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Upgraded valorization of copper (II) immobilization onto Schiff base-functionalized pectin grafted magnetic nanoparticles: A thermostable, reusable, and efficient nanocatalyst for the green synthesis of 1,2,3-triazole in pure water

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Upgraded valorization of copper (II) immobilization onto Schiff base-functionalized pectin grafted magnetic nanoparticles: A thermostable, reusable, and efficient nanocatalyst for the green synthesis of 1,2,3-triazole in pure water

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Abstract

In this project, the new catalyst copper defines as Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) was successfully manufactured and fully characterized by different techniques, including FT-IR, XRD, TEM, FESEM, EDX, VSM, and ICP analysis. All results showed that copper was successfully supported on the polymer-coated magnetic nanoparticles. One of the most important properties of a catalyst is the ability to be prepared from simple materials such as pectin that's a biopolymer that is widely found in nature. The catalytic activity of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) was examined in a classical, one pot, and the three-component reaction of terminal alkynes, alkyl halides, and sodium azide in water and observed, proceeding smoothly and completed in good yields and high regioselectivity. The critical potential interests of the present method include high yields, recyclability of catalyst, easy workup, using an eco-friendly solvent, and the ability to sustain a variety of functional groups, which give economical as well as ecological rewards. The capability of the nanocomposite was compared with previous works, and the nanocomposite was found more efficient, economical, and reproducible. Also, the catalyst can be easily removed from the reaction solution using an external magnet and reused for five runs without reduction in catalyst activity

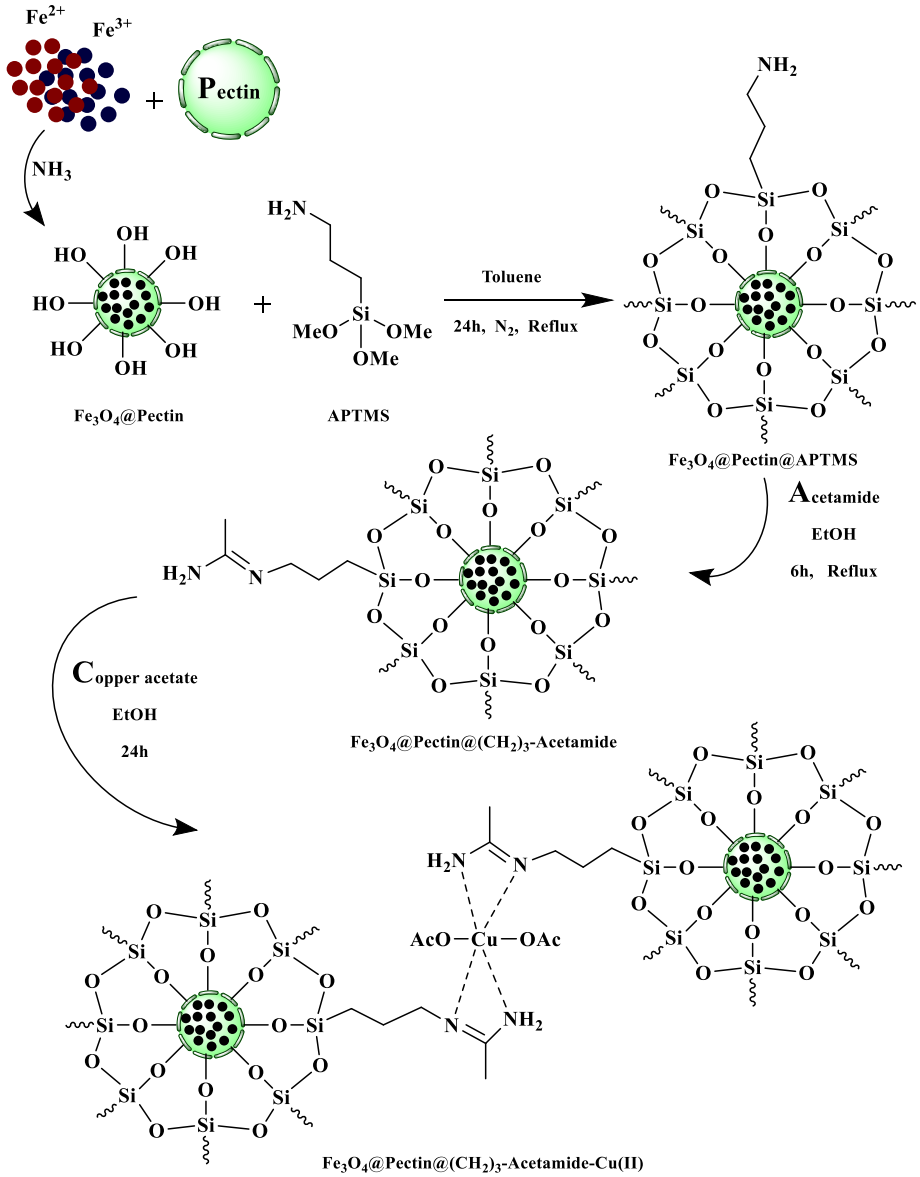
Keywords: Click reaction, Heterogeneous catalyst, Magnetic nanoparticles, Pectin, Polymer, Triazole

Introduction

Over the last decade, much interest has been shown in the synthesis of 1,2,3-triazole unit. 1,2,3-Triazoles are important and useful heterocycles. Apart from pharmaceutical applications, where these units are important for their biological activity or as an amide bond isostere, they are also important in material science and chemical biology [1, 2]. Also, other uses include: as chemical agents, dyes, corrosion inhibitors, photo stabilizers and photographic materials. Several 1,2,3-triazole derivatives show interesting biological activities. [3–7] One of the most general methods for the syntheses of 1,2,3-triazole derivatives is the classical Huisgen [8] cycloaddition reaction that involves the thermal 1, 3-dipolar cycloaddition of organic azides with alkynes. However, it is in low efficiency and mixed regioselectivity. Research groups of Sharpless [9] and Meldal's [10], later independently developed the Huisgen 1, 3-dipolar cycloaddition reaction method with a copper (I) catalyzed, which the "click" reaction is widely studied. Also, according to several recent studies in the literature since 2010, the catalyzed reaction of click with copper has been widely reflected in various branches of science. [11] To make the CuAAC reactions functional, many efforts have been made, concentrating on discovering new and more significant synthetic strategies [12-14]. In CuAAC reactions, copper has an outstanding role in the synthesis of 1,2,3-triazole derivatives. On the basis of the work of Sharpless and Medal, different copper sources such as Cu (I) [15-20], MNP@PIL-Cu [21], Cu-complex [22], Cu NPs [23], and HMS-DP-Cu(II) [24] have been tested. Moreover, in recent years, in order to synthesize triazoles, many other methods have been suggested [25-27]. Although these simple procedures are feasible for many reactions, they have a major drawback; when copper salts are used as a homogeneous catalyst, it faces problems such as difficult separation and recycling of the catalyst, cytotoxicity, and environmental pollution. Since removing trace amounts of metal contaminants from the products is necessary, particularly in the pharmaceutical industry, copper catalysts should be fully separated from the products. Thus, the heterogeneously catalyzed procedures are advantageous for such

reactions. During the past few years, copper ions have been immobilized onto a large variety of solid supports, including agarose [28], polymers [29], chitosan [30], silica [31], cellulose [32], eggshell [33], and graphene [34] that assist in controlling reactivity and selectivity besides the advantage of easy workability. However, it is complicated to remove a homogeneous copper catalyst from the reaction medium after the reaction has been completed. While removing a small amount of metal contamination from products, especially pharmaceuticals, is essential, copper catalysts should be completely removed from the product [35-38]. To solve this problem, heterogeneous copper catalysts should be used instead of homogeneous copper catalysts. The choice of materials that have been used for immobilization of copper complexes is essential, which can be referred to as magnetic nanoparticles. Magnetic nanoparticles are a group of advanced nanomaterials with specific applications, properties and sizes and are very efficient in the synthesis of heterogeneous catalysts. Among the properties of magnetic nanoparticles are biological, biomedical, environmental, low toxicity and cost-effectiveness. [39] The magnetic nanoparticles have been the focus of much research recently because they possess attractive properties which could see potential use in catalysis, including nanomaterial-based catalysts,[40] biomedicine [41] and tissue-specific targeting,[42] magnetically tunable colloidal photonic crystals,[43] microfluidics,[44] magnetic resonance imaging,[45] magnetic particle imaging,[46] data storage,[47][48] environmental remediation,[49] nanofluids,[50,51] optical filters,[52] defect sensor,[53] magnetic cooling[54][55] and cation sensors.[56] One of the significant problems of magnetic nanoparticles is their nakedness problem, which is due to the small distance between the particles and to some extent the high surface energy and the presence of van der Waals forces. The above points cause the nanoparticles to be subjected to the accumulation of the reaction mixture. [57]. The accumulation of particles affects their properties. The effect is accompanied by catalytic reactions. To maintain these properties, magnetic nanoparticles are continuously modified by placing stabilizing coatings in active sites to prevent their irreversible accumulation. Iron oxide-like outer shells such as polymers [58], zeolites [59], titanium dioxide [60], silica [61] and carbon [62] being investigated. The choice of supporting materials for the catalyst is essential because it determines the activity, thermal durability, and reproducibility of the catalyst in catalytic reactions. [63] Hence, magnetic nanocomposites are very important as a substrate for catalysts due to their wide surface area, easy preparation and green nature. [64] Pectin is a natural polysaccharide copolymer that is present in the walls of primary cells and is extracted from fruits and vegetables. [65] The structure of pectin depends on its source and extraction process. Pectin has properties such as biodegradable, biocompatible, bioactive, and is used in food, cosmetics, medicine, and biology. [66]

In this study, a highly efficient and recyclable copper catalyst first designed from pectin, a low-cost, harmless, and green biopolymer for organic reactions. In summary, amino-functionalized pectin (Pectin-NH_2) was obtained by mixing pectin with (3-Aminopropyl) trimethoxy silane (APTMS) in toluene. Schiff base reaction was performed with the reaction of NH_2-grafted pectin with acetamide. Finally, the copper catalyst was easily prepared by stirring of Schiff base functionalized pectin (Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide) and copper acetate in ethanol (Scheme 1). This novel catalyst was fully analyzed by several instrumental techniques and applied as a water-dispersible/magnetically reusable copper (II) catalyst for the 1,2,3-triazole click reactions in aqueous media. The designed copper catalyst showed highly efficient catalytic activity for click reactions of aryl halides, Sodium azide, and alkynes; in addition, the copper catalyst showed superior reusability by producing high-efficiency products even after five cycles.



