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# SYNTHESIS OF CHALCONE 1-(2, 4-DIHYDROXYPHENYL)-3-(3- HYDROXY-4-METHOXYPHENYL) PROP-2-EN-1-ONE VIA CONVENTIONAL AND SONOCHEMICAL METHODS: A COMPARATIVE STUDY

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## ABSTRACT

In present work chalcone was synthesized by Nonultrasonic (NUS) and Ultrasonic (US) methods in order to evaluate and compare the two methods in relation to %yield, time of reaction and total energy consumed. Chalcone was synthesized by Claisen–Schmidt condensation using potassium carbonate ($K_2CO_3$) as basic catalyst. The same reaction was run by using another catalyst Potassium hydroxide (KOH) to observe the effect of two catalysts in terms of yield of chalcone, and former was found better and hence $K_2CO_3$ was chosen as a catalyst for the study. Synthesized chalcone was characterized by FT-IR, NMR, X-RD, PSM, and SEM analysis .Total time taken for the synthesis of chalcone was 20 min in US and 4h in NUS method. It was found that the average crystallinity of US synthesized chalcone was approximately three times (33.33%) to that of NUS synthesized chalcone (12.49%). Moreover sonochemical (US) method of chalcone synthesis is more energy efficient ($7.11 \times 10^{-2}$ kJ/g) than conventional (NUS) method ($89.24 \times 10^{-2}$ kJ/g) and a net 82.13 kJ/g energy was saved in this process.

**Keywords: Chalcone, Sonochemistry, Acoustic Cavitaion**

## INTRODUCTION

Chalcones, a well known natural phenol Chalconoids. They act as vital intermediates for a variety of important biological compounds viz: antibacterial, antifungal, antitumor and anti-inflammatory properties **[1-4]**. Chalcones are also natural aromatase inhibitors **[5]**. Chalcones are usually synthesized via the Claisen–Schmidt condensation between acetophenone and benzaldehyde and are catalyzed by acids and bases under homogeneous conditions **[4]**. However, the traditional synthetic procedure for chalcone was done by the Claisen–Schmidt condensation with a longer reaction period and a lower product yield in the presence of KOH as a basic catalyst. Researchers around the corner also reported about the synthetic procedure of chalcones by using new and effective catalysts, such as Zinc oxide **[6]**, organolithium **[7]**, KF–$Al_2O_3$ **[8]**, modified phosphate **[9]**, zeolites and hydrotalcites **[10]** to get a higher product yield, but the preparation of the catalysts is difficult and the cost is also higher.

In the recent past scientists reports the use of ultrasound that may accelerate chemical reactions to provide improved yields, shortened reaction times and increased selectivity, therefore ultrasound irradiation has been recognized as an proficient technique in organic synthesis **[11–14]**. Usually, ultrasound works by the physical mechanism called cavitation; involving the growth, oscillation, and collapse of bubbles under the act of an acoustic field. It has been experimentally proved that, the cavitational collapse creates drastic conditions within the reaction medium for an extremely short time and temperatures of 2,000–5,000 K, pressures up to 1,800 atmosphere pressure. Inside the collapsing cavity have been produced under sonic conditions **[15, 16]**. Cavitation induced effects may causes physical and chemical changes owing to strong shear forces, jets and shock waves. Thus, ultrasound technique has found applications in materials science, life sciences, synthetic chemistry, as well as in medicinal chemistry **[17]**.

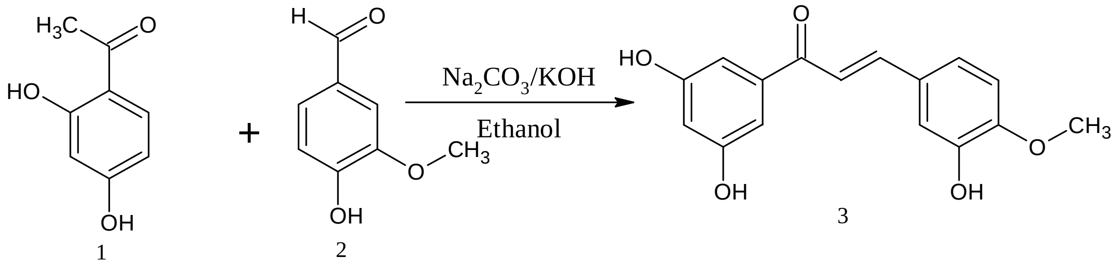
In present paper chalcone was synthesized by using US and NUS methods to observe % yield, time of reaction, % crystallinity, crystallite size, morphology and energy consumption by these two processes were also calculated and compared.

