IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Thermal, Spectral, Antibacterial And Antioxidant Studies On Inclusion Complexes Of 2- (Thiazolidinone-2') Imino-3-Allyl 5-Arylidene-4-Thiazolidinone With β-Cyclodextrin)

Chinmaya Guru, Nutan Maharana, Rabinarayana Sahu, Bamakanta Garnaik

P. G. Department of Chemistry, Berhampur University, Bhanja Bihar, Odisha, India, 760007

Corresponding author: guruchinmay6@gmail.com

Abstract: Novel Arylidene derivatives of 2-(Thiazolidinone-2') imino-3-allyl-4-thiazolidinone were synthesized. To enhance solubility, β-cyclodextrin was utilized to form inclusion complexes. The presence of mixes and inclusion complexes was confirmed by analyzing the analytical data and spectrum properties. We used a cup-and-plate experiment to measure the antibacterial and antioxidant effects against Bacillus subtilis, Escherichia coli, and Proteus vulgaris. When compared to the parent chemicals, the inclusion complexes showed far better antioxidant and antibacterial capabilities.

Index Terms **- β-cyclodextrin, Escherichia, antibacterial activity, inclusion complexes, cup plate method**

1. INTRODUCTION

Yearly reports on synthetic heterocyclic structures encompass a variety of both well-established and newly discovered frameworks. These novel compounds, known for their diverse biological activities, have garnered significant attention from researchers. Chemists are delving into their complete synthesis and potential in chemotherapy. Utilizing advanced analytical and spectroscopic tools, scientists are able to analyze structural modifications and assignments based on synthetic efforts. Thiazolidinone serves as a pivotal pharmacophore, with its five-membered ring containing both sulfur and nitrogen. The research on thiazolidinones is expansive due to their unique biological activities, exemplified by antimicrobial properties and various others such as substituted thiazolidinones have been discovered.[1-2], antioxidant[3], anti-HIV[4], antihistaminic[5], anti-convulsant[6-7], anti-inflammatory [8-10] effects. In this current study, an assortment of arylidene derivatives of 2-(Thiazolidinone-2') imino-3-allyl-4-thiazolidinone have been synthesized from asymmetrical thiourea. However, the challenge of poor solubility in polar media may impede their bioavailability and efficacy as medicinal agents. To address this issue, a promising strategy involves enhancing the bioavailability of these compounds by forming inclusion complexes with cyclodextrin[11], a hydrophobic cavity. Cyclodextrins are commonly used as model hosts to improve the solubility of water-insoluble guests, making them more easily assimilated in water. Among cyclodextrins, β-cyclodextrin stands out as a cost-effective and safe option for creating inclusion complexes [12-13]. Thus, this study aims to synthesize several derivatives of 2-(Thiazolidinone-2') imino-3-allyl-5-arylidene-4-thiazolidinone from asymmetrical thiourea[14] and investigate their complexation with β-cyclodextrin to enhance their properties and potential applications. The analysis of the compound's logical and spectral data has led to the characterization of the compound and its inclusion complexes. In addition, studies have been conducted to determine if the drug's antioxidant and antibacterial effects are amplified during complex formation.

2. EXPERIMENTAL SECTION

2.1 Apparatus and Materials: This work made use of synthetic reagents that are easily accessible. Following two rounds of filtering, the solvent was deionized distilled water. Infrared spectra of KBr pellets were collected in the range of 400-4000 cm-1 using a Shimadzu 840 FTIR, while electronic spectra were acquired using a Shimadzu UV-170 Spectrophotometer. There was clear, although unclear, absorption bands for the synthetic chemicals. Using cup-plate tests, we looked at the compounds' and inclusion structures' antioxidant and antibacterial capabilities.

2.2 Synthesis of Compound:

The compounds were synthesized using the procedure outlined in Scheme 1 by Minati Sen et.al. 14.

