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Review Article

QUERCETIN, ENCAPSULATED QUERCETIN AND ITS APPLICATION- A REVIEW

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ABSTRACT

Flavonoids are plant secondary metabolite shows a wide range of pharmacological and biological functions. Among the flavonoids, quercetin gained special attention for its potential therapeutic activities. The aim of this work was to summarize the medicinal property of quercetin, role of quercetin in synthesizing the silver and gold nanoparticles, pros and cons of quercetin, nanoencapsulation of quercetin and its advantages. This review article summarizes the published experimental research and scientific literature from the databases including PubMed, Google and local library searches. The results of these studies provide a complete understanding of the biological action of quercetin. Pharmaceutical effects of quercetin such as anti-oxidant, anti-inflammatory, anti-cancer, anti-toxic and immunomodulatory effects prove that quercetin has potential therapeutic value, though it has several beneficial effects on human health, it possesses some disadvantages like poor solubility, low bioavailability, the hydrophobic nature and poor permeability. To overcome the disadvantages of quercetin, it is encapsulated in the polymers to enhance its bioavailability and to increase its solubility. In this paper, a brief description about the encapsulation of quercetin and its application were focused.

Keywords: Quercetin, Encapsulated Quercetin, Nanoencapsulation, Flavonoid.

INTRODUCTION

Quercetin is one of the major bio flavinoid and forms the backbone of many other flavonoids [1]. It is frequently studied dietary flavonoid, distributed in onion, apple, berries, tea and brassica vegetables, as well as many nuts, seeds, barks, flowers, and leaves [2]. It is also seen in medicinal botanicals such as *Solanum trilobatum*, *Ginkgo biloba, Hypercerium perforatum* and in many others. The predictable standard daily dietary intake of quercetin by a person in the United States is 25mg. In addition, Quercetin is a major constituent of countless food supplements and other nutraceuticals. Quercetin is an anti-oxidant, which very efficiently scavenges highly reactive biological species such as peroxynitrite and hydroxyl radical [3].

Quercetin belongs to the flavonoids family, and its IUPAC name is 3, 5, 7, 3', 4'-pentahydroxy flavones. It consists of 3 rings and 5 hydroxyl groups, two aromatic rings A and B, linked by oxygen containing heterocyclic ring C (Fig. 1). There are number of hydroxyl groups and the presence of a methoxy group in the B ring [4]. It is also a building block for other flavonoids.

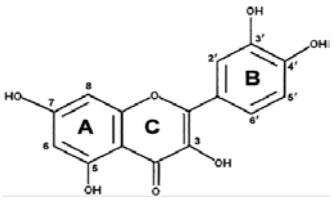

Fig. 1: Structure of Quercetin

Inspite of the presence of five –OH, quercetin has lipophilic and lipo-hydrophilic derivatives. The glands located on the surface of leaves, flowers or fruits of plants synthesize it. They can be easily isolated from hydrophilic compounds by immersing plant tissue in acetone [5]. Glycosylation of at least one hydroxyl group of quercetin derivatives result in an increase of its hydrophilicity and it may be transported to various parts of the plant and stored in vacuoles [6]. Widely investigated chemical property of phenolic compounds is their anti-oxidant activity, and it is capable of neutralizing free radicals, which are at all times there in the food within cells of the human body [7]. The anti-oxidant properties of phenolic compounds are connected with their capability to transport hydrogen or an electron, in addition to chelation of metal ions and inhibition of the activity of oxidases [6-7]. The amplified hydrophilicity of quercetin glycosides changes the coefficients of the distribution among the aqueous and lipid phase, which is of immense implication in lipid systems such as TEAC or β-carotene emulsion [8]. Molecular Formula: $C_{15}H_{10}O_7$, Molecular Weight: 302.2357, Common Name: 3, 5, 7, 3', 4'-pentahydroxyflavon (quercetin), Quercetin 3-O-glucoside (isoquercetin), Quercetin 3-O-rhamnoside (quercetin), Quercetin 3-O-rhamnozyl-(1→6)-glucoside (rutin), Quercetin 7-O- glucoside, Quercetin 3-O-rhamnoside-7-O-glucoside, Quercetin 6-C-glucoside, Quercetin 3-(2''-acetylgalactoside), Quercetin 3-sulfate-7-O-arabinoside, Quercetin 3-O-glucoside-3'-sulfate, Quercetin 5-methyl ether (azaleatin), Quercetin 7-methyl ether (rhamnetin), Quercetin 3'- methyl ether (isohramnetin), Quercetin 4'-methyl ether (tamarixetin), Quercetin 7-methoxy-3-O-glucoside, Physical State: Yellow crystalline powder, Melting Solubility: Slightly in diethyl ether; in ethanol acetone, Vapor Density: 8.1, Flash Point: 112°C, Stability: Stable under moisture.

