Jundishapur J Nat Pharm Prod. 2022 February; 17(1):e121619. doi: 10.5812/jjnpp.121619.

Published online 2022 January 5. **Editorial**

Biopharmaceutical Application of Microwave Technology and the Scalability Concerns

Olalere Abayomi Olusegun [1, *] and Gan Chee-Yuen [1, **]

[1] Analytical Biochemistry Research Centre (ABrC), Innovation Incubator Building, University of Science, Penang, Malaysia

[*] *Corresponding author*: Analytical Biochemistry Research Centre (ABrC), Innovation Incubator Building, University of Science, Penang, Malaysia. Email: olabayor@gmail.com
[**] *Corresponding author*: Analytical Biochemistry Research Centre (ABrC), Innovation Incubator Building, University of Science, Penang, Malaysia. Email: cygan@usm.my

Received 2021 December 02; **Accepted** 2021 December 22.

Keywords: Biopharmaceuticals, Electromagnetics, Drug Products, Microwave, Scalability

Since their invention, microwaves have found significant use in different fields, including medicines and food processing, as well as sterilization of microorganisms for use in biomedical treatment and research. Various scientific studies have demonstrated microwave application's capability as clean technology and a veritable solution for producing a pure and desirable drug candidate in bionutraceuticals processing. Microwave treatment, therefore, offers an efficient approach by combining electromagnetic waves with multi-directional heating technologies. It provides the prospect of shorter processing times, a better degree of selectivity, lower and greener energy use for producing high-quality medicinal products. Ionic conduction and dipole rotation have been identified as critical fundamental phenomena underlying microwave processing technology (1). In far too many cases, these two phenomena occur concurrently, with ionic conduction providing a substantial opposition to ionic flow. This, in essence, creates an impedance and heat generation in the microwave cavity (2). Moreover, the dipole rotation automatically readjusts the molecular magnetic dipole to the instantaneous electric field, prompting an ionic displacement as the dipole spins about its axis. The electric field generated inside the microwave cavity induces an ionic current to flow through the medium, which is generally the cause of its quick processing time and high-quality biopharmaceutical production.

Ever since the development of industrial microwave ovens in the late 1940s, the pharmaceutical and food industries have shown significant potential in utilizing the technology due to their quick heating capabilities in enhancing product quality (3). In recent years, microwave technology has gained attraction in the drying process, biopharmaceutical synthesis, decontamination, drug extraction, sample preparation via digestion, and microwave thawing. For example, the use of microwave dryers by pharmaceutical industries has proven to be an effective and quality-enhancing technology (3). Due to the sensitivity of pharmaceutical powders, the drying conditions are generally governed by strict quality factors such as microwave power, temperature, and irradiation duration (3). Because of the distinctive mechanism of microwave irradiation, controlled heating of different materials is feasible during drying. Microwave drying can thus be thought of as a 'self-regulating' heating process that allows for more efficient energy use (4). Because of the intrinsic capability to 'moisture level,' the optimum moisture content within the material is significantly smaller than in a traditionally dried product, and the quality of these thermally sensitive pharmaceutical products is sustainably retained. Moreover, the designing of sustained-release medication delivery systems like matrix and encapsulated tablets can be strongly influenced by using microwaves technology with the polymeric coating on the matrix altering tablet's drug-releasing properties. Microwave drying can be utilized to dry polymer coating on the tablet. The standard solution or dispersion of polymer is typically used to add the polymer coat to the capsule. The resulting drug product is more pliable, with a shorter drying time and greater tensile strength than the oven- or air-dried films, but a significantly reduced level of tensile strength than that dried by hot airstream (5).

Contemporary heavy metal regulatory standards have mandated that the pharmaceutical sector screen a variety of elemental contaminants in their raw materials, medication products, and multivitamins (5). In furtherance to this, microwave digestion is another application of microwave technology that is usually employed as one of

the basic material preparation processes in pharmaceutical applications for elemental determination. However, it is important to note that the exact heating procedure is dependent on the sample's composition and quantity. Heating digestion solutions using microwave has grown in popularity in recent years. The digestions are conducted in a closed system composed of chemically inert materials that are microwave-transparent. Apart from accelerating the reaction kinetics via the use of a closed vessel, immediately heating the sample solution reduces digestion durations even more. As a result, normal microwave digestion only takes around an hour. Nevertheless, because the fast heating is followed by a similarly quick pressure increase and presumably spontaneously produced exothermic processes, the temperature development of each sample must be continually measured, and the microwave power must be adjusted correspondingly. Pressure and temperature should be tracked together for the sake of safety, and this monitoring may also be utilized to control microwave power. The best possible process control may be obtained in this manner. Understanding the advantages and disadvantages of various microwave digesting processes is vital, especially for pharmaceutical formulations, due to the stringent validation procedures.

