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Scutellaria baicalensis extracts alleviate zymosan-induced irritable bowel syndrome symptoms by modulating inflammation and ion channel activity

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ABSTRACT

Scutellaria baicalensis extracts (SBE) have demonstrated potential therapeutic effects against gastrointestinal disorders. This study evaluated the effects of SBE on zymosan-induced irritable bowel syndrome (IBS) symptoms and the underlying mechanisms involved. The major components of SBE, baicalin and baicalein, were quantified using high-performance liquid chromatography. SBE inhibited pacemaker potentials in interstitial cells of Cajal in vitro, with an IC_{50} value of 27.48 μg/mL. In an animal model of IBS, SBE administration restored colonic length, weight, and stool consistency. Furthermore, SBE reduced tumor necrosis factor-α expression and alleviated pain-associated behaviors. Histological analysis revealed that SBE treatment restored normal colon tissue structure and significantly reduced inflammation. Electrophysiological recordings demonstrated that SBE inhibited the activity of transient receptor potential (TRP) channels, including TRPV1, TRPV4 and TRPA1, as well as voltage-gated sodium channels (NaV1.5), which are associated with visceral pain hypersensitivity. These findings suggest that SBE has therapeutic potential, making it a promising candidate for the management of IBS.

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Introduction

Irritable bowel syndrome (IBS) is a prevalent digestive condition that manifests as symptoms, such as abdominal discomfort, bloating, and irregular bowel habits, all of which significantly affect quality of life (Akbari et al. 2025; Jeong et al. 2025; Pellegrino and Gravina 2025). Although the exact pathophysiology of IBS remains unclear, it is thought to be influenced by multiple factors, such as abnormal gut motility, heightened visceral sensitivity, and inflammation (El-Salhy et al. 2025; Fan et al. 2025; Sánchez-Pellicer et al. 2025). Current treatments primarily aim to alleviate symptoms but often have limited efficacy and may cause adverse effects (Almabruk et al. 2024; Brenner et al. 2024; Wang et al. 2024). Therefore, there is growing interest in identifying alternative therapies that can offer more effective and safer solutions.

Scutellaria baicalensis, a traditional medicinal herb, has shown potential therapeutic effects in the treatment of gastrointestinal (GI) disorders (Ganguly et al. 2022; Wang et al. 2022; Zhao et al. 2024). Its bioactive compounds, such as baicalin and baicalein, possess anti-inflammatory, antioxidant, and analgesic properties, making them promising candidates for IBS management (Shieh et al. 2000; Lee et al. 2015; Dinda et al. 2017). *Scutellaria baicalensis* extract (SBE) modulates various biological pathways, including the regulation of inflammation and pain sensitivity (Gao et al. 2023; Jo et al. 2024).

This study aimed to investigate the effect of SBE in a zymosan-induced IBS mouse model by focusing on its impact on colon function, inflammatory markers, and pain-associated behaviors. Additionally, we explored the underlying mechanisms of action, particularly the involvement of interstitial cells of Cajal (ICCs), transient receptor potential (TRP) channels, and voltage-gated sodium channels (NaV). The findings of this study offer valuable insights into the potential use of SBE as a treatment strategy for IBS.

Materials and methods

Materials

SBEs were purchased from the Korea Plant Extract Bank (Cheongju, Korea). Baicalin and baicalein were

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purchased from Sigma-Aldrich (St. Louis, MO, USA). High-performance liquid chromatography (HPLC)-grade acetonitrile and water were purchased from J.T. Baker (Phillipsburg, NJ, USA). Formic acid was purchased from DAEJUNG Chemicals and Metals (Seoul, Korea).

HPLC analysis

The major components of SBE were determined as previously reported (Islam et al. 2012). SBE and all standard compounds were fully dissolved in 100% MeOH. Chromatographic analysis was performed using a JASCO HPLC system. The UV detection wavelength was set at 280 nm. A 10 µL aliquot of the standard or SBE sample solution was directly injected onto a Symmetry300™ C18 column (4.6 × 250 mm × 5 µm). The flow rate was set at 1 mL/min at 35°C. The mobile phase comprised acetonitrile and 0.1% formic acid in deionized water (30:70, v/v). The total running time for the analysis was 30 min.

Preparation of ICC cultures

The large intestine was extracted from both male and female ICR mice aged 3–6 d. The mucosal layer was carefully removed via precise dissection. To isolate the smooth muscle layers, tissues were treated with an enzyme solution containing collagenase (Worthington Biochemical Corporation, Lakewood, NJ, USA). The dissociated cells were then cultured in a smooth muscle growth medium (Clonetics Corp., San Diego, CA, USA) supplemented with 5 ng/mL murine stem cell factor (Sigma-Aldrich) at 37°C. All ICC experiments were performed after 12 h of culture.

Induction of colitis

Colitis was induced by administering 0.1 mL of a 30 mg/mL zymosan solution (Sigma-Aldrich, St. Louis, MO, USA) directly into the colon for three consecutive days. The mice were then divided into six groups: (a) naïve (n = 25), (b) control (n = 22), (c) SBE 250 mg/kg (n = 26), (d) SBE 500 mg/kg (n = 23), (e) amitriptyline (AMT) (n = 24), and (f) sulfasalazine (SSZ) (n = 24). AMT (Iqbal et al. 2025) and SSZ (Pruzanski et al. 1997), both frequently used in the clinical management of IBS, were used as positive controls.

Assessment of body weight changes and food intake

Body weight was measured on days 1, 4, 8, and 12 to track fluctuations over time. In addition, total food consumption during this period was recorded to evaluate dietary intake.

Evaluation of colon and stool conditions

To assess the effects of zymosan on the colon, colonic weight and length were measured, with length defined as the distance from the cecal end to the anus. Stool characteristics were evaluated by three independent researchers who were blinded to the study conditions, using a scoring system adapted from the Bristol Stool Scale. Stool consistency was classified into four categories: zero (normal), one (moist), two (sticky), and three (diarrheal).

Histological analysis of the colon

Colon tissue sections were fixed, embedded in paraffin, and stained with hematoxylin and eosin for histological evaluation. The stained samples were examined under a visible light microscope (Nikon, Tokyo, Japan).

Quantification of tumor necrosis factor (TNF)-α expression level by RT-qPCR

To evaluate TNF-α gene expression, total mRNA was extracted from colonic tissue using TRIzol reagent (Invitrogen, Waltham, MA, USA). The isolated RNA was used to synthesize cDNA using a cDNA reverse transcription kit (M-MLV Reverse Transcriptase; Promega, Madison, WI, USA).

Assessment of pain-associated behaviors

Pain-associated behaviors were evaluated following the methods described in a previous study (Laird et al. 2001). The assessment included specific movements, such as abdominal licking, full-body stretching, pressing the abdomen against the floor, and arching because of abdominal contractions. To ensure reliable observations, two independent researchers monitored behavior for 10 min.

