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SYNTHESIS OF NOVEL 1, 3-INDANEDIONE DERIVATIVES AND PHARMACOLOGICAL EVALUATION AS ANTI-MICROBIAL, ANTI-OXIDATIVE AGENTS

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ABSTRACT: 1,3-Indanedione derivatives, which are of wide interest because of their diverse biological and chemical applications. A series of novel 1,3-Indanedione derivatives are synthesized via KNOEVENAGEL condensing reaction mechanism by condensing 1,3-Indanedione with the 1-(4-aminophenyl) ethanone to form a styrylated indanedione leading to the formation of different Schiff base (imine) preparation by using different aldehydes with the appropriate solvent mix at a suitable temperature. All the synthetic derivatives were fully characterized by spectral analysis data (FT-IR, NMR, and Mass). The newly synthesized compounds are evaluated for their antimicrobial activity (by using Cup-Plate method against selected bacterial strains amongst *S. aureus*, *E. coli* among total compounds, compounds 7 was found to have higher activity against selected strains and the results were found to be as moderate activity, for anti-fungal activity-compounds 2,8 are more potent, compounds are evaluated for their antioxidant NO scavenging (compound 7 is having more activity), for DPPH scavenging (compound 8 is having more activity), and inhibition of lipid peroxidation (compounds 3 and 9 are having more activity), for anti-oxidative activity moderate results are demonstrated. The potential importance of the pharmacophore, styryl, imine notices a role in the development of new potential anti-bacterial, anti-fungal, and anti-oxidative agents.

INTRODUCTION: 1,3-Indanedione, a potent pharmacophore, with an anticoagulant activity with an aromatic nucleus has gained prominence in medicinal chemistry during the years, 1,3-Indanedione has become a vital component in multicomponent chemical reactions in developing various drugs, bioconjugates, agrochemicals, etc.

The β -dicarbonyl moiety of the Indanedione is established as an important starting material in various organic transformations because of its cost-effective, eco-friendliness and operational simplicity, easy to handle, and low toxicity properties and affording higher yields of corresponding products ¹.

It is structurally similar to that of the heterocyclic pharmacophore isatin and its derivatives, which is known from the literature isatins were found to have a variety of pharmacological activities ² including anti-convulsant, anti-microbial, anti-cancer, anti-inflammatory, anti-oxidative, etc. with their diverse biological and chemical application

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was created interest in researchers who have prepared derivatives on pharmacophore based synthesis. 1,3-Indanedione itself is an anticoagulant, but it can possess pharmacophore based activities like isatin derivatives. At the 2nd position of the 1,3-indanedione structure serves as a key group for the synthesis of structurally complex compounds via condensation, the styryl moiety which is introduced by the synthesis of Indanedione (the active methylene group) condensed with that of the different aldehydes will possess antimicrobial³, anti-oxidative activities. The azo methane moiety containing derivatives (Schiff bases) were prepared by condensing the styrylated indanedione derivatives with various aldehydes with appropriate solvent mix and suitable atmospheric conditions, prepared compounds are ready for the screening of different biological activities here I have highlighted anti-bacterial, anti-fungal, anti-oxidative and anti-inflammatory activities. In this study, we have designed and synthesized a novel series of 1,3-indanedione derivatives and evaluated for their

pharmacological activities such as antioxidant, antimicrobial and antifungal activities. Jayachandran *et al.* had recently reported antibacterial and anticoagulant activities of 2-(arylsulfonyl) indane-1,3-diones⁴.

Similarly, Chen *et al.*, has reported anticoagulant activity of fluorine-containing Indanedione containing rodenticides⁵. In 2017, Dhayabaran and colleagues reported the efficiency of the binding interaction of Co(II), Cu(II), Ni(II) and Zn(II) complexes with Schiff Base compounds derived from 1,3-Indandione complexes with calf thymus DNA (CT-DNA)⁶. Other biological activities include cholinesterase inhibition, anti- β -amyloid aggregation, and neuroprotection properties against Alzheimer's disease⁷ hGlyT1 inhibition⁸, embryotoxic and teratogenic activities⁹, and anti-allergic activity¹⁰. In this study, we have designed and synthesized a novel series of 1,3-indanedione derivatives and evaluated for their pharmacological activities such as antioxidant, antimicrobial and antifungal activities.