Microwave-aided drug extraction is another important technique for selective separation of active and inactive components usually from plant materials. The conventional procedures are usually time-consuming, solvent intensive, and thermally degrading, which limits elucidation of myriads of bioactive components in different plant materials. The microwave-based technology, on the other hand, enables an efficient and rapid extraction while using less solvent and protecting against dangerous pollutants. This involves the use of 'micro waves' to heat solvents and plant materials during the extraction process, thus increasing the recovery kinetics of the bioactive constituents. This is typically influenced by the interactions of extracting agents (solvents) and electromagnetic/electric field cycles (6). Due to the heat of activation and frictional effect, the solvents-ions can migrate, and the affinity of the solvent to absorb the energy generated by the microwave electric and magnetic field is thus triggered by the extracting agent's dipole moment (7). Furthermore, microwaves are one approach for thawing-freezing stored drugs. Microwave thawing is the process of bringing frozen medications to their normal physiological temperature before delivery for injection purposes (5). One advantage of microwave thawing is that the physical and chemical stability of pharmaceutical drugs is not affected, while processing costs and time are reduced (8). Because of the uniformity of the heating, precise thawing from the internal structure to the outermost layer occurs, thus reducing undesirable side reactions.

Microwave technology, therefore, offers a novel technique for controlling the physicochemical characteristics and the therapeutic agents profiles without the use of extreme heat, long processes, or harmful intermediate products. This has unambiguously shown a bright future in the design of pharmaceutical formulations such as granules, gel pellets, nanoparticles, micro-emulsion, capsules, and film coatings (5). Thus, the microwave has the prospect to adjust the physical and chemical properties of active ingredients to achieve the desired oral bioavailability of pharmaceutical products. However, the most significant drawback of microwaves, particularly in the drug development field, is scalability (5). In pharmaceutical research, synthesis scale-up from smaller to a large scale is critical, as this is a frustrating barrier for today's industrial biopharmaceutical technologists. Many small-scale syntheses cannot be replicated for large-scale processing, or even explored due to safety and cost considerations. There are currently limited documented cases of microwave technology being used for biopharmaceutical synthesis on an industrial scale. As a result, the scalability of microwave processes remains unexplored, particularly in the fields of industrial biopharmaceuticals with inherent techno-economic considerations

Footnotes

Authors' Contribution: O.A. drafting of the editorial. C.Y. critical revision of the manuscript for important intellectual content.

Conflict of Interests: The authors declare no conflict of interest.

Funding/Support: Not declared by authors.

References

1. Olalere OA, Gan C; Inamuddin. Microwave reflux extraction—An alternative approach for phenolic-rich oleoresins extraction from functional plants. In: Boddula R, Asiri AM, editors. *Green Sustainable Process for Chemical and Environmental Engineering and Science*. Amsterdam: Elsevier; 2021. p. 661–78. doi: 10.1016/b978-0-12-819848-3.00016-5.
2. Alara OR, Abdul Mudalip SK, Olalere OA. Optimization of mangiferin extrated from Phaleria macrocarpa fruits using response surface methodology. *J Appl Res Med Aromat Plants*. 2017;**5**:82–7. doi: 10.1016/j.jarmap.2017.02.002.
3. McLoughlin CM, McMinn WAM, Magee TRA. Microwave-Vacuum Drying of Pharmaceutical Powders. *Drying Technology*. 2003;**21**(9):1719–33. doi: 10.1081/drt-120025505.
4. Solanki HK, Prajapati VD, Jani GK. Microwave technology—a potential tool in pharmaceutical science. *ChemInform*. 2011;**42**(24):no.
5. Bonde MN, Sohani AC, Daud AS, Sapkal NP. Microwave: An emerging trend in pharmaceutical processes and formulations. *Int J Pharm Tech*. 2011;**3**(4):3499–520.

6. Olalere OA, Abdurahman HN, Gan C. Microwave-enhanced extraction and mass spectrometry fingerprints of polyphenolic constituents in Sesamum indicum leaves. *Ind Crops Prod*. 2019;**131**:151–9. doi: 10.1016/j.indcrop.2018.12.024.
7. Olalere OA, Gan C. Microwave-assisted extraction of phenolic compounds from Euphorbia hirta leaf and characterization of its morphology and thermal stability. *Sep Sci Technol*. 2020;**56**(11):1853–65. doi: 10.1080/01496395.2020.1795678.
8. Tapas AR, Magar DD, Kawtikwar PS, Sakarkar DM, Kakde RB. Microwaves in drug discovery and development: A. *Int J Pharmtech Res*. 2009;**1**(4):1039–50.