3.3.2.1 Number of Research Papers per teachers in the Journals notified on UGC website during the year 2022-2023.

Sr. No.	Title of the Paper	Name of the author/s	Department of the teacher	Name of journal	Year of publication	ISSN number
1	Silica Chemisorbed Bis(Hydrogensulphato)Benzene (SiO2-BHSB) New, Environmentally Benign and RecyclableCatalyst for an Efficient Synthesis of BiscoumarinScaffolds in Water Based Solvent	K. R. Kadam, G. R. Pandhare, A. S. Waghmare, V. D. Murade, N. R. Kamble ,	Chemistry	Polycyclic Aromatic Compounds	2022	1040-6638
2	Antimicrobial Potential of Carbazole Derivatives	Vijay A. Kadnor	Chemistry	Croatica. Chemica. Acta	2023	0011-1643
3	Novel Pumice Supported Perchloric Acid Promoted Protocolfor the Synthesis ofTetrahydrobenzo[b]pyran viaMulticomponentApproach	Adinath Tambe, ChaitaliDange, JayshriGavande, RavindrDhawale, VijayKadnor,Anil Gadhave , and Gopinath Shirole	Chemistry	Polycyclic Aromatic Compounds	2023	1040-6638
4	Tea Powder Waste: As A Green Catalyst For The Synthesis Of 1-Amidoalkyl 2-Naphthols	A. G. Gadhave, V. A. Kadnor, G. D. Shirole, B. K. Uphade	Chemistry	Heterocyclic Letters,	2022	2232-3087
5	Gc-MS based Phytoconstituents profiling and phytochemical investigation of Annomamuricata L.	H.S. Tambe, A. M. Bhosale, R. D. Borse, S. L. Kakad	Botany	International Journal of Biosciences	2022	2220-6655
6	Wild Edible Vegetables from western hilly region of Ahmednagar	R. D. Borse, M. B. Gunjal	Botany	International Journal of Food and Nutritional Sciences	2022	2320-7876
7	Assessment of Tourism potential ,and Its Impacts On Aurangabad District	R. S. Bhadakwad	Geography	Madhya Pradesh journal Of Social Sciences	2023	0973-855X

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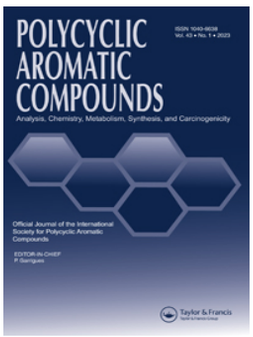

Polycyclic Aromatic Compounds

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/gpol20

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Silica Chemisorbed Bis(Hydrogensulphato)Benzene (SiO_2-BHSB) as a New, Environmentally Benign and Recyclable Catalyst for an Efficient Synthesis of Biscoumarin Scaffolds in Water Based Solvent

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ABSTRACT

The immobilization of homogeneous catalytic material over the inert heterogeneous support is a recent strategy to overcome the drawbacks and unite the merits associated with the homogeneous as well as heterogeneous catalysts. However the physisorption-induced immobilization does not serve the purpose because of its sensitive reversible nature, a tiny change in reaction parameters may revert the physisorption and so the immobilization. In this work, a new catalytic material silica chemisorbed bis(hydrogensulphato)benzene (SiO_2-BHSB) was achieved through the chemisorption of bis(hydrogensulphato)benzene as an active catalytic part on the surface of porous silica. Structural features, purity, thermal stability, and acid strength of the synthesized SiO_2-BHSB material were established by adequate analytical techniques, such as FT-IR, solid-state CP-MAS ^{13}C NMR, solid-state CP-MAS ^{29}Si NMR, EDX, DTG, TGA, and acid–base volumetric studies. An environmentally benign catalytic protocol for the synthesis of biscoumarin scaffolds through a tandem reaction between 4-Hydroxycoumarin and structurally diverse aldehydes was developed in which the synthesized material SiO_2-BHSB was observed to work as an efficient and reusable catalyst. The structures of the synthesized biscoumarin derivatives were established from their physical and spectrometric data. The synthesized catalytic material was observed to show sustained catalytic activity even after five cycles of its recovery and reuse. In comparison with the earlier reported methods, a tiny amount (2.5 mol%) of catalyst is sufficient to bring out the transformation smoothly in an aqueous-based solvent, ease of recovery, and reusability of the catalyst are additional salient features of the present protocol.

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Biscoumarins; 4-hydroxycoumarin; silica chemisorbed bis(hydrogensulphato)benzene; silica-supported catalyst

Introduction

Acid catalysis constitutes a major class of catalyzed chemical transformations, in industry, it is widely used in oil refinements, biomass transformations, and in various synthetic processes of

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pharmaceuticals, fine chemicals, polymers, and commodity chemicals.[1,2] Conventional strong mineral acids viz. HCl, HI, HNO_3, H_2SO_4, $HClO_4$, etc., exhibit great catalytic potentials, however, their industrial catalytic use is constrained due to associated inherited problems, such as safety hazards, equipment corrosion, difficulty in work up separation, toxicity, cost of disposal, waste management, and environmental concerns.[3,4] A catalytic material, which is environmentally benign, sustainable, low cost, convenient, and efficient has remained of great demand.[5] In the catalytic transformations, heterogeneous solid acid catalysts aid high selectivity, low corrosivity, less toxicity, facilitate the post workup isolation and subsequent reuse.[6,7] Consequently replacing conventional liquid acids by heterogeneous solid acids is a good strategy to overcome the associated problems but despite having other attractive properties, heterogeneous solid acids also carry a major drawback of having a poor catalytic activity due to lesser active sites and smaller contact area than their liquid acid analogous.[8] A rational approach to unite the merits of homogeneous and heterogeneous acid catalysts is to immobilize the active homogeneous catalytic material over the porous heterogeneous support.[9] In this respect the highly porous and large surface area materials, such as activated carbon, silica, alumina, titania, zirconia, grapheme oxide, cellulose, starch, chitosan, functionalized nano-materials, etc., have attracted immense attention of the researchers as the heterogeneous support candidates to immobilize the homogeneous active catalytic part. Among the available support materials, silica has been widely studied and used as a heterogeneous support due to its anticipated properties, such as a large contact area, high porosity, compatibility with a wide range of chemicals, insolubility in most of the organic solvents, ease of separation, good stability, reusability, and affordable price.[10,11]

Coumarin and its derivatives are placed among the most privileged scaffolds in pharmacology and therapeutics due to exhibit a wide spectrum of biological activities, such as antibacterial,[12,13] antimicrobial,[14] antitumor,[15] anticancer,[16] antiviral against 'chikungunya',[17] antihepatitis,[18] anticoagulant[19,20] vasorelaxant,[21] spasmolytic,[22] free radical scavengers,[23] HIV integrase inhibitor,[24] α-glucosidase inhibitor[25,26] enzymatic inhibition activity,[27] and snake's venom inhibition activity.[28] In addition to biological activities coumarins are known to show their applications in optoelectronics,[29–31] cellular imaging,[32] lasers,[33] optical whitening materials,[34] fluorescent markers for proteins,[35] effective luminescent materials,[36] and detection of Co (II) and Ni (II).[37]

More specifically, good number of articles exploring medicinal importance of heterocycle coupled biscoumarins are widely published, which described the antibacterial property of biscoumarin-pyrazole compounds,[38] antioxidant and antibacterial effect of thiazolyl-pyrazole-biscoumarin structures,[39] antimicrobial potential of chalcone coupled biscoumarin copolyster,[40] α-glucosidase inhibitor action of biscoumarin-thiourea hybrid,[41] anti-cancer, anti-leishmanial, and alkaline phosphatase inhibition activity of biscoumarin-iminothiazole conjugates,[42] semiconductors and reducing nature of biscoumarins,[43] biscoumarin derivatives as a ligand in terbium (III) complexes,[44] and biscoumarine as a chemosensor for detection of Zn(II) and Cu(II).[45] Some of the biscoumarin based representative drug molecules in the market are presented in Figure 1.[46]

Due to diverse biological activities and other applications, production of coumarins has been paid good attention. Many articles have described the extraction of coumarins from its natural sources, which includes extraction from sweet woodruff (*Galium odoratum)*,[47] sweet-clover *(Genus Melilotus)*,[48] sweet grass *(Hierochloe odorata)*,[49,50] tonka beans *(Dipteryxodorata)*,[51] and vernal grass*(Anthoxanthum odoratum)*.[52] A huge numbers of catalytic protocols have been developed for the laboratory synthesis of coumarin scaffolds, in which the use of acids,[53–59] bases,[60,61] salts,[62–64] porous materials,[65–67] Ionic liquids,[68–70] magnetic nano-composites,[71–73] metal organic frameworks[74,75], and functionalized heterogeneous materials[76–79] are described as the catalytic systems for the synthesis of biscoumarins.

As our interest in the development of environmentally benign catalytic materials as well as catalytic protocols for the synthesis of fine chemicals and bioactive compounds.[80,81] Recently, we

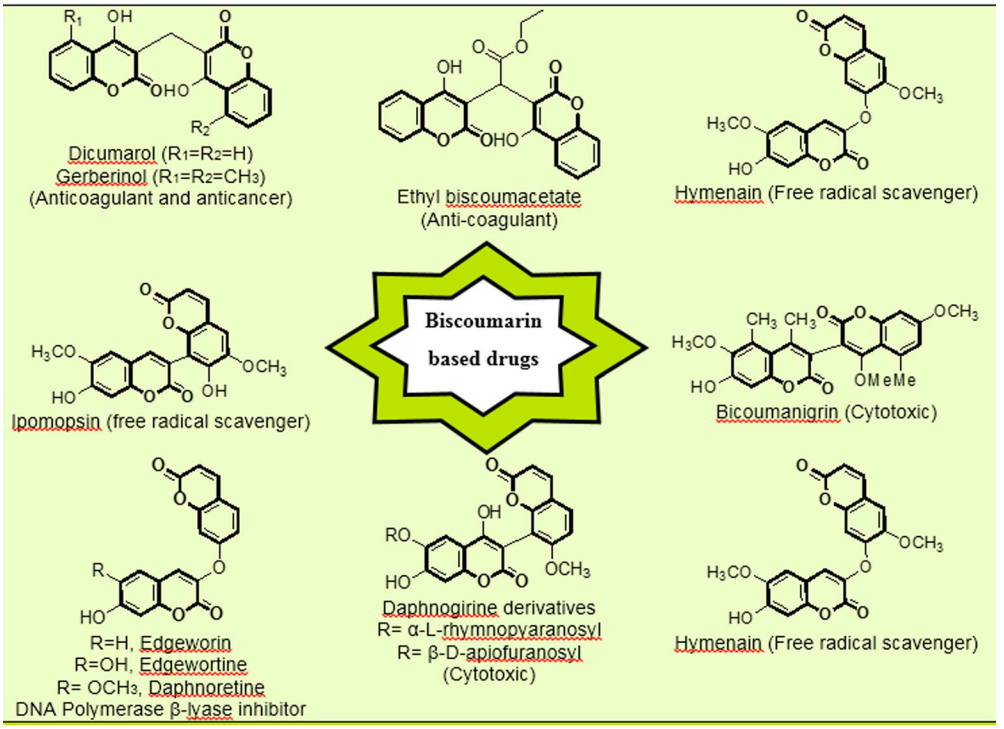
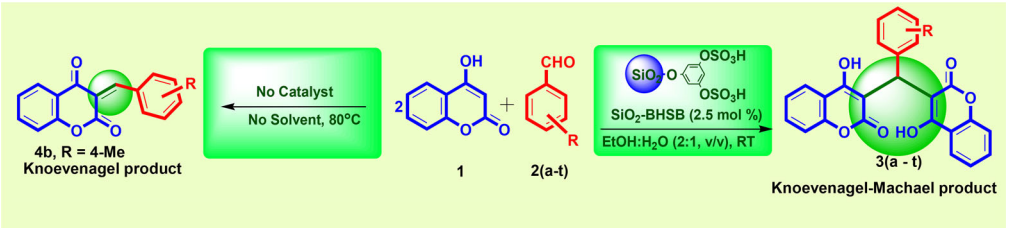


Figure 1. Biscoumarin based representative drug molecules in market.[46]



Scheme 1. Silica chemisorbed Bis(hydrogensulphato)benzene catalyzed synthesis of biscoumarin derivatives.

explored our work on the development of a new catalytic material 'silica chemisorbed bis(hydrogensulphato)benzene (SiO_2-BHSB)' and its catalytic potential for the synthesis of bis(indolyl)methanes.[82] As a next link in this chain, herein we wish to present our observations on the development of an efficient catalytic protocol for the synthesis of biscoumarin derivatives using SiO_2-BHSB as a green catalyst. In this study, we observed that a small amount of SiO_2-BHSB (2.5 mol%) is sufficient to promote the synthesis of biscoumarin scaffolds (3) efficiently from a pseudo three-component Knoevenagel–Michael reaction between two moles of 4-Hydroxycoumarin (1), and one mole of aldehyde (2) at room temperature (Scheme 1). Variety of structurally diverse aldehydes underwent the catalytic protocol smoothly to offer good to excellent yields of corresponding biscoumarin derivatives in aqueous ethanol as a water based solvent. As SiO_2-BHSB being a hybrid organo-inorganic heterogeneous material can be recovered conveniently and quantitatively from the reaction mixture. The recovered catalyst when employed for further cycles of catalytic reuse showed sustained reaction promotion activity even after five cycles of its reuse.

Materials and methods

Materials and experimentals

4-Hydroxycoumarin, phloroglucinol, chlorosulfonic acid, silica gel, malononitrile, substituted aldehydes, and rest of the chemicals used, were obtained from the Sigma-Aldhrich, Merck, or Loba chemical companies and used as received, without further refinement. The ^{1}HNMR spectra were recorded on Bruker Avance FT-NMR (400 or 500 MHz) spectrometer, ^{13}C NMR (75 MHz) spectra were scanned on Varian-NMR-Mercury 300 FT-NMR spectrometer while the solid state CP MAS ^{13}CNMR and CP MAS ^{29}Si NMR spectra were scanned on JEOL ECZR FT-NMR spectrometer. The IR spectra were obtained from Perkin Elmer RX-I FTIR spectrometer. The EDX study of the catalyst was performed on JEOL JSM 6100 FESEM while the TGA-DTA study on Shimadzu TGA-50H thermo-gravimetric analyzer. The elemental analysis of the synthesized compounds was done on Truspec Micro Analyzer. Melting points were carried out in open capillary tubes by gradual heating in paraffin bath. Cambridge software Ultra Chem Draw version 0.8 of Perkin Elmer Informatics, Waltham, USA was used to draw the structures involved.

Procedure for the synthesis of silica chemisorbed bis(hydrogensulphato)benzene (SiO_2-BHSB)

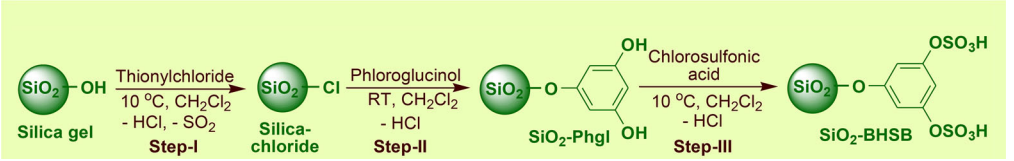
Synthesis of SiO_2-BHSB was achieved through a sequence of three steps, by taking support of a literature report on the synthesis of 'morpholinated and 8-hydroxyquilonited silica gel'.[83]

Step-I: synthesis of silica chloride (SiO_2-Cl)

Ice cold thionyl chloride (10 g) was added drop wise to a vigorously stirring mixture of oven-dried silica gel (100–200 mesh, 10 g) and ice-cold dichloromethane (50 ml) taken into a round bottom flask (250 ml) equipped with water condenser and a calcium chloride guard tube (Scheme 2, Step-I). After stirring the mixture for 24 h at room temperature, the unconsumed thionyl chloride and solvent were removed under reduced pressure, so obtained light gray particles of silica chloride (SiO_2-Cl) are flame dried and immediately stored in a previously weighed air-tight glass bottle. The yield of SiO_2-Cl was found 10.380 g and it can be used for months without decrease in its activity. The silica chloride (SiO_2-Cl) being a moisture-sensitive compound, can easily convert into original silica gel if come in contact with the moisture. Therefore, it needs to be stored in an airtight glass bottle. The amount of chloride in the SiO_2-Cl sample was determined using the simple acid–base titration, in which the liberated HCl from silica chloride (100 mg) in 50 ml deionized water was titrated against the standardized alkali solution, obtained result revealed that 1.666 milli-equivalent of chloride was found per gram of SiO_2-Cl sample.

Step-II: synthesis of SiO_2-phloroglucinol

Silica chloride (SiO_2-Cl, 8.30 mmol) from step-I and phloroglucinol (7.5 mmol) were stirred in dry CH_2Cl_2 (30 ml) taken into a round bottom flask equipped with a drying tube (Scheme 2, Step-II). Evolving HCl bubbles from the reaction mixture indicate progress of the reaction. After



Scheme 2. Systematic synthesis of Silica chemisorbed Bis(hydrogensulphato)benzene (SiO_2-BHSB).

2 h stirring, the resulting silica bound phloroglucinol (SiO_2-Phgl) was filtered at the pump, washed with CH_2Cl_2 (3 × 10 ml), dried at 60–70 °C and weighed. A 5.520 g yield of SiO_2-Phgl was obtained.

Step-III: synthesis of silica chemisorbed bis(hydrogensulphato)benzene (SiO_2-BHSB)

A 10% solution of chlorosulphonic acid (15 mmol) in CH_2Cl_2 was added drop wise to a magnetically stirring, cold suspension of SiO_2-phloroglucinol (7.5 mmol) in CH_2Cl_2 (30 ml) with the help of a constant dropping funnel (Scheme 2, Step-III). The immediate evolving HCl gas was trapped by an acid scavenger assembly arranged along. After completion of the addition, the mixture was stirred for further 2 h, the resulting suspension was filtered at the pump, washed thrice with methanol and once with distilled water in order to remove even a last fraction of an unconsumed or physisorbed chlorosulfonic acid. Obtained brown solid was dried at 60 °C for 6–8 h, the resultant free-flowing particles of SiO_2-BHSB that weighed 6.240 g as a final yield and stored in a glass bottle. The formation of SiO_2-BHSB was confirmed by qualitative as well as quantitative analytical methods.

Procedure for the synthesis of biscoumarin derivatives

A mixture of 4-hydroxycoumarin (4 mmol), aldehyde (2 mmol), and catalytic amount of SiO_2-BHSB (2.5 mol%) was stirred magnetically in ethanol:water (2:1 v/v) at room temperature for the time mentioned in Table 2. Progress of the reaction was checked by TLC using *n*-hexane and ethyl acetate as the mobile phase. Upon completion of the reaction, as denoted by TLC, the solvent was removed by filtration. Hence obtained crude product was dissolved in ethanol in order to recover the catalyst SiO_2-BHSB by filtration and the filtrate was subjected to recrystallization, obtained crystalline product was dried, examined on TLC for its purity and further purified by column chromatography if necessary. The structures of the representative synthesized compounds were confirmed from their physical, analytical, and spectroscopic data.

The recovered catalyst from the reaction mixture was washed with ethanol (3 × 5 ml), dried at 60 °C, tested quantitatively for its acid strength, and employed further for the next cycle of its reuse.

Result and discussion

In the first phase of study, synthesis of SiO_2-BHSB was achieved by referring a report which deals with the synthesis of 'Morpholinated and 8-Hydroxyquinolinated silica gel'.[83] Initially, we were uncertain about the formation of expected catalytic material 'SiO_2-BHSB' due to the possible formation of a competitive side product SiO_2–O–SO_3H from Step-III (Scheme 2). To check the fact a parallel blank reaction along with Step-III (Scheme 2) was carried out using pure silica gel (5 g) at the place of SiO_2-Phgl. The resultant products of both these reactions were analyzed volumetrically for their acid strengths. Only a trace amount of acid was observed with the product of the parallel blank reaction while 3 milli-equivalents of acid per gram of the main reaction product (SiO_2-BHSB) were observed. This fact strongly testified the chemisorption of bis(hydrogensulphato)benzene (BHSB) on silica and denied the possible share of SiO_2–O–SO_3H in the main reaction product SiO_2-BHSB. The percentage of carbon and sulfur in the EDX analysis of SiO_2-BHSB (Figure 2, C_2) also supports strongly the presence of BHSB fragment in the final product of Scheme 2. The four signals appeared at 102, 106, 157, and 159 ppm in the solid state ^{13}C NMR spectrum (Figure 2, B1) also addressed for presence of four types of sp^2 carbons in the material, in which two (157 and 159 ppm) carbons appeared at down field. Presence of only four signals in the ^{13}CNMR reflected the expected symmetric nature of the substituted benzene while down field nature of two carbons revealed their attachments with the electron-withdrawing elements/groups. One down field carbon is due to the attachment of benzene ring to silica skeleton through oxygen linkage while next down field carbon signal is due to two symmetric carbons attached with

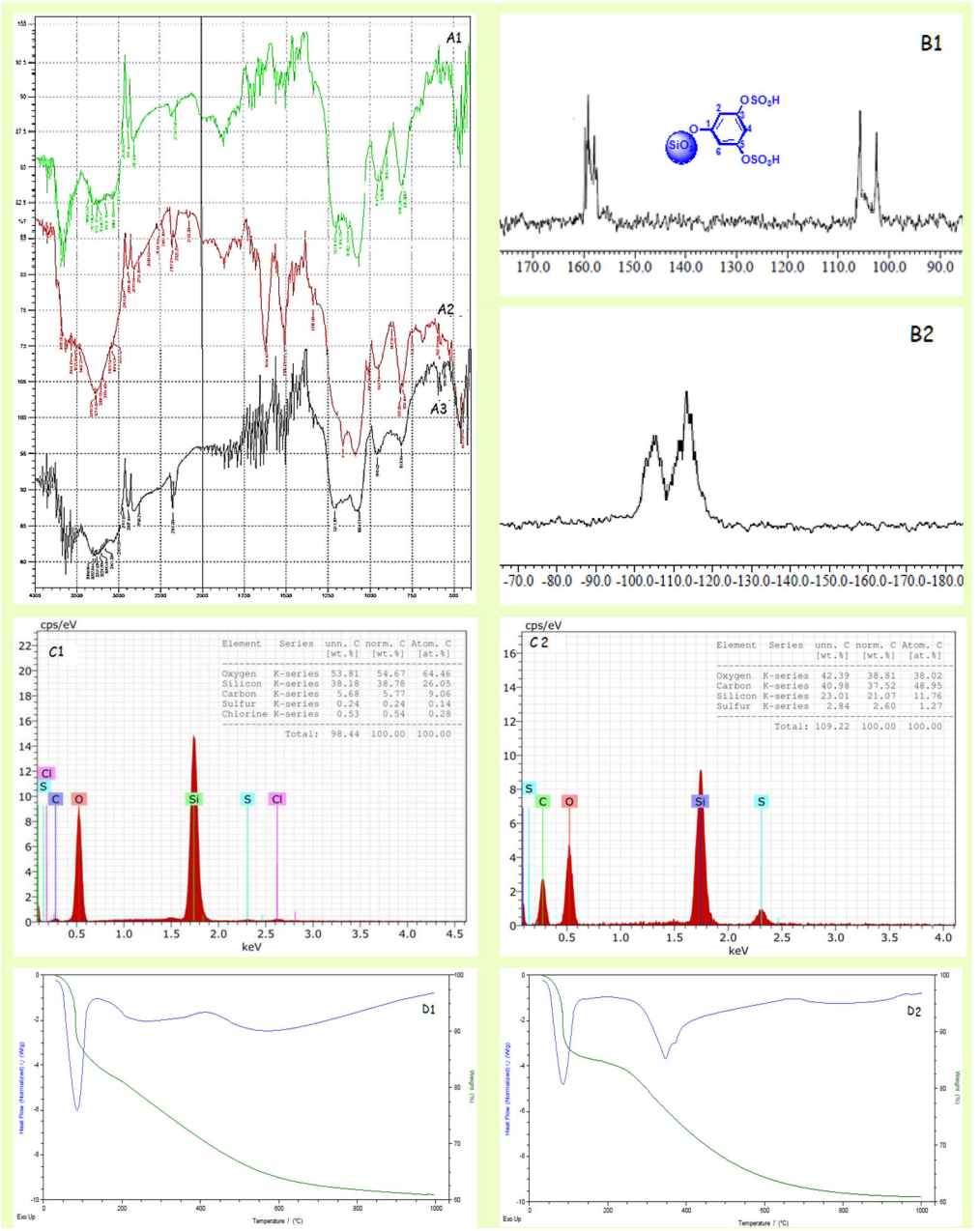


Figure 2. A1, A2, and A3 are FTIR spectra of SiO_2–Cl, SiO_2-Phgl and SiO_2-BHSB, respectively, B1 and B2 are CPMAS ^{13}C NMR and ^{29}Si NMR spectra of SiO_2-BHSB, C1 and C2 are EDX scans of SiO_2–Cl and SiO_2-BHSB, D1 and D2 are TGA-DTA plots of SiO_2–Cl and SiO_2-BHSB.

