International Research Journal of Human Resource and Social Sciences
ISSN(O): (2349-4085) ISSN(P): (2394-4218)
Impact Factor 6.924 Volume 9, Issue 11, November 2022
Website- www.aarf.asia, **Email** : editoraarf@gmail.com

A CRITICAL STUDY AOBUTTHE SYSNTHESIS AND ITS PHARMACOLOGICAL EVALUATION

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ABSTRACT

Medicinal and pharmaceutical chemistry are subfields of chemistry that focus on the design, chemical synthesis, and development of bio-active molecules with the eventual goal of getting them authorised as prescribed and market purchasable medicinal medicines. Being the most significant organic compounds, heterocyclic compounds are often found in molecules of interest in medical chemistry. Nitrogen heterocyclic compounds have long been of interest to synthetic organic chemists because of the wide range of biological activities they display. Given their prevalence in natural goods, notably alkaloids, they have attracted significant interest from the synthetic community, particularly those working on the entire synthesis of natural products.There aren't clear boundaries between the many branches of chemistry, and heterocyclic chemistry serves as an illustration of this. Heterocycles are fundamental to all biological functions. Heterocycles' ubiquity in nature is sometimes linked to the intense attention they get from the pharmaceutical and agricultural industries. In this work, we focus on the synthesis of several heterocyclic nitrogen compounds with basic nucleus such imidiazole, pyrazole, and thiazole.

Keywords: - Medicinal, Pharmaceutical, Synthesis, Product, Hetercycles.

I. INTRODUCTION

Nitrogen-based heterocyclic chemistry is an important and unique class among the applied branches of organic chemistry, with a significant amount of research dedicated to the development of novel molecules and composites. These molecules have received increasing attention over the past two decades. They contributed to the development of numerous organic synthesis protocols and found abundant applications in the chemical sciences. Many N-heterocyclic compounds that are broadly distributed in Nature, possess physiological and

pharmacological properties and are constituents of many biologically important molecules, including many vitamins, nucleic acids, pharmaceuticals, antibiotics, dyes and agrochemicals, amongst many others. Moreover, they form an integral part of many pharmacologically active molecules. The base pairs of DNA and RNA (guanine, cytosine, adenine, and thymine) are also made up of N-heterocyclic compounds, namely purines, pyrimidines, etc. These nitrogen-containing heterocyclic molecules with distinct characteristics and applications have gained prominence in the rapidly expanding fields of organic and medicinal chemistry and the pharmaceutical industry. Furthermore, the electron-rich nitrogen heterocycle is not only able to readily accept or donate a proton, but it can also easily establish diverse weak interactions. Some of these intermolecular forces, such as like hydrogen bonding formation, dipole-dipole interactions, hydrophobic effects, van der Waals forces and π-stacking interactions of nitrogen compounds have increased their importance in the field of medicinal chemistry and allows them to bind with a variety of enzymes and receptors in biological targets with high affinity due to their improved solubility. The structural features of their derivatives are beneficial since they exhibit broad bioactivities.

II. SYNTHESIS OF 5-6 MEMBERED NITROGEN HETEROCYCLES

Five membered nitrogen heterocycles can be prepared by chalcones which are precursor of flavones and flavonoids. These are aromatic ketones bearing 1,3-diaryl-2-propen-1one framework (Di et al., 1999; Sahu et al., 2012). Chalcones have *α-β* unsaturated system in which three carbons join two aromatic rings (Nasir et al., 2013). It contains keto-ethylinic group (-CO-CH=CH) and exists in *cis* and *trans* form due to the presence of double bond in which *trans* form is thermodynamically more stable (MT Albuquerque et al., 2014). The conjugated double bond produces the delocalization of π electrons which reduces its electrophilic character and makes it an intermediate for the synthesis of various biologically important heterocycles such as pyrazoline, oxazoline, thiazine, oxazine, pyrimidine and much more. Thus synthesis of chalcones has generated vast interest of organic as well as medicinal chemists (Mathew et al., 2014). Formation of these nuclei involves cyclization of *α-β* unsaturated system of chalcones. Chalcones and its analogues have numerous pharmacological activities such as anti-microbial (Fang et al., 2014; Tran et al., 2012), anti-inflammatory (Bandgar et al.,2010; Zhang et al., 2010), analgesic (Samshuddin et al., 2012; Yadav et al., 2012), anti-viral, anti-oxidant (Bandgar et al.,2010; Doan and Tran, 2011; Samshuddin et al., 2012), anti-cancer (Bandgar et al.,2010; Zhang et al., 2010), anti-malarial (Hans et al., 2010; Yadav et al., 2012), anti-protozoal (Aponte et al., 2010; Hayat et al., 2011) and anti-convulsant (Beyhan et al., 2013).

Biological properties of chalcones are related to their structural features. As in case of antimalarial activity the double bond present between the *α, β* is required for the activity and substitution of electron donating and lipophilic group on both the rings A and B increases the activity (Motta et al., 2006). For the antibacterial activity compounds having hydroxyl group

have shown good activity and their methylation decreases the activity. The hydrophobic substitution also plays key role in the antibacterial potential as presence of hydrophobic group enhances inhibitory action (Avila et al., 2008). In case of anticancer activity cyclization to pyrazole enhances the cytotoxic activity as introduction of pyrazole moiety between the two rings enhances the rigidity which plays an integral role for the increase in cytotoxic potential. Pyrazole derivatives have been found to be more active than their corresponding chalcones (Bhat et al., 2005).

