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Biogenic Ag-nanoparticles as heterogeneous catalyst for synthesis of 2-aryl benzimidazoles at room temperature

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A green, straightforward and rapid method of synthesizing silver nanoparticles in an aqueous medium has been developed using *Syzygium jambos* (L.) Alston (Bogi Jamu) leaves extract and aqueous $AgNO_3$ solution. The silver nanoparticles were characterized by UV–vis spectroscopy, transmission electron microscopy, X-ray diffraction and scanning electron microscopy. The results indicate the formation of spherical, nano-sized particles, with average particle size of 20 nm based on TEM analysis. The Ag-nanoparticles efficiently catalyze the synthesis of 2-substituted benzimidazoles by the reaction of aldehydes with *o*-phenylenediamine in DMSO at room temperature. Simple workup, mild reaction conditions, low cost, easy separation, and reusability of the catalyst are some advantages of this method.

Keywords: Biogenic synthesis, Catalysts, Heterogeneous catalysts, Nanoparticles, Silver nanoparticles, Benzimidazole

2-Aryl benzimidazoles and their derivatives have received extensive interest in diverse areas of chemistry as these structural motifs are the main constituent in numerous pharmaceutical agents possessing a wide range of biological applications[1] such as antihistamine, antiulcer agents, topoisomerase inhibitors[2], anticancer[3], antihypertensive[4], antimicrobial[5] drugs. Also, 2-aryl benzimidazole derivatives are industrially used as fluorescent acid-base indicators[6], dopants for plastic scintillation applications[7] and subunits of polybenzimidazoles as thermally stable polymers[8]. Due to their biological and industrial importance and wide applications, the synthesis of these benzimidazole derivatives has been extensively studied in synthetic organic chemistry in recent years. In all of the reported procedures, two main synthetic routes could be observed; one route in general involves direct coupling of a carboxylic acid or carboxylic acid derivatives with an appropriate *o*-phenylenediamine under the influence of a strong acid such as hydrochloric acid[9] or polyphosphoric acid[10] at high temperature or under microwave irradiation[11]. The second route involves a two-step procedure that includes the oxidative cyclodehydrogenation of Schiff bases, which are often generated from the condensation of *o*-phenylenediamines and aryl aldehydes. The direct condensation of *o*-aryldiamines and aromatic aldehydes at room temperature is less developed because as previously reported this apparently simple reaction is a complex sequence of competing reactions and leads to the formation of a complex mixture of products containing 1,2-disubstituted benzimidazoles and 1,2-disubstituted benzimidazolines as main byproducts[12]. Therefore, in the second route various oxidative and catalytic reagents have been employed[13-23]. The main drawback of these methods is that a large part of the catalyst is not recoverable and is destroyed in the work-up procedure.

However in recent years, many heterogeneous catalysts, viz., animal bone meal,[24] $FeCl_3$-doped polyaniline nanoparticles,[25] CuO nanoparticles supported on silica[26], etc. have been reported for the synthesis of 2-aryl benzimidazole derivatives. These synthetic organic routes using heterogeneous catalysts have advantages over their counterparts like ease of handling of the catalyst, enhanced reaction rates, greater selectivity, simple work-up and recyclability of the catalyst[27].

Current advances in nanoscience and nanotechnology have also led to the expansion of an efficient synthesis of bioactive compounds using nanoparticles in an ecologically and economically favorable way which is an immense challenge in modern chemistry[28]. In our continuous search for a better catalyst for the synthesis of benzimidazoles in terms of operational simplicity, reusability, and economic viability, herein we report Ag-nanoparticles as a new and reusable heterogeneous catalyst, synthesized by using aqueous *Syzygium jambos* (L.) Alston (Bogi Jamu) leaves extract. This heterogeneous catalyst system exhibits an excellent catalytic activity and recyclability for the construction of the 2-aryl benzimidazoles framework. Moreover, synthesis of Ag-nanopaticles is easy, cheap and green.

There are many reports on synthesis of Ag, Au, Pd nanoparticles using various plant leaves extracts[29]. To the best of our knowledge, this is the first synthetic report for the synthesis of silver nanoparticles using *S. jambos* (L.) Alston plant leaves extract and successfully utilized for synthesis of 2-arylbenzimidazoles at room temperature.

Materials and Methods

All the substituted aldehydes, diamines, DMSO, ethanol, ethyl acetate and hexane were obtained from Aldrich or Merck and used without further purification.

