in the pipeline stages. The indole derivatives were evaluated for their in-vitro glucosidase inhibitory activity by the In-vitro glucosidase inhibitory activity assay. The acarbose use as a standard drug.The available in vitro studies have led to the recognition that the new Indole derivatives might be considered to be more effective glucosidase inhibitory activity agents.

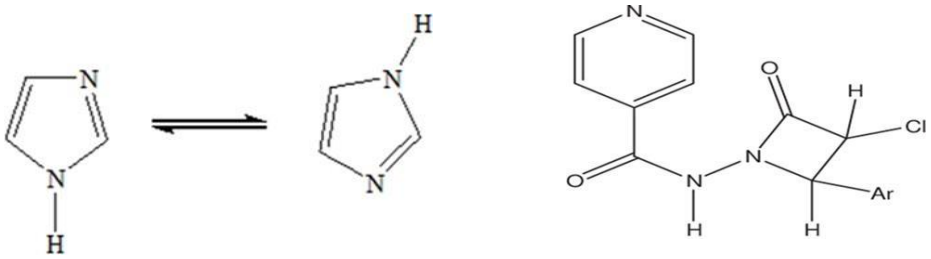
Keywords: Imidazoles, azetidines, Indole, analgesic, Glucosidase inhibitory, Acarbose.

Introduction

Imidazole

Imidazole (1, 3-diaza-2, 4-cyclopentadiene) is a five-member ring system containing 3 Carbon and 2 Nitrogen atoms at 1 and 3 positions with molecular formula $C_3H_4N_2$. The systemic name for the imidazole is 1, 3 diazole. It exists in two equivalent tautomeric forms because the hydrogen atom can be located on either of the two nitrogen atoms. Heterocycles are organic compounds containing at least one atom of carbon, and at least one element other than carbon, such as sulfur, oxygen or nitrogen within a ring structure. The diverse biological activities of imidazole derivatives made an impact to direct the attention of medicinal chemist as a promising class of a heterocyclic compounds with profound biological activities. Varied bioactivities exhibited by imidazole, efforts have been made from time to time to generate libraries of these compounds and screened them for potential biological activities. Also it is well documented that imidazole nucleus is associated with a variety of pharmacological actions.

Imidazole **2-Azatidinone**

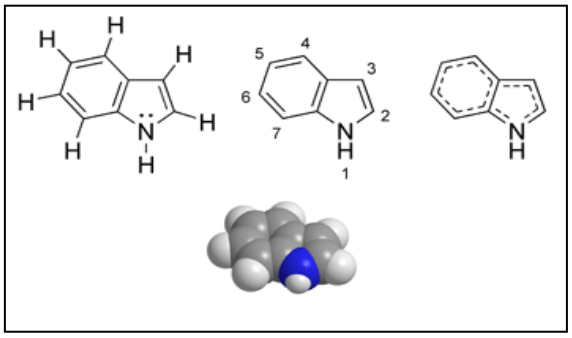


AZETIDINE

Azetidine can be taken into consideration as a fairly typical cyclic amine. strain inside the 4-membered ring is much less than that in the 3-4-membered aziridine machine, and as a result azetidines show few, if any, of the extremely good properties related to aziridines. as a result, ring cleavage reactions occur with greater ease than in larger ring cyclic amines, but much less easily than with aziridine; for example, in contrast to aziridines, azetidines do not function as alkylating agents.

INDOLE

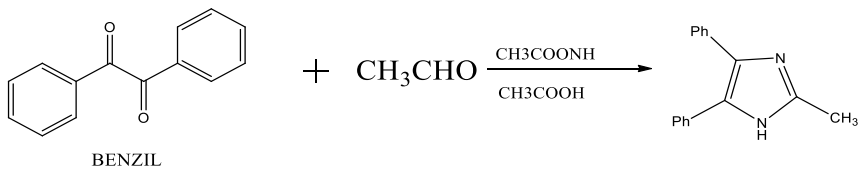
The indole scaffold is a structural motif that is shared by many different forms of bioactive heterocycles. However, there are many distinct types of bioactive heterocycles. The indole moiety is thought to be the energy principle that underlies the entire structural architecture of a number of different alkaloids, ranging from the straightforward serotonin, which is a well-known neurotransmitter, to the complex mitomycin C, which is an anticancer drug, and the reserpine alkaloid, which is used to treat hypertension. Because of the wide variety of compounds that have demonstrated impressive pharmacological activity over the course of the past decade, scientists have taken a keen interest in indole-containing compounds. This has given rise to the hope that these compounds may one day be used in the treatment of disease in the form of therapeutic medications.



Experimental

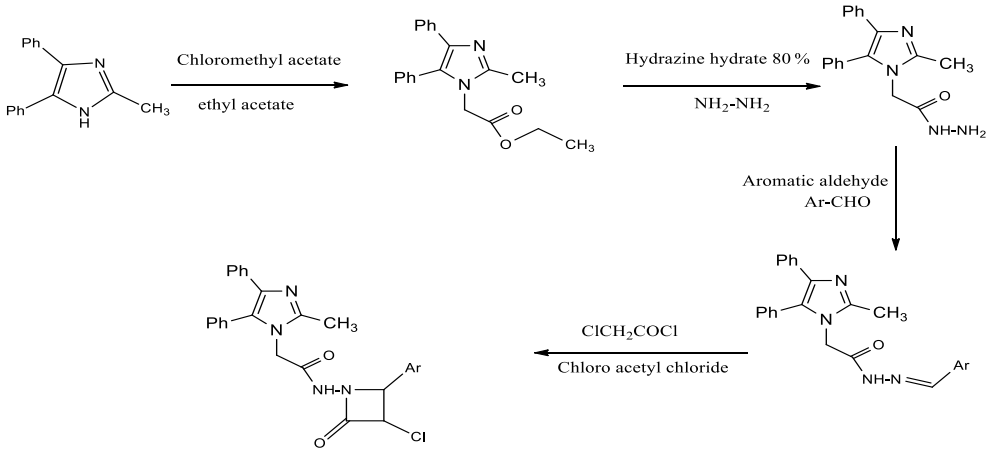
SCHEME for synthesis-Imidazole-azetidine

Step-I



BENZIL

Step-II



SCHEME for synthesis-Indole

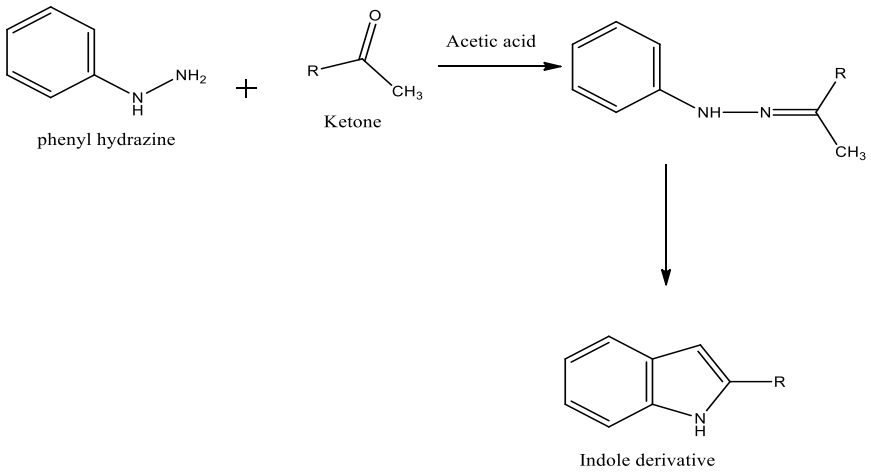
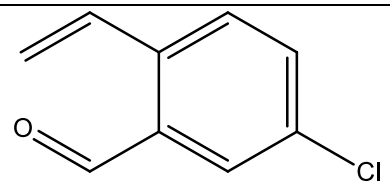
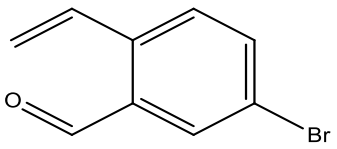
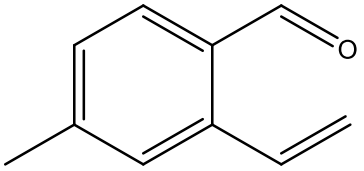
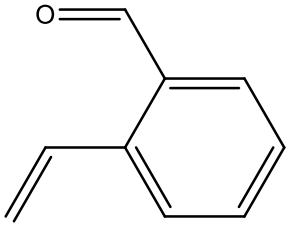
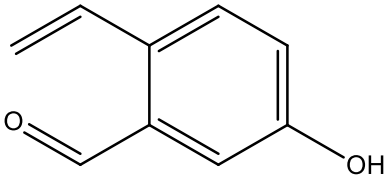
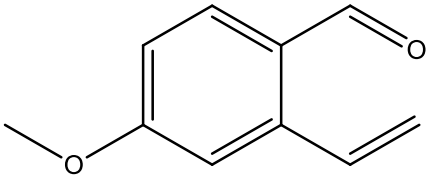


