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FUSION OF AMIDE COMPOUNDS WITH ARYL CHLORIDE: ITS CHEMISTRY AND BIOLOGICAL ACTIVITY

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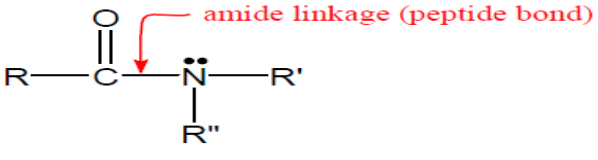
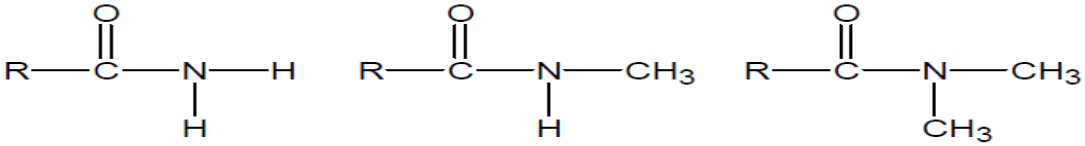
ABSTRACT

An antimicrobial is an agent that kill microorganism or stops their growth. Antimicrobial medicines can be grouped according to the microorganisms they act mainly against bacteria. For example, antibiotics are used beside bacteria and antifungal are used against fungi. They can also be classifying according to their function. Agents that kill microbes are called microbicidal, they mostly inhibit their growth are called biostatic. The utilization of antimicrobial medicines to treat infection is known as antimicrobial chemotherapy, whereas the use of antimicrobial medicines to stop infection is known as antimicrobial prophylaxis Amides have nitrogen which is directly attached to a carbon in a carbonyl group.

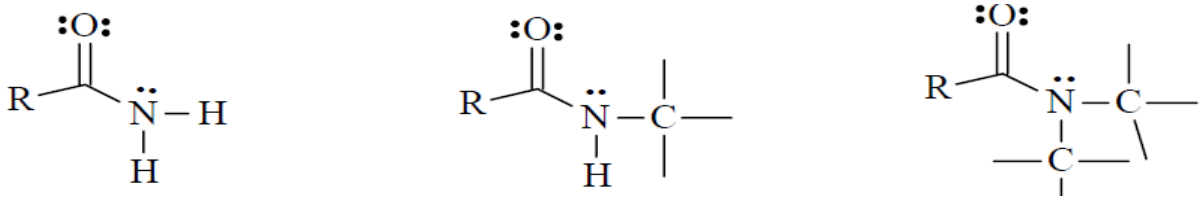


Amide



N,N-unsubstituted amide N-substituted amide N,N-disubstituted amide

Amides can be classify as "primary", "secondary" or "tertiary" depends upon the degree of carbon which is substituted on nitrogen.



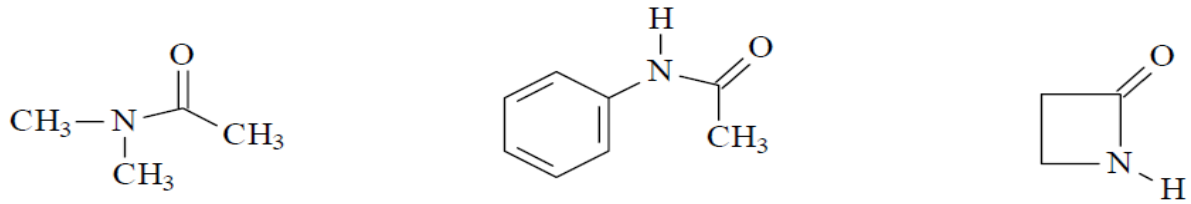
Primary Amide **Secondary Amide** **Tertiary Amide**

KEYWORDS: Antimicrobial, Amide.

