Article

# Effect of Celecoxib Combined With Escitalopram on Depressive Symptoms and Peripheral Inflammatory Markers in Patients With AIDS and Depression: A Retrospective Exploratory Study

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## Abstract

Background: To investigate the potential effects of celecoxib combined with escitalopram on neuroinflammatory status in patients with acquired immunodeficiency syndrome (AIDS) and depression, generating hypotheses for future prospective trials.

Methods: In this retrospective study, 120 individuals with AIDS and depression who were treated between September 2024 and September 2025 were classified into a control group (escitalopram monotherapy) or an observation group (escitalopram plus celecoxib) according to treatment regimen, with 60 patients in each group. Depressive symptom severity was assessed using the Hamilton Depression Rating Scale (HAMD). Serum levels of 5-hydroxytryptamine (5-HT), orphanin FQ (OFQ), high-sensitivity C-reactive protein (hs-CRP), tumour necrosis factor-alpha (TNF-$\alpha$), and interleukin-1 beta (IL-1$\beta$) were measured before and after 8 weeks of treatment.

Results: After treatment, the observation group had significantly lower HAMD scores than the escitalopram monotherapy group (9.50 $\pm$ 1.64 vs. 12.50 $\pm$ 1.94, $p < 0.001$), along with higher 5-HT (2.03 $\pm$ 0.23 vs. 1.62 $\pm$ 0.32 $\mu$mol/L, $p < 0.001$), lower OFQ (14.72 $\pm$ 2.31 vs. 17.56 $\pm$ 2.12 ng/L, $p < 0.001$), and lower hs-CRP (8.42 $\pm$ 1.79 vs. 12.56 $\pm$ 2.62 mg/L, $p < 0.001$), TNF-$\alpha$ (6.74 $\pm$ 1.26 vs. 10.31 $\pm$ 1.53 pg/mL, $p < 0.001$) and IL-1$\beta$ (23.54 $\pm$ 3.04 vs. 31.72 $\pm$ 3.84 pg/mL, $p < 0.001$) levels. No significant difference was found in adverse events (8.33% vs. 10.00%, $p = 0.752$). After adjusting for baseline age, sex, and disease duration using analysis of covariance (ANCOVA), the intergroup difference in post-treatment HAMD scores remained significant (adjusted mean difference: $-3.02$, 95% CI: $-3.68$ to $-2.36$, $p < 0.001$). Significant adjusted differences were also preserved for 5-HT, OFQ, hs-CRP, TNF-$\alpha$, and IL-1$\beta$ (all adjusted $p < 0.001$).

Conclusions: In this retrospective exploratory study, celecoxib combined with escitalopram was associated with greater improvement in depressive symptoms and more favourable changes in neurobiological and inflammatory markers compared with escitalopram alone, with acceptable short-term safety. The findings are preliminary and require confirmation in prospective randomised controlled trials.

## Keywords

celecoxib; escitalopram; AIDS; depression; neuroinflammation; exploratory study

## Introduction

With the widespread use of antiretroviral therapy (ART), the survival rate of human immunodeficiency

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virus/acquired immunodeficiency syndrome (HIV/AIDS) patients has improved substantially; however, mental health problems, particularly depression, have become increasingly prominent [1]. The prevalence of depression among patients with AIDS has been documented to reach 30%–60%, markedly higher than that in the general population [2]. Depressive symptoms not only impair quality of life and treatment adherence but may also accelerate HIV replication and disease progression [3]. Therefore, identifying safe and effective antidepressant strategies is important for improving the overall prognosis of patients with AIDS.

Selective serotonin reuptake inhibitors (SSRIs) are first-line agents for depressive disorders [4,5]. However, in clinical practice, some patients with AIDS and comorbid depression respond inadequately to SSRI monotherapy. Evidence suggests that proinflammatory cytokines produced during HIV-induced immune activation may interfere with serotonin metabolic pathways and thereby affect the efficacy of conventional antidepressants [6]. Recently, the neuroinflammation hypothesis has garnered growing interest in the pathogenesis of depression, and anti-inflammatory therapy has emerged as a potential adjunctive strategy [7,8]. Celecoxib, a selective cyclooxygenase-2 (COX-2) inhibitor, was chosen as an adjunctive agent for several reasons: (1) it has proven anti-inflammatory and neuroprotective effects in preclinical models of neuroinflammation; (2) it readily crosses the blood–brain barrier and reduces prostaglandin E2 synthesis in the central nervous system (CNS); (3) a meta-analysis has suggested its potential antidepressant augmentation effect in non-HIV populations [9]; and (4) its safety profile in HIV-infected individuals has been documented in some studies [10].

