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REGULAR ARTICLE

Copper nanoparticles (CuNPs) catalyzed chemoselective reduction of nitroarenes in aqueous medium

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Abstract. A procedure for practical synthesis of CuNPs from $CuSO_4 \cdot 5H_2O$ is established, under appropriate reaction conditions, using rice (*Oryza sativa*) as an economic source of reducing as well as a stabilizing agent. Optical and microscopic techniques are employed for the characterization of the synthesized CuNPs and the sizes of the particles were found to be in the range of 8 ± 2 nm. The nanoparticles are used as a catalyst for chemoselective reduction of aromatic nitro compounds to corresponding amines under ambient conditions and water as a reaction medium.

Keywords. Rice; copper nanoparticles; chemoselective reduction; nitroarenes; water medium.

1. Introduction

Aromatic amino derivatives are important raw materials and pivotal intermediates for the synthesis of pharmaceuticals, agrochemicals, dyes, polymers and various other industrially important chemicals.[1] In general the required aromatic amines are achieved by reductions of their corresponding nitroarenes using a stoichiometric amount of metals such as Mn, Fe, Zn, etc.[2] Use of stoichiometric amounts of transition metals as a source of reduction agent leads to the production of a large amount of waste. There are several catalytic methods to carry out the reduction process. But, the selective reduction of the nitro group in presence of other reducible functional groups in a nitroarene is a challenging task. The use of noble metal catalysts (Pd, Pt, Au, Ir, Rh, etc.) for chemoselective reduction of nitroarenes using various reducing agents such as $NaBH_4$, H_2, $N_2H_4 \cdot H_2O$ and isopropyl alcohol is well documented.[3] Regardless of the high activities displayed by noble metal catalysts, their use is limited due to low abundance, high price and toxicity.[4] This fact motivated researchers to shift their attention towards the developments of earth-abundant metal (Fe, Co, Ni and Cu) based catalysts. Immense progress has been made towards the development of non-noble metal-based active and chemoselective catalysts for the reduction of nitroarenes to their corresponding amines.[5] In spite of that, for many catalytic systems drastic conditions such as elevated temperature and high pressure are often required.[5f,6] Alternative catalysts that are cheap, simple and active at room temperature for chemoselective nitroarene reduction to corresponding amines is, therefore, highly appreciated.

In the last few decades, synthesis and applications of copper-based nanoparticles have attracted great attention, as compared to noble metal-based nanoparticles, from an economic viewpoint. Further, the functional diversity and low toxicity have boosted the synthesis of Cu-based functional nanomaterials enthusiastically all over the world. Copper-based nanoparticles have potential applications in catalysis, health and the environment. In catalysis, it is used to carry out various organic transformations.[7] Copper-based nanoparticles are also employed in the polymerization reaction,[8] decompositions of toxic dye,[9] CO oxidation,[10] hydrogen evolution reaction,[11] and conversion of CO_2 to CO.[12] Sensing property of copper nanoparticles have also been well explored. Ma *et al.* developed CuNPs@NiF electrode and explored their glucose sensing potential with a low detection limit of 0.5 μM.[13] On the other hand, Li *et al.*,

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developed copper nanoparticles based colorimetric sensor for Hg(II) ion with a limit of detection of 0.052 μM.[14] On top of that copper holds a position in the list of micronutrients and it is essential for plants, animals and human health.[15] Hence, exposure of copper from the workspace to the environments resulting in its entry into the food chain is not a matter of great concern.

Herein, we report a simple and economical method for the synthesis of copper nanoparticles-based material and its use in the chemoselective reduction of nitroarenes to their corresponding amines in water.

2. Experimental

2.1 *Synthesis of copper nanoparticles (CuNPs)*

A mixture of 3 g of rice and 10 mL of water was taken in a 100 mL round bottom flask followed by slow addition of 1 mL of concentrated H_2SO_4. The reaction mixture was heated at 100 °C for 1 h with continuous stirring and then 10 mL of 5 N NaOH (aq) was added dropwise to neutralize (pH = 7, checked using pH paper) the acid content. Subsequently, 1.25 g $CuSO_4 \cdot 5H_2O$ dissolved in 20 mL water was added to the above-mentioned reaction mixture followed by the addition of 2.5 mL of 5 N NaOH and the resulting mixture was stirred at the same temperature for another one hour whereupon a reddish-brown coloured solid (CuNPs) was formed. The reaction mixture was cooled to room temperature and the product was collected by centrifugation, washed twice with water and dried under vacuum at room temperature. The material was characterized by techniques including UV-vis, powder XRD and TEM.

