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Bogachev I.A.[1]
Krolevets A.A.[2]

PROPERTIES OF NANO ENCAPSULATED L-ARGININE AND RESVERATROL IN WATER-SOLUBLE POLYMERS

1) PG student, Department of Pharmacology, Belgorod National Research University, 85 Pobedy St., Belgorod, 308005, Russia, e-mail: bogachev91@yandex.com
2) Doctor of Chemical Sciences, Associate Professor, Department of Food Chemistry, Belgorod National Research University 85 Pobedy St., Belgorod, 308005, Russia, e-mail: a_krolevets@inbox.ru

Abstract: This article analyzes properties of nano encapsulated L-arginine and resveratrol using a Nanoparticle Tracking Analysis method, and studies their supramolecular properties using a self-organization method.
Key words: nanocapsules, self-organization, L-arginine, resveratrol, NTA-method (Nanoparticle Tracking Analysis method).

Introduction. The micro-encapsulation process is mostly used in the pharmaceutical industry due to the fact that the drugs enclosed inside polymer coatings have a number of health properties. Here are the benefits of micro-encapsulated medications:

a) protection of unstable medications from ambient effects (vitamins, antibiotics, enzymes, vaccines, sera, etc.);

b) taste masking of bitter and nauseating medications;

c) drug substance release in the required part of the gastrointestinal tract (enterosoluble microcapsules);

d) prolonged action. A mixture of microcapsules which differ in size, thickness and coat nature is put into the same capsule and sustains a certain level of the drug in the body as well as effective therapeutic action for a long time;

e) combination of incompatible-in-substance drugs in the same space (use of parting coating) [1, 2, 3, 5].

Micro-encapsulation is enclosure of small amounts of a substance inside a coating of film forming material (microcapsule) [3]. The content of microcapsules can be in a hard, solid, or gaseous state and be either an individual substance or a mixture; size of microcapsules varies from μm fractions to several mm; content of the encapsulated substance is usually 70 to 85 per cent of the capsule weight (sometimes 95 to 99 per cent). Microcapsules can have a one- or multi-layer coating (thickness varies from μm fractions to tens of μm), and either an elastic coating or a rigid one due to the properties of coat-forming substance [2].

Micro-encapsulation methods can be divided into three basic groups. The first group comprises physicochemical methods including coacervation, nonsolvent addition, new phase formation with temperature changes, solvent evaporation, melt hardening in fluid media, extraction diffusion, spray drying, and physical adsorption [5]. The second group includes chemical methods: new phase formation by cross-linking, polycondensation and polymerization. And finally, the third group includes physical methods: film coating in a fluidized bed, extrusion and condensation of vapors. This classification based on the nature of processes carried during microencapsulation is quite conventional. In practice, a combination of different methods is often used [2].

Surface active substances are mostly used in microencapsulation processes to increase sustainability of dispersion systems, chiefly those in which emulsion is formed at dispersion stages of the substance encapsulated. In systems where water is one of the stages, implication of surface active substances has been studied quite well [4].

To define the most suitable method in each particular case, tailor-made properties of the end product, cost of the process, and many other factors are being relied upon. However the method is mostly chosen due to the properties of the initial substance being encapsulated [3].

Body of Article. This article performs properties of the obtained nano encapsulated L-arginine and resveratrol in various coatings of sodium alginate, or xanthan and konjac gums.

Self-organization of microcapsules has been studied as follows. *Coffee* flavoring powder encapsulated inside carboxymethylcellulose sodium has been solved in water, a drop has been applied upon a cover-glass and evaporated. The dried surface has been scanned by a confocal microscopy method using an *OmegaScope* microspectrometer manufactured by AIST-NT (Zelenograd, Russia) and integrated with a confocal microscope. The results obtained are represented in Figures 1 and 2.

