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Fabricated Fe_3O_4 as an efficient catalyst for the synthesis of naphthapyranopyrimidines and 5-aryl-1, 2, 4-triazolidine-3-thione under microwave irradiation

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This study describes the use of iron oxide decorated with SiO_2@SO_3H as an efficient heterogeneous catalyst for bioactive heterocycles synthesis. The present work describes eco-friendly preparation of magnetic nanoparticles Fe_3O_4 (MNPs), further functionalized to Fe_3O_4@SiO_2-SO_3H. The prepared MNPs and their functionalized materials are fully characterized by FT-IR, XRD, FE-SEM, EDX, HR-TEM, and VSM (published).The modified iron oxide provide faster rate of the reaction for the synthesis of naphthopyranopyrimidine and 5-aryl-1, 2, 4-triazolidine-3-thione (**4a**, **4**c & **4d**, and **6d**, **6e, 6g,** & **6h**) in the presence of EtOH and microwave irradiation with excellent product isolation. The synthesized derivative has been recrystallized using ethanol, and homogeneity of the product has been examined by various spectroscopic techniques. Further, the selected derivatives (**4a**, **4e**, **4f**, **4g** & **4k,** and **6a**, **6b** & **6c**) were tested for their antioxidant activities and showed comparable scavenging ability.

Keywords: 1,3-Dimethylbarbituric acid, Iron oxide, Magnetic nanoparticles, MWI, Naphthopyranopyrimidine, Thiosemicarbazide

Introduction

Nanoparticles have attracted significant attention due to their unique properties like high surface area, activities and easily recoverable[1]. Heterogeneous nanocatalyst with high surface area can be separated from the reaction mixture easily by the filtration or external magnate. This property can be achieved by different preparation condition by which different size and shape can be synthesised[2]. Recent years magnetic nanoparticles (MNPs) emerged as special category of nanoparticles, due to their advanced application in cancer treatment and medicine, and also as a heterogeneous catalyst to synthesize various chemical compounds, colour pigments, natural remediation, etc[3]. MNPs are special class of materials treated, due to their easy separation from the reaction mixture, after the reaction[4]. Iron oxide exists in different forms (Fe_3O_4, α-Fe_2O_3 and γ-Fe_2O_3), Fe_3O_4 owing very good biocompatibility and magnetic permeability, easy to prepared and extensively used as a core-shell choice for the further extension[5]. Various surface fabricated iron oxide (alone or composite) materials have been well documented and demonstrated to exhibit sensing, biomedical and environmental remediation applications[6]. One of the fabrication materials well studied is MNPs with silica.

Ready availability of a vast number of silica derivatives and clean and easy reaction on iron oxide impel fabrication of core-shell Fe_3O_4-silica nanoparticles[7]. Researchers reported modified Fe_3O_4 gave better stability, prevented agglomeration and further oxidation[8]. Several publications on Fe_3O_4 and its fabrication emerged as a heterogeneous catalysts employed in various organic reactions involved either step-wise or multi-component reactions (MCRs)[9]. MCRs emerged as a promising synthetic route for the construction of wide range of complex heterocycles in one-pot by the reaction of three or more reactants in single step[10]. It is the first choice for the chemist to preferred, due to their high productivity, simple procedure, facile and atom economy are the advantageous compared to step wise reactions[11].

Microwave irradiation (MWI) is a prominent technique used in the organic reactions and well-developed MW reactor is used to reduce reaction times, as well as attain high atom economy of the organic transformations[12]. In the last two decades, wide range of organic reactions performed accelerated

by MWI has been well documented[13]. Nowadays heterocycles have emerged as promising skeletons, and widely distributed both in synthetic and natural drugs, due to several natural heterocyclic molecules exhibiting various applications such as hormones, vitamins, antibiotics ,nucleic acids, pharmaceuticals, dyes, agrochemicals, and more[14]. Among, nitrogen atom containing heterocycles have emerged superior in terms of bioactivities and abundant. The FDA reported data shows that nearly 70% of the small drug molecules used in the pharmaceuticals contain N-atom in one or more of their ring systems[15]. This is due to their H-bonding capability and specific target receptor binding capacity. Some of the well-known heterocyclic like 1,2,4-trizoles, pyrazoles[16], imidazole[17], β-lactams[18], quinolines[19], pyrimidine [20], and many more skeletons containing N-atom in the ring systems are well documented[21]. Naphthopyranopyrimidine is an important structural motif containing N-heteroatom in their skeleton, and showed promising biological applications like antimicrobial[22], antifungal[23], anticonvulsant[24], inflammatory[25], and anticonvulsant properties (Fig. 1). Recently[26], it has been reported as a neuropeptide receptor antagonist, and also emerged as a novel drug for the treatment of sleep[27], anxiety and addiction disorders[28]. In spite of the increasing demand and importance of this molecule, only limited number of synthetic routes are available in the literature[29]. The major route for the synthesis of naphthopyranopyrimidine describes single step reaction of aryl aldehyde, β-naphthol, and 1, 3-diethyl barbituric acid catalysed by $InCl_3$[30], hetero polyacid (HPA)[31], Al $(H_2PO_4)_3$[32], and L-Pro [33].

