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CLINICAL TRIAL REPORT

Efficacy and Safety of Toludesvenlafaxine Hydrochloride Sustained-Release Tablets on Somatic Symptoms of Major Depressive Disorder: A Prospective, Single-Arm, Multicenter Clinical Study

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Importance: Depression is a significant global public health issue, with somatic symptoms being a common and challenging aspect of its management.

Objective: This study aimed to evaluate the efficacy and safety of toludesvenlafaxine hydrochloride sustained-release tablets (Roxylin®) for somatic symptoms of major depressive disorder (MDD).

Design, Setting, and Participants: Prospective, single-arm, multicenter clinical study conducted between June 1, 2023 and May 1, 2024, enrolling patients diagnosed with MDD with somatic symptoms at four hospitals across China.

Intervention: All participants received toludesvenlafaxine hydrochloride monotherapy for 8 weeks.

Main Outcomes and Measures: The primary outcomes were improvements in somatic depression symptoms measured by PHQ-15 and SSS-CN at baseline and weeks 2, 4, and 8, while secondary outcomes included changes in depressive symptoms (HAMD-17), pain intensity (VAS), fatigue (MFI-20), and functional impairment (SDS), with adverse events monitored.

Results: Out of 72 screened patients, 61 were enrolled. The mean age of the participants was 30.1 ± 9.0 years, ranging from 18 to 53 years, with 29.6% being male and 70.4% female. After 8 weeks of treatment, significant reductions were observed in PHQ-15 scores (−5.8 ± 4.4, $P < 0.001$) and SSS-CN scores (−12.8 ± 10.3, $P < 0.001$), indicating improvement in somatic symptoms. Secondary outcomes also showed significant improvements in depressive symptoms (HAMD-17: −15.3 ± 7.4, $P < 0.001$), pain intensity (VAS: −1.97 ± 2.44, $P < 0.001$), fatigue (MFI-20: −12.8 ± 14.1, $P < 0.001$), and functional disability (SDS: −8.3 ± 6.5, $P < 0.001$). The occurrence of adverse events was 52.5%, with no serious adverse events reported.

Conclusion: Toludesvenlafaxine hydrochloride significantly improved somatic symptoms in patients with MDD and somatic symptoms, with a favorable safety profile, supporting its use as an effective treatment option.

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Keywords: major depressive disorder, somatic symptoms, toludesvenlafaxine, clinical trial, safety, efficacy

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Introduction

Depressive disorder is a significant global public health issue. According to the World Health Organization, approximately 280 million people worldwide suffer from depression.[1] The 2019 China Mental Health Survey reported a lifetime prevalence of depressive disorder at 6.8%, with major depressive disorder (MDD) accounting for 3.4%.[2] Depression manifests through emotional, cognitive, and somatic symptoms.[3] Studies have shown that the prevalence of somatic symptoms in depression ranges from 66% to 93%, with over 30% of patients experiencing at least 14 different somatic symptoms, categorized into pain, fatigue, autonomic, and central nervous system symptoms.[4–9] In East Asia, including China, 51.8% of depressive patients exhibit somatic symptoms.[10] A survey of 3273 Chinese MDD patients revealed common symptoms such as insomnia (64.6%), unexplained bodily discomfort (46.9%), weight loss (38.5%), and appetite loss (37.6%).[11] Hence, somatic symptoms in MDD represent a significant clinical issue.

The factors contributing to somatization in depression are complex, involving biological and non-biological influences that interact. Central nervous system dysfunction, particularly imbalances in serotonin (5-HT) and norepinephrine (NE), is a core mechanism in depression, which may also heighten sensitivity to somatic sensations. Dysfunction in neurotransmitters such as dopamine (DA), acetylcholine, and histamine in brain regions like the caudate nucleus and cerebellum are also associated with symptoms like fatigue.[12] Sexual dysfunction is common, affecting 70% of depression patients, with 59.1% developing it during antidepressant treatment, due to mechanisms involving 5-HT, DA, and other pathways.[13–16] These neurotransmitters are closely related to the pathogenesis of depression and the development of somatic symptoms.

Somatization symptoms severely impact patients' physical and mental health. Research indicates that these symptoms exacerbate depression severity, particularly pain, which is highly correlated with depression outcomes.[9] Somatic symptoms also contribute to cognitive impairment and lower health-related quality of life.[10] Moreover, they are often more challenging to treat than emotional symptoms, with residual somatic symptoms persisting after depressive symptoms improve, thereby reducing treatment efficacy and hindering recovery.[17,18] Thus, addressing the management of somatic symptoms in the treatment of MDD is critical.

