

Synthesis of fluorescently-labelled poly(2-ethyl-2-oxazoline)-protected gold nanoparticles

Article

Published Version

Creative Commons: Attribution-Noncommercial-No Derivative Works 4.0

Open Access

Nurgaziyeva, E. K., Kudaibergenov, S. E., Mun, G. A. and Khutoryanskiy, V. V. ORCID: <https://orcid.org/0000-0002-7221-2630> (2021) Synthesis of fluorescently-labelled poly(2-ethyl-2-oxazoline)-protected gold nanoparticles. Chemical Bulletin of Kazakh National University, 100 (1). pp. 12-20. ISSN 2312-7554 doi: 10.15328/cb1185 Available at <https://centaur.reading.ac.uk/97705/>

It is advisable to refer to the publisher's version if you intend to cite from the work. See [Guidance on citing](#).

Identification Number/DOI: 10.15328/cb1185 <<https://doi.org/10.15328/cb1185>>

Publisher: Kazakh National University

All outputs in CentAUR are protected by Intellectual Property Rights law, including copyright law. Copyright and IPR is retained by the creators or other copyright holders. Terms and conditions for use of this material are defined in the [End User Agreement](#).

www.reading.ac.uk/centaur

CentAUR

Central Archive at the University of Reading

Reading's research outputs online

Synthesis of fluorescently-labelled poly(2-ethyl-2-oxazoline)-protected gold nanoparticles

E.K. Nurgaziyeva¹, S.E. Kudaibergenov²,
G.A. Mun¹, V.V. Khutoryanskiy^{1,3*}

¹Al-Farabi Kazakh National University,
Almaty, Kazakhstan

²Institute of Polymer Materials and
Technologies, Almaty, Kazakhstan

³Reading School of Pharmacy, University of
Reading, Reading, United Kingdom

*E-mail: v.khutoryanskiy@reading.ac.uk

Gold nanoparticles (GNPs) protected by poly(2-ethyl-2-oxazoline) (POZ) of different molecular weights (M_w = 5, 50, 200 and 500 kDa) were synthesised and characterised by dynamic light scattering, nanoparticle tracking analysis, zeta potential measurement and transmission electron microscopy. It was established that the use of POZ with 50 kDa resulted in formation of GNPs with low polydispersity while POZ with greater molecular weights led to formation of more polydisperse GNPs. Fluorescent labelling of these nanoparticles was achieved through their reaction with polyethyleneglycol dithiol (8-12 kDa) as a linker molecule with subsequent reaction with 6-(iodoacetamido) fluorescein. The fluorescent nature of obtained GNPs was confirmed by the appearance of the fluorescence peak at 510 nm that is typical for fluorescein molecules and glowing of the aqueous solution under the UV irradiation. The fluorescently-labelled GNPs are promising tool in biomedical application to monitor the biological systems using fluorescent microscopy.

Keywords: poly(2-ethyl-2-oxazoline); gold nanoparticles; fluorescent label; polyethylene glycol; colloidal stability; fluorescein.

Поли (2-этил-2-оксазолинмен тұрақтандырылып, флуоресцентті-белгіленген алтын нанобөлшектерінің синтезі

Э.К. Нұрғазиева¹, С.Е. Құдайбергенов²,
Г.А. Мұн¹, В.В. Хуторянский^{1,3*}

¹Әл-Фараби атындағы Қазақ ұлттық
университеті, Алматы, Қазақстан

²Полимерлі материалдар мен
технологиялар институты,
Алматы, Қазақстан

³Рединг қаласының Фармациялық
мектебі, Рединг Университеті,
Рединг, Ұлыбритания

*E-mail: v.khutoryanskiy@reading.ac.uk

Бұл жұмыста әр түрлі молекулалық массадағы (5, 50, 200 and 500 кДа) поли(2-этил-2-оксазолинмен) тұрақтандырылған алтын нанобөлшектері синтезделді. Бұл нанобөлшектер физикалық-химиялық талдаудың бірнеше әдістерімен сипатталды, соның ішінде динамикалық жарық шашырау әдісі, трекингтік талдау, дзета-потенциалды өлшеу және электронды микроскопия қолданылды. Молекулалық салмағы 50 кДа болатын поли(2-этил-2-оксазолинды) қолдану полидисперстігі төмен алтын нанобөлшектерінің түзілуіне әкелетіні анықталды, ал молекулалық массасы жоғары полимерді қолдану полидисперстіктің доғарылауына әкеледі. Флуоресцентті-белгіленген бөлшектерді олардың байланыстырушы ретінде қолданылған полиэтиленгликоль дитиолымен (8-12 кДа) реакциясынан кейін 6-(йодоацетамидо)флуоресцеинмен әрекеттестіру арқылы алу әдістемесі жасалды. Бұл нанобөлшектердің флуоресцентті табиғаты сулы дисперсиясына тән ультракүлгін сәулесінде жарқылымен, сондай-ақ флуоресцентті спектроскопиямен расталды. Бұл нанобөлшектер биомедициналық зерттеулер үшін пайдалы және олардың биологиялық жүйелердегі жағдайын флуоресцентті микроскопия арқылы зерттеуге болады.

Түйін сөздер: поли(2-этил-2-оксазолин); алтын нанобөлшектері; флуоресцентті белгі; полиэтиленгликоль; коллоидты тұрақтылық; флуоресцеин.