–OSO_3H groups. The symmetric nature of the involved benzene nucleus and down field nature of two carbons strongly justifies the presence of 3,5-BHSB in the synthesized catalytic material.

Vibrational spectroscopic (FTIR) study of SiO_2-BHSB

A1, A2, and A3 represent the FT-IR spectra of silica chloride (SiO_2–Cl), silica chemisorbed phloroglucinol (SiO_2-Phgl), and SiO_2-BHSB, respectively (Figure 2). The spectrum A1 reflects all the

features of silica chloride such as strong absorptions at 3550 and 3334 cm^{-1} represent silanol O–H stretches, absorptions at 1201 and 1053 cm^{-1} are for anti-symmetric and symmetric stretches of Si-O–Si linkage, peaks at 950 and 812 cm^{-1} are for Si–OH stretch, while absorption at 450 cm^{-1} represents the Si–Cl stretch. The new absorptions appeared in spectrum A2 at 1505, 1614, and 3000–3600 represent C = C and O–H stretch, respectively, which testifies the replacement of chloride by phloroglucinol from the silica surface. In addition to the peaks discussed earlier, the extended absorption from 2000 to 3630 cm^{-1} in spectrum A3 clearly indicates the highly hydrogen-bonded (acidic) nature of OH. Strong absorptions at 1220 and 1140 cm^{-1} are due to the antisymmetric and symmetric stretch of O = S=O moiety which supports the incorporation of the '–SO_3H' group in the material. The FT-IR spectroscopy strongly manifests the formation of the SiO_2-BHSB.

Solid state ^{13}C and ^{29}Si NMR studies of SiO_2-BHSB

The nature of carbon and silicon in the synthesized material was studied with the help of solid-state NMR spectroscopy.

The four signals at 102, 106, 157, and 159 ppm in CP MAS ^{13}C NMR spectrum (Figure 2, B1) correspond for carbon-4, carbon-2/6, carbon-1, and carbon-3/5, respectively (Figure 2, B1). This is a good agreement of ^{13}C NMR spectrums with the structure of SiO_2-BHSB. The CP MAS ^{29}Si NMR spectrum (Figure 2, B2) reveals the presence of two different silicon atoms in the sample. Signal appearing at −104.813 ppm is due to the interior silicon Si–$(OSi)_4$ and the next at −113.269 ppm is for the surface silicon $(SiO)_3$–Si–OH/OAr of silica gel. Conventionally, the interior silicons (−104 ppm) are described as Q_3 while that of surface silicons (−113 ppm) as Q_4.

Thermogravimetric analysis (TGA) and differential thermal gravimetry analysis (DTG) of SiO_2-BHSB

The thermal stability of the SiO_2-BHSB has been studied with the help of thermo-gravimetric analysis (TGA) and the differential thermal gravimetric (DTG) experiments. The data obtained reveal that the 3,5-bis(hydrogensulphato)benzene group is stable up to 240 °C, beyond this temperature and up to 800 °C about 25% weight loss was observed (Figure 2, D2), which reflects the decomposition of organic backbone and sulfonic groups of BHSB. This weight loss is in good agreement of the 1.5 mmol of 3, 5-bis(hydrogensulphato)benzene per gram of SiO_2-BHSB. Earlier at around 90 °C, about 11% weight loss was observed, which represents the removal of surface water attached with the silica gel. In TGA plot D1 (Figure 2), the early loss of 15% of weight represents the evaporation of attached chloride and water molecules from the surface of SiO_2–Cl. The further gradual loss in weight is due to the decomposition of the silica skeleton.

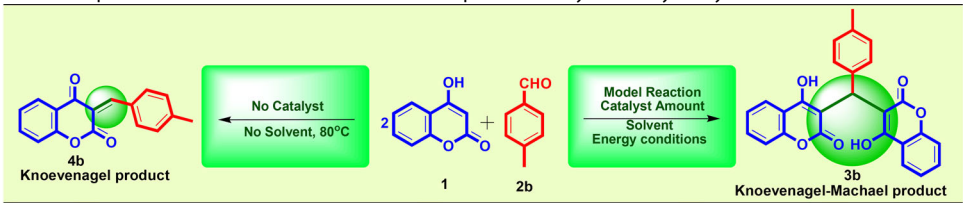
Energy dispersive X-ray (EDX) study of SiO_2-BHSB

The purity and stoichiometry of synthesized SiO_2-BHSB was confirmed from its EDX analysis. No other element than C, O, S, and Si in the EDX spectrum of SiO_2-BHSB (Figure 2, C2) is in support of its purity. The enhancement in the intensities and percentages of carbon and sulfur signals (Figure 2, C2) than the EDX spectrum of silica chloride (Figure 2, C1) is the clear indicatives of stoichiometry as well as the chemisorption of 3,5-bis(hydrogensulphato)benzene on silica gel.

SiO_2-BHSB catalyzed synthesis of biscoumarin derivatives

After establishing the structure of SiO_2-BHSB, we were interested to study the catalytic role of SiO_2-BHSB in the synthesis of biscoumarin scaffolds, for this study a reaction between 4-Hydroxycoumarin (4 mmol) and 4-Methylbenzaldehyde (2 mmol) was selected as a model

Table 1. Optimization of reaction conditions and comparative catalytic activity study for the model reaction.



Entry	Catalyst	Solvent and Reaction condition†	Reaction time (min.)	Yield* of 3b (%)
a.	No Catalyst	No solvent, 80°C	12 h	4b (58)
b.	No Catalyst	EtOH	12 h	4b (32)
c.	SiO_2 (100 mg)	EtOH	12 h	4b (30)
d.	SiO_2-BHSB (10 mol %)	EtOH	150	90
e.	SiO_2-BHSB (10 mol %)	MeOH	130	92
f.	SiO_2-BHSB (10 mol %)	$CHCl_3$	360	62
g.	SiO_2-BHSB (10 mol %)	CH_2Cl_2	12h	58
h.	SiO_2-BHSB (10 mol %)	CH_3CN	360	80
i.	SiO_2-BHSB (10 mol %)	THF	12h	52
j.	SiO_2-BHSB (10 mol %)	Dioxane	12h	55
k.	SiO_2-BHSB (10 mol %)	DMF	360	72
l.	SiO_2-BHSB (10 mol %)	H_2O	12 h	68
m.	SiO_2-BHSB (10 mol %)	MeOH:H_2O (1:1 v/v)	300	90
n.	SiO_2-BHSB (10 mol %)	EtOH:H_2O (1:1 v/v)	180	92
o.	SiO_2-BHSB (10 mol %)	EtOH:H_2O (2:1 v/v)	120	94
p.	SiO_2-BHSB (10 mol %)	EtOH:H_2O (3:1 v/v)	140	92
q.	SiO_2-BHSB (1 mol %)	EtOH:H_2O (2:1 v/v)	390	88
r.	SiO_2-BHSB (2 mol %)	EtOH:H_2O (2:1 v/v)	160	92
s.	SiO_2-BHSB (3 mol %)	EtOH:H_2O (2:1 v/v)	120	94
t.	SiO_2-BHSB (4 mol %)	EtOH:H_2O (2:1 v/v)	120	94
u.	SiO_2-BHSB (5 mol %)	EtOH:H_2O (2:1 v/v)	120	93
v.	**SiO_2-BHSB (2.5 mol %)**	**EtOH:H_2O** (2:1 v/v)	**120**	**94** [xx]
w.	PTA, 15 mol%	H_2O, 80 °C heat,	23	90 [53]
x.	PFPA, 40 mol %	H_2O, reflux	80	89 [54]
y.	CPSA, 20 mol %	EtOH-H_2O,	120	94 [55]
z.	PDBSA, 25 mol %	EtOH-H_2O, reflux	78	85 [56]
aa.	CLSA , 20 mg	H_2O, reflux	120	83 [57]
bb.	CAN, 10 mol %	H_2O	8h	82 [64]

† Unless mentioned the reaction condition is stirring at 28-30°C, * Isolated yields, [xx] present work,
PTA: $_{1\,\text{pinch}}$ Phosphotungstic acid, PFPA: Pentafluropropanoic acid, CPSA: Campher sulphonic acid, PDBSA: p-Dodecylbenzene sulphonic acid, CLSA: Cellulose sulphonic acid, CAN: Ceric ammonium nitrate

reaction. In the preliminary trial study, four sets of the model reaction with different amounts of catalyst in EtOH and without solvent were studied (Table 1, Entries **a–d**). The TLC of the model reaction without solvent and without catalyst showed no change in its composition even after 12 h stirring at room temperature while the same set of the reaction produced Knoevenagel product (Scheme 1, **4b**) with 48% yield when further stirred at 80 °C for next 12 h (Table 1, Entry **a**). The second and third model reactions in EtOH with no catalyst and SiO_2 as catalysts respectively, after 12 h of stirring each produced small yields of Knoevenagel products (Table 1, Entries **b and c**) only. The fourth model reaction in ethanol and using SiO_2-BHSB (10 mol%) as a catalyst surprisingly produced a good yield of biscoumarin derivative at room temperature in a smaller reaction time (Table 1, Entry **d**) than the earlier three model reactions (Table 1, Entries **a–c**). The obtained results demonstrate the catalytic role of SiO_2-BHSB in the formation of the desired

Knoevenagel–Michael product. The earlier three reactions without SiO_2-BHSB could only produce Knoevenagel product and not Knoevenagel–Michael product.

In earlier study, ethanol was used as a trial solvent to perform preliminary studies, thereafter in order to select the most suitable solvent for the under investigation protocol, various polar and non-polar solvents were employed for the model reaction using SiO_2-BHSB (10 mol%) as a catalyst at stirring, obtained results are summarized in Table 1 (Entries **e–o**). It is noteworthy to mention that the model reaction offered superior results in methanol and ethanol:water (2:1 v/v) system (Table 1, Entries **e and o**) than rest of the solvents employed. As ethanol:water (2:1 v/v) system being greener than methanol, we decided to explore further dimensions of this study using ethanol:water (2:1 v/v) as the reaction media.

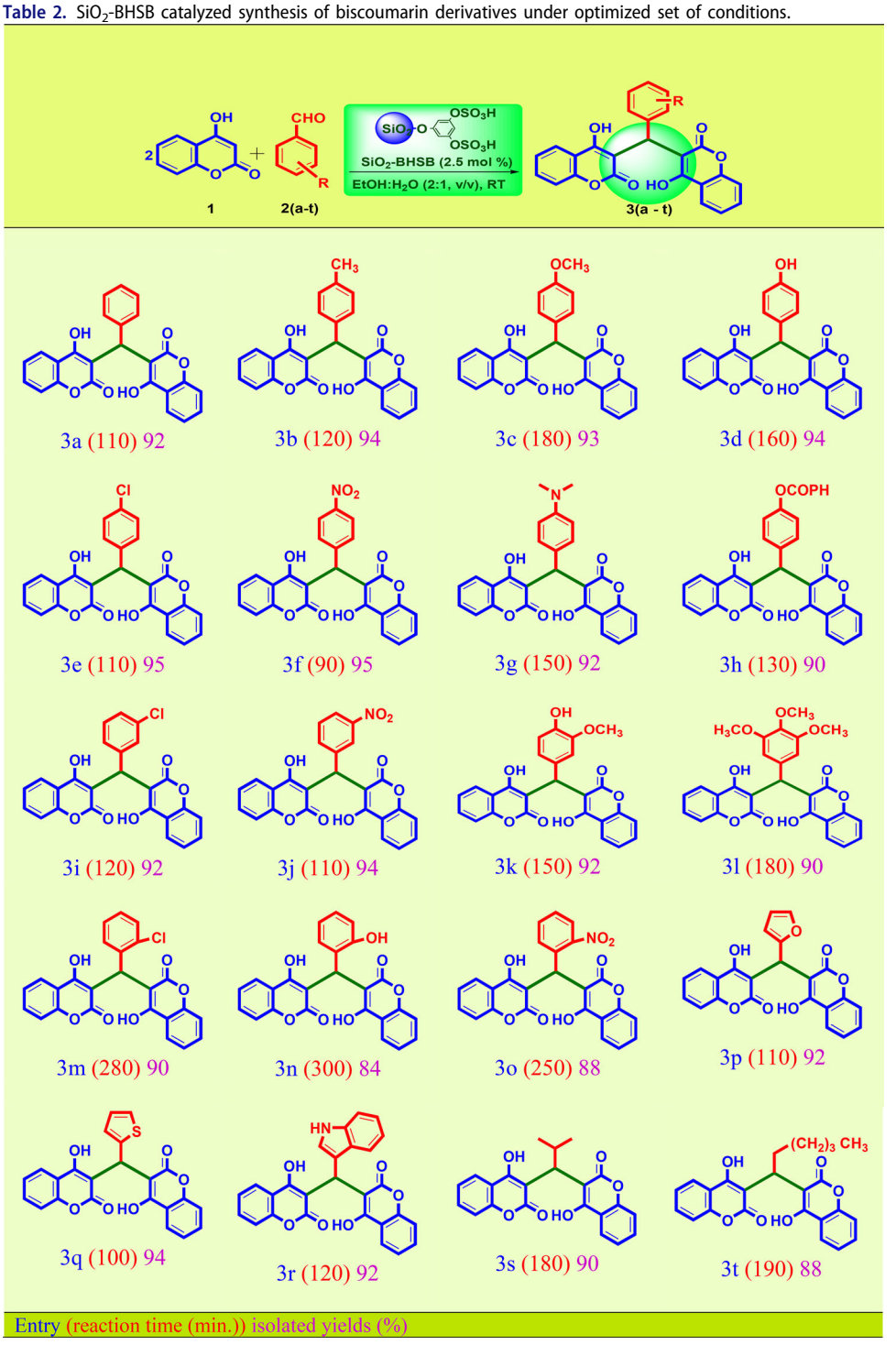
To fix an optimal amount of catalyst for under investigation protocol, the model reaction was examined for various amounts of SiO_2-BHSB (1–10 mol%) as a catalyst under stirring in ethanol:-water (2:1) solvent system. The direct proportional of yields and inverse proportional of reaction times were noted as the amount of SiO_2-BHSB increased from 1 to 3 mol% (Table 1, Entries **n–p**), further increase in the amounts of catalyst did not display improvements in results. It indicates that the optimal amount of catalyst falls in 2–3 mol% range. A microanalysis of this range revealed that the 2.5 mol% of catalyst produced the best results of the model reaction (Table 1, Entry **s**).

A comparative study between herein described catalytic protocol and various reported catalytic protocols for the model reaction has been presented in Table 1. The study revealed that under stirring, a small amount (2.5 mol%) of SiO_2-BHSB is sufficient to bring better results than the cited catalytic protocols, whereas majority of the reported protocols need 10–40 mol% of catalysts (Table 1, Entries **w–z** and **bb**) even under harsh energy conditions. Present catalytic protocol offers superiority and convenience over the cited protocols in terms of catalyst amount, reusability of catalyst, environmental compatibility of the solvent, and reaction conditions (Table 2). The probable reasons for the superiority of the present catalytic protocol include the large surface to volume ratio, organo–inorganic hybrid nature, dibasic, and strong acidic character of the catalytic material SiO_2-BHSB. The large surface-to-volume ratio provides ample active sites for substrates to react among. The dibasic and strong acidic character of the sulfonic acid could release ample number of H^+ by dissociating irreversibly, which could assist to form greater number of the acid-induced active intermediates, which later convert in to the stable product (Figure 3). According to the thumb rule of solubility 'like dissolves like' the organo-inorganic hybrid nature of the SiO_2-BHSB may assist the organic substrates to attend the closest approach with the catalyst at normal energy conditions. The dibasic nature of the catalyst could release double amount of H^+ in the reaction media, which in turn could utilize to form double amounts of acid-promoted intermediate species. These are the most plausible reasons to explain the sufficiency of a small amount (2.5 mol%) of catalyst for this protocol. The plausible working mechanism of SiO_2-BHSB for the synthesis of biscoumarin derivatives is described in Figure 3.

A range of structurally diverse aldehydes were employed to establish the generality of the above-developed catalytic protocol. It was observed that all the employed aldehydes smoothly underwent the catalytic transformation and offered well to excellent yields in **2–5** h. Steric crowding at reaction site and electronic effect of substituents showed a notable effect in terms of reaction times and yields. Aldehydes with electron-donating substituents took longer to complete the reaction (Table 2, compounds **3c, 3d, 3g,** and **3 l**) than those bearing electron-withdrawing substituents (Table 2, compounds **3e**, **3f, 3i, and 3j**). Increased steric hindrance at the reaction site of aldehydes caused notable influence in terms of decrease in yields and increase in reaction times (Table 2, **4m–4o**).

In the catalyst reuse study, the filtered catalyst from the reaction media was first washed with ethanol (3×5 ml) and then with plenty of water, dried in a hot air oven at 60 °C and employed further for the next run of its reuse. Such six cycles of catalyst recovery and reuse were tested for

Table 2. SiO_2-BHSB catalyzed synthesis of biscoumarin derivatives under optimized set of conditions.



the model reaction under optimized set of reaction conditions, the obtained results are summarized in the graphical format (Figure 4). It was noted that the model reactions produce about identical yields with a little extension of reaction time for each subsequent cycle of catalyst reuse.

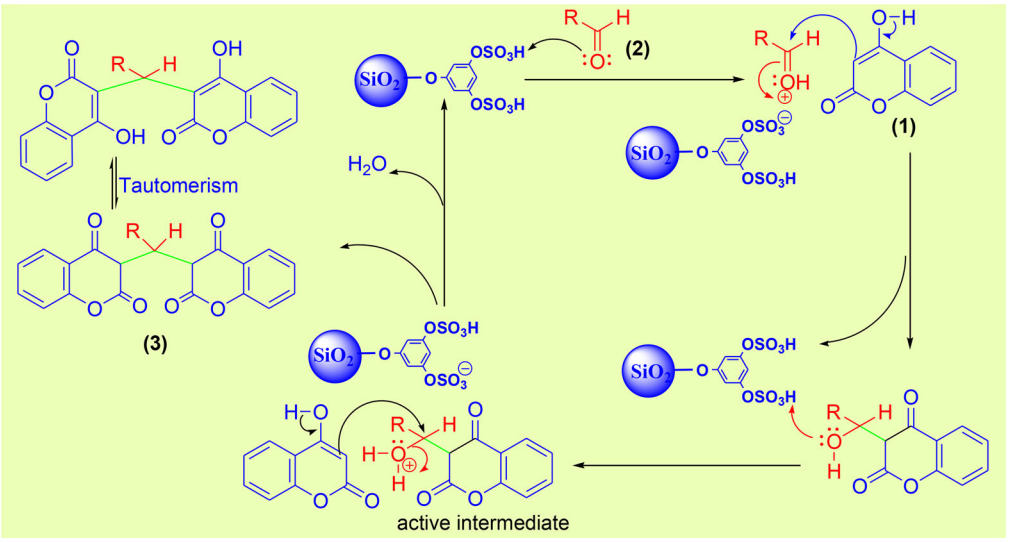


Figure 3. Plausible mechanism showing catalytic role of SiO_2-BHSB in the synthesis biscoumarin derivatives.

Figure 4. SiO_2-BHSB reuse study for the synthesis of **3b**.

In order to examine whether the catalyst material underwent any change during the catalytic synthesis of target scaffolds? The recovered catalyst from the last cycles of its reuse was analyzed by FTIR and EDX techniques. Obtained results (Figure 5) upon comparison with that of fresh catalyst revealed that there are conservations of functional groups as well as elemental composition in the reused catalyst.

Physical and analytical data of some representative biscoumarins

3, 3′-Benzylidene-bis-(4-hydroxycoumarin) (3a)

Colorless solid; M.P.: 217–219 °C; FTIR (KBr, ν_{max}): 3445 (O–H), 1672 (C = O), 1604 (C = C), 1562 (C = C), 1352, 1097 (C–O), 756 cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$, δ): 6.10 (s, 1H, Ar-CH), 7.21– 7.34 (m, 7H, Ar-H), 7.41 (d, 2H, Ar-H), 7.64 (m, 2H, Ar-H), 8.07 (d, 2H, Ar-H) 11.30 (s, 1H, –OH), 11.53 (s, 1H, –OH) ppm; ^{13}CNMR (75 MHz, $CDCl_3$, δ): 36.04 (Ar-CH), 103.74, 105.46, 116.50, 117.91, 124.23, 124.75, 126.33, 126.72, 128.48, 132.74, 135.06, 151.21, 164.44,

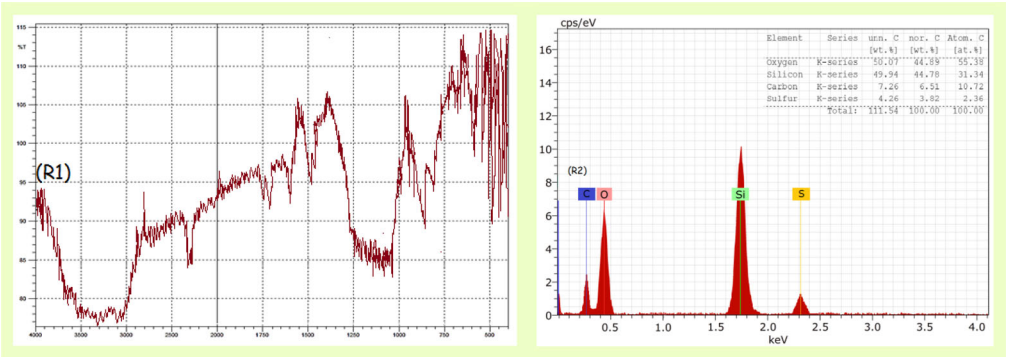


Figure 5. FTIR spectrum (R1) and EDX scan (R2) of recovered SiO_2-BHSB after the cycles of its reuse.

165.66, 166.76 (C = O), 169.11(C = O) ppm; MASS (ES+): 413 (8. 65%, M + H^+), 273 (10.23%), 251 (28.02%), 185 (27.74%), 163 (95.67%), 140 (4.83%) *m/z*; Elemental analysis: calculated (%) for $C_{25}H_{16}O_6$: C, 72.81; H, 3.91; found: C, 72.76; H, 3.85.

3, 3′-(p-Tolylmethylene)bis(4-hydroxy-2H-chromen-2-one) (3b)

White solid; M.P.: 265–267 °C; ^{1}HNMR (400 MHz, $CDCl_3$, δ): 2.33 (s, 3H, Ar-CH_3), 6.06 (s, 1H, Ar-CH), 7.17 (m, 4H, Ar-H), 7.25 (s, 2H, Ar-H), 7.40 (d, 8.40 Hz, 4H, Ar-H), 7.62 (m, 2H, Ar-H), 8.00 (d, 6.40 Hz, 1H, Ar-H), 8.06 (d, 6.4 Hz, 1H, Ar-H), 11.29 (s, 1H, –OH), 11.51 (s, 1H, –OH) ppm; ^{13}CNMR (75 MHz, $CDCl_3$, δ): 21.10 (Ar-CH_3), 35.97 (Ar-CH), 104.18 105.86, 116.56, 116.74, 117.07, 124.49, 124.97, 126.48, 129.45, 132.14, 136.59, 152.40, 152.63, 164.65, 165.83, 166.95 (C = O), 169.44 (C = O) cm^{-1}; Elemental analysis: calculated (%) for $C_{26}H_{18}O_6$: C, 73.23; H, 4.25; found: C, 73.15; H, 4.19.