Table no-1. For Compounds: 5a-f (Imidazole-azetidines)

Comp.code	**Ar**	**Comp. code**	**Ar**
5a	 5-chloro-2-vinylbenzaldehyde	5d	 5-bromo-2-vinylbenzaldehyde

5b	 4-methyl-2-vinylbenzaldehyde	5e	 2-vinylbenzaldehyde
5c	 5-hydroxy-2-vinylbenzaldehyde	5f	 4-methoxy-2-vinylbenzaldehyde

Step I-Synthesis of 2-(2 methyl, 4,5 diphenyl)-1H- Imidazole):

In a mixture of acetamide (0.01mole) and glacial acetic acid (0.01mole), 2.10 grams of benzil and 0.44 milliliters of acetaldehyde were dissolved. There was 27 minutes of stirring at 450wolt power used to bring the reaction mixture to completion. Ice was poured with this solution in an effort to create crystals. The acetone solution allowed for a re-crystallization. Product was filtered, dried, and kept in an airtight container at room temperature.

2-(2-Methyl-4,5-Diphenyl)-1H-Imidazole-1-yl) acetate, Synthesis, Step II:

Compound I (0.01mol,2.3gm) in (5ml) ethanol (0.01mol,1.085gm) of chloromethyl ethyl acetate was added to the solution, and the combination was heated in the microwave for 15 minutes at 450wolt power. To facilitate crystallization, this solution was put into ice. By dissolving it in acetone, it was able to recrystallize. The product was filtered, dried, and kept at room temperature in an airtight container.

As a last step acetahydrazide, we must:

Compound II (0.01mol, 3.2gm) was dissolved in ethanol (15ml), and then hydrazine hydrate (0.01mol, 0.32gm) was added to the mixture to get the concentration up to 80%. Overnight, we stirred the reaction mixture at room temperature.

Synthesis of Schiff's bases: IV. General Method (4a)

The reaction was carried out by adding different aromatic aldehydes (0.01mole) to a stirred solution of compound 2 in (30ml) ethanol and heating the mixture at 450wolt power for 30 minutes. The mixture was cooled to the standard laboratory temperature. After a residue was poured over broken ice, the solid crystals expanded as water was slapped on them, and they were then recrystallized with water and ethanol. 4 (a-f).

Compounds containing azetidines may be synthesized by following the standard operating process, which we will discuss in the (5a)

The compounds of the Schiff base (0.001mole) were dissolved in anhydrous 1,4-dioxane, and then chloroacetyl chloride (0.0015 mole,0.169 g) was added drop by drop over the course of 20 minutes. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. For the cost-effective procurement of 3-chloro-4-oxoazetidin Schiff base derivatives.

SYNTHESIS OF COMPOUND 5B

Synthesis of Schiff's bases compounds (4b)

Compound 2 (0.01mole, 2.9gm) was dissolved in ethanol (30ml) using a mechanical stirrer, and then 2-metyl-2-vinyl benzaldehyde (0.01mole) was added. The mixture was heated at 450wolt power for 30 minutes, during which time the reaction was completed. The mixture was cooled to the standard laboratory temperature. If a residue were sprinkled on top of crushed ice, Crystals were dissolved in water and sprayed, then afterwards reformed using water and ethanol.

Making Azetidine Compounds (5b)

After dissolving the Schiff base compounds (0.001mole) in anhydrous 1,4-dioxane for 20 minutes, chloroacetyl chloride (0.0015 mole,0.169 g) was added in a slow, steady stream. After 3 hours at room temperature, the reaction mixture was mixed. The solvent was evaporated under low pressure after the solution was heated in a refluxing vessel for 25 minutes at 450wolt power. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. This is necessary in order to purchase 3-chloro-4-oxoazetidin Schiff base analogues.

5C: A SYNTHESIS

Making compounds from Schiff's bases (4c)

To a 2.9-gram (0.01 mole) solution of Compound 2 in 30 milliliters (ml) of ethanol, 0.01 mole of 5-Hydroxy-2-vinyl benzaldehyde was added, and the mixture was heated at 450 °C (90 °F) for 30 minutes, while being agitated. The mixture was cooled to the standard laboratory temperature. Crushed ice with a residue poured on top, Once the solid crystals were diluted and sprayed with water, they underwent a recrystallization process using water and ethanol.

Compounds containing azetidines synthesized (5c)

The compounds of the Schiff base (0.001mole) were dissolved in anhydrous 1,4-dioxane, and then chloroacetyl chloride (0.0015 mole,0.169 g) was added drop by drop over the course of 20 minutes. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. That you may purchase 3-chloro-4-oxoazetidin Schiff base analogs.

SYNTHESIS OF CHEMICAL ENTITY 5d

Compounds based on Schiff's theory of synthesis (4d)

Compound 2 (0.01mol, 2.9gm) was dissolved in ethanol (30ml), and then 0.01mol of 5-bromo-2-vinyl benzaldehyde was added to the mixture, which was then heated at 450wolt power for 30 minutes while being agitated (TLC monitoring using ethyl acetate and n-hexane 3:1 ratio). The mixture was cooled to the standard laboratory temperature. After a residue was poured over broken ice, the solid crystals expanded as water was slapped on them, and they were then recrystallized with water and ethanol. ,

Compounds containing azetidines synthesized (5d)

The compounds of the Schiff base (0.001mole) were dissolved in anhydrous 1,4-dioxane, and then chloroacetyl chloride (0.0015 mole,0.169 g) was added drop by drop over the course of 20 minutes. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. For the cost-effective procurement of 3-chloro-4-oxoazetidin Schiff base derivatives.

SYNTHESIS OF COMPOUND 5e

Synthesis of Schiff's bases compounds (4e)

Compound 2 (0.01mol, 2.9gm) was dissolved in ethanol (30ml), and then 0.01mol of 5-bromo-2-vinyl benzaldehyde was added to the mixture, which was then heated at 450wolt power for 30 minutes while being agitated. The mixture was cooled to the standard laboratory temperature. Crushed ice with a residue poured on top, Crystals were dissolved in water, splashed about, then re-crystallized in a mixture of water and ethanol.

Compounds containing azetidines synthesized (5e)

The compounds of the Schiff base (0.001mole) were dissolved in anhydrous 1,4-dioxane, and then chloroacetyl chloride (0.0015 mole,0.169 g) was added drop by drop over the course of 20 minutes. After allowing the reaction mixture to sit at room temperature for 3 hours, it was stirred. After heating the solution under reflux for 25 minutes at 450wolt power, the solvent was evaporated under low pressure. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. That you may purchase 3-chloro-4-oxoazetidin Schiff base analogs.

