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Green synthesis of Pd/Fe₃O₄ nanoparticles using *Euphorbia condylocarpa M*.

bieb root extract and their catalytic applications as magnetically recoverable and

stable recyclable catalysts for the phosphine-free Sonogashira and Suzuki

coupling reactions

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ABSTRACT

This work reports on the green synthesis of Pd/Fe₃O₄ nanoparticles using *Euphorbia condylocarpa M. bieb* root extract as reducing agents and stabilizers and their catalytic applications in ligand- and copper-free Sonogashira and Suzuki coupling reactions. This method has such advantages as high yields, simple methodology and easy work up. In addition, the catalyst can be recovered by using a magnet and reused several times without significant loss of its catalytic activity. The catalyst was characterized using UV-vis, powder XRD, SEM and EDS techniques.

Keywords: Pd/Fe₃O₄; Bio-reduction; Coupling reaction; Copper-free; Ligand-free

1. Introduction

The Sonogashira reaction is probably one of the most important, powerful and straightforward methods for the synthesis of arylated internal alkyne compounds, $C(sp^2)-C(sp)$ bond, and has been widely applied to diverse areas such as natural product synthesis, pharmaceuticals and material science [1-3].

The Sonogashira reaction is generally carried out in an organic solvent such as an amine, benzene, THF, or DMF with a complex palladium catalyst in conjunction with CuX (X = Cl, Br, I) as a co-catalyst and in the presence of toxic phosphine ligands and a stoichiometric amount of base under inert conditions, which make it economically and environmentally malignant [4,5].

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However, there are several disadvantages in the literature methods such as the use of expensive and toxic ligands, low yields, long reaction times, harsh reaction conditions, environmental pollution due to the side products formed and tedious work-up [4,5]. In Sonogashira coupling reaction, the presence of copper salt as the co-catalyst can result in the formation of diyne side products via Glaser-type oxidative dimerization of *in situ* generated copper acetylide and can also decrease the efficiency to cross-coupling products [4,5].

Among various catalysts for the coupling reactions, homogeneous palladium catalysts have been widely investigated [6-9] while less expensive heterogeneous palladium catalysts have received scanter attention. The problem with homogeneous catalysis is the difficulty of separation of the catalyst from the reaction mixture and the incapability of its application in consecutive reactions. Thus, the use of ligand- and copper-free heterogeneous palladium catalysts is often desirable from the perspective of process development due to their easy handling, simple recovery, and recycling.

Since catalysis takes place on metal surface, nanoparticles (NPs) are much more reactive than the particulate metal counterpart due to their small sizes and large surface areas. Therefore, heterogeneous catalysts are mostly used in the form of nanoparticles. Among various catalysts, iron oxide magnetic nanoparticles (Fe_3O_4 -MNPs) have been paid attention to in the past few years due to their unusual magnetic, physical and surface chemical and catalytic properties, high stability and ease of recovery with an external magnet [10]. The potential advantage of Fe_3O_4 -supported metal catalysts is that it can be separated from the reaction medium by an external permanent magnet without using any filtration or centrifugation. We have recently reported simple synthesis of Pd/Fe₃O₄ nanoparticles and their applications in recyclable Sonogashira and Stille coupling reactions and *N*-arylureas preparation [11,12].

There are several methods for the synthesis of Pd/Fe₃O₄ nanoparticles using toxic and expensive chemicals. Thus, environmentally benign production methods of Pd/Fe₃O₄ nanoparticles without the use of harsh, toxic reducing agents (eg. hydrazine hydrate, sodium borohydride, dimethylformamide, ethylene glycol, and so on), and expensive chemicals are very desirable. Recently, extensive research effort has been made in utilizing various biological systems such as bacteria, fungus and plant extracts for the green synthesis of metal nanoparticles [13,14]. Green synthesis of NPs has several advantages over conventional synthetic methods, such as simplicity, very mild reaction conditions, and use of non-toxic solvents such as water, elimination of toxic and dangerous materials and cost effectiveness as well as compatibility for biomedical and pharmaceutical applications [15-19]. In addition, in this method, there is no need to use high pressure, energy, temperature and

toxic chemicals. Despite the availability of methods for the synthesis of Pd/Fe_3O_4 NPs by various toxic and expensive chemicals, there is no report on the biosynthesis of Pd/Fe_3O_4 NPs by utilizing the plants extract.

The plants of the *Euphorbiaceae* contain acrid, milky, or colorless juice. Chemical data are available for several genera, especially *Eubhorbia*, in which more than 120 species have been investigated. The family *Euphorbiaceae* is rich in flavonoids, particularly flavones and flavonols, which have been identified from several genera. Furthermore, the previous studies in 1970 on *Euphorbia condylocarpa* demonstrated the presence of phytochemicals such as flavonoids, tetracyclic triterpenoids, and trifolin in different parts of the plant [20-22].