Synthesis of Ag-nanoparticles

Fresh leaves of *S. jambos* (L.) Alston (Bogi Jamu) were collected from the nearby areas of Dibrugarh University and washed thoroughly with distilled water and shade dried. Dried leaves (10 g) were crushed in a mortar into fine powder.

Leaves extract of *S. jambos* (L.) Alston was prepared by taking 10 g of the powdered sample in 100 mL deionised water and heated for 4 h at 40 °C. After cooling at room temperature, the solution was filtered and the filtrate was used for supplementary experiment.

The *S. jambos* (L.) Alston leaves extract (2 mL) was added to 30 mL of 1 mM aqueous $AgNO_3$ solution (5.1 mg of $AgNO_3$ in 30 mL water) and stirred at room temperature for 4 hours. The color of the reaction product turned dark brown due to the reduction of Ag^+. Finally the reaction mixture was centrifuged and washed three times with distilled water to give 3.0 mg Ag nanoparticles (93% yield). The nanoparticles were characterized using UV-vis spectroscopy, FT-IR, XRD, SEM and TEM.

Characterization

The formation of nanoparticles was monitored by UV-vis spectroscopy recorded in the range between 200–900 nm using UV-1700 (Shimadzu) spectrophotometer. The Ag nanoparticles synthesized after 2–4 h of reaction with the *S. jambos* (L.) Alston leaves extract were centrifuged at 10,000 rpm for 15 min to isolate the Ag-nanoparticles from other compounds present in the solution, followed by redispersion in sterile distilled water to remove any uncoordinated biological molecules. To ensure better separation, this process was repeated three times. The purified particles were then dried and the powder was characterized by FT-IR spectra recorded as KBr pellets on a Shimadzu IR-Prestige-21 FT-IR spectrophotometer operating from 400 to 4000 cm^{-1}. The ^1H NMR spectra of the sample were recorded on a Bruker Avance II 400 MHz spectrometer using TMS as an internal standard in DMSO-d_6. Electronic absorption spectra were obtained with Shimadzu UV-1700 UV-vis spectrophotometer at room temperature.

X-ray diffraction (XRD) patterns were obtained on a Rigaku X-ray diffractometer (model: ULTIMA IV, Rigaku, Japan) with Cu K_α X-ray source ($\lambda = 1.54056$ Å) at generator voltage of 40 V, generator current 40 mA with the scanning rate as 2° min^{-1}. The SEM and TEM analysis were carried out to study the morphology, shapes and size of the nanoparticles using SEM (model 6390 LV JEOL Asia PTE Ltd., Singapore/JEOL JSM) and TEM (model TECNAI G2 20 S-TWIN (200KV); Resolution: 2.4 Å).

General procedure for synthesis of 2-aryl benzimidazole:

To a mixture of *o*-phenylenediamine (1.0 mmol) and aldehyde (1.0 mmol) in DMSO (2 mL), 5 mol% of Ag-nanoparticles catalyst were added. The resulting mixture was stirred at room temperature for appropriate time. After completion of the reaction as monitored by TLC, the reaction mixture was diluted with ethanol and centrifuged to separate the catalyst. To the reaction mixture, water was added to precipitate out the desired product which was filtered, washed several time with water and then dried.

2-Phenyl-1H-benzimidazole (1): IR (KBr, cm^{-1}): 1620, 3444. ^1H NMR (DMSO-d_6): δH 7.14–7.25 (m, 2H), 7.44–7.61 (m, 5H), 8.20 (d, 2H), 12.94 (s, 1H); ^{13}C NMR (DMSO-d_6): δC 122.1, 126.4, 128.4, 128.9, 129.2, 129.8, 130.1, 151.2.

2-(4-Chlorophenyl)-1H-benzimidazole (2): IR (KBr, cm^{-1}): 3350, 2920, 1630, 1600; ^1H NMR (DMSO-d_6): δC 12.90 (bs, 1H, NH), 8.18 (d, 2H), 7.65-7.55 (m, 4H, arom.), 7.13-6.99 (m, 2H, arom.);^{13}C NMR (DMSO-d_6): δC 150.6, 134.9, 131.6, 129.5, 129.2, 128.5.