Animal models and ethical approval

For ICC experiments, 28 ICR mice (15 males and 13 females, aged 3–6 d) were sourced from Samtako Bio Korea Co., Ltd. (Osan, Republic of Korea). In this zymosan-induced IBS model study, 81 male mice (aged 5–6 weeks, weighing 20–25 g) were used. All procedures involving animal care and experimentation were approved by the Institutional Animal Care and Use Committee of Pusan National University (approval no. PNU-2023-0266; Busan, Republic of Korea).

Plasmid transfection

HEK293T cells were cultured in six-well plates, and plasmid transfection was performed the following day. Plasmids (1.5–2 μg/well) containing human TRPV1, TRPV4, TRPA1, or NaV1.5/1.7 genes were introduced into the cells, along with pEGFP-N1, using a transfection reagent (Thermo Fisher Scientific, Waltham, MA, USA).

Electrophysiological experiments

Whole-cell patch-clamp recordings were performed. Current-clamp mode was used to assess the pacemaker potential of ICCs. TRP currents were recorded with a holding voltage of −60 mV, applying ramp pulses from −100 to 100 mV. For NaV channel measurements, currents were recorded from −120 to 0 mV, with a holding voltage of −120 mV. The specific compositions of the internal and external solutions can be found in previous studies (Kim et al. 2013; Choi et al. 2023).

Statistical analysis

The data are presented as mean ± SE. Variance was evaluated by one-way analysis of variance, followed by Dunnett's multiple comparison test. Statistical analyses were performed using GraphPad Prism 8 software, with significance set at $p < 0.05$.

Results

Quantification of major components in *SBE by HPLC-UV*

A previous study identified baicalin and baicalein as major components of SBE (Islam et al. 2012). Chromatographic analysis was performed to confirm these major components. Chromatograms of the extract and standard mixture showed that all standards were completely separated within 30 min. HPLC results showed that the concentrations of baicalin and baicalein were found to be 28.35 ± 0.58 and 78.1 ± 1.04 mg/g in SBE, respectively (Figure 1).

Effects of SBE on the pacemaker potentials of ICCs from murine large intestines

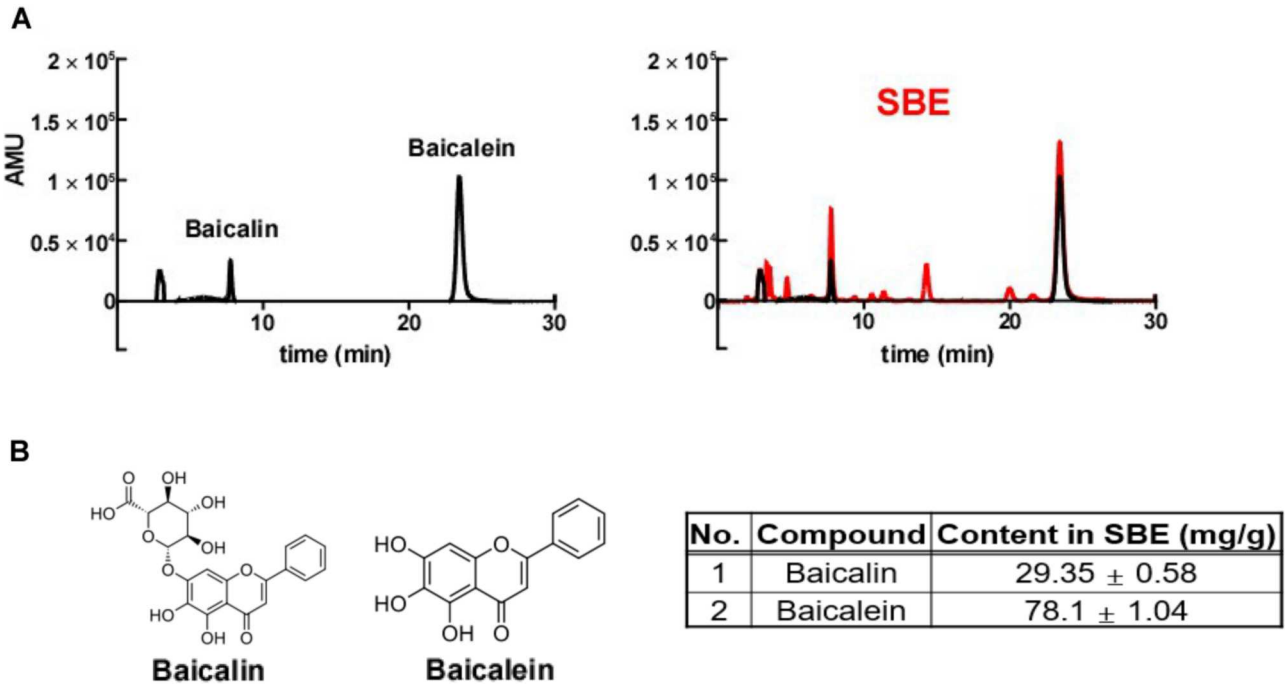
We used a whole-cell patch-clamp technique to evaluate the characteristics of ICCs in the large intestine. Under current-clamp mode (I = 0), ICCs generated pacemaker potentials, and SBE (10–100 μg/mL) inhibited these pacemaker potentials (Figure 2(A)). Summarizing the results, the IC_{50} of the frequency effect of SBE on ICCs was 27.48 μg/mL (Figure 2(B)). These findings suggest that SBE regulates ICCs by inhibiting pacemaker potentials.

Effects of SBE on zymosan-induced colonic changes

We conducted experiments using an animal model of zymosan-induced IBS to examine colonic length, weight, and stool condition following SBE administration. SSZ and AMT, both used in the clinical treatment of IBS, served as positive controls. The colon length of zymosan-induced mice was shorter than that of naïve mice; however, upon SBE administration, colon length was restored [7.43 ± 0.43 cm in naïve mice, 6.51 ± 0.34 cm in control mice (##$p < 0.01$), 7.74 ± 0.44 cm at 250 mg/kg SBE (***$p < 0.001$), 7.71 ± 0.20 cm at 500 mg/kg SBE (***$p < 0.001$), 7.31 ± 0.21 cm at AMT (*$p < 0.05$), and 7.40 ± 0.21 cm at SSZ (*$p < 0.05$); Figure 3(A)]. Similarly, zymosan-induced mice exhibited a significant increase in colonic weight; however, SBE administration restored it to baseline levels [0.94 ± 0.11 g in naïve mice, 1.14 ± 0.1 g in control mice (#$p < 0.05$), 0.94 ± 0.10 g at 250 mg/kg SBE (*$p < 0.05$), 1.02 ± 0.03 g at 500 mg/kg SBE (*$p < 0.05$), 0.92 ± 0.04 g at AMT (**$p < 0.01$), and 0.93 ± 0.10 g at SSZ (* $p < 0.05$); Figure 3(B)]. Stool condition was also improved following SBE administration [(2.25 ± 0.50 in naïve mice, 4.33 ± 0.66 in control mice (## $p < 0.01$), 3.50 ± 0.57 at 250 mg/kg SBE, 2.75 ± 0.50 at 500 mg/kg SBE (*$p < 0.05$), 2.75 ± 1.26 at AMT (*$p < 0.05$), and 2.33 ± 0.58 at SSZ (* $p < 0.05$); Figure 3(C)]. Additionally, SBE administration reversed zymosan-induced weight loss (Figure 3(D)), and food intake remained unchanged across experimental conditions (Figure 3(E)). These findings suggest that SBE treatment restores colonic alterations, prevents weight loss, and has no effect on food consumption in a zymosan-induced IBS mouse model.

