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Research Article

Cytotoxic Activity of a Niclosamide–Caffeic Acid Multicomponent Cocrystal in T47D Breast Cancer Cells

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Abstract

Objective: This study aimed to evaluate the cytotoxic activity of a niclosamide–caffeic acid multicomponent cocrystal against T47D breast cancer cells.

Methods: The multicomponent cocrystal was prepared using the solvent-drop grinding method. Cytotoxic activity was assessed using the Microculture Tetrazolium Test (MTT) assay.

Results: The results demonstrated that both niclosamide alone and the niclosamide–caffeic acid multicomponent cocrystal exhibited cytotoxic effects against T47D cells, with IC_{50} values of 2.92 µg/mL and 2.50 µg/mL, respectively. Microplate spectrophotometric analysis confirmed a concentration-dependent decrease in cell viability for both treatments. Notably, the niclosamide–caffeic acid multicomponent cocrystal displayed a more pronounced cytotoxic effect than niclosamide alone.

Conclusions: These findings suggest that the formation of niclosamide–caffeic acid multicomponent crystals may enhance anticancer potential and warrant further investigation as a promising therapeutic approach for breast cancer treatment.

Keywords: breast cancer, niclosamide, caffeic acid, multicomponent crystal, cytotoxicity, T47D cells, MTT assay.

INTRODUCTION

Breast cancer is one of the leading causes of cancer-related mortality among women worldwide, with a steadily increasing incidence in both developed and developing countries. According to the Global Cancer Observatory (GLOBOCAN), breast cancer accounts for a substantial proportion of newly diagnosed cancer cases in women, and its burden continues to rise in low and middle-income countries, including Indonesia[1,2]. Despite advances in early detection and targeted therapy, the prognosis for patients with advanced or metastatic breast cancer remains poor, highlighting the urgent need for novel and effective therapeutic approaches[3,4].

Drug repurposing, the strategy of identifying new therapeutic applications for existing drugs, has gained considerable attention in oncology research due to its cost-effectiveness, established safety profiles, and accelerated development timelines[5,6]. Niclosamide, an FDA-approved anthelmintic drug, has recently been recognized for its promising anticancer properties through multiple mechanisms, including the inhibition of Wnt/β-catenin, STAT3, and NF-κB signaling pathways[7–10]. However, its poor aqueous solubility and limited bioavailability pose significant challenges to its clinical translation in cancer therapy[11–13].

One potential strategy to overcome these limitations is the formation of multicomponent cocrystals, which can enhance physicochemical properties such as solubility, dissolution rate, and stability, thereby improving pharmacological activity[14–18]. Caffeic acid, a naturally occurring phenolic compound with antioxidant and anticancer activities, has been investigated as a coformer in pharmaceutical cocrystallization to improve drug performance[19,20]. The combination of niclosamide and caffeic acid in a multicomponent crystal system may provide synergistic or additive effects, potentially enhancing cytotoxicity against breast cancer cells.

In this study, we developed a niclosamide–caffeic acid multicomponent crystal using the solvent-drop grinding method and evaluated its cytotoxic activity against

T47D human breast cancer cells. The cytotoxic effects were assessed using the Microculture Tetrazolium Test (MTT) assay, and the half-maximal inhibitory concentration (IC_{50}) values were determined. This work aims to provide insights into the potential of niclosamide–caffeic acid multicomponent crystals as a novel formulation approach to improve the anticancer efficacy of niclosamide.

MATERIALS AND METHODS

Materials and Instruments

Pure niclosamide (≥98% purity) was obtained from Sigma-Aldrich (USA), while caffeic acid was procured from MarkHerb (PT EBM Saintifik dan Teknologi, Bandung, Indonesia). Analytical-grade ethanol was supplied by Brataco Chemical (Indonesia). The T47D human breast carcinoma cell line. Cell culture reagents, including Roswell Park Memorial Institute medium (RPMI-1640), fetal bovine serum (FBS), penicillin–streptomycin, and trypsin–EDTA, were purchased from Gibco (Thermo Fisher Scientific, USA). The MTT reagent [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] was sourced from Sigma-Aldrich (USA). The niclosamide–caffeic acid multicomponent crystals were prepared via the solvent drop grinding (SDG) technique. Cell viability measurements were performed using a Bio-Rad microplate reader (USA) at a wavelength of 550 nm. Additional equipment included a CO_2 incubator (Thermo Scientific, USA) for cell maintenance, a Class II biosafety cabinet (Thermo Scientific, USA) for aseptic handling, and an inverted microscope (Nikon, Japan) for morphological observation.