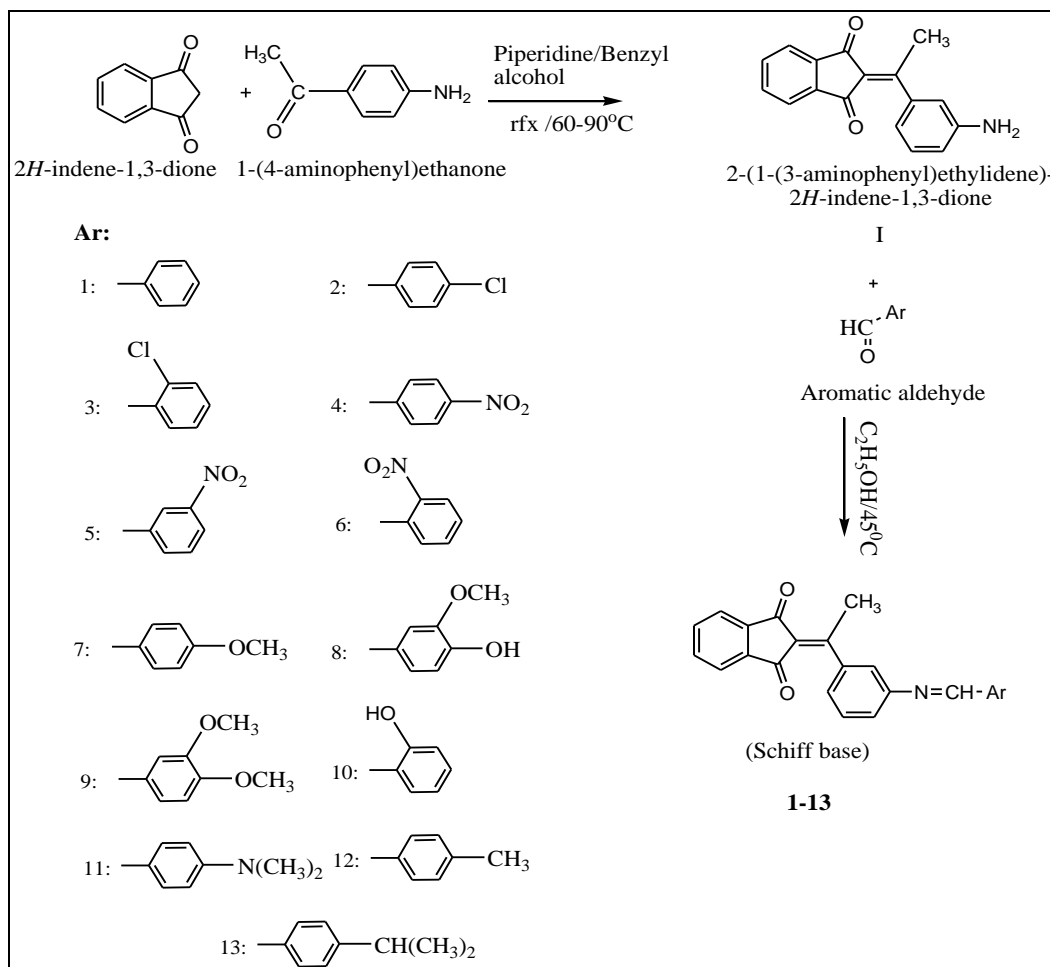


FIG. 1: SYNTHESIS OF THE NOVEL SERIES 1,3-INDANEDIONE DERIVATIVES IS SHOWN IN SCHEME

MATERIALS AND METHODS: All the chemicals used in the synthesis of the intermediates and final derivatives are of analytical grade and obtained from S.D fine chem. Limited (Mumbai). All melting points were determined in open capillary and are uncorrected. The purity of the synthesized compounds was analyzed by using TLC on silica gel-G plate as adsorbent and solvent system (or) mobile phase was used with various ratios of hexane, chloroform, ethanol, ethyl acetate appropriately.

