Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 4 [10] September 2015: 79-85

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.533
Universal Impact Factor 0.9804

ORIGINAL ARTICLE **OPEN ACCESS**

Lemon Juice catalyzed Ultrasound assisted synthesis of Schiff's base: A Total Green approach

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ABSTRACT
A classical Schiff's base was prepared from Ortho-amino benzoic acid (Anthranilic acid) and 4- hydroxy-3-methoxy benzaldehyde using lemon juice as a green acid catalyst, by conventional/nonultrasonic (NUS) and ultrasonic methods. Percentage yield, time of reaction and total energy consumed in both methods were calculated and compared. Synthesized Schiff's base was characterized by FT-IR and ^{1}H-NMR, X-RD, PSM, and SEM analysis were performed to understand the particle physical characteristics i.e. particle size, crystallinity and morphology of the two methods. Experimental data indicates that ultrasound assisted method was better in terms of high yield, economical, mild reaction condition, eco-friendly, and easy work-up procedures. It was also found that ultrasonically synthesized Schiff's base have more crystalline compared to conventional one. Most importantly ultrasonically (US) synthesized Schiff's base was more energy efficient than conventional/nonultrasonic (NUS) method. Thus a total green approach was achieved.
Keywords: *Green chemistry, Lemon juice, Schiff's base, Sonochemistry.*

Received 20.08.2015 Revised 01.09.2015 Accepted 07.09.2015

INTRODUCTION

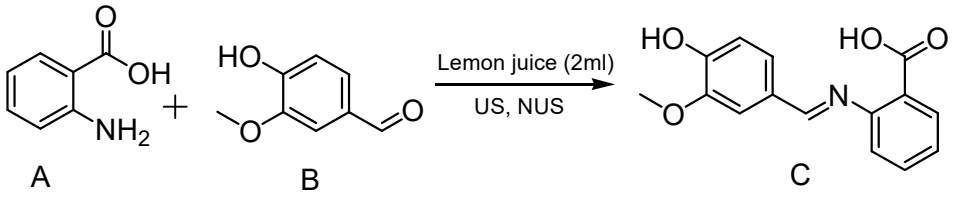
Green chemistry approach as an eco-friendly approach has tremendous application for the synthesis of various organic compounds and key intermediates in recent past [1]. This technique involves as an alternative reaction media to replace hazardous and expensive solvents routinely used in organic synthesis [2-4]. Recently fruit juice is known to be potential organic solvents for the synthesis of compounds of pharmaceutical interest [5]. The widespread applications of different fruit juices are due to their non toxic, safe, inexpensive and environmentally benign nature [6]. Fruit juice is being used on regular basis in various organic transformation reactions [7-10]. Among fruit juices, Lemon juice is the most familiar in different important organic reactions like Knoevenagel condensation reaction [11], synthesis of triazoles [12] and synthesis of Dihydropyrimidinone [13] and many more.

Schiff's bases are important member of organic compounds possesses varieties of biological activities such as anticancer [14], antibacterial [15,16] anti-fungal [17]. If we look, the literature's relating to Schiff's base synthesis many different techniques has been adopted [18,19]. There are numerous environmental friendly, solvent free and metal catalyzed reactions were reported [20-22]. So far, these methods have number of limitations pertaining to environmental pollution, cost effectiveness, low yield of products. Ultrasound technique is invariably fasten the reaction rate, improved yields, shorten the reaction time and using low energy input[23]. Mechanism involves in ultrasonic reactions is cavitation, a type of physical force producing growth, oscillation, and bubble collapse inside the reaction [24]. Present work reports the synthesis of classical Schiff's base using lemon juice as a green catalyst. Schiff's base were synthesized by conventional as well as ultrasonic methods in order to observe percentage yield, reaction time, morphology and energy consumption by these processes to achieve total green approach.

MATERIALS AND METHODS

Ortho-amino benzoic acid (Anthranilic acid) was purchased from Win-lab, UK and 4- hydroxy-3-methoxy benzaldehyde was purchased from BDH laboratory supplies, England. Fresh fruit of lemon purchased from local market.

Scheme: Lemon Juice catalyzed synthesis of Schiff's base.



Ultrasound Set-up

For sonochemical synthesis ultrasound was generated with the help of ultrasonic instrument set-up (Probe). The specification of ultrasound set-up, processing parameters used during the experiments are;

Make: ACE, USA.

Operating frequency: 20 kHz.

Rated output power: 130W.

Diameter of stainless steel tip of Probe: 8×10^{-2} m.

