Techno-Economic Analysis and Life Cycle Assessment of Bioactive Extract Production from Spent Coffee Grounds via Soxhlet Extraction

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ABSTRACT

Spent coffee grounds (SCG) represent a substantial by-product produced every day by the coffee industry and are frequently disposed of, while containing valuable bioactive compounds. This study investigates the viability of recovering these compounds at a pilot scale via Soxhlet extraction, comparing ethanol and hexane as solvents through laboratory investigation, process simulation, techno-economic analysis, and life cycle assessment. Laboratory extractions were conducted using 10 g of dried SCG. Ethanol extraction yielded 21.77% on a dry basis, exceeding the 15.06% obtained with hexane, and the ethanol extract exhibited stronger antioxidant activity, with DPPH and ABTS IC_{50} values of 892.1 ± 65.4 and 565.0 ± 25.9 µg/mL, respectively, compared to 3,841.6 ± 199.5 and 3,566.6 ± 211.8 µg/mL for hexane. Caffeine content was also higher in the ethanol extract (892.46 ± 2.86 µg/g) than in the hexane extract (272.69 ± 3.06 µg/g), by a factor of 3.3. Process simulation using BioSTEAM was conducted on a continuous equivalent basis of 166.67 kg/hr wet SCG. Techno-economic analysis over 10 years at a 10% discount rate showed the ethanol process achieved an internal rate of return of 164.2% with a payback period of 0.54 years, while the hexane process showed 68.0% IRR and 1.27 years payback. Life cycle assessment following ISO 14040/14044 indicated the ethanol extraction route had a lower global warming potential (0.95 vs. 2.54 kg CO2-eq per kg extract), reduced cumulative energy demand, and lower human toxicity, though it consumed more water due to the upstream water footprint of ethanol production. Overall, Soxhlet extraction with ethanol is recommended as the preferred method for producing nutraceutical-grade extracts from spent coffee grounds.

Keywords: Spent coffee grounds/ Soxhlet extraction/ Nutraceuticals/ Techno-economic analysis/ Life cycle assessment/ BioSTEAM/ Antioxidant activity

1. INTRODUCTION

The global coffee industry produces millions of tonnes of spent coffee grounds (SCG) each year. Most of this material ends up in landfills, even though it still contains a considerable amount of phytochemicals [1]. Landfilling SCG carries real environmental costs. The decomposing grounds acidify soil and raise biological oxygen demand in nearby waterways. This is both an ecological problem and a missed economic opportunity, which circular bioeconomy frameworks aim to address [2]. SCG itself is rich in bioactive compounds, including phenolic acids, caffeine, trigonelline, melanoidins, and lipid fractions. With this profile, it can serve as a low-cost feedstock for high-value ingredients rather than just a waste management issue.

Among these, phenolic acids and flavonoids stand out for nutraceutical applications. They are well documented antioxidants with anti-inflammatory properties [3]. Caffeine is a widely consumed bioactive alkaloid linked to cognitive performance and metabolic benefits [4]. The lipid fraction, recovered with non-polar solvents, contains diterpenes such as cafestol and kahweol. Both have shown anti-carcinogenic activity in in vitro models [5]. Having chemically distinct compound classes in one agricultural waste matrix makes SCG a versatile feedstock. Depending on the solvent chosen, the same starting material can supply ingredients to several different product categories.

The global nutraceutical and functional food market was valued at around USD 400 billion in 2020. It is projected to grow at a compound annual rate above 7% through 2030, driven by consumer demand for plant-derived bioactive ingredients with proven health benefits [6]. SCG-derived extracts rich in antioxidant

phenolics and caffeine fit well into this market, especially for dietary supplements and functional beverages where consumers increasingly want to know where the raw material comes from. SCG valorization sits at the intersection of waste reduction and high-value bioproduct manufacturing. That combination is what sets it apart from conventional extraction feedstocks and makes the case for investment at pilot scale.