R_f values produced for each compound were correlating with the literature and assumed to be pure. Characterizations of synthesized compounds were interpreted by FT-IR, ¹H-NMR, ¹³C-NMR, and Mass Spectral data.

General Procedure for Synthesis of Styrylated Indanedione Derivatives:

Synthesis of 2-(1-(3-aminophenyl)ethylidene)-2H-indene-1,3-dione: KNOEVENAGEL condensation reaction¹¹ (I): 2-(1-(3-aminophenyl)ethylidene)-2H-indene-1,3-dione was synthesized by condensation of 1,3-indanedione (0.1 mol) with the 1-(4-aminophenyl) ethanone (0.1 mol) piperidine as a base and benzyl alcohol as a solvent (6ml) under reflux for 4 to 8 hours at 70- 90 °C, a solid yellow to greenish yellow product was collected. Moisture was removed by Rota evaporator or by air dry process, the percentage yield of dried products are calculated and determined the melting points of the compounds.

Yield: 92%, m.p.: 126 °C; FT-IR (KBr, cm⁻¹): 3300, 3348 (NH₂); 3068 (C=C); 3344, 1695 (C=O); 2922 (CH₃), 956 (Ar-H); 1357 (C-N), ¹HNMR (300 MHz, CDCl₃, δ ppm): 3.8 (s, 3H); 5.38 (s, 2H); 7.30-7.44 (t, 2H); 7.37 (d, 1H); 7.71-7.72 (d, 2H); 8.26(d, 1H); 8.67-8.68(d, 2H). ¹³C NMR (CDCl₃): 14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 262.

Synthesis of Schiff bases (1-13): Schiff bases (1-13) were prepared¹² by the equimolar concentrations of the compound I condensed with various aromatic aldehydes under probe sonication for 3 h at 37 °C or 5-8 hours at 40 °C under reflux and ethanol as solvent. The mobile phase used for collecting of pure compounds by using hexane and ethyl acetate with the various ratios.

Synthesis of 2-(1-(3-(benzylideneamino) phenyl)ethylidene)-2H-indene-1,3-dione (1): Synthesis of 2-(1-(3-(4-chlorobenzylideneamino) Yield: 91%, m.p.:156-158 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1346 (C-N), 1670 (C=O); 2926 (CH₃), 992 (Ar-H); 1695 (N=C). ¹HNMR (300 MHz, CDCl₃, δ ppm): ¹³C NMR (CDCl₃): 14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 353.

Synthesis of 2-(1-(3-(4-chlorobenzylideneamino) phenyl)ethylidene)-2H-indene- 1, 3- dione (2): Yield: 89%, m.p.:160-163 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1321 (C-N), 1670 (C=O); 2906 (CH₃); 932 (Ar-H); 1685 (N=C), 762 (Chlorine). ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 7.3-7.86 (d, 6H); 7.71-7.74 (t, 4H); 8.1-8.3 (d, 2H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 385.

Synthesis of 2-(1-(3-(2-chlorobenzylideneamino) phenyl)ethylidene)-2H-indene- 1, 3- dione (3): Yield: 87%, m.p.:160-163 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1321 (C-N), 1685 (C=O); 2906 (CH₃); 932 (Ar-H); 1685 (N=C), 762 (Chlorine). ¹HNMR (300 MHz, CDCl₃, δ ppm): ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 7.28-7.29 (d, 2H); 7.3-7.86 (d, 6H); 7.71-7.74 (t, 4H); 8.1,-8.3 (d, 2H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 385.

Synthesis of 2-(1-(3-(4-nitrobenzylideneamino) phenyl)ethylidene)-2H-indene- 1, 3- dione (4): Yield: 88%, m.p.:168-173 °C; FT-IR (KBr, cm⁻¹): 1348, 1795 (NO₂); 1350 (C-N), 1685 (C=O);2974 (CH₃); 992 (Ar-H); 1631 (N=C). ¹HNMR (300 MHz, CDCl₃, δ ppm): ¹HNMR (300 MHz, CDCl₃, δ ppm) 1.7(s, 3H); 7.28-7.29(d, 2H); 7.3-7.86 (d, 6H); 7.71-7.74(t, 4H); 8.1,-8.3 (d, 2H) 8.4 (S, 1H). ¹³C NMR (CDCl₃):14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 396.

