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SYNTHESIS, CHARACTERISATION, AND BIOLOGICAL EVALUATION OF SOME CURCUMIN-BASED 4H-PYRAN DERIVATIVES USING DOPED POLYANILINE AS A NANO-CATALYST

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ABSTRACT

A collection of novel curcumin-based 2-amino-4H-pyran-3-carbonitrile was synthesized, characterized by ^{1}H-NMR, MS, FT-IR, and tested for antimicrobial activity. The literature review realized that many synthetic methods exist however, most of these are associated with difficulties like harsh reaction conditions and longer reaction times. This fact motivated us to prepare a novel nano-catalyst i.e., Cobalt doped polyaniline (Co-PANI) and subsequently used as a catalyst for the preparation of curcumin-based pyrans through a one-pot reaction at room condition. The polyaniline and Co-PANI were prepared and confirmed by FTIR, FEG-SEM, TEM, and XRD.

Keywords: Pyran, Curcumin, Catalyst, Malononitrile, Polyaniline.

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INTRODUCTION

Among the heterocyclic family, Oxygen-containing six-membered heterocycles are widespread in nature. Many naturally occurring compounds possessing pyran moiety exhibit interesting biological and pharmaceutical activity, which attracted the research community to its structure, reactivity, synthesis, and properties.[1] Currently, multifaceted biological and pharmaceutical applications of pyrans like antibacterial, antitumor, antitubercular, pigmentation, and antiviral were shown by the different groups of researchers.[2] As a consequence, a number of attempts have been taken to design a variety of 4H-pyran analogs, particularly consisting one-pot three-component system using aldehyde, reactive methylene compounds, and malononitrile was attracted much attention.[3,4] 1,5-dicarbonyl compounds or their analogs are majorly used for this purpose by ring closure.

Multicomponent reaction (MCR) is efficiently used to afford polyfunctionalized pyrans with 1,3-dicarbonyls, malononitrile, and aldehydes using heterogeneous catalysts. 4H-pyrans having free $-NH_2$ group have been synthesized using Cu(II) based catalyst.[5] Organic synthesis assisted by heterogeneous catalysts attracts much attention due to its ease of functionalization, eco-friendliness, recyclability, toxic-free, commercially acceptable, and most important easy extraction from the reaction mixture.[6,7] Pd and Pt doped PANI mediated organic transformations like hydrogenation of nitrobenzene[8], 2-ethylanthroquinone[9], oxidation of methanol,[10] glycerol,[11] etc. showed useful application in organic synthesis. One of the groups synthesized Co-PANI nano-structure using Cobalt acetate as a metal precursor and reported its application in the oxidation of alkenes.[12,13,14]

However, till date Co-PANI system was not yet reported for the 4H- pyran synthesis. In the course of developing a novel and efficient catalytic system, we have recently reported the synthesis of some bioactive curcumin-based 4H-pyran derivatives using Co-PANI as a catalyst as shown in Fig.-2. Cobalt Chloride is used as a metal precursor for the doping of PANI.

The prepared Co-PANI nano-composite was confirmed by SEM, TEM, FTIR, and XRD techniques. The functional characterization of compounds was confirmed using different characterization techniques like ^{1}H-NMR, MS, and FTIR and tested for anti-microbial activity.

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EXPERIMENTAL

Material and Methods

AR grade chemicals of Merck have been used for synthesis as received. FT-IR spectra have been recorded on a Bruker Germany 3000 Hyperion microscope. The ^{1}H-NMR (500MHz) spectra from a Bruker Avance Neo NMR Spectrometer. Mass spectra collected from SYNAPT-XS DBA064 instrument. FEG-SEM images of PANI (ES) and doped PANI were collected from JSM- 7600F instrument. HR-TEM was recorded at 300 kV on FEI Tecnai G2, F30 instrument. XRD data found on XPERT-PRO Diffractometer. Antimicrobial sensitivity of synthesized compounds tested against some Gram +ve, Gram -ve bacteria, and fungus.