Another five-membered heterocycle triazole skeleton contains 1C and 3N atoms with two double bonds with $C_2H_3N_3$ formula. Numerous 1, 2, 4-triazole containing heterocycles have been reported with various pharmacological applications like CNS stimulants[34], anticancer **(I)**, anticonvulsant **(II)**, anti-inflammatory**(III)**, anti-microbial **(IV)**, anti-anxiety**(V)**, and anti-mycotic activities**(VI)** (Fig. 2). 5-Aryl-1,2,4-triazolidine-3-thione was synthesised by the reactions of aryl aldehyde with thiosemicarbazide catalysed by various catalysts[35]. Most of the reported catalysts acidic in nature such as $[C_{16}MPy]$ $AlCl_3Br$ [36], sulfamic acid[37], PEG-400[38], [2-HMPyBSA] HSO_4[39], glycine nitrate[40], $[(Py)_2SO_2]$

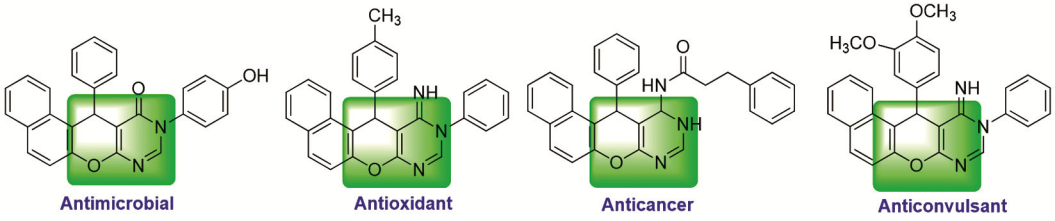


Fig. 1 — Selected bioactive naphthopyranopyrimidine derivatives

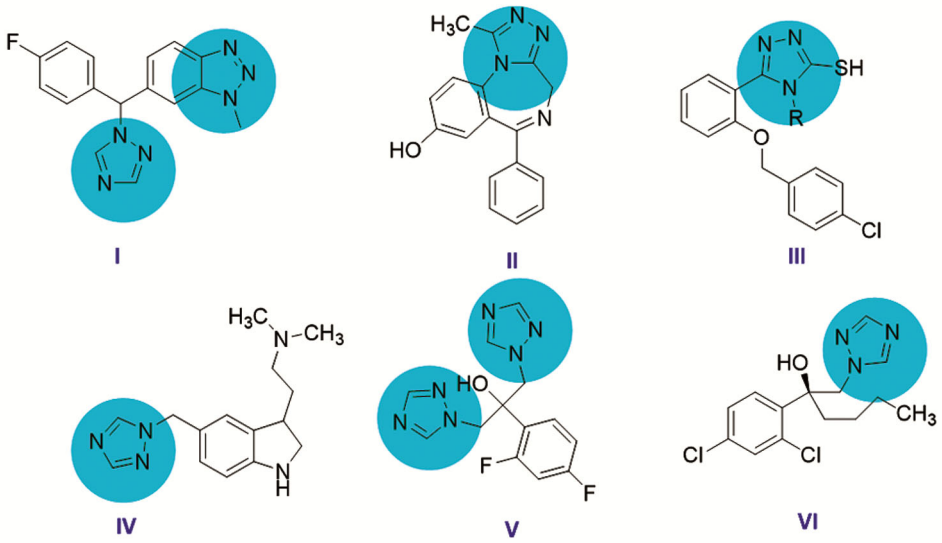


Fig. 2 — Selected Triazolidine-based bioactive derivatives

$[HSO_4]_2$[41], (BTPTB)[42], and Sm_2O_3/fluorapatite. Some of these reported methods involve slow reaction, hazardous solvents, and expensive catalysts[43]. Present work describes greener protocol for the synthesis of naphthopyranopyrimidine under MWI by 3CRs of aryl aldehyde, β-naphthol and 1,3-diethyl barbituric acid, and synthesis of 5-aryl-1,2,4-triazolidine-3-thiones derivatives *via* 2CRs of aryl aldehyde and thiosemicarbazide in the presence of iron oxide decorated silica-sulfonic acid gave excellent product isolation.

Experimental Section

The required chemicals of analytical grade were purchased from commercial vendors, and were used as received. Open capillary method was used for melting point determination and are uncorrected. FT-IR spectra were recorded in KBr pellet (Thermo Fischer).^{1}H- &^{13}C-NMR spectra were collected in Agilent spectrometer (400 MHz, in DMSO-d_6 solvent). LC-MS data was collected in Waters Synapt G2 high detection mass spectrometer.

Catalyst Fe_3O_4@SiO_2-SO_3H preparation

Water extract of lemon peel ash preparation (WELFSA)

Fresh lemon was collected from the local market. The peel was washed with tap water and distilled water to remove the dirt particle, then dried on open sunlight and burnt on a Bunsen burner to get lemon peel ash. The obtained 10 g of finely powdered ash was soaked in 100 mL of double distilled water, suspended, and stirred at room temperature for 1 h. The suspension was dark brown in colour, then the suspension was filtered to get a Water Extract of Lemon Fruit Shell Ash (WELFSA), and it was directly used for the preparation of Fe_3O_4 NPs[44].