Effects of SBE on colon tissue, TNF-α levels, and pain-associated behaviors

Hematoxylin and eosin staining revealed significant histological changes in the colons of zymosan-treated control mice, which displayed increased tissue thickness compared with that of naïve mice. However, tissue thickness was restored to levels comparable to those observed in the naïve group following SBE administration (Figure 4(A and B)). Colon tissues were collected during autopsy on day 4 after zymosan-induced colitis. The control group exhibited a marked elevation in TNF-α expression, indicating a significant rise in TNF-α levels associated with inflammation. However, TNF-α



No.	Compound	Content in SBE (mg/g)
1	Baicalin	29.35 ± 0.58
2	Baicalein	78.1 ± 1.04

Figure 1. Identification of the major components of SBE using HPLC-UV. (A) HPLC-UV chromatograms of baicalin and baicalein in standard solutions (left) and SBE (right). (B) Structural formulas and concentrations of baicalin and baicalein in SBE. SBE: *Scutellaria baicalensis* extract; HPLC, high-performance liquid chromatography.

levels were significantly reduced in the 250 and 500 mg/kg SBE groups, as well as in the positive control group (Figure 4(C)). Additionally, on day 4, the average frequency of pain-associated behaviors was elevated in zymosan-treated mice but was significantly reduced following SBE administration (Figure 4(D)). These findings suggest that SBE treatment effectively restored colonic tissue structure, reduced TNF-α levels, and alleviated pain-associated behaviors in a zymosan-induced IBS mouse model.

Effects of SBE on TRP channel currents

To investigate the potential regulatory effects of SBE on TRPV1 channels, whole-cell electrophysiological recordings were conducted using HEK293 T cells overexpressing TRPV1. The current–voltage relations were obtained by applying a ramp pulse from −100 to 100 mV. BCTC, a specific TRPV1 inhibitor, was used to confirm TRPV1 involvement (Heber et al. 2020). Capsaicin was used to activate the TRPV1 current (Abdel-Salam and Mózsik 2023), and under these conditions, SBE at concentrations of 100,

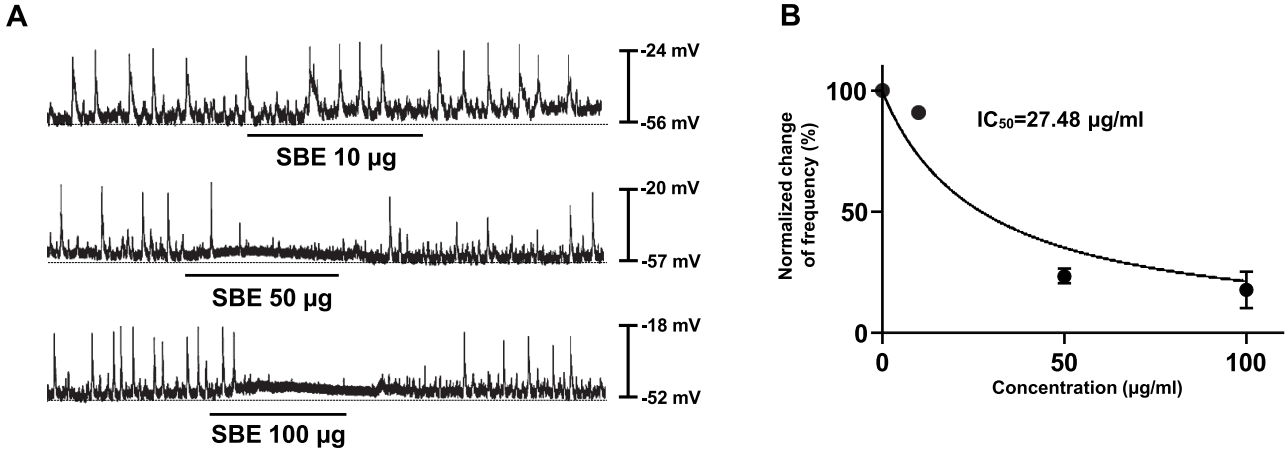


Figure 2. Effects of SBE on pacemaker potential in ICCs from the murine colon.(A) SBE suppressed ICC pacemaker potential in a dose-dependent manner. (B) Summary of normalized frequency changes in pacemaker potentials induced by SBE. Bars indicate mean ± SE. SBE: *Scutellaria baicalensis* extract; ICC, interstitial cells of Cajal.