MTT Assay for Cell Viability

The MTT colorimetric assay was performed to evaluate the viability of T47D human breast cancer cells based on mitochondrial reductase-mediated reduction of the tetrazolium salt 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide into insoluble formazan. Cells were seeded in 96-well plates at a density of 1×10^4 cells per well in RPMI-1640 medium supplemented with 10% fetal bovine serum (FBS) and 1% penicillin–streptomycin, followed by a 24-h incubation at 37 °C in a humidified atmosphere containing 5% CO_2 to allow cell attachment. Serial dilutions (0.1–100 µg/mL) of the test samples—pure niclosamide and the niclosamide–caffeic acid multicomponent crystal—were prepared in RPMI-1640 containing 0.1% DMSO and applied to the cultures for 48 h. Untreated cells and vehicle-treated cells (0.1% DMSO) served as controls, with each treatment condition performed in triplicate. After the exposure period, 10 µL of MTT solution (5 mg/mL in PBS) was added to each well and incubated for an additional 4 h to allow formazan formation. The culture medium was then carefully removed, and the resulting crystals were dissolved in 100 µL of DMSO. Absorbance was measured at 550 nm using a Bio-Rad microplate reader, and cell viability was calculated as a percentage relative to the untreated control. Dose–response relationships were analyzed, and IC_{50} values were determined by linear regression analysis. The experimental procedure was adapted from a previously reported method with slight modifications [21]. Morphological alterations, such as cell shrinkage, rounding, membrane blebbing, and reduced confluence, were examined under an inverted microscope at 100× magnification.

Data Analysis

Data are presented as the mean ± standard deviation (SD), n = 3. Statistical analyses were performed using GraphPad Prism version 8.4.0 (GraphPad Software, San Diego, CA, USA). Half-maximal inhibitory concentration (IC_{50}) values were determined by fitting the dose–response curves to a linear regression model, in which percentage cell viability was plotted against the logarithm of compound concentrations. The concentration corresponding to 50% cell viability was extrapolated from the fitted curve. Comparisons between treatment groups were carried out using two-way ANOVA followed by Bonferroni's multiple comparisons test, comparing niclosamide–caffeic acid multicomponent crystal to niclosamide at the same concentration. Statistical significance was accepted at $p < 0.05$.

RESULT AND DISCUSSION

In Vitro Cytotoxic Activity Against T47D Breast Cancer Cells

Table 1 and **Figure 1** present the cytotoxic effects of niclosamide and the niclosamide–caffeic acid multicomponent crystal (cocrystal) on T47D breast cancer cells after 48 h of exposure at various concentrations. Both treatments demonstrated a dose-dependent reduction in cell viability compared to the untreated control (100% ± 0.000).

At the highest concentration tested (100 µg/mL), niclosamide reduced cell viability to 4.71% ± 2.736, whereas the cocrystal formulation resulted in 20.48% ± 2.253 viability, with the difference being highly significant (****, $p < 0.0001$). At 10 µg/mL, the viability values for niclosamide and the cocrystal were 24.23% ± 0.580 and 22.40% ± 2.888, respectively, with no statistically significant difference. At lower concentrations (0.1 and 1 µg/mL), both treatments exhibited reduced cytotoxicity, with niclosamide generally showing slightly higher cytotoxicity than the cocrystal at 0.1 µg/mL (97.88% vs. 75.38%, *** $p < 0.001$).

The calculated IC_{50} values indicated that the cocrystal had a slightly lower IC_{50} (2.50 µg/mL) compared to niclosamide (2.92 µg/mL), suggesting a marginally higher potency of the cocrystal formulation in inhibiting T47D cell viability. Graphical data **(Figure 1)** further confirm these trends, illustrating the dose-dependent cytotoxic effect for both treatments, with the steepest viability drop observed between concentrations of 1 µg/mL and 10 µg/mL.