Синтез флуоресцентно-меченых поли(2-этил-оксазолин)-протектированных наночастиц золота

Э.К. Нұрғазиева¹, С.Е. Кудайбергенов²,
Г.А. Мұн¹, В.В. Хуторянский^{1,3*}

¹Казахский национальный университет
им. аль-Фараби, Алматы, Казахстан

²Институт полимерных материалов и
технологий, Алматы, Казахстан

³Редингская школа фармации,
Университет Рединга,
Рединг, Великобритания

*E-mail: v.khutoryanskiy@reading.ac.uk

В работе синтезированы наночастицы золота (НЧЗ), проектированные поли(2-этил-2-оксазолином) (ПОЗ) с различными молекулярными массами (M_w = 5, 50, 200 и 500 кДа), и охарактеризованы методами динамического светорассеяния, трекинг-анализа наночастиц, измерения дзета-потенциала и просвечивающей электронной микроскопии. Установлено, что использование ПОЗ с низкой молекулярной массой 50 кДа приводит к образованию НЧЗ низкой полидисперсности, в то время как использование полимера с большей молекулярной массой приводит к получению более полидисперсных НЧЗ. Разработана методика получения флуоресцентно-меченых НЧЗ посредством их реакции с полиэтиленгликоль дитиолом (8-12 кДа) в качестве линкера при последующем взаимодействии с 6-(йодоацетамидо)флуоресцеином. Флуоресцентная природа полученных наночастиц подтверждена появлением флуоресцентного пика при 510 нм, который характерен молекулам флуоресцеина и свечением водного раствора в ультрафиолетовом свете. Флуоресцентно-меченые НЧЗ являются обещающим объектом для биомедицинского применения при мониторинге биологических систем с помощью флуоресцентной микроскопии.

Ключевые слова: поли(2-этил-2-оксазолин); наночастицы золота; флуоресцентная метка; полиэтиленгликоль; коллоидная стабильность; флуоресцеин.



Synthesis of fluorescently-labelled poly(2-ethyl-2-oxazoline)-protected gold nanoparticles

E.K. Nurgaziyeva¹ , S.E. Kudaibergenov² , G.A. Mun¹ , V.V. Khutoryanskiy^{1,3*}

¹Al-Farabi Kazakh National University, 71 al-Farabi Ave., Almaty 050040, Kazakhstan

²Institute of Polymer Materials and Technologies, 1/3 microdistrict "Atyrau 1", Almaty 050019, Kazakhstan

³Reading School of Pharmacy, University of Reading, Whiteknights, PO Box 224, Reading RG66DX, United Kingdom

*E-mail: v.khutoryanskiy@reading.ac.uk

(This paper is dedicated to 70th anniversary of Professor Sarkyt E. Kudaibergenov)

1. Introduction

One of the first studies of colloidal gold was reported by Michael Faraday who was fascinated by unique properties of this material [1]. In 1951 Turkevich *et al* [2] reported an easy and highly-reproducible synthetic method of GNPs, which involves reaction of hydrogen tetrachloroaurate (HAuCl₄) with citric acid (CA) in boiling water where CA acts as both reducing and stabilizing agent. Later, it was demonstrated by Frens that the size of nanoparticles can easily be controlled by varying gold-to-citrate ratios [3]. The GNPs have received a great deal of interest due to their unique physicochemical properties. In particular they are very useful for various biomedical applications, including therapeutic and diagnostic areas [4-6]. Moreover, the GNPs are widely applied in catalysis [7-8].

The use of water-soluble polymers in the synthesis of GNPs dates back to 1718, when starch was used to stabilize the colloidal gold in aqueous dispersions [9]. Since then different synthetic and natural water-soluble polymers such as poly(N-vinyl pyrrolidone) [10-12], poly(ethylene glycol) [13-14], gellan gum [15-16], κ -carrageenan and pectin [12] were used to prepare gold nanoparticles for various applications.

Poly(2-oxazolines) are an emerging class of polymers that recently attracted a lot of attention for biomedical applications [17]. Nanoparticles decorated with poly(2-methyl-2-oxazoline) and poly(2-ethyl-2-oxazoline) were previously shown to exhibit 'stealth' properties and facilitate penetration through biological tissues [18-19]. Previously, de la Rosa *et al* reported the functionalisation of GNPs with xanthate-functional poly(2-alkyl-2-oxazoline) [20].

In the present work we have synthesised and characterised GNPs stabilised with commercially available poly(2-ethyl-2-

oxazoline) (POZ) using different concentrations and molecular weights of the polymer. We also have developed the methodology for preparation of fluorescently-labelled POZ-protected GNPs using poly(ethylene glycol) dithiol as a linker and 6-(iodoacetamido)fluorescein as fluorescent label.

2. Experiment

2.1. Materials

Poly(2-ethyl-2-oxazoline) (POZ) with M_w = 5, 50, 200 and 500 kDa, poly(ethylene glycol) dithiol (PEG-dithiol) with M_w = 8-12 kDa, 6-(iodoacetamido)fluorescein and tetrachloroauric acid (HAuCl₄) were purchased from Sigma-Aldrich (UK) and used without further purification.

2.2. Synthesis of gold nanoparticles

Synthesis of GNPs was carried out by mixing 0.3 mL (10 mmol) HAuCl₄ and 10 mL 0.1, 0.5, 1, 2, or 4 w/v % poly(2-ethyl-2-oxazoline) (POZ) at room temperature. After dropwise addition of aqueous solution of NaOH (0.5 M) the reaction mixture was stirred for several minutes until the colour of the solution changed which confirmed the formation of GNPs. When 0.1% POZ solution was used the formed GNPs underwent quick aggregation and precipitation pointing at too low concentration of the POZ for stabilisation of the GNPs. The synthesized GNPs were purified by dialysis against 4 L deionised water for 48 hours using cellulose membranes (molecular weight cut off 12-14 kDa, Medicell International Ltd, UK).