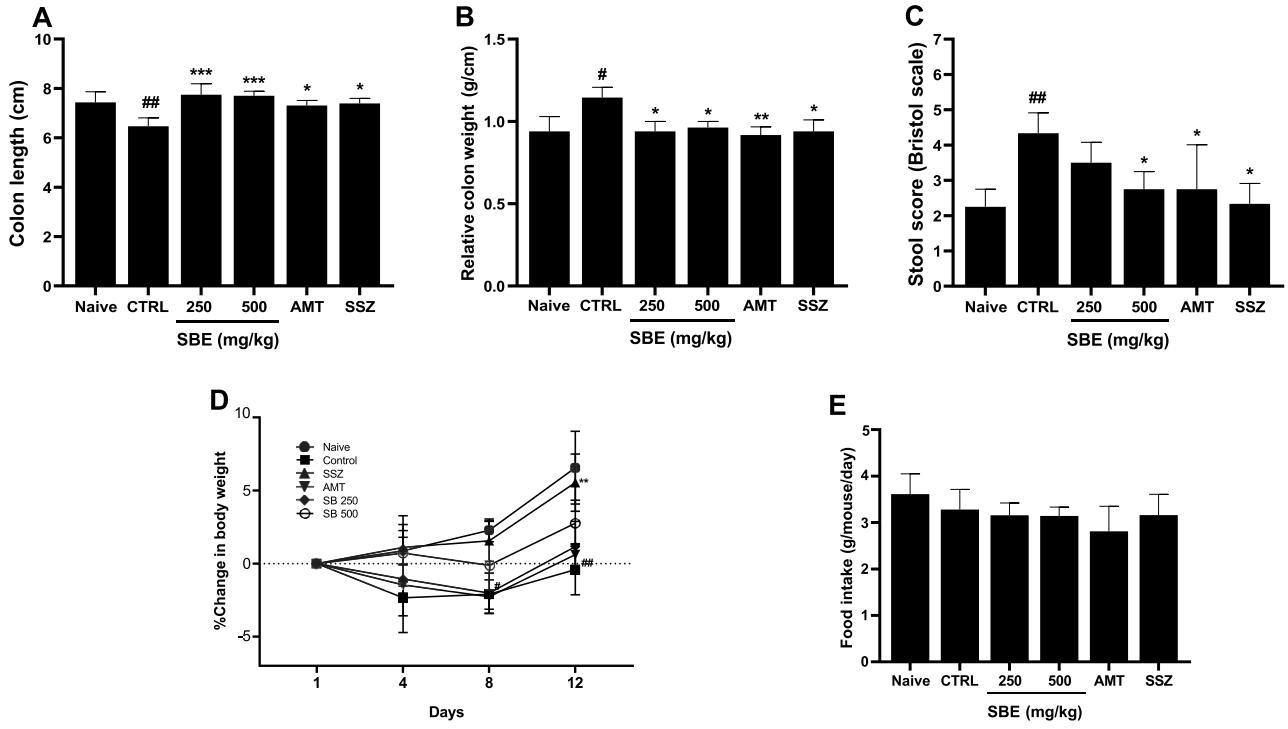


Figure 3. Effects of SBE on colonic parameters, stool score, body weight, and food intake.(A) Colon length, (B) colon weight, and (C) stool scores were evaluated in an animal model of zymosan-induced IBS. In addition, changes in body weight (D) and food intake (E) were measured. Bars indicate mean ± SE. #$p < 0.05$, and ##$p < 0.01$ vs naïve. *$p < 0.05$, **$p < 0.01$, and *** $p < 0.001$ vs control. SBE: *Scutellaria baicalensis* extract. CTRL: Control. IBS, irritable bowel syndrome.

200, and 500 µg/mL (****$p < 0.0001$) significantly decreased the TRPV1 current (Figure 5(A and B)). Normalized current amplitudes at +100 mV for each concentration are shown in the plot (Figure 5(C)). To examine the potential effects of SBE on TRPV4 channels, whole-cell electrophysiological recordings were performed on HEK293T cells overexpressing TRPV4. Ruthenium red, a selective TRPV4 inhibitor, was used to confirm TRPV4

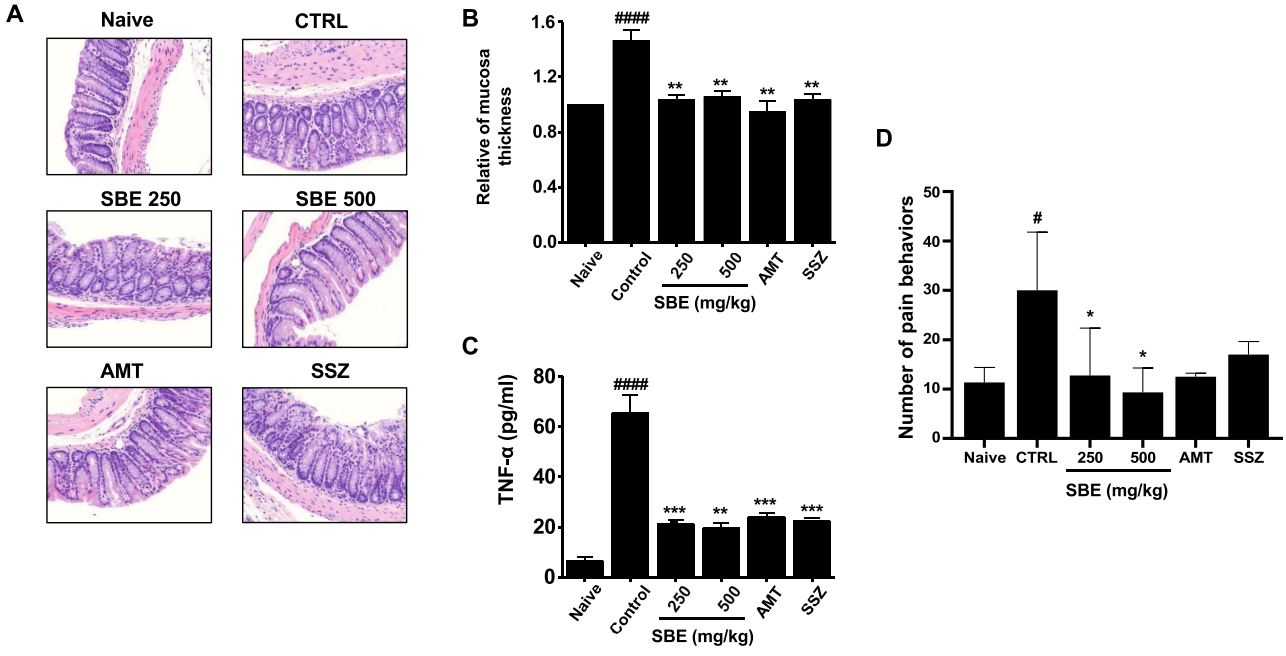


Figure 4. Effects of SBE on tissue alterations and TNF-α expression levels. Hematoxylin and eosin staining was used to assess (A) histological changes (50× magnification) and (B) quantitative measurements of colon mucosa thickness. (C) TNF-α expression levels were analyzed using RT-qPCR. (D) Pain-related behavior was evaluated. Bars indicate mean ± SE. # $p < 0.05$, #### $p < 0.0001$ vs naïve. *$p <$ 0.05, **$p < 0.01$, and ***$p < 0.001$ vs control. SBE: *Scutellaria baicalensis* extract. CTRL: Control. TNF-α: tumor necrosis factor-α.

