International Journal of Chemical Science
www.chemicaljournals.com
Online ISSN: 2523-2843, Print ISSN: 2523-6075
Received: 04-03-2021, Accepted: 06-04-2021, Published: 08-05-2021
Volume 5, Issue 3, 2021, Page No. 01-03

Comparative studies on conventional and microwave assisted synthesis of N-(phenylcarbamothioyl) benzamide derivatives and its anti-inflammatory activity

Shivani Khairmode[1], Radha Khade[2], Firoj Tamboli[1*], Harinath More[1], Dhanashri Patil[1], Karuna Dhuri[1], Namrata Kanse[1], Shrinivas Mohite[2]

[1] Department of Pharmaceutical Quality Assurance, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Maharashtra, India
[2] Rajarambapu College of Pharmacy, Kasegaon, Sangli, Maharashtra, India

Abstract
The current research work was aimed to design and development of substituted N- (phenylcarbamothioyl) benzamide derivatives by QSAR approach and its In-vitro anti-inflammatory activity. The series of substituted N-(phenylcarbamothioyl) benzamide derivatives ($2a_1$-$2a_4$) was designed, and synthesized by using conventional and microwave method.The percentage yield by microwave assisted method was more compared to conventional method.TLC and IR spectra of synthesized products was performed and showed satisfactory results. *In vitro* anti-inflammatory activity of synthesized products was done by protein denaturation method.

Keywords: N- (phenylcarbamothioyl) benzamide, microwave synthesis, protein denaturation

Introduction

Synthesis of novel chemical compounds is major step in drug discovery. Conventional methods for various chemical synthesis is very well documented and practiced. The use of microwave in organic synthesis increase the pharmaceutical and academic arenas, it is new technology for drug discovery and development [1-3]. In microwave method heat is directly contact with molecule entire reaction mixture, leading to rise in temperature. The microwave assisted synthesis is eco-friendly with higher yields [4-5]. The importance of microwave synthesis is short reaction time, wide range of reactions, and minimum exposure of hazardous chemicals and maximum utilization of energy [6-7]. Microwave assisted synthesis is mainly used in the industry as well as academic research. Microwave assisted organic synthesis (MAOS) has emerged as a new "lead" in organic synthesis. The technique offers simple, clean, fast, efficient, and economic for the synthesis of a large number of organic molecules. In the recent year microwave assisted organic reaction has emerged as new tool in organic synthesis. Important advantage of this technology include highly accelerated rate of the reaction, Reduction in reaction time with an improvement in the yield and quality of the product [7-10].

Material and Methods

All chemicals and solvents were procured from commercial sources, purified and dried using standard procedures from literature whenever required the reagents were procured from store department of Institute.

Experimental

Synthesis of N-(phenylcarbamothioyl) benzamide derivatives:

Synthesis by conventional Method [11]

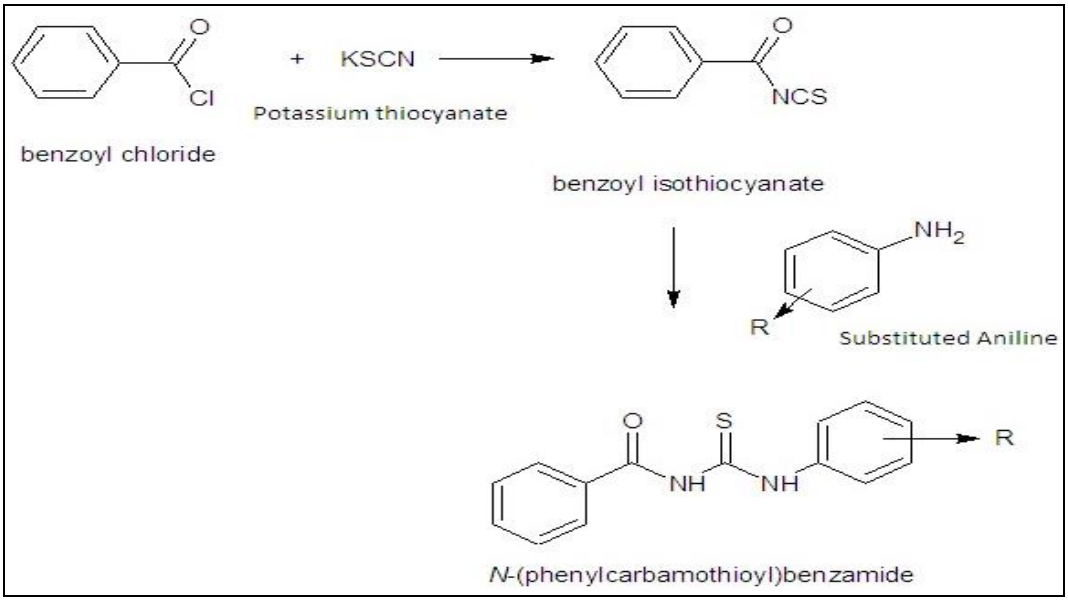
A solution of aroyl chloride (10mmol) in acetone (50mL) was added dropwise to a suspension of potassium thiocyanate (10mmol) in acetone (30 mL) and the reaction mixture was refluxed for 30 min. After cooling to room temperature, a solution of the substituted aniline (10mmol) in acetone (10 mL) was added and the resulting mixture refluxed for 2-3 h. After completion of reaction (checked by TLC). The reaction mixture was poured into cold water and the precipitated N-(phenylcarbamothioyl) benzamide derivatives were recrystallized from aqueous ethanol.