2.2.1 N_1- (Thiazolyl-2')-N_6 – allyl thiourea (C-I)"

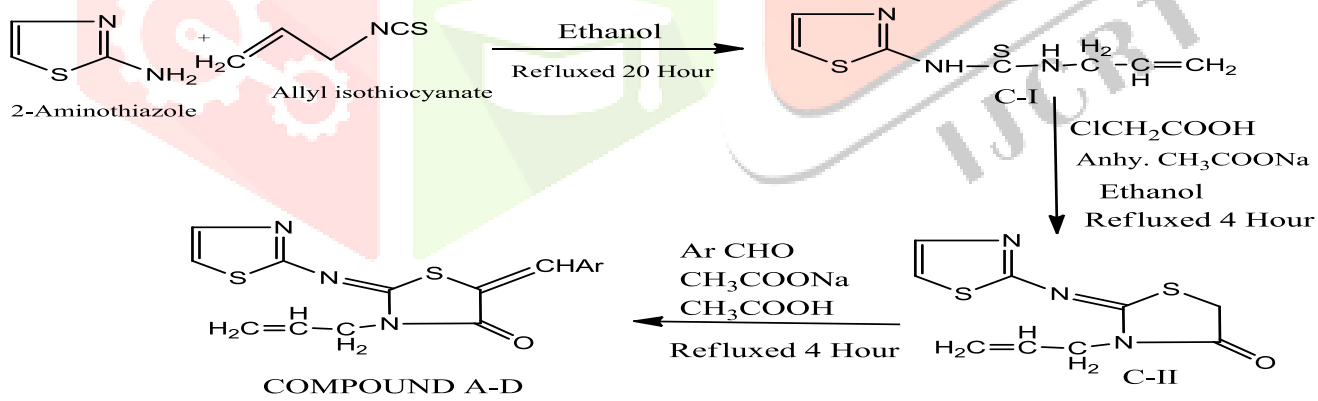
A solution containing 5-grams of 2-aminotthiazole in 15 milliliters of hot rectified spirit was prepared by slowly adding 5 milliliters of allyl isothiocyanate over the course of five minutes. After 20 hours of refluxing, the mixture was removed. After filtering, washing with spirit, drying, and recrystallization from ethanol, the precipitate that had settled to the bottom of the condensation jar was removed. M.P. 13^{o}C, yield-5.7gm (60%), (Found S, 31.90 $C_7H_9N_3S_2$ requires S, 32.16%)

2.2.2 2-(Thiazolyl-2'imino)-3-allyl-4-thiazolidinone (C-II)

0.2 grams of C-I was dissolved in 20 ml of ethanol, followed by the addition of 0.1 grams of monochloroacetic acid. The mixture was refluxed for 4 hours under anhydrous conditions. After removing the excess solvent by distillation, the remaining slurry was transferred to ice-cold water. The filtered material was washed several times with warm water, dried, and recrystallized from ethanol to obtain colourless needles. M.P.-98 ^{o}C, yield-1.4gm (60%), (Found S, 20.8 $C_9H_9N_3S_2O$ requires S, 23.27%)

2.2.3 2-(Thiazolyl-2'imino)-3-allyl-5-benzylidene-4-thiazolidinone (A)

The following was refluxed for four hours: 1 gram of C-II, 0.5 ml of benzaldehyde, 0.32 gram of anhydrous NaOAc in 5.0 ml of glacial acetic acid. The solution turned a vivid blue after cooling and being put into cold water after concentration. The vivid yellow needles were obtained by recrystallizing the precipitate from alcohol after it had been air-dried and rinsed with warm water. M.P.-175^{o}C, yield-0.86 gm (60%), (Found S, 19.3 $C_{16}H_{13}N_8S_2O$ requires S, 19.57%) . ", Similarly, the other compounds of the series (B, C & D) were prepared by using p-chlorobenzaldehyde, p-nitrobenzaldehyde and p-methoxy benzaldehyde, respectively which is elucidated in bellow.



COMPOUND A, Ar = Phenyl
COMPOUND B, Ar = p-chloro phenyl
COMPOUND C, Ar = p- nitro phenyl
COMPOUND D, Ar =p-methoxy phenyl

SCHEME-1

2.3 Synthesis of Inclusion complexes:"

A method known as co-precipitation was employed to generate inclusion complexes of IIIA, IIIB, IIIC, and IIID with β-cyclodextrin [15-17]. A solution of β-cyclodextrin was agitated while the chemicals were added dropwise, with a concentration of.03mM. The mixture was stirred at room temperature for 48 hours before being filtered and chilled for a further 48 hours. After a 24-hour air drying period, the

