

SYNTHESIS, UV-VIS, IR SPECTRAL AND ANTIBACTERIAL ANALYSIS OF 5-ARYLIDENE BARBITURIC ACID DERIVATIVES AND THEIR METAL COMPLEXES

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ABSTRACT: Barbituric acid is the paternal compound of barbiturate medications, while barbituric acid pharmacologically is inactive. Adolf von Baeyer was the first one who produced these compounds and can be involved in Knoevenagel type condensation reaction. Barbituric acid used as a reactant to form a large class of barbiturate drugs which are used as hypnotics, sedatives, anaesthetics and as central nervous system. Due to applications of barbiturates, exploration of new focus for the synthesis of these compounds is axiomatic. Thus, we selected way of green chemistry followed by grinding method along with aryl aldehyde treating with barbituric acid to get products, further these derivatives have been treated with metal salts to examine their ligand-metal connections under reflux conditions, antibacterial properties demonstrated the future scopes of these metal complexes.

Keywords: *barbituric acid, aryl aldehyde, grinding, IR, UV-Vis spectroscopy.*

I. INTRODUCTION

Barbiturates are the subordinates of barbituric acid which acquired by the basic alteration of barbituric acid. The basic barbiturates can be gotten by the replacement at 1,3 and at fifth situation of barbituric acid (Figure 1.1). The different subsidiaries of barbituric acids can be ordered into 1, 3 di substituted barbiturates, 1, 3, 5 tri substituted barbiturates, 5,5'- disubstituted barbiturates and so on. Thiobarbituric acid is a subordinate of barbituric acid and is acquired by the substitution of oxygen molecule at C-2 of barbituric acid with Sulfur. Like barbiturates, thiobarbiturates have been acquired by the basic alteration of thiobarbituric acid at 1, 3 and fifth positions. The different utilitarian gatherings, for example, alkyl, aryl, alkenyl and so forth might be presented at first, third and at fifth situation of barbituric acid or thiobarbituric acid. The C-5 situation of barbituric acid/thiobarbituric acid contain profoundly acidic hydrogen atoms and can experience Knoevenagel buildup to give barbiturates and thiobarbiturates [1-2].

The natural amalgamation of Arylidene barbituric acids have built up significant thought for their likely pharmacological applications, for example, cell reinforcement [3] and anticancer[4] operators; inhibitors of methionine aminopeptidase-1 (MetAP-1),[5] urease[6] and mushroom tyrosinase:[7] and against non-alcoholic greasy liver infection (NAFLD)[8]. As a result of the nearness of a firmly spellbound exocyclic twofold security, they are likewise flexible antecedents of a wide assortment of atoms through responses with carbanions[9] and ordinary Lewis bases, for example, alkoxides,[10] amines,[11a,12] thiols,[13] water[14] and hydrogensulfite ion.[15] Moreover, the simple reducibility of the twofold bond[16] offers these mixes as reasonable competitors in the amalgamation of 5-monoalkylbarbiturates, for example, Uridine Phosphorylase (UrdPase) hindering 5-benzylbarbiturates,[17] unsymmetrical disulfides[18] and for the gentle oxidation of alcohols.[19]

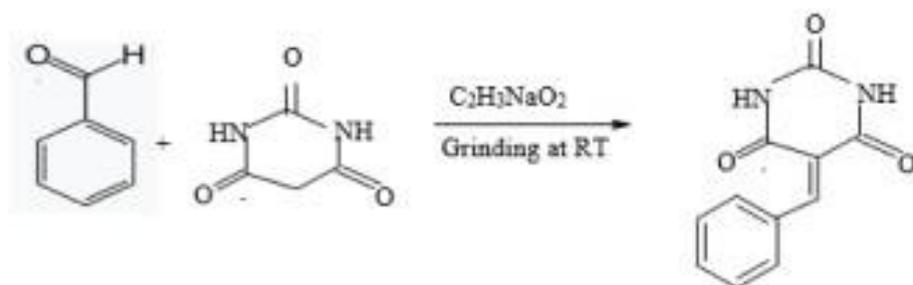
Sinn et al. revealed the precious stone structure of [Pd(en)barb] (H₂O)₄, arranged from an answer initially containing [enPd (H₂O)₂]SO₄, barbituric acid, and hydroxide particle in a 1:2:2 molar proportion. In the mind boggling Pd (II) structures bonds to both a deprotonated amide nitrogen and a deprotonated tetrahedral carbon.[20]

