UDC 577.1 https://doi.org/10.15407/biotech14.05.021

CURCUMIN-BASED MULTIFUNCTIONAL NANOSYSTEMS

M. I. KANIUK

Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine, Kyiv

E-mail: kanyukni@ukr.net

Received 02.08.2021
Revised 11.10.2021
Accepted 30.10.2021

The use of multifunctional nanosystems in medicine and research is of contemporary interest.

Aim. The purpose of the work was to summarize publications on the prospects of creating and using nanocontainers based on curcumin (Cur). Cur fluorescence in nanoparticles (NP) makes it possible to investigate the distribution of fluorescent and non-fluorescent components, significantly accelerating the study and implementation of drugs in practice. Particular attention is paid to the use of hydrophobic substances in NP, to penetrate into a living cell.

Understanding the interaction of NP with living cells is extremely important when these particles are used to transport and deliver water-insoluble drugs to cells. Cur is one of the drugs with various and very promising pharmaceutical effects, it is poorly soluble in aqueous media, and the use of nanocarriers is an effective way to significantly increase its bioavailability. Cur has its own fluorescence, which enables to use it in multifunctional fluorescent nanosystems, for example, with Pluronic® micelles.

The use of the fluorescence method makes it possible to trace the stages of interaction of Cur-loaded NP with cultured cells and their localization in cell organelles.

With this approach, nanoscale dynamics of drug distribution and stability is observed over time.

Conclusions. The main conclusion is that for unstable in the aquatic environment drugs such as Cur, it is necessary to use the most hydrophobic nanostructures without traces of water, which include the nuclei of Pluronic® micelles. This method makes it possible to use other poorly water-soluble drugs.

A promising area of nanomedicine is the creation of complex bio-compatible nanomaterials based on several active drugs that reduce the toxicity of preparations to normal cells.

Key words: multifunctional nanosystems, nanocontainers for medical preparations, curcumin.

Modern problems of nanomedicine have been reviewed in the works of Ukrainian scientists [1–9]. Particular attention is drawn to complex nanostructured materials with different functional biological properties [3–6, 10, 11].

Fluorescent nanomaterials, which have medical applications, are used to create fluorescent images of biological objects [7–9, 12–14], and for targeted transportation of drugs [2–6, 8–11, 15, 16]. The creation of complex biocompatible nanomaterials with antitumor activity is developing rapidly. They are used to deliver drugs to the localization of pathological processes. Using several drugs enhances the effect of the main preparation [8, 16, 17]. New combined preparations of nanomaterials, which are characterized by high biocompatibility, low toxicity and high specificity, are used increasingly in practice [5, 6].

The nanonization of drugs and the emergence of new nanomaterials as safe and effective drugs are developments of the recent decades. [18]. Among nanocarriers, synthetic polymer structures are of particular interest due to their universal and unique properties, which can be customized for certain practical needs [19]. The modern concept of drug delivery is based on the localization of drugs in the affected area in humans or animals. Thus, the therapeutic effect is achieved by increasing the drug concentration in the affected areas and simultaneously reducing it in the surrounding tissues. The process of administration of pharmaceutical

compounds occurs at a predetermined rate, and localized action increases the effectiveness of the drug and reduces systemic toxic effects on tissues [20].

Nanoscale multifunctional systems

The combined approach to treatment consists of co-encapsulation of several drug compounds in order to create multifunctional nanostructures for the long-term therapeutic efficacy and reduction of side effects [21, 22].

Modern nanomedicine is increasingly studying nanocarriers that can be loaded with several drugs [22], which have both hydrophobic and hydrophilic properties. The complex formulation enhances drug activity by reducing the required dose of drugs, which makes such systems more attractive and useful as treatments [23]. For example, co-encapsulation in niosomes of gallic acid and Cur, or a mixture of ascorbic acid and quercetin affects their physicochemical properties and has a synergistic antioxidant effect, which is more advantageous than the one-component nanostructures [22]. But the development of multifunctional, more specific and effective carriers, leading to a significant increase in the productivity of therapy, requires precise methods and simple techniques of control and production [8].

Molecular imaging technologies, such as fluorescence techniques, are needed to study nanobio interactions. These methods are sensitive, accurate, fast and relatively inexpensive. In modern research on the creation and determination of the lifetime of multifunctional systems, two fluorescent components are increasingly used [7], which significantly improves the receipt of scientific information about the parameters of nanocomposites [22, 24].

Various types of NP based on organic material, such as Cur complexes [9], flavonoids with ions of both transition and non-transition metals [25], or inorganic material, such as nanodiamonds [7, 8] are distinguished among the promising nanomaterials for visualization of drug delivery and use in scientific works. Most of the existing large arsenal of NP can be modified by applying an additional polymer coating [26].

Vesicles: liposomes and niosomes

Vesicles consist of two-layer amphiphilic molecules that surround the water core. Liposomes and niosomes are vesicular systems [1], which consist of a two-layer membrane that surrounds the aqueous core. The vesicular system is a platform for drug delivery, which provides effective bioavailability by controlled release of therapeutic drugs over a long period [1, 24].

Liposomes are prepared using phospholipids and have been widely used as vehicles to deliver drugs and genes for the past few years. Limitations for their widespread use are associated with phospholipid degradation, low liposome stability, and difficulties in preparation technologies [1, 18, 28]. Another major disadvantage of liposomes is their instability and short half-life in the bloodstream [1].

Niosomes are polymers that in aqueous solutions have the properties of nonionic surfactants and create vesicles [27]. Niosomes, for example, of the polymers Span (20, 40, 60, 80), Tween 20–80, Brij, consist of a hydrophilic nucleus formed from an aqueous solution and a bilayer hydrophobic shell that replaces phospholipids used in liposomes [27]. The unique amphiphilic nature of niosomes contributes to their effectiveness in the encapsulation of lipophilic or hydrophilic drugs. Other additives, such as cholesterol, can be used to maintain the rigidity of the niosome structure [18, 20, 24].

Niosomes versus liposomes

Recently, niosomes have been widely used in drug delivery as an alternative to liposomes due to their better stability, biodestructiveness, biocompatibility and low toxicity [1, 24]. Compared to liposomes, niosomes do not require special conditions for processing and storage [20]. Liposomes with phospholipids are replaced by vesicular structures of non-phospholipids of various amphiphilic molecules, namely surfactants, surfactant ionic liquids, or polymers [18, 28]. Drugs loaded into niosome vesicles showed high stability and good ability to load drug compounds, both individually and in combination. It was found that micelle-based drugs are stable for 24 hours [21], and have a smaller diameter compared to that of classical micelles, which is about 400 nm [19].

Besides, niosomes offer a number of major advantages over liposomes. Niosomes have high stability, ease of preparation and relatively low cost of surfactants [24]. Niosomes are advantageous because of their non-toxicity and biodegradability [28], which makes these systems attractive for many

chemical, biological and industrial applications [24, 28]. Niosomes enable encapsulation of a wide range of drugs [20] and thus they are a more effective tool for drug delivery in a therapeutic mode than liposomes [20].

Pharmaceutical nanocarriers: Span®, Tween®, Brij®, Pluronic®

Pharmaceutically and scientifically valuable nanocarriers include such biocompatible structures as liposomes, niosomes and multicomponent polymers [28].

Among the macromolecular systems used for targeted drug delivery, the most suitable for the creation of multifunctional devices are niosomes based on Span, Tween, Brij and Pluronic® polymers, which have the most studied characteristics. Lately, special attention is paid to amphiphilic triblock polymers Pluronic®, which have become of increased interest in the development of drug delivery systems [21].

Pluronic® polymers are triblock polymers that in aqueous solution have the properties of nonionic surfactants and form small micelles with a hydrophobic nucleus and a hydrophilic outer shell. The polymers are able to accumulate and transfer to cells both hydrophobic and hydrophobic substances. Such polymer micelles are usually less than 100 nm [19, 21].

Pluronic® are triblock copolymers with different molecular weights of polyethylene oxide (PEO), polypropylene oxide (PPO) and polyethylene oxide (PEO), which can self-assemble in an aqueous medium in the form of micelles and has the ability to increase drug solubility [29, 30].

The amphiphilic copolymer Pluronic® F127, which contains a hydrophilic part that ensures the solubility of micelles in water [31], PEO, and a hydrophobic part, PPO, has attracted attention due to its low toxicity and ability encapsulate hydrophobic agents [32]. The micelles of Pluronic® F127 are very stable in the aquatic environment, so that the critical concentration of their micelles (CMC) is 0.023% [33]. The hydrophobic core can accept water-insoluble compounds and serve as a nanocontainer for the inclusion of lipophilic therapeutic drugs. The micellar structure of this copolymer in an aqueous medium can be used to introduce hydrophilic and hydrophobic [34] drugs and release them over time [29, 35]. Micelles with carriers penetrate cells better than the drugs themselves [36–41], and conjugation of drugs with micelles is a successful self-assembly platform for future therapeutic use [42–44].

Pluronic® (PLU) micelles are used to improve Cur delivery. The micelles significantly enhance Cur availability compared to crude Cur due to protection against degradation on the way to target cells. Pluronic® F127 micelles are an effective way to cross the membranes of endothelial cells that form the blood-brain barrier [45–47].

Hydrophobic layers better store Cur in an anhydrous medium. However, due to the small number of water molecules present in the hydrophobic layer of micelles and vesicles [24], this leads to the gradual degradation of Cur. The most hydrophobic nucleus in polymers is present in Pluronic® micelles. The triblock polymer Pluronic® F 127 loaded with Cur retains active Cur in aqueous solution better than niosomes and protects Cur for 24 hr [21, 24]. Thus, hydrophobic substances that decompose rapidly in water are better preserved by Pluronic® micelles.

Multi-dye systems

The use of niosomes and block polymers makes it possible to include and transfer both hydrophobic and hydrophilic molecules and particles, and to create multicomponent nanocarriers based on them.

Fluorescent probes make it possible to remotely study the processes of transfer of NP and substances through the cell wall and their location in the middle of cells. It is especially interesting to use several dyes with different properties.

