RESEARCH PAPER

Accepted 25 May 2005
Revised 11 December 2004
Received 16 April 2004
Indian J. Pharm. Sci., 2005, 67(3): 307-310

# New Microwave Methods for Rapid Quantitative and Qualitative Analysis and Loss on Drying

S. BADAMI*, S. RAMASWAMY, S. V. SHARMA, R. K. CHOKSI, S. H. DONGRE AND B. SURESH

Department of Pharmaceutical Chemistry, J. S. S.College of Pharmacy, Rocklands, Ootacamund-643 001

**Reactions carried out under microwave irradiation are found to be faster and the technique is being used in laboratories for a variety of purposes. In order to introduce microwave technique for pharmaceutical chemistry practical, its use in quantitative and qualitative analysis and loss on drying is discussed. Quantitative estimation of amide, ester, and carbonyl compounds was successfully carried out. The percent purity obtained for all the samples was higher than those obtained through conventional methods and the time consumed was also found to be less by the microwave technique. Preparation of nitrate, oxime and hydrazone derivatives of organic molecules was successfully completed in a short duration. Determination of loss on drying was also achieved in a shorter duration. The procedures developed can be used for routine analysis in Pharmaceutical Chemistry laboratories.**

Microwave-induced organic reaction enhancement (MORE) has emerged as a simple, clean, fast, efficient, economic, environmental friendly and non-traditional method for the synthesis of a large number of organic molecules[1]. Microwave technique finds a variety of applications in chemical laboratories. Synthesis of drugs, intermediates[1], chemicals, activation of chromatographic adsorbents, drying of glass ware, sterilization of glass wares and auxiliaries[2], microscopic staining of tissues[3], drying of medicinal plants[4], extraction of essential oils from plants[5], drying of granules for the preparation of tablets[6], and enzyme inactivation of food products[7] are a few examples of the use of microwaves in laboratories. Earlier, we have successfully adopted the use of microwave technique for determination of saponification value[8], for organic synthesis[9], degradation of natural products and quantitative analysis[10] in our laboratory. In continuation of these studies, and with an objective of introducing this technique for the routine use in pharmaceutical chemistry practical, herewith, we report the use of MORE technique for exercises in quantitative analysis, qualitative analysis, and loss on drying.

*For correspondence,
E-mail: shribadami@rediffmail.com

## MATERIALS AND METHODS

All chemicals used were obtained from E-Merck Ltd., Mumbai and S. D. Fine Chem. Ltd., Mumbai, while other reagents and solvents used were of analytical grade quality. Heating was done in a domestic microwave oven (LG-Healthwave system, MG- 605 AP, 900 W, 230 V~ 50Hz).

The reaction mixture in quantitative and qualitative analysis was placed in a domestic microwave oven along with a beaker containing 200 ml of water, which served as a heating sink. This was done to avoid overheating of the samples. The intensity of microwaves and duration for each experiment were arrived at using the trial-and-error approach. The reactions under microwave irradiation were carried out at various intensities and for different durations for standardization. After the irradiation, the reaction mixture was removed and TLC was performed to confirm the completion of reaction. Further work up was carried out as per the conventional procedure. The particular microwave

intensity and the duration, which gave a similar or better result as that of conventional method is considered as the best condition for that microwave reaction. Using this condition, each experiment was repeated thrice and the average values were shown in Tables 1-3.

**Quantitative analysis:**

Quantitative analysis of organic molecules can be performed based on the chemical nature of the functional groups. Estimation of amide, ester and carbonyl compounds[11,12] was carried out using MORE technique by adopting standard procedures available in the literature. The estimations were also carried out using the same samples following the conventional methods[11,12]. In each of these estimations, a blank titration was performed separately and the percent purity was determined using the standard formula. Results are given in Table 1 and the standardized procedures developed by microwave technique are given below.

**Estimation of amides:**

A mixture of an amide (0.5 g), methanol (5 ml) and sodium hydroxide (2 N, 20 ml) was taken in a 250 ml borosil beaker covered with a petridish containing few pieces of ice. The ice in the Petri dish helped to minimize evaporation of solvent from the reaction mixture. It was placed in the microwave oven and subjected to irradiation at 360 W for a period of 15-20 min (Table 1). The reaction mixture was cooled and titrated against hydrochloric acid (1 N) solution using phenolphthalein as indicator.

**Estimation of esters:**

A mixture of an ester (1.5 g), methanol (5 ml) and alcoholic potassium hydroxide (0.5 N, 50 ml) was prepared as per the conventional procedure in a 250 ml borosil beaker covered with a petridish containing few pieces of ice. It was placed in the microwave oven and subjected to irradiation at 540 W for a period of 6-9 min (Table 1). The reaction mixture was cooled and titrated against hydrochloric acid (0.5 N) solution using phenolphthalein as indicator.

