Microwave-Promoted Synthesis Of Quinoline Heterocycles From Anilines

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Abstract

The production of biologically active heterocyclic compounds has attracted significant attention in the field of medicinal chemistry due to their diverse spectrum of biological effects and potential applications in treatment. Microwave-assisted techniques have emerged as very efficient tools in the area of organic synthesis, enabling rapid and skillful modifications. The aim of this research is to examine the use of microwave-assisted techniques in creating bioactive heterocyclic compounds. The focus will be on using starting materials derived from natural sources. The use of natural starting materials offers several advantages, including as sustainability, availability, and the potential for discovering novel compounds with unique biological characteristics. The objective of this research is to clarify the basic principles of microwave-assisted synthesis, with a particular focus on the latest advancements in this area. Moreover, this review will demonstrate the process of creating bioactive heterocyclic compounds from natural starting materials. Additionally, this study will analyze the biological characteristics and potential practical applications of these compounds, specifically emphasizing the significance of microwave-assisted synthesis in the realm of pharmaceutical investigation and progress.

Keywords: Bioactive heterocyclic compounds; microwave-assisted methodology; natural compounds; biological properties.

1. Introduction

Recently, there has been a change in research emphasis towards the creation of environmentally sustainable solutions. The multicomponent reaction approach is a technique that combines the economic aspects of new reactions with their related environmental factors. The technique indicated above consists of many synthetic steps, where the exclusion of any intermediate separation occurs. Hence, this method efficiently reduces response time, energy use, and utilization of raw materials (Ganpatrao, 2023).

Over the last several decades, there has been a notable surge in the emphasis and concentration on eco-friendly chemical processes, both in academic circles and the industrial sector. Highly unstable, toxic, and hazardous organic solvents are being regularly replaced via the use of solvent-free methods, as well as the application of ionic liquids, water, and phase-transfer catalysts. Polyethylene glycol (PEG) is advantageous as a reaction solvent because of its neutral properties. This allows for the preservation of susceptible functional groups that may be affected by acidic or basic conditions (Mathew et al., 2020).

Heterocyclic chemistry has great significance in the realm of organic chemistry, accounting for about one-third of current academic publications. Approximately two-thirds of organic molecules may be categorized as heterocyclic compounds. A carboxylic compound is an organic molecule with a cyclic structure where all carbon atoms are grouped in a ring form. A compound is considered heterocyclic if it has a ring structure in which at least one element, other than carbon, is present. Nitrogen, oxygen, and sulfur are widely acknowledged as the most frequent heteroatoms found in heterocyclic rings. However, it is important to mention that heterocyclic rings containing other heteroatoms have also received considerable attention in academic literature. A substantial number of heterocyclic compounds have been found, and this number is seeing rapid rise (Alamgir & Alamgir, 2018; Bansal, 2020; Taterao, 2023).

Heterocyclic chemistry originated from the fields of organic synthesis, natural products chemistry, and medicinal chemistry. A considerable proportion of heterocyclic chemists consider themselves to be organic chemists, and a substantial percentage also see themselves as natural products chemists and

medicinal chemists. The relationship across disciplines arises from the fundamental role that heterocyclic molecules play in biological systems. Heterocyclic chemistry has found widespread use in several fields such as biology, dyes, optical sensitizers, coordination compounds, polymeric materials, and many more domains. Given that a large proportion of physiologically active molecules include heterocyclic features, it is essential to recognize their importance in the area of combinatorial chemistry. The benefit of this resides in the capacity to identify prospective beginning points and improve the structures of these molecules (Rao et al., 2018). The goal of this project is to explore the use of microwave-assisted techniques in synthesizing bioactive heterocyclic compounds. The focus will be on using starting materials obtained from natural sources.

2. Microwave-assisted Synthesis of Complex Heterocyclic Molecules

In the 19th century, chemical reactions were carried out via a Bunsen burner. The exothermic flame enabled the execution of a chemical reaction by supplying heat energy. Later on, oil baths and hot plates were developed as substitutes, thus removing the need for open flames and therefore reducing the potential dangers linked to fire accidents (Adhikari et al., 2022). In the late 1980s, scientific literature started to record cases of chemical synthesis being carried out using household microwave ovens. Although the reduction in response time was substantial, there were difficulties in measuring the reaction parameters (Shalaby et al., 2023).

