

## ORIGINAL RESEARCH

# Effects of Sufentanil on proliferation, migration and epithelial-mesenchymal transition of endometrial cancer

Chen Cheng<sup>1</sup>, Mimi Dai<sup>2,\*</sup>, Shishi Zheng<sup>1</sup>, Yujie Wu<sup>1</sup>, Li Shu<sup>2</sup>, Huimin Wu<sup>3</sup>

<sup>1</sup>Department of Pharmacy, The 2nd Affiliated Hospital of Wenzhou Medical University, 325000 Wenzhou, Zhejiang, China

<sup>2</sup>Department of Obstetrics and Gynecology, The 2nd Affiliated Hospital of Wenzhou Medical University, 325000 Wenzhou, Zhejiang, China

<sup>3</sup>Department of Anesthesiology, The 2nd Affiliated Hospital of Wenzhou Medical University, 325000 Wenzhou, Zhejiang, China

**\*Correspondence**

Daimimi\_666@163.com  
(Mimi Dai)

**Abstract**

To investigate the impact of Sufentanil on the progression of endometrial cancer (EC), including its proliferation, migration, epithelial-mesenchymal transition and underlying mechanism. The effects of Sufentanil on EC cell growth were evaluated using Cell counting kit-8 (CCK-8) and colony formation assays, while wound healing and transwell assays were performed to assess the influence on motility. In addition, immunoblot assays were performed to determine its role in EC cell epithelial-mesenchymal transition (EMT) and the associated underlying mechanism. Sufentanil demonstrated the ability to inhibit EC cell growth, migration, invasion and EMT process through the inhibition of the Protein Kinase B (AKT)/nuclear factor kappa-B (NF- $\kappa$ B) axis, thereby contributing to the repression of EC progression. Sufentanil effectively inhibited the proliferation, migration and EMT of endometrial cancer, demonstrating a potentially effective approach against EC.

**Keywords**

Endometrial cancer (EC); Sufentanil; Migration; EMT; AKT/NF- $\kappa$ B pathway

## 1. Introduction

Endometrial cancer (EC) comprises a cluster of epithelial malignancies in the uterine lining, predominantly manifesting in perimenopausal and postmenopausal women [1], and is one of the most common tumors of the female reproductive system [2]. Globally, EC is ranked 15th among all malignancies and represents the most common type of gynecological malignancy in developed countries [3]. The established treatment protocol for EC involves surgical intervention and subsequent adjuvant therapy, for instance hysterectomy and bilateral salpingo-oophorectomy followed by conventional chemotherapy using paclitaxel and platinum agents [4]. The common pharmaceutical agents used to treat EC includes high-potency progesterone, anti-cancer chemicals and anti-cancer Chinese medicine [4]. However, women with recurrent or advanced diseases often suffer from a low response rate with conventional treatment and demonstrate poor clinical outcomes [5–7]; therefore, urging the need for new and more efficacious drugs to improve patients' outcomes.

Sufentanil finds its applicability in diverse pain management scenarios, serving as an effective choice for postoperative analgesia, particularly following surgical and gynecological procedures, and is indispensable in the fields of anesthesia and pain management [8]. Its principal mechanism of action involves targeting opioid  $\mu$  receptors, making it frequently used as an opioid analgesic [9]. It has been reported that the analgesic potency of Sufentanil surpasses that of fentanyl by

a magnitude of 5–10 times [9] and that Sufentanil, as a fat-soluble substance, has high binding rates to plasma protein [9]. In addition, research has shown that Sufentanil preconditioning exerts a protective effect on brain-related diseases [10], as well as antitumor effects [9, 11]. Notably, Sufentanil has been shown to inhibit gastric cancer cell proliferation and induce apoptosis [12], affect the proliferation and epithelial-mesenchymal transition (EMT) of lung cancer cells through modulation of the Wnt/ $\beta$ -catenin axis [13], inhibit the proliferation and metastasis of esophageal cancer by suppressing NF- $\kappa$ B and Snail pathways [14], and inhibits the proliferation and promotes apoptosis of cervical cancer cells by regulating the phosphoinositide 3 kinase (PI3K)/Akt/mammalian target of rapamycin (mTOR) axis [15] at concentrations ranging between 1 nM–20 nM [11–15]. Nevertheless, the specific role of Sufentanil in the context of endometrial cancer and its underlying mechanisms remain inadequately understood. The present study was designed to investigate the role and underlying mechanism of Sufentanil in EC.