There is currently a lack of systematic exploration and targeted management of somatization symptoms in depression. Studies suggest that serotonin and norepinephrine reuptake inhibitors (SNRIs) may be more effective than selective serotonin reuptake inhibitors (SSRIs) in alleviating somatic symptoms and achieving remission.[19,20] Given the sexual dysfunction associated with many antidepressants, careful selection of treatment is crucial, with SNRIs generally having a lower occurrence of sexual side effects compared to SSRIs.[16]

Torludivoxetine hydrochloride sustained-release tablets (Roxylin®), a novel antidepressant developed in China, inhibits the reuptake of 5-HT, NE, and DA. Clinical trials have shown torludivoxetine to significantly reduce fatigue symptoms in MDD patients with minimal impact on sexual function, weight, or sleep.[21] This study builds on these findings, using a single-arm, multicenter design to further evaluate efficacy and safety of torludivoxetine in treating somatic symptoms in patients with MDD and somatic symptoms, aiming to strengthen evidence-based treatment strategies.

Materials and Methods

Study Design

This prospective, single-arm, multicenter clinical study was conducted between June 1, 2023 and May 1, 2024 at four hospitals in China. The study enrolled patients who met the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria for MDD and had somatic symptoms. It was performed in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki. All patients provided written informed consent prior to enrollment. Ethical approval was obtained from the local research ethics committees (ClinicalTrials.gov Identifier: NCT05849272). (Include Shanghai Mental Health Center Ethics Committee, Renji Hospital Ethics Committee, Nanjing Brain Hospital Ethics Committee and Suzhou Guangji Hospital Ethics Committee).

Participants

Participants were required to be between 18 and 65 years of age, with no restrictions on gender. Inclusion criteria included a confirmed diagnosis of MDD according to DSM-5 by a senior psychiatrist, a moderate to severe level of depressive symptoms, indicated by a Hamilton Depression Rating Scale-17 item (HAMD-17) total score greater than 17 and an Anxiety/Somatization factor score of at least 3 (HAMD-17 scores in the range of 0 to 7 are generally accepted as healthy). Additionally, patients were required to have a Patient Health Questionnaire-15 (PHQ-15) score of 5 or higher, clear consciousness, no severe cognitive impairment, and the ability to communicate independently without significant signs of dementia.

Exclusion criteria included known allergies to venlafaxine or desvenlafaxine, previous ineffective treatment with venlafaxine or failure to respond to at least two different classes of antidepressants, comorbid psychiatric disorders, personality disorders, intellectual disabilities, or substance dependence or abuse within the past six months. Patients with clinically significant unstable diseases, such as hepatic or renal insufficiency, or cardiovascular, pulmonary, gastrointestinal, endocrine, neurological, rheumatological, immunological, infectious, dermatological, or metabolic disorders, were also excluded. Additional exclusion criteria involved severe self-harm or suicidal ideation or behavior, blood pressure greater than 140/90 mmHg, and clinically significant abnormalities in screening laboratory tests or electrocardiograms (ECGs). Women who were pregnant, breastfeeding, or planning to become pregnant, as well as those unable to ensure effective contraception during the study, were also excluded. Finally, patients with a history of moderate to severe head trauma, other neurological or systemic conditions that could affect central nervous system function, or any other conditions deemed unsuitable by the investigator were excluded.

Participants could withdraw from the study at any time without providing a reason. Reasons for withdrawal included safety concerns where the investigator deemed it beneficial to stop the study, violation of the study protocol, lack of efficacy, loss to follow-up, or withdrawal of informed consent.

Interventions

All participants received monotherapy with torludivoxetine for 8 weeks. For those not on antidepressants at enrollment, the treatment began with 40 mg daily for 2 days, increasing to 80 mg daily on the third day if well-tolerated. For those on other antidepressants, a cross-tapering method was used, starting with 40 mg of torludivoxetine daily, increasing to 80 mg within a week while tapering off the previous medication. The timing of tapering depended on individual circumstances. For those on monoamine oxidase inhibitors (MAOIs), a 2-week washout period was required before starting torludivoxetine. Torludivoxetine was administered at a consistent time each day, either on an empty stomach or after a meal, with the entire tablet swallowed whole. The recommended dose was 80 mg to 160 mg daily, starting at 40 mg and increasing to 80 mg within a week, with a maximum dose of 160 mg per day. The treatment duration was 8 weeks.

