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ANTIBACTERIAL STUDIES OF THE POLYMERIC PHENOLIC SCHIFF BASES CONTAINING AMINOTHIAZOLE MOIETY

Debasis Mohanty*[1]

[1*]Department of Chemistry, Dhenkanal (Auto) College, Dhenkanal, Odisha, India.

ABSTRACT

Three new chelating resins *o*-hydroxybenzaldehyde-2-aminothiazole-formaldehyde (*o*-HB-AT-HCHO), *o*-hydroxybenzaldehyde-6-methyl - 2 - aminobenzothiazole-formaldehyde (*o* – HB – MABT - HCHO), and *o*-hydroxybenzaldehyde-6-chloro - 2 - aminobenzothiazole-formaldehyde (*o* – HB – CABT - HCHO) having heterocyclic ring systems and multiple functional groups are synthesized by condensing the Schiff bases of *o*- hydroxybenzaldehyde- 2- aminothiazole (*o*- HB - AT), *o*-hydroxybenzaldehyde – 2 – amino - 6-methylbenzothiazole (*o* – HB - MABT), and *o*-hydroxybenzaldehyde-2-amino-6-chlorobenzothiazole (*o*-HB-CABT) with formaldehyde. All the resins were employed to study the activity against the pathogenic bacteria *Escherichia coli* and *Staphylococcus aureus*. It is found that, all the resins show antibacterial activity against the tested bacterial species and the antibacterial activity of *o*-HB-MABT-HCHO resin is highest among the tested resins.

KEYWORDS

Schiff base chelating resins, Aminothiazole, Antibacterial activity, Polymeric resins and heterocyclic resins.

Author for Correspondence:

Debasis Mohanty,

Department of Chemistry,

Dhenkanal (Auto) College,

Dhenkanal, Odisha, India.

Email: maildebasismohanty@gmail.com

INTRODUCTION

Due to the strong aromaticity of the ring system, greater *in vivo* stability[1] and Structural similarity to the imidazolyl moieties of the histidyl residue present in proteins[2] thiazole, substituted thiazoles and thiadiazole possess very interesting biological activity. Among thiazoles 2-aminothiazoles are very interesting heterocyclic amines with odor similar to pyridine, soluble in water, alcohol and ether. Many sulphur drugs, biocides, fungicides, dyes and chemical reaction accelerators are synthesized from 2-aminothiazoles. These are also act as very good

ligands and provide many potential binding sites for complexation of diverse metal ions like Cu (II), Co(II), Ni(II), or Zn(II) among others with well established biological roles[3-9]. It is also a well known fact that aminothiazoles and aminothiazole Schiff bases have very good antibacterial, antiviral and anti fungal property and upon complexation with metal ions its antibacterial antiviral and antifungal properties increases many folds[10-14]. Schiff-bases of amino thiazoles and their transition metal complexes play a significant role in pharmaceuticals chemistry along with co-ordination chemistry[15-18]. A brief review of literature of antimicrobial activities of aminothiazole, thiazole, substituted thiazoles and thiadiazole is given below.

Pattern and co workers[19] studied the antibacterial activity and antifungal activity of chloro and methoxy substituted 2-aminohiazole against *Escherichia coli* and *Staphylococcus aureus* and *Candida albicans* and *Aspergillus niger* respectively and compared their antibacterial and antifungal activities against some known chemotherapeutic agent like norfloxacin, grieseofulvin and DMF. They found that the substituted thiazoles have very good antibacterial and antifungal activity against all the tested samples whereas chemotherapeutic agents are active against some specific samples. Sherman and Dicken[20] have reported a series of 2-amino-4(5-nitro- 2-furyl) thiazole and their chloro, hydroxyl and methoxy derivatives. Pronounced activities are observed against *Escherichia coli*, *Salmonella* and *Staphylococcus aureus*. 2- Aminothiazole. R. V. R. Mekala et al.[21] synthesized and studied antibacterial activity of a series of phenyl-(6*H*-thiazolo) and benzooxazole-2-yl)-amines. They concluded that the antimicrobial activity of these compounds vary with introduction or elimination of a specific group. Many more such evidences are presented in the review the antibacterial activities of thiazoles, substituted thiazoles and their metal complexes[22].

