RASĀYAN J. Chem.
Vol. 18 | No. 2 |926-931| April - June | 2025
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

KINETIC MODELLING OF ULTRASOUND-ASSISTED EXTRACTION OF PHENOLIC COMPOUNDS FROM NEEM

Sunita S. Patil[1,2,✉] Shambala Gadekar-Shinde[3] and Nayana Menon[4]

[1]Department of Chemical Engineering, Dr. D.Y. Patil Institute of Engineering, Management and Research, Akurdi, Pune (Maharashtra), India

[2]Department of Chemical Engineering, D.Y. Patil International University, Akurdi, Pune (Maharashtra), India

[3]Department of Chemical Engineering, Bharati Vidyapeeth (Deemed to be University) College of Engineering, Pune (Maharashtra), India

[4]Hindustan Platinum, Mumbai (Maharashtra), India

✉Corresponding author: sunitapatil_9@rediffmail.com

ABSTRACT

Polyphenols are the plant secondary metabolites that function as anti-inflammatory, antioxidant, and antimicrobial compounds. These compounds possess high antioxidant activity due to their chemical structure. Recently, it was investigated that there is potential for the use of polyphenols as antiviral agents to inhibit the development of coronavirus disease. Hence, the extraction of phenolic compounds is essential. Ultrasound-assisted extraction is a novel extraction technique that is used for the recovery of phenolic compounds from neem leaves. The effect of temperature (30 - 60 ° C) and methanol-water composition (25 – 100 % v/v) was studied. The highest yield of polyphenols, 25.016 mg GAE/g of plant material, was achieved at 60 °C. The kinetics of ultrasound-assisted polyphenol extraction were well described by the Peleg model, showing a strong agreement between experimental and calculated data, as indicated by low root mean squared error values.

Keywords: Polyphenols, Ultrasound-Assisted Extraction, Neem, Kinetic Modelling, Temperature, Solvent Composition.

RASĀYAN *J. Chem.*, Vol. 18, No. 2, 2025

INTRODUCTION

Polyphenols are a diverse group of natural compounds that serve as secondary metabolites in plants, originating from the pentose phosphate, shikimate, and phenylpropanoid pathways. These phenolic compounds play an essential part in plant development and reproduction, offering protection against pathogens and predators while contributing to the colour and sensory qualities of fruits and vegetables. Additionally, phenolic compounds have numerous health advantages, such as antimicrobial, anti-allergenic, antioxidant, and anti-inflammatory.[1] They are broadly categorized into four main groups: “phenolic acids, flavonoids, stilbenes, and lignans”. They possess medicinal properties that benefit in reducing the risk of several pathological disturbances such as diabetes, cancers, osteoporosis, cardiovascular diseases, and neurodegenerative diseases.[2] The polyphenols possess high antioxidant activity due to their chemical structure. These are described as antioxidant, anti-inflammatory, and immunomodulatory bioactive compounds. Dietary polyphenols occur in fruits, vegetables, cereals, legumes, tea, coffee, herbs, and spices.[3] The entire global population had suffered due to coronavirus disease 2019 (COVID-19), a highly contagious illness caused by a newly emerged coronavirus. There is potential for the use of polyphenols as antiviral agents in inhibiting the development of COVID-19 induced by the coronavirus. Quercetin, rutin, methyl gallate, gallic acid, (+)catechin, (-)epicatechin, and (-)epigallocatechin gallate (EGCG) derived from different herbal plants are found to be potentially effective antiviral agents that may be used in the development of severe acute respiratory syndrome (SARS) drugs or preventive preparations.[4,5] Hence, in recent years, there has been an increased interest in the exploration of competent and cost-effective phenolic compounds that act as natural antioxidants and antiviral agents possessing beneficial health effects, nutritional value, and safety. Phenolic compounds can be extracted from traditional and novel extraction

http://doi.org/10.31788/RJC.2025.1829217

Vol. 18 | No. 2 |926-931| April - June | 2025

techniques. The most used traditional techniques include Soxhlet and maceration, which require more extraction time, energy, and a large quantity of solvent. Ultrasound-assisted extraction (UAE) is a novel extraction technique that requires less time, energy, and solvent quantity; reduces industrial pollution, increases efficiency, and is environmentally friendly. Due to these advantages, this novel technique is termed a green extraction technique.[6,7] Process variables like particle size, temperature, solid-to-liquid ratio, sonication time, solvent, and frequency affect the efficiency of the extraction process.[8-10] The kinetics of the UAE process can be studied by the application of empirical modelling. Modelling is an invaluable engineering tool for explaining systems, analysing the impact of various parameters, and predicting behaviour for future applications.[11] The studies on kinetic modelling of UAE of phenolic compounds from neem leaves by the Peleg model are less, hence the objective of this research paper is to explore the kinetic modelling of phenolic compounds from neem leaves using the Peleg model.