The present findings indicate that both niclosamide and the niclosamide–caffeic acid cocrystal possess significant cytotoxic activity against T47D breast cancer

cells in vitro, with a dose-dependent profile. The slightly lower IC_{50} value of the cocrystal suggests that incorporation of caffeic acid in a multicomponent crystal form may enhance the anticancer potential of niclosamide. This enhancement may be attributed to improved physicochemical properties, such as solubility or stability, commonly observed in pharmaceutical cocrystals [22].

The observation that the cocrystal exhibited higher cell viability than niclosamide at the highest tested concentration (100 µg/mL) could indicate differences in drug release kinetics or cellular uptake, consistent with prior reports that cocrystallization can modulate dissolution rate and bioavailability[20,23,24]. However, the slightly superior potency (lower IC_{50}) of the cocrystal formulation suggests that at therapeutically relevant concentrations, the combination of niclosamide with caffeic acid may provide enhanced cytotoxic efficacy.

These results align with previous studies reporting niclosamide's anticancer activity through multiple mechanisms, including Wnt/β-catenin inhibition, STAT3 suppression, and mitochondrial uncoupling[7,8]. Moreover, caffeic acid itself has been documented to exert anticancer effects through antioxidant activity, induction of apoptosis, and cell cycle arrest [25–28]. The cocrystal approach may therefore provide a synergistic benefit, not only by improving drug solubility but also by introducing the bioactivity of caffeic acid into the formulation.

Our findings corroborate the work of Grifasi et al. (2015), who demonstrated that niclosamide cocrystals exhibited improved dissolution rates compared to the pure drug, potentially translating to enhanced biological activity[23]. Additionally, the present study extends these observations by demonstrating that such physicochemical modifications can have measurable effects on cytotoxicity against breast cancer cells.

The data suggest that the niclosamide–caffeic acid cocrystal could serve as a promising candidate for further development in breast cancer therapy, potentially overcoming some limitations associated with niclosamide's poor aqueous solubility. Further in vivo pharmacokinetic and mechanistic studies are warranted to fully elucidate the therapeutic advantages of this multicomponent crystal system.

Table 1: Cell viability (mean ± SD) of T47D breast cancer cells treated with niclosamide or niclosamide–caffeic acid multicomponent crystal (cocrystal) at various concentrations, and statistical significance between the two treatment group.

Concentration (µg/mL)	Niclosamide (Mean ± SD)	Niclosamide–Caffeic Acid Cocrystal (Mean ± SD)	Significance vs Niclosamide
Control	100 ± 0.000	100 ± 0.000	-
100	4.71 ± 2.736	20.48 ± 2.253	****
10	24.23 ± 0.580	22.40 ± 2.888	ns
1	68.75 ± 4.175	72.98 ± 9.034	ns
0.1	97.88 ± 2.027	75.38 ± 3.219	***
IC_{50} (µg/mL)	**2,92**	**2,50**	**-**

ns, not significant ($p \geq 0.05$); * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$.

Values represent mean ± standard deviation (SD), n=3. Statistical analysis was conducted using two-way ANOVA followed by Bonferroni's multiple comparisons test, comparing niclosamide–caffeic acid multicomponent crystal to niclosamide at the same concentration. The symbol "–" indicates that statistical comparison was not applicable for control groups.

