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FULL PAPER

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# Multi-component reaction-functionalized chitosan complexed with copper nanoparticles: An efficient catalyst toward $A^3$ coupling and click reactions in water

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A novel bio-nanocomposite nanocatalyst with highly dispersed particles is synthesized through covalent functionalization of chitosan biopolymer by the multicomponent reaction (MCR) strategy. Surface functionalization of chitosan through MCR is led to the grafting of carboxamide type ligands with a high affinity toward complexation with copper nanoparticles. The catalytic activity of the synthesized catalyst was explored in various transformations such as $A^3$ coupling and click reactions in water. Reusability and non-hazardous nature of the catalyst, mild reaction conditions, operational simplicity, high yielding, and using water as a solvent are the main advantages of this catalytic protocol.

**KEYWORDS**
bio-nanocomposite, chitosan, copper nanoparticles, green reaction, multi-component reaction

## 1 | INTRODUCTION

Chitosan as a product of partial deacetylation of chitin is the second most abundant biopolymer in the world.[1] Due to the chitosan biocompatibility and biodegradability as well as its insolubility in alkaline water and organic solvents,[2] this naturally occurring polysaccharide have attracted tremendous attention in various fields such as water treatment,[3] textile industry,[4] optical and electronic devices,[5] drug delivery[6] and catalysis.[7] The presence of amine groups in the structure of chitosan provides a unique opportunity for metal ion sorption through chelation mechanisms and removing hazardous metals from aquatic environments.[8] Although most studies on chitosan have been conducted on the high absorption capacity of this polymer for the removal of environmental pollutants; from the year of 1980, a high number of publications have remarkably grown in the field of chitosan for supported catalysis.[9] So far, a wide variety of transition metals such as palladium,[10] copper,[11] silver,[12] platinum, and iridium[13] were placed on chitosan and used as a heterogeneous catalyst to promote various reaction types. Among these efforts only a few examples gave satisfactory results considering environmental standards and green chemistry principles.[9a,14] In fact, the low transfection efficiency of native chitosan and the lack of some functionalities that are highly desired for strong chelation leads to the significant leaching of metal ions in the reaction medium, which causes the environmental pollution and decreasing the recyclability of the preferred catalyst.[15] In this regard and to overcome these shortcomings of chitosan, the post-modification process can provide an efficient solution to the utilization of full capability of this natural polymer through the grafting of functional groups with the high coordination potency of metal ions.[15,16]

In the presence of organic ligands, copper(I) catalysts could well improve the productivity of click and coupling reactions under mild conditions.[17] However, some limitations and drawbacks of homogeneous copper catalytic

systems, for instance, usage of expensive or toxic ligands and reusing restriction of catalysts limit the application in catalytic systems. In recent years, heterogeneous copper-based catalysts have been widely studied, which can overcome these shortcomings.[8,18] $Cu_2O$ nanoparticles (NPs) as an environment-friendly catalyst, has attracted great attention owing to its high activity and extensive applicable areas.[19] Nevertheless, poor stability of $Cu_2O$ NPs, especially in solution is one of the significant drawbacks that affected the applicability of it in the catalytic systems. Chitosan has exhibited the distinct capability to stabilize metastable NPs such as Cu and $Cu_2O$.[2,20] Besides, chitosan as a support in many of catalytic reactions has been successfully used because of low cost, biocompatibility, biodegradability, nontoxicity and high surface area.[8,15,16]

Multi-component reactions (MCRs) represent superior robust synthetic procedures to produce high value-added scaffolds from readily available precursor components with a minimum number of chemical steps.[21] These types of reactions have long been the subject of medicinal chemistry and molecular biology due to their high productivity and inherent convergence.[22] The advancement, development, and application of MCRs are right now an essential and irrefutable part of the work of any pharmaceutical research unit. By utilizing these types of reactions in the preparation of novel functional materials, the union of material science has recently developed a new dimension in MCRs framework.[23] Functionalization of materials by MCRs is an innovative strategy which benefits all the advantages of multi-component reaction such as substrate diversity, degree of atomic economy, simplicity of operation, low cost, and reduced waste productions.[24] In recent years, significant progress has been made in expanding the scope of this strategy in various fields such as polymer chemistry,[25] drug delivery,[26] enzyme immobilization,[27] water treatment,[28] biosensors, and catalysis.[29] Although, at present significant advances are dramatically being made in this regard, this strategy is still at an early stage and there are a few numbers of reports in this context.

By concerning the shortcomings mentioned for chitosan as an ideal support and advantages of material functionalization by MCRs and also in continuation of our ongoing interest in developing catalytic systems for synthetic methodologies,[30] herein, we report a new strategy by utilization of multi-component reaction to construct carboxamide-ligands on chitosan skeleton to improve its ligation towards metal ions. This novel material represented the high affinity to coordination with copper NPs, leading efficient novel nanocatalyst to promote various transformations such as $A^3$ coupling and click reactions in water without significant loss of activity and metal leaching.