2-(2-Hydroxyphenyl)-1H-benzimidazole (3): IR (KBr, cm^{-1}): 3325, 3043, 1604, 1530, 1489, 1279; ^1H NMR (DMSO-d_6): δC 12.92 (bs, 1H, NH), 8.06 (d, 2H), 7.41-7.23 (m, 4H, arom.), 7.08–7.00

(m, 2H, arom.), 5.39 (s, 1H, OH); ^{13}C NMR (DMSO-d_6): δC 158.5, 152.2, 132.2, 126.7, 119.5, 117.6, 113.1.

2-(2-Nitrophenyl)-1H-benzimidazole (5): IR (KBr, cm^{-1}): 1338, 1516, 1620, 3421; ^{1}H NMR (DMSO-d_6): δH 13.05 (bs, 1H, NH), 8.19-7.97 (m, 2H), 7.89-7.62 (m, 2H), 7.52-7.26 (m, 4H); ^{13}C NMR (DMSO-d_6): δC 149.4, 147.7, 133.1, 131.3, 124.7, 124.6.

2-(2-Chlorophenyl)-1H-benzimidazole (6): IR (KBr, cm^{-1}): 3413, 1620, 1589, 1440, 1274, 1047, 743. ^{1}H NMR (DMSO-d_6): δH 12.74 (s, 1H), 7.89-7.92 (m, 2H), 7.51-7.67 (m, 4H), 7.20-7.24 (m, 2H); ^{13}C NMR (DMSO-d_6): δC 149.5, 132.5, 132.0, 131.6, 130.8, 130.4, 127.9.

5-Nitro-2-phenyl-1H-benzimidazole (7): IR (KBr, cm^{-1}): 3377, 1625, 1519, 1335, 694, 735 ^{1}H NMR (DMSO-d_6): δ H 7.57 (m, 2H), 7.59 (m, 1H), 7.74 (d, 1H), 8.09-8.12 (m, 1H), 8.18-8.2 (m, 2H), 8.45 (s, 1H), 13.60 (s, 1H). ^{13}C NMR (DMSO-d_6): δC 151.2, 147.2, 143.5, 136.6, 132.2, 129.3, 127.5, 117.6, 113.3.

2-(4-Chlorophenyl)-5-nitro-1H-benzo[d]imidazole (8): IR (KBr, cm^{-1}): 3375, 1623, 1518, 1334, 692, 736. ^{1}H NMR (DMSO-d_6): δH 10.01 (1 H, NH), 8.85 (s, 1H), 8.12-8.04 (m, 2H), 7.95-7.91 (dd, 1H), 7.55-7.39 (m, 2H); ^{13}C NMR (DMSO-d_6): δC 151.6, 148.2, 143.8, 136.3, 135.4, 133.9, 131.5, 129.2, 128.6, 124.9.

4-(5-Nitro-1H-benzo[d]imidazol-2-yl)phenol (9): IR (KBr, cm^{-1}): 3377, 1622, 1524, 1333, 692, 735. ^{1}H NMR (DMSO-d$_6$): δH 13.34 (1H, NH), 8.47-8.44 (d, 1H), 8.43 (s, 1H), 8.30-8.04 (m, 2H), 7.67-7.64 (d, 1H), 6.97-6.84 (m, 2H), 5.60 (s, 1H, OH); ^{13}C NMR (DMSO-d$_6$): δC 152.6, 149.2, 140.8, 135.3, 134.4, 133.9, 130.5, 129.2, 127.6, 122.9.

5-Nitro-2-(2-nitrophenyl)-1H-benzo[d]imidazole (10): IR (KBr, cm^{-1}): 3379, 1621, 1520, 1336, 696, 734. ^{1}H NMR (DMSO-d$_6$): δH 9.05 (1H, NH), 8.46-8.43 (d, 1H), 8.10-8.09 (d, 1H), 8.00-7.75 (m, 5H); ^{13}C NMR (DMSO-d$_6$): δC 156.5, 151.4, 149.7, 136.4, 140.0, 133.9, 132.4, 130.8, 130.3, 125.3, 124.8, 114.1, 113.6.

2-(5-Nitro-1H-benzo[d]imidazol-2-yl)phenol (11): IR (KBr, cm^{-1}): 3377, 1622, 1524, 1333, 692, 735. ^{1}H NMR (DMSO-d$_6$): δH 12.90 (1H, NH), 8.37-8.34 (d, 1H), 8.23 (s, 1H), 7.79-7.64 (m, 2H), 7.66-7.24 (m, 3H), 5.50 (s, 1H, OH); ^{13}C NMR (DMSO-d$_6$): δC 154.1, 152.6, 149.2, 140.8, 135.3, 134.4, 133.9, 130.5, 129.2, 127.6, 122.9, 117.2, 113.1.