III. PHARMACOLOGICAL EVALUATION OF SYNTHETIC NITROGEN HETEROCYCLES

- **Antibacterial activity:**

The antibacterial activity of substances will be tested using the agar cup-plate technique. The diffusion of the test substance from a cavity through a hardened agar layer on a petri plate is the basis for this procedure.

Compounds used

2-aryl-4,5-disubstituted imidazoles and their N-Manmch bases, 1,3-diphenyl-5-substituted phenyl-4-bromo-2-pyrazomes and their corresponding pyrazolm-4-ones, and 2,3,5,6-tetraaryl-3,3a,5,6-tetrahydro-2H-pyrazolo[3,4-d]pyrazolo[3,4-thiazoles

Methods adopted

The in vitro testing will carry out using bacteria from the Post Graduate Department of Microbiology, Orissa University of Agriculture and Technology, Bhubaneswar, Onssa. Gram positive bacteria (Actmomycuspyogenes, Staphylococcus aureus, Streptococcusvmdance) and gramme negative bacteria (Klebsiellaaerogenes, Eschenchiacoh, Enterobacteraerogenes) will obtained from Standard microbiological procedures were used to identify these species. During the research, the following media will used:

1. Nutrient broth

2. Mueller Hinton agar medium

- **Antifungal activity:**

The antifungal activity of substances will be easily determined utilising the poison food approach.

Compounds used

2-aryl-4,5-dimethyl imidazoles and their N-Manmch bases, 1-(2,4-dinitrophenyl)-3-(3-mtropheny!)-5-substituted phenyl-4-bromo-2-pyrazolines and their corresponding pyrazoIm-4-ones.

Methods adopted

Selected human pathogenic fungus, such as Candida albicans, Aspergillusniger, and Tnchodermavindiae, will obtained from the Post Graduate Department of Microbiology, University of Agriculture and Technology, Bhubaneswar, Orissa, for in vitro testing. Sabouraud's dextrose agar will utilized as the study's medium (SDA)

- **Anti-Inflammatory Activity**

The anti-inflammatory activity of selected synthesised compounds, such as 2-aryl-4,5-diphenyl imidazoles, 2-aryl indolylimidazoles and their N-Manmch bases, 1,3-diphenyi-5-substituted phenyl-4-bromo-2-pyrazolines and their corresponding pyrazolin-4-ones, will evaluated using carrageenan as an oedematogenic agent, as suggested by Winter. The rats will be male Wistar albino rats weighing 180-200 g.

The results will statistically be assessed using the student’s t-test. The data will report as the mean SEM of six observations, with p-values less than 0.01 indicating statistical significance. At the end of the three hours, the percentage inhibition of paw oedema will determine.

IV. PHARMACOLOGICAL EVALUATION OF HERBAL EXTRACTS

- **Anti-Inflammatory Activity**

In this study, the anti-inflammatory activity of crude petroleum ether, chloroform, and ethanolic extracts of Pterospermumacenfolium Wild flowers, Martyniaannua Linn fruits, and BryonopsislaciniosaNaud roots will evaluated using carrageenan.

The gathered data will statistically analysed using the Student's t-test. The data will report as the mean SEM of six observations, with p-values less than 0 01 indicating statistical significance. At the end of the three hours, the percentage inhibition of paw oedema will determine.

- **Analgesic Activity**

The analgesic activity of crude extracts of Pterospermumacenfolium Wild flowers will be assessed using the acetic acid-induced writhing technique in this study.

Male Swiss albino mice, weighing 18-22 g, will be randomly divided into six groups of six animals each.

The significance will be determined using the student's t-test. The data will report as a mean ± SEIVI from six observations, with p-values less than 0.001 indicating statistical significance. The percentage of protection will determine as well.

V. CONCLUSION

The chemistry of heterocyclic compounds currently constitutes a very Important area of research It is a vast and expanding of chemistry because of the obvious applications of heterocyclic compounds in pharmacy, medicine, agriculture and many other fields Synthesis of heterocyclic compounds containing nitrogen atoms continues to be a field of enormous Interest to synthetic organic chemists due to Its varied antimicrobial and pharmacological activities.

With the changing scenario and the threat of several diseases to mankind and In View of the tremendous broad spectrum therapeutic properties coupled with the diverse synthetic modes available in the construction of nitrogen heterocycles, the area of heterocyclic chemistry research has become a challenging one in recent years.

The paramount Importance of heterocycles In natural product chemistry and pharmacology constantly encourages the search for new methods for the construction of these units and evaluation of their therapeutic activities Although a vast amount of pioneering work has been reported for the synthesis and structure-activity relationship of diverse ring structures in the last few decades, the recent Investigations still reman unabated The construction of diverse heterocyclic compounds from easily available starting materials, as well as evaluation of their possible antimicrobial and pharmacological activities is the main theme of the Synthetic Nitrogen Heterocycles of this thesis.

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