Applied Pharmacology and Pharmaceutical Technology (APPT)
Research Article
ISSN XXXX-XXXX

Optimization of Ultrasonic Assisted Extraction Method for the Extraction of Quercetin from *Malus domestica*

Yovi Guanse[1]*
[1] Universitas 17 Agustus 1945 Jakarta, Jakarta Utara, Indonesia, 14350
*Corresponding author: yovi.guanse@uta45jakarta.ac.id

*Submitted: 18/02/2026 *Accepted: 22/02/2026 *Published: 23/02/2026*

Abstract
This study optimized ultrasound-assisted extraction (UAE) of quercetin from *Malus domestica* (red apples) using central composite design, targeting ethanol-in-water concentration (41.7–98.3%) and sonication time (8.8–51.2 min). Quercetin was quantified by UV-Vis at 372 nm, with response surface methodology yielding a significant quadratic model ($p<0.05$). Higher ethanol concentrations coupled with shorter sonication durations maximized quercetin extraction yields, as confirmed by ANOVA with the most influential factor was ethanol concentration ($F = 38.14$).

Keywords: *Malus domestica*, Ultrasound-Assisted Extraction, Central Composite Design, ANOVA.

Introduction

Indonesia, a tropical nation renowned for its abundant natural resources, extensively cultivates apples (*Malus domestica*). According to data from the Central Bureau of Statistics (2023), annual apple production reached 392,563 tons in 2023. Apples are rich in bioactive compounds, including flavonoids, specifically quercetin [1,2] The plentiful availability of apples in Indonesia presents a substantial opportunity to harness them as a source of active ingredients for developing natural product-based formulations.

Quercetin, a ubiquitous flavonoid abundant in various vegetables and fruits, has gained prominence in recent topical cosmetic formulations due to its multifaceted pharmacological properties. It exhibits potent antioxidant activity through free radical scavenging and modulation of oxidative stress pathways, alongside anti-inflammatory effects via inhibition of pro-inflammatory cytokines such as TNF-α and NF-κB signaling. Additionally, quercetin demonstrates selective antibacterial action against acne-causing pathogens like *Propionibacterium acnes* and *Staphylococcus epidermidis*, making it particularly valuable for acne management. In topical preparations, nanoemulsion or liposomal delivery systems enhance its poor aqueous solubility, dermal penetration, skin barrier function, erythema reduction, and wound healing [3–5].

Ultrasound-assisted extraction (UAE) is an advanced, green extraction technique that utilizes high-frequency ultrasonic waves to induce acoustic cavitation, facilitating efficient release of bioactive compounds from plant matrices through enhanced mass transfer, cell disruption, and solvent penetration [6]. Prior research indicates that the quantity of extracted natural compounds is markedly affected by sonication time and solvent concentration [7]. Zakaria et al. (2021) optimized UAE of *Mitragyna speciosa* leaves, demonstrating that sonication duration extension from 15 to 50 min boosted yield from ~18% to 27.88% through enhanced cavitation, while solvent concentration influenced solubility matching [8]. Wang et al. (2025) reviewed UAE of bioactive compounds from Muxu (*Medicago sativa*), reporting optimal flavonoid yields at 30 min sonication with 1:30 solid-liquid ratios and 50°C, where prolonged times beyond optimal reduced efficiency due to degradation, and solvent ratios modulated extraction rates [9].

This study aims to determine the optimal sonication time and ethanol concentration conditions to achieve maximum quercetin extraction yield from natural sources. A Response Surface Methodology, specifically Central Composite Design was selected to systematically investigate the interactive effects of sonication duration and ethanol concentration on the resultant quercetin concentration. This approach enables precise modeling of the extraction process, facilitating identification of the most efficient parameter combinations for pharmaceutical formulation applications

Materials and Method

Materials

The instrument used in this study included a UV-Vis spectrophotometer (Shimadzu UV mini-1240), a laptop (Acer Aspire 3) equipped with Design Expert® 13 software, ultrasonication (Branson 3800), centrifuge, and glassware. The materials used were red apples (*Malus domestica*), ethanol, and aquadest.