Fluorescent studies include FRET studies, which have shown significant potential for determining true and reliable information on NP behavior *in vitro* and *in vivo* [48]. In recent decades, FRET has been widely used to characterize various heterogeneous assemblies, including micelles, vesicles, proteins, lipids, DNA, nucleic acids, microemulsions, etc. [28]. In multifunctional NP, dyes can be combined into a system that creates fluorescent resonant energy transfer (FRET). The efficiency of FRET processes depends on the superposition of the fluorescence spectra of donor molecules and the absorption spectra of acceptor molecules [28]. In the micellar system, differences in the microheterogeneous environment of the probe molecule (donor/acceptor) can be understood by solvatochromic shift in their fluorescent spectra [28]. Such a system can be used both in solution to study the accumulation of various substances inside

the micelle, its stability, the rate of release of drug compounds, and to visualize their transfer together with the micelle *in vitro* and *in vivo* [49].

On the example of F127, studies were conducted to control changes in the microheterogeneity of the F127 micelle with the addition of various compositions. The resulting differences in spectra clearly indicate the structural transitions in the micelles, niosomes and polymers of Pluronic® [28]. By studying such effects, it is possible to remotely control the processes occurring in nanomaterials. Thus, FRET can provide a better understanding of the structural characteristics and dynamics of changes in various self-assembling systems and nanocomposites [28].

Curcuma (*Curcuma longa*) is a member of the family *Zingiberaceae* and is widely used in Asia as a traditional medicine [50] and in cooking as a dietary supplement [23, 51–53]. Curcuma is known to have been used in India and China for at least 2500 years to treat [54] infections, stress, depression, and dermatological diseases [55]. The most active component of turmeric is Cur [42, 55–57].

Curcumin (diferuloylmethane) is a yellow compound that is lipophilic, phenolic, and practically insoluble in water [55]. Cur has a molecular weight of 368.37 g/mol and a melting point of 183 °C. It is known that Cur is more stable in cell culture or human blood and unstable in alkaline media [51].

The small Cur molecule is a multi-purpose antioxidant with various functional groups. Phenolic hydroxyl and methoxy groups [55], diketone and double bonds contribute to its antioxidant activity [9, 56, 58]. The b-keto-enol tautomer of Cur has triple chelation sites of metals, including a double phenolic group and keto-enol fragments, which can form chelates with redox metal ions Cu^{2+}, $Fe^{2+}$and other ions [9, 51, 58]. Based on various experimental and theoretical results, it has been shown that the phenolic OH group plays an important role in the antioxidant mechanism of Cur, neutralizing ROS [9, 23, 59]. Cur affects many important enzymatic reactions, which is manifested in various biological properties of Cur [60].

The main obstacle to the therapeutic effects of Cur on the way to its introduction is its rapid metabolism in the body [56, 57, 61], chemical instability and low solubility [61]. The main metabolite of Cur in the body is the Cur glucuronide, and other metabolites include Cur sulfate, hydroxycurcumin, hexahydrocurcuminol and hexahydrocurcumin glucuronide [56].

Curcumin has a long-established safety record

The European Food Safety Authority (EFSA), the US Food and Drug Administration (FDA), the UN Expert Committee on Food Additives and the World Health Organization report that Cur is generally recognized as safe (GRAS) [50, 51, 55, 62], and acceptable and safe doses are from 4 to 8g per day [51, 63].

Dose studies have shown the safety of Cur at doses up to 12 g per day for 3 months [64] without adverse effects on humans. Despite this well-established safety, there are some concerns when consuming Cur in large doses about the possibility of inhibiting certain enzymes, which may lead to the toxic effects of Cur. Some negative side effects of Cur have been reported in the literature. For example, nausea and diarrhea, headache, rash, increased serum alkaline phosphatase and lactate dehydrogenase have been reported with 0.45 to 3.6 g per day of Cur for one to four months [50, 63].

The potential of curcumin against human diseases

Cur has been shown to target many signaling molecules and to show activity at the cellular level [50]. Extensive clinical trials over the last quarter of a century have been concerned with the pharmacokinetics, safety and efficacy of Cur against numerous human diseases [64]. Cur has a wide range of therapeutic effects [9, 17, 57, 61, 65], which includes antioxidant [50, 54, 56, 58, 65–68], anti-inflammatory [23, 50, 54, 56 58, 63, 66], antidiabetic, antiangiogenic, immunomodulatory [56], antitumor [42, 56, 61, 65, 67–69], antiproliferative, antimetastatic, antibacterial [50, 54–56], chemoprophylactic, chemotherapeutic activity [61], antifungal, antiviral, antimalarial and hepatoprotective ability and the ability to alleviate cardiovascular and neurodegenerative disorders [42, 51, 55, 61, 70, 71]. At present, Cur plays an important role in the prevention and treatment of various diseases, including cancer [55, 69], autoimmune [54, 55], neurological, cardiovascular, diabetic and lung diseases [55], and psoriasis [23].

Curcumin has antitumor activity for the colon, cervical, uterine, ovarian, prostate head and neck, breast, pulmonary, stomach and

gastric, pancreatic, bladder oral, oesophageal, and bone cancer [72]. It contains a mixture of strong bioactive molecules known as curcuminoids, which have the ability to reduce cancer in the early stages and progression of tumor development. In particular, these compounds block several enzymes required for tumor growth and may therefore be involved in the treatment of tumors [72].

Curcumin for the treatment of chronic diseases

To date, there are more than 200 clinical trials of Cur, which have shown a pronounced protective role of this compound against cardiovascular disease, metabolic diseases, neurological, skin, liver diseasei, various cancers, etc. [57]. Clinical use of native Cur is limited due to low solubility, physicochemical instability, poor bioavailability, rapid metabolism, and poor pharmacokinetics [50, 54, 63, 73]. However, these problems can be overcome using an efficient delivery system [42]. The therapeutic potential of Cur during clinical trials trumped the myth that poor bioavailability of Cur is a problem because the low bioavailability of Cur is eliminated in the treatment of chronic diseases [57]. In many clinical studies, Cur in nanoforms effectively improves its bioavailability [42, 57], which has been described for the combination of Cur with many natural and synthetic compounds and for various Cur formulations that have shown significant efficacy. Thus, Cur is a safe, inexpensive and effective drug for the treatment of various chronic diseases [51, 57, 61, 74].

Curcumin and pleiotropic effects

Cur is perhaps one of the most diverse therapeutic agents so far isolated from natural sources. The therapeutic benefits of this extraordinary natural compound have been demonstrated in the treatment of various diseases [53, 54], including cancer, inflammation, immunological disorders [54], diabetes and oxidative stress, which are often associated with hyperlipidemia [75]. Cur is effective for the treatment of various inflammatory diseases by inhibiting inflammatory cell proliferation, metastasis and angiogenesis through various molecular targets [55]. Due to its unique molecular chemical structure and functional groups, Cur can bind and subsequently either inhibit or activate various endogenous biomolecules, including enzymes, receptors, signaling molecules, metal ions, transcription factors, and even certain proteins found in cell membranes [75]. To date, many proteins are known as a target for Cur [76, 77].

Cur's pleiotropic activity derives from its ability to modulate numerous signaling molecules, such as proinflammatory cytokines, apoptotic proteins, NF-κB, cyclooxygenase-2, 5-LOX, STAT3, C-reactive protein, prostaglandin E2, prostate-specific antigen, adhesive molecules, phosphorylase kinase, transforming growth factor-β, triglycerides, ET-1, creatinine, HO-1, AST and ALT in human [64]. Cur regulates numerous transcription factors, cytokines, protein kinases, redox status, and enzymes associated with inflammation [74].

Much of the pharmacologically beneficial effects of Cur occur through non-covalent interactions with biomolecules. With so many different biological targets, Cur (polyphenol) causes numerous pleiotropic effects, which is therapeutically beneficial because many pathological conditions, such as COVID-19, involve more than one signaling pathway, receptor, protein/enzyme or gene [75, 78].

Recently, Cur has been found to have beneficial properties for the prevention and treatment of several disorders. The relevant feature here is the structural α-β-unsaturated carbonyl system, which is necessary to establish contacts with critical cysteine residues of several targets. This excellent mechanism of action gives the molecule the ability to affect a large number of targets, given its pleiotropic behavior [79]. Due to its antioxidant and anti-inflammatory properties, Cur plays a significant beneficial and pleiotropic regulatory role through synergistic binding to multiple network targets [61]. In practice, Cur has shown a beneficial effect on the progression of inflammatory diseases through numerous mechanisms of action: antiviral, anti-inflammatory, anticoagulant, antiplatelet and cytoprotective. Such effects of Cur make it promising as a new adjunctive therapy for the treatment of COVID-19 [78].

Bioavailability due to biopolymers

Despite its therapeutic benefits, Cur, as a highly pleiotropic molecule with an excellent safety profile targeting multiple diseases with strong evidence at the molecular level, has not been able to achieve its optimal therapeutic result in past clinical trials mainly due to its poor solubility and poor bioavailability [50,

54, 63, 73]. These problematic properties are primarily associated with poor absorption, rapid metabolism and rapid excretion from the gastrointestinal tract [50, 51, 58, 62].For further research, it is recommended to use the method of increasing the bioavailability of Cur [51] in combination with other substances [54].

Innovative Cur drugs based on the nanotechnology approach will increase both its bioavailability and therapeutic efficacy [79]. In clinical trials, carriers have been developed that improve the release of Cur and enhance its bioavailability. To this end, various Cur formulations have been studied, including capsules, tablets, powders, emulsions, NP, and liposomal encapsulation [64]. Cur was used both alone and in combination with other drugs [64]. Thus, the effect of Cur was significantly enhanced [50]. For example, piperine blocks the metabolic pathway of Cur and has been used to delay its metabolism [50, 51, 80, 81].

There are known methods for efficient delivery of Cur using compositions that include liposomes, niosomes, micelles, conjugates, NP and nanoglobules [27]. Cur encapsulation methods in various self-assembled biologically active systems, such as micelles, vesicles, proteins and cyclodextrins, have shown high efficacy in increasing the solubility, stability and bioavailability of Cur [24]. The increased intensity of Cur fluorescence during encapsulation in hydrophobic micro-media of micelles and niosomes is a consequence of reduced interaction of Cur with water molecules [24].

