

RESEARCH PAPER

## Biosynthesis and Characterization of Fe<sub>3</sub>O<sub>4</sub>/CaO Nanoparticles and Investigation of Its Catalytic Property

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### ABSTRACT

The principal aim of this research is the green synthesis and application of Fe<sub>3</sub>O<sub>4</sub>/CaO magnetic nanoparticles (MNPs) for heterocyclic reactions. Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs have been prepared using FeSO<sub>4</sub> and quail eggshell waste powder in solvent-free conditions. Morphology and structure of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs were determined by FT-IR, X-ray diffraction (XRD), transmission electron microscopy (TEM), and scanning electron microscopy (SEM). It was used as a highly efficient catalyst for the synthesis of triazole carbohydrate derivatives. (1S, 2R, 3R, 4R)-1-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl) pentane-1,2,3,4,5-pentanol (3) was synthesized by the reaction of thiocarbohydrazide and D-gluconic acid- $\delta$ -lactone in the presence of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs (7% mol) in ethanol under reflux conditions. Compound (3) was used as an intermediate for the synthesis of [1,2,4] triazolo[3,4-b][1,3,4]thiadiazin and thiadiazol derivatives. The assigned structure was further established by CHN analyses, NMR, and FT-IR spectra. Because of excellent capacity, the exceedingly simple workup, and good yield, eco-friendly catalyst Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs were proved to be a good catalyst for this reaction.

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### INTRODUCTION

Recently, considerable research has been focused on the Fe<sub>3</sub>O<sub>4</sub> magnetic nanostructure due to its unique physical and chemical properties, such as high surface energy, large surface area, and superparamagnetic behavior. Magnetic nanoparticles have been widely used in several areas, including gene delivery [1,2], cell therapy [3], drug delivery [4,5], recording material, sensor,

and catalyst [6–8]. These magnetic nanoparticles have been used as an efficient catalyst in many organic reactions [9-13]. The magnetic properties of the catalyst provided a convenient and easy route for the separation of the catalyst from the reaction mixture by an external bar magnet [11]. Fe<sub>3</sub>O<sub>4</sub> nanoparticles need to be modified because of their easy aggregation and oxidation in the pure form [14].

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On the other hand, CaO is one of the heterogeneous base catalysts and the only alkaline earth metal oxide which can be easily derived from the environment, waste sources such as ashes [15], crab shell [16,17], sand [18], oyster shell [19], animal bones [20], snail shell [21], and also eggshell [22]. The most chemical component of the calcined waste eggshell is CaO (about 97%), which can be obtained from calcium carbonate in the eggshell under high temperature (in the range of 700–1000 °C) [23]. CaCO<sub>3</sub> is not fully decomposed to CaO. Just a few minutes after calcination, CaO is hydrated and carbonated by absorption of H<sub>2</sub>O and CO<sub>2</sub> in room air [24,25]. Quail egg is very small with a large amount of strong basic sites. CaO from quail eggshell waste has exhibited the highest catalytic activity under mild reaction conditions, low cost, and long lifetime [26].

Furthermore, nitrogen-containing heterocyclic compounds such as triazole derivatives play very important roles in medicinal, pesticidal, and organic chemistry [27,28]. Triazole derivatives are very important due to fewer adverse effects, low toxicity, high biological, and pharmacological activities [29–30]. The presence of three nitrogen atoms allows triazoles to interact with a variety of enzymes and receptors [31,32]. 1,2,4-triazoles possess various bioactivities, such as anticancer, antidepressant, antitumor, fungicidal, antibacterial, anticonvulsant, and antioxidant [33–35].

Herein, in continuation of our previous works and studies for discovering new procedures for the synthesis of important organic compounds [36–38], we present a simple and inexpensive biosynthesis of well-crystallized Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs as an effective catalyst for the synthesis of some 1,2,4-triazole derivatives by mixing the waste natural quail eggshell powder and D-gluconic acid- $\delta$ -lactone in acetic acid.

## MATERIALS AND METHODS

### Chemicals and Instrumentation

All chemicals and solvents were purchased from Merck and Aldrich. TLC silica gel 60, aluminum sheets were purchased from Merck. The production of nano compounds was determined by powder X-ray diffraction (XRD) PW 3040/60 X'Pert PRO diffractometer system, using Cu K $\alpha$  radiation with ( $\lambda = 1.5418 \text{ \AA}$ ) in the range of  $2\theta = 20\text{--}80^\circ$  at room temperature. The morphology and sizes

of NPs were evaluated using a scanning electron microscope (SEM) and transmission electron microscope (TEM, 150 kV, and Philips-CM 10) by Day Petronic Company-Iran. FT-IR measurements were recorded on a Shimadzu 8400s spectrometer with KBr plates. The NMR spectra were recorded on Bruker XL 400 (400 MHz) instruments. The C, H, N analyses were performed by the microanalytical service of Daypetronic Company. Melting points were determined on an Electrothermal 9100 without further corrections.

