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SYNTHESIS, ANTIMICROBIAL, ANTIOXIDANT AND ADME EXPOSURE OF 4-OXOAZETIDIN BENZOPYRONES

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ABSTRACT

As we detailed in this article, 2-[(4-Methyl-2-oxo-2H-chromen-7yl)oxy-N'-(substituted methylene)acetohydrazide **(4a-4f)** was used in the synthesis with chloroacetyl chloride in presence of DMF (Dimethyl formamide) and TEA (triethyl amine) to form new 4-oxoazetidin-benzopyrone derivatives **(5a-5f)**. Mass spectra, ^{1}H NMR, FTIR, and elemental analysis were analyzed to confirm 4-oxoazetidin derivatives. The Kirby-Bauer disc diffusion technique was used to examine the biological activity of the synthesized compounds against bacterial strains (*Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli,* and *Pseudomonas aeruginosa*) against control Ampicillin, Using the DPPH test, the antioxidant characteristics of synthetic 4-oxoazetidin derivatives **(5a–5f)** were examined. Additionally, this innovative 4-oxoazetidin (azetidinones) was evaluated using an in-silico approach for ADME (Absorption Distribution Metabolism Excretion). These synthesized compounds **(5a – 5f)** show good antibacterial potency, also show better Anti-oxidants compared to the well-known antioxidant ascorbic acid, and show high results in computational studies of ADME.

Keywords: Azetidinone, Antioxidant Properties, Antimicrobial Activity, ADME Studies, Benzopyrone.
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INTRODUCTION

The broad spectrum of pharmacological effects exhibited by heterocyclic compounds continues to attract scientists in the area of medicinal chemistry.[1] Azetidin-2-one or Azacyclobutanone (β-Lactum) is an essential part of many antibiotics. Derivatives of azatidin-2-one show a wide range of biological activities, such as sedatives, muscle relaxants, analgesic, antifungal, anticonvulsant, anti-tubercular, anti-parkinson[2-6,] and numerous pharmacological activities.[7-10] They are advantageous in the central nervous system and function as enzyme inhibitors.[11-13] Moreover, Azetin-2-one compounds have been reported for their antiviral, antithrombotic, and inhibitory effects on cholesterol absorption. A derivative of azetidinone, ezetimibe lowers cholesterol levels.[14] β-lactum antibiotics, such as monobactams penicillin I, Carbapenems III, norcadicin A-IV, and cephalosporins II, have been extensively utilized as chemotherapeutic agents to treat microbial illness and bacterial infections.[15,16] The potency of 2-azetidinone derivatives to suppress proliferation by either activating are causing DNAdamage[17] which is linked to their anticancer properties. PI3K/AKT/GSK-3β (glycogen synthase Kinase) and signaling pathways are brought downstream by adenosine monophosphate-activated protein Kinase (AMPK).[18] Looking towards their medicinal aspects, we synthesized new 4-oxoazetidin derivatives and postulated that azetidinone rings with benzopyrone rings. So, their impact would be advantageous when examining their antibacterial efficacy, Antioxidant properties, and ADME evaluation.

EXPERIMENTAL

Materials and Instrumentation

The starting materials and solvents for the target compounds came from easily accessible sources and were used without additional purification. The melting point was measured using the equiptronics model EQ-730 instrument. The reaction was monitored by thin layer chromatography (TLC) and was carried out on Merck silica gel 60 F254 plates. Visualization of the plates was done using an Ultraviolet (UV) lamp (λmax = 254 or 365 nm). Fourier-transform (FTIR) infrared spectra were obtained and analyzed in the 4000–400 cm^{-1} area using an Infrared (IR) Shimadzu spectrophotometer in the KBr pallet. All ^{1}H NMR spectra were recorded at 25°C using a Bruker Ultra Shield 400MHz spectrometer with DMSO–d_6 as the solvent and TMS (Tetramethyl silane) acting as the internal standard. Mass spectra were recorded using a Shimadzu

LC2010 mass analyzer and C, H, and N elemental analyses revealed that values were consistent within 0.4% of their theoretical counterparts and analyses were conducted using a Perkin Elmer PE 2400.

