Review Article

Encapsulated Polymers Used as Nanomaterials Regarding *In vivo* Studies in Fishes

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ABSTRACT

The main and prior objective of encapsulating the nanoparticles is to enhance their effectiveness regarding drug delivery mechanism of therapeutic molecules to specific site by synchronizing early drug degradation, to keep optimum quantities of compound at the specific tissue to take much better medicinal effects, with obstructing adverse effects. The traditional drug administration methods have several limitations, which hold, fluctuations in drug quantity, low degree of bioavailability, side-effects, weak individual compliance, fast metabolism, and chemical toxicity. Instead of these limitations conditions can be resolved by implementation of object-specific encapsulated nanoparticles systems, e.g. solid lipid nanoparticles (SLNs), niosomes, liposomes, ethosomes, bilosomes, transferosomes, colloidosomes, pharmacosomes, herbosomes, layerosomes, sphingosomes, ufosomes, and polymeric nanoparticles. Since the invention of non-ionic surfactant vesicles in 1975, the development of nanomaterials was used for specific drug conveyance with biomedical procedure increasing exponentially. Encapsulated nanoparticles shows so many benefits, e.g. increased surface area, firmness and bioavailability of hydrophobic molecules, which may need less quantity of drug through controlled and sustained release of therapeutic agents, and it results reduced negative effect and drug toxicity. So that encapsulation technology is definitely proved much more efficient regarding the efficiency maintenance of compounds by means of their activity.

Keywords: Encapsulation, Nanoparticles, Nanomaterials, Therapeutics, Polymers.