In continuation of our efforts to develop environmentally friendly synthetic methodologies [23-29], we now wish to report a new and rapid protocol for the preparation of Pd/Fe_3O_4 NPs by using *Euphorbia condylocarpa M. bieb* extract (Figure 1) as a reducing and stabilizing agent and the application of these NPs as novel and stable heterogeneous catalysts in the copper- and phosphine-free Sonogashira and Suzuki coupling reactions.



Figure 1. Image of Euphorbia condylocarpa M. bieb.

2. Experimental

2.1. Instruments and reagents

All reagents were purchased from the Merck and Aldrich Chemical Companies and used without further purification. Products were characterized by comparison of their physical and spectral data with those of authentic samples. The NMR spectra were recorded in DMSO as the solvent. ¹H NMR spectra were recorded on a Bruker Avance DRX 300 MHz instrument. The chemical shifts (δ) are reported in ppm relative to TMS as the

internal standard and *J* values are given in Hz. ¹³C NMR spectra were recorded at 75 Hz. FT-IR (KBr) spectra were recorded on a Perkin-Elmer 781 spectrophotometer. Melting points were taken in open capillary tubes with a BUCHI 510 melting point apparatus and were uncorrected. TLC was performed on silica gel polygram SIL G/UV 254 plates. X-ray diffraction measurements were performed with a Philips powder diffractometer type PW 1373 goniometer, equipped with a graphite monochromator crystal. The X-ray wavelength was 1.5405 A° and the diffraction patterns were recorded in the 2 θ range (10-60) with scanning speed of 2°/min. Morphology and particle dispersion was investigated by scanning electron microscopy (SEM) (Cam scan MV2300). The chemical compositions of the synthesized nanostructures were measured by EDS performed in SEM.

2.2. Preparation of Euphorbia condylocarpa M. bieb root extract

50 g of dried powder of *E. condylocarpa M. bieb* was extracted by boiling in 300 mL double distilled water for 20 min and the aqueous extract was centrifuged at 7000 rpm to obtain the supernatant as extract (Figure 2).



Figure 2. Photograph of Euphorbia condylocarpa M. bieb root extract.

2.3. Preparation of Pd/Fe₃O₄ nanoparticles

For green synthesis of Pd supported on magnetite nanocatalyst, 0.5 g FeCl₃·6H₂O and 0.1 g PdCl₂ were dissolved in 30 mL aqueous extract of the *E. condylocarpa* at 60 °C under vigorous stirring. Then, a solution of 1.0 M Na₂CO₃ was added dropwise to the mixture to obtain alkaline pH while changing the color to dark brown and monitoring the product formation using UV-vis at times raining 5 to 35 min. After being stirred again for 5 hours at the same temperature, a suspension was formed which gave precipitate of Pd/magnetite nanoparticles on centrifugation at 7000 rpm and the obtained nanoparticles were washed with ethanol and distilled water, respectively, and then dried.

2.4. General procedure for Sonogashira coupling reaction

To a stirred solution of 1.0 mmol of aryl halide in 4 mL of DMF, 1.0 mmol of terminal alkyne, 1.5 mmol of piperidine and 0.2 mol% of Pd/Fe₃O₄ NPs were added and the mixture was heated on an oil bath at 110 °C for

24 h under inert atmosphere (N_2). After completion of the reaction (as monitored by TLC), the reaction mixture was cooled to room temperature and the catalyst was separated using a magnetic separator. The solvent was evaporated at reduced pressure, and the residue was subjected to gel permeation chromatography to afford pure products. All the products are known compounds and the spectral data and melting points were identical to those reported in the literature [30-33].

2.5. General procedure for Suzuki coupling reaction

To the stirred solution of arylboronic acid (0.6 mmol), aryl halide (0.5 mmol), and K_3PO_4 (1.5 mmol) in 5 mL of MeOH at room temperature was added Pd/Fe₃O₄ NPs (0.1 mol%). The reaction mixture was stirred at 60 °C for the appropriate times under a dry nitrogen atmosphere. After completion of the reaction (as monitored by TLC), the reaction mixture was cooled to room temperature and the catalyst was separated using a magnetic separator. The solvent was evaporated at reduced pressure to obtain the product in crude form which was purified afterwards by column chromatography. The purity of the compounds was checked by ¹H NMR and yields are based on aryl halide. All the products are known and the spectroscopic data (FT-IR and NMR) and melting points were consistent with those reported in the literature [34-36].

3. Results and discussion

3.1. Reduction of metal ions

Reduction kinetics play a key role in controlling the nucleation and growth of nanoparticles. In this work, we have employed *Euphorbia condylocarpa M. bieb* root extract as a reducing and stabilizing agent for the synthesis of Pd/Fe₃O₄ NPs. As shown in Scheme 1, metal ions were reduced to nano zero valent (NZV) metallic particles using flavonoid (FlOH) contents of the plant as green (without any hazardous impact on the environment) chemicals (reducing agents) as an alternative to the commonly used hydride reducing agent, sodium borohydride.