SYNTHESIS OF THE 5f COMPOUND

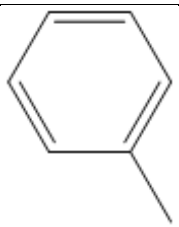
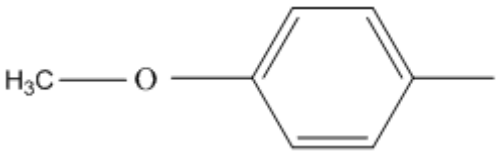
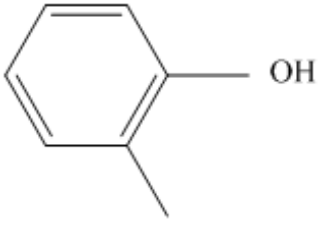
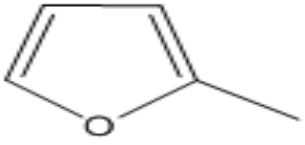
Compounds based on Schiff's theory of synthesis (4f)

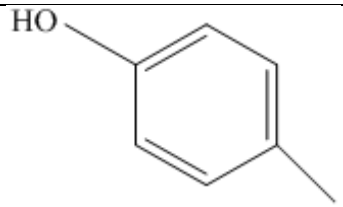
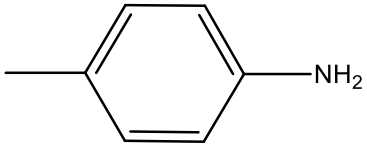
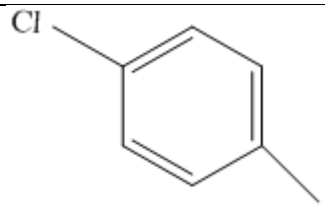
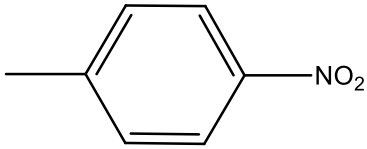
Compound 2 (0.01mole, 2.9gm) was dissolved in ethanol (30ml) and heated with 4-Methoxy-2-vinyl benzaldehyde (0.01mole) during a 30-minute period at 450wolt power until the reaction was complete. The mixture was cooled to the standard laboratory temperature. Crushed ice with a residue poured on top, Crystals were dissolved in water and sprayed, then afterwards reformed using water and ethanol

Compounds containing azetidines synthesized (5f)

The compounds of the Schiff base (0.001mole) were dissolved in anhydrous 1,4-dioxane, and then chloroacetyl chloride (0.0015 mole,0.169 g) was added drop by drop over the course of 20 minutes. Absolute ethanol was used to wash the solid product, which was then filtered, dried, and recrystallized. That you may purchase 3-chloro-4-oxoazetidin Schiff base analogs.

Table no-2. For Compounds: A1-A8 (INDOLE DERIVATIVES)

Comp.code	R	Comp. code	R
A1		**A5**	
A2		**A6**	

A3		**A7**	
A4		**A8**	

SYNTHESIS OF INDOLE DERIVATIVES (A1-A8)

SYNTHESIS OF SCHIFF'S BASE (Ia)

A sodium acetate and water solution of 1 gram of phenyl hydrazine. Then, acetophenone is added as a 0.5ml solution in 8ml of water.

INDOLE SYNTHESIS (A1)

There was a 30-minute reflux of 0.01 mole of Schiff's base and 0.01 mole of PPA. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

INSTRUCTIONS FOR MAKING SCHIFF'S BASE (Ib)

Dissolve 1 gram of phenyl hydrazine in 10 milliliters of sodium acetate and water. Then, a 0.5-milliliter O-hydroxy-Acetophenone solution in 8 milliliters of water is added. Hydrazone crystals, which are odorless and colorless, formed when the liquid was chilled in ice and agitated for 5 minutes.

INDOLE SYNTHESIS (A2)

In a 30-minute reflux, 0.01 mole of Schiff's base and 0.01 mole of PPA were combined. After that, the mixture is brought down to room temperature. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

A CHEMICAL APPROACH TO THE SYNTHESIS OF SCHIFF'S BASE (Ic)

A sodium acetate and water solution of 1 gram of phenyl hydrazine. Then, p-hydroxy-Acetophenone is added as a 0.5ml solution in 8ml of water. Hydrazine was produced by filtering and washing the product with diluted acetic acid and water.

Synthesis of Indole (A-3): A 0.01 mole amount of Schiff's base and a 0.01 mole amount of PPA have been refluxed for 30 minutes. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

Schiff's base may be synthesized by dissolving 1 gram of phenyl hydrazine in 10 milliliters of sodium acetate in water. After that, you'll pour in a p-choloro-Acetophenone solution that's 0.5 milliliters in size and 8 milliliters in volume.

INDOLE SYNTHESIS (A4)

There was a 30-minute reflux of 0.01 mole of Schiff's base and 0.01 mole of PPA. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

SYNTHESIS OF SCHIFF'S BASE (Ie)

One gram of phenyl hydrazine dissolved in ten milliliters of sodium acetate and water. A p-methoxy-Acetophenone solution (0.5 ml in 8 ml of water) is then added. For 30 minutes, 0.01 mol of Schiff's base and 0.01 mol of PPA were refluxed to create indole (A5). When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

The SCHIFF'S BASE may be synthesized by dissolving 1 gram of phenyl hydrazine in 10 milliliters of sodium acetate solution. Then we add a 0.5 ml solution of Furyl-Acetophenone in 8 ml of water. After 5 minutes of stirring in freezing water, the liquid crystallized into clear hydrazone. After filtering, washing with diluted acetic acid, and rinsing with water, hydrazine was finally created.

INDOLE SYNTHESIS (A6)

There was a 30-minute reflux of 0.01 mole of Schiff's base and 0.01 mole of PPA. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

A CHEMICAL APPROACH TO THE SYNTHESIS OF SCHIFF'S BASE (Ig)

A sodium acetate and water solution of 1 gram of phenyl hydrazine. Then, you add p-amino-Acetophenone solution (0.5 ml in 8 ml of water) to the mixture. Crystalline hydrazone formed in the liquid after being agitated for five minutes and chilled in ice. Filtration of the product was followed by a wash in diluted acetic acid and water, after which the hydrazine was recovered.

INDOLE (A7) SYNTHESIS After 30 minutes of refluxing 0.01 mol of Schiff's base and 0.01 mol of PPA, indole (A7) has been synthesized. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

Solution of 1 gram of phenyl hydrazine in 10 milliliters of sodium acetate and water is the starting point for the synthesis of Schiff's base. Then we add a p-nitro-Acetophenone solution of 0.5 ml in 8 ml of water. Clear hydrazone crystals formed when the liquid was chilled in ice and agitated for 5 minutes. Hydrazine was produced when the substance was filtered, washed with diluted acetic acid, and then rinsed with water.

INDOLE SYNTHESIS (A8)

There was a 30-minute reflux of 0.01 mole of Schiff's base and 0.01 mole of PPA. When the combination reaches room temperature, it is ready to use. An open capillary technique was used to record the compound's melting point after the result was filtered, purified, and characterized.

SPECTRAL DATA-

Material and Method:

All of the materials used were of the greatest commercial quality and were either synthesized or synthetically derived. The synthesized chemical was successfully identified, purified, and characterized.

Identification and Characterization:

The following procedures were used to identify and characterize the compounds:

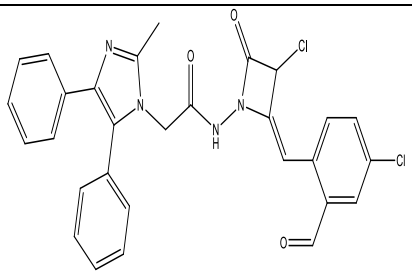
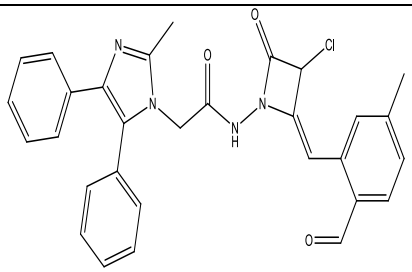
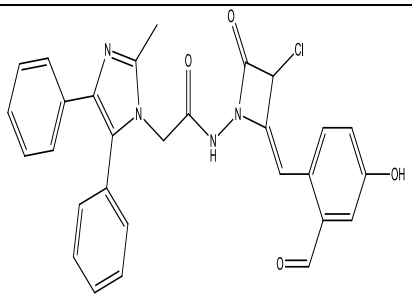
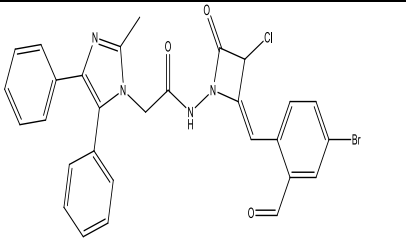
1) Melting point