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INTRODUCTION

To define nanoencapsulation one should focus on the procedure to make a coat covering on nanomaterials with different suitable compounds. The technology is fore mostly occupied for pharmaceutical, chemical and industrial interest. In field of therapeutics encapsulation procedure may play a pivotal role due to proper use of polymeric particles which can exhibit tremendous positive effects with respect to conventional methods. Before the exposure of the drug the encapsulation with polymer or any other compound gives it steadiness and more stability for not to degrade early, instead it also gives the drug a defense mechanism against premature metabolism. Despite of apparent benefits of encapsulation of therapeutic agent is continued over days to months, this is much more useful for perpetuating plasma drug concentration at therapeutic levels to extend time period[1,2,3]. When biodistribution kinetics is important within the particles it needs encapsulation with natural polymers for its maximum effect. The encapsulated nano-particles with polyethylene glycol (PEG) is increased specifically, the concentration of particular therapeutic agents in blood, particularly in brain, kidney, and intestine[4,5,6]. The main virtue of polyethylene glycol coating is to elude the reticuloendothelial clearance system. The encapsulation secured insulin from partial degradation and displayed continued exposure of the hormone exhibiting more efficient mucus conjugate between mucin and nano-particles. Drug oriented nanomaterials or general nanoparticles can be modified with the help of several types of procedures among them nano encapsulation is very liable and accurate method. On the other hand, in some methods synthetic or natural polymers can be targeted to sustainable organic or liquid state which may be emulsion polymerization. After encapsulation nanoparticle drug conjugate should be selected on the basis of its physical and chemical properties with respect to its specific effect. In the sustainable aqueous state, most probably antibiotic or therapeutic agents are encapsulated in the nanoparticles using aqueous solution without precipitant or emulsifiers[5,7,8]. Through nanoencapsulation the reduction in particle size increases the surface area of the molecule provides more activity, with increased chemical, electrical, biological and overall structural efficacy of the constructed material[9,10]. Radical emulsion polymerization of particular nanoparticle may be used to carry drug conjugate after its synthesis. e.g. polymethyl methacrylate (PMMA) which is synthesized through sustainable aqueous state polymerization. On the other hand, one of the best antigen examples for drugs such as doxorubicin, ketoprofen, and insulin were also encapsulated through nano-particles[5]. Nano-encapsulation provides the manipulated exposure of encapsulated active nanoparticles with continuous transport of therapeutic agent with increased stability, appropriate pH and temperature for specific tissues and cells[11,12]. Encapsulated nanoparticles used as drug carriers consists of metal and metal oxide are very good option to replace the presently used inorganic substances used as nanodrug carriers[9]. The intrinsic specificities of particular drug can be customized with the help of encapsulation of nanoparticles[13]. In visible zone of electromagnetic solar spectrum, the metallic nanoparticle (MNPs) such as Cu, Au, Ag, shows very broad absorption band due to their alkaline and less reactive properties. MNPs hold localized surface plasmon resonance (LSPR) specificity; as well as unique optoelectrical virtues, as they were consist of metal precursors[14,15,16]. The process of fabrication of polymeric nanoparticles by the resource of biodegradable natural polymers such as, poly(lactide) (PLA), poly(lactide-co-glycolide) (PLGA) copolymers, poly (ε-caprolactone) (PCL), and poly(amino acids) and also some natural polymers like alginate, chitosan, gelatin, and albumin[17,18,19]. Some of the specific therapeutic agents in form of macro and micro molecules hold property to recognize three steps of drug release manners that make the drug delivery paradigms that form the basis of contemporary drug delivery; the paradigms definitely take contribution for drug release during living cell treatments[18,19,20,]. The phenomenon in which the bioactive lipid oriented compounds packed through a heterogeneous or homogeneous material in form of tiny capsule like structure with size of less than one thousand nanometer is known as encapsulation. The process of encapsulation gives so many beneficial characteristics to the compound which have been encapsulated[21,22]. For achievement of extended therapeutic benefit from particular drug at specific target, the drug must be delivered with the help of nanoparticles in proper continuation. However the research already explained the effect of continue drug delivery *in-vitro* after implement of nanoencapsulation technique[23,24]. In field of therapies for intracellular infections the encapsulated polymeric nanocarriers (PNs) have exhibit the confirmed option as well as they showed the tremendous antimicrobial administration between the cells and they hold capacity to maintain accurate level of drug to enhance its efficacy and competency. Polymeric nanocarriers have quality to obstruct unusual interaction of therapeutic agents and premature deterioration of particular drug before release at the specific cell of the tissue, which results the low level resistance in microorganisms regarding that particular drug[25,26]. To increase hydrophobic drug solubility the encapsulation of self assembled block copolymer based nanoparticles were employed technically, whereas the process of nanoprecipitation used to occupy high encapsulation efficiency. On the other hand to optimize natural polymer drug and solvent the process of selection requires facilitated frame work of therapeutic nanocarriers[27,28]. The natural polymer based nanoparticles have efficiency to transport antigens, imaging agents, nucleic acid, pharmaceutical compounds, active biomolecules, as well as a variety of cargos with other chemical compounds of cellular interest either in form of blends or in combination of different nanoparticles[29]. Recently it is somehow difficult to select consistently stable base material for adequate completion of encapsulation process with its overall specificity during release. One of the most common challenges is to get the base compound for encapsulation due to their self-sensitivity with other atmospheric factors which may led to weak encapsulation quality. In this scenario the short time period of microcapsules and unprogrammed drug transport kinetics also affects the properties of encapsulation, when encapsulation focused on specific and continued transport of therapeutic agents for particular area. The natural polymer based nanocarriers with special core-shell structure were very suitable, because they have tremendous capacities for multiple functions with specific physico-chemical properties regarding complete encapsulation process[30,31,32,33]. Due to randomly low and high molecular weight of polymers and nanoparticles, the polymer nanoparticles have proper and specific immune response induction. To get rid from uneven molecular weight problem the lipid polymer hybrid nanoparticles (LPNs) were innovated and brought in practice[34,35,36]. As researchers saw the utility of core-shell structure regarding encapsulation of MNPs, they use sol-gel coating of thin layer of silica to get encapsulated metal nanoparticle[37]. Metallic nanoparticles have very good absorbance capacity especially in intestinal tissues and cells regarding polyphenols, so that, it is proved that the nanoparticles are much more appropriate with comparison to micro capsule as drug transport system. Tapioca starch nanoparticles (TSNs) conjugated with polyphenols and undergoing on adsorption kinetic, adsorption isotherm, adsorption capacity, antioxidant activity, and in vitro studies through therapeutic transport[38,39]. Encapsulated nanoparticles have quality to stabilize, a drug for more time period regarding photogenic or chemical premature depletion and mannered therapeutic transport, with adequate therapeutic interaction as well as less of adverse effects. The Nanospheres are made up of polymeric matrix led to core to surface, and nanocapsules are consist of polymeric thin layer covered on a hollow core both are natural polymer based encapsulated structures which were completely spherical and having sizes of 10 to 1000 nanometers and more[11,14,40,41]. Natural polymers were employed for nanoencapsulation because they are beneficial for environment and consistently used as nanofillers due to their biodegradability. The technique nanoencapsulation is very significant due to its increased stability, fabricated therapeutic transport of encapsulated nanocompounds, so that it is also applicable in food industry successfully[42,43,44]. At the time of characterization process of nanoparticles the observation should taken on the basis of encapsulation efficiency, morphology, particle size, and polydispersity, zeta potential and structural integrity of loaded pDNA. In this context, the comparison between synthesis processes and resources should also be focused. To conserve integration activity of plasmid there is only one technique being implied that is nanoprecipitation which protects large pDNA from shear and mechanical pressure, depletion during double emulsification[45,46,47]. Through nanoencapsulation any biologically active compound (BAC) can be embedded in liquid, solid or gaseous states within a semi-liquified matrix or inert material for conserved the coated compound (molecules/ingredients). Through the mechanism of nanoencapsulation technique the stability of biologically active compounds will increase with their enhanced regulation and motion in terms of physiological activity[21,48,]. In advancement of nanotechnology the nanoencapsulation method employed to make safe product from high temperature, excess moisture, and uneven oxygen supply. Nanoencapsulation technology modified positively the product stability and obstructs unpleasant smell sensing with conservation of exact property of the compound. The incorporation of nanoparticles by hydrophilic or hydrophobic active compounds for preservation of food in agricultural interest is also an important point for study in field of nanotechnology[48,49,50]. The construction of carbon-based nanomaterials (CNMs) the huge type of nanomaterials with wide range spectrum utilization with specific significance in agricultural field. The carbon based nanoparticles can be characterized in huge amount through different synthetic and biological resources both. The characterization through green route or biological resources acquires much more attention due to positive effects towards environment with their cost-effectiveness[51,52,53].