2.2 *General procedure for aromatic nitro compounds reduction*

In a typical procedure, a mixture of 5 mL of water, an aromatic nitro compound (1 mmol) and CuNPs (5 mg) was taken in a 50 mL round-bottomed flask and then stirred at room temperature followed by the addition of $NaBH_4$ (200 mg) with constant stirring. Progress of the reaction was monitor by TLC, after completion of the reaction the product was extracted by ethyl acetate and purified by column chromatography on silica gel to afford the amine. A variety of amines were prepared in this manner and characterized by analyzing their ^1H and ^{13}C NMR spectral data. The reported compounds were confirmed by comparing the spectral data with literature values whereas new compounds were additionally characterized by analyzing HR-MS data.

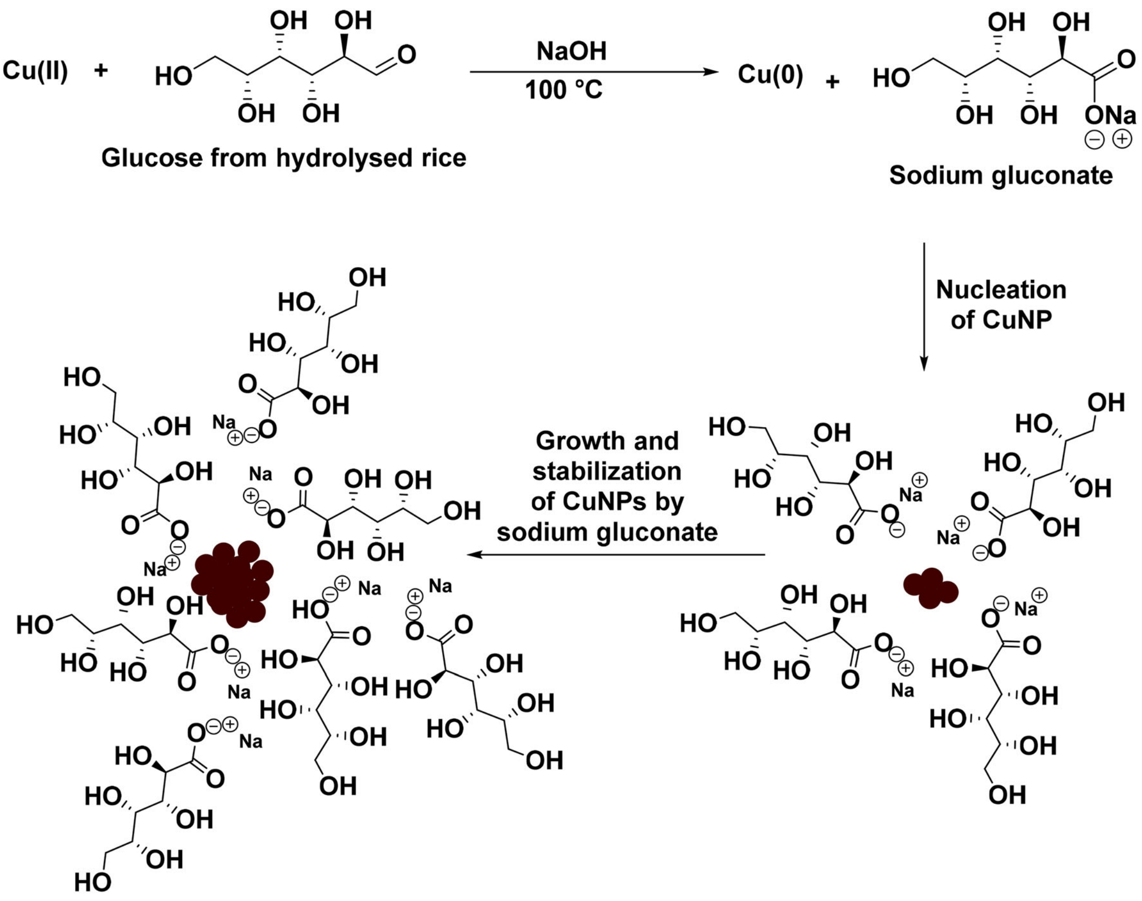
2.3 *Characterization techniques*

UV-vis spectra of samples were recorded using a JASCO V-650 Bio instrument. Powder XRD patterns were obtained using a Bruker D8 Advance instrument. CuNPs samples suitable for TEM studies were prepared by the dip and lift-off methods. In a typical procedure, a sample was dispersed in distilled water by sonicating and a TEM grid was dipped into it with the help of Forceps and then lifted off air-dried. ^1H NMR and ^{13}C NMR spectra of the amines were recorded on Bruker Avance 400 MHz NMR or Bruker Avance 500 MHz NMR instruments. Mass spectral data of new compounds were obtained using a High-Resolution Q-Tof Mass instrument.

