*Osmangazi Journal of Med, 2025;47(4):593-599*
*DOI: 10.20515/otd.1651353*

*Research Article*
*Araştırma Makalesi*

**Osmangazi Journal of Medicine**
**e-ISSN: 2587-1579**

# Evaluating The Cytotoxic and Metastatic Actions of Cannabinol on HCT-116 Colon Cancer Cells

HCT-116 Kolon Kanseri Hücreleri Üzerinde Kannabinolün Sitotoksik ve Metastatik Etkilerinin Değerlendirilmesi

Gamze Turna Saltoglu[1], Serap Yalcın Azarkan[2], Bayram Furkan Coskun[3], Habibe Sema Arslan[4]

[1]Kirsehir Ahi Evran University, Faculty of Medicine, Department of Medical Biochemistry, Kirsehir,Türkiye
[2]Kirsehir Ahi Evran University, Faculty of Medicine, Department of Medical Pharmacology, Kirsehir, Türkiye
[3]Kirsehir Ahi Evran University, Institute of Health Sciences, Department of Medical Biology, Kirsehir, Türkiye
[4]Kirsehir Ahi Evran University, Faculty of Medicine, Department of Medical Genetics, Kirsehir, Türkiye

***ORCID ID of the authors***
GTS. 0000-0002-7847-2898
SY. 0000-0002-9584-266X
BFC. 0009-0004-8885-543X
HSA. 0000-0002-2052-9345

**Correspondence / Sorumlu yazar:**
Gamze TUNA SALTOĞLU

Kirsehir Ahi Evran University, Faculty of Medicine, Department of Medical Biochemistry, Kirsehir,Türkiye

**e-mail:** gamze-trn@hotmail.com

**Ethics Committee Approval:** The cell cultere used in the study was purchased. Since the study was conducted on cell cultere, ethical committee approval was not required.

**Informed Consent:** The authors declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

**Authorship Contributions:** Idea and design: G.T.S., S.Y.A.; Data collection and processing: G.T.S., S.Y.A. B.F.C.,; Analysis and interpretation of data: G.T.S., S.Y.A., B.F.C.,H.S.A., Writing of significant parts of the article: G.T.S., S.Y.A.,B.F.C.,H.S.A

**Copyright Transfer Form:** Copyright Transfer Formwas signed by all authors.

**Conflict of Interest:** The authors declare that the research was conducted in an environment in which there was no commercial or financial relationship with any institution or person that could be construed as a potential conflict of interest.

**Received** : 05.03.2025

**Accepted** 13..05.2025

**Published** :26..05.2025

**Abstract:** It aims to evaluate the cytotoxic and metastatic effects of cannabinol (CBN) on HCT-116 colon cancer cells in this study. Colorectal cancer is one of the leading causes of cancer-related mortality worldwide, with high recurrence and metastasis rates despite current treatment approaches. In recent years, the antitumor potential of cannabinoids has gained attention; however, the specific effects of CBN remain largely unexplored. HCT-116 colon cancer cells were cultured under laboratory conditions and treated with CBN. Cell viability was assessed using the XTT cytotoxicity assay, while cell migration and invasion capabilities were analyzed through the wound healing assay and invasion assay, respectively. The acquired data were quantified using ImageJ software and statistically evaluated with GraphPad Prism 8. The $IC_{50}$ value of CBN was determined to be 69.14 µM, and CBN treatment was found to significantly reduce cell viability ($p<0.05$). Wound healing assay results demonstrated that CBN treatment markedly inhibited cell migration ($p<0.05$). Invasion analyses revealed that CBN significantly reduced invasiveness and provided a notable inhibition compared to the control group ($p<0.05$). This provides significant evidence that CBN suppresses metastatic processes in HCT-116 cells. This study supports the potential of CBN as an inhibitor of cytotoxic and metastatic activity in colon cancer cells. The findings indicate that CBN reduces cell proliferation, migration, and invasion, suggesting its potential as a therapeutic agent in colorectal cancer treatment. However, further research is needed to elucidate the underlying molecular mechanisms and validate these effects in in vivo models.
**Keywords:** Colon cancer, Cannabinol, Cytotoxicity, Migration, Invasion, Anticancer agents.

