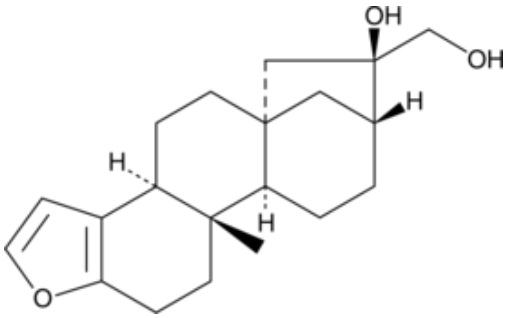
Product Data Sheet

Product Name: Cafestol
Cat. No.: GC40352

Chemical Properties

Cas. No.	469-83-0		
SMILES	O[C@]1(CO)C[C@]23[C@](CC[C@]1([H])C3)([H])[C@@](CCC4=C5C=CO4)(C)[C@]5([H])CC2		
Formula	$C_{20}H_{28}O_3$	M.Wt	316.4
Solubility	DMF: 12 mg/ml,DMF:PBS (pH 7.2) (1:50): 0.02 mg/ml,DMSO: 5 mg/ml,Ethanol: 5 mg/ml	Storage	4°C, protect from light
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		

Structure



Protocol

Cell experiment [1]:

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Cell lines	Human renal carcinoma cells (Caki), human breast carcinoma cells (MDA-MB231), human glioma cells (U251MG), human colon carcinoma cells (HCT116), human leukemia cells (U937), and human prostate carcinoma (PC3) cells
Preparation Method	Human renal carcinoma cells (Caki), human breast carcinoma cells (MDA-MB231), human glioma cells (U251MG), human colon carcinoma cells (HCT116), human leukemia cells (U937), and human prostate carcinoma (PC3) cells were obtained from the American Type Culture Collection. All cells were cultured in Dulbecco's Modified Eagle's Medium containing 10% fetal bovine serum, 20mM HEPES buffer, 100U/ml penicillin, 100μg/ml streptomycin, and 100μg/ml gentamicin. A cell death detection ELISA plus kit was used for assessing apoptotic activity by detecting fragmented DNA within the nucleus in ABT-737-, cafestol-, and combination of ABT-737 and cafestol-treated cells. Briefly, cells were treated with different concentrations of cafestol(20 or 30μM) and ABT-737 alone or in combination. After 24h, each culture plate was centrifuged for 10min at 200×g, the supernatant was removed, and the pellet was lysed for 30min. After centrifuging the plate again at 200×g for 10min, the supernatant that contained the cytoplasmic histoneassociated DNA fragments was collected and incubated with an immobilized anti-histone antibody. The reaction products were incubated with a peroxidase substrate for 5min and measured by spectrophotometry at 405 and 490nm (reference wavelength) with a microplate reader. The signals in the wells containing the substrate alone were subtracted as the background.
Reaction Conditions	20 or 30μM; 24h
Applications	Cafestol significantly potentiated ABT-737-induced apoptosis.

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Animal experiment [2]:

Animal models	Wistar albino experimental rats
Preparation Method	A total of 32 Wistar albino experimental rats of both sexes aged 6 weeks with an average weight of 150g were used in this study; animals were acquired and kept under controlled conditions of a light/dark cycle (12h) at a temperature of 23°C±2°C and humidity of 50% ± 5%. Experimental animals were randomly assigned into four groups (n = 8) as follows: Group I: each rat was given vehicle only (5% Tween in DDW) orally via oral gavage for 14 consecutive days. Then, a single dose of NaCl (0.9%), 10mL/kg, was injected intraperitoneally 1h after the last vehicle administration on day 14. This group served as the normal (negative control) group. Group II: each rat was orally given cafestol (5mg/kg/day) for 14 consecutive days. Group III: each rat was given vehicle only (5% Tween in DDW) via oral gavage for 14 consecutive days. Then, a single dose of doxorubicin (15mg/kg) was injected intraperitoneally 1h after the last vehicle administration on day 14 to serve as the positive control group. Group IV: each rat received cafestol (5mg/kg/day) orally for 14 consecutive days, and then, a single dose of doxorubicin (15mg/kg) was injected intraperitoneally 1h after the last cafestol treatment on day 14. 24 hours after doxorubicin dose administration (i.e., day 15), the animals were anaesthetized and samples were collected for further analysis.
Dosage form	5mg/kg/day for 14 days; p.o.
Applications	Cafestol significantly protected against doxorubicin-induced cardiotoxicity by attenuating oxidative stress, activating the Nrf2/HO-1/NQO-1 pathway, suppressing inflammation, and improving cardiac biomarkers and histopathology.