## MATERIALS AND METHODS

### Materials

1-(2, 4-dihydroxyphenyl) ethanone was obtained from sigma Aldrich; 4-hydroxy-3-methoxy benzaldehyde was purchased from BDH laboratory supplies, England. Potassium Carbonate ($K_2CO_3$), Potassium hydroxide (KOH), Hydrochloric acid (HCl) and Ethanol was obtained from Loba Chem.

**Reaction Scheme** 1-(2, 4-dihydroxyphenyl) ethanone **1** and 4-hydroxy-3-methoxybenzaldehyde **2** is reacted in ethanol in presence of Potassium Carbonate or Potassium hydroxide as a catalysts.



## Ultrasound Set-Up

Ultrasound for sonochemical synthesis was generated with the help of ultrasonic instrument set-up (Probe). The specification and details of the Ultrasound set-up, processing parameters used during the experiments were;

**Make: ACE, USA.**

**Operating frequency: 20 kHz.**

**Rated output power: 130W.**

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

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

## Synthesis of Chalcone Via Conventional (NUS) Method

A combination of 1-(2,4-dihydroxyphenyl) ethanone (0.013 mole) and 4-hydroxy-3-methoxybenzaldehyde (0.013 mole) was taken in ethanol (20mL). Potassium carbonate (40%, 20 mL) solution was added drop-wise over 2 min under constant stirring using magnetic stirrer (rpm = 1200). The same reaction was run by using another catalyst Potassium hydroxide to check its influence on the yield of chalcone.The reaction mixture was stirred at room temperature ($30\pm2^{0}$C) till completion of the reaction monitored by thin layer chromatography (TLC). It was found that almost 5h were needed to completion of the reaction. The temperature of the reaction was maintained at $30\pm2^{0}$C by using lab air condition (AC). The time of reaction was estimated by repeating the same reaction not less than three times. The reaction mixture after completion was poured into chilled water (100 mL) and neutralized with hydrochloric acid. The product obtained is in the form of yellowish-white solid, was separated using pump filtration and dried at $60^{0}$C in an oven. The dried product so obtained was then weighed and characterized by FT-IR, $^{1}$HNMR, $^{13}$C NMR to authenticate the formation of desired chalcone. The obtained chalcone was further studied by X-ray diffraction (XRD) and Scanning Electron Microscopy (SEM). The synthesized chalcone by conventional method (NUS) was repeated three times and the results were computed by averaging the individual results and were presented with possible error (±variation).The above reaction was also carried out by using potassium hydroxide as catalyst and the yield% and time taken to completion of reaction is drastically varied.

**Synthesis of Chalcone via sonochemical (US) Method**

A mixture of 1-(2,4-dihydroxyphenyl) ethanone (0.013 mole) and 4-hydroxy-3-methoxybenzaldehyde (0.013 mole) was taken in ethanol (20mL). Potassium Carbonate (40%, 20mL) solution was added dropwise under sonication probe (ACE probe, 20 kHz frequency) at 40% amplitude for 4 min with a 5s ON and 5s OFF cycle from time t = 0 h. After complete addition of potassium Carbonate solution (addition time 4 min), the reaction mixture was again exposed to acoustic cavitation (by using ACE ultrasonic probe) for further 16 min, by keeping all sonication parameter constant which was used during mixing, to complete the reaction of 1-(2,4-dihydroxyphenyl) ethanone and 4-hydroxy-3-methoxybenzaldehyde. The temperature of the reaction was maintained at $30\pm2^0$C by using lab air condition (AC). The reaction progress was monitored by using thin layer chromatography (TLC). After 20 min, reaction between 1-(2, 4-dihydroxyphenyl) ethanone and 4-hydroxy-3-methoxybenzaldehyde were found to be completed. To validate the reaction time, process was repeated thrice. The rest of the procedure was same as described in conventional (NUS) method.