Specialized reactors were eventually created to facilitate chemical reactions, including the capacity to monitor the reaction's temperature and pressure (Zarecki et al., 2020). The microwave-assisted synthesis technique rapidly became popular because it can fully convert the chemicals used in chemical approaches, leading to a substantial decrease in reaction time. Moreover, the molecules are produced with exceptional efficiency. This procedure operates by aligning the dipoles in the reagents via the effect of an external field, which is induced by microwaves. It follows a well-established chemical method for synthesizing particular compounds.

Microwave radiation refers to a spectrum of electromagnetic radiation frequencies that vary from 30 gigahertz (GHz) to 300 megahertz (MHz). The use of microwave-assisted organic processes in combination with organic reactions done in

water or under dry conditions was first shown in 1990 by Verma (1999), and then investigated by later researchers. Literature often presents several examples of successful utilization of microwave irradiation in organic synthesis inside eco-friendly reaction medium, as shown by Sharma et al. (2018), as well as in solvent-free conditions, as indicated by Shaikh (2018). Utilizing microwave irradiation in harmless reaction solvents provides notable advantages, such as improved time efficiency and increased yields, in the domains of traditional medicinal chemistry and the production of heterocyclic systems.

3. Synthesis of Bioactive Heterocyclic Compounds from Natural Starting Materials

Alkaloids are a class of naturally-occurring compounds known for their wide array of biological effects, such as their ability to fight cancer, kill germs, and provide pain relief. Microwave-assisted synthesis has shown to be an effective method for synthesizing several alkaloids obtained from natural sources. Indole alkaloids are a notable group of alkaloids that exhibit a wide range of biological activities, such as anticancer, anti-inflammatory, and antibacterial effects. Microwave-assisted techniques have shown to be efficient in the synthesis of indole alkaloids, providing a rapid and effective approach to acquiring these very important chemical molecules. Microwave irradiation has been used to synthesize reserpine, a significant indole alkaloid known for its antihypertensive and antipsychotic effects, using natural sources like Rauvolfia serpentina (Bellavita et al., 2022).

Quinoline alkaloids are a unique group of physiologically active compounds that may be found in many natural sources, including plants, fungi, and marine organisms. Alkaloids have a broad spectrum of pharmacological properties, such as antimalarial, anticancer, and antiviral activities. Microwave-assisted synthesis has been used as an efficient technique to obtain quinoline alkaloids produced from natural sources. Camptothecin is an exemplary instance of a successful synthesis, since it is a potent quinoline alkaloid with remarkable anticancer effects. The synthesis of this molecule has been achieved using microwave irradiation, a technology that provides a quicker and more environmentally friendly approach to manufacture (Mahato et al., 2018).

Terpenoids, also known as isoprenoids, include a wide range of naturally occurring compounds that exhibit significant biological features, including anticancer, anti-inflammatory, and antiviral effects. Microwave-assisted synthesis has been used to enhance the efficiency of synthesizing terpenoids sourced from natural sources. Furan-based terpenoids are a specific kind of terpenoids that are distinguished by their existence of a furan ring structure. These chemicals have shown a wide variety of biological actions, such as anticancer and antibacterial effects. Microwave-assisted techniques have been used to synthesize terpenoids based on furan, enabling faster and more targeted conversions. A literature example demonstrates the use of microwave irradiation technology for the synthesis of artemisinin, a well-known furan-based terpenoid with antimalarial effects, derived from Artemisia annua. The use of this approach shown significant efficacy in promoting the synthesis of this crucial chemical (Kasmi et al., 2018).

Pyran-based terpenoids are a specific kind of terpenoids that have a diverse array of biological effects, including anticancer, antifungal, and anti-inflammatory activities. Microwave-assisted synthesis has been used to efficiently synthesize pyran-based terpenoids sourced from natural sources. A demonstration of the effective combination of microwave irradiation to produce paclitaxel, a well acknowledged pyran-based terpenoid known for its anti-cancer capabilities, has been achieved. This technology offers a more expedient and ecologically sound approach to synthetic synthesis (Eckl, 2022).

