# Synthesis, Characterization and biological evaluation of some Novel 2, 3-disubstituted quinazolin-4(*3H*)-ones derivatives.

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**Abstract**

In recent years, there has been a growing interest in researching and developing new synthesized agents having various biological activities, In view of this we have undertake synthesis of various new quinazolin-4(3*H*)-one derivative from substituted anthranalic acid and aniline. All the synthesized compounds were characterized by physical and spectral analysis.

In this research study, some of the synthesized compounds of 2, 3-disubstituted quinazolin-4(3*H*)-one were screened for their possible pharmacological activities like antibacterial, antifungal, anti-inflammatory and anti-cancer activity. Antibacterial activity was evaluated against *E. coli* and *S. aureus,* and antifungal activity was evaluated against *A. niger, and C. albicans* by Well diffusion method.

**Keywords:** Quinazoline-4-(3H)-ones,

## INTRODUCTION

In the field of medicinal chemistry Quinazolinone is a heterocyclic compound with a unique place. This Quinazolinone compound having anticonvulsant, analgesic, antihypertensive, diuretic, sedative, analgesic, activity. Quinazolinone are considered as a privileged scaffold in drug discovery and drug development. Among the two isomers of quinazolinone, 4-(3H)-Quinazolinone being more common show various biological activities and its major application in the field of medicine. Pharmaceutical chemistry is order of chemistry, specially synthetic organic chemistry, It also involves pharmacology and various other biological specialties, where it is concerned with design, chemical synthesis and development of pharmaceuticals agent i.e drugs. Pharmaceutical chemistry is constant to the invention and growth of novel agents for treating disease.

### Chemicals

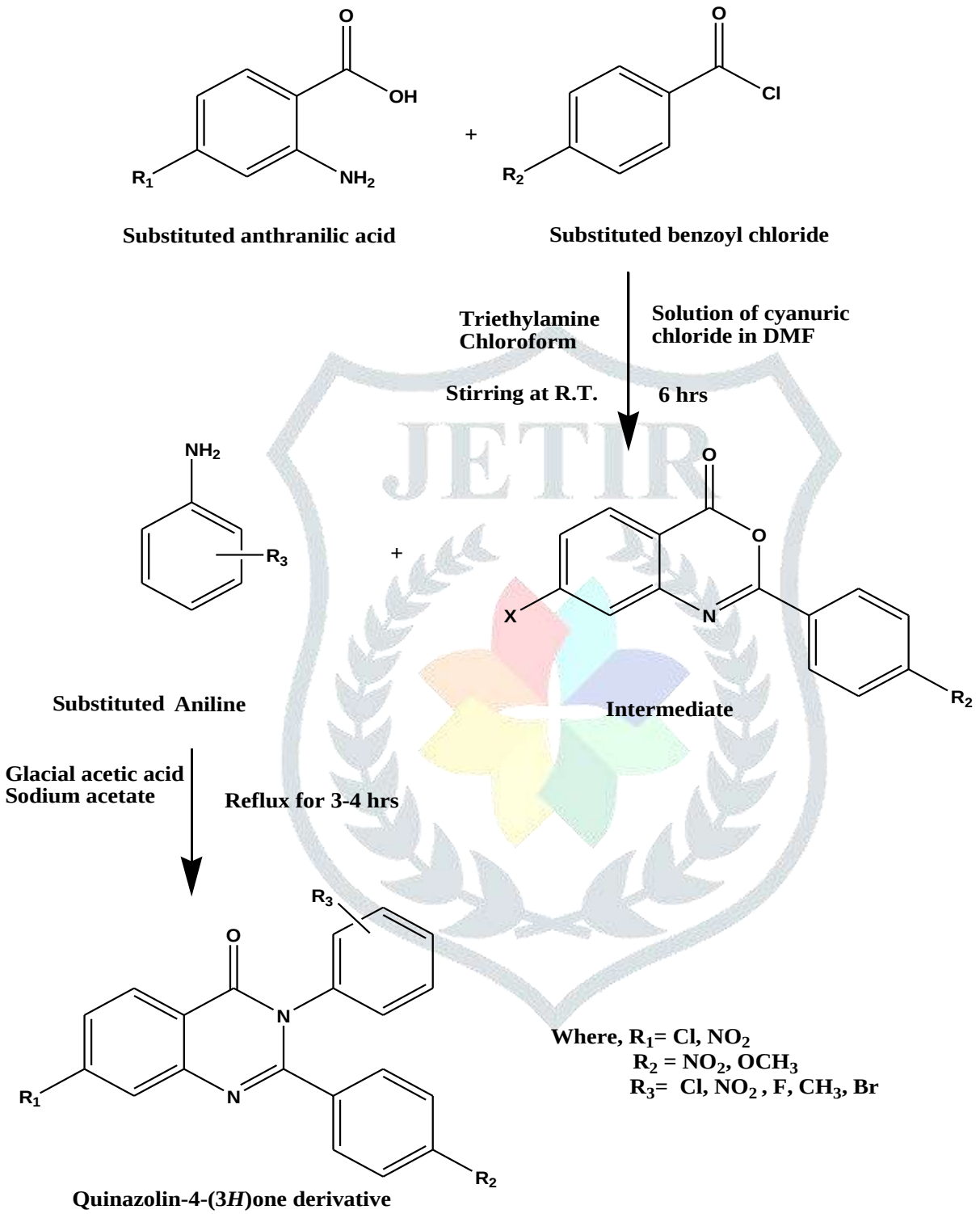
The required starting materials, chemicals and solvents were purchased from Alfa, SDFCL, Spectrochem.