precipitate was filtered through a G-4 crucible after being rinsed with distilled water. We used Higuchi-Connors [18] solubility assay to find out how the compounds dissolved in water. Using a rotary flask shaker, each chemical was subjected to room temperature shaking for 48 hours in a series of conical flasks. Filtration using Whatman-42 filter paper was followed by analysis of the solutions using a UV-visible spectrophotometer in the 200-400 nm range. The maximum absorbance (λ-max) was then compared to the β-cyclodextrin concentrations. Benesi Hilderbrand relation determines inclusion complexes' thermodynamic stability constant K_T. $1/\Delta A = 1/\Delta Є + 1/K_T$ [Guest] o ΔЄ. $[\beta\text{-CD}]_0$ "Where ΔA is change in absorbance, ΔЄ is change in molar extension coefficient, [Guest]o is concentration of compound in inclusion complex and $[\beta\text{-CD}]_0$ is molar concentration of β-CD.

2.4 Antibacterial evaluation

Cup-plate method examined compound antibacterial activity. [19] The test chemicals were dissolved in 500µg/ml DMSO. Escherichia coli (MTCC 40), Proteus vulgaris (MTCC 87), and Bacillus subtilis (MTCC 321) were introduced to a 100 ml sterile nutritive stock and cultured at 371°C for 24 hours. It was McFarland who standardized the thickness of bacterial suspensions. Agar plates were sterile-injected with test organisms prior to creating 6-mm-diameter wells. Micropipette-encapsulated drug and test synthetics (500 g/ml) were chilled to 8-10 °C in the chiller for diffusion into the medium. The Petri dishes were heated to 372 degrees Celsius for 18 to 24 hours after an initial two-hour cold incubation phase. The venire scale was used to determine the size of inhibition zones in petri dishes. Analyzing the difference between the test compounds' and the reference medication's zone of inhibition allowed researchers to account for the results (Antibiotic medication). Tagashira and Ohtake[20] suggested assessing cell reinforcement activity by DPPH (2, 2-diphenyl-1-picrylhydrazyl) radical seeking. Figure 4.22 depicts the DPPH's no-cost, no-obligation extreme search experiment of synthetic blends and composite structures. To form 1, 1-diphenyl-2-picryl hydrazine, cell reinforcement, with its speedy hydrogen gift, combines with DPPH, a nitrogen-focused extremist with a specific absorbance at 517 nm. Cellular reinforcement rummaging is suggested by staining. At concentrations of 100 and 500 g/mL, we tested the cell reinforcement capacity of the mixtures and candidate structures, respectively. Synthetic and incorporation structures' cell reinforcement or extreme rummaging action (RSA) is shown in Table 4.4.

3. RESULTS AND DISCUSSION

Limited solubility in polar solvents can restrict the pharmacological effectiveness of thiazolidinone derivatives. However, by creating inclusion complexes with cyclodextrins, these molecules can improve their solubility and therapeutic potential. Both Table-I and Table-II include analytical and spectral data for the compounds that were produced and their inclusion complexes, correspondingly. The compound forms are distinguished based on their spectral characteristics and the presence of elemental sulfur, with infrared and sulfur content measurements aligning with expectations. Their melting points provide evidence of the presence of chemical inclusion complexes with β-cyclodextrin. The compounds A, B, C, and D have melting points of 175°C, 158°C, 145°C, and 92°C, respectively. In contrast, the inclusion complexes of these compounds have melting temperatures of 180°C, 162°C, 152°C, and 98°C, respectively. The fact that the molecules need more heat to be released from the β-cyclodextrin cavity suggests that the complex has been successfully formed, which explains the discrepancy in melting points. The solubility of compounds in a β-cyclodextrin solution in the aqueous phase showed a linear dependence on concentration. The slopes of the graphs were all less than 1, suggesting a possible 1:1 stoichiometry for these compounds. For each inclusion complex, the Benesi-Hilderband relation was used to find its thermodynamic stability constant (K_T). [21]. Through the plot of 1/A vs $1/[\beta\text{-CD}]_o$ for the substances, strong linear relationships were observed, enabling the calculation of K_T values for each complex. In Table I, we can see that the K_T values for the inclusion complexes of compounds with β-cyclodextrin were 588.69, 725.5, 575.9, and 805.4 M^{-1} for A, B, C, and D, specifically. The inclusion complexes shown stability as a consequence of host-guest interactions such hydrophobic contacts and van der Waals forces, since these findings were within the usual range of 100-1000 M^{-1}. [20,21]. The calculation of the corresponding thermodynamic parameters, including the ΔG value at 298K,(△G = -2.303RT log K) was facilitated by determining the stability constant (K_T values) at various temperatures assuming a 1:1 stoichiometry.