## 2. Materials and methods

### 2.1 Cell culture and drug treatment

The two types of human endometrial cancer (EC) cells, namely HEC1A and Ishikawa cells, were purchased from the American Type Culture Collection (ATCC, USA), which were then cultivated in Dulbecco's Modified Eagle's Medium (DMEM, Gibco, USA) supplemented with 10% fetal bovine

serum (FBS, 10099-141, Gibco, Grand Island, NY, USA) and incubated at 37 °C in a 5% CO<sub>2</sub> incubator. All cell lines were negative for mycoplasma, and the cell passage number in this study was less than 10. Then, Sufentanil (Sigma, I134, St. Louis, MO, USA) at concentrations of 0.5, 1 and 2 nM was used to treat EC cells for 24 hours.

## 2.2 Cell counting kit-8 (CCK-8) assay

HEC1A and Ishikawa cells were seeded onto 96-well plates, allowed to adhere for 48 hours, and exposed to CCK-8 (C0038, Beyotime, Beijing, China) for 4 hours, following which the optical density (OD450 value) of the cells was quantified using a microplate reader (Envision, Bio-Rad, Hercules, CA, USA).

## 2.3 Colony formation assay

HEC1A and Ishikawa cells were seeded at a density of 1000 cells per well in 6-well plates and cultured with 10% FBS media for 14 days at 37 °C. Afterward, cells were fixed with paraformaldehyde (PFA) for 20 minutes and stained using 0.1% crystal violet (Beyotime, Beijing, China) for 20 minutes. Images of the cell colonies were then captured using a microscope (LSM810, Zeiss, Oberkochen, Baden-Wurtberg, Germany) and analyzed using ImageJ v9.0 (National Institutes of Health, Bethesda, MD, USA), wherein more than 100 cells were defined as a colony.

## 2.4 Transwell assay

BD Falcon inserts (BD Biosciences, Inc., New Jersey, USA) were utilized for the upper chambers, while 24-well plates served as the lower chambers. The cell culture inserts were coated with 50  $\mu$ L of 20% Matrigel and incubated at 37 °C for 30 minutes. Subsequently, cells were introduced into the upper chamber with serum-free medium, while the lower chamber contained complete medium. Invaded cells on the lower side were fixed using 4% paraformaldehyde for 25 minutes, followed by staining with a 2% crystal violet solution for 25 minutes, and images were captured using a microscope.

## 2.5 Wound-healing assay

The cells were plated onto glass coverslips until they reached 100% confluence. Then, a 10- $\mu$ L pipette tip was used to create a scratch, after which it was washed twice with phosphate balanced solution (PBS) to remove cell debris. The cells were then cultured in a serum-free media for 24 h, and the wound closure was imaged using a light microscope at 0 and 24 h and assessed using the ImageJ v9.0 software. The wound healing percentage was calculated as follows: Healing area/total area.

## 2.6 Immunoblot assay

The cells were lysed using a buffer comprising 1% Triton X-100, 150 mM Sodium chloride (NaCl) and 50 mM Tris (pH 7.5). The extracted proteins were then transferred onto polyvinylidene difluoride membranes (Millipore Sigma), which were then blocked at room temperature for 2 hours using Tris-buffered saline containing 0.2% Tween 20 (TBST) and 5% nonfat milk, followed by incubation with primary

antibodies specific to E-cadherin (1:1000, ab231303, Abcam), N-cadherin (1:1000, ab76011, Abcam), Vimentin (1:500, ab92547, Abcam), Snail (1:500, ab216347, Abcam), AKT (1:1000, ab8805, Abcam), p-AKT (1:500, ab38449, Abcam), p65 (1:500, ab16502, Abcam), p-p65 (1:500, ab76302, Abcam), and  $\beta$ -actin (1:3000, ab8226, Abcam) for 1.5 hours, then incubated with horseradish peroxidase (HRP)-labeled secondary antibodies (cat. nos. ab6721 and ab6728, 1:3000; Abcam) for an additional 1 hour. Protein bands were visualized using an enhanced chemiluminescence (ECL) detection reagent (Pierce; Thermo Fisher Scientific, Inc.) and analyzed using ImageJ 9.0 software.

## 2.7 Statistics

Data analysis was conducted using GraphPad 8.0 software (GraphPad Software, Inc., La Jolla, CA, USA). The unpaired Student's *t*-test was used to determine statistical significance between two groups, and the error bars in the graphs represent the mean  $\pm$  standard deviation (SD). A significance level of *p* < 0.05 was used to indicate statistical significance.

