Synthesis and characterization of core-shell Fe_3O_4@collagen nanoparticle, and application as catalyst in green synthesis of benzimidazoles and benzothiazoles

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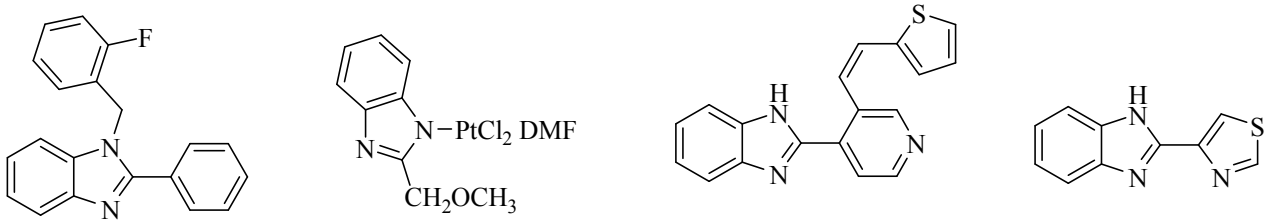
Abstract: Nanoparticles are nanostructures with at least one dimension being less than 100 nm. In this research, nanomagnetic Fe_3O_4@Collagen was prepared and characterized by Fourier transforms infrared spectroscopy (FT-IR) spectra, Scanning electron microscopy (SEM) images, energy dispersive X-ray spectroscopy (EDX) spectra, X-ray diffraction (XRD) measurements. Fe_3O_4@collagen is a new and green nano catalysis and using in synthesis of benzimidazoles and benzothiazoles. This method offers several advantages including high yields, short reaction times, easy work up procedure, reusability of catalyst and environmentally benign reaction conditions.

Keywords: Green synthesis,Nanoparticle, Fe_3O_4@Collagen,benzimidazoles, benzothiazoles.

1.Introduction

The benzimidazoles and benzothiazoles have attracted much interest in diverse areas of chemistry.
These heterocycles have shown different pharmacological activities such as antibacterial, antiulcers, antihypertensives, antivirals, antifungals, anticancers, and antihistaminics. These compounds are also used as ligands for asymmetric transformations, exhibit nonlinear optical and luminescent/fluorescent. Benzimidazole derivatives exhibit significant activity against several viruses such as HIV, herpes (HSV-1), RNA, potential antitumor agents, antimicrobial agents and influenza. They also act as topoisomerase inhibitors, selective neuropeptide YY1 receptor antagonists, angiotensinII inhibitors and smooth muscle cell proliferation inhibitors and have much more importance in organic synthesis [1].



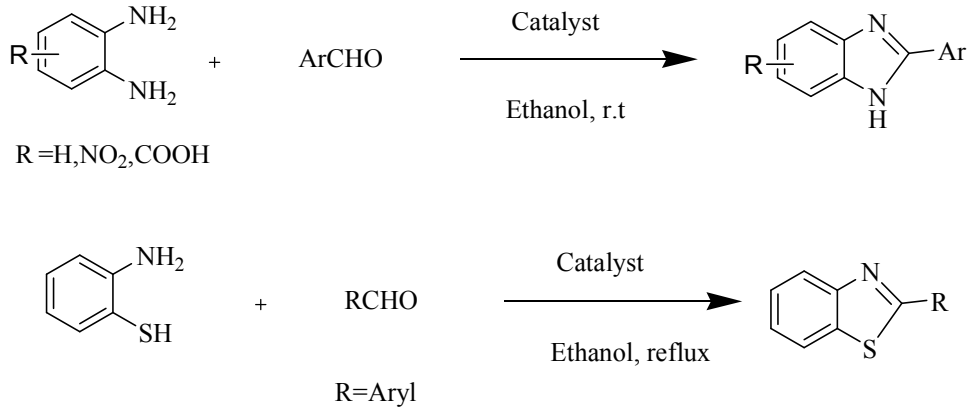
antiviral HIV | antiviral | anticancer | antimicrobial