**Özet:** Bu çalışma kannabinolün (CBN) HCT-116 kolon kanseri hücreleri üzerindeki sitotoksik ve metastatik etkilerini değerlendirmeyi amaçlamaktadır. Kolorektal kanser dünya genelinde kanserle ilişkili ölümlerin en yaygın nedenlerinden biridir ve mevcut tedavi yaklaşımlarına rağmen yüksek nüks ve metastaz oranları görülmektedir. Son yıllarda, kannabinoidlerin antitümöral potansiyeli araştırılmakta olup, CBN'nin bu konudaki etkileri henüz tam olarak aydınlatılmamıştır. HCT-116 kolon kanseri hücreleri laboratuvar koşullarında kültüre edilerek CBN ile muamele edildi. Hücre canlılığı XTT sitotoksisite testi ile,hücre göçü ve invazyon yeteneği sırasıyla yara iyileşme testi (wound healing assay) ve invazyon analizi ile değerlendirildi. Elde edilen veriler, ImageJ yazılımı ile sayısallaştırıldı ve GraphPad Prism 8 programı kullanılarak istatistiksel olarak değerlendirildi. CBN'nin $IC_{50}$ değeri 69.14 µM olarak belirlendi ve CBN uygulamasının hücre canlılığında anlamlı bir azalmaya neden olduğu belirlendi. ($p<0.05$). Yara iyileşme testi sonuçları, CBN uygulamasının hücre migrasyonunu belirgin şekilde inhibe ettiğini ortaya koymuştur ($p<0.05$). İnvazyon analizleri, CBN'nin invaziviteyi belirgin derecede azalttığını ve kontrol grubuna kıyasla anlamlı bir inhibisyon sağladığını göstermektedir ($p<0.05$). Bu bulgular, CBN'nin HCT-116 hücrelerinde metastatik süreçleri baskıladığına dair önemli kanıtlar sunmaktadır. Bu çalışma CBN'nin kolon kanseri hücreleri üzerinde sitotoksik ve metastatik aktiviteyi inhibe edici potansiyelini desteklemektedir. Bulgular, CBN'nin hücre proliferasyonunu, migrasyonunu ve invazyonunu azalttığını göstermekte olup, kolorektal kanser tedavisinde CBN'nin olası terapötik bir ajan olarak değerlendirilebileceğini düşündürmektedir. Ancak, bu etkinin altta yatan moleküler mekanizmalarının daha ayrıntılı olarak araştırılması ve in vivo modellerde test edilmesi gerekmektedir.
**Anahtar Kelimeler:** Kolon kanseri, Kannabinol, Sitotoksisite, Migrasyon, İnvazyon, Antikanser ajanlar.

**How to cite/ Atıf için:** Turna Saltoglu G, Yalcın Azarkan S, Coskun BF, Arslan HS, Evaluating The Cytotoxic and Metastatic Actions of Cannabinol on HCT-116 Colon Cancer Cells,, Osmangazi Journal of Medicine, 2025;47(4):593-599

## 1. Introduction

Colorectal cancer represents a significant global public health concern due to its high incidence and mortality rates. As one of the most common malignancies, colorectal cancer ranks third among all cancer types in terms of morbidity and mortality (1). Over the past 25 years, a significant increase in the incidence and mortality of colorectal cancer has been observed among young adults under the age of 50 (2). Research indicates that this increase is largely associated with lifestyle factors, such as changes in dietary habits and insufficient physical activity (3). According to GLOBOCAN data, in 2020, newly reported colorectal cancer cases accounted for 10% of all cancer cases worldwide, ranking third with 1,931,590 cases. Additionally, colorectal cancer was reported as the second leading cause of malignancy-related deaths, with 935,173 deaths (9.4%) (4). Colon cancer is considered one of the most aggressive and lethal cancer types, particularly due to its potential to metastasize to distant organs such as the gastrointestinal system and lungs (5). Therefore, early diagnosis and the development of effective treatment strategies are critically important for reducing disease incidence and improving survival rates (6).