## 3. Results

### 3.1 Sufentanil blocks EC cell growth

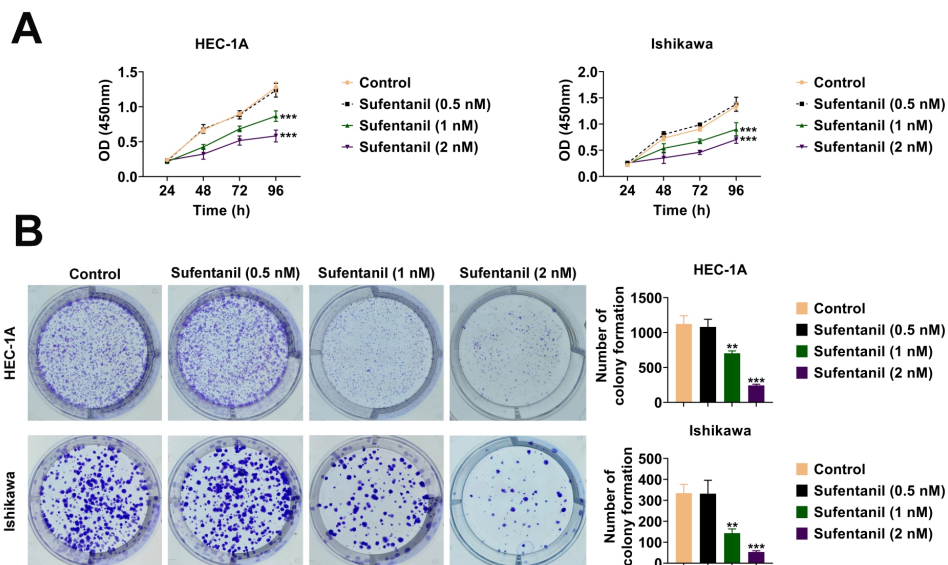
Sufentanil was used to treat EC cell lines, HEC1A and Ishikawa, at concentrations of 0.5, 1 and 2 nM, following which it was shown that it effectively suppressed the proliferation of HEC1A and Ishikawa cells in CCK-8 assays (Fig. 1A), as indicated by decreased OD450 values (Fig. 1A), and reduced the colony numbers of both cell lines in colony formation assays (Fig. 1B); thereby demonstrating promising efficacy in impeding EC cell growth.

### 3.2 Sufentanil inhibits EC cell migration and invasion

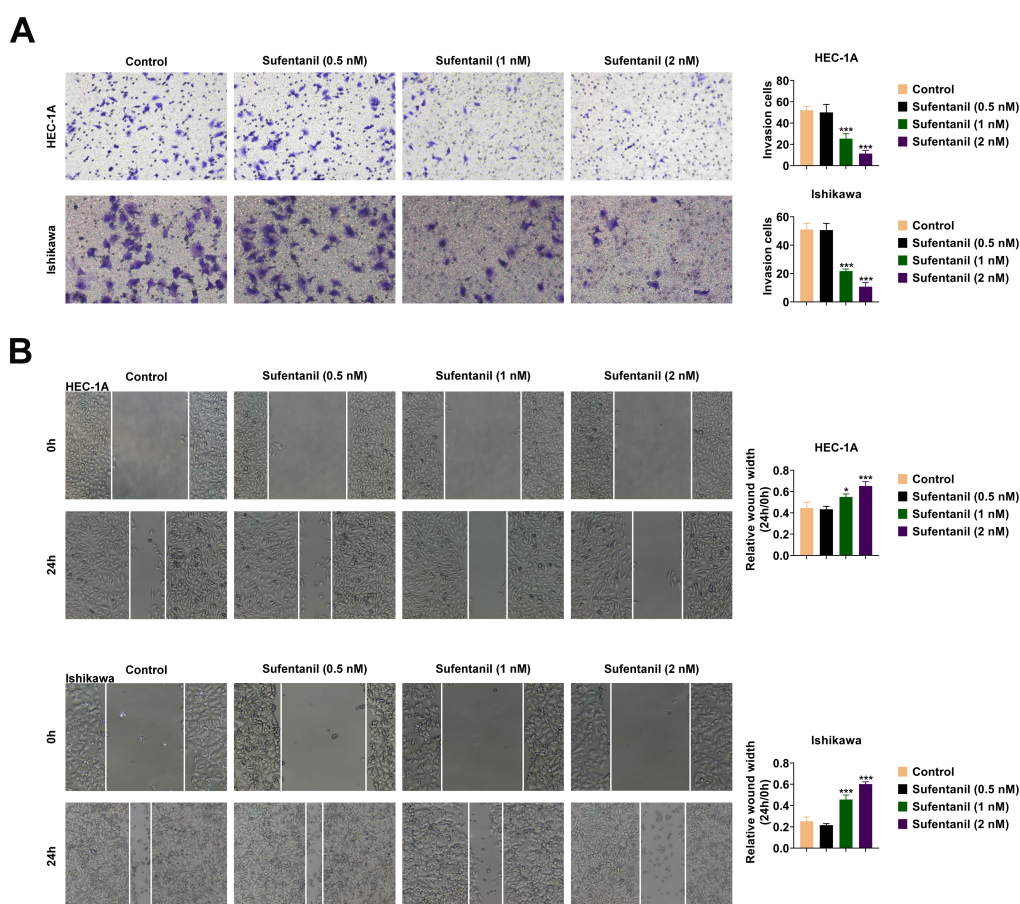
Next, we evaluated the impact of Sufentanil on the motility of EC cells. Transwell assay results showed that sufentanil treatment inhibited the invasion of EC cells, evident from the reduced count of invasive cells in both HEC1A and Ishikawa cells (Fig. 2A). In parallel, wound healing assays demonstrated that Sufentanil treatment inhibited the migration of HEC1A and Ishikawa cells (Fig. 2B). Taken together, these findings highlight the inhibitory effects of Sufentanil on the migration and invasion of EC cells.

