

SYNTHESIS AND CHARACTERISATION OF MAGNETIC BIO-NANOCOMPOSITE BASED POLYMER SUPPORT FOR BIGINELLI REACTION**Faisal Atique¹, Dr. Sarita Tiwari²**¹Research Scholar, Department of Chemistry, School of Applied Sciences, Singhania University, Pacheri Bari, Jhunjhunu, Rajasthan²Assistant Professor, Department of Chemistry, School of Applied Sciences, Singhania University, Pacheri Bari, Jhunjhunu, Rajasthan**Abstract**

The Fe₃O₄ nanoparticles were synthesized using the co-precipitation method. The synthesized Fe₃O₄ nanoparticles were incorporated into Chitosan (CS) based polymer matrix to generate the magnetic biocomposite (CS-MNP) catalyst. The nano biocomposite (CS-MNP) was characterized using different spectroscopic techniques such as FT-IR, XRD, SEM, TEM, DSC, and TGA analyses. Dihydropyrimidine (DHMP's) derivatives using the Biginelli reaction were synthesized using the magnetic nanocomposite-based heterogeneous catalyst. This generated heterogeneous catalyst provided an effective yield and reduced the reaction time effectively. The most significant benefits of this technique for synthesizing DHMP derivatives are its catalyst reusability. The reused catalyst was characterized using the FTIR technique to understand the structure change and its efficacy. Therefore, an eco-friendly strategy was adopted to synthesize biologically active component dihydropyrimidine (DHMPs) derivatives efficiently.

1. Introduction

Researchers have found new organic chemistry approaches for the design and synthesis of novel heterocyclic compounds by using the multicomponent reaction known as MCR with an ecologically acceptable perspective. Chemical reactions known as MCRs occur when three or more reactants react at the same time to create a single product.[2] MCRs have gained attention in recent years due to their ability to efficiently produce complex molecules with high yields and fewer by-products than traditional stepwise reactions. In addition, MCRs can be performed using a wide range of starting materials, making them attractive for synthesizing diverse chemical structures.[3] The use of MCRs in organic synthesis has been shown to have several advantages from an ecological perspective. Firstly, MCRs typically require fewer steps than traditional reactions, reducing the waste generated during the synthesis process.[4] Secondly, MCRs can be performed using mild reaction conditions, reducing energy consumption and using hazardous solvents. [5-6] Thirdly, MCRs can be used to produce novel heterocyclic compounds, which have potential applications in various fields such as drug discovery, material science, and catalysis. [7].

Proteins and polysaccharides are examples of natural biopolymers that have undergone extensive research and are employed in green chemistry.[8] These biopolymers are renewable resources and have specific characteristics and distinctive efficiencies that make them attractive candidates for green chemistry applications. [9] They have unique physical and chemical

properties, making them suitable for applications such as drug delivery, food packaging, and tissue engineering. Some examples of biopolymers that have been used in green chemistry include silk fibroin, collagen, and acasein. Polysaccharides, on the other hand, are complex carbohydrates that are made up of simple sugar molecules. They are abundant in nature and have unique physicochemical properties, such as high-water solubility and biodegradability, that make them attractive for various industrial applications. Chitosan (CS) is among the most versatile biopolymers abundantly found in nature and has a lot of diverse applications. [10-11] By modifying chitosan, it is possible to improve its properties for specific applications. For example, CS can be modified with organic ligands or inorganic compounds to create heterogeneous nanocatalysts with improved catalytic activity and selectivity. CS-based nanocatalysts were studied for a range of applications, including environmental remediation, chemical synthesis, and energy conversion.[12] In addition to their improved catalytic properties, chitosan-based nanocatalysts also have several advantages over traditional catalysts. For example, they are environmentally friendly, biodegradable, and non-toxic, which makes them attractive for sustainable applications. Overall, chitosan can be modified in various ways to improve its properties for the applications such as the synthesis of heterogeneous nanocatalysts. With continued research and development, chitosan-based nanocatalysts have the potential to replace traditional catalysts and contribute to a more sustainable future.[13] But they have some leaching issues, and it is difficult to extract them as such because of high hydrophilicity.

