A New Supported Manganese-Based Coordination Complex as a Nano-Catalyst for the Synthesis of Indazolophthalazinetrienes and Investigation of Its Antibacterial Activity

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Abstract

A new magnetic supported manganese-based coordination complex ($\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$) was prepared in consecutive stages, characterized via various techniques (VSM, SEM, TEM, XRD, FT-IR, EDX, TG-DTA and ICP) and used as a capable nano-catalyst for the fast and green synthesis of divers *2H*indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-triones in a simple and efficient procedure from the one pot three-component condensation reaction of aldehydes, dimedone and phthalhydrazide in refluxed ethanol in excellent yields and fast reaction times. The Mn catalyst can be recycled and reused without notable loss of the catalytic activity. Also, the antibacterial properties of the Mn supported nano-catalyst were studied against a number of gram-positive and gram-negative bacterial strains.

1 Introduction

Phthalazine derivatives have an important role in heterocyclic compounds that have received terrific interests in the field of pharmaceutical and biological activities that leads to clinical application¹ such as antifungal², anti-inflammatory,³ anticonvulsant,⁴ anticancer,⁵ cardiotonic. ⁶ In addition, these compounds represents specific optical properties. ⁷

Multi-component reactions (MCRs) are notable mechanism for preparation of wide variety of organic compounds via better efficiency in one step with at least three or more starting materials.⁸ Using a large number of different type of catalysts which accelerate or proceed the reaction in smooth condition have been extensively developed for these reactions.^{9–11} Several synthetic routes have been reported for the synthesis of Phthalazine derivatives such as one-pot three- or four- component condensation reactions.^{12–16} For example, $\text{Fe}_3\text{O}_4@\text{Cys}-\text{SO}_3\text{H}$ was used by Kefayati and coworker as a catalyst for the one-pot three-component condensation of aromatic aldehydes, phthalhydrazide and 1,3-dicarbonyl compounds for the synthesis of *2H*indazolo[2,1-*b*]phthalazinetriones derivatives in ethanol at refluxed condition.¹⁷ Shirini and coworkers applied $[\text{PVP}]\text{HClO}_4$ as an efficient and reusable solid acid polymeric catalyst for the synthesis of *2H*indazolo[2,1-*b*]phthalazine- triones in the same way of using initial regents through the one-pot reaction at 100°C in solvent-free conditions.¹⁸ Heirati and coworkers investigated implementation of O-sulfonic acid poly(4-vinylpyrrolidonium) chloride as an effective catalyst for the same synthesis at 80°C in solvent-free conditions.¹⁹ Rostamnia and co-worker synthesized a series of *1H*indazolo[1,2-*b*]phthalazine-1,6,11-triones by similar regents and using the $\text{Fe}_3\text{O}_4@\text{GO}-\text{Pr}-\text{SO}_3\text{H}$ catalyst in refluxed ethanol.²⁰ 5-sulphosalicylic acid was used by Karhale and coworkers as an organocatalyst catalyst for the one-pot synthesis of *2H*indazolo[2,1-*b*]phthalazinetriones from the previous substrates.²¹ Varghese and coworkers through a noticeable method synthesized *2H*indazolo[2,1-*b*]phthalazine-1,6, 11(13*H*)-triones by similar regents in the presence of iodine under ultrasonic irradiation.²² Mosaddegh and coworkers succeeded to synthesize phthalazinetriones derivatives through a rapid, one-pot, four-component route by using $\text{Ce}(\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ at 125°C and under solvent free condition.²³ However, some methods suffer from some limitations such as

tedious workup procedures, using corrosive catalysts, low product yields, long reaction times, formation of side products and difficulties in recovery of catalysts.²⁴

Due to concerns on environmental issues different strategies were applied to reduce side-effects of chemical industries, for instance using solvent-free techniques, eco-friendly materials, ultrasound or microwave methods and finally recyclable catalysts.²⁵ In recent years the application of magnetic nanoparticles (MNPs) according to the super magnetic property and facile separation from reactions media, high surface area, low toxicity, biocompatibility, good stability, low cost has obtained noticeable regards for chemists using as catalysts in chemical reactions. Moreover, MNPs can be functionalized completely via proper surface modifications. Based on mentioned properties, many MNPs-supported catalysts have been effectively applied for improving a large number of chemical reactions.^{26,27} Among the heterogeneous catalysts, the magnetic supported metal complexes have special places,²⁸ so we would like to announce the synthesis a novel Mn supported nano-catalyst ($\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$) in consecutive stages (Scheme 1).