### Preparation of Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles

The Fe<sub>3</sub>O<sub>4</sub> MNPs were prepared according to a previously reported procedure [19]. Typically, FeCl<sub>3</sub>·6H<sub>2</sub>O (0.02 mol) and FeCl<sub>2</sub>·4H<sub>2</sub>O (0.01 mol) was dissolved in distilled water (100 ml) in a three-necked round-bottom flask (250 ml). The resulting transparent solution was heated at 90 °C with rapid mechanical stirring under N<sub>2</sub> atmosphere for 1h. A solution of concentrated aqueous ammonia (10 ml, 25 wt %) was then added to the solution in a dropwise manner over a 30 min period using a dropping funnel. The reaction mixture was then cooled to room temperature and the resulting magnetic particles were collected with an external magnet and rinsed thoroughly with distilled water.

### Preparation of Fe<sub>3</sub>O<sub>4</sub>/CaO magnetic nanoparticles

Waste quail eggshells were thoroughly cleaned and air-dried after the removal of the inner membrane layer. Cleaned eggshells were crushed into small pieces and dried at 80°C for 24 h in the oven. The dried eggshells (3 g) and FeSO<sub>4</sub> (4 g) were added to 50 ml of acetic acid in a flask. The mixture was kept in an ultrasonic bath for 30 min and then slowly stirred outside the ultrasonic device for another 2 hours, under reflux conditions. The solvent was evaporated and the resulting precipitate was calcined at 600°C for 2 hours to obtain Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs.

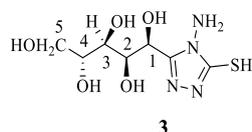
### Synthesis of (1S, 2R, 3R, 4R)-1-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)pentane-1,2,3,4,5-pentanol (3)

Thiocarbohydrazide (1 mmol), D-gluconic acid- $\delta$ -lactone (1 mmol), and a catalytic amount of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs (7 mol %) were mixed and reacted in ethanol (10 ml) under reflux conditions. The progress of the reaction was monitored by TLC using n-hexane: ethyl acetate (1:1) and detected by a UV lamp (254 & 366 nm). At the end of the

reaction, the catalyst was separated by an external magnet, filtered, washed with ethanol and water, dried at 80 °C for 1h, and reused for the same reaction. The residue of the reaction mixture was evaporated, and the crude product was purified by short-column chromatography on silica gel (n-hexane: ethyl acetate / 4:1). The products were determined by CHN analyses, NMR, and FT-IR spectra.

#### CHARACTERISATION METHODS

(1*S*, 2*R*, 3*R*, 4*R*)-1-(4-amino-5-mercapto-4*H*-1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazin-7-ylidene)pentane-1,2,3,4,5-pentanol (3)



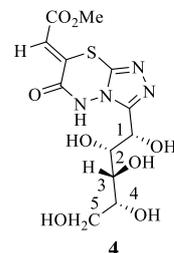
White powder, yield 92% , m.p. 189-193°C. IR (KBr) ( $\nu_{\max}$  cm<sup>-1</sup>): 3440 (OH), 3375 (NH<sub>2</sub>), 1613 (C=N). <sup>1</sup>H-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 3.06 (d, J = 7.5 Hz, 1H, H-3), 3.39 (dd, J = 5.4 Hz, 1H, H-5'), 3.50 (m, 1H, H-4), 3.52 (dd, J = 5.4 Hz, 1H, H-5), 4.18 (d, J = 7.5 Hz, 1H, H-2), 4.33 (m, 3H, OH-3,4,5), 4.62 (d, J = 5.4 Hz, 1H, OH-2), 4.79 (d, J = 7.5 Hz, 1H, H-1), 5.48 (s, 2H, NH<sub>2</sub>), 5.49 (s, 1H, OH-1), 13.59 (s, 1H, SH). <sup>13</sup>C-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 64.21, 67.57, 68.56, 70.65, 72.28, 154.27, 165.71. Anal. Calc. for C<sub>7</sub>H<sub>14</sub>N<sub>4</sub>O<sub>5</sub>S (266.27): C, 31.58; H, 5.30; N, 21.04, found: C, 31.52; H, 5.33; N, 21.12.

