JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

A mini-review on Chemistry, Pharmacokinetics and Antioxidant properties of quercetin

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Abstract

Quercetin, a polyphenolic compound, has garnered significant attention in recent times due to its presence in various everyday foods and medicinal plants. This minireview presents a comprehensive examination of the chemistry, pharmacokinetics, and antioxidant properties of quercetin. In this analysis, we will examine the pharmacokinetics of quercetin within the human body, focusing on its processes of intake, distribution, metabolism, and elimination. The study of bioavailability is conducted in a comprehensive manner, with specific emphasis on the examination of delivery systems and dietary co-factors that exert an influence on it. This paper provides a comprehensive analysis of the antioxidant capabilities of quercetin, focusing on its major topic. This text emphasises the capacity of quercetin to effectively eliminate free radicals and its significant role in mitigating oxidative stress. The elucidation of its connections to key cellular processes and enzymes is being progressively undertaken, particularly in relation to antioxidant defence mechanisms. The objective of this concise review is to present a comprehensive overview of the chemistry, pharmacokinetics, and antioxidant properties of quercetin. The intention is to elucidate the potential therapeutic advantages of quercetin in preventing illnesses associated with oxidative stress. The expanding literature on quercetin highlights its importance as a natural antioxidant and its potential to improve human health and well-being.

Keywords: Natural products, Quercetin, Pharmacokinetics, Antioxidant activity

Introduction

By the course of human history, various infectious illnesses have been successfully treated by the usage of medicines derived from plants [1, 2]. The general public's acceptance of and interest in natural treatment has seen a substantial uptick over the last 10 years, and this trend can be seen in both emerging countries and established ones. As a result, one may get these natural treatments not only from pharmacies but also from supermarkets and other types of food retailers that fall under the category of hypermarkets. It is estimated that over 80 percent of people living in Africa and other poor countries resort to traditional herbal remedies for the treatment of a variety of illnesses [3,4]. This preference is largely attributable to the ease of availability to these treatments as well as the relatively lower costs connected with them in comparison to those of current pharmaceutical medications. In addition, these compounds have a variety of beneficial qualities that are beneficial to human health and contribute to its maintenance. Effects such as anti-inflammatory, spasmolytic, antioxidant, sedative, antibacterial, antiviral, antiseptic, anti-diabetic, immunostimulant, and hepatoprotective are included among these qualities [5,6,7]. From therapeutic plants, a large number of phytoconstituents and chemical compounds that display fascinating biological and pharmacological effects have been isolated and described [8,9,10]. Both chalcones and ellagic acid were examined by Batiha et al. [8] and Beshbishy et al. [9] for their potential to inhibit the growth of protozoa in the course of their different research projects. These phytoconstituents that occur naturally were obtained from the extracts of several herbs. The researchers investigated the effects of these compounds on a variety of protozoan parasites such as Plasmodium, Leishmania, Trypanosoma, Babesia, and Theileria. The findings of both research came to the same conclusion: chalcones and ellagic acid have antiprotozoal efficacy. According to the information that is now available, these phytochemicals have the potential to be used as a basis for the synthesis of new synthetic molecules that display increased efficacy while exhibiting lower toxicity [11].

Chemistry

The chemical structure of quercetin, also known as 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4-Hchromen-4-one, is seen in figure 1. quercetin is a flavonoid compound. This substance is classified as a flavonol, which is one of the six unique forms of flavonoid compounds. Flavonols are also known as flavanones. The