Flavonoids, a class of naturally-occurring compounds, demonstrate a wide array of biological effects in several plant species. These actions include antioxidative, anticancer, and anti-inflammatory characteristics. Microwave-assisted synthesis has been used to enhance the efficiency of synthesizing flavonoids obtained from natural sources. Flavones, a kind of flavonoid subclass, exhibit a diverse variety of pharmacological effects, including but not limited to their ability to combat cancer, reduce inflammation, and fight against viruses. Microwave-assisted techniques have been used to synthesize flavones, providing a rapid and efficient approach to generate these chemical compounds. An instance of this is the accomplished production of apigenin, a widely acknowledged flavone molecule famous for its ability to combat cancer and reduce inflammation. This synthesis

technique employs microwave irradiation and leverages naturally occurring sources such as chamomile (Orsat and Routray, 2017).

Isoflavones are a specific group of flavonoids that possess a wide range of biological characteristics, such as estrogenic, anticancer, and anti-inflammatory effects. Microwave-assisted synthesis has been successfully used as an efficient approach for synthesizing isoflavones obtained from natural sources. In the realm of organic chemistry, researchers have effectively used microwave irradiation to produce genistein, an isoflavone molecule known for its potential as an anticancer and neuroprotective drug. This novel technique provides a rapid and eco-friendly means of synthesizing genistein (Kshatriya et al., 2015).

Overall, microwave-assisted synthesis has emerged as a dominant and efficient technique for producing bioactive heterocyclic compounds sourced from natural sources, while also encouraging sustainability. Research has shown that using microwave irradiation may speed up and selectively alter substances, resulting in significant advantages such as shorter reaction times, increased product yields, and improved environmental sustainability. The versatility and potential of microwave-assisted methods in the production of diverse bioactive compounds are shown by the showcased examples of alkaloids, terpenoids, flavonoids, and other natural starting materials. Technological advancements are very important in the field of medicinal chemistry and drug discovery. They allow for the creation of novel therapeutic agents that may be used to treat various diseases and disorders. (Seth et al., 2017).

4. Biological Activities and Potential Applications

Bioactive heterocyclic compounds from natural sources have shown significant efficacy in inhibiting cancer growth, preventing apoptosis, and preventing cell spread. These compounds can be developed by targeting molecular pathways involved in cancer formation and progression. Indole alkaloids, such as vinblastine and vincristine, have shown anticancer efficacy by disrupting microtubule assembly in malignant cells. Similarly, paclitaxel, a terpenoid from Taxus brevifolia, has been used as a chemotherapeutic agent to impede cellular proliferation by promoting microtubule stabilization.

These compounds also possess antibacterial and anti-inflammatory properties, controlling inflammation pathways, reducing pro-inflammatory mediator synthesis, and inhibiting enzyme activation. Curcumin, a polyphenolic substance from Curcuma longa, has shown significant anti-inflammatory efficacy by inhibiting inflammatory enzymes and reducing pro-inflammatory cytokine production.

Antioxidants, such as flavonoids and terpenoids, play a crucial role in protecting cellular integrity against oxidative stress. Flavonoids, like quercetin and catechins, have potent antioxidant properties, while terpenoids and alkaloids also exhibit antioxidant properties. In addition to their anticancer and antimicrobial properties, these compounds also exhibit additional bioactivities, such as neuroprotective effects, antidiabetic effects, cardioprotective properties, antiviral capabilities, antiparasitic properties, and antifungal properties.

3. Conclusion

Ultimately, bioactive heterocyclic compounds derived from natural sources possess a wide range of biological characteristics and have significant potential for many applications. These compounds have shown potential in inhibiting the growth and spread of cancer by specifically targeting many molecular pathways that are involved in the development and advancement of the disease. In addition, they possess notable antibacterial properties against bacteria, fungi, viruses, and parasites, which makes them very suitable for the creation of antimicrobial agents.

Overall, this research study demonstrates the successful creation of biologically active compounds with diverse ring structures by the use of microwave-assisted synthesis methods, using naturally occurring raw materials. The technique has several advantages, such as improved reaction efficiency and reduced reaction durations, which make it a valuable asset in the field of pharmaceutical research. Possible areas for future research might include investigating other natural source materials, optimizing reaction conditions, and conducting more extensive studies of the biological features shown by the synthesized compounds.

Nevertheless, further research is required to fully understand the processes by which these actions occur, optimize their efficacy, and ensure the safety of humans. Furthermore, it is essential to do

research on sustainable and eco-friendly methods of production to meet the increasing demand for these materials.

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