EXPERIMENTAL

Materials and Methods

The cleaned and dried neem leaves (*Azadirachta indica* L.) were ground using a Bajaj grinder and sieved to obtain 72 mesh-sized particles (0.212 mm). The sample was stored in closed containers at 5 °C to prevent air exposure. Analytical grade sodium carbonate, Folin-Ciocalteu reagent (to determine total polyphenol content), methanol, and standard gallic acid were purchased from Sourav Scientific, Pune, India.

Ultrasound-Assisted Extraction (UAE)

An ultrasonic probe sonicator (diameter 12 mm) with power 120 W and frequency 20 kHz, supplied by Dakshin, Mumbai, India, was used for the extraction of total phenolic compounds. It was operated in pulse mode to avoid heat dissipation. The temperature was regulated by providing a stirred water bath. During ultrasound-assisted extraction, 5 g of 0.212 mm particle-size plant material was mixed with 200 mL of solvent.[12] The mixture was sonicated for 90 minutes with a collection of samples at regular intervals for analysis. The impact of temperature (30, 40, 50, 60 °C) and methanol-water composition (25%, 50%, 75%, 100% v/v) on the yield of total phenolic content (TPC) was investigated.

Analysis

The calibration curve was prepared using standard gallic acid in the range 50 -1000 mg GAE/L. The concentration of TPC was determined by the Folin-Ciocalteu method as reported[13], using a Shimadzu UV double beam spectrophotometer (Model -UV 1800). Each sample was analysed in triplicate, and the average results were recorded along with the standard error, and TPC was measured in milligram gallic acid equivalent per gram of plant material (mg GAE/g of plant material).

Kinetics of Ultrasound-Assisted Extraction of TPC

Peleg Model

Peleg, a semi-empirical kinetic model, was used here to determine the kinetic parameters of extraction. The Peleg model is used to describe the kinetics of solid-liquid extraction since sorption and extraction curves are comparable.[14] The kinetics of polyphenol extraction from soybeans[15] and grape seeds[11] have been explained by this model. The Peleg model equation is:

$$c_t = c_o + \frac{\mathrm{t}}{\mathrm{k_1+k_2(t)}} \qquad (1)$$

Where c_t= quantity of TPC at time t (mg GAE/ g of plant material), c_o = quantity of TPC (mg GAE/g of plant material) at time t = 0, k_1 = Peleg's rate constant, which describes the initial rate of extraction, and k_2 = Peleg's capacity constant, which represents the maximum extraction yield. Since the initial quantity of TPC in the fresh solvent is zero, the term c_o can be omitted from the (1). Therefore, Eq. (1) was modified to Eq. (2) as:

$$c_t = \frac{\mathrm{t}}{\mathrm{k_1+k_2(t)}} \qquad (2)$$

The Peleg constants in the above equation were determined by plotting the graph of $\frac{1}{c_t}$ Vs. $\frac{1}{t}$. The c_tValues were calculated at various time points to assess the model's fit.

Statistical Analysis

The alignment between the estimated and experimental data was assessed using the root mean squared error (RMSE), which is defined.

$$RMSE = \sqrt{\frac{1}{m}\sum_{i=1}^{m}\left(y_j - \hat{y}_j\right)^2} \quad (3)$$

Where m is the number of samples, y_j Is the experimental value of the jth sample, $\hat{y}_j i$Is the estimated value of the jth sample. A high level of consistency is indicated by a low RMSE score between the estimated and experimental data.