Surface area of ultrasound irradiating face: 8×10^{-4} m^2.

Preparation of Lemon Juice from the Fruits of Citrus Lemon

A fruit of fresh Citrus lemon was purchased from the local market. The juice was extracted mechanically and centrifuged using Centrifuge machine (EBA-20, Hettich, Germany). Clear portion of the juice was used as a catalytic solvent for the above reaction.

Synthesis of Schiff's base via Conventional (NUS) Method

A mixture of ortho-amino benzoic acid (Anthranilic acid) A (0.01mole) and 4- hydroxy-3- methoxy benzaldehyde B (0.01 mole) was reacted using lemon juice (2mL) and refluxed about 1h and monitored with TLC (*n*-hexane : EtOAc, 80 : 20) till completion of the reaction by observation of single new spot and disappearance of staring materials. A white solid obtained after the recrystallization with ethanol. Schiff's base so obtained was characterized by FT-IR, ^{1}H-NMR and ^{13}C-NMR to authenticate the desired product. X-ray diffraction (XRD) technique and scanning electron microscopy (SEM) was used for further study of Schiff's base. The reaction was repeated at least three times to assess the time of reaction. Results were computed by averaging the each result and were presented with promising error (±variation).

Synthesis of Schiff's base via ultrasonic (US) Method

A mixture of *ortho*-amino benzoic acid (Anthranilic acid) A (0.01 mole) and 4- hydroxy-3- methoxy benzaldehyde B (0.01 mole) was taken in sonicating flask and then lemon juice (2mL) was added drop wise under sonication probe (ACE probe, 20 kHz frequency) at 40% amplitude for 2 min with a 5s ON and 5s OFF cycle from time t = 0 h. After complete addition of lemon juice (up to 2 min), the reaction mixture was again exposed to acoustic cavitation (by using ACE ultrasonic probe) for further 10 min, by keeping all sonication parameters constant. The temperature of the reaction was maintained at 30±2^{o}C by using lab air condition (AC). Approximately after 10 min reaction was completed and confirmed by thin layer chromatography (*n*-hexane: EtOAc, 80: 20). Reaction was repeated three times to authenticate the process. Rest of the procedure was followed as described earlier in NUS method of Schiff's base synthesis.

Characterization

The Schiff's base was characterized by studying their X-ray diffraction (XRD) patterns using Rigaku Ultima IV X-ray Diffractometer. XRD patterns of Schiff's base were recorded at angles between 2^o and 80^o; with a scan rate of 2^o/min. Debye–Scherrer equation were applied to determine crystalline sizes of the compound. Particle size measurement (PSM) of the Schiff's base sample was calculated by using microtrack nanowave particle size analyzer instrument.

Fourier Transform Infra Red Spectroscopy (FTI-R) spectra of the Schiff's base were recorded using KBr discs using FT/IR - 4100 JASKO model in the ratio of 1:100. ^{1}H-NMR, ^{13}C-NMR spectra for elucidating total proton and carbon were recorded by modern NMR instrument BRUCKER-PLUS (500MHz) using TMS as internal standard. Scanning electron microscopy (SEM) analysis was done to know the surface characteristics of the compound using Carl Zeiss EVO LS10 (Oberkochen, Germany). Coating was carried out using quorum Q150 R S (Quorem Technologies Ltd, 2 Acorn House, The Broyle, Ringmer, East, Sussex, United Kingdom) sputter coater by deposition of gold on the samples.

RESULTS AND DISCUSSION

Reaction time and % Yield

Total time taken for conventionally and ultrasonically synthesized Schiff's base were found 1h and 10 min, respectively (Table 1).The time of reaction and % yield was also checked in ultrasonically synthesized Schiff's base by considering effect of amplitude (Power density). It was observed that as the

% amplitude increased from 30% to 50%, time of completion of reaction decreased from 780 to 540 s (Table 2).

It was also found that % yield of the reaction in case of ultrasonically (US) synthesized Schiff's base (83.71±1.47%) was higher as compared to conventional (NUS) (74.16±2.70%) Table1.The less time taken to the formation of desired compound by ultrasonic method as compared to conventional might be due to acoustic energy produced under ultrasonic irradiation.

Furthermore, effect of % amplitude (power density) variation on the % yield of synthesized Schiff's base was also marked. It was found that % amplitude increased from 30% to 50%, yield of the reaction was increased up to 40% amplitude and then constant up to 50% amplitude (Table 2).Therefore, 40% amplitude was considered best for the Schiff's synthesis.