2.3. Preparation of fluorescently-labelled gold nanoparticles

2 mL of GNPs solution and 1 mL of poly(ethylene glycol) dithiol (0.7 w/v %) were mixed and stirred at room temperature

overnight. The reaction mixture was then dialyzed against deionised water using cellulose membrane for a week. 0.5 % 1 mL of 6-(iodoacetamido) fluorescein was added to this solution and was stirred overnight. Then the reaction mixture was dialyzed using a float-a-lyzer membrane (with 3.5-5 kDa molecular weight cut off) for a week to get rid of unreacted dye.

2.4. Dynamic light scattering (DLS) and zeta potential measurements

Particle size distributions and zeta-potential of GNPs in aqueous dispersions were measured using Zetasizer NanoZS (Malvern Instruments Ltd., UK). The results are presented as the mean \pm standard deviation for three repeated measurements. All experiments were performed at 25 °C. DTS-1070 cuvettes were used for zeta potential measurements.

2.5. Nanoparticle tracking analysis (NTA)

The size of GNPs was additionally characterised using nanoparticle tracking analysis using LM10 system with temperature-controlled module, green 532 nm laser, and syringe pump (Malvern, UK).

2.6. UV-vis spectroscopy

Absorption spectra of GNPs were recorded at room temperature using UV-Vis spectroscopy (Specord 210 plus BU, Germany).

2.7. Transmission electron microscopy (TEM)

TEM images of GNPs were recorded using a Philips CH 200 microscope operated at an accelerating voltage of 160 kV. Samples were prepared by dropping a dispersion of the particles on Formvar coated copper grids.

2.8. Fluorescence spectra

Fluorescence spectra were recorded for fluorescently-labelled POZ-protected nanoparticles using a FP-6200 Spectrofluorometer (Jasco, UK) over the wavelength range 505-700 nm (λ_{ex} = 308 nm).

3. Results and Discussion

Formation of GNPs is usually accompanied by changes in colour of solutions, the intensity of which depends on the concentration and size of nanoparticles. In our case the color of POZ solutions containing GNPs changes is shown in Figure 1.

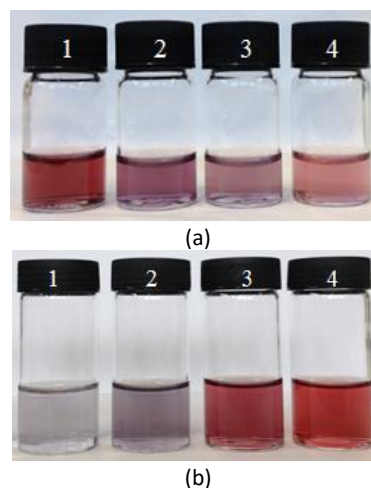


Figure 1 – Photographs of aqueous solutions containing GNPs, which were synthesised using (a) 1 w/v % POZ of different M_w = 5 (1); 50 (2); 200 (3); 500 kDa (4); (b) POZ (M_w = 200 kDa) of different concentrations 0.5 w/v % (1); 1 w/v % (2); 2 w/v % (3); 4 w/v % (4)

The reduction of Au^{3+} to Au^0 probably proceeds through the ionization of tertiary amine groups of POZ by $HAuCl_4$ followed by formation of $AuCl_3(OH)^-$ that is reduced into atomic gold [21] and stabilized via chemisorbed lactame ring, as schematically illustrated in Figure 2. In our mind the negative charge of the system is accounted for chemisorbed chloride and/or hydroxide ions on the surface of GNPs. The exact mechanism of this

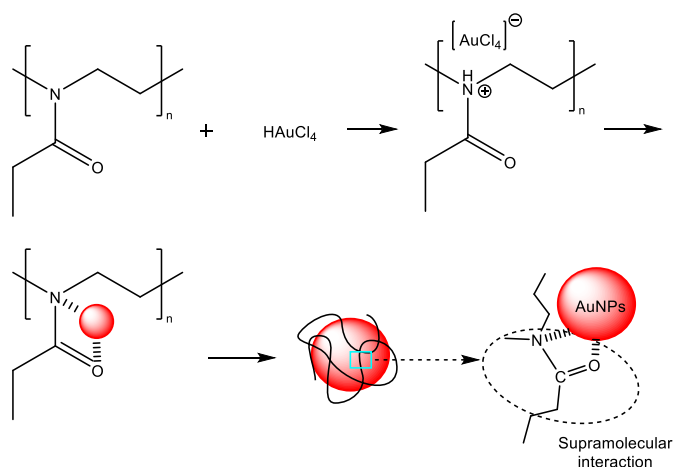


Figure 2 – Proposed stabilization mechanism of GNPs by POZ

reaction and which species act as a reducing agent for Au^{3+} is currently unclear. This will require further studies.

All nanoparticles were characterized using dynamic light scattering, nanoparticle tracking analysis (NTA), zeta-potential measurements and transmission electron microscopy. Figure 3 shows typical size distributions of GNPs measured by dynamic light scattering in aqueous solutions. In most cases the size distributions are monomodal, which indicates good colloidal stabilisation of the nanoparticles. According to recent results [12] the average hydrodynamic diameters of GNPs stabilized with a series of synthetic and natural polymers varied from 5 to 30 nm, while the zeta-potentials were negative and range between -28 and -42 mV. The colloidal stability of GNPs protected by these polymers is very good over an extended period of 36 days. A long-time stability of GNPs for our system was also observed but was not studied in detail in this work. A polymodal size distribution, on the contrary, indicates poor colloidal stability, polydisperse nature and possible aggregation of nanoparticles to form larger species. For example, polymodal size distribution was observed for the GNPs synthesised in the presence of 0.5 w/v % POZ with $M_w = 50$ kDa.