RESULTS AND DISCUSSION

Effect of Temperature on Total Polyphenols Content

Effect of temperature on ultrasound-assisted extraction kinetics of TPC from neem leaves powder of particle size 0.212 mm, solid-to-solvent ratio 1:40 g/mL, and 50% (v/v) methanol-water solvent composition is depicted in Fig.-1. The yield of TPC increased with increasing temperature from 30 °C to 60 °C. The temperature had a positive influence on TPC. After 90 minutes of ultrasound-assisted extraction, the extraction yield of TPC at 30 °C was 17.031 mg GAE/g of plant material, while the yield increased to 25.016 mg GAE/g of plant material at 60 °C. Similar results were reported in ultrasound-assisted extraction of total phenolic content at 50, 60, and 70 °C from eggplant (*Solanum melongena L.)* peel.[16] Belwal *et al.*[17] also noticed the positive effect of methanol concentration (20, 50, 80%) and temperature (30, 55, 80 °C) on solid-liquid extraction of phenolic compounds from *Berberis asiatica* fruits. The increase in temperature increases the mass transfer of polyphenols from the plant matrix into the solvent by enhancing the solubility and diffusivity of polyphenols. The rising temperature also affected the softening and swelling of the plant tissue. In ultrasound-assisted extraction, the thermal and cavitation effects play an important role in increasing the efficiency of the process. Cavitation destroys plant material, which in turn releases the solute content from the interior pores of the plant material into the solvent. Though high temperature in an appropriate range can promote ultrasound-assisted extraction, its adverse effect on cavitation cannot be neglected. Because the increase in vapor pressure of the solvent at high temperature decreases the efficiency of the implosion of cavitation bubbles on the plant surface.[18] Figure-1 demonstrates a strong correlation between the experimental and model-predicted TPC yield values. Table-1 presents the Peleg model constants (k_1 and k_2), along with the experimental and estimated equilibrium yield values at different temperatures and the RMSE.

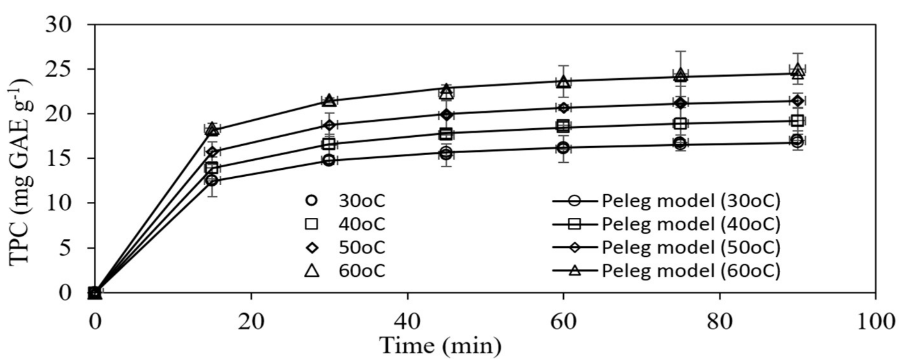

Fig.-1: Effect of Temperature on the Extraction of TPC (mg GAE/g of Plant Material)

Table-1: Kinetic Parameters, Experimental and Estimated Equilibrium Concentrations at Various Temperatures (mg GAE/g of Plant Material)

Temperature °C	k_1 (g min/mg)	k_2 (g/mg)	Experimental c_e	Estimated c_e	RMSE
30	0.368	0.055	17.031	16.780	0.191
40	0.358	0.048	19.212	19.166	0.120
50	0.304	0.043	21.474	21.428	0.098
60	0.252	0.038	25.016	24.469	0.327