2-(2-Chlorophenyl)-5-nitro-1H-benzo[d]imidazole (12): IR (KBr, cm^{-1}): 3377, 1625, 1519, 1335, 694, 735. ^{1}H NMR (DMSO-d$_6$): δH 9.01 (1H, NH), 8.42 (s, 1H), 8.41-8.40 (d, 1H), 7.97-7.93 (m, 1H), 7.58-7.39 (m, 4H); ^{13}C NMR (DMSO-d$_6$): δC 149.2, 141.0, 139.6, 138.6, 132.7, 131.6, 130.9, 130.6, 130.0, 128.6, 128.1, 128.1, 119.4.

Results and Discussion

Characterization of the Ag-nanoparticles

The formation of Ag-nanoparticles was visually confirmed by color change from light yellow to dark brown which arises due to surface plasmon resonance phenomenon of the silver nanoparticles[30]. The formation of nanoparticle was monitored by recording the UV-vis spectra. Figure 1 shows the UV-vis spectra of silver nanoparticles after 4 h of reaction with a characteristics peak at 451 nm, which confirms the fairly rapid bio-reduction of Ag$^+$ to Ag^0 major part of the reduction of Ag$^+$ ions wase completed within 4 hs, after addition of the *S. jambos* (L.) Alston leaves extract to the metal ion solutions (Fig. 1). The inset of Fig. 1 shows the visible color change after 4 h during Ag-nanoparticles synthesis.

The FT-IR analysis was carried out to identify the possible biomolecules responsible for the reduction of Ag$^+$ ions and capping of the bioreduced Ag-nanoparticles synthesized by the *S. jambos* (L.) Alston leaves extract. Figure 2(a) shows the FT-IR spectrum of the Ag nanoparticles synthesized using *S. jambos* (L.) leaves extract. Ag nanoparticles formed by reduction of Ag$^+$ ions using the leaves extract showed peaks at 3259 cm^{-1} (weak peak for OH vibration), 1680 cm^{-1}, 1442 cm^{-1}, 1557 cm^{-1}, 1515 cm^{-1}, 1392 cm^{-1}, 1090 cm^{-1}, 1051 cm^{-1}. The FTIR spectra of 2(b) only the aqueous extract of *S. jambos* (L.) Alston leaves shows the peaks at 3248 cm^{-1} (strong peak for OH vibration), 2095 cm^{-1}, 1608 cm^{-1}, 1409 cm^{-1}, 1267 cm^{-1} and 1092 cm^{-1}. This result suggests the presence of flavonoid adsorbed on the surface of metal

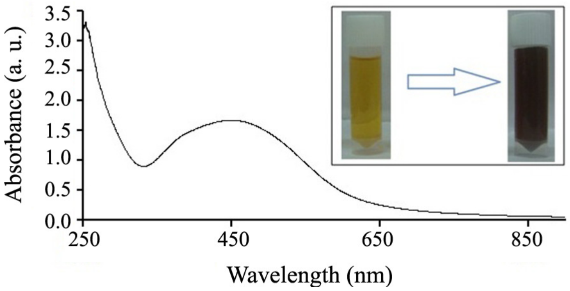


Fig. 1 – UV-vis spectrum of Ag-nanoparticles formed on reacting 1 m*M* aqueous solution of AgNO$_3$ with *Syzygium jambos* (L.) Alston leaves extract. [Inset: Formation of Ag-nanoparticles. Left: AgNO$_3$ solution after addition of plant extract; Right: AgNO$_3$ solution and plant extract after 4 h].