## Materials and Methods.

1. All the chemicals used were purchased from commercial sources such as Himedia, SD fine Chemicals, Merck, Spectrochem and purified using standard procedure if required.
2. Melting points were verified on an open capillary tube on Super Fit melting point apparatus and are uncorrected.
3. The purity of all the final compounds was evaluated by using TLC.
4. Readymade TLC plates were secured from Merck [TLC silica gel 60 on aluminium sheets ( 20 x 20 cm) and cut to suitable size as required.]
5. Completion of the reaction was monitored by TLC by Ethyl Acetate: n-hexane ( in varying proportions i.e 1.5:3.5/1:4) system.
6. TLC plates were visualized using UV lamp, Iodine chamber.
7. IR spectra were recorded in KBr disk on "Shimandzu FTIR model I.R. affinity" and are reported in centimeters ($cm^{-1}$)

## SCHEME FOR SYNTHESIS

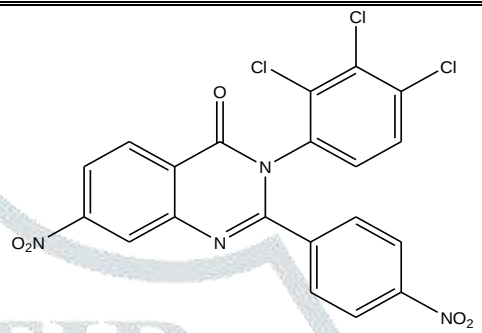
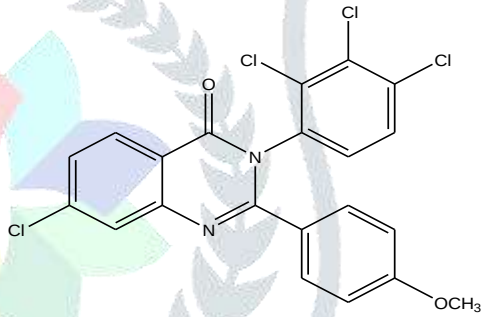
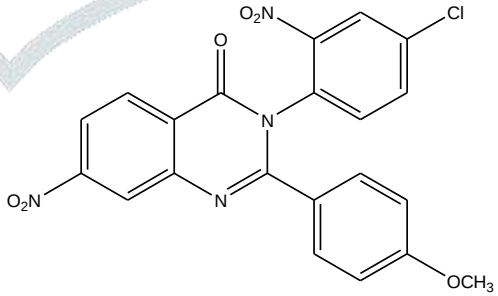
### Scheme for synthesis of quinazolin 4 (3H)-one