3. Results and Discussion

3.1 *Copper nanoparticles*

Reducing sugar present in hydrolysed rice played a dual role of, under optimized conditions, reduction of Cu(II) to Cu(0) as well as stabilization of ensuing nanoparticles. Glucose acts as a reducing agent and its oxidised form, gluconate, acts as a stabilizing agent (Scheme 1). and In our previous report, it has been observed that the use of 1 g of rice and 1.25 g of $CuSO_4 \cdot 5H_2O$ (5 mmol) produced spherical Cu_2ONPs (9-10 nm) exclusively.[16] In this work we observed that, with 2 g of rice and other conditions being unchanged a mixture of Cu_2ONPs and CuNPs is formed. However, increasing the amount of rice to 3 g produced CuNPs exclusively. The formation of NPs was confirmed by analysing UV-Vis absorption spectra of the samples where a characteristic surface resonance peak at 478 nm indicates the formation of Cu_2ONPs and that at 600 nm confirms the presence of CuNPs (Figure 1a). Hung *et al.,* reported spherical CuNPs of 8 nm size where the UV-Vis absorption spectrum showed a peak at 600 nm.[17] Formation of a mixture of Cu_2ONPs and CuNPs by using 2 g of rice may be correlated to insufficient amount of hydrolysed rice constituent that caused an incomplete reduction of Cu_2O to Cu. Powder X-Ray diffraction (Figure 1b) for Cu_2ONPs shows the entire characteristic of Bragg's reflection at appropriate 2θ, (110), (111), (200), (220), (311) and (222) (JCPDS No. 05-0667). For CuNPs, Powder X-Ray diffraction show 2θ pick position corresponding to Cu, which is in good agreement with



Scheme 1. Schematic representation of gluconate stabilized (oxidized product of glucose, rice) CuNPs.

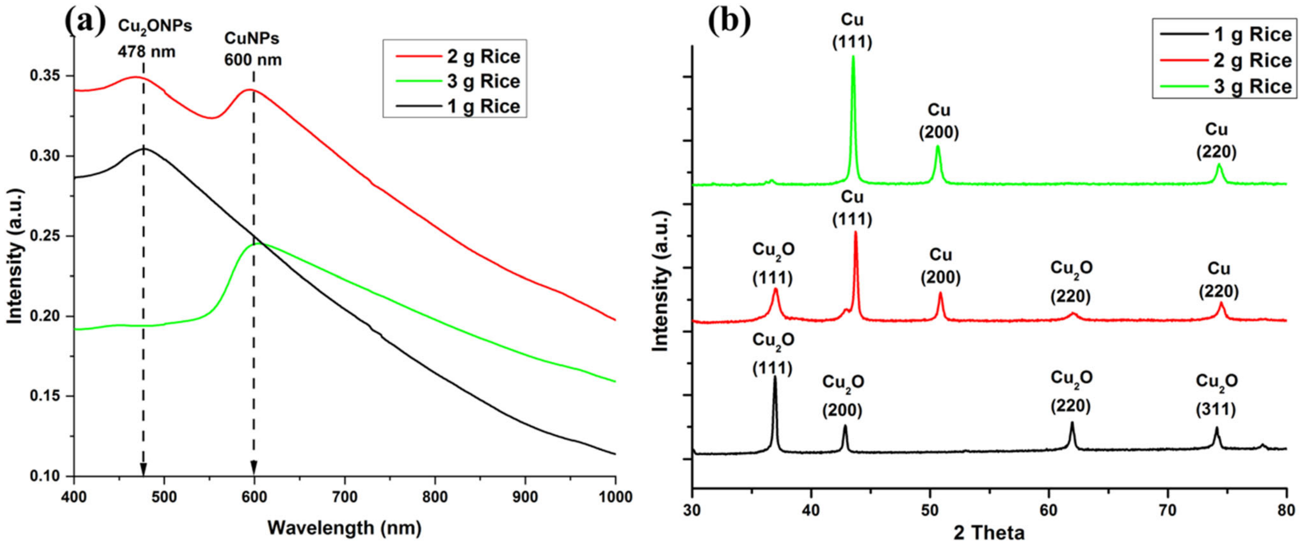


Figure 1. Monitoring the formation of CuNPs by (a) UV-Vis absorption and (b) Powder X-Ray diffraction techniques.