Effect of Solvent Concentration on Total Polyphenols Content

The selection of a correct extraction solvent is one of the most important steps to obtain a better yield. This selection of a solvent mostly depends upon the polarity of the solvent, affinity towards the solute, cost, and safety. Alcohols and acetone, combined with varying proportions of water, have been extensively used to extract polyphenols from plant material.[15] In extraction assisted by ultrasound, the cavitation phenomena will be affected by the physical properties of the solvent. With the increase in vapour pressure and surface tension of the solvent, cavitation intensity decreases.[19] This study investigated the effect of methanol-water concentrations (25%, 50%, 75%, and 100% v/v) on the yield of total polyphenols, using a particle size of 0.212 mm, a solid-to-liquid ratio of 1:40 g/mL, and room temperature. The total polyphenols yield at 25% methanol-water concentration was found to be 17.784 mg GAE/g of plant material, and the yield was increased with the increase in methanol-water concentration from 25-75%, whereas a lower yield of total polyphenols was obtained for absolute methanol. In the extraction of polyphenols from the peel of kinnow (*Citrus reticulata L.*) by UAE and maceration techniques, the maximum yield was obtained for 80% methanol concentration, and absolute methanol showed less yield. Our results are coordinating with the earlier report. This variation in the yield of total polyphenols obtained depends on the polarities of solvents and their concentration levels, either aqueous or absolute. The addition of a small amount of water weakens the strong hydrogen bond between the protein and polyphenols and enhances the solubility.[20] The total phenolic content recovery from different agrowastes using 80% methanol concentration was investigated. Among the various agrowastes, pomegranate peels exhibited the highest recovery of 36.4 $\pm$ 0.7 g GAE/ 100 g of dry matter.[21] Figure-2 shows the comparison between the experimental data and extraction curves obtained from the Peleg model. The Peleg model constants k_1 and k_2 for different methanol concentrations are shown in Table-2. The lower values of RMSE in Table-2 depict a good agreement between the experimental and estimated equilibrium values of total polyphenols.

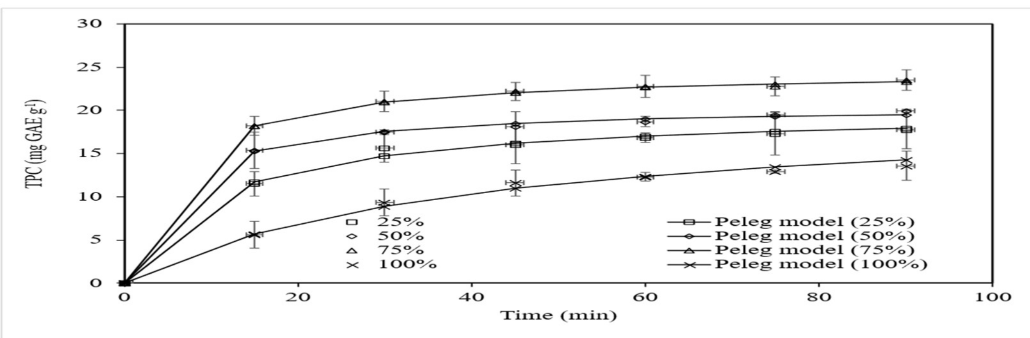

Fig.-2: Effect of Solvent Concentration on Extraction of TPC (mg GAE/g of Plant Material)

Table-2: Kinetic Parameters, Experimental and Estimated Equilibrium Concentrations at Various Solvent Compositions (mg GAE/g of Plant Material)

Solvent composition (methanol/water, %v/v)	k_1 (g min/mg)	k_2 (g/mg)	Experimental c_e	Calculated c_e	RMSE
25	0.537	0.050	17.784	17.931	0.379
50	0.254	0.048	19.957	19.521	0.208
75	0.219	0.040	23.510	23.344	0.100
100	1.900	0.049	13.573	14.263	0.442

CONCLUSION

Interest in plant polyphenols has been growing due to their antioxidant, anti-inflammatory, immunomodulatory, and antiviral properties. The traditional techniques used for the extraction of phenolic compounds required longer extraction times, higher amounts of solvents, and more energy. The ultrasound-assisted extraction of phenolic compounds has the advantages of less time, low solvent requirement, higher extraction yield, and being environment-friendly. The experimental investigations showed that the maximum extraction yield of TPC from the neem leaves obtained at 60 °C was 25.016 mg GAE/g of plant material, and for 75% (v/v) methanol-water concentration yield was 23.51 mg GAE/g of plant material. The

Peleg model showed a good fit between the experimental and calculated values. The phytotherapy with polyphenols extracted from natural resources can be used in the prevention of COVID-19. Though ultrasound-assisted extraction has been studied extensively on a laboratory scale, further study is needed in the design and scale-up of UAE for industrial application.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID ids, given below:

Sunita Patil https://orcid.org/0000-0002-9709-1927
Shambala Gadekar- Shinde https://orcid.org/0000-0001-7090-4097
Nayana Menoni https://orcid.org/0009-0001-6276-8168