Synthesis of 2-(1-(3-(3-nitrobenzylideneamino) phenyl)ethylidene)-2H-indene- 1, 3- dione (5): Yield: 86%, m.p.:168-173 °C; FT-IR (KBr, cm⁻¹): 1348, 1795 (NO₂); 1350 (C-N), 1670 (C=O); 2974 (CH₃); 992 (Ar-H); 1631 (N=C). ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 7.28-7.2 9(d, 2H); 7.3-7.86 (d, 6H); 7.71-7.74 (t, 4H); 8.1-8.3 (d, 2H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 396.

Synthesis of 2-(1-(3-(2-nitrobenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (6): Yield: 85%, m.p.:168-173 °C; FT-IR (KBr, cm⁻¹): 1348, 1795 (NO₂); 1350 (C-N), 1670 (C=O); 2974 (CH₃); 992 (Ar-H); 1631 (N=C). ¹HNMR (300 MHz, CDCl₃, δ ppm): ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 7.28-7.29 (d, 2H); 7.3-7.86 (d, 6H); 7.71-7.74 (t, 4H); 8.1-8.3 (d, 2H, 8.4 (S, 1H). m/z: 396.

Synthesis of 2-(1-(3-(4-methoxybenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (7): Yield: 85%, m.p.:178 °C; FT-IR (KBr, cm⁻¹): 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2808 (CH₃). ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 3.25 (s, 3H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 56, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 384.

Synthesis of 2-(1-(3-(3-methoxy,4-hydroxybenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (8): Yield: 84%; m.p.: 183 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2850(CH₃); (300 MHz, CDCl₃, δ ppm): 2.17 (s, 1H); 3.2-3.3 (s, 3H); 4.9 (s, 1H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H), 8.4 (S, 1H)¹³ CNMR (CDCl₃): 15, 54, 115.5, 122.2, 130.1, 135.4, 137, 140, 152.1, 190. m/z: 387.

Synthesis of 2-(1-(3-(3,4-dimethoxybenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (9): Yield: 84%; m.p.: 185 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2860 (CH₃). ¹HNMR (300 MHz, CDCl₃, δ ppm): 3.86-3.89 (S, 6H); 7.1-7.36 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H); 8.4 (S, 1H). ¹³CNMR (CDCl₃): 16, 50, 115.5, 122, 130, 135, 137, 140, 152.1, 190. m/z: 413.

Synthesis of 2-(1-(3-(2-hydroxybenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (10): Yield: 90%, m.p.:161 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 3200-3550 (OH); 1350 (C-N), 1670 (C=O); 3250 (OH); 992 (Ar-H); 1679 (N=C). ¹HNMR (300 MHz, CDCl₃, δ ppm): 2.17(s, 3H); 4.9 (s, 1H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1,-8.3 (d, 3H) 8.4 (S, 1H). ¹³CNMR (CDCl₃): 16, 50, 115.5, 122.2, 130, 135.1, 137, 152, 190 m/z: 367.

Synthesis of 2-(1-(3-(4-(dimethylamino)benzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-

dione (11): Yield: 80%; m.p.: 139-140 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2450 (N-H 0; 2050, 2098(CH₃). ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.57(s, 3H); 2.6, 2.8 (s, 6H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 40, 115.5, 122.2, 130, 135.1, 137, 152, 190 m/z: 394.

Synthesis of 2-(1-(3-(4-methylbenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (12): Yield: 80%, m.p.:145- 149 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2858 (CH₃); ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 2.25 (s, 3H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H), 8.4 (S, 1H). ¹³C NMR (CDCl₃): 14, 26, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 365.

