ANTIMICROBIAL SCREENING AND SYNTHESIS OF QUINAZOLINONE DERIVATIVES

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ABSTRACT
The present work deals with synthesis of 2- Pyridyl – 4 Quinazolone (NN) (A1), 2-Pyrazinyl – 4 – Quinazolone (A2). The synthesis is based on Niementowski Reaction which involves condensation of the reactants under varying thermal conditions. The synthesis of 2-hetero substituted Quinazolone is based on Niementowski Reaction involves thermal condensation and cyclisation of a drug amide and Anthranilic acid / 3, 5 di bromo anthranilic acids at elevated temperatures to yield the various hetero-moieties. The drug amides used are Nicotinamide, Pyrazinamide and Carbamezepine. The products formed were recrystallized using ethanol. Thin layer chromatography was carried out using Benzene: ethanol. The melting points of the products were found by capillary tube method. The values are uncorrected. The synthesized compounds have been characterized using UV, IR, NMR and MASS. The literature review indicates that Substituted Quinazolinones have wide spectrum of pharmacological activity such as anti-bacterial, antimicrobial, antiviral and antifungal. Hence antimicrobial study was carried out. The antibacterial activity of the synthesized compounds was determined. The pathogens used in this study included both gram positive and gram negative organisms. Namely Negative coagulase staphylococci, Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia, all the synthesized compounds showed antibacterial activity to varying degree against the organisms tested. Zone of inhibition was carried out using Antibiotic disc diffusion assay method Amikacin (5 g/ml) was used as control.

KEYWORDS: Quinazolone, Niementowski Reaction, Pyrazinamide, Carbamezepine, thermal condensation, capillary tube method.

INTRODUCTION
The course of study and research has been on the synthesis of 2- Pyridyl – 4 quinazolone, 2-pyrazinyl – 4 – quinazolone, 2-carbamazepinyl – 4- quinazolone , 6,8 - Dibromo - 2-carbamazepinyl - 4- quinazolone by using Niementowski Reaction and screening for their antimicrobial, antifungal, anti-tubercular and anti-inflammatory activities with the standard drugs by using standard methods.

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Quinazolinone is a heterocyclic compound chemically known as 4-Hydroxyquinazoline. There are two structural isomers, 2-quinazolinone and 4-quinazolinone, with the 4-isomer. Quinazolinone is a building block for approximately 150 naturally occurring alkaloids isolated to date from a number of families of the plant kingdom, from animals and from microorganisms. Quinazolinone and its derivatives have also attracted a widespread interest due to the diverse biological activities associated with them. They are pharmaceutically important as antituberculars (thromboxane A2 synthetase inhibitors), antibacterial anti Parkinson’s, and anthelmintic (and they also show blood platelet anti-aggregating activity). In the light of recent studies, it might be expected that a combination of quinolones moiety with such structures may increase their biological activities or create new medicinal properties. It is worthy to mention that the combination of this moiety, formulated a unique structure, which showed different biological activities, such as anti-tumour activity, cytotoxic toward the leukaemia P388 cells, etc. Quinolone is frequently integrated into an organic compound in order to have enhanced or unexpected biological activities.

EXPERIMENTAL METHODS

**Instruments:**

The melting points were determined on a Veego apparatus and are uncorrected. The reactions were monitored by TLC. The mass spectra were taken on a Macro mass spectrometer (Waters). The IR spectra were recorded in Nujol on Schimatzu 8000 spectrophotometer. $^1$H NMR spectra were recorded on a Bruker 400 MHz instrument in DMSO and TMS as an internal standard. Elemental analysis was performed on Perkin–Elmer EAL-240 elemental analyzers.

**Methods:**

The compounds NN (A1), NP (A2) and NC (A3) were synthesized by following mechanism using Niementowski Reaction.
The compound NCB (A4) was synthesized by following mechanism:

**Recrystallisation:**
To small amount of precipitate ethanol was added and heated so as to dissolve completely. The clear solution thus formed after filtration was set aside for natural cooling. As the temperature decreases crystals were found to appear. The process was repeated to obtain a pure crystalline form.

**Thin layer chromatography:**
Precoated aluminium TLC-GF binder was used. Solution of the reactants and products in ethanol were prepared. Various mobile phases were tried out.

**Stationary phase:** Silicagel–GF

**Mobile phase:** Benzene:ethanol

**Detection of spots:** UVlight

The product was obtained as a single spot without any secondary spot indicating the purity of the synthesized compound.

**Niementowski Reaction synthesis of following Quinazolinones.**

**2- Pyridyl – 4 quinazolone (A1)**
RESULTS AND DISCUSSION

The synthesis is based on Niementowski Reaction which involves condensation of the reactants under varying thermal conditions. The synthesis of 2- hetero substituted Quinazolone is based on Niementowski Reaction involves thermal condensation and cyclisation of a drug amide and anthranilic acid / 3,5 di bromoanthranilic acid at elevated temperatures to yield the various hetero-moieties. The drug amides used are Nicotinamide, Pyrazinamide and Carbamazepine. The products formed were recrystallised using ethanol. Thin layer chromatography was carried out using Benzene: ethanol. The melting points of the products were found by capillary tube method. The values are uncorrected. The synthesized compounds have been characterized using UV, IR, NMR and MASS. The antibacterial activity of the synthesized compounds was determined. The pathogens used in this study included both gram positive and gram negative organisms. Namely Negative coagulase staphylococci, Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia.

CONCLUSION

The present work deals with synthesis of 2- Pyridyl – 4 Quinazolone (NN) (A1), 2-Pyrazinyl – 4 – Quinazolone (A2), 2-carbamazepinyl – 4- quinazolone (A3) and 6, 8 - Di bromo - 2-carbamazepinyl - 4- quinazolone (A4). The synthesis is based on Niementowski Reaction which involves condensation of the reactants under varying thermal conditions. The synthesized compounds have been characterized using UV, IR, NMR and MASS. All the synthesized compounds showed antibacterial activity to varying degree against the organisms tested. Zone of inhibition was carried out using Antibiotic disc diffusion assay method. Amikacin (5 g/ml) was used as control.

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