INTRODUCTION

Antimicrobial agent shows disinfectant properties which is used to kill a large range of microbes on non-living surfaces and used to prevent the spread of illness, antiseptics are applied to living tissue and help decrease infection during surgery and antibiotics demolish microorganisms within the body. The term "antibiotic" initially described only those formulations imitative from living micro organisms but is now also useful to synthetic antimicrobials, such as the sulphonamides, or fluoroquinolones. The term also used to be controlled to antibacterial. Antibacterial agents can be promoting subdivided into bactericidal agents, who kill bacteria, and bacteriostatic agents, which slow down or stop bacterial growth.[4]

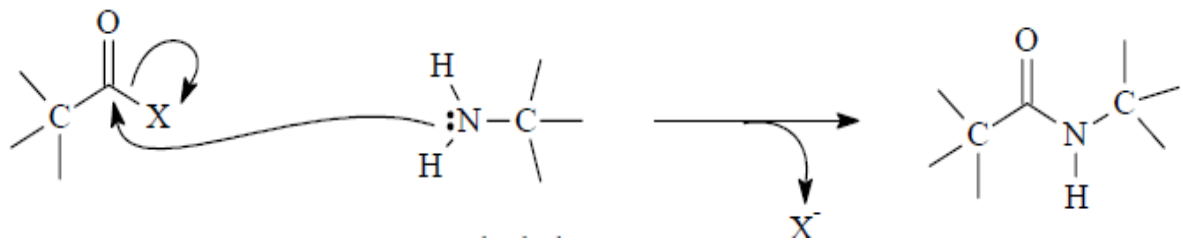
Amides are sub divided as aliphatic, aromatic (benzamides) or cyclic (lactams), based on the nature of the nitrogen substituents and its structure. Aliphatic amides are those amide having hydrocarbon substitution auch as alkyl group while aromatic amides have at least aromatic ring substituent as exposed in the example below. Lactams cyclic structure contain an amide group.[7,8]



Tertiary aliphatic amide **Secondary Analide (Benzamide)** **Lactam (Cyclic Amide)**

Figure 4.

There are many methods to develop the preparation of amides. Most of these methods are involve reaction of an amine with an "activated carbonyl" compound (i.e. acid chloride) very similar to the method which is used to prepare esters.[8]



Activated acid (X=Cl) **Alcohol** **Amide**

(Electrophile) **(Nucleophile)**

MATERIAL AND METHOD

1. Material

The chemicals used in this work are listed below with their suppliers

Table 2: The chemicals and reagents used

Materials		Company	Origin
Acetanilide		Central drug house (CDH)	New Delhi, India
Urea		Central drug house (CDH)	New Delhi, India
aniline		Central drug house (CDH)	New Delhi, India
Sulphonamide		Central drug house (CDH)	New Delhi, India
Propanol		Himedia Pvt. Ltd.	Mumbai, India
Ethylacetate		Himedia Pvt. Ltd.	Mumbai, India
n-Hexane		Himedia Pvt. Ltd.	Mumbai, India
Silica gel (60-120)		Himedia Pvt. Ltd.	Mumbai, India
Hydrochloric acid		Himedia Pvt. Ltd.	Mumbai, India
Methanol		Himedia Pvt. Ltd.	Mumbai, India
Sodium hydroxide		Central drug house (CDH)	New Delhi, India
Chloroform	Central drug house (CDH)		New Delhi, India

With their origin.

2. Instruments used

Instruments	Company	Origin
Double beam UV spectrometer	Elico SL 210, India	India
TLC chamber	Himgiri traders	India
Percoted TLC plate	Merck	India
Melting point apparatus	Scientific traders	New Delhi, India
pH meter	Eutech	New Delhi, India
Optical rotary apparatus	Rudolph research	New Delhi, India
Hot air oven	Scientific traders	New Delhi, India
UV chamber	Scientific traders	New Delhi, India
Mechanical stirrer	Scientific traders	India
Hot plate	Himgiri traders	New Delhi, India
Electronic balance	Shimadzu corporation	Ambala, India

3. Sources of data

Database like chemical abstract, Journal of Chemistry, Indian Journal of Heterocyclic Chemistry, European Journal of Chemistry, Asian journal of Pharmaceutical chemistry, Journal of Heterocyclic Chemistry, Journal of Molecular Structure, Bio-organic and Medicinal Chemistry, Unique Research Journal of Chemistry etc.

