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Gold Nanoparticles-based Extraction of Phenolic Compounds from Olive Mill Wastewater: A Rapid and Sustainable Method

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Abstract. Olive Mill WasteWater (OMWW) is an important by-product of the Olive Oil production. Its high concentration in Phenolic Compounds (PC) gives OMWW antimicrobial and phytotoxic properties. The aim of this work is to develop a rapid, simple and sustainable method based on the use of gold nanoparticles (AuNPs) chosen to extract PC from OMWW. AuNPs can be used taking advantage of their unique surface properties and high surface/volume ratio. They also offer high stability, easy chemical synthesis and use of water or eco-friendly solvents for their synthesis procedures. Two different stabilizing layers were used on the AuNPs surface: Cysteamine hydrochloride (Cys), and 4,4'-dithiolterphenyl (TR) obtaining AuNPs-Cys and AuNPs-TR, respectively. The extraction with AuNPs-Cys achieved 70% of the PC present in OMWW, allowing to make the by-product available for land fertilization and giving the possibility to use PC for other aims, as nutraceutical, active packaging, cosmetic or pharmaceutical.

INTRODUCTION

Olive oil production is one of the most important in Italy, with 428.900 tons of oil produced in 2017 [1]. Several techniques are involved in the oil production but, for extra virgin olive oil, only mechanical or physical extraction is allowed [2]. High quality productions, or protected geographical indications, require the use of a specific variety of olives and "traditional" production techniques. The first step is the olive harvest, preferably handmade and at the right ripening stage. After that, a machine provides the defoliation as well as the washing. Olives are then sent to the grinding step, where a millstone works the drupes for 30-40 minutes. In this step the right milling level is reached and larger droplets of oil with the typical oil flavor. The following extraction step involves the use of hydraulic presses. This technique allows to maintain a low temperature. The products of this step are olive pomace (40%) and oily pulp (60%). Oily pulp is centrifuged, allowing the separation of the oil from Olive Mill WasteWater (OMWW). The pomace, instead, is involved in another extraction system to obtain the pomace oil. By using this technology system, the OMWW achieved 42% (w/w) of the initial amount of olives used in the oil production process (Figure 1) [3, 4].

OMWW is composed of water (83-96 %), organic compounds (3-16%) and minerals (0.4-7%) [5, 6]. It is characterized by violet-dark brown to black color, strong olive oil fragrance, high organic pollution, pH range 3-6 and high electrical conductivity. The OMWW includes high nutrient content (e.g., nitrogen, phosphorus, potassium,

and magnesium) and no evidence of heavy metal concentration [7]. In the Mediterranean area, the disposal of the OMWW is one of the main problems from an environmental point of view. The interest in the recovery of OMWW has increased in recent years; examples include the production of biofuel from the OMWW, as well as the purification of the OMWW from potentially harmful molecules. The aim of these studies is to obtain an easier and safer disposal [8, 9] or the re-use for alternative purposes [10, 11]. Among all the substances present in olive mill wastewater there are Phenolic Compounds (PC) in high concentrations, in the range between 5 and 25 gL⁻¹ [12]. The research on these compounds is very interesting because of its excellent characteristics, which make them usable in different sectors: cosmetic, food and pharmaceutical. In fact, PC represent one of the most important and ubiquitous groups of plant metabolite and they have been studied for their anti-microbial, anti-carcinogenic and antioxidant activity [13]. For these reasons, the extraction of polyphenols from the OMWW is a great way to recover the PC and re-use them for different applications. Several studies on the recovery of the polyphenols were conducted in order to develop and to optimize the extraction method of these compounds. For example, the hydrothermal pre-treatments with steam explosion and subcritical water [14], ultrasound or microwave assisted extraction [15], extraction with supercritical fluid [16], solid phase extraction [17] and the liquid/liquid extraction [18] are usually used for this purpose. In this framework, nanoparticles can be used, taking advantage of their unique surface properties and high surface/volume ratio [19].