Then, the Mn supported nano-catalyst was characterized by various techniques (VSM, SEM, TEM, XRD, FT-IR, EDX, TG-DTA and ICP) and used as a capable nano-catalyst for the synthesis of divers 2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-triones in a simple and efficient procedure from the one pot three-component condensation reaction of aldehydes, dimedone and phthalhydrazide in refluxed ethanol in good yields and fast reaction times (Scheme 2).

2 Results And Discussion

2.1 Characterization of the Mn supported nano-catalyst

Structure of the Mn supported nano-catalyst was approved utilizing the FT-IR, ICP, VSM, XRD, EDX, TEM, SEM, and TG-DTA.

2.1.1 ICP analysis of the Mn supported nano-catalyst

The Mn content in $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$ was achieved about 0.27% by The ICP analysis.

2.1.2 FT-IR spectroscopy of the Mn supported nano-catalyst

Figure 1 illustrates the FT-IR spectra for each step of preparation of nano catalyst that includes **A**) Fe_3O_4 MNPs, **B**) $\text{Fe}_3\text{O}_4@\text{SiO}_2$, **C**) $\text{Fe}_3\text{O}_4@\text{SiO}_2@ \text{CPTMS}$, **D**) $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}$ and **E**) $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$. In part **A** existence of stretching vibrations peak for Fe-O is characteristic at about 578 cm^{-1} . Appearing of a wide peak close by 1087 cm^{-1} in part **B** indicates the coating of silica with magnetite nanoparticles. Part **C** exhibits a unique peak at about 583 cm^{-1} confirming the presence of the C-Cl bond. Part **D** shows two newly discovered peaks at 1345 and 1664 cm^{-1} which are corresponded to the C-N and C = N bonds, respectively. Part **E** indicates a shift from 1664

to 1602 cm^{-1} which could be in accordance of the new interaction of manganese with the nitrogen of the C = N bond. Also at 408.93 cm^{-1} a weak peak was appeared in corresponding to the Mn-N band. Therefore, comparison of the all IR spectra approved the successful formation of the Mn supported nano-catalyst.

2.1.3 XRD analysis of the Mn supported nano-catalyst

In order to evaluate the crystallographic structure of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$, the XRD analysis was carried out for $\text{Fe}_3\text{O}_4@\text{SiO}_2$ (grey, **A**), $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}$ (red, **B**), $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}$ (blue, **C**) and $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$ (green, **D**) and shown in Fig. 2. The diffraction peaks at $2\theta =$ at 10, 30, 35, 45, 53, 57 and 63 approve the silica coated on the cubic spinel crystal planes of Fe_3O_4 effectively. The XRD pattern of $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{M}$ indicates the crystalline nature of the nano catalyst at $2\theta =$ 30, 35, 39, 43, 56 which responded to the Mn catalyst. Through Debye Scherrer formula the particle size was obtained about 34.68 nm. In fact, due to the reduction of intensity the core-shell structure could be anticipated and the Fe_3O_4 MNPs particles were coated with ligand profitably.^{29–31}

2.1.4 EDX analysis of the Mn supported nano-catalyst

The elemental structure of the Mn supported nano-catalyst was disclosed by the EDX analysis (Fig. 3). The results ratified the existence of the predictable elements in the construction of the catalyst, including C, N, O, Si, S, Fe and Mn. Generally the sample will be usually coated with a very thin layer of gold that leads appearing of the Au peak in the EDX graph analysis, as well.

2.1.5 SEM and TEM analysis of the Mn supported nano-catalyst

In another evaluation, the morphology and size of the Mn supported nano-catalyst were determined by SEM and TEM images (Fig. 4–5). The spherical shape of the $\text{Fe}_3\text{O}_4@\text{SiO}_2@\text{CPTMS}@\text{MBOL}@\text{Mn}$ is conceived through the uniform nanometer-sized particles. In the SEM images, formation of sintered grains with the 35–47 nm size range was apparent. The core–shell structure of nano catalyst could be observed via TEM images. However, magneto static interactions of the particles could be the reason of some particle aggregations. At an exact scrutiny, according to distribution histograms (Fig. 6), the average sizes of the nanoparticles is anticipated between 19.1 and 29.7 nm.