Methods

Ultrasound-Assisted Extraction

Ultrasound-assisted extractions were conducted using a ultrasonication (Branson 3800) operating at 40 kHz and 100 W nominal power, 1 gram of red apples powder was suspended in solvent mixtures (varying proportions). Independent variables, including ethanol and sonication time were optimized, with extractions followed by centrifugation (1500×g, 5 min) [10]. The central composite design extraction scheme is presented in the following table:

Table 1. Central composite design extraction scheme

Independent Variable	Coded Levels					Unit
	Axial (-α)	**Low**	**Centre**	**High**	**Axial (+α)**	
X_1: Ethanol in water	41.7157	50	70	90	98.2843	%
X_2: Sonication Time	8.7868	15	30	45	51.2132	min

Analysis of the Quercetin by Spectrophotometer UV-Vis

Quercetin standard stock solution (100 ppm) was serially diluted to prepare calibration standards at 20, 30, 40, 50, and 60 ppm; the absorption of the extracted sample solution, consisted of *Malus domestica* extract determined using Spectrophotometer UV Vis at 372 nm [11].

Experimental Design

The Central Composite Design was used to determine the optimal extraction conditions. For this purpose, 2 factors were considered, representing the independent variables at different levels. The independent variables were % ethanol in water (X_1), and sonication time (X_2). A total of thirteen experiments were derived from CCD through Design Expert 13 software. The response variables were total quercetin concentration which represent the concentrations of the majority compounds in the *Malus domestica* samples quantified by spectrophotometry UV-Vis. A polynomial equation (Equation (1) was generated to predict the correlation between the independent variables and the response.

$$y = \beta_0 + \sum_{i=1}^{k} \beta_i X_i + \sum_{i=1}^{k} \beta_{ii} X_i^2 + \sum \sum_{i<j}^{k} \beta_{ij} X_i X_j \qquad (1)$$

Where y is the predicted response (quercetin concentration), β_0 is the model constant; X_i and X_j are the independent variables; β_i are the linear coefficients; β_{ij} are the coefficients corresponding to the interactions; and β_{ii} are the quadratic coefficients.

Statistical Analysis

Analysis of variance (ANOVA) was employed to assess the significance of differences among the independent variables. Significant effects of independent variables ($p < 0.05$) were incorporated into the reduced model. Two-dimensional response surface plots were generated to illustrate the interaction effects of these variables on the responses. An R^2 value of at least 0.8 was considered indicative of a good model fit [12].

Applied Pharmacology and Pharmaceutical Technology (APPT)
Research Article
ISSN XXXX-XXXX

Result and Discussion

Response Surface Model

Response surface methodology (RSM) was applied to predict variations in quercetin concentration, as these responses were influenced by sonication time and ethanol concentration in water. All data underwent statistical analysis to identify the best-fit model for the independent variables affecting quercetin concentration. The regression coefficient, and p-value are presented below. Non-significant linear terms ($p > 0.05$) were retained in the final reduced model when associated quadratic or interaction terms were significant ($p < 0.05$).

Table 2. Equation and p-value for the final reduced model

Model	Value
Equation	$Y = 0.131155X_1 - 0.0587548X_2 + 0.011X_1X_2 - 0.0254875\,X_1^2 - 0.0532375X_2^2$
p-value	<0.05

Analysis of variance (ANOVA) was conducted to evaluate the significance of the quadratic polynomial models (Table 3). The elevated F-values and low p-values ($p < 0.05$) for all main effects confirmed their significant effects on the response variables. Results indicated that ethanol concentration and sonication time exerted positive influences on quercetin concentration. Two-dimensional response surface plots depicting the interplay between ethanol concentration and sonication time provided further insight into the factor interactions (Figure 1).

Table 3. ANOVA of regression coefficient of the fitted quadratic equation for UAE

Variables		Quercetin Concentration	
		F value	**p-value**
Main Effects	A	38.14	0.0005
	B	7.65	0.0278
Quadratic Effects	A^2	1.25	0.3000
	B^2	5.46	0.0520
Interaction Effect	AB	0.1341	0.7250

Identifying the optimal combination of sonication time and ethanol-in-water concentration is crucial, as elevated quercetin concentrations were observed with increasing ethanol-in-water levels and decreasing sonication time. The most influential factor was ethanol concentration, with an F-value of 38.14. Thus, extractions yielding high quercetin concentrations can be achieved using high ethanol concentrations and short sonication durations.