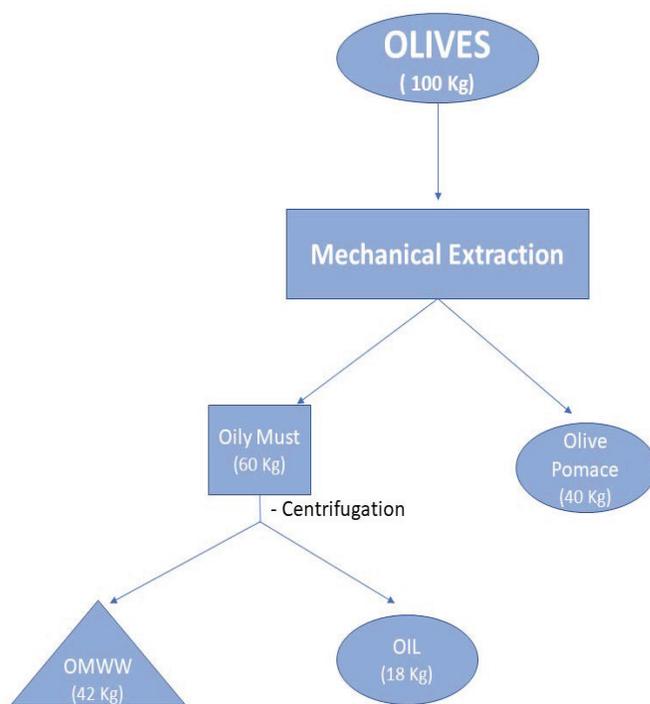


FIGURE 1. Traditional olive oil production process

Among others, functionalized gold nanoparticles (AuNPs) [20] offer high stability, easy chemical synthesis and tunable surface functionalizations which, as a consequence, have strong effects on applications [21-23]. Nowadays, nanoparticles are considered as suitable tool for the extraction of food contaminants as acrylamide in fried food [24], pyrethroid residues in apples [25] or bisphenol A [26]. Moreover, limited papers have been found on the extraction of food intrinsic compounds as glutathione [27], minerals [28] and amines [29].

In particular, one of the emerging fields of study is the use of nanoparticles for food control [30-31] and for extraction of active molecules such as polyphenols from olive oil [32-33]. It is noteworthy that they can also be extracted from olive mill wastewater (OMWW) and, in this framework, AuNPs represent a new tool for an efficient extraction process [34].

The aim of this work is to develop a rapid, simple and sustainable extraction procedure of polyphenols from olive mill wastewater (OMWW), based on the use of AuNPs functionalized with hydrophilic or hydrophobic thiol

ligands, *i.e.* Cysteamine (Cys) or 4,4''-dithiolterphenyl (TR), obtaining AuNPs-Cys and AuNPs-TR, respectively. A comparison between the hydrophilic or hydrophobic AuNPs is presented.

Several papers have been found on the isolation and purification of phenolic compounds from olive mill wastewaters. Many techniques have been usually involved such as membrane processes [35-37], filtration [38-39], exchanging resins [40], chemical oxidation [41]. Moreover, new techniques use biomass for their absorption [42-43]. Also magnetic nanoparticles have been used to treat OMWW [44], but to the best of our knowledge this is the first paper proposing the use of gold nanoparticles as efficient extraction tool of phenolic compounds from OMWW.

MATERIALS AND METHODS

Materials

Methanol (CH₃OH), n-Hexane (C₆H₁₄), Folin-Ciocalteu reagent (H₃[P(W₃O₁₀)₄]/ H₃[P(Mo₃O₁₀)₄]), Gallic acid (C₇H₆O₅), chloridric acid (HCl), sodium hydroxide (NaOH) and sodium carbonate (Na₂CO₃) were purchased from Sigma Aldrich Chemical Co. Tetrachloroauric(III) acid trihydrate (HAuCl₄·3H₂O, 99.9%), sodium borohydride (NaBH₄, 98%), Toluene, Tetraoctylammonium bromide (TOAB) (99%), Cysteamine hydrochloride (HSCH₂CH₂NH₂·HCl, Cys 98%), and 4,4''-dithiolterphenyl (HS-C₆H₄-C₆H₄-C₆H₄-SH, TR 98%) were used as received (Aldrich reagent grade). Deionized water was used for the synthesis procedures.