2) “Thin layer chromatography”

3) “Infra-red spectroscopy”

4) “Nuclear magnetic resonance spectroscopy”

Table.no-3. spectral study of the synthesized compounds.5a-f

Sr.no	**Comp. code**	**Structure**	**I R**	**N M R**
1	5a		3029-(Ar-CH),3064 (Ar-CH) ,2916, 2848 (CH2-CH) ,1681 (-C=O) ,3400(-NH) ,1325 (-N Imidazole), 1660(-C=OAzatadine),779,773(-Cl),1288(-CNAzatadine)	1.57(3H,d,CH3),3.75(1H,q,CH),4.51(2H,d,CH2)7.25-7.78(11H,m,Ar-H),8.57(1H,s,NH),9.23(1H,s,NH attpaind to imine),8.11(1H,s,CH=N).
2	5b		3029(Ar-CH) ,3064(Ar-CH),2916,2848(CH2-CH),1681(-C=O),3400(-NH),1325(-NImidazole),1660(-C=OAzatadine),2785(-CH3),1288(-CNAzatadine)	1.57(3H,d,CH3),3.75(1H,q,CH),4.51(2H,d,CH2),7.28-7.91(11H,m,Ar-H),8.59(1H,s,NH),9.01(1H,s,NHattpaind toimine),8.11(1H,s,CH=N).
3	5c		3029-(Ar-CH),3064(Ar-CH) ,2916, 2848 (CH2-CH) ,1681 (-C=O), 3400(-NH) ,1325 (-N Imidazole), 1660 (-C=OAzatadine) ,3317(-OH), 1288 (- CN Azatadine);	1.61 (3H, d,CH3),3.77(1H,q,CH),4.44-4.52(2H,d,CH2),7.287.82(12H,m, ArH),8.13(1H,s,NH),8.38(1H,s,OH),9.55(1H,s,CH=N).
4	5d		3029-(Ar-CH)3064(Ar-CH)2916,2848(CH2-CH)1681(-C=O)3400(-NH)1325(-NImidazole)1660(-C=OAzatadine)560(-Br)128(-CNAzatadine)	1.57(3H,d,CH3),3.75(1H,q,CH),4.51(2H,d,CH2),7.548.45,9.50(1H,s,NHattpaindtoimine),8.11(1H,s,CH=B)

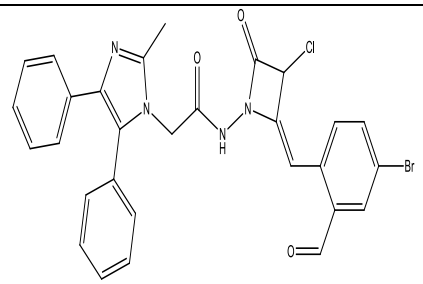
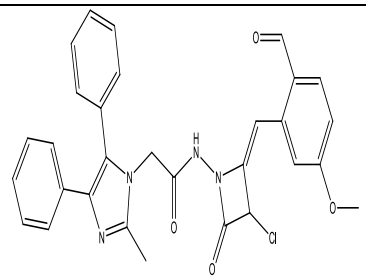
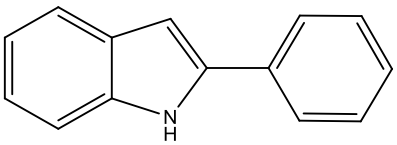
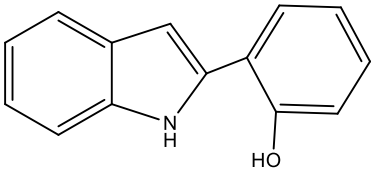
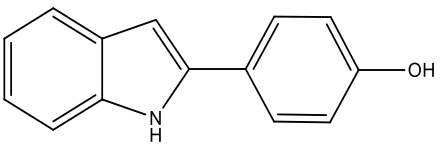
5	5e		3029-(Ar-CH),3064 (Ar-CH), 2916, 2848 (CH2-CH) ,1681 (-C=O) ,3400(-NH) ,1325 (-N Imidazole) ,1660(-C=OAzatadine),1288(-CNAzatadine)	1.57(3H,d,CH3),3.75(1H,q,CH), 4.51(2H,d,CH2),7.487.88(11H,m, Ar-H),8.44 (1H,s,NH),8.59(H,s,NHattpaindtoimine),8.11(1H,s,CH=N).
6	5f		3029-(Ar-CH),3064(Ar-CH),2916,2848(CH2-CH),1681(-C=O),3400(-NH),1325(-NImidazole) ,1660(-C=OAzatadine),2785(-OCH3),1288(-CNAzatadine)	1.56(3H,d,CH3),3.7(1H,q,CH),3.89(3H,s,OCH3),7.28-7.96(11H,m,Ar-H),8.28(1H ,s,N=CH),8.57(1H,s,NH),9.61(1H, s,NH-N=CH).

Table.no-4.spectral study of the synthesized compounds.(A1-A8)

Sr. No	**Comp. Name**	**Structure**	**I R**	**N M R**
1	A1		3245.23(-CH Str.), 1080(-C-N str.), 2283(C=C str.), 3540(N-H str.), 3110(C-C str.)	11.36(NH), 7.79-6.77(9H-CH), 7.51(8H-indole),
2	A2		3240(CH str.), 2273(C=C str.), 3583(NH str.), 3650(C-O str.), 1245(CN str.)	11.0 (1H of –NH); 6.54-8.35 (8H of phenyl); 6.27 (1H of –indole); 5.0 (1H of –OH);
3	A3		3241(CH str.), 2240(C=C str.), 1360(CN str.), 3641(C-O str.), 3548(NH str.), 3655(OH str.)	5.00(Ar-OH), 11.36(NH), 7.26-7.40(5H-Indole), 6.86-7.49(3H-Benzene)

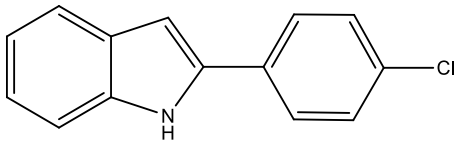
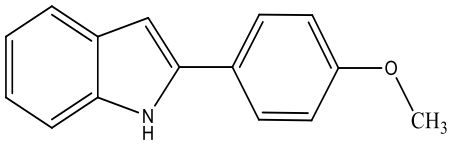
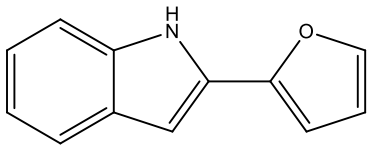
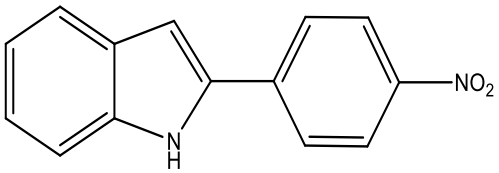
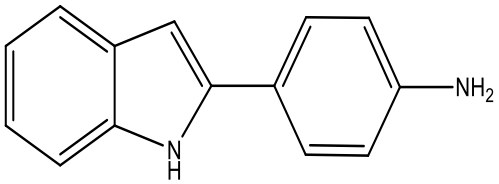
4	A4		3255(CH str.), 2281(C=C str.), 745.20(C-Cl str.), 3550(NH str.), 1160(CN str.)	11.36(NH), 7.55-7.98(3CH-Benzene), 6.45-7.55(3H-Indole)
5	A5		3243(CH str.), 2215(C=C str.), 1300(CO str.), 3588(NH str.), 1122(CN str.)	11.0 (1H of –NH); 6.4-7.6 (8H of phenyl); 6.2 (1H of Indole); 3.6-3.8 (3H of –CH3)
6	A6		3245(CH str.), 2210(C=C str.), 1120(CN str.), 1000(C=C str.), 3060(C-C str.), 3573(NH str.)	7.30-6.38(3H-Furan), 6.99-7.49(5H-Indole)
7	A7		3251(CH str.), 1620(C-C str.), 2270(C=C Str.) 1220(C-N str.), 1460(N-O str.),	11.0 (1H of –NH); 6.6-7.8 (8H of phenyl); 6.4 (1H of indole)
8	A8		1600(C-C str.), 2281(C=C str.), 1200(C-N str.), 3440(N-H str.)	11.0 (1H of –NH); 6.6-7.5 (8H of phenyl); 6.3 (1H of indole); 6.1 (2H of –NH2)

Table no. 5: Structure and IUPAC Name of (Scheme): -(5a-5f).