 $nFlOH + M^{+n} \longrightarrow nFlO (radical) + nM^{0}$ $nFlO (Radical) + M^{+n} \longrightarrow nFlOX + nM^{0} (Nucleation)$ $nM^{0} + M^{+n} \longrightarrow M_{n}^{+n} (Growth)$ $M_{n}^{+n} + M_{n}^{+n} \longrightarrow M_{2n}^{+2n}$ $(M_{2n}^{+2n})_{n} + (FlOH)_{n} \longrightarrow metalic NZV$

Scheme 1. Reducing ability of antioxidant phenolics to produce metalic NPs where FIOH and NZV are flavonoid and nano zero valent, respectively.

3.2. Characterization of catalyst

The stable Pd/Fe₃O₄ NPs obtained were fully characterized by UV-vis, SEM, EDS and XRD and their behavior as catalyst was tested in the Sonogashira and Suzuki coupling reactions.

3.2.1. UV-vis and FT-IR analysis

Figure 3 shows the UV-vis spectra of *Euphorbia condylocarpa M. bieb* root extract. The UV spectrum with bands at λ_{max}^{nm} 387 (band 1) which is due to the transition localized within the B ring of cinnamoyl system; whereas the one depicted at 283 (band 2) is consistent with absorbance of ring A of benzoyl system (Scheme 2). They are related to the $\pi \rightarrow \pi$ transitions and these absorbent bands demonstrate the presence of flavon nuclei.



Figure 3. UV-vis spectrum of Euphorbia condylocarpa M. bieb root extract.



The FT-IR analysis was carried out to identify the possible biomolecules responsible for the reduction of Au/Pd nanoparticles and capping of the bioreduced Au and Pd nanoparticles synthesized by the root extract (Figure 4). The FT-IR spectrum depicted some peaks at 3436 to 3000, 1643, 1561, 1413 and 1277 cm⁻¹, which represent free OH in molecule and OH group forming hydrogen bonds, carbonyl group (C=O), stretching C=C aromatic ring and C-OH stretching vibrations, respectively. These peaks suggested the presence of flavonoid and phenolics acids in the *Euphorbia condylocarpa M. bieb* root extract. The presence of flavonoid and phenolics acids in the extract could be responsible for the reduction of metal ions and formation of the corresponding metal nanoparticles. Flavonoid and phenolics acids could be adsorbed on the surface of metal nanoparticles, possibly by interaction through π -electrons in the absence of other strong ligating agents.



Figure 4. FT-IR spectrum of Euphorbia condylocarpa M. bieb root extract.

The UV-vis spectra of Pd/Fe_3O_4 bimetallic nanoparticles synthesized using the aqueous extract of *Euphorbia condylocarpa* at different times have been shown in Figure 5. The surface plasmon resonance peak is centered at 380 nm and developed with increasing the time ranging 5 min to 35 min in which the appearance of the maxima in 35 min indicates the end of the reaction.



Figure 5. UV-vis spectra of Pd/Fe₃O₄ bimetallic NPs.

3.2.2. X-ray powder diffraction analysis

The crystalline structure of Pd/Fe₃O₄ NPs was confirmed with powder XRD (X-ray Powder Diffraction) measurements. The presence of palladium and iron was confirmed with powder XRD measurements (Figure 6). The X-ray diffraction pattern revealed that iron nanoparticles are very air-sensitive and easily oxidized to Fe_3O_4 . The results showed that the products consisted of a face-centered cubic (fcc) structure.



Figure 6. XRD pattern of Pd/Fe₃O₄ NPs.

3.2.3. Scanning electron microscopy (SEM) of Pd/Fe₃O₄ nanoparticles

The shape and size of the Pd/Fe₃O₄ NPs were determined by scanning electron microscopy (SEM). Figure 7 shows FE SEM images of the Pd/Fe₃O₄ NPs. It is clearly observed that the Pd grain pervaded on Fe₃O₄ surface, which displays a good combination between Fe₃O₄ and Pd NPs. Hence, Pd nanoparticles appear as bright dots over the surface of Fe₃O₄ with average sizes of less than 39 nm.



Figure 7. FE SEM images of Pd/Fe₃O₄ NPs.

3.2.4. The EDS analysis

The elemental composition of the Pd/Fe_3O_4 NPs was also analyzed by the Energy Dispersive X-ray Spectroscopy (EDS). This technique further confirmed that Pd/Fe_3O_4 NPs was composed of palladium, iron and oxygen (Figure 8). The EDS results show that Fe, Pd and oxygen concentrations are about 22.7, 12.2 and

62.7%, respectively. The excess oxygen is due to physical absorption of oxygen from the environment during sample preparation.



Figure 8. EDS spectrum of Pd/Fe₃O₄ NPs.