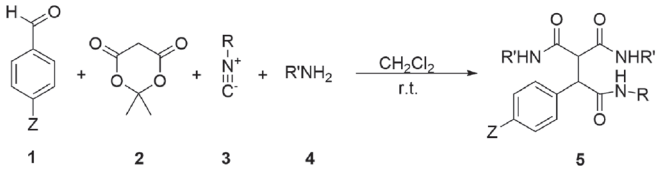
## 2 | RESULTS AND DISCUSSION

Recently, we have designed and reported an efficient method for the synthesis of triamide derivatives **5** *via* an isocyanide based MCR using aldehydes **1**, Meldrum's acid **2**, isocyanides **3** and amines **4** (Scheme 1).[31] This reaction presented a high potential for the construction of *pseudo* peptide skeletons that could be used for the strong chelation to the metals. In continuation of our recent works in developing catalytic systems based on material functionalizations with MCRs,[23] modification of chitosan as a natural polymer can be accomplished using MCR above to construct carboxamide-ligands on chitosan skeleton to improve its ligation towards copper ions. (Figure 1).

### 2.1 | Characterization of CS-MCR/$Cu_2O$ bio-nanocomposite

#### 2.1.1 | FT-IR analysis

Figure 2 represents the FT-IR spectra of CS, CS-MCR, and CS-MCR/$Cu_2O$ bio-nanocomposite. In the neat CS, FT-IR spectra can be seen a broad band of multiple peaks between 3200–3600 $cm^{-1}$ that can be related to the stretching of $-NH_2$ and –OH groups and hydrogen bonds of intramolecular and intermolecular. The peak about methane hydrogen atoms (C–H stretching) appeared at 2914 $cm^{-1}$. The absorption band of the carbonyl stretching of the secondary amide and the N-H bending vibrations of the *N*-acetylated residues (amide) appeared in the regain of the 1638 and 1626 $cm^{-1}$, respectively. The polysaccharide skeleton of the -C-O- and -C-N- stretching were respectively assigned between 1300–1450 $cm^{-1}$ and 1000–1200 $cm^{-1}$.[32] Compared to the FT-IR spectra of neat CS, CS-MCR expose a peak at




