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SYNTHESIS, ANTIMICROBIAL AND ANTIOXIDANT ACTIVITIES OF SOME NEW5, 6-DIAMINO-1, 3-DIMETHYLPYRIMIDINE-2, 4(1*H*, 3*H*)-DIONE DERIVATIVES

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ABSTRACT

A series of 5, 6-Diamino-1, 3-dimethylpyrimidine-2, 4(1*H*,3*H*)-dione derivatives were synthesized. An efficient synthesis of 5, 6-diamino-1,3-dimethylpyrimidine-2,4(1H,3H)-dione bridge substituted to indole nucleus was described antioxidant of synthesized compounds (3 and 4) were determined by various *in vitro* assays such as 1,1-diphenyl-2-picryl hydrazyl free radical (DPPH), Reducing ability by Fe^{3+} to Fe^{2+} method, Ferrous ion (Fe^{2+}) chelating activities. Antimicrobial activity was carried out by cup plate method. These results were compared with the respective standards. Compounds 3a and 4a showed good radical scavenging activity (RSA). Compounds 3b, 4b and 4c exhibited good reducing power activity, whereas, the compound 3a, exhibited good metal chelating activity. Among the all compounds 4a exhibited promising antibacterial, antifungal activities.

KEYWORDS: Pyrimidine, Indole, Antibacterial, Antifungal, Antioxidant activity.

1. INTRODUCTION

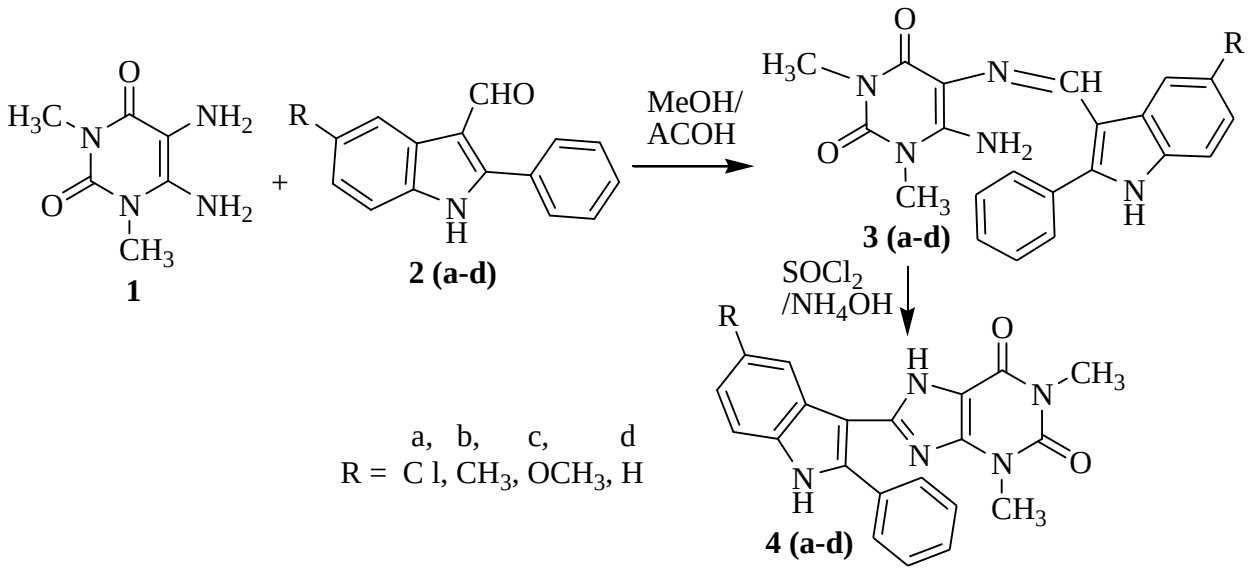
Pyrimidine is the parent nucleus of a large group of heterocyclic compounds, which have attracted the attention for a long time. Pyrimidine derivatives occur in natural products [1] like nucleic acids and vitamin B_1 which have remarkable pharmaceutical importance because of their biological activities. [2-5] Some of the pyrimidine derivatives e.g., antitumor agent, fluorouracil and its analogues contains pyrimidine ring in their structures. They also have applications in liquid crystal composition. [6] The indole derivatives possess a wide variety of

biological properties *viz.*, anti-inflammatory, [7,8] anticonvulsant, [9] antibacterial, [10] COX-2 inhibitor [11,12] and antiviral [13] activities.