Escitalopram, a highly selective SSRI, was selected because it has the fewest drug–drug interactions with ART and is widely used in HIV-positive patients with depression [11].

Serum 5-hydroxytryptamine (5-HT) and orphanin FQ (OFQ) were selected as depression-related biomarkers because 5-HT is the primary neurotransmitter targeted by SSRIs, and its levels correlate with depressive severity; OFQ (nociceptin) is an endogenous opioid peptide that modulates stress responses and has been linked to depression-like behaviours through the hypothalamic–pituitary–adrenal axis and mesolimbic dopamine system. Both markers are measurable in peripheral blood and have been reported to change with antidepressant treatment in HIV-positive populations [12–14].

This retrospective exploratory study aimed to examine the effects of celecoxib combined with escitalopram on depressive symptoms, as well as neurobiological and peripheral inflammatory markers in patients with AIDS and depression, with the goal of generating hypotheses for future prospective trials.

## Materials and Methods

### *Study Population*

This retrospective study included 120 patients with AIDS and depression who were treated at Fujian Medical University Affiliated First Quanzhou Hospital between September 2024 and September 2025. According to treatment regimen, patients were divided into a control group (escitalopram monotherapy) and an observation group (escitalopram combined with celecoxib), with 60 patients in each group.

The inclusion criteria were as follows: (1) meeting the diagnostic criteria for AIDS [15]; (2) age 18–65 years; (3) meeting the diagnostic criteria for a depressive episode in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [16]; (4) first episode of depression with no previous antidepressant treatment; and (5) complete clinical data.

The exclusion criteria were as follows: (1) comorbid psychiatric disorders; (2) known allergy to the study medications; (3) use of other antidepressants within 1 month before enrolment; and (4) incomplete clinical data.

This study was approved by the Ethics Committee of Fujian Medical University Affiliated First Quanzhou Hospital (institution review board number, No. 2026-K158) and was performed in accordance with the principles of the Declaration of Helsinki. Because of the retrospective nature, the committee waived the requirement for individual informed consent.

### *Sample Size and Statistical Power*

This retrospective study included all eligible patients available during the study period. No a priori sample size calculation was performed. An exploratory post-hoc power analysis was conducted using G*Power version 3.1.9.7 (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany) for an independent-samples *t*-test (two-tailed, $\alpha$ = 0.05). With 60 patients per group, the study had approximately 80% power to detect an effect size (Cohen's d) of 0.52. The observed effect size for Hamilton Depression Rating Scale (HAMD) change was approximately 1.8, sug-


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gesting adequate power for the primary outcome.

*Treatment Regimens*

Patients in the control group received escitalopram oxalate (Shandong Jingwei Pharmaceutical Co., Ltd., Tai'an, Shandong, China; National Medical Products Administration approval No. H20103327). Treatment was initiated at 10 mg/day for the first 2 weeks and then increased to 20 mg/day for 4 consecutive weeks as one treatment course, for a total of two courses [17].

Beyond the same escitalopram regimen, patients in the observation group additionally received oral celecoxib capsules (CSPC Ouyi Pharmaceutical Co., Ltd., Shijiazhuang, Hebei, China; National Medical Products Administration approval No. H20203297) at 200 mg once daily after meals for 8 consecutive weeks [18].

*Outcome Measures*

Outcome data were extracted from the medical record system, including baseline and post-treatment assessments.

17-Item Hamilton Depression Rating Scale (HAMD-17)

The HAMD-17 was used to assess depression symptoms. The scale includes 17 items, evaluating depressed mood, sleep disturbance, and somatic symptoms, with a total score range of 0–52 [19].

*Serum Depression-Related Biomarkers*

Serum 5-HT levels were measured in fasting venous blood collected from the cubital vein before and after treatment using high-performance liquid chromatography with electrochemical detection. Serum OFQ levels were measured using radioimmunoassay.