3.3. Evaluation of the catalytic activity of Pd/Fe_3O_4 NPs through the Sonogashira coupling reaction

In most transition metal catalyzed reactions, ligands play a key role. Various ligands such as phosphine and nonphosphine used in palladium catalyzed coupling reactions are described in the literature. Most of these ligands are air and moisture sensitive, difficult to prepare, and expensive. Thus, catalysis under ligand-free conditions is an area of high importance. In this work, the prepared Pd/Fe₃O₄ NPs were used as heterogeneous catalysts in the copper- and ligand-free Sonogashira coupling reaction.

Initially, we employed *p*-iodoanisole and phenylacetylene as model substrates for the development of optimized conditions. Control experiments show that there is no reaction in the absence of catalyst (Table 1, entry 10). However, addition of the catalyst to the mixture has rapidly increased the formation of product in high yields. The reactivity of the catalyst in the presence of different bases was also investigated. The results indicated that base had a demonstrative effect on the yield of product. Among the tested bases (DMAP, NaHCO₃, Et₃N, piperidine, NaOH, KOH, pyridine), piperidine was found to be superior since it gave the highest yield of product (Table 1, entry 7). A decrease in the catalyst loading from 0.2 to 0.08 mol% afforded the product in lower yield (Table 1, entry 8). No significant improvement on the yield was observed using higher amounts of the catalyst (Table 1, entry 9) and 0.2 mol% of the catalyst was found to be optimum. The best result was obtained with 1.0 mmol of *p*-iodoanisole, 1.0 mmol of phenylacetylene, 0.2 mol% of Pd/Fe₃O₄ NPs and 1.5 mmol of piperidine at 110 °C, which gave the product in an excellent yield. No surfactant or ligand was

required. Since no copper salt was used, the undesired formation of Glaser-type oxidative homocoupling product, which is a diyne, was also avoided.

Table 1.

Copper-free Sonogashira reaction of phenylacetylene with *p*-iodoanisole in the presence of different solvents and bases^a

Entry	Pd/Fe ₃ O ₄ NPs (mol %)	Solvent	Base	$\text{Yield}^{b}(\%)$
1	0.2	DMF	DMAP	0
2	0.2	DMF	Pyridine	0
3	0.2	DMF	NaHCO ₃	39
4	0.2	DMF	NaOH	Trace
5	0.2	DMF	КОН	Trace
6	0.2	DMF	NEt ₃	36
7	0.2	DMF	piperidine	85
8	0.08	DMF	piperidine	40
9	0.5	DMF	piperidine	86
10	0.0	DMF	piperidine	0

^a Reaction conditions: *p*-iodoanisole (1.0 mmol), phenylacetylene (1.0 mmol), Pd/Fe₃O₄ (0.2 mol%), base (1.5 mmol), DMF (4.0 mL), 110 °C, 24 h.

Having optimized the conditions, we explored the general applicability of Pd/Fe_3O_4 NPs as catalysts for copper-free coupling of different alkynes with aryl iodides and bromides containing electron-withdrawing or donating substituents. As indicated in Table 2, it is evident that our method is reasonably general and can be applied to several types of aryl halides. In all cases, the reaction gave the corresponding products in good to excellent yields. In addition, steric hindrance of the substituent did not influence the product yield in the copper-free Sonogashira reaction of deactivated aryl halides using Pd/Fe_3O_4 NPs (Table 2, entries 4 and 9). Good yield is also found with chlorobenzene (Table 2, entry 19).

Table 2.

Sonogashira coupling reaction of different aryl halides with terminal alkynes^a

$$R \xrightarrow{-X + RC} = CH \xrightarrow{-Pd/Fe_3O_4 NPs, DMF} R \xrightarrow{-C} C = CR$$

Entry	Aryl halide	Alkyne	Yield ^b (%)	
1			88	
2	MeO		85	
3	Me		83	
4	Me		84	
5	O ₂ N I		80	
6	F ₃ CI		83	
7	I I		87	
8	MeO		90	
9	Me		85	
10		=	85	
11		≡ − ⊘ −Br	86	
12	Br	=	81	
13	MeO		80	
14	Me		74	
15	O ₂ N Br		73	
16	NC-Br		71	
17	Br		81	
18	MeO		83	
19	-Cl		70	

^a Reaction conditions: Aryl halide (1.0 mmol), alkyne (1.0 mmol), Pd/Fe₃O₄ (0.2 mol%), piperidine (1.5 mmol), DMF (4.0 mL), 110 °C.
^b Yields after work-up.

To show the advantages of proposed method in comparison with other reported methods, we summarized some of results for Sonogashira coupling reaction between chlorobenzene with phenylacetylene in Table 3,

which shows that Pd/Fe_3O_4 NPs is an equally or more efficient catalyst with respect to reaction time and yield than previously reported ones.

Table 3.