Procedure

Step 1: Prepare the developing container

The developing container for TLC can be a specially designed chamber, a jar with a lid, or a beaker with a watch glass on the top (the latter is used in the undergrad labs at CU). Pour solvent into the chamber to a depth of just less than 0.5 cm. To aid in the saturation of the TLC chamber with solvent vapors, you can line part of the inside of the beaker with filter paper. Cover the beaker with a watch glass, swirl it gently, and allow it to stand while you prepare your TLC plate.

Step 2: Prepare the TLC plate

TLC plates used are purchased as 5 cm x 20 cm sheets. Each large sheet is cut horizontally into plates which are 5 cm tall by various widths. Measure 0.5 cm from the bottom of the plate. Using a pencil, draw a line across the plate at the 0.5 cm mark.

Step 3: Spot the TLC plate

Dissolve about 1 mg of sample in 1 mL of methanol. Dip the microcap into the solution and then gently touch the end of it onto the proper location on the TLC plate.

Step 4: Develop the plate

Place the prepared TLC plate in the developing beaker, cover the beaker with the watch glass, and leave it undisturbed on your bench top. The solvent will rise up the TLC plate by capillary action. Make sure the solvent does not cover the spot. Allow the plate to develop until the solvent is about half a centimeter below the top of the plate. Remove the plate from the beaker and immediately mark the solvent front with a pencil. Allow the plate to dry.

Step 5: Visualize the spots

Hold a UV lamp over the plate and circle any spots you see.

4.8. Total antioxidant activity (TAA)

The antioxidant activity of the extracts were evaluated by the phosphomolybdenum method (Jayaprakasha et al; 2002).

Reagents

(a) Sulfuric acid (0.6M)

(b) Sodium phosphate (28mM)

(c) Ammonium molybdate (4mM)

Procedure

The assay is based on the reduction of Mo(VI)–Mo(V) by the extract and subsequent formation of a green phosphate/Mo(V) complex at acidic pH. The extract 0.3 ml was combined with 3 ml of reagent solution (0.6 M sulfuric acid, 28 mM sodium phosphate and 4mM ammonium molybdate). The tubes containing the reaction solution were incubated at 95°C for 90 min. Then the absorbance of the solution was measured at 695 nm using spectrophotometer (UV Cary 100) against blank after cooling to room temperature. The antioxidant activity is expressed as µg of ascorbic acid equivalents/g of sample.

Standard ascorbic acid solution graph

The standard ascorbic acid graph solution for estimation of total antioxidant content is shown in Appendix B. From the graph, mathematical relationship was established between ascorbic acid concentration and absorbance, which is given as follows:

$Y = 1.056\ A - 2.3065$ $(R^2 = 0.989)$

Where; Y is concentration and A is absorbance

4.9. Anti bacterial activity

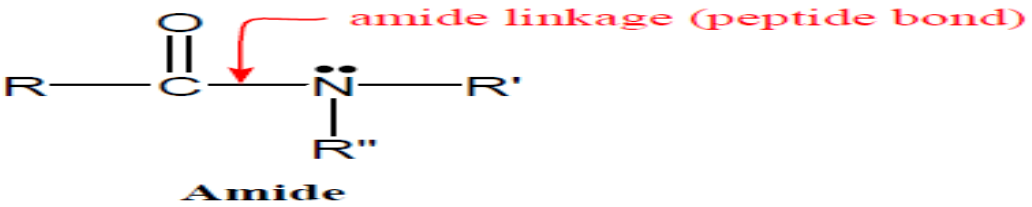
The antibacterial activity of these compound was carried out by disc diffusion method.[10] In this technique the filter paper (Whatman No.1) sterile disc of 5 mm diameter, impregnated with the test compounds (10 µg/ml of ethanol) along with standard were placed on the nutrient agar plate at 37oC for 24 hrs in BOD incubator. The inhibition around dried impregnated disc was measured after 24 hrs. The bacterial activity was classifieds as highly active (dia = > 15 mm), moderate active (dia =10-15 mm) and partially active (dia = 5-10mm).