Sr.No	**Comp. Name**	**Structure**	**IUPAC Name**

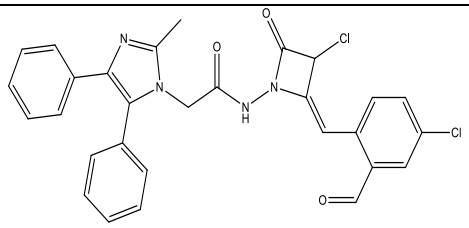
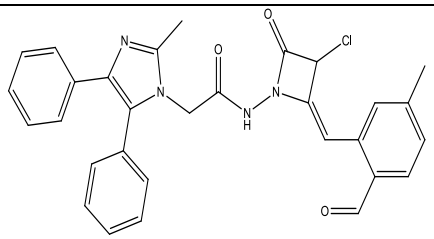
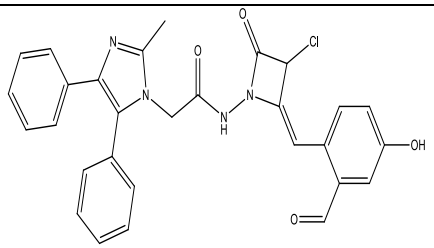
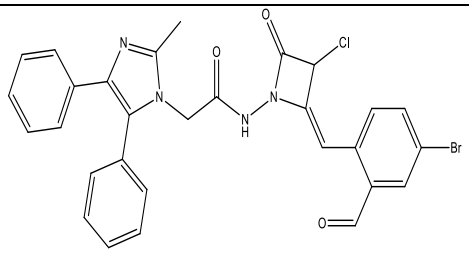
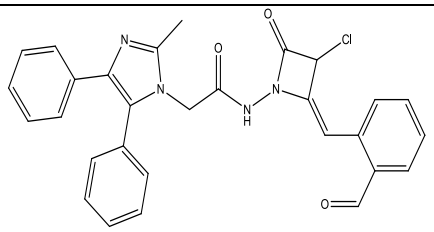
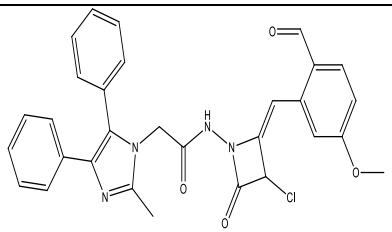
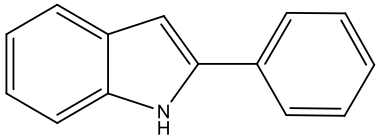
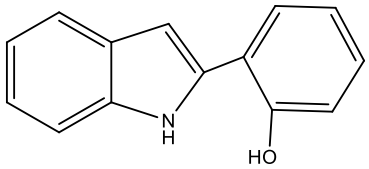
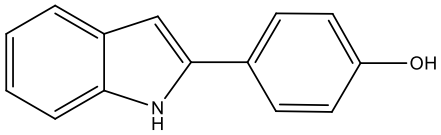
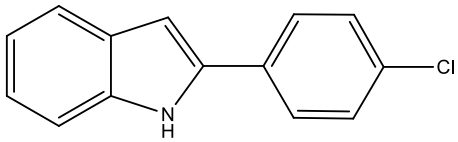
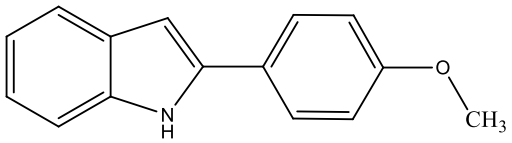
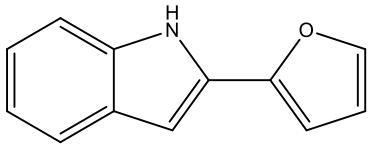
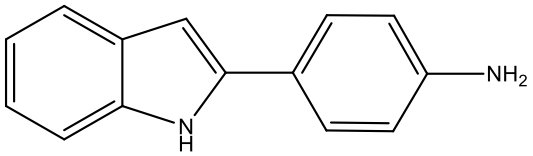
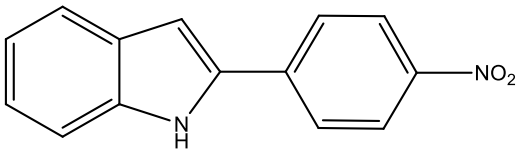
1	5a		[N-(2-(4-chloro-2-formylbenzylidene)-3-chloro-4-oxoazetin-1yl)-2- (2methyl-4,5diphenyl-1H-imidazol-1-yl) acetamide]
2	5b		[N-(2-(2-formyl-5-methylbenzylidene)-3-chloro-4-oxoazetin-1yl)-2- (2methyl-4,5diphenyl-1H-imidazol-1-yl) acetamide]
3	5c		[N-(2-(4-hydroxy-2-formylbenzylidene)3-chloro-4-oxoazetin1yl)-2- (2methyl-4,5diphenyl-1H-imidazol-1-yl) acetamide]
4	5d		[N-(2-(4-bromo-2-formylbenzylidene)-3-chloro-4-oxoazetin-1yl)-2- (2methyl-4,5diphenyl-1H-imidazol-1-yl) acetamide]
5	5e		[N-(2-(2-formylbenzilidene)-3chloro-4-oxoazetin-1yl)-2-(2methyl- 4,5diphenyl -1H-imidazol-1-yl) acetamide]
6	5f		[N-(2-(2-formyl-5-methoxybenzylidene)-3-chloro-4-oxoazetin-1yl)-2- (2methyl-4,5diphenyl -1H-imidazol-1-yl) acetamide]

Table no.6: Structure and IUPAC Name of (Scheme A1-A8):

Sr.No	**Comp. Name**	**Structure**	**IUPAC Name**

1	A1		2-phenyl- 1H-indole
2	A2		2-(1H-indole-2-yl)phenol
3	A3		4-(1H-indole-2-yl)phenol
4	A4		2-(4-chlorophenyl)-1H-indole
5	A5		2-(4-methoxyphenyl)-1H-indole
6	A6		2-(furan-2-yl)-1H-indole
7	A7		4-(1H-Indol-2-yl)aniline
8	A8		2-(4-Nitrophenyl)-1H-indole

Biological activities:

Pharmacological Activity:Imidazole-azetidines

Materials and Methods:

Analgesic activity activity of all synthesized compounds was evaluated by using Swiss albino mice as well as S. Aureus bacteria.

All of the 5(a-f) compounds, totaling 120 mg, were dissolved in distilled water just before being taken orally, and 0.06% glacial acetic acid solution, 0.06% pentazocine, and 0.9% normal saline were all utilized for intraperitoneal injections. The mice were randomly assigned to one of three groups, with a total of three groups having a total of 18 mice (n = 18). (control, standard, and test group). Two hours before the test, the subjects were given an oral dose of 120 mg/kg of the synthetic compounds 5(a-f) and 25 ml/kg of normal saline. Pentazocine, a standard medication, was injected intraperitoneally at a dose of 10 mg/kg 15 minutes before the trial began. Approximately 15–30 minutes after administration, pentazocine begins to significantly alleviate pain.

The research was done with the blessing of the Institutional Animal Care and Use Committee (IAEC). number 1091/G0/Bt/S/07/CPCSEA indicating that it has been approved under the CPSEA. Male and female albino mice weighing 30-50 g at 8-12 weeks of age were utilized in tests. Albino mice were raised at the Pravara Rural College of Pharmacy's main animal facility in Loni.