### 3.3 Sufentanil suppresses EMT in EC cells

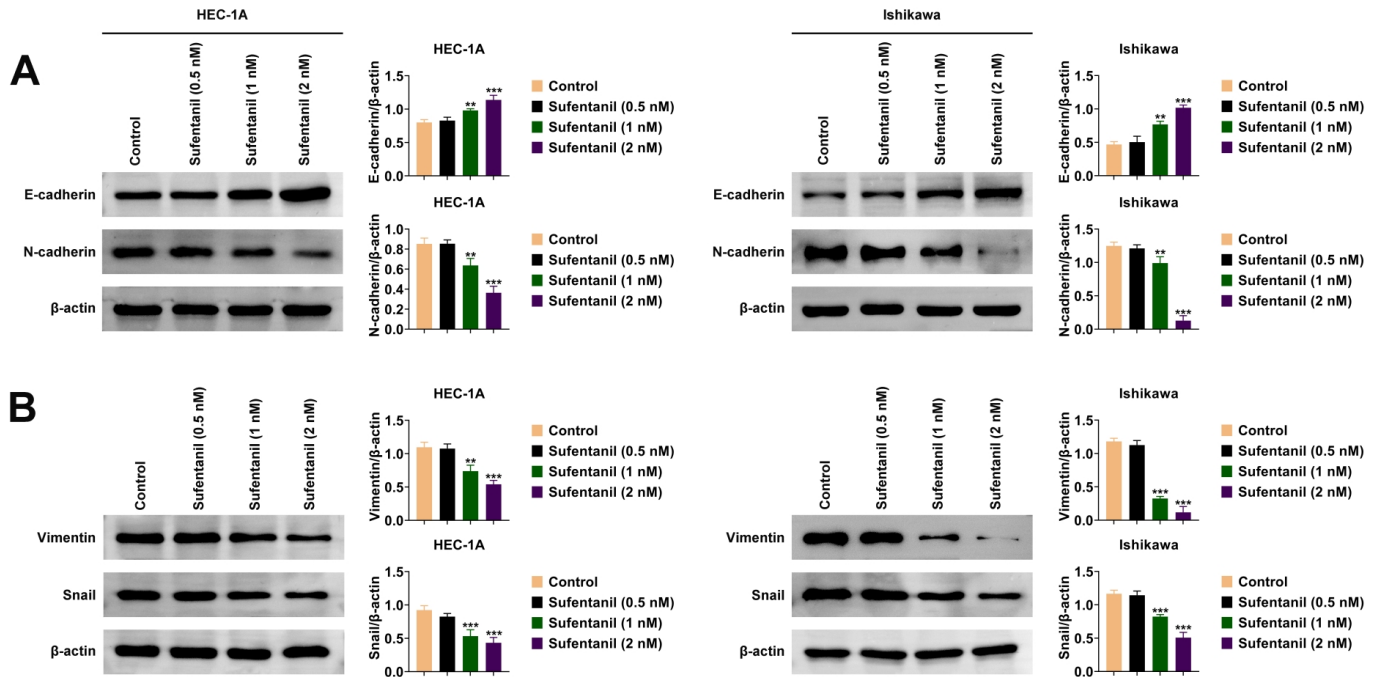
Immunoblot assays were subsequently conducted to examine the impact of Sufentanil on the epithelial-mesenchymal transition (EMT) of EC cells. Our findings revealed that Sufentanil treatment led to the suppression of N-cadherin expression and an increase in E-cadherin expression (Fig. 3A), as well as reduced levels of Vimentin and Snail expression in both HEC1A and Ishikawa cells (Fig. 3B). These results collectively provide evidence that Sufentanil exerts a suppressive influence on the EMT process in EC cells.