Selected nanoparticles were additionally characterised using transmission electron microscopy (TEM). Figure 4 shows the TEM images of some GNPs. It is clearly seen that all of them

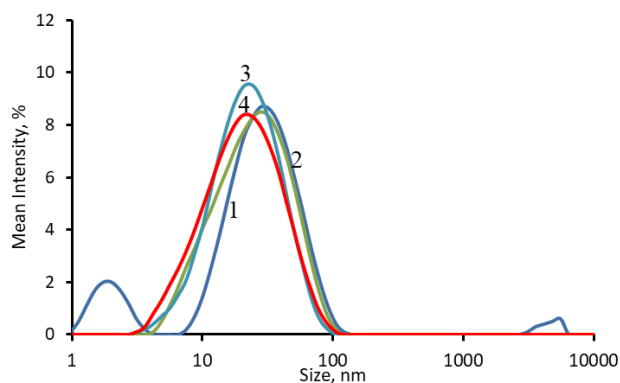


Figure 3 – Size-distribution of POZ-protected GNPs prepared using 50 kDa POZ of different concentrations: 0.5 w/v % (1-blue); 1 w/v % (2- green); 2 w/v % (3- bright blue), 4 w/v % (4-red)

are spherically shaped polydisperse nanoparticles. The average sizes of GNPs evaluated using TEM image analysis, NTA, DLS together with polydispersity index (PDI) and zeta-potential data are summarized in Table 1.

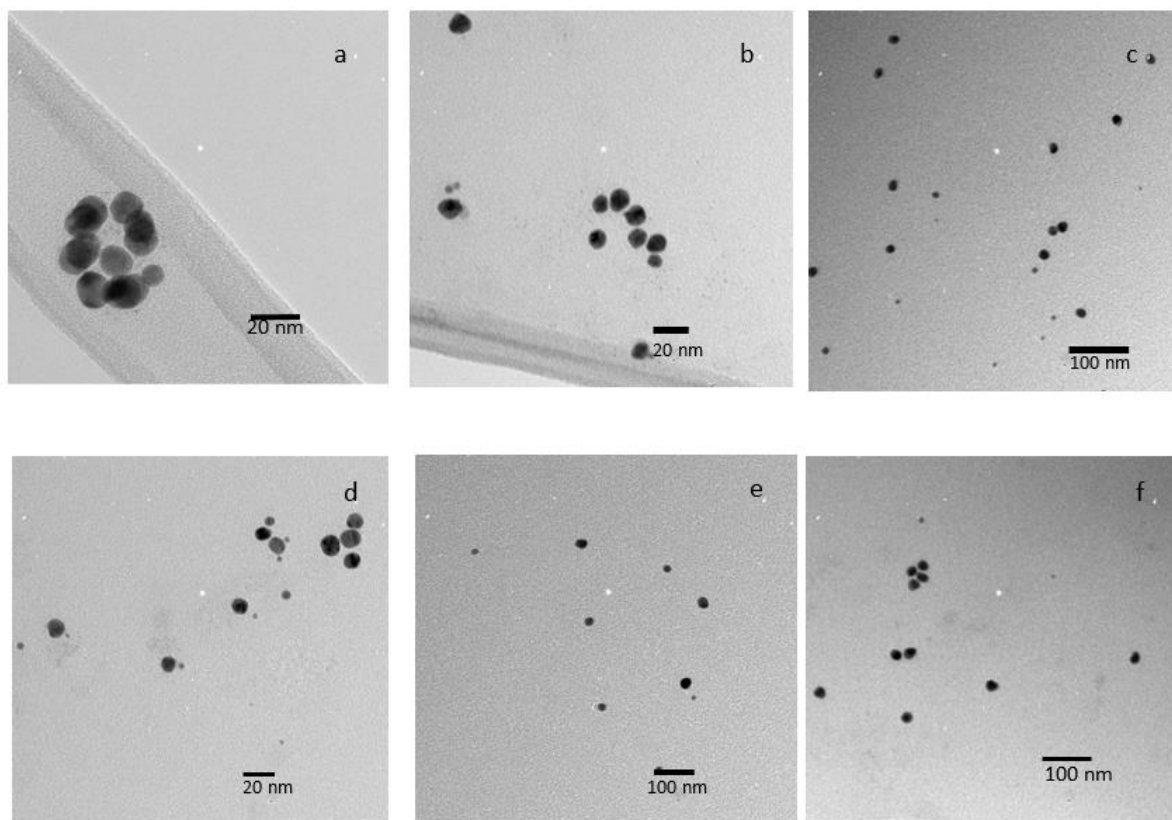


Figure 4 – TEM images of GNPs prepared using POZ 5 kDa (a, b, d), 50 kDa (c, e, f) at the polymer concentration of 0.5 (a) and 2 w/v % (b, c, d, e, f)

Table 1 – The average sizes of GNPs determined by NTA, DLS, TEM together with their PDI and zeta-potential