2. MATERIALS AND METHODS

2.1 Chemistry

The synthetic strategy was planned as depicted in Scheme 1. The requisite starting materials, 5, 6-Diamino-1, 3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione 1 reported method. [14,15] Compound (1) on condensation with various 5-substituted 2-phenyl-1*H*-indole-3-carbaldehyde (2a-d) using reported procedure [16] in methanol and acetic acid (4:1) yielded 5-[(5-substituted 2-phenyl-1H-indol-3-yl)methyleneamino]-6-amino-1,3-dimethylpyrimidine-2,4(1H,3H)-diones (3a-d). Compounds (3a-d) refluxed in thionylchloride for 30-40 min afforded the target compounds 8-(5-substituted 2-phenyl-1H-indol-3-yl)-1, 3-dimethyl-1H-purine-2,6(3H,7H)-diones (4a-d) respectively.



Scheme-1 Schematic pathway for the synthesis of compounds (1-4).

2.l Experimental Protocol

All the reagents were obtained commercially and used by further purification. Melting points were determined by an open capillary method and are uncorrected. Purity of the compounds was checked by thin layer chromatography using silica gel-G coated Al plates (Merck) and spots were visualized by exposing the dry plates in iodine vapors, using Benzene:Ethylacetate (1:1) and/or Tolune:Ethylacetate (1:1). The IR (KBr pellet) spectra were recorded on a Perkin-Elmer (Spectrum ONE) FT-IR Spectrometer. The ^{1}H NMR (DMSO-d_6) spectra were recorded with a BRUKER NMR 500 MHz spectrometer the chemical shift values are

expressed in ppm (δ scale) using tetramethylsilane as an internal standard. The mass spectral measurements were carried out by Electron Impact method on JEOL GC mate spectrometer at 70 eV. Elemental analyses were performed on flash EA 1112 series elemental analyzer.

2.2 Synthesis

2.2.2. 5, 6-diamino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (1) was by following literature procedure. [14,15]

2.2.3. 5-Substituted 2-phenyl-1*H*-indol-3-carboxaldehydes (2a-d) were prepared by literature method. [16]

2.2.4. General procedure for the synthesis of various 5-[(5-Substituted2-phenyl-1*H*-indol-3-yl) methyleneamino]-6-amino-1, 3-dimethylpyrimidine-2, 4(1*H*, 3*H*)-diones (3a-d).

To a stirred solution of 5,6-Diamino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione (**1**) (1.0g, 5.87 mmol) in MeOH-AcOH (4:1 40 ml) was slowly added 5-substituted 2-phenyl-1*H*-indole-3-carbaldehyde (**2a-d)** in methanol (24 ml). The reaction mixture was further stirred overnight at room temperature. The residue obtained after removal of solvent under reduced pressure was dissolved in ice-cold water and alkalized with sodium hydroxide. The resultant turbid solution was cooled in ice for complete precipitation. The precipitate obtained was filtered off, washed with ice cold water and dried to obtained pure 3a-d.

2.2.5. 5-[(5-Chloro-2-phenyl-1*H*-indol-3-yl)methyleneamino]-6-amino-1,3-dimethyl pyrimidine-2,4(1*H*,3*H*)-dione 3a

Yield: 42 %, mp 209-210 ºC; FTIR (KBr) cm^{-1}: 3417, 3214 (indole-NH, NH_2); 1701, 1650 (C=O); 1620 (C=N); ^{1}H NMR (DMSO-d_6, δ, ppm) 12.10 (s, 1H, indole NH); 9.61(s, 1H, N=CH); 7.10-8.20 (m, 8H, Ar-H); 5.79 (br s, 2H, NH_2); 3.60 (s, 3H, CH_3); 2.69(s,3H, CH_3); MS (EI) *m/z* 407 (M^+); 409 (M^++2). Anal. % $C_{21}H_{18}N_5O_2Cl$: C, 61.84; H, 4.45; N, 17.11; Found: C, 61.85; H, 4.48; N, 17. 15.