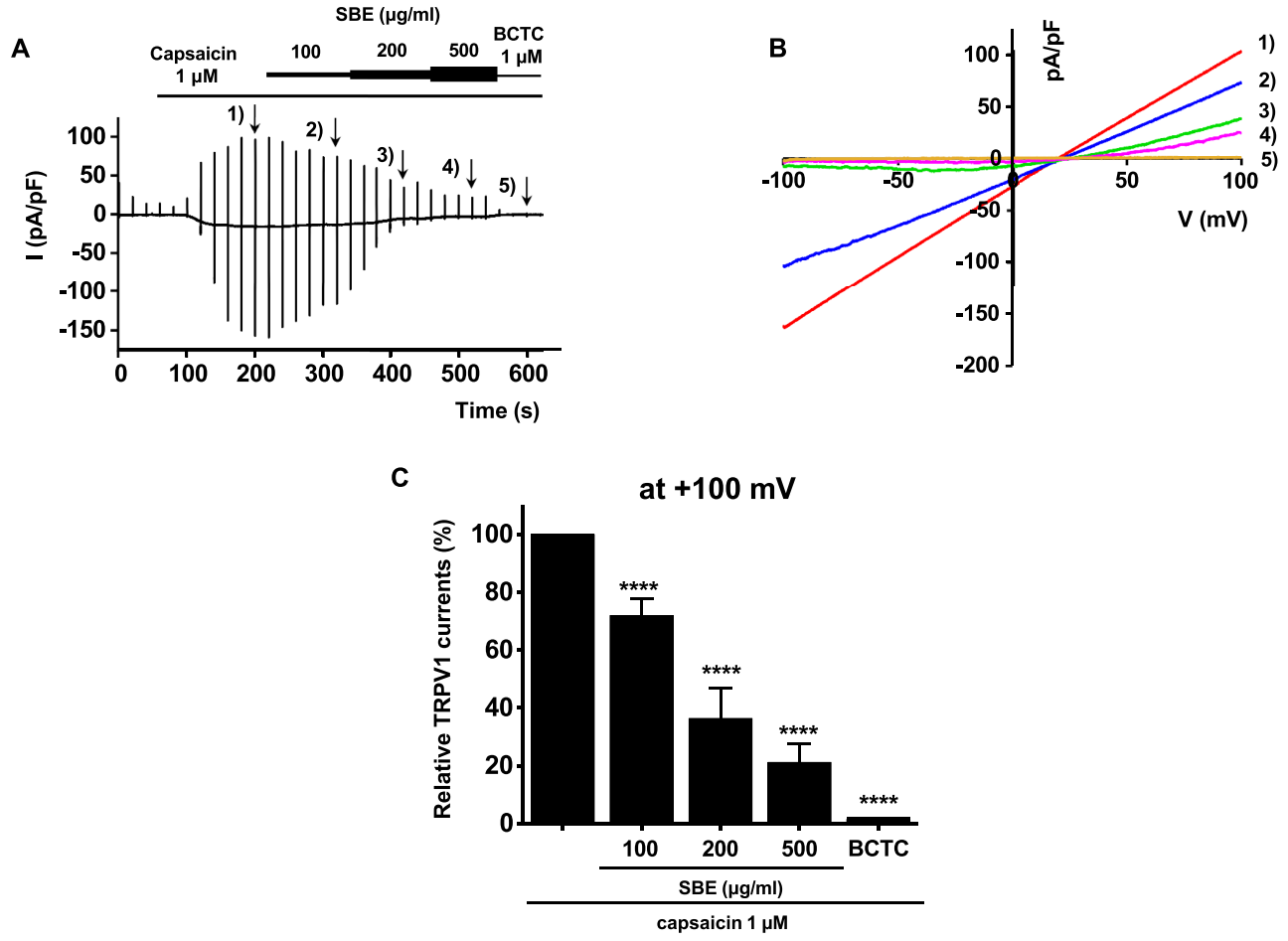


Figure 5. Effects of SBE on TRPV1 currents. (A) Representative TRPV1 current trace demonstrating the effects of 100, 200, and 500 μg/mL SBE. Capsaicin was used as a TRPV1 agonist, whereas BCTC served as a TRPV1 antagonist. (B) Representative current–voltage (I–V) curve illustrating the impact of 100, 200, and 500 μg/mL SBE. (C) Statistical analysis of changes in relative TRPV1 current. Bars indicate mean ± SE. ****$p < 0.0001$ vs naïve. SBE: *Scutellaria baicalensis* extract. TRP, transient receptor potential.

involvement (Cho et al. 2014). GSK101 was applied to activate the TRPV4 current (Baratchi et al. 2019), and under these conditions, SBE at concentrations of 100, 200, and 500 μg/mL (**$p < 0.01$) significantly reduced the TRPV4 current (Figure 6(A and B)). Normalized current amplitudes at +100 mV for each concentration are shown in the plot (Figure 6(C)).

To explore the regulatory effects of SBE on TRPA1 channels, whole-cell electrophysiological recordings were performed on HEK293 T cells overexpressing TRPA1. A967079, a specific TRPA1 inhibitor, was used to confirm TRPA1 involvement (Gyamfi et al. 2020). AITC activated the TRPA1 current (Ohashi et al. 2023), and under these conditions, SBE at concentrations of 200 μg/mL (**$p < 0.01$) and 500 μg/mL (****$p < 0.0001$) significantly suppressed the TRPA1 current (Figure 7(A and B)). Normalized current amplitudes at +100 mV for each concentration are shown in the plot (Figure 7(C)). These results suggest that TRPV1, TRPV4 and TRPA1 channels may play critical roles in SBE-induced attenuation of visceral pain hypersensitivity.

Effects of SBE on NaV1.5 and NaV1.7 currents

In NaV1.5 currents, SBE notably decreased the peak inward current by 84.6 ± 0.4% (0.1 mg/mL), 72.2 ± 16.5% (0.3 mg/mL; *$p < 0.05$), 58.7 ± 14.9% (1 mg/mL; **$p < 0.01$), and 25.7 ± 7.8% (5 mg/mL; **$p < 0.01$), with an IC_{50} value of 1.3 mg/mL (Figure 8). In addition, NaV1.7 current was inhibited by SBE only at high (5 mg/ml) concentrations by 97.3 ± 3.8% (0.1 mg/mL), 99.1 ± 11.7% (0.3 mg/mL), 96.1 ± 8.2% (1 mg/mL), and 65.2 ± 6.9% (5 mg/mL; **$p < 0.01$) (Figure 9). These findings suggest that NaV1.5 may play a primary role in the visceral pain-suppressive effects of SBE.

Discussion

This study aimed to evaluate the effects of SBE in a zymosan-induced IBS mouse model, focusing on its impact on colonic function, inflammation, and pain-associated behaviors. Our findings indicate that SBE exhibits significant therapeutic potential for alleviating

