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Review Article

Therapeutic aspects of taxifolin – An update

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ABSTRACT

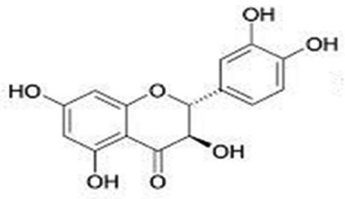
Taxifolin is a potent plant flavonoid. The main sources of taxifolin include onions, French maritime bark, tamarind seeds, and milk thistle and are also commercially available in semisynthetic forms. The main pharmacological actions of taxifolin are antibacterial, antifungal, anti-inflammatory, antioxidative, and even anticancer actions. Hence, an attempt was taken to review the pharmacological actions of taxifolin.

Keywords: Taxifolin, flavonoid, pharmacological actions, antibacterial, anticancer

Introduction

Flavanones and flavonoids have been extensively researched for their biological role. Flavonoids are derivatives of phenol and taxifolin is a plant derivative. It is known for various properties which it exhibits including antimicrobial activity, antioxidative functions. It is commonly found in conifers such as larix sibirica, cedrus deodara, and pinus roxburghii.[1]

Molecular structure



taxifolin

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Pharmacological actions

Taxifolin has a wide range of pharmacological actions; in recent studies, it is known to have a potential antibacterial, antifungal, anti-inflammatory, analgesic, antioxidant, antipyretic, platelet inhibitory, and even anticancer actions. Taxifolin was found to enhance the efficacy of antibiotics. Some of its pharmacological actions are discussed below.

Antibacterial action

Taxifolin is found to have antibacterial activity, effective against a wide range of bacterial spectrum such as *Streptococcus sobrinus*.[2]

It is also found to have antibacterial action against six known clinical pathogens *Escherichia coli, Listeria* sp., *Pseudomonas auregenosa, Bacillus* sp., and *Staphylococcus aureus*.[3]

Enterococcus faecalis KAS III (ef KAS III) and one flavanone and 11 hydroxyflavanones with hydroxy groups were tested. The minimum inhibitory concentration (MIC) values of these flavanones for *E. faecalis* and vancomycin-resistant *E. faecalis* were measured, and binding affinities to ef KAS III were determined. Naringenin, eriodictyol, and taxifolin, with high-scoring functions and good binding affinities, docked well with ef KAS III, resulting in MIC values in the range 128−512 μg/mL. These flavanones are good candidate KAS III inhibitors and may be utilized as effective antimicrobials.[4]

Antifungal action

Five flavonoids, namely, (-)-epicatechin-3-O-β-glucopyranoside (1), 5-hydroxy-3-(4-hydroxylphenyl)pyrano[3,2-g]chromene-4(8H)-one (2), 6-(p-hydroxybenzyl)taxifolin-7-O-β-D-glucoside (tricuspid) (3), quercetin-3-O-α-glucopyranosyl-(1 → 2)-β-D-glucopyranoside (4), and (-)-epicatechin(2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol (5), were isolated from the leaves of mango (*Mangifera indica* L.). Antifungal activity of these compounds was evaluated against five fungal species, namely, *Alternaria alternata* (Fr.) *Keissler, Aspergillus fumigatus Fresenius, Aspergillus niger van Tieghem, Macrophomina phaseolina* (Tassi) Goid., and *Penicillium citrii*. Six concentrations, namely, 100, 300, 500, 700, 900, and 1000 ppm of each of the five flavonoids were employed by means of the poisoned medium technique. All concentrations of the five test flavonoids significantly suppressed fungal growth. In general, antifungal activity of the flavonoids was gradually increased by increasing their concentrations.[5]

Anti-inflammatory action

Taxifolin is also found to have anti-inflammatory actions.[6] The mechanism behind its anti-inflammatory action is that it blocks the synthesis of prostaglandins by inhibiting cyclooxygenase, which converts arachidonic acid to cyclic endoperoxides, precursors of prostaglandins. Thus, the inhibition of prostaglandin synthesis accounts for its anti-inflammatory actions as well as its other pharmacological actions such as antipyretic, analgesic, and platelet-inhibitory actions.