Instruments

UV-vis spectra (190-750 nm) were run in H₂O solutions by using quartz cells with a Varian Cary 100 Scan UV-vis spectrophotometer. FESEM images were acquired on cast deposited samples with a Zeiss Auriga 405, (7.5 keV, working distance 2.5 mm). Size distribution of AuNPs in H₂O solution (0.1-0.2 mg/mL) was investigated at the temperature of (25.0 ± 0.2) °C by means of dynamic light scattering (DLS) measurements by using a Malvern Nano ZS90 scattering apparatus (Malvern Zetasizer Nanoseries Instruments Ltd., Worcestershire, UK). An ultrasonic bath has been used to mix the suspensions (Transonic T 460 Elma) at r.T.. A Scilogex refrigerated microcentrifuge was used for the purification of AuNPs samples (5000 rpm, 10 min, 4°C, 5 times with deionized water). pH measurements were made with a CyberScan pH 600 (Eutech Instruments). Deionized water was obtained from Zeener Power I Scholar-UV (18.2 MΩ).

Methods

Synthesis and characterization Of Aunps-Cys And Aunps-TR

AuNPs were prepared according to already published methods, adapted to the specific ligand characteristics[45], [46]. Briefly, AuNPs-Cys were prepared with an Au/S molar ratio equal to 1/1.5. The synthesis was carried out starting from 200 mg of HAuCl₄·3H₂O solved into deionized water (10 mL) and 0.0865 g of Cys solved into 10 mL of deionized water. After stirring 10 minutes at r.T., for a homogeneous solubilisation, and after 10 min of bubbling with nitrogen, a solution of the reducing agent NaBH₄ (0.1437 g in 10 mL of deionized water) was added dropwise under vigorous stirring. After 2 h stirring at r.T. a solid product was recovered by centrifugation with ultrapure water for 5 times at 5000 rpm for 10 minutes. The total time of purification is about 75 minutes. Yield: 35 ± 5% wt.

In the case of AuNPs-TR, nanoparticles were prepared with an Au/S molar ratio equal to 4/1. The synthesis was carried out in a two phases system, by adding to a HAuCl₄·3H₂O solution (0.1140 g in 5 mL of deionized water), the phase transfer agent tetraoctylammonium bromide (TOAB) (0.1678 g) in toluene (10 mL). After vigorous mixing of the two-phases mixture, the tetrachloroaurate was transferred into the organic layer and a solution of 4,4''-dithiolterphenyl (0.0199 g) in toluene (10 mL) was added. At this step, a freshly prepared aqueous solution of the reducing agent NaBH₄ (0.1051 g in 5 mL of deionized water) was added under vigorous stirring. The reaction mixture was allowed to react for 3 h, then the organic phase was separated and washed with water. The organic phase was reduced to 2 mL in a rotary evaporator, and 40 mL of ethanol were added. The mixture was kept overnight at T = -18 °C and then centrifuged at 5000 rpm for 15 min to remove excess thiol and TOAB. The supernatant was eliminated, and the precipitate was washed by centrifugation at 13,400 for 10 min, with ethanol for 10 times. A solid powder was recovered with a yield 28 ± 4% wt.

Main Characterizations:

AuNPs-Cys : DLS (H₂O, $\langle 2R_H \rangle$ [nm]): 20±8; UV-vis (H₂O, [nm]): 550

AuNPs-TR: DLS (CH₂Cl₂, $\langle 2R_H \rangle$ [nm]): 10±3 and 90±15; UV-vis (CH₂Cl₂, [nm]): 610.

Sampling

Three olive mill wastewaters samples was collected from oil mills of Lazio Region, where it's produced a Protected Designation of Origin (PDO) olive oil denominated "Sabina PDO". After the procurement, the samples have been preserved refrigerated at -28 °C.