Outcome Assessment

The primary outcomes were the improvement in somatic symptoms of depression, as assessed by the Patient Health Questionnaire-15 (PHQ-15) and the Chinese Somatic Symptom Scale (SSS-CN). These scales were used to evaluate the severity and frequency of somatic symptoms at baseline and at weeks 2, 4, and 8. Secondary outcomes included changes in depressive symptoms as measured by the Hamilton Depression Rating Scale (HAMD-17), pain intensity assessed by the Visual Analog Scale (VAS), fatigue levels evaluated using the Multidimensional Fatigue Inventory (MFI-20), and functional impairment assessed by the Sheehan Disability Scale (SDS). Adverse events, defined as any unfavorable medical occurrence after administration of the study drug, were recorded throughout the study and up to 30 days after the last dose, regardless of the causal relationship with the drug. Demographic and general clinical data were also collected, including age, gender, vital signs, medical history, and laboratory test results.

Sample Size

Sample size calculation was based on an assumed mean reduction in PHQ-15 score of 6.2 points after 8 weeks of treatment and standard deviation of 7.4, with reference to similar study.[22] Using PASS software, with a power of 0.9 and an alpha level of 0.005, the estimated sample size was 28. Considering a 20% dropout rate, the required sample size was approximately 35. The final sample size of 61 participants was deemed sufficient for statistical analysis.

Statistical Analysis

Statistical analysis were performed using SAS 9.2. All statistical tests were two-sided, with a *P*-value of ≤ 0.05 considered statistically significant, and 95% confidence intervals were used. Continuous data were described using mean ± standard deviation. The primary efficacy outcomes were analyzed using the last observation carried forward (LOCF) method, with paired *t*-tests comparing within-group changes from baseline.Efficacy outcomes were analyzed using paired *t*-tests. The correlation between the main efficacy indicators and HAMD-17 was analyzed using Spearman correlation. Safety analyses included the occurrence of adverse events, and describing laboratory test results before and after treatment, noting any abnormal changes and their potential relationship to the study drug.

Results

Demographic and Baseline Clinical Characteristics

Out of 72 screened subjects, 61 were successfully enrolled in the study, with 11 failing to meet the inclusion criteria. All enrolled patients had somatic symptoms and were administered sustained-release tablets of toludesvenlafaxine hydrochloride (Figure 1). The demographic and baseline clinical characteristics are detailed in Table 1. The mean age of the patients was 30.1 ± 9.0 years, ranging from 18 to 53 years, with 29.6% being male and 70.4% female. All patients were of Han ethnicity, and 81.5% were covered by basic health insurance, while 18.5% were self-financed. The educational background of the cohort was predominantly higher education, with 64.8% having completed college or university and 18.5% holding a graduate degree. In terms of employment status, 53.7% were employed full-time, and 25.9% were students.

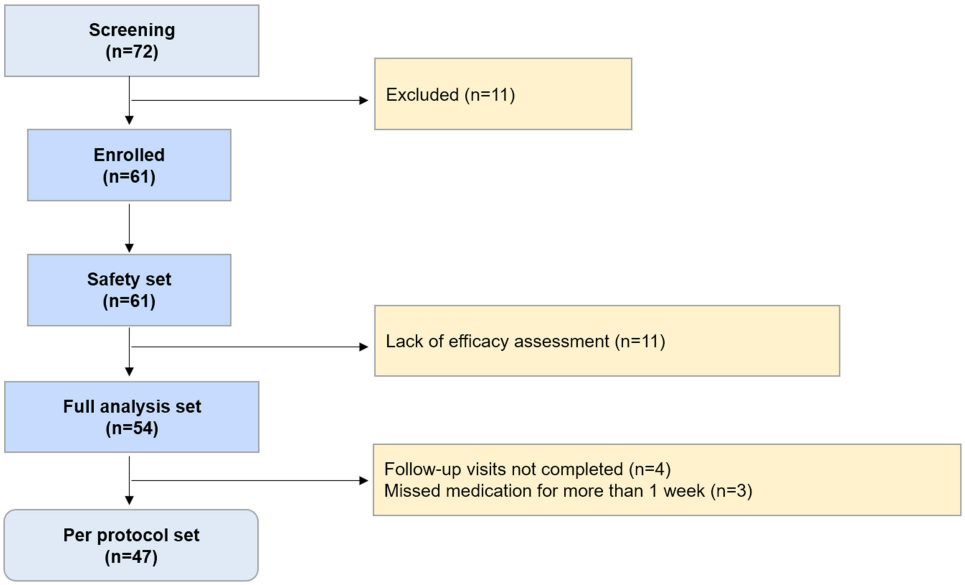

Figure 1 Study participant flow diagram. The diagram illustrates the progression of participants from screening (n = 72) to the per protocol set (n = 47). Reasons for exclusion and dropouts at various stages are provided.