**FIGURE 1. Sufentanil blocks endometrial cancer cell growth.** (A) CCK-8 assays illustrating the proliferation capacity of HEC1A and Ishikawa cells following treatment with Sufentanil at concentrations of 0.5, 1 and 2 nM. The OD450 value was quantified through three independent experiments. (B) Colony formation assays revealing colony counts in HEC1A and Ishikawa cells treated with Sufentanil at concentrations of 0.5, 1 and 2 nM. These experiments were conducted three times. Data are presented as mean  $\pm$  SD,  $**p < 0.01$ ,  $***p < 0.001$ . OD: optical density.



**FIGURE 2. Sufentanil inhibits endometrial cancer cell migration and invasion.** (A) Transwell assays demonstrating the impact of Sufentanil on the invasive potential of HEC1A and Ishikawa cells at concentrations of 0.5, 1 and 2 nM. Invasive cell counts were determined based on three separate experiments. (B) Wound healing assays depicting the influence of Sufentanil on the migratory behavior of HEC1A and Ishikawa cells at concentrations of 0.5, 1 and 2 nM. Wound width rate was calculated from three independent experiments. Data are presented as mean  $\pm$  SD,  $*p < 0.05$ ,  $***p < 0.001$ .



**FIGURE 3. Sufentanil suppresses EMT in endometrial cancer cells.** (A) Immunoblot assays revealing the expression of E-cadherin and N-cadherin in HEC1A and Ishikawa cells treated with Sufentanil at concentrations of 0.5, 1 and 2 nM. (B) Immunoblot assays depicting the expression of Vimentin and Snail in HEC1A and Ishikawa cells treated with Sufentanil at concentrations of 0.5, 1 and 2 nM. These experiments were conducted three times. Data are presented as mean  $\pm$  SD, \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

### 3.4 Sufentanil restrains the AKT/NF- $\kappa$ B pathway in EC cells

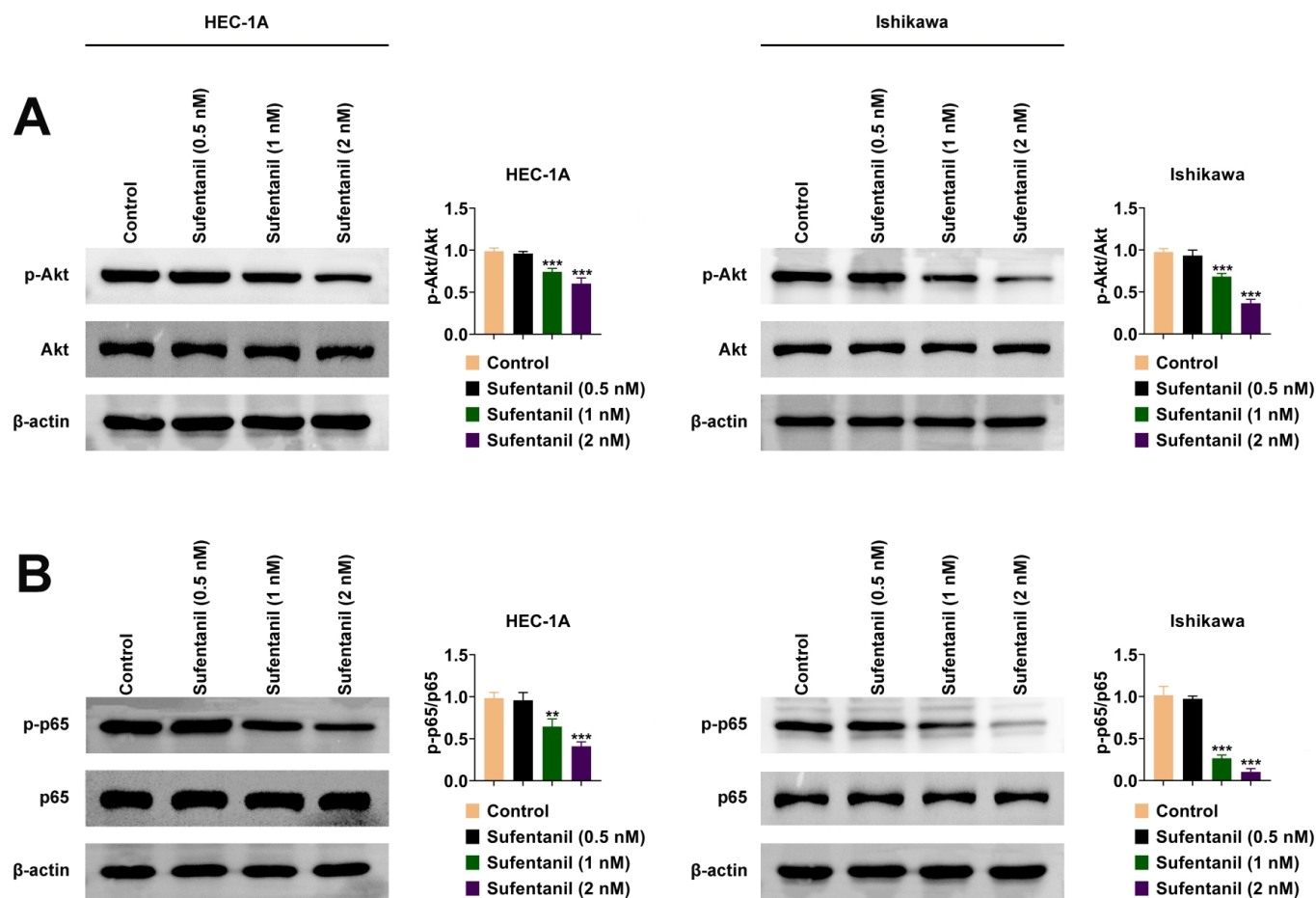
We subsequently investigated the mechanism underlying Sufentanil's inhibition of EC progression. Our immunoblot assays revealed that Sufentanil treatment reduced AKT phosphorylation in both HEC1A and Ishikawa cells (Fig. 4A) and also suppressed the phosphorylation of p65 (Fig. 4B), thereby providing additional evidence of Sufentanil's regulatory effect on the AKT/NF- $\kappa$ B pathway in EC cells. Thus, Sufentanil may also effectively reduce the activity of EC cells by modulating the AKT/NF- $\kappa$ B pathway.