**Estimation of carbonyl compounds:**

A mixture of a sample containing carbonyl group (1.0 g), hydroxylamine hydrochloride solution (0.5 N, 30 ml), methanol (20 ml) and pyridine (10 ml) was prepared in a 250 ml borosil beaker covered with a petridish containing few pieces of ice. It was placed in the microwave oven and was subjected to irradiation at 540 W for 6-20 min (Table 1). The reaction mixture was cooled and titrated against alcoholic sodium hydroxide (0.5 N) solution using methyl orange as indicator.

**Qualitative analysis:**

Preparation of derivatives is an important step in qualitative analysis, which helps in the identification of organic compounds. Several derivatives for various compounds were prepared by both conventional[13] and microwave methods. Reactions under microwave irradiation were performed at 900 W for various durations. The compounds used for nitrate, oxime and hydrazone derivatives, the reagents used and the duration of reaction for both by conventional and microwave methods is shown in Table 2. The microwave reactions were carried out separately for each derivative in 100 ml beaker covered with a petri dish in a microwave oven. After irradiation, the mixture was cooled and poured in to cold water (20 ml) with stirring. The products obtained were recrystalized with alcohol and identified by comparing their physical constants with authentic samples. These results are shown in Table 2.

**Determination of loss on drying:**

Loss on drying (LOD) is defined as the loss in %w/w resulting from water and volatile matter of any kind that can be driven off under specified conditions[12]. Loss on drying of potassium iodide, sodium salicylate and sodium benzoate was determined by both conventional[12] and newly developed microwave methods. The sample substance of specific weight was taken in a crucible with covering. It was irradiated with microwaves at 900 W for various durations. The sample was weighed each time and the weight loss was calculated in %w/w loss on heating. The duration required to obtain results similar to conventional procedure was noted and shown in Table 3.

## RESULTS AND DISCUSSION

The quantitative analysis of amides, esters and carbonyl compounds were successfully carried out in less than 20 min heating using microwave irradiation. The corresponding heating time by conventional method was found to vary from 1-3 h for these estimations. All the samples analyzed showed slightly higher percent purity when compared to conventional method.

The results obtained in qualitative analysis were achieved in less than 3 min by microwave technique. However, the same reactions by conventional methods required more duration of heating. In the determination of loss on drying the results were achieved at 5-25 min of heating by

TABLE 1: QUANTITATIVE ANALYSIS OF AMIDES, ESTERS AND CARBONYL COMPOUNDS BY CONVENTIONAL AND MICROWAVE METHODS

| Experiment | Reagents | Test Sample | Conventional method | Microwave method | |
|---|---|---|---|---|---|
| | | | % Purity* (Heating time, h) | Duration (min) (Microwave intensity,W) | % Purity* |
| Estimation of amides | Sample (0.5 g)+ methanol (5 ml)+ NaOH (2 N, 20 ml) | Acetamide | 98.2 (2-3) | 20 (360) | 99.1 |
| | | Benzamide | 99.8 (2-3) | 20 (360) | 99.9 |
| | | Formamide | 99.4 (2-3) | 15 (360) | 99.7 |
| Estimation of esters | Sample (1.5 g)+ methanol (5 ml)+ alcoholic KOH (0.5 N, 50 ml) | Dibutyl phthalate | 98.7 (1) | 9 (540) | 99.1 |
| | | Diethyl phthalate | 98.3 (1) | 8 (540) | 99.1 |
| | | Benzyl benzoate | 97.9 (1) | 6 (540) | 98.7 |
| | | Methyl benzoate | 97.7 (1) | 6 (540) | 98.2 |
| | | Ethyl cyanoacetate | 96.0 (1) | 8 (540) | 98.3 |
| | | Diethyl malonate | 97.5 (1) | 9 (540) | 98.7 |
| | | Triethyl orthoformate | 98.1 (1) | 9 (540) | 99. 3 |
| Estimation of carbonyl compounds | Sample (1.0 g)+ Alc. $NH_2OH.HCl$ (0.5 N, 30 ml)+ methanol (20 ml)+ pyridine (10 ml) | Benzophenone | 98.6 (2) | 20 (540) | 98.9 |
| | | Acetophenone | 98.8 (2) | 20 (540) | 99.2 |
| | | Cyclohexanone | 97.2 (2) | 10 (540) | 98.2 |
| | | Cyclopentanone | 97.4 (2) | 10 (540) | 99.5 |
| | | Benzaldehyde | 98.4 (2) | 6.5 (540) | 98.5 |
| | | Cinnamaldehyde | 97.7 (2) | 10 (540) | 98.8 |