To fully exhibit the healing properties of Cur (anti-inflammatory, antitumor and antioxidant) [50], a targeted delivery system is required [23]. Polymeric nanoscale drug delivery systems are widely used due to their reduced adverse effects and increased drug bioavailability [23]. Polymeric NP with Cur are already known, in which significant therapeutic activity has been recorded *in vitro* and *in vivo* [23].

It has become known that poly-ε-caprolactone NP together with the stabilizing surfactant Pluronic® F-68 (Cur–PCL) load Cur well and have antioxidant and cytoprotective properties [23]. Pluronic® F-68 triblock copolymer provides steric stabilization of the nanopreparation, which allows the system to function for a long time and increase the transport of drugs across cellular barriers. These NP did not induce cell death of dermal fibroblasts, but they did reduce cell proliferation without affecting cell migration and adhesion [23].

Curcumin as a potential agent in cancer therapy

The broad therapeutic efficacy of Cur is associated with synergistic interactions with different biological targets, as well as the modulation of several signaling pathways. This kind of behavior can be useful in the treatment of multifactorial diseases such as cancer [69, 79]. The combination of Cur with antitumor drugs is a valuable strategy for obtaining an enhanced response with minimized side effects [56, 65, 67, 68, 79, 82].

Mixed ligand-Cur complexes with lanthanum (curcumin-terpyridyl-lanthanum (La^{3+}) and rare earth metals such as Sm^{3+}, Eu^{3+} and Dy^{3+} are toxic to cancer cells [83, 84] and have antibacterial activity [83–86]). Cur complexes have shown enhanced photocytotoxicity in HeLa cells [83, 84].

The antitumor activity of Cur depends on the dose and time. Cur has the ability to target the molecular pathways that are responsible for the growth and survival of cancer. Cur can impair the proliferation and metastasis of cancer cells, causing cell cycle arrest and other effects. The inhibitory effect of Cur on the viability and colony formation of cancer cells is important to increase the sensitivity of cancer cells to chemotherapy [56]. Cur nanoplatforms can lead to enhanced therapeutic efficacy while reducing systemic toxicity [42] of chemotherapeutic agents [56]. For example, Cur reduces the activity and expression of p-glycoprotein (P-gp) and multidrug resistance-1 (MDR1) of MCF-7 tumor to promote the accumulation of paclitaxel in [56, 82]. The complex action of calcitriol with Cur enhanced the response of MCF-7 cancer cells to paclitaxel [56, 82].

Cur is well tolerated by humans. Cur concentration peaks 1–2 hours after oral administration and begins to decline after 12 hours [87]. Oral administration of 8 g of Cur leads to a serum concentration of 0.5 to 1.8 μm, which indicates its poor bioavailability [56, 87].

Cur has antitumor properties, but a number of problems with the drug delivery regime limit its therapeutic use. Chemical complex formation can be considered as a strategy to increase the potency of Cur in the treatment of breast cancer [88]. The study showed the antitumor properties of two Cur complexes – iron-curcumin [Fe (Cur) 3] and boron-curcumin [B (Cur) 2] in the breast cancer cell line MDA-MB-231 [88]. Cell proliferation, migration, and invasion were also analyzed. All three compounds inhibited cell invasion, and

only Cur and B (Cur) 2 inhibited cell migration. Taken together, these results showed that Fe (Cur) 3 and B (Cur) 2 may exhibit similar antitumor properties as Cur and suggests that chemical complexation may be considered as a strategy to increase Cur potential in the treatment of breast cancer [88]. Cellular localization of Cur and B and Fe complexes was determined by fluorescence microscopy. The results showed that the three compounds were localized in the perinuclear and cytoplasmic regions of the cell, and showed cytotoxicity with IC50 values of 25, 35 μM and 8 μM (μM) for Cur, B (Cur) 2 and Fe (Cur) 3, respectively [88]. The use of literature sources makes it possible to compare the desired concentration of Cur to combat some cancers. For example, *in vivo* Cur at a concentration of 20 μm significantly contributes to the antitumor activity of doxorubicin against triple negative breast cancer cells, inhibiting the transition of the epithelium to the mesenchyme and metastasis [56]. However, in practice, oral administration of pure Cur results in the concentration in serum from 0.5 to 1.8 μm [87], which is insufficient in this case.

Many recent studies have focused on the development and synthesis of Cur analogues that improve bioavailability and target selectivity [98]. Synthetic Cur derivatives have been obtained to develop effective therapeutic agents in the treatment of cancer and neurodegenerative diseases [61].

Further *in vitro* and *in vivo* studies are needed to study the effects of Cur, to mitigate the treatment of various cancers [72]. Cur can be developed as a therapeutic drug by improving the properties of the formulation or delivery systems, which ensure its enhanced absorption and cellular assimilation [63]. These features, combined with pharmacological safety and low cost, make Cur an attractive agent for further research [74].

Curcumin as a fluorescent dye

Cur is a dye with a solvent-dependent absorption band that ranges from 408 to 430 nm. The maximum fluorescence is even more dependent on the solvent and occurs between 480 and 560 nm. Cur is very poorly soluble in water, where it emits weak fluorescence, and the quantum yield of Cur fluorescence in most solvents is low and decreases significantly in the presence of water [90].

In a hydrophobic medium, Cur's own fluorescence is an order of magnitude greater than in an aqueous medium, and the intensity of Cur's fluorescence can reveal the change in the hydrophobicity of the medium in which it is located [24].

Cur is highly degradable in aqueous solution. In phosphate buffer solution (pH 7.4), the level of Cur degradation after 1 h is more than 80% [24]. Spectrally, this is determined by the rapid decrease in the intensity of Cur absorption and the decrease in fluorescence. The greater the degree of interaction of Cur with water, the greater the degree of degradation [24].

When Cur is in a non-aqueous medium with high viscosity or in phospholipid membranes, the intensity of its fluorescence increases significantly [24, 91]. It is expected that in cellular images, its radiation can be observed only when it is in a composite with hydrophobic nanocarriers, or contained in membranes or intracellular hydrophobic structures.

Using various Cur nanocomplexes with carriers, it is possible to study the encapsulation of hydrophobic substances in liposomes, niosomes and Pluronic® micelles by the intensity of Cur fluorescence, and to visualize their interaction with cells in microscopic studies. The results show that nonionic surfactants that form micellar compounds significantly reduce the level of Cur degradation from 12 to 24 h by including it in the hydrophobic part of the micelles [21, 24]. This increased fluorescence intensity, along with a significant shift in the maximums of Cur emissions during encapsulation in hydrophobic microenvironments of micelles and niosomes, is a consequence of reduced interaction of Cur with water molecules. A more rigid and limited niosome microenvironment increases the intensity and fluorescence time of Cur against micelles with hydrophilic nucleus [24].

ROS

Free radical oxidation plays an important role in our lives. Large amounts of produced free radicals condition lipid peroxidation, protein denaturation, neurodegenerative, fibrous and other pathological changes. Overproduction of reactive oxygen species (ROS) and reactive nitrogen (RNS), which are potent oxidants, causes DNA damage and lipid oxidation. This leads to oxidative stress and cell damage. Oxidative stress is a major factor leading to the development of various diseases such as neurodegenerative and heart diseases, diabetes, and cancer [92, 93].

The anti-inflammatory and antioxidant properties of Cur, which have a wide range

of therapeutic potentials *in vitro* and *in vivo*, have been studied in order to create drugs that counteract free radical oxidation [51, 54, 94]. In *in vivo* systems, Cur acts by regulating the levels of enzymatic and non-enzymatic antioxidants in target tissues [58]. Experimental results *in vitro* and *in vivo* indicate a protective effect of Cur on experimentally induced inflammation, hepatotoxicity and cardiotoxicity in rats [66]. The studies of rat myocardium under Cur treatment have shown inhibition of free radical distribution and increased levels of SOD (superoxide dismutase), CAT (catalase) and glutathione peroxidase [58, 66].

The Cur molecule may exhibit prooxidant properties, depending on the environment and environmental conditions in which it is located. Cur has many biological functions, and many of these functions are related to the induction of oxidative stress. However, how Cur causes oxidative stress in cells is not fully understood [53]. The antitumor effect of Cur was confirmed *in vitro* on the example of leukemic cells. Curcumin targets several enzymes involved in the metabolic pathway of ROS, as a result of its action inhibits the growth of tumor cells [95].

The effective activity of Cur was studied against the fungus *Botrytis cinerea*, which causes gray rot of plants. It has been shown that the ROS produced by Cur caused apoptosis in hyphae of the fungus *Botrytis cinerea*. Cur has been suggested to cause oxidative stress through a NADPH oxidase-dependent mechanism [96].

The Cur-Cu (II) complex can cause DNA breakdown due to the uncontrolled production of both ROS and RNS, which ultimately leads to oxidation of DNA by the oxidative chain [79]. It should be emphasized that intracellular ROS levels do not necessarily correlate with the strength of Cur's antitumor activity. It is possible that the molecules that actually killed the leukemic cells were obtained during the production of ROS, such as reactive carbonyls and reactive aldehydes [97].

In recent years, a number of derivatives have been developed and patented, aimed both at improving Cur's multifaceted biological profile and at overcoming its undesirable effects [61]. The studies revealed antitumor activity of the allylated monocarbonyl analogue Cur CA6 against gastric cancer cells. The CA6 showed significant cytotoxicity to gastric cancer, which was considered as induction of G2/M cell cycle arrest, apoptosis and induction of endoplasmic reticulum stress. CA6 increased ROS levels by directly binding and inhibiting thioredoxin reductase R1 (TrxR1) [98].

ROS are by-products of biochemical processes in aerobic organisms. The concentration of ROS is regulated by the activity of such antioxidant enzymes as superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) [51]. The imbalance between the production and disposal of ROS leads to oxidative stress, which leads to negative consequences for cells, tissues, namely inflammatory reactions and apoptosis [51].

Large-scale studies have shown that inflammation alters signaling pathways and increases the number of inflammatory biomarkers, lipid peroxides and free radicals. Acute and chronic inflammation are an important risk factor for some types of cancer [55]. Membrane lipid peroxidation [58] and free radical-mediated oxidative damage to DNA and proteins are thought to be associated with a variety of chronic pathological complications such as cancer, atherosclerosis, and neurodegenerative diseases [52]. Oxidative damage and inflammation in preclinical studies indicate the root cause of cancer and other chronic diseases, such as diabetes, hypertension, Alzheimer's disease, etc. [63].