Polyaniline (PANI) Synthesis

The chemical oxidation method was used for the preparation of PANI at low temperatures (from 0 to 5°C) using APS and HCl as oxidants. The aniline monomer was prepared by adding 0.0547 mol aniline in 30 ml HCl (2 mol) and cooling it below 5°C in the ice bath. Then 0.0078 mole aqueous APS solution was added to it with continuous stirring. After the completion of polymerization within 3-4 hours, the green color PANI was obtained. It was washed several times with the hot dilute HCl and oven dried for 24 hours[15](Fig.-1).

Fig.-1: Freshly Prepared PANI (Emeraldine Salt)

Doping of PANI

An oven-dried anhydrous CoCl2 (1.0 mmol) was dissolved in acidified methanol solution (pH=1). PANI powder (0.2 g) was mixed with a dopant solution of different concentrations for 2-3 hours with constant stirring. The product was dried in two steps, firstly room temperature drying for 12 hr and further in the oven at 50°C for 6 hours. Finally, green color powder of doped PANI was obtained. It was ground to a fine powder.[16]

Preparation of 4H-pyran using nano-catalyst

The compounds 2-amino-4H-pyran-3-carbonitrilea (4a), (4b), and (c) are synthesized as reported in the literature.[17] In an oven-dried reaction flask, 10 mmol curcumin (1), 10 mmol malononitrile (2), 10 mmol aldehyde (3), ethanol (3mL), and a catalytic quantity of doped PANI were transferred sequentially at room conditions. This admixture is allowed to stir for 12 hours. The TLC technique was used to judge the reaction progress.[18] After reaction completion, a solid product precipitated out on the addition of distilled water into the resulting mixture. It was filtered, and washed with aqueous alcohol (4a-c). The products were recrystallized from alcohol for further purification Fig.-2.

RESULTS AND DISCUSSION

Scanning Electron Microscopy (SEM) Characterization

The prime aim of SEM is to determine the surface characteristics and morphological properties of the nanomaterial. Figure-3(a) and 4(a) show the morphology of bare PANI (Emeraldine Salt) and Co-doped PANI respectively. From the SEM images, a condensed spherical-shaped bunch of inter-connected PANI nanotubes were observed and for the Co-PANI composite spherical-shaped cobalt nanoparticles were evenly distributed along the PANI surface.[19] This confirms the successful formation of the Co-PANI Composite.

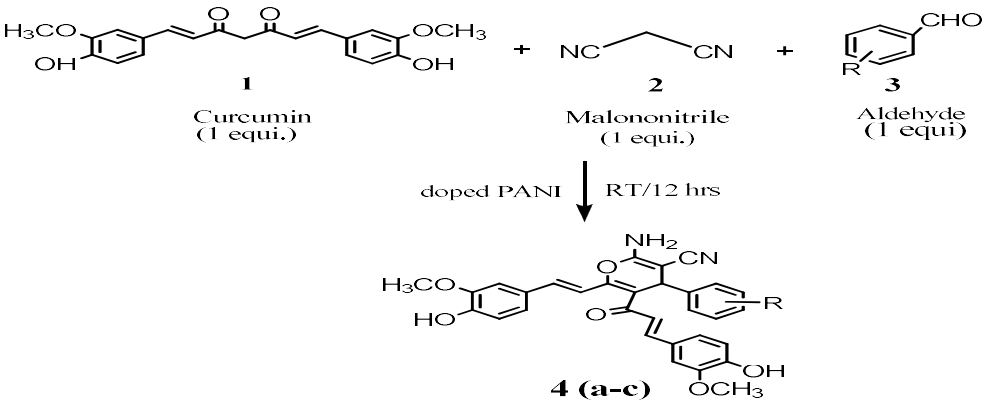


Fig.-2: Schematic Representation of the Synthesis of 4H-pyran derivatives

Transmission Electron Microscopy (TEM) Characterization

The HR-TEM images of PANI (ES) and Co-PANI are shown in Fig.-3(b).and 4(b) PANI (ES) represented a regular spherical shape interconnected agglomerated structure.[20] While Co-PANI nanocomposite reveals the light shell nature of PANI in which dark Cobalt nanoparticles are embedded.[21]

