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Review article

Molecular mechanisms underlying anticancer effects of myricetin

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ABSTRACT

Dietary guidelines published in the past two decades have acknowledged the beneficial effects of myricetin, an important and common type of herbal flavonoid, against several human diseases such as inflammation, cardiovascular pathologies, and cancer. An increasing number of studies have shown the beneficial effects of myricetin against different types of cancer by modifying several cancer hallmarks including aberrant cell proliferation, signaling pathways, apoptosis, angiogenesis, and tumor metastasis. Most importantly, myricetin interacts with oncoproteins such as protein kinase B (PKB) (Akt), Fyn, MEK1, and JAK1–STAT3 (Janus kinase–signal transducer and activator of transcription 3), and it attenuates the neoplastic transformation of cancer cells. In addition, myricetin exerts antimitotic effects by targeting the overexpression of cyclin-dependent kinase 1 (CDK1) in liver cancer. Moreover, it also targets the mitochondria and promotes different kinds of cell death in various cancer cells. In the present paper, a critical review of the available literature is presented to identify the molecular targets underlying the anticancer effects of myricetin.

Contents

1. Introduction

The term “cancer” refers to a pleiotropic disease that is caused by abnormal growth of cells, which then potentially invade and/or spread to other organs and tissues [1]. According to GLOBOCAN data, cancer affects 14.1 million people worldwide each year [2]. Pathophysiological studies have shown that about 90–95% of cancers are caused by epigenetic factors such as smoking, diet, infections, radiation, and environmental pollutants [3–8]. Various therapeutic protocols are currently available for treating cancer such as surgery, chemotherapy, phototherapy, and radiotherapy. However, the current therapeutic strategies have certain limitations such as poor outcome, high cost, risk of relapse,

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as well as emergence of drug resistance. Hence, natural dietary compounds are being increasingly studied for their significant anticancer activity and negligible side effects [9–15].

Increasing evidence in recent years has shown that phytochemicals exhibit significant therapeutic activity with negligible side effects [16–19]. Polyphenols constitute an important class of natural bioactive compounds abundantly found in different plant species [9,20–23]. Thus far, flavonoids are the most common polyphenolic antioxidants [22,24]. There is considerable evidence that flavonoids possess potent anticancer effects via various molecular pathways. Structurally, flavonoids contain a basic benzo-γ-pyrone structure [25–28], and they are divided into different groups such as flavones, flavonols, flavanols, flavononols, flavanones, anthocyanidins, isoflavones, dihydroflavonols, flavan-3,4-diols, coumarins, chalcones, dihydrochalcones, and aurones [29,30].

Myricetin (3,5,7-trihydroxy-2-(3,4,5-trihydroxyphenyl)-4-chromenone) is a common dietary flavonoid abundantly found in plant sources (Fig. 1) [31]. Studies have shown the different protective effects of myricetin including its antioxidant, cytoprotective, antiviral, antimicrobial, and antiplatelet activities [32]. Moreover, myricetin exhibits an anticarcinogenic effect against several types of cancers in various ways. The aim of the present article was to review scientific reports on the molecular targets of myricetin in various types of human cancers.

2. The chemistry and source of myricetin

Flavonoids are ubiquitous, natural polyphenolic compounds based on a 15-carbon skeleton (**1**) (Fig. 2). Their structure comprises two aromatic rings (rings A and B) joined together by a three-carbon chain that often cyclize to form ring C (**1**). Based on the presence or absence of the 4-ketone functional group, the C2–C3 double bond, oxygenation at C-3, etc., flavonoids are further divided into many structural subclasses. For example, the common flavonoid luteolin (**2**), which contains a C2–C3 double bond and a catecholic ring B, belongs to the flavone group.

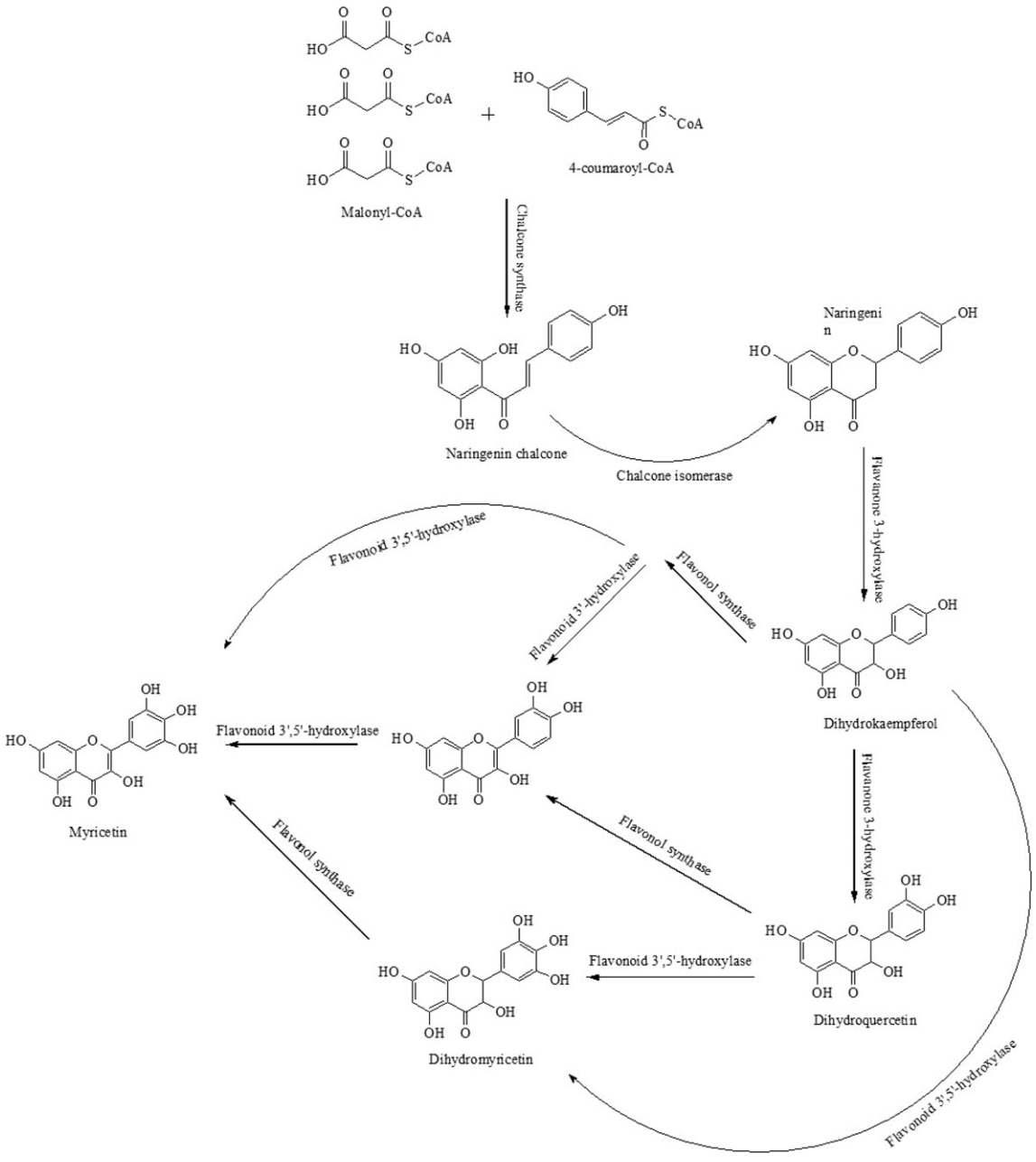

Fig. 1. Biosynthetic pathways of myricetin.