Scheme 1: The general synthetic approach for preparation of the Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

Experimental

Materials and physicochemical characterization

Ferric chloride hexahydrate ($FeCl_3 \cdot 6H_2O$, >99%) and ferrous chloride tetrahydrate ($FeCl_2 \cdot 4H_2O$) were used as an iron source. Pectin with the degree of esterification of 76% and other materials used in this article were from Merck (Germany) and Sigma Aldrich and were used without further purification. The reaction progress and purity of the products were determined using TLC on silica-gel Polygram SILG/UV254 plates. FT-IR spectra were recorded with a Nicolet system 800 beam splitter KBr SCAL = 800 in the 400– 4000 cm^{-1}. Transmission electron microscope (TEM) investigations were performed using a Philips EM 208S Transmission Electron Microscope. Thermogravimetric analysis (TGA) was also recorded under argon and air atmosphere using TGA/TDA Q600 TA Instruments. Melting

points were determined using an electrothermal 9100 device. The powder X-ray diffraction (XRD) was performed within Philips PW1730 with a Cu Kα (λ = 1.54060 Å) radiation. SEM-EDX was recorded by Fe-SEM TESCAN MIRA3. The ^{1}H NMR (250 MHz) and ^{13}CNMR (62.9 MHz) analyses were performed on a Bruker Avance DPX-250 spectrometer in $CDCl_3$ and DMSO-d_6 as solvent and TMS as internal standard.

1.2 Synthesis of Fe_3O_4@Pectin

Core-shell Fe_3O_4@Pectin nanospheres were prepared in terms of the previously described method.[67] According to this, 0.5 g of pectin dissolves in 50 ml of distilled water under stirring until a homogeneous dispersion of pectin is obtained .$FeCl_3.6H_2O$ (3 g) and $FeCl_2.4H_2O$ (1.6 g) dissolve in 25 ml of distilled water separately and then add them. Then slowly added them to the mixture containing pectin, which resulted in a brown gel. The reaction mixture was stirred under a gentle flow of N_2 at 85 ° C for 2 h. After which an excess of ammonium hydroxide (25 wt%) to the reaction mixture was added until the pH reaches 11-12 and the mixture becomes black indicating the formation of magnetite and again the mixture was under a gentle flow of N_2 at 85° C for 30 min. At the end , the precipitate was removed from the reaction vessel and to reduce the pH washed with distilled water until pH reached the range of 7, then precipitate dried under vacuum.

2.2 Synthesis of Fe_3O_4@Pectin@APTMS

In the first step, synthesized Fe_3O_4@Pectin (1.7 g) was sonicated in dry toluene (30 ml) for 30 min, and then 3-aminopropyl trimethoxy silane (APTMS: 1.1 ml) was added slowly to the mixture. Then the mixture was stirred for 1 h at room temperature. After stirring, the product obtained from Fe_3O_4@Pectin and APTMS was exposed for 24 h under N_2 gas at reflux conditions. After finishing the reaction, the solid obtained is separated by an exterior magnet and washed three times with 15 ml of toluene. At the end, solid dried at 70 ºC in oven under vacuum for 4h.

3.2. Synthesis of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide

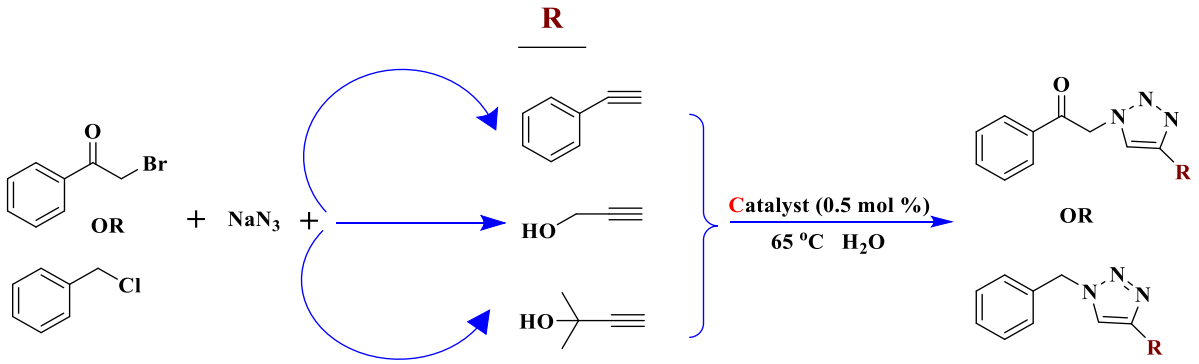
In the beginning, Acetamide (2.12mmol, 0.129 g) was dissolved in dry ethanol (5 ml) and then slowly added to a 100 ml flask containing 45 ml of ethanol and Fe_3O_4@Pectin@APTMS (1.97 g), which were dispersed using ultrasound for 30 min. The reaction mixture was refluxed for 6 h. After, the mixture was cooled to room temperature. The resulting Schiff base immobilized on Fe_3O_4@Pectin was separated by an external magnet, washed three times with ethanol and dried under vacuum.

4.2 Synthesis of Fe_3O_4@Pectin@ $(CH_2)_3$-Acetamide-Cu (II)

The synthesized Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide (1g) was dissolved in dry ethanol (5 ml) under sonication. Copper acetate was also dissolved separately in ethanol (15ml). The metal solution was slowly added to the solution containing the substrate under sonicate conditions. Then the reaction mixture is subjected to vigorous stirring for 24 h to place the copper metal on substrate Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide. Finally, it separated the solid product from the solution and washed it with ethanol several times to remove excess copper from the catalyst, and it dried under vacuum (Scheme 1).

5.2The method of synthesizing triazole derivatives

To a test tube on a magnetic stirrer containing catalyst (0.5 mol %) and H_2O (2ml) as a green solvent, Alkyl halides (1.0 mmol), Sodium azide (1.2 mmol), alkyne (1.0mmol) added. The reaction mixture was stirred at 65 ° C and the progress of the reaction was monitored by thin-layer chromatography (TLC). After the reaction is complete and the reaction mixture has cooled, the catalyst is removed from the reaction medium by an external magnet. A pure product was obtained by recrystallization from EtOAC-Water. The products were identified by comparing their melting points with those previously reported because the products are known compounds. The spectral data for the selected compounds are as follows:



Scheme 2: Reaction of synthesis triazole derivatives in the presence of catalyst Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

1-benzyl-4-phenyl-1H-1,2,3-triazole (4a):

^{1}HNMR (DMSO, 300 MHz): δ= 5.66 (s, 2H, CH_2), 7.34-7.45(m, 8H, H-Ar), 7.48 (s, 1H, CH of triazole), 7.85-7.87 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 53.51, 122.03, 125.65, 128.37, 129.59, 133.22, 147.14 ppm.

Anal. calcd for $C_{13}H_{15}N_3$: C, 75.57; H, 5.57; N, 17.86; found: C, 75.52; H, 5.58; N, 18.9. Mp (°C): 127-129. [71]

1-(4-methylbenzyl)-4-phenyl-1H-1,2,3-triazole (4b):

^{1}HNMR (DMSO, 300 MHz): δ= 2.308 (s, 3H, CH_3), 5.607 (s, 2H, CH_2), 7.25(q, 3H, H-Ar), 7.36 (t, 2H, H-Ar), 7.45 (t, 2H, h-Ar), 7.69 (s, 1H, CH of triazole), 7.86 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 21.18, 53.30, 128.42, 129.36, 129.80, 131.16, 133.48, 137.98, 147.09 ppm.

Anal. calcd for $C_{16}H_{15}N_3$: C, 77.08; H, 6.06; N, 16.85; found: C, 77.11; H, 6.04; N, 16.85. M.p (°C): 103-105. [72]

1-(4-chlorobenzyl)-4-phenyl-1H-1,2,3-triazole (4c):

^{1}HNMR (DMSO, 300 MHz): δ= 5.76 (s, 2H, CH_2), 7.24 (d, 2H, H-Ar), 7.34 (d, 2H, H-Ar), 7.62 (q, 3H, H-Ar), 7.77 (s, 1H, CH of triazole), 7.86 (d, 2H, H-Ar) ppm.

Anal. calcd for $C_{15}H_{12}ClN_3$: C, 66.79; H, 4.48; Cl, 13.14; N, 15.58; found: C, 66.59; H, 4.72; N, 15.54. M.p (°C): 145-147 [73]

1-(2-chlorobenzyl)-4-phenyl-1H-1,2,3-triazole (4d):

^{1}HNMR (DMSO, 300 MHz): δ= 5.77 (s, 2H, CH_2), 7.34 (3H, H-Ar), 7.45 (3H, H-Ar), 7.57 (d, 1H, H-Ar), 7.67 (s, 1H, CH of triazole), 7.86 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 51.27, 125.68, 127.24, 128.28, 129.38, 130.76, 130.99, 133.66, 138.79, 146.94 ppm.

Anal. calcd for $C_{15}H_{12}ClN_3$: C, 66.79; H, 4.48; Cl, 13.14; N, 15.58; found: C, 66.61; H, 4.53; N, 15.561. Mp (°C): 88-90. [73]

2-(1-benzyl-1H-1,2,3-triazol-4-yl)propan-2-ol (4e):

^{1}HNMR (DMSO, 300 MHz): δ= 1.45 (s, 6H, CH_3), 5.09 (s, 2H, CH_2), 5.55 (s, 1H, OH), 7.40 (5H, H-Ar), 7.91(s, 1H, CH of triazole) ppm.