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References:
[1] Woo, S. M., Min, K. J., Seo, B. R., Nam, J. O., Choi, K. S., Yoo, Y. H., & Kwon, T. K. (2014). Cafestol overcomes ABT-737 resistance in Mcl-1-overexpressed renal carcinoma Caki cells through downregulation of Mcl-1 expression and upregulation of Bim expression. *Cell death & disease*, *5*(11), e1514.
[2] Al-Kenany, S. A., & Al-Shawi, N. N. (2023). Protective effect of cafestol against doxorubicin-induced cardiotoxicity in rats by activating the Nrf2

Background

Cafestol, one of the major components of coffee, is a coffee-specific diterpene form and an inhibitor of ERK2[1]. Cafestol has elevated blood lipids [2], anti-inflammatory[1], anti-angiogenic[3] and anti-diabetic[4] activities. In addition, Cafestol induces tumor cell apoptosis and autophagy, which can be used in the study of cancer[5].

In vitro, Cafestol (0–100μM; 1–24h) dose-dependently suppressed PGE_2 production and reduced COX-2 mRNA levels in LPS-stimulated RAW 264.7 cells, while concurrently inhibiting AP-1 activation and ERK2 activity after 1h treatment[1]. Cafestol (30μM, 24h) significantly potentiated ABT-737-induced apoptosis in Mcl-1-overexpressed human renal carcinoma Caki cells, human glioma U251MG cells, and human breast carcinoma MDA-MB231 cells by downregulating Mcl-1 protein expression (via promoting protein degradation) and upregulating Bim expression, while showing no cytotoxicity in normal human skin fibroblasts[6].

In vivo, Cafestol (40–80mg/kg; i.g.; 20 days) markedly reduced tumor growth in a colon cancer xenograft mouse model[5]. Oral administration of Cafestol (5mg/kg/day for 14 days) in Wistar albino rats significantly protected against doxorubicin-induced cardiotoxicity by attenuating oxidative stress (downregulate MDA, upregulate GSH/SOD/CAT/Gpx-1), activating the Nrf2/HO-1/NQO-1 pathway (downregulate Keap1/NF-κB), suppressing inflammation (downregulate TNF-α/IL-1β), and inhibiting apoptosis (downregulate Bax/Casp3, downregulate TUNEL-positive cells), while improving cardiac biomarkers (CK-MB/LDH/ALP/ALT) and histopathology[7].

References:

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[1] Shen, T., Lee, J., Lee, E., Kim, S. H., Kim, T. W., & Cho, J. Y. (2010). Cafestol, a coffee-specific diterpene, is a novel extracellular signal-regulated kinase inhibitor with AP-1-targeted inhibition of prostaglandin E2 production in lipopolysaccharide-activated macrophages. *Biological & pharmaceutical bulletin*, *33*(1), 128–132.
[2] Urgert, R., Schulz, A. G., & Katan, M. B. (1995). Effects of cafestol and kahweol from coffee grounds on serum lipids and serum liver enzymes in humans. *The American journal of clinical nutrition*, *61*(1), 149–154.
[3] Wang, S., Yoon, Y. C., Sung, M. J., Hur, H. J., & Park, J. H. (2012). Antiangiogenic properties of cafestol, a coffee diterpene, in human umbilical vein endothelial cells. *Biochemical and biophysical research communications*, *421*(3), 567–571.
[4] Mellbye, F. B., Jeppesen, P. B., Shokouh, P., Laustsen, C., Hermansen, K., & Gregersen, S. (2017). Cafestol, a Bioactive Substance in Coffee, Has Antidiabetic Properties in KKAy Mice. *Journal of natural products*, *80*(8), 2353–2359.
[5] Feng, Y., Yang, J., Wang, Y., Wang, X., Ma, Q., Li, Y., Zhang, X., Wang, S., Zhang, Q., Mi, F., Wang, Y., Zhong, D., & Yin, J. (2024). Cafestol inhibits colon cancer cell proliferation and tumor growth in xenograft mice by activating LKB1/AMPK/ULK1-dependent autophagy. *The Journal of nutritional biochemistry*, *129*, 109623.
[6] Woo, S. M., Min, K. J., Seo, B. R., Nam, J. O., Choi, K. S., Yoo, Y. H., & Kwon, T. K. (2014). Cafestol overcomes ABT-737 resistance in Mcl-1-overexpressed renal carcinoma Caki cells through downregulation of Mcl-1 expression and upregulation of Bim expression. *Cell death & disease*, *5*(11), e1514.
[7] Al-Kenany, S. A., & Al-Shawi, N. N. (2023). Protective effect of cafestol against doxorubicin-induced cardiotoxicity in rats by activating the Nrf2 pathway. *Frontiers in pharmacology*, *14*, 1206782.

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