AuNps Extraction of Phenolic Compounds from OMWW

Starting from the optimized condition [45] 4 mg of AuNPs were added to 3 mL of aqueous fraction of OMWW, sonicated for 1 min and then stirred for 15 min. After the contact the OMWW/AuNPs solution was centrifuged at 2500 rpm for 5 min, then the supernatant was separated from the charged AuNPs [45].

Determination of Total Phenolic Compounds (Folin-Ciocalteu)

Total phenolic content (TPC) was determined using the Folin-Ciocalteu method [13]. The method was modified for OMWW as follows: 1 mL of hydroalcoholic extract was added to 0.25 mL of FC reagent, 0.5 mL of Na₂CO₃ (7.5% w/v), in a 10 mL volumetric flask reaching the final volume with purified water. Each sample was stored for 45 min at room temperature, and the spectrophotometric analysis was performed at $\lambda = 750$ nm. Total phenolic content was expressed as milligrams GA equivalent (GAE) per Kg, the results were obtained through a calibration curve with range from 15 to 500 mg L⁻¹ (R² = 0.9925).

Statistical Analysis

For ANOVA analysis JMP 13 (SAS, USA) software was used, the experiments considered were only been the ones with RSD < 5%.

RESULTS AND DISCUSSION

Functionalized Gold Nanoparticles: AuNPs-Cys and AuNPs-TR Synthesis and Characterization

Functionalized AuNPs were on purpose prepared for this study in the presence of hydrophilic or hydrophobic thiol ligands, suitable for interaction with polyphenols present in OMWW. The different functionalization was selected in order to have an ammonium terminal group in the case of AuNPs-Cys, that should have affinity with aqueous phase and a phenyl functionality in the case of AuNPs-TR, with affinity for organic phase. In figure 2, a chemical sketch of the prepared nanoparticles is presented, together with the UV-vis spectra of the nanoparticles and FESEM images.

From UV-vis absorption spectra it is possible to observe a broad Surface Plasmon Band at about 550 nm for AuNPs-Cys and 610 nm for AuNPs-TR, respectively, that could be ascribed either to large size nanoparticles and to very close nanoparticles [47]. The size and morphology of the nanoparticles was studied with FESEM instrument and low sized NPs can be observed, with more regular shape and size in the case of AuNPs-TR sample. In this sample the diameter of AuNPs-TR was observed in the range 5-10 nm, whereas in AuNPs-Cys sample a population of low sized NPs (about 5 nm diameter) is present together with more dispersed size nanoparticles, up to 20 nm. The DLS study evidenced a population with hydrodynamic diameter of about 20 nm for AuNPs-Cys and 10 nm for AuNPs-TR, together with higher aggregates due to the interconnecting thiol used.