Comparison present methodology with other reported methods in the Sonogashira coupling reaction between chlorobenzene with phenylacetylene

Entry	Catalyst	Time (h)	Temperature (°C)	Yield ^a (%) [Ref.]
1	Polystyrene resin supported palladium(II) complex	3	r.t.	35 [37]
2	Polystyrene anchored Pd(II) azo complex	12	80	6 [38]
3	Pd(0)-MCM-41	24	100	29 [39]
4	Pd(II)-MCM-41	24	90	47 [40]
5	Pd@agarose-Fe ₃ O ₄	24	130	53 [41]
6	Pd/Fe ₃ O ₄ NPs	24	110	70 [This work]
<u> </u>				· · ·

^a Yields after work-up.

3.4. Evaluation of the catalytic activity of Pd/Fe₃O₄ NPs through the Suzuki coupling reaction

The Suzuki coupling reaction catalyzed by palladium (Pd) catalysts in the presence of phosphine ligands is one of the most powerful tools for selective C-C bond formation for the construction of biaryl skeletons, which are often considered as partial structures in pharmaceuticals, natural products, polymers and material science [34-36]. However, Pd-catalyzed Suzuki coupling under ligand-free conditions is a topic of considerable interest because of both economic and environmental reasons. The efficiency and stability of Pd/Fe₃O₄ NPs prompted us to use the catalyst for the commercially important Suzuki coupling reactions.

For optimization of the reaction conditions, we chose the reaction of 0.5 mmol of iodobenzene with 0.6 mmol of phenylboronic acid in the presence of 0.1 mol% of Pd/Fe₃O₄ nanoparticles and 1.5 mmol of base at 60 °C in MeOH (5 mL) as the model reaction and the effects of the various bases (K_3PO_4 , Et₃N, NaHCO₃, NaOAc) on the reaction were examined. The reaction was significantly influenced by the base employed and the best result was obtained in the case of K_3PO_4 . In the absence of base, the reactions did not proceed after a long period of time. Increasing the amount of catalyst showed no substantial improvement in the yield. The best result was obtained with iodobenzene (0.5 mmol), phenylboronic acid (0.6 mmol), catalyst (0.1 mol%), K_3PO_4 (1.5 mmol) and MeOH (5 mL), which gave the product in a good yield (93%).

Next, using the optimized procedure, a variety of arylboronic acids and aryl halides possessing both electronreleasing and electron-withdrawing groups were employed. As shown in Table 4, reactions of aryl iodides were complete at 60 °C after 12 h, while the aryl bromides and aryl chlorides required longer reaction times.

Table 4.

Suzuki coupling reaction of different aryl halides with arylboronic acids^a



^a Reaction conditions: Aryl halide (0.5 mmol), arylboronic acid (0.6 mmol), Pd/Fe₃O₄ (0.1 mol%), K₃PO₄ (1.5 mmol), MeOH (4.0 mL), 60 °C.

^b Yields after work-up.

^c Yields after the fifth cycle.

The present method offers several notable features, compared with the other literature works [42-49] on the Suzuki coupling reaction, i.e., (1) The use of plant extract as an economic and effective alternative represents an interesting, fast and clean synthetic route for the large scale synthesis of Pd/Fe₃O₄ NPs, (2) avoidance of the toxic ligands and homogeneous catalysts, (3) wide substrate scope and generality, (4) higher yields, (5) higher turnover number (TON) (6) in our method, because of the magnetic nature of the Pd/Fe₃O₄ NPs catalyst, it can be recovered by simply using external magnets, with high efficiency and up to 99% recovery of catalyst. Also, According to the UV-vis results, the synthesized Pd/Fe₃O₄ NPs by this method are quite stable and can be kept under inert atmosphere for several months.

3.5. Catalyst recyclability

The reusability of the catalysts is one of their most important advantages, which makes them useful for commercial applications. We studied the reusability of these heterogeneous Pd/Fe_3O_4 NPs catalysts in Sonogashira coupling reaction (Figure 9). After completion of the reaction, the catalyst was recovered by the application of an external magnet, then washed with ethyl acetate, and dried in a hot air oven at 100 °C for 2 h. The recovered catalyst was reused under similar conditions for the next run, and the catalytic behavior of the Pd/Fe_3O_4 NPs was found to be unaltered over five consecutive cycles. Thus, the magnetic nanocatalyst is stable during the Sonogashira coupling reaction. The reusability of the catalyst was also studied for the Suzuki coupling reaction under the present reaction conditions (Table 4, entry 3).



Figure 9. Reusability of Pd/Fe₃O₄ NPs for Sonogashira coupling reaction.