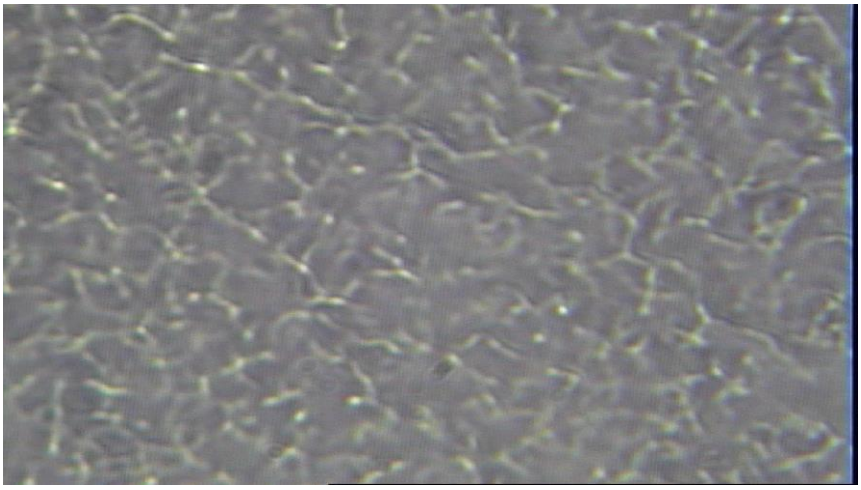

Figure 1. Self-organization of L-arginine inside sodium alginate with concentration 0.125% and a core-to-coating ratio 1:3 when magnified 2830 times

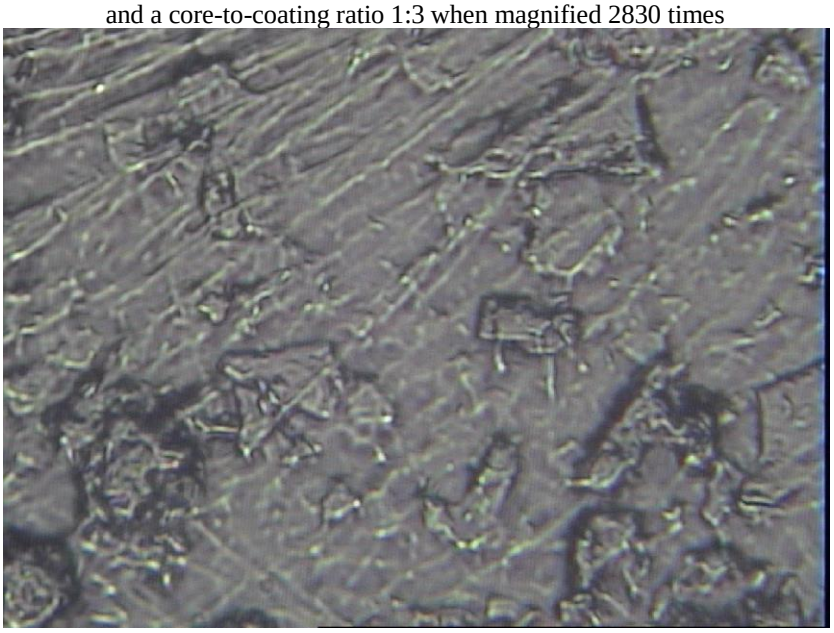

Figure 2. Self-organization of resveratrol inside xanthan gum with concentration 0.25% and a core-to-coating ratio 1:3 when magnified 2830 times

To measure sizes of nanoparticles, a method of Nanoparticle Tracking Analysis has been used. This is a method of imaging and study of nanoparticles in solutions which was devised by the Nanosight Company (the UK). It is based upon observation of Brownian motion of single nanoparticles when motion velocity depends on fluid viscosity and temperature as well as nanoparticle size and shape. This permits to use this principle to measure sizes of nanoparticles in colloid solutions. Beside the size, light scattering intensity for a separate nanoparticle can be measured at the same time which allows to discriminate nanoparticles against their material. A third parameter to measure is concentration of each fraction of nanoparticles [6].