JCPDS card no. 04-0836. TEM image of CuNPs (Figure 2) shows a particle size distribution in the range of 8 ± 2 nm which is consistent with the peak observed in the corresponding UV-Vis spectrum.

The relation between the quantity of rice and the formation of Cu_2ONPs and CuNPs can also be understood from redox chemistry. As described earlier, rice is a source of glucose (reducing sugar). The

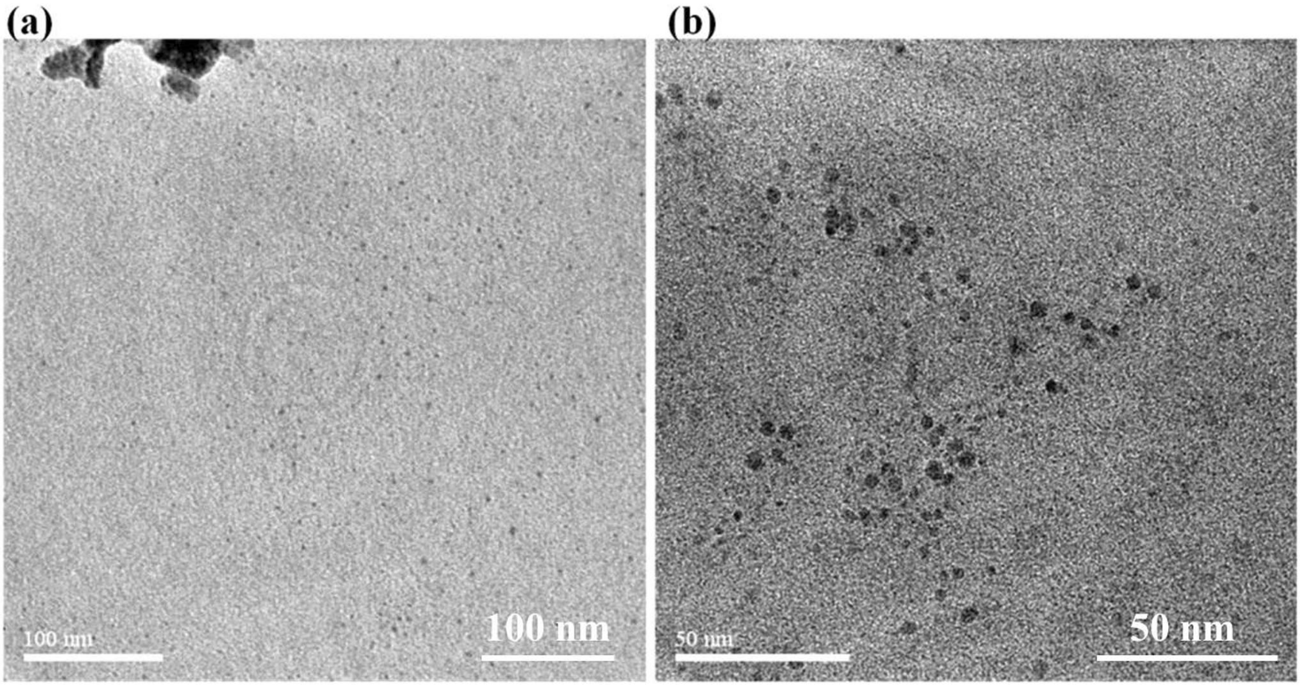


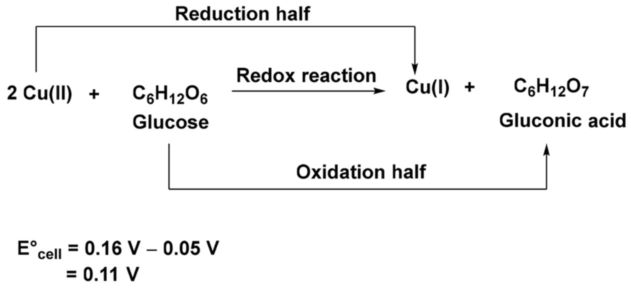
Figure 2. TEM image of CuNPs (a) with scale 100 nm (b) with scale 50 nm.

standard reduction potential of Cu(II) to Cu(I), Cu(I) to Cu(0), and gluconic acid to glucose are 0.16, 0.52 and 0.05 V, respectively.[25] The following redox reaction takes place between copper precursor and glucose (Schemes 2 and 3). E^{o}_{cell} for production of Cu_2O and Cu are 0.11 and 0.47 V, respectively.