Table 1 Demographic and Baseline Characteristics (FAS)

Characteristic		Study Patients (n = 54)
Age	Mean ± SD	30.1 ± 9.0
Gender, n (%)	Male	16 (29.6)
	Female	38 (70.4)
Ethnicity, n (%)	Han	54 (100.0)
Height (cm)	Mean ± SD	164.4 ± 7.2
Weight (kg)	Mean ± SD	60.66 ± 10.43
BMI (kg/m^2)	Mean ± SD	22.41 ± 3.49
Educational level, n (%)	High school or less	9 (16.7)
	Undergraduate	35 (64.8)
	Post-graduate or higher	10 (18.5)
Employment status, n (%)	Full-time	29 (53.7)
	Part-time	2 (3.7)
	Householder	1 (1.9)
	Student	14 (25.9)
	Retirement	0 (0.0)
	Unemployed	8 (14.8)
Marital status, n (%)	Single	27 (50.0)
	In love	6 (11.1)
	Married	15 (27.8)
	Divorce	6 (11.1)
Smoking history, n (%)	Never	40 (74.1)
	Former smoker	4 (7.4)
	Current smoker, ≤10 cigarettes per day	5 (9.3)
	Current smoker, >10 cigarettes per day	5 (9.3)
Drinking history, n (%)	Never	34 (63.0)
	Former drinker	2 (3.7)
	Light drinking	17 (31.5)
	Heavy drinking (daily alcohol intake ≥50g)	1 (1.9)
Drug allergy history, n (%)	Yes	6 (11.1)
Drug abuse history, n (%)	Yes	0 (0.0)
Family history of mental illness, n (%)	Yes	5 (9.3)

Abbreviations: BMI, body mass index; SD, standard deviation; FAS, full analysis set.

Primary Outcome Measures

The primary outcomes were the changes in somatic symptoms determined using the PHQ-15 and SSS-CN scores from baseline across all follow-up visits. The study demonstrated a statistically significant reduction in PHQ-15 and SSS-CN scores at each visit, indicating less important somatic symptoms with treatment time. At 2 weeks, the PHQ-15 score decreased by −3.5 ± 3.8 points from baseline, and by the end of the 8-week treatment period, the reduction reached −5.8 ± 4.4 points ($P < 0.001$). Similarly, the SSS-CN score decreased by −7.9 ± 8.0 points at two weeks, with a further reduction to −12.8 ± 10.3 points at the 8-week endpoint ($P < 0.001$), indicating significant improvement in somatic symptoms (Table 2 and Figure 2).

Secondary Outcome Measures

Secondary outcome measures included changes in the HAMD-17, VAS for pain, MFI-20, and SDS. There was a significant reduction in HAMD-17 scores across all visits, with a decrease of −9.3 ± 5.7 points at two weeks, and a total reduction of −15.3 ± 7.4 points by the end of the 8-week treatment period ($P < 0.001$), reflecting marked improvement in depressive symptoms. Pain levels, as measured by VAS, also improved significantly. The VAS score

Table 2 The Change From Baseline of Outcome Measures at Each Visit Point (FAS)