The effect of Cur on free radicals is carried out by several different mechanisms. It can absorb various forms of free radicals, such as ROS [9, 50, 52, 58, 66] and remove free radicals of reactive nitrogen (RNS) [50, 51]. The decrease in ROS depends on the dose of Cur and time [23]. The anti-inflammatory effect of Cur, directed against pathological conditions, is most likely mediated by its ability to inhibit the activity of enzymes that generate ROS, such as xanthine hydrogenase/oxidase [50, 51, 55], and the ability to inhibit cyclooxygenase [50–52, 55, 58], lipoxygenase (LOX) [50–52, 55, 58], induced nitric oxide synthase (iNOS) [52, 55, 58]. Cur inhibition of the activity of important enzymes that mediate inflammatory processes [52] is important for the downregulation of oxidative stress [50-52].

Poly-ε-caprolactone NP enhance the mechanism of action of Cur to reduce ROS in dermal fibroblasts [23]. Interestingly, Cur-PCL NP and poly-ε-caprolactone reduce oxidative stress caused by hydrogen peroxide and have a cytoprotective effect, so these NP may have clinical application in disorders associated with the formation of reactive oxygen species [23].

Cur has been shown to improve systemic markers of oxidative stress [50, 99]. There

is evidence that it may enhance the serum activity of antioxidants such as SOD [50–52, 58, 80, 99], catalase [50, 58, 99], glutathione peroxidase (GSH) [50, 51, 58] and at the same time favorably increase the serum activity of antioxidants of lipid peroxides [51]. Curcuminoids in serum increased GSH concentrations [80, 99], significantly reduced lipid peroxides [99] and significantly reduced malonic dialdehyde concentrations [80].

Cur, which has a strong antioxidant and anti-inflammatory effect, can be a prophylactic and chemotherapeutic agent for cancer of the colon, skin, mouth and intestines [58], as well as other chronic diseases [63]. Cur inhibited iron ion-catalyzed lipid peroxidation [58] in *in vitro* experiments in liver homogenates and inhibited heat-induced hemolysis of rat erythrocytes [66]. This may be one of the mechanisms by which Cur exhibits anti-inflammatory and antitumor activity. Cur can reduce the toxicity of iron ions, possibly by chelating iron ions, reducing oxidative stress caused by lipid peroxidation, and improving the antioxidant defense mechanism [100].

Toxicity caused by lead ions in various organ systems occurs due to increased oxidative stress due to the formation of ROS and RNS. Lead poisoning causes numerous clinical consequences for almost all organs, but the main targets are the brain, liver and kidneys. Lead is a multi-organ toxicant that is involved in various types of cancer, damage to reproductive organs in both humans and animals [51]. For the treatment of diseases or poisonings caused by heavy metal ions (Pb, Cu, Fe), standard chelator drugs are used, which often show numerous side effects from mild to severe. In the treatment of lead toxicity, Cur acts as a chelator [51].

Cur can be effective in treating various skin conditions such as dermatitis, psoriasis and scleroderma [55]. A study in mice indicates that Cur can protect the skin, removing free radicals and reducing inflammation by inhibiting nuclear factor NF- B and cytokines such as IL-1b and IL-6 [55].

Neurodegenerative diseases: Alzheimer's, Parkinson's and multiple sclerosis

Aging is a significant risk factor for neurodegenerative diseases [70]. It is believed that Cur can be effective in the mechanisms associated with aging, preventing changes in cellular proteins that occur due to aging, helping to maintain protein homeostasis [55]. Experimental studies have shown that Cur can be used for the prevention and treatment of Alzheimer's disease [58]. Nasal administration enables the drug to be delivered across the blood-brain barrier. Cur can be administered likewise and has anti-inflammatory, antitumor, antioxidant and cytoprotective effects [23]. Cur reduces neurodegenerative damage due to its antioxidant and anti-inflammatory properties [70]. Previous studies have shown that Cur interacts with several targets involved in inflammation of the nervous system, reducing inflammation, relieving neuropathic pain, nerve ischemia, and demyelination [50, 51].

Millions of people worldwide suffer from autoimmune diseases. In recent decades, Cur has been shown to be used by a variety of mechanisms [54] as a therapeutic agent against autoimmune diseases such as multiple sclerosis (MS) or rheumatoid arthritis (RA) [55].

Multiple sclerosis is a chronic inflammatory autoimmune disease characterized by degradation of the myelin sheath [55]. Differentiated effector memory T cells (TEM) have the pathogenic property to quickly infiltrate tissues or organs, which leads to their damage [54]. In recent years, there has been increasing evidence *in vitro* and *in vivo* that Kv1.3 channels in TEM cell control T cell proliferation and activation [54]. In activated TEM cells, the number of channels per cell increases from about 250 to 1500 [54]. Thus, Kv1.3 is a key player in the modulation of autoimmune disorders, and the blockade of Kv1.3 represents a promising approach to immunosuppression for the treatment of autoimmune diseases [54]. Cur is able to inhibit the proliferation and proinflammatory secretion of cytokines [55] in TEM cells by directly blocking the open hKv1.3 channels, depending on time and concentration (5–100 mM) [54]. This leads to an anti-inflammatory effect, which is an important pharmacological mechanism for the treatment of autoimmune diseases [54]. Collectively, Cur has an immunosuppressive effect on various pathogenic subgroups of T lymphocytes, so in the future Cur can be used as a powerful anti-inflammatory agent for the treatment of autoimmune diseases [54].

A neurodegenerative disease such as Alzheimer's is characterized by inflammation, oxidative damage, and abnormal protein production [55]. Neurodegenerative diseases, such as Alzheimer's and Parkinson's disease, are the main results of increased ROS production in the body [51]. Cur having antioxidant and anti-inflammatory properties

can improve cognitive function by reducing b-amyloid plaques [55]. Cur, due to its neuroprotection and antioxidant properties, can attenuate the course of Parkinson's disease, which is characterized by the loss of dopaminergic neurons in the substantia nigra [55]. It protects the neurons of the substantia nigra, improves dopamine levels in the 6-OHDA model of rats from Parkinson's disease (Figure) [55].

Experimental studies have shown that Cur can be used for the prevention and treatment of Alzheimer's disease [58]. In the experiment, Cur was administered peripherally *in vivo* to Tg mice, crossed the blood-brain barrier and bound to amyloid plaques in the brain, significantly reducing amyloid levels by inhibiting b-amyloid peptide aggregation [51, 58, 70].

Cur reduces the generation of ROS, inhibits lipid peroxidation and reduces the level of malonic dialdehyde. Cur has been shown to reduce plaque pathogenesis and inhibit the production of oligomers and fibrils [51, 70] and promote microglia formation, delaying neuronal deterioration in patients [55]. Cur alleviates neuroinflammation [101], thus it is indicated as a potential neuroprotective agent [55].

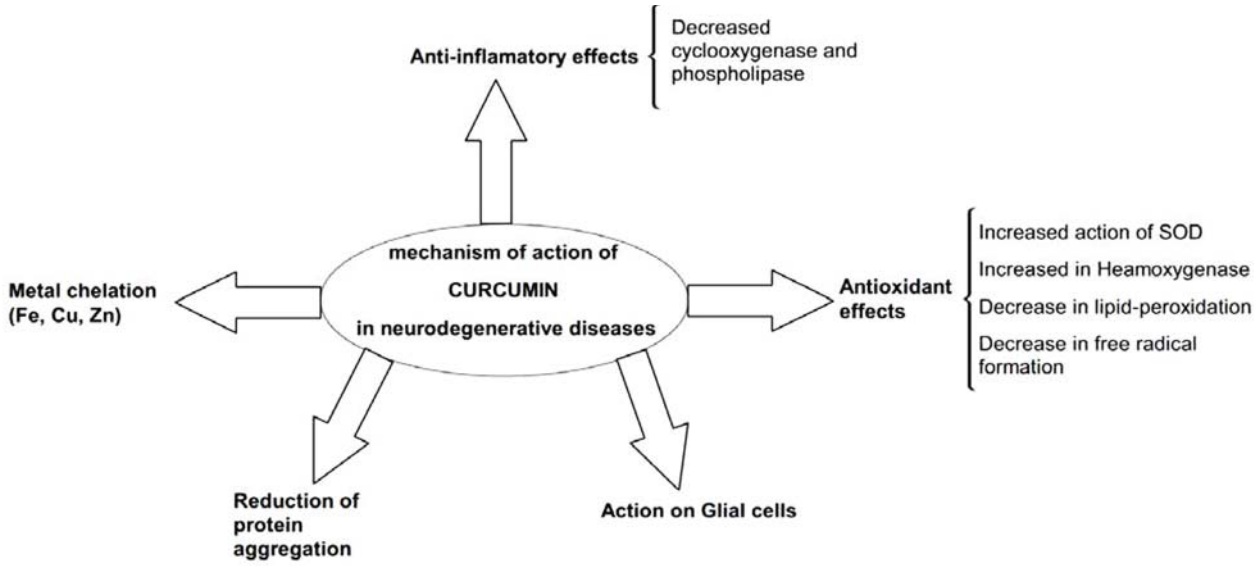
The neuroprotective mechanism of Cur against neurodegenerative disorders of the brain is also due to the ability to bind redox-active metal ions, such as Fe^{2+}, Cu^{2+}, Zn^{2+} [58], Mn^{2+}, Cd^{2+}, Pb^{2+} and Hg^{2+} [51]. The formation of Cur chelates with redox metal ions [71] leads to a decrease in ROS generation and a decrease in edema around the neuronal cells of the body [51].

Conclusions

The work summarized the literature data on the prospects of using curcumin in therapy by methods that improve its solubility. Particular attention was paid to the use of Cur as a complex drug together with other drugs in the composition of nanomaterials. Due to fluorescence, Cur makes it possible to trace the processes that occur during the penetration of the nanostructure into the cell and its interaction with the components of cellular organelles.