*General procedure for the synthesis of [1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazin and thiadiazol derivatives*

Compound 3 (1 mmol), dialkylacetylen dicarboxylate or isatin (1 mmol), and a catalytic amount of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs (7 mol %) were mixed and reacted in methanol (compound 4) or ethanol (compound 5, 6) (10 ml) under reflux condition. The progress of the reaction was monitored by TLC using n-hexane: ethyl acetate (1:1) and detected by a UV lamp (254 & 366 nm). At the end of the reaction, the catalyst was separated by an external magnet, filtered, washed with ethanol and water, filtered, washed with ethanol and water, dried at 80 °C for 1h, and reused for the same reaction. The residue of the reaction mixture was evaporated, and the crude product was recrystallized by ethanol or methanol. The products were determined by CHN analyses, NMR, and FT-IR spectra.

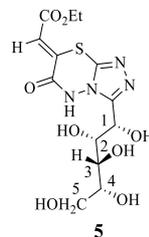
*Methyl (Z)-2-(6-oxo-3-((1*S*,2*R*,3*R*,4*R*)-1,2,3,4,5-*

*pentahydroxypentyl)-5,6-dihydro-7*H*-(1,2,4)triazolo[3,4-*b*][1,3,4]thiadiazin-7-ylidene)acetate (4)*



Reaction time 60 min, yellow powder, yield 95%, m.p. 59-63°C. IR (KBr) ( $\nu_{\max}$  cm<sup>-1</sup>): 3400 (OH), 3350 (NH), 1750 (C=O), 1710 (C=N). <sup>1</sup>H-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 3.18 (d, J = 8.3 Hz, 1H, H-3), 3.39 (dd, J = 5 Hz, 1H, H-5'), 3.54 (m, 1H, H-4), 3.57 (dd, J = 5 Hz, 1H, H-5), 3.77 (s, 3H, CH<sub>3</sub>), 4.04 (m, 3H, OH-3,4,5), 4.26 (d, J = 8.3 Hz, 1H, H-2), 4.62 (d, J = 5 Hz, 1H, OH-2), 4.87 (d, J = 8.3 Hz, 1H, H-1), 5.49 (s, 1H, OH-1), 6.90 (s, 1H, CH), 7.00 (s, 1H, NH). <sup>13</sup>C-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 53.35, 64.68, 67.46, 68.88, 71.13, 73.54, 123.62, 154.72, 158.87, 158.21, 164.62, 165.21. Anal. Calc. for C<sub>12</sub>H<sub>16</sub>N<sub>4</sub>O<sub>8</sub>S (376.34): C, 38.30; H, 4.29; N, 14.89, found: C, 38.37; H, 4.34; N, 14.46.

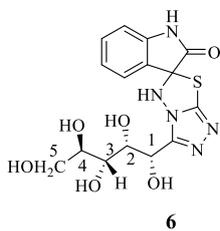
*Ethyl (Z)-2-(6-oxo-3-((1*S*,2*R*,3*R*,4*R*)-1,2,3,4,5-pentahydroxypentyl)-5,6-dihydro-7*H*-(1,2,4)triazolo[3,4-*b*][1,3,4]thiadiazin-7-ylidene)acetate (5)*



Reaction time 60 min, yellow powder, yield 94% , m.p. 68-73°C. <sup>1</sup>H-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 1.24 (t, J = 7.1 Hz, 3H, CH<sub>3</sub>), 3.15 (d, J = 8. Hz, 5, 1H, H-3), 3.37 (dd, J = 4.3 Hz, 1H, H-5'), 3.43 (q, J = 7.1 Hz, 2H, CH<sub>2</sub>), 3.51 (m, 1H, H-4), 3.55 (dd, J = 4.3 Hz, 1H, H-5), 4.13 (d, J = 8.5 Hz, 1H, H-2), 4.24 (m, 3H, OH-3,4,5), 4.85 (d, J = 4.3 Hz, 1H, OH-2), 4.89 (d, J = 8.5 Hz, 1H, H-1), 5.49 (s, 1H, OH-1), 6.85 (s, 1H, CH), 7.12 (s, 1H, NH). <sup>13</sup>C-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 17.36, 60.78, 65.18, 67.15, 68.62, 70.44, 72.88, 122.73, 154.65, 157.50, 158.69, 163.16, 165.34. Anal. Calc. for C<sub>13</sub>H<sub>18</sub>N<sub>4</sub>O<sub>8</sub>S (390.08): C, 40.00; H, 4.65; N, 14.35, found: C, 40.31; H, 4.73; N, 14.08.