2.2.6. 5-[(5-Methyl-2-phenyl-1*H*-indol-3-yl)methyleneamino]-6-amino-1,3-dimethyl pyrimidine-2,4(1*H*,3*H*)-dione 3b

Yield: 50%, mp 200-201 ºC; FTIR (KBr) cm^{-1}: 3330, 3210 (indole-NH, NH_2); 1691, 1650 (C=O); 1618 (C=N); ^{1}H NMR (DMSO-d_6, δ, ppm) 12.09 (s, 1H, indole NH); 8.91 (s, 1H, N=CH); 6.95-8.15 (m, 8H, Ar-H); 5.54 (br s, 2H, NH_2); 3.75 (s, 3H, CH_3); 3.69 (s,3H, CH_3);

2.25 (s,3H, CH_3); Anal. % $C_{22}H_{21}N_5O_2$: C, 68.20; H, 5.46; N, 18.01. Found: C, 68.23; H, 5.47; N,18.04.

2.2.7. 5-[(5-methoxy-2-phenyl-1H-indol-3-yl)methyleneamino]-6-amino-1,3-dimethyl pyrimidine-2,4(1H,3H)-dione 3c

Yield: 51%, mp 220-222 ºC; FTIR (KBr) cm^{-1}: 3245, 3145 (indole-NH, NH_2); 1690, 1640 (C=O); 1632 (C=N); ^{1}H NMR (DMSO-d_6, δ, ppm) 11.69 (s, 1H, indole NH); 9.54 (s, 1H, N=CH); 7.15-8.25 (m, 8H, Ar-H); 6.14 (br s, 2H, NH_2); 3.90 (s, 3H, OCH_3); 3.69 (s,3H, CH_3); 2.30 (s, 3H, CH_3); Anal. % $C_{22}H_{21}N_5O_3$: C, 65.50; H, 5.25; N, 17.36. Found: 65.57; H, 5.29; N, 17.33.

2.2.8. 5-[(2-Phenyl-1*H*-indol-3-yl)methyleneamino]-6-amino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione 3d

Yield: 62%, mp 250-251 ºC; FTIR (KBr) cm^{-1}: 3404, 3110 (indole-NH, NH_2); 1700, 1690 (C=O); 1620 (C=N); ^{1}H NMR (DMSO-d_6, δ, ppm) 12.41 (s, 1H, indole NH); 9.80 (s, 1H, N=CH); 7.20-8.00 (m, 9H, Ar-H); 7.00 (br s, 2H, NH_2); 3.50 (s, 3H, CH_3); 3.69 2.45 (s, 3H, CH_3); Anal. % $C_{21}H_{19}N_5O_3$: C, 67.55; H, 5. 13; N, 18.76. Found: C, 67.60; H, 5.13; N, 18.76.

2.2.9. General procedure for the synthesis of various 8-(5-Substituted 2-phenyl-1*H* indol-3- yl)-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-diones 4(a-d).

Compounds (3a-d) (1.0g, 2.5 mmol) obtained were refluxed separately in thionly chloride (20 ml) for 30-40 min to affect cyclization. The excess thionly chloride was removed under reduced procedure to obtain a solid product. Ice cold water was added to it and resultant suspension was neutralized with ammonium hydroxide solution. The precipitate obtained was collected by filtration, dried and recrystallized from a mixture of DMF and methanol to afford the desired products **4a-d**.

2.2.10. 8-(5-Chloro-2-phenyl-1*H*-indol-3-yl)-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione 4a

Yield: 68%, mp 233-235 ºC; FTIR (KBr) cm^{-1}: 3421 (indole-NH); 17100, 1640 (C=O); ^{1}H NMR (DMSO-d_6, δ, ppm) 12.41 (s, 1H, indole NH); 7.10-8.20 (m, 8H, Ar-H); 3.50 (s, 3H, CH_3); 2.50 (s, 3H, CH_3); MS (EI) *m/z* 405 (M^+); 407 (M^++2). Anal. % $C_{21}H_{18}N_5O_2Cl$: C, 62.15; H, 3.97; N, 17.26. Found: C, 62.18; H, 3.95; N, 17.24.