Synthesis by Microwave method [11]

A solution of aroyl chloride (5mmol) in acetone (25mL) was added dropwise to a suspension of potassium thiocyanate (5mmol) in acetone (15mL) and the reaction mixture was heated in microwave under reflux for 5-10min at 340 watt. After cooling to room temperature, a solution of the substituted aniline (10 mmol) in acetone (10 mL) was added and the resulting mixture refluxed for 20-25min. After completion of reaction (checked by TLC). The reaction mixture was poured into cold water and the precipitated N-(phenylcarbamothioyl) benzamide were recrystallized from aqueous ethanol.

Table 1: List of Aniline

Sr. No	Compound 2a	Substituted Aniline
1	$2a_1$	o-chloro
2	$2a_2$	m-Nitro
3	$2a_3$	o-Nitro
4	$2a_4$	4-Ethyl



Reaction scheme

***In-Vitro* Anti-inflammatory screening** [12-13]

in vitro anti-inflammatory activity by protein denaturation Method.

The mixture (10ml) consisted of 0.4ml of egg albumin (from fresh hen's egg), 5.6ml of Phosphate buffered solution (PBS, pH 6.4) and 4ml of varying concentration of test Samples so that final concentration become 50 µg/ml, 100 µg/ml. similar volume of DMSO served as control. Then the mixtures were incubated at (37 ^{0}C ± 2) for 15 min. and then heated at 70 ^{0}C for 5min. After cooling, their absorbance was measured at 660nm (JASCO UV Spectrophotometer) by using vehicle as blank and their viscosity was determined by using Ostwald viscometer. Diclofenac sodium at the final concentration of 50 µg/ml, 100 µg/ml was used as reference drug and treated similarly for determination of absorbance and viscosity. The % inhibition of protein denaturation was calculated by using the following formula,

$$\% \text{ Inhibition protein denaturation:} \frac{\text{Absorbance of control} - \text{Absorbance of test}}{\text{Absorbance of control}} X\ 100$$

Result and Discussion

In this present inquisition various substituted Thiourea derivatives were synthesized by microwave and Conventional method for *in-vitro*anti-inflammatory activity. By using microwave method gives more yield in less time.All synthesized compounds were recrystallized in acetone, methanol, ethanol and butanol by slow evaporation method. Compounds showed best result in butanol with needle shaped crystals.

Table 2: Conventional and Microwave method ($2a_1$-$2a_4$)

Sr No	Compounds	Molecular formula	Molecular weight	Melting point	Percentage yield		Rf value	Mobile
					conventional	microwave		(T:A)
1	$2a_1$	$C_{14}H_{10}Cl_2N_2OS$	325.21	170- 172 ^{0}C	78.60%	81.20%	0.67	9:1
2	$2a_2$	$C_{14}H_{10}ClN_3O_3S$	335.76	162- 164 ^{0}C	94.48%	95.10%	0.64	9:1
3	$2a_3$	$C_{14}H_{10}ClN_3O_3S$	335.76	167-169 ^{0}C	83.84%	86.20%	0.83	9:1
4	$2a_4$	$C_{16}H_{15}ClN_2OS$	318.82	188- 190 ^{0}C	81.20%	83.09%	0.67	9:1

Thin layer chromatography was performed by using toluene and acetone as a solvent.

