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The Hybrid Drug Concept and Recent Advances in Anticancer Hybrids

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Abstract

Cancer is a complex disease, and treating it is difficult due to the variable efficacy of conventional anticancer drugs. A two-drug cocktail hybrid approach is a recent drug discovery strategy that involves combining two drug pharmacophores into a single molecule. The hybrid molecule acts on multiple targets simultaneously through distinct modes of action, resulting in greater efficacy and less susceptibility to resistance. As a result, there is enormous potential for using hybrid compounds to address the current challenges in cancer medicine. Recent research has used this technique to discover some intriguing molecules with significant anticancer properties. We present data on a number of promising hybrid anti-proliferative/anti-tumor agents developed over the previous ten years in this study. Quinazoline, indole, carbazole, pyrimidine, quinoline, quinone, imidazole, selenium, platinum, hydroxamic acid, ferrocene, curcumin, triazole, benzimidazole, isatin, pyrrolo benzodiazepine (PBD), chalcone, coumarin, nitrogen mustard, pyrazole, and pyridine-based anticancer hybrids are examples. Overall, this review demonstrates the potential benefits of combining pharmacophoric subunits from various known chemical prototypes to create more potent and precise hybrid compounds. This is useful information for researchers working on complex diseases like cancer.

Keywords: Molecular hybridization • Anticancer agents • Cell lines • Pharmacophore

Introduction

Cancer is a complex group of diseases characterised by uncontrolled cell proliferation and replication, which eventually disrupts normal physiology, metabolism, or structure. Benign tumours are self-limiting and do not invade or metastasize; however, in advanced stages, groups of cells exhibit uncontrolled growth, invasion, and metastasis. Cancer cells migrate from one organ to another of the body through the circulatory and lymphatic systems during the metastasis stage. Cancer is caused by a series of harmful mutations that alter cell functions. These mutations frequently result in abnormal proliferation. Cancer is a major global health issue that continues to be a leading cause of morbidity and mortality, with various cancer types.

Literature Review

Due to resistance and a lack of selectivity, cancer chemotherapy with single-agent or single monofunctional 'targeted' drugs has a low success rate. Combination therapy was developed to address this limitation. Two or more medicines that act on distinct sites simultaneously or concurrently are used; multi-targeting or promiscuous drug treatment is used; and hybridization drugs are used. Despite the use of drug-combination medicines, tumour heterogeneity, drug-drug interactions, unpredictable pharmacokinetic safety profiles, and poor patient compliance pose a problem for cancer treatment. As a result, improving drug selectivity while eliminating drug resistance has become critical for successful cancer treatment. Cancer care presents unique challenges in both developing and developed countries. These issues include healthcare financing, patient awareness, and treatment delivery.

One approach to increasing the efficacy of a two-drug cocktail is to use so-called hybrid drugs. The hybridization of biologically active molecules is a novel concept and a potent tool in drug design and development, with applications in a wide range of diseases. It is a rational design strategy for such ligands or prototypes based on the identification of pharmacophoric subunits that retain pre-selected properties of the original templates. "Single molecule multiple targets" or "multiple ligands" are other terms for hybrid drugs. Hybrid molecules have the structural characteristics of two "parent" molecules. Two biologically active parent molecules that act on two distinct pharmacological targets.

Discussion

Furthermore, hybrid drugs have a high molecular mass and lipophilicity, which violates Lipinski and Veber's rules. However, hybrid anticancer drugs have significant advantages over conventional anticancer drugs because they are designed to act on a different bio target or interact with multiple targets at the same time, reducing the likelihood of drug-drug interactions, with fewer side effects and a lower propensity to elicit resistance compared to the parent drugs. These novel hybrid molecules have increased affinity, efficacy, and safety. Nowadays, hybrid drugs have sparked interest in the purposeful and logical design of ligands that function selectively on multiple targets, as evidenced by an increase in the number of relevant publications in the field.

Inflammation activates the vascular endothelium in response to infection or injury, resulting in pro-inflammatory signalling, coagulation, increased barrier permeability, and excessive leukocyte trafficking to vital organs such as the lungs, liver, and kidneys. Increased leukocyte trafficking is linked to tissue damage, organ dysfunction, and increased mortality. As a result, the endothelium plays an important role in cytokine-induced changes and is an important therapeutic target. While endothelial cells share many characteristics, EC heterogeneity causes organ-specific variations in EC structure, function, and mechanisms that regulate leukocyte trafficking into key organs.

While several studies have examined the functional changes in ECs of various organs during cytokine-induced changes such as those seen in sepsis, the underlying molecular mechanisms of this differential response have not been investigated. Because inflammation is a highly dynamic process, the level of protein alterations may vary across disease stages. In contrast to genetic analyses, which often provide indirect clues about cell function, proteomic analysis can provide direct insight into protein expression in organ-specific ECs

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and aid in the closure of the genotype-phenotype gap. Despite this, few previous studies have identified potential protein regulation patterns or assessed the interaction and differential expression of various proteins in organs such as the lungs, liver, and kidneys during inflammation.

Quinazoline is a heterocyclic compound with anticonvulsant, anticancer, analgesic, sedative, antihypertensive, anti-inflammatory, anti-histaminic, antimicrobial, antiviral, and anti-tubercular properties. Quinazoline-containing compounds were studied for their ability to inhibit kinases, which are important targets for cancer medicine development.It created and tested quinazoline-based imidazole hybrids for anticancer activity against Epidermal Growth Factor Receptor and HT-29 cells. The majority of the synthesised compounds exhibited potent anticancer activity. Among them, compound excellent activity in comparison to gefitinib control [1-5].

Conclusion

For a long time, medicinal chemists from around the world have been attempting to develop new and effective cancer treatments. Because a complex disease like cancer cannot be effectively treated with a single drug, combination therapy and hybrid chemotherapeutics have become more common. This study explains the rationale behind the design of anticancer agents using molecular hybridization. Because it combines two moieties to create new molecular scaffolds, this method has promise. Because it can produce compounds with distinct and/or multiple modes of action and minimal side effects, molecular hybridization has a wide range of applications. The few examples in this article are not meant to be an exhaustive list of anticancer hybrids, but rather to provide a quick explanation of the concept.

Acknowledgement

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Conflict of Interest

There are no conflicts of interest by author.

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