**Structure of synthesized compounds 2, 3-disubstituted quinazolin-4(3*H*)- one derivatives**

## Synthesis and characterization of novel quinazolinone derivatives

**Scheme-1 General procedure for the synthesis of quinazolin-4(3*H*)-one derivative .**

| Compound | $R_1$ | $R_2$ | $R_3$ | Structure |
|---|---|---|---|---|
| 1 | 7-Nitro | 4-nitro phenyl | 2, 3, 4 - trichloro phenyl |  3-( 2, 3, 4 –trichlorophenyl)-7-nitro-2-(4-nitrophenyl)quinazolin-4(3*H*)-one |
| 2 | 7-chloro | 4-methoxy Phenyl | 2,4,5-trichloro phenyl |  7-chloro-3-(2, 3, 4- trichlorophenyl)-2-(4-methoxyphenyl)quinazolin-4(3*H*)-one |
| 3. | 7-Nitro | 4-methoxy Phenyl | 4-chloro,2-Nitro phenyl |  3-(4-chloro-2-nitrophenyl)-2-(4-methoxyphenyl)-7-nitroquinazolin-4(3*H*)-one. |

**Step - I**

The solution of 4-chloro/4-nitro anthranilic acid (1mmol) and trimethylamine (1 mmol) in chloroform (50 ml) was prepared. To this solution were added 1 mmol of 2-Methoxy benzoyl chloride. The resulting mixture was stirred at room temprature for 2 hr. after completion of 2 hrs add mixture of cyanuric chloride (1mmol) in DMF. The mixture was stirred for 4 hrs and the reaction was washed with ice water. Mixture was set aside for few hrs, filtered and finally the product was collected.

**Step –II**

To the product of step I substituted aniline (1mmol), glacial acetic acid (20 ml) and sodium acetate (0.25 mg) were added. This mixture was refluxed for 3-4 hr at $60^0$C-$70^0$C temprature. The reaction was monitored by TLC. The reaction mixture was cooled after completion of reaction, cool the reaction mixture. The combined organic layer was evaporated under reduced pressure and then obtained crude product was further purified by recrystallization from hot ethanol. The product was confirmed by melting point, $^1$HNMR, IR, and Mass analysis.

## Spectral Data of Synthesized Compound

**Compound-1 3-(2, 3, 4-trichlorophenyl)-7-nitro-2-(4-nitrophenyl)quinazolin-4 (3*H*)-one.**

IR (KBr): ν $cm^{-1}$ 3078 (C-H Stretching), 1747 (C=O stretching), 1703 (C=C Stretching), 1697 (C=N), 1361 (-$NO_2$), 781 (C-Cl), 729 (C-Cl). Filtered the solid residue, washed with water, dried affording 55 % yield as yellow solid and melting point was found to be 238- $240^0$C. TLC-Ethyl acetate: n-hexane (1.5:3.5) and $R_f$ value = 0.4.

**Compound-2 7-chloro-3-(2, 3, 4-trichlorophenyl)-2-(4-methoxyphenyl)quinazolin - 4(3*H*)-one**.

IR (KBr): ν $cm^{-1}$ 3360 ($OCH_3$), 3115 (C-H stretching), 1732 (C=O), 1668 (C=C), 1614 (C=N), 775 (C-Cl), 744 (C-Cl) aromatic 1, 3, 5, trisubstituted chloride filtered the residue, washed with water and dried. Percentage yield was found to be 65% as a white solid. Melting point was found to be 195-196 $^0$C. TLC- Ethyl acetate: n-hexane (1.5:3.5) and $R_f$ = 0.31.