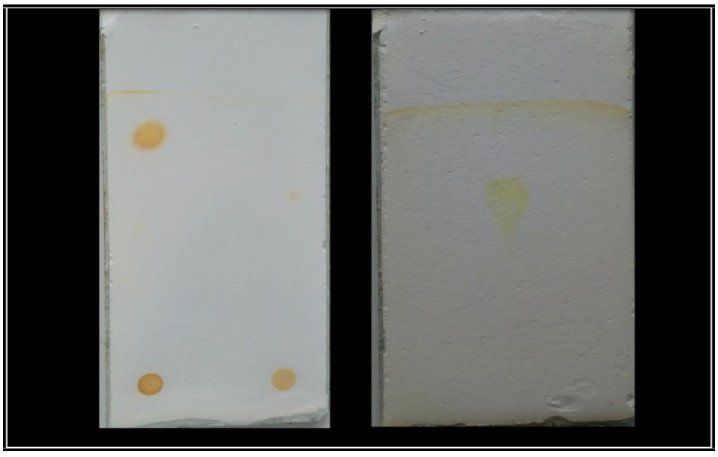


Fig 1: TLC profile of synthesized compounds

The structural characterization of the synthesized compounds was done by the interpretation of IR spectra analysis. All compound showed satisfactory results

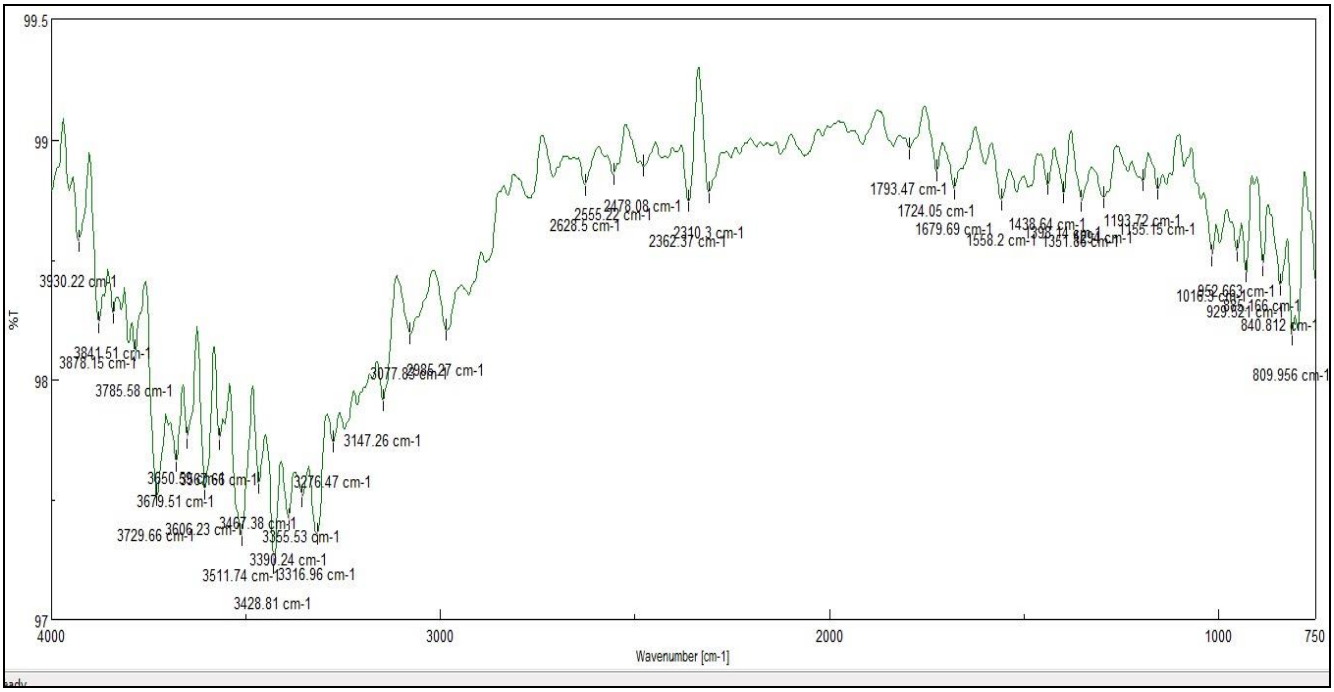


Fig 2: IR Spectra

Table 3: IR Value of compound $2a_2$

Sr. No.	Value (cm-1)	Functional group
1	3365.32	-NH-C stretch
2	1795.4	C-NH stretch
3	1685.66	C=O stretch
4	1317.14	N-(CH3)2bend
5	755.95	C-CL stretch

Table 4: *In-vitro* anti-inflammatory activity of synthesized compounds

Compounds	% inhibition of protein denaturation		Viscosity(cps)	
	50µg/ml	100µg/ml	50µg/ml	100µg/ml
Standard	52.22%	61.11%	0.52	0.56
$2a_2$	41.11%	47.77%	0.43	0.49
Viscosity of control = 1.52cps				

Conclusion

In this present work microwave synthesis showed more yields. The purity and homogeneity of synthesized compounds were judged by their sharp melting points and Rf value. The structural characterization of the synthesized compounds was done by the interpretation of IR spectra. All synthesized compounds were screened for *in- vitro* anti-inflammatory activity showed satisfactory result.

References

1. Santagada V, Perissutti E, Caliendo G. The application of microwave irradiation as new convenient synthetic procedure in drug discovery. Curr Med Chem, 2002;9(13):1251-83. doi: 10.2174/0929867023369989. PMID: 12052166.
2. Krstenansky JL, I. Cotterill I. Recent advances in microwave-assisted organic syntheses. Curr Opin Drug Discov Devel,2000;3(4):454-461.