Iron oxide nanoparticles are commonly employed in catalysis because of their distinctive physical and chemical characteristics. [14] Iron oxide nanoparticles possess high surface area, high reactivity, magnetic properties, and good thermal stability, making them suitable for various catalytic applications.[15] One of the most common applications of FeO NPs in the area of catalysis is in the oxidation of organic compounds. Iron oxide nanoparticles can catalyze reactions such as the oxidation of alcohols, aldehydes, and other organic compounds under mild conditions.[15] The chemical industry is very interested in this reaction because it can be used to make useful compounds like ketones, aldehydes, and carboxylic acids. The Fischer-Tropsch synthesis has also employed iron oxide nanoparticles.[16]

Due to their noteworthy and promising diversity in therapeutic and pharmacological activities, including geroprotective, anticancer, antitubercular, analgesic, and antidiabetic activities, researchers have recently focused more on developing novel synthetic methods for privileged N-heterocyclic Polyhydroquinoline and 1,4-dihydropyridine compounds. [17] For the production of these chemical and biological compounds, a variety of novel synthetic techniques and several types of catalysts, including salicylic acid [18], L-proline, [19] LiBr [20], and Fe₃O₄ [21] nanoparticles have been described. Due to its use in biomedical and catalytic applications, diverse functionalization techniques, and creation of core-shell magnetic structures, the attention on Fe₃O₄ magnetic nanoparticles (Fe₃O₄ MNPs) has recently grown.[22] Here, we discuss efforts to create new biopolymer-based nanocomposites, the introduction of novel tactics based on green chemistry viewpoints, the design, and synthesis of a new magnetic biopolymer-based nanocomposite biopolymer and magnetic nanoparticles, as well as attempts to develop novel biopolymer-based nanocomposites. This study effectively created and produced a brand-new magnetic chitosan bionanocomposite. Synthesis of Fe₃O₄ magnetic

nanoparticles incorporated into CS polymeric substrate. The magnetic bio-nanocomposite has been successfully characterized using a variety of spectral and analytical techniques, including FT-IR, EDX, FE-SEM, TEM, XRD, and TGA analyses. This innovative magnetic bio nanocomposite's catalytic effectiveness and performance in condensation and symmetric processes were assessed in addition to outlining its special and particular properties. This heterogeneous nanocatalyst with high potential magnetic properties and environmentally benign nature may be employed successfully for one-pot synthesis of diverse libraries when compared to conventional catalysts and past investigations.

2. Material and Methods

Methods

Chitosan (Cs, \geq 98% deacetylated, M_w 130 kDa), Analytical grade Ferric chloride, Ferrous chloride, 2-aminoterephthalic acid (ATA, $C_8H_7NO_4$) from Sigma-Aldrich, acetic acid. The chemicals, reagents, and solvents were used for the reaction and synthesis as received. Fourier transforms infrared (FTIR) spectra were recorded with a Nicolet iS5 spectrometer. Fourier transforms infrared (FTIR) spectra were captured with a resolution of 8 cm^{-1} in the range of 4000 to 400 cm^{-1} . X-ray diffraction (XRD) was carried out on Rigaku Smart Lab X-Ray Diffractometer using CuK radiation. Using a Perkin Elmer Diamond STG-DTA and a nitrogen environment at a heating rate of $10\text{ }^\circ\text{C}/\text{min}$, thermal behavior was examined in the temperature range of 60-680 $^\circ\text{C}$. Using a high-resolution transmission electron microscope (HRTEM, JEOL-2100F) with an acceleration voltage of 200 kV and a scanning electron microscope (SEM) (Zeiss EVO MA20) with a voltage of 50 kV, the surface morphology of materials was investigated.

Preparation of Iron oxide nanoparticles

A mixture of $FeCl_3$, $FeCl_2$, and ATA (2-amino-terephthalic acid) was added to the 500 mL round bottom flask in deionized (DI) water. The reaction mixture was heated at 100 $^\circ\text{C}$ for 2 hours under an inert atm. NH_4OH was taken in 30% of water and added to the resulting mixture, which caused SPIO particles to form. The resultant reaction mixture became a suspension and was vigorously stirred at the same temperature for a duration of 2 h. Afterward, the suspension was cooled to room temperature. The pH of the final solution was measured and found to be basic. The so-formed magnetic nanoparticles were magnetically isolated and repeatedly washed with a solution of DI water and ethanol (10 mL, 1:1 vol/vol) over a period of four washings, resulting in the isolation of 3.25 g of coated Fe_3O_4 .