Cur is non-toxic and has many beneficial effects so it is considered as a drug or pharmaceutical agent. The use of various methods to improve the solubility of hydrophobic Cur in the aquatic environment and reduce the rate of its metabolism in the body are effective for the treatment of chronic diseases. The use of niosomes and block polymers makes it possible to include and transfer both hydrophobic and hydrophilic molecules and particles. it is possible to create multicomponent nanocarriers with scientific and medical applications, based on the niosomes and block polymers.

Multifunctional nanosystems penetrate into cells in a targeted and controlled manner and are used to reduce drug toxicity to normal cells. Effective use of the capabilities of multifunctional nanosystems is possible under



The proposed mechanisms of neuroprotective activity of curcumin and curcumin-like molecules [58] https://doi.org/10.2174/092986732102131206115810.

the condition of scientific substantiation of the features of joint use of components and in-depth study of the properties of these substances. Cur has a wide range of possibilities when used as the main component or part of a combination in hybrid NP, which makes it a promising drug, and such structures are promising nanomaterials. The developed Cur complexes with metal ions are more soluble in water than pure Cur and increase the target effect of the drug. Complexes of Cur-ions of metal show different biochemical activity, which depends on the nature of the metal ion. Based on Cur, double combinations with synergistic reinforcement with Cur have already been developed: Cur-quercetin, Cur-piperine, Cur-silibinin and Cur-doxorubicin. Created multifunctional therapeutic nanosystems will be widely used in medicine in the future.

A number of biologically active polymer conjugates and polymer compositions, such as micelles, hydrogels, and polymer-coated NP that can deliver multiple drugs are currently in clinical development. Nanoscale multifunctional systems have been created, which consist of several substances that have an advantage over one-component due to the synergistic action of components. The results showed that co-encapsulation of preparations affected their physicochemical properties and could produce a synergistic effect. Thus, the combined approach to treatment consists of co-encapsulation of several drug compounds into multifunctional nanostructures, which led to long-term therapeutic efficacy, reducing side effects. The development of multifunctional, more specific and effective carriers for therapy requires precise methods and simple techniques, which are primarily aimed at research to control and study their various characteristics in order to obtain the necessary parameters. The creation of optimal drug delivery systems requires such research systems that would provide the ability to quickly obtain the necessary information, including optical methods.

Developments on purposeful transport of nanocomplexes from several drugs proceed. The current direction is the development of methods for creating hydrophilic structures with a hydrophobic core containing Cur, which are aimed at increasing the amount and duration of action of the drug. Of greatest interest are monodisperse nanocarriers with a hydrophobic core without traces of water with well-known characteristics, biodegradable and with minimal toxic effects, which include Pluronic®. The use of self-assembling structures is a modern strategy for creating nanostructures in order to transfer them across the cell membrane. Particular attention is paid to the non-toxicity of polymers used for self-assembly. Among the macromolecular systems useful for targeted drug delivery are Pluronic® multifunctional amphiphilic triblock polymers, which have studied characteristics. Pluronic® F-127 provides an attractive route for encapsulation and delivery of hydrophobic compounds or ingredients. Its micelles with loaded carriers penetrate cells better than the preparations themselves. Practice-oriented tasks are aimed at creating and in-depth study of various functional properties of such combined nanomaterials to improve the therapeutic effect of drugs. The new tasks are related to multifunctional nanocarriers (nanocontainers), which carry a combination of already known medical or natural preparations. The creation of multifunctional structures makes it possible to add different components, and fluorescence makes it possible to monitor the processes occurring in the cell and track the time and location of drug unload.

The work was done according to the topic No. 3 of the Department of Neurochemistry "Molecular mechanisms of regulation and multidirectional modulation of transport of excitatory and inhibitory neurotransmitters in presynapse in normal and neuropathological conditions" of Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine.

REFERENCES

1. *Priskoka A. O., Checkman I. S.* Nanotechnologies in development of drug delivery systems. *Ukr. Med. J.* 2010, 1 (75), I–II, 14–18.(In Ukrainian).
2. *Chekman* I. *S.* Nanopharmacology. K.: *Zadruga*. 2011, 424 p. (In Ukrainian).
3. *Prylutska S. V., Grynyuk I. I., Grebinyk S. M., Matyshevska O. P., Prylutskyy Yu. I., Ritter U., Siegmund C., Scharff P.* Comparative study of biological action of fullerenes C_{60} and carbon nanotubes in thymus cells. *Mat.-wiss. u. Werkstofftech.* 2009, V. 40, P. 238–241. https://doi.org/10.1002/mawe.200900433
4. *Prylutska S. V., Burlaka A. P., Prylutskyy Yu. I., Ritter U., Scharff P.* Comparative study of antitumor effect of pristine C_{60} fullerenes and doxorubicin. *Biotechnol.* 2011, V. 4, P. 82–87.

5. *Prylutska S. V.* Using of C_{60} fullerene complexes with antitumor drugs in chemotherapy. *Biotechnol. acta*. 2014, 7 (3), 9–20. https://doi.org/10.15407/biotech7.03.009
6. *Prylutska S. V., Didenko G. V., Kichmarenko Yu. M., Kruts O. O., Potebnya G. P., Cherepanov V. V., Prylutskyy Yu. I.* Effect of C_{60} fullerene, doxorubicin and their complex on tumor and normal cells of BALB/c mice. *Biotechnol. acta*. 2014, 7 (1), 60–65. https://doi.org/10.15407/biotech7.01.060 (In Ukrainian)
7. *Kanyuk M. I.* Ultrafine fluorescent diamonds in nanotechnology. *Biotechnol. acta*. 2014, 7 (4), 9–24. https://doi.org/10.15407/biotech7.04.009 (In Ukrainian).
8. *Kanyuk M. I.* Use of nanodiamonds in biomedicine. *Biotechnol. acta*. 2015, 8 (2), 9–25. https://doi.org/10.15407/biotech8.02.009
9. *Kaniuk M. I.* Prospects of Curcumin use in Nanobiotechnology. *Biotechnol. acta*. 2016, 9 (3), P. 23–36. http://dx.doi.org/10.15407/biotech9.03.023.
10. *Prylutska S. V., Remeniak O. V., Honcharenko Yu. V., Prylutskyy Yu. I.* Carbon nanotubes as a new class of materials for nanobiotechnology. *Biotechnol.* 2009, 2 (2), 55–66. (In Ukrainian).
11. *Prylutska S. V., Remenyak O. V., Burlaka A. P., Prylutskyy Yu. I.* Perspective of carbon nanotubes application in cancer therapy. *Oncology*. 2010, 12 (1), 5–9. (In Ukrainian).
12. *Sagnou M., Benaki D., Triantis C., Tsotakos T., Psycharis V., Raptopoulou C. P., Pirmettis I., Papadopoulos M., Pelecanou M.* Curcumin as the OO bidentate ligand in "2+1" complexes with the $[M(CO)_3]^+$ (M = Re, 99m Tc) tricarbonyl core for radiodiagnostic applications. *Inorg. Chem.* 2011, 50 (4), 1295–1303. https://doi.org/10.1021/ic102228u
13. *Asti M., Ferrari E., Groci S., Atti G., Rubagotti S., Lori M., Capponi P. C., Zerbini A., Saladini M., Versari A.* Synthesis and characterization of ^{68}Ga-labeled curcumin and curcuminoid Complexes as potential radiotracers for imaging of cancer and Alzheimer's disease. *Inorg. Chem*. 2014, 53 (10), 4922–4933. https://doi.org/10.1021/ic403113z
14. *Priyadarsini K. I.* The Chemistry of Curcumin: From Extraction to Therapeutic Agent. *Molecules*. 2014, 19 (12), 20091–20112. https://doi.org/10.3390/molecules191220091
15. *Golub A., Matyshevska O., Prylutska S., Sysoyev V., Ped L., Kudrenko V., Radchenko E., Prylutskyy Yu., Scharff P., Braun T.* Fullerenes immobilized at silica surface: topology, structure and bioactivity. *J. Mol. Liq*. 2003, 105 (2–3), 141–147. https://doi.org/10.1016/S0167-7322(03)00044-8
16. *Moorthi C., Kathiresan K.* Curcumin–Piperine/Curcumin–Quercetin/Curcumin — Silibinin dual drug- loaded nanoparticulate combination therapy: A novel approach to target and treat multidrug-resistant cancers. *J. Medical Hypotheses and Ideas*. 2013, 7 (1), 15–20. https://doi.org/10.1016/j.jmhi.2012.10.005
17. *Mullaicharam A. R., Maheswaran A.* Pharmacological effects of curcumin. *Int. J. Nutr. Pharmacol. Neurol. Dis.* 2012, 2 (2), 92–99. https://doi.org/10.4103/2231-0738.95930
18. *Moghassemi S., Hadjizadeh A.* Nanoniosomes as nanoscale drug delivery systems. An illustrated review. *J. Controlled Release*. 2014, V. 185, P. 22–36. https://doi.org/10.1016/j.jconrel.2014.04.015
19. *Pitto-Barry A., Barry N. P. E.* Pluronic® block-copolymers in medicine: from chemical and biological versatility to rationalisation and clinical advances. *Polym. Chem.* 2014, V. 5, P. 3291–3297. https://doi.org/10.1039/c4py00039k
20. *Yeo P. L., Lim C. L., Chye S. M., Ling A. P. K., Koh R. Y.* Niosomes: a review of their structure, properties, methods of preparation, and medical applications. *Asian Biomed. (Res. Rev. News)*. 2017, 11 (4), 301–14. https://doi.org/10.1515/abm-2018-0002
21. *Tavano L., Mauro L., Naimo G. D., Bruno L., Picci N., Andò S., Muzzalupo R.* Further Evolution of Multifunctional Niosomes Based on Pluronic Surfactant: Dual Active Targeting and Drug Combination Properties. *Langmuir*. 2016, 32 (35), 8926–8933. https://doi.org/10.1021/acs.langmuir.6b02063
22. *Tavano L., Muzzalupo R., Picci N., Cindio B.* Co-encapsulation of antioxidants into niosomal carriers: Gastrointestinal release studies for nutraceutical applications. *Colloids and Surfaces B: Biointerfaces*. 2014, V. 114C, P. 82–88. https://doi.org/10.1016/j.colsurfb.2013.09.058
23. *Del Prado-Audelo M. L., Rodríguez-Martínez G., Martínez-López V., Ortega-Sánchez C., Velasquillo-Martínez C., Magaña J. J., González-Torres M., Quintanar-Guerrero D., Sánchez-Sánchez R., Leyva-Gómez G.* Curcumin-loaded poly- ε-caprolactone nanoparticles show antioxidant and cytoprotective effects in the presence of reactive oxygen species. *J. Bioactive and Compatible Polymers*. 2020, 35 (3), 270–285. https://doi.org/10.1177/0883911520921499
24. *Mandal S., Banerjee C., Ghosh S., Kuchlyan J., Sarkar N.* Modulation of the photophysical properties of curcumin in nonionic surfactant (Tween-20) forming micelles and niosomes: a comparative study of different microenvironments. *J. Phys. Chem. B*. 2013, 117 (23), 6957–6968. https://doi.org/10.1021/jp403724g
25. *Pusz J., Wolowiec S.* Solid compounds of Ce(III), Pr(III), Nd(III), and Sm(III) ions with