*3'-((1*S*,2*R*,3*R*,4*R*)-1,2,3,4,5-pentahydroxypentyl)-*

5'H-spiro[indoline-3,6'-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol]-2-one (6)



Reaction time 80 min, orange powder, yield: 96%, m.p. 210-217°C. FT-IR (KBr) ( $\nu_{\max}$  cm<sup>-1</sup>): 3350 (OH), 3300 (NH), 1700 (C=O), 1640 (C=N). <sup>1</sup>H-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 3.06 (d, J = 8 Hz, 1H, H-3), 3.39 (dd, J = 4 Hz, 1H, H-5'), 3.51 (m, 1H, H-4), 3.59 (dd, J = 4 Hz, 1H, H-5), 4.13 (d, J = 8 Hz, 1H, H-2), 4.16 (m, 3H, OH-3,4,5), 4.20 (d, J = 4 Hz, 1H, OH-2), 4.81 (d, J = 8 Hz, 1H, H-1), 5.48 (s, 1H, OH-1), 6.95 (d, J = 8 Hz, 1H, CH), 7.09 (t, J = 4 Hz, 1H, CH), 7.36 (t, J = 8 Hz, 1H, CH), 7.68 (d, J = 4 Hz, 1H, CH), 11.21 (s, 1H, NH), 13.62 (s, 1H, NH).

<sup>1</sup>H-NMR (D<sub>2</sub>O exchange):  $\delta$  (d<sub>6</sub>-DMSO), 3.06 (d, J = 8.2 Hz, 1H, H-3), 3.39 (dd, J = 7.7 Hz, 1H, H-5'), 3.51 (m, 1H, H-4), 3.53 (dd, J = 7.7 Hz, 1H, H-5), 4.15 (d, J = 8.2 Hz, 1H, H-2), 4.81 (d, J = 8.2 Hz, 1H, H-1), 6.95 (d, J = 7.8 Hz, 1H, CH), 7.09 (t, J = 7.5 Hz, 1H, CH), 7.36 (t, J = 7.8 Hz, 1H, CH), 7.68 (d, J = 7.5 Hz, 1H, CH). <sup>13</sup>C-NMR:  $\delta$  (d<sub>6</sub>-DMSO), 63.88, 66.47, 71.54, 72.03, 72.28, 111.64, 120.28, 122.96, 131.98, 133.23, 142.95, 152.30, 165.99, 171.47, 178.62. Anal. Calc. for C<sub>15</sub>H<sub>17</sub>N<sub>5</sub>O<sub>6</sub>S (395.09): C, 45.57; H, 4.33; N, 17.71, found: C, 45.61; H, 4.38;

N, 17.80.

RESULTS AND DISCUSSION

The principle aim of this study is the application of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs in the synthesis of some triazole derivatives. Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs were prepared by a simple, low cost, and convenient method from the reaction of FeSO<sub>4</sub> and quail eggshell waste in acetic acid. The FT-IR spectra of prepared Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs are shown in Fig. 1.

The result in this spectra shows that the data are the same as reported in the literature [39]. The absorption band at 400–679 cm<sup>-1</sup> is related to the Fe-O and Ca-O, which confirms the formation of the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs. The contact of trapped water in the nanoparticles with CO<sub>2</sub> originated from the air can lead to the formation of carbonate ions characterized by a peak situated at 1543 and 1572 cm<sup>-1</sup>. The absorption bands at 713 (C-O), 875 (OCO), and 1445 (C-O) cm<sup>-1</sup> are related to the carbonate group, The broad absorption band at around 3447 cm<sup>-1</sup> is related to O–H and H–O–H molecules absorbed physically on the surface of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs.

The crystalline structure and average size of nanoparticles of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs were identified with the XRD technique. As shown in Fig. 2, the XRD pattern of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs shows high intense peaks in the whole spectrum of 2 $\theta$  values ranging from 20° to 80°, which correspond to the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs. They are consistent with the standard pattern for JCPDS Card No. (19-0629