Potential uses of Quercetin

New researches of natural substances with pharmacological activity have become a promising development in nutritional and pharmacological research [9]. There has been growing interest in quercetin in sports, science and athletic communities and pharmacological activities of quercetin were presented in (Table 1).

Anti-oxidant effects

The anti-oxidant activity of this molecule is higher than other well-known anti-oxidant molecules such as ascorbyl, trolox and rutin [22] because of the number and position of the free hydroxyl groups in the quercetin [36]. The flavonoid glycosides are vastly hydrolyzed in the small intestine or by bacterial activity in the colon, to produce the quercetinaglycones, and it's metabolized into a glucuronidated or sulfated form of quercetin [37]. Anjaneyulu & Chopra [20] studied that the antioxidant activity of quercetin is well recognized as it possesses an appropriate structure for free radical scavenging and ion chelation activity [38]. Calender [21] observed that the catechin or quercetin plus CPF (Chlorpyrifos) treated groups in rats resulted in increased anti-oxidant activity. These protective effects may be due to anti-oxidant effects of catechin and quercetin. Boots [39] investigated the possible anti-inflammatory effects of physiologically attainable quercetin concentrations. It increased the anti-oxidant capacity *in vivo* and displays anti-inflammatory effects *in vitro*. Hollman [40] estimated the protective effect of quercetin against oxidative neuronal injuries induced in primary cultured rat cortical cells and their anti-oxidant activities by using three different cell-

free bioassays. These outcomes specify that quercetin. (+) - Dihydroquercetin, and quercetin 3-methyl ether possess the active anti-oxidant values. In addition, quercetin 3-methyl ether shows to be the mainly powerful neuroprotectant of the three flavonoids isolated from this plant.

Table 1: Pharmacological Activities of Quercetin

S. No.	Pharmacological Activities	References
1.	Analgesia	[10, 11]
2.	Anti-bacterial	[12, 13]
3.	Anti-viral	[14]
4.	Anti-diabetic	[15]
5.	Anti-inflammation	[16, 17]
6.	Anti-oxidant	[18-28]
7.	Anti-cancer	[23-28]
8.	Coronary Functions	[29]
9.	Hypoglycemic	[30]
10.	Immunosupressor	[31]
11.	Anti-thyroid	[32]
12.	Anti-toxic	[33, 34]
13.	Photo protective	[35]

Anti-cancer effects

The mechanism responsible for the cancer-preventive effects of quercetin are mediated by removing free radicals [41], inhibition of enzymes that activate carcinogens, modification of signal transduction pathways, interactions with estrogen receptors [42], transcription factors [43], and other proteins [25].

Anti-cancer activity of quercetin including inhibition of cell proliferation [44, 45], induction of apoptosis [46], fatty acid synthase (FAS) [47], decreasing metalloproteinase-2 (MMP-2) and metalloproteinase-9 (MMP-9) expression [26] was studied in prostate cancer cells. The suppression of carcinogenesis is suggested to be due to its radical scavenging activity [48] and quercetin is reported to reduce CYP450 family of enzyme, which plays a key role in the activation of a number of suspected human carcinogens. Q-Cl and Q-OCH3 also show some activity against the breast cancer cell line MCF-7 with 50.3% and 24.9% cell survival, respectively and active against prostate cancer.