Appropriate substances and compounds to encapsulate metallic nanoparticles

In order to facilitate biologically active compounds with their conjugates polysaccharides can be converted in to nanogels. There are numerous challenges associated with the development of efficient functional encapsulated nanoparticles which were able to give constancy and stability with retention of compound carrying capacity. To resolve these issues and challenges, ideal encapsulation and transport systems such as lipid-based techniques (e.g., nanoemulsions, liposomes), biopolymer-based techniques (e.g., single biopolymer nanocarriers, complex nanocarriers), nature-inspired techniques (e.g., cyclodextrins, caseins), and specialized equipment-based techniques (e.g., nanospray dryer, electrospinning) have currently been used for micro/nanoencapsulation biologically active chemical substances[54,55,56]. Against intracellular organisms in order to develop pharmaceutical properties, researchers use to focus on construction of nanoconjugates and nanoplatforms due to object specific drug transport and their active principles with increased therapeutic quality. Nanoencapsulation is only effective way to increase the pharmaceutical effects against intracellular infectious diseases because it is a major issue in health care due to the poor efficacy of abundant treatments and the drug resistant microbes create the bar for the present therapeutic agents[25,57,58]. As we know that size and weight matters too much in terms of effects so that nanoencapsulation technology is highly valuable in framing drugs because of encapsulated nanoparticles were very efficient to approach any part of human body easily. Nanoencapsulation is much better with comparison to any other technology because it has capacity to increase drug solubility, making drug more viable, and mannered drug transport systems with active passive mode of biologically active substances at particular place of action. Encapsulation technology, either in form of micro or nanoencapsulation is employed for the traditional therapeutics, biopharmaceuticals, food supplements, medicinal compounds, or bioactive drugs from natural sources as well as for chemically synthesized such as biomarkers[8,59,60]. Researchers choose chitosan in first priority as a nanocarrier resource due to its biocompatibility, ecofriendly qualities and other ideal objective fulfillment. It is well known that Chitosan is a natural polysaccharide, with cation rich properties. Chitosan is a wonderful biologically active compound which is very suitable for drug transport material with almost no or slight toxic effects and low degradability[61,62,63]. The biopolymers are very attractive resource for nanoencapsulation due to their chemical balance, enzymatic quality with tremendous potential to modify them. The biopolymers are very useful alone or with combination to other natural or synthetic polymers. They made this technology very important regarding improved stabilizing properties. Due to this type of combination of basic materials chitosan has been exclusively fabricated and gives base for nanoencapsulation technique used in so many chemical substances[63,64,65,66]. Encapsulation is a method to coat or cover active molecules in a carrier material to benefit the final application of the encapsulated system. Although the characterization of the physical properties of encapsulated systems offers meaningful information, it is also helpful to predict and precisely design tailored encapsulation systems and operating conditions[67,68]. The deactivation of metallic nanoparticles during catalysis reaction through migration coalescence, because imposition of high surface energy regarding heterogeneous catalysis procedures. The encapsulation of metallic nanoparticles in form of Nanocapsules, nanoshells and nanopores proved its importance over several other methods regarding the stability factor of the nanoparticle. In order to increase the efficiency of the encapsulated compound the adjustment, biological activity, molecular sieving and specific selectivity plays the key role. Instead of the bonding between nanoparticle and material used for encapsulation also very important factor[37,69,70]. Nano-technology has emerged as a wide spectrum of technolized materials composite where particle size is defined at the nano-scale[71].