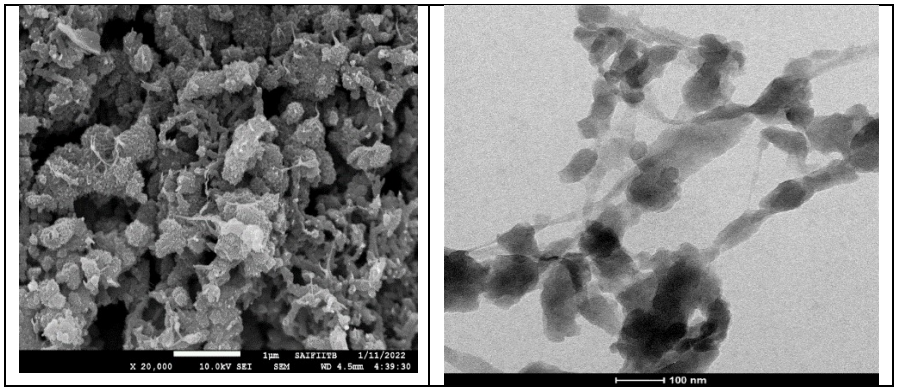


Fig.-3: (a) FEG-SEM of PANI (1µm) (b) TEM image of PANI (100 nm)

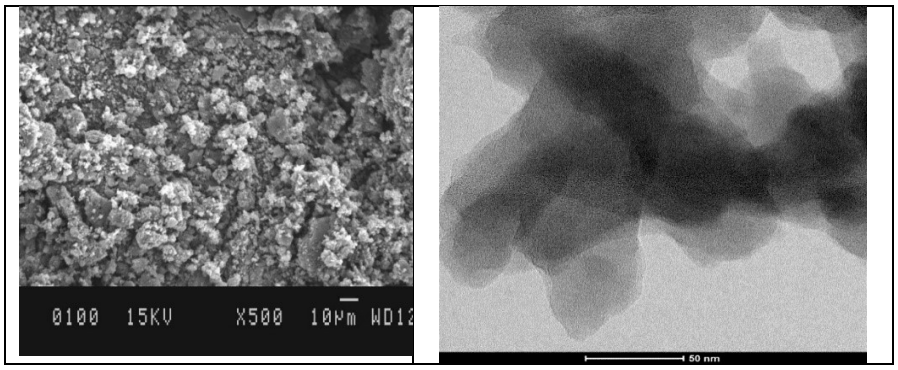


Fig.-4: (a) FEG-SEM of Co-PANI (10 nm) (b) TEM image of Co-PANI (50 nm)

FTIR Analysis

The functionality of synthesized material was confirmed by FT-IR spectroscopic technique (Fig.-5). The band at 1560/cm is attributed to C=C (quinoid) stretching while C=C (benzenoid) stretching appears at 1485/cm, the frequency at 1284/cm for C-N aromatic amine stretching and C-N-C stretching vibration at 1230/cm for the polar ion of PANI.[22,23] C-H bending vibrations confirmed by the band at 1117/cm. Benzene ring substitution by different groups was indicated by various absorption bands lying between 500-700/cm. The attachment of the phenyl moiety with $–NH_2$ groups mainly occur in the para position, consequently, it shows the linear mode of polymerization.[24] The overall FT-IR data confirm the successful synthesis of PANI.