3, 3′-((3, 4, 5-Trimethoxyphenyl)methylene)bis(4-hydroxy-2H-chromen-2-one) (3l)

Colorless solid; M.P.: 240–242 °C; FTIR (KBr, ν_{max}):1662 (C = O), 1618 (C = C), 1566 (C = C), 1348, 1126 (C–O), 759 (Ar-H bending) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$, δ): 3.58 (s, 6H, 2 × Ar-OCH_3), 3.63 (s, 3H, Ar-OCH_3), 6.28 (s, 1H, Ar-CH), 6.45 (s, 2H, Ar-H), 7.30–7.36 (m, 4H, Ar-H), 7.56–7.60 (m, 2H, Ar-H), 7.91 (t, 7.20 Hz, 2H, Ar-H) ppm; ^{13}CNMR (75 MHz, $CDCl_3$, δ): 35.73 (Ar-CH), 55.69 (Ar-OCH3), 60.24 (Ar-OCH3), 103.88, 104.23, 116.09, 123.71, 124.46, 131.38, 132.45, 136.47, 152.08, 153. 76, 164.67 (C = O), 167.49 (C = O) ppm; MASS (ES+): 503 (3.85%, M + H^+), 363 (41.46%), 341 (127. 33%), 207 (7.17%), 167. 1 (10.36) *m/z*; Elemental analysis: calculated (%) for $C_{28}H_{22}O_9$: C, 66.93; H, 4.41; found: C, 66.88; H, 4.36.

3, 3′-(2-Nitrobenzylidene)-bis-(4-hydroxycoumarin) (3o)

Yellow solid. M.P.: 206–208 °C; FTIR (KBr, ν_{max}): 2603-2586 (OH), 3078 (Ar-H), 1658 (C = O), 1602 (C = C), 1558 (C = C), 1521 (–NO_2), 1354 (–NO_2), 1213, 1097, 829, 754 (Ar-H bending) cm^{-1}; ^{1}HNMR (400 MHz, $CDCl_3$, δ): 6.66 (s, 1H, Ar-CH), 7.31–7.70 (m, 10 H, Ar-H), 7.98–8.11 (m, 2H, Ar-H), 10.42–11.54 (br s, 2H, OH) ppm; ^{13}CNMR (75 MHz, $CDCl_3$, δ): 33.10 (Ar-CH), 103.82, 116.76, 124.73, 128.09, 129.12, 132.39, 132.55, 149.88, 152.16, 164.46 (C = O), 166.14 (C = O), 167.49 ppm; MASS (ES+): 458 (24.94%, M + H^+), 318 (19.16%), 185 (24.98%), 163 (97.60%), 120 (3.44%) *m/z*; Elemental analysis for $C_{25}H_{15}NO_8$: calculated (%): C, 65.65; H, 3.31; N, 3.06; found (%): C, 65.69; H, 3.33; N, 3.12.

3, 3′-(Furan-2-ylmethylene)-bis-(4-hydroxy-2H-chromen-2-one) (3p)

White solid; M.P.: 198–199; ^{1}HNMR (500 MHz, $CDCl_3$, δ): 6.10 (s, 1H, Ar-CH), 6.31 (m, 1H, Ar-H), 6.35 (dd, J = 8.5 Hz, 1.5 Hz, 1H, Ar-H), 7.34 to 7.37 (m, 2H, Ar-H), 7.38 to 7.39 (m, 2H, Ar-H), 7.49 (t, J = 1 Hz, 1H, Ar-H), 7.60–7.64 (m, 2H, Ar-H), 7.96 (dd, *J* = 8 Hz, 1.5 Hz, 2H, Ar-H), 9.80 (br, 2H, –OH) ppm; ^{13}CNMR (75 MHz, $CDCl_3$, δ): 32.54 (Ar-CH), 107.77, 110.62, 116.76, 124.45, 124.98, 133.02, 148.85, 152.50 (C = O), 164.92 (C = O) ppm; Elemental analysis for $C_{23}H_{14}O_7$: calculated (%): C, 68.66; H, 3.51; found (%): C, 68.61; H, 3.44.

Conclusion

Physisorption induced immobilization of the active catalytic part on an inert support is highly sensitive toward reaction conditions. Even a small change in a reaction parameter may cause the mobilization of the active catalytic part from the surface of the support. In order to overcome this problem of physisorption we have synthesized SiO_2-BHSB as a new silica-supported catalytic material based on the chemisorption phenomenon. Structural features, elemental composition, thermal stability, and acid strength of the synthesized catalytic material were established with the help of suitable analytical techniques. The synthesized material was observed to act as a potential catalyst for the synthesis of biscoumarins. An environmentally benign catalytic protocol for the synthesis of biscoumarin scaffolds was developed, in which a small amount 2.5 mol% of SiO_2-BHSB is sufficient to act as an efficient and reusable catalyst for the transformation in aqueous-based ethanol as a solvent. Structurally, diverse aldehydes underwent the developed catalytic protocol smoothly to produce the corresponding biscoumarin derivatives in good to excellent yields. Structures of the synthesized compounds were confirmed from their physical and analytical studies. At the end, it is worthy to remark that there is a wide scope to develop catalytic protocols for the synthesis of fine chemicals and bioactive compounds using SiO_2-BHSB as a recyclable heterogeneous catalyst.

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Disclosure statement

No conflict of interest was reported by the author(s).

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REVIEW

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Antimicrobial Potential of Carbazole Derivatives

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Abstract: Amongst many nitrogen-containing heterocycles, carbazole frame is the building block of various biologically active compounds, including both synthetic and natural products of which its antimicrobial and antifungal activities are the most examined. In this review, 3, 4 and *N*- substituted carbazole derivatives and their antimicrobial activities are discussed (articles published from 2013 to 2022).

Keywords: carbazole derivatives, biological potential, antibacterial, antifungal.

INTRODUCTION

RESEARCH on novel chemotherapy has been very important in controlling different types of diseases in humans and animals caused by microorganisms. Various chemotherapeutic agents are isolated from living organisms known as antibiotics such as penicillin and tetracycline or they are certain synthetic organic compounds such as sulpha drug.[1] Microorganisms generated disease have the capacity to resist these chemotherapeutic agents, thus such microbial strains produce a major effort in the treatment of microbial infections.[2] To overcome this intricacy study of new antimicrobial agents is a continual process, which led to develop new chemical compounds with good antimicrobial activities and suitable to be used as chemotherapeutic agents.

The heterocyclic framework of aromatic carbazole is an advantageous pharmacophore skeleton found in various biologically active compounds from different sources, covering both natural and synthetic sources. The parent compound 9*H*-carbazole was first described by Graebe and Glaser in 1872, which was obtained from the anthracene fraction of coal tar distillate.[3] This outline has since grown the consideration by researchers as it has been highlighted in molecules that intervene a wide range of biological activities.[4,5] The biological properties of active carbazole alkaloids, isolated mainly from taxonomically similar plants of the genus *Murraya,*[6–9] *Clausena*[10–12] and *Glycosmis*[13–15] that belongs to the citrus family *Rutaceae* caused that many research groups became interested in the structural modifications of natural compounds and synthesis of new derivatives of carbazole.[16] The biologically active fused aromatic systems are known of natural origin (alkaloids) or synthetic drugs containing component of carbazole[17–26] in their structure which possess anti-cancer, antibacterial, antifungal, anti-inflammatory, hepatoprotective, anti-HIV, antiprotozoan and sedative properties, or topoisomerase II inhibition ability.

In this article I will present the antimicrobial potential of carbazole derivatives reported from the years 2013 to 2022, which are interesting because of their biological and photophysical properties.[27–46] Some of carbazole compounds have a very high activity against many organisms, bacteria, fungi, parasites.[34–38]

Antibacterial and Antifungal Activities of Carbazoles

A potent antibacterial activity of *N*-substituted benzimidazole incorporating with carbazole namely *N*-((1-(4-(9*H*-carbazol-9-yl) butyl)-1*H*-benzo[d]imidazol-2-yl) methyl)-2-fluoroaniline **1** and its corresponding salt **1a** (Figure 1.) reported by HuiZhen and coworkers in 2013.

The antibacterial activity revealed that carbazole **1** gave good antibacterial activity against *B. subtilis* (MIC = 64 µg/mL) and *P. aeruginosa* (MIC = 64 µg/mL), than the reference drug chloromycin. Corresponding salt compound **1a** showed the best antibacterial activity, at the concentrations of 8–32 µg/mL, it is more sensitive to the

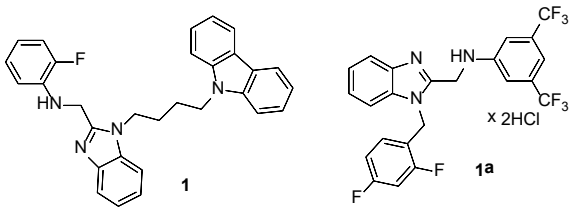


Figure 1. Structures of carbazole frame benzimidazole and its salt.[47]

S. aureus, *B. subtilis*, and *M. luteus* species (MIC = 8 μg/mL) which was nearly equipotent or even higher to the reference drug chloromycin 8 μg/mL. The study has shown the introduction of carbazole ring was advantageous to the benzimidazole for enhancement antimicrobial activity.[47]

Synthesis and spectral characterization of sulfonamide and carbamate derivatives of 4-(oxiran-2-ylmethoxy)-9*H*carbazole (**2a–d** and **3a–f**) as shown in Figure 2. were described by

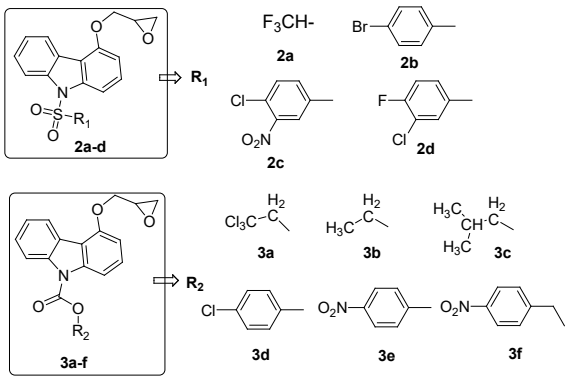
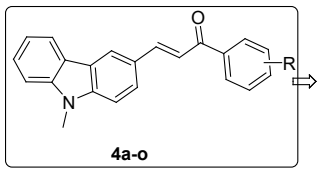


Figure 2. Structures of carbazole based sulfonamide and carbamate (**2a–d** and **3a–f**) derivatives.[48]

Venkata *et al*. in 2013, in order to study the change in substituent might affect the antimicrobial activity. Antimicrobial property of all the synthesized compounds (**2a–d** and **3a–f**)



Comp.	R	Comp.	R
4a	H	**4i**	2,4-Cl
4b	4-OCH_3	**4j**	3,4-Cl
4c	3,4-OCH_3	**4k**	2,5-Cl
4d	2,4,6- OCH_3	**4l**	4-Br
4e	4-F	**4m**	4-NO_2
4f	2,4-F	**4n**	2-Thiophene
4g	3,4-F	**4o**	2-pyridine
4h	4-Cl		

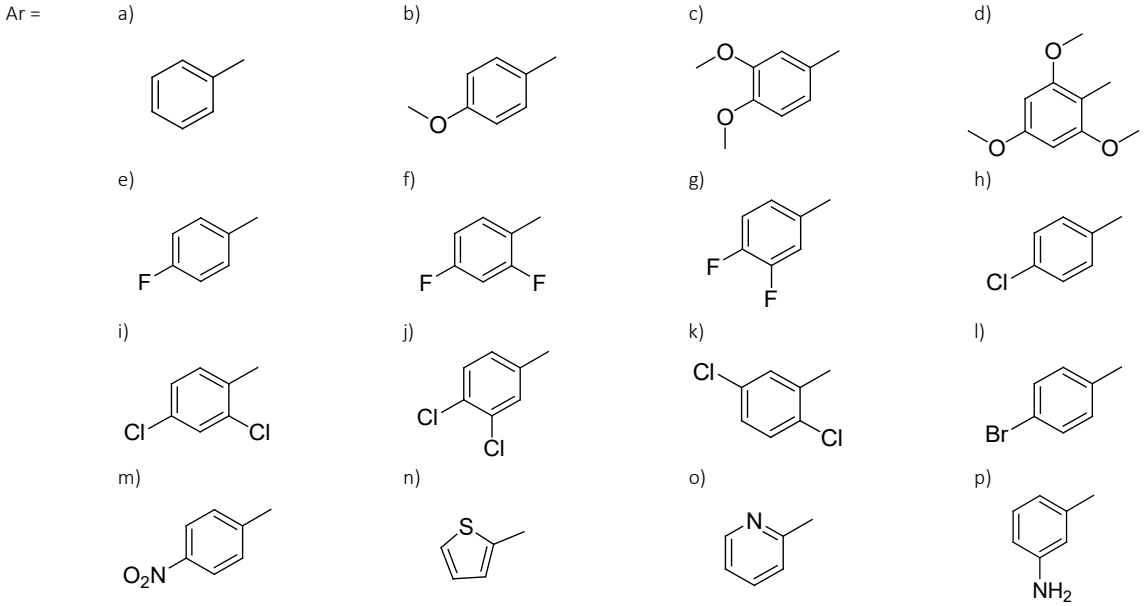
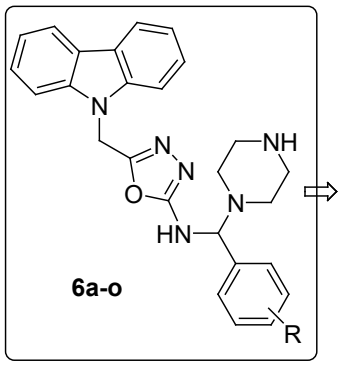


Figure 3. Structures of the carbazole derivatives reported by Bandgar et al.[49,50]



Comp.	R	Comp.	R
6a	4-NO_2	6i	2-OH
6b	4-OH	6j	3-Cl
6c	3,4, 5-OCH_3	6k	2-Cl
6d	4-Cl	6l	3 -OCH_3
6e	4- $N(CH_3)_2$	6m	4 -OCH_3
6f	2- NO_2	6n	4-F
6g	4-OH	6o	H
6h	3- NO_2		

Figure 4. Structures of carbazole incorporated oxadiazole derivatives (**6a**–**o**).[51]

examined against (*S. aureus*, *B. subtilis*, and *E. coli*) bacterial and (*F. oxysporum*, *C. albicans*, and *A. niger*) fungal strains through the agar well diffusion method. All the compounds (**2a**–**d** and **3a**–**f**) discovered modest to strong antimicrobial activities at a concentration of 200 µg/mL, and the results were comparable to the standard drugs ciprofloxacin and fluconazole. Amongst the synthesized compounds, the functional groups such as *p*-NO_2 in **2a** and **3e**, *p*-Cl-*m*-NO_2 in **2c** against *C. albicans*, *p*-Br in **2b** against *E. coli*, *p*-F-*m*-Cl in **2d**, CCl_3 in **3a** and isobutyl in **3c** against *B. subtilis* might be responsible for good activity.[48]

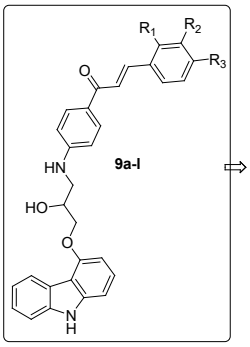
In 2013, Bandgar *et al*. evaluated the antimicrobial activities of a series of novel carbazole chalcones (**4a**–**o**) (Figure 3.). The antibacterial screening data of the compounds **4a**, **4e** and **4m** displayed significant inhibition zone (4.5 ± 2.5 mm) against all the three bacterial growth. Whereas compounds **4b**, **4g** and **4h** inhibited (6.0 ± 1.5 mm) zone against *P. vulgaris* and *E. coli* selectively, but compounds **4c** and **4o** had valuable results against *S. aureus* with inhibition zone (2.5 ± 2.0 and 4.5 ± 1.5 mm) respectively. Compounds **4h** and **4m** showed good antifungal activity with inhibition zone (5.5 ± 5.0 mm), while the rest of the compounds were inactive against *C. albicans*.[49]

The pyrimidine moiety is one of the most exposed structures found in the nucleic acid. The same year, Bandgar *et al*. also described the antimicrobial activity of a series of new carbazole substituted aminopyrimidines (**5a**–**p**) as drawn in Figure 3. using the disk diffusion method. Carbazole derivatives **5c**, **5g**, **5j** and **5o** showed upright activity in the range of inhibition zone (18.0 ± 8.00 mm) against all designated bacterial strains at a concentration of 1 mg/mL as compared to standard drug tetracycline. Notably carbazole derivative **5o** showed comparable activity with inhibition zone (18 ± 10 mm) as that of standard, against *B. subtilis*. *S. aureus* and *S. flexenari*. On the other hand, compounds **5b**, **5c**, **5m** and **5o** showed good activity with inhibition zone (15 ± 10 mm) against selected fungal strains at a concentration of 1 mg/mL as compared to standard drug nystatin. Compounds **5m** and **5o** showed comparable activity with inhibition zone (14 ± 10 and 15 ± 12mm) respectively as that of standard, against *C. albicans* and *A. niger*.[50]

In 2014, Sharma *et al*. evaluated the antimicrobial activity of a series of new carbazole derivatives (**6a**–**o**) (Figure 4.) with oxadiazole moiety is one of the most perceptible pharmacophore integrated at position 9 of carbazole nucleus. The antimicrobial activity was interpreted in terms of diameter (mm) of the zone of inhibition by disc diffusion method on nutrient agar medium against four bacterial and two fungal strains. Among the screened carbazoles, **6a, 6d,** and **6n** were found to be more potent with inhibition zone (16.2 ± 0.1, 24.2 ± 0.1 and 23.6 ± 0.1mm) against all tested bacterial and fungal strains at a concentration 50 µg/mL respectively.[51]

Synthesis of solvent–free carbazole chalcones (**7a**–**i**) and its benzofuran derivatives (**8a**–**i**) (Figure 6) described by Ashok *et al*. in 2014. The antimicrobial activity was examined against Gram positive *S. aureus* (ATCC 6538), *B. subtilis* (ATCC 6633) and Gram negative *E. coli* (ATCC 25922), *K. pneumoniae* (ATCC 13883) bacterial and three pathogenic fungi, *F. oxysporum*, *A. nigerzeae*, and *A. flavus* strains at 20 and 40 µg/mL concentrations. All the compounds (**7a**–**i** and **8a**–**i**) revealed moderate to strong antimicrobial activities at concentration of 20 µg/mL, and the results were comparable to the standard drugs ciprofloxacin and amphotericin-B.[52]

In 2014, Malani *et al*. explored the antimicrobial activities of carbazonyloxy *β*-hydroxy amine-based chalcones (**9a**–**l**) as shown in Figure 5. by the broth dilution method. New chalcones were examined with bacteria *E. coli* (MTCC 443), *P. aeruginosa* (MTCC 1688), *S. aureus* (MTCC 96), *S. pyogenus* (MTCC 442C), Fungi *C. albicans* (MTCC 227), *A. clavatus* (MTCC 1323) taking ampicilin, chloramphenicol, ciprofloxacin, gentamycin, norfloxacin and nystatin as standard drugs respectively. From this study, it was determined that compounds **9b** and **9j** proved at least as persuasive as the reference drug ampicillin in the

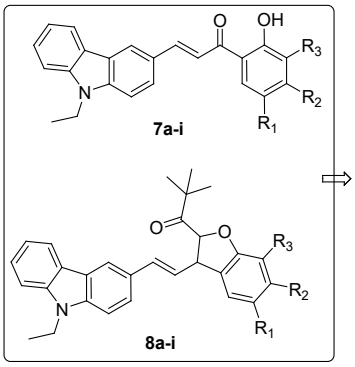


Comp.	R_1	R_2	R_3	Comp.	R_1	R_2	R_3
9a	H	H	OCH_3	**9g**	H	NO_2	OCH_3
9b	OH	H	H	**9h**	H	H	CH_3
9c	H	H	H	**9i**	H	H	H
9d	Cl	H	H	**9j**	H	H	OH
9e	H	H	Cl	**9k**	H	OCH_3	OCH_3
9f	H	NO_2	H	**9l**	H	H	NO_2

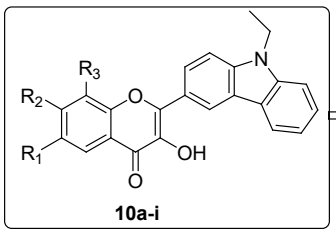
Figure 5. Structures of carbazonyloxy *β*-hydroxy amine-based chalcones (**9a–l**).[53]

case of *E*. *Coli*. The antifungal activity of compounds **9a**, **e**, **g** and **j** that they were comparable with the standard drug greseofulvin in the case of *C*. *albicans*, while compounds **4d** and **f** are more active compared with Greseofulvin in the case of *C*. *albicans*.[53]

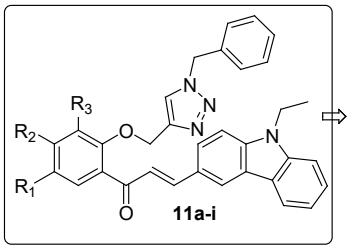
Antimicrobial activities of carbazole incorporated chromones (**10a–i**) as drawn in Figure 6. reported by Ashok and colleagues in 2015**.** The antimicrobial activity examined against four bacterial and two fungal strains using agar diffusion and poison plate technique express in terms



Comp.	R_1	R_2	R_3	Comp.	R_1	R_2	R_3
7a	H	H	H	**8a**	H	H	H
7b	F	H	H	**8b**	F	H	H
7c	Cl	H	H	**8c**	Cl	H	H
7d	Br	H	H	**8d**	Br	H	H
7e	CH_3	H	H	**8e**	CH_3	H	H
7f	Cl	CH_3	H	**8f**	Cl	CH_3	H
7g	Cl	H	H	**8g**	Cl	CH_3	H
7h	H	OCH_3	Cl	**8h**	H	OCH_3	H
7i	H	OC_2H_5	H	**8i**	H	OCH_3	H

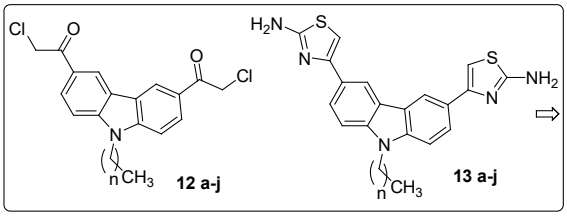


Comp.	R_1	R_2	R_3	Comp.	R_1	R_2	R_3
10a	H	H	H	**10f**	Cl	CH_3	H
10b	F	H	H	**10g**	Cl	H	Cl
10c	Cl	H	H	**10h**	H	OCH_3	H
10d	Br	H	H	**10i**	H	OC2H5	H
10e	CH_3	H	H				



Comp.	R_1	R_2	R_3	Comp.	R_1	R_2	R_3
11a	H	H	H	**11f**	Cl	CH_3	H
11b	F	H	H	**11g**	Cl	H	Cl
11c	Cl	H	H	**11h**	H	OCH_3	H
11d	Br	H	H	**11i**	H	OC2H5	H
11e	CH_3	H	H				

Figure 6. Structures of the carbazole derivatives reported by Ashok *et al* (2014, 2015, 2016).[52,54,55]



12, 13:

a, *n* = 1 b, *n* = 2 c, *n* = 3

d, *n* = 4 e, *n* = 5 f, *n* = 6

g, *n* = 7 h, *n* = 9 I, *n* = 15

J, *n* = 17

Figure 7. Structures of carbazole aminothiazoles (**13a–j**), their forerunner (**12a–j**).[56]

zone of inhibition diameter (mm). Amongst all, compounds **10a**, **10h** and **10i** showed maximal zones of inhibition in the range of (30–12 mm, 32–13 mm, 33–14 mm), respectively, against the tested bacterial and fungal strains. The study exposed the importance of 3-hydroxy chromenones with electron releasing groups, such as methoxy, ethoxy and unsubstituted compounds, showed the maximum activity.[54]

In 2016, Ashok et al. also reported the novel series of 1,2,3- triazolo- carbazole chalcones (**11a–i**) as depicted in Figure 6. and examined against a panel of bacterial and fungal microorganism by the agar diffusion and poison plate technique using ciprofloxacin, tetracycline and hymexazole standard drugs respectively. The zone of inhibition (in mm) was compared with standard drugs, antimicrobial data revealed that compounds **11e**, **11g**, and **11h** showed maximum zone of inhibition in the range of (23.5–15.8mm, 24.2–16.7mm and 24.5–14.2mm) respectively against Gram-positive and negative bacterial strains at the concentration of 20 µg/mL, as compared the standards tetracycline. Among all, compounds **11e**, **11f**, **11g**, **11h** and **11i** showed maximum activity against the tested fungal strains.[55]

