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BENZOTHIAZOLE ANALOGUES: POTENT ANTICANCER AGENTS IN CONTEMPORARY PHARMACEUTICAL RESEARCH

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Abstract:
Cancer encompasses a diverse group of disorders characterized by uncontrolled proliferation of abnormal cells, which can originate in any organ or tissue of the body. The process of metastasis, where cancer cells spread to distant organs, significantly contributes to cancer-related mortality. Cancer is also referred to commonly as neoplasm or malignant tumor.
In 2018, cancer accounted for approximately 9.6 million deaths globally, making it the second leading cause of death. Benzothiazole, a significant class of pharmaceutical compounds, exhibits a wide array of biological activities, including antibacterial, anticonvulsant, anticancer, antifungal, antimitotic, and antitumor properties. Benzothiazole and its derivatives, such as the indole ring, have demonstrated promising anticancer activities. Studies on structure-activity relationships of benzothiazole derivatives have provided valuable insights into their efficacy against various cancer cell lines, enhancing our understanding of their potential in cancer therapy.

KEYWORDS: Benzothiazole antibacterial, anticonvulsant, anticancer, antifungal, antimitotic, and antitumor

INTRODUCTION:

Malignant tumors have the ability to invade nearby tissues and metastasize to distant parts of the body. They are synonymous with cancerous tumors. Unlike blood cancers such as leukemia, which typically do not form solid tumors, many other types of cancer can develop into solid tumors.
Benign tumors, in contrast, do not invade neighboring tissues. They are generally non-threatening and rarely recur after surgical removal, although they can grow quite large. Some benign tumors, like those found in the brain, can still pose serious health risks or symptoms.
Cancer encompasses a wide range of diseases that can originate in any organ or tissue of the body when abnormal cells proliferate uncontrollably, breach normal boundaries, and potentially metastasize to other organs. Metastasis, the process by which cancer spreads, is a leading cause of cancer-related deaths. Cancer is also known as neoplasm or malignant tumor.

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In 2018, cancer was responsible for approximately 9.6 million deaths globally, making it the second most common cause of death worldwide. Men commonly develop cancers such as lung, prostate, colorectal, stomach, and liver cancers, while women are more prone to breast, colorectal, lung, cervical, and thyroid cancers.

The global burden of cancer continues to rise, placing significant physical, emotional, and financial strain on individuals, families, communities, and healthcare systems. Many healthcare systems in low- and middle-income countries are inadequately equipped to handle this burden, resulting in limited access to timely and high-quality diagnosis and treatment for many cancer patients worldwide. Countries with strong healthcare systems have seen improved survival rates through accessible early detection, effective treatment, and comprehensive survivorship care.

LUNG CANCER

Timely medical intervention plays a crucial role in preventing severe health complications associated with lung cancer. Treatment approaches are determined by the patient's medical history and the stage of the disease. Lung cancer manifests primarily in two forms: small cell carcinoma (SCLC) and non-small cell carcinoma (NSCLC). SCLC, though less common, tends to grow rapidly, while NSCLC, more prevalent, progresses more slowly.

Lung cancer remains a significant global health challenge and the leading cause of cancer-related mortality. In 2020, it accounted for 1.8 million deaths, constituting 18% of all cancer-related deaths worldwide, according to the International Agency for Research on Cancer (IARC) GLOBOCAN 2020 estimates.

The primary cause of lung cancer is tobacco use, encompassing pipes, cigars, and cigarettes, although it can also affect non-smokers. Additional risk factors include pre-existing chronic lung diseases, exposure to air pollution, genetic predispositions to cancer, secondhand smoke exposure, and occupational hazards such as asbestos, radon, and certain chemicals.

BREAST CANCER

Breast cancer originates from abnormal proliferation of breast cells that form tumors capable of spreading throughout the body, potentially leading to fatal outcomes if left untreated. These cancerous cells typically begin in the milk ducts or milk-producing lobules of the breast. Early-stage breast cancer, known as "in situ," can be detected early and is generally not life-threatening. However, invasive breast cancer cells can invade nearby breast tissue, causing thickening or lumps. Metastasis occurs when these invasive tumors spread to nearby lymph nodes or other organs, posing a significant threat.

In 2020, approximately 2.3 million women worldwide were diagnosed with breast cancer, resulting in 670,000 deaths. Breast cancer affects women of all ages post-adolescence, with its incidence increasing with age.

Global statistics reveal substantial disparities in breast cancer incidence based on human development indices. In countries with very high Human Development Index (HDI), approximately 1 in 12 women may be diagnosed with breast cancer during their lifetime, with 1 in 71 succumbing to the disease. In contrast, in low HDI countries, 1 in 48 women die from breast cancer, despite only 1 in 27 receiving a diagnosis in their lifetime.