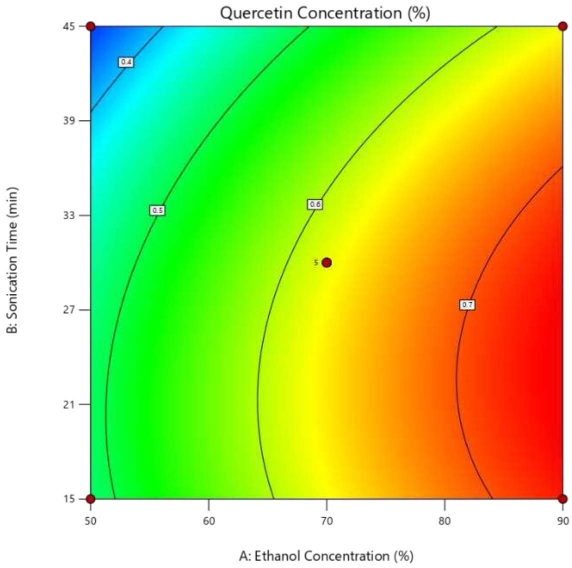

Figure 1. Response surface plots showing the effect of interaction between sonication time (min) and ethanol concentration (%) on quercetin concentration (%)

Conclusion

The central composite design successfully optimized ultrasound-assisted extraction of quercetin from *Malus domestica*, revealing that elevated ethanol-in-water concentrations combined with reduced sonication times significantly quercetin concentration. This green UAE approach offers a reproducible, efficient method for isolating quercetin. Future studies could validate these conditions at pilot scale and explore additional factors such as temperature, cycle, amplitude, and sample-to-solvent ratio.

Conflict of Interest Statement

The authors declare no conflict of interest related to this work.

References

[1] Pandey J, Bastola T, Tripathi J, Tripathi M, Rokaya RK, Dhakal B, et al. Estimation of Total Quercetin and Rutin Content in Malus domestica of Nepalese Origin by HPLC Method and Determination of Their Antioxidative Activity. J Food Qual. 2020;0(0):1–13.

[2] Soetadipura AD. Skrining Fitokimia dan Karakterisasi Simplisia Buah Apel Hijau (Malus sylvestris (L.) Mill). Bandung Conf Ser Pharm. 2022;2(2):1–6.

[3] Alshebremi M, Babiker AY, Rahmani AH. The Role of Quercetin , a Flavonoid in the Management of Pathogenesis Through Regulation of Oxidative Stress , Inflammation , and Biological Activities. Biomolecules. 2025;15(151):1–56.

[4] Handoyo TR, Resmi JK, Hutabarat R, Guanse Y. Sciences of Pharmacy Effect of Tween 80 and Span 80 Surfactants Systems on the Malus domestica Emulsions for Anti-Cutibacterium acnes. Sci Pharm. 2026;5(1):60–7.

[5] Bo Y, Li Y. Multi-target mechanisms and potential applications of quercetin in the treatment of acne vulgaris. Front Pharmacol. 2025;1–19.
[6] Demesa AG, Saavala S, Pöysä M, Koiranen T. Overview and Toxicity Assessment of Ultrasound-Assisted. Foods. 2024;13(19):1–13.
[7] Roobab U, Muhammad R, Sreedhara S, Maqsood S. Ultrasonics Sonochemistry Comparative evaluation of ultrasound-assisted extraction with other green extraction methods for sustainable recycling and processing of date palm bioresources and by-products : A review of recent research. Ultrason Sonochem [Internet]. 2025;114(January):107252. Available from: https://doi.org/10.1016/j.ultsonch.2025.107252
[8] Zakaria F, Tan J kit, Munirah S, Faudzi M, Basyaruddin M, Rahman A, et al. Ultrasonics Sonochemistry Ultrasound-assisted extraction conditions optimisation using response surface methodology from Mitragyna speciosa (Korth .) Havil leaves. Ultrason Sonochem [Internet]. 2021;81(September):105851. Available from: https://doi.org/10.1016/j.ultsonch.2021.105851
[9] Wang H, Deng L, Huang G. Ultrasonics Sonochemistry Ultrasound - assisted extraction and value of active substances in Muxu. Ultrason Sonochem [Internet]. 2025;113(January):107220. Available from: https://doi.org/10.1016/j.ultsonch.2024.107220
[10] Gonzalez-gonzalez M, Yerena-prieto BJ, Carrera C, Mercedes V, Velasco A, Miguel Á, et al. Optimization of an Ultrasound-Assisted Extraction Method for the Extraction of Gingerols and Shogaols from Ginger. Agronomy. 2023;13(1787):1–16.
[11] Ellycornia A, Tri Y, Reubun A, Warti L. Quantitative analysis of quercetin in tea mistletoe (Scurrula oortiana Dans.) Analisis kuersetin pada ekstrak benalu teh (Scurrula oortiana Dans.) secara kuantitatif. J Pharm Sci. 2025;8(1):67–75.
[12] Hassan H, Adam SK, Alias E, Mohd M, Meor R, Affandi M. Central Composite Design for Formulation and Optimization of Solid Lipid Nanoparticles to Enhance Oral Bioavailability of Acyclovir. Molecules. 2021;26(5432):1–19.