General Procedure for Synthesis

7-hydroxy-4-methyl-coumarin **(1)** synthesized via the Pechmann condensation.[19] Compound **(1)** (1 gm, 5 mmol) on reaction with Ethyl chloroacetate (1.22 gm, 10 mmol) using Anhydrous K_2CO_3 (Potassium carbonate) (1.38 gm, 10 mmol) in acetone at reflux for 6 hrs gives Ethyl[(2-oxo-2H-chromen-4-yloxy)]acetate **(2)**. Then, compound ethyl[(2-oxo-2H-chromen-4-yl)oxy]acetate (1 gm, 3 mmol) **(2)** reacts with hydrazine hydrate (0.14 gm, 4.5 mmol) in ethanol, reflux for 4 hrs gives 2-[(2-oxo-2H-chromen-4-yl)oxy]acetohydrazide **(3)**.[20] Finally compound **(3)** (2.32 gm, 10 mmoles) on condensation with different aromatic aldehydes (1mmole) in chloroform/methanol (1:1) (30 mL), stirring the reaction mixture for 2-3 minutes the precipitates of 2-[(4-methyl-2-oxo-2H-chromen-7yl)-oxy-N'-(substituted benzylidene) acetohydrazide **(4a – 4f)** was started to form which was then filtered and dried.[21] Then after the final cyclization process was carried out.

Synthesis of 4-oxoazetidin Benzopyrone Derivatives (5a – 5f)

Compound 2-[(4-methyl-2-oxo-2H-chromen-7yl)-oxy-N'-(substituted benzylidene)acetohydrazide **(4a-4f)** (2 mmol) with Chloro acetyl chloride (4 mmol) and TEA (triethyl amine) (4 mmol) in 20 mL of DMF (N,N-dimethyl formamide), stirred and refluxed for 20 hrs. The reaction mixture was cooled, poured into crushed ice and filtered. Recrystallized from ethanol.

N-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5a) Yield. 72%; Light yellow solid; M.P. 305°C; FTIR (KBr) ν: 1684 (C=O Stretch), 1615 (Substituted Benzene), 1392 (Alkane), 1272 (C=O Stretch), 976 (Trans Bond), 833 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.74 (1H, s, NH), 8.02 (1H, d, C_5-H) 7.78 (CH, m, 3H ($C_6\underline{H}_5$ – C_2-H′, C_4-H′, C_6-H′)), 7.52 (CH, d, 3H, C_6-H, ($C_6\underline{H}_5$ – C_3-H′, C_5-H′)), 7.06 (CH, d, 1H, C_8-H), 6.24 (1H, s, C_3-H), 5.31 (1H, d, CH-Cl), 4.92 (2H, s, CH_2), 4.82 (1H, d, -N-CH-Ar), 2.40 (3H, s, CH_3) ppm; Elemental Analysis calculated: C, 61.11; H, 4.13; N, 6.80. Found: C, 61.25; H, 4.08; N, 6.88. MS: m/z 411 (M-H); $C_{21}H_{17}ClN_2O_5$ requires 412.08.

N-(3-chloro-2-(4-chlorophenyl)-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5b): Yield. 76%; Light brown solid; M.P. 350°C; FTIR (KBr) ν: 2922 (C-H Stretch), 1684 (C=O Stretch), 1615 (Substituted Benzene), 1392 (Alkane), 1272 (C=O Stretch), 976 (Trans Bond), 833 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.78 (1H, s, NH), 8.022 (2H, d, ($C_6\underline{H}_4$-Cl – C_3-H′, C_5-H′)), 7.76 (3H, d, C_5-H($C_6\underline{H}_4$-Cl – C_2-H′, C_6-H′)), 7.60 (1H, d, C_8-H), 7.533 (1H, d, C_6-H), 7.00 (2H, s, CH_2), 6.24 (1H, s, C_3-H), 5.32 (1H, d, CH-Cl), 4.94 (1H, d, -N-CH-Ar), 2.414 (3H, S, CH_3) ppm; Elemental Analysis calculated: C, 56.39; H, 3.62; N, 6.26. Found: C, 61.25; H, 4.08; N, 6.88. MS: m/z 446 (M+); $C_{21}H_{16}Cl_2N_2O_5$ requires 446.04.