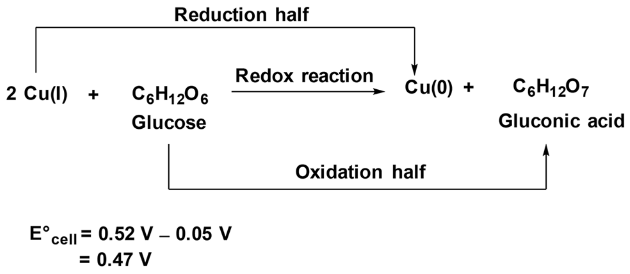
Based on E°_{cell} values shown in Schemes 2 and 3, the conversion of Cu(I) to Cu(0) is more spontaneous than Cu(II) to Cu(I). However, increases in rice content by two-fold resulted in only a mixture of Cu_2ONP and CuNPs. This may be attributed to the fact that hydrolysed rice contents are not sufficient to stabilize the formed CuNPs and reverse reaction (aerial oxidation) takes place as the reaction was carried out at 100 °C in open air. By increments of the rice content to three-fold, the production of CuNPs got optimized.

3.2 *Chemoselective reduction of nitroarenes*

Reduction of nitroarenes to corresponding anilines using sodium borohydride require hazardous solvent (DMSO, sulfolane) and high temperature (85-100 °C).[26] Catalytic activity of the synthesized CuNPs for reduction of nitroarenes was evaluated by reacting a model nitroarene with $NaBH_4$ (as a reducing agent). The reaction was carried out in a flask containing an aqueous suspension of CuNPs at room temperature and under open air with continuous stirring. First, we chose 4-nitrophenol as a model substrate and the progress of the reaction was monitored by TLC. Another set of reactions was carried out in glass vials without and with CuNPs (Scheme S1, Supplementary Information). At the end of 30 mins, the products of each reaction were analysed by ^1H NMR and it was

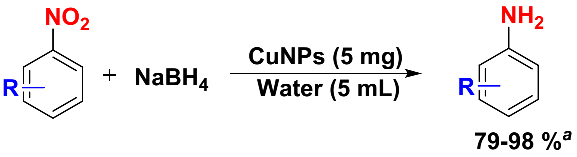


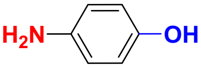
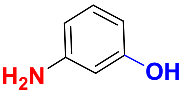
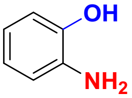
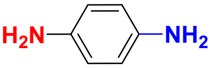
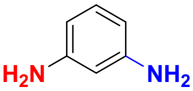
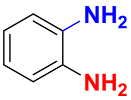
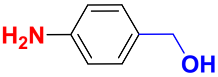
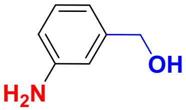
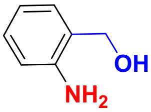
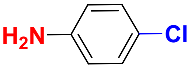
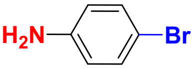
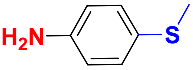
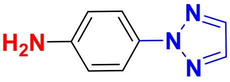
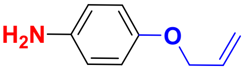
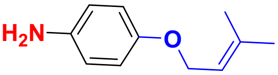
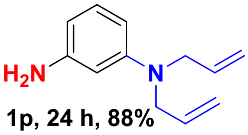
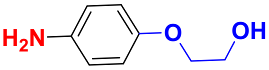
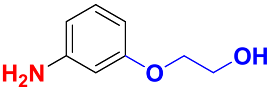
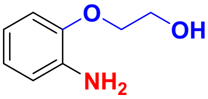
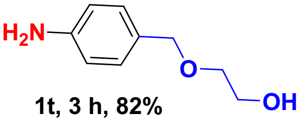
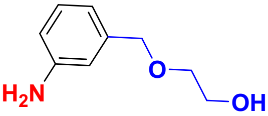
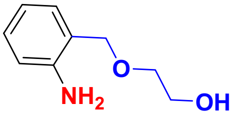
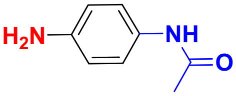
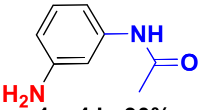
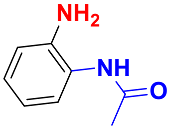
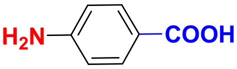
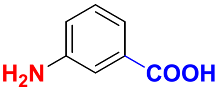
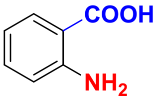
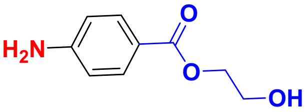
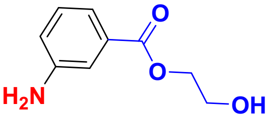
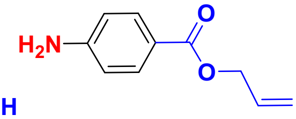
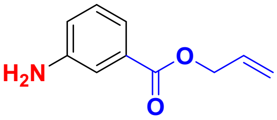
Scheme 2. Redox reaction between Cu(II) and glucose (with 1 g rice).