Anal. calcd for $C_{12}H_{15}N_3O$: C, 66.34; H, 6.96; N, 19.34; O, 7.36; found: C, 66.41; H, 7.01; N, 19.41. Mp (°C): 75-77. [72]

2-(1-(4-methylbenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (4f):

^{1}HNMR (DMSO, 300 MHz): δ= 1.44 (s, 6H, CH_3), 2.30 (s, 3H, CH_3), 5.09 (s, 2H, CH_2), 5.49 (s, 1H, OH), 7.23 (5H, H-Ar), 7.87 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 22.90, 31.94, 58.86, 78.40, 122.41, 125.68, 129.38, 131.04, 133.66, 134.80 ppm.

Anal. calcd for $C_{13}H_{17}N_3O$: C, 67.51; H, 7.41; N, 18.17; O, 6.92; found: C, 67.53; H, 7.50; N, 17.98.

2-(1-(4-chlorobenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (4g):

^{1}HNMR (DMSO, 300 MHz): δ= 1.46 (s, 6H, CH_3), 5.13 (s, 2H, CH_2), 5.67 (s, 1H, OH), 7.42 (4H, H-Ar), 7.88 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 31.17, 58.64, 78.40, 122.41, 129.38, 130.99, 132.19, 133.66 ppm.

Anal. calcd for $C_{12}H_{14}ClN_3O$: C, 57.26; H, 5.61; Cl, 14.08; N, 16.69; O, 6.36; found: C, 57.31; H, 5.62; N, 16.82.

2-(1-(2-chlorobenzyl)-1H-1,2,3-triazol-4-yl)propan-2-ol (4h):

^{1}HNMR (DMSO, 300 MHz): δ= 1.46 (s, 6H, CH_3), 5.15 (s, 2H, CH_2), 5.66 (s, 1H, OH), 7.27 (d, 1H, H-Ar), 7.51 (d of d, 1H, H-Ar), 7.63 (d of d, 1H, H-Ar), 7.73 (d, 1H, H-Ar), 7.90 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 31.17, 52.89, 78.40, 121.05, 127.24, 127.25, 128.28, 130.76, 131.04, 133.66, 139.41 ppm.

Anal. calcd for $C_{12}H_{14}ClN_3O$: C, 57.26; H, 5.61; Cl, 14.08; N, 16.69; O, 6.36; found: C, 57.34; H, 5.59; N, 16.79.

1-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanone (4i):

^{1}HNMR (DMSO, 300 MHz): δ= 6.29 (s, 2H, CH_2), 7.35–7.40 (t, 1H, H-Ar), 7.46–7.68 (m, 4H, H-Ar), 7.75–7.81 (t, 1H, H-Ar), 7.88–7.92 (d, 2H, H-Ar), 8.11–8.15 (d, 2H, H-Ar), 8.55 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 56.49, 123.53, 125.64, 128.36, 128.72, 129.45, 129.51, 131.24, 134.61, 134.79, 146.78, 192.70 ppm. Mp (°C): 170-172 [71].

Anal. calcd for $C_{16}H_{13}N_3O$: C, 72.99; H, 4.98; N, 15.96; found: C, 72.67; H, 5.01; N, 15.94. Mp (°C): 170-172 [71].

1-(4-Bromophenyl)-2-(4-phenyl-1H-1,2,3-triazol-1-yl) ethanone (4j).

^{1}HNMR (DMSO, 300 MHz): δ= 6.27 (s, 2H, CH_2), 7.35–7.52 (t,t, 3H, H -Ar), 7.85–7.91 (m, 4H, H-Ar), 8.03– 8.07 (d, 2H, H-Ar), 8.33–8.37 (d, 2H, H-Ar), 8.54 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 56.47, 121.53, 127.54, 128.06, 128.86, 129.82, 129.85, 130.51, 131.54, 133.61, 148.78, 192.70 ppm. Mp (°C): 116-120 [71].
Anal. calcd for $C_{16}H_{12}BrN_3O$: C, 56.16; H, 3.53; N, 12.28; found: C, 56.24; H, 3.55; N, 12.14. Mp (°C): 116-120 [71].

1-(4-Nitro phenyl)-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanone (4k):

^{1}HNMR (DMSO, 300 MHz): δ= 6.37 (s, 2H, CH_2), 7.35– 7.41 (t, 1H, H-Ar), 7.47–7.52 (t, 2H, H-Ar), 7.89–7.92 (t, 2H, H-Ar), 8.33–8.37 (d, 2H, H-Ar), 8.44–8.48 (d, 2H, H-Ar), 8.55 (s, 1H, CH of triazole) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 56.47, 121.23, 123.54, 128.06, 128.76, 129.72, 129.80, 130.41, 140.58, 148.88, 150.51, 192.71 ppm.

Anal. calcd for $C_{16}H_{12}N_4O_3$: C, 62.33; H, 3.92; N, 18.17; found: C, 61.94; H, 3.62; N, 18.21. Mp (°C): 184-185. [74]

2-(4-(2-Hydroxypropan-2-yl)-1H-1,2,3-triazol-1-yl)-1- phenylethanone (4l).

^{1}HNMR (DMSO, 300 MHz): δ= 1.51 (s, 2×3H, CH_3), 5.16 (s, 1H, OH), 6.15 (s, 2H, CH_2), 7.61–7.66 (t, 2H, H-Ar), 7.73–7.79 (t, 2H, CH-Ar), 7.86 (s, 1H, CH of triazole), 8.08–8.11 (d,d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 31.30, 56.46, 78.32, 122.92, 128.75, 130.78, 133.14, 133.53, 134.53, 190.90 ppm.

Anal. calcd for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34; found: C, 60.79; H, 5.13; N, 19.37. Mp (°C): 96–98. [74]

1-(4-Bromophenyl)-2-(4-(2-hydroxypropan-2-yl)-1H-1,2,3- triazol-1-yl)ethanone (4m).

^{1}HNMR (DMSO, 300 MHz): δ= 1.51 (s, 6H, CH_3), 5.16 (s, 1H, OH), 6.13 (s, 1H, CH_2), 7.84–7.87 (d, 3H, CH of triazole and H-Ar), 8.00–8.03 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 31.29, 56.50, 78.29, 122.52, 127.32, 128.75, 129.88, 131.54, 133.53, 152.58, 190.91 ppm. Mp (°C): 167–169 [75].

Anal. calcd for $C_{13}H_{14}N_4O_4$: C, 53.79, H, 4.86; N, 19.30; found: C, 53.63; H, 4.80; N, 19.39.

2-(4-(2-Hydroxypropan-2-yl)-1H-1,2,3-triazol-1-yl)-1-(4- nitrophenyl)ethanone (4n).

^{1}HNMR (DMSO, 300 MHz): δ= 1.38 (s, 6H, CH_3), 4.90 (s, 2H, CH_2), 5.53 (s, 1H, OH), 7.75 (s, 1H, CH of triazole), 8.31–8.33 (d,d, 2H, H-Ar), 8.41–8.44 (d, 2H, j ¼ 8.7, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 31.18, 56.49, 78.29, 122.82, 123.83, 129.75, 131.24, 140.58, 152.58, 190.90 ppm.

Anal. calcd for $C_{13}H_{14}N_4O_4$: C, 53.79, H, 4.86; N, 19.30; found: C, 53.63; H, 4.80; N, 19.39. Mp (°C): 126-128 [74].

2-(4-(Hydroxymethyl)-1H-1,2,3-triazol-1-yl)-1- phenylethanone (4o).

^{1}HNMR (DMSO, 300 MHz): δ= 4.58–4.59 (d, 2H, CH_2–OH), 5.23–5.27 (t, 1H, OH), 6.18 (s, 2H, CH_2), 7.60– 7.66 (t, 2H, H-Ar), 7.73–7.79 (t, 1H, H-Ar), 7.95 (s, 1H, CH of triazole), 8.08–8.11 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 55.57, 56.20, 124.87, 128.64, 129.47, 134.67, 148.41, 192.76 ppm.

Anal. calcd for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.34; found: C, 60.79; H, 5.13; N, 19.37. Mp (°C): 111-113 [75].

1-(4-Bromophenyl)-2-(4-(hydroxymethyl)-1H-1,2,3-triazol-1- yl)ethanone (4p).

^{1}HNMR (DMSO, 300 MHz): δ= 4.38 (s, 2H, CH_2), 5.00 (s, 2H, CH_2–OH), 5.75 (s, 1H, OH), 7.98 (s, 1H, CH of triazole), 8.33–8.37 (d, 2H, H-Ar), 8.44–8.48 (d, 2H, H-Ar) ppm.

^{13}CNMR (DMSO, 75 MHz): δ= 55.57, 56.20, 122.77, 127.72, 129.47, 131.41, 134.67, 147.41, 192.76 ppm.

Anal. calcd for $C_{11}H_{10}BrN_3O_2$: C, 44.62; H, 3.40; Br, 26.98; N, 14.19; found: C, 44.48; H, 3.44; N, 14.21. Mp (°C): 156–158 [74].

Result and discussion

1.2) Catalyst characterization

We synthesized a catalyst that is very efficient, selectivity, green and suitable for the synthesis of triazole derivatives under aqueous conditions, because organic reaction design in aqueous environments is another project of progress in green chemistry. Finally, with the help of an external magnet, the catalyst can be removed from the reaction medium with high efficiency and reused. A general schematic for the synthesis of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)is shown (Scheme 1).