Quercetin can demethylate the p161NK4a gene promoter, whose hypermethylation is present in human colon cancer cells [49]. Quercetin also activates histone deacetylase enzymatic activity, thus reducing the acetylation of histone H3 could be responsible for the inhibition of surviving expression, and for the subsequent sensitization to TRAIL-induced apoptosis. Tanigawa et al [28]. Considered that the role of p53 in the anti-proliferative and proapoptotic action of quercetin on tumor cell lines. In HepG2 cells, Quercetin causes cell-cycle arrest and apoptosis by inducing p53 phosphorylation and by stabilizing p53 both at the mRNA and protein level.

To eradicate the prospect that quercetin may cause any nonspecific, toxic effects on prostate cancer cell lines, Nair et al [50]. Resolute the viabilities of PC-3 cells cultured with quercetin for 8 days and the statistics found with viable PC-3 cells and demonstrated that quercetin is nontoxic at the concentrations used and does not affect the constitutive expression of the β-actin housekeeping gene.

Quercetin inhibits expression of cell cycle genes, up-regulates the expression of tumor suppressor genes and down-regulates expression of oncogenes in prostate cancer cell line. The androgen receptor (AR) is concerned in the progression of prostate cancer and the AR protein expression at the transcription level was reduced by quercetin, which reduced the secretion of the prostate-specific, androgen-regulated tumor markers, PSA and hK2 [27]. Nevertheless, many anti-cancer drugs are mitochondria toxic and provoke reactive oxygen species, which in turn can lead to cancer cell death [51, 52] and also induce activation of anti-oxidant and detoxifying enzymes, thus protecting cells against oxidative damage from carcinogenic compounds [53]. Using molecular dynamics (MD) simulation, Joshi *et al* [38] studied the effect of anti-oxidant, anti-inflammatory and anti-cancer activity in two modified groups of Q-Cl and Q-OCH3 in quercetin compound. They conclude that the anti-cancer activity observed in Q-Cl analogue, which is showing good activity in HepG2 cell lines, compared to other cell lines and notably reduction in anti-inflammatory activity in the structural modification.

The multidrug resistance (MDR) is the main causes in cancer treatment failure; because it involves an increased activity of ATP-binding cassette family transportors (ABC) [54]. The quercetin can inhibit P-group function and *ABCB1* gene expression in many cell lines [55, 56]. Quercetin has been investigated in a number of animal models and human cancer cell lines, and has been found to have anti-proliferative effects in numerous cell types, including breast [57], leukemia, colon [58], squamous cell [59], endometrial [60], gastric and non-small cell lung. Quercetin has also an immunosuppressive effect on dendritic cells function [31]. Thus quercetin plays a major role in treating the cancer.

Anti-toxic activities

Apart from several therapeutic functions quercetin involved in scavenging toxic metabolites. Mi et al [33], concluded that quercetin inhibited oxidative damage in spermatogonial cells exposed to 3-methyl-4-nitrophenol, a toxic found in diesel exhaust. They analyzed the intracellular anti-oxidant system of cells from embryonic chickens after treatment with 3-methyl-4-nitrophenol. The toxin induced condensed nuclei and vacuolated cytoplasm, decreased testicular cell viability, spermatogonial cell numbers and induced lipid peroxidation. Supplementation with quercetin restored these parameters and showed anti-toxic effects.

The quercetin protected kidney tissue against the nephrotoxic effects of the antibiotic gentamicin. The clinical use of the antibiotic is limited by its nephrotoxicity. The researchers theorized that gentamicin acted by forming free radicals and the anti-oxidant quercetin protects the cells against these free radicals. They found that injection of rats with quercetin ameliorated histopathological changes and normalized biochemical parameters of the kidneys [34].