RESULT

We developed new synthetic methodologies for the synthesis of amide derivatives. The starting material aniline was reacted with benzoyl chloride to give corresponding amide group, the schotten boumann reaction were take place in presence of sodium hydroxide as a catalyst.

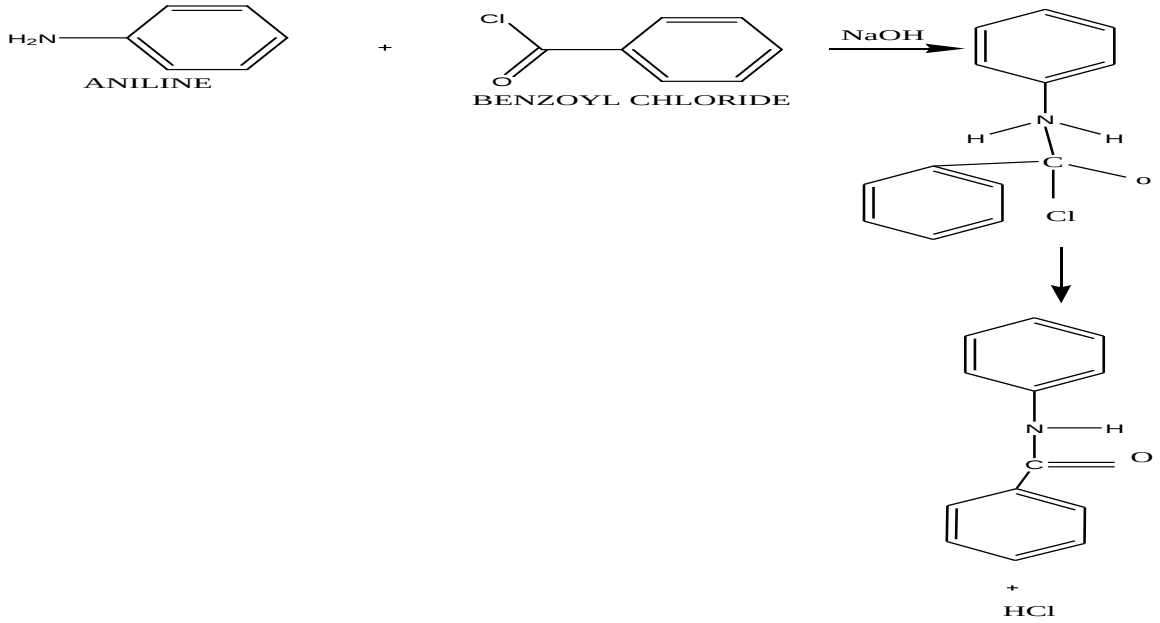
1. Reaction mechanism of schotten boumann reaction