The Schiff bases having multiple coordination sites are known to form complexes with transition metal ion readily[23-25]. Present in a polymeric matrix they are expected to show affinity selectivity towards the metal ions at an appropriate pH. This simple idea inspired our research group to synthesize a number of chelating resins containing Schiff base moiety and study their metal ion uptake behavior[26-31]. Literature studies reveal that metal ion uptake behavior of resins containing Schiff bases of heterocyclic compounds especially amino thiazole Schiff bases are yet to be studied.

Three new chelating resins *o*-hydroxybenzaldehyde-2-aminothiazole-formaldehyde (*o*-HB-AT-HCHO), *o*-hydroxybenzaldehyde-6-methyl-2-amino benzo thiazole - formaldehyde (*o*-HB-MABT-HCHO), and *o*-hydroxybenzaldehyde-6-chloro-2-aminobenzothiazole-formaldehyde (*o*-HB-CABT-HCHO) containing aminothiazole moiety, which have multiple functional groups are synthesized by condensing the Schiff bases of *o*-hydroxybenzaldehyde-2-aminothiazole (*o*-HB-AT), *o*-hydroxybenzaldehyde-2-amino-6 methyl benzo thiazole (*o*-HB-MABT), and *o*-hydroxybenzaldehyde-2-amino-6-chloro benzo thiazole (*o*-HB-CABT) with formaldehyde. Thermal and analytical characterization techniques like FTIR, ^{1}HNMR, TGA, and DSC studies were adopted to ascertain the structural features of these resins. The idea is to use the resins simultaneously both for separation of heavy metal cations like Cu^{2+}, Ni^{2+}, UO_2^{2+}, Co^{2+}, $Fe^{3+}$and toxic anions like AsO_4^{3-} in drinking water. The synthesis, characterization and metal ion uptake studies and arsenate uptake studies are presented elsewhere.

As aminothiazoles show good antibacterial activity, so to increase the dimension of application of the resin it is thought that to study the antibacterial activity of the resin. Although the literature is full with antibacterial study of aminothiazole compounds and their Sciff bases but there is no report of antibacterial activity of thiazole compounds present in a resin matrix. In this paper antibacterial activity of the above three resins against pathogenic bacteria like *Escherichia coli* and *Staphylococcus aureus* is reported.

The study of antibacterial activity of these resins is aiming to increase the dimension of application of these resins in many fold and these resins can be effective in the purification of drinking waters in

rural regions which are contaminated with heavy metals and various pathogenic bacteria.

EXPERIMENTAL

MATERIAL

The starting materials such as, 2-aminothiazole (Merck, Germany), 2-amino-6-methyl benozo thiazole, and 2-amino-6-chlorobenzothiazole were of Aldrich (USA). The *o*-hydroxybenzaldehyde, sulphate and nitrate salts of copper, nickel, uranyl and iron (Merck/BDH, India, AnalR grade) were used as received. Doubly distilled deionised water was used for the preparation of the solutions. The agar used for preparation of agar plate for antibacterial study was MacConkey agar, Merck, Germany.

RESULTS AND DISCUSSION

Antibacterial studies

The synthesized chelating resins *o*-HB-AT-HCHO, *o*-HB-MABT-HCHO, *o*-HB-CABT-HCHO (Figure No.1a - 1c), were screened for the test of the antibacterial activity against the pathogenic bacterial strains of *Escherichia coli* and *Staphylococcus aureus*. For the study paper disc diffusion method was adopted as described by Chohan and coworkers[10,13,32].

Preparation of the discs

The chelating resins (30 µg) in DMF (0.01 mL) were applied on a paper disc (prepared from blotting paper 5 mm diameter) with help of the micropipette. The discs were put in a vacuum incubator for 48 h at 37ºC and then applied on the bacteria grown agar plates.

