




Review

# Therapeutic Potential and Pharmaceutical Development of a Multitargeted Flavonoid Phloretin

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**Abstract:** Phloretin is a flavonoid of the dihydrogen chalcone class, present abundantly in apples and strawberries. The beneficial effects of phloretin are mainly associated with its potent antioxidant properties. Phloretin modulates several signaling pathways and molecular mechanisms to exhibit therapeutic benefits against various diseases including cancers, diabetes, liver injury, kidney injury, encephalomyelitis, ulcerative colitis, asthma, arthritis, and cognitive impairment. It ameliorates the complications associated with diabetes such as cardiomyopathy, hypertension, depression, memory impairment, delayed wound healing, and peripheral neuropathy. It is effective against various microbial infections including *Salmonella typhimurium*, *Listeria monocytogenes*, *Mycobacterium tuberculosis*, *Escherichia coli*, *Candida albicans* and methicillin-resistant *Staphylococcus aureus*. Considering the therapeutic benefits, it generated interest for the pharmaceutical development. However, poor oral bioavailability is the major drawback. Therefore, efforts have been undertaken to enhance its bioavailability by modifying physicochemical properties and molecular structure, and developing nanoformulations. In the present review, we discussed the pharmacological actions, underlying mechanisms and molecular targets of phloretin. Moreover, the review provides insights into physicochemical and pharmacokinetic characteristics, and approaches to promote the pharmaceutical development of phloretin for its therapeutic applications in the future. Although convincing experimental data are reported, human studies are not available. In order to ascertain its safety, further preclinical studies are needed to encourage its pharmaceutical and clinical development.

**Keywords:** phloretin; therapeutic potential; physicochemical properties; pharmaceutical development; toxicity

## 1. Introduction

Flavonoids are biologically active molecules widely present in foodstuffs of herbal origin. Several health benefits are associated with the regular intake of flavonoids—in particular, decreased risk of various diseases [1]. Therefore, interest has been growing in dietary flavonoids, primarily in fruit- and vegetable-rich diets. Phloretin is a dihydrogen chalcone flavonoid naturally present in ample amounts in apples and strawberries [2]. This



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