N-(3-chloro-2-(4-fluorophenyl)-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5c) Yield. 88%; White solid; M.P. 345°C; FTIR (KBr) ν: 2969 (N-H Stretch), 1683 (C=O Stretch), 1615 (Substituted Benzene), 1540 (C=O Stretch), 1390 (Tertiary Amine), 1286 (Ether), 1086 (F Stretch), 752 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.70 (1H, s, NH), 8.02 (1H, d, C_5-H) 7.72 (3H, m, 3H, C_8-H, ($C_6\underline{H}_4$-F – C_2-H′, C_6-H′)), 7.45 (3H, d, C_6-H, ($C_6\underline{H}_4$-F – C_3-H′, C_5-H′)), 6.22 (1H, s, C_3-H), 7.05 (2H, s, CH_2), 5.34 (1H, d, CH-Cl), 4.82 (1H, d, -N-CH-Ar), 2.40 (3H, s, CH_3) ppm; Elemental Analysis calculated: C, 58.57; H, 3.74; N, 6.51. Found: C, 56.25; H, 3.71; N, 6.70. MS: m/z 431 (M+H); $C_{21}H_{16}ClFN_2O_5$ requires 430.07.

N-(3-chloro-2-(3-nitrophenyl)-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5d) Yield. 77%; Light brown solid; M.P. 355°C; FTIR (KBr) ν: 3075 (N-H Stretch), 1683 (C=O Strong Stretch), 1615 (Substituted Benzene), 1510 (C=O Bend), 1389 (N=O Stretch), 1342 (Tertiary Amine), 1265 (Ether), 674 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.93 (1H, s, NH), 8.53 (1H, d, C_5-H), 8.39 (1H, d, $C_6\underline{H}_4$-NO_2 – C_6-H′), 8.23 (2H, m, C_8-H, ($C_6\underline{H}_4$-NO_2 – C_5-H′)), 8.15 (1H, d, ($C_6\underline{H}_4$-NO_2 – C_2-H′)), 7.76 (2H, s, C_6-H, ($C_6\underline{H}_4$-NO_2 – C_4-H′)), 7.074 (2H, d, CH_2), 6.23 (1H, s, C_3-H), 5.37 (1H, d, CH-Cl), 4.86 (1H, d, -N-CH-Ar), 2.40 (3H, s, CH_3) ppm; Elemental

Analysis calculated: C, 55.07; H, 3.52; N, 9.20. Found: C, 55.15; H, 3.57; N, 4.51. MS: m/z 457 (M+); $C_{21}H_{16}ClN_3O_7$ requires 457.07

N-(3-chloro-2-(4-methoxyphenyl)-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5e) Yield. 68%; dark brown solid; M.P. 280°C; FTIR (KBr) ν: 2930 (N-H Stretch), 2362 (OCH_3 Stretch), 1682 (C=O), 1613 (Substituted Benzene), 1508 (C=O Stretch), 1254 (Ether), 1155 (Ester CO Stretch), 832 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.57 (1H, s, NH), 7.73 (CH, m, 3H, C_5-H, ($C_6\underline{H}_4OCH_3$ – C_2-H′, C_6-H′)), 7.061 (CH, m, 4H, C_6-H, C_8-H, ($C_6\underline{H}_4OCH_3$ – C_3-H′, C_5-H′), 6.23 (1H, s, C_3-H), 5.28 (1H, d, CH-Cl), 4.80 (1H, d, -N-CH-Ar), 3.803 (2H, s, CH_2), 2.50 (3H, s, OCH_3), 2.40 (3H, s, CH_3) ppm; Elemental Analysis calculated: C, 59.68; H, 4.32; N, 6.30. Found: C, 59.86; H, 4.51; N, 8.15. MS: m/z 441 (M-H); $C_{22}H_{19}ClN_2O_6$ requires 442.09.

