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Applications of microwaves in pharmaceutical processes

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Abstract

Microwaves are the electromagnetic waves with frequencies that lie between 300 MHz and 300 GHz. They have wide applications in pharmaceutical field. The basic theory behind this is dipole rotation and ionic conduction. It attempts a great focus on many fields like drying, synthesis, extraction, sterilization etc. By the use of these microwaves, highest yield can be obtained in lesser time and lesser solvent consumption with great efficiency.

Keywords: microwaves, electromagnetic, dipole rotation, ionic conduction, applications

1. Introduction

Microwaves are electromagnetic waves with frequencies that lie between 300 MHz and 300 GHz with wavelengths that vary from 1 millimeter to 1 meter. Microwaves are not forms of heat but rather forms of energy that appear as heat through their interaction with materials. (Chang, 2000) [2]

Microwaves initially excite the outer layers of molecules. Microwaves are a form of electromagnetic energy with frequencies between 300 MHz and 300 GHz, generated by magnetrons under the combined force of an electric and a magnetic field perpendicular to each other. In the electromagnetic spectrum they fall between radio waves and optical waves. For domestic, scientific, medical and industrial purposes two frequencies are allocated that do not interfere with communications frequencies i.e.: 915 MHz and 2450 MHz. (Ankit *et al*., 2012) [4]

In the pharmaceutical industry the most common frequency used is 2450 MHz, because of the advantages which this frequency offers in conjunction with vacuum. Microwave fields are reflected off metals, which they do not heat. For this reason metals are used as conductors for the microwaves, or wave-guides, and or as wall for a microwave oven.

2. Microwave assisted extraction principle and mechanism

Principle: The basic principle of microwave extraction is the changes in cell structure caused by electromagnetic waves. The target of microwave extraction is the heating in dried plant material and the minute microscopic traces of moisture that occurs in plant cells. The heating up of this moisture inside the plant cell due to microwave effect results in evaporation and generates tremendous pressure on the cell wall. This pressure then ruptures the cell wall results in exudation of active constituents from the ruptured cells occurs hence increasing the yield of phytoconstituents (Veggi *et. al*., 2013; Yuan *et. al*., 2011) [13, 14]

Mechanism

The mechanism of microwave heating is the dipole rotation and ionic conduction through reversals of dipoles and displacement of charged ions present in the solute and the solvent. Ionic conduction is the electrophoretic migration of ions when an electromagnetic field is applied, and the resistance of the solution to this flow of ions results in friction that heats the solution. Dipole rotation means rearrangement of dipoles with the applied field (Mandal *et. al*., 2007) [10]

Advances in microwave-assisted extraction (MAE) have led in the development of various techniques such as compressed air microwave distillation (CAMD), vacuum microwave hydro distillation (VMHD), microwave hydro distillation (MWHD), solvent-free microwave extraction (SFME), microwave accelerated steam distillation (MASD), microwave by hydro diffusion and gravity (MHG).

Microwave energy to the samples may be performed using two technologies: either closed vessels under controlled pressure and temperature, or open vessels at atmospheric pressure. The two technologies are commonly named pressurised MAE (PMAE), with a multi-mode cavity, or focused MAE (FMAE) using the waveguide as a single-mode cavity, respectively. Both systems are shown in Fig. 6. Whereas in open vessels the temperature is limited by the boiling point of the solvent at atmospheric pressure, in closed vessels the solvent can be heated above its boiling point at atmospheric pressure by simply applying suitable pressure, thus enhancing both extraction speed and efficiency. However, after extraction with closed vessels, one needs to wait for the temperature to decrease before opening the vessel, thereby increasing the overall extraction time (by approximately 20 min). Open systems use focused microwaves, resulting in homogenous and very efficient heating of the sample. In closed systems using diffuse microwaves, the electric field in the cavity is non-homogenous, and therefore the vessels are placed on a turntable. Recently, the respective advantages of high-pressure vessels and focused microwave heating have led to the development of systems that combine both approaches. These so-called ''focused high-pressure, high temperature microwave systems'' comprise an integrated closed vessel and a focused microwave-heated system operating at very high pressure and temperature. (Sticher, 2008) [12]

3. Applications of Microwaves in Pharmaceutics

Microwave sterilization

There is great utilization & significance of a new method i.e., microwave sterilization in Pharmaceutical industry. The sterilization is brought about by microwave dielectric heating effect. Microwave sterilization is now utilized for sterilization of heat labile drugs where a high temperature is generated for sterilization in a shorter period of time. That creates a possibility of making the process continuous. Such a process can benefit the industry due to its economy & lesser production time (Jurgen *et al*., 2003) [6]

Microwave Thawing

Thawing is process where freeze stored drugs brought to normal Physiological temperature before administration especially if an injection. One of the methods for thawing is the use of microwave. Stability of majority of drug preparation was unaffected except for some preparations, thus providing criticism for microwave thawing. The stability of many drugs both physical and chemical was not affected after microwave thawing

Drug extractions

Microwave-Assisted Extraction (MAE) has been a developing extraction technique for the isolation of semivolatile organic compounds from solid matrices. With MAE, the sample is placed in an open vessel and heated by microwave energy, using a microwave absorbing solvent. The hallmark feature of MAE is accelerated dissolution kinetics as a result of the relatively high extraction temperature. Microwave-assisted extraction (MAE) is a relatively new extraction technique which utilizes microwave energy to heat the solvent and the sample to increase the mass transfer rate of the solutes from the sample matrix into the solvent.