## 4. Discussion

The primary treatment of choice for EC patients involves surgical intervention, followed by chemoradiotherapy and targeted therapeutics [16]. Targeted therapies act at specific sites, inducing specific tumor cell death while sparing the adjacent normal tissues [16]. Under normal conditions, targeted drugs such as anastrozole are commonly used in clinical settings [17]. The other targeted drugs used in EC include rapamycin, sirolimus, everolimus, *etc.* [18]. In this study, we found that Sufentanil could effectively inhibit EC progression, indicating promising potential for clinical settings as a potent drug against EC. Moving forward, combining Sufentanil with chemotherapy, anastrozole, flutesterone or other medications could hold promise in improving EC treatment but necessitates thorough exploration at both the cellular and animal levels.

Through comprehensive experiments involving CCK-8, colony formation, transwell and Immunoblot assays, we

have established that Sufentanil effectively suppressed the functional activities of EC cells. Sufentanil, due to its primary interaction at  $\mu$ -opiate receptors, is recognized as a very efficient analgesic agent [10]. Its lipophilicity, approximately twice that of fentanyl, enables easier blood-brain barrier penetration, and it exhibits a higher binding affinity to plasma proteins than fentanyl [14]. In contrast to the classical cancer pain medication morphine, Sufentanil offers advantages such as rapid onset, effective attenuation of pain-induced stress response, and favorable hemodynamic stability, making it increasingly prominent in cancer pain management [15]. Numerous studies have confirmed the anti-cancer potential of Sufentanil [12, 13]. Sufentanil inhibited proliferation and also induced apoptosis of gastric cancer cells [19]. For instance, it has been shown to inhibit the proliferation of lung cancer cells [13], the proliferation and metastasis of esophageal cancer [14], the metastasis of breast cancer [20], and the proliferation and metastasis of breast cancer cells by modulating EMT [11] at concentrations ranging between 1 nM–20 nM [11–15]. Likewise, our findings reveal that even at low concentrations (0.5, 1 and 2 nM), Sufentanil can induce EMT in EC cells, underscoring its potent antitumor activity against EC. Moreover, it suppressed proliferation and EMT in lung cancer cells through the Wnt/beta-catenin axis. These collective evidences suggest Sufentanil's potential as a broad-spectrum antitumor agent applicable across diverse tumor types. Nonetheless, given the unique phenotypes and signaling pathways across different tumors, further exploration of the specific pathways and molecular mechanisms against EC is warranted. In addition, considering that Sufentanil acts as a



**FIGURE 4. Sufentanil restrains the AKT/NF- $\kappa$ B pathway.** (A) Immunoblot assays illustrating the expression and phosphorylation of AKT in HEC1A and Ishikawa cells treated with Sufentanil at concentrations of 0.5, 1 and 2 nM. (B) Immunoblot assays revealing the expression and phosphorylation of p65 in HEC1A and Ishikawa cells treated with Sufentanil at concentrations of 0.5, 1 and 2 nM. These experiments were conducted three times. Data are presented as mean  $\pm$  SD, \*\* $p < 0.01$ , \*\*\* $p < 0.001$ .

robust ligand for  $\mu$ -opiate receptors and exerts its influence on EC progression *via* these receptors, it could be considered that Sufentanil's suppression of EC progression might also occur through its interaction with  $\mu$ -opiate receptors.