Soxhlet extraction is one of the most common methods for recovering bioactive compounds from solid plant matrices. The continuous reflux cycle gives complete solvent-solid contact, and no high-pressure equipment is needed [7]. The simple operation and high reproducibility make it a good benchmark technique at laboratory and pilot scale. Solvent choice, on the other hand, drives both extract composition and downstream commercial value. Ethanol favors polar phenolics, antioxidants, and alkaloids, which are the bioactive fraction of interest for nutraceuticals. Hexane, by contrast, selectively pulls out the lipid fraction. The lipid extract suits cosmetic and oleochemical applications but carries much lower antioxidant capacity [8]. Many laboratory studies have characterized each extract type on its own. However, a side-by-side evaluation of techno-economic performance and environmental impact at a commercially relevant scale has not been reported.

Thailand is a particularly relevant setting for this analysis. It is one of the growing specialty coffee markets in Southeast Asia. Domestic coffee consumption and production are both rising steadily, which means SCG generation at the point of consumption is rising in proportion [9]. The Bio-Circular-Green (BCG) Economy Model, adopted as a national priority strategy in 2021, identifies agricultural waste valorization as a key route toward sustainable industrial development [10]. Running TEA and LCA with Thai-specific data, including EGAT grid electricity tariffs, regional solvent market prices, and the Thai Baht exchange rate, gives results directly applicable to investment decisions inside the country. It also avoids the inflated feasibility estimates that often come from applying generic international cost data to the Thai industrial context.

This work has three aims. First, to measure and compare extraction yield, antioxidant activity, and caffeine content for SCG extracts obtained with ethanol and hexane. Second, to simulate both processes at pilot scale using BioSTEAM [11]. Third, to evaluate their techno-economic performance and gate-to-gate environmental impacts across four LCA midpoint indicators following ISO 14040/14044 [12, 13]. One distinguishing feature of this study is the use of Monte Carlo simulation under simultaneous parametric uncertainty. This gives probabilistic feasibility estimates alongside deterministic outputs, which is a sturdier basis for scale-up decisions than single-point analysis alone.

2. METHODOLOGY

2.1 Raw Materials and Chemicals

Spent coffee grounds were collected from a local coffee shop in Bangkok, Thailand. The collected SCG had a moisture content of about 55 wt%, measured gravimetrically by oven-drying at 105 °C to constant weight. After drying, the material was stored in sealed containers at room temperature. All chemicals used were analytical-grade or higher. Ethanol and hexane were obtained from Sigma-Aldrich (St. Louis, MO, USA) and used without further purification. Reagents for the antioxidant assays, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), were supplied by Merck (Darmstadt, Germany).

2.2 Soxhlet Extraction and Extract Characterization

Soxhlet extractions were performed with 10 g of dried SCG loaded into a cellulose thimble. Each extraction lasted 6 hours at the reflux temperature of the respective solvent (ethanol: 78.4 °C; hexane: 69 °C). After extraction, the liquid phase was separated from the spent coffee cake using vacuum filtration. The solvent was then removed with a rotary evaporator under reduced pressure to yield the crude extract. The extracts were stored at -20 °C until further analysis.

The antioxidant capacity of the crude extracts was evaluated using DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)) radical scavenging assays

[14, 15]. Caffeine content was measured by HPLC-DAD (Ultimate 3000SL, Dionex, USA) and reported as µg/g of crude extract [16].

2.3 Process Modeling Using BioSTEAM

Process simulation was performed using BioSTEAM in Python, a steady-state platform that integrates process modeling with techno-economic analysis and life cycle assessment [11]. The simulation was built on a continuous equivalent basis of 1,000 kg wet SCG per cycle, corresponding to a continuous flow of 166.67 kg/hr over 7,200 operating hours per year. For this preliminary scale-up, a linear scaling assumption was applied. It was assumed that the extraction yields, mass transfer behavior, and thermodynamic equilibrium achieved at the 10-g laboratory scale remain constant at the pilot scale.