chrysin. *J. Therm. Anal. Calorim*. 2012, V. 110, P. 813–821. https://doi.org/10.1007/s10973-011-1989-4
26. *Mathew A. P., Uthaman S., Cho K. H., Cho C. S., Park I. K.* Injectable hydrogels for delivering biotherapeutic molecules. *Int. J. Biol. Macromol.* 2018, V. 110, P. 17–29. https://doi.org/10.1016/j.ijbiomac.2017.11.113
27. *Xu Y. Q., Chen W. R., Tsosie J. K., Xie X., Li P., Wan J. B., He C. W., Chen M. W.* Niosome Encapsulation of Curcumin: Characterization and Cytotoxic Effect on Ovarian Cancer Cells. *J. Nanomaterials*. 2016, V. 2016, P. 1–9. https://doi.org/10.1155/2016/6365295
28. *Roy A., Kundu N., Banik D., Sarkar N.* Comparative Fluorescence Resonance Energy-Transfer Study inPluronic Triblock Copolymer Micelle and Niosome Composed ofBiological Component Cholesterol: An Investigation of Effect ofCholesterol and Sucrose on the FRET Parameters. *J. Phys. Chem. B.* 2016, 120 (1), 131–142. https://doi.org/10.1021/acs.jpcb.5b09761
29. *Le T. M. P., Pham V. P., Dang T. M. L., La T. H., Le T. H., Le Q. H.* Preparation of curcumin-loaded pluronic F127/chitosan nanoparticles for cancer therapy. *Adv. Nat. Sci.: Nanosci. Nanotechnol.* 2013, 4 (2), 025001. https://doi.org/10.1088/2043-6262/4/2/025001
30. *Hosniyeh H., Fatemeh A., Rassoul D., Aeyed N. O.* Chitosan–Pluronic nanoparticles as oral delivery of anticancer gemcitabine: preparation and *in vitro* study. *Int. J. Nanomed.* 2012, V. 7, P. 1851–1863. https://doi.org/10.2147/IJN.S26365.
31. *Kozlov M. Y., Melik-Nubarov N. S., Batrakova E. V., Kabanov A. V.* Relationship between pluronic block copolymer structure, critical micellization concentration and partitioning coefficients of low molecular mass solutes. *Macromolecules*. 2000, 33 (9), 3305–3313. https://doi.org/10.1021/ma991634x
32. *Prados J., Melguizo C., Ortiz R., Vélez C., Alvarez P. J., Arias J. L., Ruíz M. A., Gallardo V., Aranega A.* Doxorubicin-loaded nanoparticles: new advances in breast cancer therapy. *Anti-cancer Agents Med. Chem.* 2012, 12 (9), 1058–70. https://doi.org/10.2174/187152012803529646
33. *Ganguly R., Kunwar A., Dutta B., Kumar S., Barick K., Ballal A., Aswal V., Hassan P.* Heat-induced solubilization of curcumin in kinetically stable pluronic P123 micelles and vesicles: An exploit of slow dynamics of the micellar restructuring processes in the aqueous pluronic system. *Colloids and surfaces B: Biointerfaces.* 2017, V. 152, P. 176–182. https://doi.org/10.1016/j.colsurfb.2017.01.023
34. *Chiappetta D. A., Sosnik A.* Poly (ethylene oxide)–poly (propylene oxide) block copolymer micelles as drug delivery agents: improved hydrosolubility, stability and bioavailability of drugs. *Eur. J. Pharmac. Biopharmac.* 2007, 66 (3), 303–317. https://doi.org/10.1016/j.ejpb.2007.03.022
35. *Wenzel J. G. W., Balaji K. S. S., Koushik K., Navarre C., Duran S. H., Rahe C. H., Kompella U. B.* Pluronic F127 gel formulations of deslorelin and GnRH reduce drug release and effect in cattle. *J. Control. Release*. 2002, V. 85, P. 51–59. https://doi.org/10.1016/S0168-3659(02)00271-7
36. *Verma G., Hassan P. A.* Self assembled materials: design strategies and drug delivery perspectives. Cite this: *Phys. Chem. Chem. Phys.* 2013, V. 15, P. 17016–17028. https://doi.org/10.1039/c3cp51207j
37. *Zhang X., Burt H. M., Mangold G., Dexter D., Von Hoff D., Mayer L., Hunter W. L.* Anti-tumor efficacy and biodistribution of intravenous polymeric micellar paclitaxel. *Anticancer Drugs*. 1997, 8 (7), 696–701. https://doi.org/10.1097/00001813-199708000-00008
38. *Shin I. G., Kim S. Y., Lee Y. M., Cho C. S., Sung Y. K.* Methoxy poly (ethylene glycol)/ϵ-caprolactone amphiphilic block copolymeric micelle containing indomethacin.: I. Preparation and characterization. *J. Control. Release*. 1998, 51 (1), 1–11. https://doi.org/10.1016/S0168-3659(97)00164-8
39. *Yu B. G., Okano T., Kataoka K., Sardari S., Kwon G. S.* In vitro dissociation of antifungal efficacy and toxicity for amphotericin B-loaded poly(ethylene oxide)-block-poly(beta benzyl L aspartate) micelles. *J. Control. Release.* 1998. 56 (1–3), 285–291. https://doi.org/10.1016/S0168-3659(98)00095-9
40. *Jeong Y. I., Nah J. W., Lee H. C., Kim S. H., Cho C. S.* Adriamycin release from flower-type polymeric micelle based on star-block copolymer composed of poly(γ-benzyl l-glutamate) as the hydrophobic part and poly(ethylene oxide) as the hydrophilic part. *Int. J. Pharm.* 1999, 188 (1), 49–58. https://doi.org/10.1016/S0378-5173(99)00202-1
41. *Allen C., Han J., Yu Y., Maysinger D., Eisenberg A.* Polycaprolactone–b-poly(ethylene oxide) copolymer micelles as a delivery vehicle for dihydrotestosterone. *J. Control. Release.* 2000, 63 (3), 275–286. https://doi.org/10.1016/S0168-3659(99)00200-X
42. *Yallapu M. M., Bhusetty Nagesh P. K., Jaggi M., Chauhan S. C.* Therapeutic Applications of Curcumin Nanoformulations. *AAPS J.* 2015, 17 (6), 1341–1356. https://doi.org/10.1208/s12248-015-9811-z
43. *Selvam P., El-Sherbiny I. M., Smyth H. D.* Swellable hydrogel particles for controlled release pulmonary administration using propellant-driven metered dose inhalers. *J. Aerosol Med. Pulm. Drug Deliv.* 2011, 24 (1), 25–34. https://doi.org/10.1089/jamp.2010.0830