Synthesis of 2-(1-(3-(4-isopropylbenzylideneamino)phenyl)ethylidene)-2H-indene-1, 3-dione (13): Yield: 80%, m.p.: 152 °C; FT-IR (KBr, cm⁻¹): 3068 (C=C); 1350 (C-N), 1670 (C=O); 992 (Ar-H); 1679 (N=C), 2808 (CH₃): ¹HNMR (300 MHz, CDCl₃, δ ppm): 1.7 (s, 3H); 1.25 (s, 6H); 7.3-7.86 (d, 6H); 7.72-7.73 (t, 2H); 8.1-8.3 (d, 3H), 8.2 (S, 1H). ¹³C NMR (CDCl₃):14, 24, 115.5, 122.2, 130, 135.1, 137, 152, 190. m/z: 393.

Pharmacological Evaluation:

In-vitro Antioxidant Activity:

Assay of Nitric Oxide Scavenging Activity: Sodium nitroprusside (10 mM) in phosphate buffer (pH 7.4) was incubated with the newly synthesized compounds (100 μM) dissolved in a suitable solvent (dioxane/methanol) at 25 °C for 2 h. Control experiment was conducted similarly. 2 ml of incubation solution was diluted with 2 ml Griess Reagent (1% sulfanilamide, 2% H₃PO₄ and 0.1% N-(1-naphthyl) ethylenediamine dihydrochloride)). The absorbance of the chromophore formed during diazotization of nitrite with sulphanilamide and subsequent N-naphthalene diamine was read at 546 nm¹³.

Interaction with Stable Free Radical DPPH:

Diphenylpicrylhydrazyl (DPPH) radical scavenging assay was carried out by adding 100 μl of the test compound to the standard solution. 100 μl of DPPH solution was added to the earlier mixture. Control was performed with 100 μl of DMSO and

DPPH. Sample blank and control blank were also performed. The mixture was incubated at 37 °C for 30 min without exposing to light, and the absorbance of each solution was measured at 540 nm¹⁴.

Lipid Peroxidation: Formation of lipid peroxide was measured by a modified thiobarbituric acid-reactive species (TBARS) assay using egg yolk homogenate (lipid-rich medium). 0.5 ml of egg homogenate (10% v/v) and 0.1 ml of the test compound were added to a test tube and made up to 1 ml with distilled water. Lipid peroxidation was induced by adding FeSO₄ (0.07 M) to the mixture and incubated for 30 min. To this, 1.5 ml of 20% acetic acid (pH adjusted to 3.5 with NaOH), 1.5 ml of 0.8% (w/v) TBA in 1.1% sodium dodecyl sulphate and 0.5 ml 20% TCA were added and heated for 60 min at 95 °C. Butanol (5 ml) was added to each tube after cooling and centrifuged at 3000 rpm for 10 min. The absorbance of the organic upper layer was measured at 532 nm¹⁵.

Anti-Microbial Activity: The antibiotic potency of the newly synthesized compounds was determined by using Cup-Plate method and *Pseudomonas aureus* (Gram-positive) and *Escherichia coli* (Gram negative) as test organisms. Initially, the prepared nutrient agar medium was sterilized by autoclaving at 15 lbs pressure and 121 °C for 25 min. Agar media was cooled to room temperature, and the organism was inoculated to the media. 15 ml of media was transferred to a Petri plates aseptically. Synthesized Compounds were dissolved in water and diluted to get 10 mg/ml of concentration, whereas, streptomycin is used as a standard drug at a concentration of 10 µg/ml. The culture plates were incubated at 37 °C for 24 h. The zone of inhibitions produced by test compounds was recorded in mm¹⁶.

Anti-Fungal Activity: Anti-fungal activity of the newly synthesized derivatives was evaluated by Disc diffusion method. Sabour and dextrose agar plates (5-6 mm) were prepared aseptically and were dried at 37°C before inoculation. *Candida albicans* were inoculated into sabour and dextrose agar plates by using sterile inoculation loop and were incubated at 37 °C for about 24 h. Ketoconazole (10 µg/disc) was used as the standard. Sterile Whatman no. 2 filter paper disc (5 mm diameter)

was soaked into synthesized compounds (20 µg/disc) separately and evaporated to dryness and placed on the media. One more disc immersed in dimethyl sulphoxide and placed on the media as a control. The Petri dishes were incubated at 37 °C for 24 h. Cooled them for an hour in a refrigerator to facilitate uniform diffusion.