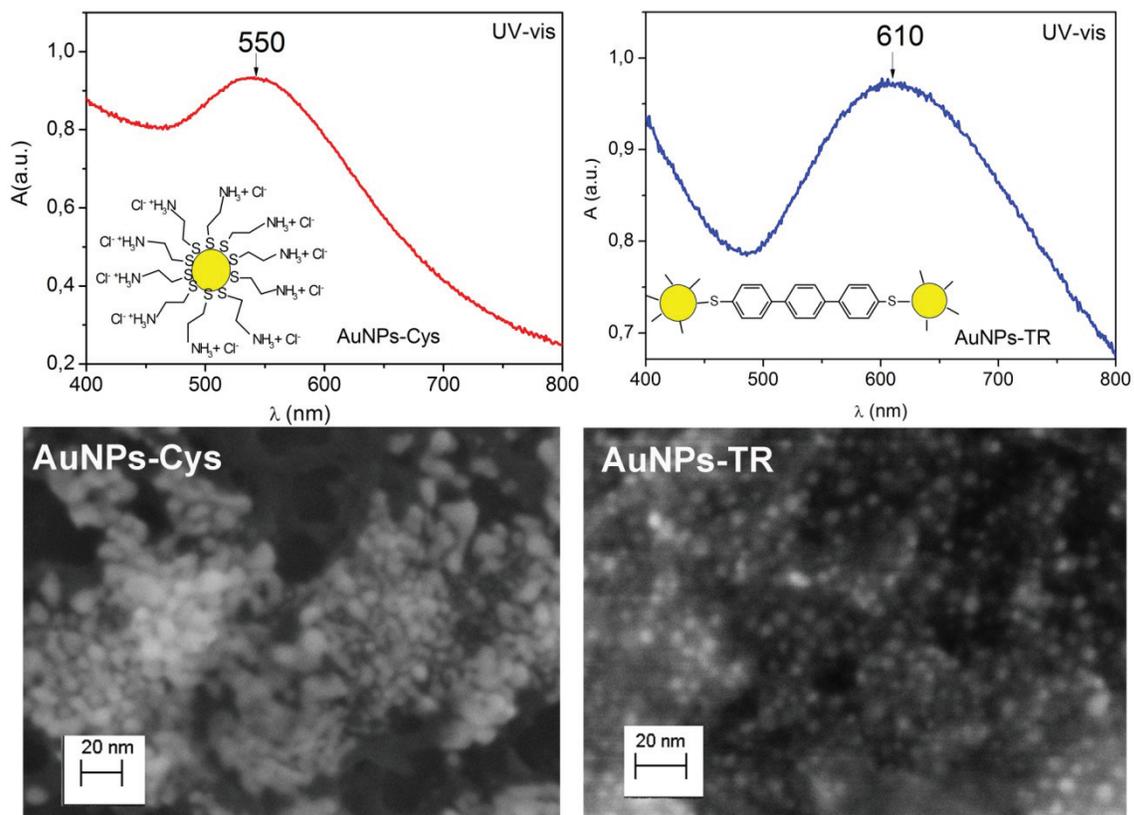


FIGURE 2. AuNPs-Cys and AuNPs-TR: chemical structures, UV-vis spectra and FESEM images.

Extraction of Phenolic Compounds by Au-NPs: Comparison Between AuNPs-Cys and AuNPs-TR

It is noteworthy that OMWW have a high concentration of PC, coming from the oil production. Three OMWW samples were collected from oil mills of Lazio Region, where it's produced a Protected Designation of Origin (PDO) olive oil denominated "Sabina PDO". At first, an aliquot of 10 mL of each OMWW sample were centrifuged at 2,500 rpm for 15 min, in order to separate the fatty portion and the solid one from the aqueous solution containing the PC. The aqueous fractions (around 8 mL for each aliquot) of OMWW were mixed in an amber flask. In order to assess the PC extraction, a comparison on the TPC content was performed before and after the contact with AuNPs. Therefore, four aliquots of each samples were collected in amber vials and for each aliquot a TPC determination was carried out three times. The results of TPC determination were reported in Table 1, the mean value for the three samples was 391.85 ± 2.98 (RSD% = 0.76%).