44. *Ye Y., Li Y., Fang F.* Upconversion nanoparticles conjugated with curcumin as a photosensitizer to inhibit methicillin-resistant Staphylococcus aureus in lung under near infrared light. *Int. J. Nanomedicine.* 2014, V. 9, P. 5157–5165. https://doi.org/10.2147/IJN.S71365
45. *Pardridge W. M.* Blood–brain barrier delivery. *Drug Discovery Today*. 2007, 12 (1), 54–61. https://doi.org/10.1016/j.drudis.2006.10.013
46. *Andrieux K., Couvreur P.* Nanomedicine as a promising approach for the treatment and diagnosis of brain diseases: the example of Alzheimer's disease. *Ann. Pharm. Fr. Elsevier*. 2013, 71 (4), 225–233. https://doi.org/10.1016/j.pharma.2013.04.001
47. *Tsai Y. M., Chien C. F., Lin L. C., Tsai T. H.* Curcumin and its nano-formulation: the kinetics of tissue distribution and blood–brain barrier penetration. *Int. J. Pharmac.* 2011, 416 (1), 331–338. https://doi.org/10.1016/j.ijpharm.2011.06.030
48. *Gravier J., Sancey L., Hirsjärvi S., Rustique E., Passirani C., Benoît J. P., Coll J. L., Texier I.* FRET Imaging Approaches for *in Vitro* and *in Vivo* Characterization of Synthetic Lipid Nanoparticles. *Mol. Pharmac.* 2014, 11 (9), 3133–3144. https://doi.org/10.1021/mp500329z
49. *Charron D. M., Zheng G.* Nanomedicine development guided by FRET imaging. *Nano Today.* 2018, V. 18, P. 124–136. https://doi.org/10.1016/j.nantod.2017.12.006
50. *Hewlings S. J., Kalman D. S.* Curcumin: A Review of Its' Effects on Human Health. *Foods.* 2017, 6 (10), 92, 1–11. https://doi.org/10.3390/foods6100092
51. *Kabeer A., Mailafiya M. M., Danmaigoro A., Rahim E. A., bu Bakar M. Z. A.* Therapeutic potential of curcumin against lead-induced toxicity. A review. *Biomed. Res. Therapy*. 2019, 6 (3), 3053–3066. https://doi.org/10.15419/bmrat.v6i3.528
52. *Menon V. P., Sudheer A. R.* Antioxidant and anti-inflammatory properties of curcumin. *Adv. Exp. Med. Biol.* 2007, V. 595, P. 105–125. https://doi.org/10.1007/978-0-387-46401-5_3
53. *Cai W., Zhang B., Duan D., Wu J., Fang J.* Curcumin targeting the thioredoxin system elevates oxidative stress in HeLa cells. *Toxicol. Appl. Pharmacol*. 2012, 262 (3), 341–348. https://doi.org/10.1016/j.taap.2012.05.012
54. *Lian Y. T., Yang X. F., Wang Z. H., Yang Y., Yang Y., Shu Y. W., Cheng L. X., Liu K.* Curcumin serves as a human kv1.3 blocker to inhibit effector memory T lymphocyte activities. *Phytother. Res.* 2013, 27 (9), 1321–1327. https://doi.org/10.1002/ptr.4863
55. *Kocaadam B., Sanlier N.* Curcumin, an active component of turmeric (Curcuma longa), and its effects onhealth. *Crit. Rev. Food Sci. Nutr.* 2017, 57 (13), 2889–2895. https://doi.org/10.1080/10408398.2015.1077195
56. *Ashrafizadeh M., Zarrabi A., Hashemi F., Zabolian A., Saleki H., Bagherian M., Azami N., Bejandi A. K., Hushmandi K., Ang H. L., Makvandi P., Khan H., Kumar A. P.* Polychemotherapy with Curcumin and Doxorubicinvia Biological Nanoplatforms: EnhancingAntitumor Activity. *Pharmaceutics.* 2020, 12 (11), 1084. https://doi.org/10.3390/pharmaceutics12111084
57. *Kunnumakkara A. B., Harsha C., Banik K., Vikkurthi R., Sailo B. L., Bordoloi D., Gupta S. C., Aggarwal B. B.* Is curcumin bioavailability a problem in humans: lessons from clinical trials. *Expert Opinion on Drug Metabolism & Toxicology*. 2019, 15 (9), 705–733. https://doi.org/10.1080/17425255.2019.1650914
58. *Marchiani A., Rozzo C., Fadda A., Delogu G., Ruzza P.* Curcumin and curcumin-like molecules: Fromspice to drugs. *Curr. Med. Chem.* 2014, 21 (2), 204–222. https://doi.org/10.2174/092986732102131206115810
59. *Priyadarsini K. I., Maity D. K., Naik G. H., Kumar M. S., Unnikrishnan M. K., Satav J. G., Mohan H.* Role of phenolic O-H and methylene hydrogen on the free radical reactions and antioxidant activity of curcumin. *Free Radic. Biol. Med.* 2003, 35 (5), 475–484. https://doi.org/10.1016/s0891-5849(03)00325-3
60. *Kunwar A., Barik A., Mishra B., Rathinasamy K., Pandey R., Priyadarsini K.* Quantitative cellular uptake, localization and cytotoxicity of curcumin in normal and tumor cells. *Biochim. Biophys. Acta*. 2008, 1780 (4), 673–679. https://doi.org/10.1016/j.bbagen.2007.11.016
61. *Di Martino R. M. C., Bisi A., Rampa A., Gobbi S., Belluti F.* Recent progress on curcumin-based therapeutics: a patent review (2012-2016). Part II: curcumin derivatives in cancer and neurodegeneration. *Expert Opinion on Therapeutic Patents.* 2017, 27 (8), 953–965. https://doi.org/10.1080/13543776.2017.1339793
62. *Anand P., Kunnumakkara A. B., Newman R. A., Aggarwal B. B.* Bioavailability of curcumin: problems and promises. *Mol. Pharm*. 2007, 4 (6), 807–818. https://doi.org/10.1021/mp700113r
63. *Basnet P., Skalko-Basnet N.* Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment. *Molecules.* 2011, 16 (6), 4567–4598. https://doi.org/10.3390/molecules16064567
64. *Gupta S. C., Patchva S., Aggarwal B. B.* Therapeutic roles of curcumin: lessons learned from clinical trials. *The AAPS J.* 2013, 15 (1), 195–218. https://doi.org/10.1208/s12248-012-9432-8

65. *Joe B., Vijaykumar M., Lokesh B. R.* Biological properties of curcumin-cellular and molecular mechanisms of action. *Crit. Rev. Food Sci. Nutr.* 2004, 44 (2), 97–111. https://doi.org/10.1080/10408690490424702
66. *Naik S. R., ThakareV. N., Patil S. R.* Protective effect of curcuminon experimentally induced inflammation, hepatotoxicity and cardiotoxicityin rats: Evidence of its antioxidant property. *Exp. Toxicol. Pathol.* 2011, 63 (5), 419–431. https://doi.org/10.1016/j.etp.2010.03.001
67. *Gupta S. C., Patchva S., Koh W., Aggarwal B. B.* Discovery of curcumin, a component of golden spice, and its miraculous biological activities. *Clin. Exp. Pharmacol. Physiol.* 2012, 39 (3), 283–299. https://doi.org/10.1111/j.1440-1681.2011.05648.x
68. *Goel A., Aggarwal B. B.* Curcumin, the golden spice from Indian saffron, is a chemosensitizer and radiosensitizer for tumors and chemoprotector and radioprotector for normal organs. *Nutr. Cancer.* 2010, 62 (7), 919–930. https://doi.org/10.1080/01635581.2010.509835
69. *Fang J., Lu J., Holmgren A.* Thioredoxin reductase is irreversibly modified by curcumin: a novel molecular mechanism for its anticancer activity. *J. Biol. Chem.* 2005, 280 (26), 25284–25290. https://doi.org/10.1074/jbc.M414645200
70. *Shi L. Y., Zhang L., Li H., Liu T. L., Lai J. C., Wu Z. B., Qin J.* Protective effects ofCurcumin on acrolein-induced neurotoxicity in HT22 mousehippocampal cells. *Pharmacol. Reports.* 2018, 70 (5), 1040–1046. https://doi.org/10.1016/j.pharep.2018.05.006
71. *Mary C. P. V., Vijayakumar S., Shankar R.* Metal chelating ability and antioxidant properties of Curcumin-metal complexes – A DFT approach. *J. Mol. Graph. Model.* 2018, V. 79, P. 1–14. https://doi.org/10.1016/j.jmgm.2017.10.022
72. *Imran M., Ullah A., Saeed F., Nadeem M., Arshad M. U., Suleria H. A. R.* Cucurmin, anticancer, and antitumor perspectives: A comprehensive review. *Crit. Rev. Food Sci. Nutr.* 2018, 58 (8), 1271–1293. https://doi.org/10.1080/10408398.2016.1252711
73. *Naksuriya O., Okonogi S., Schiffelers R. M., Hennink W. E.* Curcumin nanoformulations: A review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. *Biomaterials.* 2014, 35 (10), 3365–3383. https://doi.org/10.1016/j.biomaterials.2013.12.090
74. *Aggarwal B. B., Harikumar K. B.* Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *Int. J. Biochem. Cell Biol.* 2009, 41 (1), 40–59. https://doi.org/10.1016/j.biocel.2008.06.010
75. *Hatamipour M., Johnston T. P., Sahebkar A.* One molecule, many targetsand numerous effects: the pleiotropy of curcumin lies in its chemicalstructure. *Curr. Pharm. Des.* 2018, 24 (19), 2129–2136. https://doi.org/10.2174/1381612824666180522111036
76. *Perrone D., Ardito F., Giannatempo G., Dioguardi M., Troiano G., Russo L. L., DE Lillo A., Laino L., Muzio L. L.* Biological and therapeutic activities, and anticancer properties of curcumin. *Exp. Ther. Med.* 2015, 10 (5), 1615–1623. https://doi.org/10.3892/etm.2015.2749
77. *Sa G., Das T.* Sa G.,Das T.Anti cancer effects of curcumin: cycle of life and death. *Cell Division.* 2008, 3 (14). https://doi.org/10.1186/1747-1028-3-14
78. *Rattis B. A. C., Ramos S. G., Celes M. R. N.* Curcumin as a Potential Treatment for COVID-19. *Front. Pharmacol.* 2021, P. 12. https://doi.org/10.3389/fphar.2021.675287
79. *Di Martino R. M. C., Luppi B., Bisi A., Gobbi S., Rampa A., Abruzzo A., Belluti F.* Recent progress on curcumin-based therapeutics: a patent review (2012–2016). Part I: Curcumin. *Expert Opinion on Therapeutic Patents.* 2017, 27 (5), 579–590. https://doi.org/10.1080/13543776.2017.1276566
80. *Panahi Y., Alishiri G. H., Parvin S., Sahebkar A.* Mitigation of systemic oxidative stress by curcuminoids in osteoarthritis: Results of a randomized controlled trial.*J. Diet. Suppl.* 2016, 13 (2), 209–220. https://doi.org/10.3109/19390211.2015.1008611
81. *Shoba G., Joy D., Joseph T., Majeed M., Rajendran R., Srinivas P. S.* Influence of piperine on the pharmacokinetics of curcumin inanimals and human volunteers. *Planta Med.* 1998, 64 (4), 353–356. PMID: 9619120. https://doi.org/10.1055/s-2006-957450
82. *Attia Y. M., El-Kersh D. M., Ammar R. A., Adel A., Khalil A., Walid H., Eskander K., Hamdy M., Reda N., Mohsen N. E., Al-Toukhy G. M., Mansour M. T., Elmazar M. M.* Inhibition of aldehyde dehydrogenase-1 and p-glycoprotein-mediated multidrug resistance by curcumin and vitamin D3 increases sensitivity to paclitaxel in breast cancer. *Chemico-Biological Interactions.* 2020, V. 315, P. 108865. https://doi.org/10.1016/j.cbi.2019.108865
83. *Priyadarsini K. I.* The Chemistry of Curcumin: From Extraction to Therapeutic Agent. *Molecules.* 2014, 19 (12), 20091–20112. https://doi.org/10.3390/molecules191220091
84. *Hussain A., Somyajit K., Banik B., Banerjee S., Nagaraju G., Chakravarthy A. R.* Enhancing the photocytotoxic potential of curcumin on terpyridyl-lanthanide(III) complex formation.