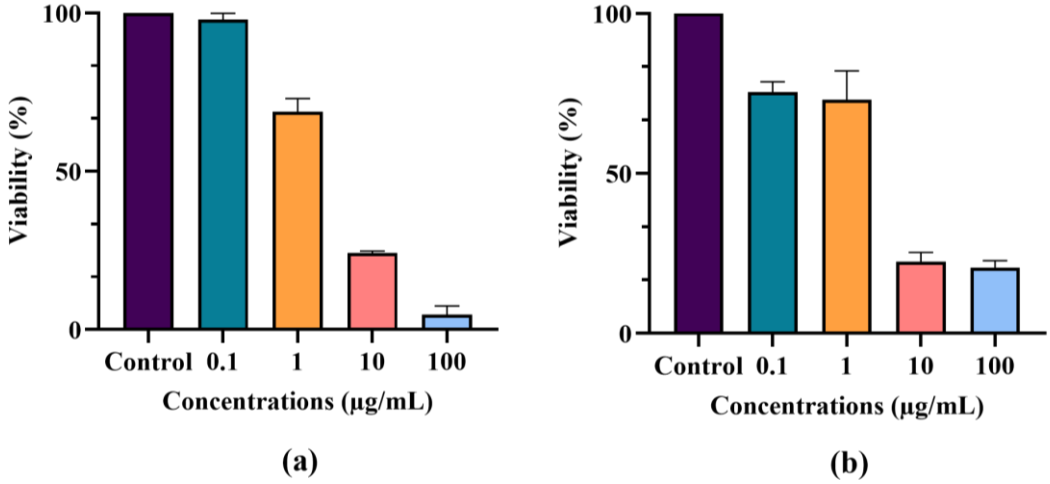
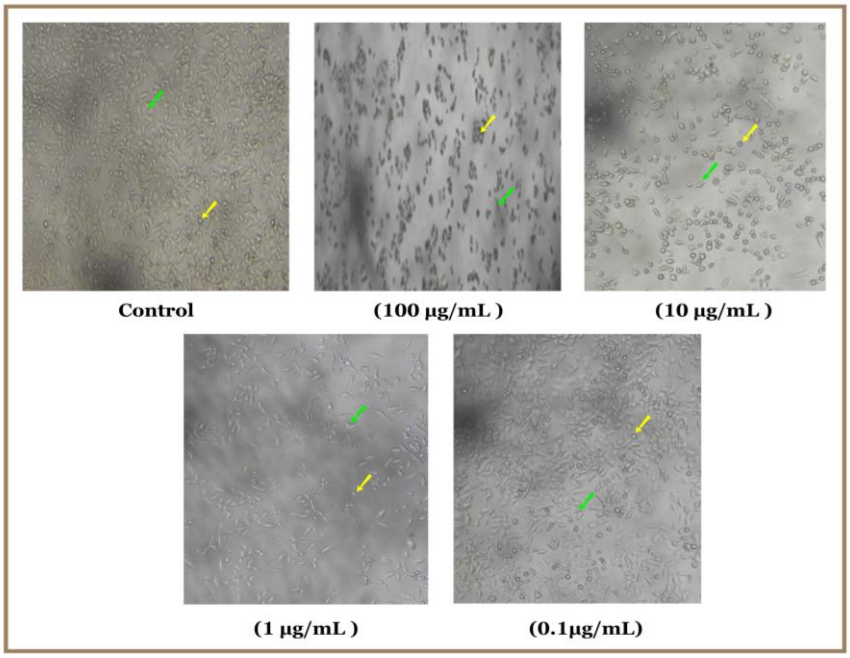


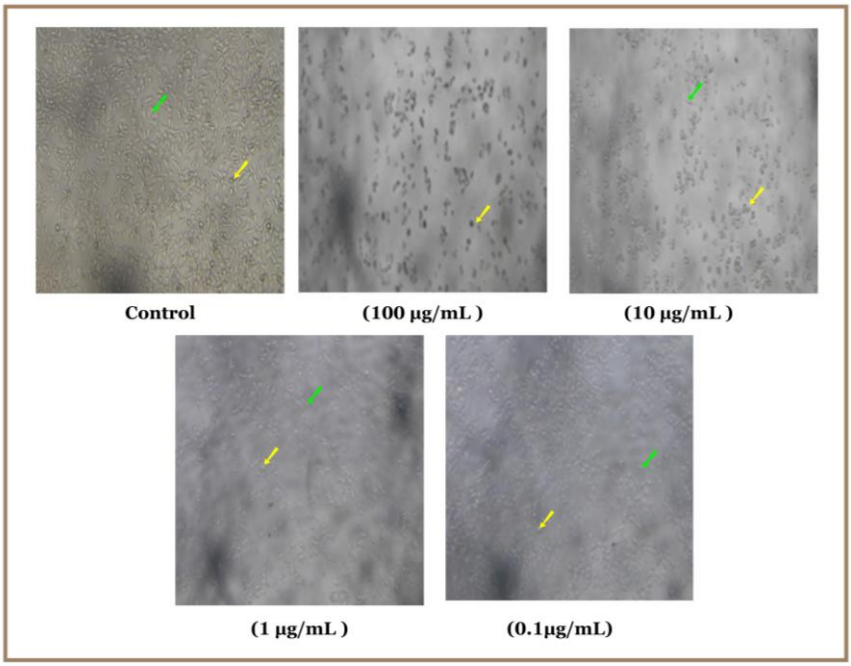
Figure 1: Percentage viability of T47D breast cancer cells after 48 h exposure to (a) niclosamide and (b) niclosamide–caffeic acid cocrystal. All values are expressed as means (n = 3) ± SD.