Visit point	Score (Mean ± SD)	Change from Baseline (Mean ± SD)	*P*
PHQ-15			
Baseline	13.7 ± 4.4	—	
Week 2	10.0 ± 4.8	−3.5 ± 3.8	<0.001
Week 4	9.4 ± 4.5	−4.1 ± 4.1	<0.001
Week 8	8.0 ± 4.8	−5.8 ± 4.4	<0.001
SSS-CN			
Baseline	50.1 ± 9.7	—	
Week 2	42.2 ± 11.1	−7.9 ± 8.0	<0.001
Week 4	41.0 ± 10.9	−9.1 ± 8.9	<0.001
Week 8	37.3 ± 10.5	−12.8 ± 10.3	<0.001
HAMD-17			
Baseline	22.7 ± 4.7	—	
Week 2	13.4 ± 5.7	−9.3 ± 5.7	<0.001
Week 4	10.5 ± 5.4	−12.2 ± 7.1	<0.001
Week 8	7.6 ± 5.7	−15.3 ± 7.4	<0.001
VAS			
Baseline	4.42 ± 2.45	—	
Week 2	3.22 ± 2.31	−1.20 ± 1.99	<0.001
Week 4	2.98 ± 2.22	−1.41 ± 1.68	<0.001
Week 8	2.42 ± 2.09	−1.97 ± 2.44	<0.001
MFI-20			
Baseline	75.6 ± 9.7	—	
Week 2	71.9 ± 11.7	−3.7 ± 9.3	0.0046
Week 4	69.8 ± 10.2	−5.8 ± 11.0	<0.001
Week 8	63.2 ± 14.2	−12.8 ± 14.1	<0.001
SDS			
Baseline	17.9 ± 6.6	—	
Week 2	13.3 ± 7.4	−4.6 ± 5.9	<0.001
Week 4	12.9 ± 7.5	−5.0 ± 6.3	<0.001
Week 8	9.9 ± 6.7	−8.3 ± 6.5	<0.001

Abbreviations: PHQ-15, Patient Health Questionnaire-15; SSS-CN, Somatic Symptom Scale-China; HAMD-17, 17-item Hamilton Depression Rating Scale; VAS, Visual Analog Scale; MFI-20, Multidimensional Fatigue Inventory-20; SDS, Sheehan Disability Scale.

decreased from a baseline of 4.42 ± 2.45 to −1.97 ± 2.44 by the end of the 8-week period ($P < 0.001$), indicating a significant reduction in pain intensity. The MFI-20 scores, which assess fatigue, showed a significant reduction from baseline, with a decrease of −12.8 ± 14.1 points by week eight ($P < 0.001$), indicating a considerable reduction in fatigue symptoms. The SDS scores decreased significantly at all time points, with a reduction of −8.3 ± 6.5 points by the end of the study ($P < 0.001$), demonstrating significant improvements in functional disability (Table 2 and Figure 2).

Pearson's correlation analysis showed that at the end of the second week of treatment, PHQ-15 ($r = 0.49$, $P < 0.001$) and SSS-CN ($r = 0.32$, $P = 0.027$) scores were significantly correlated with the improvement of HAMD-17 scores. At the

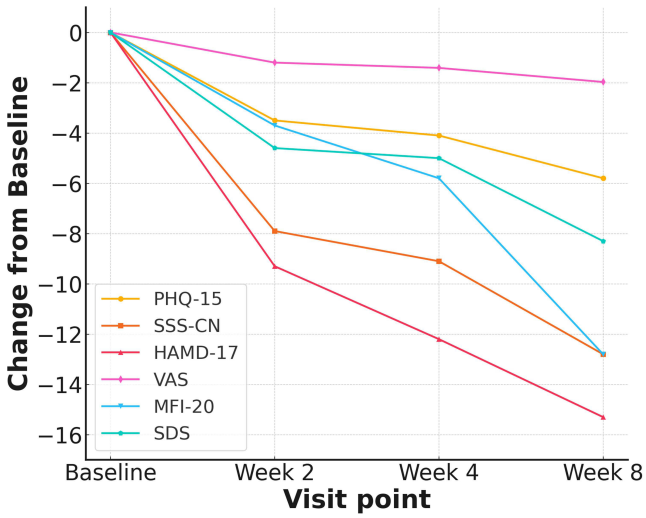

Figure 2 The change from baseline of different outcome measures at each visit point (FAS). The graph shows the mean change in scores from baseline to Week 8 for the following assessments: PHQ-15 (Patient Health Questionnaire-15), SSS-CN (Somatic Symptom Scale-China), HAMD-17 (17-item Hamilton Depression Rating Scale), VAS (Visual Analog Scale), MFI-20 (Multidimensional Fatigue Inventory-20), and SDS (Sheehan Disability Scale). Each line represents the trajectory of score changes over time, with each marker corresponding to Baseline, Week 2, Week 4, and Week 8. FAS, full analysis set.

end of the eighth week of treatment, the correlation became more significant with the continuation of treatment, with correlation coefficients of $r = 0.56$ ($P < 0.001$) and $r = 0.53$ ($P < 0.001$), respectively (Table 3).