Miscellaneous activities

Giuliani et al [32] identified that quercetin may be a novel disruptor of thyroid function, which has potential effects on, or use in, the therapy of thyroid diseases. Quercetin inhibited thyroid growth acting, at smallest amount in part, by inhibiting PI3K/Akt activity and down-regulates NIS gene RNA levels. The action quercetin might be helpful to recognize the powerful use in anti-thyroid therapy.

The immunomodulatory activity of quercetin has been investigated in NK cells (Natural Killer cells) [61]. Macrophages [62], mast cells [63], neutrophils [64], B cells [65], and T cells [66]. Dendritic cells (DCs) play a vital function in linking innate and adaptive immunity. Quercetin efficiently repressed LPS (Lipopolysaccharide)-induced DCs activation by reducing the production of pro inflammatory cytokines and the expression of MHC class II and revoked the ability of LPS-stimulated DCs to induce Ag-specific T cell activation in both *in vitro* and *in vivo*. These results showed that quercetin might be powerful immunosuppressive agent and helpful in the avoidance of chronic inflammation, autoimmunity and transplantation [31].

Huang et al [31] reported for the first time that quercetin is an immune suppressor of DCs by inhibiting endocytosis and provided sturdy confirmation that quercetin may be a gifted agent for the prevention and treatment of inflammatory and autoimmune diseases. Muthian & Bright [67] stated that quercetin ameliorates EAE (Experimental Allergic Encephalomyelitis) by blocking IL-12 signaling and Th1 differentiation and utilized in the treatment of Th1 cell-mediated autoimmune diseases. Intimal type VSMC (Vascular Smooth Muscle Cells) showed increased JNK (Jun amino terminal kinases) activation, which was repressed by quercetin. This might play a role in the anti-atherogenic and anti-hypertensive effects of quercetin[68]. Saija et al [35]. stated that the quercetin is renowned to have the strongest protective effect against UV light induced lipoperoxidation. The stability following UV light exposure of quercetin and its three esters was examined along with their lipophilicity and water solubility. They demonstrated that the esterification with an opportune aliphatic side chain of the OH

function located at C-3 position and thus may be good applicants as photo protective agents.

Biosynthesis of Gold and Silver Nanoparticles - Role of Quercetin

Biosynthesis of gold nanoparticles (AuNPs) was found by an easy chemical reduction method by a plant-derived aglycone flavonoid, quercetin, as a reducing agent. The aqueous chloroauric acid while exposed to quercetin, it was reduced and changed to AuNPs in the size range from 20 to 45 nm. AuNPs was distinguished by UV-visual spectroscopy, transmission electron microscopy, atomic force microscopy and dynamic light scattering method. It has wide biomedical and pharmaceutical applications [69].

Quercetin, an anti-oxidant compound present in *Medicago sativa,* contains the readily oxidized hydroxyl group in the C-ring next to the carboxyl group, which is involved in the synthesis of AuNPs [70]. It also was proposed that the *Mentha piperita* might decrease the silver and gold nanoparticle into metallic nanoparticles. It was reported that the ketone is the main part in *Cymbopogon flexuosus* extract that renders the liquid similar to characteristics of the spherical gold nanoparticle [71].

Drug delivery is a main crisis in macrophage specific leishmanial parasite infections. Das et al [69], were effectively, evaluated that new quercetin conjugated gold nanoparticles against leishmanial macrophage infections. Nowadays, extensive consideration has been paid to the synthesis and characterization of gold nanoparticles; as they can be used in diverse chemical science and technologies [11]. Gold nanoparticles are biologically static and cause no severe side effects in genetic systems. In several studies, gold nanoparticles have been used for drug delivery [73, 74]. Quercetin was conjugated with gold nanoparticle throughout synthesis of the particle by citrate reduction of chloroauric acid. The conjugates were distinguished by various techniques like Atomic Force Microscopy, Dynamic Light Scattering, Transmission Electron Microscopy, Absorption Spectroscopy, Differential Scanning Calorimetry and Thermal Gravimetric Analysis [75]. Silver nano particles being most exploited and newer methods for synthesis of highly mono-disperse particles [76]. It has been intensively focused of owing to their wide range of applications in catalysis, optics, antimicrobials and biomaterials [77, 78]. Biosynthesis of silver nanocubes was carried out using leaf extract of *Peltophorum pterocarphum* containing Quercetin-3-O-β-d-galactopyranoside compound. It shows the potential effect on antifungal activity against commercial antifungal agent fluconazole [79].