Some Mn(II), Zn(II), Cd(II), Co(II), Ni(II), Cu(II), Fe(III), Cr(III) edifices of barbituric acid have been integrated yet the sub-atomic structures of these buildings were not investigated.[21] The X-ray structure examination of nonpartisan Cu(II) complex, [Cu(Hbarb)₂(H₂O)₃], incorporated by the response of sodium barbiturate (NaHbarb) and CuSO₄ in water, shows that the Cu(II) particle, in the somewhat mutilated square-pyramidal geometry, is composed by two O atoms of two monodentate barbiturates and three O molecules of three water particles. By and large, the negative charge of free barbiturate anion (Hbarb⁻) is for the most part situated at carbon, which is fortified with H particles, while that of the present facilitated Hbarb⁻ was predominantly focused on one oxygen. This showed, during the time spent coordination, copper particles initiate movement of the negative charge from C to O; as such, one carbonyl gathering turns into a hydroxyl anion. This tautomerism is first merited model for a metal complex of Hbarb. The expansion of a methanol arrangement of H₂barb to the fourfold overabundance of PPh₃AuCl and sodium methoxide in methanol brought about the development of a few edifices by the progressive end of every one of the four hydrogen particles of 1.[22]

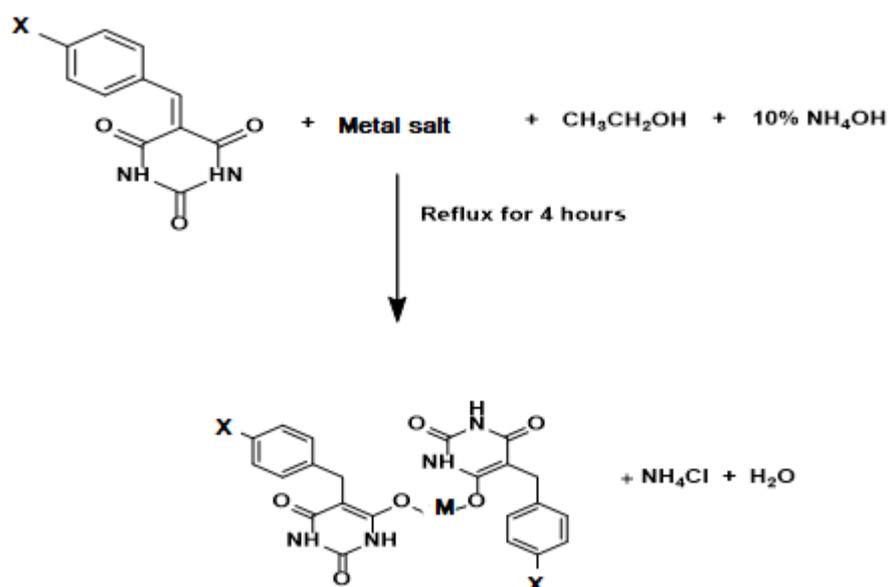
Reason for approaching green chemistry: In most of the organic experiments, it has been found that they produce high amounts of harmful and poisonous solvents. Eco-friendly reactions are the need of today's world. Reactions in an aqueous condition are definitely area of interest of many analysts and are the main viewpoints of green chemistry. Organic solvents are predictably used

in organic synthesis and in industrial processes on a huge amount. Less/no use of organic solvents can be resulted into reduce the generation of waste, which is a requirement of one of the values of green chemistry.

We have focused on these points and which make this process more suitable for preparation of Barbituric acid derivatives further to make enhancement of synthesized derivatives treated with Cu, Mn and Ni metal salts under reflux conditions.



General reaction for preparation of 5-Arylidene Barbituric acid



X= NO₂, Br, F, CH₃

General reaction for preparation of 5-Arylidene Barbituric acid and metal complex

II. MATERIALS AND METHOD

Study has been done that Synthesis 5-Arylidene Barbituric acid derivatives were prepared by reported method of simple grinding method [14]. Amongst many them, we used the best which is eco-friendly and solvent free; we got appropriate yield and which was easier. The method used for synthesis of 5-Arylidene Barbituric acid derivatives involves one pot synthesis phase.