Preparation of Magnetic Bionanocomposite

The combination of Fe_3O_4 MNPs to the chitosan solution is accompanied by magnetic bionanocomposite. In order to do this, 1% weight percent of chitosan powder was dissolved in an acetic acid solution (pH-6) in 500 mL of the round bottom flask. The mixture was then swirled while being heated up to 70 $^\circ\text{C}$. Water was carefully added at the temperature of 70 $^\circ\text{C}$ drop by drop, and the mixture was neutralized.

3. Result and Discussion

3.1. Synthesis and Characterisation of Magnetic Nanoparticles

Chemical preparation through co-precipitation is the most widely used technique for creating NPs because it is easy, practical, economical, and effective. The method makes it simple to alter the reaction parameters and change the composition and shape of NPs. By co-precipitating

**SYNTHESIS AND CHARACTERISATION OF MAGNETIC BIO-NANOCOMPOSITE BASED POLYMER
SUPPORT FOR BIGINELLI REACTION**

water solutions of Fe^{2+} and Fe^{3+} ions, iron oxide NPs were created. The chemical oxidation of NPs can be prevented by surface modification and capping agents, giving rise to stability benefits, ease of dispersion in solvents, and compatibility with the organic matrix to mediate their processing, and further functionalization. To create Fe_3O_4 at the surface of magnetite, manufactured NPs were coated with an organic aromatic acid called aminoterephthalic acid (ATA), which has carboxylic acid groups. The dispersion picture is mentioned in Fig. 1a. The molecular makeup of the nanoparticles, the type of functions, and the existence of a coating were all confirmed by FTIR spectrum, Fig. 1b. All of the produced nanoparticles exhibit a peak at 590 cm^{-1} , which is connected to the Fe-O stretch. A broad peak at $3200\text{--}3600\text{ cm}^{-1}$ suggested the presence of N-H due to amine groups, bound water, and surface hydroxyl groups on iron. In the range of $2500\text{--}3000\text{ cm}^{-1}$, the O-H stretch brought on by carboxylic groups first showed. The aromatic C-H stretch of ATA between 3098 and 3000 cm^{-1} , which is absent in Fe^0 , suggested that Fe_3O_4 has a capping. The presence of symmetric and asymmetric C-O stretches in the area of 1410 cm^{-1} and 1548 cm^{-1} , respectively, point to the presence of a carboxylate ion. Moreover, the large peak near 1440 may be the result of O-H bending vibrations brought on by water molecules near the Fe^0 . The surface coating in Fe_3O_4 suggested its existence. Figure 1 shows the SEM and TEM analysis of images of the Fe_3O_4 , Fig. 1c and 1d. As can be observed, the Fe_3O_4 are uniformly distributed and have a spherical shape. The TEM study of NPs also showed that the average particle size was 10 nm .

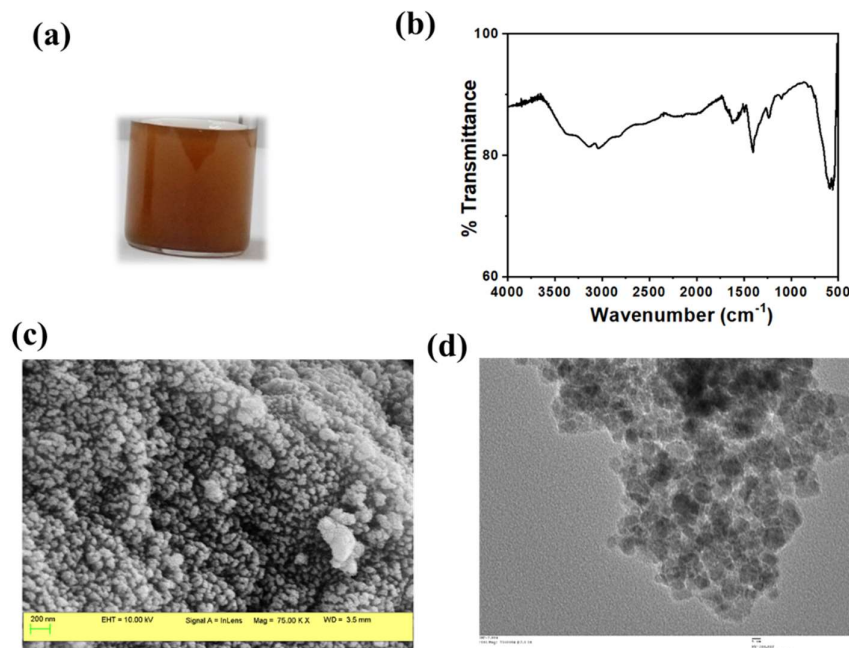


Figure 1: Characterisation of Magnetic nanoparticles: (a) dispersion of Fe_3O_4 nanoparticles into water (1 mg/mL); (b) FTIR spectrum ;(c) SEM images and ;(d) TEM images of Fe_3O_4 nanoparticles.