2.2.11. 1,3-Dimethyl-8-(5-methyl-2-phenyl-1*H*-indol-3-yl)-1*H*-purine-2,6(3*H*,7*H*)-dione 4b

Yield: 47%, mp190-191 ºC; FTIR (KBr) cm^{-1}: 3335 (indole-NH); 1660, 1640 (C=O); ^1H NMR (DMSO-d_6, δ, ppm) 12.41 (s, 1H, indole NH); 7.30-8.10 (m, 8H, Ar-H); 3.50 (s, 3H, CH_3); 2.89 (s, 3H, CH_3); 2.50 (s, 3H, CH_3); Anal. % $C_{22}H_{19}N_5O_2$: C, 68.56; H, 4.97; N, 18.17. Found: 68.60; H, 4.95; N, 18.20.

2.2.12. 8-(5-methoxy-2-phenyl-1H-indol-3-yl)-1,3-dimethyl-1H-purine-2,6(3H,7H)-dione 4c

Yield: 66%, mp 240-241 ºC; FTIR (KBr) cm^{-1}: 3404 (indole-NH); 1700, 1630 (C=O); ^1H NMR (DMSO-d_6, δ, ppm) 12.00 (s, 1H, indole NH); 6.80-7.60 (m, 8H, Ar-H); 3.90 (s, 3H, OCH_3); 3.15 (s, 3H, CH_3); 2.55 (s, 3H, CH_3); Anal. % $C_{22}H_{19}N_5O_3$: C, 65.83; H, 4.17; N, 17.45. Found: C, 65.85; H, 4.19; N, 17.50.

2.2.13. 1,3-Dimethyl-8-(2-phenyl-1*H*-indol-3-yl)-1*H*-purine-2,6(3*H*,7*H*)-dione 4d

Yield: 55 %, mp > 259-260 ºC; FTIR (KBr) cm^{-1}: 3240 (indole-NH); 1695, 1650 (C=O); ^1H NMR (DMSO-d_6, δ, ppm) 12.11 (s, 1H, indole NH); 7.00-8.00 (m, 9H, Ar-H); 3.25 (s, 3H, CH_3); 2.85 (s, 3H, CH_3); Anal. % $C_{21}H_{17}N_5O_2$: C, 67.91; H, 4.61; N, 18.86; Found: C, 67.94; H, 4.62; N, 18.89.

3. RESULTS AND DISCUSSION

3.1 Antimicrobial Activities

Antimicrobial screening of the compounds 3, 4 (a-d) was performed by cup-plate method at a concentration of 1mg/ml following reported procedure. [17] The bacteria *Escherichia coli, Bacillus subtilis* and *Klebsiella pneumoniae* and fungal *Asperigillus niger, Asperigillus flavus and Asperigillus fumigates* were used. The zones of inhibition were compared with the standards. Streptomycin and flucanazole were used as standards for antibacterial and antifungal activities, respectively. The results are presented in Table-1.

The investigation of antibacterial screening revealed that, compounds 3a, 4a and 4c exhibited maximum zone of inhibition against *E. coli.* Compounds 3a, 4a and 4c showed maximum zone of inhibition against *B. subtilis* and compounds 3a, 3c and 4a exhibited the maximum zone of inhibitory against *K. pneumonia.*

In case of antifungal screening, compounds 3a, 3c, 3d and 4a exhibited promising activity against *A. niger*, whereas compounds 3a, 4a and 4c exhibited maximum zone of inhibition against *A. flavus*. The compounds 3a, 3b, 4a and 4c exhibited maximum zone of inhibition against *A. fumigatus*. The results of enhanced antimicrobial activities may be due to presence of chloro or methyl group substitution.

Table 1: Antimicrobial activities for 5, 6-Diamino-1,3-dimethylpyrimidine-2,4(1*H*,3*H*)-dione derivatives 3, 4 (a-d).