Inhibition of intestinal mobility

Intraperitoneal administration of taxifolin 100−200 mg/kg reduced (23−41%; $P < 0.05$−0.01) intestinal transit at doses of 100−200 mg/kg.This effect was antagonized by yohimbine (87−96%) and phentolamine (87–91%) but not by prazosin, propranolol, atropine, hexamethonium, mepyramine, cyproheptadine, and naloxone.Yohimbine (92–96%) also antagonized the inhibitory effect of flavonols (12.5–50 mg/kg) ($P < 0.05$–0.01) on intraluminal accumulation of fluid and diarrhea induced by castor oil. By contrast, verapamil potentiated the flavonol effect. It is suggested that these effects, influenced by the structure of the molecules, are mediated by alpha-2 adrenergic receptors and calcium.[7]

Anticancer action

Several flavonoids were examined for their activity of induction of terminal differentiation of human promyelocytic leukemia cells (HL−60) by nitro blue tetrazolium (NBT) reducing, non-specific esterase, specific esterase, and phagocytic activities. 10 flavonoids were judged to be active (percentage of NBT reducing cells was more than 40% at a concentration of 40 microM), taxifolin exerted its activity in a dose-dependent manner. HL−60 cells treated with flavonoids differentiated into mature monocyte/macrophage. The structure-activity relationship established from comparison between flavones and flavanones revealed that ortho-catechol moiety in ring B and C2−C3 double bond had an important role for induction of differentiation of HL−60. In polymethoxylated flavones, hydroxyl group at C3 and methoxyl group at C8 enhanced the differentiation-inducing activity.[8]

Metabolism of taxifolin

The enzyme taxifolin 8 - monooxygenase uses taxifolin, NADPH, NADH, H+, and O_2 to produce 2,4-dihydrogossypetin and NAD+, NADP+, and H_2O.

Taxifolin is also known as taxifoliol, dihydroquercetin (DHQ), distylin, etc.

Leucocyanidin [(2R,3S,4R)-3,4,5,7,3,4-hexahydroxyflavan] is synthesized from taxifolin by sodium borohydride reduction.[9]

Taxifolin and other flavonoids

Taxifolin is a flavonoid which has various biological functions, some of which are shared by other flavonoids.

Taxifolin acts as a chemopreventive agent, however, is not mutagenic and considerably less toxic when compared to the flavonoid quercetin.[10]

This chemopreventive effect is caused by ARE-dependent gene regulation.[11]

Taxifolin is also one of the flavonoids which possess an anticarcinogenic effect.

Taxifolin is said to have a dose-dependent effect on inhibiting the ovarian cancer cells.[12]

It also has a strong correlation between the antiproliferative effects of DHQ derivatives on murine skin fibroblasts and human breast cancer cells.[13]

Taxifolin has also been known to inhibit the cellular melanogenesis as effectively as arbutin, one of the most widely used hypopigmenting agents in cosmetics. However, arbutin is also highly mutagenic, carcinogenic, and toxic.[14]

Taxifolin also enhances the efficacy of certain antibiotics such as levofloxacin and ceftazidime which are known to have a potential for combined therapy of patients infected with a strain of methicillin-resistant *S. aureus* (MRSA).[15]

Although many flavonoids such as quercetin and arbutin have been known to be used due to their positive effects on health, taxifolin could be used as a substitute of these due to its lack of mutagenicity or toxicity.

Taxifolin as a supplement

Taxifolin or DHQ has been known for its positive role in health and a number of articles have been done researching their effects on health. Not only are taxifolin supplements good for general well-being due to their antioxidative and anticarcinogenic properties,

unlike certain other flavonoids. Taxifolin does not have any side effects at all.

Quercetin and other such compounds are similar to taxifolin but are more toxic in nature. Compared to them, taxifolin is completely free of any harmful effects.

No side effects have been proven to be caused due to taxifolin.

As a supplement, taxifolin can be used in various ways.

It can be used along with vitamins like Vitamin C to enhance its effects.

Vitamin C tablets with enhanced DHQ are being sold in the market.[16]

In a study done in 2006, taxifolin was used in athletes during exercise and it showed an increase in the recovery period from exhaustion to normalcy.

Along with its antioxidative capacity, taxifolin has also been shown to have a great positive effect on the immune system. The immunity is greatly increased due to intake of flavonoid supplements, especially taxifolin.[17]

Conclusion

Taxifolin can be used instead of various other flavonoids which are currently in use today and also have no side effects at all, along with better action as an antioxidant or an anticarcinogen and so helps in increasing immunity of the body. Hence, it must be incorporated into the daily diet as it will greatly increase the incidence of disease.

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