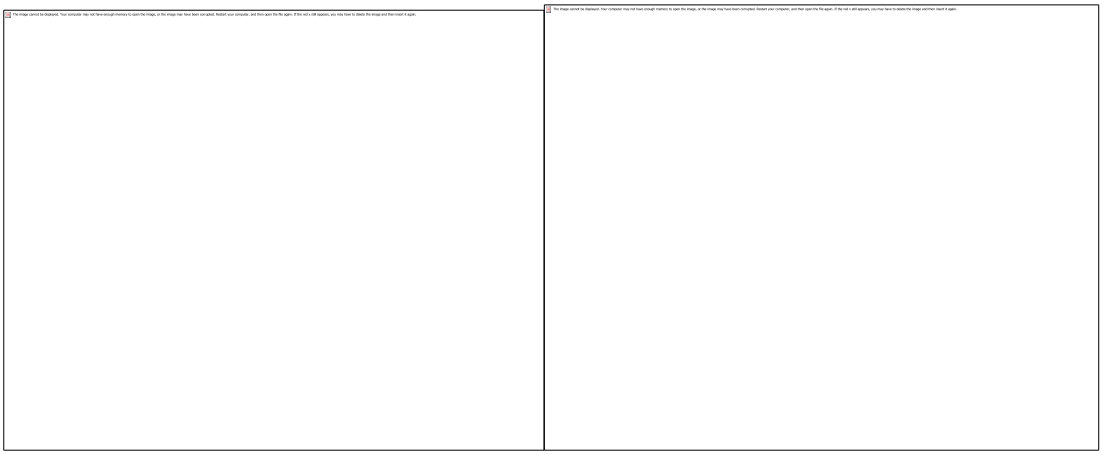


Figure: 1 A Figure: 1B

The obtained activation energies for all inclusion complexes in Table-I are negative, indicating that the process of inclusion is thermodynamically favorable. "Analysis of the IR data in Table II of Compound A shows characteristic bonds such as C-S, C-C, C-N, C=O, C-H, and N-H at 680, 126, 159, 170, 296, and 3109 cm^{-1}, respectively. Similarly, the IR spectra of I.C. A display distinctive absorptions at 745, 124, 1597, 172, 2965, and 312 cm-1, confirming the presence of C-S, C-C, C-N, C=O, C-H, and N-H bonds. The IR analyses of complexes B, C, and D along with their inclusion complexes, also exhibit characteristic absorption frequencies in accordance with the spectral data. In all cases, a reduction in the IR frequencies of the C=O bonds is observed, accompanied by broadening, weakening, and smoothing of the peaks. Conversely, upon formation of the inclusion complex, the N-H stretching vibration frequency shifts to a higher wavenumber. Weak interactions including hydrogen bonding, van der Waals forces, and hydrophobic contacts between the host and guest molecules are formed as a result of these alterations, which show that the compounds have been effectively contained within the β-cyclodextrin cavity. [19-20].

3.1 Antibacterial Study

The results of the antibacterial tests indicate that the zones of inhibition against three bacterial strains (Proteus vulgaris, Escherichia coli, and Bacillus subtilis) increase in size from simple to complex structures for both the combinations and their corresponding inclusion complexes (Table III, Figs. 2, 3, and 4). The drugs are effective against sensitive bacteria, while showing no activity against resistant strains. Additionally, the compounds tend to exhibit greater stability and bioavailability compared to the pure medication. By encapsulating the drug molecules within the hydrophobic core of β-cyclodextrin, and allowing the hydrophilic surface to interact with the surrounding environment, there is an enhancement in bioavailability and sensitivity to bacteria.

3.2 Antioxidant results

In Table-IV, we can see the antioxidant activities, which are shown as radical scavenging activity (RSA), for the compounds and their inclusion complexes at concentrations of 100 µg/ml (Figure-6) and 500 µg/ml (Figure-5). Improvements in solubility and bioavailability are responsible for the chemicals' increased RSA when inclusion complexes are formed. An improvement in bio-accessibility enhances the antioxidant activity of the compounds. All compounds exhibit dose-dependent DPPH radical scavenging activity.