Scheme 3. Redox reaction between Cu(II) and glucose (with 2 g and 3 g rice).

Table 1. Chemoselective reduction of aromatic nitro compounds to aromatic amines.



 1a, 0.5 h, 98%	 1b, 2 h, 95%	 1c, 1 h, 95%	 1d, 0.5 h, 95%
 1e, 1 h, 94%	 1f, 0.5 h, 96%	 1g, 1.5 h, 89%	 1h, 2 h, 85%
 1i, 1.5 h, 88%	 1j, 4 h, 87%	 1k, 6 h, 84%	 1l, 18 h, 89%
 1m, 18 h, 90%	 1n, 15 h, 83%	 1o, 15 h, 82%	 1p, 24 h, 88%
 1q, 1 h, 92%	 1r, 3 h, 87%	 1s, 3 h, 81%	 1t, 3 h, 82%
 1u, 4 h, 79%	 1v, 4 h, 81%	 1w, 4 h, 92%	 1x, 4 h, 90%
 1y, 4 h, 90%	 1z, 1 h, 87%	 1aa, 1 h, 91%	 1ab, 1 h, 89%
 1ac, 5 h, 91%	 1ad, 4 h, 79%	 1ae, 18 h, 83%	 1af 18 h, 81%

Reaction condition: Nitro-arene (1 mmol), $NaBH_4$ (200 mg), Room temperature, open air, 0.5-24 h; [a]Isolated yield.