**Characterization**

The chalcone samples (powder form) were first characterized by studying their X-ray diffraction (XRD) patterns on a Rigaku Ultima IV X-ray Diffractometer. XRD patterns were recorded at angles between $2^0$ and $80^0$, with a scan rate of $2^0$/min. Crystallite sizes were determined using the Debye–Scherrer equation. Particle size measurement (PSM) of the chalcone samples was measured by using microtrack nanowave particle size analyzer instrument. Fourier Transform Infra Red Spectroscopy (FTIR) spectra of the chalcone samples were recorded in KBr discs using FT/IR - 4100 JASKO model in the ratio of 1:100. $^1$H-NMR, $^{13C}$NMR, for elucidating total proton and carbon was done by modern NMR instrument BRUCKER-PLUS (500MHz) using TMS as internal standard. Elemental analysis was done to evaluate the presence of C, H, and N by Perkin Elmer-series-II and the results found were within ±0.4% of the theoretical values.

For SEM analysis 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. Scanning electron microscopy was done using Carl Zeiss EVO LS10 (Oberkochen, Germany) scanning electron microscope to know the surface characteristics of the chalcone.

## RESULTS AND DISCUSSION

### Reaction time and % Yield

The time of reaction for conventionally and sonochemically synthesized chalcone were found 5h and 20 min respectively **(Table1)**. Temperature was maintained throughout the reaction in both cases by means of lab air condition at 30±2$^0$C, so effect of temperature variation on the chalcone has not been studied. In another way some experiments were carried out to check the completion of the reaction with varying % amplitude increased from 30% to 50%, time taken for completion of the reaction is considerably decreased from 1500 to 1200s **(Table 2)**.

The % yield of the reaction was calculated in both sonochemical as well as conventional method. Yield was estimated on the basis of initial weight of the raw materials taken and the final weight of the chalcone obtained after the complete drying. During washing unreacted materials like salt is formed were separated before complete drying. It was observed that %yield of the reaction in case of sonochemically (US) synthesized chalcone (89.04±1.02%) was higher as compared to conventionally (NUS) synthesized chalcone (83.07±1.25%) **(Table1)**. The reduction of time in case of sonochemicallly chalcone was possibly due to formation of acoustic energy which in turn produces rapid micromixing as well as faster reaction rate. Furthermore effect of % amplitude (power density) variation on the % yield of synthesized chalcone was also evident. It was observed that % amplitude increases from 30% to 50%, percent yield of the reaction was increases upto 40% amplitude and it was found to be constant up to 50% amplitude **(Table 2)**. Consequently, 40% amplitude is considered to be ideal amplitude for the synthesis of chalcone in present context.

### X-ray Diffraction (XRD) Analysis

X-ray scattering technique is a non-destructive analytical technique which gives the information about the crystalline structure, chemical composition, and physical properties of many synthesized compounds. X-ray diffraction is helpful in determining the % crystallinity and crystalline size of the compound under investigation. From the XRD patterns **(Figure 1)**, it is also possible to compute the % crystallinity and crystallite size. The amorphous phase portion of the sample may be determined by taking the ratio of the amorphous area of the X-ray diffractogram to the total area. The area covered by the amorphous region means that the area of the diffractogram predominantly not belongs to any sharp diffraction peaks. Method for the estimation of amorphous phase part from XRD has been reported in literature **[15, 18]**. Crystallite size of the samples may be obtained using the Debye–Scherrer equation. This equation has been applicable for the assessment of crystallite size of nano metal oxide **[19, 20]**. The Debye–Scherrer equation relates the peak breadth of a specific phase of a material to the mean crystallite size of that material. Quantitatively better the material's crystallites are, sharper are the XRD peaks. According to the full width at half-maximum (FWHM) rule of the diffraction peaks, particles average size can be estimated from the Scherrer equation.