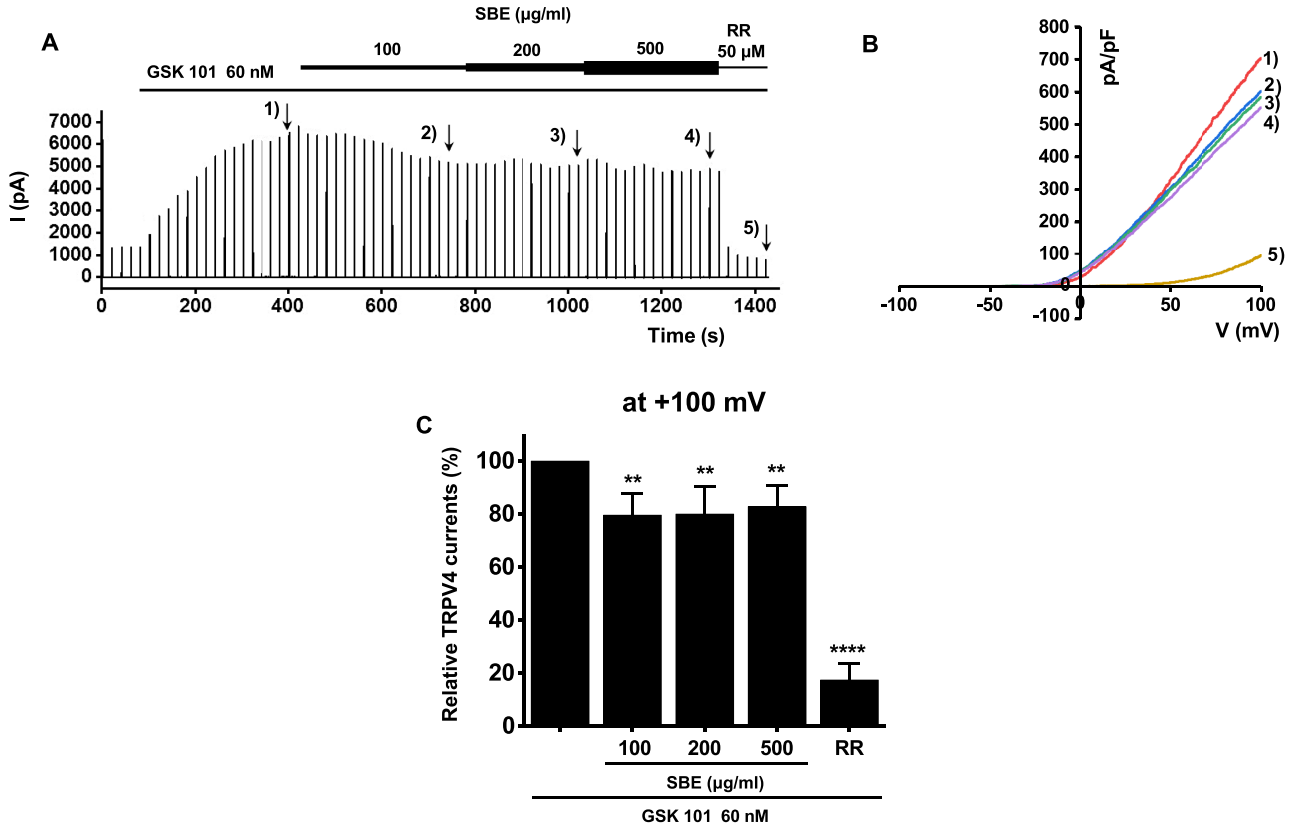


Figure 6. Effects of SBE on TRPV4 currents. (A) Representative TRPV4 current trace demonstrating the effects of 100, 200, and 500 μg/mL SBE. GSK101 was used as a TRPV4 agonist, and ruthenium red served as a TRPV4 antagonist. (B) Representative current–voltage (I–V) curve illustrating the impact of 100, 200, and 500 μg/mL SBE. (C) Statistical analysis of the relative changes in TRPV4 current. Bars indicate mean ± SE. $^{**}p < 0.01$; $^{****}p < 0.0001$ vs naïve. SBE: *Scutellaria baicalensis* extract. TRP, transient receptor potential.

IBS-related symptoms by modulating key physiological pathways involved in gut motility, inflammation, and pain perception.

One of the key findings of this study was the quantification of baicalin and baicalein as the major bioactive compounds in SBE, using HPLC-UV analysis (Figure 1). These compounds have been previously reported to possess anti-inflammatory and analgesic properties, suggesting their potential role in IBS management (Shieh et al. 2000; Lee et al. 2015; Dinda et al. 2017). The observed effects of SBE on ICC pacemaker potentials further support the hypothesis that SBE influences gut motility by modulating rhythmic intestinal contractions. Specifically, SBE inhibited ICC pacemaker potentials in a dose-dependent manner (Figure 2), indicating its potential to regulate gut motility, which is often disrupted in patients with IBS.

In this zymosan-induced IBS model, SBE administration effectively restored colonic length and weight, which were significantly altered by inflammation (Figure 3(A and B)). These findings suggest that SBE plays a crucial role in maintaining colonic structural integrity, comparable to clinically used treatments, such as AMT and SSZ. Additionally, the improvement in stool condition and prevention of weight loss further highlight SBE's potential as a therapeutic agent for IBS (Figure 3(C and D)). Histological analysis of colon tissues revealed that SBE treatment mitigated the thickening of colonic tissues observed in IBS mice (Figure 4(A and B)), suggesting a protective effect against inflammation-induced structural alterations. Moreover, SBE significantly reduced TNF-α levels (Figure 4(C)), a key proinflammatory cytokine associated with IBS pathophysiology. The reduction in TNF-α expression aligns with previous studies demonstrating the anti-inflammatory effects of *Scutellaria baicalensis* and its bioactive compounds, further supporting its potential role in IBS treatment (Liao et al. 2021; Gao et al. 2023; Jang et al. 2023; Zhu et al. 2023; Jo et al. 2024).

Several studies have highlighted the anti-inflammatory properties of *Scutellaria baicalensis* against GI disorders. For example, one study demonstrated that *Scutellaria baicalensis* root extract inhibited NO production, iNOS, and COX-2 expression in LPS-induced macrophages, reducing inflammation via modulation

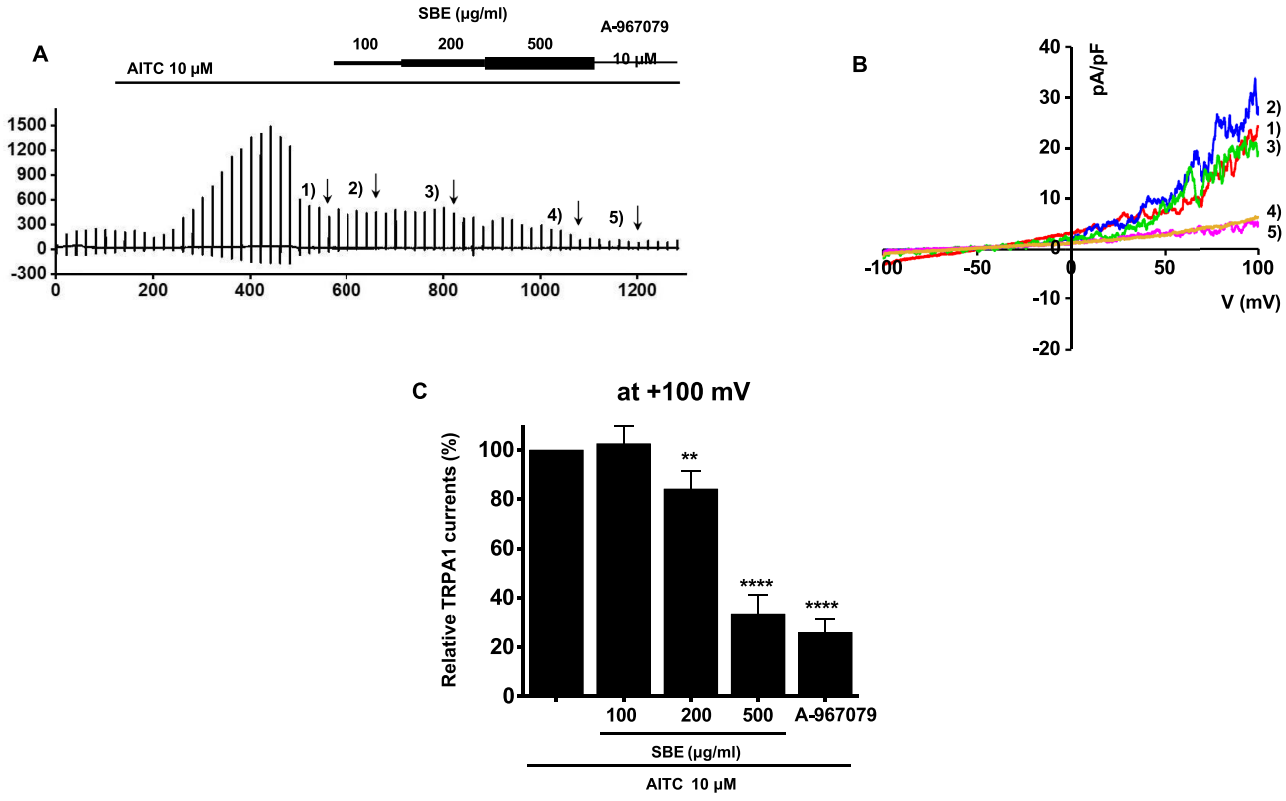


Figure 7. Effects of SBE on TRPA1 currents.(A) Representative TRPA1 current trace demonstrating the effects of 100, 200, and 500 μg/mL SBE. AITC was used as a TRPA1 agonist, whereas A-967079 served as a TRPA1 antagonist. (B) Representative current–voltage (I–V) curve illustrating the impact of 100, 200, and 500 μg/mL SBE. (C) Statistical analysis of the relative TRPA1 current changes. Bars indicate mean ± SE. $^{**}p < 0.01$; $^{****}p < 0.0001$ vs naïve. SBE: *Scutellaria baicalensis* extract. TRP, transient receptor potential.

