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An Overview On Evaluation Of Biological Activity Of Quinazoline Based Heterocycles

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Abstract

This paper reveals about the quinazolines, benzaimides and thiazolidinediones which comprise diverse therapeutically potent applications in the field of medicinal chemistry and synthetic applications in the field of the organic chemistry. This paper briefly reviews an appropriate balance between the broad spectrum pharmacological profile and synthesis of drugs that should be economical, harmless and environmental friendly.

With the idea in mind, it is projected in the present work to synthesize various series of quinazolines, benzaimides and thiazolidinediones based, pyrimidines, thiazoles. This study is expected to hopefully produce analogues with better biological profiles and with the minimal requirement to maintain the activity.

1. Introduction

Heterocyclic chemistry is a chemistry involving the heterocyclic compounds which contain atoms of atleast two different elements as number of ring. The heterocyclic may be inorganic, though the compound has carbon atoms in the ring, the word hetero means different from carbon and hydroge Nitrogen containing heterocyclic compounds plays an important role in medicinal chemistry. As shown in Figure 1, Quinazoline is one the most important compound of this class. It consists of two fused benzene and pyramidine ring. It is a yellow colour compound which is found in crystalline form. Quinazoline is known for its antimalarial activities.

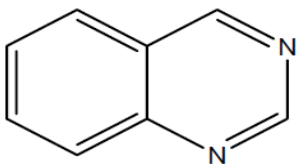

Figure 1. Quinazoline

Gabreil was first researcher who attempted and synthesized in the year 1903 and isolated from the Chinese plant Aseru. The biological activities of Quinazoline recognized after the synthesis of 2-methyl-1,3-aryl-4-quinazoline derivatives. This compound acts as sleep inducing agent and sedative in nature. Many researchers worked about the significant advances of medicines in the last 10-15 years of research. In 1968, only two derivatives of quinazoline i.e., methaqualone and diuretic quinathozone were used as soporific and anticonvulsant. More than 50 different kind of derivatives of same class were identified by 1980. These derivatives have different biological activities [1] such as analgesic, anticonvulsant, antitussive, soporific, sedative, tranquilizing, myorelexant, antirheumatic, hypotensive, antiallergic, bronchodilating, antidiabetic, cholagogue, diuretic, cystatic, antimalarial, spermicidal etc.

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As well known, Quinazolines play a versatile and important role in various biological activities [2-6]. It comprises many biological properties including antihypertensive [7], antimicrobial [8], antihyperlipidemic [9], anti-inflammatory [10] and anticonvulsant [11] activities. It also draws a great attention due to their wide range of therapeutic activities including antiviral [12], antibacterial [13], antifungal [14], antimalarial [15], anticancer [16], antihypertensive [17], diuretic [18], inhibition of derived growth factor receptor phosphorylation [19], anticonvulsant [20], antagonism of ghrelin receptor [21], anti-inflammatory, analgesic and COX-2 inhibitory activities [22].

Similarly, the derivatives of quinazoline are also potential bioactive agents and have been reported to exhibit a wide spectrum of pharmalogical properties. Quinazolin-4(3H)-ones with 2,3-disubstitution are reported to have significant anti-inflammatory [23] . The different derivatives of quinazoline has already been reported by various researchers in past in which some of them are 2-phenyl-3-substituted quinazolines [24], 2-methyl-3-substituted quinazolines, 2-methylthio-3-substituted quinazolines [25] and 2,3-disubstituted quinazolines [26]. All these derivatives exhibit anti-inflammatory activities. The known anti-inflammatory drug, Proquazone I, chemically known as 1-isopropyl-7-methyl-4-phenylquinazolin-2(1H)-one [27], and the recently developed derivatives of 2,3-diarylquinazolinone II chemically known as 3-(4-methanesulfonyl-phenyl)-2-(4-methoxy-phenyl)-3H-quinazolin-4-one [28] are good examples of quinazolinone derivatives with potent anti-inflammatory activity (Fig. 2).

