International Journal of Botany Studies
ISSN: 2455-541X; Impact Factor: RJIF 5.12
Received: 09-01-2021; Accepted: 09-02-2021: Published: 18-02-2021
www.botanyjournals.com
Volume 6; Issue 1; 2021; Page No. 536-539

Comparative study of conventional and microwave assisted green synthesis of 6- amino flavones

Fouzia Tehseen[1*], Syed Safiullah Ghori[2], Ruqaiya Khatoon[1], Saneela Sajid[1], Huda Nafees[3]
[1] Department of Pharmaceutical Chemistry, Anwarul Uloom College of Pharmacy, Hyderabad, Telangana, India
[2] Department of Pharmacology, Anwarul Uloom College of Pharmacy, Hyderabad, Telangana, India
[3] Department of Saidla, Faculty of Unani Medicine, Aligarh Muslim University, Aligarh, Uttar Pradesh, India

Abstract
Green chemistry focuses on synthesis of chemical compounds to get maximum yield with minimal waste, atom economy, usage of less toxic chemicals, less wastage, high efficiency, Green catalysts. The basic aim of our study is to compare the synthesis of amino flavanones by conventional and microwave Assisted method. Microwave assisted synthesis is a green tool for organic synthesis providing clean, economic, enhanced reaction rate and percentage yields. In the present study, Paracetamol was taken as the starting material which after a series of steps gave 6-amino flavanones. The microwave method was found to be highy efficient where the reaction time reduces from hours to minutes when compared to the conventional organic synthesis. The rate of reaction of microwave assisted reaction increases by 10-1000 times and the yield is found to be increased by 10-40 percent than the conventional method. All the compounds synthesized were characterized by melting point, TLC, IR, (1) H NMR spectroscopy. Study was done by comparing reaction time and percentage yield in both methods. It is observed that the microwave assisted method is greener, cheaper, more convenient method than conventional method.

Keywords: comparison, microwave, conventional, amino flavanones

Introduction
Green chemistry can be defined as the design of chemical processes which can effectively minimize or reduce or eliminate the usage or generation of hazardous subtances [1]. Conventional synthetic method of synthesis utilizes various equipments like oil bath, sand bath and heating mantle where the process is tedious, long and involves utilisation of massive chemicals. This results in higher cost of the processes and immoderate use of chemicals/ solvents and reagents. Microwave assisted methods utilizes conversion of electromagnetic radiation into heat resulting in enhanced reaction rates due to selective microwave energy absorption by the polar groups in the molecules [2]. It is an evolving alternative source of energy to bring about chemical reactions in minutes. Now a days it is adopted for the synthetic reactions so as to increase productivity and efficacy. The usage of microwave irradiation results in good yields, enhanced rate of reaction, minimized solvents usage and cleaner reactions when compared to classical heating methods [3].

Flavonoids are a group of naturally occurring hydroxylated phenolic substances that are classified into flavonones, iso flavonones, flavonols and anthocyanins. They are produced by plants in response to microbial infections [4]. Flavones are a class of flavonoids based on the backbone of 2-phenylchromen-4-one. Flavanone is the major intermediate responsible for the synthesis of secondary metabolites in plants. The activity shown by them depends on their chemical structure, chemical class, degree of hydroxylation, substitution and other chemical modifications like polymerization, conjugation and rearrangements [5]. Flavonoids show various pharmacological properties like antimicrobial, antioxidant, antimutagenic, cardiotonic, anticancer and other age related diseases [6, 7]. They also regulate gene expression and modulate enzymatic reactions [8]. Flavonoids are found to effective in prevention of age related neurodegerative diseases like Parkinson's and Alzheimers disease [9]. Generally flavonoids are synthesized by the treatment of 2'- hydroxychalcones with acidic or basic reagent or oxidative cyclisation. Cyclization of 2'-hydroxychalcone to flavanone is reported by using various reagents like amino acid [10], triflouroacetic acid [11], sulfuric acid in methanol [12], polyphosphoric acid [13], triethyl amine under reflux [14] NaOH [15], KOH in methanol [16], potassium carbonate in acetone under reflux [17] and many other methods. These reported conventional methods have disadvantages like low yield, longer reaction time, high temperature and expensive catalysts. However, the use of microwave irradiation, an effective green tool resulted in enhanced reaction rate, solvent economy, higher purity, higher yields and use of easily available catalysts [18].