Sample	Average size of GNPs, nm			PDI	Z-potential, mV
	NTA	DLS	TEM		
AuNPs /0.5% -POZ 5 kDa	20±5	19±1	13.9±1.2	0.259	-5.37
AuNPs /1% - POZ 5 kDa	26±14	22±1	*	0.342	-14.10
AuNPs /2% - POZ 5 kDa	52±5	85±20	13.3±1.2	0.168	-10.30
AuNPs /0.5 % - POZ 50 kDa	40±4	82±4	11.5±1.2	0.191	-5.63
AuNPs /1% - POZ 50 kDa	25±7	57±20	*	0.198	-10.20
AuNPs /2% - POZ 50 kDa	90±9	61±6	12.5±1.0	0.138	-10.90
AuNPs /4% - POZ 50 kDa	133±8	29±5	*	0.168	-8.92
AuNPs /0.5% - POZ 200 kDa	55±1	44±13	*	0.197	-12.10
AuNPs /1% - POZ 200 kDa	84±5	29±1	*	0.480	-5.34
AuNPs /2% - POZ 200 kDa	67±6	32±2	*	0.341	-10.50
AuNPs /4% - POZ 200 kDa	67±15	37±6	*	0.485	-7.99
AuNPs /0.5% - POZ 500 kDa	61±5	43±8	*	0.468	-10.9
AuNPs /1% - POZ 500 kDa	75±15	52±12	*	0.602	-9.96
AuNPs /2% - POZ 500 kDa	71±6	30±1	*	0.429	-7.03
AuNPs /4% - POZ 500 kDa	67±18	36±12	*	0.530	-2.65

*Samples were not characterised

It is clearly seen that POZ with 50 kDa results in formation of GNPs with lower PDI = 0.138 – 0.198, whereas the POZ with greater molecular weights produces nanoparticles with higher PDI = 0.341-0.602. The latter can be explained by the greater size of macromolecular coils of POZ that are associated with bigger aggregates of GNPs. The discrepancy between the particle sizes of GNPs determined by DLS, NTA and TEM is observed. The particle size registered by TEM represents the core of GNPs without a hydrated polymer-based shell. While both DLS and NTA results show greater size of GNPs due to the presence of a polymer shell. However, there is also some discrepancy between DLS and NTA data. This is probably related to application of different techniques used for calculation of particle size. NTA tracks the motions of each individual particle and then calculates the particle size, whereas DLS is based on light scattering of all particles in the suspension. In this case DLS is more biased to larger particles and NTA can provide information on more polydisperse samples. These discrepancies between DLS, NTA and TEM data are well documented in the literature for similar systems composed of dense solid core and hydrated polymer shells [22].

Overall, the GNPs prepared using 5 kDa and 50 kDa POZ have a core-shell structure with 10-15 nm gold core and polymer-based shell, whose thickness ranges within 3-40 nm depending on molecular weight and concentration of POZ. The greater values of the GNPs shell thickness are observed for POZ with higher molecular weights due to bigger size of macromolecules stabilising these particles.

Zeta potential measurements indicate that all GNPs have negative charge due to chemisorption of chloride ions onto GNPs. The low values of zeta potentials are probably accounted

for non-ionic nature of POZ, which shields the negatively charged surface of GNPs. The main advantage of our approach over developed in [12, 23] methods is formulation of POZ-stabilized GNPs in the absence of any other reducing agents and the possibility achieve the Au³⁺ reduction process at room temperature.

Previously, we reported the behaviour of thiolated silica nanoparticles functionalised with poly(ethylene glycol) or with poly(2-oxazolines) and their penetration through various biological tissues such as the cornea [24], stomach mucosa [18-19] and hair follicles [25]. The GNPs decorated with hydrophilic polymer shells are also of great interest for tissue penetration studies. However, conventional polymer-protected GNPs are not fluorescent, which limits their detection by fluorescent microscopy.

In the present work we developed a facile synthesis of polymer-protected and fluorescently labelled GNPs using PEG-dithiol as a linker. Thiol containing molecules have excellent affinity to gold [26] and give an opportunity to link PEG-dithiol macromolecules to gold surface leaving the other thiol end intact. The possibility of some PEG-dithiol macromolecules binding to GNPs surface with both thiol groups cannot be fully ruled out. However, this binding will be sterically less favourable.

The free thiol groups present on the surface of GNPs after this modification were used to conjugate with 6-(iodoacetamido) fluorescein (6-IAFC), which resulted in formation of fluorescently labelled GNPs (Figure 5).

The fluorescence ability of the fluorescently-labelled GNPs was tested under UV light (Figure 6). The fluorescently-labelled GNPs solution displays characteristic green glowing under UV light, which is not observed for the unlabeled GNPs.