Our pharmacology experts conducted this investigation. Experimental animals were exposed to the laboratory setting for at least 1 hour prior to any testing. Paget and Barnes' method of converting human daily doses to mouse doses served as the basis for the medication dosages. (1962).

Drugs and chemicals:

All of the synthetic compounds 5(a-f) were dissolved in 120 mg of distilled water right before being taken by mouth. Compounds 5a–f were used to make the test drug, which was given by mouth 2 hours earlier with a dose of 120 mg/kg and 25 ml/kg of normal saline. 15 minutes before the experiment, the standard drug pentazocine (10 mg/kg) was given intraperitoneally. Between 15 and 30 minutes, pentazocine starts to relieve pain in a big way.

• Group 1: 25 ml/kg of normal saline (oral)

• Group 2: Pentazocine -10 mg/kg (intra-peritoneal)

• Group 3: All compounds 5(a-j) made in a lab, 120 mg/kg (intra-peritoneal).

Analgesic Activity:

Eddy's Hot Plate Method:

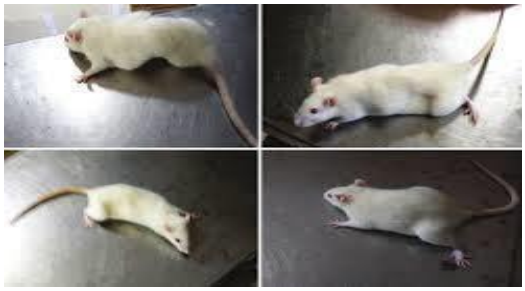
Thus, the latency duration of all synthetic compounds 5(a-j) was considerably (P 0.05) better than the control at 30-120 min, and the latency period of the standard was more significantly (P 0.05) better than that of synthesized compounds 5(a-f) at all time intervals of the experiment.

Fig.1: Eddy's Hot Plate Test on Mice

Writhing Method:

All of the synthetic compounds 5(a-f) substantially decreased the amount of writhes when administered orally 2 hours prior to intraperitoneal injection of acetic acid. It was found that synthesized compounds 5(a-f) at a dose of 120mg/kg significantly reduced the writhing response compared to the normal saline control group. Synthetic compounds 5(a-f) had fewer writhes than the standard, whereas the standard medication (pentazocine) had fewer writhes than both the synthesized compounds and normal saline. Synthesized compounds 5(a-f) had a 56.39% inhibition rate compared to the control, whereas the standard had an 84.35% rate.

Fig. 2: Writhing Test on Mice



Tail Clip Method:

As a result, the average response time of all synthesized compounds was considerably (P 0.05) better than the control at 30-120 min, while the latency duration of the standard was more significant (P 0.05) when compared to all synthetic compounds at all- time intervals of experiments.

Fig. 3: Tail Clip Test on Mice

Table No.7: The analgesic activity of synthesized compound 5(a-f) in thermal pain model- Eddy's hot plate:

Groups	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
Control	0.89+/-0.07	1.080+/-0.060	2.10+/-0.070	2.310+/-0.040	2.190+/-0.060
Standard	2.950+/-0.110*	6.480+/-0.060*	7.040+/-0.070	8.250+/-0.040*	10.210+/0.050*
5a	0.9+/-0.03	4.04+/-0.10*	6.01+/-0.08*	7.03+/-0.06*	5.44+/-0.08*
5b	0.6+/-0.02	2.02+/-0.03	5.03+/-0.07	5.08+/-0.04	4.34+/-0.06
5c	0.7+/-0.04	2.03+/-0.05	4.02+/-0.05	6.07+/-0.06	6.03+/-0.04

5d	1.06+/-0.07	5.32+/-0.02	6.07+/-0.08	5.08+/-0.04	1.66+/-0.07
5e	0.9+/-0.08	3.09+/-0.03	3.09+/-0.06	4.02+/-0.05	3.15+/-0.08
5f	1.8+/-0.04	4.07+/-0.04	5.08+/-0.04	6.01+/-0.03	5.18+/-0.07

Table No.8: The % analgesic activity of synthesized compound 5(a-f) and control when compared to standard – Eddy's Hot Plate:

Groups	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
Control	30.16	16.66	29.82	28	21.44
5a	30.50	62.34	85.36	85.21	53.28
5b	30.45	62.24	85.30	85.18	53.22
5c	30.25	62.14	85.16	85.06	53.07
5d	30.38	62.08	85.04	85.02	53.03
5e	28.57	61.40	83.42	84.28	52.34
5f	30.20	62.03	85.06	85.01	53.04

Table No.9: The analgesic activity of synthesized compound 5(a-f) in visceral pain model- Writhing method:

Groups	**No. Of Wriths**	**% Of Inhibition**
Control	35.16+/-2.850	0
Standard	5.5+/-2.420	84.35
5a	15.33+/-2.16	56.39
5b	20.45+/-1.85	74.66
5c	28.36+/-1.92	83.22
5d	30.02+/0.68	86.65
5e	18.35+/-1.76	67.02
5f	19.35+/-2.04	70.93

Table No.10: The analgesic activity in mechanical pain mode – Tail clip method:

Groups	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
Control	0.890+/-0.070	0.730+/-0.230	2.810+/-0.220	2.710+/-0.160	2.950+/-0.210
Standard	2.950+/-0.110*	8.840+/-0.120*	10.060+/0.130*	10.200+/0.070*	10.210+/0.090*
5a	0.9+/-0.03	2.03+/-0.11*	6.14+/-0.16*	6.50+/-0.18*	5.53+/-0.23*
5b	0.6+/-0.02	4.04+/-0.10*	7.03+/-0.07	7.08+/-0.04	8.34+/-0.06
5c	0.7+/-0.04	6.02+/-0.03	5.02+/-0.05	8.07+/-0.06	6.03+/-0.04
5d	1.06+/-0.07	4.03+/-0.05	6.07+/-0.08	6.08+/-0.04	6.66+/-0.07
5e	0.9+/-0.08	3.32+/-0.02	7.09+/-0.06	7.02+/-0.05	8.15+/-0.08
5f	1.8+/-0.04	5.09+/-0.03	9.08+/-0.04	10.01+/-0.03	7.18+/-0.07

Table No.11: The % analgesic activity of synthesized compound 5(a-f) & control when compared with standard Tail clip method:

Groups	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
Control	30.16	8.25	27.93	26.36	29.47
5a	30.50	22.96	61.03	63.72	55.24
5b	30.35	22.76	61.08	63.50	55.64
5c	28.85	22.82	60.07	63.45	55.23
5d	30.58	22.98	61.05	62.78	54.65
5e	30.19	22.56	60.03	62.84	53.98
5f	30.28	22.26	60.02	60.89	54.86

Table No.12: The % analgesic activity of synthesized compound 5(a-f) when compared to control- Eddy's hot plate method:

Groups	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
5a	0.34	45.68	55.54	57.21	31.84
5b	0.32	44.78	54.65	57.14	31.54
5c	0.28	45.56	55.58	56.85	30.94
5d	0.23	43.52	53.89	54.65	31.25
5e	0.33	41.98	54.87	55.68	31.34

5f	0.32	44.87	55.25	55.79	30.84

The experimental protocol conducted according to the guideline for the use and care of the experimental animals.

In all three of the well-established experimental models of pain, the test drug of every azetidine derivative exhibits considerable analgesic effect compared to the control. After 60 and 90 minutes, the analgesic effect was at its peak. The potential process may include a reduction in central sympathetic tone, an increase in spinal cord enkephalin and endorphin release, a rise in angiotensin 1-7 levels, and a fall in prostaglandin E2 and cyclooxygenase 2 (PGE2 and COX2) levels.

All azetidine derivatives may, therefore, show analgesic effect in two distinct ways: (a) centrally, by the release of -endorphin and enkephalins in the Eddy's hot plate and tail clip as well as (b) peripherally, via the suppression of COX 2 and PGE2.