N-(3-chloro-2-(4-hydroxyphenyl)-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide (5f) Yield. 91%; white solid; M.P. 210°C; FTIR (KBr) ν: 3214 (O-H Stretch), 1687 (C=O Stretch), 1611 (Substituted Benzene), 1511 (N-H Bend), 1389 (Tertiary Amine C-N Stretch), 1258 (Ether), 835 (C-Cl stretch in β-Lactum) cm^{-1}; DMSO-d_6, 400MHz ^{1}H NMR, δ = 11.47 (1H, s, NH), 10.36 (1H, s(broad), OH), 7.72 (1H, d, C_5-H), 7.56 (CH, d, 2H, ($C_6\underline{H}_4OH$– C_2-H′, C_6-H′)), 7.0 (CH, d, 2H, C_6-H, C_8-H), 6.87 (CH, d, 2H, ($C_6\underline{H}_4OH$– C_3-H′, C_5-H′), 6.23 (1H, s, C_3-H), 5.25 (1H, d, CH-Cl), 4.81 (1H, d, -N-CH-Ar), 4.261 (2H, s, CH_2), 2.40 (1H, s, CH_3) ppm; Elemental Analysis calculated: C, 58.80; H, 4.03; N, 6.51. Found: C, 58.96; H, 3.86; N, 6.76. MS: m/z 428 (M+); $C_{21}H_{17}ClN_2O_6$ requires 428.08.