Fig 1.Biologically active benzimidazol derivatives

A number of methods have been developed for the synthesis of benzimidazoles. Generally 2-substituted benzimidazoles are synthesized by 1,2-phenylendiamine with an aldehydes, acyl chlorides, carboxylic acids or orthoesters which comprise the use in acidic medium with microwave irradiation [2], refluxing in acetic acid [3], silica supported sulfuric acid [4], zinc-proline [5], $Yb(OTf)_3$ [6].
In addition a number of methods have been reported for the synthesis of the benzothiazole by 2-aminothiophenol with acyl chlorides or aldehydes which comprise the use of ionic liquid [7], refluxing in

acetic acid [8], oxygen/active carbon in the presence of toxic solvents xylene [9], Sio_2 with microwave irradiation [10].
Many of the synthetic methods for benzimidazoles and benzothiazoles suffer from one or more disadvantages such as low yields, strict reaction conditions, long time period and expensive catalysts and difficult workup. Thus, the development of environmentally benign, high-yielding, and fast synthesis of benzimidazole and benzothiazole derivatives still remains a desired goal in organic synthesis. we wish to report herein a highly efficient procedure for the preparation of benzimidazole and bezothiazole derivatives using Fe_3O_4@Collagen, in EtOH solvent (Scheme 1).

Scheme 1. Synthesis of benzimidazole derivatives catalysed by Fe_3O_4@Collagen at room temperature (25 °C) and synthesis of benzothiazole derivatives catalysed by Fe_3O_4@Collagen at reflux.



2.Experimental

2.1. *Materials and methods*

All chemicals were purchased from Merck, Fluka and Sigma-Aldrich companies and were used without further purification. All reactions and the purity of benzimidazole and benzothiazole derivatives were monitored by thin-layer chromatography (TLC) using aluminum plates coated with silica gel F254 plates (Merck) using ethyl acetate , n-hexane and methanol as eluents. Melting points were determined in open capillaries using an Electro thermal 9100 instrument. IR spectra were recorded on a Shimadzu FT-IR400s. 1H NMR spectra were recorded on a Bruker 400 Ultrasheild NMR and DMSO-d6 was used as solvent.

2.2.*General procedure for the synthesis of benzimidazoles derivatives*

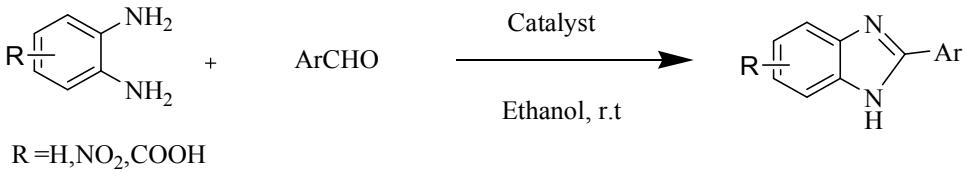
A mixture of aromatic aldehyde (1.0 mmol), 1,2-phenylendiamine (1.0 mmol) were employed as reactants in the presence of catalytic amount of Fe_3O_4@Collagen (50 mg) and 4 mL of EtOH as solvent was stirred at room temperature for 10–60 min, the progress of the reaction was monitored by thin-layer chromatography (TLC). the catalyst washed with EtOH and after drying could be ready to use for the next reaction without loss in activity. After evaporation of the solvent, the resulting solid product was recrystallized from ethanol to obtain pure product. The products were characterized by FT-IR spectra and melting point.

2.3.*General procedure for the synthesis of benzothiazole derivatives*

A mixture of aromatic aldehyde (1.0 mmol), 2-aminothiophenol (1.0 mmol) were employed as reactants in the presence of catalytic amount of Fe_3O_4@Collagen (50 mg) and 4 mL of EtOH as solvent was stirred at reflux for 35–140 min, the progress of the reaction was monitored by thin-layer chromatography (TLC). the catalyst washed with EtOH and after drying could be ready to use for the next reaction without loss in activity. After evaporation of the solvent, the resulting solid product was recrystallized from ethanol to obtain pure product. The products were characterized by FT-IR spectra and melting point.