Cannabinoids, first derived from the Cannabis sativa plant, have been used for centuries as a fiber source and for medicinal purposes (7, 8). In the mid-19th century, O'Shaughnessy and Moreau reported the therapeutic effects of cannabinoids on conditions such as muscle spasms, vomiting, rheumatism, and tetanus (9, 10). In recent years, cannabinoids have also been utilized for the treatment of chemotherapy-induced nausea and vomiting, among other indications (11, 12). Cannabinoids are classified into three main categories. These categories are plant-derived phytocannabinoids (e.g. Δ9-tetrahydrocannabinol (Δ9-THC), cannabidiol (CBD), cannabinol (CBN)), endogenous cannabinoids (e.g. anandamide (AEA) and 2-arachidonoylglycerol (2-AG)), and synthetic cannabinoids. (13). Endocannabinoids exert their biological effects by binding to cannabinoid receptors CB1 and CB2, which are members of the G-protein-coupled receptor family (14). Endocannabinoids play a role in regulating various physiological functions, including cardiovascular regulation, reproduction, inflammatory response, and the immune system (15). Phytocannabinoids and synthetic cannabinoids can bind to CB1 and CB2 receptors due to their structural similarity to endocannabinoids, thereby modulating various signaling pathways in the body (14).

Phytocannabinoids are C21 terpenophenolic compounds (16). To date, more than 120 types of cannabinoids have been identified, with the most abundant including Δ9-tetrahydrocannabinol (Δ9-THC), cannabinol (CBN), cannabidiol (CBD), cannabichromene (CBC), cannabidivarin (CBDV), cannabigerol (CBG), cannabivarin (CBV), Δ8-tetrahydrocannabinol (Δ8-THC), and Δ9-tetrahydrocannabivarin (THCV) (17). Recent studies have shown that cannabinoids induce autophagy and apoptosis, while playing a crucial role in regulating signaling pathways that suppress cancer cell proliferation, angiogenesis, and metastasis (18).

Cannabinol (CBN) is a compound formed as a result of the metabolic degradation of Δ9-tetrahydrocannabinol (Δ9-THC), which exhibits psychoactive properties (19). Cannabinoids exert their anticancer effects by binding to cannabinoid receptors and modulating cellular signaling pathways (18, 20). CBN has been reported to inhibit cancer cell growth and invasion by regulating the MAPK/ERK and PI3K/AKT pathways, which are associated with cell proliferation in various cancer cell types (21).

In light of this information, this study aims to evaluate the cytotoxic effects of cannabinol on HCT-116 colon cancer cells, as well as its impact on cell proliferation, migration, and invasion.

## 2.Materials and Methods

### 2.1.Cell Culture

The HCT-116 human colon cancer cell line was cultured in RPMI-1640 medium supplemented with 10% Fetal Bovine Serum (FBS) and 1% antibiotic (penicillin-streptomycin) under standard conditions in a 37°C incubator with 5% $CO_2$. Once the cells reached 80% confluence, they were enzymatically dissociated using 0.05% trypsin-EDTA and passaged.

### 2.2.Cytotoxicity Assay

To determine the $IC_{50}$ value of cannabinol in HCT-116 colon cancer cells, the XTT (2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-2H-tetrazolium-5-carboxanilide) cell viability assay was performed. The cells were seeded in 96-well culture plates at a density of 5,000 cells per well and allowed to adhere and establish their morphology. Cannabinol (Sigma-Aldrich, 521-35-7) was prepared in dimethyl sulfoxide (DMSO) and diluted with the appropriate culture medium before treatment. The compound

was applied to the cells in serial dilutions at varying concentrations. The XTT assay was conducted according to the manufacturer's protocol, and absorbance values were measured using a spectrophotometer (BioTek, USA) at 450 nm (22).

