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# MICROWAVE ASSISTED SYNTHESIS, A GREEN PROTOCOL FOR DEVELOPMENT OF NEW AND ADVANCED DRUG DELIVERY SYSTEMS, A REVIEW

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## ABSTRACT

Medicinal Chemistry community is considering new chemical processes, which are environmentally benign. Environmentally benign synthetic protocols have become the primary concern during complex drug discovery processes. Green chemistry is providing algorithms for protecting the environment, not by cleaning it, but by inventing new chemical processes that fuel the Economy and lifestyles, without causing any damage to the environment. Microwave assisted techniques has opened up new opportunities to the synthetic chemists in the form of new improved reaction pathways, that are not otherwise feasible. MAOS has reduced the reaction times from hours or days to minutes leading to efficient economic way for synthesis of large number of molecules. Present Review article attempts to focus on what is MAOS, how it is generated and works going on in this area.

**Keywords:**
*Environmentally benign,Microwave assisted techniques, green protocol.*

## INTRODUCTION

Microwave assisted synthesis enhances the rate of the reaction leading to higher yields, and improved selectivity, with respect to the conventional reaction conditions.1, 2.Solvent –free reactions using either organic or inorganic solid supports have gained grounds in the recent years3, 4.Synthesis in dry media is economically advantageous because no solvent is used and it still have short reaction times and are safer, clean and efficient. Synthesis of new molecules is a major concern in the drug discovery. Conventional methods for various chemical syntheses are well documented and practiced 5. The researchers are working day and night to modify these methods for synthesis of molecules. New protocols have been discovered, Microwave assisted synthesis is considered as an important green protocol for the development of advanced drug synthesis and delivery methods. This technology is still under-used in the laboratory and has the potential to have a large impact on the fields of screening, combinatorial chemistry, medicinal chemistry and drug development. The technology shows plethora of opportunities to the chemists, in the form of new reactions which are not possible through conventional heating. The technology well obeys 12 principles of Green chemistry" which are as follows:

• Prevention of waste

- Atom Economy
- Less Hazardous Chemical Syntheses
- Design Safer Chemicals
- Safer Solvents and Auxiliaries
- Design for Energy Efficiency
- Use Renewable Feedstocks
- Reduce Derivatives
- Catalysis
- Design for Degradation
- Real-time Analysis for Pollution Prevention
- Inherently Safer Chemistry for Accident Prevention

**PRINCIPLE**

Microwave radiations are non-ionizing form of electromagnetic radiations. These radiations do not alter the molecular structure of compound being heated and provide thermal activation only. Radiations have ability to couple directly with the reaction molecule and by-passing thermal conductivity leading to a rapid rise in the temperature, microwave irradiation has been used to improve many organic syntheses. The microwave region of the electromagnetic spectrum lies between infrared and radio frequencies6, 7. The heating effect utilized in microwave assisted transformations is mainly due to change in the dipole moment of the molecule caused due to the interaction of the molecule with the radiation. The ability of a material to convert electromagnetic energy into thermal energy is dependent on the dielectric constant. Solvents with high dielectric constants such as water, methanol, DMF, ethyl acetate, acetone, acetic acid, etc. are all heated rapidly with microwave radiation. However, solvents with low dielectric constants do not couple and therefore do not heat that rapidly under microwave irradiation, leading to the use of Microwave heating as very convenient thermal source in a chemical laboratory. Kappe CO, Dallinger D.reported many advantages of using rapid "Microwave flash heating for chemical synthesis.One of them being dramatic reduction in reaction time from days and hours to minutes and seconds. They also reported the reasons for using Micowave radiations by pharmaceutical companies into their drug discovery efforts.8,9. The phenomena of producing heat by electromagnetic irradiation are either by collision or by conduction, sometimes even by both10, 11 Chemists have explored the possibility of the application of a conventional microwave oven to carry out chemical reactions. However, the advantages of using microwave dielectric heating for performing organic transformations have only emerged since the mid- 1980s.

**MICROWAVES FOR DRUG SYNTHESIS**

In the past few years, use of microwave energy as green protocol for drug synthesis has been an increasingly popular theme in the scientific community. Since the first published reports on the use of microwave irradiation by the groups of Gedye 12, more than 5000 articles have been published in this fast moving and exciting field, today generally referred to as microwave assisted organic synthesis13-15. The applications of this enabling technology have, more recently, been exploited in the context of multistep total synthesis16 and medicinal chemistry/drug discovery17. Santagada V, Frecentese F, Perissutti E, Fiorino F, Severino B, Caliendo G. 18,19Showed through well designed equipments and experiments and through examples that microwave assisted synthesis is very useful for the synthesis of biologically active compounds both in heterocyclic and in peptide and peptidomimetic optimization. They showed that technique is of great

importance in high-speed combinatorial and medicinal chemistry. Traditional methods of synthesis of heterocyclic compounds are orders of magnitude too slow to satisfy the demand for these compounds. Speed is of the essence. The efficiency of microwave flash-heating chemistry in dramatically reducing reaction times (reduced from days and hours to minutes and seconds) has recently been proven in several different fields of organic chemistry. We believe that the time saved by using focused microwaves is potentially important in traditional organic synthesis but could be of even greater importance in high-speed combinatorial and medicinal chemistry.

Larhed M, Hallberg A. 20 reported the use of microwave assisted synthesis for new organic molecules needed in both lead identification and lead optimization processes emphasizing the fact that traditional methods of organic synthesis are orders of magnitude too slow to satisfy the demand for these compounds.

Kappe CO 21 unravellled the mysteries of microwave chemistry using silicon carbide reactor technology and confirmed through the data obtained from these investigations that in the overwhelming majority of cases a bulk temperature phenomenon drives the enhancements in microwave chemistry and that the electromagnetic field associated with the microwave radiation has no direct influence on the reaction pathway, nullifying the speculation of direct influence of radiation on a chemical transformation.

Feng Chen, Peng Huang, Chao Qi et.al 22 synthesized multifunctional mesoporous microspheres of europium-doped amorphous calcium phosphate ($Eu^{3+}$-doped ACP) using a natural biomolecule adenosine triphosphate (ATP) by the rapid microwave-assisted solvothermal method. This method has advantages such as surfactant-free, rapid and energy-saving.

## CONCLUSION

Microwave radiations donot effect the chemical environment of the reaction as proved from the work done by researchers, however MAOs follow all the parameters of green chemistry,providing excellent heating effect in a decreased duration of time.Microwave assisted synthesis can be used as the green protocol for conventional reactions utilized in the drug delivery and drug synthesis.

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