RESULTS AND DISCUSSION:

Chemistry: All the novel 1,3-indanedione derivatives were synthesized, purified and separated by using column chromatography or recrystallization method. Synthesized compounds were characterized by using IR, ¹H NMR, ¹³C NMR, and Mass Spectrometric studies. The integration curves fully support the orientation of protons in the analyzed compounds. Furthermore, all the compounds demonstrated the characteristic chemical shifts for the indanedione nucleus. Additionally, synthesized compounds were analyzed by mass spectra under ESI conditions and indicated no difference in the fragmentation pattern among the set of synthesized series.

Anti-Oxidative Activity: The antioxidant activity of the newly synthesized 1, 3-indanedione derivatives is determined regarding % scavenging of NO and DPPH, and % inhibition of lipid peroxidation **Table 1** and **Fig. 2**. All the tested compounds exhibited moderate to low scavenging activity of NO and DPPH, and substantial inhibition of lipid peroxidation. NO scavenging is ranged between 11.5% (compound 1) and 29.9% (compounds 7), whereas, DPPH scavenging is from 11.6% (compound 1) to 26.16% (compound 8). Highest antioxidant activity regarding inhibition of lipid peroxidation is observed with compound 3 (53.85%), followed by compound 9 (52.98).

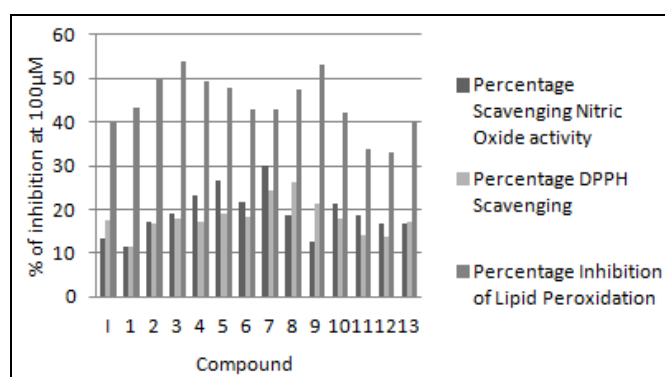
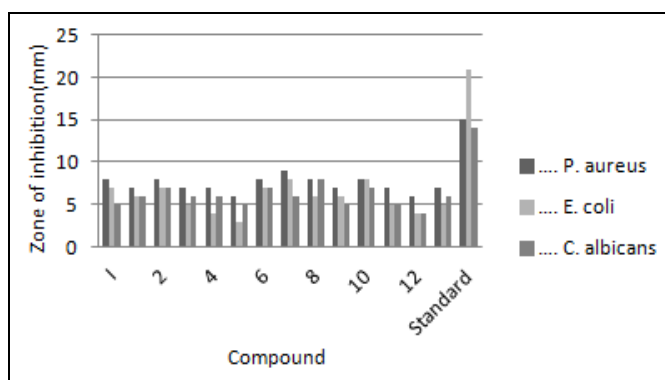


FIG. 2: ANTIOXIDANT ACTIVITY OF NEWLY SYNTHESIZED 1,3-INDANEDIONE DERIVATIVES

TABLE 1: ANTIOXIDANT ACTIVITY OF NEWLY SYNTHESIZED 1,3-INDANEDIONE DERIVATIVES

| Compound | Percentage scavenging nitric oxide activity | Percentage DPPH scavenging | Percentage inhibition of lipid peroxidation |
|----------|---|----------------------------|---|
| I | 13.5 | 17.5 | 39.99 |
| 1 | 11.54 | 11.6 | 43.24 |
| 2 | 17.3 | 16.65 | 49.75 |
| 3 | 18.9 | 17.9 | 53.85 |
| 4 | 23.21 | 17.28 | 49.34 |
| 5 | 26.8 | 19.12 | 47.65 |
| 6 | 21.82 | 18.24 | 43.06 |
| 7 | 29.9 | 24.21 | 42.73 |
| 8 | 18.7 | 26.16 | 47.43 |
| 9 | 12.5 | 21.23 | 52.98 |
| 10 | 21.4 | 17.81 | 42.25 |
| 11 | 18.5 | 14.3 | 33.98 |
| 12 | 16.9 | 13.6 | 32.90 |
| 13 | 16.87 | 17.21 | 40.06 |