In our laboratory, we synthesized 6-amino flavone derivatives from Paracetamol by both conventional method [19] and microwave enhanced method [20]. Conventional synthesis was done in a four step procedure. Likewise, the microwave irradiation method was performed in domestic microwave oven (Onida) for the synthesis of the compounds and compared with the conventional method shown in figure 1. The compound codes are given in tablw 1. It was observed that the reaction time was reduced from hrs to few minutes and % yields were found to be higher when compared to conventional method.

Material and Methods
The chemicals required for the synthesis were purchased from Standard Chemicals, Hyderabad and were of laboratory grade. Melting points were determined by open capillary method and are uncorrected, expressed in °C.

Purity of synthesized compounds was checked by thin layer chromatography. Analysis was done by IR spectra (recorded using Bruker FTIR spectrophotometer) and NMR.
Procedure:

Method 1: Conventional method (5a, 5b, 5c, 5d, 5e, 5f by CM)

Method 2: Microwave method (5a, 5b, 5c, 5d, 5e, 5f by MW)

Step1: Synthesis of 5'-acetamido-2'-Hydroxyacetophenone (2a-2f) from Paracetamol

1. Conventional Method(CM): To a mixture of paracetamol (0.66 mol) and anhydrous aluminium chloride (0.016 mol) contained in a conical flask, was added aluminium chloride (0.016 mol) in nitrobenzene (50 ml) slowly for duration of 0.5 hr. the temperature was slowly increased to 130ºover half an hour period and heated for 2.5 hrs. It was cooled to 40 ºC for 0.5 hr time. Poured in a mixture of crushed ice snd 30 ml comc. HCl with vigorous stirring and then filtered, washed with water to make it free from any acid residue followed by toluene and recrystallized from isopropanol to get light brown needles.
2. Microwave assisted method: to a mixture of paracetamol (0.066 mol) and anhydrous aluminium chloride (0.016 mol) in nitrobenzene (10mL), acetyl chloride (0.066 mol) was added over a period of 0.5 hr. The reaction mixture was kept then microwave irradiated for 30 seconds (3times) at 80 watts. After cooling, it was added to a mixture of crushed ice and 30 ml conc. HCl and stirred. Filtered, washed with water followed by toluene, recrystallized using isopropanol.

Step2: Synthesis of 5'-Acetamido-2'-Hydroxychalcones (3a-3f)

1. Conventional Method: To a mixture of 5' acetamido-2'-Hydroxy acetophenone (0.01mol) and aryl aldehyde (0.01mol) dissolved in 30 ml ethanol was added aqueous potassium hydroxide solution (0.03 mol) slowly. It was then stirred for 24 hrs at room temperature. The reaction mixture was then poured into crushed ice and acidified with 5 N HCl. The crystals separated were filtered and crystallised from ethanol.
2. Microwave irradiation method: Equimolar quantities (0.01 mol) of of 5'-acetamido-2'-Hydroxyacetophenone and respective aldehydes (0.001 mol) were mixed and dissolved 3 ml of alcohol. Aqueous potassium hydroxide solution (0.003mol) was added slowly and mixed. The entire reaction mixture was microwave irradiated for about 6 minutes at 180 watts and then poured on crushed ice and acidified with 5 N HCl. The crystals are filtered and recrystallised using ethanol.

Step3: Synthesis of 6-Acetamidoflavones (4a-4f)

1. Conventional Method: Catalytic amount of iodine dissolved in Dimethyl sulfoxide (10ml) and added 5'-Acetamido -2'Hydroxychalcone, refluxed for 30 minutes to 1 hour. Then cooled and 10% sodium thiosulfate solution added to remove excess iodine. The product obtained was purified by recrystallization from methanol.
2. Microwave irradiation method: To 5'-Acetamido -2'-Hydroxychalcone was added catalytic amount of Iodine and 3 ml of Dimethyl Sulfoxide. It was microwave irradiated for 3 min at 360 watts and then poured on crushed ice. The excess Iodine was removed using sodium thiosulphate (10%) and filtered and crystallised using methanol.