Comp. No.	R	Diameter of zone of inhibition in mm[#]					
		Antibacterial Activity			Antifungal Activity		
		E. coli	B. *subtilis*	*K. pneumoniae*	A. *niger*	*A. flavus*	*A. fumigates*
3a	Cl	20	23	19	18	20	17
3b	CH_3	17	09	13	08	11	18
3c	OCH_3	19	17	18	17	05	16
3d	H	15	14	10	18	13	08
4a	Cl	22	25	20	19	21	18
4b	CH_3	10	09	07	15	09	13
4c	OCH_3	20	23	16	18	19	17
4d	H	13	10	05	05	05	13
Std_1	-	23	26	22	-	-	-
Std_2	-	-	-	-	20	22	19

Including diameter of well[#], control (DMF) = no activity, streptomycin (Std_1) and flucanazole (Std_2) were used as standards for antibacterial and antifungal activities, respectively.

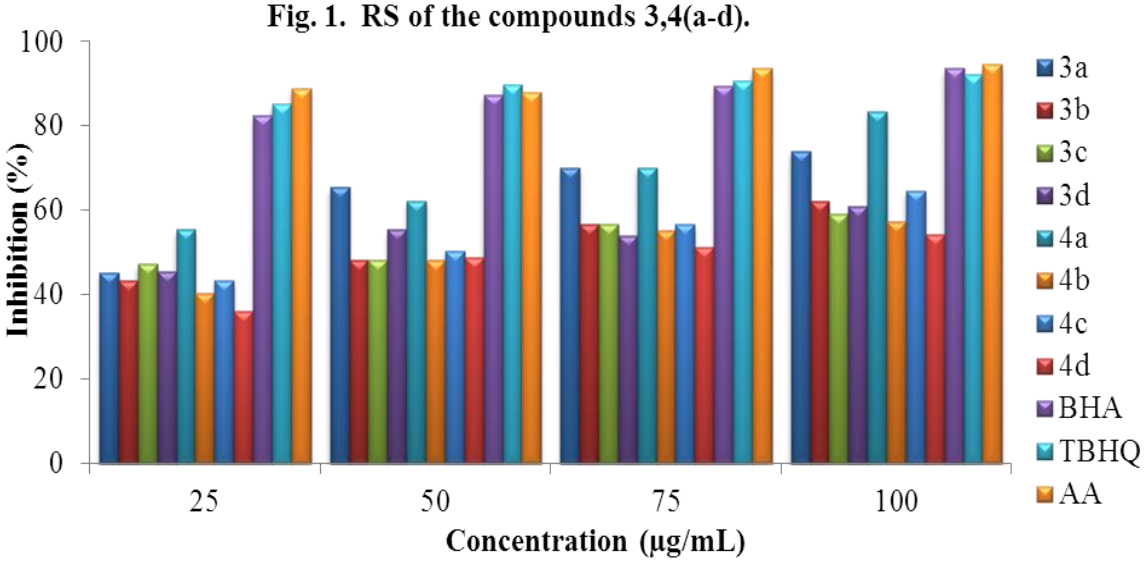
3.2. 1, 1-Diphenyl-2-Picryl Hydrazyl (DPPH) Radical Scavenging Activity (RSA)

The free radical scavenging activity (RSA) of compounds **3, 4 (a-d)** at concentration (25, 50, 75 and 100 µg/mL) was carried out in the presence of freshly prepared solution of stable free radical DPPH (0.04% w/v) following Hatano's method[18], using 2-tert-butyl-4-methoxyphenol (butylated hydroxy anisole, BHA) and 2-(1,1-dimethylethyl)-1,4-benzenediol (2-tert. butyl hydroquinone, TBHQ) as standards. All the test analyses were performed on three replicates and results are averaged. The results in percentage are expressed as the ratio of absorption decrease of DPPH in the presence test compounds and absorption of DPPH in the absence of test compounds at λ 517 nm on ELICO SL 171 Mini Spec spectrophotometer. The percentage scavenging activity of the DPPH free radical was measured using the following equation.

DPPH radical scavenging (%) = [(Ac-As/Ac)X100]

Where, Ac is the absorbance of the control reaction and As is the absorbance of the sample or standards. The activity of results revealed that, compound 3a and 4a (70.18 and 70.15 %) exhibited good radical scavenging activity at conc. of 75 µg/ml concentration. Compounds 3a and 4a showed good radical scavenging activity (74.14, 83.35%, respectively) at 100 µg/ml concentration. The results are shown in the fig. 1.