X-ray Diffraction (XRD) Analysis

X-ray diffraction analysis is helpful in determining crystalline and amorphous nature of synthesized compounds. It provides idea about structure, chemical composition and physical properties of compounds under examination. X-ray diffraction is also useful in elucidating crystalline size and % crystallinity of the synthesized compounds. From the XRD pattern it was evident that the ratio of the amorphous area of the X-ray diffractogram to the total area gives amorphous phase portion of the sample. Crystallite nature (size) of the compound may be determined by the Debye–Scherrer equation. The Debye–Scherrer equation compares the peak breadth of a particular phase of a compound to the mean crystallite size. As per the rule of full width at half maximum (FWHM) of the diffraction peaks, average size of the particles can be measured from the Scherrer equation.

The equation represented as:

$\beta hkl = K\lambda / (Dhkl \times Cos\theta hkl)$.....(1)

Where:

β is the width of the peak at half
maximum intensity of a Specific phase (hkl) in radians,
.K is a constant that varies with the method of taking the breadth
$(0.89 < K < 1)$ for calculation purpose in this experiment $K = 0.9$,
k is the wavelength of incident X-rays,
θ is the center angle of the peak,
D is the crystallite length

Results obtained from x-ray diffraction analysis in the form of % crystallinity and crystalline size has been presented in Table 1. Crystalline area found in US synthesized Schiff's base was more than NUS. Average cryastallinity was also found more in US (37.36%) synthesized Schiff's base than NUS (14.56%) as in Fig 1. Possibility behind the more crystalline area found in US synthesized Schiff's base may be due to energy, obtained from cavitational phenomena and rapid micromixing during sonication. As a result well defined shaped crystals were formed in less time, increasing in overall crystallinity of synthesized Schiff's base. On the other hand less crystalline nature of Schiff's base formed by conventional method might be due to the fact that the compound was exposed for longer time (1h) in comparison to sonochemical method. As a result of which used more energy which may convert crystalline form of compound into amorphous, resulting into a decreased in the crystallinity of the NUS Schiff's base. Moreover, reason to form crystalline nature of compound could not be confirmed, and still needs investigation.

Particle Size Measurement (PSM)

Schiff's base synthesized via conventional as well as ultrasonic method also carried out for particle size analysis using water as dispersing medium. Average particle size for NUS and US synthesized Schiff's base were found to be 431 and 19.36 nm, respectively. Particle size distribution for US at 10% PSM completion, 50% PSM completion and 90% PSM completion were 14.78, 17.89 and 21.64 nm respectively and for NUS sample at 10% PSM completion, 50% PSM completion and 90% PSM completion were 168, 385 and 498nm, respectively. Much larger differences in particle size of two methods might be linked to the effects of ultrasound in US driven Schiff's base as compared to NUS. Physical phenomena such as cavitation, agglomeration, shear forces and attrition produced during chemical reaction might have played significant role to the reduction of particle size in US mediated synthesis of Schiff's base.

Scanning Electron Microscopy (SEM)

Morphology of synthesized Schiff's base by conventional (NUS) and ultrasonic (US) method was done by scanning electron microscopy (SEM) micrograph. SEM images were produced at two different magnifications 2000x and 5000x, respectively to check the variation in size & shape as well as probable agglomeration (Fig 2). Shape of particle in an ultrasonically (US) synthesized compound was appeared as rod shaped (Fig 2, M), but not well defined shape (Fig 2, N) was found in conventionally (NUS) synthesized compound. Attrition and cavitation played an important role in former case to make final compound in a definite shape, while in case of NUS method due to aggregation particle was not showed as

a definite shape. Therefore particles obtained from ultrasonic method were more uniform and crystalline than the conventionally formed particles.

FT-IR and NMR

The FT-IR and NMR were carried out as analytical tools to confirm the formed Schiff's base. The FT-IR spectrum of compound gives an absorption band near 1538cm^{-1} which was a characteristics of C=N group of synthesized Schiff's base. The ^{1}H- NMR and ^{13}C- NMR data of synthesized Schiff's base by NUS and US methods gives: ^{1}H-NMR (500MHz, DMSO-d_6, δ/ ppm): 3.85 (s, 3H, OCH_3), 6.49-7.70(m, 7H, aromatic), 7.72(1H, s, OH),7.92(s, 1H, N=CH), 9.78(1H, s, COOH),^{13}C-NMR (500MHz, DMSO-d_6, δ/ ppm):169.5(CO),151.4 (N=CH),148.9, 148.1, 147.8, 134.1, 131.6, 130.4, 128.6, 126.5, 126.0, 116.2, 115.5, 114.5, (aromatic Carbon), 56.0 (OCH_3).