Safety Assessments

The overall occurrence of adverse events during the study period was 52.5%, of which adverse events greater than 5% included dizziness (11.5%), diarrhea (8.2%), and nausea (6.6%). All adverse events were mild to moderate. There were no serious adverse events, and no participants withdrew from the study due to adverse events. In addition, Toludesvenlafaxine hydrochloride sustained-release tablets had no significant effects on blood pressure, electrocardiogram, blood biochemistry, blood routine (Table 4).

Table 3 Correlation Between the Improvement of HAMD-17 Score and the Change of PHQ-15 and SSS-CN Score

	n	*r*	*P*
Baseline			
PHQ-15	54	0.1416	0.3069
SSS-CN	54	0.1819	0.1881
After 2 weeks of treatment			
PHQ-15	54	0.4987	0.0001
SSS-CN	54	0.349	0.0097
After 4 weeks of treatment			
PHQ-15	53	0.6298	<0.0001
SSS-CN	50	0.6284	<0.0001
After 8 weeks of treatment			
PHQ-15	50	0.6483	<0.0001
SSS-CN	54	0.4987	0.0001

Abbreviations: PHQ-15, Patient Health Questionnaire-15; SSS-CN, Somatic Symptom Scale-China; HAMD-17, 17-item Hamilton Depression Rating Scale.

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Table 4 Occurrence of Adverse Events During the Treatment (SS)

Adverse Events		N=61	%
Digestive system	Gastrointestinal discomfort	1	1.6
	Stomachache	1	1.6
	Distention	1	1.6
	Celialgia	1	1.6
	Diarrhea	5	8.2
	Nausea	4	6.6
	Dry mouth	2	3.3
	Poor appetite	2	3.3
	Belching	1	1.6
	Constipation	1	1.6
Mental system	Tired	1	1.6
	Be irritable	1	1.6
	Be on edge	1	1.6
	Intense	1	1.6
Nervous system	Insomnia	1	1.6
	Headache	2	3.3
	Giddy	7	11.5
Whole body system	Fatigue	1	1.6
	Perspire	3	4.9
Hepatobiliary system	Abnormal liver function	1	1.6
	Alanine aminotransferase increased	1	1.6
	Glutamyltransferase was elevated	1	1.6
Cardiovascular system	Palpitation	1	1.6

Notes: Drug-related adverse events are those that are definitely related, likely related, or possibly related to the drug.
Abbreviations: AEs, adverse events; SS, safety set.

Discussion

This single-arm, multicenter clinical trial demonstrated significant reductions in both somatic and depressive symptom severity according to improvements in PHQ-15, SSS-CN, HAMD-17, VAS for pain, MFI-20, and SDS scores, highlighting the potential of this treatment approach for the management of MDD and somatic symptoms. This study innovates by focusing on the improvement in somatic symptoms, an approach that could help manage the severity of MDD.[9] Furthermore, toludesvenlafaxine hydrochloride demonstrated a favorable safety profile with no serious adverse events reported.

Toludesvenlafaxine hydrochloride, a new triple reuptake inhibitor, is designed as an extended-release oral tablet for treating MDD in adults. It inhibits the transport proteins responsible for clearing dopamine, serotonin, and norepinephrine from the synaptic cleft, thereby increasing the levels of these neurotransmitters in the brain's striatum.[23] Toludesvenlafaxine exhibits high binding affinities and inhibitory effects on serotonin (SERT), norepinephrine (NET), and dopamine (DAT) transporters. The IC50 values for ansofaxine show different potencies: 31.4 nM for SERT, 586.7 nM for NET, and 733.2 nM for DAT, respectively. Compared to venlafaxine, toludesvenlafaxine demonstrates a stronger and more balanced inhibition across the three types of transporters, potentially offering enhanced efficacy in treating MDD.[24] Toludesvenlafaxine alleviates somatic symptoms in MDD through its balanced inhibition of serotonin and norepinephrine reuptake. For serotonin, the inhibition increases its levels, helping to reduce pain perception, alleviate gastrointestinal disturbances, and improve overall emotional stability, which in turn diminishes physical symptoms like headaches and GI issues. For norepinephrine, the increased levels enhance energy, focus, and cognitive function, while

also playing a critical role in descending pain modulation pathways, effectively reducing chronic pain and fatigue associated with depression.