*Inflammatory Markers*

Before and after treatment, 6 mL of fasting morning venous blood was collected and centrifuged. Tumour necrosis factor-alpha (TNF-$\alpha$) and interleukin-1 beta (IL-1$\beta$) levels were detected by enzyme-linked immunosorbent assay using kits (TNF-$\alpha$: Cat. No. LM812hu; IL-1$\beta$: Cat. No. LM802hu; Shanghai Lianmai Biotechnology Co., Ltd, China). High-sensitivity C-reactive protein (hs-CRP) levels were detected using radioimmunoassay kits (Cat. No. JLC7644; Shanghai Jingkang Biotechnology Co., Ltd, Shanghai, China).

*Adverse Events*

Based on the known safety profiles of the two study drugs, the primary monitoring adverse events were prespecified as dizziness, nausea/vomiting, and gastrointestinal discomfort [4,20]. All adverse events were assessed for their causality with the study drugs by the attending physicians in accordance with the Technical Guideline for Causality Assessment of Adverse Events in Drug Clinical Trials issued by the National Medical Products Administration (NMPA) [21]. Adverse events classified as "possibly related" or above were considered drug-related adverse reactions. Severity of adverse events was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [22].

*Statistical Analysis*

Data were analysed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Variables that followed a normal distribution were presented as mean $\pm$ standard deviation (SD) and were compared using parametric tests; variables that deviated from normality were presented as median (interquartile range) and were analysed using non-parametric tests. For between-group comparisons of normally distributed data, independent-samples *t*-tests (two-tailed) were used; for within-group pre-post comparisons, paired-samples *t*-tests (two-tailed) were used. For non-normally distributed data, the Mann–Whitney U test and Wilcoxon signed-rank test were used for between-group and within-group comparisons, respectively. Categorical data are expressed as rates (%) and were compared using the chi-square test. Furthermore, analysis of covariance (ANCOVA) was employed to adjust for potential confounding factors, including baseline values of the respective outcome measures, age, sex, and disease duration, reporting adjusted mean differences and their 95% confidence intervals. A two-sided $p$ value $< 0.05$ was considered statistically significant.

## Results

*Baseline Characteristics*

Baseline characteristics of the study population are summarised in Table 1. A total of 120 patients with AIDS


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**Table 1. Comparison of baseline characteristics between the two groups.**

| Characteristics | Control group (n = 60) | Observation group (n = 60) | $t/\chi^2$ | $p$ |
|---|---|---|---|---|
| Age (years), mean ± SD | 34.51 ± 4.67 | 35.02 ± 4.28 | 0.592 | 0.555 |
| Sex, n (%) | | | 0.137 | 0.711 |
| Male | 35 (58.33%) | 33 (55.00%) | | |
| Female | 25 (41.67%) | 27 (45.00%) | | |
| BMI (kg/m$^2$), mean ± SD | 24.35 ± 2.62 | 24.61 ± 2.74 | 0.531 | 0.597 |
| Disease duration (years), mean ± SD | 1.89 ± 0.52 | 1.92 ± 0.63 | 0.284 | 0.777 |
| Education level, n (%) | | | 0.836 | 0.361 |
| High school or below | 26 (43.33%) | 31 (51.67%) | | |
| College or above | 34 (56.67%) | 29 (48.33%) | | |
| Marital status, n (%) | | | 0.302 | 0.583 |
| Married | 28 (46.67%) | 25 (41.67%) | | |
| Unmarried/Divorced/Widowed | 32 (53.33%) | 35 (58.33%) | | |
| CD4+ cell count (cells/$\mu$L), mean ± SD | 312.43 ± 84.91 | 307.80 ± 79.29 | –0.309 | 0.758 |
| Plasma HIV RNA ($\log_{10}$ copies/mL), mean ± SD | 4.19 ± 0.63 | 4.07 ± 0.67 | –1.012 | 0.314 |
| ART regimen, n (%) | | | 0.164 | 0.685 |
| NNRTI-based | 42 (70.00%) | 44 (73.33%) | | |
| PI-based | 18 (30.00%) | 16 (26.67%) | | |

Note. BMI, body mass index; ART, antiretroviral therapy; NNRTI, non-nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; SD, standard deviation.

and depression (60 in each group) were included, with 60 patients in each group. The mean age was 34.51 ± 4.67 years in the control group and 35.02 ± 4.28 years in the observation group. The majority of patients were male (58.33% in the control group vs. 55.00% in the observation group). The mean disease duration was 1.89 ± 0.52 years and 1.92 ± 0.63 years, respectively. The mean CD4+ cell count was 312.43 ± 84.91 cells/$\mu$L in the control group and 307.80 ± 79.29 cells/$\mu$L in the observation group. Regarding ART, non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens were used in 70.00% of the control group and 73.33% of the observation group, whereas protease inhibitor (PI)-based regimens accounted for the remainder. No significant differences were found between the two groups in any baseline demographic or clinical characteristics (all $p > 0.05$), indicating that the two groups were comparable at baseline.