In 2016, Addla *et al*. reported the preparation of new carbazole aminothiazoles and their precursor's (**13a–j** and **12a–j**) as DNA-targeting prospective antimicrobial agents (Figure 7.). All new compounds were examined against four Gram-positive bacteria, four Gram-negative bacteria and five fungi by the standard two folds serial dilution method using chloromycin, norfloxacin and fluconazole as standard drugs. The antimicrobial data revealed that, better antibacterial efficacies in preliminary active screening displayed by the carbazole aminothiazoles (**13a–j**) than their precursors (**12a–j**) which exposed that the 2-aminothiazole fragment was important in exerting antimicrobial activities. Noticeably heptyl derived carbazole aminothiazole **13f** could efficiently inhibit the growth of methicillin-resistant *S. aureus* (MRSA) with a MIC value of 4 µg/mL, which was greater to the reference drugs. Compounds **13h** and **13i** exhibited good activities against fluconazole-insensitive *A. flavus* with MIC value 128 µg/mL as compared to that fluconazole (MIC = 256 µg/mL). Study also exposed moderation in length of alkyl groups exhibited good activities against some tested bacteria. Specifically, *N*-pentyl carbazole aminothiazole **13d** displayed strong inhibition against *P. aeruginosa* with a MIC value of 2 µg/mL, which was 8-fold more active than reference drug chloromycin (MIC = 16 µg/mL). From this study, it was determined that prepared compounds with long hydrophobic alkyl chains such as pentyl and heptyl groups showed superior antimicrobial activities.[56]

In 2017, Clausen *et al*. reported four *N*-substituted carbazoles (**14a–d**) (Figure 8.) in order to study the inhibition activity of the fungal plasma membrane H^+-ATPase, which is necessary for fungal growth and survival**.** The H^+-ATPase inhibitory activity of the synthesized compounds conducted at a concentration of 20 µM. The compounds were characterized for H^+-ATPase inhibition and antifungal activity by means of an ATP hydrolysis assay and a fungal growth inhibition assay, respectively. The study has shown that compounds (**14a–d**) were identified as novel H^+-ATPase inhibitors and the ATP hydrolysis IC_{50} was determined together with antifungal activity against *S. cerevisiae* and *C. albicans.* Notably compound **14d** with two chloro substituents was recognized as the most potent antifungal compound, which displayed H^+-ATPase inhibitory activity. Also compound **14a** displayed the highest potency for H^+-ATPase inhibition, with IC_{50} values of 1.1 and 2 mM for *C. albicans* and *S. cerevisiae* H+-ATPase, respectively, as compared to the parent compounds.[57]

PLX01107 and **PLX01008** are xenomycins as drawn in Figure 9., new subclass of antimicrobial carbazole derivatives were designed and prepared by Zhanataev *et al.* in 2017. Both newly synthesized compounds showed strong antifungal activity *in vitro* and examine potential genotoxicity. The

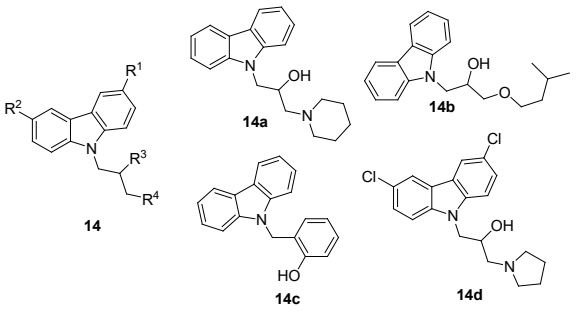


Figure 8. Carbazole scaffold (left) and structures of initial H^+-ATPase inhibitor hits.[57]

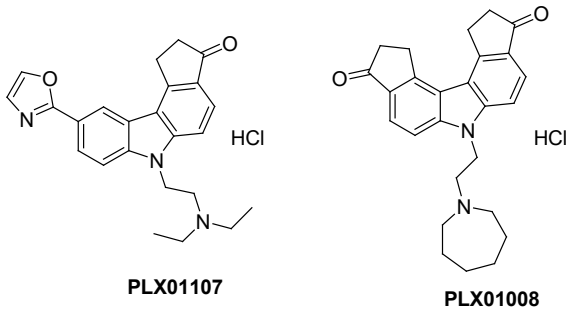


Figure 9. Structures of xenomycins **PLX01107** and **PLX01008**.[58]

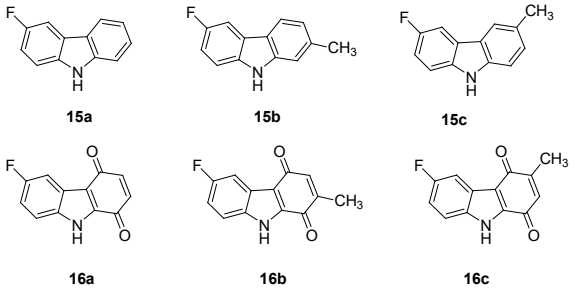


Figure 10. Structures of fluorocarabazole and its quionone derivatives (**15a–c** and **16a–c**).[59]

antimicrobial activity performed by bacterial reverse mutation assay (Ames test), *in vitro* cytokinesis-block micronucleus assay, and chromosome aberration test in mouse bone marrow cells, to investigate the possible genotoxicity of these compounds. The bacterial reverse mutation assay was performed with *S. typhimurium* TA98, TA100, TA1535, TA1537 and combination of *E. coli* WP2 uvrA and WP2 [pKM101] bacterial strains using the Ames MPF™ PENTA I kit and Aroclor 1254-induced rat liver fraction S9. The results obtained by Ames assays observed that, **PLX01107** did not show a progressive response for *S. typhimurium* or *E. coli* strains in the absence or presence of S9, but it displayed a cytotoxic response for strains TA98, TA100, and TA1535 without S9. In contrast, **PLX01008** was found to be mutagenic in *S. typhimurium* strains TA98 and TA1537, with or without S9 activation. The strain TA1535 indicated optimistic response only at 0.4 µg/mL in the absence of S9.[58]

In 2017, Chakraborty *et al*. reported the preparation and antimicrobial activities of fluorocarabazole and their respective quinone derivatives (**15a–c** and **16a–c**) as presented in Figure 10. using standard agar well diffusion method (NCCLS 2000).

Compound **15b** and its corresponding quinone compound **16b** showed the positive activity against *E. coli*, *B. subtilis* and Methicillin-resistant *S. aureus* with MIC value 25 µg/mL. Also compound **15c** and **16c** showed optimistic activity against *E. coli* and *S. aureus* with MIC value 50 µg/mL. The present study lead to the conclusion that properly substituted fluorocarbazole and fluorocarbazole quionones are highly promising scaffolds for further antimicrobial evaluation.[59]

Chromone is a natural molecule existing in the diet of human and animals and shows less toxicity to mammalian cells. In 2018, Kadnor *et al*. examined the antimicrobial activity of new carbazole substituted chromone derivatives (**17a–d, 18a–d** and **19a–d**) as drawn in Figure 11. using agar diffusion method ampicillin as standard drug. Carbazole derivatives **17b** and **17d** exhibited strong activities against Gram positive bacteria *S. lactis* and inhibit the growth of *Penicillium sp.* and *C. albicans* fungal strain as compare to the standard drug ampicillin. Notably, Compound **18a** gave nearly equipotent antibacterial broader bioactive spectrum against *P. putide B. subtilis* and *S. lactis* strains as compared to the standard drugs, while compounds **19b** and **19c** exhibited a broad spectrum against *S. lactis* bacterial strain. The results also suggested that electron withdrawing substituent chlorine and bromine on aromatic ring were more active against all test microbes than compounds with electron donating ones.[60] The same year, Kadnor and coworkers also investigated new 9-ethyl-9*H*-carbazole-3-carboxylic acid derivatives (**20a–e, 21a–e** and **22a–e**) as depicted in Figure 11. Carbazole acid derivatives were examined against four bacteria (*E. coli, P. putide, B. subtilis*, and *S. lactis*) and three fungi (*A. niger, Penicillium sp.* and *C. albicans*) by agar well diffusion method using ampicillin and greseofulvin as positive control. Compounds **20a**, **20b** and **20c** gave stronger antibacterial efficacies and broader bioactive spectrum

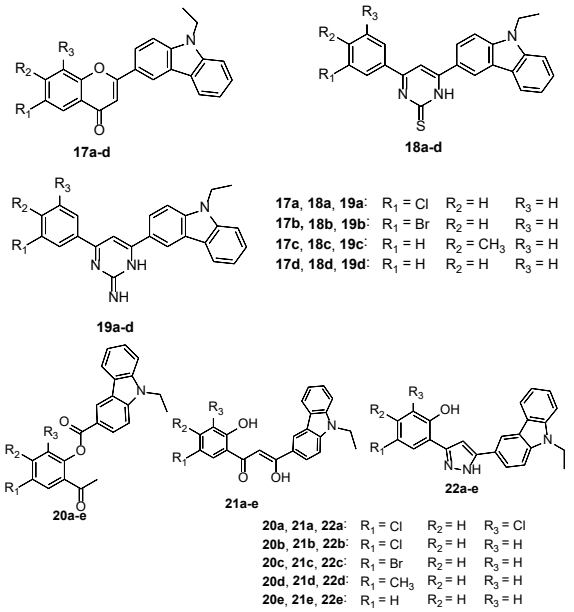


Figure 11. Structures of the carbazole derivatives reported by Kadnor *et al*.[60,61]

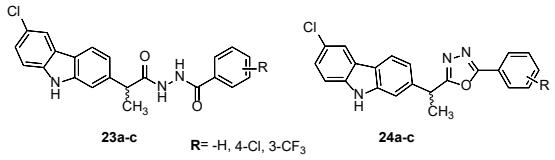
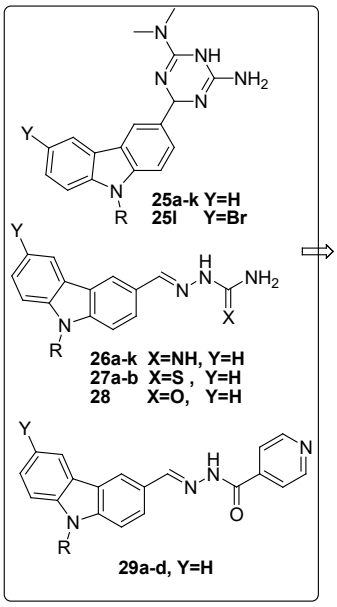


Figure 12. Structures of 6-chloro-9*H*-carbazol and 1,3,4-oxadiazol derivatives.[62]

against *S. lactis*, and *B. subtilis* with the MIC values in the range (30–40 μg/mL) and broad spectrum of antifungal activities (45–55 μg/mL) against *C. albicans* and *Penicillium sp.* as comparable to the standard drug ampicillin and griseofulvin (25 μg/mL) respectively. Compounds **21a**, **21b**, **21c, 21d** and **21e** displayed significant inhibition activities with a MIC ≥ 30 μg/mL against all tested fungal strains, while compounds **21d** and **21e** are passive for *C. albicans* fungal strain. Carbazole based pyrazoles **22a** and **22b** show remarkable antibacterial activity against tested pathogens, namely *S. lactis*, *B. subtilis* and *P. putide* compared to standard drug ampicillin at lowest concentration ranging from (35−55 μg/mL) with nearly equipotent of inhibition zone.[61]

In 2020, Bordei Telehoiu *et al*. reported the synthesis of 6-chloro-9*H*-carbazol and 1,3,4-oxadiazol scaffolds (**23a–c** and **24a–c**) as drawn in Figure 12. This novel adducts were examined against a panel of Gram-negative *E. coli* (ATCC 25922), *P. aeruginosa* (ATCC 27853) and Gram-positive *S. aureus* (ATCC 25923), *E. faecalis* (ATCC 29212) bacteria, as well as the fungal strain *C. albicans* (ATCC 90029) using the microdilution method in liquid Mueller Hinton medium at a concentrations in the range of 5–0.009 mg/mL. The best antibacterial was recorded for **23a** against *E. coli*, with MIC of 1.25 mg/mL and for **24c** against *C. albicans*, with MIC of 0.625 mg/mL.[62]

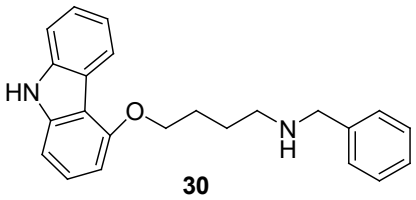
In 2021, Xue and coworkers synthesized a collection of 30 compounds with carbazole moiety containing an aminoguanidine, dihydrotriazine, thiosemicarbazide, semicarbazide or isonicotinic moiety (**25a–l**, **26a–k**, **27a–b**, **28**, and **29a–d**) as depicted in Figure 13. These thirty derivatives were screened against two Gram-positive strains *S. aureus* (4220), *S. mutans* (3289), one clinical isolate of multidrug-resistant Gram-positive bacterial strain *Methicillin-resistant S. aureus* (CCA*RM* 3167), one Gram-negative strain *E. coli* (1924) and one fungus *C. albicans* (7535). The MIC values were obtained using a 96-well microtiter plate and a serial dilution method, with positive controls gatifloxacin and moxifloxacin and DMSO as a negative control. All microorganisms showed susceptibility to most of the compounds with MICs in the range of 1–64 μg/ml. Compounds **25f**, **25l**, **26d** and **26e** exhibited strong antibacterial activity against Gram-positive strains and one Gram-negative strain with MIC values of 0.5 or 1 μg/ml. In addition, compound **25f** demonstrated a strong inhibitory activity (MIC of 0.5 μg/ml) against *E. coli* 1924, which was four-fold greater than the activities of moxifloxacin and gatifloxacin with (MIC of 2 μg/mL). The phenyl ring substituted compounds **25a–l** and **26a–k** exhibited significant effect on the potency of antimicrobial activities. The antibacterial activities were as follows order: phenyl group > 2,4-dichloro-substitutions > 4-CH_3> halogen substitutions>benzyl group > 4-CN > alkyl group. Moreover,



⇨ R=

25a	CH_3-	**26d**	4-$CH_3C_6H_4CH_2$-
25b	C_2H_5-	**26e**	2-$FC_6H_4CH_2$-
25c	$C_6H_5CH_2$-	**26f**	2,4-$Cl_2C_6H_3CH_2$-
25d	4-$CH_3C_6H_4CH_2$-	**26g**	2$ClC_6H_4CH_2$-
25e	2-$FC_6H_4CH_2$-	**26h**	3-$ClC_6H_4CH_2$-
25f	2,4-$Cl_2C_6H_3CH_2$-	**26i**	4-$ClC_6H_4CH_2$-
25g	2$ClC_6H_4CH_2$-	**26j**	4-$BrC_6H_4CH_2$-
25h	3-$ClC_6H_4CH_2$-	**26k**	4-$CNC_6H_4CH_2$-
25i	4-$ClC_6H_4CH_2$-	**27a**	CH_3-
25j	4-$BrC_6H_4CH_2$-	**27b**	C_2H_5-
25k	4-$CNC_6H_4CH_2$-	**28**	C_2H_5-
25l	C_6H_5-	**29a**	$C_6H_5CH_2$-
26a	CH_3-	**29b**	4-$CH_3C_6H_4CH_2$-
26b	C_2H_5-	**29c**	2-$FC_6H_4CH_2$-
26c	$C_6H_5CH_2$-	**29d**	2,4-$Cl_2C_6H_3CH_2$-

Figure 13. Structures of the carbazole derivatives reported by Xue and coworkers.[63]



30

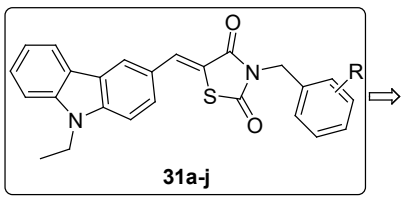
Figure 14. Structure of (4-(4-(benzylamino)butoxy)-9*H*-carbazole) derivative **30**.[64]

bromo- and chloro-substitutions on the phenyl ring in compounds **25a–l** were observed to improve their antifungal activity against *C. albicans* 7535.[63]

In 2021, Zawadzka and collegues reported (4-(4-(benzylamino)butoxy)-9*H*-carbazole) derivative **30** (Figure 14.) was prepared in two substitution steps from commercially available 4-hydroxycarbazole following standard procedures. This new adduct was studied against a Gram-positive *S. aureus* (ATCC 29213), *S. aureus* (ATCC 25923), *S. aureus* (ATCC 6358), *S. aureus* (ATCC 700699), *S. aureus* (ATCC 43300), *S. epidermidis* (ATCC 12228), *S. pyogenes* (ATCC 19615) and Gram-negative *E. coli* (ATCC 25922), *P. hauseri* (ATCC 13315), *P. aeruginosa* (ATCC 15442) bacteria, as well as fungi *C. albicans* (ATCC 10231), *A. flavus* (ATCC 9643).

Antimicrobial study exposed, that fungi and Gram-negative bacteria were more resistant than Gram-positive strains, although a positive control is needed to fully assess these bacterial strains.[64]

Lastly, Kamala and coworkers reported the series of novel carbazole thiazolidinedione hybrid derivatives (**31a–j)** as drawn in Figure 15. This adduct were examined against gram-positive bacterial strains (*S. aureus*) and gram-negative bacterial strains (*P. aeruginosa*, *E. coli*, *K. pneumonia*) at concentration of 100 µg/mL. The results were compared with the activity of the standard antibiotic ciproflaxacin and expressed as zone of inhibition in millimeter. Compounds **31c** and **31h** with nitro at second and bromo at fourth position on phenyl ring respectively have shown good antibacterial activity. On the other hand unsubstituted **31a**, chloro substituted **31d**, **31e**, **31f**, **31i**, fluoro substituted **31g** and cyano substituted **31j** compound have shown modest zone of inhibition.[65]



31a-j

31a	R = H	**31f**	R = 4-Cl
31b	R = 4-NO_2	**31g**	R = 4-F
31c	R = 2-NO_2	**31h**	R = 2-Br
31d	R = 2-Cl	**31i**	R = 2,4-Cl
31e	R = 3-Cl	**31j**	R = 4-CN

Figure 15. Structures of carbazole-thiazolidinedione hybrid derivatives (**31a–j**).[65]

CONCLUSIONS

This review summarizes acknowledged reports about various carbazole derivatives and their antimicrobial activities that are attractive structural patterns in synthetic organic chemistry due to their tunable electronic and steric properties. As summarized above, the existence of carbazole moieties has confirmed operative in improving the antimicrobial activity of various compounds. Several carbazole derivatives displayed strong *in vitro* inhibitory activity against bacteria and fungi with analogous or even greater activity when compared to the standard drugs. Consequently, this review may therefore propose an important resource to assist scientists in designing of new, convincing, and safe carbazole derivatives against microbial diseases in the near future**.**

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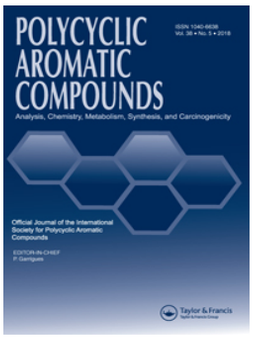

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Novel Pumice Supported Perchloric Acid Promoted Protocol for the Synthesis of Tetrahydrobenzo[*b*]pyran via Multi-component Approach

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ABSTRACT

A novel heterogeneous pumice supported perchloric acid catalyzed synthesis of tetrahydrobenzo[*b*]pyran has developed via multi-component condensation of aromatic aldehydes, dimedone and malononitrile. The catalyst was characterized by IR, XRD, EDS, SEM, and TGA techniques which confirmed the formation novel pumice supported perchloric acid. The present protocol proved to have numerous advantages like one-pot reaction, good yield, short reaction time, inexpensive catalyst, recyclability and reusability of the catalyst, simple experimental and work up procedure, and purification of targeted molecules without column chromatography.

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KEYWORDS
Pumice supported perchloric acid; tetrahydrobenzo[*b*]pyran; multi-component reaction; dimedone; malanonitrile

Introduction

In the last two decades, volcanic pumice and pumice based materials have been employed in divergent organic transformations such as reduction reaction, oxidation reaction, photo catalytic degradation, multi-component condensation reaction and also water treatment process. These varied reactions are achieved because large silica content of the pumice which was converted into active catalytic material. The appreciable advantages of pumice supported catalytic materials are heterogeneous nature, good surface area, excellent catalytic activity, thermal stability, high porosity, high absorption capacity, recyclability and reusability, etc.[1–9]

Multi-component reaction (MCR) approach has gained excellent impact in the discovery of heterocyclic compounds due to the synthetic efficiency and economy. The MCR strategy is a one step synthetic operation with incredibly well-designed and quick approach to discover highly functionalized and complex biologically active molecules. It has also advantages like high flexibility, high atom economy and high selectivity.[10–12] The synthesis of tetrahydrobenzo[*b*]pyrans is also an important illustration of the multi-component reaction.

The tetrahydrobenzo[*b*]pyran derivatives are extremely significant to the organic chemists because of their prominent biological and pharmacological activities. They are fascinating polyfunctionalized compounds which possess a wide variety of biological activities like anti-allergic, antibacterial, anti-coagulant, anti-tumor, calcium channel antagonists and diuretic etc. Along with biological activities, some derivatives of tetrahydrobenzo[*b*]pyran have been employed as photoactive materials and agrochemicals. They are also used in cosmetics and pigments.[13–18] The some illustration of biologically active tetrahydrobenzo[*b*]pyran derivatives shown in Figure 1.

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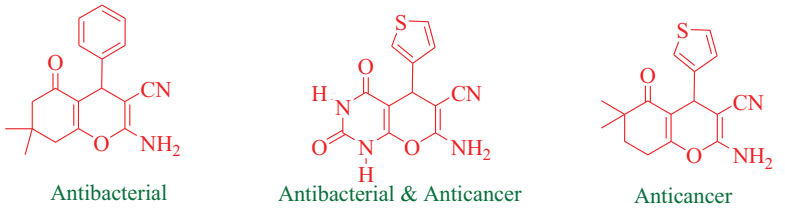


Figure 1. Some examples of biologically active tetrahydrobenzo[*b*]pyran derivatives.

In a vision of the enormous scope of tetrahydrobenzo[*b*]pyrans there is increased attention in developing new routes for their synthesis. The synthetic protocols include numerous catalyst such as tetraethylammonium perchlorate,[19] CTMAB-bentonite,[20] nano-titania sulfuric acid,[21] ultrasound,[22] MNPs–$PhSO_3H$,[23] molecular sieve-supported zinc catalyst,[24] silica nanoparticles,[25] oxyammonium-based ionic liquid,[26] $MeSO_3H$,[27] PEG-SO_3H,[28] WEMFSA,[29] tungstic acid functionalized mesoporous SBA-15,[30] amine-functionalized SiO_2@Fe_3O_4 nanoparticles,[31] choline chloride-oxalic acid,[32] L-proline,[33] chitosan,[34] xanthum gum supported Fe_3O_4,[35] phosphotungstic acid supported on SiO_2@$NHPhNH_2$ functionalized nanoparticles of $MnFe_2O_4$,[36] poly(Ethyleneoxide)-based magnetic nanocomposite,[37] magnetic aluminosilicate nanoclay,[38] amine-functionalized silica-supported magnetic nanoparticles,[39] etc.

In continuation of our work in developing new methodologies for the synthesis of active compounds[40] herein, we have reported an efficient and sustainable protocol for the synthesis of tetrahydrobenzo[*b*]pyrans via multi-component reaction of aromatic aldehyde, dimedone and malononitrile in the presence of novel pumice supported perchloric acid. The present work has a number of advantages in comparison with the literature reported protocols, such as good yields, high atom economy, smooth reaction conditions, simple work-up procedure and purification of targeted molecule without column chromatography.

Experimental procedures

General

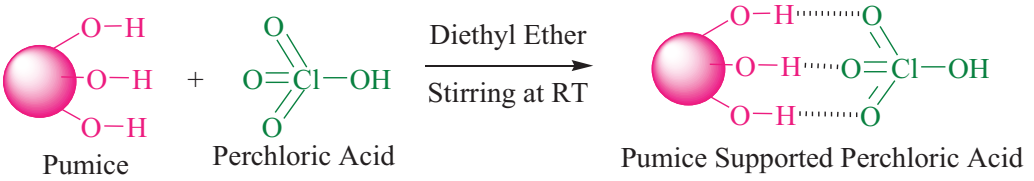
The progress of the reaction was monitored by thin-layer chromatography (TLC) by using silica gel coated aluminum plates and plates are visualized with UV light. Melting points were taken in an open capillary and are uncorrected. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were recorded with the BRUCKER AVANCE NEO 500 MHz in $CDCl_3$ using TMS as an internal standard. IR spectra were taken on PerkinElmer FTIR Spectrometer. The pumice supported perchloric acid catalyst was prepared in the laboratory. Mass spectra were recorded on a MALDI SYNAPT XS HD Mass spectrometer.