Result and discussion

Imidazole-azetidine-

The azetidine derivatives 5(a)–5(f) were synthesized according to the methodology below. Initially, 2methyl, 4,5-diphenyl imidazole was produced by reacting benzil and acetaldehyde with acetamide and glacial acetic acid. After subjecting compound (I) to chloro methyl ethyl acetate. The chemical (II) 2-(2-methyl, 4,5-diphenyl)-1H-imidazole-1-yl) acetate was obtained by amination of 2-(2-methyl, 4,5-diphenyl)-1H-imidazole in pure ethanol. Imidazole-1-yl)-2-(2-methyl, 4,5-diphenyl)-acetahydrazide is a chemical that serves as an example of a heterocyclic aromatic hydrazide (III). compounds of the Schiff's base type were obtained by condensing compound (III) with a number of different aromatic aldehydes (4a-f). The compounds (4a-f) then produced 2-Azetidinones compounds5 after reacting with chloracetyl chloride (a-f).

Spectroscopic analysis using both IR and NMR techniques revealed distinctive peaks for each component.

Eddy's Hot Plate Method:

At 30–120 minutes, the latency period of all manufactured compounds 5(a-f) was considerably (P 0.05) better than the control, whereas at all other times, the latency duration of the standard was more significant (P 0.05) than that of the synthesized compounds 5(a-f).

Tail ClipMethod:

All manufactured compounds had considerably better mean response times than the control at 30–120 minutes, whereas the latency duration of the standard was significantly longer than that of all created compounds across all time periods.

Writhing Method:

It was shown that synthesized compounds 5(a-f) at a dose of 120mg/kg significantly reduced the writhing response compared to the normal saline control group. Synthetic compounds 5(a-f) had fewer writhes than the standard, whereas the standard medication (pentazocine) had fewer writhes than both the synthesized compounds and normal saline. Synthesized compounds 5(a-f) had a percentage inhibition of 56.39 compared to the control, whereas the standard had an inhibition percentage of 84.35.

Pharmacological activity-indole

IN-VITRO GLUCOSIDASE INHIBITORY ACTIVITY

α-Glucosidase Inhibition Assay

The -glucosidase enzyme was used in vitro to test the inhibitory activity of all eight synthesized new indole derivatives (A1-A8). The majority of substances showed some level of -glucosidase inhibition, with IC50 values ranging from 20.70 M to 61.1 M when compared to acarbose.

Adding 50 µl of Na2CO3 halted the reaction (0.1M).

Multipal Reader was used to measure the 405 nm absorbance of the freed p-nitro phenol.

Various concentrations of acarbose (0.1-0.5mg/ml) were provided as a reference.

Each experiment was conducted in triplicate and a control set up in parallel without the test drug served as a comparison.

Table no.13: In-vitro glucosidase inhibitory activity evaluation of synthesized compounds(A1 – A8).

Compound	IC50 (mM ± SEMa)
A1	17.850±1.20
A2	21.80±0.60
A3	36.80±1.10
A4	11.90±0.50
A5	37.20±2.20
A6	27.50±0.60
A7	42.50±0.90
A8	21.60±0.50
Acarbose	30.60±1.20

Result and discussion

Imidazole-azetidine-

The azetidine derivatives 5(a)–5(f) were synthesized according to the methodology below. Initially, 2methyl, 4,5-diphenyl imidazole was produced by reacting benzil and acetaldehyde with acetamide and glacial acetic acid. After subjecting compound (I) to chloro methyl ethyl acetate. The chemical (II) 2-(2-methyl, 4,5-diphenyl)-1H-imidazole-1-yl) acetate was obtained by amination of 2-(2-methyl, 4,5-diphenyl)-1H-imidazole in pure ethanol. Imidazole-1-yl)-2-(2-methyl, 4,5-diphenyl)-acetahydrazide is a chemical that serves as an example of a heterocyclic aromatic hydrazide (III). compounds of the Schiff's base type were obtained by condensing compound (III) with a number of different aromatic aldehydes (4a-f). The compounds (4a-f) then produced 2-Azetidinones compounds5 after reacting with chloracetyl chloride (a-f).

Spectroscopic analysis using both IR and NMR techniques revealed distinctive peaks for each component.

Eddy's Hot Plate Method:

At 30–120 minutes, the latency period of all manufactured compounds 5(a-f) was considerably (P 0.05) better than the control, whereas at all other times, the latency duration of the standard was more significant (P 0.05) than that of the synthesized compounds 5(a-f).

Tail ClipMethod:

All manufactured compounds had considerably better mean response times than the control at 30–120 minutes, whereas the latency duration of the standard was significantly longer than that of all created compounds across all time periods.

Writhing Method:

It was shown that synthesized compounds 5(a-f) at a dose of 120mg/kg significantly reduced the writhing response compared to the normal saline control group. Synthetic compounds 5(a-f) had fewer writhes than the standard, whereas the standard medication (pentazocine) had fewer writhes than both the synthesized compounds and normal saline. Synthesized compounds 5(a-f) had a percentage inhibition of 56.39 compared to the control, whereas the standard had an inhibition percentage of 84.35.

INDOLES

The synthesized new compound structures, yields and melting points have been given in the table. Melting points of the synthesized compounds were sharp indicating that the compounds were pure; the yield value of the compounds also suggested that the chemical methods were reliable for the synthesis of the compound.All spectral data were in accordance with assumed structure. The synthesized compounds were screened for their In-vitro glucosidase inhibitory activity in treatment of diabetic Mellatis. The Acarabose was used as standard control.We investigated the importance of functional group substitutions, in the structural framework of the compounds for their In-Vitro glucosidase inhibitory activity. All compounds showed significant glucosidase inhibitory activity.

Summary and conclusion

IMIDAZOLE-AZETIDINE

Literature reveals that imidazole-azetidine passes a wide range of pharmacological activity.It was also found that 3-chloro-4-oxo azetidine-1-yl)-2-(2-methyl-4,5-diphenyl-1H-Imidazole-1-yl) acetamide derivatives have pharmacological importance.Promoted by thetherapeutic importance of imidazole-azetidine one, it was planned to synthesise imidazole-azetidine one derivatives by microwave method and to screen the synthesise for analgesic activity.The compounds plan for synthesis where prepared under available laboratory conditions and where confirmed by physical and spectral.2-(2-methyl,4,5diphenyl)-1H-Imidazole) was synthesized from Benzene and acetamide in presence of glacial acetic acid and formaldehyde. The synthesised 2-(2-methyl,4,5diphenyl)-1H-Imidazole-1-yl)acetate from2-(2-methyl,4,5diphenyl)-1H-Imidazole)Was reacted with chloromethyl ethyl acetate. For the synthesis of 2-(2-methyl, 4,5 diphenyl)-1H-Imidazole-1-yl) acetahydrazide, 2-(2-methyl, 4,5 diphenyl)-1H-Imidazole-1-yl) acetate reacts with hydrazine hydrate.For synthesis of intermediate Schiff's bases,2-(2-methyl,4,5diphenyl)-1H-Imidazole-1-yl)acetahydrazide reacts with various aldehyde and formed substituted with various aromatic aldehyde 3-chloro-4-oxo azetidine-1-yl)-2-(2-methyl-4,5-diphenyl-1H-Imidazole-1-yl)acetamide derivatives.

Across all three standard experimental models of pain, the test medication of the azetidine derivatives 5(a-f) demonstrates considerable analgesic effect compared to the control. After 60 and 90 minutes, the analgesic effect was at its peak. The potential process may include a reduction in central sympathetic tone, an uptick in spinal cord enkephalin and endorphin release, an increase in angiotensin 1–7, and a decrease in prostaglandin E2 and cyclooxygenase 2 (PGE2 and COX).

Therefore, it can be concluded that all azetidine derivatives likely show their analgesic activity in a variety of ways.

INDOLES-

The present research work is a Bonafide novel for the synthesis of indole.The extensive literature review suggests the utilization of these heterocycles as a lead in treatment of wide variety of diseases and disorders. The method

of synthesis of these heterocycles starting from different substrate had been established. Around Eight newer derivatives of before mentioned heterocycles were synthesized. The purity of synthesized compounds was checked with the help of TLC.The physical constants (m.p.) of the synthesized compounds were determined using open capillary method.The structures of the synthesized compounds were established by using IR, H^1NMR and CHN analysis.