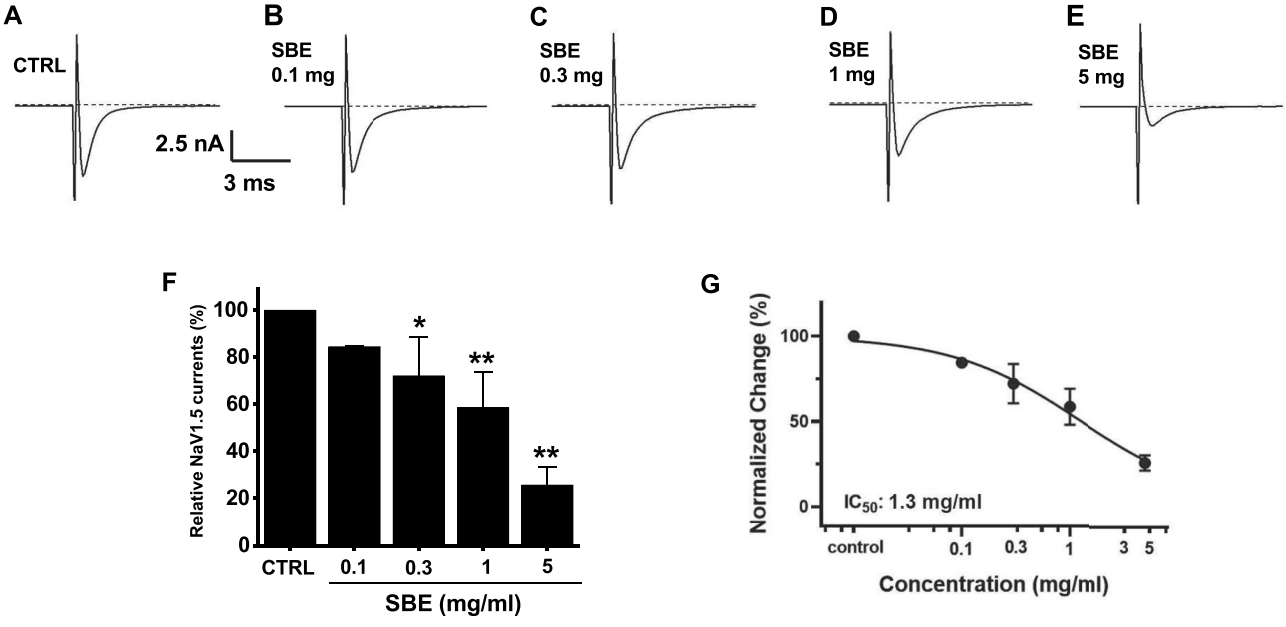


Figure 8. Effect of SBE on NaV1.5 currents. (A) Representative plot of NaV1.5 currents in HEK293 T cells. (B–E) Representative plots showing the effects of SBE at 0.1, 0.3, 1, and 5 mg/mL. (F) Summary of the relative current changes in NaV1.5 induced by SBE. (G) Normalized changes in NaV1.5 currents following SBE treatment. $IC_{50} = 1.3$ mg/mL. Bars indicate mean ± SE. $^{*}p < 0.05$; $^{**}p < 0.01$ vs control. SBE: *Scutellaria baicalensis* extract. CTRL: Control. Nav, voltage-gated sodium channel.

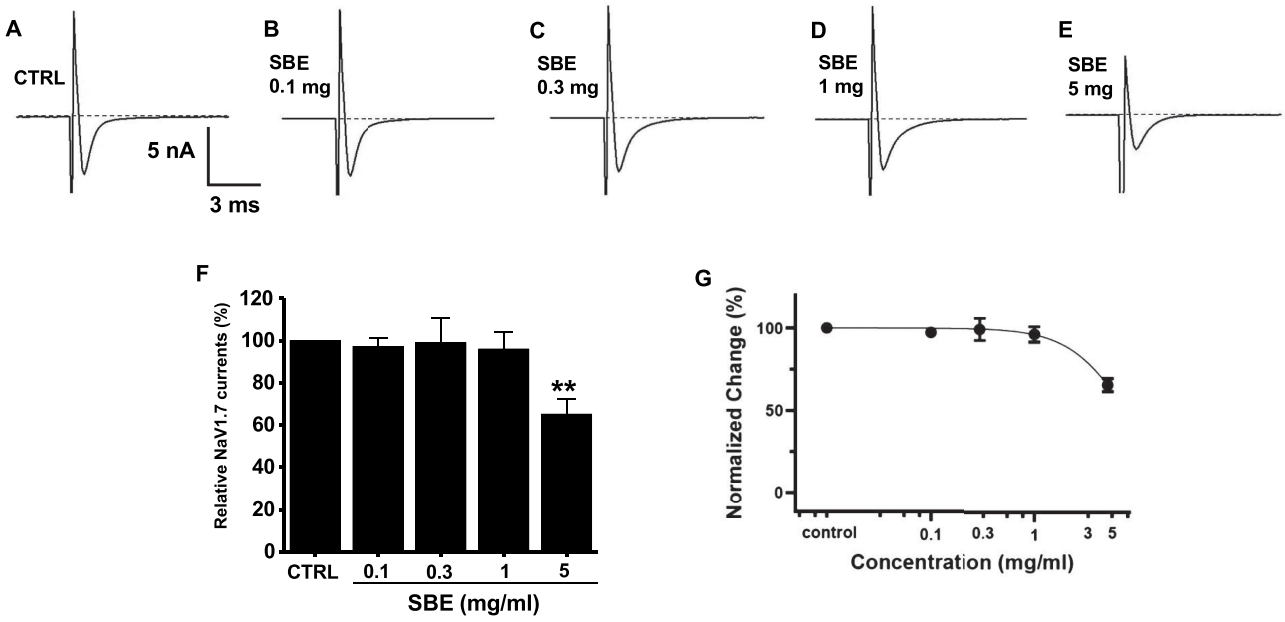


Figure 9. Effect of SBE on NaV1.7 currents. (A) Representative plot of NaV1.7 currents in HEK293 T cells. (B–E) Representative plots showing the effects of SBE at 0.1, 0.3, 1, and 5 mg/mL. (F) Summary of the relative NaV1.7 current changes induced by SBE. (G) Normalized changes in NaV1.7 currents following SBE treatment. Bars indicate mean ± SE. $^{**}p < 0.01$ vs control. SBE: *Scutellaria baicalensis* extract. CTRL: Control. Nav, voltage-gated sodium channel.