polyphenolic flavonoid known as quercetin may be discovered in a wide variety of fruits and vegetables, including apples, berries, lovage, capers, cilantro, dill, and onions [12]. Additionally, it may be found in a wide variety of different kinds of fruits and vegetables. The chemical is completely soluble in lipids and alcohol, but only partially soluble in hot water and not at all in cold water. It is only partially soluble in hot water. The colour of the thing is a beautiful shade of yellow that brings to mind the colour of the sky on a bright and sunny day. The origin of the word "quercetin" may be traced back to the Latin word "quercetum," which means "oak forest." Flavonol is the correct nomenclature for this compound, and the human body does not produce it endogenously [13]. In accordance with the guidelines established by the International Union of Pure and Applied Chemistry (IUPAC), the following is the quercetin chemical formula: C15H10O7 and 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one are two examples of molecules that are structurally similar to one another. A significant number of pharmacological effects may be attributed to the chemical quercetin, which is found in plants. These include its shown effectiveness in anticancer and antiviral applications, as well as its potential for treating allergy, metabolic, and inflammatory diseases, ophthalmic and cardiovascular illnesses, and arthritic issues [14]. Additionally, it has the potential to cure ocular and cardiovascular ailments, as well as arthritic conditions. In addition, a wealth of data suggests that it has a wide variety of anticancer characteristics, and a large number of studies have unequivocally proved that it is useful in warding off cancer. In addition to its capabilities as a psychostimulant, research has demonstrated that quercetin also has the capacity to lower capillary permeability and lipid peroxidation and to induce mitochondrial biogenesis. The purpose of this article is to provide a better knowledge of the clinical uses and safety concerns of quercetin, in addition to its pharmacological and therapeutic benefits.

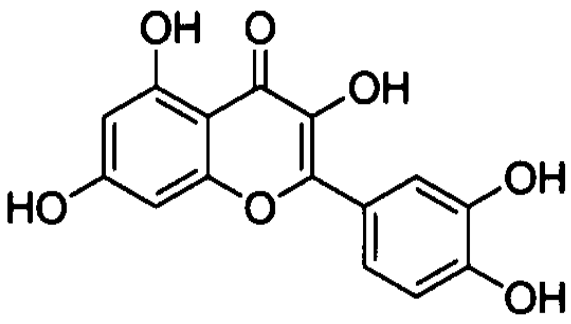

Figure 1 illustrates the molecular structure of the compound known as quercetin.

The pharmacokinetics and bioavailability of quercetin.

Quercetin has been shown to have a poor oral bioavailability after a single dose of oral administration, according to studies that have been carried out on both animals and people [16]. It is thought that this is mostly caused by a disruption in the body's ability to absorb macronutrients. When quercetin is taken in the form of glycosides, the glycosyl groups are freed as a byproduct of the mastication, digestion, and absorption processes. The process of converting quercetin glycosides into aglycone takes place inside the colon and is facilitated by enzymes known as glycosidases. Enterocytes are the cells that end up absorbing this aglycone. Previous studies have shown, as indicated by Walle et al. [17], that bacteria that are present in the mouth and stomach are responsible for the enzymatic breakdown that takes place in the body. Because it is a lipophilic molecule, quercetin has a greater potential for absorption compared to its glycoside cousins, which are subject to breakdown in the digestive system [18]. In the context of the human population, a great number of research have been carried out to investigate the bioavailability of quercetin glycosides obtained from a variety of species. In patients with ileostomies, Hollman et al. [19] found that quercetin glycosides produced from onions had a much greater absorption rate when compared to pure aglycone. After eating a meal that included onions, Scholz and Williamson [20] discovered significant levels of aglycone in the fluid that was collected from the ileostomies of the participants. It was noted that the fluid did not include any quercetin glycosides; nonetheless, the test results revealed the existence of a substantial quantity of quercetin glycosides as well as a small amount of quercetin aglycone. Hydrolysis of the glycosides is a possible step in the conversion of quercetin glycosides to aglycone, which is catalysed by the enzymes known as -glycosidases. The vast majority of these enzymes proceed through the process of absorption after they have been found inside the small intestine. In order to explore the pharmacokinetic effects of the chemical, Ferry et al. [21] gave cancer patients intravenous injections of quercetin at dosages ranging from 60 to 2000 mg/m2 of the substance in order to find out how the compound behaves in the body. According to the findings of a research, the most effective and secure quantity of quercetin to take is 945 mg/m2, which is measured in milligrammes per square metre. In contrast, going beyond the prescribed dosage led to undesirable consequences such as nephrotoxicity, increased blood pressure, nausea, and a drop in potassium levels in the blood. It was discovered that the distribution and elimination half-lives of quercetin administered intravenously varied anywhere from 0.7 to 7.8 minutes and 3.8 to 86 minutes, respectively. In