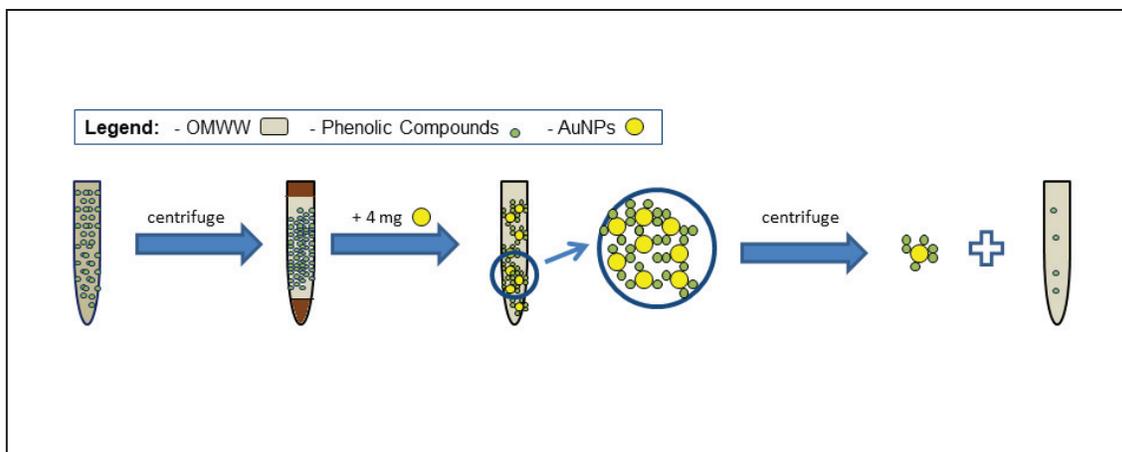


FIGURE 3. Procedure scheme for Phenolic Compounds AuNPs based extraction from OMWW.

TABLE 1. TPC determination on 3 different Sabina PDO OMWW samples, before the AuNPs recovery.

<i>Samples</i>	<i>Aliquots</i>	<i>TPC (mg/L)</i>
Sabina PDO 1	<i>A</i>	386.21 ± 1.54
	<i>B</i>	388.56 ± 1.87
	<i>C</i>	389.54 ± 2.66
	<i>D</i>	390.73 ± 3.15
	<i>Mean</i>	388.76 ± 1.91
Sabina PDO 2	<i>A</i>	391.42 ± 3.40
	<i>B</i>	392.76 ± 3.89
	<i>C</i>	393.16 ± 4.12
	<i>D</i>	390.74 ± 2.78
	<i>Mean</i>	392.02 ± 1.13
Sabina PDO 3	<i>A</i>	397.25 ± 5.50
	<i>B</i>	392.86 ± 5.20
	<i>C</i>	394.33 ± 3.67
	<i>D</i>	394.72 ± 4.68
	<i>Mean</i>	394.79 ± 1.82

The optimized conditions, previously published [45], were used to extract phenolic compounds on AuNPs-Cys. Briefly, 3 mL of aqueous fraction of OMWW were added to 4 mg of AuNPs-Cys, sonicated for 1 min and then stirred for 15 min. After the contact the OMWW/AuNPs-Cys solution was centrifuged at 2500 rpm for 5 min, then the TPC determination was carried out on supernatant three times. The same procedure was executed for the contact with AuNPs-TR (Figure 3).

The extraction was performed twice on three separate tests for each sample and the mean value and SD were calculated. The results of TPC content after OMWW-AuNPs are reported in Table 2.

TABLE 2 TPC determination on 3 different Sabina PDO OMWW samples, after the AuNPs recovery.

<i>Samples</i>	<i>Aliquots</i>	AuNPs-Cys	AuNPs-TR
		TPC (mg/L)	TPC (mg/L)
Sabina PDO 1	<i>A</i>	111.23 ± 3.65	231.23 ± 1.68
	<i>B</i>	114.57 ± 2.67	233.65 ± 2.35
	<i>C</i>	120.36 ± 4.32	236.64 ± 4.56
	<i>Mean</i>	115.39 ± 4.61	233.84 ± 2.71
Sabina PDO 2	<i>A</i>	118.61 ± 1.58	239.45 ± 4.85
	<i>B</i>	117.29 ± 2.41	237.45 ± 3.97
	<i>C</i>	113.75 ± 2.98	238.79 ± 4.27
	<i>Mean</i>	116.55 ± 2.51	238.56 ± 1.01
Sabina PDO 3	<i>A</i>	114.92 ± 5.22	235.34 ± 5.81
	<i>B</i>	115.93 ± 1.92	233.65 ± 2.69
	<i>C</i>	117.06 ± 4.67	237.71 ± 1.52
	<i>Mean</i>	115.97 ± 1.07	235.57 ± 2.04

The TPC content in OMWW after contact with NPs was **115.97 ± 2.73 mg/L** (RSD% = 2.35%) for AuNPs-Cys and **235.99 ± 2.72 mg/L** (RSD% = 1.15%) for AuNPs-TR.