Using FT-IR spectroscopy to investigate the steps of catalyst synthesis and confirm the formation of the expected functional groups has been done. The spectra of Fe_3O_4 (a), Pectin (b), Fe_3O_4@Pectin (c), Fe_3O_4@Pectin@APTES (d),

Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide (e) and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanocomposites (f) are shown in Figure 1. FT-IR spectrum of Fe_3O_4 (Fig. 1a) the stretching vibrations Fe-O and O-H at 574 cm^{-1} and 3420 cm^{-1} that allow the establishment of Fe_3O_4 nanoparticles. The FT-IR spectrum of Pectin (Fig. 1b) shows characteristic peaks at 3400-3600 cm^{-1} (O-H stretching alcoholic and acidic), 2923 cm^{-1} (C-H stretching), 1725 cm^{-1}(C=O of ester), 1618 cm^{-1} (COO^- asymmetric stretching), 1412 cm^{-1} (COO^- symmetric stretching). After core-shell, the Pectin with Fe_3O_4 shows the peaks at 3422 cm^{-1} (O-H stretching),2923 cm^{-1} (C-H stretching), 1626 cm^{-1} (COO^- asymmetric stretching) and 577 cm^{-1} cans be assigned to Fe_3O_4 (Fig. 1c). As predicted (Fig. 1d), several new bands have been detected in 1100, 1200 and 3200 cm^{-1} that were corresponding to the stretching vibrations of the C-N, Si-O functional group and NH_2 (that overlap with peaks of OH in pectin) bond that approval of surfaces chemical modification of the Fe_3O_4@pectin with the (3-Aminopropyl) triethoxysilane. FT-IR spectrum Of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide nanoparticles (Fig. 1e), the presence of a weak peak of 1650 cm^{-1}, which is covered by peaks of carbonyl group of pectin and peaks of NH_2 , overlap with peaks of OH in pectin, indicates the formation of a Schiff base in the structure of this catalyst. In the FT-IR spectrum of the Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II), the shifting of the stretching vibration of the C=N groups to lower wave-number confirms the coordination of Cu metal ions to the nitrogen atoms of the Schiff base.

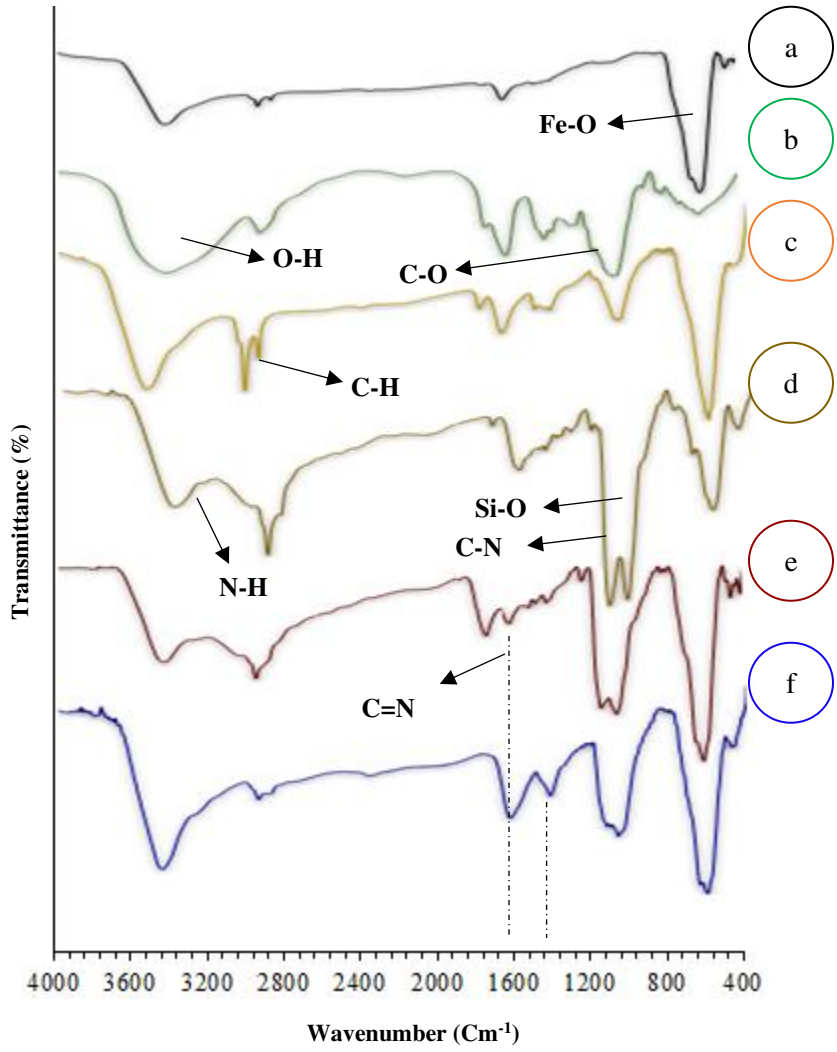


Fig. 1: FT-IR spectra of a)Fe_3O_4, b) Pectin, c) Fe_3O_4 @ Pectin, d) Fe_3O_4 @ Pectin@APTES, e) Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide, f) Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

The TEM method was used to gain further insight into the structure of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanostructures. Monodispersed nanoparticles were identified with a relatively uniform morphology (Fig. 2). The average diameter of nanostructures is obtained based on the 15 nm particle size distribution histogram (Fig. 2).

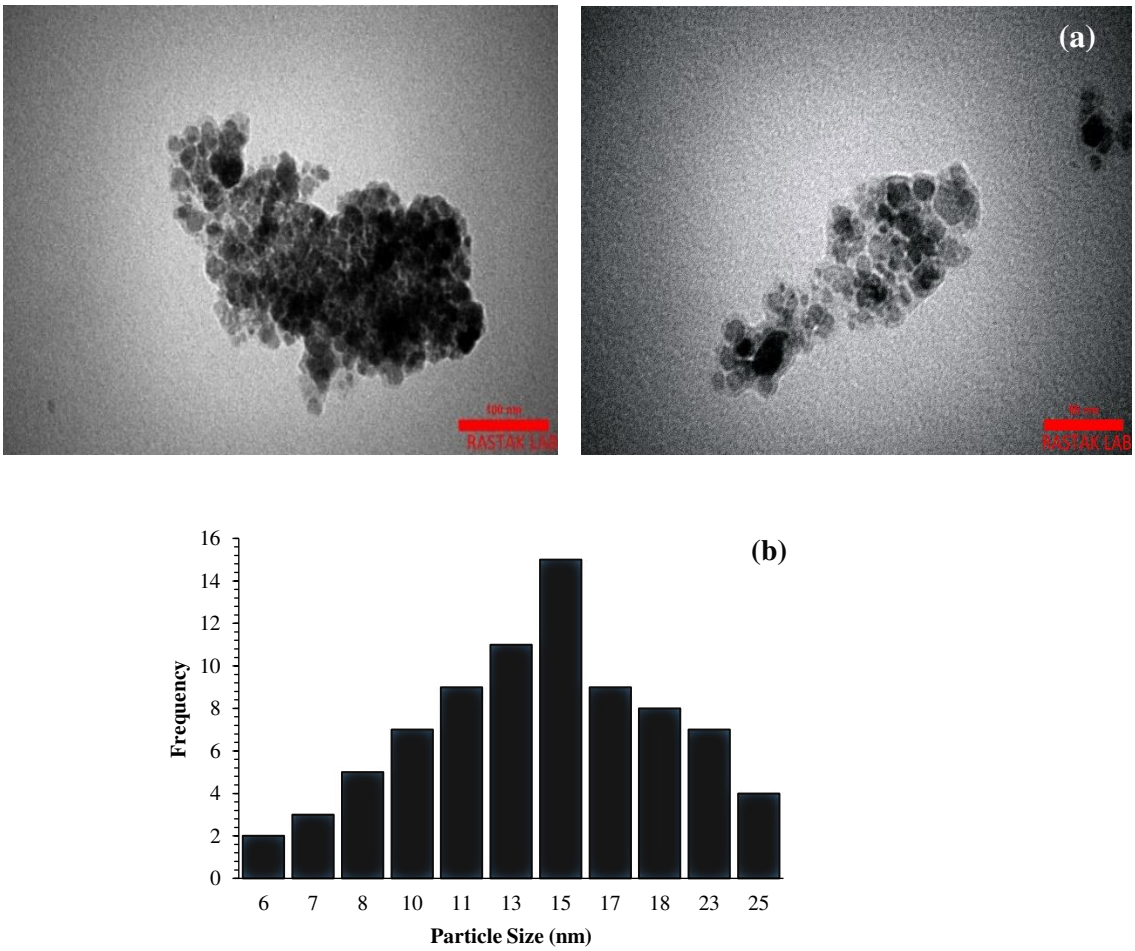


Fig. 2: TEM images (a) Particle size distribution histogram (b) of the Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

The thermal degradation behavior of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) catalyst was investigated by TGA analysis, and its curve is shown in Figure 3 that there are three thermal stages. In the first stage that occurs at temperatures of 50 to 100°C, mass loss of about 4% due to the desorption of water molecules in the nanocatalyst surface. The second stage, which weight loss of about 10%, occurs in the temperature range of 200 to 350°C, is related to the major degradation of pectin, because pure pectin is degraded at a temperature of 300 to 500 °C. The third stage of the weight loss of 8% in the temperature range between 330 and 630 °C may be due to the thermal crystal phase alteration from Fe_3O_4 to γ-Fe_2O_3. Other stages of the weight loss of about 11% at the temperature with a gentle slope of 400–800 °C were assigned due to the decomposition of the immobilized organic moieties on the surface of the Fe_3O_4@Pectin core-shell nanoparticles.

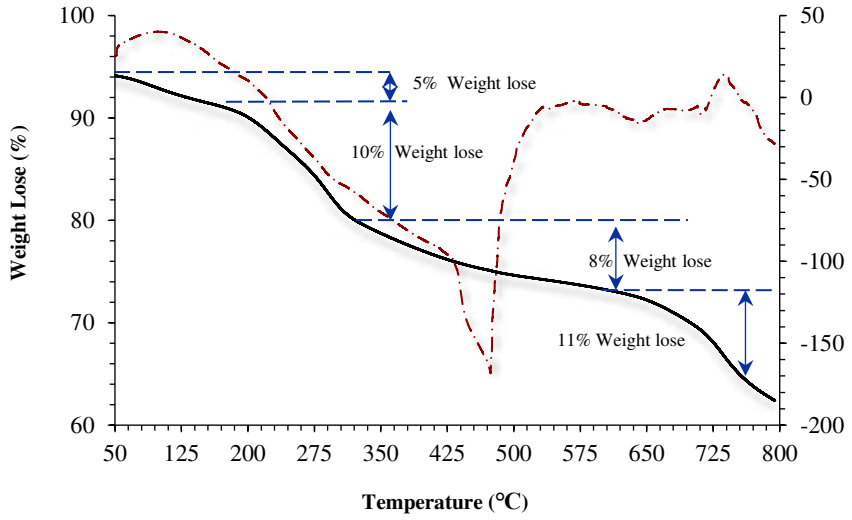


Fig. 3: The TGA curve of the Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

The Field Emission Scanning Electron Microscopy image and Energy Dispersive X-Ray analysis of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) were characterized by FESEM and EDX (Fig. 4). FESEM analysis of products (Fig. 4a) provides information on the size and morphology of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II). The results showed the average product size of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanoparticles was less than 24 nm. By EDX analyzing, the distribution of elements in Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) were studied (Fig. 4b). As can be seen, elements of Fe, Si, O, C, N, and Cu are present in the structure of the catalyst, indicating that our catalyst is well synthesized.