*Average of three determinations

TABLE 2: REACTION TIME FOR NITRATION, OXIME AND HYDRAZONE TESTS BY CONVENTIONAL AND MICROWAVE METHODS

| Test | Observation | Test sample | Heating time* | | Melting point (°) | | |
|---|---|---|---|---|---|---|---|
| | | | Conventional (min) | Microwave[a] (sec) | Conventional | Microwave | Reported[13] |
| Nitration test aromatic compounds | Pale yellow precipitate | Toluene | 2 | 20 | 53 | 53-54 | 53-54 |
| | | Naphthalene | 5 | 60 | 59 | 59-60 | 59-61 |
| | | Chlorobenzene | 10 | 80 | 52 | 52 | 52 |
| Oxime test carbonyl compounds | Pale white precipitate | Acetaldehyde | 15 – 30 | 120 | 46 | 47 | 47 |
| | | Benzaldehyde | 15 – 30 | 150 | 35 | 35 | 35 |
| | | Acetone | 15 – 30 | 60 | 59 | 59 | 59 |
| | | Benzophenone | 15 – 30 | 80 | 142 | 143 | 144 |
| Hydrazone test carbonyl compounds | White crystalline precipitate | Benzaldehyde | 10 – 15 | 60 | 157 | 158 | 158 |
| | | Acetone | 10 – 15 | 40 | 42 | 42 | 42 |
| | | Benzophenone | 10 – 15 | 40 | 135 | 135 | 135 |

*Average of three determinations; [a]Microwave heating was carried out at 900 W. Nitration was carried out with sample (0.5 ml)+nitration mixture (5 ml). Oxime test reagents were, sample (0.5 g)+hydroxylamine HCl (0.5 g)+methanol (8 ml)+pyridine (0.2 ml). Hydrazone test was done using sample (0.4 g)+phenylhydrazine HCl (0.5 g)+sodium acetate (0.8 g)+water (5 ml)

TABLE 3: COMPARISON OF LOSS OF WEIGHT AND DURATION BY CONVENTIONAL AND MICROWAVE METHODS.

| Test sample | Loss on drying (% w/w)* by | |
|---|---|---|
| | Conventional method[a] | Microwave method[b] (duration, min) |
| Potassium iodide | 0.896 | 0.898 (9) |
| Sodium salicylate | 0.349 | 0.351 (25) |
| Sodium benzoate | 4.042 | 4.028 (5) |

***Average of three determinations; [a]Heating was done up to constant weight (2-3 h, at 105°), [b]Microwave heating – 900 W**

microwave technique, while the conventional procedure needed 2-3 h. The values obtained in both the methods were in the range of standard limits given in the Pharmacopoeia[12].

In conclusion, using microwaves as the source of heating, we have developed simple, efficient and rapid methods for quantitative/qualitative analysis and loss on drying of several organic samples. These new methods were found to be very convenient for their use in routine practicals. The conventional procedures for the same experiments require elaborate apparatus set-up like reflux assembly. However, microwave procedures can be carried out using simple apparatus like a beaker. Thus, these new procedures offer an additional advantage of simple apparatus set-up without any compromise on safety of the experiments. These procedures can be used in various laboratories for routine analysis.

## ACKNOWLEDGEMENTS

The authors thank His Holiness Jagadguru Sri Sri Shivarathri Deshikandra Maha Swamigalawaru of Sri Suttur Matt, Mysore, for providing the facilities. One of us (RKC) thanks The Tamilnadu Pharmaceutical Welfare Trust for providing partial research grant.

## REFERENCES

1. Sharma, S.V., Rama Sarma, G.V.S. and Suresh, B., **Indian J. Pharm. Sci.,** 2002, 64, 337.
2. Sasaki, K., Wonda, N., Ohsawa, S., Miyake, Y. and Kawashima, Y., **Arch. Pract. Pharm.,** 1998, 58, 125.
3. Van Ginncken, C., Dc Smet, M., Van Moir, F. and Weyns. A., **Histochem. J.,** 1998, 30, 703.
4. Brantner, A. and Lucke, W., **Pharmazie,** 1995, 50, 762.
5. Jean, F.I., Collin, G.T. and Lord, D., **Perfum. Flavour,** 1992, 17, 35.
6. David, A., Benkoczy, Z., Acs, Z., Creskovits, D. and David, A.Z., **Drug Develop. Ind. Pharm.,** 2000, 26, 943.
7. Rodriguez-Lopez, J.N., Fenoll, L.G., Tudela, I., Devece, C., Sanchez-Hernandez, D., de Los Reyes, E. and Gracia-Canovas, F., **J. Agr. Food Chem.,** 1999, 47, 3028.
8. Badami, S., Reddy, M.S.A., Sharma, S.V. and Suresh, B., **Indian Drugs,** 2002, 39, 451.
9. Sharma, S.V., Badami, S., Venkateshwaralu, L. and Suresh, B., **Indian Drugs**, 2003, 40, 450.
10. Badami, S., Mathew, A.M., Thomas, S., Purushotham, K.V., Geo Mathew, K., Sharma, S.V. and Suresh, B., **Indian J. Pharm. Edu.,** 2003, 37, 199.
11. Ahluwalia, V.K. and Aggarwal, R., In; Comprehensive Practical Organic Chemistry - Preparation and Quantitative analysis, Universities Press (India) Ltd., Hyderabad, 2002, 248.
12. Indian Pharmacopoeia, Vol. II, The Controller of Publications, Govt. of India, New Delhi, 1996, A89.
13. Furniss, B.S., Hannaford, A.J., Rogers, V., Smith, P.W.G. and Tatchell, A.R., Vogel's Textbook of Practical Organic Chemistry, 4th Edn., ELBS and Longmann, 1978, 1234.