General procedure for the preparation of pumice supported perchloric acid

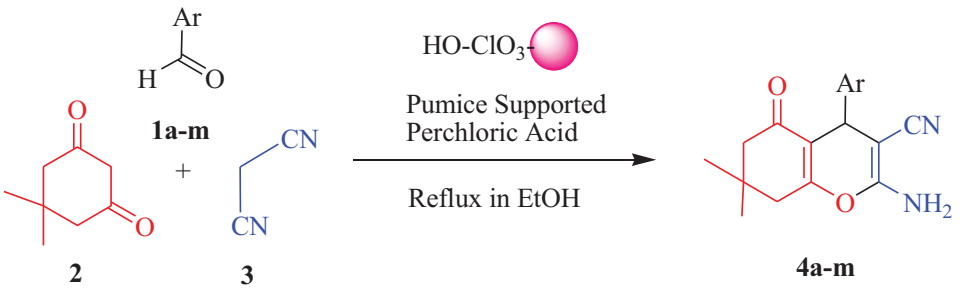
Perchloric acid (3.0 gm) was added to the suspension of pumice (45 gm) in diethyl ether (60 mL) with constant stirring for 2 h. The mixture was concentrated and the residue was washed with acetone to remove unreacted perchloric acid. The resultant residue was dried under vacuum at 80 °C for 6 h to afford free Pumice Supported Perchloric acid (Pumice@$HClO_4$) (Scheme 1).

General procedure for the synthesis of tetrahydrobenzo[b]pyran derivatives (4a–m)

In a 100 mL round bottom flask, the mixture of substituted benzaldehyde (2 mmol), dimedone (2 mmol), malanonitrile (2 mmol) and pumice supported perchloric acid (100 mg) was taken in 10 mL of ethanol (Scheme 2). The resulting reaction mixture was refluxed for appropriate time.



Scheme 1. Preparation of pumice supported perchloric acid.



Scheme 2. Synthesis of tetrahydrobenzo[*b*]pyran derivatives (**4a–m**).

The progress of the reaction was confirmed by TLC. To separate out the catalyst pumice supported perchloric acid, the content was filtered at hot condition. After cooling the filtrate, the solid was separate out which was dried and purified by recrystalization using ethanol.

Result and discussion

The pumice supported perchloric acid was prepared from volcanic pumice and perchloric acid by simple agitation in diethyl ether which has characterized by various analytical techniques such as FTIR, XRD, EDAX, SEM, and TGA. The FTIR spectra of pumice supported perchloric acid showed that, the significant absorption band at 3413.95 cm^{-1} corresponding to the acidic proton in Pumice@$HClO_4$. In addition to this, the band appeared at 1637.53 cm^{-1} is due to the (Cl = O) bond and the bands at 1147.39 and 1090.09 cm^{-1} are related to Si–O–Si bonds (Figure 2(a)). These bands are not observed in FTIR of plane pumice (Figure 2(c)) except the band at 1036.86 cm^{-1}due to Si–O–Si bonds. This clearly indicates that, the perchloric acid was supported on pumice. Also the FTIR of recycled pumice@$HClO_4$ (Figure 2(b)) did not show any noteworthy deviation from pure pumice@$HClO_4$.

The EDAX analysis showed the composition of Pumice supported perchloric acid. This indicates that the synthesized catalyst composed of Si, O, Al, K, and Cl elements. The higher percentage of chlorine and oxygen proved that the perchloric acid was supported on Pumice (Figure 3(a)). Also the EDAX of recycled pumice@$HClO_4$ (Figure 3(b)) did not show any noteworthy composition of elements.

The XRD pattern of the catalyst was exhibited the broad characteristic peak between diffraction angle $2\theta = 15\text{-}30$ which demonstrated the amorphous nature of the Pumice supported perchloric acid (Figure 4(a)). Also the XRD of recycled pumice@$HClO_4$ (Figure 4(b)) did not show any significant change.

The SEM image showed that, pure as well as recycled pumice supported perchloric acid has no particular size and morphology (Figure 5(a,b)).

To investigate the thermal stability of the newly prepared pumice supported perchloric acid and pumice, the thermogravimetric analysis (TGA) was performed in the temperature range from 30 to 650 °C as shown in Figure 6(a,b). The literature survey revealed that, the –OH groups

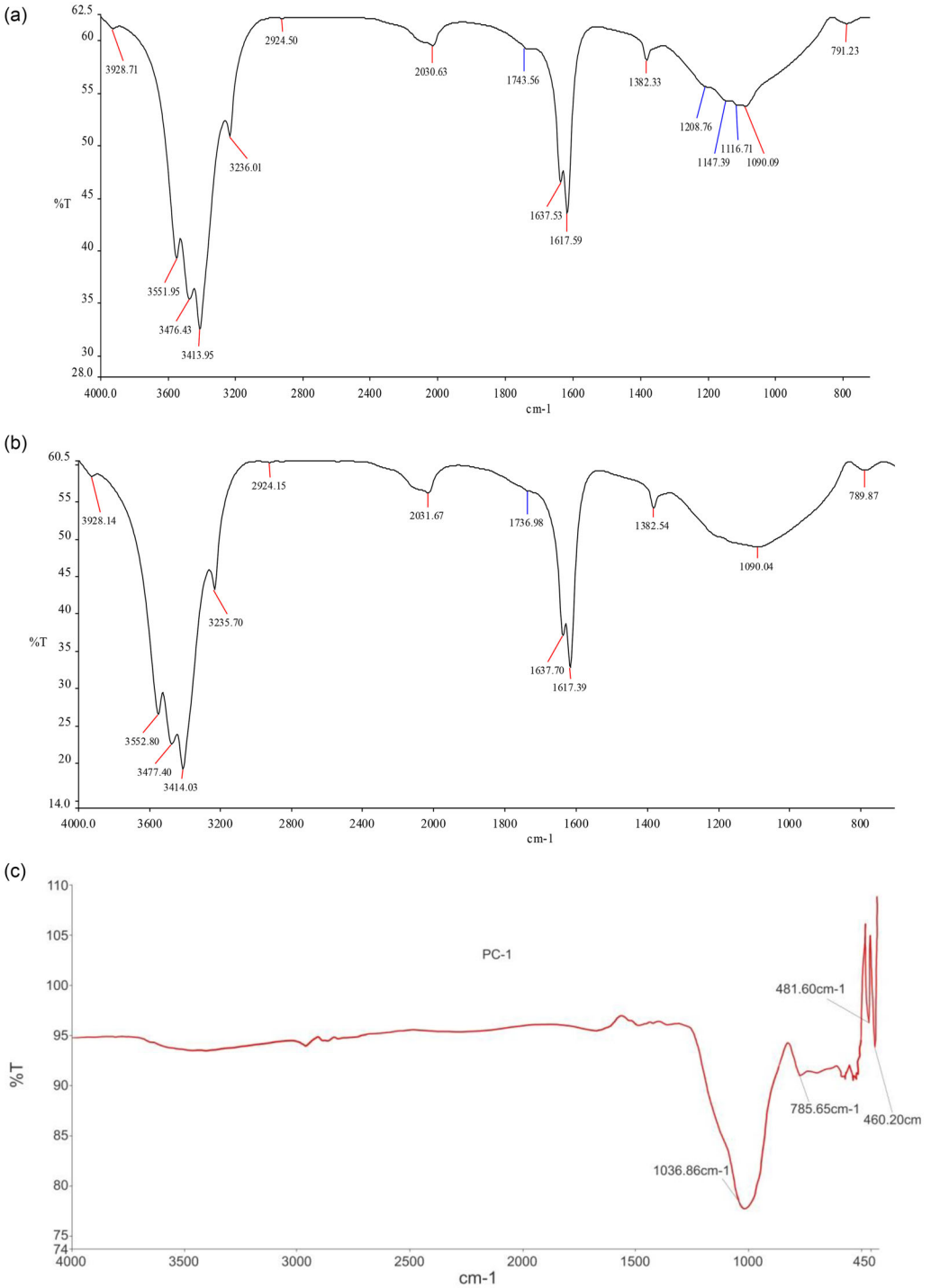


Figure 2. (a) FTIR of pumice supported perchloric acid (Pumice@$HClO_4$). (b) FTIR of recycled pumice supported perchloric acid (Pumice@$HClO_4$). (c) FTIR of pure pumice.

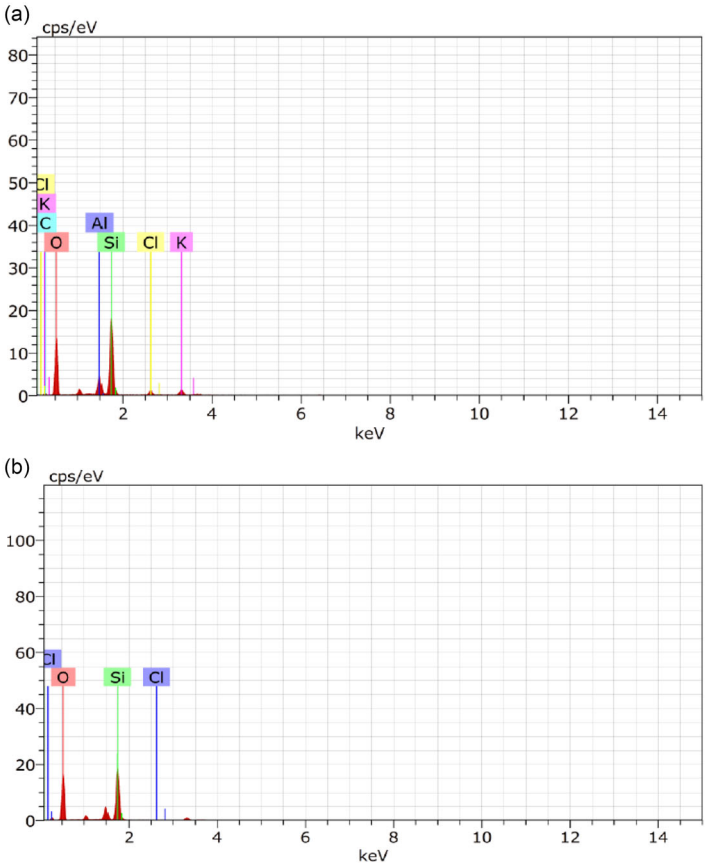


Figure 3. (a) EDAX of pumice supported perchloric acid (Pumice@$HClO_4$). (b) EDAX of recycled pumice supported perchloric acid (Pumice@$HClO_4$).

present in the catalytic material leave the structure by dehydration reaction at high temperature. The TGA of pumice supported perchloric acid (Figure 6(a)) and pumice (Figure 6(b)) showed that, 2.1% weight lost below 140 °C due to the removal of –OH groups in the form of water molecule present in the catalyst.

Study of acidic nature of pumice Supported perchloric Acid

The acidic nature of the catalyst was determined potentiometrically by following the standard method.[4] Initially the 0.1 g of pumice supported perchloric acid catalyst was taken in a titration flask containing 10 ml distilled water and the resultant mixture was titrated against the 0.1 N NaOH solution. The reading data of titration was used for plotting the graph of ΔE/ΔV against the volume of 0.1 N NaOH. From the graph, the acidic nature of catalyst was found to be 0.9 mmol/g at the equivalence point (Figure 7).

Optimization of the Reaction condition

The multi-component condensation reaction of 4-methyl benzaldehyde, dimedone and malononitrile was selected as pilot reaction (Scheme 3) to choose the optimize conditions for the synthesis of tetrahydrobenzo[*b*]pyran. Initially, the reaction was carried out under varying conditions such

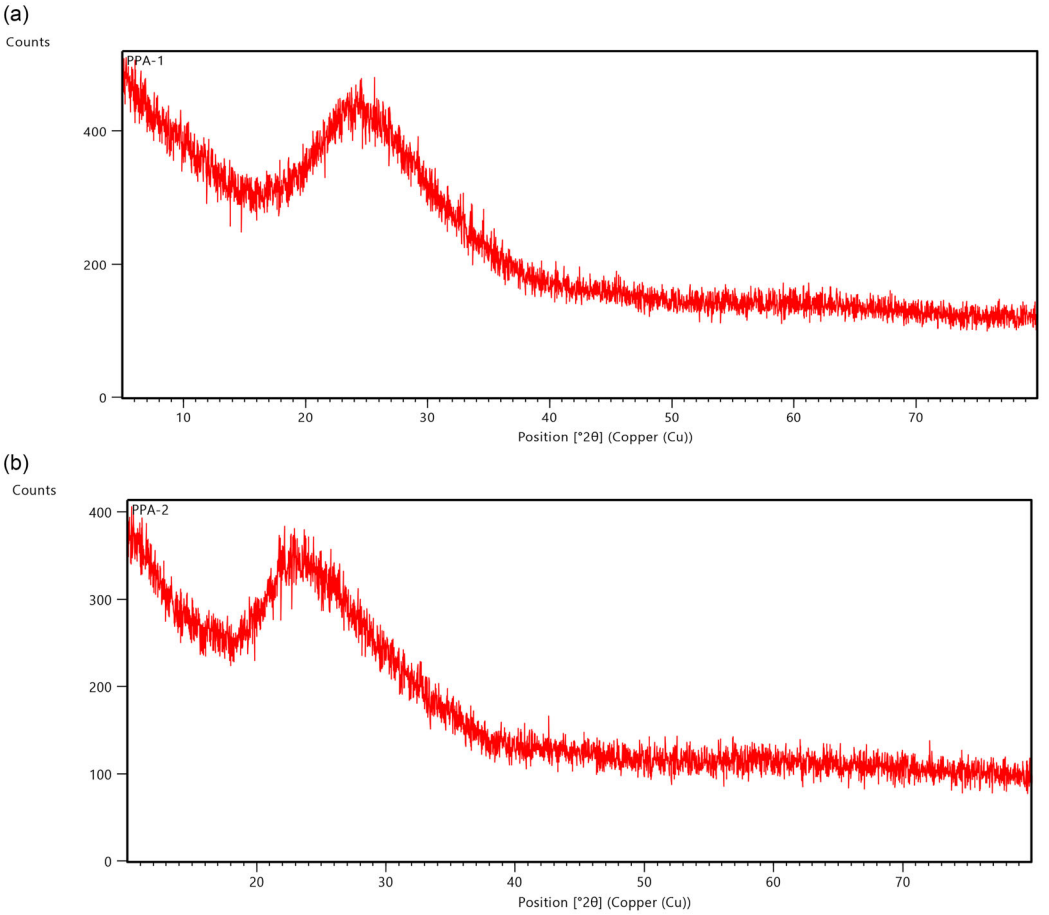


Figure 4. (a) XRD of pumice supported perchloric acid (Pumice@$HClO_4$). (b) XRD of recycled pumice supported perchloric acid (Pumice@$HClO_4$).

as the amount of catalyst, time, temperature and solvent medium (Table 1). The good result was obtained for pilot reaction with 100 mg of pumice supported perchloric acid catalyst (Table 2) in the presence of ethanol under reflux condition.

After the investigation of the exact optimized condition, it was employed for the synthesis of different tetrahydrobenzo[*b*]pyran derivatives by one-pot three component condensation of diverse aromatic aldehydes with malononitrile and dimedone. The best result was obtained for aldehydes containing electron donating as well as electron withdrawing groups in high yields and short period of time without appearing side product (Table 3).

Spectral data selected compounds

4a: 2-amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-phenyl-4H-chromene-3-carbonitrile

White color; m.p. 222–224 °C; FTIR (cm^{-1}): 3396.57 (N–H), 2198.93 (CN), 1680.23 (C = O), 1660.44 (C = C), 1603.25 (C = C), 1451.14 (C = C), 1369.68 (C–O), 1213.49 (C–N); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.04 (s, 3H, $-CH_3$), 1.11 (s, 3H, $-CH_3$), 2.18–2.25 (m, 2H, $-CH_2-$), 2.45 (s, 2H, $-CH_2-$), 4.40 (s, 1H, –CH–), 4.57 (s, 2H, $-NH_2$), 7.19–7.30 (m, 5H, Ar–H) ; MS (ESI): m/z = 295.1469 [M + H].

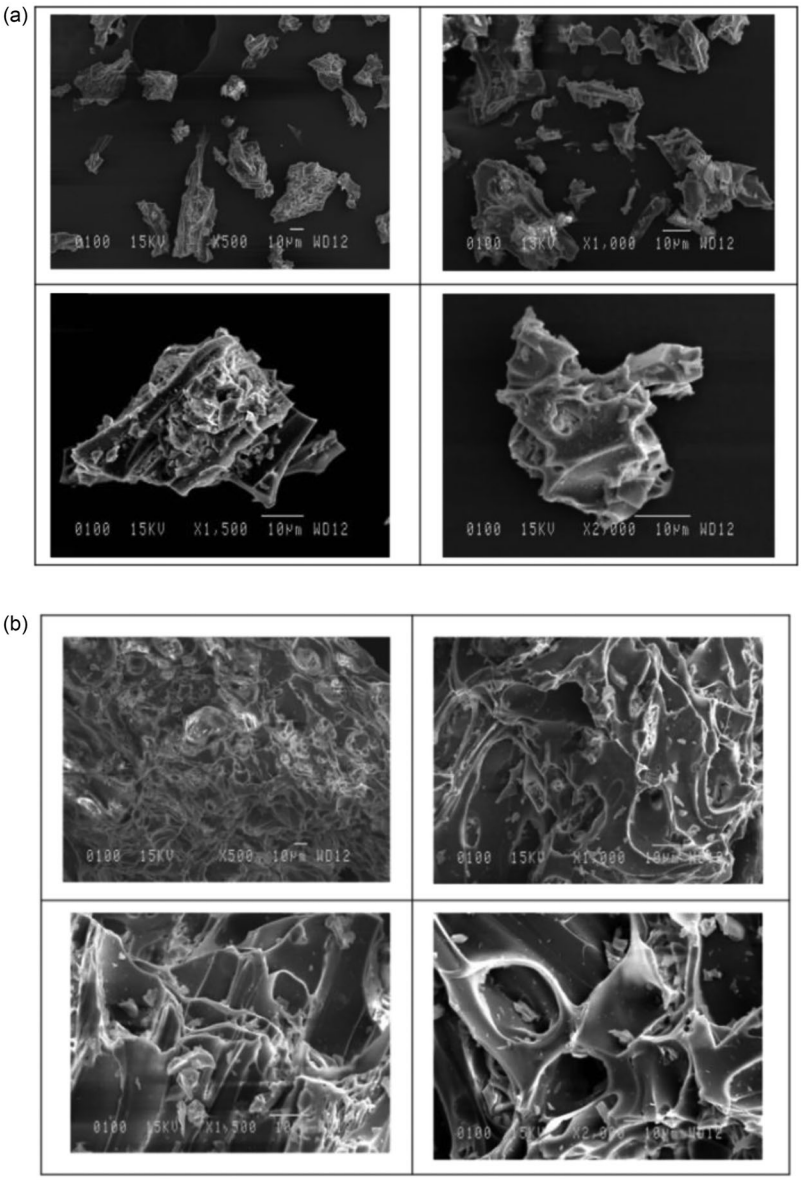


Figure 5. (a) SEM of pumice supported perchloric acid (Pumice@$HClO_4$). (b) SEM of recycled pumice supported perchloric acid (Pumice@$HClO_4$).

4b: 2-amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4-p-tolyl-4H-chromene-3-carbonitrile

White color; m.p. 214–216 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 1.04 (s, 3H, $-CH_3$), 1.11 (s, 3H, $-CH_3$), 2.17 (m, 2H, $-CH_2-$), 2.21 (s, 2H, $-CH_3$), 2.44 (s, 2H, $-CH_2-$), 4.36 (s, 1H, –CH–), 4.51 (s, 2H, $-NH_2$), 7.08 (m, 4H, Ar–H).

4c: 2-amino-4-(4-ethylphenyl)-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-4H-chromene-3-carbonitrile

White color; m.p. 222–224 °C; FTIR (cm^{-1}): 3410.74 (N–H), 2188.62 (CN), 1682.53 (C = O), 1652.20 (C = C), 1618.21 (C = C), 1509.02 (C = C), 1369.47 (C–O), 1214.05 (C–N); ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.99 (s, 3H, $-CH_3$), 1.10 (s, 3H, $-CH_3$), 1.26 (t, 3H, $-CH_3$), 2.19 (q, 2H,

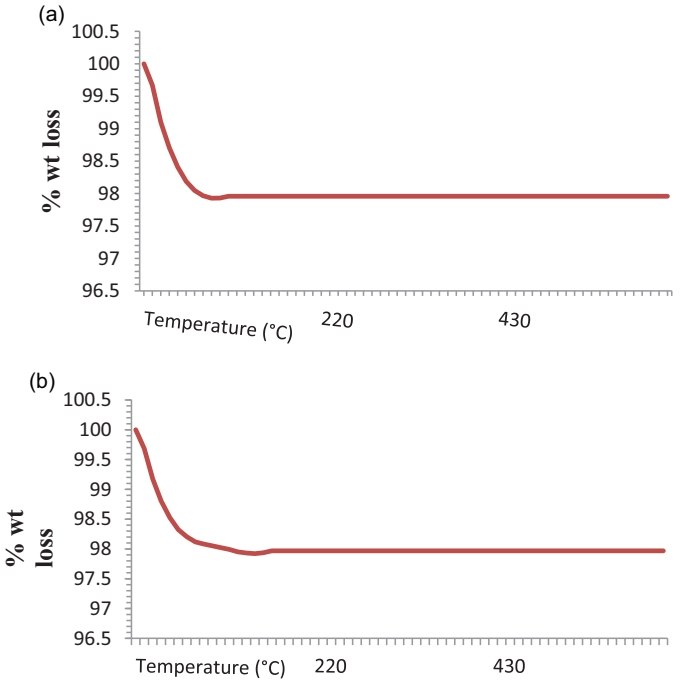


Figure 6. (a) TGA of pumice supported perchloric acid (Pumice@$HClO_4$). (b) TGA of pure pumice.

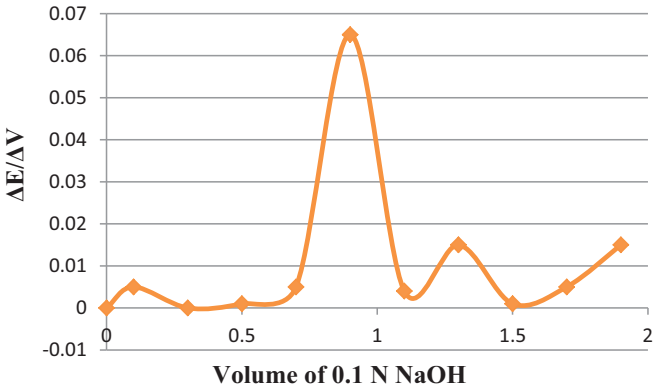
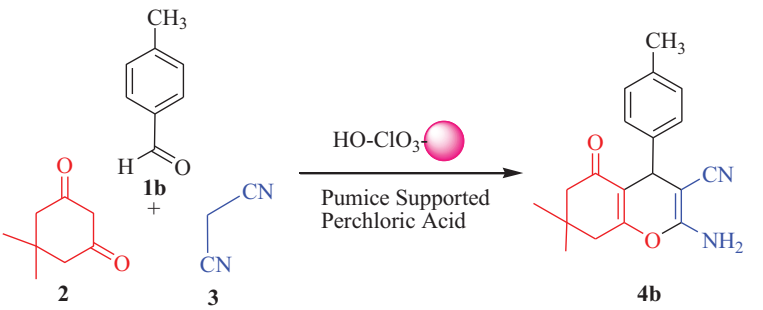


Figure 7. Study of acidic nature of pumice@$HClO_4$ by potentiometric titration.



Scheme 3. Pilot reaction for the synthesis of tetrahydrobenzo[*b*]pyran (**4b**).

Table 1. Optimization of reaction conditions for the synthesis of tetrahydrobenzo[*b*]pyran (**4b**).

Entry	Solvent system	Temperature	Time (min)	Yield (%)
1	Grinding	RT	60	NR
2	H_2O	RT	120	NR
3	EtOH	RT	120	NR
4	EtOH + H_2O (50%)	RT	120	NR
5	H_2O	Reflux	120	Trace
6	EtOH	Reflux	60	88
7	EtOH + H_2O (50%)	Reflux	60	40

Reaction condition: 4-methyl benzaldehyde (2 mmol), malononitrile (2 mmol), and dimedone (2 mmol), pumice supported perchloric acid catalyst (100 mg).

Table 2. Optimization of amount of catalyst for the synthesis of tetrahydrobenzo[*b*]pyran.