Pros and Cons of Quercetin

The main disadvantages of using quercetin in therapeutically are poor solubility in water and instability in physiological medium, which restricts the use of this flavonoid to oral administration [80]. And it is not potential to solubilize these two compounds in a single nontoxic solvent [81]. Over the last decade, there has been increase in the number of newly developed drug molecules that exhibit poor water solubility as well as poor availability. Most challenging tasks in drug development are to improve solubility and oral bioavailability of these novel drugs.

Ader et al [82] investigated the bioavailability of the flavonol quercetin after intravenous and oral application in pig by giving 0.4 – 5mg of quercetin in different time intervals and the blood samples were analyzed for quercetin in HPLC. The results indicate absorption of the flavonol quercetin from the small intestine mainly in the form of glucuronides. The solid dispersion of quercetin with polyvinyl pyrrolidone kollidon® 25 (PVP K25) suggests an interesting way to increase quercetin solubility, antioxidant activity, and consequently bioavailability by various techniques, and it was possible because of the quercetin solubility increasing due to the solid dispersion formation. Hu et al [83] experimented that the instability of quercetin in the cell culture in which would manipulate the *in vitro* studies. They observed the transport behavior of quercetin in Neuro-2a (N2a) cells, as an exemplification to confirm quercetin stable conditions and the structure is steadier in weak acid and less stable in DMEM (Dulbecco's Modified Eagle Medium) than H_20 at the pH of 7, which will enhance the stability of quercetin.

Nanotechnology

Nanotechnology is the disciple of science that deals with molecules of nanometric size i. e. 10^{-9} of a meter [84]. In the past three decades, the explosive development of nanotechnology has exploded into difficult innovations in pharmacology, which is in the development of revolutionizing the delivery of biologically active compounds. The systems are exploited for therapeutic function to take the drug in the body in a controlled manner from the site of administration to the therapeutic target. This involves the passage of the drug molecules and drug delivery system across numerous physiological barriers, which signify the most difficult goal in drug targeting [84]. Preclinical characterization of nanoparticles intended for medical applications is complicated due to the variety of materials used, their unique surface properties and multifunctional nature.

Nanotechnology has to conclude and definitely pierced the empire of drug delivery. Acts of intellectual drug delivery system are constantly enhanced with the principle to exploit curative action and to reduce adverse side effects. Now a days, the advanced drug delivery system based on micelles, polymeric nanoparticles and dendrimers, liposomes, nanotubes, quantum dots etc. for the manipulation of various diseases and their metabolic pathway [85]. Besides, the nano-size too permits for access into the cell and various cellular compartments as well as in the nucleus. Nanoparticles are also well thought-out to have the possible as new intravascular or cellular probes for both analytical and therapeutic functions, which is predictable to produce novelty and play a significant role in medicine. Target-specific drug/gene delivery and early verdict in cancer treatment is one of the main concern research areas in which nanomedicine will play a vital role [86].

Nanoparticles

Nanotechnology and nanoparticulate carriers recommend unique promises in many biomedical fields, such as in disease prevention, diagnosis and controlled drug delivery. Nano-sized particles have novel physiochemical properties, which have been developed for plentiful applications in a variety of fields, especially in pharmaceutical and cosmetic industries.