Preparation of Fe_3O_4

Iron oxide (NPs) obtained by the reaction of $FeSO_4.7H_2O$ (3g) and $FeCl_3.6H_2O$ (3g) dissolved in 50 mL water taken in a 100 mL beaker. To this 10 mL of WELPSA added, and heated to 80-85°C for 45 min, and cooled to room temperature, NaOH (1 M) solution was added drop wise till the formation of the black precipitate, and kept aside to settle. The black solid was collected externally using a magnet, and washed several times with DDW, and then with ethanol, dried and calcinated at 400 °C for 3h.

Preparation of Fe_3O_4@SiO_2

Fe_3O_4@SiO_2 NPs were prepared by treating Fe_3O_4 NPs with tetraethyl orthosilicate (TEOS). Briefly, the prepared Fe_3O_4 (1 g) was taken and dispersed in water (20 mL), ethanol (60 mL), NH_4OH (2 mL, 25 wt%), and homogenized by ultra-sonication. Then the solution of TEOS in ethanol (1 mL/10 mL) was added drop wise into the dispersion solution under mechanical stirring. The product (Fe_3O_4@SiO_2) was washed water and ethanol and separated using an external magnet, and finally dried.

Preparation of Fe_3O_4@SiO_2@SO_3H

The Fe_3O_4@SiO_2 NPs (0.5 mL) prepared above was dispersed in dry CH_2Cl_2 (30 mL) by ultrasonic bath for 20 min. Subsequently, chlorosulfonic acid (0.8 mL) was added to the dispersed solution in ice bath for 30 min. The HCl gas evolved was removed by a vacuum pump, with NaOH trap and the residue was washed with dichloromethane (DCM), dried, and characterized further.

Synthesis of naphthopyranopyrimidine derivatives

In a 50 mL RB flask, β-naphthol (1 mmol), arylaldehyde (1 mmol), 1,3-dimethylbarbituric acid (1 mmol), and 25 mg of Fe_3O_4@SiO_2-SO_3H catalyst in ethanol (2 mL) subjected to MWI. The reaction was monitored by TLC ($CHCl_3$: MeOH), after the reaction completion, poured cold water (10 mL) into RB flask, separated solid was filtered, washed with water, and recrystallized in alcohol.

Synthesis of 5-aryl-1, 2, 4-triazolidine-3-thione derivatives

In a 50 mL RB flask arylaldehyde (1mmole), thiosemicarbazide (1 mmol), and 25 mg (Fe_3O_4@SiO_2-SO_3H) catalyst in ethanol (2 mL) exposed to MWI. The reaction was monitored by TLC ($CHCl_3$: MeOH), after the reaction, poured cold water (10 mL) into the RB flask, separated product was filtered, washed with water, and recrystallized with ethanol.

Spectral data of representative compounds

12-Phenyl-8,10-dimethyl-12H-naphtho[1',2':5,6]pyrano[2,3-d]pyrimidine-9,11-dione (4a)

White solid; FT-IR (KBr, cm^{-1}): 3172, 2888 (CH), 1747 (C=O), 1685 (C=C), 1564, 1465 (Ar CH=CH); ^{1}H NMR (400 MHz), (DMSO-d_6): δ = 2.46 (s, 3H, CH_3), 3.30 (s, 3H, CH_3), 6.88 (s, 1H, CH), 7.04 (*J* = 7.2 Hz, t, 1H, Ar-H), 7.22 (*J* = 7.2 Hz, t, 2H, Ar-H), 7.26 (*J* = 7.8 Hz, d, 2H, Ar-H), 7.35 (*J* = 7.4 Hz, t, 1H, Ar-H), 7.52 (*J* = 7.0 Hz, t, 1H, Ar-H), 7.61 (*J* = 8.8 Hz, d,1H, Ar-H), 7.69 (*J* = 7.8 Hz, d, 1H, Ar-H), 8.22 (*J* = 9.2 Hz, d,1H, Ar- H), 8.39 (d, *J* = 8.4 Hz, 1H, Ar-H); ^{13}C-NMR (DMSO-d_6): δ31 (CH_3-C), (CH_3-C=O-N), 35 (CH_3-N), 39 (C=O), (C=C) , 90

(C-O),119 (CH-C), (CH-O), 124 (CH-C), 125 (CH-C), (CH-O), 126 (CH-O), 127, 128 (C-Ar), 129 (CH-C), (CH-Ar) 130 (C-C), 131 (CH-C), 132, 133 (C-O), 145, 147, 150, 151 (C-C), 153, 162 (C-C), 163; LC-MS: m/z (Calcd.) = 370.0142 Da; m/z (Obs.) = 370.1030 Da.