### *Comparison of Depressive Severity Before and After Treatment*

Both groups showed significant reductions in HAMD scores from baseline to 8 weeks after treatment (control: 22.42 ± 3.36 to 12.50 ± 1.94, $t = 27.514$, df = 59, $p < 0.001$; observation: 21.95 ± 3.17 to 9.50 ± 1.64, $t = 21.681$, df = 59, $p < 0.001$). After 8 weeks of treatment, the observation group had lower HAMD scores than the control group (mean difference −3.24, 95% CI −3.91 to −2.57, $t = 9.133$, df = 118, $p < 0.001$; ANCOVA adjusted difference −3.02, 95% CI −3.68 to −2.36, F = 54.3, $p < 0.001$) (Table 2).

### *Comparison of Serum Depression-Related Biomarkers*

After treatment, the observation group had significantly higher 5-HT levels than the control group ($t = -8.028$, df = 118, $p < 0.001$) and significantly lower OFQ levels than the control group ($t = 7.013$, df = 118, $p < 0.001$). Both groups showed significant increases in 5-HT levels and decreases in OFQ levels after treatment (control group: 5-HT: $t = 4.093$, OFQ: $t = -22.917$, both $p < 0.001$; observation group: 5-HT: $t = 10.706$, OFQ: $t = -27.101$, both $p < 0.001$) (Table 3).

### *Comparison of Inflammatory Markers*

Within the control group, significant reductions were observed after 8 weeks of treatment in hs-CRP (from 16.96 ± 2.35 to 12.56 ± 2.62 mg/L, $t = 10.906$, df = 59, $p < 0.001$), TNF-$\alpha$ (from 14.67 ± 3.21 to 10.31 ± 1.53 pg/mL, $t = 9.482$, df = 59, $p < 0.001$), and IL-1$\beta$ (from 43.22 ± 4.62 to 31.72 ± 3.84 pg/mL, $t = 15.147$, df = 59, $p < 0.001$). Similarly, within the observation group, significant reductions were also found in hs-CRP (from 16.83 ± 2.47 to 8.42 ± 1.79 mg/L, $t = 22.355$, df = 59, $p < 0.001$), TNF-$\alpha$ (from 14.28 ± 2.89 to 6.74 ± 1.26 pg/mL, $t = 18.366$, df = 59, $p < 0.001$), and IL-1$\beta$ (from 42.79 ± 4.52 to 23.54 ± 3.04 pg/mL, $t = 25.997$, df = 59, $p < 0.001$).


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**Table 2. Comparison of depressive severity before and after treatment (mean ± SD).**

| Group | Before treatment | After 8 weeks of treatment |
|---|---|---|
| Control group | 22.42 ± 3.36 | 12.50 ± 1.94 |
| Observation group | 21.95 ± 3.17 | 9.50 ± 1.64 |
| Intergroup *t* (df = 118) | 0.783 | 9.133 |
| Intergroup *p* | 0.435 | <0.001 |
| Paired *t* within control (df = 59) | - | 27.514 |
| Paired *p* within control | - | <0.001 |
| Paired *t* within observation (df = 59) | - | 21.681 |
| Paired *p* within observation | - | <0.001 |

Note. HAMD, Hamilton Depression Rating Scale. Intergroup comparisons were performed using independent-samples *t*-tests; within-group pre-post comparisons were performed using paired *t*-tests.

**Table 3. Comparison of serum depression-related biomarkers between the two groups (mean ± SD).**

| Group | 5-HT before treatment ($\mu$mol/L) | 5-HT after treatment ($\mu$mol/L) | OFQ before treatment (ng/L) | OFQ after treatment (ng/L) |
|---|---|---|---|---|
| Control group | 1.26 ± 0.62 | 1.62 ± 0.32* | 28.58 ± 3.14 | 17.56 ± 2.12* |
| Observation group | 1.25 ± 0.54 | 2.03 ± 0.23* | 28.15 ± 2.86 | 14.72 ± 2.31* |
| Intergroup *t* (df = 118) | −0.063 | 8.028 | −0.780 | −7.013 |
| *p* value | 0.950 | <0.001 | 0.437 | <0.001 |

Note. *$p < 0.001$ compared with baseline within the same group (paired-samples *t*-test). 5-HT, 5-hydroxytryptamine; OFQ, orphanin FQ; SD, standard deviation.