**SCHEME 1** Synthesis of triamide derivatives *via* an isocyanide based MCR

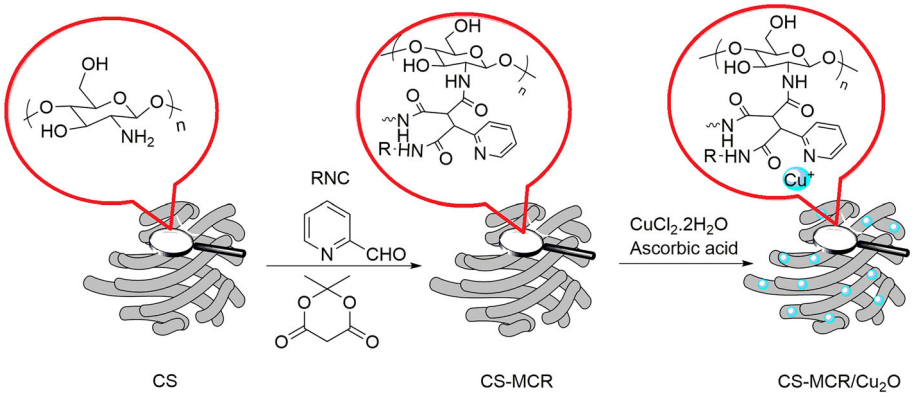



**FIGURE 1** Preparation of CS-MCR-Cu2O

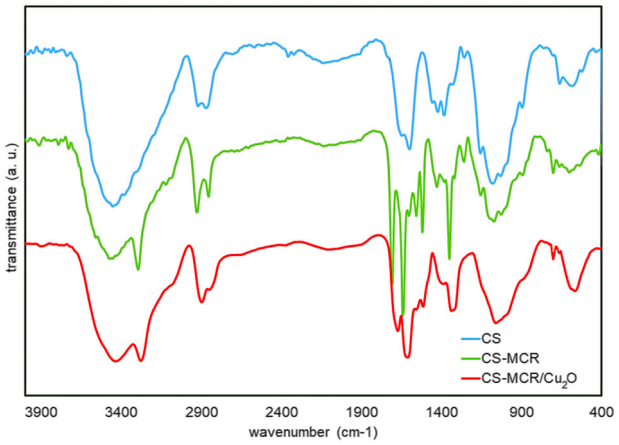



**FIGURE 2** FTIR spectra for the CS and CS-MCR/Cu2O bio-nanocomposite

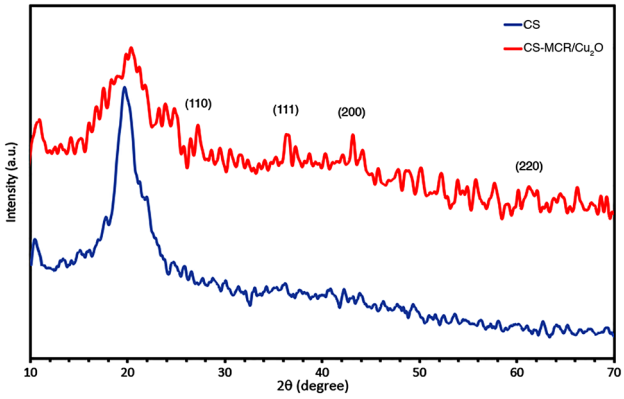



**FIGURE 3** XRD patterns of the CS and CS-MCR/Cu2O bio-nanocomposite

1650 $cm^{-1}$ and 3080 $cm^{-1}$ regions, which attributed to the amid band formation. Also, the intense characteristic bands of C–H stretching at 2800 and 2900 $cm^{-1}$ increased after the modification of CS through MCR. The spectra of CS-MCR and the CS-MCR/$Cu_2O$ bio-nanocomposite is similar with a little difference. The successfully *in situ* formation of $Cu_2O$ nanoparticle within the CS polymeric network is verified by the strong characteristic adsorption peak at 599 $cm^{-1}$ that related to the Cu-O bond vibration of $Cu_2O$.

### 2.1.2 | XRD analysis

The XRD pattern of the pure CS and CS-MCR/$Cu_2O$ bio-nanocomposite is shown in Figure 3. The neat CS shows the characteristic peaks of typical fingerprints of semi crystallinity CS at 2θ values of about 11° and 20°.[33] For the XRD pattern of CS-MCR/$Cu_2O$ bio-nanocomposite, the diffraction peaks at 2θ = 29.7°, 36.6°, 42.4°, 61.5° are respectively well corresponding to (110), (111), (200), (220) planes of cubic-structured $Cu_2O$.[34] Besides, the wide peak at 2θ value of 11° and 20° are related to the typical nature of CS. These results revealed the *in situ* formation of $Cu_2O$ NPs within CS-MCR/$Cu_2O$ bio-nanocomposite with preservation of crystal structures of $Cu_2O$ NPs.

### 2.1.3 | TGA analysis

TGA diagrams of the CS and CS-MCR/$Cu_2O$ bio-nanocomposite are shown in Figure 4. Both samples demonstrated three distinct stages under air from room temperature to 600 °C. In the first stage (removing the trace of water consequence), between 50 and 150 °C with loss of water the inter- and intramolecular anhydride bonds forming occurs. Also, in this stage, by decarboxylation process of the free carboxylic groups and anhydride, $CO_2$ is released. For CS and CS-MCR/$Cu_2O$, the first weight loss was respectively observed 18.1 and 15.2%. In the second stage (range from 155 to 400 °C) can be seen 60.3 and 45.2% weight loss for CS and CS-MCR/$Cu_2O$ that is due to the heat decomposition of sample carboxyl

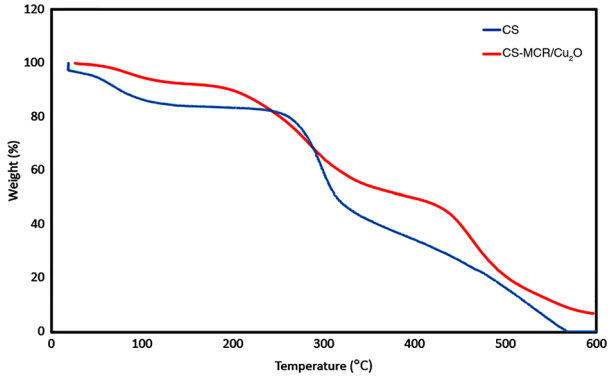



**FIGURE 4** TGA diagrams of the CS and CS-MCR/Cu2O bio-nanocomposite

groups, respectively.[35] According to the TGA data, by polymeric modification with MCR and the presence of $Cu_2O$ NPs in the polymeric matrix, the second step weight loss were decreased from ~280 °C for CS to ~210 °C for CS-MCR/$Cu_2O$, which is probably because of the creation of solidarity and disorders that altered the composite's degradation mechanism. Meanwhile, more study is required to clarify the exact mechanism to fully understand. The pure CS destroyed around 580 °C, but for the prepared bio-nanocomposite, there are still up to ~6% weight of bio-nanocomposite stayed in the container after the burning process. That is probably attributed to the reduction of $Cu_2O$ by polymer through the thermal reduction process.