12-(4-Methylphenyl)-8,12-dihydro-8,10-dimethyl-9H-naphtho[1-Œ,2-Œ:5,6]pyrano[2,3-d]pyrimidine-9,11-(10H)- dione (4c)

White solid; FT-IR (KBr, cm^{-1}): 3150, 3067, (CH), 1699 (C=O), 1646 (C=C), 1552 1454 (Ar CH=CH); ^{1}H NMR (400 MHz), (DMSO-d_6): δ = 2.46 (s, 3H, CH_3), 3.30 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 6.82 (s, 1H, CH), 7.04 (J = 8.0 Hz, d, 2H, Ar-H), 7.13 (J = 8.0 Hz, d, 2H, Ar-H), 7.61-7.69 (m, 2H, Ar-H), 7.67 (J = 8.8 Hz, d, 1H, Ar-H), 7.72-8.43 (m, 3H, Ar-H);^{13}C-NMR (DMSO-d_6): δ 30 (C-N), 31 (CH_3-N), 34 (C-C), 82 (C-O), 120 (CH-C), 121 (CH-O), 122 (C-C), 123 (CH-C), 124, 126 (CH-C), 127 (CH-O), 128 (C-O), 129 (CH-Ar), 130 (CH-Ar), 131, 136 (C-Ar), 144, 145, 154, 155 (C-O), 163 (C-C), 164 (C-O);LC-MS: m/z (Calcd.) = 384.0478 Da; m/z (Obs.) = 384.2547 Da.

12-(4-Methoxyphenyl)-8,12-dihydro-8,10-dimethyl-9H-naphtho [1',2':5,6]pyrano[2,3-d]pyrimidine-9,11- (10H)-dione (4d)

White solid; IR (KBr, cm^{-1}): 3168, 3062 (CH), 1728 (C=O), 1668 (C=C), 1592, 1455, 1247, 1175; ^{1}H NMR (400 MHz), (DMSO-d_6): δ = 2.04 (s, 3H, CH_3), 3.45 (s, 3H, CH_3), 3.34 (s, 3H, OCH_3), 5.71 (s, 1H, CH), 7.61 (J = 8.8 Hz, d, 1H, Ar-H), 7.85 (J = 8.8 Hz, d,1H, Ar-H), 7.96 (J = 8.0 Hz, t, 1H, Ar-H), 7.97 (J = 7.5 Hz, t,1H, Ar-H), 8.02 (J = 8.8 Hz, d,1H, Ar-H), 8.11 (J = 8.4 Hz, 1H, d, Ar-H), 8.22 (J = 8.8 Hz, d,1H, Ar-H), 8.39 (J = 8.4 Hz, d, 1H, Ar-H); ^{13}C-NMR (DMSO-d_6): δ29 (CH_3-N), 31 (CH_3-O), 38 (CH-C=C), 84 (C-C), 114 (CH-O-C), 119 (CH-C),122 (CH-C), 123 (CH-C), 125 (CH-O), 126, 127 (CH-C), 128, 129, 131, 135 (C-C), 137, 139, 143, 150 (C-O), 151 (C-C), 164 (C-O);LC-MS: m/z (Calcd.) = 400.0145 Da; m/z (Obs.) = 401.2010 Da.

5-(4-Pyridinyl)-1, 2, 4-triazolidine-3-thione (6d)

Yellow solid; 3412 (NH, stretching), 3133 (CH), 1610 (C=C), 1533, 1219 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 7.10 (s,1H, CH), 7.12 (s, 1H, CH), 7.43 (s, 1H, CH), 7.63-7.65 (d, 2H, Ar-H, J = 7.0 Hz), 8.17 (d, 1H, NH J = 5 Hz), 8.24(d, 1H, NH, J = 5 Hz), 11.43 (s,1H, NH); ^{13}C-NMR (DMSO-d_6): δ 40 (CH-N), 128 (CH-C), 131 (CH-C), 138 (CH-C), 177 (C-N), (C-C);LC-MS: m/z (Calcd.) = 179.4516 Da; m/z (Obs.) = 180.0956 Da.

5-(5-Methylthiazol-4-yl)-1, 2, 4-triazolidine-3-thione (6e)

White solid; FT-IR: 3446, 3268 (NH), 3026 (CH), 1615 (C=C), 1541, 1296 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 2.50 (s,3H, CH_3), 6.86 (s, 1H, CH), 7.60 (s, 1H, CH), 8.21 (d, 1H, CH), 8.36 (s, 1H, NH), 9.03 (d, 1H, NH), 11.39 (s,1H, NH); ^{13}C-NMR (DMSO-d_6): δ 15(CH_3-C), 127 (C-C), 136 (C-C), 154 (C-C), 155 (CH-C), 178 (C-S-NH_2);LC-MS: m/z (Calcd.) = 199.248 Da; m/z (Obs.) = 200.0257 Da.

5-(1H-Pyrrol-2-yl)-1, 2, 4-triazolidine-3-thione (6g)

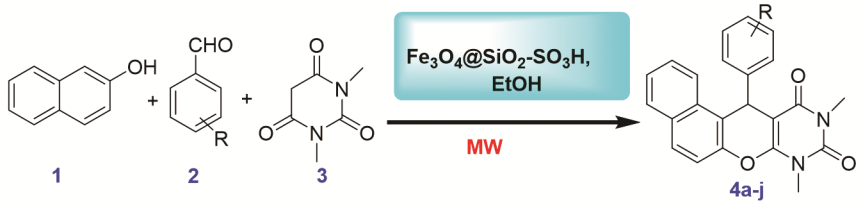
Yellow solid; FT-IR: 3474, 3333 (NH), 2972 (CH), 1690 (C=C), 1296 (C=S) cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.10 (s,1H, NH), 6.39 (s, 1H, CH), 6.40 (s, 1H, CH), 7.83 (d, 1H, CH), 7.94 (s, 1H, NH), 8.04 (d, 1H, NH), 11.24 (s,1H, NH); ^{13}C-NMR (DMSO-d_6): δ 40 (CH-CN), (CH-N) 109 (CH-C), 129 (C-C), 113 (CH-C), 128 (C-C), 134 (C-C), 177 (C-SCN);LC-MS: m/z (Calcd.) = 168.4758 Da; m/z (Obs.) = 169.0821 Da.