To start with the experimentation part all the chemicals and solvents were used without any kind of alteration in them. Experiment part was done without any special conditions. To prepare 5-Arylidene Barbituric Acids aromatic aldehyde (25 mmol) was mixed with barbituric acid (25 mmol) and catalyst sodium acetate (25 mmol) after addition of all these chemicals were grinded at room temperature just one precaution was taken that this mixture was not supposed to absorb air moisture. To monitor the reaction TLC was performed with the help of solvent system- [N-hexane + Ethyl acetate + Ethanol]

III. RESULT AND DISCUSSION

Following were the aromatic aldehydes were used to prepare derivatives:

Table 1. Synthesized 5-Arylidene Barbituric acid derivatives

Compound code	IUPAC name
D1	5-(4-nitrobenzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione
D2	5-(4-bromobenzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione
D3	5-(4-fluorobenzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione
D4	5-(4-methylbenzylidene)pyrimidine-2,4,6(1H,3H,5H)-trione

5-Arylidene Barbituric acid derivatives form a coloured complex with metal salts in the presence of an ammonia solution. The solution is a transparent solution whereas the complex form is stable. The method can be used for determining the trace amounts of metal salts which is further proved by Beer's law that the complex obeys. In addition to this, the composition of manganese metal to 5-Arylidene Barbituric acid derivatives complex is established by adopting Job's method of continuous variation and mole ratio method. The composition of the metal to ligand ratio is found to be 1:2.

In the second part, we have synthesized metal complexes by reaction 5-Arylidene Barbituric acid derivative with Copper, Manganese and Nickel metal salts under reflux condition for 4 hours further kept them in oven to dry and washed with ethanol to recrystallize them.

Spectral results:

The UV spectrum of all 5-Arylidene Barbituric acid derivatives in DMSO. The UV absorption and assignments related to the ligand D1 to D4 listed in Table 3.6. The Derivative 1 possessed two bands $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ at wavelength 211,250 and 312 respectively, Derivative 2 possessed two bands $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ at wavelength 220, 280 and 325 respectively, in Derivative 3 showed only one band $\pi \rightarrow \pi^*$ at 225, 237, 270, Derivative 4 possessed two bands $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ at wavelength 220, 283 and 335 respectively whereas ;The UV spectrum of all metal complexes of 5-Arylidene Barbituric acid derivatives done with the help of DMSO. The UV absorption and assignments related to the Copper, Manganese and Nickel metal complexes D1 to D4 listed in Table 3.36. The metal complexes exhibited two absorption bands which may be attributed to $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ excitation of electrons and one absorption band at higher wavelength and higher intensity because of the ($d \rightarrow d$) transition of metal and $\pi \rightarrow \pi^*$ or $n \rightarrow \pi^*$ transition of ligands with higher intensity than their corresponding ligands. This extra absorption band and higher intensity of absorbance reveals that the ligands were coordinated to metals.

Table 2. The UV-Visible Spectral data synthesized metal complexes for D1-D4

Compound name	Band Position (nm)	Band assignment
D1Cu	237	$\pi \rightarrow \pi^*$
	350	$n \rightarrow \pi^*$
	423, 614	$d \rightarrow d$
D2Cu	247	$\pi \rightarrow \pi^*$
	353	$n \rightarrow \pi^*$
	442,529, 611	$d \rightarrow d$
D3Cu	229	$\pi \rightarrow \pi^*$
	339	$n \rightarrow \pi^*$
	456, 659	$d \rightarrow d$
D4Cu	319	$n \rightarrow \pi^*$
	431, 576	$d \rightarrow d$
D1Mn	251, 293	$\pi \rightarrow \pi^*$
	429	$d \rightarrow d$
D2Mn	219, 259	$\pi \rightarrow \pi^*$
	403, 471	$d \rightarrow d$

D3Mn	224, 261	$\pi \rightarrow \pi^*$
	406	$d \rightarrow d$
D4Mn	227, 287	$\pi \rightarrow \pi^*$
	416	$d \rightarrow d$
D1Ni	243	$\pi \rightarrow \pi^*$
	350	$n \rightarrow \pi^*$
	425, 659	$d \rightarrow d$
D2Ni	223	$\pi \rightarrow \pi^*$
	357	$n \rightarrow \pi^*$
	429, 559, 676	$d \rightarrow d$
D3Ni	235, 255	$\pi \rightarrow \pi^*$
	439, 576, 700, 710	$d \rightarrow d$
D4Ni	251	$\pi \rightarrow \pi^*$
	362	$n \rightarrow \pi^*$
	467, 550, 677	$d \rightarrow d$