### 2.1.4 | Morphological characteristic

Figure 5 displays the SEM images of the CS-MCR/$Cu_2O$ bio-nanocomposite surface at low and high magnification. As seen in Figure 5a, the surface morphology of the bio-nanocomposite is tightly and smoothly severe wrinkles with many cavities. This could be related to the interfacial interactions between CS chains and $Cu_2O$ NPs that possibly act as intermolecular cross-linkers (Figure 1). As shown in the high magnification image (Figure 5b), in the surface of CS-MCR/$Cu_2O$ because of wrapped $Cu_2O$ NPs in CS matrix can be seen roughly and porously cubic shape powders similar to ellipsoidal with a diameter of ~40–60 nm. For catalytic administration of $Cu_2O$, this structure could has a suitable affinity for the diffusion of reagent into the bio-nanocomposite without aggregation of $Cu_2O$ NPs.

Figure 6 represents the transmission electron microscopy (TEM) image of CS-MCR/$Cu_2O$ bio-nanocomposite. As shown in Figure 6, copper species disperse as dark spherical-like shapes over the string shape of the chitosan fibers.

### 2.1.5 | EDX, CHN and ICP-OES analysis

The element information about CS-MCR/$Cu_2O$ bio-nanocomposite was achieved by using EDX analysis (Figure 7). The successful formation of the $Cu_2O$ nanoparticle in the bio-nanocomposite with high purity was indicated by the EDX spectrum which presented the only existence of C, O, N and Cu. We have also performed CHN analysis for CS and CS-MCR/$Cu_2O$ composites in which the C: H: N ratio in CS is ~40.0: 7.7: 7.41 whereas for CS-MCR/$Cu_2O$, C: H: N ratio is ~44.2: 6.8: 8.1 indicating the surface functionalization of chitosan. Furthermore, to determine the loading of copper in the catalyst, the inductively coupled plasma-optical emission