5-(p-Tolyl)-1, 2, 4-triazolidine-3-thione (6h)

White solid; FT-IR: 3210 (NH), 3037 (CH), 1647 (C=C), 1490, 1293 (C=S) cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 2.47 (s, 3H, CH_3), 7.37 (d, 2H, Ar-H, J = 8.7 Hz), 7.51 (d, 2H, Ar-H, J = 8.4 Hz), 7.67 (s, 1H, CH), 8.01 (s, 1H, NH), 8.12 (s, 1H, NH), 11.41 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 24 (CH_3-C), 72 (CH-N), (CH-C), 126 (CH-CN), 127 (CH-C), 128 (CH-Ar), 129 (CH-C), 136 (C-C), 141 (C-CN), 184 (C-SCN); LC-MS: m/z (Calcd.) = 193.0326 Da; m/z (Obs.) = 193.1439 Da.

Results and Discussion

The required Fe_3O_4 for the present work was prepared by starting with $FeCl_3$ and $FeSO_4$ in an agro waste solvent medium (WELPSA). The detailed preparation of WELPSA is discussed in the experimental section. The method showed added advantageous like eco-friendly, inexpensive, and iron oxide isolated as free-flowing nanoparticles. Further, iron oxide prepared was surface functionalized to increase its catalytic activity as well as stability using TEOS followed by $ClSO_3H$ (chlorosulfonic acid) treatment gave Fe_3O_4@SiO_2-SO_3H[45]. The prepared catalyst is fully characterized by various analytical and spectroscopic tolls such as FT-IR, XRD, FE-SEM & EDX, HR-TEM, TGA and VSM[45]. The catalytic activity of the prepared catalyst was demonstrated herein for the one-pot synthesis of naphthopyranopyrimidine by the reaction of β-naphthol (1 mmol), aryl/ heterocycle aldehyde



Scheme 1 — Naphthopyranopyrimidine synthesis

Table 1 — Quantity of the catalyst required in a model reaction.

S. No	Catalyst quantity (mg)	Time (min)	Yield%
1	0	5	Nil
2	5	5	20
3	10	5	30
4	20	5	65
5	**25**	**5**	**90**
6	30	5	90

Table 2 — Microwave power optimization

Entry	MW Power (W)	Time (min)	Yield (%)
1	180	5	75
2	300	5	85
3	**450**	**5**	**90**
4	600	5	90

(1 mmol), and 1,3-diethyl barbituric acid (1 mmol) as a model reaction (Scheme 1). After 1 h stirring in the reaction vessel solid product separation noticed (TLC monitored). It was diluted with ethanol, filtered, and evaporated to isolate product with low yield.

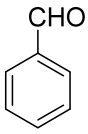
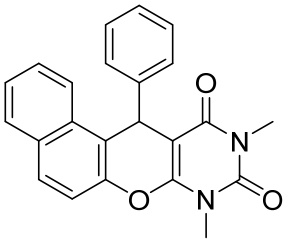
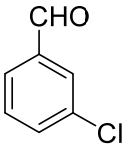
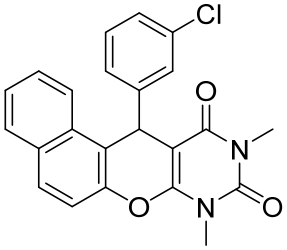
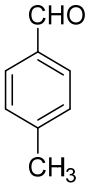
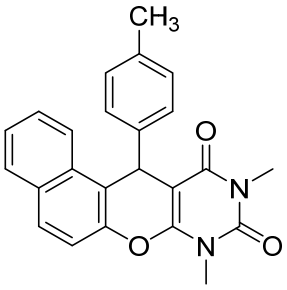
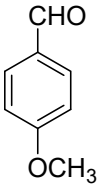
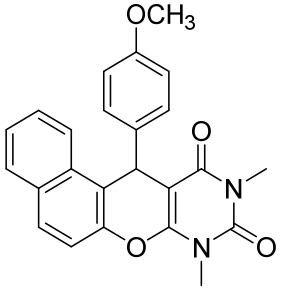
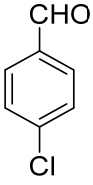
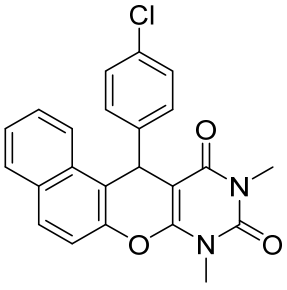
Further to speed up the reaction, MWI was used. Surprisingly, the formation of the product noticed in a few min, and isolated excellent yield. To optimize condition required for the reaction, different wt% of catalyst was employed in a series of model reaction carried out starting 0, 5, 10, 20, 25 and 30 mg catalysts under MWI at 450 W (Table 1). The optimization condition revealed that, catalyst starting from 5 mg to 25 mg gave gradual increase of the product yield (entries 2-5**,** Table 1), but in 30 mg of catalyst used in a model reaction gave no noticeable increase in the product isolation. Furthermore, to optimize microwave power suitable for this reaction, a model reaction was performed with varying MWI power (180, 300, 450, and 600 W) (Table 2) using optimized catalyst (25 mg). This study revealed that, the reaction carried out at 450 W gave highest yield of the product in 5 min exposure in EtOH (2mL) solvent. Moreover, to find the tolerance of this protocol, various substituted aryl aldehyde was taken for the reaction in the optimized condition. The product isolated using the substituted aromatic benzaldehyde containing electron withdrawing groups (EWG) and electron donating groups (EDG) are presented in Table 3. This observation revealed that, either EWG or EDG group present on the aromatic aldehyde does not influence any major difference in the final product isolation. Hence, the optimized reaction is not influenced by the substitution present on the aryl aldehyde, and the method can be applied to aryl as well heterocyclic aldehyde. The plausible pathway of the reaction involved in the product formation is appended in the supplementary Information (Fig. S25).