The synthesized compounds were screened for their In-vitro glucosidase inhibitory activity in treatment of diabetic Mellatis.We investigated the importance of functional group substitutions, in the structural framework of the compounds for their In-Vitro glucosidase inhibitory activity. All compounds showed significant glucosidase inhibitory activity. The compounds (A1, A3 and A6) showed better activity.

Finally, the encouraging result of the glucosidase inhibitory activity displayed by these compounds may be of interest for further structural modifications to the lead compound and next level studies in the hope of. Finding a new potent glucosidase inhibitor.

References

1. A.R.Bhat,et al "Synthesis of 4-thiazolidinones and azetidin-2-ones and their biological activities," *Indian Journal of Pharmaceutical Sciences*, vol. 49, no. 5, pp. 194–197, 2002.
2. N. S. Mahajan, et al "Synthesis of some thiazole compounds of biological interest containing mercapto group," *International Journal of Chemical Sciences*, vol. 6, no. 2, pp. 800–806, 2008.
3. K. M. Basavaraja, et al "Synthesis and biological activity of some 2-[3substituted-2-thione-1,3,4-thiazole-5-yl) amino benzothiazoles," *Indian Journal of Heterocyclic Chemistry*, vol. 18, pp. 69–72, 2008.
4. Satyanarayana V S, Sivakumar A, Ghosh A R, Journal of Pharmacy Research, 2010, 3, 2327-2331.
5. Hemlata Bhawar, Nachiket Dighe *et al* Synthesis and Evaluation of Some New Imidazole Derivatives for their Anti-Microbial and Anti-Inflammatory activities.Asian J.Pharm. Tech. 2014; Vol. 4: Issue 4, Oct.-Dec.,Pg 189-194.
6. Amira S. Abd El-A., 2Fatma A.F. Ragab, Asmaa A. Magd El-Din, Design, Synthesis and Anticancer Evaluation of Some Selected Schiff Bases Derived from Benzimidazole Derivative, Global Journal of Pharmacology 7 (2): 143-152, 2013.
7. Malleshappa Noolvi a, Suresh Agrawal a, Harun Patel a, Aravind Badiger b, Monika Gaba a, Azit Zambre c, Synthesis, antimicrobial and cytotoxic activity of novel azetidine-2-one derivatives of 1H-benzimidazole, Arabian Journal of Chemistry (2014) 7, 219–226.
8. Snehal Lokhandwala and Nikhil M. Parekh, Synthesis and microbial studies of imidazolone based azetidinone analogues, Scholars Research Library Der Pharma Chemica, 2014, 6(6):139-142.
9. Ayse, U. O. et al Comparative study of microwave-assisted and conventional synthesis of ibuprofen-based acyl hydrazone derivatives. Turkish Journal of Chemistry Turk. J. Chem. 2013. Vol. 37. Pp: 927 – 935.
10. Oana, M. D, et al Synthesis and Biological Evaluation of New 2Azetidinones with Sulfonamide Structures. Molecules. 2013, Vol.18. Pp: 4140-4157.
11. Oana, M. D, et al Synthesis and Biological Evaluation of New 2Azetidinones with Sulfonamide Structures. Molecules. 2013, Vol.18. Pp: 4140-4157.
12. Mukherjee s m Singh et al organic chemistry, Volume II, International(P) Limited, publisher, 2003, 586- 587.
13. G. R. Chatwal, et al instrumental method of chemical analysis, Himalaya publishing house, 2.5 99- 2.6 16
14. A.V. Kasture, et al pharmaceutical analysis, Volume II, instrumental method, Nirali Prakashan, 267, 268, 281, 289, 305, 306, 308.
15. Knepper K.; Vanderheiden S.; BraseS(2012).Synthesis of diverse indole libraries on polystyrene resin–Scope and limitations of an organometallic reaction on solid supports.J.Org. Chem.; 2012; 8; 1191.
16. Pews-Davtyan A.; Annegret T.; Anne-Caroline S.; Stefanie O.; Frech M. J.; Rolfs. A.; BellerM(2010). A new facile synthesis of 3- amido indole derivatives and their evaluation as potential GSK-3β inhibitors. Org. Biomol. Chem.; 2010; 8; 1149.
17. Houlin W. J(1972). Indoles Wilry-Interscience, New York. Part I (1972).
18. Joule J. A.; Mills K.; Smith G. F(1995). Het.Chem., 3rd edit; Chapman and Hall, (1995).
19. Baeyer A. V(1866). Ann. Chem.; 1866; 140; 295-313.

20. Sanz, R.; Escribano, J.; Pedrosa, M. R.; Aguado, R.; Arnáiz, F. J.; *Adv*. *Synth*. *Catal*. 2007, *349*,713.

21. Silveira C. C.; Mendes S. R.; Soares J. R.; Victoria F. N.; Martinez D. M.; Savegnago L(2013). Synthesis and antioxidant activity of new C-3 sulfenyl indoles. Tetrahedron Letts.; 2013; 54; 4926–4929.

22. Tichy M.; Pohl R.; Xu H. Y.; Chen Y.; Yokokawa F.; Shi P.; Hocek M(2012). Synthesis and antiviral activity of 4,6-disubstituted pyrimido[4,5-b]indole ribonucleosides. Bioorg.Med. Chem.; 2012; 20; 6123–6133.

23. Xue S.; Ma L.; Gao R.; Li Y.; Li Z(2014). Synthesis and antiviral activity of some novel indole-2-carboxylate derivatives.ActaPharmaceuticaSinica B; 2014; 4; 313–321.

24. Wang R.; Shi H.; Zhao J.; He Y.; Zhang H.; Liu J(2013). Design, synthesis and aromatase inhibitory activities of novel indole- imidazole derivatives.Bioorg. Med. Chem. Letts.; 2013; 23; 1760–1762.

25. Nguyen T.; German N.; Decker A. M.; Li J.; Wiley J. L.; Thomas B. F.; Kenakin T. P.; Zhang Y(2015). Structure–activity relationships of substituted 1H-indole-2-carboxamides as CB1 receptor allosteric modulators.Bioorg.Med. Chem.; 2015; 23; 2195– 2203.

26. Palmerini C. A.; Tartacca F.; Mazzoni M.; Granieri L.; Goracci L.; Scrascia A.; Lepri Susan(2015). Synthesis of new indole-based bisphosphonates and evaluation of their chelating ability in PE/CA-PJ15 cells. Eur. J. Med. Chem.; 2015; 102; 403-412.

27. Song Y.; Wu F.; Zhang C.; Liang G.; Zhou G.; Yu J(2015). Ionic liquid catalyzed synthesis of 2-(indole-3-yl)-thiochroman-4-ones and their novel antifungal activities.Bioorg. Med. Chem. Letts.; 2015; 25; 259–261

28. Pooja; Prasher P.; Singh P.; Pawar K.; Vikramdeo K. S.; Mondal N.; Komath S. S(2014). Synthesis of amino acid appended indoles: Appreciable anti-fungal activity and inhibition of ergosterol biosynthesis as their probable mode of action. Eur. J. Med. Chem.; 2014; 80; 325-339.

29. Zhang M.; Mulholland N.; Beattie D.; Irwin D.; Gu Y.; Chen Q.; Yang G.; Clough J(2013). Synthesis and antifungal activity of 3- (1,3,4-oxadiazol-5-yl)-indoles and 3-(1,3,4-oxadiazol-5-yl)methyl-indoles. Eur. J. Med. Chem.; 2013; 63; 22-32.

30. Mukherjee s m Singh et al organic chemistry, Volume II, International(P) Limited, publisher, 2003, 586- 587.

31. G. R. Chatwal, et al instrumental method of chemical analysis, Himalaya publishing house, 2.5 99- 2.6 16

32. A.V. Kasture, et al pharmaceutical analysis, Volume II, instrumental method, Nirali Prakashan, 267, 268, 281, 289, 305, 306, 308.

33. W. Kemp, et al organic Spectroscopy 3rd edition, 52, 55,56,102,286.