This method keeps strongly growing in popularity in the scientific community. Thus, by early autumn in 2012, a number of scientific papers using the Nanoparticle Tracking Analysis method has reached 400 ones while above 100 papers among them have been only published within 2012 [7].

The measurements have been made using a nanoparticle multiparameter analyzer Nanosight LM0 manufactured by Nanosight Ltd (the UK) and configured as HS-BF (high-sensitivity camera Andor Luca, semiconductor laser with wave length 405 nm and power 45 mW). The device operates on the basis of the Nanoparticle Tracking Analysis (NTA) method described in ASTM E2834.

The optimum dilution ratio 1:100 has been chosen. To make measurements, the following parameters have been chosen for the device: Camera Level = 16, Detection Threshold = 10 (multi), Min Track Length: Auto, Min Expected Size: Auto, single measurement duration = 215s, syringe pump use.

Figures 3 and 4 show measurement results for nanocapsules of L-arginine and resveratrol in various coatings.

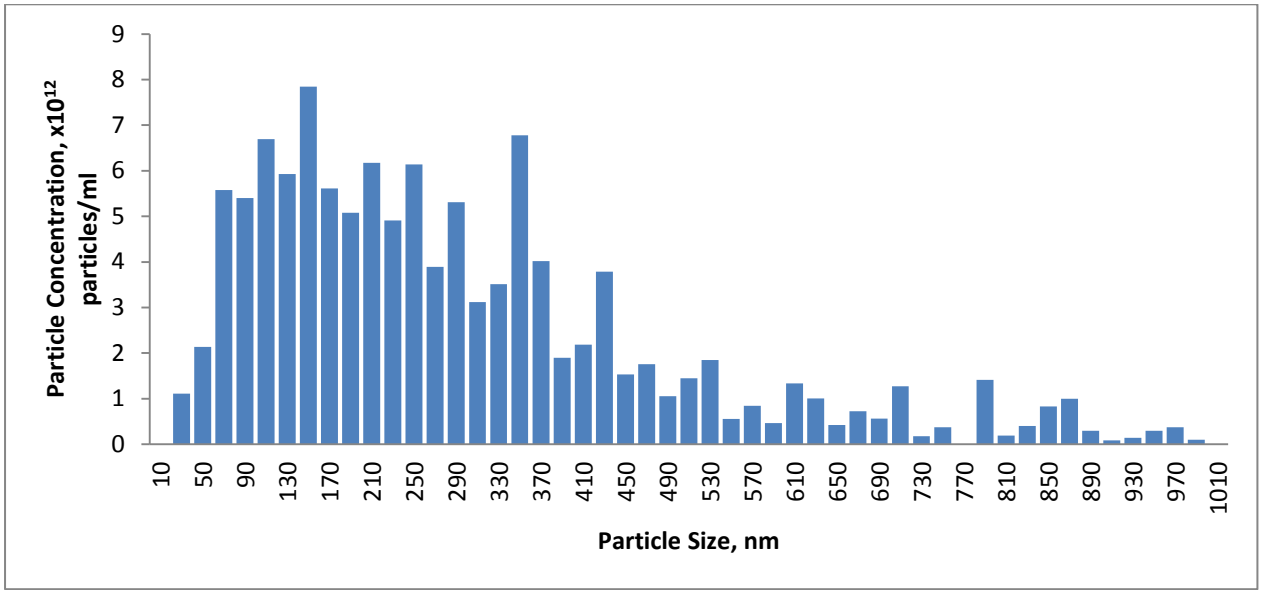

Figure 3. Distribution of particles by size in a sample of L-arginine nanocapsules inside alginate sodium (core-to-coating ratio is 5:1)

Statistical characteristics of the distributions are represented in Table 1

Table 1

Statistical characteristics of particles in L-arginine samples inside alginate sodium (core-to-coating ratio is 5:1)

Parameter	Value
Average size, nm	330
D10, nm	94
D50, nm	274
D90, nm	661
Polydispersity index, (D90- D10)/D50	2.07
Total particle concentration, $\times 10^{12}$ particles/ml	1.26