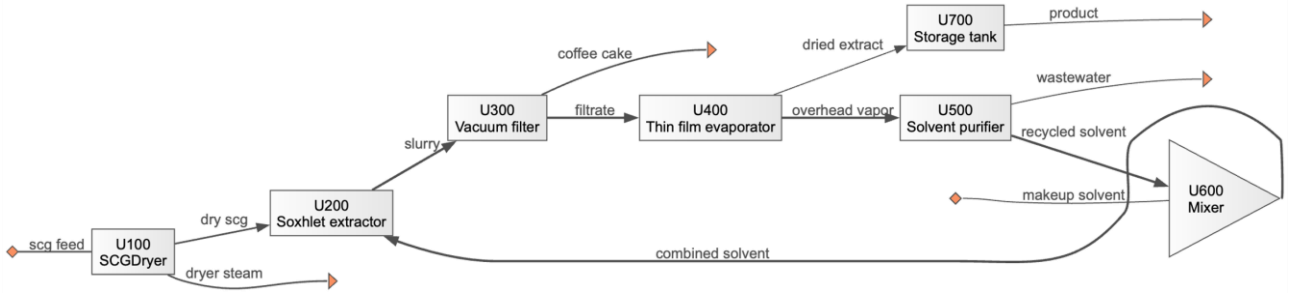

Figure 1. BioSTEAM process flowsheet for SCG Soxhlet extraction with closed-loop solvent recycle.

The process flowsheet, illustrated in Figure 1, comprises seven unit operations: U100 SCG Dryer; U200 Soxhlet Extractor; U300 Vacuum Filter; U400 Thin-Film Evaporator; U500 Solvent Purifier; U600 Recycle Mixer; and U700 Storage Tank. A solvent recycle loop from U500 back to U600 maintains solvent balance via a makeup specification function. The identical makeup solvent flow in both cases reflects a fixed 2.5% loss specification applied uniformly, as solvent-specific pilot-scale loss data were unavailable.

2.4 Techno-Economic Analysis (TEA)

Techno-economic analysis was conducted using the SimpleTEA module within BioSTEAM, which computes capital and operating costs, revenue, and profitability indicators over a defined project lifetime. Variable operating costs covered makeup solvent and utility expenses, while fixed operating costs were set at 10% of the fixed capital investment per year. Key economic metrics reported include total capital investment (TCI), fixed capital investment (FCI), annual revenue, net present value (NPV), internal rate of return (IRR), simple payback period, return on investment (ROI), and minimum selling price (MSP). The financial assumptions and input prices used throughout the analysis are summarized in Table 1.

Table 1. Financial assumptions and input prices used in the techno-economic analysis.

Parameter	Value
Project duration	10 years
Income tax rate	20%
Working capital	15%FCI
Minimum acceptable IRR	10%
Fixed operating cost (FOC)	10% of FCI per year
Electricity price	0.1256 USD/kWh
Exchange rate	32.36 THB/USD
Product price — Ethanol extract	10 USD/kg
Product price — Hexane extract	7 USD/kg

Sensitivity analysis was performed using a one-at-a-time approach over five parameters, including extraction yield, solvent removal efficiency, product selling price, solvent purchase price, and annual operating days. Monte Carlo simulation with 200 iterations using Latin Hypercube sampling was subsequently applied to estimate the probability distributions of IRR and NPV under simultaneous uncertainty in extraction yield, product price, and solvent price.

2.5 Life Cycle Assessment (LCA)

A gate-to-gate LCA was conducted in accordance with ISO 14040/14044, with the functional unit defined as 1 kg of purified extract. The system boundary covered all unit operations from SCG drying through product storage, excluding upstream SCG production and downstream product end-of-life. Four midpoint impact categories were assessed, namely global warming potential (GWP_{100}, kg CO_2-eq), cumulative energy demand (CED, MJ), water consumption potential (WCP, L), and human toxicity (HT, CTUh, USEtox method) [7]. SCG was treated as a zero-burden waste feedstock under an allocation-free approach. The characterization factors applied to electricity and foreground solvent inputs are summarized in Table 2; steam and cooling-water utilities were not characterized and are excluded.

Table 2. Characterization factors for foreground inventory inputs used in the LCA.

Parameter	GWP_{100} (kg CO_2-eq)	CED (MJ)	WCP (L)	HT (CTUh)
Electricity	0.5178	9.44	2.0	4.0×10^{-8}
Ethanol	1.45	33.9	10.5	5.0×10^{-9}
Hexane	2.85	50.0	2.0	1.5×10^{-8}

3. RESULTS AND DISCUSSION

3.1 Extraction Yield and Bioactivity

The yields and bioactivity data for both extracts are summarized in Table 3. Ethanol extraction produced a higher yield than hexane, due to its broader polarity, which enables the extraction of polar phenolics, alkaloids, and semi-polar compounds as well as lipids. Hexane extraction was highly selective for the coffee oil fraction.