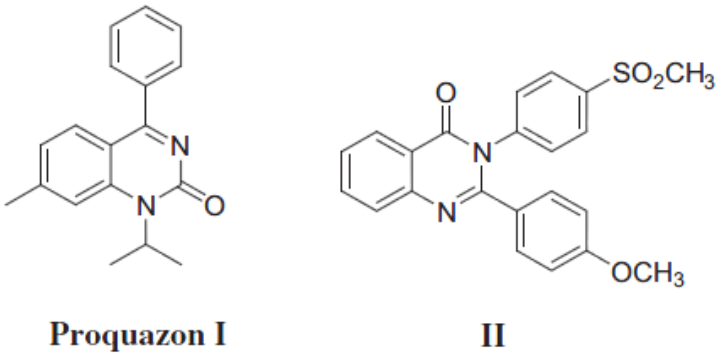

Fig 2: Quinazoline derivatives with potent anti-inflammatory activity

It is hoped that the synthesis and biological evaluation of heterocyclic compounds would provide a rational approach to the study of structure activity relationship of these molecules. Design and synthesis of bioactive molecules is a prime object of medicinal and organic chemists, who are interested to design a drug with minimum side effects and to find appropriate balance between the broad spectrum pharmacological profile and synthesis of drugs that should be economical and harmless. At present scenario, the major health problem in developing and developed countries is contributed by cancer and a wide range of drugs possessing different mode of action which are used to treat cancer either alone or in combination [29]. Quinazolines have merged as a versatile model for inhibition of a diverse range of receptor tyrosine kinases. Tyrosine kinases are enzymes concerned in many cellular processes such as cell proliferation, metabolism, survival, and apoptosis. Several tyrosine kinases are activated in cancer cells and results in tumor growth and progression [30]. So, many pharmaceutical industries, scientists and researchers are focusing on the inhibition of receptor tyrosine kinases (RTKs). They can be broadly classified as receptor such as epidermal growth factor receptor (EGFR), or non-receptor kinases. An important mediator of growth factor signaling pathways is the epidermal growth factor receptor. The most widely studied of epidermal growth factor receptor (EGFR), with the small-molecule inhibitor Gefitinib (as shown in Fig 3) is the first agent from this class which is to be approved for the treatment of Non-Small Cell Lung Cancer refractory to chemotherapeutic intervention [31]. Further 4-anilinoquinazoline is reported to be potent and highly selective inhibitors of RTKs [3]. The most promising small molecule selective EGFR-TK inhibitors include quinazolines. Some examples shown in Figure 3 includes which are currently approved drugs or in clinical trials [33].

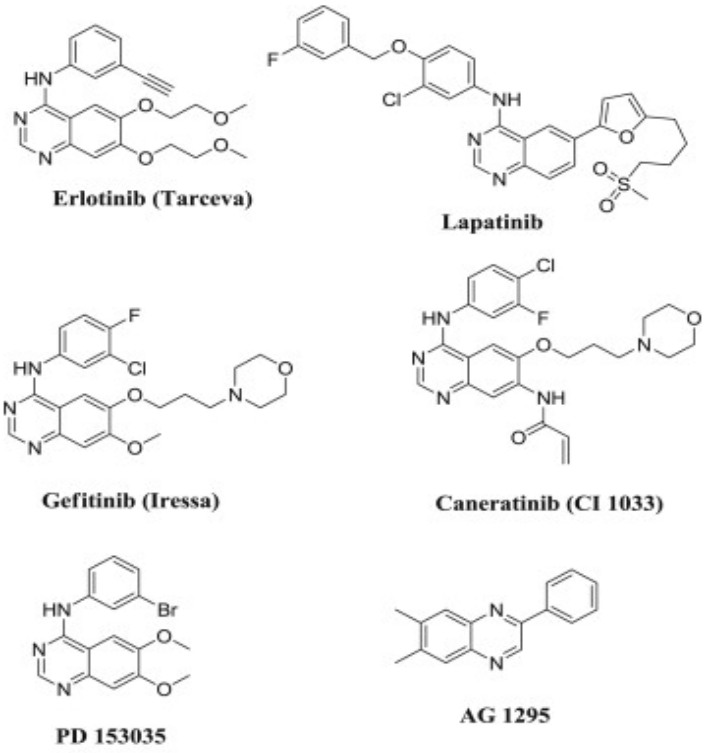

Fig 3: Chemical structures of EGFR-TKIs- quinazolines.