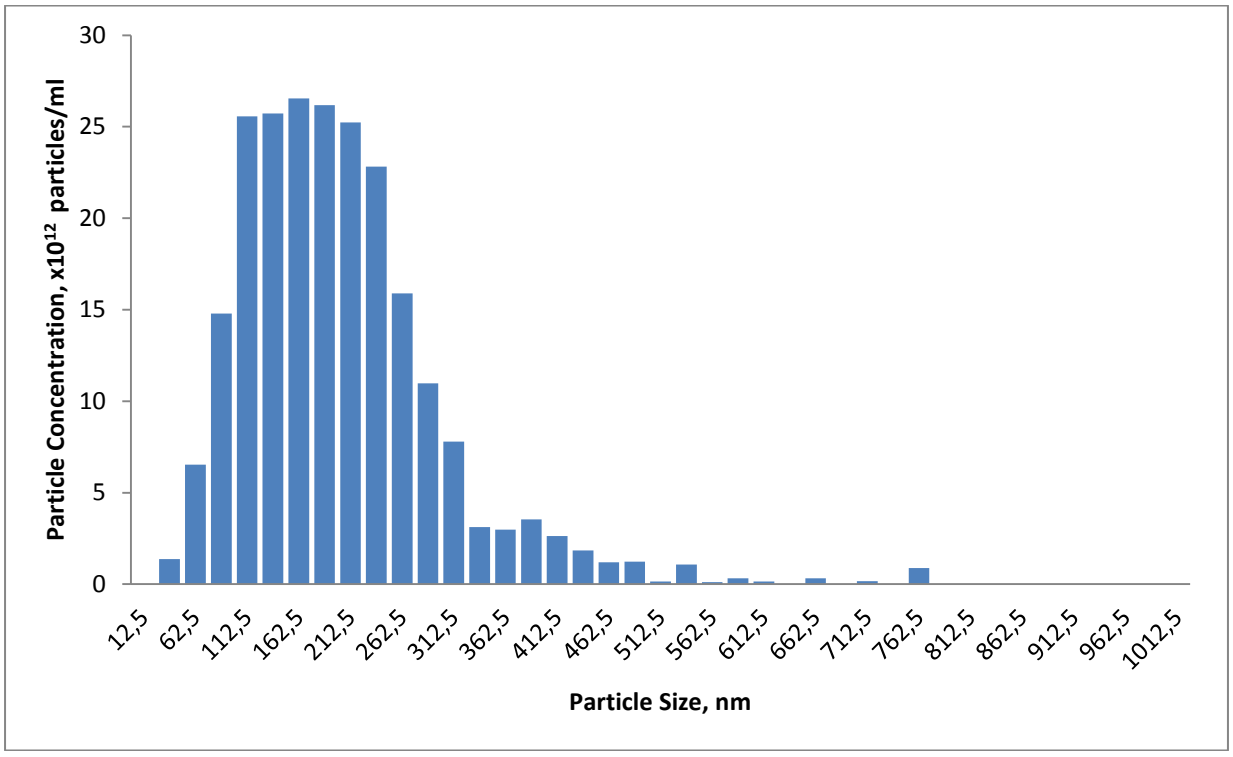

Figure 4. Distribution of particles by size in a sample of resveratrol nanocapsules inside apple pectin (core-to-coating ratio is 5:1)

Statistical characteristics of the distributions are represented in Table 2

Table 2

Statistical characteristics of particles in resveratrol samples inside apple pectin (core-to-coating ratio is 5:1)

Parameter	Value
Average size, nm	204
D10, nm	99
D50, nm	187
D90, nm	318
Polydispersity index, (D90- D10)/D50	1.17
Total particle concentration, $\times 10^{12}$ particles/ml	2.29

Thus, nano encapsulated L-arginine and resveratrol have supramolecular properties and nano-size of particles. Distribution of particles by size shows possible exchange of a two-chamber pharmacokinetic model to a one-chamber one due to the fact that substance particles would stay within a blood stream.

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