The formation of Schiff's base was identified by the presence of N=CH appeared at δ 7.92 and 149.6 at ^{1}H-NMR and ^{13}C-NMR respectively.

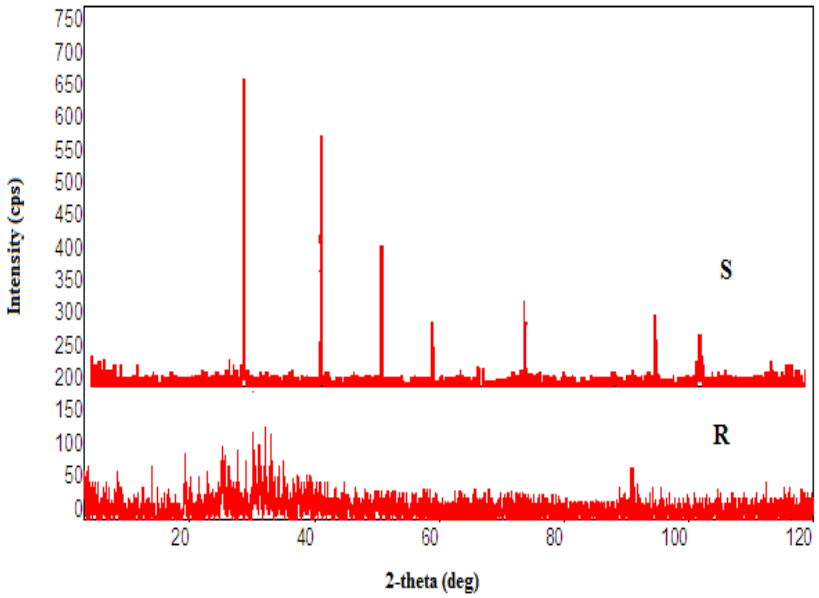


Figure 1 XRD Pattern of the Conventionally (NUS) and Sonochemically (US) Synthesized Chalcone Showing as R and S Respectively.

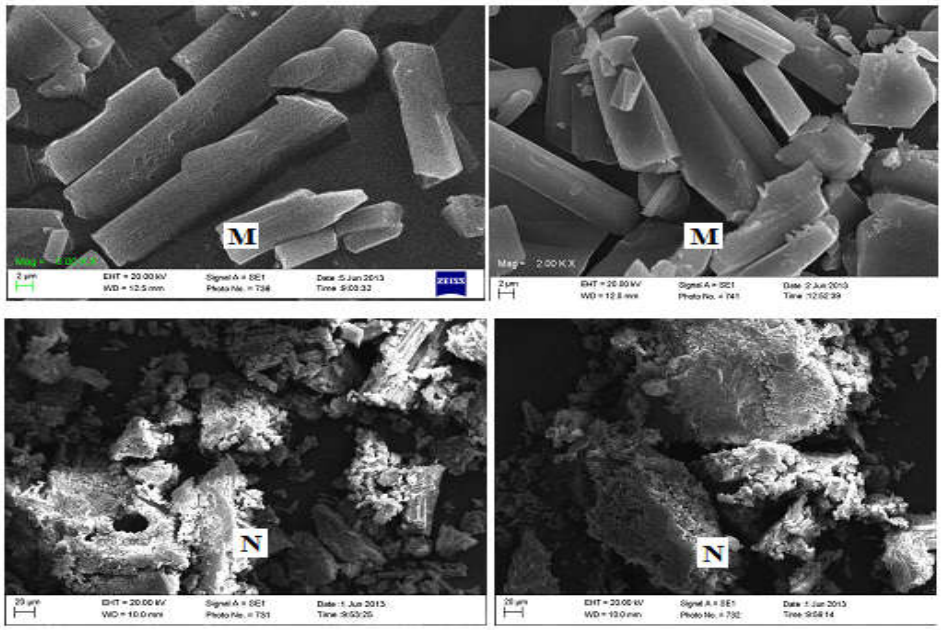


Fig 2: SEM micrograph of synthesized shiffs base.

Table 1: % Crystalinity, Crystalline Size and % Yield of the Conventionally (NUS) and Ultrasonically (US) Synthesized Shiffs base.

Method	Time taken for the completion of the reaction	Crystallinity (%) (Average)	Crystallite size *d* (nm) (Average)	Yield (%)	Energy (J)	Power input (W)
Conventional(NUS)	1hr	14.56	20	74.16±2.70%	-	-
Ultrasonic (US)	10 min	37.36	36	83.71±1.47%	19.74	32.90

Table 2: Effect of % Amplitude (Power Density) on % Yield of Synthesized Shiffs base.