The Elemental composition confirms the presence of Fe ion along with the other organic components such as C, N, and O. XRD was used to examine the structural phase composition and coating efficiency on iron NPs. The peaks of the produced iron nanoparticles and the

magnetite (Fe_3O_4) nanoparticles were in good agreement. The co-formation of magnetite (Fe_3O_4) and maghemite (Fe_2O_3) in the case of Fe^0 is confirmed by a highly intense peak at 32.60 (420) plane and the associated XRD peaks, which are attributed to the environmental oxidation of Fe^{2+} ions to generate Fe^{3+} ions due to the bare surface. Fe_3O_4 confirmed the inverse spinel structure of the Fe_3O_4 phase by displaying the most intense 311 crystal plane along with other broad planes 110, 220, 511, and 440. The capping agent ATA was included in Fe nanoparticles to prevent the development of maghemite. Thermogravimetry analysis (TGA) was used to quantify the organic coating on nanoparticle surfaces. When heated from 50 to 200 °C, Fe nanoparticles showed a slight mass loss that was attributed to the elimination of physico-sorbed water and hydrogen-bound molecules because of the NP surface's polarity.

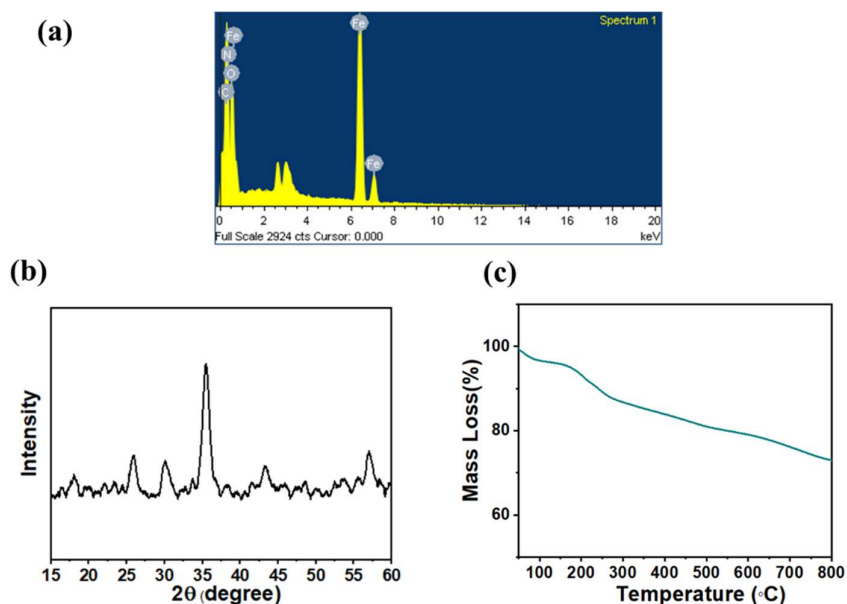


Figure 2: Characterisation of Magnetic nanoparticles: (a) EDX analysis to determine the elemental composition of Fe_3O_4 nanoparticles; (b) Powder XRD spectrum and (c) TGA spectrum of Fe_3O_4 nanoparticles.

3.2. Synthesis and Characterisation of Magnetic Bionanocomposite

In this study, a novel bifunctional creatine-based magnetic bionanocomposite was created for the first time, based on functionalized chitosan polymeric strands as a sustainable and environmentally friendly substrate. In this context, fabricating the magnetic bio-nanocomposite was done with chitosan substrate has been functionalized with Fe_3O_4 MNPs to create the magnetic bionanocomposite. The magnetic bio-nanocomposite was characterized using a variety of spectroscopic and analytical techniques. FT-IR spectra, shown in Fig. 3a, were provided at this step to confirm the emergence of new functional groups and the presence of the existing functional groups. Fig. 3b shows the FE-SEM analysis. A synthetic magnetic bionanocomposite's form and size were determined using the pictures in Fig. 3b. The material's thermal stability was described using DSC and TGA analyses, as shown in Fig. 3c-d.