RESULTS AND DISCUSSION

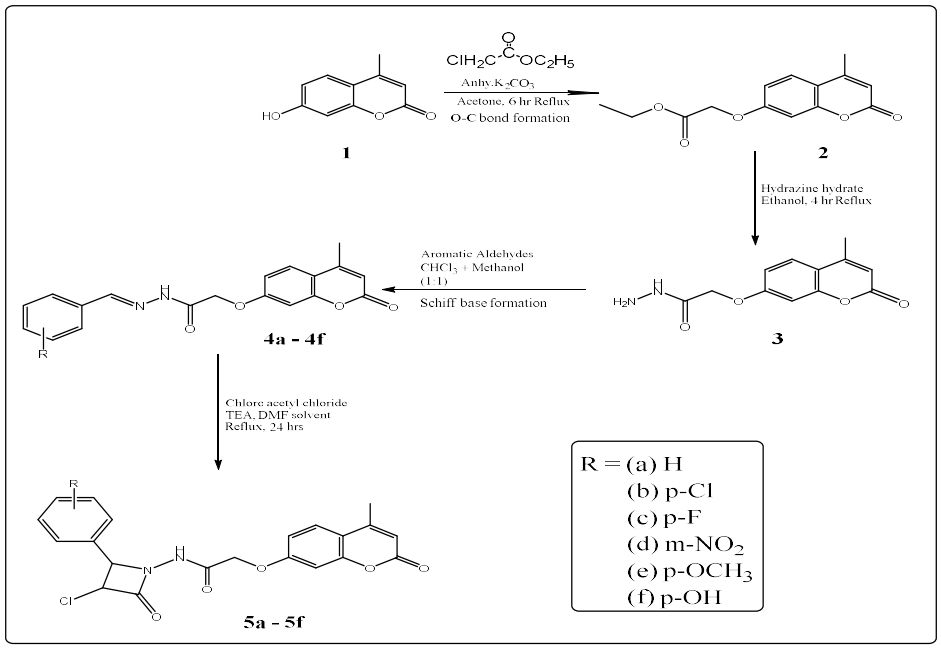

Fig.-1: Synthesis of 4-oxoazetidin Benzopyrone Derivatives

The process of Pechmann condensation is used to synthesize 7-hydroxy-4-methyl-2H-chromene-2-one **(1)**.[19] This is followed by condensation O-C bond formation reaction with ethyl chloro acetate to yield Ethyl[(2-oxo-2H-chromen-4-yloxy)] acetate **(2)**, which is then subjected to hydrazinolysis to yield 2-[(2-oxo-2H-chromen-4-yl) oxy] acetohydrazide **(3)**.[20] To synthesize Schiff's bases, 2-[(4-Methyl-2-oxo-2H-chromen-7yl) oxy-N'- (substituted benzylidene) acetohydrazide **(4a – 4f)**, compound **3** was condensed with various aromatic aldehydes.[21] Compounds **(4a - 4f)** undergo cyclization using chloroacetyl chloride in the presence of triethylamine (TEA) and dimethyl formamide (DMF). Resulted in the final compounds **(5a – 5f)**, as shown in **Figure 1**, being N′-(3-chloro-2-aryl-4-oxoazetidin-1-yl)-2-((4-methyl-2-oxo-2H-chromen-7-yl)oxy)acetamide **(5a – 5f)** derivatives. Compound **5f** was one of the characteristic bands found in the IR spectra of the synthesized compounds. The IR (KBr, in cm^{-1}) peaks at 3214.69 for O-H stretch, 1687.68 for lactone grp, 1611.51 for C=O stretch in CONH, 1389.48 for C-N bend, and 835.46 for C-Cl gives all

the desired frequencies of the different functional groups. The ^{1}H NMR (DMSO-d_6, δ in ppm) of **5f** indicated peaks at δ 4.81 ppm for CH of 4-oxoazetidin ring, δ 5.25 ppm for CHCl of 4-oxoazetidin ring, δ 7.03 - 7.72 ppm for aromatic protons, δ 10.36 ppm for OH proton, δ 11.47 ppm for NH proton & supports the synthesis. The Mass spectra are 428 (M+). Same way compounds **(5a – 5e)** were validated by IR, Mass, ^{1}H NMR, and Elemental analyses. We investigated the 4-oxoazetidin-benzopyrones derivatives microbial screening against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli,* and *Pseudomonas aeruginosa* strains. We explored the antioxidant properties of synthesized 4-oxoazetidin-benzopyrones derivatives and in-silico ADME (Absorption Distribution Metabolism Excretion) study.

Antibacterial Activity

The antibacterial activity of synthesized compounds was examined against bacterial strains *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli,* and *Pseudomonas aeruginosa* using the Kirby-Bauer disc diffusion method at a concentration of 1mg/mL in DMSO.[22] Ampicillin was used as a standard drug. 0.1 mL of each solution was used to fill in the wells on agar plates. Agar plates were kept in an incubator at 37°C for 24 hrs. Bacterial strains that showed sensitivity to the synthesized chemicals were found to have a zone of inhibition, which is shown in Table-1.

Table-1: Bacterial Proliferation of the Synthesized Compounds

	Zone of Inhibition			
Compound	*Bacillus subtilis (gm+ve)*	*Staphylococcus aureus (gm+ve)*	*Escherichia coli (gm-ve)*	*Pseudomonas aeruginosa (gm-ve)*
5a	13mm	12mm	12mm	13mm
5b	12mm	13mm	14mm	13mm
5c	11mm	13mm	13mm	15mm
5d	10mm	13mm	13mm	14mm
5e	12mm	15mm	15mm	12mm
5f	14mm	12mm	13mm	11mm
Ampicillin (standard)	10mm	11mm	10mm	11mm

According to the findings, compound **5a** had the least anti-*E. coli* activities when measured against other synthetic compounds; compounds **5b**, **5c**, **5d**, and **5f** showed moderate potency due to insertion of Cl, F, NO_2, and OH grp, while compound **5e** showed higher potency due to OCH_3 grp insertion. Compounds **5c** showed high potency in relation to *P. aeruginosa* due to the insertion of fluoro grp which is highly penetrator, whereas compounds **5a**, **5b,** and **5d** are moderately active, and compounds **5e** and **5f** are marginally active. The synthetic compounds **5a**, and **5f** exhibited the lowest levels of activity and **5e** highest against *S. aureus*, respectively, whereas compounds **5b**, **5c**, and **5d** showed moderate potency against *S.aureus*. Compounds except **5f** showed good potency against *B. subtilis*. **5a** also indicates a modest degree of activity which has no substitution on the phenyl ring.