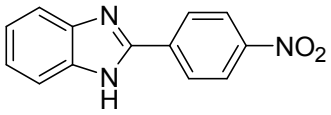
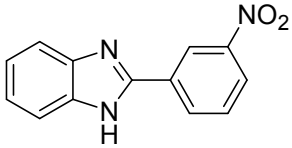
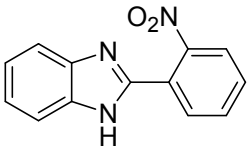
3. Results and discussions

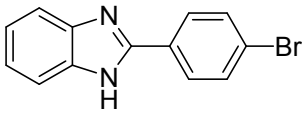
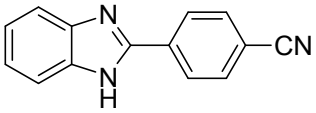
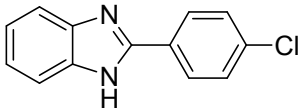
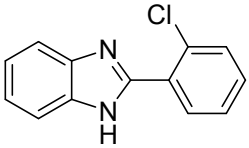
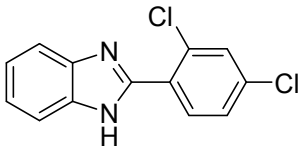
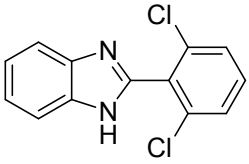
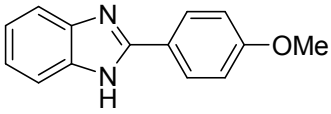
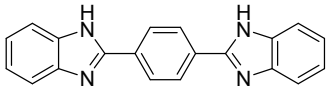
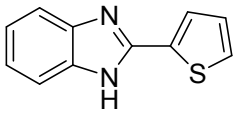
In a pilot experiment, a mixture of 1.0 mmol of 1,2phenylendiamine, 1.0 mmol of 3-nitrobenzaldehyde and Fe_3O_4@Collagen (0.05 g) in 4 mL of EtOH as solvent in a vial was stirred under room temperature conditions. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the solid product were collected by a simple filtration and washed with EtOH. In order to show the general applicability of the method a variety of benzimidazoles were synthesized using different aldehydes. Various halogens and electron withdrawing groups on the aldehydes were well tolerated and yields are almost quantitative in all cases (Table 1).

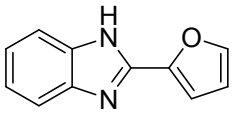
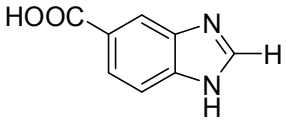
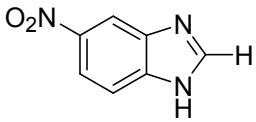


R =H,NO_2,COOH

Table 1. Synthesis of benzimidazole derivatives the presence of Fe_3O_4@Collagen

Entry	Ar	R	Product	Time (min)	Yield[a] (%)	MP(°C)	
						Found	Reported
1	4-$NO_2C_6H_4$	H		12	78	314-318	315-317 [11]
2	3-$NO_2C_6H_4$	H		15	97	186-188	185-187 [12]
3	2-$NO_2C_6H_4$	H		15	78	260	261-263 [13]

4	4-BrC_6H_4	H		15	85	296.5-298	297-298 [14]
5	4-CNC_6H_4	H		20	90	261	262 [15]
6	4-ClC_6H_4	H		20	60	281-282	281-283 [12]
7	2-ClC_6H_4	H		20	50	222-223	225 [16]
8	2,4-$Cl_2C_6H_4$	H		18	87	218-220	220 [17]
9	2,6-$Cl_2C_6H_4$	H		25	73	218-222	220 [18]
10	$OCH_3C_6H_4$	H		30	55	181	180-182 [1]
11	$CHOC_6H_4$	H		20	83	>400	456-458 [19]
12	Thiophen	H		25	97	345	342-343 [20]

13	Furan	H		60	65	234-238	234-235 [21]
14	4-CNC_6H_4	COOH		30	70	185	183-185 [14]
15	4-CNC_6H_4	NO_2		25	73	189	191-192 [14]

[a] Isolated yields.