The advantages of using nanocrystals like increased saturation solubility and dissolution velocity recognized to their higher surface area and good adhesion to biological surfaces. Gupta [87] compared the efficiency of production, the size and quality of the products. The compensation in using this kind of materials in drug delivery lie in the possibility of obtaining a target-specific delivery of drugs and genes to various sites in the body, in the increase of the drug residence at the target site and in the improvement of cellular uptake and intracellular stability [86], and its renowned that the enhanced permeability and retention (EPR) effect of the tumor vasculature allows the nanoparticulate carriers accumulate in cancer tissue and to release the loaded drug in the target site [88]. Sahoo et al [89] found that the dissolution of the drug nanocrystals was much higher than that of the pure drug at pH 6.8 (quercetin nanocrystals) and 1.2 (original quercetin) and increased antioxidant activity of the quercetin nanocrystals were more effective than the original quercetin. Their studies found that the enhanced dissolution rate was attributed to the increased effective surface area due to the decreased particle size.

Nanoencapsulation and its Advantages

Encapsulation is known as one of the "nature made" techniques for shielding biological organization. Encapsulation is used in product formulation to trap important ingredients into a carrier, so as to pass on protection against oxidation, isomerization and degradation and to broaden the shelf life of materials over a period of time and it is used for controlled/sustained delivery of functional substances when ingested in the body [90].

Nanoencapsulation improve the solubility and pharmacokinetics profiles of insoluble drugs. In many cases, targeted drug delivery is greatly enhanced, bioavailability to the target tissues and cells are significantly improved, while toxicity is reduced. It can considerably increase the delivery of such drugs to tumor tissue and reduce their toxic side effects to normal cells. Several choices for polymers that

can be selected to encapsulate the drug however it is significant that the polymer have capability to bind the drug without altering its activity. Bovine Serum Albumin (BSA) is appropriate carrier for drug as the nanoparticle produced from a protein base is simply adjustable to human body [91]. In general, the large particle is simply removed by liver and spleen. Reducing the size of colloidal particle carriers; enhance the stability of the carrier nanoparticles. The nanoencapsulation of quercetin, a strong antioxidant and radical scavenger, via methyl methacrylate miniemulsion polymerization, using miglyol 812 as costabilizer and lecithin as surfactant was studied and the effect of the monomer/co-stabilizer ratio and different types of initiator, and redox pair composed of hydrogen peroxide and ascorbic acid, was investigated. Higher quercetin recovery was obtained for nanocapsules when compared with nanospheres [92].

The communication of the molecular memory to a polymer network is called Molecular Imprinting, which is a very useful and straightforward method. Molecular Imprinted Polymers (MIP) has been used in a wide number of research areas such as in chromatographic separation and solid-phase extraction. Recently, researchers make attempts to obtain nano-sized imprinted particulates to be used in drug delivery. Curcio et al [93] reported that the synthesis and characterization of imprinted nanospheres with high swelling properties obtained using quercetin, MAA and ethylene glycol dimethacrylate (EGDMA) as template, functional monomer and cross-linking agent respectively. The removal of the template leaves in the polymer organization binding cavities that sustain the size and shape of the template molecule present elevated selectivity for the release of quercetin and Curcio et al [93] investigated the possibility of employing these monodispersed imprinted nanoparticles as devices for the controlled/sustained release of quercetin. The imprinted polymers to be used in drug delivery should possess a certain degree of flexibility, in order to minimize potential irritation to surrounding tissues and obtain a fast equilibrium between the release and re-uptake of the template in the cavity, but also maintain the conformation of the imprinted cavities also in absence of the template, to preserve their selectivity properties [94]. Flavin & Resmini [95] reported that the *in vitro* release studies in plasma simulating fluids and the cytotoxicity tests indicated the suitability of these materials as devices for the controlled/sustained delivery of quercetin in biological fluids and anti-proliferative activity of quercetin were preserved after loading onto MIP materials.

Kumari et al [96] studied the encapsulated the quercetin on poly D, L-lactide (PLA) nanoparticles by solvent evaporation method. The nanoencapsulation efficiency of quercetin evaluated by HPLC and antioxidant assay is showed 96.7%. PLA is extensively used for the encapsulation of many therapeutic agents due to its high hydrophobicity, biodegradability, biocompatibility, low toxicity, strong mechanical strength and slow drug release and have reported on successful encapsulation of quercetin into liposomes [97] and chitosan nanoparticles [98]. The quercetin loaded PLA nanoparticles have been characterized by scanning electron microscope, atomic force microscope, and UV-Vis spectrophotometer. Effect of quercetin loaded PLA nanoparticles on fluorescence quenching of BSA protein has also been evaluated. The quantification of encapsulation efficiency, antioxidant activity and *in vitro* release was also carried to improve its function in pharmaceuticals field. PLA encapsulated quercetin molecule shows higher aqueous solubility and constant release [96].