Table 1: Examples of metal NPs coated with nutraceuticals and their associated applications and biological activities for the specific nutraceuticals conjugated with the nanoparticles[72].

S.NO	NPs	Capping Agent	Biological activity
1.	Silver	Curcumin	Antimicrobial
2.	Silver	Plumbagin	Antimicrobial
3.	Silver	Plumbagin	Anticancer
4.	Silver	Curcumin	Antiviral
5.	Gold	Gallic acid	Anticancer
6.	Gold	Gallic acid	Antimicrobial
7.	Gold	Resveratrol	Anticancer
8.	Magnetic	Curcumin	Anticancer
9.	Magnetic	Gallic acid	Antioxidant
10.	TiO_2	Curcumin	Antimicrobial

Encapsulation of nanoparticles for stability issue

In order to focus on stability factor of encapsulated metal nanoparticles the zeolite encapsulated metal nanoparticle catalysts exhibits great promise for several green and sustainable processes, its parameters from environmental changes regarding rectification and conversion of biomass in preservative ways up to its surrounding factors. The binding of microporous zeolite framework is much more durable so that it is able to control selective measures as well as it can be able to obstruct sintering also in high temperature and pressure. However, encapsulation process of zeolite holds expensive and tough characterization processes[73,74,75]. In field of encapsulation of MNPs ceria (CeO_2) is a tremendous compound for this technology due to its miraculous qualities like high stability, extremely active catalysis and selectivity towards therapeutic agents, it is very low expensive and has anomalous property to generate active oxygen. Researchers have trying to develop better CeO_2 nanoshell due to its specificity in encapsulating MNPs and a unique electronic configuration for generation of active oxygen. CeO_2 is very important in encapsulation technology because of its catalytic applications and efficacy in encapsulating MNPs[37,76,77]. Moreover chitosan is also an appropriate suitable base material for encapsulation of natural compounds essential oils and naturally abundant and typically original substances. The chitosan is used for basic fabrication and coating for encapsulation of various natural substances. And chitosan is also suitable encapsulation supportive compound for green originated compounds with its multiple beneficial properties[78,79,80]. For mannered encapsulation of Ag and Au nanoparticles researchers use the procedure based on basic seeded emulsion polymerization, due to specific obstructions like degree of solubility in biological fluids, specific degree of stability, bio-affinity and effect of physiological condition. Although in studies of plasmonic nanoparticles shows some extra limitations while they implied *in-vivo* regarding their capacity to bind, solubility and stability inside. The encapsulation technique enables the involvement of single nanoparticle to cluster of nanoparticles inside the natural polymer covering, with their dimensional size of 50-200nm. Encapsulated nanoparticles efficiently working with metals and exhibit their efficacy with different hybrid nanocomposites and holding tremendous stability in high ionic strength, oxidation procedures, and high cellular uptake and negligible toxicity within the cells. In this context the encapsulated nanostructures were very efficient for plasmonic applications with biologically correlated factors and conditions[81,82,83]. Nutraceutical in combination with MNPs can increase their efficacy to obstruction against antibiotic resistivity regarding cancer therapy and viral infections. This wonderful bonding of nanoparticles and nutraceuticals used in encapsulation technology of bioactive compounds for increasing their properties and also used to exhibit ideal imaging. In present scenario the use of plant-based methods for characterization of encapsulated nanoparticles is more reliable safer and cost-effective with respect to other synthetic and chemical procedures. This is also a difficult subject matter to find-out the exact toxicity and beneficiary profiles of metallic nanoparticles and metal-oxide nanostructures to prevent their toxic effect on biological systems they may be *in-vivo* or *in-vitro*[60,72,84,85,86].