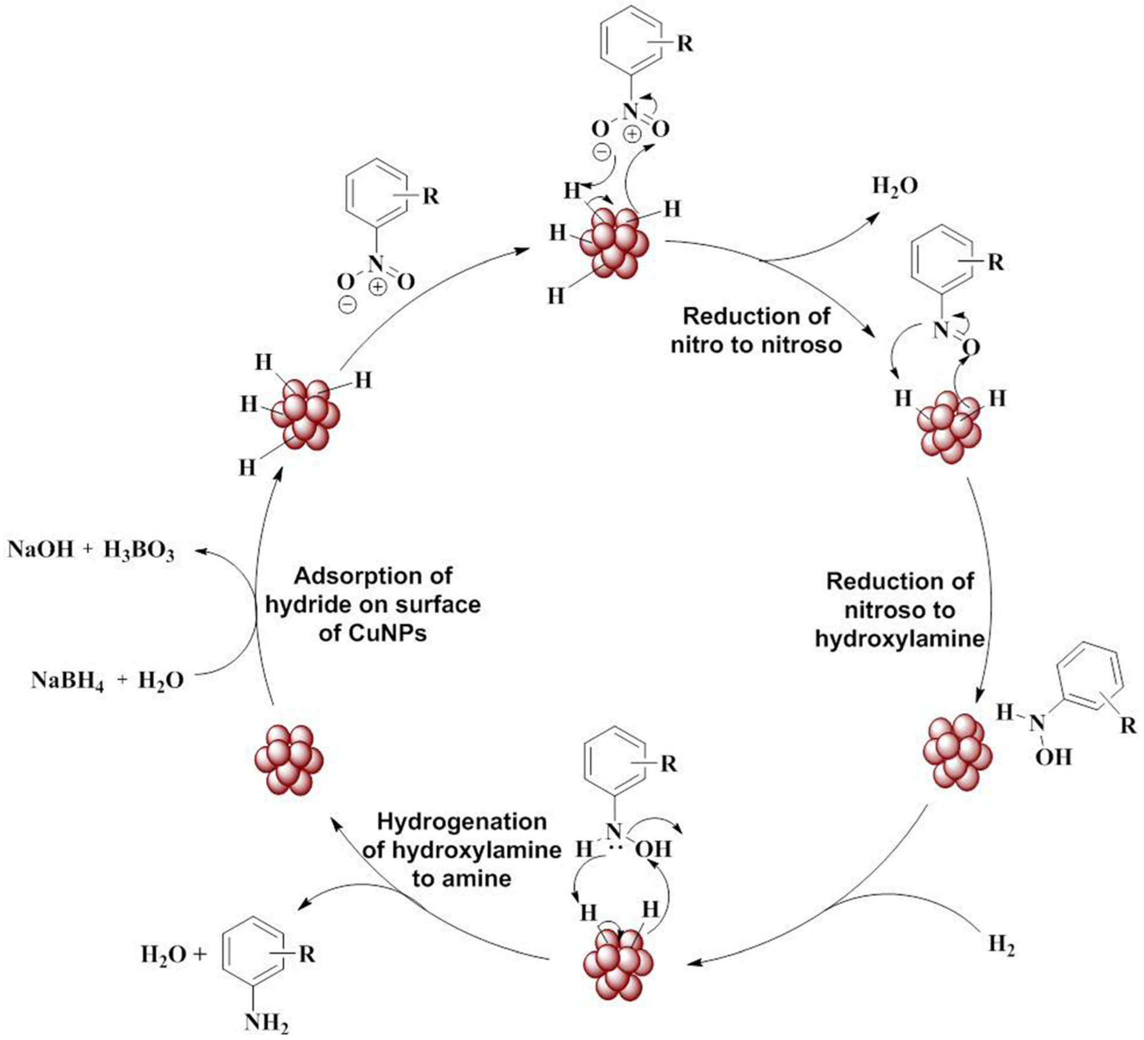
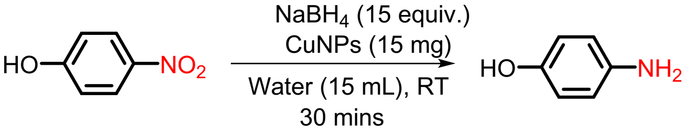


Figure 3. Proposed catalytic reaction mechanism of nitroarene reduction.

found that the reaction did not move forward in absence of CuNPs catalyst (Figure S1, Supplementary Information). As we moved ahead with a variety of substrates, reaction time appears to be substrate-dependent. The substrate with high solubility in water required less time and substrates which are less soluble or insoluble required a longer time. This is possibly due to variation in catalyst-substrate interaction frequency with a variety of substrate, as a highly soluble substrate will have high catalyst-substrate interaction frequency and less soluble substrate will have less of this interaction frequency. Excellent chemoselective reduction of nitro to amine was achieved for substrates containing additional functional groups (chloro, bromo, ether, thioether, acetamides, carboxylic acid and ester) as shown in Table 1. Most of the substrates used here are raw materials for the synthesis of industrially important and biologically active molecules. Reduction of 4-nitrophenol to 4-aminophenol is the first step for the synthesis of paracetamol.[18] We too obtain an excellent yield of 4-aminophenol from 4-nitrophenol (Table 1, entry 1a). 3-Aminophenol (Table 1, entry 1b), (3-aminophenyl)methanol (Table 1, entry 1h) and 2-(3-aminophenoxy)ethanol (Table 1, entry 1r) are also important ingredients for the synthesis of macrocyclic compounds bearing kinase inhibition potential and antineoplastic agents.[1d],[19] Halogen substituted nitroarenes were selectively reduced to corresponding haloaromatic amines (Table 1, entry 1j and 1k) without undergoing dehalogenation. 4-chloroaniline is an important constituent for the synthesis of proguanil, an antimalarial drug.[20] Bhagwat *et al*., in 2019 claimed 4-chloroaniline (Table 1, entry 1j), 4-bromoaniline (Table 1, entry 1k), N-(4-aminophenyl)acetamide (Table 1, entry 1w) and 4-(2H-1,2,3-triazol-2-yl)aniline (Table 1, entry 1m) as indispensable intermediates for the synthesis of various valuable compounds used to treat or prevent

Table 2. Recycling of the CuNPs catalyst.