The extraction efficiency was calculated as:

$$E.E. = 100 - (TPC_{\text{after}} / TPC_{\text{before}}) \times 100, (1)$$

according to literature. The extraction efficiency results are shown in Table 3.

TABLE 3. Extraction efficiency results for AuNPs-Cys and AuNPs-TR for 3 different Sabina PDO OMWW samples.

<i>Samples</i>	<i>Aliquots</i>	AuNPs-Cys	AuNPs-TR
		E.E. (%)	E.E. (%)
Sabina PDO 1	<i>A</i>	71,39	40,52
	<i>B</i>	70,53	39,90
	<i>C</i>	69,04	39,12
	<i>Mean ± S.D.</i>	70.32 ± 1.19	39.85 ± 0.70
Sabina PDO 2	<i>A</i>	69,74	38,92
	<i>B</i>	70,08	39,43
	<i>C</i>	70,98	39,09
	<i>Mean ± S.D.</i>	70.27 ± 0.64	39.14 ± 0.26
Sabina PDO 3	<i>A</i>	70,89	40,39
	<i>B</i>	70,63	40,82
	<i>C</i>	70,35	39,79
	<i>Mean ± S.D.</i>	70.62 ± 0.27	40.33 ± 0.52

Hence, the extraction efficiency was **70.40 ± 0.71 %** (RSD % = 1.01 %) for AuNPs-Cys and **39.77 ± 0.69 %** (RSD % = 1.73 %) for AuNPs-TR. The obtained results suggest that a higher extraction rate can be obtained for the more hydrophilic AuNPs. The polar end group of the Cys ligand demonstrated affinity with PC, probably due to the dipolar interaction between them. On the contrary, AuNPs-TR showed a lower extraction efficiency, due to their hydrophobic and non-polar structure.

AuNPs-Cys appears to be a suitable tool to recover PC from OMWW with higher extraction efficiency compared to AuNPs-TR. A rapid and sustainable method was developed, short time for the PC extraction was achieved (16 min for contact and 5 min of centrifugation) and a small amount of NPs was used.

It's noteworthy that AuNPs synthesized are stable, so the AuNPs charged with PC could be involved in many processes. Phenolic compounds can be released in a specific solution, the charged NPs can be used as carrier of antioxidants in cosmetics, in nutraceutical or in active packaging for food.

CONCLUSIONS

OMWW is an important by-product of olive oil production (42% of total amount), with a high PC concentration. The disposal of OMWW is one of the main problems of oil production industry, in relation to their environmental impact and economic cost. In this work, the extraction of bioactive compounds from OMWW, such as PC was achieved with the use of AuNPs. AuNPs functionalized with hydrophilic or hydrophobic thiols, *i.e.* Cys or TR, respectively, were tested to extract PC from OMWW. TPC content was determined in the OMWW aqueous fraction (391.85 ± 2.98 mg/L), then 4 mg of AuNPs were added to 3 mL of this solution. After 15 min of contact by stirring, the AuNPs were separated. The TPC content in OMWW after contact with AuNPs was 115.97 ± 2.73 mg/L for AuNPs-Cys and 235.99 ± 2.72 mg/L for AuNPs-TR. Then the extraction rate achieved was 70.40 ± 0.71 % for AuNPs-Cys and 39.77 ± 0.69 % for AuNPs-TR. The obtained results suggest that a higher extraction rate can be obtained for the more hydrophilic AuNPs. The polar end group of the Cys ligand demonstrated affinity with PC, probably due to the dipolar interaction between them. On the contrary, AuNPs-TR showed a lower extraction efficiency, due to their hydrophobic and non-polar structure. Starting from a production of 100 kg of olives, it is possible to obtain 9.76 g ÷ 11.30 g of PC. In relation to high production of olive oil, the extraction based on the use of AuNPs allows the possibility to make the by-product available for land fertilization and give the possibility to use PC for other aims (nutraceutical, cosmetic and pharmaceutical sectors). Future perspectives could involve this NPs application to different waste matrices, for PC or other bioactive compounds too.

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