Antioxidant Activity

A popular, fast, accurate, and trustworthy method for assessing the antioxidant properties of synthetic materials in vitro is the DPPH test.[23] The sample solution was mixed at several dosages (250–1000 µg/mL) with a 0.1 mM DPPH solution in methanol in a 1 mL container. The mixture was left to develop in a dark atmosphere for around 30 minutes. The control included all of the reagents, but the sample was absent, and methanol was used as the blank. 1mL of DPPH solution was mixed with a solvent to create the blank.[24] The DPPH-H radical scavenging activity was taken at an absorbance of 517 nm by using the UV-VIS spectrophotometer. In contrast, it was also determined how well ascorbic acid scavenged DPPH radicals. The following formula was used to determine each sample's percentage inhibition of DPPH, or its proportion of potential to scavenge DPPH radicals which is shown in Table-2

$$\text{Percentage Inhibition} = \{(Ao-As)\div Ao\}\times 100$$

Where, Ao: absorption of control (0.914)

As: is the absorption of the sample solution

Table-2: Absorbance and % Inhibition of The Synthesized Compounds with Respect to Different Concentration

Compound	Concentration (µg/mL)	Absorbance	%Inhibition
5a	250 µg/mL	0.570	37.63
	500 µg/mL	0.510	44.20
	750 µg/mL	0.320	64.98
	1000 µg/mL	0.170	81.40
5b	250 µg/mL	0.524	42.60
	500 µg/mL	0.430	52.95
	750 µg/mL	0.300	67.17
	1000 µg/mL	0.125	86.32
5c	250 µg/mL	0.670	26.69
	500 µg/mL	0.510	44.20
	750 µg/mL	0.370	59.51
	1000 µg/mL	0.150	83.58
5d	250 µg/mL	0.560	38.73
	500 µg/mL	0.350	61.70
	750 µg/mL	0.220	75.92
	1000 µg/mL	0.120	86.87
5e	250 µg/mL	0.630	31.07
	500 µg/mL	0.500	45.29
	750 µg/mL	0.310	66.08
	1000 µg/mL	0.030	96.71
5f	250 µg/mL	0.525	42.56
	500 µg/mL	0.450	50.76
	750 µg/mL	0.200	78.11
	1000 µg/mL	0.060	93.43
Standard (Ascorbic Acid)	250 µg/mL	0.622	32.00
	500 µg/mL	0.421	54.00
	750 µg/mL	0.293	68.00
	1000 µg/mL	0.15	83.00

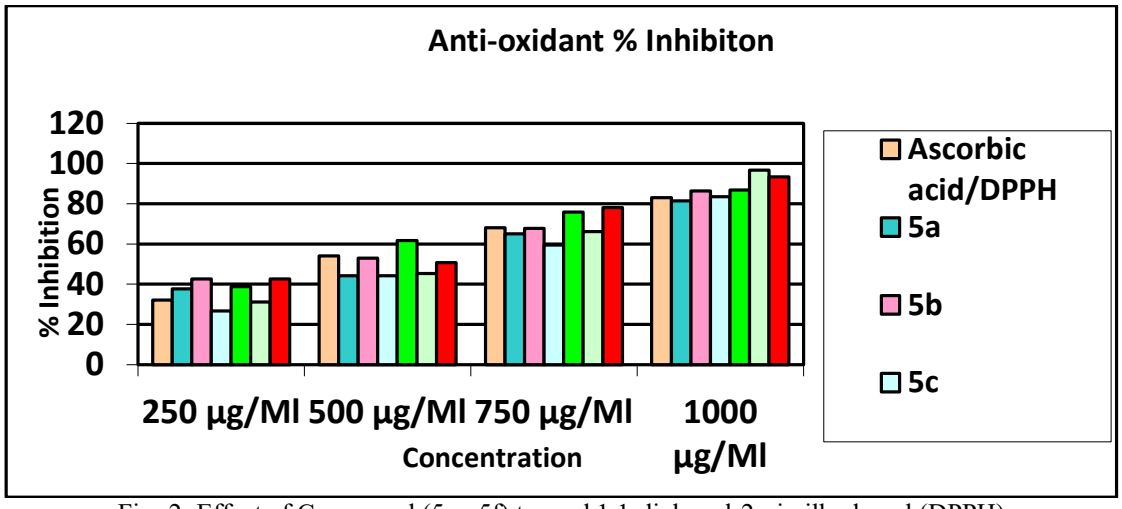

Fig.-2: Effect of Compound (5a - 5f) toward 1,1-diphenyl-2-picrilhydrazyl (DPPH)