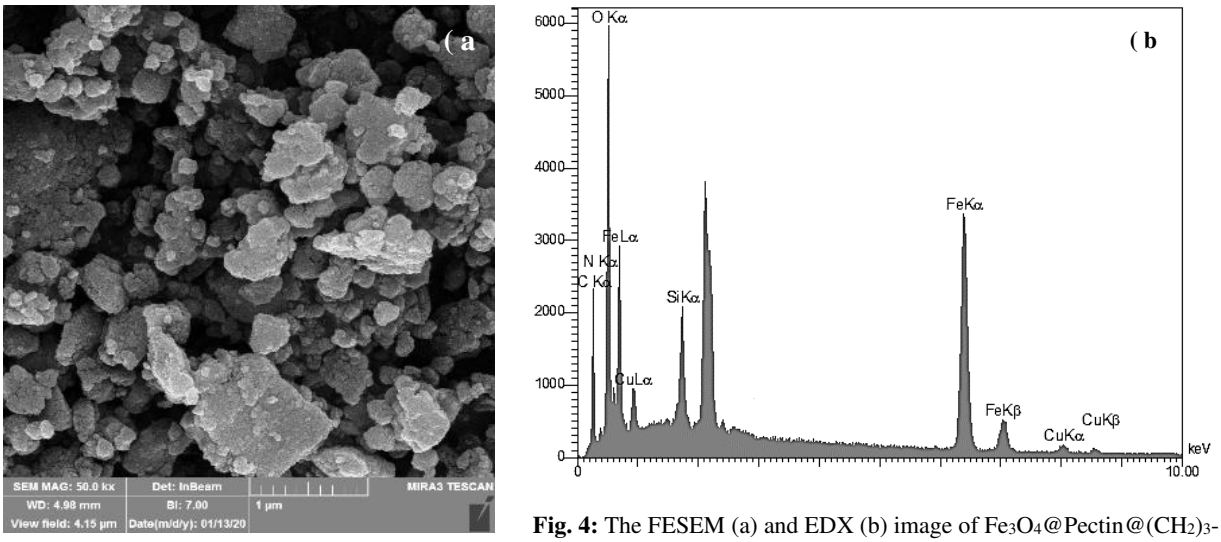


Fig. 4: The FESEM (a) and EDX (b) image of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

The magnetic properties of Fe_3O_4 (Fig. 5a), Fe_3O_4@Pectin (Fig. 5b) and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanoparticles (Fig. 5c) were recorded at room temperature using the VSM method (Fig. 5). 63.23, 53.23 and 36.93 emu/g were the saturation magnetization values for Fe_3O_4, Fe_3O_4@Pectin and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanoparticles. Therefore the saturation magnetization value of Fe_3O_4 after coating with pectin, APTMS and acetamide (Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)) decreases significantly from about 63.23 emu/g to 36.93

emu/g. The pectin shell that surrounds the Fe_3O_4 nanoparticles reduce the interactions between these particles. However, despite the decrease in saturation magnetism, the catalyst can still be rapidly and easily removed from the reaction media using an external magnetic field.

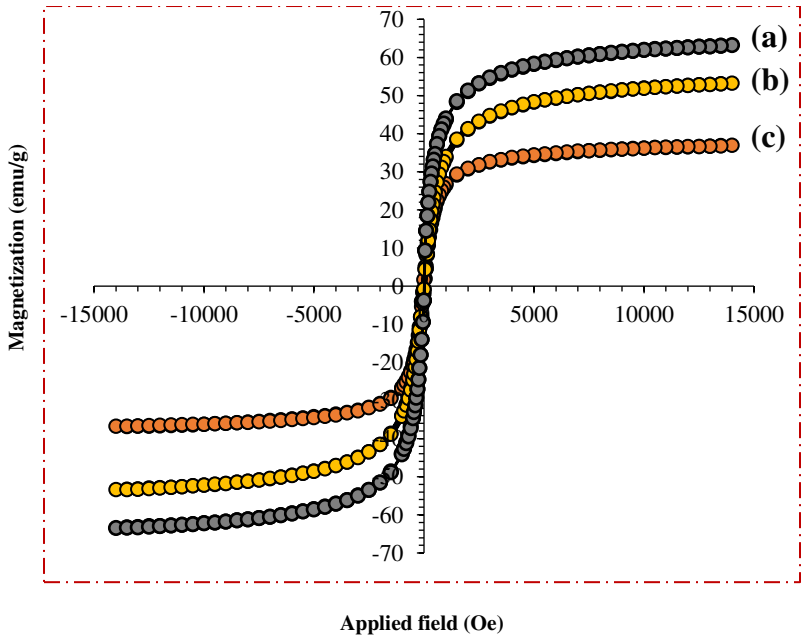


Fig. 5: The magnetic properties of a) Fe_3O_4 b) Fe_3O_4@Pectin c) Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

X-ray diffraction patterns of Fe_3O_4, CuO, and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) in the 2θ range between 10° and 80° are shown in Figure 6. The XRD pattern of Fe_3O_4 shows six characteristic diffraction peaks according to the cubic crystal system at 30.3°, 35.8°, 43.6°, 54.8°, 57.3°, and 63.2° (2Θ), corresponded respectively to the (220), (311), (400), (422), (511), and (440) miller indices, according to the database of maghemite (See Fig. 7)[67,68]. Also, the XRD pattern of the CuO (Fig. 7) shows the peaks at 2θ = 32.07°, 35.47°, 35.82°, 48.72°, 52.97°, 58.02°, 62.47°, 67.87° and 69.32° corresponding to the (110), (111), (022), (202), (202), (113), (022), (220) and (222) crystallographic phases in PXRD pattern are related to CuO.[69,70] The XRD pattern of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) was also examined as shown in Figure 7 that matches well with the characteristic peaks of bare Fe_3O_4 and CuO, these explanations, these results imply that the spinel structure of Fe_3O_4 and Cu(II) has been retained during the process of catalyst preparation. Also, the peak at 18°, which is related to pectin in Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II), indicates that it is also present in the structure of the pectin catalyst[67].

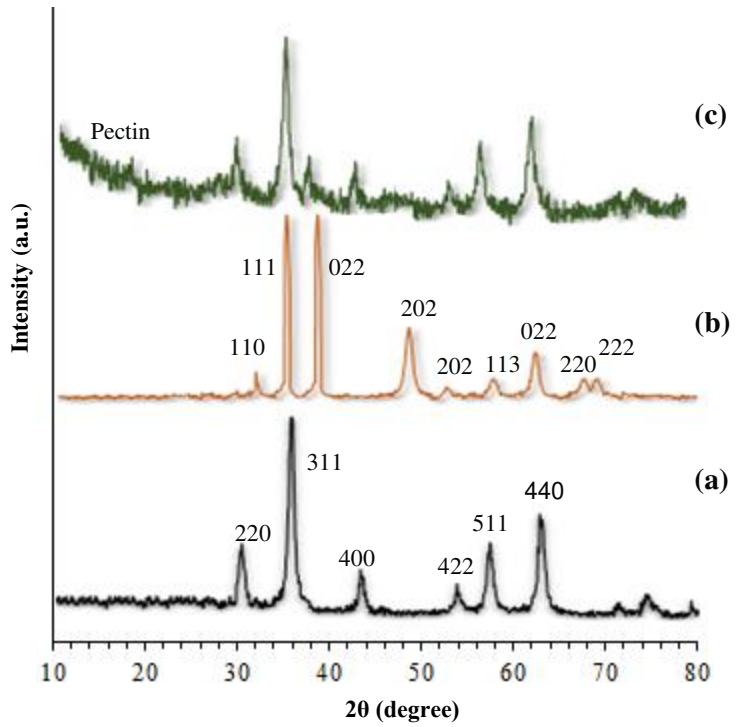


Fig. 6 : XRD of a) Fe_3O_4 b) CuO c) Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

2.2. Evaluation of the catalytic actuality of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) in the reactions of synthesis of triazole derivatives

The catalytic activity of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanocatalysts in the synthesis of 1,2,3-triazole derivatives were investigated. The reaction of benzyl chloride, sodium azide and phenyl acetylene in the presence of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) catalyst was selected as a model. The effect of different parameters on the catalytic activity of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) was investigated. Reactions were performed with various solvents such as ethanol, methanol, H_2O, n-Hexane and in solvent-free conditions (Fig. 7-I). Ethanol and methanol showed moderate activity, whereas solvent-free and n-Hexane were not suitable for this reaction. Further investigation of solvents showed that when used H_2O as a solvent, the yield of the desired product increases significantly. Therefore, water, which is the cheapest, safest, and environmentally green solvent, is the best choice for this reaction. Then the effect of the amount of catalyst was investigated. The reaction was performed at different levels of the amount of catalyst at 75 °C (Fig. 7-II). 0.5 mol% of the amount catalyst was most effective in providing high yield. Increasing the amount of catalyst decreased the reaction efficiency even after a longer reaction time. Also, the product was not obtained when the reaction was performed without the presence of catalyst. In the next step, the effect of temperature on the reaction was investigated (Fig. 7-III). At room temperature no improvement was observed, however, the best efficiency was observed at 65 °C. After several experimental optimizations, the optimal reaction conditions for the synthesis of 1,2,3- triazole derivatives are as follows: 0.5 mol% of catalyst in H_2O and 65 ºC.