Step4: Synthesis of 6-Amino Flavones (5a-5f)

1. Conventional Method: A mixture of concentrated HCl and water (1:1) was added to 5'-Acetamido-2'-Hydroxychalcone, and boiled for 1-2 hrs. After reaction was complete, ice cold water was added and the reaction mixture was cooled to room temperature. The solution was made alkaline by adding 10% sodium carbonate solution to obtain brown colored precipitate of 6-aminoflavone having an aromatic fruity smell. It was washed with water, dried and recrystallized from ethanol.
2. Microwave irradiation method: A mixture of 5'-Acetamido-2'-Hydroxychalcone in 5 ml ethanol is addedto silica gel moistened with few drops of conc HCl. This was microwave irradiated for 4 minutes to get a fruity aroma 6 aminoflavone. The product was then added to Crushed ice, filtered and dried and recrystallized using ethanol.

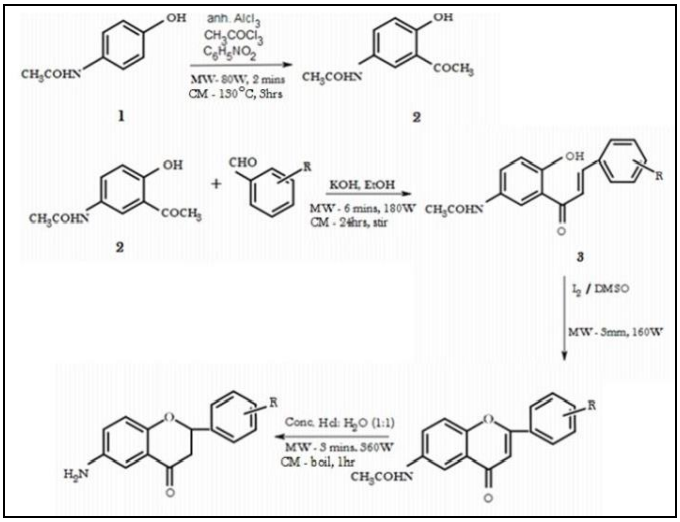

Fig 1: Microwave Assisted and Conventional route for 6 -Amino flavone synthesis.

Table 1: Compound codes synthesised

Compound code by CM	Compound code by MW	R
5a	5a	H
5b	5b	NO_2
5c	5c	OCH_3
5d	5d	Cl
5e	5e	$C_6H_5NO_2$
5f	5f	OC_2H_5

Results and Discussions

The comparison between final products, molecular weights, melting points, time and yields obtained by conventional method and microwave assisted method are compared in the table 2.

The synthesised products were characterised and compared by Fourier Transform Infrared (FTIR) spectroscopy and NMR. The values are discussed in table 3. When the data is analysed it can be clearly seen that the time required for the synthesis by conventionl method is in hrs whereas microwave assisted method takes few minutes for the same reactions. The percentage yields of the compounds 5a-5d are appreciably better in case of microwave method than conventional method.

Table 2: Comparison of end products of CM and MW

Compound code	Compound name	Molecular Weight (gms)	Melting Point Range °C	(Method 1) Conventional method(CM)		(Method 2) Microwave assisted method(MW)	
				Time (hr)	% Yield	Time (min)	% Yield
5a	6-Amino-2-phenyl-4H-chromen-4-one	237	172-178	1	72	2.5	78
5b	6-Amino-2-(3'-nitrophenyl)-4H-chromen-4-one	289	180-184	1	50	2	60
5c	6-Amino-2-(3'-methoxy)phenyl-4H-chromen-4-one	267	150-156	1	72	3	82
5d	6-Amino-2-(4'chlorophenyl)-4H-chromen-4-one	271	154-160	1	68	1.5	76