Microwave-assisted organic synthesis (MAOS)

Microwave-assisted organic synthesis (MAOS) is clearly a method by which the laboratory chemist can achieve goals in a fraction of time as compared to traditional conductive heating methods. Reactions times in the best cases have been reduced from hours or days to minutes.

Microwave-assisted Hydrodistillation

The ability of microwave radiation to heat solid material effectively can also be used for obtaining essential oils. Thus, the herb is placed in a microwave cavity and irradiated with microwaves. This process yields essential oils consisting of relatively low volatile fractions as compared to hydrodistillation. For instance, in coriander oil, the percentage of tetradecanoic and hexadecanoic acid increased whereas that of linalool decreased. This is possibly due to the poor stability of linalool, a tertiary alcohol. Dill seed oil obtained by microwave-assisted hydrodistillation (MWAHD) contained greater quantities of compounds with higher boiling points and lesser quantities of compounds of lower stability. These and other findings indicate that MWAHD is better for extracting stable, high-boiling point components, whereas it is not suitable for recovering chemically unstable compounds.

Microwave Drying

The mechanism for drying with microwave energy is quite different from that of conventional drying. In conventional drying heat is transferred to the surface of the material by conduction, convection or radiation and into the interior of the material by thermal conduction. Moisture is initially flashed off from the surface and the remaining water diffuses to the surface. This is often a *slow process* in conventional drying and the diffusion rate is limited, requiring high external temperatures to generate the temperature differences required (Larhed, 2001) [8].

Few examples of MAE in herbal extractions

Microwave-assisted extraction (MAE) has been recognized as a technique with several advantages over other extraction methods, such as reduction of costs, extraction time, energy consumption, and CO2 emissions. In this study, MAE was performed to obtain essential oils from two different herbs (basil and epazote). Amount of solvent and heating time significantly affected the yields ($p<0.05$). Chemical composition and physical properties of the essential oils from basil and epazote were not affected by the extraction method (MAE or SD), with similar yielding obtained by both methods ($p<0.05$) (Cardoso-Ugarte, 2013) [3].

A few sesquiterpenes lactones and monoterpenes when subjected to microwave irradiation on solid surface undergo facile carbon – carbon double bond migration from exo-to endo position. Moreover the reactions have proved to be cleaner concomitant with improvement in yield and selectivity (Kaur *et al*., 2011) [7]

Urtica dioica's conventional extraction is usually performed using reflux, cold maceration, soxhlet and simple distillation techniques. These methods which have been used for many decades are very time consuming and require relatively large quantities of solvents5. Extraction using non-conventional methods (microwave assisted extraction and ultrasound assisted extraction) can result in a yield increase in shorter time using less solvent (Badnar *et al*., 2013) [5].

Fresh tea shoots (one shoot and two or three young leaves) were extracted using microwave-assisted extraction method (MAE). Several factors such as ethanol concentrations (0-99.5o (volume percentage)), material: solvent ratio (1:4 to 1:12), extraction time, oven power were studied to optimise conditions at laboratory scale. MAE archived good yield (82.46 %) after 6 minutes microwave radiation, that was higher than that of extraction at room temperature in 24 hours, conventional heating extraction at reflux temperature in 60 minutes or ultrasound-assisted extraction in 60 minutes (Quan *et al*., 2006) [11].

The use of microwaves comprises more than the simple application of a goal-oriented, innovative tool, it is crucial to be aware of the fundamentals of chemistry in the microwave field before investigating challenging reaction mechanisms. Therefore, the following overview focuses mostly on reaction engineering in the microwave field. Parallel reactions and scale-up are also discussed. The last section of this review is dedicated to the development of experimentally sound protocols on microwave-assisted syntheses and separations, which are illustrated through experiments (Nuchter *et al*., 2004) [9].

4. Economics of Microwave Systems

Several criteria for successful microwave drying systems are related to reduce cost. Cost saving may be realized through:

1. Energy savings
2. Faster batch processing
3. Operational efficiencies
4. Increased throughput
5. Labor reduction
6. Reduction in heat load in the plant
7. Reduced maintenance costs
8. Reduction in product fouling
9. Less floor space needed

5. Conclusion

Although microwave technology has been around a long time, its application in the pharmaceutical industry is relatively recent. On the other hand, its acceptance and evolution are progressing at developing rate. The modern microwave drying systems are all equipped with the necessary safety measures to ensure completely safe processing for both operator and product. However, careful design of the process parameters is necessary to obtain optimal results from the microwave technology in pharmaceutical production (Bonde *et al*., 2011) [1]. The main advantages of Microwave assisted techniques are faster and cleaner procedure, higher yields, development of new pathways and green chemistry.

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