Like the quinazolines, Benzaldimines (Schiff's bases or Mannich bases) and 4-thiazolindinones also represent the most active class of compounds possessing a broad spectrum of pharmacological properties like anticancer, antitubercular activity. These Schiff bases (imines) can be achieved by the reaction of aldehydes and amines in acidic medium and involves the formation of carbon–nitrogen double bond .The development of carbon–nitrogen double bond plays important role in organic synthesis. Schiff bases have attracted considerable attention of organic chemists due to their significant biological activities like including antimalarial [34], HIV-inhibitory [35], analgesic, anti-inflammatory [36], anti-microbial [37], antifungal [38], anti-bacterial [39], anticancer activities [40]. The Schiff bases are also used as flexible components in nucleophilic addition with organometallic reagents [41] and in cycloaddition reactions [42].Schiff bases are active against a wide range of organisms for example; Candida Albicans, Escherichia coli Staphylococcus aureus, Bacillus polymxa, Trychophyton gypseum, Mycobacteria, Erysiphe graminis and Plasmopora viticola [43]. Figure 4 includes some examples of mannich bases that are currently in clinical trials.

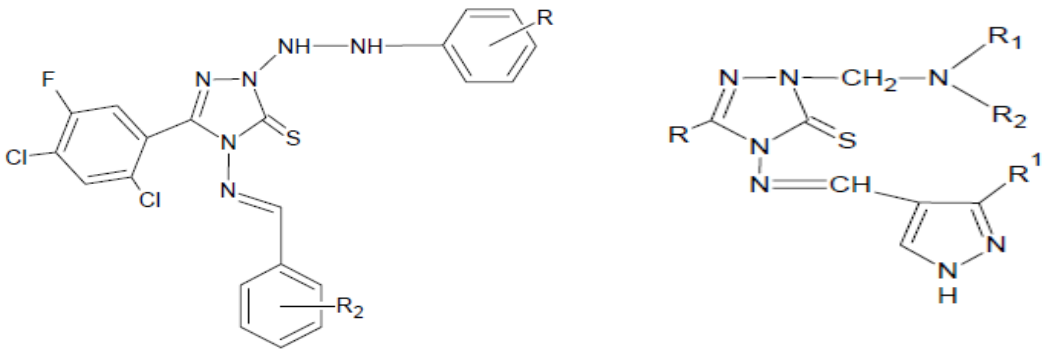

Fig 4: Chemical Structure of Some Mannich Bases

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Similar to six-membered heterocycles, the five-membered heterocycles i.e., 4-thiazolidinoneare has also attracted considerable attention for its wide range of pharmaceutical activities. These are the derivatives of thiazolidine which belong to an important group of heterocyclic compounds having sulfur and nitrogen in a five member ring. The activities of 4-

Thiazolidinones are due to the –C-N-S- linkage. Various thiazoline derivatives occupy an important role in medicinal chemistry as they show a variety of pharmaogical and microbiological activities like antibacterial [44], anticancer [45], antitubercular [46], antifungal [47], anti-inflammatory [48], antiviral [49], and analgesic [50].

Conclusion

The paper concludes that the quinazolines, benzaimides and thiazolidinediones contributes diverse therapeutically potent applications along with less economical, harmless and environmental friendly. It reflects with careful investigation that a new strategy or new route can be developed to synthesize medicinally potent new drug molecules. Also these heterocycles plays important and great potentials in the field of the organic chemistry as well as medicinal chemistry. These are considered as magic moieties which not only possess almost all types of biological activities but also have wide diversity in the biological profile which is the base to explore these heterocyclic to their multiple potentials against several activities.

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