4. Conclusions

In conclusion, we have established that the Pd/Fe_3O_4 NPs generated by Euphorbia condylocarpa M. bieb extract used as a reducing agent and stabilizer is a highly efficient, magnetically recoverable and recyclable catalyst for the phosphine-free Sonogashira and Suzuki coupling reactions. The use of a green, renewable reagent such as Euphorbia condylocarpa M. bieb provides a great advantage in terms of safety, economy, and sustainability. The present method has the advantages of readily available starting materials, straightforward and easy work-up procedures, elimination of dangerous and toxic ligands and homogeneous catalysts, high yields, low catalyst loading, and tolerance for a wide variety of functionalities. The catalyst is eco-friendly because it produces little waste and can be recovered by a magnet and successively reused without significant loss of activity.

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References

- [1] K. Sonogashira, Y. Tohda, N. Hagihara, Tetrahedron Lett. (1975) 4467.
- [2] M. Nasrollahzadeh, M. Maham, M. M. Tohidi, J. Mol. Catal. A: Chem. 391 (2014) 83.
- [3] E. Negishi, L. Anastasia, Chem. Rev. 103 (2003) 1979.
- [4] K. Sonogashira, in: B.M. Trost, I. Fleming (Eds.), Comprehensive Organic Synthesis, vol. 3, Pergamon, New York, 1991.
- [5] S. Shylesh, V. Schunemann, W. R. Thiel, Angew. Chem., Int. Ed. 49 (2010) 3428.
- [6] C. Yi, R. Hua, Catal. Commun. 7 (2006) 377.
- [7] H. F. Chow, C. W. Wan, K. H. Low, Y. Y. Yeung, J. Org. Chem. 66 (2001) 1910.
- [8] A. Corma, H. Garciá, A. Primo, J. Catal. 241 (2006) 123.
- [9] B. Liang, M. Dai, J. Chen, Z. Yang, J. Org. Chem. 70 (2005) 391.
- [10] V. Polshettiwar, B. Baruwati and R. S. Varma, Green Chem. 11 (2009) 127.
- [11] M. Nasrollahzadeh, M. Maham, A. Ehsani and M. Khalaj, RSC Advance 4 (2014) 19731.
- [12] M. Nasrollahzadeh, A. Azarian, A. Ehsani, S.M. Sajadi, F. Babaei, Mat. Res. Bull. 55 (2014) 168.
- [13] Y. Konishi, K. Ohno, N. Saitoh, T. Nomura, S. Nagamine, H. Hishida, Y. Takahashi, T. Uruga, J. Biotechnol. 128 (2007) 648.
- [14] M. Rai, A. Yadav, A. Cade, Critic. Rev. Biotechnol. 28 (2008) 277.

- [15] S. S. Shankar, A. Ahmad, M. Sastry, Biotechnol. Prog. 19 (2003) 1627.
- [16] S. P. Dubey, M. Lahtinen, M. Sillanpa, Process Biochem. 45 (2010) 1065.
- [17] D. Philip, Spectrochim. Acta, Part A 73 (2009) 374.
- [18] J. Kesharwani, J. K. Yoon, J.; Hwang, M. Rai, J. Bionanosci. 3 (2009) 1.
- [19] V. K. Sharma, R. A. Yngard, Y. Lin, Adv. Colloid Interface Sci. 145 (2009) 83.
- [20] A. Rizk, Bot. J. Linn. Soc. 94 (1987) 293.
- [21] A.R. Jasbi, Phytochem. 67 (2006) 1977.
- [22] M. Nasrollahzadeh, S.M. Sajadi, M. Maham, P. Salaryan, A. Enayati, S.A. Sajjadi, K. Naderi, Chem. Nat. Compd. 47 (2011) 434.
- [23] M. Nasrollahzadeh, A. Ehsani, A. Rostami-Vartouni, Ultrason. Sonochem. 21 (2014) 275.
- [24] P. Fakhri, B. Jaleh, M. Nasrollahzadeh, J. Mol. Catal. A: Chem. 383-384 (2014) 17.
- [25] M. Nasrollahzadeh, A. Rostami-Vartooni, A. Ehsani, M. Moghadam, J. Mol. Catal. A: Chem. 387 (2014) 123.
- [26] M. Nasrollahzadeh, A. Zahraei, A. Ehsani and M. Khalaj, RSC Adv. 4 (2014) 20351.
- [27] M. Nasrollahzadeh, RSC Adv. 4 (2014) 29089.
- [28] M. Nasrollahzadeh, M. Enayati, M. Khalaj, RSC Adv. 4 (2014) 26264.
- [29] M. Nasrollahzadeh, B. Jaleh, A. Jabbari, RSC Adv. 4 (2014) 36713.
- [30] M. Cai, J. Sha, Q. Xu, Tetrahedron 63 (2007) 4642.
- [31] P. Appukkuttan, W. Dehaen, E. V. d. Eycken, Eur. J. Org. Chem. (2003) 4713.
- [32] T. Suzuka, Y. Okada, K. Ooshiro, Y. Uozumi, Tetrahedron 66 (2010) 1064.
- [33] K. R. Reddy, N. S. Kumar, P. S. Reddy, B. Sreedhar, M. L. Kantam, J. Mol. Catal. A: Chem. 252 (2006) 12.
- [34] P.K. Mandali, D.K. Chand, Catal. Commun. 31 (2013) 16.
- [35] T.S.A. Heugebaert, S. De Corte, T. Sabbe, T. Hennebel, W. Verstraete, N. Boon, C.V. Stevens, Tetrahedron Lett. 53 (2012) 1410.
- [36] Y.-Y. Peng, J. Liu, X. Lei, Z. Yin, Green Chem. 12 (2010) 1072.
- [37] M. Bakherad, A. Keivanloo, B. Bahramian, S. Jajarmi, Appl. Catal. A: Gen. 390 (2010) 135.
- [38] S. M. Islam, P. Mondal, A. Singha Roy, S. Mondal, D. Hossain, Tetrahedron Lett. 51 (2010) 2067.
- [39] S. Jana, B. Dutta, R. Bera, S. Koner, Inorg. Chem. 47 (2008) 5512.
- [40] B. Susmita, K. Subratanath, Ind. J. Chem. 50A (2011) 1380.