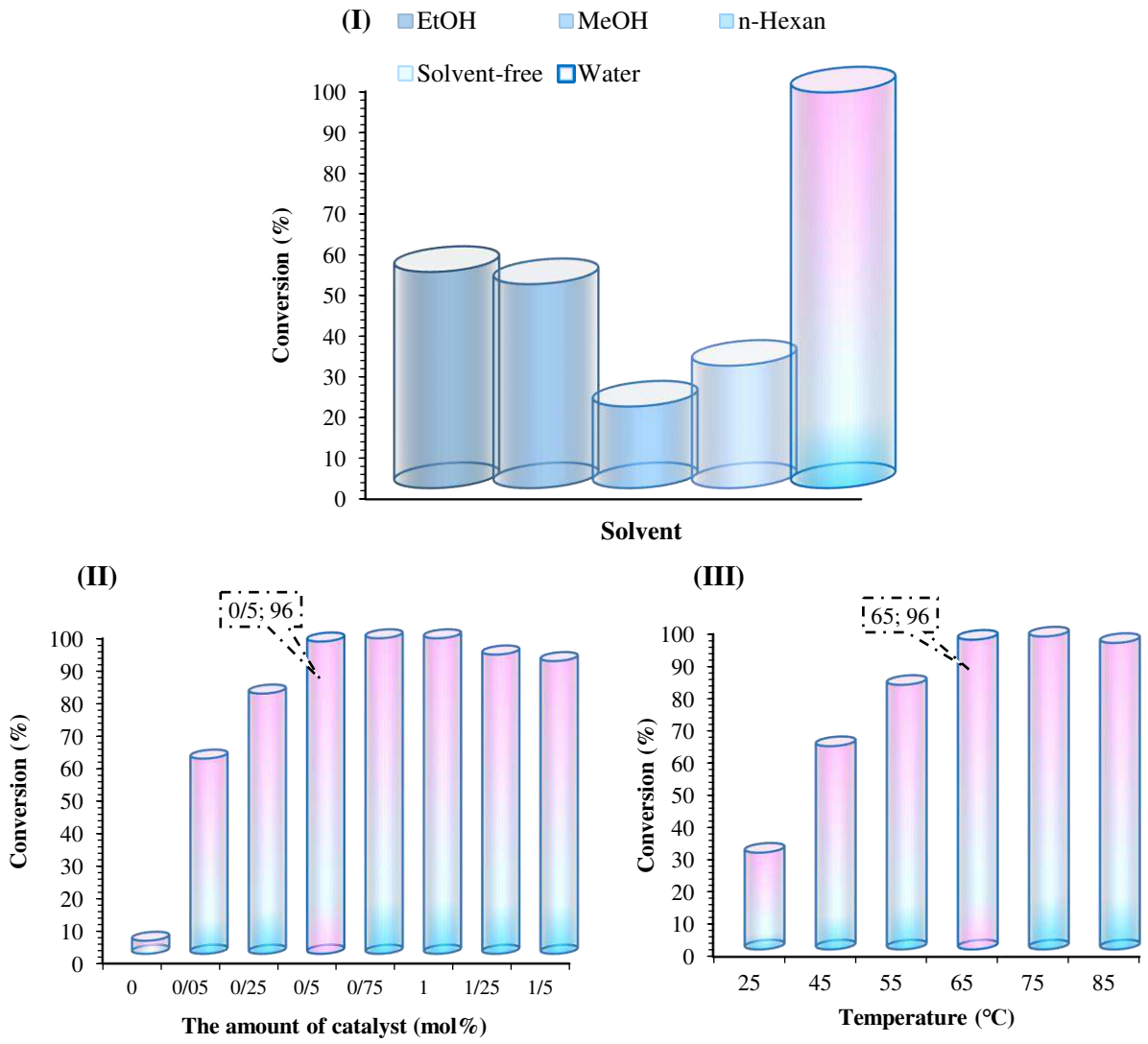
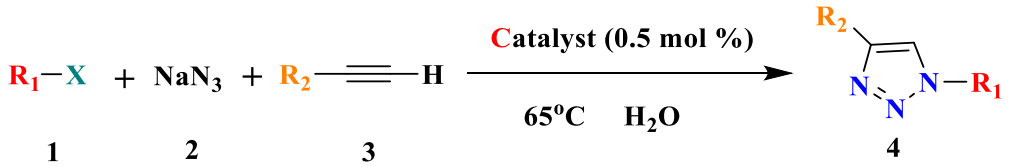


Fig. 7: Screening of solvent, amount catalyst, and temperature for click reaction with a molar ratio of benzyl chloride, sodium azide, phenylacetylene and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) as catalyst

After determining the optimized reaction conditions, the general use of the Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) catalytic system with different aryl or alkyl halides and alkynes for the synthesis of 1, 2, 3-triazole derivatives was studied. Reactions of benzyl chloride with sodium azide and phenylacetylene afforded the corresponding triazoles in high to excellent yields (Table 1, entries 1-4). Also, reactions of benzyl chloride with aliphatic alkynes required longer reaction times than aromatic alkynes to give high yields of the corresponding cycloaddition reactions (Table 1, entries 5, 6). Furthermore, the reaction of phenacyl bromide with alkynes, like benzyl chloride, proceeded well and provided the corresponding products at 87-98 % isolated yields (Table 1, entries 7-14). Generally, all the substrates had the related products in high yields, But the benzyl chloride and phenacyl bromide with electron-donating substituents (such as methyl) or no substituents, have higher reaction efficiencies than benzyl chloride and phenacyl bromide with electron-withdrawing substituents.

Table 1. Multi-component synthesis of 1,2,3-triazole derivatives at 65 °C temperature using water as solvent and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) as catalyst [a]



Entry	R_1	R_2	X	Products	Time (min)	Yield [b] (%)	TON	TOF
1	Ph-CH_2	Ph	Cl	4a	120	97	194	97
2	4-Me-Ph-CH_2	Ph	Cl	4b	125	95	188	90.25
3	4-Cl-Ph-CH_2	Ph	Cl	4c	130	93	188	87.03
4	2-Cl-Ph-CH_2	Ph	Cl	4d	135	92	184	81.77
5	Ph-CH_2	Me_2C–OH	Cl	4e	140	94	188	80.68
6	4-Me-Ph-CH_2	Me_2C–OH	Cl	4f	140	93	186	79.82
7	4-Cl-Ph-CH_2	Me_2C–OH	Cl	4g	120	95	190	95
8	2-Cl-Ph-CH_2	Me_2C–OH	Cl	4h	130	96	192	87.27
9	Phenacyl	Ph	Br	4i	90	98	196	130.66
10	4-Br-Phenacyl	Ph	Br	4j	90	91	182	121.33
11	4-NO_2-Phenacyl	Ph	Br	4k	90	90	180	120
12	Phenacyl	Me_2C–OH	Br	4l	100	90	180	108.43
13	4-Br-Phenacyl	Me_2C–OH	Br	4m	100	87	174	104.81
14	4-NO_2-Phenacyl	Me_2C–OH	Br	4n	100	87	174	104.81
15	Phenacyl	CH_2OH	Br	4o	100	92	184	110.84
16	4-Br-Phenacyl	CH_2OH	Br	4p	100	89	178	107.23

[a] Alkyl halides (1.0 mmol), Sodium azide (1.2 mmol), alkyne (1.0mmol), catalyst (0.5 mol %) were placed in a test tube on a stirrer at 65 °C for 120 minutes under H_2O (2ml) as a solvent
[b] Yields of isolated product

Also, to confirm the performance of the catalyst in comparison with its components, the efficiency of Fe_3O_4, Pectin, Fe_3O_4@Pectin and Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) were separately studied in the model reaction (Fig. 8).As shown in Figure 8, no product was gained by using Fe_3O_4, Pectin and Fe_3O_4@Pectin species. However, in the presence of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II), the reaction efficiency was very favorable. These findings indicate that the efficiency and strength of the catalyst increase with the presence of copper metal.