### 2.3.Cell Invasion Assay

The effect of cannabinol (CBN) on the invasion capacity of HCT-116 colon cancer cells was evaluated using the $IC_{50}$ value (69.14 µM) determined from the XTT assay. For this purpose, a control group and a CBN-treated experimental group (at $IC_{50}$ concentration) were established, and the cells were incubated at 37°C for 72 hours. At the end of the incubation period, the cells were fixed with 10% formaldehyde for 10 minutes and subsequently stained with Giemsa stain (23). Following the staining process, microscopic images of the cells were captured, and cell numbers were analyzed within a fixed area using ImageJ software. The data obtained from the control and experimental groups were statistically analyzed and visualized using GraphPad Prism 8.

### 2.4.Wound Healing Assay

The wound healing assay was performed to evaluate cell migration and wound closure in vitro. A six-well culture plate was used, with $1.5 \times 10^5$ cells seeded into each well and incubated for 24 hours. After incubation, three wells were designated as the control group, while the remaining three wells were treated with cannabinol (CBN). A wound model was created in the cell monolayer, and images were captured every 24 hours throughout the healing process. The collected images were analyzed using ImageJ software. This protocol was applied to quantitatively assess cell motility and wound closure. (24).

### 2.5.Statistical Analysis

Data analysis was performed using IBM SPSS Statistics 29. Non-parametric data were analyzed using the Mann-Whitney U and Kruskal-Wallis tests. Graphs were generated using GraphPad Prism 8. All experiments were independently repeated at least three times. A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant.

## 3.Results

In this study, the cytotoxic and metastatic effects of cannabinol (CBN) on HCT-116 colon cancer cells were evaluated. Cell viability, proliferation, migration, and invasion analyses were performed.

XTT cell viability assay was used to assess cytotoxicity, while cell invasion and migration capacities were determined through migration and invasion assays. The XTT assay results showed that the $IC_{50}$ value of CBN was calculated as 69.14 µM (Figure 1).

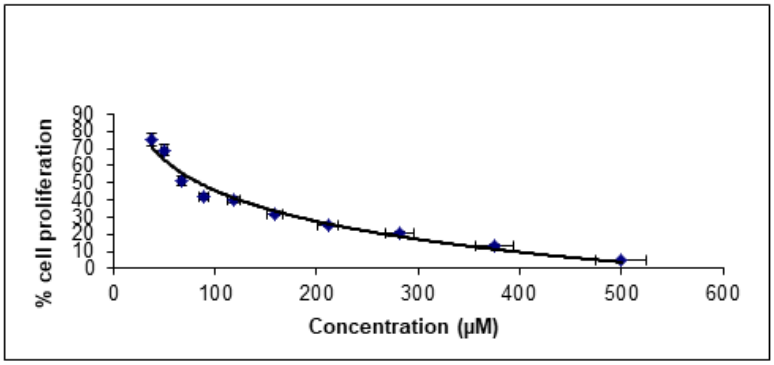


**Figure 1.** XTT assay results and determination of the $IC_{50}$ value. The effect of different concentrations of cannabinol (CBN) on the viability of HCT-116 colon cancer cells was assessed using the XTT assay. The graph illustrates the decrease in cell proliferation percentage (y-axis) in response to increasing CBN concentrations (x-axis). The $IC_{50}$ value was calculated as 69.14 µM, representing the concentration at which CBN reduces cell viability by half.

A wound healing assay was performed to evaluate the metastatic potential of HCT-116 colon cancer cells. This protocol is widely used for the in vitro assessment of cell migration and wound healing. Cell cultures that reached 80% confluence were treated with cannabinol (CBN) at a concentration of 69.14 µM to examine cell migration. Cell motility was observed microscopically at 24 and 48 hours and analyzed using ImageJ software. The results demonstrated a significant reduction in migration in CBN-treated cells compared to the control group at 48 hours ($p=0.002$) (Figure 2).