CERVICAL CANCER

Cervical cancer ranks as the fourth most common cancer in women worldwide, with over 660,000 new cases estimated in 2020. Approximately 94% of the 350,000 cervical cancer-related deaths that year occurred in low- and middle-income countries. Regions such as South-East Asia, Central America, and sub-Saharan Africa (SSA) exhibit the highest incidence and mortality rates of cervical cancer. Disparities in access to vaccination, screening, and treatment facilities, along with risk factors like HIV prevalence, and social and economic determinants including gender bias and poverty, contribute to regional variations in cervical cancer incidence.

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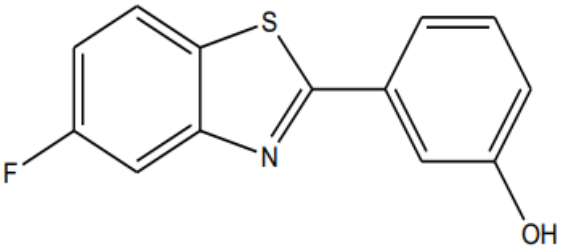
Women living with HIV are six times more likely to develop cervical cancer compared to the general population. Cervical cancer disproportionately affects younger women, with an estimated 20% of children whose mothers died from cancer being due to cervical cancer.
Researchers have synthesized fluorinated 2-aryl benzothiazole derivatives and evaluated their anti-tumor activities against cancer cell lines like MDA-MB-468 (derived from metastatic mammary gland/breast tissues) and MCF-7 (human breast adenocarcinoma). Among these derivatives, compounds 1 (3-(5-fluorobenzo[d]thiazol-2-yl)phenol) and 2 (4-(5-fluorobenzo[d]thiazol-2-yl)phenol) showed promising anti-tumor activity, with low GI50 values against the MCF-7 cell line. Additionally, N-bis-benzothiazole and benzothiazolyl thiocarbamide derivatives demonstrated significant cytotoxic activities against human cell lines U-937, THP-1, and B16-F10, highlighting their potential therapeutic applications in cancer treatment.



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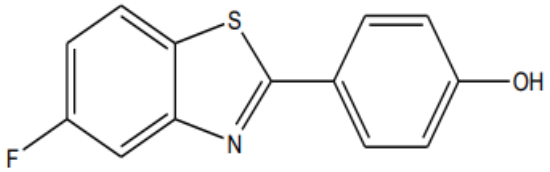

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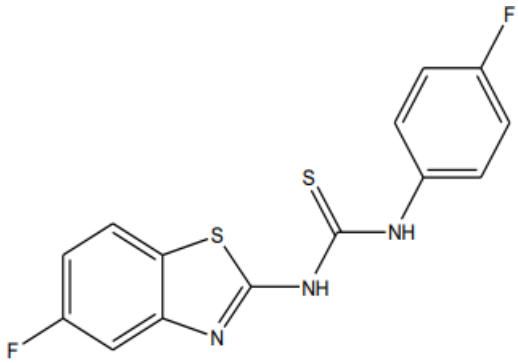

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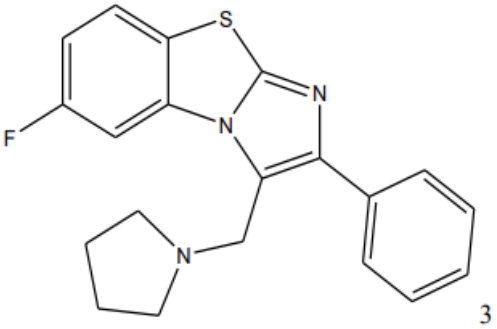

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CONCLUSION

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Benzothiazole, a versatile pharmacophore in medicinal chemistry, has garnered significant interest for its potential as antiproliferative and anticancer agents. This review underscores the increasing exploration and development of lead or hybrid structures incorporating the benzothiazole (BTA) moiety. The study highlights the promising role of BTA scaffolds in combating various types of cancers including ovarian, prostate, central nervous system, renal, gastric, pancreatic, liver, breast, and colon cancers. Structure-activity relationship (SAR) studies have elucidated that the anticancer efficacy of BTA derivatives hinges on the specific nature of substituents present in these molecules, which often involve multifactorial mechanisms not easily rationalized. The extensive research detailed in this review on the anticancer properties of BTA derivatives, along with insights into their drug targets where feasible, provides a valuable foundation for the development of novel therapeutic agents in cancer treatment.

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