TAXIFOLIN IN MEDICAL PRACTICE

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The article provides information about Taxifolin, which plays an important role in the prevention and treatment of various diseases. Studies have revealed a wide range of pharmacological activities of taxifolin: antioxidant, anti-inflammatory, hepatoprotective, antiangiogenic properties, antidiabetic, cardioprotective, neuroprotective, etc. By inhibiting enzymes responsible for the infection and inflammatory response in the brainstem, Taxifolin also plays a neuroprotective role supporting its activity against Alzheimer's disease. Taxifolin has been shown to have excellent antioxidant activity, preventing lipid peroxidation, causing cleavage of poly(ADP-ribose) polymerase by H2O2.

Keywords: Taxifolin, flavonoid, antioxidant activity, oxidative stress.

In recent years, bioactive compounds derived from plants have been identified as new agents that play an important role in the prevention and treatment of various diseases, including cardiovascular and neurodegenerative diseases [1]. Flavonoids, which are hydroxylated phenolic compounds, have been shown to be beneficial to human health [2]. Studies have shown a wide range of pharmacological activities of flavonoids, including antioxidant, anti-inflammatory, hepatoprotective, antiangiogenic, antidiabetic, cardioprotective, and neuroprotective properties. In addition, flavonoids have a positive effect on Alzheimer's disease. This activity mainly depends on the degree of their polymerization, as well as the degree of hydroxylation, structural class, other substitutions and conjugations, and metal chelation activity [3]. Recent studies show that higher dietary flavonoid intake is inversely associated with the risk of death and some types of depression [4]. Taxifolin is a subclass of flavonoids, isoflavones of the flavonoid family. The structure contains a 3-hydroxyl group in the C ring, which is attached to the B ring at carbon-2 [5]. Taxifolin consists of two aromatic rings containing two phenolic groups (-OH). This phenolic group accounts for the strong antioxidant activity [6]. The strong antioxidant activity of taxifolin is mainly due to its conjugated structures and resonance stability of both phenolic rings [7]. The presence of the C2-C3 double bond is crucial for the inhibitory activity of flavonoids. Taxifolin lacks the C2-C3 double bond, which makes it highly susceptible to inactivation by forming strong hydrogen bonds with macromolecules. The presence of the 3-OH group in the C ring is responsible for the modulating effect against the oxidative burst of neutrophils [8]. Various studies have been conducted on the bioavailability of taxifolin upon oral administration to rats. Plasma taxifolin concentration was found to be very low after oral administration of 10-100 mg/kg body weight in an experiment by Wang and colleagues [9]. The bioavailability was estimated to be 0.17% compared to intravenous administration. Another study where taxifolin was administered to male rats intravenously at a dose of 50 mg/kg or orally at doses of 12.5, 25 or 50 mg/kg as a single dose, the highest concentration of taxifolin was found in plasma, kidney, liver, heart, spleen, brain, skeletal muscle and lung within 24 hours of administration. In this study, the bioavailability of taxifolin was 24% [10]. Toxicity studies of taxifolin have been conducted by various investigators and optimal doses for humans and animals have been obtained. Toxicity study was conducted before determining the toxic dose considered for use as a food additive in various marketed products [11]. Taxifolin is associated with antioxidant activity and protective vascular effects [12].

In the study, taxifolin-treated rats showed decreased lipid peroxidation in the liver and serum through thiobarbituric acid reaction, demonstrating the antioxidant properties of taxifolin [13]. The antioxidant activity of taxifolin is also demonstrated through its neuroprotective effects by inhibiting oxidative damage to neurons in rat cortical cells, which is supported by DPPH radical scavenging activity and inhibition of lipid peroxidation [14]. The antioxidant potential of taxifolin was also evaluated by deoxyribose degradation assay for electrochemical redox potentials [15]. According to the experiment of Wang et al., taxifolin can regulate NF-κB activation in rats diagnosed with cerebral

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ischemia-reperfusion injury. In addition, taxifolin is associated with inhibition of leukocyte infiltration and COX-2 and iNOS expression in the brain [16]. This proves the antioxidant activity of taxifolin through the activation of NF-κB pathway. It is also effective against osteoclastogenesis, which was studied in vivo and in vitro models [17]. Taxifolin was found to cause inhibition of osteoclastogenesis through the suppression of RANKL-induced gene expression without significant cytotoxicity [18]. Silymarin is a widely used hepatoprotective drug of which taxifolin is a key component. Various studies have reported that taxifolin at doses of 0.25, 0.5 and 1 mg/kg exhibited significant hepatoprotective activity in rotenone-induced rats. Significant decrease in total protein concentration, bilirubin activity, alanine aminotransferase (ALT), alkaline phosphate (ALP), gamma-glutamyl transferase and aspartate aminotransferase (AST) were observed in taxifolin-treated animals [19].