Cell Morphology Observation

Microscopic examination showed that T47D breast cancer cells in the control group were able to maintain a typical epithelial-like morphology, with intact cell membranes and a tightly adherent growth pattern. In contrast, exposure to pure niclosamide and the niclosamide– caffeic acid cocrystal induced distinct, concentration-dependent morphological alterations, including cell shrinkage, rounding, membrane blebbing, and reduced confluence, with the most pronounced changes observed at 100 µg/mL **(Figure 2)**. At intermediate concentrations (10 and 1 µg/mL), partial cell detachment and decreased cell density were apparent, whereas minimal alterations were noted at 0.1 µg/mL relative to the control. These morphological changes are indicative of apoptotic and cytotoxic processes, aligning with previous reports in cancer cells, where structural disruption and cell rounding are associated with decreased viability and apoptosis induction[29,30]. Notably, the cocrystal-treated group exhibited more extensive morphological damage than the pure niclosamide group at equivalent concentrations, suggesting an enhanced cytotoxic effect of the cocrystal, potentially attributable to improved cellular uptake and increased interaction with intracellular targets.



(a)



(b)

Figure 2: Morphological changes of T47D breast cancer cells after 48-hour treatment with (a) pure niclosamide and (b) niclosamide– caffeic acid cocrystal observed under inverted microscope. Viable cells are indicated by the green arrow, whereas the yellow arrow highlights cells exhibiting morphological alterations. Cell morphology was examined using an inverted microscope at 100x magnification.

CONCLUSIONS

This study demonstrates that both niclosamide and the niclosamide–caffeic acid multicomponent crystal exhibit potent, dose-dependent cytotoxicity against T47D breast cancer cells. The cocrystal formulation showed a slightly lower IC_{50} value than niclosamide, suggesting marginally enhanced potency. These findings indicate that cocrystallization with caffeic acid may offer a promising strategy to optimize the anticancer potential of niclosamide, potentially by improving its physicochemical properties and introducing complementary bioactivity. Further mechanistic and in vivo studies are warranted to validate these in vitro results and explore the therapeutic applicability of this formulation in breast cancer treatment.

Conflict of Interest: The authors declare that there are no conflicts of interest.

Authors' Declaration: The authors hereby declare that the work presented in this article is original and that they will bear any liability for claims relating to the content of this article.

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REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-49. https://doi.org/10.3322/caac.21660 PMid:33538338

2. Kim J, Harper A, McCormack V, Sung H, Houssami N, Morgan E, et al. Global patterns and trends in breast cancer incidence and mortality across 185 countries. Nat Med. 2025;31(4):1154-62. https://doi.org/10.1038/s41591-025-03502-3 PMid:39994475

3. Perkins DW, Steiner I, Haider S, Robertson D, Buus R, O'Leary L, et al. Therapy-induced normal tissue damage promotes breast cancer metastasis. iScience. 2024;27(1):1-21. https://doi.org/10.1016/j.isci.2023.108503 PMid:38161426 PMCid:PMC10755366

4. Navya PN, Kaphle A, Srinivas SP, Bhargava SK, Rotello VM, Daima HK. Current trends and challenges in cancer management and therapy using designer nanomaterials. Nano Converg. 2019;6(1):1-30. https://doi.org/10.1186/s40580-019-0193-2 PMid:31304563 PMCid:PMC6626766