**Table 4. Comparison of inflammatory markers between the two groups (mean ± SD).**

| Group | hs-CRP before treatment (mg/L) | hs-CRP after treatment (mg/L) | TNF-$\alpha$ before treatment (pg/mL) | TNF-$\alpha$ after treatment (pg/mL) | IL-1$\beta$ before treatment (pg/mL) | IL-1$\beta$ after treatment (pg/mL) |
|---|---|---|---|---|---|---|
| Control group | 16.96 ± 2.35 | 12.56 ± 2.62* | 14.67 ± 3.21 | 10.31 ± 1.53* | 43.22 ± 4.62 | 31.72 ± 3.84* |
| Observation group | 16.83 ± 2.47 | 8.42 ± 1.79* | 14.28 ± 2.89 | 6.74 ± 1.26* | 42.79 ± 4.52 | 23.54 ± 3.04* |
| Intergroup *t* (df = 118) | 0.295 | 10.108 | 0.699 | 13.947 | 0.515 | 12.933 |
| *p* value | 0.769 | <0.001 | 0.486 | <0.001 | 0.607 | <0.001 |

Note. *$p < 0.001$ compared with baseline within the same group (paired-samples *t*-test). hs-CRP, high-sensitivity C-reactive protein; TNF-$\alpha$, tumour necrosis factor-alpha; IL-1$\beta$, interleukin-1 beta; SD, standard deviation. For ANCOVA-adjusted results, see the Results section.

After adjustment for baseline values using ANCOVA, the observation group had significantly lower post-treatment levels of hs-CRP (adjusted mean difference: –4.122 mg/L, 95% CI: –4.927 to –3.317; F = 102.857, $p < 0.001$), TNF-$\alpha$ (adjusted mean difference: –3.571 pg/mL, 95% CI: –4.081 to –3.060; F = 191.868, $p < 0.001$), and IL-1$\beta$ (adjusted mean difference: –8.187 pg/mL, 95% CI: –9.446 to –6.928; F = 165.895, $p < 0.001$) compared with the control group (Table 4).

*Comparison of Adverse Events*

All adverse events were grade 1–2 according to CTCAE v5.0, and no serious adverse events, bleeding events, or drug-related grade ≥3 events were recorded in either group. The incidence of adverse events was 10.00% (6/60) in the control group and 8.33% (5/60) in the observation group, with no significant between-group difference ($\chi^2 = 0.100$, df = 1, $p = 0.752$) (Table 5).

## Discussion

Patients with AIDS and depression experience both the physiological burden of immune dysfunction and the psychological stress associated with social discrimination, stigma, and disease prognosis. Consequently, the prevalence of depressive disorders in this population is higher than the general population [23]. Depressive symptoms not only seriously affect treatment adherence and quality of life but may also accelerate HIV replication and disease progression through neuroimmune pathways, contributing to a vicious cycle [24,25].

The neuroinflammation hypothesis has drawn increas-


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**Table 5. Comparison of adverse events between the two groups [n (%)].**

| Group | Dizziness | Nausea/Vomiting | Gastrointestinal discomfort | Total incidence |
|---|---|---|---|---|
| Control group | 2 (3.33%) | 1 (1.67%) | 3 (5.00%) | 6 (10.00%) |
| Observation group | 1 (1.67%) | 2 (3.33%) | 2 (3.33%) | 5 (8.33%) |
| $\chi^2$ (df = 1) | | | | 0.100 |
| *p* value | | | | 0.752 |

ing attention in studies of depression pathogenesis. HIV infection can activate immune cells in the CNS, which may contribute to depressive symptoms, neurotoxic damage, and the production of inflammatory mediators [26–28]. Celecoxib, a selective COX-2 inhibitor, has anti-inflammatory and neuroprotective effects and may target neuroinflammatory pathological processes in patients with AIDS and depression [29]. The present study found a potential association between celecoxib add-on therapy and greater improvement in depressive symptoms.