2.1.6 Thermal properties of the Mn supported nano-catalyst

The thermo-gravimetric analysis shows the thermal stability and decomposition behavior of the Mn supported nano-catalyst beyond heating (Fig. 6). As observed there are about four weight loss stages for the catalyst in the ranges of 100, 185, 300, and 360 °C, respectively. The initial weight reduction at about 100 °C probably corresponds to the residual water, the second weight loss at about 180 °C is possibly attributed to the thermal decomposition of the complex, the third weight loss at about 300 °C is attributed

to the thermal decomposition of the two CPTMS and MBOL ligands, and the fourth weight reduction at about 360 °C is probably resulted from the de-coating of Fe₃O₄.

2.1.7 VSM analysis of the Mn supported nano-catalyst

Due to comparison of magnetic properties, the VSM analysis was performed for the five steps of preparing including A) Fe₃O₄ MNPs, B) Fe₃O₄@SiO₂, C) Fe₃O₄@ SiO₂-CPTMS, D) Fe₃O₄@SiO₂@CPTMS@MBOL and E) Fe₃O₄@SiO₂@CPTMS@MBOL@Mn (Fig. 7). Generally, all five steps of formation show magnetic possessions and a clear decrease from A to E (65, 35, 30, 10 and 4.35 emu/g, respectively) can be observed. In fact the dipolar–dipolar interactions reduce between the magnetic nanoparticles due to coating of Fe₃O₄ MNPs via different layers and complexation.

3 Experimental

3.1 General

All chemicals (starting materials, reagents, solvents, etc) were acquired from the chemical companies and used in the absence of additionally purification.

3.2 Preparation of the Mn supported nano-catalyst

The Mn supported nano-catalyst was prepared according to the procedure described.³²

3.3 General Procedure for the synthesis of indazolophthalazinetriones

Phthalhydrazide (0.162 g, 1.0 mmole), dimedone (0.140 g, 1.0 mmole), an aldehyde derivative (1.0 mmole) and the Mn supported nano-catalyst (20 mg) were mixed in ethanol (5 mL), stirred and heated at reflux condition in appropriate times which depends on the substrate (Table 2), and completion of the reaction was monitored with TLC. After cooling, the Mn supported nano-catalyst was separated by a super magnet, H₂O (10 mL) added, and a white precipitate filtered and recrystallized in EtOH.

3.4 Optimization

To obtain the best result, effects of different conditions were investigated for this reaction. The one-pot three-component condensations of phthalhydrazide (1.0 mmole), 4-methylbenz-aldehyde (1.0 mmole) and dimedone (1.0 mmole) was chosen as a model reaction in different reaction conditions (amount of the catalyst temperature and solvent). The best result was achieved with 1.0 mmole of 1:1:1 of benzaldehyde: dimedone: phthalhydrazide in presence of 20 mg of the Mn supported nano-catalyst in EtOH at reflux condition (Table 1, entry 5).

Table 1
Optimization of the reaction conditions

Entry	Solvent	Catalyst (mg)	Temperature (°C)	Time (min)	Yield (%)
1	EtOH/H ₂ O	10	80	15	71
2	EtOH/H ₂ O	20	80	15	82
3	EtOH/H ₂ O	30	80	15	74
4	EtOH/H ₂ O	40	80	15	74
5	EtOH	20	80	15	90
6	H ₂ O	20	80	15	76
7	Toluene	20	80	15	53
8	DMF	20	80	15	49
9	EtOH	20	60	15	72
10	EtOH	20	40	15	37
11	EtOH	20	rt	15	21

Also, two additional reactions were performed under the optimum conditions as below:

1. The synthesis of indazolophthalazinetriones carried out in the absence of Fe₃O₄@SiO₂@CPTMS@MBOL@Mn: The reaction efficiency was very low (trace).
2. The reaction was done in the presence of (Fe₃O₄@SiO₂@CPTMS@MBOL) and no product was observed.