2. Physicochemical properties

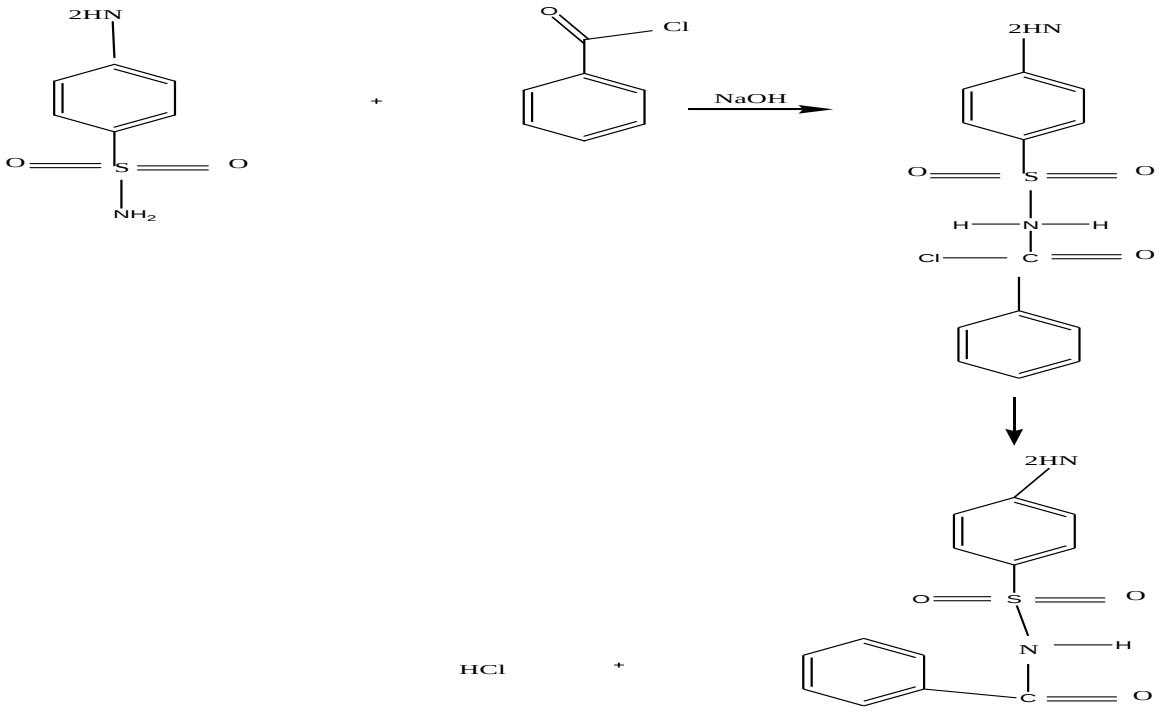


Amide

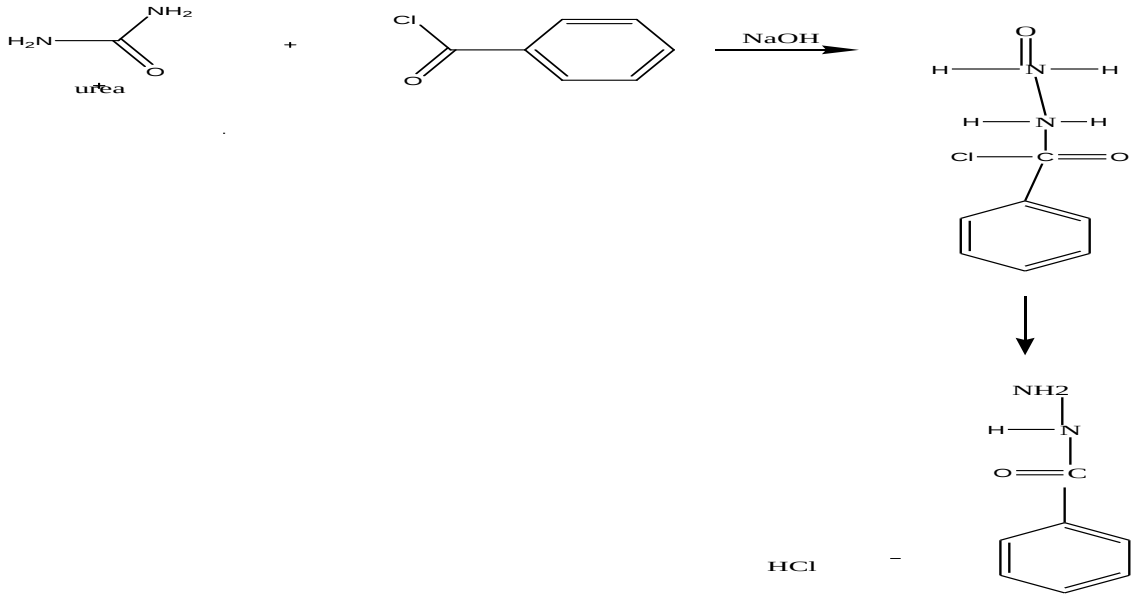
2.1 Synthesis of amide derivative from aniline and benzoyl chloride