**Compound-3 3-(4-chloro-2-nitrophenyl)-2-(4-methoxyphenyl)-7-nitroquinazolin-4(3*H*)-one.**

IR (KBr): ν $cm^{-1}$ 3111 (C-H Stretching), 2833 (C=O), 1618 (C=N), 1516 ($NO_2$), 717 (C-Cl). Filtered the solid residue, washed and dried, percentage yield 71% as a orange crystal. melting point was found to be 204-$206^0$C. TLC- Ethyl acetate: n-hexane (1.5: 3.5) and $R_f$ value = 0.39.

## BIOLOGICAL EVALUATION

In recent years, there has been a growing interest in researching and developing new antimicrobial agents from various sources to fight microbial resistance.

Microbiological assay may be defined as qualitative or quantitative determination of any chemical compound from a simple or even complex material with the use of microorganisms. It is necessary to assay the anti-microbiological agent for determination of its potency. Biological activity of the synthesized novel quinazolinone derivatives were screened for antibacterial, antifungal, anticancer, and anti inflammatory activity. Total 15 compounds were subjected for antimicrobial and antifungal evaluation.

### Antibacterial Activity:

The inhibition of microbial growth under standardized conditions may be utilized for demonstrating the therapeutic efficacy of drug compound. The microbiological activity is based upon a comparison of the inhibition of the growth of microorganism by measured concentrations of the drug compound to be examined with that produced by known concentrations of standard preparation of the antibiotic having a known activity.

### Materials and Method.

**Material used :-**

**Material**

Material used for antimicrobial work- Sterilized test tube, graduated pipettes and watch glasses, 18-27 hr. old grown culture in nutrient broth, Sterilized fine pointed forceps, Sterilized Petri dishes, Sterilized 6 mm corck borer, Sterilized inoculation loop, Autoclave for sterilization, Incubator, Burner.

**Method: - Well diffusion method**

The well diffusion agar method tests the effectiveness of antimicrobial or synthesized compound on a specific microorganism. The synthesized compound is allowed to diffuse out into the medium in a plate which was freshly seeded with the test organisms. Then resulting zones of inhibition of growth of test organism can be measured in millimeters. [28].

**Medium used: - Nutrient agar**

Agar is a long chain polysaccharide obtained from seaweeds algae. It also contains calcium, Chloride, magnesium, sulphate, iron etc. Agar or agar–agar is known commonly used for preparation of solid media. Agar act as good solidifying agent [29]

**Micro-organism used:-**

Gram positives- *S. aureus,*

Gram negative- *E. coli,*

**Antibacterial Activity of Synthesized 2, 3-disubstituted quinazolin -4(3*H*)-one derivative.**

| Compound Code | *E. Coli* | Compound Code | Recoding of Compound. | *S. Aureus* |
|---|---|---|---|---|
| Compound 1 | 14 | Compound 1 | A | 12 |
| Compound 2 | 15 | Compound 2 | B | 13 |
| Compound 3 | 13 | Compound 3 | C | 11 |

**Photograph of Antibacterial Activity Plates of Synthesized 2, 3-disubstituted -quinazolin-4(3*H*)-one Derivatives**

***1) E. Coli***

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**2.Antifungal Activity**

The antifungal activity of synthesized compound were determined by screening them against the, *Aspergillus niger* and *Candida ablicans* using Well Diffusion Method.

**Diffusion method**

**Medium:-** Potato dextrose agar

Potato Dextrose Agar is used for the cultivation of fungi in a laboratory setting. Potato Dextrose Agar is not intended for use in the diagnosis of disease or other conditions in human.[26]

**Organism used: -** *Aspergillus flavus.* and

*Candida albicans.*

**Preparation of stock solution**

Prepared in dimethyl sulphoxide for both synthesized compound and standard compounds.

| Compound Code | *A. niger* | *C. albicans* |
|---|---|---|
| Compound 1 | 10 | 10 |
| Compound 2 | 12 | 15 |
| Compound 3 | 13 | 12 |