Table 3. Extraction results and bioactivity of SCG extracts.

Parameter	Ethanol Extract	Hexane Extract
Extraction yield (% dry basis)	21.77 ± 0.77	15.06 ± 0.52
DPPH IC_{50} (µg/mL)	892.1 ± 65.4	3,841.6 ± 199.5
ABTS IC_{50} (µg/mL)	565.0 ± 25.9	3,566.6 ± 211.8
Caffeine content (µg/g extract)	892.46 ± 2.86	272.69 ± 3.06

The ethanol extract showed stronger antioxidant activity than the hexane extract, with DPPH and ABTS IC50 values approximately four and six times lower, respectively. This result aligns with the polarity principle in solvent extraction: polar solvents like ethanol are more effective at extracting phenolic compounds, the main contributors to radical scavenging activity in plant materials [3]. In contrast, hexane extracts lipophilic compounds such as triglycerides and waxes, which have lower antioxidant potency [8]. The caffeine content in the ethanol extract was 3.3 times higher than in the hexane extract, reflecting solvent selectivity. Caffeine, a hydrophilic xanthine alkaloid, partitions into polar media and contributes significantly to the antioxidant capacity of coffee extracts [4].

3.2 Process Simulation

The BioSTEAM simulation results, presented in Table 4, show that both solvent scenarios produced identical upstream performance, as the drying and filtration stages depend solely on the SCG feed composition rather than the choice of solvent. The key difference between the two cases emerged at the extraction stage, where the higher extraction yield of ethanol resulted in a 44.6% greater annual extract output compared to hexane. This advantage compounds directly into revenue, since both processes share the same capital investment and operating structure, meaning that any gain in product throughput translates proportionally to improved economic performance.

Table 4. BioSTEAM stream summary for both solvent scenarios.

Stream / Parameter	Ethanol Case	Hexane Case
Wet SCG feed (kg/hr)	166.67	166.67
Moisture evaporated (kg/hr)	87.72	87.72
Dry SCG to extractor, dry basis (kg/hr)	75.00	75.00
Solvent flow to extractor (kg/hr)	375.00	375.00
Recycled solvent (kg/hr)	365.66	365.66
Makeup solvent (kg/hr)	9.34	9.34
Extract product rate (kg/hr)	16.33	11.30
Coffee cake by-product (kg/hr)	58.67	63.70
Annual extract production (t/yr)	117.56	81.32

3.3 Techno-Economic Analysis

TEA results are summarized in Table 5. Both Scenarios required similar capital investment because they share the same equipment setup. The profitability gap therefore comes from differences in product yield and market value, not from capital costs. The ethanol process gave an IRR of 164.2% with a payback period of 0.54 years. The hexane process gave 68.0% IRR and 1.27 years payback. These IRR values are well above what is typical for chemical processes [17]. Two factors explain this. Capital requirements are low at pilot scale, and nutraceutical-grade extracts command a high market price. The wide margin means the process stays viable even if product prices drop noticeably.

Table 5. Techno-economic analysis comparison for SCG ethanol and hexane extraction.

Category	Parameter	Unit	Ethanol	Hexane
Capital Investment	Total Capital Investment (TCI)	USD	468,511	468,522
	Fixed Capital Investment (FCI)	USD	407,401	407,410
Operating Costs	Annual Variable Operating Cost (VOC)	USD/yr	104,002	118,804
	Annual Fixed Operating Cost (FOC)	USD/yr	40,740	40,741
Revenue & Income	Annual Revenue	USD/yr	1,175,580	569,268
	Net Income per Year	USD/yr	824,670	327,779
Profitability Indicators	Net Present Value (NPV)	M USD	4.58	1.58
	Internal Rate of Return (IRR)	%	164.2	68.0
	Payback Period (PBP)	Yr	0.54	1.27
	Return on Investment (ROI)	%	176.0	70.0
Product Pricing	Minimum Selling Price (MSP)	USD/kg	1.93	2.96
	Assumed Product Selling Price	USD/kg	10.00	7.00