3. Giguere RJ, Bray TL, Duncan SM, Majetich G. Application of commercial microwave ovens to organic synthesis, Tetrahedron Lett,1986;27:4945–4948.
4. Ravichandran S, Karthikeyan E. Microwave Synthesis-A Potential Tool for Green Chemistry. Int J Chem Tech Res,2011;3(1): 466-470.
5. Gaba M, Dhingra N. Microwave Chemistry: General Features and Applications, Indian J Pharm Educ Res,2011; 5(2):175-183.
6. Willert-Porada M. Advances in Microwave and Radio Frequency Processing, Springer Berlin Heidelberg, 2007, 359-369.
7. Chemat-Djenni Z, Hamada B, Chemat F. Atmospheric pressure microwave assisted heterogeneous catalytic reactions. Molecules,2007;12(7):1399-1409.
8. Collins MJ Jr. Future trends in microwave synthesis, Future Med Chem,2010;2(2):151-155.
9. Larhed M, Hallberg A. Microwave-assisted high-speed chemistry: a new technique in drug discovery. Drug Discov Today,2001;6(8):406-416.
10. Ajmer Singh Grewal, Karunesh Kumar, Sonika Redhu, Shashikant Bhardwaj. Microwave assisted synthesis: a green chemistry approach. Int. Res J Pharm. App Sci,2013;3(5):278-285.
11. Algul O, Kaessler A, Apcin Y, Yilmaz A, Jose J. Comparative studies on conventional and microwave synthesis of some benzimidazole, benzothiazole and indole derivatives and testing on inhibition of hyaluronidase. Molecules,2008;13(4):736-748.
12. A. Anbarasi, R. Vidhya. Evaluation of *In Vitro* Anti-Inflammatory Activity of *Tephrosia purpurea* (Seed). Asian J. Pharm. Res,2015;5(2):83-89.
13. K. Teja, T. Satyanarayana, B. Saraswathi, B. Goutham, K. Mamatha, P. Samyuktha, S. Tharangini. Phytochemical and *In vitro* Anti-inflammatory Activity on *Abrus precatorius.* Asian J Res. Pharm. Sci,2019;9(1):50-54.