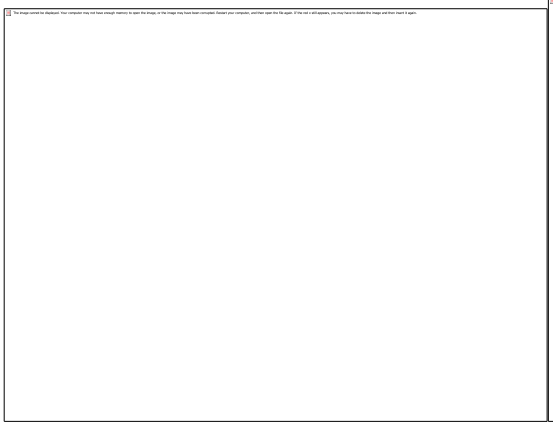


Figure: 2

Figure: 3

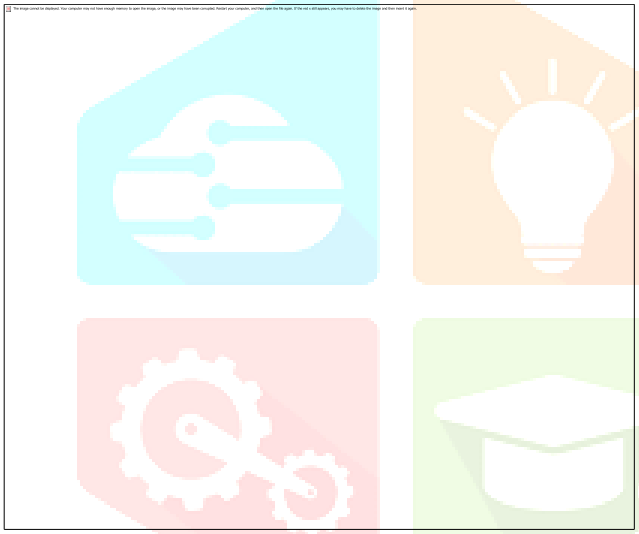


Figure: 4

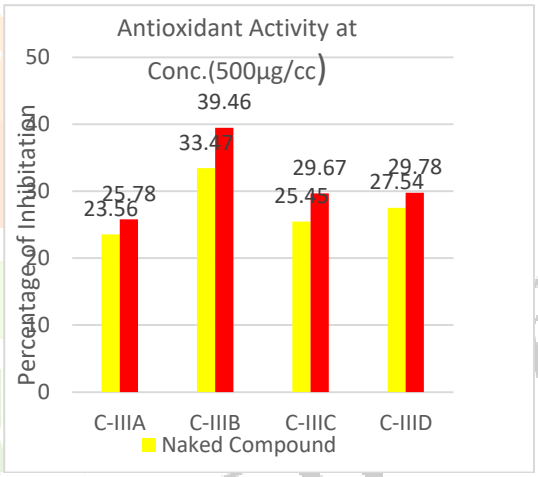


Figure: 5

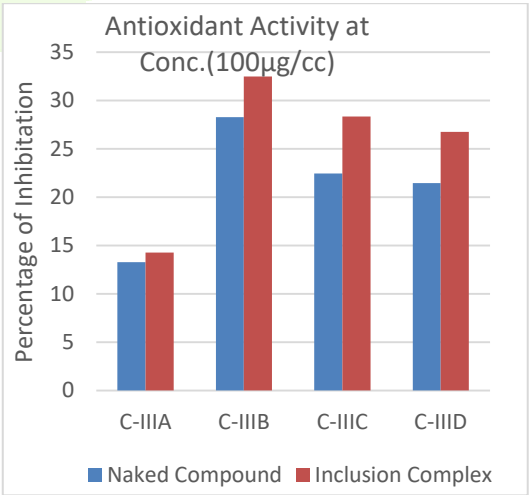


Figure: 6

Table: 1 Physical properties and thermodynamics parameter of the synthesized compounds and their complexes

Sl	Compound/ Complex	Ar.	Color	M.P. in ^0C	% of yield	K	△G (kj/ mol)
1	A	Phenyl	Brownish red	175	60	-	
2	I.C.A		Light yellowish	208	40	588.69	-15.804
3	B	p-Cl-C_6H_4	Deep yellow	158	65		
4	I.C. B		Brownish yellow	162	41	725.5	-16.33
5	C	p–NO_2 C_6H_4	Dull brown	145	55		
6	I.C- C		Pale yellow	152	45	575.9	-15.737
7	D	p-OCH_{3}-C_6H_4	Dull white	92	54		
8	I.C.- D		White	98	39	805.4	-16.58