Based on the present findings and prior mechanistic studies, we hypothesise that the potential mechanisms underlying the observed association may involve several interrelated pathways. Escitalopram, as an SSRI, mainly exerts antidepressant effects by increasing synaptic 5-HT concentrations; however, it has limited effects on the HIV-associated neuroinflammatory state [4]. HIV infection can induce persistent activation of microglia and astrocytes, which may upregulate COX-2 expression through the nuclear factor-kappa B (NF-$\kappa$B) signalling pathway, increase prostaglandin E2 synthesis, and enhance the release of proinflammatory cytokines, directly damaging neurons and impairing neuroplasticity [20]. Additionally, HIV infection can activate indoleamine 2,3-dioxygenase (IDO), shifting tryptophan metabolism toward the kynurenine pathway, reducing 5-HT synthesis and increasing the neurotoxic metabolite quinolinic acid. Prostaglandin E2-stimulated signalling may also contribute to hypothalamic–pituitary–adrenal (HPA) axis dysregulation, further reducing hippocampal neural plasticity [26–28]. Celecoxib may counter these effects by blocking prostaglandin E2 synthesis, inhibiting NF-$\kappa$B activation, reducing proinflammatory factor release, and potentially restoring HPA axis negative feedback regulation [30,31].

Additionally, the reduction in OFQ levels observed in the observation group may be associated with reduced inflammation-mediated NF-$\kappa$B activation, potentially contributing to the modulation of the reward neural circuits [32]. However, these proposed mechanisms involving the NF-$\kappa$B pathway, IDO, and the HPA axis were not directly assessed in the present study. Our assessments relied on peripheral blood markers, and no molecular or animal experiments were performed to validate these pathways. Therefore, these mechanistic interpretations remain speculative and should be investigated in future studies using direct CNS measurements, molecular assays, and animal models.

This study has several limitations. First, all participants came from a single medical facility, and the sample size was small. Furthermore, no a priori sample size estimation was performed; although the post-hoc power analysis suggested sufficient power for the primary outcome, the study had limited ability to detect smaller effects or subgroup differences. Second, the observation period was short and only reflected the short-term efficacy and safety of combination therapy; long-term follow-up data were unavailable, preventing evaluation of recurrence of depressive symptoms and longitudinal changes in neuroinflammation. Third, this was a retrospective, non-randomised study without blinding. Clinicians' decision to add celecoxib may have been influenced by unmeasured factors such as symptom severity, introducing selection bias that cannot be fully corrected by statistical adjustment. Although ANCOVA was used to control for baseline variables, residual confounding cannot be excluded. Moreover, the subjective nature of HAMD assessment may have introduced measurement bias. Fourth, neuroinflammation was assessed mainly through peripheral blood inflammatory markers, which may not fully reflect inflammatory alterations in the CNS. Fifth, other clinically relevant outcomes, such as sleep quality and somatic symptom burden, were not assessed using dedicated scales (e.g., PSQI for sleep, or PHQ-15 for somatic symptoms), and potential drug–drug interactions were not systematically evaluated.

Future studies should include neuroimaging methods or cerebrospinal fluid analyses, expand sample size, extend follow-up periods, and adopt prospective randomised controlled designs. Although this study suggests that celecoxib may exert synergistic antidepressant effects possibly through regulating the NF-$\kappa$B pathway, affecting tryptophan metabolism, and modulating OFQ expression, these mechanisms have not yet been verified at the molecular level or in animal models and require further investigation.


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## Conclusions

Within the constraints of this retrospective exploratory study, celecoxib combined with escitalopram was associated with greater improvements in depressive symptoms in patients with AIDS and depression compared with escitalopram alone. The underlying mechanisms may involve upregulation of 5-HT, downregulation of OFQ, and inhibition of neuroinflammatory responses; however, these mechanistic interpretations remain hypothetical and require further validation. The combination therapy showed a favourable short-term safety in this study and may provide preliminary evidence supporting future prospective randomised controlled trials.

## Availability of Data and Materials

The datasets used and/or analysed during the current study were available from the corresponding author on reasonable request.

## Author Contributions

YPG and FFZ designed the study; all authors conducted the study; JFL and FFZ collected and analysed the data. YPG and YNL participated in drafting the manuscript, and all authors contributed to critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work were appropriately investigated and resolved.

## Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Fujian Medical University Affiliated First Quanzhou Hospital (institution review board number, No. 2026-K158) and was performed in accordance with the principles of the Declaration of Helsinki. Because of the retrospective nature, the committee waived the requirement for individual informed consent.

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## Conflict of Interest

The authors declare no conflict of interest.

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