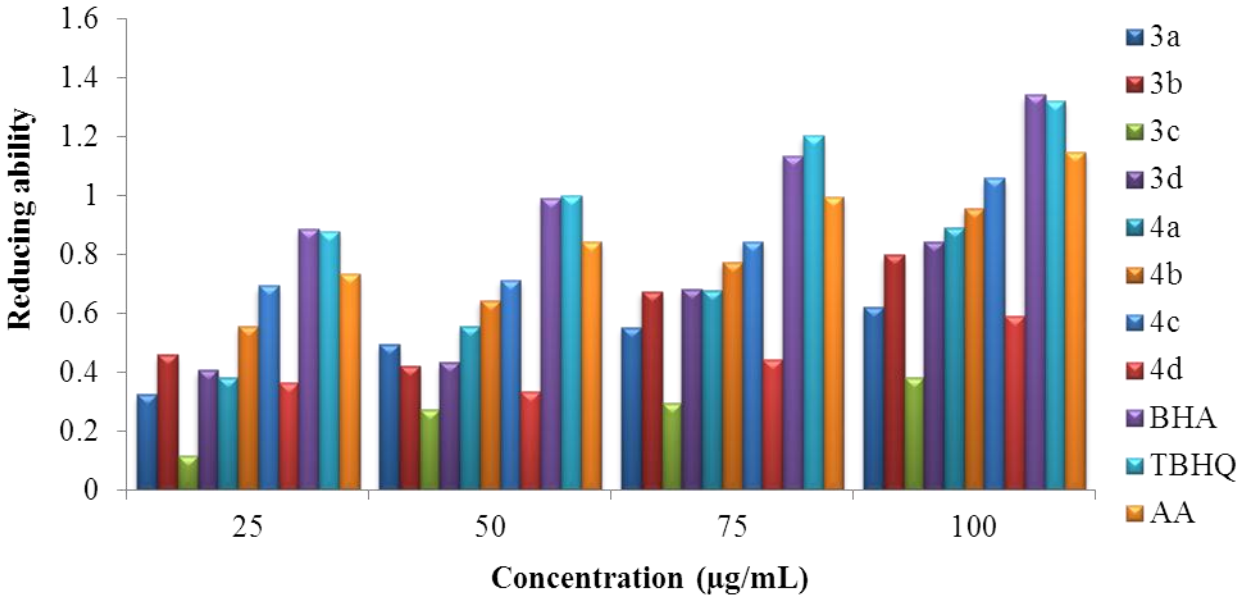
Fig. 1. RS of the compounds 3,4(a-d).



3.3. Ferric ions (Fe^{3+}) Reducing Antioxidant Power (FRAP) Activity

The reducing power of the synthesized compounds was determined according to the Oyaizu method[19]. Different concentration of samples (25, 50, 75 and 100 µg/mL) in DMSO (1 mL) were mixed with phosphate buffer (2.5 mL, 0.2 M, pH=6.6) and potassium ferricyanide (2.5 mL, 1%). The mixture was incubated at 50°C for 20 min. After which a portion of trichloroacetic acid (2.5 mL, 10%) was added to the mixture and centrifuged for 10 min, at 1000 Xg. The upper layer of solution (2.5 mL) was mixed with distilled water (2.5 mL) and ferric chloride (0.5 mL, 0.1 %). Then absorbance at λ 700 nm was measured in spectrophotometer. Higher absorbance of the reaction mixture indicated greater reducing power. The FRAP of synthesized compounds were determined at four different concentrations (25, 50, 75 and 100 µg/mL) at pH 6.6 by literature method[20] using BHA, TBHQ and AA as standards. Higher absorbance of the reaction mixture indicated greater reducing power of the test compounds. The analysis of results indicated that, compound 4c exhibited good reducing activity at 25 µg/ml concentration, whereas compounds 4b and 4c showed reducing power at 50 µg/ml concentration. Compounds 3b, 4b and 4c shows promising activity at 75 and 100 µg/ml concentration, respectively. The results are shown in the fig. 2.

