European Journal of Medicinal Chemistry xxx (xxxx) 117424

Contents lists available at ScienceDirect

European Journal of Medicinal Chemistry

journal homepage: www.elsevier.com/locate/ejmech

Review article

Multifunctional metal-organic frameworks in breast cancer therapy: Advanced nanovehicles for effective treatment

Shefali Shukla [a,*], Dipankar Bagchi [a], Divya [a], Khushi [a], Y. Veera Manohara Reddy [a,**], Jong Pil Park [b,***]

[a] Department of Chemistry, Sri Venkateswara College, University of Delhi, New Delhi, India
[b] Department of Food Science and Technology, GreenTech-based Food Safety Research Group, BK21 Four, Chung-Ang University, Anseong, 17546, Republic of Korea

ARTICLE INFO

Keywords:
Breast cancer
Chemotherapy
Metal-organic frameworks
Phototherapy
Theranostics

ABSTRACT

Breast cancer is the second-most common cause of cancer-related death among women worldwide, with a gradual annual increase of 0.5 % in its occurrence rate in recent years. This complex ailment exhibits considerable diversity, with a mortality rate of 2.5 %. One promising area of research for its treatment is the development of MOFs, which are intricate three-dimensional (3D) structures constructed from metal ions or clusters joined with organic ligands through coordinate bonds. MOFs have emerged as versatile platform overcoming the limitations of conventional chemotherapeutics including poor drug solubility, non-specific targeting, and multidrug resistance. These applications are attributed to their adjustable porosity, chemical makeup, dimensions, straightforward surface customization capabilities, biocompatibility, nontoxicity etc. These properties position MOFs as excellent candidates for diverse regimes of cancer therapeutics including innovative approaches such as phototherapy, chemotherapy, immunotherapy, gene therapy, sonodynamic therapy, and various combination therapies. The article emphasizes the functionalization and applications of MOFs, with a primary focus on their therapeutic capabilities, synergistic approaches, and theranostic strategies that integrate diagnostic and therapeutic functions. Strategies to improve MOF biocompatibility and stability, such as surface modifications and biocompatible coatings are also discussed. Insights on various challenges and future prospects are provided to address current limitations and inspire further research, paving the way for clinical translation of MOF-based breast cancer therapies.

1. Introduction

Breast cancer is the most frequently identified form of carcinoma, affecting approximately one million women annually. Its prevalence, affecting nearly one in eight women, underscores its significance worldwide [1,2]. This cancer primarily originates in the inner layer of milk-producing glands or lobules, as well as the ducts, which are small conduits responsible for transporting milk [3]. The age group of 40–60 years is the prime target for different types of in situ and invasive breast cancers. The advancement of anticancer medications that target critical proteins such as human epidermal growth factor receptor 2 (HER2), vascular endothelial growth factor (VEGF), insulin-like growth factor binding proteins-3 (IGFBP-3), and estrogen receptor (ER) and gene suppression using aptamers and small interfering RNA (siRNA) has caused a significant shift in breast cancer therapy. This has shifted the focus from merely addressing tumor size to a more biologically centered approach [4]. Tumors that express ER and/or the progesterone receptor (PR) are categorized as hormone receptor-positive breast cancers, whereas those that do not express ER, PR, or HER2 are categorized as triple-negative breast cancer (TNBC).

Among the various treatment methods, chemotherapy is one of the most traditional therapies for breast cancer and is now ingeniously combined with the Fenton reaction [5,6]. The prolonged use of traditional chemotherapeutic drugs, such as DOX, poses several major challenges such as non-selectivity, development of multidrug resistance (MDR) over time, compromised loading efficiency, non-biocompatibility etc. Additionally, toxicity in the liver, kidneys, and heart owing to the excessive production of reactive oxygen and nitrogen species can harm both cancer and healthy cells through oxidative stress, leading to DNA damage and reduced protein synthesis [7–9]. To address these limitations, researchers are exploring advanced drug de-

* Corresponding author.
** Corresponding author.
*** Corresponding author.
E-mail addresses: shefali.shukla@yahoo.co.in (S. Shukla), dr.yvmanohararedy@gmail.com (Y.V. Manohara Reddy), jppark@cau.ac.kr (J.P. Park).

https://doi.org/10.1016/j.ejmech.2025.117424
Received 12 January 2025; Received in revised form 10 February 2025; Accepted 18 February 2025
0223-5234/