The PI3K/AKT axis participates in various biological processes, encompassing cell growth, survival, metabolism, invasion and migration [21, 22]. Studies have demonstrated the PI3K axis's role in modulating Akt's downstream substrates, including NF- $\kappa$ B, a key player in several molecular signaling pathways linked to EMT [21]. Alterations in the NF- $\kappa$ B axis have been shown to be closely associated with tumor cell occurrence, proliferation, differentiation, apoptosis, invasion and metastasis [20]. In addition, NF- $\kappa$ B functions as a potent driver of tumorigenesis and has emerged as a novel target in cancer therapy [20], and activation of post-translocation events to the nucleus, triggered by various stimuli, can promote oncogene transcription [20, 23]. The downregulation of the Akt/NF- $\kappa$ B pathway has been shown to inhibit EC cell migration, invasion and proliferation [24]. Although we did not directly confirm the effects of Sufentanil on EC cell apoptosis, its modulation of the PI3K/AKT pathway is likely to influence apoptotic processes. Thus, we speculate that Sufentanil can affect EC cell apoptosis, and further investigations would be

required to confirm this, potentially through flow cytometry (FCM) and TdT-mediated dUTP nick end labeling (TUNEL) assays. Interestingly, we observed that Sufentanil inhibited EC cell progression by impeding the Akt/NF- $\kappa$ B pathway, which has been reported to influence EC cell migration, invasion and proliferation [24]. However, the precise underlying mechanisms warrant further investigation.

An important limitation of this study is the absence of animal experiments. Our subsequent steps would involve confirming whether Sufentanil can indeed suppress EC progression in mice, further elucidating the underlying mechanism, and using an AKT/NF- $\kappa$ B axis inhibitor to confirm its underlying mechanism.

## 5. Conclusions

In summary, our findings demonstrate that Sufentanil effectively inhibits the proliferation, migration, invasion and EMT of EC cells through the targeted suppression of the AKT/NF- $\kappa$ B axis, thereby supporting Sufentanil as a promising therapeutic agent for EC treatment.

## AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

## AUTHOR CONTRIBUTIONS

CC and MMD—designed the study and carried them out; prepare the manuscript for publication and reviewed the draft of the manuscript. CC, MMD, SSZ, YJW, LS and HMW—supervised the data collection, analyzed the data, interpreted the data. All authors have read and approved the manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article does not contain any studies with human participants or animals performed by any of the authors.

## ACKNOWLEDGMENT

Not applicable.

## FUNDING

This research received no external funding.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