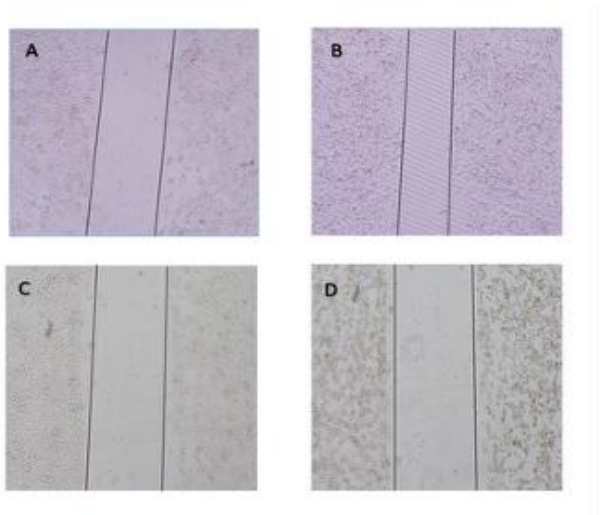


**Figure 2.** Representative light microscopy images (10×) of cell migration in the control group at (A) 24 hours and (B) 48 hours, and in the CBN-treated group at (C) 24 hours and (D) 48 hours.

Figure 3. percentage migration change in control and CBN-treated groups. While the control group maintained normal migration ability during the 24- and 48-hour incubation period, a significant reduction in cell migration capacity was observed in the CBN-treated group at 48 h (p=0.002).

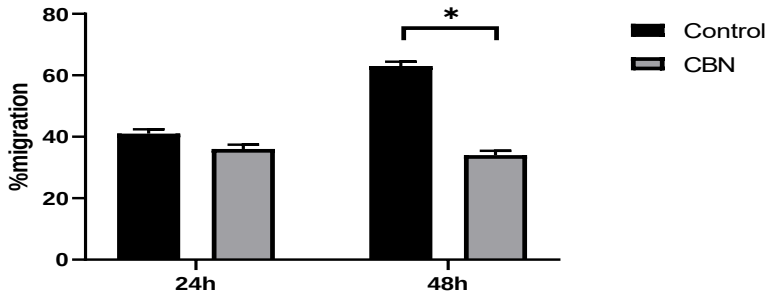


**Figure 3.** Percentage migration change in control and CBN groups. Cell migration rates (% migration) in control and CBN-treated groups were evaluated over 24 and 48 hours. At 48 hours, a significant reduction in migration was observed in the CBN-treated group compared to the control group group (p=0.002 for 48h; p<0,05) (p=0,072 for 24h).

An invasion assay was performed to evaluate the effect of CBN treatment on the invasiveness of HCT-116 cells. The results showed that the invasion capacity of CBN-treated cells was significantly reduced compared to the control group (p=0,028 for 24h, p=0,012 for 48h, p=0,009 for 72h, Figure 4 and Figure 5).

Microscopic images obtained after staining were analyzed using ImageJ software, and cell counts were performed. The data were visualized and statistically analyzed using GraphPad Prism 8. Figure 4 demonstrates that CBN treatment markedly inhibited cell invasion.

Figure 5 shows the comparison of cell invasion rates between the control and CBN-treated groups. While the invasion rate remained high in the control group at all time points, a significant reduction in cell invasion was observed in the CBN-treated groups at 24, 48, and 72 hours. The differences between the CBN-treated groups and the control group were found to be statistically significant. (p=0,028 for 24h, p=0,012 for 48h, p=0,009 for 72h).

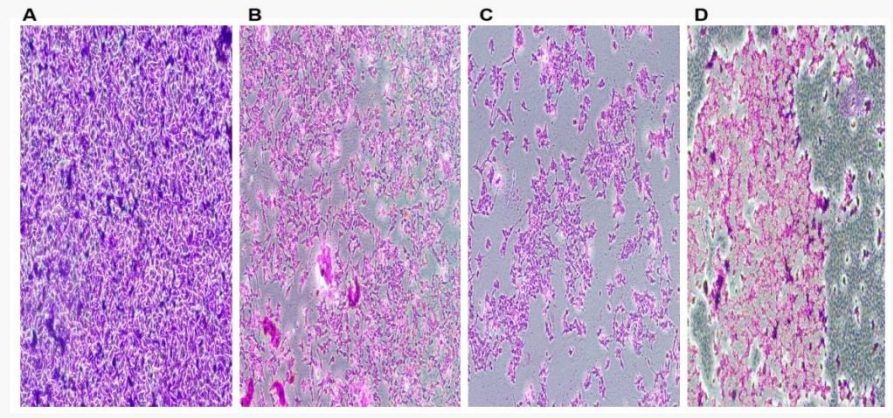


**Figure 4.** Cell invasion analysis (Control group (A); CBN-treated group at (B) 24h, (C) 48h and (D) 72h). Extensive invasion was observed in the control group (A), whereas a marked reduction in invasion capacity was detected in cells treated with 69.14 µM CBN (B,C,D). Cells were stained with Giemsa and imaged under a microscope.