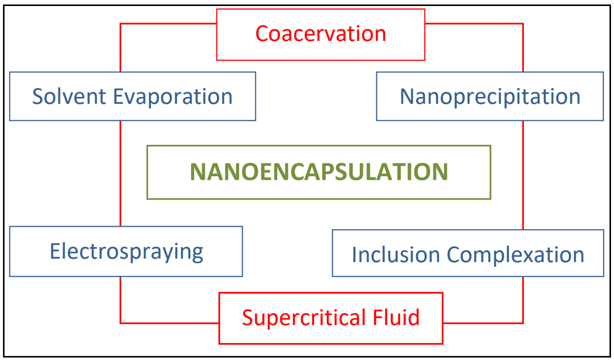

Figure 1: Applications of nanoencapsulation for agri-food industry[42].

Metal nanoparticles themselves can be use for encapsulation

If we focus on reactions based on catalysis the metal nanoparticles prove themselves as strong catalytically active compounds as they used in various catalysis reactions. On the basis of their specific qualities encapsulated MNPs hold high surface energy and pretend to coalesce by dispersion via catalysis and got deactivated by loss of energy[87,88]. Now-a-days scientist uses several procedures to increase the stability factor of MNPs, with their other efficacies. The characterization of core shell substances for encapsulation of MNPs in combination with inorganic compounds improve their electivity, remediation, biological activity, binding capacity as well as chemical affinity of both MNPs and inorganic compound, So that the encapsulation technique is much more important in overall phenomena. In present scenario the TiO_2 and SiO_2 were found suitable coating material to encapsulate various MNPs such as (Ag, Au, Cu, Pt, and Pd). Researchers involved in finding out the accurate properties such as stability, electronic transfer, tandem catalysis and selectivity of MNPs after encapsulation[87,89]. When nutraceutical combines with MNPs they exhibit the properties of both the NPs and nutraceuticals. e.g. the AgNPs combines with plumbagin, (a nutraceutical) it shows high antibacterial, Antipathogenic activity against Escherichia coli and Bacillus subtilis. Although the combination of gallic acid (an anticancer nutraceutical compound) with gold nanoparticle explored, the enhanced capacity to demolish the proliferation of cholangiocarcinoma cell with respect to anticancer nutraceutical without any conjugation. This is another very important procedure to increase the efficacy of nutraceuticals so that the gallic acid is used to encapsulate AuNPs regarding cancer therapies. However the drawback of use of gallic acid is cytotoxicity for cervical cancer cell as well as normal cell both. But when gallic acid combines with AuNPs it leaves its cytotoxicity against normal cells so that AuNPs and gallic acid combination is broadly useful in cancer therapies[72,90,91,92]. The long term toxic effects of nanoparticles and safety measures for cellular system is a major issue which needs more focus on it. In this concern biocapping and stabilization with green resources and aqueous plant extracts is an effective process during controlled development of NPs to reduce the rate of toxicity. Moreover superficial tailoring of nanostructures is essential to get monodispersible and polydispersible NPs[93,94,95]. Although the characterization and purification of NPs is very hectic from other reaction products and it is another task after employing this method on large scale. Researchers still finding out the facts of growth of capped nanocrystals and nanocomposites with reliable colloidal stability and other functions with other qualitative effects emerged after capping, regarding therapeutics and other environmental factors[93,96,97].