3.5 Synthesis of diverse indazolophthalazinetriones (2a-j)

According to the optimization of model reaction, different indazolophthalazinetriones (**2a-j**) were synthesized from the one pot three-component condensation reaction of aldehydes, dimedone and phthalhydrazide in EtOH at reflux conditions in attendance of the Mn supported nano-catalyst with good to excellent yields in fast reaction times (Table 2).

3.6 Characterization of the products

All indazolophthalazinetriones were characterized and recognized by considering to their physical and spectroscopic analysis and comparing the reported in the literature. The structures of all products were confirmed via their IR and NMR spectra (Supplementary data).

3,3-Dimethyl-13-phenyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**2a**): mp 202–206°C; FT-IR (KBr, cm⁻¹): The characteristic IR peaks: 3100, 3000, 2953, 1663; ¹H NMR (90 MHz, CDCl₃):

$\delta_{\text{H}} = 7.80\text{--}8.37$ (m, 4H), 7.26 (m, 5H), 6.45 (s, 1H), 3.30 (d, 2H, CH_2), 2.33 (s, 2H, CH_2), 1.22 (s, 6H, 2 CH_3). ^{13}C NMR (75 MHz, CDCl_3): 28.7, 34.7, 38, 5, 65, 77.5, 118, 127, 127, 127.7, 128, 128.6, 128.7, 128.8, 128.9, 129, 133.5, 134.5, 136.3, 150.8, 154.2, 156, 192.

13-(4-Chlorophenyl)-3,3-dimethyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**2b**): mp 260–263°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2957, 1660; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.81\text{--}8.41$ (m, 4H), 7.32 (m, 4H), 6.41 (s, 1H), 3.30 (d, 2H, CH_2), 2.34 (s, 2H, CH_2), 1.21 (s, 6H, 2 CH_3). ^{13}C NMR (75 MHz, CDCl_3): 28.5, 34.4, 38, 50, 61.3, 77, 118, 127.7, 128.2, 129.2, 134, 151, 154.3, 192.

13-(4-Bromophenyl)-3,3-dimethyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**2c**): mp 256–259°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2959, 1687, 1654; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.86\text{--}8.39$ (m, 4H), 7.23–7.35 (m, 4H), 6.70 (s, 1H), 3.23–3.45 (d, 2H, CH_2), 2.34 (s, 2H, CH_2), 1.23 (s, 6H, 2 CH_3).

3,3-Dimethyl-13-(3-nitrophenyl)-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**2d**): mp 267–270°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2962, 1661; ^1H NMR (300 MHz, CDCl_3): $\delta_{\text{H}} = 7.87\text{--}8.40$ (m, 4H), 6.52–7.59 (m, 4H), 6.52 (s, 1H), 3.24–3.47 (dd, 2H, CH_2), 2.35 (s, 2H, CH_2), 1.22 (s, 6H, 2 CH_3). ^{13}C NMR (75 MHz, CDCl_3): 27.3, 28.4, 28.6, 34.7, 38, 50.8, 64, 76.5, 77, 117, 121.5, 123.7, 127.7, 128.2, 128.6, 129, 129.6, 134, 134.2, 134.7, 138.6, 148.5, 151.8, 154.6, 156, 192.

13-(2,4-Dichlorophenyl)-3,3-dimethyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11-(2*H*, 13*H*)-trione (**2e**): mp 219–222°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2964, 2940, 1663; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.75\text{--}8.38$ (m, 4H), 7.13–7.26 (m, 3H), 6.6 (s, 1H), 3.3 (d, 2H, CH_2), 2.33 (s, 2H, CH_2), 1.22 (s, 6H, 2 CH_3). ^{13}C NMR (75 MHz, CDCl_3): 28.8, 34.6, 38, 50.8, 63.5, 77, 127.6, 127.7, 128, 128.6, 129, 130.4, 131.7, 133.2, 133.7, 134.6, 135, 152, 154.3, 156, 192.

3,4-Dihydro-3,3-dimethyl-13-(4-methylphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione (**2f**): mp 224–227°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2924, 1687, 1655; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.77\text{--}8.28$ (m, 4H), 7.17–7.35 (m, 4H), 6.4 (s, 1H), 3.3 (d, 2H, CH_2), 2.29–2.32 (m, 5H), 1.21 (s, 6H, 2 CH_3).