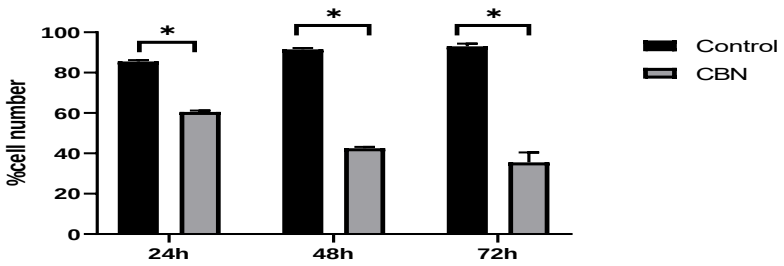


**Figure 5.** Quantitative analysis showing the effect of CBN treatment on the invasion ability of HCT-116 cells. A significant reduction in cell invasion was observed in the CBN-treated group compared to the control group at 24, 48, and 72 hours (p=0,028 for 24h, p=0,012 for 48h, p=0,009 for 72h).

## 4.Discussion

Colorectal cancer (CRC) remains one of the leading causes of cancer-related mortality worldwide and continues to be a significant global health concern (25). Although significant advancements have been made in surgical techniques and chemotherapeutic approaches in recent years, current treatment strategies for CRC have not led to substantial improvements in survival rates. Approximately 20% of patients still face poor clinical outcomes due to recurrence and metastasis (26). Therefore, the development of novel therapeutic approaches is of great importance.

Recently, the effects of cannabinoid compounds on cancer have gained increasing attention. One such compound, cannabinol (CBN), is a cannabinoid with low psychoactivity that has been shown to exhibit various biological activities. While extensive oncological research has been conducted on Δ9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD), knowledge regarding the anticancer potential of CBN, a metabolite of Δ9-THC degradation, remains highly limited (19). However, some studies suggest that CBN can modulate intracellular signaling pathways by binding to CB1 and CB2 receptors, thereby exhibiting antitumor effects. While Δ9-THC binds to CB1 and CB2 receptors at similar levels, exerting widespread effects on both the central nervous system and peripheral tissues, CBN has a lower affinity for CB1 receptors and a relatively higher affinity for CB2 receptors (27).

Studies on the antitumor effects of Δ9-THC have demonstrated that it reduces proliferation in colon cancer cell lines (28). Additionally, studies have shown that Δ9-THC reduces survival in hepatocellular carcinoma and glioblastoma cells, induces autophagy and apoptosis, and that these processes occur through the downregulation of the ERK and AKT signaling pathways (29, 30). Studies investigating the effects of CBN on cancer are still limited. In a study conducted by Wang et al. (2022), it was found that the application of CBN to neuroblastoma cells decreased cell proliferation,

invasion, and angiogenesis in a dose-dependent manner (21).

In another study conducted by Zhong et al. (2023), it was determined that CBN exhibited antitumor activity in glioma A172, hepatocellular carcinoma HepG2, and breast cancer HCC1806 cell lines. In this regard, it was shown that CBN suppressed cancer cell proliferation and regulated the expression of various cannabinoid receptors. Additionally, it was found that CBN inhibited the ERK1/2 signaling pathway in A172 and HepG2 cells, while it suppressed the AKT signaling pathway in HCC1806 cells. Moreover, it was revealed that CBN could trigger apoptotic processes and play a regulatory role in cell death mechanisms (31).