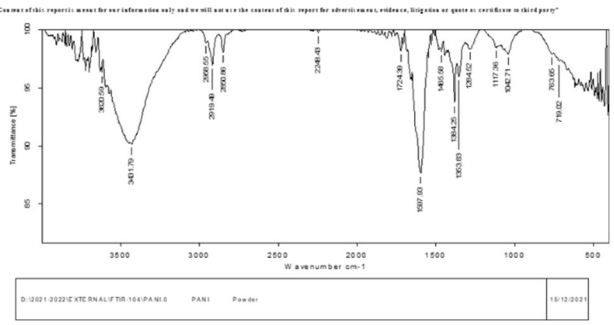


Fig.-5: FT-IR Spectrum of PANI (Emeraldine Salt)

XRD Analysis

The XRD technique was used for characterizing the nature of PANI crystallite. The X-ray diffraction pattern of PANI (ES) at room temperature shows three diffraction peaks at 14.90, 20.70, and 25.41 respectively (Fig.-6a). As sharp peaks confirm the semi-crystalline nature of PANI.[25] For PANI, the sharp peak observed is 2θ=25.41. The value of the interplanar distance is 3.352 A°. Hence, the average size of crystallite is 1.357 nm. Similarly, for Co-PANI, three different peaks are observed at 14.86, 20.77, and 25.31 respectively (Fig.-6b). The sharp peak is observed at 2θ=25.41. The interplanar distance obtained is 3.5156 A°. Hence, the average crystal size is 1.458 nm, as calculated by Debye- Scherrer Equation.[26]

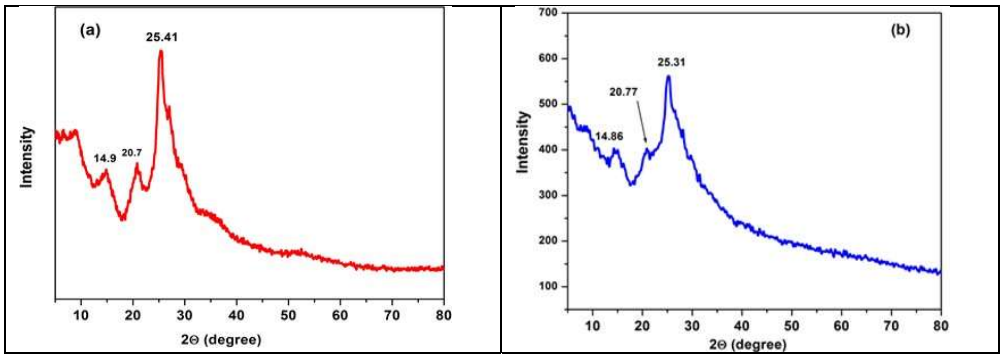
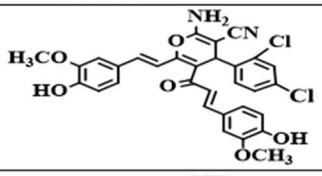
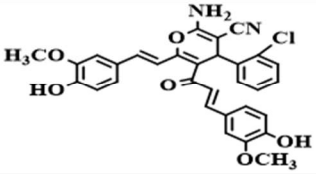
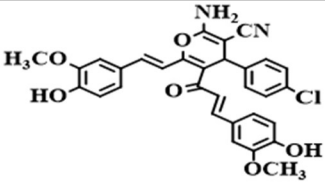


Fig.-6: (a) XRD Spectrum of PANI (ES) (b) XRD Spectrum of Co-PAN

There are Some curcumin-substituted 4H-pyran derivatives have been synthesized and they found to have a good yield.

Table-1: Representative Data of Synthesized 4H-pyrans

S.No.	Product	R in 3	Time(Hrs.)	Isolated Yield(%)
1.		o,p-C6H3Cl2	11	72
2.		o-C6H4Cl	10	78
3.		p-C6H4Cl	12	74

The Representative Physical and Spectroscopic Data of Synthesized Compounds

(Entry-1 and Table-1) Molecular Formula-$C_{31}H_{24}Cl_2N_2O_6$; Mol.Weight-590.10; Reddish brown, State-solid, m.p. 166-168 ºC, Yield-72%

Table-2: ^{1}H-FTNMR (500MHz, DMSO)

Peak observed in (δ) ppm	Multiplicity	Inference
4.28	s	1H, ─C^4- H pyran
5.07	s	2H, Ar-NH_2
9.01	br,s	2H, -OH
3.96-7.02	d	6H,Ar-OCH_3
6.99-7.19	m	4H (two HC=CH protons)
6.52-6.95	m	9H (three Aromatic protons)

FT-IR (υ max: cm^{-1}): 3450, 3276 (-NH_2), 2362 (C≡N), 1683 (CO), 1616 (C=C).