IR spectral results:

Derivative1- In the IR spectrum (KBr disc) the relatively weak bands absorption in the frequency range 3117–2958 cm⁻¹ are recognized to the $\nu(\text{NH})$ vibrations of the amine and C–H stretching vibrations of the alkyl group of the Derivative. $\nu(\text{C}=\text{N})$ peaks are found around 1615 cm⁻¹; For the three carbonyl groups $\nu(\text{CO})$ bands between 1531 and 1413 cm⁻¹ and one weak band at 1782 cm⁻¹ were observed. The bands with strong intensity between 1345 and 1240 cm⁻¹ correspond to the C-N+ C-O twist vibrations.

Derivative2- In the IR spectrum (KBr disc) the relatively strong bands absorption in the frequency range 3428–3032 cm⁻¹ are recognized to the $\nu(\text{NH})$ vibrations of the amine and C–H stretching vibrations of the alkyl group of the Derivative. $\nu(\text{C}=\text{N})$ peaks are found around 1619 cm⁻¹; For the three carbonyl groups $\nu(\text{CO})$ bands between 1517 and 1345 cm⁻¹ and one weak band at 1166 cm⁻¹ were observed. The bands with strong intensity between 1085 and 865 cm⁻¹ correspond to the C-N+ C-O twist vibrations.

Derivative3- In the IR spectrum (KBr disc) the relatively band absorption in the frequency range 3411-2975 cm⁻¹ are recognized to the $\nu(\text{NH})$ vibrations of the amine and C–H stretching vibrations of the alkyl group of the Derivative. $\nu(\text{C}=\text{N})$ peaks are found around 1704 cm⁻¹; For the three carbonyl groups $\nu(\text{CO})$ bands between 1692 and 1646 cm⁻¹ and one weak band at 1575 cm⁻¹ were observed. The bands with strong intensity between 1429 and 1200 cm⁻¹ correspond to the C-N+C-O twist vibrations.

Derivative4- In the IR spectrum (KBr disc) the relatively strong bands absorption in the frequency range 3486–3091 cm⁻¹ are recognized to the $\nu(\text{NH})$ vibrations of the amine and C–H stretching vibrations of the alkyl group of the Derivative. $\nu(\text{C}=\text{N})$ peaks are found around 1891 cm⁻¹; For the three carbonyl groups $\nu(\text{CO})$ bands between 1595 and 1434 cm⁻¹ and one weak band at 1382 cm⁻¹ were observed. The bands with strong intensity between 1282 and 1143 cm⁻¹ correspond to the C-N+ C-O twist vibrations.

The IR spectrum of D1Cu (KBr disc) shows six strong to medium intensity absorption bands at 1878, 1871, 1725 and 1631, 1575, 1492 cm⁻¹ for the six carbonyl groups. The spectrum also has resonances at 3391- 3179 cm⁻¹, assigned to $\nu(\text{N}-\text{H})$. Moreover, typical $\nu(\text{C}-\text{H})$ vibrations are observed in the range of 3012–2292 and 1412-1273 cm⁻¹. The strong band at 431 cm⁻¹ are indicative of Cu-D1 ligation in the complexes.

The IR spectrum of D2Cu (KBr disc) shows absorption bands between 1885 and 1509 cm⁻¹ for the carbonyl groups. The spectrum also has resonances at 3081-2987 cm⁻¹, assigned to $\nu(\text{N}-\text{H})$. Moreover, typical $\nu(\text{C}-\text{H})$ vibrations are observed in the range of 2455–2062 and 1419-1314 cm⁻¹. The strong bands at 486-420 cm⁻¹ are indicative of Cu-D2 ligation in the complexes.

The IR spectrum of D3Cu (KBr disc) shows strong to medium intensity absorption bands between 1606 and 1415 cm⁻¹ for the six carbonyl groups. The spectrum also has resonances at 3440- 2957 cm⁻¹, assigned to $\nu(\text{N}-\text{H})$. Moreover, typical $\nu(\text{C}-\text{H})$ vibrations are observed in the range of 2918–2897 and 1363-1196 cm⁻¹. The strong band at 417 cm⁻¹ is indicative of Cu-D3 ligation in the complexes.