In this study, the cytotoxic and metastatic effects of CBN were investigated in HCT-116 colon cancer cells. The XTT cell viability assay showed that CBN reduced cell proliferation, with an $IC_{50}$ value of 69.14 μM. These results are in line with previous studies that have highlighted the anticancer effects of cannabinoids on colon cancer cells (22). Furthermore, analyses conducted on cell migration and invasion revealed that CBN inhibited metastatic mobility. According to the results of the cell migration analysis (wound healing assay), a significant reduction in migration was observed in CBN-treated cells compared to the control group at 48 hours ($p=0.002$, Figure 2 and Figure 3). This inhibitory effect of CBN on migration is consistent with previous studies conducted on different cancer cell lines.

In our study, it was shown that CBN suppressed the migration and invasion ability of CRC cells, with this effect becoming particularly pronounced at 48 and 72 hours. Image analysis and quantitative data confirm that CBN significantly inhibited cell migration and invasion. These findings support studies suggesting that cannabinoids, through receptors may lead to anti-metastatic effects (18). As shown in Figure 4 and Figure 5, a significant reduction in invasion ability was observed in CBN-treated cells. These results support studies reporting that cannabinoids have inhibitory effects on migration and invasion (32). It is suggested that the effect of CBN may be related to the suppression of the ERK1/2 and AKT signaling pathways, which regulate focal adhesion complexes and actin cytoskeleton dynamics (31).

This study has certain limitations. The lack of validation in in vivo models and the absence of a detailed investigation into the molecular mechanisms mediating the effects of CBN limit the overall scope of the study. Nevertheless, as this work was designed as a preliminary investigation, future comprehensive studies addressing these gaps will be essential for a more in-depth understanding of the biological effects of CBN.

In conclusion, this study demonstrates that CBN exhibits cytotoxic effects in colon cancer cells and inhibits their metastatic abilities. The findings support the therapeutic potential of CBN, though further mechanistic and in vivo studies are needed.

## REFERENCES


1. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, et al. Colorectal cancer statistics, 2020. CA: a cancer journal for clinicians. 2020;70(3):145-64.
2. Ahmed M. Colon cancer: a clinician's perspective in 2019. Gastroenterology research. 2020;13(1):1.
3. Islam MR, Akash S, Rahman MM, Nowrin FT, Akter T, Shohag S, et al. Colon cancer and colorectal cancer: Prevention and treatment by potential natural products. Chemico-biological interactions. 2022;368:110170.
4. 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: a cancer journal for clinicians. 2021;71(3):209-49.
5. Kuppusamy P, Yusoff MM, Maniam GP, Ichwan SJA, Soundharrajan I, Govindan N. Nutraceuticals as potential therapeutic agents for colon cancer: a review. Acta Pharmaceutica Sinica B. 2014;4(3):173-81.
6. Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. Clinics in colon and rectal surgery. 2009;22(04):191-7.
7. Gonçalves ECD, Baldasso GM, Bicca MA, Paes RS, Capasso R, Dutra RC. Terpenoids, Cannabimimetic Ligands, beyond the Cannabis Plant. Molecules. 2020;25(7):1567.
8. Kalant H. Medicinal use of cannabis: history and current status. Pain Research and Management. 2001;6(2):80-91.
9. O'Shaughnessy WB. On the preparations of the Indian hemp, or Gunjah: Cannabis indica their effects on the animal system in health, and their utility in the treatment of tetanus and other convulsive diseases. Provincial Medical Journal and Retrospect of the Medical Sciences. 1843;5(123):363.
10. Zuardi AW. History of cannabis as a medicine: a review. Brazilian Journal of Psychiatry. 2006;28:153-7.
11. Kleckner AS, Kleckner IR, Kamen CS, Tejani MA, Janelsins MC, Morrow GR, et al. Opportunities for cannabis in supportive care in cancer. Therapeutic advances in medical oncology. 2019;11:1758835919866362.