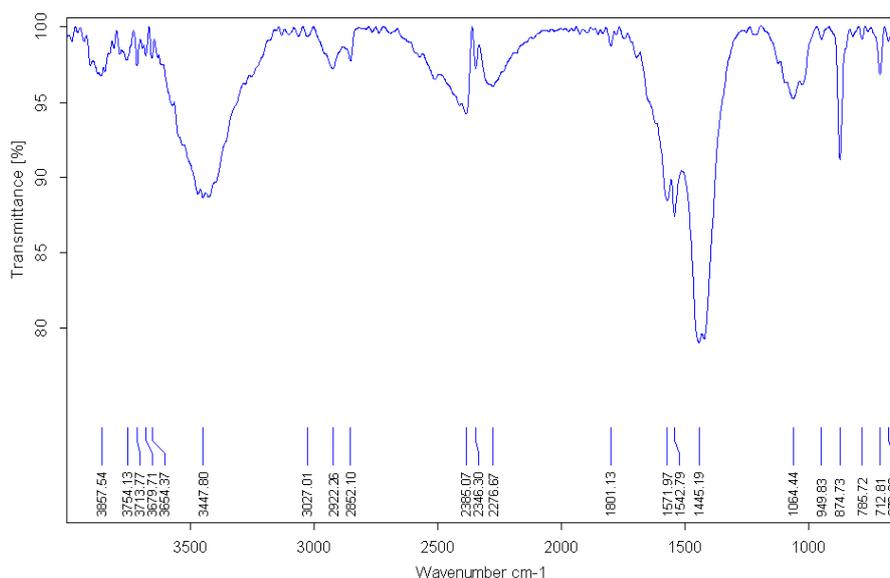


Fig. 1. FT-IR spectra of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs

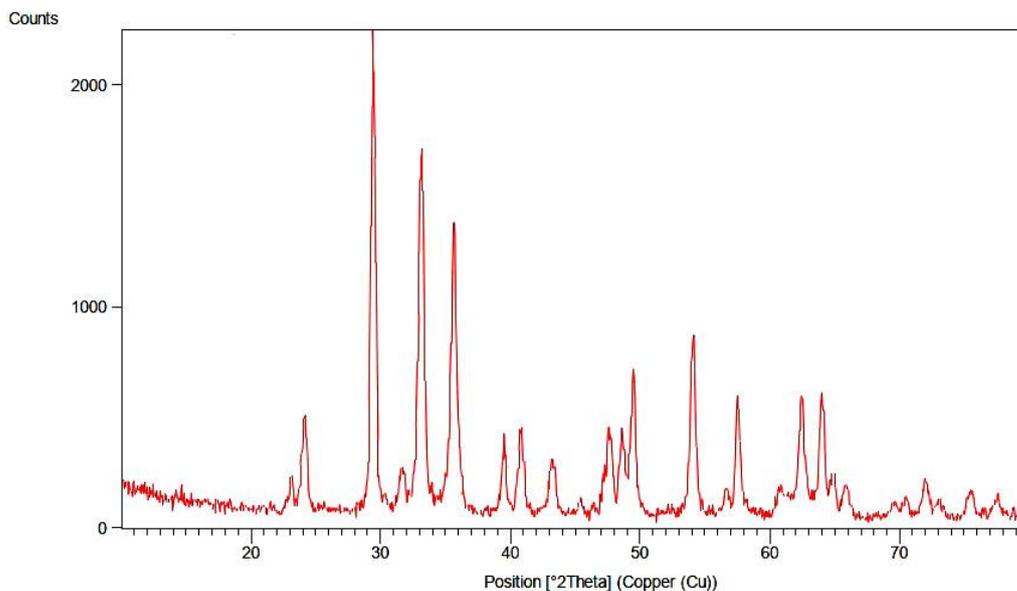


Fig. 2. XRD patterns of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs

for cubic Fe<sub>3</sub>O<sub>4</sub> and 05-0586 for hexagonal CaO) and confirmed that Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs had been formed. The average diameter is obtained about 36 nm according to the line width analysis of the diffraction peaks based on the Debye–Scherrer equation [40] ( $D = K\lambda / \beta \cos\theta$ , where K is constant,  $\beta$  is the peak width at half maximum and  $\lambda$  is X-ray wavelength).

The SEM images in Fig. 3 show the morphologies of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs. In this method, the samples are turned into spherical particles when calcined at high temperatures.

Fig. 4 shows the transmission electron microscopy (TEM) images of the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs. We can see that the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs are composed of small particles. The average particle size is about 40-60 nm.

Based on our previous works, the reaction of thiosemicarbazide or thiocarbohydrazide with aldehydes or ketones in the absents of catalyst have been obtained thiosemicarbazone or thiocarbohydrazone derivatives. In the presence of the catalyst, the one-pot ring closure reactions have been done to obtain heterocyclic derivatives [41-43]. Because of these facts, we tried to synthesis (1S, 2R, 3R, 4R)-1-(4-amino-5-mercapto-4H-1,2,4-triazol-3-yl)pentane-1,2,3,4,5-pentanol (3) and some other triazole derivatives (4-6) in the presents of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs.