Runs	Yields (%)[a]
1	96
2	93
3	91
4	91
5	87

4-nitrophenol (3 mmol); [a]Isolted yield.

diseases in need of heparin sulphate biosynthesis inhibition.[21] In addition, nitroarene bearing ether as additional functional group (ether, acid and ester) remained unaffected after completion of reaction and corresponding amines were isolated with good yields. Wang *et al.*, used 2-(4-aminophenoxy)ethanol (Table 1, entry 1q) and 2-(4-aminobenzyloxy)ethanol (Table 1, entry 1t) as an intermediate component for the synthesis of antitumor agent.[22] Our synthesized catalyst also showed a selective reduction of nitro group to amine in presence of reducible functional groups like carboxylic acid and ester. Nitrobenzoic acid was also reduced to corresponding aminobenzoic acid (Table 1, entry 1z, 1aa and 1ab) with excellent selectivity and conversion, which is a vital intermediate often used in drug evolution and drug discovery.[23] Esters of aminobenzoate (Table 1, entry 1ac, and 1ae) are also used by many researchers as important intermediate molecules for the synthesis of antibacterial agents and other biologically active molecules.[24] Table S1 (Supplementary Information) describe the importance of substrates as starting material for the synthesis of few industrially important and bio-active molecules.

3.3 *Proposed mechanism for reduction of nitroarenes compounds*

The proposed mechanism of nitroarenes reductions is described in Figure 3. The addition of $NaBH_4$ to the reaction mixture resulted in copper nanoparticles-hydride complex (CuNPs-H). The CuNPs-H complex reduced nitro to nitroso and then to hydroxylamine which on further hydrogenation ends up with amines as a final product.

3.4 *Recyclability test of the catalyst*

For practical applications, the reusability of catalyst is an important parameter. To study this parameter, reactions were performed by increasing the nitroarene constituents (4-nitrophenol, CuNPs, water and $NaBH_4$) by three-fold. By increasing the constituents, we experienced minimal loss during the isolation of the catalyst after each cycles. We successfully reused the catalyst up to five cycles without significant loss of product yields (Table 2). A slight lowering of yields upon reusing the catalyst may be due to agglomeration of nanoparticles as observed in the TEM image of the catalyst after the first cycle (Figure 4). Agglomeration of the catalyst (CuNPs) may be due to the solubility of the stabilizing agents (gluconate) in water. With the progress of the reaction, slight loss of stabilizing agent from the surface of CuNPs may also be another reason for agglomeration of CuNPs after catalytic reaction (Figure 4).

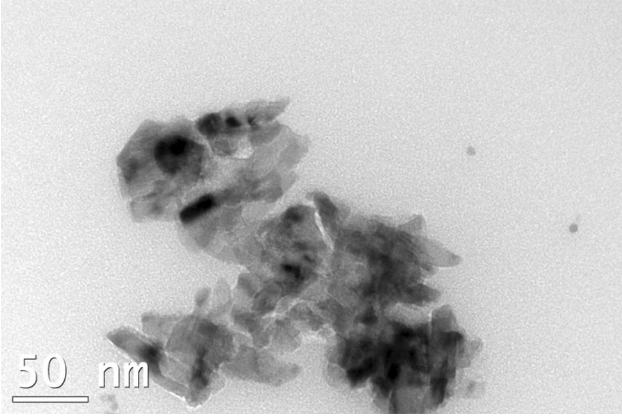


Figure 4. TEM image of CuNPs after first catalytic cycle.

4. Conclusions

We have synthesized CuNPs with homogeneous particle size distribution (8 ± 2 nm) using rice as a source of reducing and stabilizing agents by cross-fertilizing the concepts of (i) acidic hydrolysis of starch (polysaccharides) to give corresponding monosaccharide (glucose) and (ii) Fehling reactions. The catalytic activity of synthesised CuNPs showed a chemoselective reduction of nitroarenes to corresponding amines in good to excellent yields. The catalyst was recycled up to five cycles without significant loss in yields.

Supplementary Information (SI)

Supplementary information associated with this article is available at www.ias.ac.in/chemsci.

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