Fig. 2. Ferric (Fe^{3+}) ions reducing capacity of compounds 3,4(a-d).



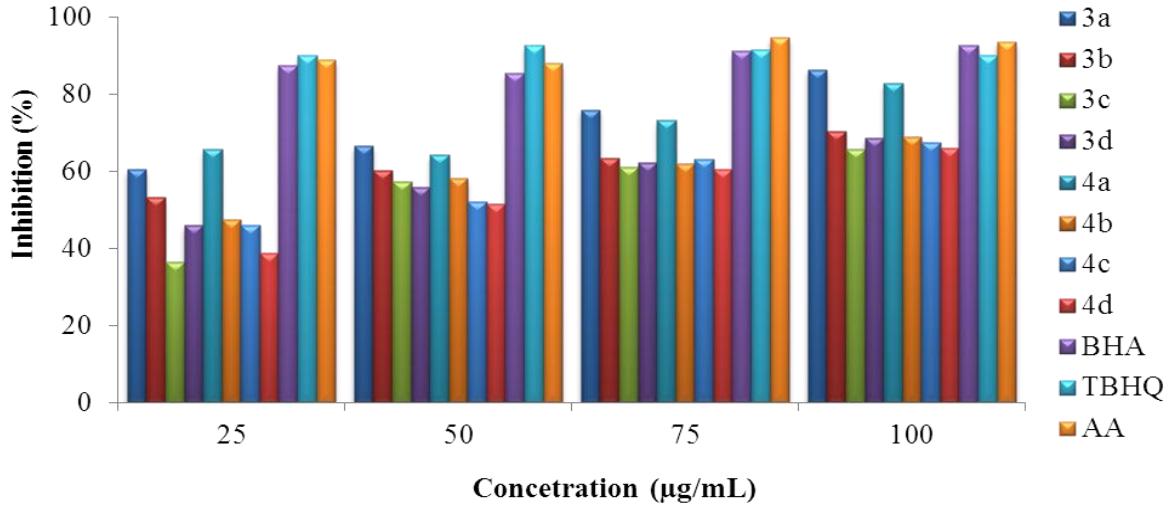
3.4. Ferrous (Fe^{2+}) Metal Ion Chelating Activity

The chelating activity of ferrous ions by synthesized compounds 3,4(a-d) was estimated by following Dinis method[21]. The test samples (25, 50, 75 and 100 µg/mL) in ethanolic solution (0.4 mL) were added to a solution of $FeCl_2$ (0.05 mL, 2 mM). The reaction was initiated by the addition of ferrozine (0.2 mL, 5 mM) and the total volume was adjusted to 4 mL with ethanol. Ferozine reacted with the divalent iron form stable magenta complex species that were very soluble in water. The mixture was shaken vigorously and kept at room temperature for 10 min. Then the absorbance of the solution was measured spectrophotometrically at λ 562 nm. All test analyses were run in triplicate and averaged. The percentage of inhibition of the ferrozine Fe^{2+} complex formations was calculated using the formula:

Ferrous ion chelating effect (%) = [(Ac-As/Ac)] X100.

Where, Ac is the absorbance of control and As is the absorbance of test sample or standards. Compounds 3a, 4a and 4c showed good metal chelating activity (75.24 and 73.18 % respectively) at 75 µg/ml concentration, whereas 3a, and 4a exhibited promising metal chelating activity (86.84 and 82.54 %) at 100 µg/ml concentration. The results are shown in the fig. 3.

Fig. 3. Metal chelating activity of compounds 3,4(a-d).



CONCLUSION

It may be concluded that the compounds having electron withdrawing and donating property showed more potent antimicrobial and antioxidant activities. Compounds bearing chloro substitution on indole nucules exhibited significant antimicrobial and antioxidant activities. Among the synthesized compound, 4a was found to be most active against all the microorganisms tested and also exhibited promising RSA and 3a showed metal chelaters. 4c showed FRAP suggesting that the presence of methoxyl substituent responsible for activities among the synthesized compounds.

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REFERENCES

1. Williams RR, Cline JK, (synthesis of vitamin B_1). J Am Chem Soc, 1936; 58(8): 1504-05.
2. Reidlinger CD, worczak R, Fabian WMF, Junek H, (Structure-Color Correlations of Penta- and Heptamethines. Syntheses with Nitriles XCIV", Dyes Pigments), 1994; 24: 185-204.