Using DPPH, the in vitro Anti-oxidant properties of compounds 5a to 5f were investigated. In Fig.-2, they exhibit strong antioxidant activity. Using DPPH radicals as the H radical acceptor, the hydrogen donating activity demonstrated a substantial correlation between the conc. of the new chemical and the % of inhibition. Compounds 5a–5f have successfully converted the stable radical DPPH to the yellow diphenyl picrylhydrazine using the DPPH test. Thus, title compounds have a great scope for the development of antioxidant medicines.

ADME Report

Using the publicly available web server Swiss ADME, the basic character and ADME values (Absorption, Distribution, Metabolism, and Excretion) were determined.[25] All compounds **(5a – 5f)** in the Table-3.

For each chemical, there are the five rules were introduced to pass the ADME test also called Lipinski's rule, those are Molecular wt. (MW), no. of H-bond acceptors (nHBA), H-bond donors (nHBD), topological polar surface area (TPSA) and no. of rotatable bonds (nRB). Lipophilicity which have ranges between -0.7 to 5.0 are the XLOGP3, molecular weight between 150 $gmol^{-1}$ to 500 $gmol^{-1}$, polarity between 20 Å2 to 130 Å2, solubility between 0 to 6 are log S (ESOL) 6, saturation between 0.25 to 1 are Fraction Csp3, and flexibility between 0 to 9 are of rotatable bonds. Are the rules by which all the ranges are to be calculated and can be decide whether fit in the rules of ADME or not. Further had done the Boiled-egg predict using the web server which also available online SwissADME model.[26] In the model Fig.-3, the yellow-colored region shows the blood brain permeant region. Looking forward none of the compounds shows the blood brain permeant, the white colored region shows the gastric absorption and all the synthesized compounds **(5a – 5f)** are comes under this region means which have less or minimum toxicity.

Table-3: ADME Values of 4-oxoazetidin-benzopyrone with Standard BHT and Dacarbazine

Compound	5a	5b	5c	5d	5e	5f	BHT	Dacarbazine
MW	412.08	446.04	430.07	457.07	442.09	428.08	428.82	182.82
Rotatable bonds	6	6	6	7	7	6	6	3
H-bond acceptors	5	5	6	7	6	6	6	4
H-bond donors	1	1	1	1	1	2	2	2
MR	110.35	115.36	110.31	119.17	116.84	112.37	112.37	44.77
TPSA	88.85	88.85	88.85	134.67	98.08	109.08	109.08	99.73
Consensus Log P	2.73	3.18	2.95	2.15	2.68	2.27	2.27	0.04
ESOL Solubility (mg/ml)	2.79E-02	7.66E-03	2.01E-02	2.65E-02	2.52E-02	3.96E-02	3.96E-02	2.27E+01
GI Absorption	+	+	+	+	+	+	+	+
Blood-brain permeant	-	-	-	-	-	-	-	-
Pgp substrate	-	-	-	-	-	+	+	-
Lipinski violations	-	-	-	-	-	-	-	-
Muegge violations	-	-	-	-	-	-	-	1
PAINS alerts	-	-	-	-	-	-	-	1
Leadlikeness violations	1	1	1	1	1	1	1	1