**Photograph of Antifungal Activity Plates of Synthesized 2, 3-disubstituted - quinazolin-4(3*H*)-one Derivatives**

***1) A.Niger*** ***2)C.Albicans***

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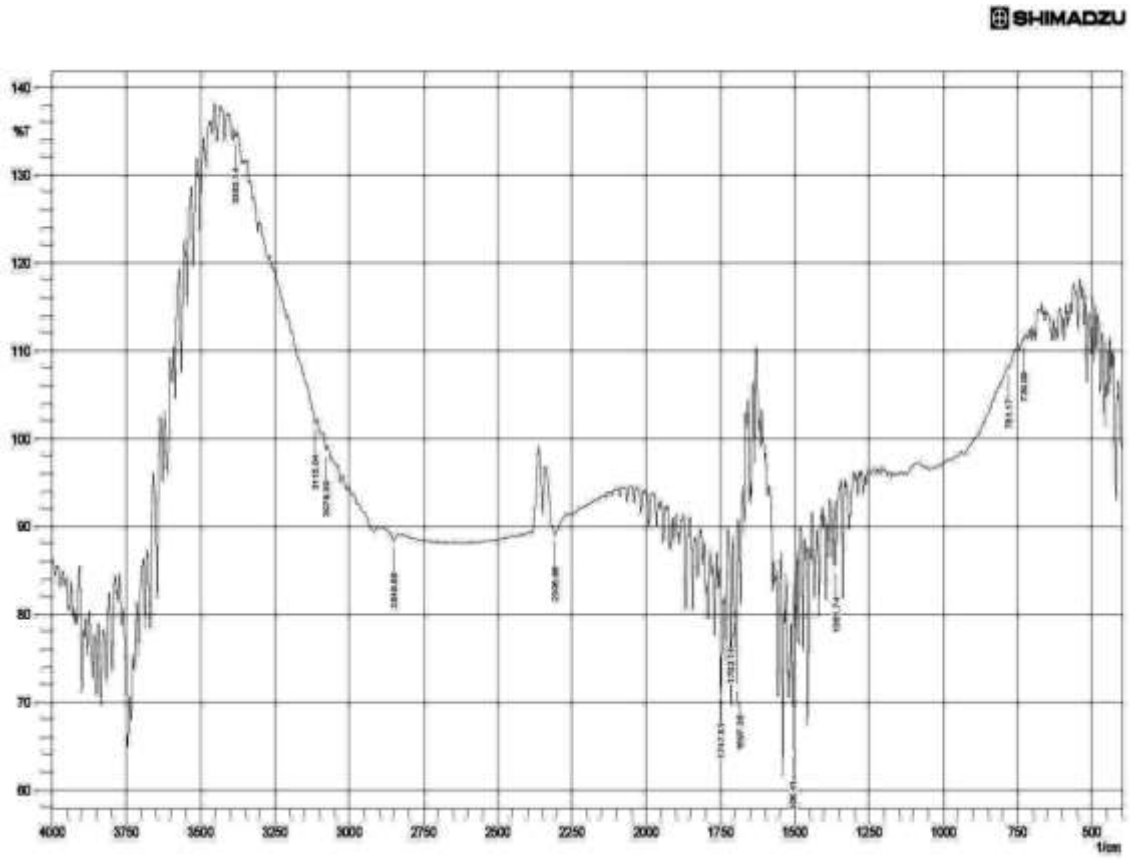
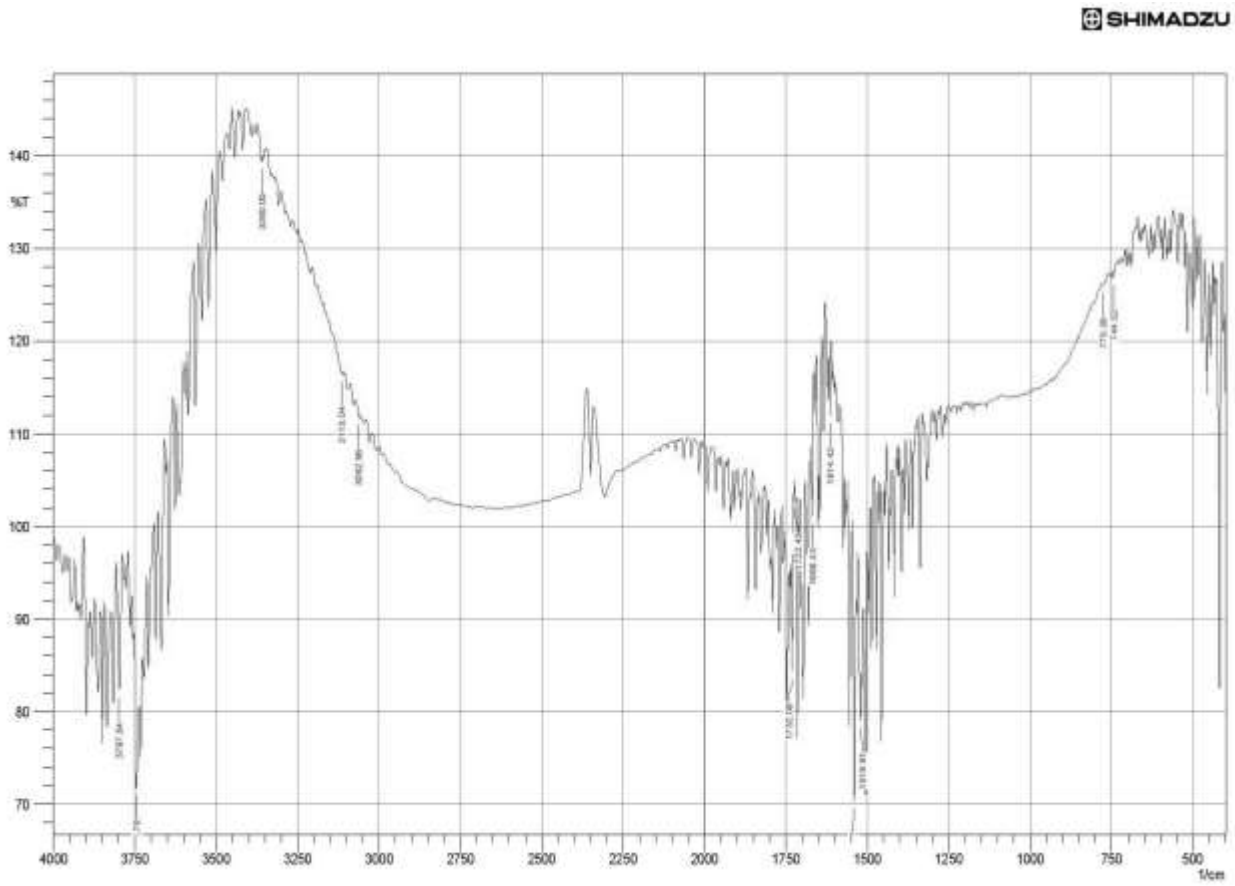
**Spectral analysis of synthesized 2, 3-disubstituted quinazolin-4(3*H*)-one**