The equation takes the form:

$\beta_{hkl} = K\lambda / (D_{hkl} \times \cos\theta_{hkl})$.........(1)

**Where:**

- $\beta$ 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). Here, in this work, for calculation purpose K = 0.9,
- k is the wavelength of incident X-rays,
- $\theta$ is the center angle of the peak,
- D is the crystallite length

All the characteristics results of chalcone including % crystallinity and crystallite size have been presented in **Table 1**. There are substantial number of crystalline area were found in US synthesized chalcone than NUS. It was also found that US synthesized chalcone shows more average crystallinity (33.33%) than NUS synthesized chalcone (12%). The reason behind this may be the nice atmosphere formed during ultrasonication. Literature **[18]** suggested that there are three possibilities behind an increase in the crystallinity of US chalcone than that of NUS chalcone. **(i)** The necessary energy dissipated due to cavitation phenomenon and micromixing of the materils may increase the randomness of the solute diffusive motion/Brownian motion of the formed chalcone raw molecules resulting into the formation of regular crystal formation in less time, increasing overall crystallinity of synthesized chalcone, **(ii)** Chalcone synthesized by NUS method is exposed to alkaline nature (potassium carbonate) for longer time (5 h) and even if chalcone crystals are formed in less time, alkalinity may affect the crystal structure and due to which overall crystallinity is found to be decreased while in case of US process, raw materials are exposed to ultrasound for only 20 min, and **(iii)** NUS synthesized chalcone was exposed for longer time, utilizing more energy which may convert crystalline form of material into amorphous, resulting into a decrease in the overall crystallinity of the NUS chalcone. Furthermore, which of the above reason is dominating for the formation of crystalline chalcone is not evident till now. Therefore there is need to carry out more discussion and validation of crystalline and amorphous synthesized materials to find out exact reasons.

**Particle Size Measurement**

Synthesized chalcone by NUS and US processes were also checked for particle size measurement (PSM). Water was used as dispersing medium to disperse chalcone for particle size analysis. It was found that average particle size of NUS and US was 427 and 18.29 nm. It was also found particle size distribution for US at 10% PSM completion, 50% PSM completion and 90% PSM completion were 15.89, 18.29 and 20.84 nm respectively and for NUS sample at 10% PSM completion, 50% PSM completion and 90% PSM completion were 152, 397 and 541nm respectively. The huge differences in particle size of two methods were observed due to effects of ultrasound in US mediated chalcone as compared to NUS. In former case small particle size is due to tendency of ultrasound to reducing the particle size as well agglomeration. This size reduction is possibly due to the ultrasound cavity collapse. Secondly there is formation of local shear forces and attrition through liquid reaction medium as a result of which size reduction of chalcone takes place.

**Scanning Electron Microscopy (SEM)**

Following particle size analysis, morphology of synthesized chalcone (US, NUS) were done by scanning Electron Microscopy (SEM). Results were obtained from SEM micrograph were compared with particle size analysis and were well supported. Outcome obtained as a SEM images for sonochemically (US) and conventionally (NUS) formed chalcone at two different magnifications 2000x and 5000x respectively in order to observe size & shape variation as well as possible agglomeration. Shape of formed particle is somewhat rounded/square in case of sonochemically (US) synthesized chalcone as indicated from **Figure 2P and Figure 3P** is due to attrition. In another way NUS synthesized chalcone particle was in aggregated form in water system and are not well defined shape **(Figure 2Q, Figure 3Q)** as compared to US formed chalcone. It was also observed that US synthesized chalcone sample has very less tendency to form aggregates than NUS chalcone. If attention has made over two methods it was clearly understand that cavitation had play a good impact in case of US synthesized chalcone, comparatively smaller crystalline size and almost no agglomeration. Therefore involvement of cavitation mechanism in the synthetic reaction has great influence to reducing the particle size while synthesis. It acts by increasing the surface area; reaction time and keeping the shape of the particle more uniform (Crystalline in this case).

### FTIR, NMR and Elemental Analysis

The FT-IR, NMR and elemental analysis of conventionally (NUS) and sonochemically (US) synthesized chalcone has been recorded. The FT-IR spectrum of dried powder gives an absorption band near 1648cm$^{-1}$ indicates the presence of C=O group. The absorption band at 1594 cm$^{-1}$ confirm the presence of aromatic C=C group of chalcone. The $^{1}$H NMR and $^{13}$C NMR of synthesized chalcone by NUS and US process give $^{1}$H NMR d = 3.92 (s, 3H), 6.93 (d, 2H), 7.09 (d, 2H), 7.42 (d, 1H, J = 15.36 Hz), 7.50 (d, 2H), 7.68 (d, 1H, J = 15.72 Hz), 8.02 (d, 2H) and $^{13}$C NMR d 52.42, 112.77, 114.89, 121.44, 129.78, 130.80, 131.0, 132.43, 141.89, 162.22, 165.66, 186.57 ppm. The coupling constant J = 15.72 Hz of chalcone indicates the presence of olefinic bond and confirm the trans isomer. The elemental analysis of synthesized chalcone is indicated below.