In a pilot experiment, a mixture of 1.0 mmol of 2-aminothiophenol, 1.0 mmol of 3-nitrobenzaldehyde and Fe_3O_4@Collagen (0.05 g) in 4 mL of EtOH as solvent in a vial was stirred under refluxing conditions. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the solid product were collected by a simple filtration and washed with EtOH. In order to show the general applicability of the method a variety of benzothiazole were synthesized using different aldehydes. Various halogens and electron withdrawing groups on the aldehydes were well tolerated and yields are almost quantitative in all cases. The results are summarized in Table 2

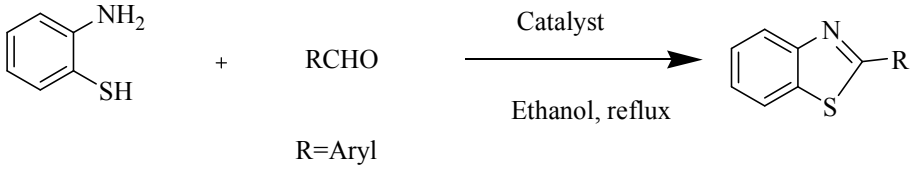
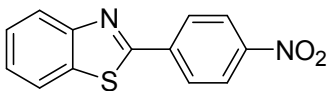
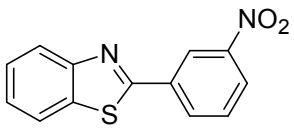
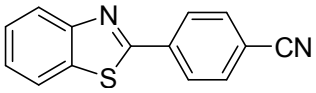
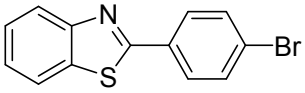
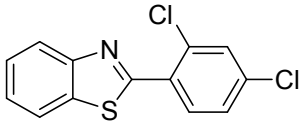
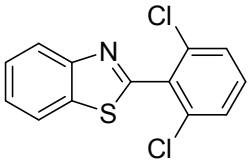
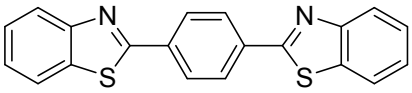


Table 2. Synthesis of benzothiazole derivatives the presence of Fe_3O_4@Collagen

Entry	Ar	Product	Time (min)	Yield[a] (%)	MP(°C)	
					Found	Reported
1	4-$NO_2C_6H_4$		90	70	223-226	224-225 [22]
2	3-$NO_2C_6H_4$		60	83	180-182	180-181[23]

3	4-CNC_6H_4		35	78	161-162	161-162 [24]
4	4-BrC_6H_4		50	75	120.9-122	120-121 [25]
5	2,4-$Cl_2C_6H_4$		65	80	140-143	144-145 [26]
6	2,6-$Cl_2C_6H_4$		100	65	89-91	87-90 [27]
7	$CHOC_6H_4$		140	63	198	196 [28]

[a] Isolated yields.

First, to optimize the reaction conditions, we carried out the reaction of 1,2-phenylendiamine (1 mmol) and 3-nitrobenzaldehyde (1 mmol) as a model reaction in the presence of different organic solvents (Table 3). The results showed that ethanol was the solvent of choice (Table 3).

Table 3. Optimization of the solvent for the Synthesis of benzimidazole .[a]

Entry	Solvent	Time(min)	Yield(%)
1	ETOH	15	97
2	H_2O	15	Trace
3	CH_2Cl_2	15	80
4	$CHCl_3$	15	48.67
5	CH_3CN	15	_

a Conditions: 1 mmol 1,2phenylendiamine, 1 mmol 3-nitrobenzaldehyde , 4 mL solvent.

4.Conclusion

In summary, we have delineated a highly efficient, procedure for the synthesis of benzimidazole and benzothiazole using Fe_3O_4@Collagen-catalyst. In other words, the most important feature of described

method is use of organic solvent, reusability of the catalyst, facile conditions, easy isolation of the products with excellent purity, increasing yields, reducing reaction time and waste-free chemical process

Acknowledgements

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