Reusability

Naphthopyranopyrimidine synthesis was achieved by the reaction of β-naphthol, benzaldehyde and 1,3-dimethylbarbituric acid in an optimized reaction. After the reaction, the reaction mixture was diluted with solvent (ethyl acetate) and centrifuged for the catalyst separation. The separated catalyst was washed with water, and ethanol twice and dried at 80°C, and then reused. The efficiency of the recycled catalyst was studied up to four cycles. It was noticed that there was no significant loss in its catalytic activity, but in case of fifth cycle comparatively, the product isolated gave low yield (Fig. 3). This study revealed that the catalyst could be used up to four cycles without loss in its catalytic activity. This method points out the requirement of less quantity of the catalyst, and significant reduction of the waste production.

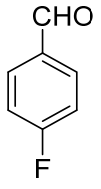
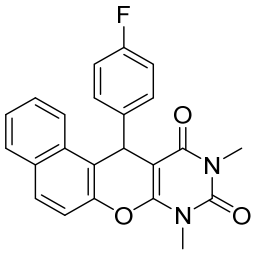
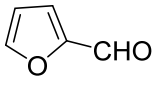
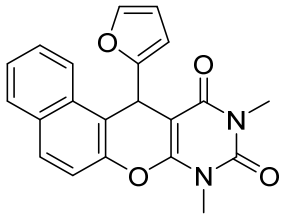
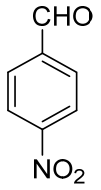
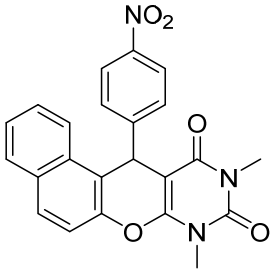
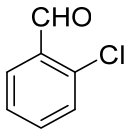
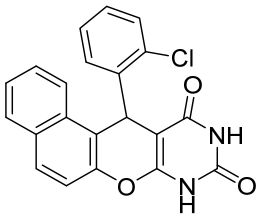
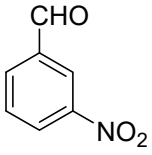
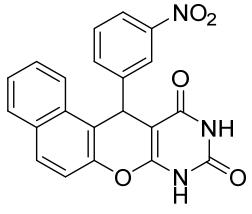
The use of the catalyst was further extended to synthesize another class of heterocycle, 5-aryl-1, 2, 4-triazolidine-3-thione in2CRsof thiosemicarbazide and benzaldehyde as a model reaction using above-optimized reaction conditions (Tables 1 & 2, Scheme 2). Notably, the final product was isolated in excellent yield with purity using optimized reaction conditions (Table 4). This revealed that, the catalyst is efficient to build 1, 2, 4-triazolidine-3-thione library. Several arylaldehydes with EDG and EWG substitution present on the aryl aldehyde gave corresponding 5-aryl-1,2,4-triazolidine-3-thione

Table 3 — Naphthopyranopyrimidine derivatives and physical constant

Entry	Aldehyde	Product	Yield (%)	M.P. (°C) Obs. / Lit.
1.	 **2a**	 **4a**	89	222-224 [new]
	 **2b**	 **4b**	90	222-224/ 223-225 [46]
2.	 **2c**	 **4c**	92	260-262 [new]
3.	 **2d**	 **4d**	87	211-213 [new]
4.	 **2e**	 **4e**	85	232-243/ 233-235[47]

(*Contd*.)

Table 3 — Naphthopyranopyrimidine derivatives and physical constant (*Contd*.)

Entry	Aldehyde	Product	Yield (%)	M.P. (°C) Obs. / Lit.
5.	 **2f**	 **4f**	86	300-302 299-301[47]
6.	 **2g**	 **4g**	90	201-203/ 200-202[48]
7.	 **2h**	 **4h**	81	277-279/ 280-281[49]
8.	 **2k**	 **4i**	86	270-272/ 269-271[49]
9.	 **2l**	 **4j**	80	303-305/ 301-303[49]

derivatives (Table 4) extending the scope of this method.