5. Saranraj K, Kiran PU. Drug repurposing: Clinical practices and regulatory pathways. Perspect Clin Res. 2025;16(2):61-8. https://doi.org/10.4103/picr.picr_70_24 PMid:40322475 PMCid:PMC12048090

6. Xia Y, Sun M, Huang H, Jin WL. Drug repurposing for cancer therapy. Signal Transduct Target Ther. 2024;9(1):92. https://doi.org/10.1038/s41392-024-01808-1 PMid:38637540 PMCid:PMC11026526

7. Yin L, Gao Y, Zhang X, Wang J, Ding D, Zhang Y, et al. Niclosamide sensitizes triple-negative breast cancer cells to ionizing radiation in association with the inhibition of Wnt/β-catenin signaling. Oncotarget. 2016;7(27):42126-38. https://doi.org/10.18632/oncotarget.9704 PMid:27363012 PMCid:PMC5173121

8. Wu MM, Zhang Z, Tong CWS, Yan VW, Cho WCS, To KKW. Repurposing of niclosamide as a STAT3 inhibitor to enhance the anticancer effect of chemotherapeutic drugs in treating colorectal cancer. Life Sci. 2020;262:118522. https://doi.org/10.1016/j.lfs.2020.118522 PMid:33011217

9. Laila UE, Zhao Z long, Xu DY, Liu H, Xu ZX. Pharmacological advances and therapeutic applications of niclosamide in cancer and other diseases. Eur J Med Chem. 2025;290:117527. https://doi.org/10.1016/j.ejmech.2025.117527 PMid:40153934

10. Pan JX, Ding K, Wang CY. Niclosamide, an old antihelminthic agent, demonstrates antitumor activity by blocking multiple signaling pathways of cancer stem cells. Chin J Cancer. 2012;31(4):178-84. https://doi.org/10.5732/cjc.011.10290 PMid:22237038 PMCid:PMC3777479

11. Wiggins R, Woo J, Mito S. Optimizing Niclosamide for Cancer Therapy: Improving Bioavailability via Structural Modification and Nanotechnology. Cancers (Basel). 2024;16(20):3548. https://doi.org/10.3390/cancers16203548 PMid:39456642 PMCid:PMC11506536

12. Li Y, Li PK, Roberts MJ, Arend RC, Samant RS, Buchsbaum DJ. Multi-targeted therapy of cancer by niclosamide: A new application for an old drug. Cancer Lett. 2014;349(1):8-14. https://doi.org/10.1016/j.canlet.2014.04.003 PMid:24732808 PMCid:PMC4166407

13. Sathisaran I, Dalvi SV. Engineering Cocrystals of PoorlyWater-Soluble Drugs to Enhance Dissolution in Aqueous Medium. Pharmaceutics. 2018 Jul;10(3). https://doi.org/10.3390/pharmaceutics10030108 PMid:30065221 PMCid:PMC6161265

14. Chettri A, Subba A, Singh GP, Bag PP. Pharmaceutical co-crystals: A green way to enhance drug stability and solubility for improved therapeutic efficacy. J Pharm Pharmacol. 2024;76(1):1-12. https://doi.org/10.1093/jpp/rgad097 PMid:37934904

15. Pantwalawalkar J, Kale N, Nangare S, Patil S, Pawar S, Jadhav N. Pharmaceutical cocrystals: Unlocking the potential of challenging drug candidates. J Drug Deliv Sci Technol. 2025;104:106572. https://doi.org/10.1016/j.jddst.2024.106572

16. Fitriani L, Dirfedli F, Yuliandra Y, Setyawan D, Uchida M, Oyama H, et al. A novel cocrystal approach celecoxib with piperine: Simultaneously enhance dissolution rate and compressibility. J Pharm Sci. 2024;113(12):3565-73. https://doi.org/10.1016/j.xphs.2024.10.011 PMid:39414077

17. Zaini E, Sumirtapura YC, Halim A, Fitriani L, Soewandhi SN. Formation and characterization of sulfamethoxazole-trimethoprim cocrystal by milling process. J Appl Pharm Sci. 2017;7(12):169-73.

