Colloid and Polymer Science
https://doi.org/10.1007/s00396-024-05357-5

RESEARCH

Biological evaluation of folic acid functionalized nano-zeolitic imidazolate framework-8 for cancer therapy

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Received: 1 October 2024 / Revised: 22 November 2024 / Accepted: 29 November 2024

Abstract

Conventional chemotherapy often results in toxicity to normal cells and hampers cancer treatment efficacy. Cancer targeting via surface-functionalized nanocarrier offers an excellent opportunity for tackling this unwanted issue. However, a comprehensive understanding of its toxicity and safety in biological entities remains limited. In this study, we report the cancer-selectivity of surface-functionalized nano-zeolitic imidazolate framework-8 (FA@nZIF-8) and its safety characteristics in small organisms including zebrafish embryos and brine shrimp. The FA@nZIF-8 exhibited higher selectivity (3.95) towards cancer cells (MCF7) compared to pure nZIF-8. Moreover, this functionalized nano-ZIF-8 not only enhanced permeability performance but also appeared to be a significant survivability advantage, 80% ($P < 0.001$) with a higher survival rate compared with pure nZIF-8 at the 96-h mark. No scoliosis appeared in healthy zebrafish embryos for both nanoparticle systems. Monitoring brine shrimps showed minimal toxicity induction at a certain level of concentration. This study suggests that surface-functionalized FA@nZIF-8, with its cancer-selective behavior and promising safety characteristics, has bright potential for further exploration in cancer therapy.

Keywords Cancer · Selectivity · Zebrafish embryos · Brine shrimps · ZIF-8

Introduction

Cancer is the most diagnosed cancer and the leading cause of cancer-related mortality among females [1–3]. Globally, the cancer burden is expected to increase significantly, with 12.7 million new cases reported in 2008 and an expected rise to 22.2 million cases by 2034 [4, 5]. It is important to note that men can also develop breast cancer, though it is considered rare, accounting for approximately 1% of worldwide cases [6]. Conventional cancer treatments, such as chemotherapy, are often inefficient and non-selective, affecting both healthy and cancerous cells. Patients frequently discontinue treatment due to unbearable side effects, such as hair loss and loss of appetite [7]. Additionally, chemotherapy drugs often exhibit low accumulation and selectivity at tumor sites, limiting their effectiveness [8]. The nonselective nature of chemotherapy has driven the development of targeted drug therapies.

Previous studies have identified a distinguishing characteristic in some cancer cells which is the overexpression of folate receptors [9–11]. Folate receptor α (FRα) is a minor glycoprotein found on cell membranes that binds to and internalizes folic acid, facilitating DNA and RNA synthesis [10, 11]. In 1991, Coney et al. first discovered FRα in human ovarian cancer cell lines, and subsequent studies revealed its discriminatory upregulation in various solid cancers, including ovarian, kidney, lung, and breast cancer [11]. With the overexpression of FRα on cancer

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Published online: 14 December 2024