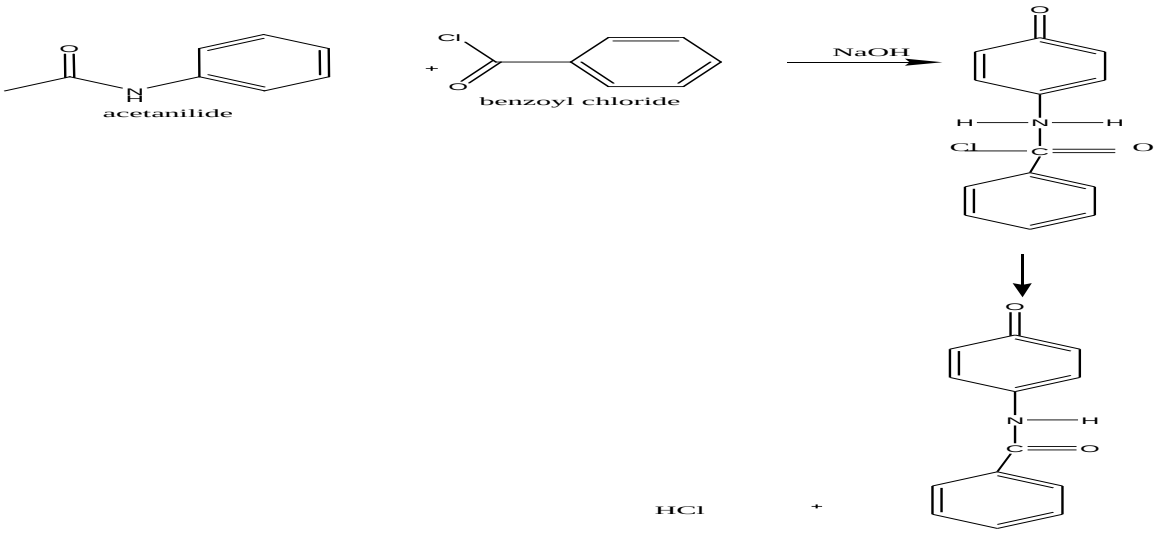
2.2 Synthesis of amide derivative from sulphonilamide and benzoyl chloride



2.3 Synthesis of amide derivative from urea and benzoyl chloride



2.4 Synthesis of amide derivative from acetinalide and benzoyl chloride



3. Antibaterial activity

Figure : Preparation of agar plate for growth of bacteria.

Figure : Growth of *E. coli* and *S. aureus* in all agar plates.