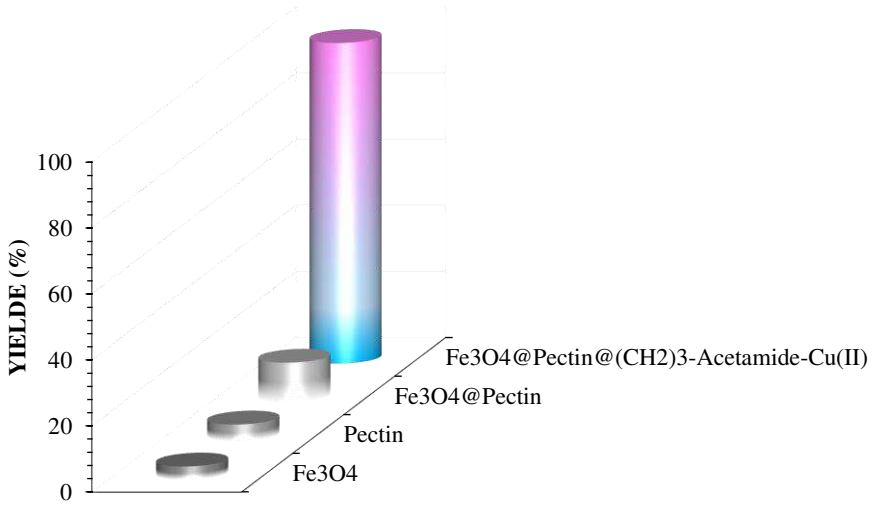
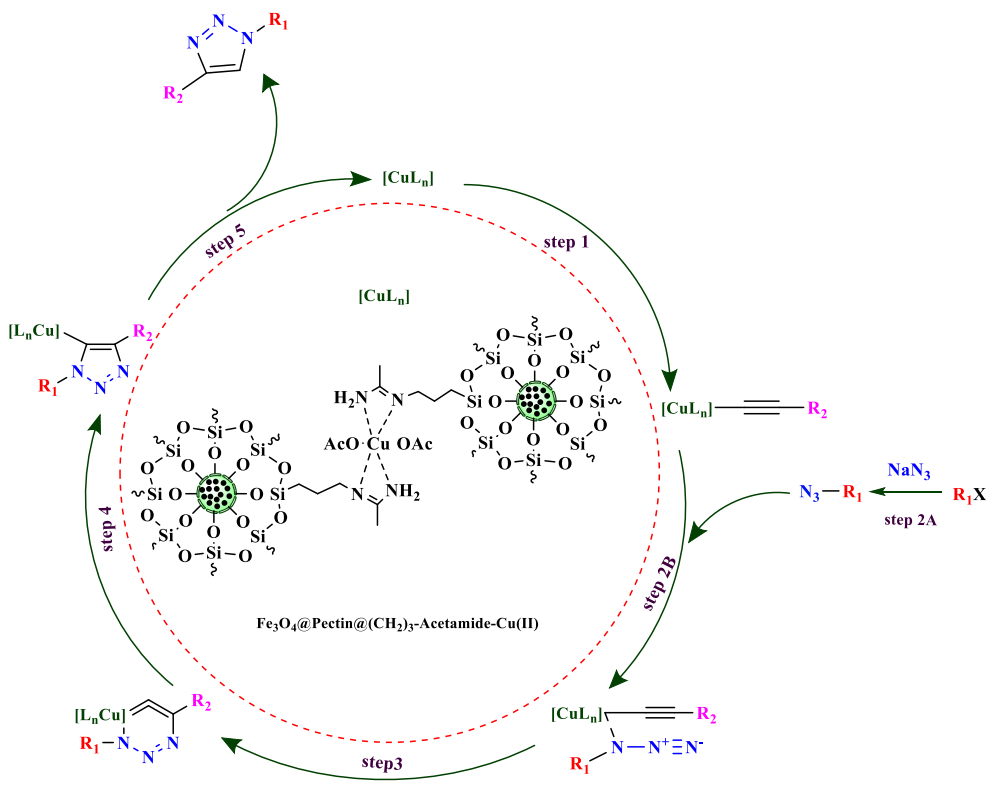


Fig. 8: Comparison of the performance of catalysts with each other. Reaction conditions: Benzyl chloride (1.0 mmol), Sodium azide (1.2 mmol), phenylacetylene (1.0mmol), catalyst (0.5 mol %), H_2O (2ml) as a solvent at 65 ° C for 120 minutes.

Based on previous reports [76] and our observations, a suggested mechanism for the synthesis of triazole derivatives catalyzed by Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) nanocatalyst is shown in Scheme3. In the first step, Cu–acetylide complex was generated from the reaction of Cu and aryl acetylene (step 1). Then, the alkyl or benzyl azide preparation in situ from sodium azide and alkyl halide [in situ formation (Step 2A)] is attached to [Cu] acetylide and a π-complex is formed as an intermediate product (step 2B). In the next step, the distal nitrogen of the azide attacks to the carbon of the Cu–acetylide to give a six-membered metallacycle (step 3). Finally, ring contraction to a Cu–triazolide complex (step 4) is followed by protonolysis that delivers the target product along with regeneration of Cu catalyst (step 5).



Scheme 3: Plausible mechanism for synthesis of 1,2,3- triazole derivatives by Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) NPs catalyst

The recyclability of the catalyst was performed for 5 cycles in optimal conditions (Fig. 9). The results indicated that the used material was also active as a catalyst for five runs without a dramatic loss of catalytic activity. These results indicate that the catalyst of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) has very good performance and stability under reaction conditions.

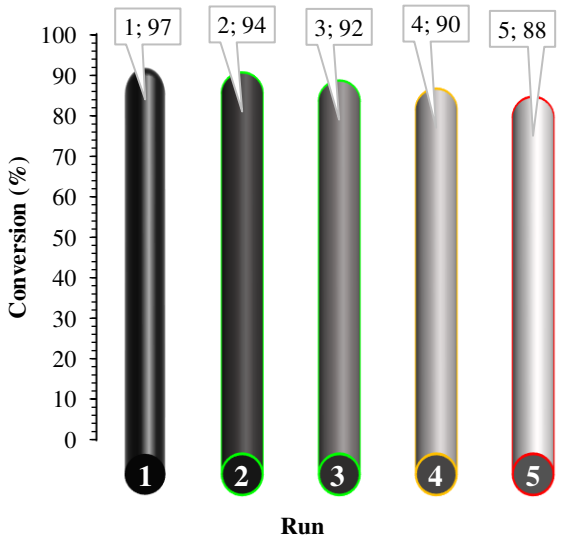


Fig. 9: Recycling potential of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)

A special property of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) is the stability of the framework under reaction conditions which preserves the heterogeneous nature of the system (Fig. 10). To evaluate the heterogeneous nature of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II), the hot leaching test was carried out for click reaction in H_2O as solvent at 65 °C. For this experiment, the catalyst was removed after 60 minutes from the reaction time, and the residual solution was stirred in the absence of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) for an additional 120 minutes. The result showed that no further increase in either the conversion or selectivity occurred in the absence of the catalyst. This finding established that Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) is a typical heterogeneous catalyst.

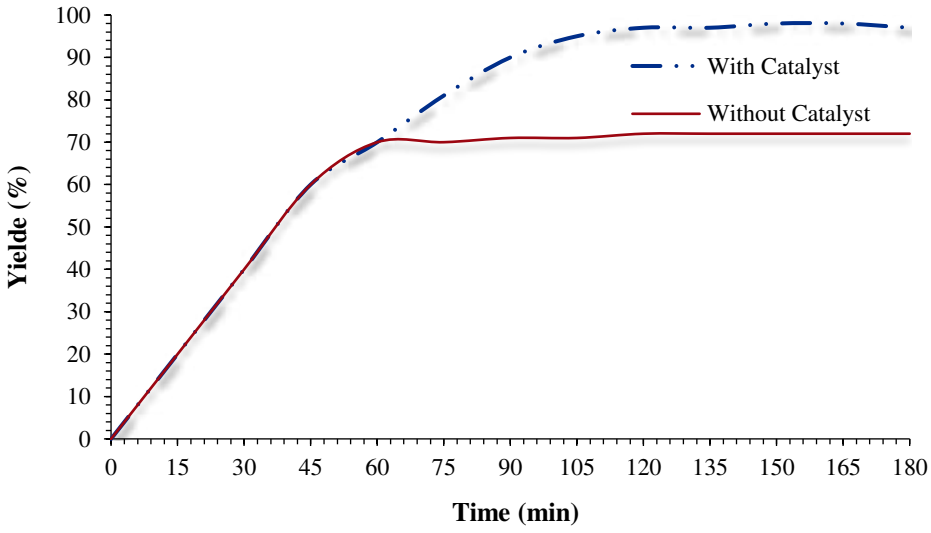


Fig. 10: Hot leaching test for click reaction using Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) under optimized conditions

Comparison of the catalytic activity of Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) catalyst in click reaction with other catalysts is shown in Table 2 for 1-benzyl-4-phenyl-1H-1,2,3-triazole and Table 3 for 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazole-1-yl)ethanone. So far, several catalysts that have been used, as well as to the advantages, also had disadvantages, such as including long reaction time, low efficiency, use of high temperature for preparing these compounds. In the last few years, many triazole derivatives have been considered in clinical trials. The synthesized Fe_3O_4@Pectin@$(CH2)_3$-acetamide-Cu(II) catalyst has many advantages over the reported catalysts such as suitable reaction conditions, short reaction time, high reaction efficiency, and lower catalyst amount.

Table 2. Synthesis of 1-benzyl-4-phenyl-1H-1,2,3-triazole (4a) using different catalysts and reaction conditions.

Entry	Catalyst	Catalyst amount	Solvent	Temp.(°C)	Time(h)	Yield[a] (%)	Ref.
1	Cu/C	1 mol%	H_2O	100	1	91	77
2	POSS–SAL–Cu	1 mol%	H_2O	70	12	95	78
3	$[Cu(tzol)_2]$	1.9 mol%	H_2O	70	12	96	79
4	CuNPs/MagSilica	4.3 mol%	H_2O	70	2	83	80
5	Catalysts 4	0.86 mol%	H_2O	70	14	76	81
6	LDH-Cu^{II}	0.004 g	H_2O	70	12	96	82
7	HCP-NHC–Cu	0.45 mol%	EtOH	80	8	91	83
8	**Fe_3O_4@Pectin@$(CH_2)_3$ -Acetamide-Cu(II)**	**0.5 mol%**	**H_2O**	**65**	**2**	**97**	**This work**

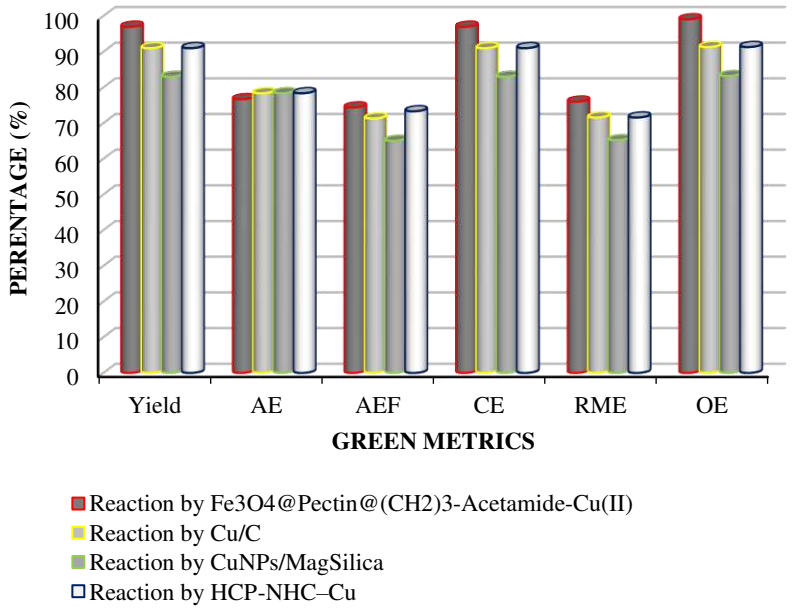
[a] Yields of isolated product

Table 3. Synthesis of 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazole-1-yl)ethanone(4i) using different catalysts and reaction conditions.