Table 2: Spectral data of synthesized compounds and their inclusions

Sl no.	Compound/ Complex	Ar.	IR(KBr) cm^{-1}	1H NMR	$UV_{\lambda max}$
1	Compound A	Phenyl	742.59(C-S str), 1492.60(C=C Str), 1589.34(C=N str), 1645.28(C=O str), 3194.12(N-H str)	1H NMR (CDCl3) : δ 6.81-8.23 (d, 6H, Ar-H), 4.23(s,1H,C-NH),7.58(s,1H,C-H),7.34-7.61 (m,8H, Ar-H) 1H NMR (CDCl3)	275
2	I.C.A		746.45(C-Sstr), 1494.83(C=C str), 1581.83(C=N str), 1714.12(C=O str), 3224.34(N-H str)	δ 6.12-7.81 (d, 6H, Ar-H), 3.83 (s,1H,C -NH),7.11(s,1H,CH),6.82-7.24 (m,8H, Ar-H)	278
3	C.B	p-Cl-C_6H_4	692.44(C-C str), 744.52(C-S str), 1487.12(C=C Str), 1583.56(C=N str), 2916.37(Ar-Hstr)1701.22, 1645.28(C=O str), 3197.89(N-H str)	1H NMR (CDCl3) : δ 6.95-8.6 (d, 6H, Ar-H), 4.4(s,1H,CNH),7.80(s,1H,C-H),7.56-7.9 (t,8H, Ar-H)	265
4	I.C. B		692.44(C-Cstr), 746.45(C-S str), 1489.05(C=C Str), 1539.20(C=Nstr), 1714.72(C=O str), 3030.17(ArHstr), 3325.28, 3194.12(N-H str)	1H NMR (CDCl3): δ 6.3 -7.45 (d, 6H, Ar-H), 3.9 (s,1H,C-NH),7.25(s,1H,CH),6.9-7.3 (t,8H, Ar-H)	267

5	Compound C	P – NO_2 C_6H_4	742.59(C-Sstr), 850.61, 1338.60(N=Ostr), 1616.35(C=C Str), 1450.26(C=N str), 1696.36 (C=Ostr), 2916.37(Ar-HStr), 3196.50 (N-Hstr)	1H NMR (CDCl3) : δ 6.72-7.44 (d, 6H, Ar-H), 4.34(s,1H,C-NH),7.91(s,1H,C-H),7.51-7.92(m,8H, Ar-H)	296
6	I.C- C		690.52(C-Cl str), 748.38(C-S str), 1157.92(C-N str), 1494.83(C=C Str), 1597.60(C=N str), 2922.16(ArHstr)	1H NMR (CDCl3): δ 6.33-7.12 (d, 6H, Ar-H), 4.14 (s,1H,C-NH),7.33(s,1H,CH),7.11-7.54 (m,8H, Ar-H)	299
7	Compound D	p-OCH_3-C_6H_4	748.38(C-Sstr), 1425.40(C=Nstr), 1494.83(C=C Str), 1593.20(C=N str), 1712.97 (C=o), 3062.96(Ar-HStr)	1H NMR (CDCl3) : δ 6.6-8.5 (d, 6H, Ar-H), 4.3(s,1H,CNH),7.65(s,1H,C-H),7.3-7.6 (t,8H, Ar-H),3.95 (s,3H,OCH_3)	271
8	I.C.- D		748.38(C-Sstr), 1417.60(C-NStr), 1456.26(C=Cstr), 1508.33(C=N str), 1699.29, 1637.56(C=O str), 3331.07(N-H str)	1H NMR (CDCl3): δ 6.1-7.8 (d, 6H, Ar-H), 3.7 (s,1H,C-NH),7.5(s,1H,CH),6.6-7.1 (t,8H, Ar-H)3.65 (s,3H,OCH3)	275

Table-3: Antibacterial activity of the synthesized compounds and their complexes

Compound/Complex	**Diameter of zone of inhibition(mm)**		
	Proteus vulgaris	***Escherichia coli***	***Bacillus subtilis***
Comp- A	7	8	10
I.C.A.	10	11	13
Comp-B	15	10	12
I.C. B	18	17	17
Comp-C	14	12	16
I.C.C	18	16	18
Comp-D	12	8	10
I.C. D	16	13	14

Table 4: Antioxidant activity of synthesized compounds and their inclusions”