(Entry-2, Table-1) Molecular Formula-$C_{31}H_{25}ClN_2O_6$; Mol. Weight-556.14; Yellowish solid; m.p. 165-168°C; Yield:78%.

Table-3: ^{1}H-FTNMR (500MHz, DMSO)

Peak observed in (δ) ppm	Multiplicity	Inference
5.79	s	1H, ─C^4- H pyran
3.93	s	6H, Two Ar-OCH_3
9.04	br	2H, -OH
8.02	s	2H, Ar-H
4.8	s	2H,Two Ar-NH_2
6.8-7.39	m	4H, Ar-H
7.78	d	4H vinyl protons(J = 15.4 Hz)
7.12	dd	4H, Ar-H

FT-IR (υ max: cm^{-1}): 3410, 3276(-NH_2), 2392 (C≡N), 1558 (C=O), 1653 (C=C).

(Entry-3, Table-1) Molecular Formula-$C_{31}H_{25}ClN_2O_6$; Mol. weight- 556.14; Faint brown solid; m.p. 156-158°C; Yield: 74%.

Table-4: ^{1}H-FTNMR (500 MHz, DMSO)

Peak observed in (δ) ppm	Multiplicity	Inference
4.28	s	1H, ─C^4- H pyran
4.07	s	6H, Two Ar-OCH_3
9.01	br,s	2H, -OH
4.2	s	2H,Two Ar-NH_2
7.52	d	4H,vinyl protons(J = 15 .7 Hz)
7.90	d	4H, Ar-H (J = 8.1 Hz)
6.99-7.19	m	4H, Ar-H
8.6	s	2H, Ar-H

FTIR (υ max: cm^{-1}): 3525,3200 (-NH_2), 2362 (C≡N), 1683 (C=O), 1616 (C=C)

Antimicrobial Studies

All synthesized compounds were screened for antimicrobial sensitivity in vitro against *S. aureus*, *B. subtilis* (Gram-ve bacteria), E. coli (Gram-ve bacterium), and Yeast cells (fungal species). Ofloxacin (20 mg) was used as a standard drug for antimicrobial activity.[27] The antimicrobial sensitivity has been reported in Table-5. Results revealed that compound 4-b is found to be equipotent against *S. aureus* and fungi compared to Ofloxacin. Compound 4-c exhibited remarkable antibacterial activity against *S. aureus* and was equipotent against fungi. Compounds 4-a display poor activity against E. coli.

Table-5: Antimicrobial Activity of 4H-pyran (a-c).

S.No.	Compound	Gram -ve	Gram +ve		Fungi
		E. coli	*S. aureus*	*B. subtilis*	*Yeast cell*
1	4-a	--	08	08	08
2	4-b	--	12	12	16
3	4-c	--	20	18	20
4	Ofloxacin (20 mg)	02	10	22	18

*The numbers show the inhibition zone in mm.

CONCLUSION

This paper focuses on the Cobalt-doped PANI-catalyzed synthesis of 4H-pyran derivatives using one pot multicomponent reaction. It was possible to synthesize curcumin-substituted 4H- pyran derivatives by tandem reaction between differently substituted aldehydes, malononitrile, and curcumin as 1,3-dicarbonyl compound under ambient conditions. The nano-catalyst polyaniline doped with Cobalt (Co-PANI) has feasible synthetic conditions, operational simplicity, safe and moderate efficiency. Synthesized materials were characterized using Nano techniques. Antimicrobial activities were done for the synthesized compounds and results reveal that curcumin-substituted 4H-pyran derivatives are remarkably sensitive when substitution is at the para position. It is noteworthy that the reaction time was appreciably reduced by using novel Co-PANI as a nano-catalyst. This catalyst is used for the first time in the synthesis of curcumin-substituted 4H- Pyran derivatives as a heterogeneous catalyst.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

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