Entry	Catalyst	Catalyst amount	Solvent	Temp.(°C)	Time(h)	Yield[a] (%)	Ref.
1	Cu NPs/Graphite	5 mol%	H_2O/CH_3OH	70	12	74	84
2	$CuFe_2O_4$	0.012 g	H_2O	70	8	78	85
3	$PANs_2FCu$	2 mol%	H_2O	60	3	91	86
4	$CuO–CeO_2$	0.1 g	EtOH	reflux	1	92	87
5	A-21CuI	0.06:1 g	acetonitrile	reflux	1	89	88
6	Cu(II)phen@SBA-15	0.5 mol%	H_2O	70	6-14	87	89
7	CuI-USY	0.02 g	H_2O	90	15	62	90
8	**Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II)**	**0.5 mol%**	**H_2O**	**65**	**1.5**	**98**	**This work**

[a] Yields of isolated product

Finally, a series of green metrics such as atom economy (AE), atom efficiency (AEF), carbon efficiency (CE), reaction mass efficiency (RME), optimum efficiency (OE), process mass intensity (PMI), E-factor (E), solvent intensity (SI), and water intensity (WI) were calculated to evaluate the greenness of the one-pot multi-component reaction of benzyl chloride, sodium azide, phenylacetylene for 1-benzyl-4-phenyl-1H-1,2,3-triazole (Fig. 11) and Phenacyl bromide, sodium azide, phenyl acetylene for 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanone (Fig. 12). To stable, the more greenness of the current catalyst over the reported catalysts in the one-pot multi-component reaction of benzyl chloride, sodium azide, phenylacetylene for 1-benzyl-4-phenyl-1H-1,2,3-triazole (Table 2, entries 1,3 and 9) and and Phenacyl bromide, sodium azide, phenylacetylene for 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanone (Table 3, entries 1, 4 and 6), the current catalyst's green metrics was compared with those of three previously reported catalysts. As it is shown in Figures 11 and 12, the high values of the AE, AEF, CE, RME, and OE for the synthesis of 1-benzyl-4-phenyl-1H-1,2,3-triazole and 1-Phenyl-2-(4-phenyl-1H-1,2,3-triazol-1-yl)ethanone, illustrate well the greenness of the process. The lower the PMI, E, and SI, the more favorable process is because of green chemistry.



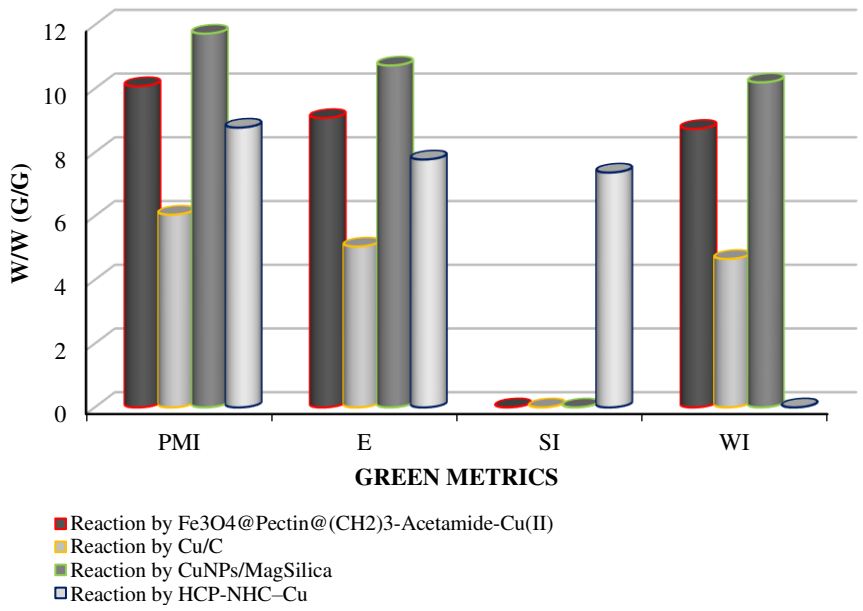
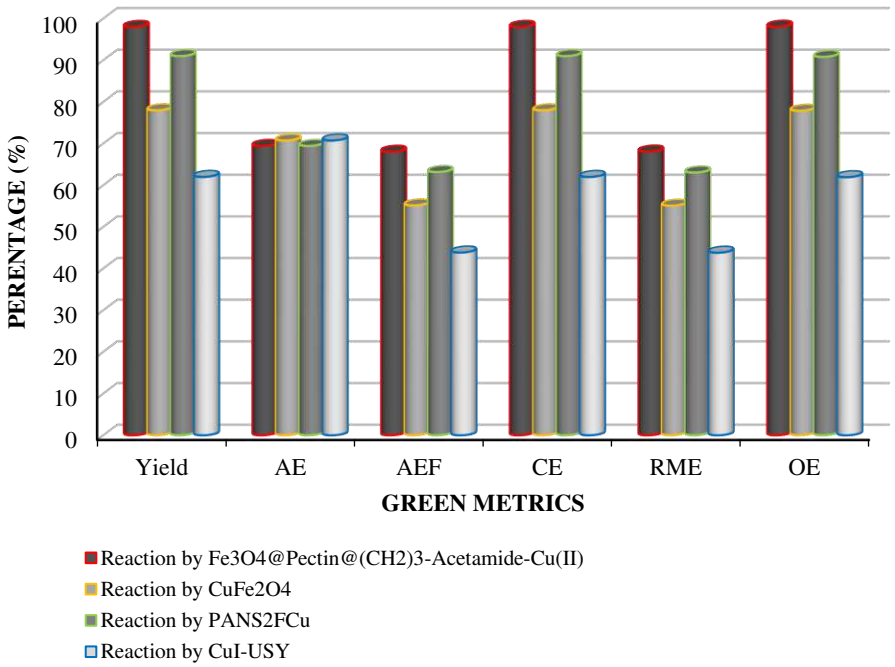


Fig. 11: Green metrics including (a) AE, AEf, CE, RME, OE and (b) PMI, E, SI and WI for the one-pot Multi-component reaction of benzyl chloride, sodium azide, phenylacetylene, and catalysed by Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) (this study), Cu/C (Table 2, entry 1), CuNPs/MagSilica (Table 2, entry 4) and HCP-NHC–Cu (Table 2, entry 7); W/W = Weight/Weight (g/g)



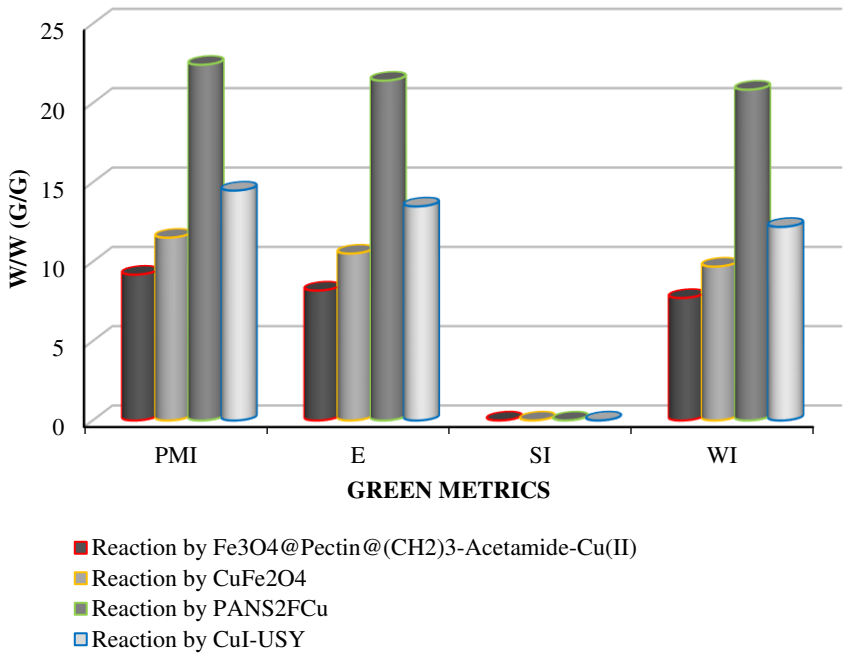


Fig. 12: Green metrics including (a) AE, AEf, CE, RME, OE and (b) PMI, E, SI and WI for the one-pot Multi-component reaction of Phenacyl bromide, sodium azide, phenylacetylene, and catalysed by Fe_3O_4@Pectin@$(CH_2)_3$-Acetamide-Cu(II) (this study), $CuFe_2O_4$ (Table 3, entry 2), $PAN_{S2}FCu$ (Table 3, entry 3) and CuI-USY (Table 3, entry 7); W/W = Weight/Weight (g/g)

Conclusions

We have successfully developed a green heterogeneous catalytic system for Huisgen cycloaddition by immobilizing of copper ions on polymer-coated magnetic nanoparticles, which can be readily prepared from simple materials. The solid support was prepared from Schiff base functionalized pectin in the presence of Fe_3O_4 magnetic nanoparticles. The presence of pectin makes the prepared catalyst more cost-effective and eco-friendlier. The prepared catalyst exhibits are used for the synthesis of 1,2,3-triazole derivatives. Under the optimized reaction conditions, a wide range of 1,2,3 triazole derivatives was synthesized from various alkyl halides and alkyne using the prepared catalyst in the presence of water as a standard green solvent. This catalyst can be considered as a heterogeneous version of Cu (II) and can be easily prepared from starting materials. Catalyst properties include: high activity, high stability, easy recovery and reusability of the catalyst. Also, the magnetic nature of the catalyst eliminates of the need for centrifugation and filtration of the catalyst from the reaction mixture, making it possible to remove the catalyst from the reaction medium with the help of an external magnet. Finally, it can be said that the catalyst is recyclable and has good stability for click reaction.

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