- [41] H. Firouzabadi, N. Iranpoor, M. Gholinejad, S. Akbari and N. Jeddi, RSC Adv. 4 (2014) 17060.
- [42] H. Li, Z. Zhu, H. Li, P. Li, X. Zhou, J. Colloid Interface Sci. 349 (210) 613.
- [43] J. Wang, B. Xu, H. Sun, G. Song, Tetrahedron Lett. 54 (2013) 238.
- [44] Y. Jang, J. Chung, S. Kim, S. W. Jun, B. H. Kim, D. W. Lee, B. M. Kim and T. Hyeon, Phys. Chem. Chem. Phys. 13 (2011) 2512.
- [45] S. Zhou, M. Johnson and J. G. C. Veinot, Chem. Commun. 46 (2010) 2411.
- [46] A. Schatz, T. R. Long, R. N. Grass, W. J. Stark, P. R. Hanson and O. Reiser, Adv. Funct. Mater. 20 (2010) 4323.
- [47] M. Cargnello, N. L. Wieder, P. Canton, T. Montini, G. Giambastiani, A. Benedetti, R. J. Gorte and P. Fornasiero, Chem. Mater. 23 (2010) 3961.
- [48] C. X. Yang, A. K. Manocchi, B. Lee and H. M. Yi, J. Mater. Chem. 21 (2011) 187.
- [49] A. Modak, J. Mondal, M. Sasidharan and A. Bhaumik, Green Chem. 13 (2011) 1317.

Scheme captions

Scheme 1. Reducing ability of antioxidant phenolics to produce metalic NPs where FlOH and NZV are flavonoid and nano zero valent, respectively.

Scheme 2. Flavon nuclei.



Scheme 1. Reducing ability of antioxidant phenolics to produce metalic NPs where FIOH and NZV are flavonoid and nano zero valent, respectively.



Figure captions

Figure 1. Image of *Euphorbia condylocarpa M. bieb*.

Figure 2. Photograph of *Euphorbia condylocarpa M. bieb* root extract.

Figure 3. UV-vis spectrum of *Euphorbia condylocarpa M. bieb* root extract.

Figure 4. FT-IR spectrum of *Euphorbia condylocarpa M. bieb* root extract.

Figure 5. UV-vis spectra of Pd/Fe₃O₄ bimetallic NPs.

Figure 6. XRD pattern of Pd/Fe₃O₄ NPs.

Figure 7. FE SEM images of Pd/Fe₃O₄ NPs.

Figure 8. EDS spectrum of Pd/Fe₃O₄ NPs.

Figure 9. Reusability of Pd/Fe3O4 NPs for Sonogashira coupling reaction.



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Figure 2. Photograph of *Euphorbia condylocarpa M. bieb* root extract.



Figure 3. UV-vis spectrum of Euphorbia condylocarpa M. bieb root extract.

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Figure 6. XRD pattern of Pd/Fe₃O₄ NPs.



Figure 7. FE SEM images of Pd/Fe₃O₄ NPs.

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Table captions

 Table 1. Copper-free Sonogashira reaction of phenylacetylene with *p*-iodoanisole in the presence of different solvents and bases.

Table 2. Sonogashira coupling reaction of different aryl halides with terminal alkynes.

Table 3. Comparison present methodology with other reported methods in the Sonogashira coupling reaction

 between chlorobenzene with phenylacetylene.

 Table 4. Suzuki coupling reaction of different aryl halides with arylboronic acids.

Table 1.