3. Hardtman GE, Otto H, U. S. Pat. 366369; Chem Abstr, 1972; **77**: 52313.
4. Brown DJ, The pyrimidines, Suppl II, Edited by Weissberger A, Taylor CE., The Chemistry of Heterocyclic Compounds (John Wiley Interscience, New York). 1985.
5. Brown DJ, pyrimidines, edited by Katritzky AR, Rees CW, Comprehensive Heterocyclic chemistry, (Pergamon Press, Oxford), 1984; 3: 57.
6. Vishnu, J. Ram, (Synthesis of Pyrimidines and Fused Pyrimidines). J Prakt Chemie Band, 1989; 331**.**
7. Misra U, Hitkari A, Saxena AK, Gurtu S, Shanker K, (Biologically active indolylmethyl-1,3,4-oxadiazoles, 1,3,4-thiadiazoles, 4H-1,3,4-triazoles and 1,2,4-triazines). Euro J Med Chem, 1996; 31(7-8): 629-634.
8. Rani Preeti, Srivastava VK, Ashok Kumar, (Synthesis and anti-inflammatory activity of heterocyclic indole derivatives). Euro J Med Chem, 2004**;** 39(5): 449-452.
9. El-Gendy Adel, Abdou Naida A, Sarhan El-Taher Z, El-Banna Hosney A, (Synthesis and biological activity of some new spio-[indoline-3,2′-thiazolidine]-2,4,-diones). J Pharm Sci, 1993; 7: 99-103.
10. Dandia A, Sehgal V, Singh P, (Synthesis of fluorine containing 2-aryl-3-pyrazolyl/pyranyl/ isoxazolinyl indole derivatives as antifungal and antibacterial agents). Indian J Chem, 1993; 32B: 1288-1291.
11. Kalgutkar AS, Crews BC, Sam Saleh, Prudhomnae D, Marnett L, (Indolyl esters and amides related to indomethacin are selective COX-2 inhibitors). J Bioorg Med Chem, 2005; 13(24): 6810-6822.
12. Sureyya Olgen, Dogu Nebioglu, (Synthesis and biological evaluation of N-substituted indole esters as inhibitors of cyclo-oxygenase-2 (COX-2)). I L Farmaco, 2002; 57(8):677.
13. Leneva IA, Fadeeva NI, Fedykina IT, Abstract 187, 7th International Conference on Antiviral Research, 1994.
14. Papesch V, Schroeder EF, (Synthesis of 1-mono- and 1,3-disubstituted 6-aminouracils. diruetic activity). J Org Chem, 1951; 16:1879-1890.
15. Blocke FF, Godt HC, (Reactions of 1, 3 -dimethyl-5, 6- diaminoluracil). J Am Chem Soc, 1954; 76: 2798-2800.
16. Hiremath SP, Biradar JS, Purohit M G, (A new routeto indolo [3, 2-b]isoquinolines). Indian. J Chem B, 1982; 21: 249-253.
17. Indian pharmacopoeia, Appendix IV, Government of India New Delhi, 3rd Ed. 1985; 90.

18. Hatano T, Kagawa H, Yasuhara T, Okuda T, (Two new flavonoids and other constituents in licorice root: their relative astringency and radical scavenging effects). Chem &Pharm. Bull, 1988; (36)6: 2090-2097,
19. Oyaizu M, (Studies on products of the browning reaction. Antioxidative activities of browning reactionproducts prepared fromglucosamine). Jap J Nutr, 1986; 44(6): 307-315.
20. Strlic M, Radovic T, Kolar J, Pihlar B, (Anti- andprooxidative properties of gallic acid in fenton-type systems). J Agr & Food Chem, 2002; 50(22): 6313-6317.
21. Dinis TCP, Madeira VMC, Almeida LM, (Action of phenolic derivatives (acetaminophen, salicylate, and 5-aminosalicylate as inhibitors of membrane lipid peroxidation and as peroxyl radical scavengers). Arch Biochem & Biophys, 1994; 315(1): 161-169.