Similar to SSRIs like fluoxetine, toludesvenlafaxine effectively reduced depressive symptoms, but the main advantage of toludesvenlafaxine is the notable efficacy in alleviating somatic symptoms, which are often less responsive to SSRIs alone.[25] This dual action on MDD and somatic symptoms aligns toludesvenlafaxine more closely with SNRIs like duloxetine, known for treating both depressive and somatic symptoms, especially in patients with coexisting pain.[26] The significant effect sizes across various symptom scales suggest that toludesvenlafaxine may offer an efficacy profile comparable to or even better than traditional SNRIs and TCAs, like amitriptyline, which has shown the largest effect size for treating somatic symptoms.[25] Additionally, toludesvenlafaxine's favorable safety profile, with no serious adverse events, compares well to SSRIs and is superior to TCAs, which have a higher risk of adverse effects.[27]

Sexual dysfunction is a significant concern with antidepressant therapy and can impact patient adherence. SNRIs like duloxetine may mitigate some of the serotonin-related sexual side effects seen with SSRIs. For instance, treatment-emergent sexual dysfunction was significantly lower with duloxetine compared to paroxetine (46% vs 61%) in both male and female patients, although both rates were higher than placebo.[28] Similarly, duloxetine showed lower rates of sexual dysfunction compared to escitalopram in short-term use, though this advantage may not persist long-term.[29] Kennedy et al reported that venlafaxine-related adverse effects were significantly lower in women compared to paroxetine and sertraline, but not in men.[30] Desvenlafaxine succinate, the major active metabolite of venlafaxine and approved as an antidepressant in the United States, similarly appears to have lower sexual adverse effects in women compared to men, though this observation is primarily based on spontaneous self-reports.[31] The Phase 3 clinical trial results indicated that after 8 weeks of treatment with toludesvenlafaxine, there was no significant difference in ASEX total score change compared to placebo, and no newly developed sexual dysfunction were reported.[21] These findings suggest that toludesvenlafaxine may offer a favorable sexual side effect profile compared to other antidepressants, potentially improving patient adherence.

While our study did not specifically assess sleep disturbances or hot flashes, existing research shows that SSRIs like citalopram and SNRIs like venlafaxine effectively reduce these symptoms in menopausal women.[32] Given toludesvenlafaxine's dual mechanism, it may offer similar benefits, potentially making it a valuable option for menopausal women with MDD who also experience these symptoms.

The findings from our study offer new insights into the treatment of MDD with prominent somatic symptoms using toludesvenlafaxine hydrochloride sustained-release tablets, which is the main innovation of the present study. This trial is notable as the first to assess the efficacy and safety of toludesvenlafaxine in this specific context, and the results are promising, demonstrating significant reductions in both depressive and somatic symptoms. The data suggest that toludesvenlafaxine could be a viable first-line treatment option for MDD, particularly in patients where somatic symptoms, such as pain, are prominent. Additionally, the potential effectiveness of toludesvenlafaxine in managing related conditions like sexual dysfunction, sleep disturbances, and hot flashes could broaden its clinical application, especially in targeted populations such as menopausal women. While this study demonstrates promising results, it is essential to acknowledge certain limitations that should guide future research endeavors. The modest sample size limits the generalizability of the findings. The single-arm design lacking a placebo group prevents definitive conclusions regarding the sole impact of drug on observed improvements. The 8-week timeframe, though showcasing significant changes, requires longer-term investigation for a comprehensive efficacy and safety profile. Future research should prioritize larger, longer-term, multi-center randomized controlled trials incorporating placebo or active controls to validate efficacy and safety of toludesvenlafaxine across diverse MDD populations. Further exploration is warranted regarding the efficacy across various somatic symptom subtypes (eg, pain, fatigue, sleep) and its synergistic potential with psychotherapy.

Conclusion

In conclusion, toludesvenlafaxine hydrochloride sustained-release tablets demonstrate strong potential as a treatment option for MDD with prominent somatic symptoms. The promising results from this study highlight its balanced efficacy and safety, suggesting it could play a significant role in future treatment strategies, especially for somatic symptoms in MDD. To solidify its place in clinical practice, further research, particularly randomized controlled trials, will be essential

in confirming these findings and determining exact position of toludesvenlafaxine in the treatment hierarchy for MDD and somatic symptoms.

Data Sharing Statement

The original contributions presented in the study are included in the article, further inquiries can be directed to the corresponding author.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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