Dalton Trans. 2013, 42 (1), 182–195. https://doi.org/10.1039/c2dt32042h

85. *Zhou S. S., Xue X., Wang J. F., Dong Y., Jiang B., Wei D., Wan M. L., Jia Y.* Synthesis, optical properties and biological imaging of the rare earth complexes with curcumin and pyridine. *J. Mater. Chem.* 2012, 22 (42), 22774–22780. https://doi.org/10.1039/c2jm34117d
86. *Song Y. M., Xu J. P., Ding L., Hou Q., Liu J. W., Zhu Z. L.* Syntheses, characterisation and biological activities of rare earth metal complexes with curcumin and 1,10-phenanthroline-5,6-dione. *J. Inorg. Biochem.* 2009, 103 (3), 396–400. https://doi.org/10.1016/j.jinorgbio.2008.12.001
87. *Cheng L., Hsu C. H., Lin J. K., Hsu M. M., Ho Y. F., Shen T. S., Ko J. Y., Lin J. T., Lin B. R., Wu M. S., Yu H. S., Jee S. H., Chen G. S., Chen T. M., Chen C. A., Lai M. K., Pu Y. S., Pan M. H., Wang Y. J., Tsai C. C., Hsieh C. Y.* Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or pre-malignant lesions. *Anticancer Res.* 2001, 21 (4B), 2895–2900.
88. *Mohammed F., Rashid-Doubell F., Taha S., Cassidy S., Fredericks S.* Effects of curcumin complexes on MDA-MB-231 breast cancer cell proliferation. *Int. J. Oncol.* 2020, 57 (2), 445–455. https://doi.org/10.3892/ijo.2020.5065
89. *Mourmoura E., Vial G., Laillet B., Rigaudiere J. P., Hininger-Favier I., Dubouchaud H., Morio B., Demaison L.* Preserved endothelium-dependent dilatation of the coronary microvasculature at the early phase of diabetes mellitus despite the increased oxidative stress and depressed cardiac mechanical function *ex vivo*. *Cardiovasc Diabetology*. 2013, 12 (49), 1169–1186. https://doi.org/10.1186/1475-2840-12-49
90. *Rebillard A., Lefeuvre-Orfila L., Gueritat J., Cillard J.* Prostate cancer and physical activity: Adaptive response to oxidative stress. *Free Radic. Biol. Med.*. 2013, V. 60, P. 115–124. https://doi.org/10.1016/j.freeradbiomed.2013.02.009
91. *Edwards R. L., Luis P. B., Varuzza P. V., Joseph A. I., Presley S. H., Chaturvedi R., Schneider C.* The anti-inflammatory activity of curcumin is mediated by its oxidative metabolites. *J. Biol. Chem.* 2017, 292 (52), 21243–21252. https://doi.org/10.1074/ jbc.RA117.000123
92. *Larasati Y. A., Yoneda-Kato N., Nakamae I., Yokoyama T., Meiyanto E., Kato J.* Curcumin targets multiple enzymes involved in the ROS metabolic pathway to suppress tumor cell growth. *Sci. Rep.* 2018, 8 (2039). https://doi.org/10.1038/s41598-018-20179-6
93. *Hua C., Kai K., Bi W., Shi W., Liu Y., Zhang D.* Curcumin Induces Oxidative Stress in Botrytis cinerea, Resulting in a Reduction in Gray Mold Decay in Kiwifruit. *J. Agric. Food Chem.* 2019, 67 (28), 7968–7976. https://doi.org/10.1021/acs.jafc.9b00539
94. *Ellis E. M.* Reactive carbonyls and oxidative stress: Potential for therapeutic intervention. *Pharmacol. Ther.* 2007, 115 (1), 13–24. https://doi.org/10.1016/j.pharmthera.2007.03.015
95. *Rajamanickam V., Yan T., Wu L., Zhao Y., Xu X., Zhu H., Chen X., Wang M., Liu Z., Liu Z., Liang G., Wang Y.* Allylated Curcumin Analog CA6 Inhibits TrxR1 and Leads to ROS-Dependent Apoptotic Cell Death in Gastric Cancer Through Akt-FoxO3a. *Cancer Manag. Res.* 2020, V. 12, P. 247–263. https://doi.org/10.2147/CMAR.S227415
96. *Priyadarsini K. I.* Photophysics, photochemistry and photobiology of curcumin: Studies from organic solutions, biomimetics and living cells. *J. Photochem. Photobiol. C: Photochem. Rev.* 2009, 10 (2), 81–95. https://doi.org/10.1016/j.jphotochemrev.2009.05.001
97. *Patra D., El Khoury E., Ahmadieh D., Darwish S., Tafech R. M.* Effect of Curcumin on Liposome: Curcumin as a Molecular Probe for Monitoring Interaction of Ionic Liquids with 1, 2-Dipalmitoyl-sn-Glycero-3-Phosphocholine Liposome. *Photochem. Photobiol.* 2012, 88 (2), 317–327. https://doi.org/10.1111/j.1751-1097.2011.01067.x
98. *Chainoglou E., Hadjipavlou-Litina D.* Curcumin analogues and derivatives with anti-proliferative and anti-inflammatory activity: Structural characteristics and molecular targets. *Expert Opin. Drug Discov.* 2019, 14 (8), 821–842. https://doi.org/10.1080/17460441.2019.1614560
99. *Sahebkar A., Serban M. C., Ursoniu S., Banach M.* Effect of curcuminoids on oxidative stress: A systematic review and meta-analysis of randomized controlled trials. *J. Funct. Foods.* 2015, V. 18 B, P. 898–909. https://doi.org/10.1016/j.jff.2015.01.005
100. *Badria F. A., Ibrahim A. S., Badria A. F., Elmarakby A. A.* Curcumin Attenuates Iron Accumulation andOxidative Stress in the Liver and Spleen ofChronic Iron-Overloaded Rats. *PLoS ONE.* 2015, 10 (7), e0134156.1–13. https://doi.org/10.1371/journal.pone.0134156
101. *Yuan J., Liu W., Zhu H., Zhang X., Feng Y., Chen Y., FengH., Lin J.* Curcumin attenuates blood-brain barrier disruption after subarachnoid hemorrhage in mice. *J. Surg. Res.* 2017, 207 (30), 85–91. https://doi.org/10.1016/j.jss.2016.08.090

МУЛЬТИФУНКЦІОНАЛЬНІ НАНОСИСТЕМИ НА ОСНОВІ КУРКУМІНУ

М. І. Канюк

Інститут біохімії ім. О. В. Палладіна
НАН України, Київ

E-mail: kanyukni@ukr.net

Використання мультифункціональних наносистем у медицині та наукових дослідженнях є актуальним.

Мета. Узагальнити дані літератури стосовно перспектив створення та використання наноконтейнерів на основі куркуміну (Cur). Флуоресценція Cur у складі наночастинок (НЧ) дає можливість дослідити розподіл флуоресцентних та нефлуоресцентних компонентів, значно пришвидшити вивчення та впровадження препаратів у практику. Особливу увагу спрямовано на використання гідрофобних речовин у НЧ, які можуть проникати всередину живої клітини.

Розуміння взаємодії НЧ з живими клітинами є вкрай важливим у тих випадках, коли ці частинки використовують для транспортування та доставлення до клітин нерозчинних у воді лікарських засобів. Cur є одним із препаратів із різноманітними і дуже перспективними фармацевтичними ефектами, але він малорозчинний у водному середовищі, а використання наноносіїв є ефективним способом для необхідного значного збільшення його біодоступності. Cur має власну флуоресценцію, що дає можливість використати його як мультифункціональну флуоресцентну наносистему, наприклад, із міцелами Pluronic®.

Використання методу флуоресценції дає можливість простежити етапи взаємодії навантажених Cur НЧ із культивованими клітинами та їхню локалізацію в клітинних органелах.

За допомогою такого підходу в часі спостерігається наноразмірна динаміка розподілу та стійкості лікарських засобів.

Висновки. Для нестійких у водному середовищі препаратів, до яких відноситься Cur, слід застосовувати найбільш гідрофобні наноструктури без слідів води, до яких належать ядра міцел Pluronic®. Такий метод дає можливість використовувати інші малорозчинні у воді лікарські препарати.

Перспективним напрямом наномедицини є створення комплексних біосумісних наноматеріалів на основі декількох діючих препаратів, які зменшують токсичність ліків щодо нормальних клітин.

Ключові слова: мультифункціональні наносистеми, наноконтейнери для медичних препаратів, куркумін.

МУЛЬТИФУНКЦИОНАЛЬНЫЕ НАНОСИСТЕМЫ НА ОСНОВЕ КУРКУМИНА

Н. И. Канюк

Институт биохимии им. А. В. Палладина
НАН Украины, Киев

E-mail:kanyukni@ukr.net

Использование мультифункциональных наносистем в медицине и научных исследованиях является актуальным.

Цель. Обобщение данных литературы относительно перспектив создания и использования наноконтейнеров на основе куркумина (Cur). Флуоресценция Cur в составе наночастиц (НЧ) дает возможность исследовать распределение флуоресцентных и нефлуоресцентных компонентов, значительно ускорив изучение и внедрение препаратов в практику. Особое внимание направлено на использование гидрофобных веществ в НЧ, которые могут проникать внутрь живой клетки.

Понимание взаимодействия НЧ с живыми клетками чрезвычайно важно в тех случаях, когда эти частицы используются для транспортировки и доставки к клеткам нерастворимых в воде лекарственных средств. Cur является одним из препаратов с различными и очень перспективными фармацевтическими эффектами, однако он малорастворим в водной среде, а использование наноносителей является эффективным способом для необходимого значительного увеличения его биодоступности. Cur имеет собственную флуоресценцию, что дает возможность использовать его в качестве мультифункциональной флуоресцентной наносистемы, например, с мицеллами Pluronic®.

Использование метода флуоресценции дает возможность проследить этапы взаимодействия нагруженных Cur НЧ с культивируемыми клетками и их локализацию в клеточных органеллах.

С помощью такого подхода во времени наблюдается наноразмерная динамика распределения и устойчивости лекарственных средств.

Выводы. Для неустойчивых в водной среде препаратов, к которым относится Cur, необходимо использовать наиболее гидрофобные наноструктуры без следов воды, к которым относятся ядра мицелл Pluronic®. Такой метод дает возможность использовать другие малорастворимые в воде лекарственные препараты. Перспективным направлением наномедицины является создание комплексных биосовместимых наноматериалов на основе нескольких действующих препаратов, которые уменьшают токсичность лекарств относительно нормальных клеток.

Ключевые слова: мультифункциональные наносистемы, наноконтейнеры для медицинских препаратов, куркумин.