S.No.	% Amplitude	Reactions completed in time (seconds) based on TLC	Energy (J)	Power (W)	Yield (%) in 10 min Average ± Variation
1.	30	780	12.63	10.50	79.27±2.21%
2.	40	600	19.74	25.30	83.71±1.47%
3.	50	540	23.68	39.50	84.03±1.78%

CONCLUSIONS

Present article described about the synthesis of Schiff's base using lemon juice as a green catalyst by conventional (NUS) heating and ultrasonic methods. Experimental data so obtained from both the methods were used to compare in terms of reaction time, percentage yield, energy and morphological data. Ultrasonically synthesized Schiff's base formed in 10 min, relatively more stable and crystalline in nature while in the conventional method more time (1h), less stable and amorphous nature of particle observed. High yield of the product, rapid, economical, environmental benign and energy efficient qualities made the ultrasonic process superior over conventional one. Conclusion is that synthesizing organic compounds by means of green chemistry approach, we can save our environment, valuable time, and money and intern utilize these concepts to form varieties of organic intermediates and final compounds in large scale industry level.

(1) Effectiveness of energy consumption

Appendix 1

A.1. Energy calculations

1. Energy delivered during 10 min for Schiff's base formation by ultrasonic method

- Energy delivered during sonication = Energy required to synthesized Schiff's base
- Electrical energy delivered during sonication using horn for 10 min (indicated by power meter) = 19.74 kJ.
- Efficiency of horn taken for calculation = 30% (estimated independently using calorimetric studies).
- Actual energy delivered by horn during sonication = Energy delivered during sonication using horn in 10 min x Efficiency of horn
  = 19.74 kJ x 30/100 = 5.92 kJ
  Quantity of material processed = Quantity of Ortho-amino benzoic acid(Anthranilic acid)+ Quantity of 4- hydroxy-3- methoxy benzaldehyde+ Quantity of lemon juice
  1.37(g) +1.52(g) +2.34(g) = 5.23 (g)
- Net energy supplied for processing of material using sonochemical method = Actual energy delivered by horn during sonication/Quantity of material processed
  5.92kJ/ 5.23(g) = 1.13 (kJ/g) ---------- (A1)

2. Energy Delivered During Conventional Method

- Voltage input in magnetic stirrer (Fisher Scientific, Model C188618443308, Made in China) = 220 V.
- Current measured using digital multimeter (Model KYORITSU, Made in Japan) = 43 mA = 43 $x10^{-3}$ (A).
  Power input in magnetic stirrer = Voltage input x Current measured
  220(V) x 43 $x10^{-3}$ (A) = 9.4 W (J/s)
- Efficiency of magnetic stirrer taken for the calculation = 40% (estimated independently using calorimetric studies).
- Actual power input in overhead stirrer = Power input in magnetic

stirrer (W) x 40/100

9.4(W) x 40/100 = 3.7 W (J/s)

- Time required for completion of reaction = 1h (3600 s).
- Net energy delivered during conventional method = Power input in magnetic stirrer x Time required for completion of reaction
- 3.7 J/s x 1h x 3600(s/h) = 13320 J= 13.32 kJ ---------- (A2)
- Quantity of material processed = Quantity of Ortho-amino benzoic acid(Anthranilic acid) + Quantity of 4- hydroxy-3- methoxy benzaldehyde + Quantity of lemon juice

1.37(g) +1.52(g) +2.34(g) = 5.23 (g)

- Net energy supplied for processing of material using conventional method = Net energy delivered during conventional method/quantity of material processed

13.32 kJ/ 5.23 = 2.54 (kJ/g) ---------- (A3)

3. Energy Saved

- Net Energy saved = (Net energy supplied for processing of material using conventional method – (Net energy supplied for processing of material using ultrasonic method

2.54(kJ/g) - 1.13 (kJ/g) = 1.41(kJ/g)

AKNOWLEDGMENT

Author is thankful to the department of Pharmaceutics for providing ultrasonic machine to synthesize Schiff's base Prince Sattam Bin Abdulaziz University.

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CITATION OF THIS ARTICLE

MOHAMMED. AFROZ B. Lemon Juice catalyzed Ultrasound assisted synthesis of Schiff's base: A Total Green approach. Bull. Env. Pharmacol. Life Sci., Vol 4 [10] September 2015: 79-85