REFERENCE

1. N. V. Zagoskina, M. Y. Zubova, T. L. Nechaeva, V.V. Kazantseva, E.A. Goncharuk, V. M. Katanskaya, E. N. Baranova, M. A. Aksenova, *International Journal of Molecular Sciences*, **24**, 13874(2023), https://doi.org/10.3390/ijms241813874
2. A. Vignesh, T. C. Amal, A. Sarvalingam, K. Vasanth, *Food Chemistry Advances*, **5,** 100749(2024), https://doi.org/10.1016/j.focha.2024.100749
3. M. Rudrapal, G. Rakshit, R. P. Singh, S. Garse, J. Khan, S. Chakraborty, *Antioxidants*, **13**, 429 (2024), https://doi.org/ 10.3390/antiox13040429
4. M. A. El-Missiry, A. Fekri, L. A. Kesa, A. I. Othman, *Phytotherapy Research,* **38,** (2020), http://doi.org/10.1002/ptr.8123
5. P. K. Agrawal, C. Agrawal, G. Blunden, *Natural Product Communications*, **15,** (2020), https://doi.org/10.1177/1934578X211042540
6. K. Chojnacka, A. Witek-Krowiak, D. Skrzypczak, K. Mikula, P. Mlynarz, *Journal of Functional Foods*, **73**, 104146 (2020), https://doi.org/10.1016/j.jff.2020.104146
7. B. K. Tiwari, *Trends Analytical Chemistry,* **71**, 100(2015), https://doi.org/10.1016/j.trac.2015.04.013
8. S. Peng, M. Zhu, S. Li, X. Ma, F. Hu, *Frontiers in Sustainable Food Systems*, **7**, 1131959(2023), http://doi.org/ 10.3389/fsufs.2023.1131959
9. H. Che, R. Zhang, X. Wang, H. Yu, X. Shi, J. Yi, J. Li, Q. Qi, R. Dong, Q. Li, *Ultrasonics Sonochemistry*, **111**,107083(2024), https://doi.org/10.1016/j.ultsonch.2024.107083
10. M. Pinelo, J. Sineiro, M. J. Nunez, *Journal of Food Engineering*, **77,** 57(2006), https://doi.org/10.1016/j. jfoodeng.2005.06.021
11. S. Jokic, D. Velic, M. Bilic, A. Bucic-Kojic, M. Planinic, S. Tomas, *Czech Journal of Food Sciences*, **28**, (2010), http://doi.org/10.17221/200/2009-CJFS
12. J. G. Gujar, S. Chattopadhya, S. J. Wagh, V. G. Gaikar, *The Canadian Journal of Chemical Engineering*, **88**, 232(2010), https://doi.org/10.1002/cjce.20271
13. V. L. Singleton, R. Orthofer, *Method in Enzymology*, **299,** 152(1999), http://doi.org/10.1016/S0076-6879(99)99017-1
14. S. S. Patil, A. Pathak. V. K. Rathod, *Ultrasonics Sonochemistry*, **70,** 105267(2021), https://doi.org/10.1016/j.ultsonch.2020.105267
15. A. Bucic-Kojic, M. Planinic, S. Tomas, M. Bilic, D. Velic, *Journal of Food Engineering,* **81**, 236(2007), http://doi.org/10. 1016/j.jfoodeng.2006.10.027

16. F. Dranca, M. Oroian, *Ultrasonics Sonochemistry*, **31,** 637(2016), https://doi.org/10.1016/j.ultsonch.2015.11.008
17. T. Belwal, P. Dhyani, I.D. Bhatt, R. S. Pande, *Food Chemistry*, **207**, 115(2016), https://doi.org/10.1016/j.foodchem.2016.03.081
18. Y. Tao, Z. Zhang, D. W. Sun, *Ultrasonics Sonochemistry*, **21,** 1461(2014), https://doi.org/10.1016/j.ultsonch.2014.01.029
19. K. Vilkhu, R. Mawson, L. Simons, D. Bates, *Innovative Food Science and Emerging Technologies*, **9,** 161(2008), http://doi:10.1016/j.ifset.2007. 04.014
20. M. N. Safdar, T. Kausar, S. Jabbar, A. Mumtaz, K. Ahad, A. A. Saddozai, *Journal of Food Drug and Analysis*, **25**, 488(2017), https://doi.org/10.1016/j.jfda.2016.07.010
21. B. Sultana, F. Anwar, M. R. Asi, S. A. *Grasas y aceites*, **59,** 2005(2008), https://doi.org/10.3989/gya.2008.v59.i3.510

[RJC-9217/2024]