Food Science & Nutrition

WILEY

Food Science & Nutrition Open Access

REVIEW OPEN ACCESS

Phloridzin as a Nutraceutical for Cancer Prevention and Therapy: A Comprehensive Review of Its Mechanisms, Bioavailability Challenges and Future Applications

Praveen Dhyani[1] | Priyanka Sati[2] | Dharam Chand Attri[3] | Eshita Sharma[4] | Ruchi Soni[5] | Javad Sharifi-Rad[6,7,8] | Daniela Calina[9]

[1]Institute for Integrated Natural Sciences, University of Koblenz, Koblenz, Germany | [2]Department of Biotechnology, Kumaun University, Bhimtal, India | [3]Department of Botany, Central University of Jammu, Rahya-Suchani (Bagla), India | [4]Department of Molecular Biology and Biochemistry, Guru Nanak Dev University, Amritsar, India | [5]Regional Centre for Organic and Natural Farming, Ghaziabad, India | [6]Universidad Espíritu Santo, Samborondón, Ecuador | [7]Centro de Estudios Tecnológicos y Universitarios del Golfo, Veracruz, Mexico | [8]Department of Medicine, College of Medicine, Korea University, Seoul, Republic of Korea | [9]Department of Clinical Pharmacy, University of Medicine and Pharmacy of Craiova, Craiova, Romania

Correspondence: Javad Sharifi-Rad (javad.sharifirad@gmail.com) | Daniela Calina (calinadaniela@gmail.com)

Received: 5 April 2025 | **Revised:** 15 May 2025 | **Accepted:** 20 July 2025

Funding: The authors received no specific funding for this work.

Keywords: anticancer activity | bioavailability | flavonoids | GLUT inhibitors | phloridzin

ABSTRACT

The global rise in cancer incidence has driven the search for safer, more effective therapies, with natural compounds gaining increasing attention. Phloridzin, a dihydrochalcone glycoside abundant in apple trees (*Malus* spp.), has demonstrated notable anticancer properties. This review summarizes its pharmacological profile, natural sources, and structural characteristics, with a focus on its mechanisms of antitumor action. We conducted a structured literature search across SCOPUS, PubMed, Google Scholar, and TRIP databases, highlighting studies on phloridzin's anti-proliferative, pro-apoptotic, anti-inflammatory, and metabolic regulatory effects across various in vitro and in vivo cancer models. Key mechanisms include glucose transporter inhibition (GLUT1/2), modulation of PI3K/AKT/mTOR and JAK2/STAT3 signaling, and suppression of metastasis and angiogenesis. Despite compelling preclinical evidence, phloridzin's clinical application is limited by low bioavailability. Novel delivery systems and synthetic derivatives, such as fatty acid esters, have shown improved pharmacokinetic profiles and efficacy. Future studies should prioritize translational research and clinical trials to validate phloridzin's potential as an adjunct or alternative therapy in oncology.

1 | Introduction

Phytochemicals are biologically active organic substances found in plants, synthesized by the secondary metabolism of cells. Phytochemicals have a broad role in plant systems, such as (among many) color, aroma, flavor, and defense mechanism. For ages, these phytochemicals were vital components in traditional health care systems worldwide, as plants were one of their essential components. Nevertheless, in modern medicine, owing to their capability to regulate various physiological processes in humans with fewer side effects, they are widely researched and used as plant-based drug molecules instead of synthetics (Tzevtkov et al. 2023). Among the various classes of phytochemicals, flavonoids have been studied in numerous clinical trials due to their multiple pharmacological activities beneficial to the human body (Bisol et al. 2020; Russo et al. 2019). Phloridzin is a flavonoid with diverse bio-effects belonging to the subclass of dihydrochalcones. It is also known as phloretin 2′-O-glucoside,