addition, the clearance and distribution volume of quercetin were calculated to be between 0.23 and 0.84 L/min/m2 and 3.7 L/m2, respectively. These values were found via pharmacokinetic modelling. In a research that was carried out by Erlund et al. [22], the pharmacokinetics of quercetin aglycone that was given to healthy persons by oral administration were looked at. During the course of the research, participants were given doses of 8, 20, and 500 milligrammes respectively. In addition, Graefe and colleagues [23] looked into the pharmacokinetic characteristics of quercetin. The maximum effective concentration (Cmax) of quercetin was determined to be 2.3 1.5 g/mL, and the maximum elimination half-life (Tmax) of quercetin was recorded to be 0.7 0.3 hours, respectively, when the drug was administered at a dose of 200 mg.

The pharmacological effects of quercetin as well as the natural sources of this compound.

More than 20 different plant species all contribute their own unique vegetables, grains, and fruits to the world's supply of the bioflavonoid molecule known as quercetin. Because of its widespread presence, quercetin is recognised as one of the bioflavonoids with the highest frequency. Foeniculum vulgare, Curcuma domesticavaleton, Santalum album, Cuscutareflexa, Withaniasomnifera, Emblica officinalis, Mangiferaindica, Daucuscarota, Momordicacharantia, and Ocimum sanctum are some of the botanical species that are featured. The text entered by the user is not seen [24]. These effects include the molecule's action as an anti-obesity agent, an anti-inflammatory agent, a vasodilator, an antioxidant, an immunostimulant, an anti-diabetic, an anti-hypertensive, an anti-atherosclerotic, and an anti-hypercholesterolemic agent. The nutritional supplement may be purchased in either pill or powder form, depending on your preference.

Antioxidant property

The connection between quercetin's benefits and the antioxidant activity it has is one of the most fascinating aspects of this compound. On the basic flavonol skeleton, quercetin is part of a varied group of flavonoids that are distinguished by the presence of hydroxyl groups in the positions 3, 5, 7, and 4'. The most important derivatives of quercetin are created when certain groups of hydroxyls go through the process of glycosylation, which results in the production of a variety of quercetin glycosides. A number of research [25] have shown that there is a connection between the structural activity of quercetin and its derivatives