Antimicrobial and Antifungal Activities: The antimicrobial and antifungal activities of the newly synthesized 1,3-indanedione derivatives against bacterial/fungal strains are shown in **Table 2**. All the tested compounds exhibited moderate to low activities when compared to that of the standard. Zone of inhibition in *P. aureus* is ranged from 6 mm (compounds 5, 12) to 9 mm (compound 7), whereas, in *E. coli* screening is from 3 mm (compound 5) to 8 mm (compound 7). Zone of inhibition of with standard is 15 mm and 21 mm

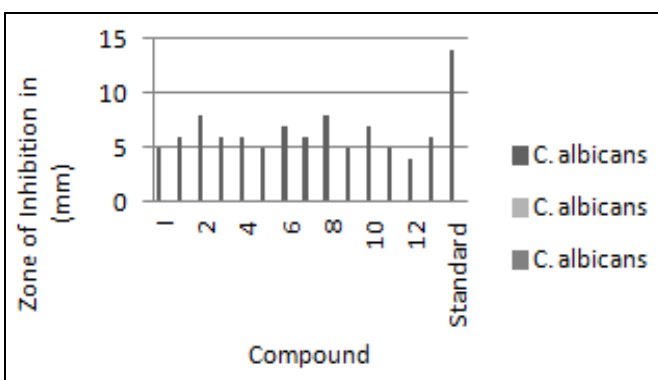
**FIG. 3: ANTIMICROBIAL ACTIVITY OF NOVEL 1,3-INDANEDIONES**

CONCLUSION: Novel series of 1,3-indanedione derivatives were synthesized by using a new procedure with an efficient catalyst and evaluated for their pharmacological potentials regarding antimicrobial and antifungal, antioxidant activities. All the compounds are showing minimum to moderate activities, among them electronegative groups on the benzene ring, the phenolic group as the terminal substitution or Meta and Para di-

against *P. aureus* and *E. coli*, respectively, and no inhibition was observed in control screening **Fig. 2**. Compound 2 and 8 has exhibited highest antifungal activity (8 mm inhibition) among the tested series against *C. albicans*, followed by compounds 6 and 10 (7 mm) **Fig. 3**. Compounds with Paramethoxy group substituted compounds were reported with higher antimicrobial activity. Additionally, compounds with Meta & Ortho substitutions, Para-substitution was found to be more active compared to other substitutions.

TABLE 2: ANTIMICROBIAL AND ANTIFUNGAL ACTIVITIES OF NOVEL 1,3-INDANEDIONES

| Compound | Zone of inhibition (mm) | | |
|----------|-------------------------|----------------|--------------------|
| | <i>P. aureus</i> | <i>E. coli</i> | <i>C. albicans</i> |
| I | 8 | 7 | 5 |
| 1 | 7 | 6 | 6 |
| 2 | 8 | 7 | 8 |
| 3 | 7 | 5 | 6 |
| 4 | 7 | 4 | 6 |
| 5 | 6 | 3 | 5 |
| 6 | 8 | 7 | 7 |
| 7 | 9 | 8 | 6 |
| 8 | 8 | 6 | 8 |
| 9 | 7 | 6 | 5 |
| 10 | 8 | 8 | 7 |
| 11 | 7 | 5 | 5 |
| 12 | 6 | 4 | 4 |
| 13 | 7 | 5 | 6 |
| Standard | 15 | 21 | 14 |

**FIG. 4: ANTIFUNGAL ACTIVITY OF NOVEL 1,3-INDANEDIONES**

substitutions were observed to have higher antimicrobial/antifungal activities.

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CONFLICT OF INTEREST: Authors declare no conflicts of interest.

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