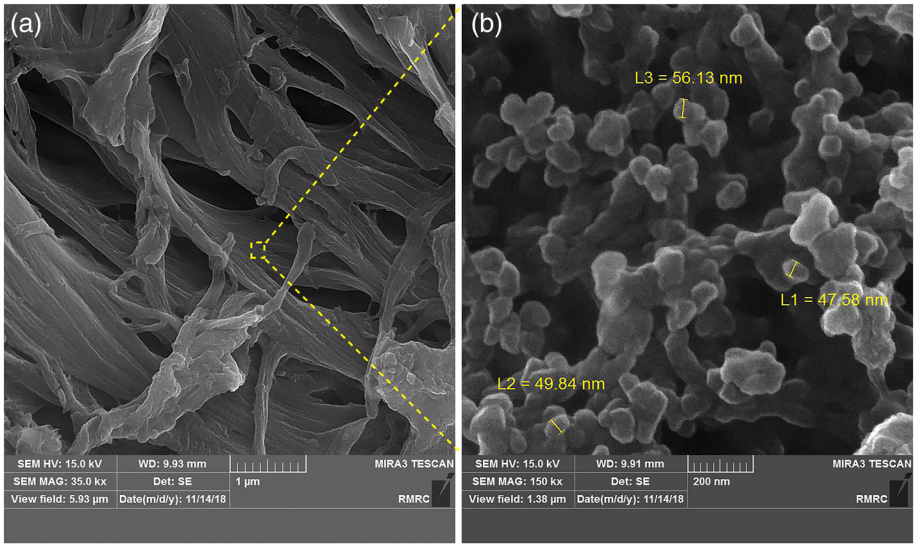



**FIGURE 5** SEM image of the CS-MCR/Cu2O bio-nanocomposite at low (a) and high magnification (b)

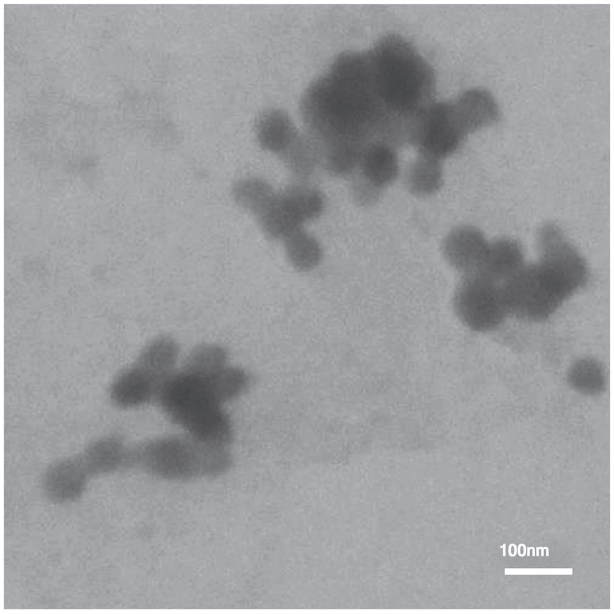



**FIGURE 6** TEM image of the CS-MCR/Cu2O bio-nanocomposite

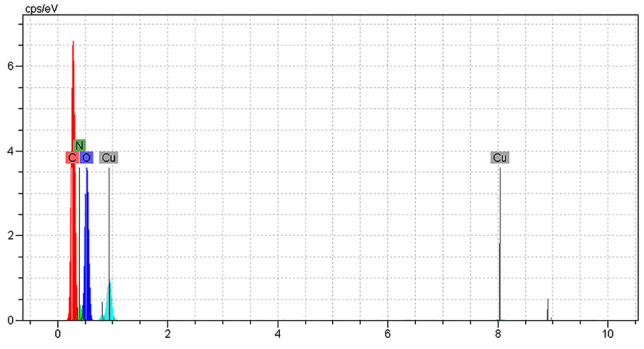



**FIGURE 7** EDX spectrum of the CS-MCR/Cu2O bio-nanocomposite

spectroscopy (ICP-OES) analysis of CS-MCR/$Cu_2O$ was carried out. The results showed 3.3 wt.% copper loading in the final catalyst.

### 2.1.6 | Catalytic activity of CS-MCR/$Cu_2O$ bio-nanocomposite

Initially, the catalytic activity of the newly synthesized CS-MCR/$Cu_2O$ bio-nanocomposite was evaluated in $A^3$ coupling reactions. The model reaction of benzaldehyde, phenylacetylene, and piperidine was investigated under various conditions (Table 1). At the outset, water was chosen as a reaction medium, and the model reaction was explored in various amounts of catalyst. In the absence of catalyst at 100 °C after 24 hr, no desired product was obtained (Table 1, entry 1). When the reaction was repeated in the presence of 5, 10, 20, and 50 mg of catalyst, no significant progress in the reaction was observed (Table 1, entry 2–5). Interestingly, when the model reaction carried out in water under ultrasonic irradiation in the presence of 20 mg of catalyst at room temperature, the desired product achieved with 98% yields in 30 minutes (Table 1, entry 8). In order to confirm the catalytic efficiency of CS-MCR/$Cu_2O$ bio-nanocomposite, the model reaction was also examined in the presence of other catalysts such as chitosan, CS-MCR, and $CuCl_2.2H_2O$ individually and the results of the comparisons revealed that CS-MCR/$Cu_2O$ has superior catalytic efficiency than the other catalysts (Table 1, entries 9–11). Considering these results, the optimal conditions for the model reaction were appointed 20 mg of the CS-MCR/$Cu_2O$ at room temperature under ultrasonic irradiation in water as a green solvent.

**TABLE 1** Optimization of reaction conditions for the synthesis of propargylamine *via* $A^3$ coupling reaction of benzaldehyde, piperidine and phenylacetylene[a]

| Entry | Catalyst (mg) | Temperature (°C) | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| **1** | - | 100 | 24 | - |
| **2** | CS-MCR/$Cu_2O$ (5) | 100 | 24 | 10 |
| **3** | CS-MCR/$Cu_2O$ (10) | 100 | 24 | 17 |
| **4** | CS-MCR/$Cu_2O$ (20) | 100 | 24 | 31 |
| **5** | CS-MCR/$Cu_2O$ (50) | 100 | 24 | 40 |
| **6**[c] | CS-MCR/$Cu_2O$ (5) | r.t. | 1 | 72 |
| **7**[c] | CS-MCR/$Cu_2O$ (10) | r.t. | 1 | 85 |
| **8**[c] | **CS-MCR/$Cu_2O$ (20)** | **r.t.** | **0.5** | **98** |
| **9**[c] | Chitosan (20) | r.t. | 0.5 | - |
| **10**[c] | CS-MCR (20) | r.t. | 0.5 | - |
| **11**[c] | $CuCl_2.2H_2O$ (20) | r.t. | 0.5 | Trace |

[a]Reaction conditions: benzaldehyde (1.00 mmol), piperidine (1.00 mmol), phenylacetylene (1.00 mmol), and catalyst in water.

[b]Isolated yield.

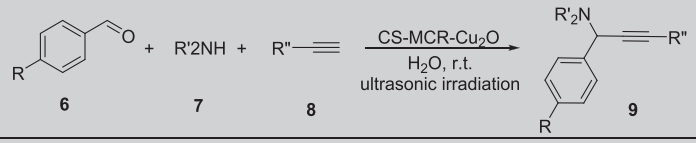
[c]Reaction under ultrasonic irradiation.

Then, the optimized conditions were used for the synthesis of propargylamines by using a series of benzaldehyde with different substituents, various secondary amines, and phenylacetylene derivatives. It can be seen that all products were obtained in high yields (Table 2).

To investigate the generality and utility of this catalytic system, the catalytic efficiency of CS-MCR/$Cu_2O$ was examined in click reaction for the synthesis of 1,2,3-triazoles. The best reaction conditions were 20 mg catalyst in the water at 40 °C Table 3.