and the anti-inflammatory and antioxidant capabilities that they possess. It was noted that the antioxidant activity of quercetin decreased as a result of the change, as demonstrated by the data that belong to the compound as a whole, which are as follows: Using the equation tamarixetin = isorhamnetin + quercetin + isorhamnetin-3-O-glucuronide + quercetin-3,5,7,3',4'-pentamethylether + quercetin-3,4'-di-glucoside = isorhamnetin + quercetin, researchers were able to illustrate the importance of the 3-hydroxyl quercetin group in connection to antioxidant activity [26]. Isorhamnetin and tamarixetin are two methylation quercetin metabolites, and according to Lesjak et al. [25], they displayed greater levels of antioxidant activity when compared to quercetin. This was shown by their capacity to efficiently lower lipid peroxidation levels. It has been shown that quercetin has the ability to remove reactive oxygen radicals from the environment, which is evidence of its antioxidant activity [27]. Through the quantitative control of oxidative stress variables and antioxidant enzymes, quercetin is able to slow the advancement of several cancers. The antioxidant power of quercetin was investigated via an in vivo experiment to see how it fared in comparison to carcinogen and testosterone. In this work, both histology and oxidative stress indicators such as reduced glutathione (GSH), lipid peroxidation (LPO), and hydrogen peroxide (H2O2) were evaluated. When compared to rats treated with quercetin, animals given carcinogens and testosterone had significantly higher levels of LPO and H2O2 but significantly lower levels of GSH, as found by the researchers. In a research that was carried out by Sharmila et al. [29], it was discovered that administering quercetin to animals that were suffering from prostate cancer caused an increase in the levels of apoptotic proteins and antioxidant enzymes. It has been shown that quercetin may affect a number of important components, such as androgen receptors (AR), protein kinase B (AKT), insulin-like growth factor receptor 1 (IGFIR), as well as anti-apoptosis proteins and proteins involved in cell proliferation. In order to provide additional protection for the heart against secondary cardiac dysfunction resulting from oxidative stress and inflammation, research has demonstrated that quercetin has the ability to lower the levels of malondialdehyde (MDA) while simultaneously enhancing the activity of catalase and superoxide dismutase (SOD) [30]. This is done in order to provide additional protection for the heart against oxidative stress and inflammation. Because of its capacity to boost TNF- production while simultaneously lowering ROS generation, quercetin may protect cardiac cells from the damage that is caused when Ca2+ levels become too high. Because of this, quercetin has the ability to reduce the damage that is brought on by oxidative stress [31].

Recent studies have presented evidence that quercetin has antioxidant effects. In trials carried out on live beings (in vivo) as well as in laboratory settings (in vitro), this study has shown that quercetin has the capacity to lessen oxidative stress and damage. [32,33] This ability can be proved by quercetin's ability to minimise and prevent oxidative stress and damage. Quercetin was shown to have substantial effectiveness in reducing lipid peroxidation generated by tert-Butyl hydroperoxide in human sperm cells in vivo, according to the research that was carried out by Moretti et al. [34]. This research was carried out by Moretti et al. In a second research involving rats, it was reported that giving dosages of quercetin at 25-50 mg/kg exhibited antioxidant capabilities in fighting the oxidative stress associated with streptozotocin-induced diabetes mellitus [35]. This was discovered in a study that indicated that quercetin had been proven to have these qualities. In addition, earlier research has shown that quercetin, when supplied at a dose of 250 g/mL, had stabilising capabilities in polyethylene, in addition to its well-established antioxidant activity [36]. This was discovered when the antioxidant impact of quercetin was tested. As a consequence of this, the polymer's residual stability over a prolonged period of time is improved. In addition, research has shown that quercetin-cadmium complexes have a remarkable stability constant (Kf) value [37] when they are used as a chelating agent in chelation treatment for the aim of removing harmful metallic ions such as cadmium. This is the case when the goal of the therapy is to eliminate poisonous metallic ions. The maintenance of a healthy balance between oxidants and antioxidants is the mechanism through which quercetin attenuates the damaging effects of oxidative stress. The protective properties of quercetin against oxidative stress and cellular damage generated by a variety of variables, such as acrylamide, radiation-induced rat brain damage, neurodegenerative diseases, cadmium fluoride, and diabetes, have been proven by a number of research studies. through efficiently managing the amounts of antioxidants, quercetin is known to protect numerous cells in the brain, nerves, and other regions of the body [31]. This is accomplished through quercetin's ability to fight free radicals. The potential of quercetin to block free radicals and increase the antioxidant defence systems of the body may be of use in the treatment of disorders such as nicotine addiction [38]. This can lead to a decrease in the amount of oxidative stress that is experienced by the body. A reduction in the formation of reactive oxygen species (ROS) is one of the effects that may be caused by nicotine stimulation. In investigations conducted with living subjects, it was shown that quercetin protected the liver against the acute damage that was caused by tertiary butyl hydrogen peroxide. It has been shown that quercetin is

capable of offering excellent protection against the genetic toxicity and damage produced by radiation [39]. This is made possible by its capacity to mop up free radicals and raise the quantities of antioxidants produced naturally by the body's cells.

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