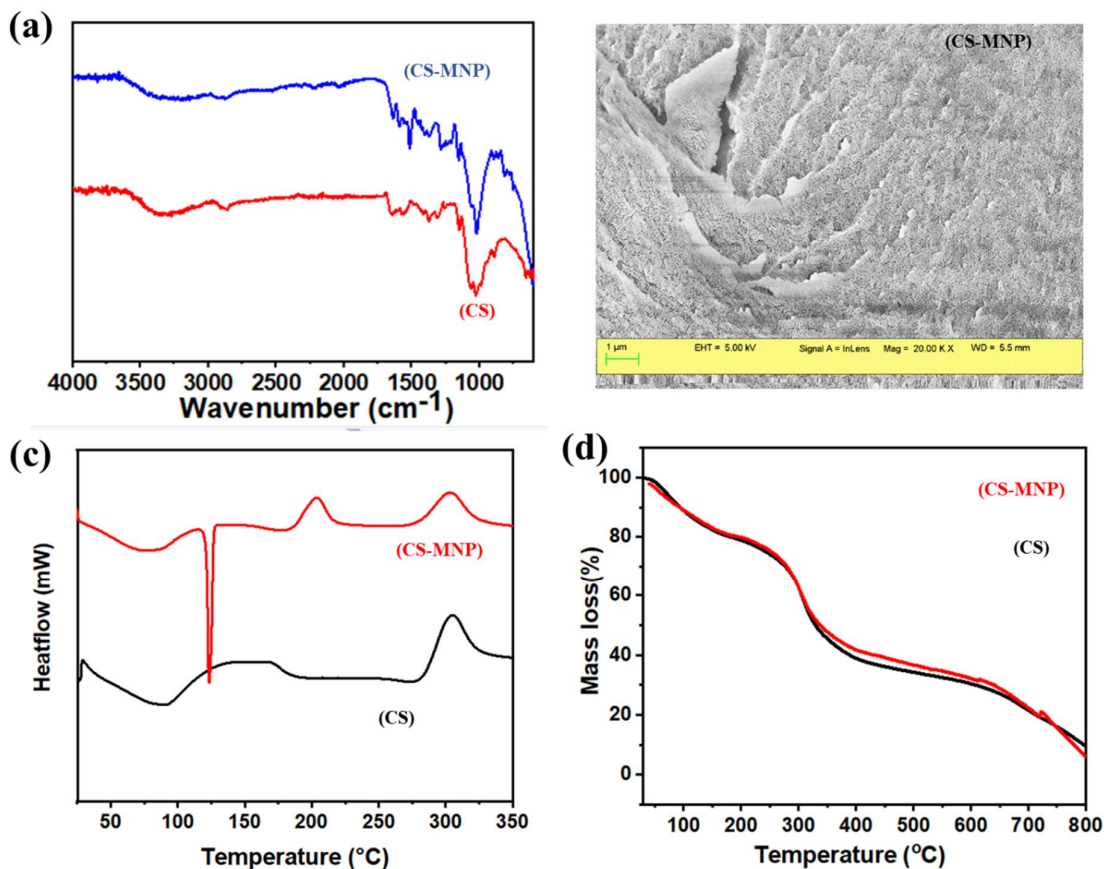


Figure 3: Characterisation of Magnetic nanoparticles: (a)FTIR spectra; (b) SEM image (c) DSC spectra; and (d) TGA spectrum of CS and CS-MNP.

3.3. Catalytic activity Studies

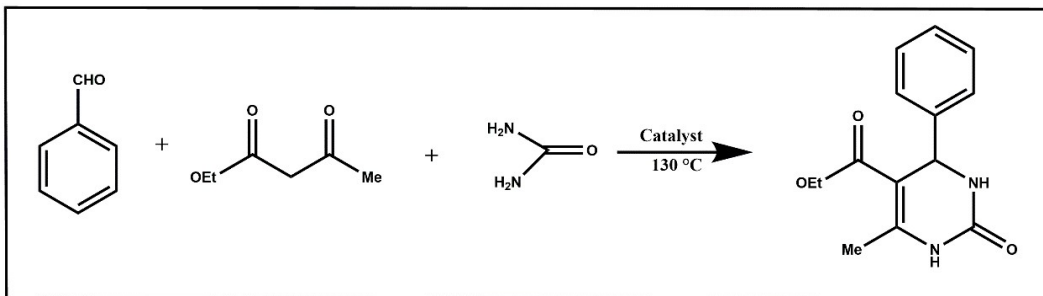


Figure 4: General Biginelli reaction for the synthesis of 3,4 dihydropyrimidinone
Over the created nanocomposites, the Biginelli reaction for the synthesis of 3,4-dihydropyrimidinone (DHMPs) was successfully carried out. About the effects of catalyst weight, temperature, and other variables on optimization studies. The reaction involving benzaldehyde, ethylacetoacetate, and urea to produce 5-ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one has the following molar ratio of reactants, Fig. 4.