The sensitivity analysis results for both scenarios are shown in Figure 2. For the ethanol case, product selling price had by far the greatest effect on IRR. The swing extended further on the upside (IRR up to 342%) than on the downside (down to 73%), mainly because the tested price range (5–20 USD/kg around a 10 USD/kg baseline) is itself asymmetric; IRR is nearly linear in price. Extraction yield came second but with a much smaller swing. Operating days had a moderate effect, whereas ethanol price and evaporator efficiency had negligible effect. The hexane case showed a different pattern. Product price and extraction yield produced

swings of similar size, which means yield is relatively more influential for the hexane process than for the ethanol process. This ranking depends on the tested ranges: the hexane price range (5–10 USD/kg) is narrower than the ethanol range (5–20 USD/kg), while the relative yield range is wider for hexane on the upside.

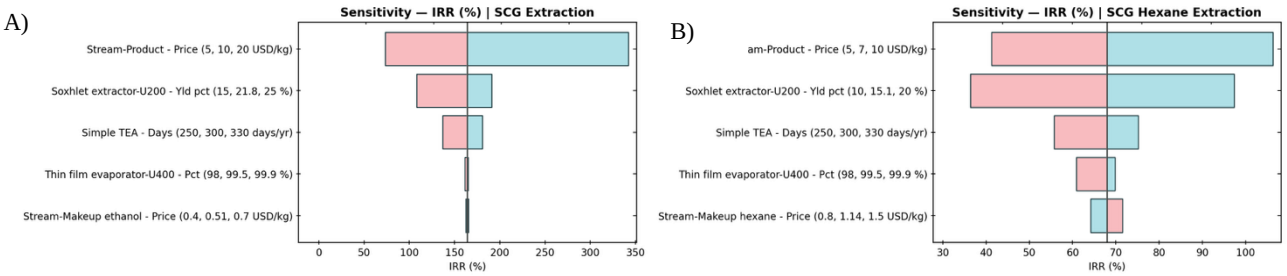

Figure 2. Tornado charts of single-point sensitivity analysis showing the effect of five process and economic parameters on IRR for (A) ethanol extraction and (B) hexane extraction. Pink and blue bars indicate the IRR response at the lower and upper bounds of each parameter, respectively.

Although IRR is highly sensitive to assumed product selling prices, both processes show good economic resilience. As shown in Table 5, the break-even MSP is only 1.93 USD/kg for the ethanol extract and 2.96 USD/kg for the hexane extract. These values sit well below the conservative baselines of 10 and 7 USD/kg, respectively. In other words, both pilot-scale extraction routes remain profitable even with a substantial drop in market price.

Monte Carlo simulation results for the ethanol case are presented in Figure 3. Across all 200 iterations, no run produced an IRR below the 10% hurdle rate or a negative NPV. Economic feasibility holds up under simultaneous uncertainty in extraction yield, product price, and solvent price. The IRR distribution ranged from about 48% to 371% with a right skew, so upside potential modestly exceeds downside risk. The NPV distribution had all values above break-even, ranging from about 1.0 to 11.2 M USD. This is consistent with the sensitivity result that product price is the dominant parameter in the system. The ethanol extraction process carries low financial risk at pilot scale and offers solid upside under favorable market conditions.