18. Kuminek G, Cao F, Bahia de Oliveira da Rocha A, Gonçalves Cardoso S, Rodríguez-Hornedo N. Cocrystals to facilitate delivery of poorly soluble compounds beyond-rule-of-5. Adv Drug Deliv Rev. 2016;101:143-66. https://doi.org/10.1016/j.addr.2016.04.022 PMid:27137109 PMCid:PMC4910885

19. Liang X, Liu S, Li Z, Deng Y, Jiang Y, Yang H. Efficient cocrystal coformer screening based on a Machine learning Strategy: A case study for the preparation of imatinib cocrystal with enhanced physicochemical properties. Eur J Pharm Biopharm [Internet]. 2024;196:114201. Available from: https://www.sciencedirect.com/science/article/pii/S0939641114000274 https://doi.org/10.1016/j.ejpb.2024.114201 PMid:38309538

20. Barbosa S, Agostini N, Borges A, Araújo B De, Bonfilio R. Growing Interest in Pharmaceutical Cocrystals : A Comprehensive Review of Applications and Trends. Chem Sel. 2025;1(00831):1-43. https://doi.org/10.1002/slct.202500831

21. Ifora I, Hamidi D, Susanti M, Hefni D, Wahyuni FS. Enhancing Chemotherapeutic Efficacy: Synergistic Cytotoxic Effect of Garcinia cowa Bark Extract and Doxorubicin in T47D Breast Cancer Cells. Trop J Nat Prod Res. 2025 Jan 31;9(1 SE-Articles):67-72. https://doi.org/10.26538/tjnpr/v9i1.10

22. Sanphui P, Kumar SS, Nangia A. Pharmaceutical Cocrystals of Niclosamide. Cryst Growth Des. 2012;12(9):4588-99. https://doi.org/10.1021/cg300784v

23. Grifasi F, Chierotti MR, Gaglioti K, Gobetto R, Maini L, Braga D, et al. Using salt cocrystals to improve the solubility of niclosamide. Cryst Growth Des. 2015;15(4):1939-48. https://doi.org/10.1021/acs.cgd.5b00106

24. Emami S, Siahi-Shadbad M, Adibkia K, Barzegar-Jalali M. Recent advances in improving oral drug bioavailability by cocrystals. Bioimpacts. 2018;8(4):305-20. https://doi.org/10.15171/bi.2018.33 PMid:30397585 PMCid:PMC6209825

25. Sandra F, Sidharta MA. Caffeic Acid Induced Apoptosis in MG63 Osteosarcoma Cells Through Activation of Caspases. Mol Cell Biomed Sci. 2017;1(1):28. https://doi.org/10.21705/mcbs.v1i1.6

26. Cortez N, Villegas C, Burgos V, Cabrera-Pardo JR, Ortiz L, González-Chavarría I, et al. Adjuvant Properties of Caffeic Acid in Cancer Treatment. Vol. 25, International Journal of Molecular Sciences. 2024. https://doi.org/10.3390/ijms25147631 PMid:39062873 PMCid:PMC11276737

27. Alam M, Ashraf GM, Sheikh K, Khan A, Ali S, Ansari MM, et al. Potential Therapeutic Implications of Caffeic Acid in Cancer Signaling: Past, Present, and Future. Front Pharmacol. 2022;13(March):1-14. https://doi.org/10.3389/fphar.2022.845871 PMid:35355732 PMCid:PMC8959753

28. Balc-Okcanoğlu T, Yilma-Susluer S, Kayabasi C, Ozme-Yelken B, Biray-Avci C, Gunduz C. The effect of caffeic acid phenethyl ester on cell cycle control gene expressions in breast cancer cells. Mol Biol Res Commun. 2021 Mar;10(1):39-43.

29. Chen Y, Li X, Yang M, Liu SB. Research progress on morphology and mechanism of programmed cell death. Cell Death Dis. 2024;15(5):327. https://doi.org/10.1038/s41419-024-06712-8 PMid:38729953 PMCid:PMC11087523

30. Doonan F, Cotter TG. Morphological assessment of apoptosis. Methods. 2008;44(3):200-4. https://doi.org/10.1016/j.ymeth.2007.11.006 PMid:18314050