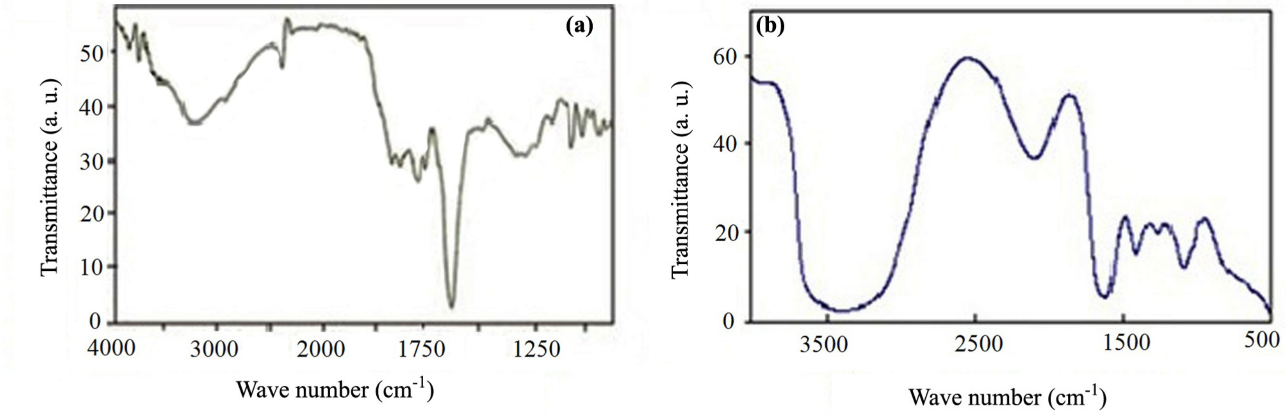


Fig. 2 – (a) FT-IR spectrum of Ag nanoparticles synthesized by reduction of Ag$^+$ ion by *Syzygium jambos* (L.) Alston leaves extract, and, (b) FT-IR spectra of aqueous extract of *Syzygium jambos* (L.) Alston leaves alone.

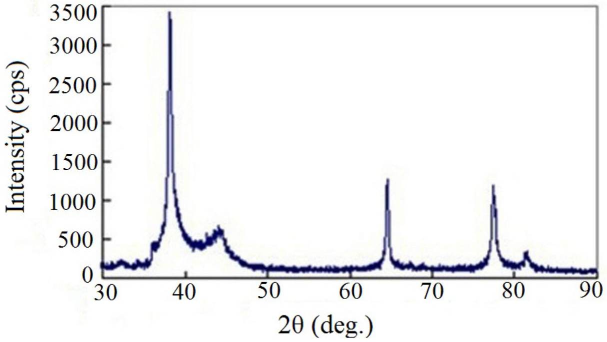


Fig. 3 – XRD pattern of Ag nanoparticles formed on reacting *Syzygium jambos* (L.) Alston leaves extract with AgNO$_3$ solution.

nanoparticles. The flavonoid and phenolic acids molecule play a major role in the synthesis of Ag-nanoparticles. Strong peak for OH vibration at 3248 cm^{-1} in Fig. 2(b) is due to the presence of phenolic group and water present in the sticky part of the aqueous extract of respective plant material.

The formation of the Ag-nanoparticles was further confirmed by the XRD analysis. The XRD patterns of Ag-nanoparticles using *S. jambos* (L.) Alston leaves extract are shown in Fig. 3. The diffraction peak at 2θ values of 38.10°, 44.16°, 64.52° and 77.40° are assigned to the (111), (200), (220) and (311) respectively of lattice plane of face centered cubic (fcc) for Ag-nanoparticle. The corresponding '*d*' spacing of Ag-nanoparticles were 2.360, 2.0492, 1.4431 and 1.2320 respectively. The high intensity diffraction peak observed at 38.10°, to Ag, confirmed that the nanoparticles were composed of pure crystalline Ag[31].

To study the size and shape of the prepared Ag-nanoparticles, SEM and TEM analysis were carried out. The SEM image (Fig. 4) confirmed that the Ag-nanoparticles exhibit spherical shape with the average size in the range of 0.60–0.70 µm. This SEM image also indicates that synthesized nanoparticles were not aggregated (monodisperse) and have high density as well as stability.

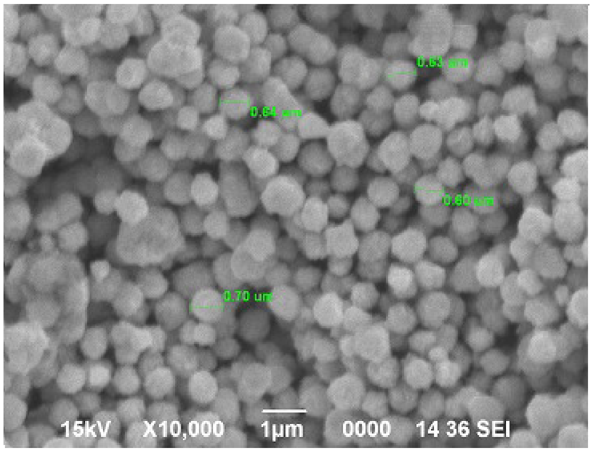


Fig. 4 – SEM image of the silver nanoparticles formed on reacting Szygium jambos (L.) Alston leaves extract with AgNO$_3$ solution.

