Chapter 6
Indazoles Chemistry and Biological Activities:
Synthesis, Properties, and Biological Activities of Indazole

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ABSTRACT

In organic and medicinal chemistry research, indazole is an essential nitrogen-containing heterocyclic unit that is also a helpful precursor molecule for the synthesis of several kinds of heterocycles. The diverse tautomeric forms and unique chemical properties make it a versatile scaffold in medicinal chemistry. Indazole's relevance in the pharmaceutical industry is underscored by its presence in currently marketed drugs and investigational compounds, highlighting its therapeutic potential. In addition, the present ring structure has already been explored for diverse biological activity, including anti-microbial, anti-viral, anti-protozoal, anti-cancer, anti-inflammatory, analgesic, antipyretic, anti-oxidant, anti-convulsant, anti-depressant, anti-emetic,

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anti-diabetic, neuroprotective, antihypertensive, and anti-arrhythmic properties. This chapter comprehensively reviews indazole's synthesis, properties, and biological applications, along with an update on recent patents and ongoing clinical trials.

1. INTRODUCTION

The world's best-selling drugs are nitrogen-containing heterocyclic moieties due to their adaptability to various biological scaffolds as well as medicinal products. Various nitrogen-containing heterocycles like indole, indazole, quinolone, quinazoline, and carbazole are essential components for numerous synthetic and semi-synthetic pharmaceuticals. Indazoles are aromatic heterocyclic organic compounds with the chemical formula $C_7H_6N_2$ (Tan et al., 2022). This moiety has 10-π electrons in its bicyclic aromatic framework. Like the pyrazole molecule, it resembles pyridine and pyrrole, and its reactivity reflects its dual behaviour(Teixeira et al., 2006). This moiety is a member of the azoles family, first introduced by Emil Fisher in 1889. They consist of a bicyclic structure formed by fusing a benzene ring and a pyrazole ring. It is also called isoindazole and benzopyrazole (Kumar et al., 2022). Indazole is a naturally occurring alkaloid, so only a few naturally isolated indazole alkaloids from Nigella have been reported. Nigellicine and Nigellidine are the main indazole phytonutrients present in Nigella sativa seeds (Niu et al., 2020). The diverse bioactivities exhibited by indazole cores, attributed to the interaction of their two successive nitrogen atoms with enzyme sites, make them valuable for drug development. These scaffolds are desirable target compounds in chemical synthesis because of their intriguing biological characteristics. Numerous indazole derivatives with biological and medicinal qualities are possible due to the remarkable selectivity with which the indazole ring can be functionalized at various positions. Compounds with indazole rings have been commonly reported to display anti-microbial (J. R. Saketi et al., 2023), anti-viral (Yin et al., 2021), anti-protozoal (Rodríguez-Villar et al., 2021), anti-cancer (Cao et al., 2022), anti-inflammatory (Cheekavolu, 2016), anti-oxidant (Sapnakumari et al., 2014), anti-convulsant (Matsumura et al., 2013), anti-depressant (Degnan et al., 2016a), anti-emetic (Basak et al., 2020), anti-diabetic (Bushra et al., 2021), neuroprotective (Jismy et al., 2021), antihypertensive (Sączewski et al., 2016), anti-arrhythmic (Uppulapu et al., 2022), analgesic (Abbady et al., 2014) and antipyretic activity (Badawey et al., 1998).