Compound	Percentage of Inhabitation			
	Conc.(100µg/cc)		Conc.(500µg/cc)	
	Naked Compound	Inclusion Complex	Naked Compound	Inclusion Complex
A	13.27	14.27	23.56	25.78
B	28.25	32.47	33.47	39.46
C	22.43	28.32	25.45	29.67

D	21.46	26.74	27.54	29.78

4. CONCLUSION:

In summary, the findings indicate that the solubility, bioavailability, thermodynamic stability, antibacterial, and antioxidant activities of the synthesized compounds, specifically 2-(thiazolidinone-2) imino-3-allyl 5-arylidene-4-thiazolidinone, are significantly enhanced through the formation of inclusion complexes with β-cyclodextrin.

ACKNOWLEDGEMENT:

The authors are thankful to Dr. J.R. Panda, Department of Pharmaceutical Science, Roland Institute of Pharmaceutical Sciences, Berhampur, Odisha, India for doing antibacterial and antioxidant study. The authors also thankful to the Department of Chemistry Berhampur University for providing needful facilities for the successful competition of the research.

REFERENCE.

[1] Desai KG and Desai KR, A facile microwave enhanced synthesis sulfur-containing 5-membered heterocycles derived from 2- mercaptobenzothiazole over $ZnCl_2$/ DMF and antimicrobial activity evaluation. Journal of Sulfur Chemistry, 27(4); 2006; 315–328.

[2] Garnaik BK and Dash S, Recent Advances and Potential Antimicrobial Activities of Thiazolidinone Derivatives: A Review. Asian Journal of Research in Chemistry. 7(4);2014;01-12.

[3] Shih MH and Ying KF, Synthesis and evaluation of antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives. Bioorganic Medicinal Chemistry. 12;2004;4633-4643.

[4] Balzarini J, Orzeszko B, Maurin JK, Orzeszko A. Synthesis and anti-HIV studies of 2-adamantylsubstituted thiazolidin-4-ones. European Journal of Medicinal Chemistry. 42;2007; 993-1003.

[5] Diurno MV, Mazzoni O, Piscopo E, Calignano A, N Giordano F and Bolognesell A. Synthesis and Antihistaminic Activity of Some Thiazolidin-4-ones. Journal of Medicinal Chemistry. 35;1992; 2910-2912.

[6] Malawska B, New anticonvulsant agents. Current Topics in Medicinal Chem.5; 2005; 69-85.

[7] Parmar SS, Dwivedi C, Chaudhari A and Gupta TK, Substituted thiazolidinones and their selective inhibition of nicotinamide dependant oxidations. Journal of Medicinal Chemistry .15;1972; 99.

[8] Ottana R, Maccari R, Barreca ML, Bruno G, Rotondo A and Rossi A, 5-Arylidene-2-imino4thiazolidinones: Design and synthesis of novel anti-inflammatory agents. Bioorganic Medicinal Chemistry. 13;2005; 4243-4252.

[9] Kumar A, Rajput CS and Bhati SK, Synthesis of 3-[4 '-(pchlorophenyl)- thiazol-2 '-yl]-2-[(substituted azetidinone/ thiazolidinone)- aminomethyl]-6-bromoquinazolin-4-ones as anti-inflammatory agent. Bioorganic Medicinal Chemistry. 15;2007; 3089–3096.

[10] Vazzana I, Terranova E, Mattioli F and Sparatore F, Aromatic Schiff bases and 2,3 disubstituted-1,3-thiazolidin- 4-one derivatives as anti-inflammatory agents. Arkivoc . 83 (v);2004;364-374.

[11] Rohini RM and Manjunath M, Synthesis and anti-convulsant activity of triazothiole/thiazolyl thiazolidinone derivatives of indole, Der Pharma Chemica., 2012;4 (6): 2438–2441.

[12] Rajendra PY, Lakshmana RA, Prasoona L, Murali K and Rav KP. Synthesis and characterization of 1-formyl-3-phenyl-5-uryl- 2-pyrazolines. Bioorganic Medicinal Chemistry letter.15; 2005; 5030-5034.

[13] Ozdemir Z Kandilici HB, Gumusel B, Calis U and Bilgin AA. Synthesis and studies on antidepressant and anticonvulsant activities of some 3-(2-furyl)-pyrazoline derivatives. European Journal of Medicinal Chemistry. 42;2007; 373-379.