Preparation of Agar plates

For the preparation of the agar plate for bacterial species, 12g of agar was soaked in 200 ml of distilled water for 15 minutes and then boiled in water bath until the agar was completely dissolved. This was autoclaved for 15 minutes at 120ºC, then poured into sterilized Petri dishes, and stored at a temperature of 40ºC for inoculation.

Inoculation

Platinum wire loop was used for inoculation. Platinum wire loop was made red hot in a flame, cooled and used for the application of bacterial strains.

Application of the discs

The paper discs were applied to the inoculated agar plates with the help of sterilized forceps. After the application of the discs, they were incubated at 37ºC for 24 h. The diameter of the inhibition zone was measured.

Antibacterial studies

The chelating resins, *o*- HB-MABT- HCHO, *o*- HB-AT- HCHO, *o*- HB-CABT- HCHO were evaluated for the antibacterial activity against the bacterial strains of *Escherichia coli* and *Staphylococcus aureus* (Table No.1a and b). Each chelating resins were individually exhibited varying degrees of inhibitory effects on the growth of the tested samples. It can be seen that the antibacterial activity of *o*-HB-MABT- HCHO is nearly 60-70 % against the tested bacterial strains. The order of activity of the resins is *o*-HB-MABT- HCHO > *o*- HB-AT-HCHO > *o*- HB-CABT- HCHO. Stability and solubility play a great role in the anti-bacterial activity of a material. During the condensation with formaldehyde, because of the +I effect of the -CH_3 group in *o*- HB-MABT Schiff bases reduces the cross linking ability. Thus *o*-HB-MABT- HCHO resin is less cross-linked than the other resins facilitating the solubility. Accessibility is also another factor which promotes the efficiency of the antibacterial activities. If cross-linking is less, the accessibility of the material to the bacteria is more. Chohan *et al*. have suggested that the accessibility, solubility, and conductivity are main factors behind the activity of materials against the bacterial species[10].

Table No.1 (a): Antibacterial activity of microbial species *Escherichia coli*

S.No	Resins	% of inhibition	Inhibition zone diameter (mm)
1	*o*-HB-MABT-HCHO	61-70	13.5-15.5
2	*o*-HB-AT-HCHO	59-68	13.0-15.0
3	*o*-HB-CABT-HCHO	52-59	11.5-13.0

Table No.1 (b): Antibacterial activity of microbial species *Staphylococcus aureus*

S.No	Resins	% of inhibition	Inhibition zone diameter (mm)
1	*o*-HB-MABT-HCHO	59-68	13.0-15.0
2	*o*-HB-AT-HCHO	57-64	12.5-14.0
3	*o*-HB-CABT-HCHO	45-57	10.0-12.5

*Percent inhibition values are relative to inhibition zone (22mm) of standard antibacterial (sulfadiazine, sulfathiazole), considered as 100% inhibition, and tested under the same conditions as the new compounds reported here.