With the optimized conditions established, the versatility of the CS-MCR/$Cu_2O$ for the 1,3-dipolar cycloaddition of structurally diverse benzyl bromides and alkynes was investigated under optimized conditions and the results are presented in Table 4.

**TABLE 2** Synthesis of propargylamines *via* $A^3$ coupling reaction catalyzed by CS-MCR/$Cu_2O$[a]

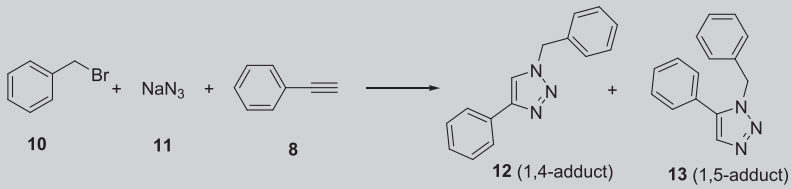



| Entry | R | Amine | R" | Yield[b] (%) | Product |
|---|---|---|---|---|---|
| **1** | H | Piperidine | Ph | 98 | **9a** |
| **2** | Me | Morpholine | Ph | 91 | **9b** |
| **3** | Me | Pyrrolidine | Ph | 93 | **9c** |
| **4** | OMe | Morpholine | Ph | 88 | **9d** |
| **5** | Cl | Morpholine | Ph | 94 | **9e** |
| **6** | H | Morpholine | Ph | 96 | **9f** |
| **7** | $NO_2$ | Morpholine | Ph | 97 | **9 g** |
| **8** | H | Piperidine | 4-$CH_3$Ph | 95 | **9 h** |

[a]Reaction conditions benzaldehyde (1.00 mmol), amine (1.00 mmol), alkyne (1.00 mmol), and 20 mg CS-MCR/$Cu_2O$ in water under ultrasonic irradiation, r.t., 0.5 hr.

[b]Isolated yield.

**TABLE 3** Optimization of reaction conditions for the synthesis of 1,2,3-triazole *via* 1,3-dipolar azide-alkyne cycloaddition of benzyl bromide, sodium azide and phenylacetylene[a]




| Entry | Catalyst (mg) | Temperature (°C) | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| **1** | - | 50 | 2 | 13 (both regioisomers) |
| **2** | CS-MCR/$Cu_2O$ (5) | r.t. | 2 | 66 (only 1,4-adduct) |
| **3** | CS-MCR/$Cu_2O$ (10) | r.t. | 2 | 78 (only 1,4-adduct) |
| **4** | CS-MCR/$Cu_2O$ (20) | r.t. | 2 | 91 (only 1,4-adduct) |
| **5** | **CS-MCR/$Cu_2O$ (20)** | **40** | **1** | **99 (only 1,4-adduct)** |

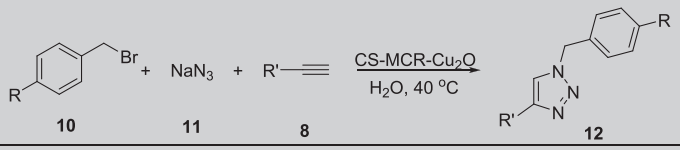
[a]Reaction conditions: benzyl bromide (1.00 mmol), sodium azide (1.00 mmol), phenylacetylene (1.00 mmol), and catalyst in water.

[b]Isolated yield.

The heterogeneity of CS-MCR/$Cu_2O$ was proved using a filtration test and $Hg^0$-poisoning experiment.[36] To investigate whether the catalyst is truly heterogeneous or acting as an active soluble copper species source, a filtration test was performed in the $A^3$ coupling reaction of benzaldehyde, piperidine, and phenylacetylene after ~50% completion of the desired reaction. The filtrate was transferred to another flask under the same initial reaction conditions. Upon further stirring of the catalyst-free solution under ultrasonic irradiation for 24 hr, only negligible progress (4% by GC analysis) was observed, confirming the heterogeneous nature of the used catalyst. In addition to the filtration test, mercury poisoning experiment was performed to determine whether the catalyst is heterogeneous or homogeneous. With standard reaction conditions for the $A^3$ coupling reaction, an experiment with CS-MCR/$Cu_2O$ nanocomposite was designed using benzaldehyde (1.00 mmol), piperidine (1.00 mmol), phenylacetylene (1.00 mmol) and CS-MCR/$Cu_2O$ (20 mg) in $H_2O$ (5 ml). After about 15 mins stirring under the optimized reaction conditions, the reaction was stopped, and the excess of $Hg^0$ (60 mmol) was added, and the reaction was then restarted. The yield for 15 minutes was 62% and for an additional 12 hr after the addition of mercury, it was 65%. This result clearly demonstrates the heterogeneous nature of the catalyst.