Importance of encapsulation of nanoparticles with natural polymers

The development of encapsulation technology with the help of natural polymers also aiming to improving the quality of therapeutic agents and preservatives used for the safety of packaged food by the incorporation of antimicrobial natural compounds and/or antioxidant natural compounds. Encapsulation technology also helps the compound from spoilage due to high temperature, high pressure and exposure to the high beam of light. To increase shelf life of the substance, suitable carriers and encapsulation techniques were employed with use of oxides nanoclays, metals and essential oils. As compared to natural antimicrobial, essential oils and nanoemulsions (10.9-100 nm) have efficiency regarding sensory disorders[98,99]. Encapsulation of curcumin shows strong affinity with the proteins specially gelatin and zein which gives rise to increased conservation effect for nanofibers. Regarding conservative encapsulation efficiencies zein hold the effects of augmentation. Among specific natural biopolymers chitosan and polyglutamicacid were showing electrospinning processes due to their elasticity and firmness, biodegradable biopolymers for electrospinning are obtained from natural biopolymers such as starches, cellulose, cellulose acetate, chitin, chitosan, proteins (gelatin, zein, silk), bio–engineered polymers (such as poly(hydroxy alkanoates (PHAs), [poly(glutamicacid) which are characterized biologically using green route], derived from monomers such as polylactic acid. Synthetic biopolymers such as poly (ethylene glycol) (PEG), poly (vinyl alcohol) (PVA), poly (ethylene oxide) (PEO), poly (caprolactone) (PCL), are also used. In order to focus on natural polymers and proteins, zein is significantly paved because its qualities such as toughness, flexibility, compressibility, hydrophobicity, nontoxicity and being cheap. In terms of natural resources, connective tissue of animals is also a very good natural source of natural biopolymers which is highly flexible and biologically protected. But polyvinyl-chloride (PVC) is a completely synthetic biopolymer with high optical sensitivity and solubility[98,100,101]. For encapsulation of compounds essential oils were also a good matrix because of their size, binding capacity and sustained release. Moreover polymeric nanofibers were extremely useful as pesticide due to improved residual effects and negligible toxicity[101,102]. Now-a-days natural polymers were used to improve the quality of drug delivery system either they may be combine with small macro-molecule or micro-molecule. In combination with MNPs the natural polymer based drug delivery system is being very efficient by all means regarding therapeutics[103,104].

As it is well known that gold nanoparticles (GNPs) are regarded as most stable and novel MNPs among all NPs. However GNPs holds unique electronic configuration, synergistic effect large surface area, endurance towards high temperature and pressure and tremendous surface energies, which were very beneficial for encapsulation technique. Rather than all these features GNPs have wonderful surface area to volume ratio and plasmonic excitation capacity. So that GNPs were the backbone of nanotechnology and encapsulation technology based on NPs. GNPs can be converted into colloidal form which has a broad range of uses in therapies due to their optical and magnetic effects. Due to broad surface area to volume ratio with specific functionalization these nanocompounds become extremely sensitive to environmental changes, so that nanosensors can detect anomalies at very low range[105,106]. Regarding encapsulation technology hydrogels are specific conjugative substances due to their capacity of water retention with capturing of structural configuration and its 3D structure. Hydrogels keeps the qualities of the living soft tissues so that they suppose to be a factor biological medication. In order to be sensitive against electric field, magnetic field, temperature, pressure, pH, external impulses and stimuli, ionic concentration, beam of light, and strong chemicals, the hydrogels system hold several chemical and structural factors. With respect to advanced technological application the natural polymeric hydrogels have capacity of conversion of their volumetric transitional phase with structural variation. As a result of external stimuli a huge potential for experimental observation may developed among these hydrogels alginate and agarose gels were proved their capacity on the basis of their morphology and physiochemical consistency. Natural polymeric hydrogels are very promising variants in field of medicine and pharmaceutical due to their synergy with living connective tissue, tolerance for biodegradability and good compatibility[107,108,109].

CONCLUSION

Encapsulation of nanoparticles through biological compounds with different carriers is a committed way to strengthen their stability, firmness, surface area and viability. Nanotechnology applied encapsulation of nanoparticles and other biologically active particles for many apparent benefits from water treatment plants to pharmaceutical and food processing, as well as other industrial uses. Encapsulation provides the stability improvements and bioavailability advancement in a controlled manner. Encapsulation also gives advantages of being safe via defensive mechanism and controlled release of biologically originated compounds used in vivo or anywhere else. Encapsulation provides different types of protective measures with different substances they may be natural compounds or modified synthetic chemicals.

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