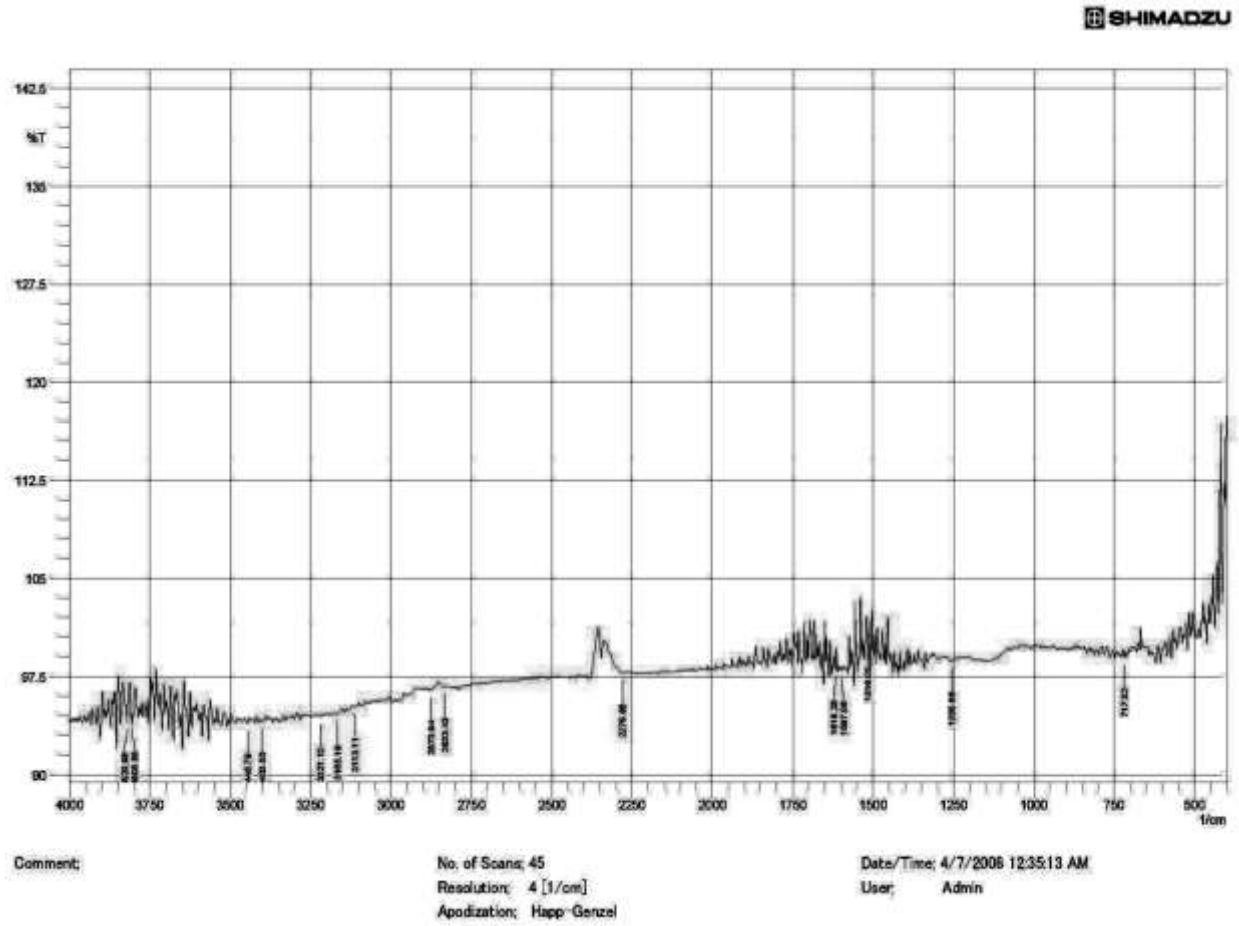
**IR spectrum of compound 1**




**IR Spectrum of Compound 1:** 3-( 2, 3, 4 –trichlorophenyl)-7-nitro-2-(4-nitrophenyl)quinazolin-4(3*H*)-one.




**IR spectrum of Compound 2:** 7-chloro-3-( 2, 3, 4- trichlorophenyl)-2-(4-methoxyphenyl)quinazolin-4(3*H*)-one.




**IR Spectrum of Compound 3:** 3-(4-chloro-2-nitrophenyl)-2-(4-methoxy-phenyl)-7-nitroquinazolin-4(3*H*)-one.

## CONCLUSION

The current status of medicinal chemistry research is directed towards the synthesis of newer heterocyclic derivatives with wide range of biological activities.

The antibacterial activity of synthesized compounds were assessed against *E. coli* and *S. aureus* using well diffusion method and The antifungal activity of synthesized compounds were evaluated against *A. niger* and *C. albicans* using well diffusion method.

# REFERENCE

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