3.4. Synthesis of Libraries of DHMPs

**SYNTHESIS AND CHARACTERISATION OF MAGNETIC BIO-NANOCOMPOSITE BASED POLYMER
SUPPORT FOR BIGINELLI REACTION**

As these reaction conditions produced a higher yield of product in a short time, they were chosen for further extending the process for synthesizing libraries of DHPMs. The catalyst weight was 0.10 g, the temperature was 130 °C, and the amount of urea used was 1.3 mmol. On top of nanocomposite, various aldehydes, 1,3-dicarbonyl compounds, and urea are used to create several

Table 1: Obtained Yield% and reaction time for the synthesis of different DHMPs derivative.

Compound	Yield (%)	Time of Reaction (min.)
(a)	90	16
(b)	93	30
(c)	85	14
(d)	90	9
(e)	82	50
(f)	87	46
(g)	81	48
(h)	86	32
(i)	91	18
(j)	83	30

types of DHPMs, Fig.5. With all different types of reactants, the catalyst produced yields that were satisfactory. The outcomes are shown in Table 1.

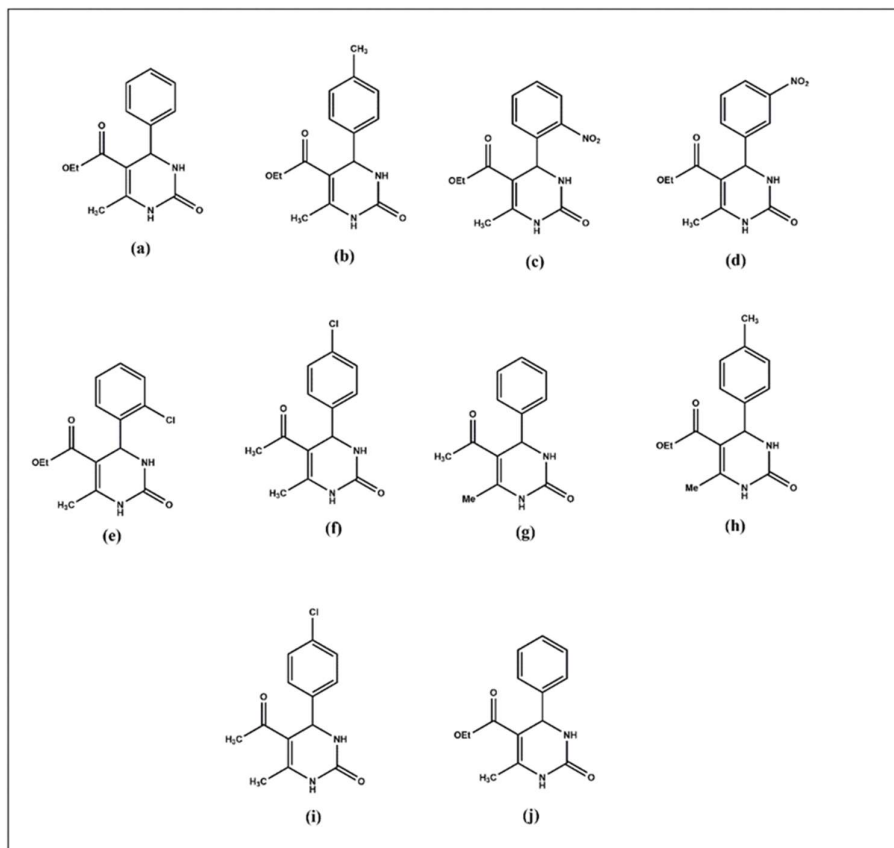


Figure 5: Library of synthesised different DHMPs derivatives.