Molecular formula: $C_{16}H_{14}0_5$

C 67.13% (calculated) and 67.09% (found)

H 4.93% (calculated) and 4.95% (found)

**Table 1: % Crystalinity, Crystalline Size and % Yield of the Conventionally (NUS) and Sonochemically (US) Synthesized Chalcone**

| Method | Time taken for the completion of the reaction | Crystallinity (%) (Average) | Crystallite size *d* (nm) (Average) | Yield (%) | Energy (J) | Power input (W) |
|---|---|---|---|---|---|---|
| Conventional | 5h | 12.49 | 18 | 83.07±1.25% | - | - |
| Sonochemical | 20 min | 33.33 | 32 | 89.04±1.02% | 21.049 | 17.50 |

**Table 2: Effect of % Amplitude (Power Density) on % Yield of Synthesized Chalcone**

| S. No. | % Amplitude | Reactions completed in time (seconds) based on TLC | Energy (J) | Power (W) | Yield (%) in 20 min Average | ± Variation |
|---|---|---|---|---|---|---|
| 1 | 30 | 1500 | 13.680 | 9.12 | 83.60 | 2.82 |
| 2 | 40 | 1200 | 21.049 | 17.50 | 89.04 | 1.02 |
| 3 | 50 | 960 | 25.039 | 26.10 | 89.56 | 1.42 |

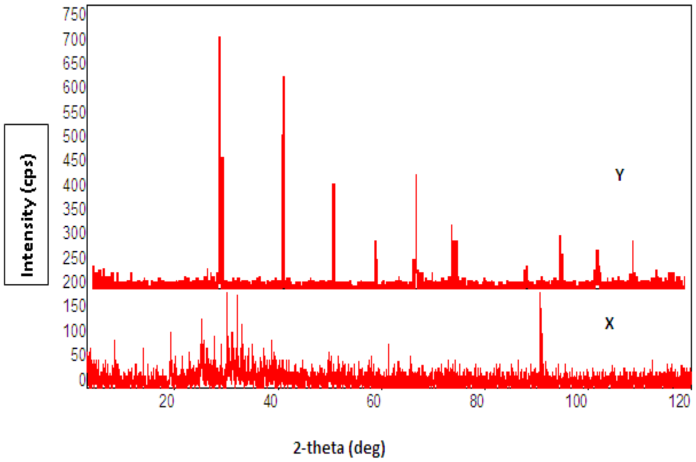


**Figure 1: XRD Pattern of the Conventionally (NUS) and Sonochemically (US) Synthesized Chalcone Showing as X and Y Respectively**