13-(4-Methoxyphenyl)-3,3-dimethyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11-(2*H*, 13*H*)-trione (**2g**): mp 219–221°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2956, 1664; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.92\text{--}8.24$ (m, 4H), 7.54–7.82 (m, 4H), 6.5 (s, 1H), 3.77 (s, OCH_3), 3.33 (d, 2H, CH_2), 2.33 (s, 2H, CH_2), 1.2 (s, 6H, 2 CH_3).

3,4-Dihydro-3,3-dimethyl-13-(2-eylnaphtalene)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione (**2h**): mp 249–251°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2967, 1681, 1664; ^1H NMR (90 MHz, CDCl_3): $\delta_{\text{H}} = 7.45\text{--}8.38$ (m, 11H), 6.62 (s, 1H), 3.24–3.5 (dd, 2H), 2.33 (s, 2H), 1.22(s, 6H). ^{13}C NMR

(75 MHz, CDCl_3): 118.6, 124, 126.2, 126.3, 126.8, 127.7, 128, 128.2, 128.7, 129, 133.2, 133.4, 133.5, 133.6, 134.5, 150.8, 156, 192.

13-Ethyl-3,3-dimethyl-3,4-dihydro-1*H*-indazolo[2,1-*b*]phthalazine-1,6,11(2*H*,13*H*)-trione (**2i**): mp 264–267°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2962, 2931, 1652; ^1H NMR (90 MHz, CDCl_3): δ_{H} = 7.81–8.35 (m, 4H), 5.69 (m, 1H), 3.16 (d, 2H, CH_2), 2.16–2.37 (m, 4H, 2 CH_2), 1.19 (s, 6H, 2 CH_3), 0.65–0.82 (t, 3H, CH_3).

3,4-Dihydro-3,3-dimethyl-13-(4-thiomethylphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione (**2j**): mp 228–230°C; FT-IR (KBr, cm^{-1}): The characteristic IR peaks: 3100, 3000, 2959, 2978, 1663; ^1H NMR (90 MHz, CDCl_3): δ_{H} = 7.84–8.37 (m, 4H), 7.1–7.35 (m, 4H), 6.4 (s, 1H), 3.21–3.45 (d, 2H, CH_2), 2.42 (s, 3H), 2.34 (s, 2H), 1.2 (s, 6H).

3.7 The plausible mechanism

A persuasive mechanism for the synthesis of diverse phthalazine-triones is illustrated as below. The reaction is followed by mixture of reagents in EtOH at reflux conditions in the presence of the Mn supported nano-catalyst (Scheme 3).

The suggested mechanism is presumably in accordance of the Lewis acidity of the Mn supported nano-catalyst by connecting to the carbonyl group to simplify the nucleophilic attack of the enolic form of dimedone (Knoevenagel condensation) to aldehyde to form the intermediate with the subsequent deletion of water, the nucleophilic attack of phthalhydrazide, deletion of water, and the final cyclization to get the product.

3.8 Comparison of Catalytic activity

Table 3 shows the comparison of the previous procedures (entries 1–9) used for the synthesis of 3,4-Dihydro-3,3-dimethyl-13-(4-methylphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione with our used method (entry 10). In general, each procedure includes some advantages that by focusing on the previous routes we could declare this method could accelerate the process of reaction and be useful and efficient as well.

Table 3

Comparison of the Mn supported nano-catalyst capability with the other catalysts in synthesis of 3,4-dihydro-3,3-mimethyl-13-(4-methylphenyl)-2*H*-indazolo[2,1-*b*]phthalazine-1,6,11(13*H*)-trione

Entry	Catalyst	Solvent ^a	T ^b (°C)	Time (min)	Yield (%)	Ref.
1	MNPs-guanidine (0.03 g)	SF	70	40	90	34
2	β-Cyclodextrin	H ₂ O	80	30	86	35
3	[Simp] ₃ PW ₁₂ O ₄₀ (0.03 g)	SF	100	60	66	36
4	PTA@Fe ₃ O ₄ /EN-MIL-101 (0.02 g)	SF	100	60	70	37
5	Fe ₃ O ₄ @Silica sulfuric acid (0.075 g)	SF	100	40	86	38
6	MNPs-PSA (0.03)	SF	100	30	90	39
7	H ₂ SO ₄ (0.015 %mmole) in EtOH/H ₂ O	EtOH	Reflux	30	86	40
8	MnFe ₂ O ₄ @SiO ₂ @NH-NH ₂ -PTA (0.03 g)	SF	80	30	87	41
9	CAN (5 %mol)	PEG	50	150	94	42
10	Fe ₃ O ₄ @SiO ₂ @CPTMS@MBOL@Mn (0.02 g)	EtOH	Reflux	15	90	PW ^c
^a SF = Solvent-free, ^b T = temperature, ^c PW = present work						