Quercetin and resveratrol (RES) stimulates a synergic inhibition of the adipogenesis and enhance apoptosis in adipocytes, and that sodium deoxycholate (SDC) has necrotic effects, the nanoencapsulation of quercetin and RES into SDC-elastic liposomes and their encapsulation efficiency of quercetin and RES into liposomes was more or less 97%, this could be a novel advance for dissolving the subcutaneous fat [99]. Quercetin has been used as a model drug. Kakran et al [100] investigated the preparation quercetin nanocrystals using three fabrication methods, such as high-pressure homogenization, bead milling and cavi-precipitation. These techniques were used to compare the partical size, saturation solubility and dissolution of the products. After fabrication, the smallest particles of around 276.7 nm* were found and saturation solubility of 25.50±1.11µg/ml, about nine times higher than coarse quercetin was obtained.

Tan et al [101] investigated lecithin-chitosan nanoparticles as a topical delivery system for quercetin. The quercetin-loaded nanoparticles showed higher permeation ability, and significantly increased accumulation of quercetin in the skin, especially in the epidermis. The interaction between nanoparticles and the skin surface changed the morphology of the stratum corneum and broke the close conjugation of the corneocyte layers, due to high permeability of quercetin into the skin. It can be concluded that the obtained formulation of chitosan-lecithin nanoparticles could be promising vehicle for topical delivery of quercetin. Song et al [102] investigated that antioxidant activity of quercetin and β-carotene by co-encapsulation in nanoparticle, they observed that nanoparticles holding quercetin, had a faster rate of reaction when compared to β-carotene encapsulated nanoparticles. Kouassi et al [103] studied that the linoleic acid (LA) was encapsulated in the presence or absence of quercetin into a dual polymer system of whey protein and Kappa-carrageenan using ultrasound. Anti-oxidant activity of quercetin and the stability of encapsulated LA were examined and 83% of the LA was efficiently encapsulated. Bioactivity of quercetin can be enhanced by nanotechnical encapsulation [104] and that liposomes be capable of firmly and professionally deliver Ag and quercetin for the Ag-specific suppression of inflammatory arthritis [105]. Ghosh et al [106] proposed oral treatment with nanoencapsulated quercetin, it has a protective role against oxidative damage by preventing the loss of pyramidal neurons from the hippocampal CA1 and CA3 subfields in ischemia reperfusion induced young and aged rats. Nevertheless, shorter durations of reperfusion produce considerably less damage. Ghosh et al [107]. investigated that nanoencapsulated formulations with quercetin and DMSO alone or coencapsulated in polylactide-co-glycolide [N (quercetin+DMSO)] were synthesized to investigate their healing function in a rat model of chronic arsenic toxicity and DMSA may provide a more effective therapeutic strategy in the management of arsenic toxicity and also presents a novel way of combining hydrophilic and hydrophobic drugs into a single delivery system. Gao et al [108] stated that quercetin exhibited anti-cancer activity in A2780S ovarian cancer cells. Encapsulation of quercetin in MPEG-PCL micelles, suppressed the growth of established xenograftA2780S ovarian tumors through causing cancer cell apoptosis and inhibiting angiogenesis *in vivo*. Thus encapsulation of quercetin using polymers will improve the therapeutic effects of quercetin.

CONCLUSION

In this paper, the complete study of the biological, physical and chemical properties of quercetin was discussed. The role of quercetin in the biosynthesis of silver and gold Nanoparticles was also presented. Brief descriptions about the encapsulation of quercetin were discussed.

CONFLICT OF INTERESTS

Declared None

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