The recyclability and reusability of CS-MCR/$Cu_2O$ were tested in six consecutive runs for the synthesis of

**TABLE 4** Synthesis of 1,4-disubstituted 1,2,3-triazoles catalyzed by CS-MCR/$Cu_2O$[a]




| Entry | R | R′ | Yield[b] (%) | Product |
|---|---|---|---|---|
| **1** | H | Ph | 99 | **12a** |
| **2** | Br | Ph | 95 | **12b** |
| **3** | H | C $(Me)_2OH$ | 92 | **12c** |
| **4** | Br | C $(Me)_2OH$ | 89 | **12d** |
| **5** | H | $CH_2N(Me)_2$ | 92 | **12e** |
| **6** | Br | $CH_2N(Me)_2$ | 90 | **12f** |
| **7** | $NO_2$ | Ph | 99 | **12 g** |
| **8** | $NO_2$ | C $(Me)_2OH$ | 95 | **12 h** |

[a]Reaction conditions benzyl bromide (1.00 mmol), sodium azide (1.00 mmol), alkyne (1.00 mmol), and 20 mg CS-MCR/$Cu_2O$ in water, 40 °C, 1 hr.

[b]Isolated yield.

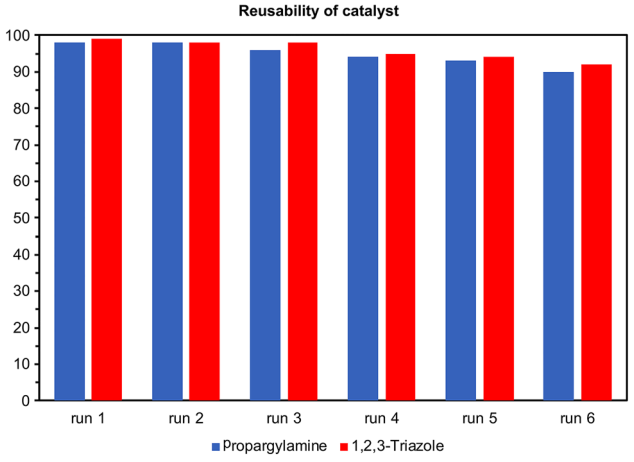



**FIGURE 8** Recycle of the CS-MCR/Cu2O for the synthesis of propargylamine 9a and triazole 12a

propargylamine **9a** and triazole **12a**. After completion of the reaction, the catalyst was separated by filtration, washed with $H_2O$, ethanol, and acetone, dried and reused in the subsequent run. As shown in Figure 8, the recycled catalyst was efficiently used in the next six consecutive runs with only an insignificant loss of activity.

To confirm the reusability and stability of CS-MCR/$Cu_2O$ during the reaction, the TEManalysis of recovered catalyst was performed and compared to that of the fresh one. In TEM images (Figure 9) no significant changes were seen. This observation confirms that the morphology and structure of recovered catalyst did not change during the reaction. Furthermore, less than 3% leaching of copper from the catalyst recovered after several runs, according to ICP-OES analysis, clearly indicates the stability of the catalyst.