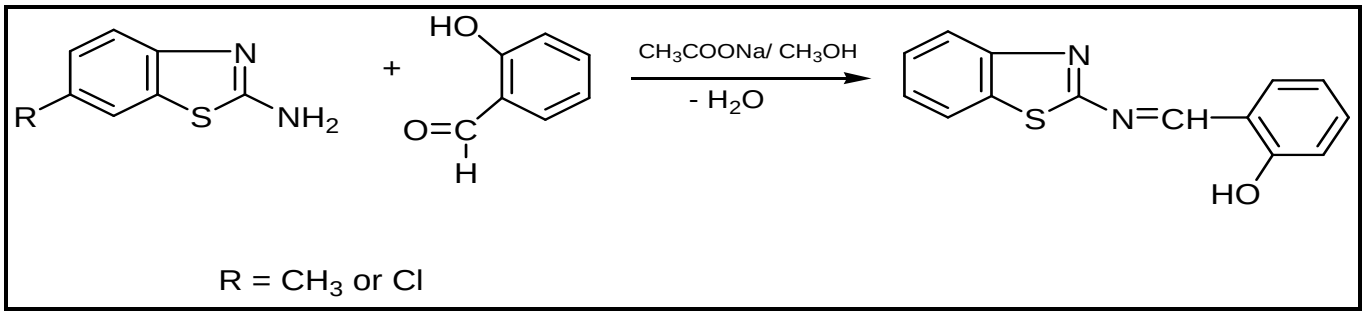

Figure No.1 (a): Reaction scheme for synthesis of Schiff base monomer

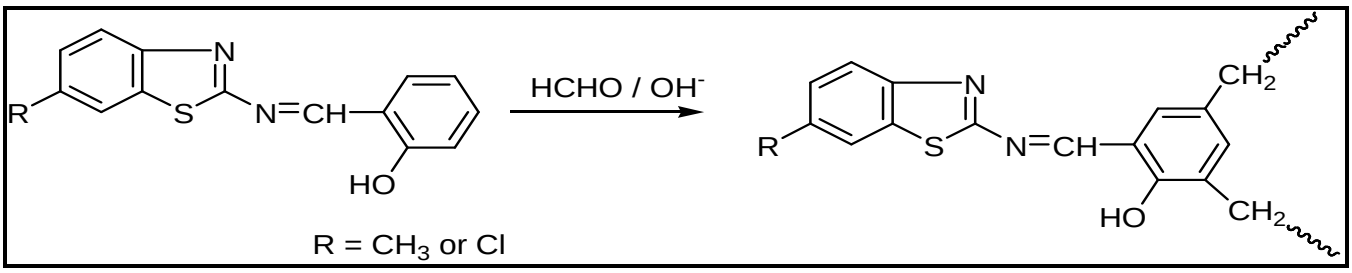

Figure No.1 (b): Reaction scheme for synthesis of resins

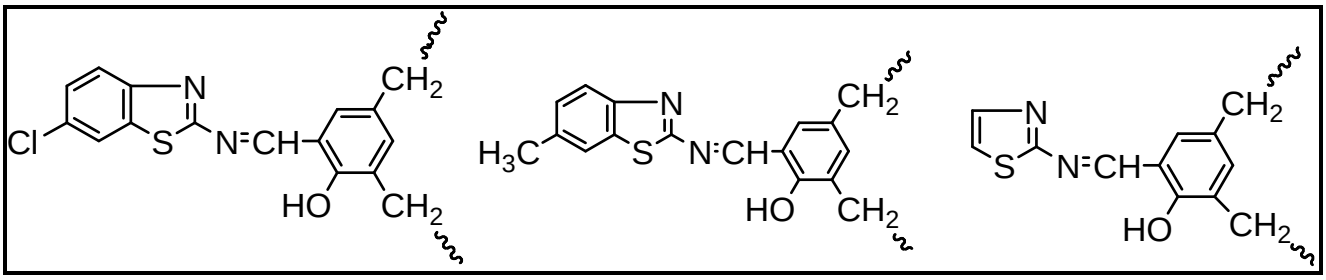

Figure No.1 (c): Structure of the, *o*-HB-AT-HCHO, *o*-HB-CABT-HCHO and *o*-HB-MABT-HCHO resins

CONCLUSION

Phenolic Schiff bases containing aminothiazole moiety were synthesized. Condensation polymerization of these multifunctional phenolic Schiff bases with formaldehyde was successfully carried out. In attempting to draw a conclusion about the structural features of such indefinite phenol-formaldehyde-type polymers, a number of routine characterization techniques such as FTIR, ^{1}HNMR, TG-DTG, and DSC studies were adopted. The resins were tested for the antibacterial activity against some common bacterial strain like *Escherichia coli* and *Staphylococcus aureus*. They show very good antibacterial activity against bacterial strain like *Escherichia coli* and *Staphylococcus aureus*. Thus in commensuration with the experimental observations, the newly synthesized resins has shown suitable application as a protector towards the activity of pathogenic bacteria present in drinking water in rural areas.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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