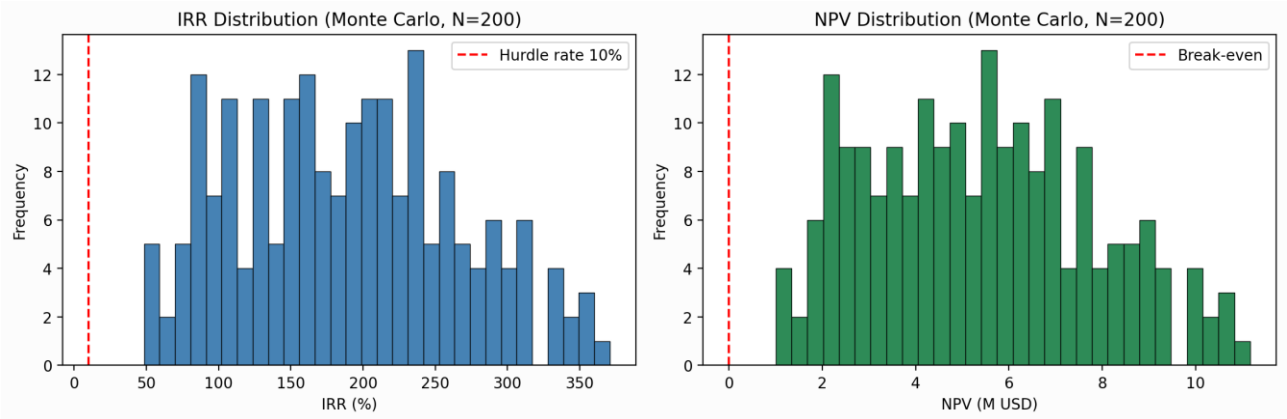

Figure 3. Monte Carlo simulation results (N = 200, Latin Hypercube sampling) showing the probability distributions of IRR and NPV for ethanol extraction. The red dashed line indicates the 10% hurdle rate for IRR and the break-even point for NPV.

3.4 Life Cycle Assessment

LCA results are presented in Table 6. The ethanol process showed much lower GWP_{100}, CED, and HT. Hexane came out lower on WCP, because of the high upstream water footprint of ethanol production. On balance, the ethanol route performs better in three of four impact categories. That supports its selection on environmental grounds, even with the water consumption trade-off.

Table 6. Gate-to-gate LCA results per 1 kg extract

LCA Indicator	Unit	Ethanol	Hexane
Global Warming Potential (GWP_{100})	kg CO_2-eq/kg extract	0.954	2.54
Cumulative Energy Demand (CED)	MJ/kg extract	21.7	44.6
Water Consumption Potential (WCP)	L/kg extract	6.49	2.35
Human Toxicity (HT)	$\times 10^{-8}$ CTUh/kg extract	1.25	2.62

The impacts in Table 6 are driven mainly by makeup solvent supply, which accounts for about 87% (ethanol) and 93% (hexane) of GWP, with electricity contributing the remainder. The results therefore reflect the foreground inputs in Table 2. Since both routes have similar thermal duties, the ranking of GWP and CED is not expected to change with the choice of energy supply; for example, applying the EU average grid factor (0.23 kg CO_2-eq/kWh) lowers the ethanol GWP by only 7% (0.95 to 0.88 kg CO_2-eq/kg).

For nutraceutical applications, where phenolic antioxidant content and caffeine concentration are the main quality criteria, the ethanol route delivers higher bioactivity, lower environmental burden across three indicators, and stronger economic returns. At this scale, it is the preferable option over hexane extraction.

4. SUMMARY

This study compared ethanol and hexane as solvents for Soxhlet extraction of SCG bioactives through laboratory experiments, process simulation, TEA, and LCA. Ethanol extraction gave higher yield, stronger antioxidant activity, and greater caffeine content. Together, these make ethanol more suitable for nutraceutical applications. Both processes were economically viable well above the 10% hurdle rate. The ethanol case delivered higher IRR and NPV, thanks to greater product throughput and market value. Sensitivity analysis identified product selling price as the dominant economic driver, and Monte Carlo simulation confirmed feasibility across a wide range of uncertainties. On the environmental side, the ethanol route produced lower impacts in three of four LCA indicators. In both cases, makeup solvent was the main contributor to the LCA impacts. Based on these findings, ethanol Soxhlet extraction is recommended as the preferred route for nutraceutical-grade SCG extract production. Process intensification is a priority for future work, to bring down the energy and solvent loads.

References:

[1] R. Campos-Vega, G. Loarca-Piña, H. A. Vergara-Castañeda, and B. Dave Oomah, "Spent coffee grounds: A review on current research and future prospects," *Trends Food Sci. Technol.*, vol. 45, no. 1, pp. 24–36, 2015, doi: 10.1016/j.tifs.2015.04.012.

[2] P. S. Murthy and M. Madhava Naidu, "Sustainable management of coffee industry by-products and value addition - A review," *Resour. Conserv. Recycl.*, vol. 66, pp. 45–58, Sep. 2012, doi: 10.1016/j.resconrec.2012.06.005.