TEM analysis was used to evaluate the morphology and size of some representative silver particles obtained. In Fig. 5, the TEM images show that the Ag-nanoparticles are well dispersed in colloidal solution with spherical particles of size 20 nm.

Optimization of synthesis parameters

We optimized various parameters including solvent, amount of catalyst and the reaction time for the reaction of *o*-phenylenediamine (1.0 mmol) with 4-chlorobenaldehyde (1.0 mmol) as a model reactant (Scheme 1) and the resultant data are listed in Table 1.

Various solvents were examined during the optimization studies and it was found that these reactions appeared to be largely dependent on the nature of the solvent. The data in Table 1 shows that amongst the five solvents investigated, viz. ethanol (EtOH), water (H_2O), dimethyl sulfoxide (DMSO), N,N-dimethylformamide (DMF), acetonitrile (AcCN), and dimethyl sulfoxide (DMSO) was found to be the best. DMSO is an aprotic polar solvent and it seems especially well suited as a medium for C-heteroatom bond formation in transition metal catalysed organic reactions[32]. Herein we have used Ag nanoparticles as a catalyst and not a transition metal complex, and the exact role of DMSO is yet to be investigated. We prepared three batches of Ag-nanoparticles to optimize the reaction and got almost the same yield of the products in each batch. For the present studies 5 mol% of Ag-nanoparticles was found to be the optimum amount of catalyst. In the absence of catalyst, no reaction takes place at room temperature. We also carried out a blank reaction using only plant extract at room temperature for 24 h, no reaction occurred for the blank reaction. The 2-arylated benzimidazole product was obtained in 95 % yield after stirring at room temperature in DMSO for 4 h. Finally, the conditions mentioned in entry 3 (Table 1) were chosen as the optimum condition for the synthesis of 2-arylated benzimidazole from *o*-phenylenediamine and 4-chlorobenaldehyde.

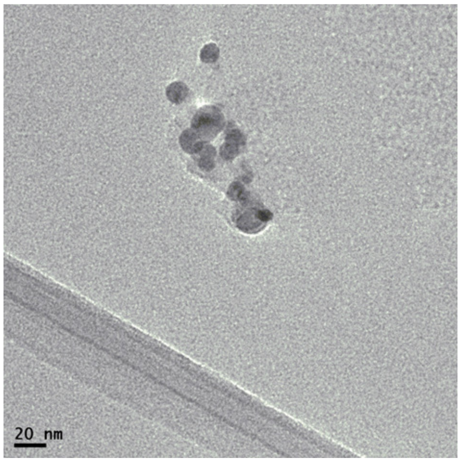
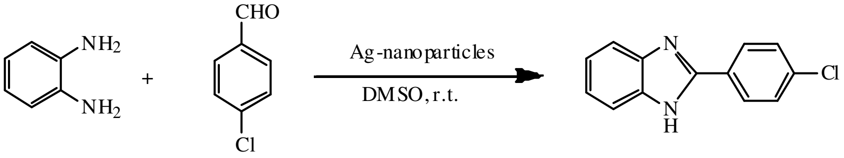


Fig. 5 TEM image of the silver nanoparticles formed on reacting S*zygium jambos* (L.) Alston leaves extract with $AgNO_3$ solution.

After optimization to expand the synthetic scope of this protocol, the reaction was extended to various aldehyde and *o*-phenylenediamine derivatives. In all cases, reactions were completed in a reasonable time (4–12 h) and 2-aryl bezimidazole derivatives were formed in good yields (82% – 96%). The use of this protocol in the reaction of *o*-phenylenediamine with different aldehydes produced only one of the possible regioisomers in almost all the cases (Table 2).