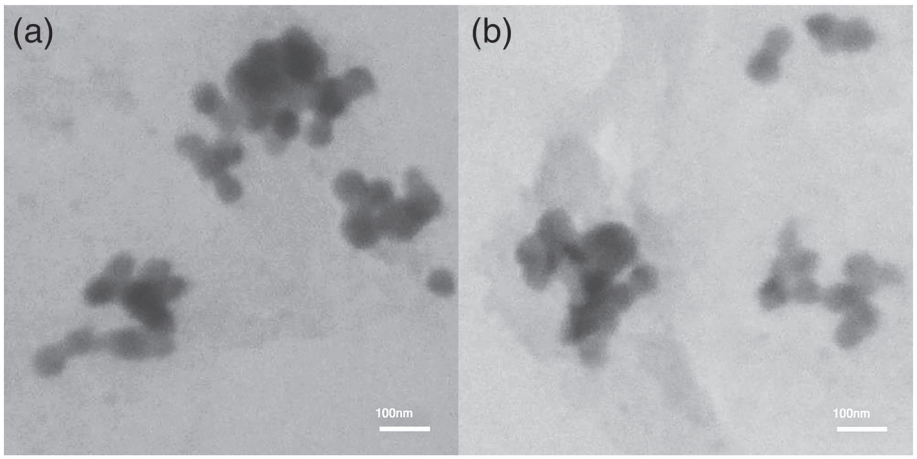



**FIGURE 9** TEM image of the CS-MCR/Cu2O bio-nanocomposite before (a), and after using (b)

## 3 | CONCLUSIONS

In summary, a novel strategy was introduced in the functionalization of biopolymer by utilizing the benefits of MCRs for the synthesis of affinity ligands with the high coordination potential based on copper metal on the surface of chitosan. CS-MCR/$Cu_2O$ bio-nanocomposite was synthesized through covalent functionalization of chitosan biopolymer by the MCR strategy; subsequently, *in situ* forming of $Cu_2O$ NPs within the biopolymeric chitosan. The preparation of materials was proved by various techniques such as FT-IR, XRD, TGA, SEM, EDS, TEM, and ICP. The resulted bio-nanocomposite can act as an effective, robust and recyclable catalyst for the synthesis of propargylamine and 1,2,3-triazole scaffolds with fairly good yields in water. In fact, complexation of the carboxamide-ligands to the copper metals improves reusability and heterogeneity of the desired catalyst by preventing the agglomeration and leaching of copper NPs. According to the results, this strategy could be employed for various biopolymers, which suffer from lack of some special functionalities. Moreover, to improve applications of biopolymers in different fields such as drug delivery, enzyme immobilization, biosensor, and catalysis, this strategy might be useful.

## 4 | MATERIALS AND METHODS

All reagents were purchased from Sigma-Aldrich and used without further purification. The FT-IR spectra were recorded on a Bomem MB-Series FT-IR spectrometer. The X-ray powder diffraction (XRD) patterns were recorded on an STOE diffractometer with Cu-Kα radiation (λ = 1.5418 Å). Thermogravimetric analysis (TGA) was carried out using STA-1500 instrument at a heating rate of 10 °C $min^{-1}$ in the air. The concentration of copper was measured using an inductively coupled plasma optical emission spectrometer (ICP-OES; Varian Vista PRO Radial) and Shimadzu AA-680 flame atomic absorption spectrophotometer. Scanning electron microscopy (SEM) observations were carried out with a Philips XL-30 ESEM electron microscope. All samples were sputtered with gold before the inspection. Elemental analysis was performed by an Elementar Analysensysteme GmbH VarioEL. The $^1H$ NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 MHz using $CDCl_3$ as solvent and tetramethylsilane (TMS) as an internal standard. The gas chromatography analyses were carried out on a Varian model 3600 gas chromatograph (GC) (Varian Iberica, Madrid, Spain) equipped with a split/splitless capillary injection port and flame ionization detector (FID).

### 4.1 | Preparation of CS-MCR

In a typical procedure, Meldrum's acid (0.72 g, 5.00 mmol) and 2-pyridinecarboxaldehyde (0.53 g, 5.00 mmol) were dissolved in $CH_2Cl_2$ (15 ml). Then, the solution was stirred at room temperature for 1 hr. Afterward, cyclohexyl isocyanide (0.54 g, 5.00 mmol) and chitosan (0.50 g) were added and the resulting mixture was stirred at room temperature for 3 days in a closed vial. On completion, CS-MCR was easily purified by washing with $H_2O$, $CH_2Cl_2$, and acetone and isolated by filtration.

### 4.2 | Preparation of CS-MCR/$Cu_2O$

The CS-MCR/$Cu_2O$ was synthesized according to a previously reported method.[37] CS-MCR (1.00 g) was dispersed in water and then ultrasonication was performed at room temperature. Then, a solution of $CuCl_2.2H_2O$ (0.09 g, 0.50 mmol) in 5 ml of $H_2O$ was added dropwise to the reaction mixture, followed by the addition of ascorbic acid (50 ml, 0.05 M). The reaction mixture was stirred on a magnetic stirrer at 80 °C for 24 hr. Then, CS-MCR/$Cu_2O$ was filtered, washed three times with deionized water and dried under vacuum at 60 °C.

### 4.3 | General procedure for the synthesis of propargylamine derivatives

To a mixture of amines (1.00 mmol), benzaldehyde (1.00 mmol) and CS-MCR/$Cu_2O$ (20 mg) in $H_2O$ (5 ml), phenylacetylene (1.00 mmol) was added and the mixture subjected to ultrasound irradiation (45 kHz) for 30 min at room temperature. After completion of the reaction, as monitored by TLC, the catalyst was separated by filtration and washed with $H_2O$, ethanol, and acetone followed by drying at 60 °C for 3 hr. The crude product was purified by column chromatography on silica gel using n-hexane/EtOAc as elution solution to afford the corresponding pure product.

### 4.4 | General procedure for the synthesis of 1,2,3-triazole derivatives

Benzyl bromide derivatives (1.00 mmol), alkynes (1.00 mmol) and sodium azide (1.00 mmol, 0.065 g) were added to a 10 ml round bottom flask fitted with a magnetic stirrer containing a suspension of catalyst (20 mg) in water (5 ml). The resultant mixture was heated at 40 °C. The progress of the reaction was followed by thin layer chromatography (TLC) (ethyl acetate/n-hexane). Upon completion, the mixture cooled to room temperature and the catalyst was separated by filtration and the

product was extracted with chloroform. The solvent was removed in vacuum to afford the pure product.

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## CONFLICT OF INTEREST

There are no conflicts to declare.

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## SUPPORTING INFORMATION

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