The IR spectrum of D4Cu (KBr disc) shows absorption bands at 1735, 1540, 1506 and 1440, 1408 cm⁻¹ for carbonyl groups. The spectrum also has resonances at 3426 and 3064 cm⁻¹, assigned to $\nu(\text{N}-\text{H})$. Moreover, typical $\nu(\text{C}-\text{H})$ vibrations are observed in the range of 2758 and 1286-1200 cm⁻¹. The strong bands at 455 and 431 cm⁻¹ are indicative of Cu-D4 ligation in the complexes.

The IR spectrum of D1Mn (KBr disc) shows six strong to medium intensity absorption bands at 1843, 1600, 1520 and 1440 cm^{-1} for carbonyl groups. The spectrum also has resonances at 3453- 3373 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 3081–2563 and 1387-1224 cm^{-1} . The strong bands at 497 and 452 cm^{-1} are indicative of Mn-D1 ligation in the complexes.

The IR spectrum of D2Mn (KBr disc) shows six strong to medium intensity absorption bands at 1864, 1794, 1721 and 1632, 1586, 1446 cm^{-1} for the six carbonyl groups. The spectrum also has resonances at 3450- 3366 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 2918–2615 and 1377-1126 cm^{-1} . The strong band at 493 and 441 cm^{-1} are indicative of Mn-D2 ligation in the complexes.

The IR spectrum of D3Mn (KBr disc) shows strong to medium intensity absorption bands at 1920, 1822, 1620 and 1523, 1474, 1443 cm^{-1} for the six carbonyl groups. The spectrum also has resonances at 3446- 3370 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 1297-1165 cm^{-1} . The strong band at 424 cm^{-1} is indicative of Mn-D3 ligation in the complexes.

The IR spectrum of D4Mn (KBr disc) shows strong to medium intensity absorption bands at 1673, 1620, 1582 and 1478, 1422, 1346 cm^{-1} for the six carbonyl groups. The spectrum also has resonances at 3408- 3380 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 2633 and 1158-1040 cm^{-1} . The strong bands at 448 and 413 cm^{-1} are indicative of Mn-D4 ligation in the complexes.

The IR spectrum of D1Ni (KBr disc) shows six strong to medium intensity absorption bands at 1857, 1627, 1513 and 1426, 1314, 1269 cm^{-1} for the six carbonyl groups. The spectrum also has resonances at 3443- 360 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 1217-1109 cm^{-1} . The strong bands at 455 cm^{-1} is indicative of Ni-D1 ligation in the complexes.

The IR spectrum of D2Ni (KBr disc) shows strong to medium intensity absorption bands at 1627, 1613, 1561 and 1509, 1460, 1419 cm^{-1} for the six carbonyl groups. The spectrum also has resonances at 3373- 3040 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 2452–2121 and 1332-1113 cm^{-1} . The strong bands at 438 and 406 cm^{-1} are indicative of Ni-D2 ligation in the complexes.

The IR spectrum of D3Ni (KBr disc) shows strong to medium intensity absorption bands at 1878, 1735, 1606, 1579, 1460 and 1440 cm^{-1} for carbonyl groups. The spectrum also has resonances at 3064- 2918 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 2733–2358 and 1262-1200 cm^{-1} . The strong bands at 462 and 431 cm^{-1} are indicative of Ni-D3 ligation in the complexes.

The IR spectrum of D4Ni (KBr disc) shows six strong to medium intensity absorption bands at 1902, 1735, 1704 and 1568, 1516, 1446 cm^{-1} for carbonyl groups. The spectrum also has resonances at 3443- 3085 cm^{-1} , assigned to $\nu(\text{N-H})$. Moreover, typical $\nu(\text{C-H})$ vibrations are observed in the range of 1293- 1161 cm^{-1} . The strong band at 455 and 424 cm^{-1} are indicative of Ni-D4 ligation in the complexes.

Antimicrobial studies:

Antibacterial activity of the synthesized 5-Arylidene Barbituric acid derivatives ligands and their corresponding Cu(II), Mn(II), Ni(II) complexes were examined against two Gram- negative (*Escherichia coli*, *Pseudomonas aeruginosa*) and two Gram- positive (*Bacillus subtilis* and *Streptococcus aureus*) bacterial strains. The antimicrobial activity was performed by agar diffusion method at the concentration level of 100 $\mu\text{g/ml}$.

Ciprofloxacin was used as standard drug at a concentration level of 100 $\mu\text{g/ml}$. Nutrient agar was used as culture media for antibacterial activity.