In the preliminary stage of the investigation, the model reaction of D-gluconic acid- $\delta$ -lactone 1 (1mmol) and thiocarbohydrazide 2 (1mmol) was carried out by using various amounts of NPs (5, 7, 10 mol%) in various solvents and solvent-free

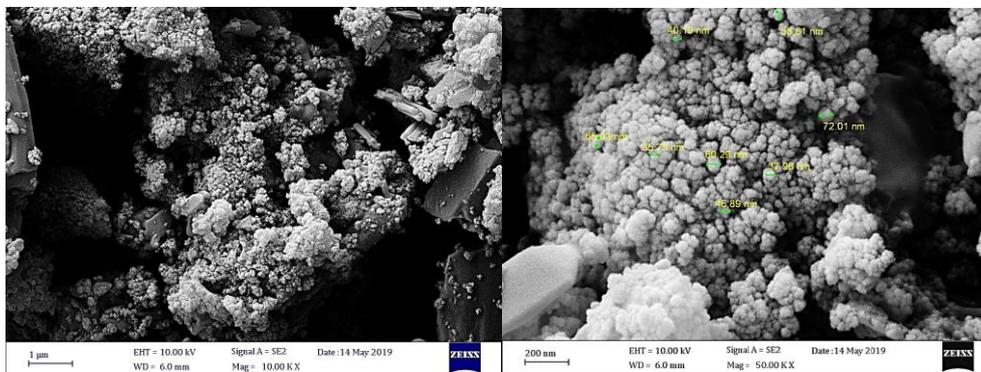


Fig. 3. SEM image of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs

conditions. As shown in Table1, 7 mol% of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs was the best amount of catalyst for this reaction, increasing the amount of catalyst

more than 7 mol% does not increase the yield of the product any further, whereas decreasing the amount of catalyst less than 7 mol% leads to a

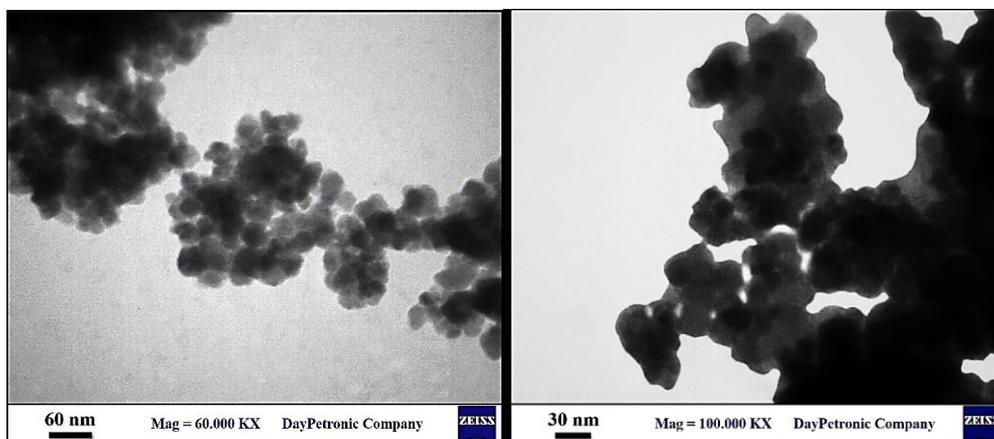


Fig. 4. TEM images of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs

Table 1. The reaction of thiocarbohydrazide (1mmol) and D-gluconic acid-δ-lactone (1mmol) under different conditions.

Entry	Solvent	Catalyst(mol%) Fe <sub>3</sub> O <sub>4</sub> MNPs	Time	Yield <sup>a</sup> (%)	Catalyst(mol%) Fe <sub>3</sub> O <sub>4</sub> /CaO MNPs	Time	Yield <sup>a</sup> (%)
1	THF <sub>dry</sub>	-	4h	trace	-	2h	trace
2	THF <sub>dry</sub>	5	4h	51	5	2h	60
3	THF <sub>dry</sub>	7	4h	58	7	2h	74
4	THF <sub>dry</sub>	10	4h	58	10	2h	75
5	EtOH	-	4h	trace	-	2h	24
6	EtOH	5	4h	53	5	2h	75
7	EtOH	7	4h	68	7	1h	93
8	EtOH	10	4h	68	10	1h	92
9	H <sub>2</sub> O	-	4h	trace	-	2h	trace
10	H <sub>2</sub> O	5	4h	40	5	2h	55
11	H <sub>2</sub> O	7	4h	48	7	1h	82
12	H <sub>2</sub> O	10	4h	46	10	1h	82
13	CH <sub>2</sub> Cl <sub>2</sub> <sub>dry</sub>	-	4h	trace	-	2h	trace
14	CH <sub>2</sub> Cl <sub>2</sub> <sub>dry</sub>	5	4h	41	5	2h	56
15	CH <sub>2</sub> Cl <sub>2</sub> <sub>dry</sub>	7	4h	55	7	2h	62
16	CH <sub>2</sub> Cl <sub>2</sub> <sub>dry</sub>	10	4h	56	10	2h	63
17	CH <sub>3</sub> CN	-	4h	trace	-	2h	28
18	CH <sub>3</sub> CN	5	4h	58	5	2h	63
19	CH <sub>3</sub> CN	7	4h	64	7	2h	71
20	CH <sub>3</sub> CN	10	4h	63	10	2h	71
21	DMF	-	4h	trace	-	3h	trace
22	DMF	5	4h	59	5	3h	69
23	DMF	7	4h	61	7	3h	73
24	DMF	10	4h	62	10	3h	74
25	Solvent-free	-	4h	trace	-	3h	trace
26	Solvent-free	5	3h	37	5	3h	45
27	Solvent-free	7	2h	45	7	2h	56
28	Solvent-free	10	2h	45	10	2h	55