3.5. Analysis of Reused Catalyst

By examining the FTIR spectrum of the recycled catalyst, the composition of the catalyst was verified. Fig.6 shows that even after multiple runs, the catalyst's functions remain unchanged, demonstrating the excellent stability of the current nanocomposites during the reaction and catalytic workup.

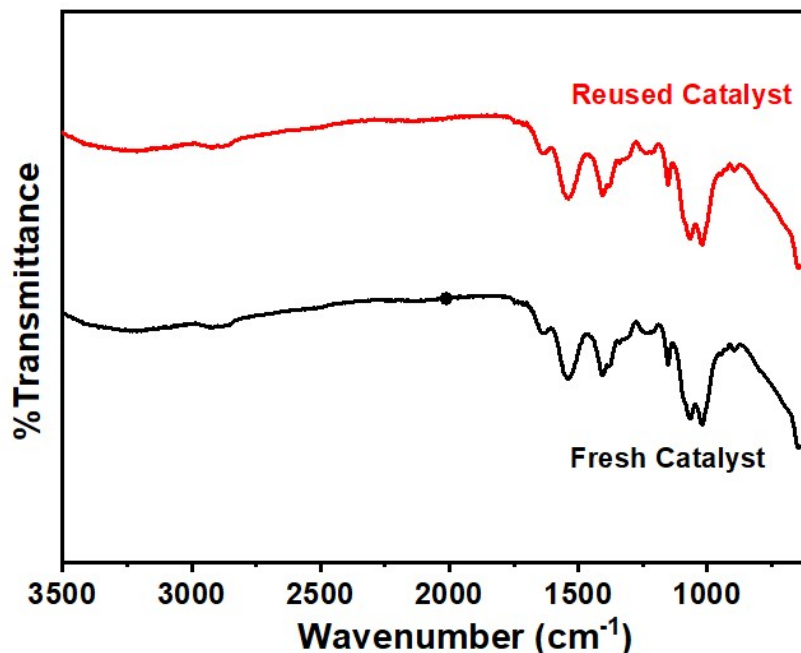


Figure 6: FTIR spectra of CS-MNP catalysts before and after their use in the catalysis process.

4. Conclusion

In a nutshell, we have shown a solvent-free, inexpensive green catalyst made of chitosan-based magnetic nanocomposite that we used to manufacture a variety of known DHPMs. The promising features of this technology are effectiveness, simplicity, clear reaction profile, compatibility with various functional groups, reaction speed, high reaction product yields, and non-chromatographic purification. The catalyst's ability to be recycled without losing any of its activity, as well as how easy it is to separate the catalyst from the reaction mixture, how cheap it is, how little the catalyst is loaded, and how environmentally friendly the catalyst is, are all crucial components of this green technique.

5. References

1. Zhu, J. (2003). Recent developments in the isonitrile-based multicomponent synthesis of heterocycles. *European Journal of Organic Chemistry*, 2003(7), 1133-1144.
2. Choudhury, L. H., & Parvin, T. (2011). Recent advances in the chemistry of imine-based multicomponent reactions (MCRs). *Tetrahedron*, 67(43), 8213.
3. Weber, Lutz. "Multi-component reactions and evolutionary chemistry." *Drug Discovery Today* 7 (2002): 143-147.
4. Farhid, H., Khodkari, V., Nazeri, M. T., Javanbakht, S., & Shaabani, A. (2021).

