**Chapter 3 Antibacterial activity: A structure-reactivity study.**

**3.1 Introduction**

Different methods have been used for the synthesis of 1,3-indandione derivatives with substitution at position 2. Previous studyreported phenylation of 1,3-indandione with diaryliodonium salts and α-alkenylation of β-dicarbonyl compounds with alkenyl triarylbismuthonium salts [1,2]. The Friedel-Crafts methods were also reported for the derivatization of 1,3-indandione at position 2 [3].In addition to these conventional methods, the electrochemical synthesis has also been used for preparation of indandione derivatives with catechol or 2,3-dimethylhydroquinone ring on their position 2 [4-6].

Studies of substituent effects on zone of inhibition against the growth of microorganisms in various substituted N-(1-piperidino benzyl) nicotinamide[7] and substituted N-(1-piperidinobenzyl)acetamide and substituted N-(1-morpholinobenzyl)acetamide[8] have been reported. The literature reveals that there is a little work done on the antimicrobial study of activated olefinic compounds. As a part of our interest in the structure-reactivity study, we have synthesized 2-benzylidene-1,3-indandiones and studied the antibacterial activity to find out the substituent effect on 2-benzylidene-1,3-indandione.

The barbituric acid derivatives are clinically useful. By substituting two protons in C-5 position during barbiturate synthesis, acidity of the whole molecule can be reduced and an unsaturated group can be added for the later incorporation of para hydrogen into the molecule [1]. Benzylidenebarbituric acids as potential organic oxidizers [2] are applied for preparing pyrimidine derivatives [3]. The benzylidene barbituric acids are the important building blocks in synthesizing pyrazolo [3,4-d]pyrimidines and pyrido[2,3-d]pyrimidines [4,5]. They also have a broad range of biological activities Some barbituric acid derivatives have been widely used as sedative, hypnotic, anticonvulsant, antispasmodic, as well as local anesthetic agents [6]. Benzylidenebarbituric acids are useful as potential organic oxidizers, for the preparation of oxadeazaflavines [7] and for the unsymmetrical synthesis of disulfides [8]. Some of them have been recently studied as nonlinear optical materials [9]. Several 5-benzylidenebarbituric acids were prepared in the absence of solvent by the influence of infrared irradiation. These molecules were obtained by means of a Knoevenagel condensation between barbituric acid and various benzaldehydes [10]. In continuation of our research interest in the structure-reactivity study, we have synthesized substituted 5-benzylidenebarbituric acids and studied the antibacterial activity to find out the substituent effect on 5-benzylidenebarbituric acid.

**3.2 Results and Discussion**

**3.2.1 (A)** **Antibacterial activity of 2-benzylidene-1,3-indandiones: A structure-reactivity**

**study.**

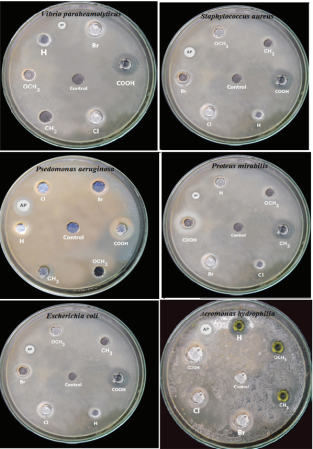
In this study a gram-positive bacteria (*Staphylococcus aureus*) and five gram-negative bacteria (*Aeromonas hydrophilia, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Vibrio paraheamolyticus*) were used. The result of the present study showed a broad range of antimicrobial activity. The data found in the literature, that the compounds with halogen substituent are the most efficient against gram-positive bacteria, particularly against *S. aureus*[11,12]. But in this study, we found more or less equal zone of inhibition values for all gram-positive and gram-negative bacteria (Figure 3.1)(Table 3.1).It shows that the antibacterial activity depends upon substituents only.Compound **6** exhibited excellent antibacterial activity. It has been established that the –COOH group has an excellent metal-binding capacity[13]. This explains the higher antibacterial activity. The results also reveal that the antibacterial activity is affected by the nature of the substituent group (X) found in the aryl ring. The chloride derivative is characterized by greater antibacterial activity than that of the methyl and methoxy derivatives. According to Mohamed et al.[14] this may be attributed to the electron-withdrawing character of the chlorine group that decreases the electron density in the indandiones group, increasing its cationic character. The derivatives with electron withdrawing groups showed strong antibacterial activity than those of electron donating group[14]. Electron-withdrawing substituent increases acidity also. Bacterial growth is inhibited by increasing the acidity of the substituents. The order of antibacterial activity of compounds (**1-6**) for all the microorganism were in the following sequence:

-OCH3<-CH3<- H <-Cl <-Br <-COOH

If atom or group attracts electrons less strongly than hydrogen, it is said to have +I effect (electron repelling or electron–releasing) viz., -OCH3, -CH3 groups showing lesser zone inhibition values compared to unsubstituted phenyl ring (-H).

**Table- 3.1**. **Antimicrobial activity (Zone of inhibition (mm) values) of substituted 2-benzylidene-1,3-indandiones**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No**. | **Name of the microorganisms** | **Inhibition zone radius (mm)** | | | | | | |
| **Standard**  **(Amphotericin – B)** | **-OCH3** | **-CH3** | **-H** | **-Cl** | **-Br** | **-COOH** |
| 1 | ***Aeromonas hydrophilia*** | 21 | 5 | 6 | 7 | 8 | 9 | 12 |
|  |  |  |  |  |  |  |  |  |
| 2 | ***Escherichia coli*** | 16 | 6 | 7 | 8 | 9 | 10 | 12 |
|  |  |  |  |  |  |  |  |  |
| 3 | ***Psedomonas aeruginosa*** | 21 | 5 | 6 | 8 | 8 | 9 | 11 |
|  |  |  |  |  |  |  |  |  |
| 4 | ***Proteus mirabilis*** | 18 | 5 | 6 | 7 | 9 | 10 | 12 |
|  |  |  |  |  |  |  |  |  |
| 5 | ***Staphylococcus aureus*** | 16 | 6 | 7 | 8 | 9 | 9 | 11 |
|  |  |  |  |  |  |  |  |  |
| 6 | ***Vibrio paraheamolyticus*** | 18 | 5 | 7 | 9 | 10 | 10 | 12 |

****

**Figure 3.1 Antibacterial activity of substituted 2-benzylidene-1,3-indandione**