- [1] Zhai L, Yang X, Cheng Y, Wang J. Glutamine and amino acid metabolism as a prognostic signature and therapeutic target in endometrial cancer. *Cancer Medicine*. 2023; 12: 16337–16358.
- [2] Oaknin A, Gilbert L, Tinker AV, Brown J, Mathews C, Press J, *et al.* A plain language summary of results from the GARNET study of dostarlimab in patients with endometrial cancer. *Future Oncology*. 2023; 19: 1709–1714.
- [3] Li Q, Wang T, Bin Y, Zhao L. Positive rate of malignant cells in endometrial cytology samples of ovarian cancer, fallopian tube cancer, and primary peritoneal cancer patients: a systematic review and meta-analysis. *Journal of Cytology*. 2023; 40: 51–57.
- [4] Huang P, Qian Y, Xia Y, Wang S, Xu C, Zhu X, *et al.* Integrated analysis identifies RAC3 as an immune-related prognostic biomarker associated with chemotherapy sensitivity in endometrial cancer. *Journal of Cellular and Molecular Medicine*. 2023; 27: 2385–2397.
- [5] Chang CS, Lai YL, Choi CH, Kim TJ, Lee JW, Kim BG, *et al.* Comparison of minimally invasive and open surgery for the treatment of endometrial cancer with a high risk of recurrence: a propensity score matching study in Korea and Taiwan. *Annals of Surgical Oncology*. 2023; 30: 6855–6864.
- [6] Brus L, Grimm-Glang D, Krawczyk N, Fehm T, Rody A, Paluchowski P, *et al.* Circulating tumor cells in metastatic breast cancer: ready for clinical practice? *European Journal of Gynaecological Oncology*. 2022; 43: 4–8.
- [7] Liu L, Huan L, Zhang Y, Wei W, Chen Z, Xu D, *et al.* Ubiquitin-specific protease 8 inhibits lipopolysaccharide-triggered pyroptosis of human bronchial epithelial cells by regulating PI3K/AKT and NF- $\kappa$ B pathways. *Allergologia et Immunopathologia*. 2022; 50: 96–103.
- [8] Liu C, Wang Q, Niu L. Sufentanil inhibits Pin1 to attenuate renal tubular epithelial cell ischemia-reperfusion injury by activating the PI3K/AKT/FOXO1 pathway. *International Urology and Nephrology*. 2023; 55: 1903–1916.
- [9] Tan H, Wang C, Jiang Y, Shi Q, Liang W, Li D. Postoperative effect of Sufentanil preemptive analgesia combined with psychological intervention on breast cancer patients. *BMC Anesthesiology*. 2023; 23: 170.
- [10] Tire Y, Sarkilar G, Esen H, Onoglu R, Uzun ST. The effect of intrathecal Sufentanil preconditioning against myocardial ischemia-reperfusion injury. *Bratislava Medical Journal*. 2018; 119: 240–244.
- [11] Xu S, Li X, Li W, Ma N, Ma H, Cui J, *et al.* Sufentanil combined with parecoxib sodium inhibits proliferation and metastasis of HER2-positive breast cancer cells and regulates epithelial-mesenchymal transition. *Clinical & Experimental Metastasis*. 2023; 40: 149–160.
- [12] Li J, Li S, Yu L, Wei J, Li S, Tan H. The effects of Resistin gene polymorphism on pain thresholds and postoperative Sufentanil consumption in gastric cancer patients. *Journal of Pain Research*. 2022; 15: 1995–2004.
- [13] Lin Y, Miao Z, Wu Y, Ge F, Wen Q. Effect of low dose naloxone on the immune system function of a patient undergoing video-assisted thoracoscopic resection of lung cancer with Sufentanil controlled analgesia—a randomized controlled trial. *BMC Anesthesiology*. 2019; 19: 236.
- [14] Tang H, Li C, Wang Y, Deng L. Sufentanil inhibits the proliferation and metastasis of esophageal cancer by inhibiting the NF- $\kappa$ B and snail signaling pathways. *Journal of Oncology*. 2021; 2021: 7586100.
- [15] Dias S, Trovisco S, Neves I, Miranda L, Valente R. Efficacy and safety of Sufentanil infusion for postoperative analgesia in cancer surgery: a retrospective cohort study. *Cureus*. 2023; 15: e38993.
- [16] Mutch DG. Targeted therapy in endometrial cancer: making progress. *Cancer*. 2016; 122: 3428–3429.
- [17] Eritja N, Chen B, Rodríguez-Barrueco R, Santacana M, Gatiús S, Vidal A, *et al.* Autophagy orchestrates adaptive responses to targeted therapy in endometrial cancer. *Autophagy*. 2017; 13: 608–624.
- [18] Zagouri F, Bozas G, Kafantari E, Tsiatas M, Nikitas N, Dimopoulos M, *et al.* Endometrial cancer: what is new in adjuvant and molecularly targeted therapy? *Obstetrics and Gynecology International*. 2010; 2010: 1–11.
- [19] Wu W, Wei N, Jiang CN, Cui S, Yuan J. Effects of Sufentanil on human gastric cancer cell line SGC-7901 *in vitro*. *Central-European Journal of Immunology*. 2014; 39: 299–305.
- [20] Li M, Gu K, Kong Q, Wang G, Gu J. Sufentanil inhibits the metastasis and immune response *via* mediating the NF- $\kappa$ B pathway. To be published in *Immunopharmacology and Immunotoxicology*. 2023. [Preprint].
- [21] Li H, Chen M, Yang Z, Xu C, Yu Q, Song J, *et al.* Amorphophalli Rhizoma inhibits breast cancer growth, proliferation, migration, and invasion *via* the PI3K/AKT pathway. *Journal of Ethnopharmacology*. 2022; 286: 114926.
- [22] Xu Y, Fang R, Shao J, Cai Z. Erianin induces triple-negative breast cancer cells apoptosis by activating PI3K/Akt pathway. *Bioscience Reports*. 2021; 41: BSR20210093.
- [23] Feng Q, Yang Y, Qiao Y, Zheng Y, Yu X, Liu F, *et al.* Quercetin ameliorates diabetic kidney injury by inhibiting ferroptosis *via* activating Nrf2/HO-1 signaling pathway. *The American Journal of Chinese Medicine*. 2023; 51: 997–1018.
- [24] Lin L, Gao Y, Hu X, Ouyang J, Liu C. Pentamidine inhibits proliferation, migration and invasion in endometrial cancer *via* the PI3K/AKT signaling pathway. *BMC Women's Health*. 2022; 22: 470.

**How to cite this article:** Chen Cheng, Mimi Dai, Shishi Zheng, Yujie Wu, Li Shu, Huimin Wu. Effects of Sufentanil on proliferation, migration and epithelial-mesenchymal transition of endometrial cancer. *European Journal of Gynaecological Oncology*. 2023; 44(6): 122-127. doi: 10.22514/ejgo.2023.106.