<sup>a</sup> Isolated yield

decrease in the yield of the product. It was found that in the absence of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs, the yield of the product on the TLC plate even after 4h of

the reaction wasn't good. The best results were obtained with 7 mol% of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs in EtOH under reflux conditions (Table 1, Entry 7).

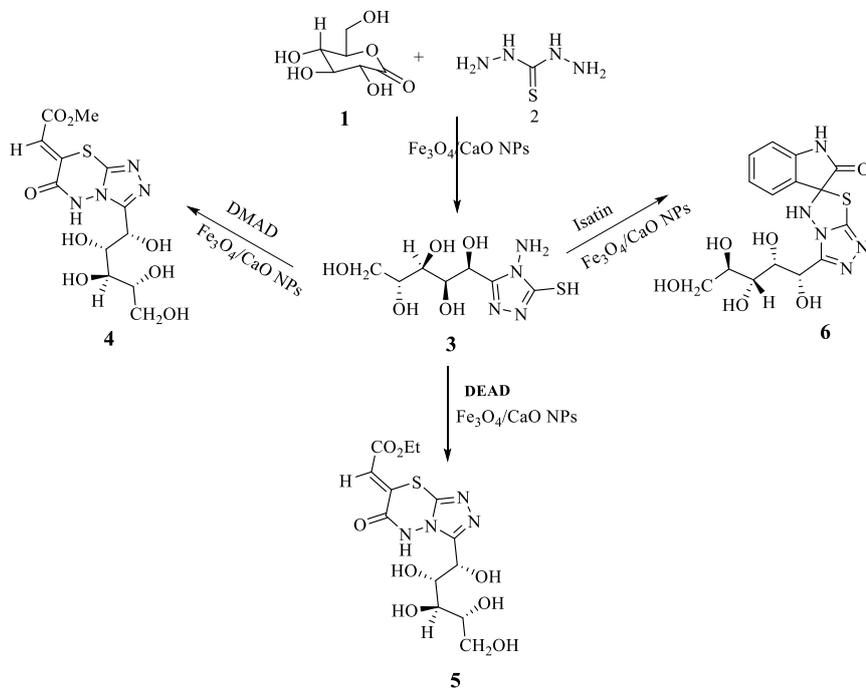


Fig. 5. Production of 1,2,4-triazole derivatives using Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs.

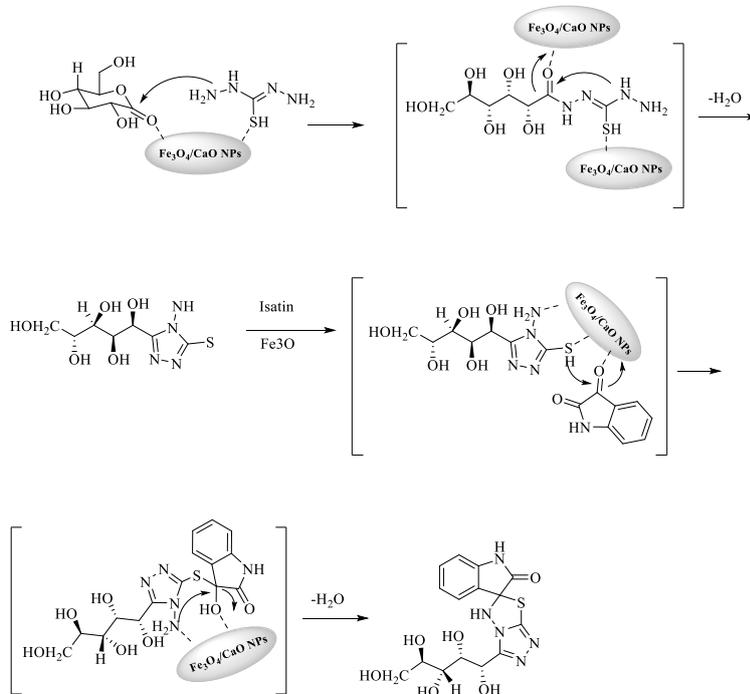


Fig. 6. A plausible mechanism for synthesis of 1,2,4-triazole derivatives using Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs.