[14] Li S and Purdy WC. Cyclodextrins and their application in analytical chemistry. Chemical Review.92;1992; 1457-1470.

[15] Sen M ,Mishra N,Behera RK and Nayak A, Synthesis and Nmr Spectral of Thiazolidinines derived from unsymmetrical thioureas.SUJ Sc. Tech. X:31-35

[16] Garnaik BK and Dash S. Synthesis and antibacterial study of inclusion complexes of 2-(benzothiazolyl-2')-azino-5-arylidene-4-thiazolidinone. Journal of Chemical and Pharmaceutical Research. 7(5);2015;102-108.

[17] Nayak SS, Panda S, Panda P and Padhy MS. Studies on acridone derivatives with and without inclusion complex formation with β-CD. Bullgerian Chemical Communication. 42(2);2010;147-152.

[18] Garnaik BK, Panda S and Behera B. Studies on Inclusion complexes of 3-[4-(4'-oxothiazolidinyl-2-imino)-aryl]-5,6-dihydro-5-oxothizolo[2,3-a] triazole derivatives with b-cyclodextrin. Journal of Chemical and Pharmaceutical Research, 4(11);2012; 4770-4773.

[19] Higuchi T and Connors K. Phase solubility technique. Adv Anal Chem Instrument. 4;1965; 117-211.16. Ekinci AS, Moncol J, Krishna VS, Sriram D and Özadali-Sari K. 5-Methyl-4- thiazolidinones, Synthesis and evaluation as antitubercular agents, J. Res. Pharm., 2020; 24(1): 30–37.

[20] Bollela, VR, Sato DN and Fonseca BAL. McFarland nephelometer as a simple method to estimate the sensitivity of the polymerase chain reaction using Mycobacterium tuberculosis as a research tool., Brazillian Journal of Medical and Biological Research. 32;1999; 1073-1076.

[21] Tagashira M and Ohtake Y. A new antioxidative 1,3-benzodioxole from *Melissa officinalis*. *Planta. Med*. **1998**, 64, 555–558.

[22] Benesi HA and Hilderband JH, A Spectrophotometric Investigation of the Interaction of Iodine with Aromatic Hydrocarbons, J. Amer. Chem. Soc. 1999;71: 2703-2707.

[23] Higuchi T. and Connors K, Phase solubility technique, Adv. Anal. Chem. Instru., 1965; 4: 117-211.

[24] Sahu R, Dash S and Garnaik BK, Thermal, Spectral, Antibacterial and Antioxidant Studies on Inclusion Complexes of 2-(Benzothiazolyl-2')hydrazono-3-phenyl 5-arylidene- 4-Thiazolidinone derivatives with β-cyclodextrin, Res. J. Pharm. Tech., 2016; 9(12): 2265-2270.

[25] Dash S, Sahu R and Garnaik BK, Studies on Inclusion complexes of 2-(Benzothiazolyl-2')hydrazono-3-phenyl-5-arylidene-4-Thiazolidinone derivatives with β cyclodextrin Asian J. Chem., 2016; 28(12):2764-2768 .

[26] Panda S, Nayak SS, Panda PM and Padhy S, Studies on acridone derivatives with and without inclusion complex formation with β-cyclodextrin, Bull. Chem. Comm., 2010;42(2):147-152.

[27] Dash S, Inclusion Complexes of Some Substituted 4-Thiazolidinones with Activating and Deactivating Group, Asian J. Chem., 2020; 32(1): 133-136.

[28] Bollela VR, Sato DN and Fonseca BAL., McFarland nephelometer as a simple method to estimate the sensitivity of the polymerase chain reaction using Mycobacterium tuberculosis as a research tool, Brazi. J.Med.Bio.Res., 1999; 32: 1073-1076.

[29] Szetli J, Molecular entrapment and release properties of drugs by cyclodextrins. Controlled Drug Bio-availability. 1985; Vol. 3: Willey Interscience publications, New York.

[30] Rajewski RA and Stella VJ, Pharmaceutical applications of cyclodextrins in vivo drug delivery, Jour. of Pharma., 1996; 85: 1142-1169.

[31] Stalin T., Vasantharani P, Shanti B, Sekhar A and Rajendiran N, Inclusion Complexes of trihydroxybenzene with α- and β- cyclodextrin, Ind. J. Chem. Sec A., 2006;45: 1113-1120.