[3] P. Esquivel and V. M. Jiménez, "Functional properties of coffee and coffee by-products," *Food Research International*, vol. 46, no. 2, pp. 488–495, May 2012, doi: 10.1016/j.foodres.2011.05.028.

[4] B. B. Fredholm, K. Bättig, J. Holmén, A. Nehlig, and E. E. Zvartau, "Actions of Caffeine in the Brain with Special Reference to Factors That Contribute to Its Widespread Use," *Pharmacol. Rev.*, vol. 51, no. 1, pp. 83–133, 1999, doi: https://doi.org/10.1016/S0031-6997(24)01396-6.

[5] C. Cavin, D. Holzhaeuser, G. Scharf, A. Constable, W. W. Huber, and B. Schilter, "Cafestol and kahweol, two coffee specific diterpenes with anticarcinogenic activity," *Food and Chemical Toxicology*, vol. 40, no. 8, pp. 1155–1163, Aug. 2002, doi: 10.1016/S0278-6915(02)00029-7.

[6] F. Shahidi and P. Ambigaipalan, "Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects – A review," *J. Funct. Foods*, vol. 18, pp. 820–897, Oct. 2015, doi: 10.1016/J.JFF.2015.06.018.

[7] M. D. Luque de Castro and F. Priego-Capote, "Soxhlet extraction: Past and present panacea," *J. Chromatogr. A*, vol. 1217, no. 16, pp. 2383–2389, Apr. 2010, doi: 10.1016/J.CHROMA.2009.11.027.

[8] A. Zuorro and R. Lavecchia, "Spent coffee grounds as a valuable source of phenolic compounds and bioenergy," *J. Clean. Prod.*, vol. 34, pp. 49–56, 2012, doi: https://doi.org/10.1016/j.jclepro.2011.12.003.

[9] International Coffee Organization, "COFFEE REPORT AND OUTLOOK," 2023.

[10] Department of International Organizations, "Thailand's Voluntary National Review," 2021. Accessed: May 14, 2026. [Online]. Available: https://image.mfa.go.th/mfa/0/OznAy3tii2/E-booking/VNR_2021__ENG_.pdf

[11] Y. Cortes-Peña, D. Kumar, V. Singh, and J. S. Guest, "BioSTEAM: A Fast and Flexible Platform for the Design, Simulation, and Techno-Economic Analysis of Biorefineries under Uncertainty," *ACS Sustain. Chem. Eng.*, vol. 8, no. 8, pp. 3302–3310, Mar. 2020, doi: 10.1021/ACSSUSCHEMENG.9B07040.

[12] International Organization for Standardization, "ISO 14040:2006 - Environmental management — Life cycle assessment — Principles and framework." Accessed: May 14, 2026. [Online]. Available: https://www.iso.org/standard/37456.html

[13] International Organization for Standardization, "ISO 14044:2006 - Environmental management — Life cycle assessment — Requirements and guidelines." Accessed: May 14, 2026. [Online]. Available: https://www.iso.org/standard/38498.html

[14] R. Re, N. Pellegrini, A. Proteggente, A. Pannala, M. Yang, and C. Rice-Evans, "Antioxidant activity applying an improved ABTS radical cation decolorization assay," *Free Radic. Biol. Med.*, vol. 26, no. 9–10, pp. 1231–1237, May 1999, doi: 10.1016/S0891-5849(98)00315-3.

[15] W. Brand-Williams, M. E. Cuvelier, and C. Berset, "Use of a free radical method to evaluate antioxidant activity," *LWT - Food Science and Technology*, vol. 28, no. 1, pp. 25–30, Jan. 1995, doi: 10.1016/S0023-6438(95)80008-5.

[16] S. M. Ribeiro, D. Bohrer, J. Lapinski, L. N. De Carvalho, P. T. Do Nascimento, and C. Viana, "Development and validation of an HPLC-DAD method to quantify caffeine in time-release dosage forms," *Indian J. Pharm. Sci.*, vol. 81, no. 4, pp. 626–632, 2019, doi: 10.36468/PHARMACEUTICAL-SCIENCES.553.

[17] T. Richard A., J. A. Shaeiwitz, D. Bhattacharyya, and W. Wallace B., *Analysis, Synthesis, and Design of Chemical Processes*, 5th ed. Prentice Hall, 2018.