Synthesis of benzimidazole by using Ag nanoparticles a model reaction

Scheme 1

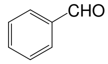
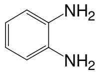
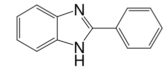
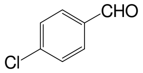
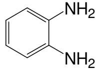
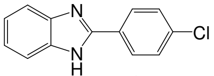
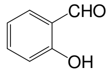
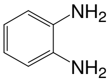
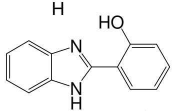
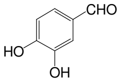
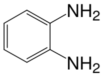
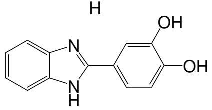
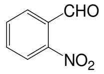
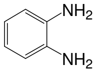
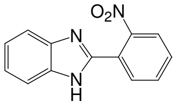
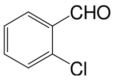
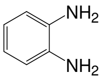
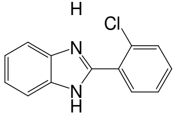
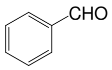
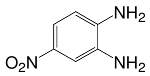
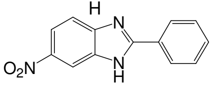
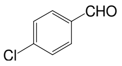
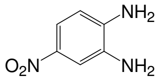
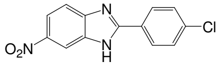
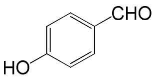
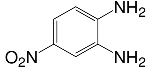
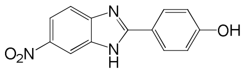
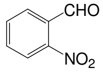
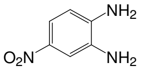
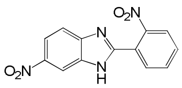
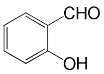
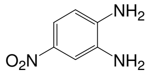
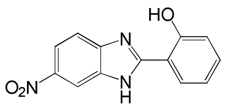
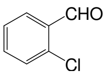
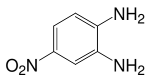
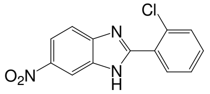
Table 1 – Effect of various solvents in the condensation reaction of *o*-phenylenediamine (1.0 mmol) with 4-chlorobenzaldehyde (1.0 mmol) at room temperature using Ag-nanoparticles

Entry	Catalyst (mol %)	Solvent	Time (h)	Yield[a] (%)	TOF[b] (h^{-1})
1	5	Ethanol	18	94	1.04
2	5	Water	24	52	0.43
3	5	DMSO	4	96	4.80
4	5	DMF	8	90	2.25
5	5	Acetonitrile	20	86	0.86
6	3	DMSO	4	89	7.40
7	1	DMSO	4	75	18.74
8	7	DMSO	4	97	3.45
9	No catalyst	DMSO	24	No reaction	-
10	No catalyst	Plant extract	24	No reaction	-

[a]Isolated yield.

[b]TOF (Turn Over Frequency) = mol of product /(time × mol of catalyst).

Table 2 – Ag-nanoparticles catalyzed synthesis of benzimidazole derivatives[a]

Aldehyde	Diamine	Product	Time (h)	Yield[b] (%)	TOF[c] (h^{-1})
			4	95	4.75
			4	96	4.80
			5	85	3.40
			24	trace	---
			8	89	2.22
			5	91	3.64
			6	89	2.96
			9	86	1.91
			10	83	1.66
			8	85	2.12
			12	82	1.36
			10	84	1.68

[a]React. cond.: *o*-phenylenediamine: (1.0 mmol); aldehyde: (1.0 mmol); Ag-nano catalyst: (5 mol%) in DMSO (2 mL).

[b]Isolated yield.

[c]TOF (Turn Over Frequency) = mol of product/ (time×mol of catalyst).

Recyclability

One of the very important industrial applications of heterogeneous catalyst is its reusability. After completion of the reaction, the mixture was diluted with ethanol and centrifuged to separate the catalyst. Then it was washed with ethylacetate and the Ag-nanoparticles were reused. With almost consistent activity, the catalyst can be used up to four times. Even at the fourth run, the yield was 90%, signifying an excellent reusability and chemical stability of the catalyst.

Conclusions

In the present study, Ag-nanoparticles were synthesized using *S. jambos* (L.) Alston leaves extract and found to be a cheap, air-stable and efficient recyclable catalyst for the synthesis of 2-aryl benzimidazole derivatives by coupling of *o*-phenylenediamine with aldehyde in DMSO as a solvent at room temperature. The mild reaction conditions, short reaction time, high yields, easy and quick isolation of the products, recyclability of the catalyst, eco-friendly and good selectivity are the main advantages of this protocol. To the best of our knowledge, this is the first synthetic report for the synthesis of silver nanoparticles using *S. jambos* (L.) Alston leaves extract and successfully utilized for synthesis of 2-arylbenzimidazoles at room temperature.

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