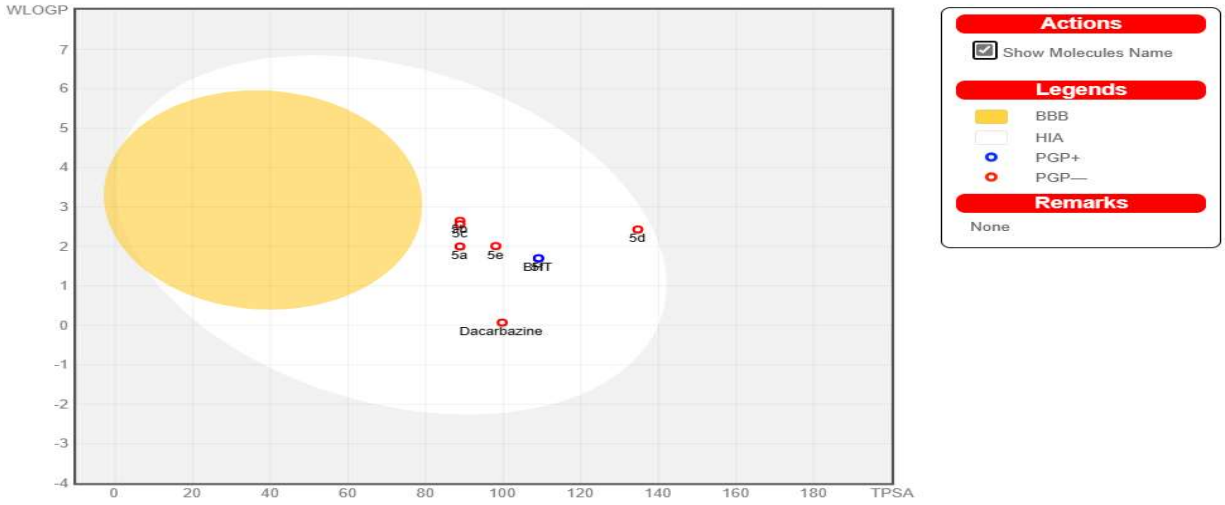

Fig.-3: BOILED-Egg Model Representation of 4-oxoazetidin-benzopyrone in Comparison with BHT and Decarbazine

CONCLUSION

Novel azetidinone (β-lactum) (5a – 5f) was designed & created by condensation of Schiff bases (4a – 4f) with chloro acetyl chloride in the presence of TEA & DMF solvent with excellent yield. Synthesized compounds were confirmed by IR, Mass, ^{1}H NMR, and elemental analyses. Title compounds (5a – 5f) showed good inhibitory effects against *Escherichia coli* & *Pseudomonas aeruginosa* (gm^{-ve}), *Bacillus subtilis* & *Staphylococcus aureus* (gm^{+ve}) strains with respect to standard Ampicillin. By using the SwissADME prediction method, we were able to predict the ADME (adsorption distribution metabolism excretion) of our synthesized compounds. Azetidinone (5a–5f) has high GI absorption. Compounds also have their lipophilicity and polarity determined with a dependable prediction model of the brain or intestine permeation method through a boiled egg model. Using 1,1-diphenyl-2-picrylhydrazyl (DPPH), the in vitro antioxidant activity of compounds 5a to 5f was examined. When compared to ascorbic acid, they showed antioxidant activity. Using these radicals as the H-acceptor, the hydrogen donating activity demonstrated a substantial correlation between the concentration of the synthesized compounds and the percent of inhibition. Compounds (5a–5f) have successfully converted the stable radical DPPH to yellow diphenyl picrylhydrazine using the DPPH test. Because the reaction produced the non-radical form of DPPH-H, a methanolic DPPH solution was decreased in the presence of an anti-oxidant that donates hydrogen. Thus, the outcome demonstrates the new compounds' strong antioxidant qualities (5a–5f). The basis for the first search for potentially new Azetidinone (β-lactam) with benzopyrone derivatives with minimum toxicity and promising biological activity is ensured by our study. The development of Azetidinone-benzopyrone derivative synthesis was investigated in this work and has great scope as broad-spectrum antibiotics & antioxidants.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly, Responsible for conceptualization, Methodology, Lab work, First Draft, Revised manuscript, Editing, analyzed data, and Editing. The research profile of the authors can be verified from their ORCID IDs, given below:

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