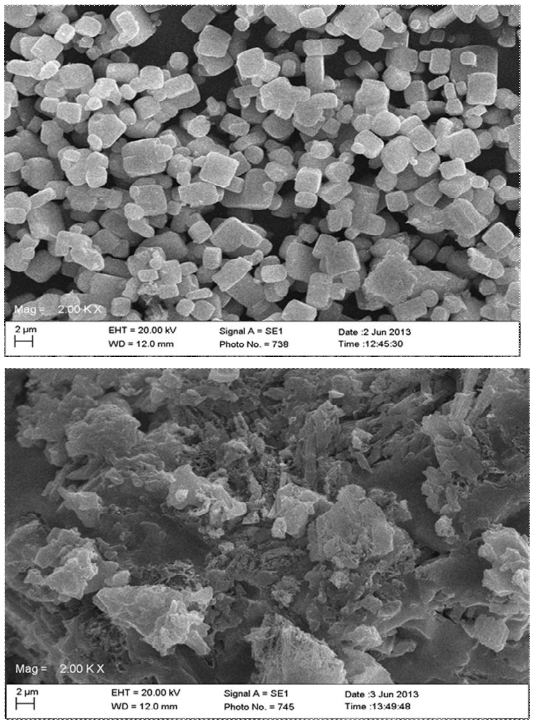


**Figure 2: Synthesiszed Chalcone Characterized by SEM**

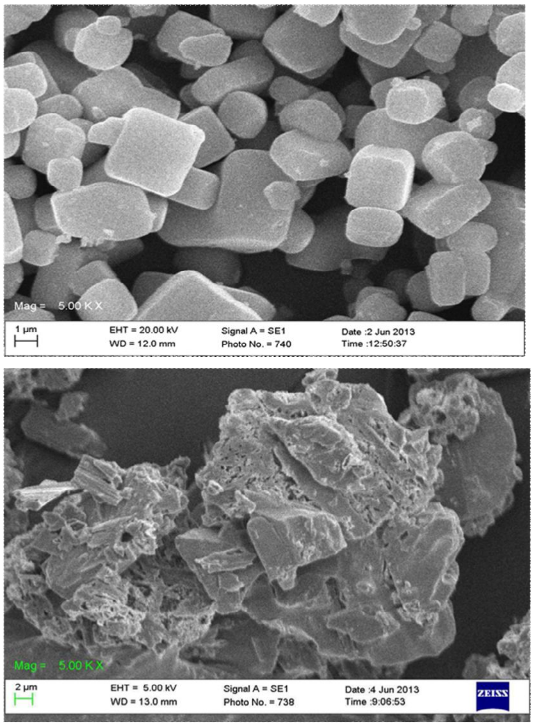


**Figure 3: Synthesiszed chalcone characterized by Micrograph at 2000x: (P) US, (Q) NUS. SEM Micrograph at 5000x: (P) US, (Q) NUS**

## CONCLUSIONS

Chalcone was synthesized by sonochemical (US) and conventional (NUS) and compared for their efficiency in terms of yield, time of reaction and stability of final product. Synthesized chalcone was well characterized and confirmed that US mediated product is formed in 20 min relatively more stable and small in particle size (Crystalline). Sonochemical method saved significant energy in comparison to conventional one. Hence, Sonochemical method of chalcone synthesis is rapid, economical (time and energy) and eco-friendly in nature

**Effectiveness of Energy Consumption**

**Appendix 1**

**A.1. Energy Calculations**

1. Energy delivered during 20 min for chalcone formation by sonochemical method

- Energy delivered during sonication = Energy required to synthesized chalcone material.
- Electrical energy delivered during sonication using horn for 20 min (indicated by power meter) = 21.049 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 20 min x Efficiency of horn
  = 21.049 x 30/100 = 6.31 kJ
- Quantity of material processed = Quantity of 4-hydroxy-3-methoxybenzaldehyde + Quantity of 1-(2,4-dihydroxyphenyl) ethanone + Quantity of Potassium Carbonate + Quantity of Ethanol
  1.98(g) +1.98(g) +69(g) +15.78(g) = 88.74(g)
- Net energy supplied for processing of material using sonochemical method = Actual energy delivered by horn during sonication/Quantity of material processed
  6.31 kJ/88.74(g) = $7.11 \times 10^{-2}$ (kJ/g)…..(I)

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)
  = 50 mA = 50 $\times 10^{-3}$ (A).
- Power input in magnetic stirrer = Voltage input x Current measured
  220(V) x $50 \times 10^{-3}$ (A) = 11W (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 11(W) x 40/100 = 4.4 W (J/s)

- Time required for completion of reaction = 5h (18000 s).
- Net energy delivered during conventional method = Power input in magnetic stirrer x Time required for completion of reaction

4.4 J/s x 5h x 3600(s/h) = 79200 J= 79.2kJ

- Quantity of material processed = Quantity of 4-hydroxy-3-methoxybenzaldehyde + Quantity of 1-(2,4-dihydroxyphenyl) ethanone + Quantity of Potassium Carbonate + Quantity of Ethanol
  1.98(g) +1.98(g) +69(g) +15.78(g) = 88.74(g)
- Net energy supplied for processing of material using conventional method = Net energy delivered during conventional method/quantity of material processed
  79.2kJ/88.74 (g) = 89.24 x $10^{-2}$ kJ/g..........(II)

3. **Energy Saved**

Net Energy saved = (Net energy supplied for processing of material using conventional method (II)) – (Net energy supplied for processing of material using sonochemical method........(III)

89.24 x $10^{-2}$ kJ/g - 7.11x$10^{-2}$ (kJ/g) = 82.13(kJ/g)

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