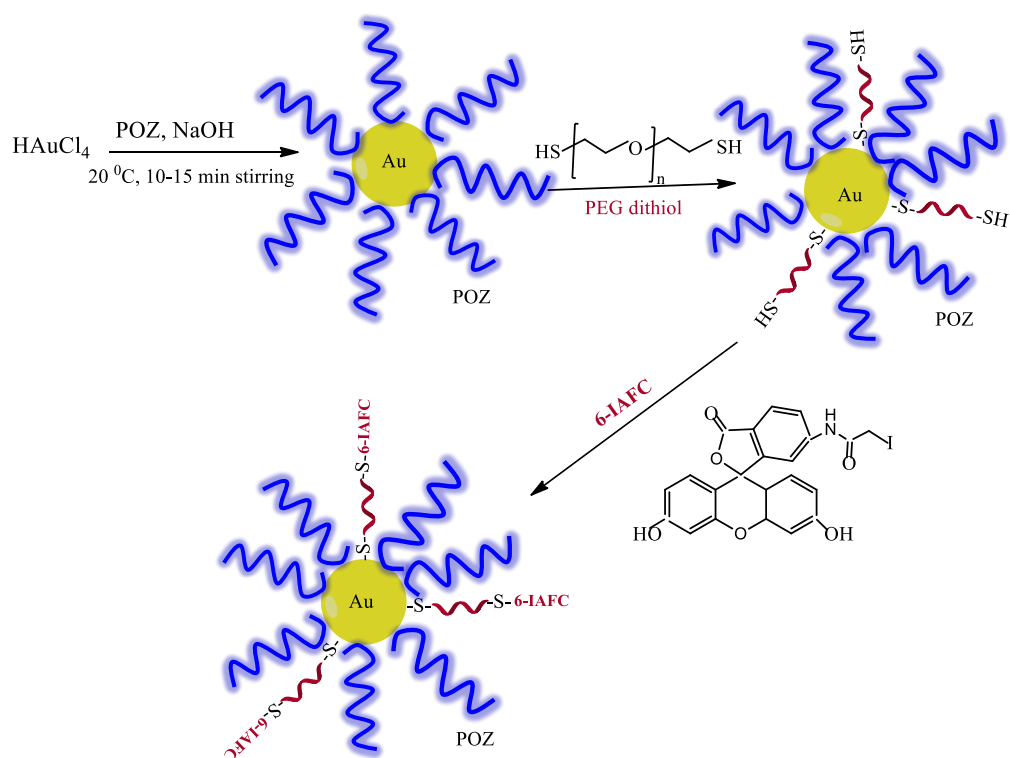


Figure 5 – Scheme of synthesis of fluorescently-labelled POZ protected GNPs

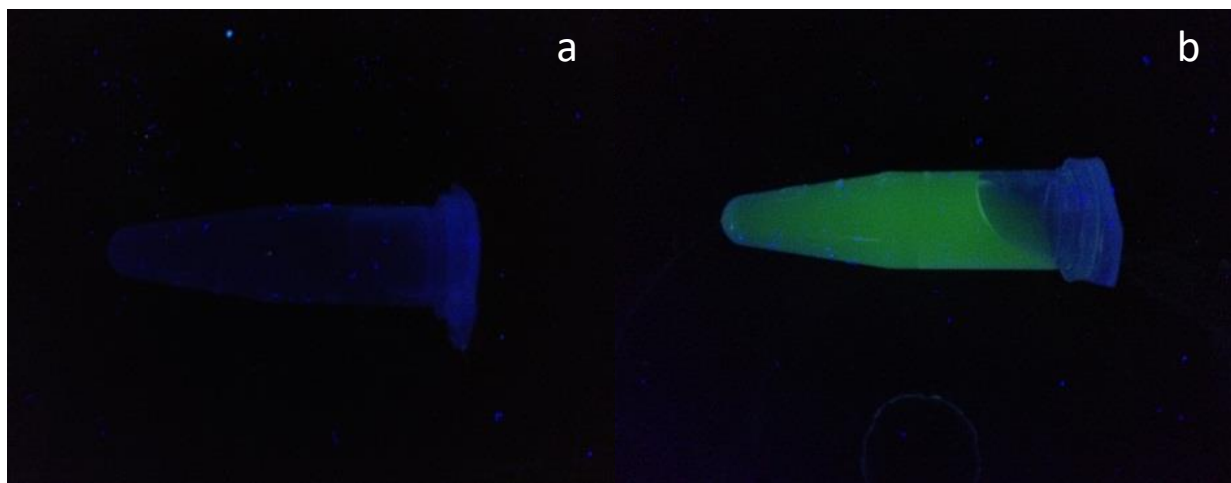


Figure 6 – Aqueous solutions of POZ-protected GNPs without (a) and with (b) fluorescent labelling under the UV irradiation

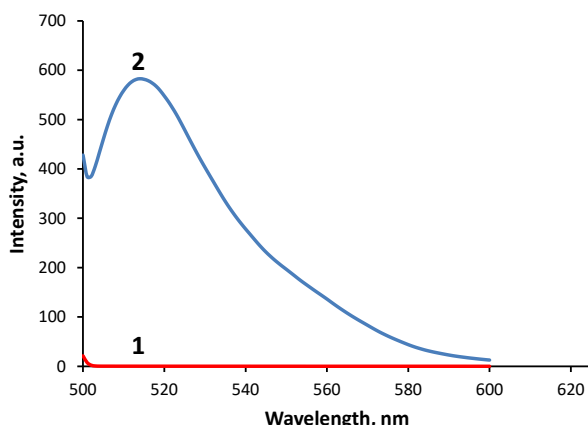


Figure 7 – Fluorescence spectra of POZ-protected GNPs without fluorescent labelling (1) and with fluorescent labelling (2)

The fluorescence spectra of fluorescently-labelled GNPs solutions clearly show the emission maximum at 510 nm, which is typical for fluorescein (Figure 7). The unlabeled GNPs do not display this characteristic fluorescence.

4. Conclusions

GNPs were synthesised in the presence of POZ with different molecular weights and concentrations. It was established that both molecular weights and concentrations of POZ affect the size and polydispersity of GNPs. Most of GNPs are spherically-shaped and have a core-shell structure. The size of gold core was around 10-15 nm and the thickness of the hydrated polymer shell was in the range of 3-40 nm. The synthetic protocol for the preparation of fluorescently-labelled GNPs using PEG-dithiol as a linker and 6-(iodoacetamido) fluorescein as fluorescent label was developed. It is expected that POZ-protected and fluorescently-labelled GNPs can be of great interest for biomedical applications, in particular as therapeutic and imaging agents in cancer therapy.

Acknowledgements

This work was supported by the Horizon 2020 research and innovation program of the European Union Maria Skłodowska-Curie (grant agreement 823883-NanoPol-MSCA-RISE-2018).