Table 3: Comparison of FTIR and NMR data of the compounds 5a-5d

S.No.	Compound code	Infrared spectroscopy values (KBr)(cm^{-1})		Nuclear magnetic resonance data: $_1$H NMR(400 MHz, DMSO) δppm	
		Conventional method (CM)	Microwave assisted green method (MW)	Conventional method (CM)	Microwave assisted green method (MW)
1	5a	1649(C=O str. flavones), 3300(NH2symstr), 3022(NH2asymstr), 1194 (C-N str), 3100(CH strAr)	1645(C=O str. flavones), 3310(NH2symstr), 3030(NH2asymstr), 1200 (C-N str), 3150(CH strAr)	5.5(s,2H,NHz at C_6),6.86(s, 1H, H3), 7.10(m,3H, H),	5.4(s,2H, NH_2 at C_6), 6.5(s,1H,3H), 7.82(m,2H, 4H)
2	5b	1650(C=O str. flavones), 3332(NH2symstr), 3402(NH2asymstr), 1194 (C-Nstr), 3069(CH strAr)	1608(C=O str. flavones), 3340(NH2symstr), 3400(NH2asymstr), 1130(C-Nstr), 3060(CH strAr)	5.5(s,2H, NH_2 at C_6), 6.8(s, 1H,H3), 7.0(m, 3H,H_3),	5.6(s,2H, NH_2 at C_6), 6.89(s, 1H,H3), 7.20(m, 3H,H_3),
3	5c	1612(C=O str. flavones), 3330(NH2symstr), 3402(NH2 asymstr), 1138 (C-N str), 3070(CH strAr)	1610(C=O str. flavones), 3340(NH2symstr), 3400(NH2 asymstr), 1140 (C-N str), 3070-H strAr)	5.4(s,2H, NH2 at C6),6.45(s,1H,3H), 7.80(m,2H,4H)	5.46(s,2H, NH2 at C6),6.5(s,1H,3H), 7.82(m,2H,4H)
4	5d	1608(C=O str. flavones), 3332(NH2symstr), 3402(NH2asymstr), 1132 (C-N str), 3069(CH strAr)	1600(C=O str. flavones), 3330(NH2symstr), 3400 (NH2asymstr), 1130 (C-N str), 3070(CH strAr)	5.42(s,2H, NH2 at C6),6.45(s,1H,3H), 7.78(m,2H,4H)	5.4(s,2H, NH2 at C6), 6.5(s,1H,3H), 7.82(m,2H,4H)

Conclusion

From the comparison hereby made, we can observe that the 6-Amino flavanones synthesised by Microwave method is a greener method when compared to conventional method. Microwave method has its advantages like more efficiency, lesser reaction times, less usage of solvent amounts and high yields. The amino flavanones can further be explored for activities like antioxidant or antimalarial or antiinfective or antitubercular in further research.

References

1. Sheldon RA, Arends I, Hanefeld U. Green Chemistry.
2. Varma RS. Solvent free accelerated organic synthesis using Microwave, Pure Appl Chem. 2001; 73:193-8.
3. Vasudevan A., Microwave assisted organic synthesis-An enabling technology with disruptive potential, Drug Disco World Fall, 2008, 83-90.
4. Dixon RA, Dey PM, Lamb CJ. "Phytoalexins: Enzymology and molecular Biology. 1983: 55:1-136.
5. Kelly EH, Anthony RT, Dennis JB. "Flavonoid antioxidants: Chemistry, metabolism and structure-activity relationships," Journal of Nutritional Biochemistry. 2002; 13:572-584.
6. Craig WJ. "Health promoting properties of common herbs," Am J Clin Nutr. 1999; 70:491S-499S.
7. Galati G. "Cancer chemoprevention and apoptosis mechanism induced by dietary polyphenolics," Drug Metabol Drug Interact. 2000; 17:311-348.
8. Shanshank Kumar, abhay K. Pandey, "Review: flavonoids- chemistry, metabolism, cardioprotective effects and dietary sources,"The Scientific World Journal. 2013; 7:66-76.
9. Aleksandra kozowska, Rocs Panstw Zakl Hig, 2014; 65:79-85.

10. Bidhendi GN, Banerjee NR, Ind. J. Chem. 1989; 28:352.
11. Patonay T, Litkei G, Zsuga M, Kiss A, Organic Preparations and procedures int. 1984; 16:315.
12. Aitmambetov A, Kubzheterova A, Russ J, Bioorg. Chem. 2002; 28:165.
13. Tanka K, Sugino T. Green Chem, 2001; 3:133.
14. Mondal R, Das Gupta A, Mallik AK, Tetrahedron Lett, 2011; 52:5020.
15. Maruyama K. Tetrahedron lett. 1989; 30:4145.
16. Makrandi JK, Bala S. Synth Commun. 2000; 30:3555.
17. Matsushima R, Kageyama HJ, Chem. Soc. Perkins Trans. 1985; 2:743.
18. Barge Varsha, Bhosale Dipak, International Journal of Applied Research. 2015; 1(7):259-261.
19. Lalitha Simon *et al*, "Synthesis and evaluation of anticancer activity of some 6-amnio flavanones," International Journal of Pharmaceutical Chemistry, 2015; 5(07):240-246.
20. Fouzia Tehseen *et al*, "Highly efficient green synthesis and characterization of 6- amino flavanones and their possible effects," IJCTRP. 2019; 7(3):95-97.