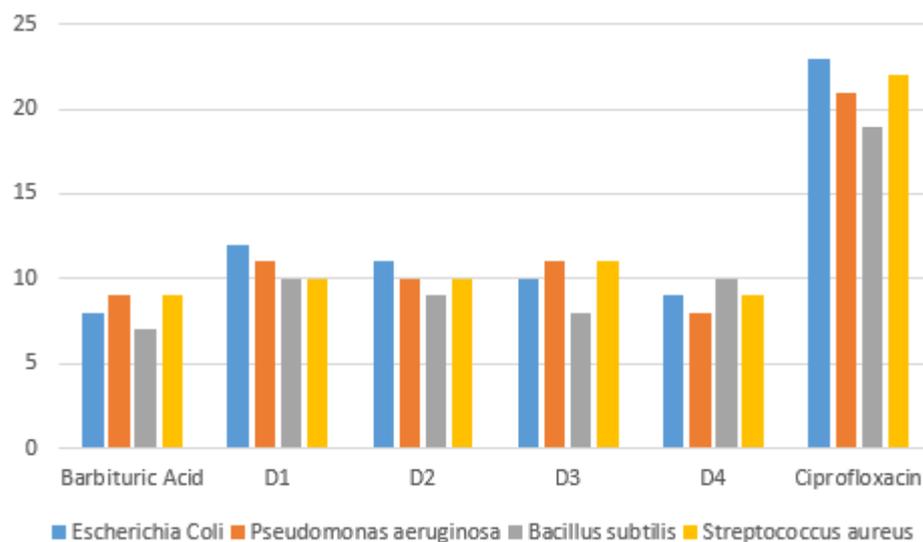


Figure 1. Antibacterial activity of derivatives of D1-D4

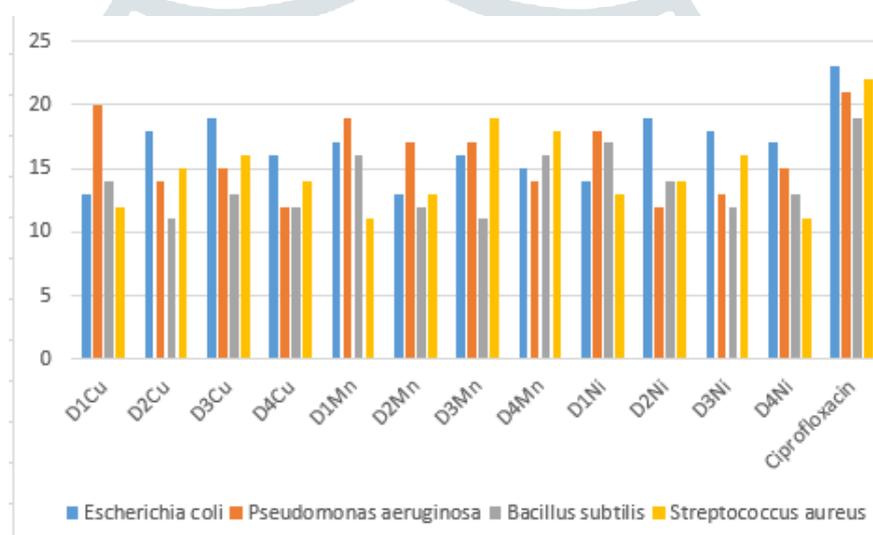


Figure 2. Antibacterial activity of synthesized metal complexes of D1-D4

IV. CONCLUSION

In conclusion, 5-Arylidene Barbituric acid derivatives and their Cu, Mn, Ni complexes were synthesized and their chemical analysis was carried out to identify derivatives (ligand) - metal ratio of these complexes in solution. Further study on this approach could cover a mode for the development of 5-Arylidene Barbituric acid derivatives-metal complex based antibacterial agent; it was found that metal showed significant antimicrobial activity than that of derivatives but still market available standards are having better growth than our synthesized compounds which concludes these compounds further can be studied in order to increase their therapeutic properties.

V. ACKNOWLEDGMENT

Shreekanth Naik and Pooja Prajapati and Komal Jarhad added to the design and operation of the research, Dr. Sushama Ambadekar and Dr. Gayatri Barabde to the analysis of the results and helped to the formatting of the manuscript. All authors had discussed the methodology and results and contributed to the final manuscript.

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