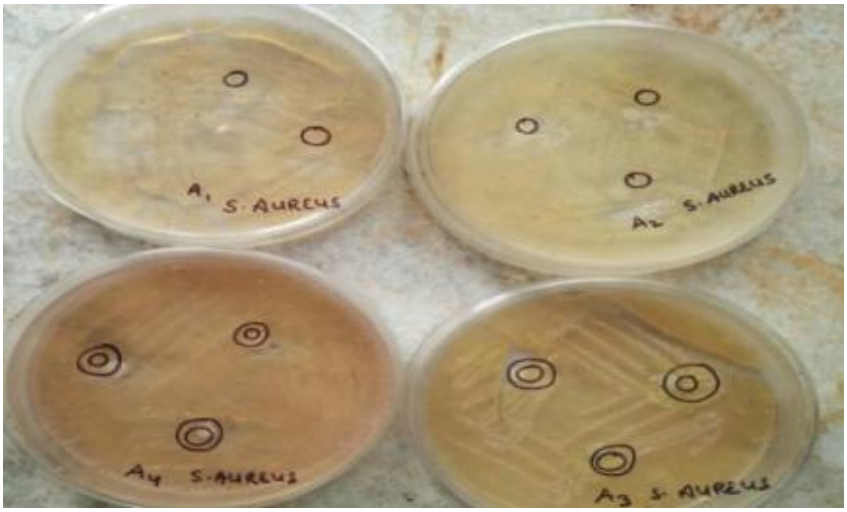
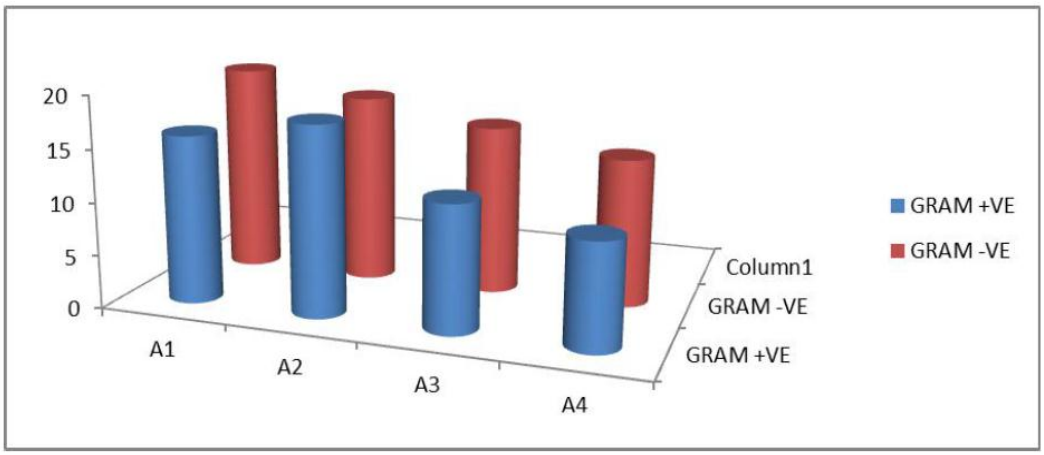


Figure: Zone of inhibition in *S. Aureus.*

Table : Screening results of the newly synthesized Compounds as antibacterial activity

S. NO.	Compound no.	Gram +Ve bacteria	Gram -Ve bacteria
1.	A1	16	20
2.	A2	18	18
3.	A3	12	16
4.	A4	10	14



DISCUSSION

All the compounds have been screened for *in-vitro* antimicrobial and antioxidant activities. All the compounds have been screened for antibacterial activities using agar disc diffusion method by measuring the zone of inhibition in mm. Sulphonamide (µg/ml) was used as standard drug for antibacterial activity. The compounds were screened for antibacterial activity against *E. coli* and *S. aureus* in nutrient agar media.

These sterilized agar media were spread with the help of sterilized loop. The disc of 6mm diameter was used. All the synthesized compounds (µg/ml) were dipped in disc for diffusion for 1hr, DMSO was used as solvent for all compounds and as control. These plates were incubated at 37oC for 24 hr and 28oC for 48 hr, for antibacterial activities. The zone of inhibition were observed around the disc after incubation and measured.

The use of SAR study helped in concluding that the different substitutions on the compound exerted varied biological activity. The electron donating groups were chosen as substitutions on the chemical structure of targeted compounds. Compounds A1, A2, A3, and A4 with substitution with different groups showed minimum inhibitory concentration against *E. coli* and *S. aureus* as compared to the standard used for antimicrobial screening. From this the result divulges that the derivatives with higher electron donating capacity show higher antimicrobial activity. The A1 and a2 derivatives shows maximum MIC against both bacteria due to presence of stronger donating group. So these support our research that the electron donating group having the capacity to increase the electron density and makes the compound more effective against microbial activity and the A3 and A4 synthesis compounds having less activity against bacteria.

CONCLUSION

The present study was design with fused synthesis and biological activity like antimicrobial studies of substituted fused benzoyl chloride and amide derivatives. The subject was assigned and the annexure were completely filled and various parameters were observed physical properties like pH, solubility, optical rotation, elemental analysis, IR, NMR, TLC and antibacterial activity.

During the study the major conclusion drawn that A1 and A2 derivatives shows maximum MIC against both bacteria due to presence of stronger donating group.

So these derivatives supported our research that the electron donating group having the capacity to increase the electron density and makes the compound more effective against microbial activity and the A3 and A4 synthesis compounds were having less activity against the microbial agents.

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