Entry	Amount of catalyst (mg)	Time (min)	Yield (%)
1	Absence of catalyst	60	NR
2	25	60	Trace
3	50	60	55
4	75	60	80
5	100	60	88
6	125	60	88

–CH_2–), 2.44 (m, 2H, –CH_2–), 2.59 (m, 2H, –CH_2–), 4.37 (s, 1H, –CH–), 4.56 (s, 2H, –NH_2), 7.09–7.14 (m, 4H, Ar–H) ; ^{13}C NMR ($CDCl_3$, 500 MHz) δ: 15.33, 27.76, 28.64, 28.87, 32.21, 35.12, 40.70, 50.70, 63.70, 114.18, 118.81, 127.41, 128.09, 140.48, 142.93, 157.47, 161.47, 195.97; MS (ESI): m/z = 323.1790 [M + H].

4d: 2-amino-5,6,7,8-tetrahydro-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-4H-chromene-3-carbonitrile

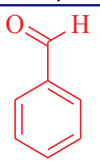
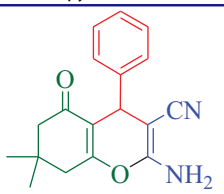
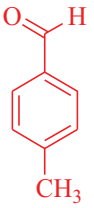
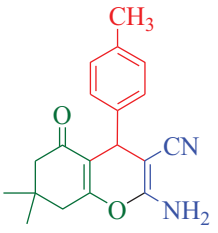
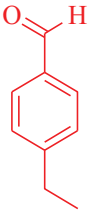
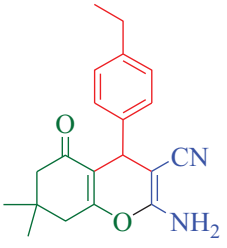
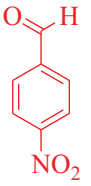
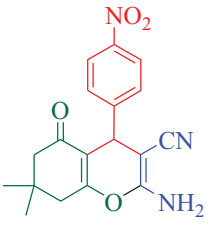
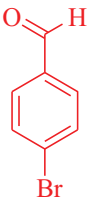
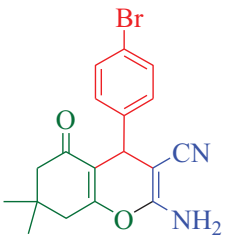
White color; m.p. 178–180 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 0.97 (s, 3H, –CH_3), 1.05 (s, 3H, –CH_3), 2.11–2.28 (m, 2H, –CH_2–), 2.54 (s, 2H, –CH_2–), 4.38 (s, 1H, –CH–), 7.17 (s, 2H, –NH_2), 7.45 (d, 2H, J = 8.7, Ar–H) , 8.17 (d, 2H, J = 8.7, Ar–H) ; ^{13}C NMR ($CDCl_3$, 500 MHz) δ: 26.83, 28.14, 31.69, 35.55, 49.75, 56.88, 111.63, 119.18, 123.53, 128.49, 146.15, 152.15, 158.47, 162.96, 195.54.

Recyclability and reusability of pumice supported perchloric acid

The recovery and reusability of the pumice supported perchloric acid catalyst make the protocol most valuable, unique and beneficial. After the completion of the reaction, the catalyst was separated from the reaction media at hot condition. It was washed with hot ethanol followed by chloroform and was dried at 80 °C temperature. The recovered catalyst was characterized by FTIR, EDAX, XRD and SEM as shown in Figures 2(b) to 5(b). The reusability of the catalyst was studied on the pilot reaction. The catalyst has been recycled and reused three times with 88, 87 and 84% of product yields, respectively.

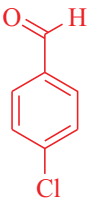
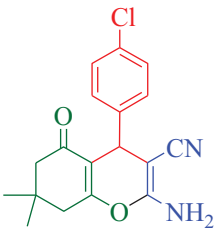
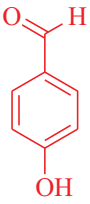
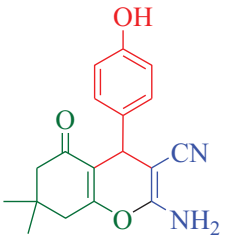
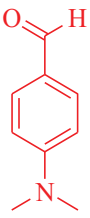
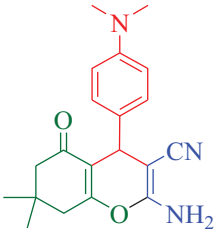
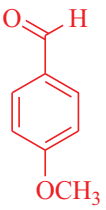
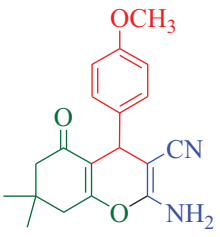
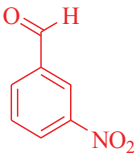
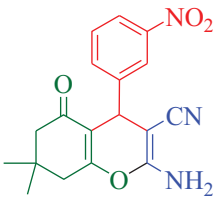
The comparison of the efficiency of pumice supported perchloric acid catalyst with the various reported protocols are mentioned in Table 4. From this investigation, it was found that the pumice supported perchloric acid catalyst showed a noteworthy activity for the synthesis tetrahydrobenzo[*b*]pyran derivatives. Also a current protocol has many advantages in comparison with

Table 3. Synthesis of tetrahydrobenzo[*b*]pyran derivatives (**4a–m**).

Entry	Aldehyde	Benzopyran derivative	Time (min.)	Yield (%)	M.P.(°C) Observed	M.P.(°C) Reported (ref.)
1		 **4a**	50	80	222–224	224[15]
2		 **4b**	60	88	214–216	213[15]
3		 **4c**	45	82	222–224	155–158[18]
4		 **4d**	50	84	178–180	179[15]
5		 **4e**	50	90	202–204	200–203[16]

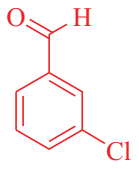
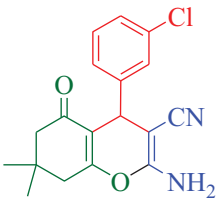
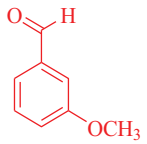
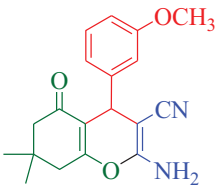
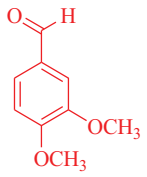
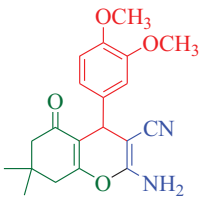
(*continued*)

Table 3. Continued.

Entry	Aldehyde	Benzopyran derivative	Time (min.)	Yield (%)	M.P.(°C) Observed	M.P.(°C) Reported (ref.)
6		 **4f**	45	90	198–200	206[15]
7		 **4g**	65	77	220–222	205[15]
8		 **4h**	60	82	188–190	198–200[15]
9		 **4i**	60	80	202–204	201[15]
10		 **4j**	60	76	212–214	210[15]

(*continued*)

Table 3. Continued.

Entry	Aldehyde	Benzopyran derivative	Time (min.)	Yield (%)	M.P.(°C) Observed	M.P.(°C) Reported (ref.)
11		 **4k**	40	82	202–204	226–228[16]
12		 **4l**	50	84	210–212	185–187[16]
13		 **4m**	65	78	164–166	132–141[18]

Reaction condition: Aldehyde (2 mmol), dimedone (2 mmol), and malanonitrile (2 mmol) were refluxed in 10 ml ethanol in the presence of pumice supported perchloric acid (100 mg)

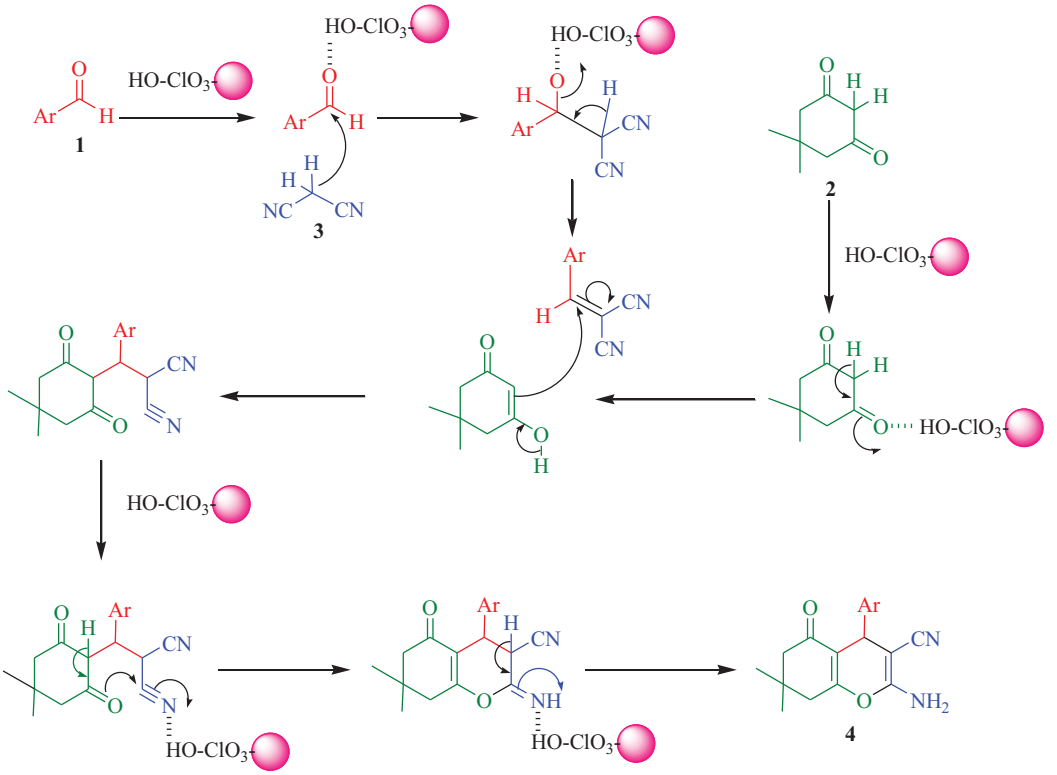
Table 4. Comparison of the efficiency of pumice@$HClO_4$ for the synthesis of tetrahydro-benzo[*b*]pyran derivative with other protocols.

Entry	Catalyst used	Reaction condition	Time (min)	Yield (%)	Ref. no.
1	CTMAB-bentonite	H_2O:EtOH (1:1) / RT	05–10	80–99	[20]
2	Nano-titania sulfuric acid	EtOH / US / 40 °C	10–30	85–97	[21]
3	MNPs–$PhSO_3H$	H_2O:EtOH (1:1) / 100 °C	10–60	65–95	[23]
4	Molecular sieve-supported Zinc	EtOH/reflux	240	85–98	[24]
5	SiO_2 nano-particles	EtOH/RT	25–30	86–98	[25]
6	Xanthum gum supported Fe_3O_4	EtOH/RT	05–20	84–96	[35]
7	Phosphotungstic acid supported on SiO_2@$NHPhNH_2$	SF/ 80 °C	25–30	85–94	[36]
8	Fe_3O_4@PEO-SO_3H	EtOH/RT	25–40	85–95	[37]
9	Magnetic aluminosilicate nanoclay	SF/ 40 °C	20–30	93–96	[38]
10	Fe_3O_4@SiO_2–NH_2	SF/ 60 °C	80–120	78–93	[39]
11	Pumice @$HClO_4$	EtOH/reflux	45–65	78–90	Present work

reported methods such as cheap and readily available volcanic material, smooth reaction condition and purification of targeted molecule without column chromatography.

Plausible mechanism

The plausible mechanism for the synthesis of tetrahydrobenzo[*b*]pyran derivatives using pumice supported perchloric acid were shown in Scheme 4.



Scheme 4. Plausible mechanism of Pumice@$HClO_4$ catalyzed synthesis of benzopyran.

Conclusion

In conclusion, we have investigated a novel, highly efficient protocol for the synthesis of tetrahydrobenzo[*b*]pyran in the presence of heterogeneous catalyst pumice supported perchloric acid via multi-component condensation of aromatic aldehydes, dimedone and malononitrile under reflux condition. The catalyst was characterized by IR, XRD, EDS, SEM, and TGA techniques which showed the formation novel pumice supported perchloric acid. The present protocol proved to have numerous advantages like one-pot reaction, quantitative yield of the targeted molecule, short reaction time, mild conditions inexpensive catalyst, recyclability and reusability of the catalyst, smooth experimental condition, simple work up procedure and purification of targeted molecule without column chromatography.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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TEA POWDER WASTE: AS A GREEN CATALYST FOR THE SYNTHESIS OF 1-AMIDOALKYL 2-NAPHTHOLS

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Abstract: Tea powder waste is used an efficient natural green catalyst for the one pot three component synthesis of amidoalkyl naphthol using aromatic aldehyde, 2-naphthol and acetamide at reflux condition. The catalyst could be recovered and reused at least five times without appreciable decreasing the catalytic activity. The nontoxic solvent, excellent yield, short reaction time, green synthesis and natural eco-friendly catalyst are the advantages of present protocol.

Keywords: Amidoalkyl naphthol, green synthesis, natural catalyst.

Introduction

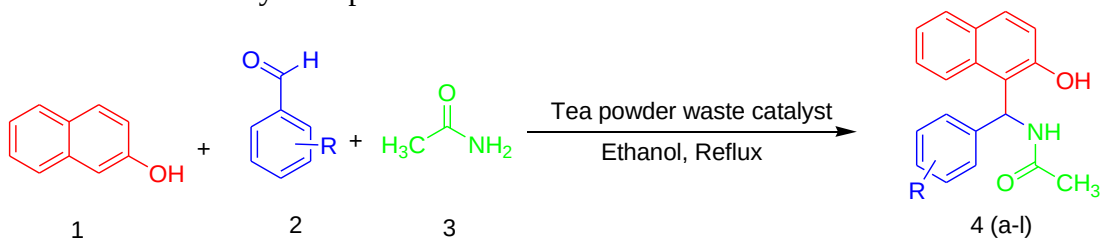
In organic synthesis multi-component reaction are used due to its selectivity and high atom economy. In Ritter type reaction the formation of C-N gives N-alkyl amide compounds are of biologically active ingredients[i]. This type of reaction is associated with condensation of aryl aldehydes, beta naphthol and acetamide in presence of different catalysts like silica sulphuric acid[ii], $Ce(SO_4)_2$[iii], $HClO_4$-SiO_2[iv], $FeCl_3$-SiO_2[v], montmorillonite K10[vi], Ag nanoparticles[vii], bismuth (III) nitrate pentahydrate[viii], nano sulphated zirconia[ix], nano-graphene oxide[x], magnetic nano-Fe_3O_4@SiO_2@Hexamethylene tetramine supported ionic liquid[xi], tetrachlorosilane[xii], $K_5CoW_{12}O_{40}\cdot 3H_2O$[xiii] and cation-exchanged resins[xiv]. The reported methods have some limitations such as use of toxic reagents, tedious work up, hazardous solvent, high reaction temperature and formation of by-products. Therefore, it become a challenge to develop new cost-effective method for synthesis of 1-amidoalkyl-2-naphthols.

According to Research Department of India the consumption of tea powder in India was approximately 1.1 billion kilograms during the financial year 2021. So, the large amount of waste tea powder was introduced in the environment. The tea powder consists of carboxylate, aromatic, phenolic, hydroxyl groups, oxyl groups, carbon and calcium[xv]. The tea waste was used as adsorbent for the removal of dyes and heavy metals[xv]. The attempt was

made in which tea powder waste was used as a heterogeneous catalyst in multi component reactions. In continuation of our research work[xvi-xviii], here we report new cost effective naturally occurring catalyst for the synthesis of 1-amidoalkyl-2-naphthols.

Results and discussion

The reaction was carried out by mixing benzaldehyde (1 mmol), 2-naphthol (1 mmol) and acetamide (1.2 mmol) in presence of 30 mg of tea waste catalyst. The mixture was refluxed with different solvents. The model reaction between benzaldehyde, 2-naphthol and acetamide in presence of tea waste catalyst was used to study the effect of solvent on synthesis of 1-amidoalkyl 2-naphthol derivatives (Table 1). The ethanol was the suitable solvent for the synthesis of 1-amidoalkyl 2-naphthol derivatives.



Scheme 1: Synthesis of 1-amidoalkyl 2-naphthols.

Table: 1 Effect of solvent on synthesis of 1-amidoalkyl 2-naphthols

Sr. No.	Solvent	Time (min)	Yield (%)
1	Solvent free	14	32
2	Water	13	61
3	Methanol	10	64
4	Ethanol	8	92
5	Chloroform	11	51
6	Dimethyl sulfoxide	10	49

The model reaction between benzaldehyde, 2-naphthol and acetamide was refluxed in presence of ethanol and tea waste catalyst to study the effect of amount of catalyst on synthesis of 1-amidoalkyl 2-naphthol derivatives (Table 2). The amount of tea waste catalyst was varied from 10-70 mg, the result shows that the 30 mg of catalyst was sufficient to carry out the reaction.

Table: 2 Effect of amount of catalyst on synthesis of 1-amidoalkyl 2-naphthols

Sr. No.	Amount of catalyst (mg)	Time (min)	Yields (%)
1	10	13	67
2	20	10	78
3	30	8	92
4	40	8	92
5	50	8	92
6	60	8	92
7	70	8	92

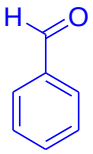
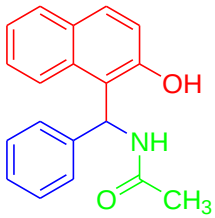
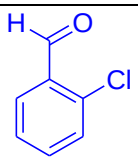
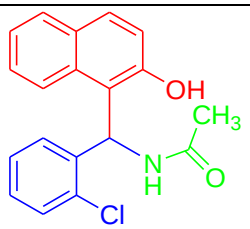
In order to study the effect of time on the synthesis of 1-amidoalkyl 2-naphthols, the model reaction between benzaldehyde, 2-naphthol and acetamide in presence of 30 mg of tea waste catalyst was carried out in the range 2-14 minutes (Table 3). The 8 minutes was the optimum time for the synthesis of 1-amidoalkyl 2-naphthol derivatives.

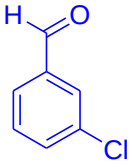
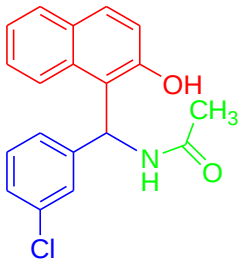
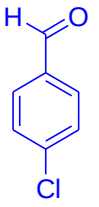
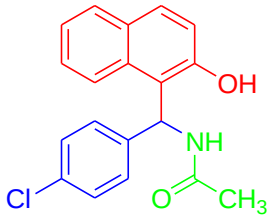
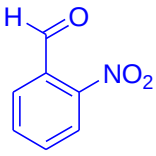
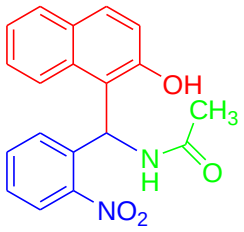
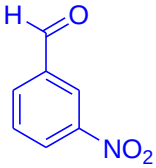
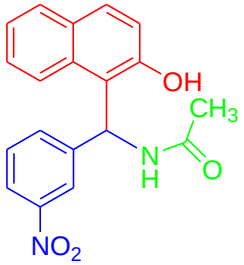
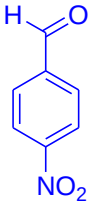
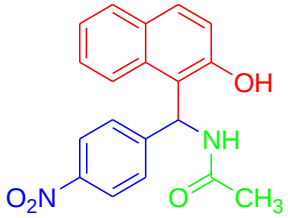
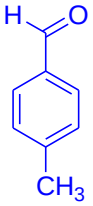
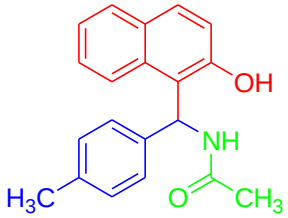
Table: 3 Effect of time on synthesis of 1-amidoalkyl 2-naphthols

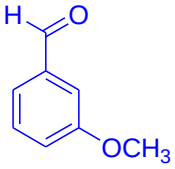
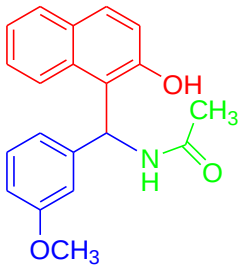
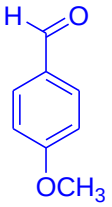
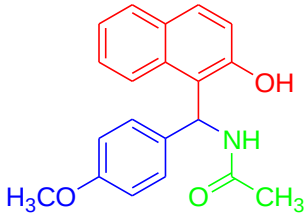
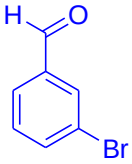
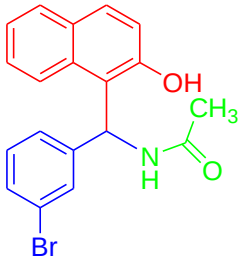
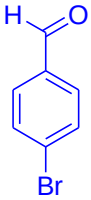
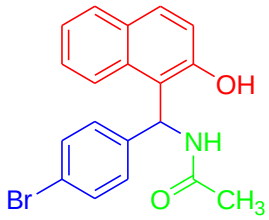
Sr. No.	Time (min)	Yields (%)
1	2	46
2	4	69
3	6	73
4	8	92
5	10	92
6	12	92
7	14	92

In order to check the applicability of the tea waste catalyst, the series of the 1-amidoalkyl 2-naphthol derivatives was synthesized (Table 4). A variety of aromatic aldehydes with electron donating and electron withdrawing groups were converted to 1 amidoalkyl 2-naphthols in excellent yields (88-95 %) with short reaction time (6-18 min). In the present method the 1-amidoalkyl 2-naphthols were the sole products and no by-product was observed.

Table: 4 Synthesis of 1-amidoalkyl 2-naphthol derivatives

Sr. No.	Aldehyde	Product	Time (min)	Yields (%)	M. P (°C)
1		 **4a**	8	92	237-239
2		 **4b**	12	94	191-194

3		 **4c**	14	91	236-238
4		 **4d**	6	90	224-226
5		 **4e**	13	91	215-217
6		 **4f**	7	94	239-241
7		 **4g**	6	95	234-236
8		 **4h**	7	91	218-220

9		 **4i**	16	89	202-204
10		 **4j**	13	90	180-182
11		 **4k**	16	88	227-229
12		 **4l**	18	90	226-228

Experimental

The commercially available chemicals were used without purification. The open capillary method was used to note the melting points. The 1-amidoalkyl 2-naphthol derivatives were matched with known compounds using their spectral data. The Perkin-Elmer FT-IR spectrometer was used to record the IR spectra. The Bruker Avance II (300 MHz) was used to record ^{1}H NMR spectra. The Varian-Saturn GC/MS instrument was used to record mass spectrum of 1-amidoalkyl 2-naphthol derivatives.

Preparation of catalyst

The tea waste was collected, washed with doubled distilled water and dried at room temperature. The waste material was heated in heating oven at 110^{o}C for 3 hrs, for the removal of adsorbed substance and water molecules. The tea waste was then grinded by using mortar and pestle. The tea waste was used again as catalyst in organic reactions.

General procedure for the synthesis of 1-amidoalkyl 2-naphthols

A mixture of aromatic aldehydes (1 mmol), 2-naphthol (1 mmol), acetamide (1 mmol) and tea waste catalyst (0.030 g) were refluxed in presence of ethyl alcohol in oil bath. The

progress of the reaction was monitored by thin layer chromatoghy technique. The solid products obtained were filtered, dried at room temperature.

Compound 4a: ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) 1.95 (s, 3H), 7.11-7.32 (m, 9H),7.75-7.84 (m, 3H), 8.36 (d, *J = 9 Hz*, 1H), 9.92 (s, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): δ (ppm) 23.2, 41.1, 118.4, 120.4, 122.2, 123.7, 124.8, 125.5, 127.4, 128.3, 128.1, 128.2, 128.4, 134.1, 144.2, 152.4, 169.4, MS: m/z 231M^+.

Compound 4f: ^{1}H-NMR (300 MHz, DMSO-d_6): δ (ppm) 2.04 (s, 3H), 7.12-7.45 (m, 6H), 7.74-8.01 (m, 5H), 8.52 (d, *J = 8.1 Hz*, 1H), 10.10 (s, 1H), ^{13}C NMR (75 MHz, DMSO-d_6): 25.51, 66.11, 108.60, 118.12, 120.24, 122.30, 123.92, 125.53, 127.41, 128.10, 129.18, 129.44, 130.81, 132.06, 134.80, 147.67, 148.01, 152.45, 191.65, MS: m/z 276 M^+.