In Table 4, the isolated yield reflects no measurable effect on the aryl substitution containing EWG and EDG group in the reaction. The plausible mechanism of product formation is given in the Supplementary Information (Fig. S26).

Evaluation of antioxidant properties

Some of the selected derivatives were screened for their antioxidant activity against DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging and Ac(ascorbic acid) as a reference[56]. The synthesized compounds showed radical scavenging activity in the test concentration range of 200 µg/µL-1000 µg/µL[57]. The

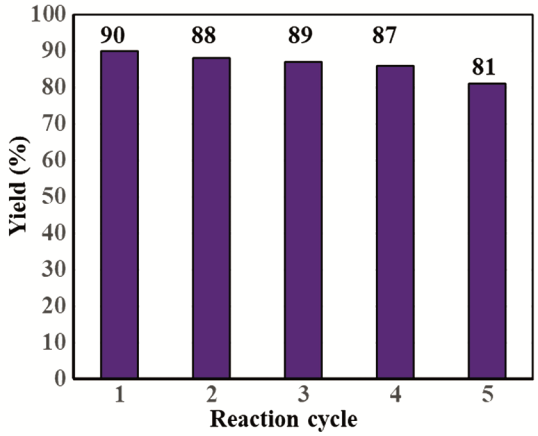
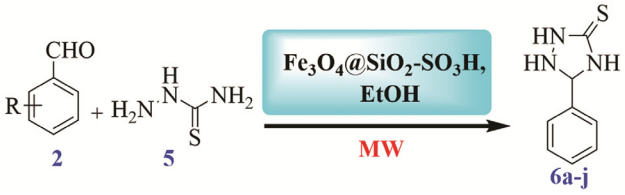


Fig. 3 — Recycle of catalysts



Scheme 2 — Synthesis of 5-aryl-1, 2, 4-triazolidine-3-thione derivatives

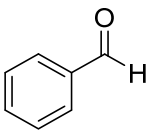
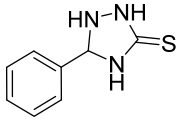
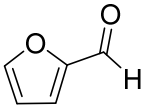
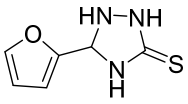
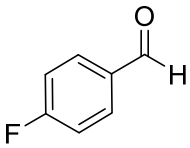
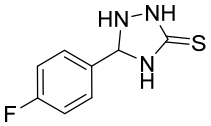
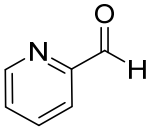
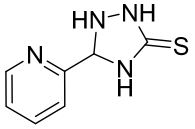
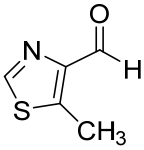
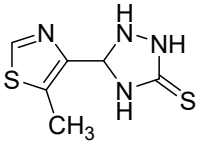
obtained results revealed that, the compounds **4a, 4g,** and **4h** (Fig. 4a), and 6a, 6b and 6c **(**Fig. 4b) showed better scavenging ability, and other compounds **4e, 4f** and**4k** (Fig.4a) showed moderate scavenging ability. The radical scavenging abilities of the tested derivatives with standard samples are appended in Fig. 4.

Reusability

The catalyst used in 5-aryl-1,2,4-triazolidine-3-thione synthesis was recycled after the first cycle, in a model reaction and reused for the successive runs. The isolated yields were 92, 90, 89, 87 and 80% for 1 to 5 cycles, respectively (Fig. 5). In the recycled reaction it was noticed that only 12 % loss of the catalytic efficiency in terms of the isolated product yield after the fourth cycle. This revealed that, the reaction required less catalyst, leading to less waste production and inexpensive method.

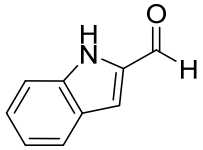
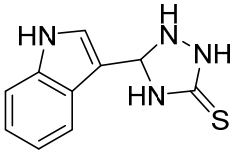
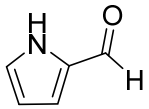
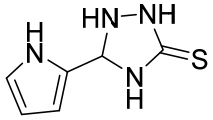
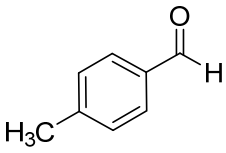
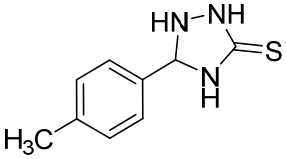
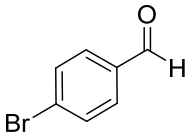
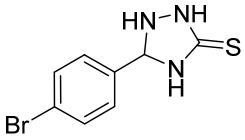
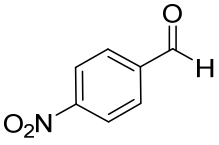
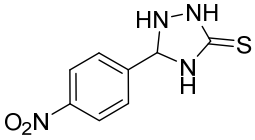
Finally, the present developed method was compared with the reported methods for naphthopyranopyrimidineand5-aryl-1,2,4-triazolidine-3-thione synthesis (Table 5). In Table 5, entries 1 and

Table 4 — 5-Aryl-1,2,4-triazolidine-3-thione physical data

S. No	Reactant 1	Product	Yield (%)	M.P (°C)
1		 **6a**	93	184-186/ 185-187[50]
2		 **6b**	90	172-174/ 172-174[51]
3		 **6c**	89	206-208/ 205-207[52]
4		 **6d**	88	202-204 [new]
5		 **6e**	82	162-164 [new]