3.9 Reusability of the Mn supported nano-catalyst

To investigate the recyclability of the Mn supported nano-catalyst for environmental and commercial applications, it was tested with the model reaction, and found that it is relatively capable even after five runs and its activity was almost similar to the fresh one (90, 90, 88, 87, and 84%) respectively (Fig. 8). The stability of the Mn supported nano-catalyst even after the 5th run was inspected by FT-IR and SEM techniques (Fig. 9–10).

3.10 Antibacterial properties

The antibacterial properties of the Mn supported nano-catalyst were studied against a number of gram-positive and gram-negative bacterial strains, and DMSO was used as a blank (Table 4). The catalyst inhibited the growth of bacterial strains, producing a zone of inhibition of diameter 5–30 mm. The Mn supported nano-catalyst was even more effective against *Serratia marcescens* in gram-negative bacteria than the standard tetracycline antibiotic. Since the comparison of the size of inhibition zones is generally not reliable, the MIC value of the compound was also determined. The results indicated that the MIC value of the Mn supported nano-catalyst against the tested organisms was about 8 mg/mL. The MIC value of standard tetracycline antibiotic is about 8 mg/mL.

Table 4 Antibacterial activity of Mn supported nano catalyst that was expressed as diameter of inhabitation zone (mm) and minimum inhibitory concentration (MIC)

Microorganisms	Standard	Blank	Zone of inhabitation (mm)
MIC (mg/mL)	Tetracycline (10 mg/mL)	DMSO	the Mn catalyst
	8	-	8
Gram (+)	30	-	10
Bacillus thuringiensis	36	-	20
Bacillus cereus	30	-	5
Staphylococcus aureus			
Gram (-)	25	-	20
Pseudomonas aeruginosa	20	-	30
Serratia marcescens	22	-	15
Escherichia coli	25	-	5
Klebsiella pneumoniae			

4 Conclusion

In conclusion, we were successful to synthesize a novel Mn nano-catalyst supported on magnetic iron oxide functionalized with mercaptobenzoxazole as an appropriate surface for synthesis of 2*H*-Indazolo[1,2-*b*]phthalazine-triones from the one pot three-component condensation reaction of aldehydes, dimedone and phthalhydrazide in refluxed ethanol in fine yields and short reaction times. In fact iron oxide nanoparticles through the noticeable properties such as small size, high magnetism and low toxicity would be a proper methods for chemistry synthesis. Also we inspected the antibacterial properties of Mn nano catalyst against a number of gram-positive and gram-negative bacterial strains and determined the nano catalyst would be more effective against *Serratia marcescens* in gram-negative bacteria than the standard tetracycline antibiotic. Environmental issues revealed that the Mn nano catalyst would be used for five runs without significant loss of the catalytic activity.

Declarations

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Tables

Due to technical limitations, table 2 is only available as a download in the Supplemental Files section.

Figures

Figure 1

FT-IR spectra of five steps of preparation of nano-catalyst (A, B, C, D and E)

Figure 2

Synthesis of a novel Mn supported nano-catalyst

Figure 4

Synthesis of diverse indazolophthalazinetriones

Figure 5

The EDX analysis of the Mn supported nano-catalyst

Figure 6

Figure 7

The SEM images of the Mn supported nano-catalyst

Figure 8

The TEM images of the Mn supported nano-catalyst

Figure 9

The particle size distribution of Mn- catalyst

Figure 10

TGA-DTA patterns of the Mn supported nano-catalyst catalyst

Figure 11

The VSM analysis of A, B, C, D and E

Figure 12

Reusability of the Mn supported nano-catalyst

Figure 13

FT-IR spectra of fresh and recovered Mn supported nano-catalyst

Figure 14

SEM image of recovered Mn supported nano-catalyst

Figure 15

Antibacterial activity of Mn supported nano catalyst

Supplementary Files

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- [Table2b.jpg](#)