Table 2. A comparison of different catalysts for the synthesis of compound 6 in EtOH

Entry	Catalyst	Amount of catalyst (mol%)	Time (hours)	Yield %
1	CuO	10	3	52
2	Fe <sub>3</sub> O <sub>4</sub> MNPs	10	3	63
3	Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> -SO <sub>3</sub> H MNPs	10	2	74
4	CaO NPs	10	2	59
5	ZnO	10	2	73
5	ZnO-CaO NPs	7	2	78
6	Fe <sub>3</sub> O <sub>4</sub> /CaO MNPs	7	1	96

Table 3. Recycling of the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs catalyst.

Number of cycles	Yield <sup>a</sup> (%)
1	92
2	90
3	89
4	87

<sup>a</sup> Isolated yield after chromatography

To evaluate the scope and limitations of this methodology, we extended our studies to the reaction of DMAD (dimethyl acetylenedicarboxylate), DEAD (diethyl acetylenedicarboxylate), and isatin with 1,2,4-triazole. The results are summarized in Fig. 5.

A plausible mechanism for the reaction is envisaged in (Fig. 6). It is proposed that the carbonyl group primarily is activated by NPs (Fe<sub>3</sub>O<sub>4</sub>/CaO), and then the nitrogen attacks to positive centers to open the ring and afford amide intermediate. At least NH or NH<sub>2</sub> groups undergo electrophilic (Fe<sub>3</sub>O<sub>4</sub>/CaO) at the more activated C=O position to react with the carbonyl group and obtain triazole derivatives.

In almost all cases, the reactions proceeded smoothly within 60-80 min, providing the corresponding products in good isolated yields. The structures of compounds are confirmed by IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR, and CHN analysis. For example, the NMR spectrum of compound 6 (scheme 1) exhibited one structure with a spiro chiral carbon. The <sup>1</sup>H NMR spectrum shows singlets at 11.21 and 13.62 ppm for NH protons and five OH signals at 4.16-5.48 ppm for OH protons. These exchangeable protons were exchanged with the

deuterium in the D<sub>2</sub>O as a solvent and disappear from the <sup>1</sup>H NMR spectrum. The aromatic protons were presented at 6.95-7.68 ppm. In the <sup>13</sup>C NMR spectrum, the resonances related to C-OH groups of 6 have appeared at 63.88, 66.47, 71.54, 72.03, and 72.28 ppm. The signals attributed to unsaturated carbon double bonds (-N=C-) have appeared at 171.47, 178.62 ppm, and aromatic carbons showed at 120.28, 122.96, 131.98, 133.23, 142.95, and 152.30 ppm, respectively. The elemental analysis result of compound 6 was satisfactory.

To investigate the efficiency of the Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs, we compared some other metal oxide NPs for the synthesis of compound 6 and the results were summarized in Table 2. The metal oxide NPs were synthesized according to the previously reported procedures [11, 44-47]. As shown in Table 2, the best catalyst for the synthesis of compound 6 is Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs. Using this magnetic metal oxide as a catalyst offers several advantages such as excellent yields, short reaction times, a simple procedure, a simple workup, and using EtOH as a green solvent in contrast with other metal oxides. Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs as an efficient heterogeneous catalyst was prepared by a simple operation from Waste quail eggshells and FeSO<sub>4</sub>.

The catalyst was simply separated by centrifugation, washed with ethanol and water, and dried at 100 °C for 2 h. The recovered catalyst was then re-entered to a fresh reaction mixture under the same conditions and recycled 5 times without considerable loss of activity (Table 3). More recycling of the nanocatalyst led to a gradual reduction during the recovering and washing steps.

## CONCLUSIONS

In summary, an efficient protocol for the synthesis of triazole derivatives was described in the presence of Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs as an inexpensive and reusable catalyst in ethanol. The reactions were carried out in short reaction time and mild reaction conditions and the corresponding products were obtained in good yields. In addition to having the general advantages attributed to the inherent property of nanocatalyst, Fe<sub>3</sub>O<sub>4</sub>/CaO MNPs exhibited exceptionally high catalytic activity in green chemistry and increases reaction speed without pollution. This method is easier and less expensive than other methods.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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