(*Contd.*)

Table 4 — 5-Aryl-1, 2, 4-triazolidine-3-thione physical data. (*Contd.*)

S. No	Reactant 1	Product	Yield (%)	M.P (°C)
6		 **6f**	79	154-156[53]
7		 **6g**	83	196-198 [new]
8		 **6h**	88	174-176 [new]
9		 **6i**	88	172-174/ 174-176[54]
10		 **6j**	90	202-204/ 203-205[55]

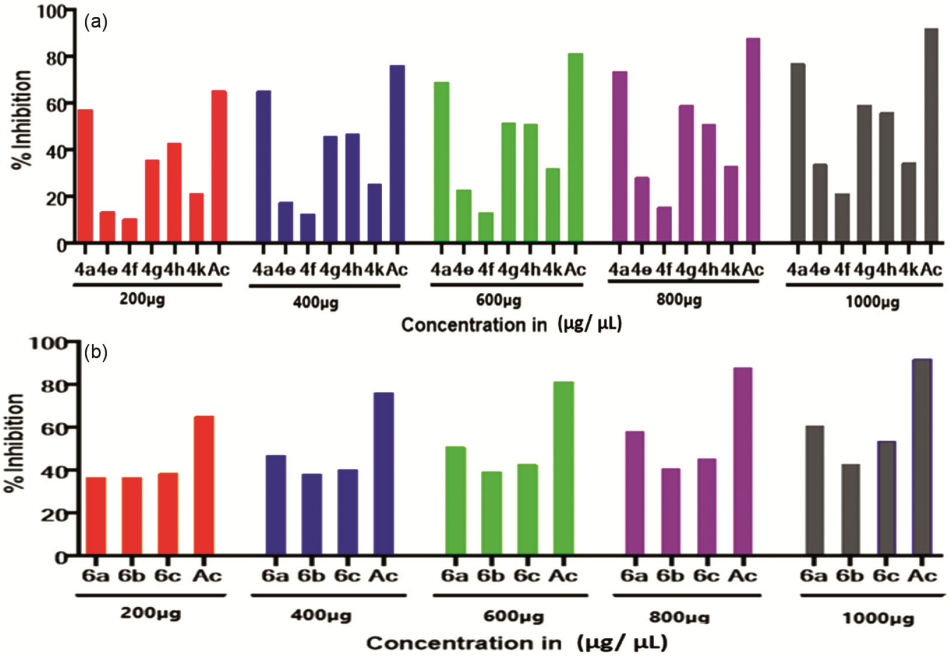


Fig. 4 — (a) Antioxidant activity of naphthapyranopyrimidines and (b) 5-aryl-1, 2, 4-triazolidine-3-thione derivatives

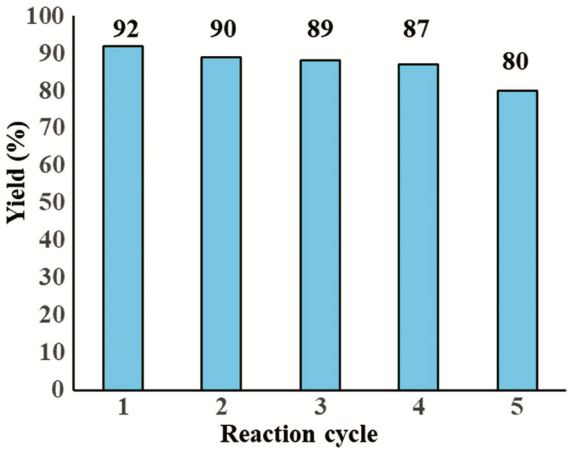


Fig. 5 — Reusability studies

4 used expensive catalyst with high temperature for the reaction, and entry 3 took long reaction time. In case of entry 6, the catalyst preparation is tedious. Overall, the reported methods have one or more limitations like being expensive, tedious catalyst preparation and slow reaction rate. The present method overcomes these limitations, and demonstrates efficient and faster synthesis of naphthopyranopyrimidine and 1, 2, 4-triazolidine-3-thione derivatives (entries **5 & 9**, Table **5**).

Conclusion

The present work demonstrates the chemical free agro-waste extract-based preparation of core iron oxide NPs, and its fabrication with silica-sulfonic acid to give stable fabricated Fe_3O_4@SiO_2-SO_3H catalyst. The prepared catalyst demonstrates the efficient synthesis of structurally diverse naphthopyranopyrimidine and 1,2,4-triazolidine-3-thione derivatives by the 3CRs of arylaldehydes, β-naphthol, and 1,3-dimethylbarbituric acid, and 2CRs of aromatic/heteroaromatic aldehyde with thiosemicarbazide, respectively under MWI in ethanol solvent. The protocol is found to be simple, faster, efficient, inexpensive, straight forward and eco-friendly. The catalyst can be recycled up to four cycles without considerable loss of catalytic activity.

Conflict of interest

The authors declare no conflict of interest.

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Supplementary Information

Supplementary information is available on the website https://nopr.niscpr.res.in/handle/123456789.

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