12. Parker LA, Rock EM, Limebeer CL. Regulation of nausea and vomiting by cannabinoids. British journal of pharmacology. 2011;163(7):1411-22.
13. Pertwee RG. Cannabinoid pharmacology: the first 66 years. British journal of pharmacology. 2006;147(S1):S163-S71.
14. Kovalchuk O, Kovalchuk I. Cannabinoids as anticancer therapeutic agents. Cell Cycle. 2020;19(9):961-89.
15. Guindon J, Hohmann AG. The endocannabinoid system and pain. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders). 2009;8(6):403-21.
16. Andre CM, Hausman J-F, Guerriero G. Cannabis sativa: the plant of the thousand and one molecules. Frontiers in plant science. 2016;7:19.
17. Morales P, Hurst DP, Reggio PH. Molecular Targets of the Phytocannabinoids: A Complex Picture. Prog Chem Org Nat Prod. 2017;103:103-31.
18. Velasco G, Sánchez C, Guzmán M. Anticancer Mechanisms of Cannabinoids. Current Oncology. 2016;23(11):23-32.
19. Pertwee R. The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids: Δ9-tetrahydrocannabinol, cannabidiol and Δ9-tetrahydrocannabivarin. British journal of pharmacology. 2008;153(2):199-215.
20. Velasco G, Sánchez C, Guzmán M. Towards the use of cannabinoids as antitumour agents. Nature Reviews Cancer. 2012;12(6):436-44.
21. Wang B, Li D, Cherkasova V, Gerasymchuk M, Narendran A, Kovalchuk I, et al. Cannabinol Inhibits Cellular Proliferation, Invasion, and Angiogenesis of Neuroblastoma via Novel miR-34a/tRiMetF31/PFKFB3 Axis. Cancers. 2022;14(8):1908.
22. Nallathambi R, Mazuz M, Namdar D, Shik M, Namintzer D, Vinayaka AC, et al. Identification of Synergistic Interaction Between Cannabis-Derived Compounds for Cytotoxic Activity in Colorectal Cancer Cell Lines and Colon Polyps That Induces Apoptosis-Related Cell Death and Distinct Gene Expression. Cannabis and Cannabinoid Research. 2018;3(1):120-35.
23. Shaw LM. Tumor cell invasion assays. Cell migration: developmental methods and protocols. 2005:97-105.
24. Rodriguez LG, Wu X, Guan J-L. Wound-healing assay. Cell Migration: Developmental Methods and Protocols. 2005:23-9.
25. Eng C, Yoshino T, Ruíz-García E, Mostafa N, Cann CG, O'Brian B, et al. Colorectal cancer. The Lancet. 2024;404(10449):294-310.
26. Wang X, Zhang L, Li H, Sun W, Zhang H, Lai M. THBS2 is a potential prognostic biomarker in colorectal cancer. Scientific reports. 2016;6(1):33366.
27. Mahadevan A, Siegel C, Martin BR, Abood ME, Beletskaya I, Razdan RK. Novel cannabinol probes for CB1 and CB2 cannabinoid receptors. Journal of medicinal chemistry. 2000;43(20):3778-85.
28. Hwang Y-N, Kwon I-S, Park J-H, Na H-H, Kwon T-H, Park J-S, et al. Cell death induction and intracellular vesicle formation in human colorectal cancer cells treated with Δ9-Tetrahydrocannabinol. Genes & Genomics. 2023;45(12):1463-74.
29. Salazar M, Carracedo A, Salanueva ÍJ, Hernández-Tiedra S, Lorente M, Egia A, et al. Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells. The Journal of clinical investigation. 2009;119(5):1359-72.
30. Vara D, Salazar M, Olea-Herrero N, Guzmán M, Velasco G, Díaz-Laviada I. Anti-tumoral action of cannabinoids on hepatocellular carcinoma: role of AMPK-dependent activation of autophagy. Cell Death & Differentiation. 2011;18(7):1099-111.
31. Zhong N, Li D, Wang B, Kovalchuk O, Kovalchuk I. Cannabinol inhibits cell growth and triggers cell cycle arrest and apoptosis in cancer cells. Biocatalysis and Agricultural Biotechnology. 2023;48:102627.
32. Yousef B, Hassan H, Guerram M, Hamdi A, Wang B, Zhang L-Y, et al. Pristimerin inhibits proliferation, migration and invasion, and induces apoptosis in HCT-116 colorectal cancer cells. Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie. 2016;79:112-9.