References (GOST)

- 1 Faraday M. X. The Bakerian Lecture. — Experimental relations of gold (and other metals) to light // Philosophical Transactions of the Royal Society of London. — 1857. — Vol.147. — P.145-181
- 2 Turkevich J., Stevenson P.C., Hillier J. A study of the nucleation and growth processes in the synthesis of colloidal gold // Discussions of the Faraday Society. — 1951. — Vol.11. — P.55-75.
- 3 Frens G. Controlled Nucleation for the Regulation of the Particle Size in Monodisperse Gold Suspensions // Nature Physical Science. — 1973. — Vol.241(105). — P.20-22.
- 4 Yeh Y.-C., Creran B., Rotello V.M. Gold nanoparticles: preparation, properties, and applications in bionanotechnology // Nanoscale. — 2012. — Vol.4(6). — P.1871-1880.
- 5 Elahi N., Kamali M., Baghersad M.H. Recent biomedical applications of gold nanoparticles: A review // Talanta. — 2018. — Vol.184. — P.537-556.
- 6 Das M., Shim K.H., An S.S.A., Yi D.K. Review on gold nanoparticles and their applications // Toxicology and Environmental Health Sciences. 2011. — Vol.3(4). — P.193-205.
- 7 Dzhardimalieva G.I., Zharmagambetova A.K., Kudaibergenov S.E., Uflyand I.E. Polymer-Immobilized Clusters and Metal Nanoparticles in Catalysis // Kinetics and Catalysis. — 2020. — Vol.61(2). — P.198-223.
- 8 Kudaibergenov S.E., Dzhardimalieva G.I. Flow-Through Catalytic Reactors Based on Metal Nanoparticles Immobilized within Porous Polymeric Gels and Surfaces/Hollows of Polymeric Membranes // Polymers. — 2020. — Vol.12(3). — ID.572.
- 9 Shan J., Tenhu H. Recent advances in polymer protected gold nanoparticles: synthesis, properties and applications // Chemical Communications. — 2007. — Vol.44. — P.4580-4598.
- 10 Pastoriza-Santos I., Liz-Marzán L.M. Formation of PVP-Protected Metal Nanoparticles in DMF // Langmuir. — 2002. — Vol.18, Is.7. — P.2888-2894.
- 11 Pal J., Deb M.K. Microwave green synthesis of PVP-stabilised gold nanoparticles and their adsorption behaviour for methyl orange // Journal of Experimental Nanoscience. — 2014. — Vol.9, Is.5. — P.432-443.
- 12 Nurakhmetova Z.A., Azhkeyeva A.N., Klassen I.A., Tatykhanova G.S. Synthesis and Stabilization of Gold Nanoparticles Using Water-Soluble Synthetic and Natural Polymers // Polymers. — 2020. — Vol.12, Is.11. — ID.2625.
- 13 Rahme K., Chen L., Hobbs R.G., Morris M.A., O'driscoll C., Holmes J.D. PEGylated gold nanoparticles: polymer quantification as a function of PEG lengths and nanoparticle dimensions // RSC Advances. — 2-13. — Vol.3, Is.17. — P.6085-6094.
- 14 Alalaiwe A., Roberts G., Carpinone P., Munson J., Roberts S. Influence of PEG coating on the oral bioavailability of gold nanoparticles in rats // Drug Delivery. — 2017. — Vol.24, Is.1. — P.591-598.
- 15 Vieira S., Vial S., Maia F.R., Carvalho M., Reis R.L., Granja P.L., Oliveira J.M. Gellan gum-coated gold nanorods: an intracellular

- nanosystem for bone tissue engineering // RSC Advances. – 2015. – Vol.5, Is.95. – P.77996-78005.
- 16 Dhar S., Mali V., Bodhankar S., Shiras A., Prasad B.L., Pokharkar V. Biocompatible gellan gum-reduced gold nanoparticles: cellular uptake and subacute oral toxicity studies // J Appl Toxicol. – 2010. – Vol.31, Is.5. – P.411-420.
 - 17 Hoogenboom R. Poly(2-oxazoline)s: A Polymer Class with Numerous Potential Applications // Angewandte Chemie-International Edition. – 2009. – Vol.48, Is.43. – P.7978-7994.
 - 18 Mansfield E.D.H., Sillence K., Hole P., Williams A.C., Khutoryanskiy V.V. POZylation: a new approach to enhance nanoparticle diffusion through mucosal barriers // Nanoscale. – 2015. – Vol.7, Is.32. – P.13671-13679.
 - 19 Mansfield E.D.H., De La Rosa V.R., Kowalczyk R.M., Grillo I., Hoogenboom R., Sillence K., Hole P., Williams A.C., Khutoryanskiy V.V. Side chain variations radically alter the diffusion of poly(2-alkyl-2-oxazoline) functionalised nanoparticles through a mucosal barrier // Biomaterials Science. – 2016. – Vol.4, Is.9. – P.1318-1327.
 - 20 De La Rosa V.R., Zhang Z., De Geest B.G., Hoogenboom R. Colorimetric logic gates based on poly(2-alkyl-2-oxazoline)-coated gold nanoparticles // Advanced Functional Materials. – 2015. – Vol.25, Is.17. – P.2511-2519.
 - 21 Agunloye E., Panariello L., Gavrilidis A., Mazzei L. A model for the formation of gold nanoparticles in the citrate synthesis method // Chemical Engineering Science. – 2018. – Vol.191. – P.318-331.
 - 22 Mansfield E.D.H., Pandya Y., Mun E.A., Rogers S.E., Abutbul-Ionita I., Danino D., Williams A.C., Khutoryanskiy V.V. Structure and characterisation of hydroxyethylcellulose-silica nanoparticles // RSCAdvances. – 2018. – Vol.8, Is.12. – P.6471-6478.
 - 23 Reis C.A., Rodrigues C.F., André F. Moreira A.F. et al. Surface modification of gold nanoparticles with small molecules for biochemical analysis // Materials Science and Engineering C. – 2019. – Vol.98. – P.960-968.
 - 24 Mun E.A., Morrison P.W.J., Williams A.C., Khutoryanskiy V.V. On the barrier properties of the cornea: A microscopy study of the penetration of fluorescently labeled nanoparticles, polymers, and sodium fluorescein // Molecular Pharmaceutics. – 2014. – Vol.11, Is.10. – P. 3556-3564.
 - 25 Al Mahrooqi J.H., Khutoryanskiy V.V., Williams A.C. Thiolated and PEGylated silica nanoparticle delivery to hair follicles // International Journal of Pharmaceutics. – 2021. – Vol.593. – ID.120130.
 - 26 Xue Y., Li X., Li H., Zhang W. Quantifying thiol-gold interactions towards the efficient strength control // Nature Communications. – 2014. – Vol.5, Is.1. – ID.4348.