In addition, taxifolin has been shown to have hepatoprotective effects in patients with carbon tetrachloride-induced acute liver injury. This has also been evaluated in mice. Taxifolin reduced liver injury, vacuole formation, neutrophil infiltration, necrosis, MDA levels, and increased antioxidant enzyme activity [20]. According to studies, taxifolin used alone or in combination with cilostazol significantly reduced high αβ and C99 levels in N2 aSwe cells. It is also associated with synergistic inhibition of amyloidogenesis by suppressing P-JAK2/P-STAT3-dependent NF-κB-associated BACE1 expression through SIRT1 activation [21]. Taxifolin restores vascular integrity and memory in cerebral amyloid angiopathy (CAA) by inhibiting amyloid-β oligomer formation [22]. A recent study by Inoue and colleagues showed that taxifolin increases cerebral blood flow, removes amyloid-β from the brain, and prevents cognitive dysfunction by suppressing the ApoE-ERK1/2-amyloid-β axis [23]. In a recent study, the ability of taxifolin against postprandial hyperglycemia and α-amylase inhibitory activity were evaluated in an alloxan-induced diabetes model in rats. The experimental result demonstrated the potent inhibitory activity of taxifolin against α-amylase and the regulation of postprandial hyperglycemia along with anti-inflammatory and antioxidant activities in the treatment of diabetes in rats

[24]. In another study, the inhibitory activity of taxifolin against three digestive enzymes was evaluated both in vitro and in vivo. A study showed that pre-treatment with taxifolin significantly improved postprandial hyperglycemia and decreased triglyceride absorption by inhibiting pancreatic lipase in rats [25]. Several studies have shown that taxifolin has antihyperlipidemic activity and this was assessed by evaluating hyperlipidemic rats treated with taxifolin. The results showed that taxifolin maintained normal serum and liver lipid profiles and fecal lipid excretion in rats fed a cholesterol-rich diet [26].

The in vivo study results also show that taxifolin-treated animals had lower liver total cholesterol levels with decreased thiobarbituric acid reactive substances levels in both serum and liver [27]. To date, taxifolin has been shown to inhibit stress-induced apoptosis, especially oxidative stress and endoplasmic reticulum stress, through the PI3K/Akt pathway, which provides cardioprotective activity against ischemia-reperfusion injury. In addition, taxifolin delays the onset of endoplasmic reticulum stress by regulating the expression of certain proteins [28]. In another study, taxifolin was evaluated to determine its effect and mechanism on myocardial ischemia/reperfusion (I/R) injury. The results showed that taxifolin significantly improved cardiac function, regulated oxidative stress, and reduced apoptosis [29]. Taxifolin also has efficacy against lung injury. The results of biochemical and histopathological analysis showed that animals treated with taxifolin were healthy and had no signs of oxidative damage to the lungs compared to the cisplatin group. These results suggest that taxifolin may be used to treat cisplatin-induced lung toxicity [30].The antifungal activity of taxifolin has also been evaluated in various studies. According to the studies, the antifungal activity of taxifolin was evaluated against five different fungal species: Alternaria Alternata (Fr.) Keissler, Aspergillus fumigatus Fresenius, Aspergillus niger van Tieghem, Macrophomina Phaseolina (Tassi) Goid. and Penicillium Citrii. Different concentrations (100, 300, 500, 700, 900, and 1000 ppm) of taxifolin were used, which showed excellent antifungal activity by significantly inhibiting fungal growth in a dose-dependent manner [31]. The antiviral activity of taxifolin has also recently been investigated against severe acute

respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of COVID-19. After a thorough in silico study, the researchers found that taxifolin could be a potential inhibitor of the major protease of SARS-CoV-2 and had the lowest calculated IC value among a series of flavonoids [32]. Another group of researchers also conducted a comprehensive computational analysis to discover the major inhibitors of SARS CoV-2 protease and found 11 potential binders, including taxifolin [33]. These findings indicate that taxifolin is a possible anti-SARS-CoV-2 drug that requires preclinical testing before being approved as a medicinal molecule against Covid-19 [34]. A number of studies have been conducted on taxifolin in humans with different physiological conditions. Taxifolin (40-120 mg/day), derived from larch, was used to treat 507 patients for 2 weeks to 3 months. At the end of the study, no adverse effects were observed in the taxifolin group [35, 36]. From human and animal studies, it has been established that taxifolin can be added to packaged foods to provide health benefits as an antioxidant and anti-inflammatory agent, as supported by various in vivo and in vitro studies. Taxifolin can also be used with vitamins such as vitamin C to enhance its effectiveness. Vitamin C tablets containing enhanced dihydroquercetin are commercially available [37]. Taxifolin also exhibits immunomodulatory activity. Immunity is significantly enhanced by taking taxifolin as a dietary supplement. The recommended daily dose of taxifolin is 100 mg/day. Over the past half century, taxifolin has become more widely used in pharmaceutical

and healthcare applications. In addition to its health benefits, taxifolin is increasingly entering the cosmetic market due to its ability to slow down skin aging. In addition, taxifolin can be developed into clinical drugs. Anti-inflammatory, antioxidant, and vascular protective properties are the remarkable qualities of this compound. It inhibits COX-2 activity and exhibits anti-inflammatory activity in animals and humans. [38] Taxifolin is a flavonol with a unique structure that distinguishes it from other flavonoids in terms of antioxidant activity, but its limited bioavailability is a significant obstacle to biological application. Many studies have been conducted on taxifolin, and numerous pharmacological properties have been found, including antioxidant, anti-inflammatory, hepatoprotective, anti-Alzheimer's, anti-angiogenic, antihyperglycemic, antimicrobial, antipsoriatic, antihyperuricemic, etc. The main action of taxifolin is related to inflammatory reactions, oxidative stress, and vascular wall protection. From the SAR of taxifolin, it was clearly determined that the structural orientation of taxifolin provides its ability to scavenge free radicals, which is consistent with its antioxidant activity. Further studies of taxifolin biochemistry and its mechanism of action on components associated with oxidative stress and inflammation may be critical. Studies of taxifolin activity in humans under various physiological conditions confirm its superior biological activity. This biological activity allows taxifolin to be used as a potential dietary supplement as an antioxidant, immune enhancer, and cardioprotector for athletes.

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XÜLASƏ

TAKSİFOLİN TİBBİ PRAKTİKADA

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Məqalədə müxtəlif xəstəliklərin qarşısının alınması və müalicəsində mühüm rol oynayan Taksifolin haqqında məlumat verilir. Tədqiqatlar Taksifolinin geniş farmakoloji fəaliyyətini ortaya qoydu: antioksidant, iltihab əleyhinə, hepatoprotektiv, antiangiogenik xüsusiyyətlər, antidiabetik, kardioprotektiv, neyroprotektiv və s. Beyin sapında infeksiya və iltihab reaksiyasına cavabdeh olan fermentləri inhibə edərək, Taksifolin həm də Alzheimer xəstəliyinə qarşı fəaliyyətini dəstəkləyən neyroprotektiv rol oynayır. Taksifolinin əla antioksidant fəaliyyəti sübut edilmişdir ki, o, lipidlərin peroksidləşməsinin qarşısını alır, H_2O_2 ilə poli(ADP-riboza) polimerazanın parçalanmasına səbəb olur.

Açar sözlər: Taksifolin, flavonoid, antioksidant aktivlik, oksidləşdirici stress.

РЕЗЮМЕ

ТАКСИФОЛИН В МЕДИЦИНСКОЙ ПРАКТИКЕ

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В статье дана информация о таксифолине, который играет важную роль в предотвращении и лечении различных заболеваний. Исследования выявили широкий спектр фармакологической активности таксифолина: антиоксидантные, противовоспалительные, гепатопротекторные, антиангиогенные свойства, антидиабетические, кардиопротекторные, нейропротекторные. За счет ингибирования ферментов, ответственных за инфекцию и воспалительную реакцию в стволе мозга, таксифолин также играет нейропротекторную роль, что подтверждает его активность против болезни Альцгеймера. Доказана превосходная антиоксидантная активность таксифолина за счет того, что он вызывает ингибирование перекисного окисления липидов, H_2O_2-индуцированное расщепление поли(АДФ-рибозы)-полимеразы.

Ключевые слова: таксифолин, флавоноид, антиоксидантная активность, окислительный стресс.