of the NF-κB and MAPK signaling pathways (Zhu et al. 2023). Another study found that *Scutellaria baicalensis* flavonoids attenuated colonic inflammation in experimental colitis models by downregulating TNF-α, IL-6, and IL-1β expression while enhancing IL-10 production (Jang et al. 2023). Collectively, these findings indicate that *Scutellaria baicalensis* exerts broad anti-inflammatory effects through multiple pathways, including cytokine regulation and oxidative stress reduction. Unlike previous studies that primarily focused on the anti-inflammatory potential of *Scutellaria baicalensis*, our study expands the therapeutic scope for IBS by evaluating its impact on ion channel activity, gut motility, and pain hypersensitivity. While earlier research demonstrated that *Scutellaria baicalensis* can reduce inflammation in colitis and other GI disorders, our study uniquely identifies its modulatory effects on TRP and NaV channels. This broader scope suggests that SBE's benefits extend beyond controlling inflammation to the direct regulation of gut function and pain perception, making it a promising candidate for IBS treatment.

Pain perception is a major concern in IBS and is often linked to hypersensitivity mediated by TRP and NaV channels. Our electrophysiological analysis demonstrated that SBE significantly inhibited TRPV1 and TRPA1 channel currents (Figures 5 and 7). Although TRPV4 channel currents also exhibited a slight inhibitory effect, the effect was not as significant as that of TRPV1 and TRPA1 (Figure 6). These TRP channels are involved in visceral pain hypersensitivity, and their inhibition by SBE suggests a mechanism by which SBE alleviates IBS-related pain. Furthermore, SBE primarily inhibited NaV1.5, with a minimal effect on NaV1.7, which is crucial for pain signal transmission. Given that NaV1.5 inhibition was more pronounced, this suggests a primary role in the visceral pain suppression effects of SBE. In addition to the TRP and NaV channels, emerging evidence suggests that other ion channels may also contribute to the effects of *Scutellaria baicalensis* on GI disorders. SBE modulates large-conductance calcium-activated potassium (BK) channels, which regulate smooth muscle relaxation and gut motility (Kim et al. 2019). Furthermore, SBE has been shown to influence chloride channels, which play a critical role in intestinal fluid secretion and barrier function (Ko et al. 2002; Yue et al. 2004). These findings suggest that the therapeutic effects of SBE extend beyond the TRP and NaV channels, contributing to its broad regulatory impact on GI function. Ion channels play a crucial role in IBS pathophysiology by regulating gut motility, pain perception, and the inflammatory response (Fuentes and Christianson 2016; Maqoud et al. 2023). Dysfunction in TRP, NaV, K^+, Cl^-, and Piezo channels has been associated with visceral hypersensitivity (de Carvalho Rocha et al. 2014; Fuentes and Christianson 2016; Bai et al. 2017), abnormal peristalsis (Beyder et al. 2016; Radulovic et al. 2015; 2016), and disrupted epithelial barrier function (Kim et al. 2021) in patients with IBS. The ability of SBE to modulate these ion channels highlights its potential as a

multitarget therapeutic agent for IBS. By restoring ion channel homeostasis, SBE may help alleviate key IBS symptoms and offer a novel approach for managing this complex disorder. Beyond its effects on GI disorders, Scutellaria baicalensis exerts various pharmacological actions in which ion channels are thought to play a significant role. For example, baicalein, a major flavonoid component of Scutellaria, has been shown to activate BK_{Ca} currents in rat mesenteric artery smooth muscle cells via the PKA and PKG signaling pathways. This activation enhances K^+ efflux, induces membrane hyperpolarization, and leads to the closure of voltage-dependent calcium channels (VDCCs), suggesting its potential therapeutic role in cardiovascular disorders (Lin et al. 2010). In addition, baicalein has been reported to protect against myocardial ischemia by reducing oxidative stress, inflammation, and apoptosis, partly through inhibition of the TLR4/MyD88/MAPK/NF-κB pathway and regulation of L-type Ca^{2+} channel activity (Li et al. 2022). In addition, a previous study demonstrated that Scutellaria baicalensis exerts neuroprotective effects against glutamate-induced excitotoxicity in primary rat cortical neurons by selectively inhibiting NMDA receptor function through interaction with its glycine binding site (Yang et al. 2014). Furthermore, a recent study suggests that baicalin, a major constituent of Scutellaria baicalensis, exerts anti-nociceptive effects by downregulating TRPV1 mRNA expression and suppressing TRPV1-mediated calcium influx in dorsal root ganglion neurons, suggesting a potential mechanism for its analgesic action (Sui et al. 2010). Finally, baicalein has been found to promote non-amyloidogenic precursor protein processing and reduce β-amyloid production by activating GABAA receptors, thereby improving cognitive performance in Alzheimer's disease models (Zhang et al. 2013). Collectively, these findings highlight the broad ion channel-modulating potential of Scutellaria baicalensis, which may contribute to its diverse therapeutic actions.

Traditional medicine has long played a vital role in treating GI disorders, including IBS. *Scutellaria baicalensis* has been used as a traditional herbal remedy because of its anti-inflammatory and gut-regulating properties. Recent studies have increasingly focused on the mechanisms underlying its therapeutic effects, particularly in GI diseases (Shao et al. 2004; Cui et al. 2021; Dmitrieva et al. 2023). *Scutellaria baicalensis* and its bioactive flavonoids can regulate the composition of gut microbiota, reduce oxidative stress, and modulate immune responses, making it a promising candidate for IBS treatment (Cui et al. 2021). Additionally, their potential synergy with probiotics and other natural compounds has been explored to enhance their efficacy in gut health management (Shao et al. 2004; Dmitrieva et al. 2023; Cho and Lim 2024). Our findings provide scientific validation for the therapeutic use of *Scutellaria baicalensis* in IBS treatment, bridging the gap between traditional knowledge and modern biomedical research. The integration of traditional medicine into contemporary IBS management strategies offers new avenues for the development of safer and more effective treatments.

Collectively, these findings suggest that SBE exerts multifaceted protective effects against IBS by modulating gut motility, reducing inflammation, and attenuating pain hypersensitivity. The suppression of TRP and NaV channel activity provides a mechanistic explanation for SBE's analgesic effects, and its ability to restore colonic structure and function underscores its therapeutic potential. Future studies should explore the molecular pathways involved and evaluate the long-term efficacy and safety of SBE in clinical settings. Further investigation of its effects on gut microbiota composition and immune modulation could provide deeper insights into its therapeutic mechanisms (Yun and Hyun 2023). Clinical trials assessing optimal dosages, formulation stability, and potential synergistic effects with conventional IBS treatments would also be valuable for translating these findings into clinical practice (Kwon et al. 2023).

Overall, our study provides compelling evidence that SBE could serve as a promising natural alternative for IBS management, offering both anti-inflammatory and analgesic benefits with minimal adverse effects. These findings pave the way for further investigations into the clinical applications of *Scutellaria baicalensis* in functional GI disorders.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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