Conclusion

We report here a green protocol for the synthesis of 1-amidoalkyl 2-naphthol derivatives by the condensation of aromatic aldehydes, 2-naphthol and acetamide in presence of naturally available tea waste as a catalyst. The non-toxic solvent, easy work up, high yield and cost effective are the advantages of present method.

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GC-MS based phytoconstituents profiling and phytochemical investigation of *Annona muricata* L.

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Key words: *Annona muricata* L., Ethanol and Hexane extract, Phyto-compound, GC-MS.

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Abstract

Annona muricata L. is conventionally used to treat various ailments. This plant shows varied medicinally valuable effects like anti-cancer, anti-hermitic, anti-spasmodic,anti-convulsant,anti-pyretic, sedative, hypotensive, digestive, anti-diabetes, anti-microbial,anti- inflammatory, anti- dysenteric, andanti- rheumatic effects. The phytochemical qualitative analysis of *Annona muricata* leaves exhibits the presence of carbohydrates, tannins, saponins, alkaloids, flavonoids, glycosides, quinines, phenols, terpenoids, coumarins, anthraquinones, steroids, phlobatannins and anthracyanine.The GC-MS analysis report shows the 22 compounds in the leaf ethanolic and hexane extract of *Annona muricata* by comparing retention time and interpretation of their mass spectra.

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Introduction

Annona muricata L. is a species of Annona muricata. It is also known as Laxman phal. It is an Annona species from the Annonaceae family of custard apple trees. Graviola, also known as soursop, is an edible fruit. *Annona muricata* is native to the Caribbean and Central America, but due to its widespread cultivation, it has become invasive in tropical and subtropical climates around the world (Hamizah *et al.*,2012).Phytochemicals are natural biological active and non-nutrient compounds found in plants that protect them from fungal and bacterial infections (Doughari *et al.*, 2009; Krishnaiah *et al.*, 2009). Recently, bioactive phyto-compounds and their effects on human health have been studied. Extracted phyto-chemicals and their mode of action as an anti-cancer agent provide useful information for future applications. As a result, it is critical to test the apoptotic potential of plants in their crude extract or as a pure compound. The plant extracts have been linked to the arrest, prevention, or reversal of carcinogenesis' molecular and cellular processes (Neergheen *et al.*, 2009; Wamidh; 2011). Anti-oxidant compounds combat diseases such as cancer, Alzheimer's, atherosclerosis, Parkinson's, diabetes, and heart disease (Valko *et al.*, 2007, Joabe *et al.*, 2010; Aboul-Enein *et al.*, 2012). Annonaceous acetogenins from *Annona muricata* have been shown in vitro to become a new anti-cancer and anti-tumor agent. These compounds are selectively toxic to different types of cancerous cells while causing no harm to healthy cells (Rieser *et al.*, 1993, Wu *et al.*, 1995; Hamizah *et al.*, 2012). *Annona muricata* leaf extracts have the potential to develop a new alternative treatment for cervical cancer (Qorina *et al.*, 2020). The current study investigates secondary metabolites of *Annona muricata* and characterization of compounds using GC-MS analysis to the presence of phytochemical constituents, with the goal of curing many diseases and disorders.

Materials and methods

Collection of plant materials

The plant material was collected from Mahatma Phule Krishi Vidyapeeth (MPKV), Rahuri(Located 19.349104°N 74.646106°E) Ahmednagar district, Maharashtra during November 2020.The plant material was authenticated by Dr.Wabale A.S., Department of Botany, P.V.P.College, Pravaranagar.

Samples preparation and Extraction

The leaves of *Annona muricata were* cleaned with water and cut into small pieces, drying was done at RT (room temperature) for three weeks and the dried samples were powdered in a grinder machine (Tiwari *et al.*, 2011; Das *et al.*, 2010). 10 grams of dried powder of leaves were suspended in 200 ml of each water, ethanol and hexane solvents. The extraction procedure was done using Soxhlet apparatus for five hours at a definite temperature for each solvent but not more thanthe boiling point. The extract was concentrated with a rotary evaporator and stored in a refrigerator throughout the experiment (Roghini and Vijayalakshmi *et al.*, 2018).

Phytochemical screening

Samples of ethanol, hexane and water extracts of *Annona muricata* were selected for the screening ofphyto constituent's viz. tannins, saponins, alkaloids, flavonoids, glycosides, quinones, phenol, terpenoids, cardiac glycosides, coumarins, anthraquinones, phlobatanin and anthracyanine.Tannins, saponins, alkaloids, flavonoids, glycosides, quinones, phenol, terpenoids, cardiac glycosides, coumarins, anthraquinones, phlobatanin, and anthracyanine were screened in ethanol, hexane, and water extracts of *Annona muricata*.

Carbohydrates Test: 2-3ml of the extract was treated with 2 ml of Molisch's reagent and 1-2 drops of conc. H_2SO_4, resulting in the formation of a purple color, confirms the presence of carbohydrates (Roghini and Vijayalakshmi *et al.*, 2018).

Tannin Test: Tannins were tested by adding 2 ml of 5 percent ferric chloride to 1 ml of extract. The presence of tannins showed by dark blue or greenish-black color (Roghini and Vijayalakshmi *et al.*,2018).

Saponins Test: 2 ml of extract was mixed with 2 ml of

distilled water and shaken in a measuring cylinder for 15 minutes. The presence of saponins is revealed by the formation of a 1 to 2 centimeter layer of foam (Roghini and Vijayalakshmi *et al.*, 2018).

Alkaloids Test: 2-3 ml of extract was mixed with 1-2 drops of conc. hydrochloric acid. 2-3ml of Mayer's reagent was then added. The presence of alkaloids is revealed by the formation of white ppt (Roghini and Vijayalakshmi *et al.*,2018).

Flavonoids Test: 2 ml of 2N NaOH was added to 3ml of extract. The presence of flavonoids is indicated by the yellow colour (Roghini and Vijayalakshmi *et al.*, 2018).

Glycosides Test: 1-2ml of plant sample was mixed with 3 ml of chloroform and 10% NH_4OH solution. The presence of glycosides is indicated by the pink colour (Roghini and Vijayalakshmi *et al.*, 2018).

Quinones Test: 2 ml of sample extract was mixed with 2 ml of conc.H_2SO_4. The presence of quinines is indicated by the presence of red color (Roghini and Vijayalakshmi *et al.*, 2018).

Phenols Test: 1-2 ml of extract, 2 ml of D/W was added, followed by a few drops of 10% $FeCl_3$. Phenols are indicated by the presence of green or blue color (Roghini and Vijayalakshmi *et al.*, 2018).

Terpenoids Test: Add 0.5 ml of extract, 1-2ml of chloroform, and 2 ml of conc. H_2SO_4 to 0.5 ml of extract. Terpenoids indicated by the presence of red or brown colour at the interface (Roghini and Vijayalakshmi *et al.*, 2018).

Glycoside Test: 1 ml of the extract was mixed with 2-3 ml of glacial CH_3COOH and 1-2 drops of $FeCl_3$. This was followed by 1-2ml of conc. H_2SO_4.Glycosides are indicated by the presence of a brown ring at the interface (Roghini and Vijayalakshmi *et al.*, 2018).

Ninhydrin Test: 1-2 drops ninhydrin reagent added to 2 ml of the extract and heated for few minutes. The presence of amino acids is indicated by blue or violet color (Roghini and Vijayalakshmi *et al.*, 2018).

Coumarins Test: 1 ml of 10% NaOH was mixed with 2ml of extract. The presence of coumarins is indicated by the presence of yellow colour (Roghini and Vijayalakshmi *et al.*, 2018).

Anthraquinones Test: 1-2ml of 10% NH_4OH solution was added to 2 ml of extract, and the formation of pinkish color ppt indicates the presence of anthraquinones (Roghini and Vijayalakshmi *et al.*, 2018).

Steroid Test: 1-2ml of extract and 1-2ml of $CHCl_3$ was added; along with 1-2 drops of conc.H_2SO_4.The formation of a brown color indicates the presence of steroids, while the formation of a bluish brown ring indicates the presence of phyto-steroids (Roghini and Vijayalakshmi *et al.*, 2018).

Phlobatannins Test: 1-2ml of extract, a few drops of HCl was added. The presence of phlobatannins is indicated by the formation of redish ppt (Roghini and Vijayalakshmi *et al.*, 2018).

Anthracyanine Test: Few ml of the extract was mixed with 1-2 ml of 2N NaOH and heated for 5 minutes. The presence of anthocyanin was indicated by the formation of a bluish-green color (Roghini and Vijayalakshmi *et al.*, 2018).

Gas chromatography–Mass spectrometry (GC-MS) analysis

Ethanol and Hexane fractions of *Annona muricata* leaf extracts were taken for the GC-MS analysis. The analysis was done on a GC clarus 500 Perkin Elmer system comprising a AOC-20i auto sampler and gas chromatograph interfaced to a mass spectrometer instrument with the following conditions: column DB 35- MS capillary standard non-polar column 30 x 0.25mm ID x 0.25µMdf operating in electron impact mode at 70eV; Helium gas 99.99% was used as a carrier gas at a constant flow of 1 milliliter per minute and employed the injection volume of 1 microliter.

The oven temperature was set from 70°c with an increase of 6°c/min to 260°c, then 5°c/min to 280°c. A mass spectrum was taken at 70eV and the total gas column running time is 37.52min. The relative percent amount of each constituent was calculated by comparing its average peak area to the total areas. Thermo GC-Trace Ultra Ver 5.0 software set to handle mass spectra and chromatograms (Shibula *et al.,* 2015).

Results

Qualitative phytochemical analysis

Qualitative phytochemical analysis of *Annona muricata* extracts is summarized in Table 1.

Table 1. Qualitative phytochemical analysis of different leaf extracts of *Annona muricata*.

Sr. No.	Test	Distilled Water Extract	Ethanol Extract	Hexane Extract
•	Carbohydrates (Molisch's Test)	+	+	+
•	Tannins	-	+	-
•	Saponins	+	-	-
•	Alkaloids	-	+	+
•	Flavonoids	-	-	+
•	Glycosides	+	-	-
•	Quinones	+	+	+
•	Phenols	-	+	-
•	Terpenoids	+	+	+
•	Ninhydrin	-	+	-
•	Coumarins	-	-	+
•	Anthraquinones	-	-	-
•	Steroids	-	+	-
•	Phlobatanin	-	-	-
•	Anthracyanine	-	+	-

The phytochemical analysis of distilled water extract confirmed the presence of secondary metabolites like carbohydrates, saponins, glycosides, quinones and terpenoids. Ethanol extract confirmed the presence of secondary metabolites like carbohydrate, Tanins, alkaloids, quinones, phenols, terpenoids, cardiac glycosides, ninhydrin, steroids and anthracyanins, while hexane extract confirmed the presence of carbohydrates, alkaloids, flavonoids, quinones, terpenoids, cardiac glycosides and coumarins.

Gas chromatography–Mass spectrometry (GC-MS) analysis

GC-MS analysis of Ethanol Extract

The total ion chromatogram of the ethanolic extract showed the GC-MS profile of the identified compounds (Table 2, Fig. 1). Twelve compounds were identified in the ethanol fraction of *Annona muricata* by GC-MS analysis.

The prevailing compounds were 1,5-heptadiene, 2,3,6-trimethyl, phytol, acetate, 3,7,11,15-tetramethyl-2-hexadecen-1-ol, n-hexadecanoic acid, 2,6,10-dodecatrien-1-ol, 3,7,11-trimethyl-, phytol, 9,12-octadecadienoic acid (z,z), octadecanoic acid, squalene, di-n-octyl phthalate, gamma.-tocopherol, cyclohexane propionic acid and 4-oxo-, ethyl ester.

The presence of hydrofurans and epoxides in the sample detected by GC-MS analysis were analyzed on the basis of different annonaceous acetogenins from *Annona muricata*.

Table 2. GCMS Analysis of ethanol leaf extract of *Annona muricata*.

Peak	R.Time	Area	Area %	Height	Height%	CompoundName
1.	24.008	22261	1.53	8906	1.90	1,5-Heptadiene, 2,3,6-trimethyl
2.	30.815	211713	14.58	78807	16.78	Phytol, acetate
3.	31.334	27851	1.92	11635	2.48	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
4.	31.704	67616	4.66	24186	5.15	3,7,11,15-Tetramethyl-2-hexadecen-1-ol
5.	33.491	169332	11.66	45017	9.58	n-Hexadecanoic acid
6.	34.100	29584	2.04	11312	2.41	2,6,10-Dodecatrien-1 ol,3,7,11-trimethyl
7.	36.212	119299	8.21	41095	8.75	Phytol
8.	36.700	38996	2.68	15024	3.20	9,12Octadecadienoicacid (Z,Z)
9.	37.194	56918	3.92	16991	3.62	Octadecanoicacid
10.	38.243	129984	8.95	22919	4.88	Squalene
11.	43.499	50280	3.46	18526	3.94	Di-n-octyl phthalate
12.	46.665	65690	4.52	14351	3.06	Gamma.-Tocopherol
13.	48.474	23917	1.65	8780	1.87	Cyclo hexane propionic acid, 4-oxo-, ethylester

GC-MS analysis of Hexane Extract

The total ion chromatogram of the hexane extract showed the GC-MS profile of the identified compounds (Table 3, Fig.2). Nine compounds were identified in hexane fraction of *Annona muricata* by GC-MS analysis. The prevailing compounds were 2-propenoic acid, butyl ester, oxalic acid, butyl propyl ester, nonane, 3-methyl-, nonane, 1-iodo-, 4-fluoro-2-trifluoromethylbenzoic acid, neope, sulfurous acid, 2-ethylhexyl hexyl ester, oxalic acid, dineopentyl ester, 6-octen-1-ol, 3,7-dimethyl-, propanoate, 1,2-benzenedicarboxylic acid and butyl octyl ester.

Table 3. GCMS Analysis of hexane leaf extract of *Annona muricata*.

Peak	R.Time	Area	Area %	Height	Height%	Compound Name
1.	6.467	33800	20.72	10088	16.45	2-Propenoicacid,butylester
2.	7.436	2506	1.54	1692	2.76	Oxalicacid,butylpropylester
3.	12.256	8515	5.22	4417	7.20	Nonane,3-methyl-
4.	23.073	5853	3.59	3649	5.95	Nonane,1-iodo-
5.	23.837	14061	8.62	4146	6.76	4-Fluoro-2-trifluoromethyl benzoicacid,neope
6.	28.030	9725	5.96	5066	8.26	Sulfurousacid,2-ethylhexylhexylester
7.	29.969	3023	1.85	2227	3.63	Oxalicacid, dineopentyl ester
8.	30.814	29365	18.00	12054	19.66	6-Octen-1-ol,3,7-dimethyl ,propanoate
9.	33.500	56317	34.52	17985	29.33	1,2-Benzenedicarboxylic acid, butyloctyl ester

Discussion

More phytochemical compounds were elucidated in the Ethanol than Hexane and Distilled water fraction of *Annona muricata*, which was in contrast to the observation of Roghini and Vijayalakshmi, 2018.The past reports of Shibula and Velavan (2015), Lali Growther (2018), Alamu *et al*. (2020); also proved 4,4-dimethyl-5-oxo-tetrahydrofuran-3-carboxylic acid, 1-dodecenoic acid, 1-octadecanoic acid, isoaromadendrene epoxide, 1-hexadecanoic acid, 1,2-benzenedicarboxylic acid, dibutyl ester, 1,2-benzenedicarboxylic acid, di isooctyl ester and 2,7,12,18-tetramethyl-3,8-diethyl-13,17-bis(3-chloroprophyl) prophyrin, 12-octadecadienoic acid, hexadecanoic acid ethyl ester, 9-octadecenoic acid, -2-hydroxy-1-(hydroxymethyl)ethyl ester, n-

hexadecanoic acid and squalene; 2-methyl-z,z-3,13-octadecadienol,tetradecanoic acid ethyl ester, n-hexadecanoic acid, 1,8,11-heptadecatriene in ethanol and ethyl acetate extract fraction of *Annona muricata* extract. among these, disparate compounds are phytol, 3,7,11,15- tetramethyl-2-hexadecen-1-ol, di-n-octyl phthalate, gamma tocopherol and nonane.

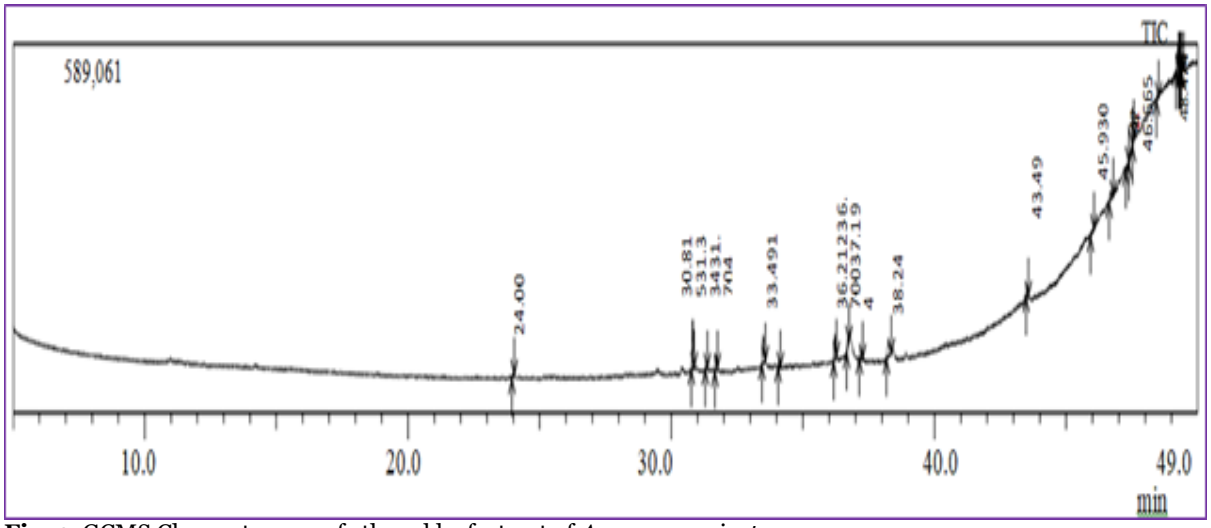

Fig. 1. GCMS Chromatogram of ethanol leafextract of *Annona muricata*.

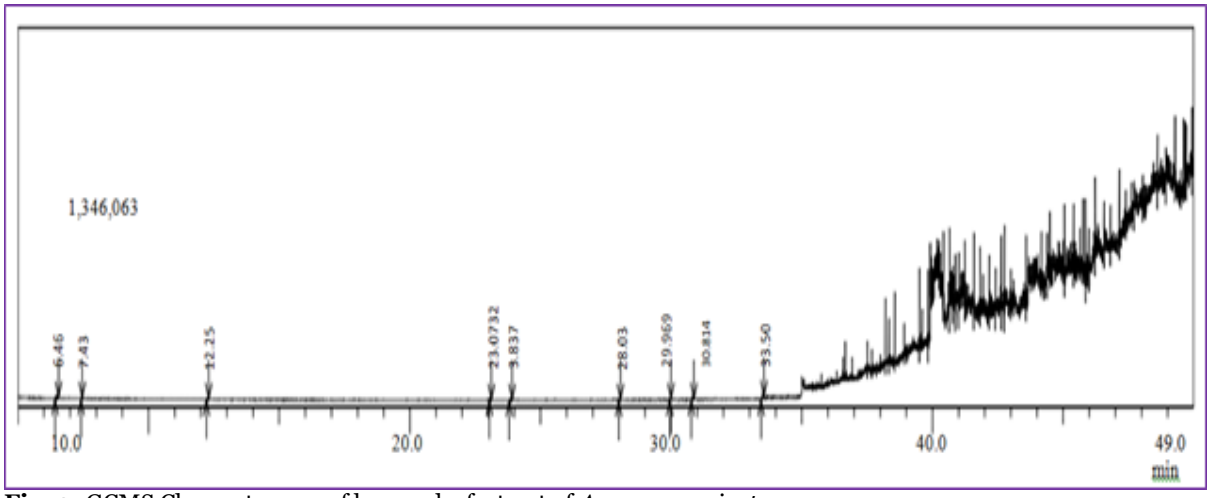

Fig. 2. GCMS Chromatogram of hexane leafextract of *Annona muricata*.

Conclusion

The presence of 5 phytoconstituents in water extract, 10 phytoconstituents in ethanol extract, and 7 phytoconstituents in hexane extract is revealed by phytochemical screening. This discovery demonstrated variation in phytochemicals as a result of solvent solubility variation and ethanolic extract as a potential source of phytochemicals. The presence of 13 compounds in ethanol extract and 9 compounds in hexane extract was confirmed by GC-MS analysis. The pharmaceutical properties of this plant are due to the presence of various phyto-bioactive compounds.

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WILD EDIBLE VEGETABLES FROM WESTERN HILLY REGION OF AHMEDNAGAR (MAHARASHTRA, INDIA)

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Abstract:

Approximately 60% of populations in underdeveloped countries residing in agricultural and forest areas, from nearby habitat they harvest various plant parts such as roots, leaves, fruits, and nuts which forms an integral part of their daily diets. Ahmednagar is one of largest districts in western Maharashtra and consists of both hilly area and deccan plateau plain land. It is situated in the rain shadow region of the Western Ghats, whereas the northwestern region comes under the hilly region of western ghats and receives plenty of rain resulting in flourishing biodiversity. A survey was conducted in Akole and Sangamner areas of Ahmednagar to find out the information about wild vegetables utilized by natives as a source of food. A total of 62 plant species of wild vegetables belonging to 59 genera and 23 families were reported edible from the selected area. The fabaceae was the most dominant family (14%), followed by Amaranthaceae (12%), Cucurbitaceae (8%), These three families contributed about 35% of the wild vegetables used in the study area.

Keywords: Wild vegetables, Akole, Sangamner, Survey, Plants

Introduction:

Earlier than Human civilization man had been using wild edible plants as a food because of their rich nutritional value and therapeutic importance. These plants play a significant role in their livelihoods [1]. Approximately 60% of populations in

underdeveloped countries reside in agricultural and forest areas and harvest various plant parts from nearby habitats such as roots, leaves, fruits, and nuts which forms an integral part of their routine diets[2]. These wild edible plants not only act as alternatives to cultivated food during periods of food scarcity but they also play as a valuable supplement for a nutritionally balanced diet [3]. There are nearly 45,000 species of wild plants out of which 9,500 species are considered as ethno-botanically important species. [4]

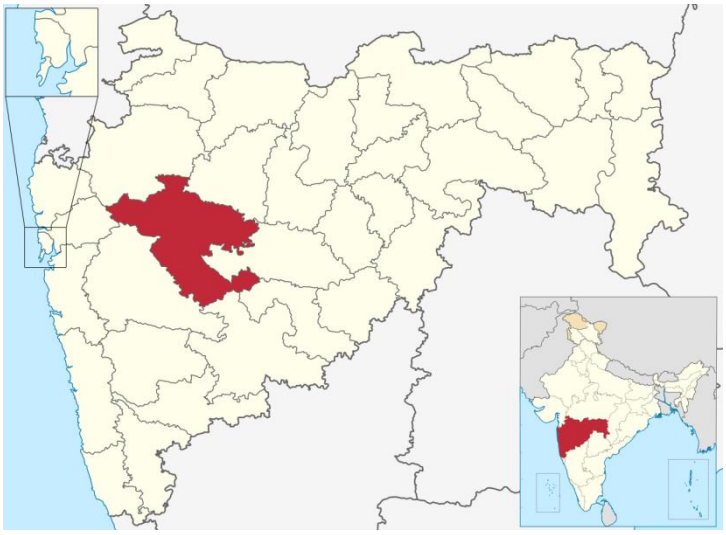
Wild edible plants consist of plant species which grow spontaneously in self-maintaining populations in natural or semi-natural ecosystems [5]. These wild species include all vegetables that are collected (not cultivated), whether they are collected in agricultural areas, barren land, non-cultivated areas, or forestland [6]. Since time immemorial, the tradition of collection of wild edible vegetables has been inculcated in many asian and african communities [7]. Rural tribal communities are considered experts in particular to make use of wild vegetables to supplement their diets, which is based on rainfed cultivation of staples cereals and pulses [8, 9]. The Western Ghats is a mountain range that covers an area of 160,000 km^2 (62,000 sq mi) in a length of 1,600 km (990 mi) parallel to the western coast of the Indian peninsula, from which Maharashtra constitutes an area of 52,000 km2 [10]. Ahmednagar is one of largest districts in western Maharashtra and consists of both hilly area and plain land. It is situated in the rain shadow region of the Western Ghats, whereas the northwestern region comes under the hilly region of Western Ghats and receives plenty of rain resulting in flourishing biodiversity. The northwestern region of Ahmednagar is composed of two tehsils Sangamner and Akole. These two tehsils consist of Hilly areas covered by three mountain ranges such as Adhala, Baleshwar and Kalsubai. By the impacts of the tallest peaks of the mountain, this region is one of the richest in terms of vegetation and diversity in western ghat. The indigenous peoples residing in the untouched and mountainous area fulfill their food needs by using the natural resources available in the nearby habitats such as uncultivated areas, grassland, mountain scape, forest and barren land. earlier studies are only concentrated in Akole tehsil and reported 31 species of wild vegetables belonging to 23 families. As the earlier studies suggested that there is need for further research, a survey was conducted in

selected areas to find out the information about wild vegetables utilized by natives as a source of food.