Copper-free Sonogashira reaction of phenylacetylene with *p*-iodoanisole in the presence of different solvents and bases^a

Entry	Pd/Fe ₃ O ₄ NPs (mol %)	Solvent	Base	$\operatorname{Yield}^{b}(\%)$
1	0.2	DMF	DMAP	0
2	0.2	DMF	Pyridine	0
3	0.2	DMF	NaHCO ₃	39
4	0.2	DMF	NaOH	Trace
5	0.2	DMF	KOH	Trace
6	0.2	DMF	NEt ₃	36
7	0.2	DMF	piperidine	85
8	0.08	DMF	piperidine	40
9	0.5	DMF	piperidine	86
10	0.0	DMF	piperidine	0

^a Reaction conditions: *p*-iodoanisole (1.0 mmol), phenylacetylene (1.0 mmol), Pd/Fe₃O₄ (0.2 mol%), base (1.5

mmol), DMF (4.0 mL), 110 °C, 24 h.

Table 2.

Sonogashira coupling reaction of different aryl halides with terminal alkynes^a

	X + RC	$\equiv CH \frac{Pd/Fe_3O_4 NPs, DMF}{Piperiding, 110 \%}$	$-\langle - \rangle - C \equiv CR$	
	R	Pipendine, 110 C	R	
Entry	Aryl balide	Allaune	Vield ^b (%)	
<u> </u>			88	
			0.5	
2	MeO		85	
3	Me		83	
4	Me		84	
5	O ₂ N-		80	
6	E-C		83	
7			87	
,	I I			
8	MeO		90	
9	Me	-OMe	85	
10		-F	85	
11		■ Br	86	
12	Pr		81	
12			00	
13	MeO————————————————————————————————————		80	
14	Me		74	
15	O ₂ N Br		73	
16			71	
17			81	
18	Br		83	
10	MeO—Br		0.5	
19	Cl		70	
	×/			

^a Reaction conditions: Aryl halide (1.0 mmol), alkyne (1.0 mmol), Pd/Fe₃O₄ (0.2 mol%), piperidine (1.5 mmol),

DMF (4.0 mL), 110 °C.

^b Yields after work-up.

Table 3.

Comparison present methodology with other reported methods in the Sonogashira coupling reaction between

chlorobenzene with phenylacetylene

Entry	Catalyst	Time (h)	Temperature (°C)	Yield ^a (%) [Ref.]
1	Polystyrene resin supported palladium(II) complex	3	r.t.	35 [37]
2	Polystyrene anchored Pd(II) azo complex	12	80	6 [38]
3	Pd(0)-MCM-41	24	100	29 [39]
4	Pd(II)-MCM-41	24	90	47 [40]
5	Pd@agarose-Fe ₃ O ₄	24	130	53 [41]
6	Pd/Fe ₃ O ₄ NPs	24	110	70 [This work]
9	2 1			

^a Yields after work-up.

Table 4.

Suzuki coupling reaction of different aryl halides with arylboronic acids^a

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$$R \xrightarrow{R'} B(OH)_2 \xrightarrow{Pd/Fe_3O_4 NPs, MeOH} R \xrightarrow{R'} R$$

Entry	Aryl halide	Arylboronic acid	Time (h)	Yield ^b (%)
1		B(OH)	12	94
2	MeO	B(OH)	12	91
3	Me	B(OH)	12	95, 92°
4	O ₂ N-I	B(OH)2	12	92
5	√I	Me0 B(OH)	12	91
6	Br	B(OH)2	18	94
7	MeO-Br	B(OH)2	18	91
8	Me	B(OH) ₂	18	92
9	O ₂ N-Br	B(OH)	18	95
10	Cl	BIOH	24	95
11	MeO-Cl		24	78
12	Me		24	83
13	O ₂ N-Cl		24	95

^a Reaction conditions: Aryl halide (0.5 mmol), arylboronic acid (0.6 mmol), Pd/Fe₃O₄ (0.1 mol%), K₃PO₄ (1.5 mmol), MeOH (4.0 mL), 60 °C.

^b Yields after work-up.

^c Yields after the fifth cycle.

Abbreviations

- XRD: X-ray Powder Diffraction
- SEM: Scanning Electron Microscopy
- EDS: Energy Dispersive X-ray Spectroscopy
- VSM: Vibrating sample magnetometer
- FT-IR spectroscopy: Fourier transform infrared spectroscopy

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NMR: Nuclear Magnetic Resonance

Graphical Abstract

Green synthesis of Pd/Fe₃O₄ nanoparticles using *Euphorbia condylocarpa M*.

bieb root extract and their catalytic applications as magnetically recoverable and

stable recyclable catalysts for the phosphine-free Sonogashira and Suzuki

coupling reactions

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Highlights:

- Green synthesis of Pd/Fe₃O₄ nanoparticles using *Euphorbia condylocarpa M. bieb*.
- Sonogashira and Suzuki coupling reactions of different aryl halides.
- > Catalyst was characterized using the powder XRD, SEM, EDS and UV-vis.
- > Catalyst can be easily recovered by using a magnet and reused.

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