- Multicomponent reactions as a potent tool for the synthesis of benzodiazepines. *Organic & Biomolecular Chemistry*, 19(15), 3318-3358.
5. Maddila, S. N., Maddila, S., Van Zyl, W. E., & Jonnalagadda, S. B. (2016). Ceria–Vanadia/Silica-Catalyzed Cascade for C–C and C–O Bond Activation: Green One-Pot Synthesis of 2-Amino-3-cyano-4H-pyrans. *ChemistryOpen*, 5(1), 38-42.
 6. Maddila, S. N., Maddila, S., Van Zyl, W. E., & Jonnalagadda, S. B. (2016). Ceria–Vanadia/Silica-Catalyzed Cascade for C–C and C–O Bond Activation: Green One-Pot Synthesis of 2-Amino-3-cyano-4H-pyrans. *ChemistryOpen*, 5(1), 38-42.
 7. Weber, L. (2000). High-diversity combinatorial libraries. *Current Opinion in Chemical Biology*, 4(3), 295-302.
 8. Shahid, M., & Mohammad, F. (2013). Green Chemistry Approaches to Develop Antimicrobial Textiles Based on Sustainable Biopolymers: A Review. *Industrial & Engineering Chemistry Research*, 52(15), 5245-5260.
 9. Cevasco, G., & Chiappe, C. (2014). Are ionic liquids a proper solution to current environmental challenges?. *Green Chemistry*, 16(5), 2375-2385.
 10. Bakshi, P. S., Selvakumar, D., Kadirvelu, K., & Kumar, N. S. (2020). Chitosan as an environment friendly biomaterial—a review on recent modifications and applications. *International journal of biological macromolecules*, 150, 1072-1083.
 11. Cui, Chen, Qingjin Fu, Lei Meng, Sanwei Hao, Rengang Dai, and Jun Yang. "Recent progress in natural biopolymers conductive hydrogels for flexible wearable sensors and energy devices: materials, structures, and performance." *ACS applied bio materials* 4, no. 1 (2020): 85-121.
 12. Li, N., Ma, J., Zhang, Y., Zhang, L., & Jiao, T. (2022). Recent Developments in Functional Nanocomposite Photocatalysts for Wastewater Treatment: A Review. *Advanced Sustainable Systems*, 6(7), 2200106.
 13. Azmana, M., Mahmood, S., Hilles, A. R., Rahman, A., Arifin, M. A. B., & Ahmed, S. (2021). A review on chitosan and chitosan-based bionanocomposites: Promising material for combatting global issues and its applications. *International journal of biological macromolecules*, 185, 832-848.
 14. Wu, W., He, Q., & Jiang, C. (2008). Magnetic iron oxide nanoparticles: synthesis and surface functionalization strategies. *Nanoscale research letters*, 3, 397-415.
 15. Wu, W., Wu, Z., Yu, T., Jiang, C., & Kim, W. S. (2015). Recent progress on magnetic iron oxide nanoparticles: synthesis, surface functional strategies and biomedical applications. *Science and technology of advanced materials*, 16(2), 023501.
 16. Akbari, A., Amini, M., Tarassoli, A., Eftekhari-Sis, B., Ghasemian, N., & Jabbari, E. (2018). Transition metal oxide nanoparticles as efficient catalysts in oxidation reactions. *Nano-Structures & Nano-Objects*, 14, 19-48.
 17. Zhao, H., Zhu, Q., Gao, Y., Zhai, P., & Ma, D. (2013). Iron oxide nanoparticles supported on pyrolytic graphene oxide as model catalysts for Fischer Tropsch synthesis. *Applied Catalysis A: General*, 456, 233-239.
 18. Asgharnasl, S., Eivazzadeh-Keihan, R., Radinekiyan, F., & Maleki, A. (2020). Preparation of a novel magnetic bionanocomposite based on factionalized chitosan by creatine and its application in the synthesis of polyhydroquinoline, 1, 4-

- dyhydropyridine and 1, 8-dioxo-decahydroacridine derivatives. *International journal of biological macromolecules*, 144, 29-46.
19. I.A. Khodja, W. Ghalem, Z.I. Dehimat, R. Boulcina, B. Carboni, A. Debache, Solvent-free synthesis of dihydropyridines and acridinediones via a salicylic acid-catalyzed Hantzsch multicomponent reaction, *Synth. Commun.* 44 (2014) 959–967.
 20. N.N. Karade, V.H. Budhewar, S.V. Shinde, W.N. Jadhav, L-proline as an efficient organo-catalyst for the synthesis of polyhydroquinoline via multicomponent reaction.
 21. D. Yadav, R. Patel, V. Srivastava, G. Watal, L. Yadav, LiBr as an efficient catalyst for one-pot synthesis of Hantzsch 1,4-dihydropyridines under mild conditions, *Chin. J. Chem.* 29 (2011) 118–122.
 22. Z. Hajizadeh, A. Maleki, J. Rahimi, R. Eivazzadeh-Keihan, Halloysite nanotubes modified by Fe₃O₄ nanoparticles and applied as a natural and efficient nanocatalyst for the symmetrical Hantzsch reaction, *Silicon* (2019) 1–10.
 23. Sonmez, M., Georgescu, M., Alexandrescu, L., Gurau, D., Fikai, A., Fikai, D., & Andronescu, E. (2015). Synthesis and applications of Fe₃O₄/SiO₂ core-shell materials. *Current Pharmaceutical Design*, 21(37), 5324-533