References

- 1 Faraday M (1857) Philosophical Transactions of the Royal Society of London 147:145-181. <https://doi.org/10.1098/rstl.1857.0011>
- 2 Turkevich J, Stevenson PC, Hillier J (1951) Discuss Faraday Soc 11(0):55-75. <https://doi.org/10.1039/DF9511100055>
- 3 Frens G (1973) Nature Physical Science 241(105):20-22. <https://doi.org/10.1038/physci241020a0>
- 4 Yeh Y-C, Creran B, Rotello VM (2012) Nanoscale 4(6):1871-1880. <https://doi.org/10.1039/C1NR11188D>
- 5 Elahi N, Kamali M, Baghersad MH (2018) Talanta 184:537-556. <https://doi.org/10.1016/j.talanta.2018.02.088>
- 6 Das M, Shim KH, An SSA, Yi DK (2011) Toxicology and Environmental Health Sciences 3(4):193-205. <https://doi.org/10.1007/s13530-011-0109-y>
- 7 Dzhardimalieva GI, Zharmagambetova AK, Kudaibergenov SE, Uflyand IE (2020) Kinet Catal+ 61(2):198-223. <https://doi.org/10.1134/S0023158420020044>
- 8 Kudaibergenov SE, Dzhardimalieva GI (2020) Polymers-Basel 12(3):572. <https://doi.org/10.3390/polym12030572>
- 9 Shan J, Tenhu H (2007) Chem Commun (44):4580-4598. <https://doi.org/10.1039/B707740H>
- 10 Pastoriza-Santos I, Liz-Marzán LM (2002) Langmuir 18(7):2888-2894. <https://doi.org/10.1021/la015578g>
- 11 Pal J, Deb MK (2014) J Exp Nanosci 9(5):432-443. <https://doi.org/10.1080/17458080.2012.667160>
- 12 Nurakhmetova ZA, Azhkeyeva AN, Klassen IA, Tatykhanova GS (2020) Polymers-Basel 12(11):2625. <https://doi.org/10.3390/polym12112625>
- 13 Rahme K, Chen L, Hobbs RG, Morris MA, O'driscoll C, Holmes JD (2013) RSC Adv 3(17):6085-6094. <https://doi.org/10.1039/C3RA22739A>
- 14 Alalaiwe A, Roberts G, Carpinone P, Munson J, Roberts S (2017) Drug Deliv 24 (1):591-598. <https://doi.org/10.1080/10717544.2017.1282554>
- 15 Vieira S, Vial S, Maia FR, Carvalho M, Reis RL, Granja PL, Oliveira JM (2015) RSC Adv 5(95):77996-78005. <https://doi.org/10.1039/C5RA13556G>
- 16 Dhar S, Mali V, Bodhankar S, Shiras A, Prasad BL, Pokharkar V (2011) J Appl Toxicol 31(5):411-420. <https://doi.org/10.1002/jat.1595>
- 17 Hoogenboom R (2009) Angew Chem Int Edit 48(43):7978-7994. <https://doi.org/10.1002/anie.200901607>
- 18 Mansfield EDH, Sillence K, Hole P, Williams AC, Khutoryanskiy VV (2015) Nanoscale 7(32):13671-13679. <https://doi.org/10.1039/c5nr03178h>
- 19 Mansfield EDH, De La Rosa VR, Kowalczyk RM, Grillo I, Hoogenboom R, Sillence K, Hole P, Williams AC, Khutoryanskiy VV (2016)

Biomater Sci-Uk 4(9):1318-1327. <https://doi.org/10.1039/c6bm00375c>

20 De La Rosa VR, Zhang Z, De Geest BG, Hoogenboom R (2015) Adv Funct Mater 25(17):2511-2519. <https://doi.org/10.1002/adfm.201404560>

21 Agunloye E, Panariello L, Gavriilidis A, Mazzei L (2018) Chem Eng Sci 191:318-331. <https://doi.org/10.1016/j.ces.2018.06.046>

22 Mansfield EDH, Pandya Y, Mun EA, Rogers SE, Abutbul-Ionita I, Danino D, Williams AC, Khutoryanskiy VV (2018) RSC Adv 8(12):6471-6478. <https://doi.org/10.1039/c7ra08716k>

23 Reis CA, Rodrigues CF, André F, Moreira AF et al. (2019) Mater Sci Eng C 98:960-968. <https://doi.org/10.1016/j.msec.2019.01.068>

24 Mun EA, Morrison PWJ, Williams AC, Khutoryanskiy VV (2014) mol pharmaceut 11(10):3556-3564. <https://doi.org/10.1021/mp500332m>

25 Al Mahrooqi JH, Khutoryanskiy VV, Williams AC (2021) Int J Pharm 593:120130. <https://doi.org/10.1016/j.ijpharm.2020.120130>

26 Xue Y, Li X, Li H, Zhang W (2014) Nat Commun 5(1):4348. <https://doi.org/10.1038/ncomms5348>