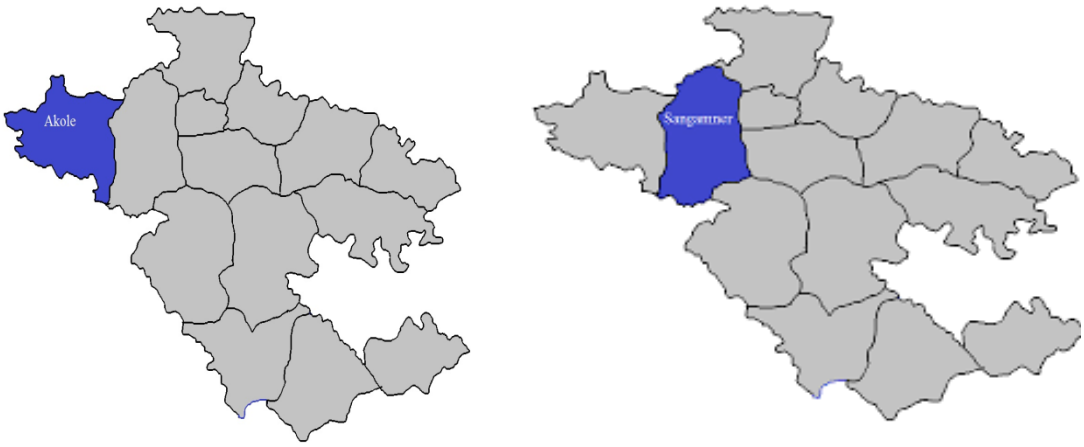
Materials and methods:

Study area:

` Geographically, Ahmednagar district is the largest district in the state of Maharashtra. Sangamner and Akole are tehsil places in Ahmednagar district, Maharashtra state, well covered by the mountains of Sahyadri Fig, 1.



Ahmednagar in Maharashtra



Akole in Ahmednagar Sangamner in Ahmednagar

Fig 1. Location map

Reconnaissance Survey and Selection of Study Sites and Informants

A reconnaissance survey was conducted throughout the year to have an overview of the terrain and potential informants, and to select study sites. Study villages were selected based on basins of three rivers. Before the survey, a semi-structured questionnaire was designed. In each selected village, a purposive sampling method was employed to identify key informants and respondents. Key informants were selected for interviews with assistance of the local villagers.

Ethnobotanical Data Collection

Ethnobotanical techniques were employed to collect data on the utilization and management of wild vegetables. The information was collected from the local community using semi-structured interviews, focus group discussions, ecological surveys, market surveys. Information regarding the local names of plant species, growth forms, part (s) used, availability in natural resources, method of processing and vegetable preparation was carefully recorded.

Ecological Surveys

For the ecological inventory of wild vegetables, forest walks were done by a team accompanied by the key informants in the different communities. The opportunistic

sampling technique was exploited in the survey for wild vegetables with each sampling site geo-referenced using a Google map. Based on the ethnobotanical information obtained from informants', plant specimens with their vernacular names were collected. Further identification of all plant specimens was done using flora such as Flora of Maharashtra and Flora of Bombay Presidency.

Results and discussion:

Indigenous Knowledge

Most of the local community members with good knowledge of and use of wild vegetables belonged to the older generation between the ages of 50 and 80. Whereas the least are the younger generation below the age of 40. It was also noted that most of the household members involved in tendering these vegetables are women across all age categories.

The wild vegetables

The diversity of plants used as vegetables in the North western region of Ahmednagar shown in Table 1. A total of 62 species in 59 genera of 32 families were identified. The most common life forms used were herbs, vegetable. Kolhe (2009) reported A total of 31 plant species of wild vegetables belonging to 23 families were reported from the study area [11]. Similar results were obtained by Khayde et al. (2009). from Akole tehsil [12].

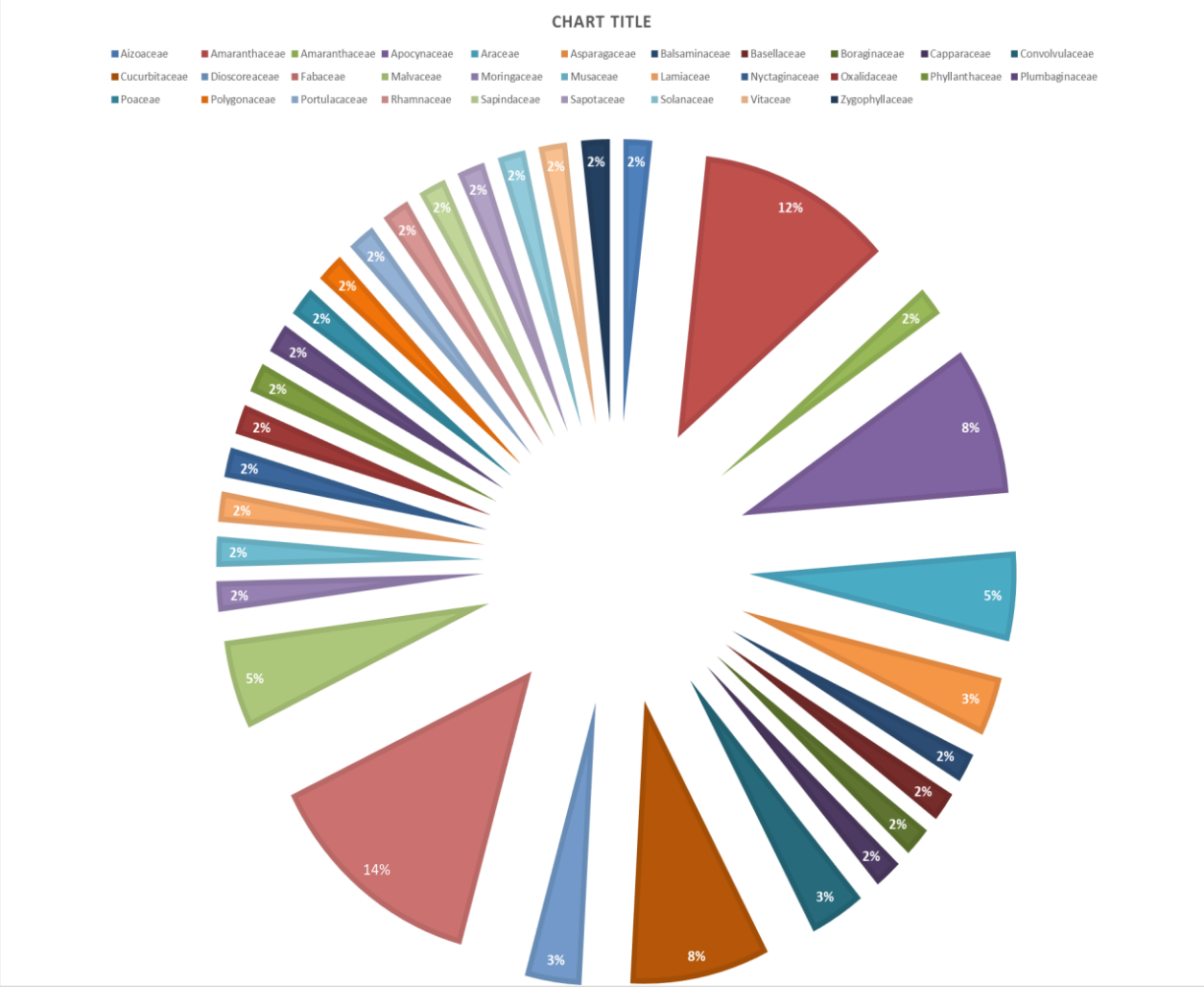


Fig 2: Families of wild vegetables with percentage of genera

The fabaceae was the most dominant (14%), followed by Amaranthaceae (12%), Cucurbitaceae (8%), These three families contributed about 35% of the wild vegetables used in the study area. The other families with their respective consumption percentages are shown in Figure 2.

Conclusion:

Most of the local community members with good knowledge of and use of wild vegetables belonged to the older generation between the ages of 50 and 80. Whereas the least are the younger generation below the age of 40. So emphasis should be given to find

out any cultivation method of these wild vegetables. Also further research should be carried out to find out medicinal properties of these vegetables.

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ASSESSMENT OF TOURISM POTENTIAL AND ITS IMPACTS ON AURANGABAD DISTRICT

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ABSTRACT

Tourism is closely related to the social and economic development of the world because of its maximum backward and forward linkages. Tourism contributes more to income and employment generation in developing nations. However, the development of the tourism sector in India has also created some problems related to society and the environment. This paper is a review of available tourism potential, Planning and Promoting tourism in Aurangabad district and its impacts of tourism development in the city. An observational approach has been used in this study. Apart from this, a photography presentation has been made to highlight the growing impact of Aurangabad on tourism. The findings of the study showed that the tourism potential was very high but mass tourism caused various environmental problems in the area. From a theoretical perspective, carrying capacity, pollution, deforestation, solid waste, etc. have been seen as important environmental impacts and social impacts of tourism development.

Key Word- Tourism Potential, Tourist Footfall, Social Impacts, Environmental Impact,

Introduction

Tourism is a field of human activity known to mankind from time immemorial. It cuts across barriers of caste, color, and creed and builds universal brotherhood. The world's oldest industry is also one of the largest and fastest growing industries today. In general terms, travel is referred to any movement of one or more people from one point to another. There is not much difference between tourism and travel; in general, both terms are used as synonyms. Many people believe that tourism is a service industry that takes care of visitors when they are away from home. Some restrict the definition of tourism by the number of miles away from home, overnight stays in paid accommodations, or travel for pleasure or leisure.

This is the first of its kind in the tourism sector in world heritage and is aimed at organizing and training service providers at tourist sites who are otherwise considered a nuisance by tourists and planners alike but are an essential part of the world heritage tourism scenario. Along with the development of infrastructure in Aurangabad, there is a need to cater to small necessities of tourists which are met by mushrooming hawkers whose service to tourists leaves much to desire. The microfinancing sub- projects are aimed at organizing, training, and financing this low-income segment. Women entrepreneurs will be given preference and suitable NGOs had been identified to train, disburse and monitor the micro-credit funding credit and recovery. The beneficiaries included in the scheme are small restaurant owners, tea shops, kiosks, guides, photographers, hawkers, fruit vendors, and taxi operators. This would make them more presentable as well as increase their entrepreneurial skills and

abilities. The loan amount will be channelized through rural banks.

Review of Literature

Tourism is one of the fastest growing industries; tourism plays a dynamic role in economic growth of many countries in the world [Flecha and et al, 2010]. Walpole & Goodwin [2000] recognized tourism as a development tool which provides economic benefits for host communities, including increased employment opportunities, improved socio- economic conditions and greater market stability. In India in the year 2015, According to Higgs [2002], socio-economic development is defined as an individual's resources, wealth, education level and degree of urbanization.

According to Madhuri Sawant tourism effect on socio-economic development in Aurangabad district in year 2016, Conference: A pathway for the new generation of tourism research - Proceedings of the EATSA Conference 2016. According to Glenn [2001] tourism impacts are not only in terms of economic impacts, jobs, and taxes but they are broad and often influence areas beyond those commonly associated with tourism. National Tourism policy of India [2002] and Tourism Policy of Maharashtra state [2006] define tourism as an engine of growth aiming high to achieve maximum sustainable tourism growth in the country.

Objectives

- To study the Tourism Potential in the Aurangabad district.
- To study the domestic and foreign tourist footfall in the district.
- To study the positive and negative impacts of tourism in the district.

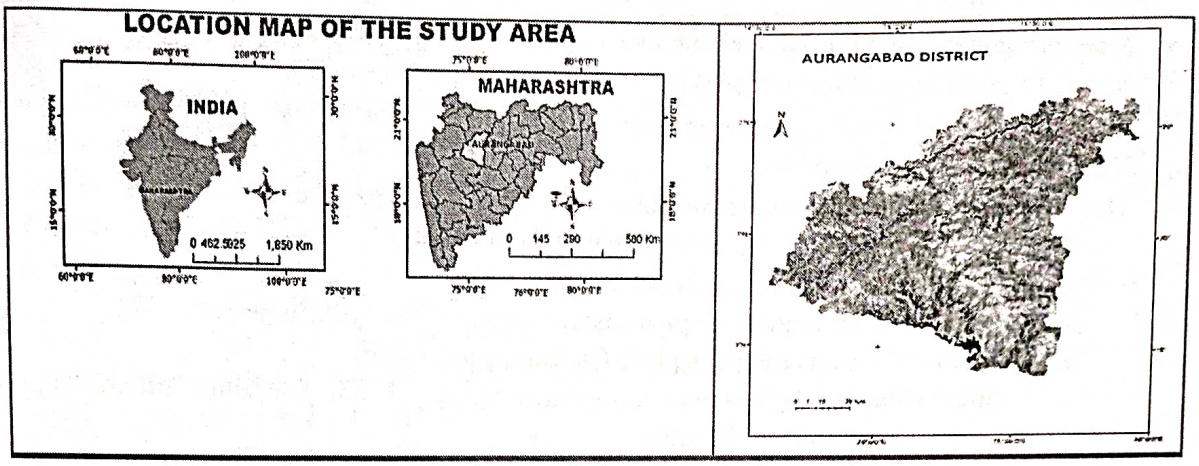
Research Methodology

The present study is based on

1. Field observation
2. Secondary data- The data has been obtained from the Government project, related articles, research papers, reports, policies and plan documents of Government of India and Maharashtra state. The data has also been obtained from websites of Govt. of India and Govt. of Maharashtra, MTDC as well as Ministry of Environment. Visits to some site have been undertaken to know the environmental status.

Location of Study Area

Aurangabad District situated in the central part of the state is an elevated land, which has been incised by the Godavari River and its tributaries in the southern part. Except for a small portion in the north and northwest, which belongs to the Tapi drainage, the entire district falls in the Godavari Basin. Aurangabad district lies between 19°17' north to 20°40' North latitude and 74°39' east to 76°40' East longitudes. It is surrounded by Jalgaon district to the north, Jalna district to the east, Ahmednagar district to the south and southwest, and Nasik district to the west. It also has small boundaries with Buldhana district in the northeast and Beed district in the south.



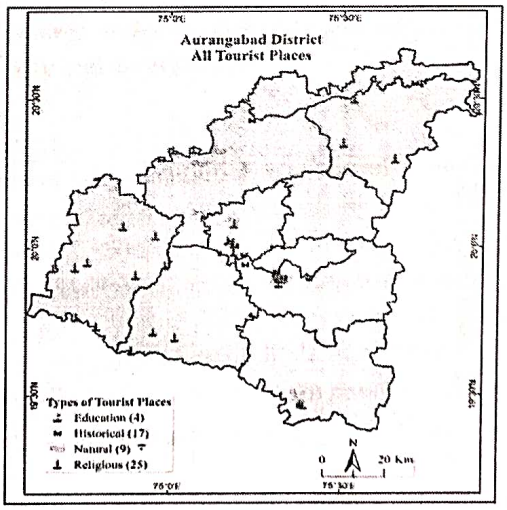
Map No.1: Locational Map of study area

Discussion

Tourism Potential in Aurangabad District

Recently declared the 'Tourism Capital of Maharashtra', Aurangabad is an important hub in the state's tourism sector with its close connection to such significant tourist destinations as the caves of Ajanta and Ellora which have been declared 'World Heritage Sites by UNESCO as well as the famous Mughal monument Bibi ka Maqbara. One of the fastest growing cities in Maharashtra, it is also emerging as a prime industrial city. The city is linked with Mumbai by air, rail, and road and an excellent road network connects Aurangabad with the rest of the state. Apart from Ajanta and Ellora, the city also serves as a transit point for Pitalkhora, Daulatabad, Khultabad, and Paithan.

Tourism Classification in Aurangabad District



Map No.2: Tourism Potential in Aurangabad District

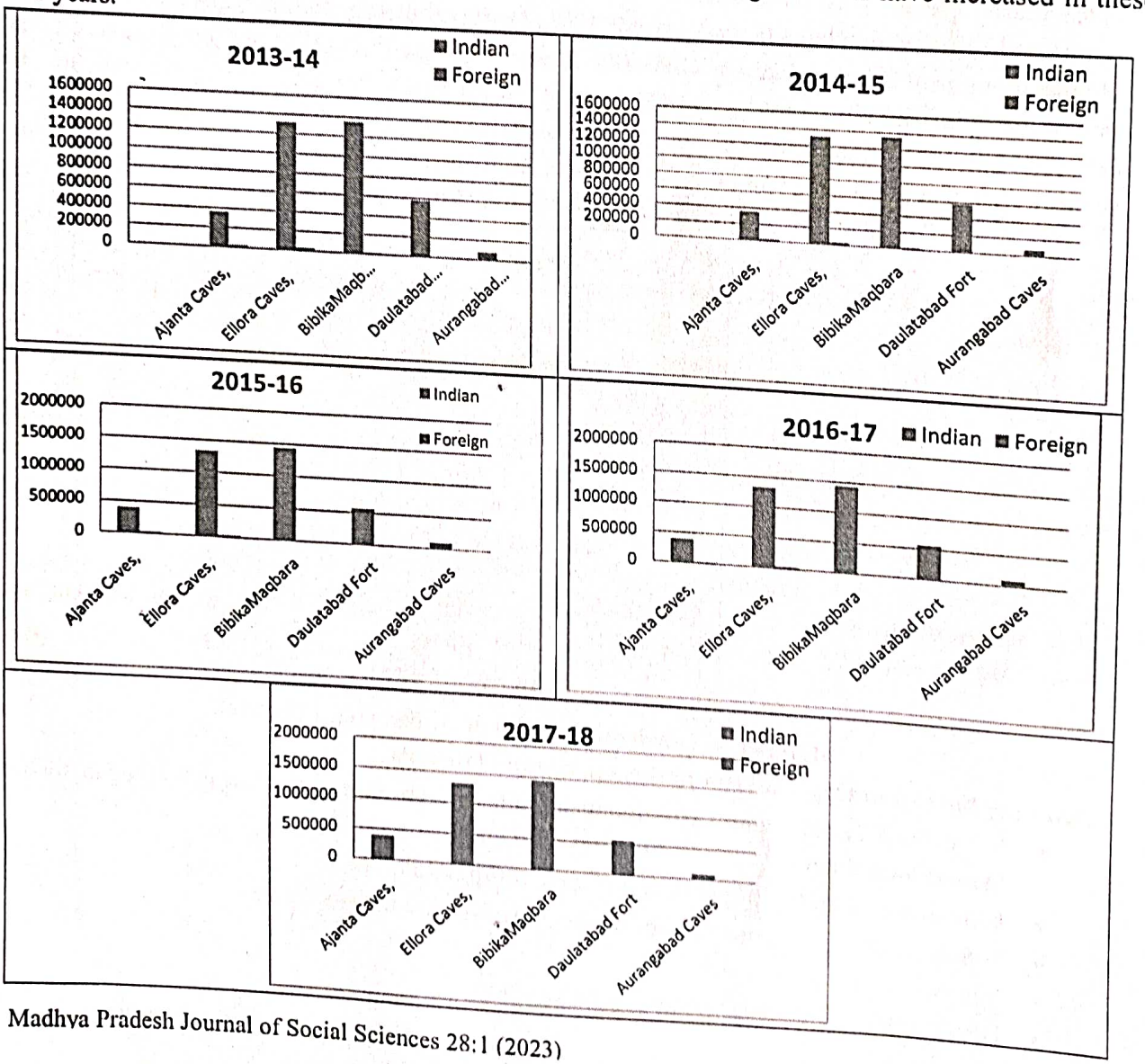
Planning for Promoting Tourism in the Aurangabad district

- In Vision 2022 following steps are taken to plan for promoting tourism in Aurangabad District Maharashtra State.
- Increased availability of public transport to tourist locations.
- Development and maintenance of public amenities and infrastructure.
- Improving the access roads.
- Development of gardens nearby tourist locations.

- Monitoring the availability of hygienic foods and eatables at reasonable rates.
- Ajanta Ellora conservation and tourism development project Phase-III
- Conservation and Tourism Developments in and around Ajanta Caves, Ellora Caves, and Daulatabad Fort, and Lonar lake.
- Development of tourism amenities in and around Newly Identified Destinations.
  - Lonar (2nd largest crater in basaltic rock in the world)
  - Shirdi (Famous religious place for Lord Saibaba)
  - Ghrishneswar (A famous religious place and one of the Jyotirlinga out of 12)
  - Khultabad (Famous religious place for Aurangzeb Tomb)
  - Paithan (Famous religious place for Samadhi of Sant Eknath) Shegaon (Famous religious place for Sant Gajanan Maharaj)

Domestic and Foreign Tourism in Aurangabad

Aurangabad district of Maharashtra state offers a variety of tourist attractions varying from pilgrimage centers, forts, dam-sites, and eco-tourism areas to world heritage sites. The famous world heritage sites of Ajanta and Ellora are located in this region. The following table shows the Tourist footfall of Aurangabad circle from 2013-2018. Domestic and Foreign tourists have increased in these five years.



Source: Archaeological Survey of India Aurangabad Circle

The above table and graph show the no. of Domestic and Foreign tourists from various states, and countries traveling to Aurangabad district from various states and also various countries. The ratio of Domestic tourists is the highest in the district. Foreign tourists visited to Aurangabad study the world-famous Archeological site in this destination.

Positive Impacts

a) Social Impacts:

The local people develop pride and appreciation for the heritage sites. They gather an understanding of the past through local guides and developed a respect for each other culture as a Muslim-based community but they develop respect for Buddhism, Jainism, and Hinduism. They are keen to develop friendships among tourists. As it lies on the way to major tourist destinations, tourists stay there for some time to view major scenic points.

b) Cultural Impact:

The tourism industry has developed a sense to respect for every culture.

Negative Impacts

a) Social Impacts:

The natural water system of this region played an important role in the lives of people but with the upcoming tourism new systems of the water supply has been formulated and abandoned the old water system. Hence tourism may be responsible for introducing new insensitive infrastructural techniques.

b) Physical Impacts:

Despite active tourism around Aurangabad, there is not much heritage conservation in the area. The village has large archaeological mounds of 10 paper mills, two mosques, and one tomb which are historically and architecturally significant and have no protection from any legal authority

Economic impacts

Neither government nor local authorities play any role in the development of finances in the area. People are very poor. The village is having maximum stakeholders for tourism like local van walas who drop the tourists at their destinations. The other stakeholders are local on-road dhaba walas who serve food and minor leisure for tourists. Few of them are guides.

Conclusion

Ajanta, Ellora, and Daulatabad are having high tourist inflow throughout the year and local people get an advantage out of the incentives and facilities provided, but what about the other historically significant places which need to be looked after most of them are begging for their survival. The place where the first handmade paper in India was manufactured after the technology was brought here by Mongol invaders to print the religious book Quran is under major threat. The place is significant and there must be much more significant related and all are dying. Even the local tradition of making paper is on the verge of varnish.

As a whole, the tourism industry has challenges in achieving a Sustainable living environment in a core heritage zone. Tourism development and in particular sustainable tourism development faces mired the following

Challenges:

- Inadequate marketing of paper and its product development;

- Overlooking and Bypassing heritage buildings in the village
- Lack of finance development
- Lack of skilled local labor related to the paper industry
- Lack of private sector incentives;
- Bureaucratic delays/no schemes planned;
- High costs of operations

The following are a few suggestions on the impacts of Aurangabad tourism development

- Need for good resorts(Star Hotels) or facilities near Ajanta Caves for Local economic growth
- Need for regular meetings and surveys of residents to understand and involve in the decision-making of tourism policies
- Need for a master plan for Homestays and local products (handicraft, items of Ajanta Caves, etc.)

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