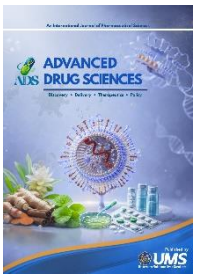
Advanced Drug Sciences

Volume 1 *https://doi.org/to be assigned* *Issue 1*

Journal Homepage: https://journals2.ums.ac.id/ads/index



REVIEW ARTICLE

Comparative Evaluation of Sertraline and Fluoxetine in Major Depressive Disorder: A Structured Review of Safety, Pharmacokinetics, and Clinical Dosing

Md. Toufiqul Islam[1]*, Fatema Akhter[1 †], Fahamida Binta Anower[1†]

1 Department of Pharmacy, Faculty of Science, Engineering & Technology, Bangladesh University, Mohammadpur, Dhaka - 1207, Bangladesh.

† These authors contributed equally.

***Corresponding Author:** Email: riyadtoufiq002@gmail.com; Tel: +889112663; Fax: +889119555.*

Citation: Islam, M. T., Akhter, F., & Anower, F. B. (2026). Comparative Evaluation of Sertraline and Fluoxetine in Major Depressive Disorder: A Structured Review of Safety, Pharmacokinetics, and Clinical Dosing. *Adv. Drug Sci., 1*(1), exxxx. DOI: to be assigned

ABSTRACT

Major depressive disorder is a prevalent psychiatric condition and a prominent cause of disability around the world. Selective serotonin reuptake inhibitors remain the first-line pharmacological options and are the most frequently used, with sertraline and fluoxetine shown to be effective and safe. Although both drugs inhibit serotonin reuptake, they have distinct pharmacokinetic and safety profiles that can affect clinical decision-making. This structured narrative review compares sertraline and fluoxetine regarding their pharmacokinetic properties, such as absorption, distribution, metabolism, elimination, peak plasma concentration, time to peak concentration, area under the concentration–time curve, and elimination half-life (t1/2), and adverse effect profiles. Systematic searches were conducted in electronic databases, such as PubMed, Scopus, ScienceDirect, Google Scholar, and the Cochrane Library, for publications from 2000 to 2025. After screening and quality assessment, 78 studies were included in the review. The synthesized evidence suggests that both drugs are equally effective in treating depression. Fluoxetine, however, has a longer half-life and more potent inhibition of cytochrome P450 2D6 (CYP2D6), which could increase drug–drug interactions, enhance adherence, and decrease discontinuation effects. In contrast, sertraline has a lower inhibition potential for the CYP450 system, fewer clinically important drug-drug interactions, and a better cardiovascular safety profile. In summary, the choice of antidepressant should be individualized based on patient-specific factors, comorbidities, tolerability, cardiovascular parameters, hepatic function, and any other drugs the patient is taking to achieve the best therapeutic effect.

ARTICLE INFORMATION

Keywords:
Sertraline
Fluoxetine
SSRIs
Pharmacokinetics

Received	21 May 2026
Revision	22 Jun 2026
Accepted	22 Jun 2026
Published	26 Jun 2026

1. INTRODUCTION

Major depressive disorder (MDD), also known as depression, is a complex and serious illness that impacts mental and physical health, characterized by a wide range of symptoms such as psychomotor retardation, loss of appetite, suicidal ideation, depressed mood, and anhedonia [1]. In 2018, over 300 million people

worldwide were affected by this disorder. The study of 30 countries showed that almost 11% of the population develops depression over the duration of their lifetime. With the onset of COVID-19, 53 million (28%) more people are affected by this disorder, indicating an alarming wave concurrently.

Conventional antidepressant treatments are available, but approximately one-third of patients with MDD do not respond, which increases the risk of further health problems and decreases the chance of successful recovery. Despite adequate knowledge of depression, researchers have not yet identified the biological causes of depression. This lack of knowledge persists, hindering the development of truly effective and innovative treatments [2]. For initial treatment, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are recommended due to their relatively mild side-effect profiles and effectiveness. Both SSRIs and SNRIs help in improving the symptoms of depression and preventing recurrences, while also offering better tolerability compared to other medications, such as tricyclic antidepressants or the monoamine oxidase inhibitors [3]. The most commonly prescribed SSRIs, such as sertraline and fluoxetine, are used in both psychiatric and general medical practice. The first SSRI to be approved by the Food and Drug Administration (FDA) for GAD (Generalized Anxiety Disorder), fluoxetine, has a well-established efficacy profile.

On the other hand, sertraline has a very good safety profile and a wide spectrum of clinical use, including FDA approval for the use in PTSD (Post-Traumatic Stress Disorder) and OCD (obsessive-compulsive disorder), social anxiety disorder, and MDD. Sertraline was the only SSRI to be approved for use in the treatment of PTSD [4, 5]. Although both drugs have the same mechanism of action: inhibiting the reuptake of serotonin in the synaptic gap, there are important differences among these drugs, clinically relevant differences in terms of pharmacokinetics, adverse effects, and drug–drug interactions. Variations in hepatic metabolism, CYP450 enzyme inhibition, and drug half-life influence the likelihood of drug-drug interactions [6].

Furthermore, there are differences in side effect profiles; for patients with cardiac issues, sertraline has a more favorable side effect profile compared to fluoxetine, which can have more early CNS activation and sexual dysfunction [7], [8]. Patient-related factors (e.g., concomitant liver disease, cardiovascular risk, age, reproductive status) should be considered when choosing between these medications. In addition, pharmacokinetic properties must be considered to explain the onset of action, efficacy, and tolerability. Comparative knowledge of these differences is critical when selecting an antidepressant for the individual, especially those with liver dysfunction, polypharmacy, and special populations, as well as in patients with cardiovascular disease. This narrative review compares the safety profiles, pharmacokinetic profiles, and clinical dosing information of these two drugs.

2. METHODS

This study was designed as a structured narrative review comparing the adverse effects, pharmacokinetic properties, and clinical dosing considerations of sertraline and fluoxetine in the treatment of major depressive disorder and related psychiatric disorders. A literature search was conducted in electronic databases, including PubMed, Scopus, ScienceDirect, Google Scholar, and the Cochrane Library, for studies published between January 2000 and 2025. The search strategy included combinations of the following terms: "sertraline" or "fluoxetine" or "selective serotonin reuptake inhibitors" or "major depressive disorder" or "pharmacokinetics" or "adverse effects" or "CYP450 interactions" or "AUC" or "Cmax" or "Tmax" or "half-life".

Published peer-reviewed English-language original articles, review articles, meta-analyses, clinical trials, and regulatory documents were considered. A total of 742 studies were initially identified. After duplicate removal, eligibility screening, and relevance assessment, 78 studies were included in the review. Priority was given to studies with clear pharmacological evidence and relevant clinical significance. Selected articles also included related references, which were consulted to ensure thorough coverage of the topic. The article was not designed as a systematic review; there has been no formal PRISMA methodology, quantitative meta-analysis, or risk-of-bias assessment. Rather, the available evidence was critically reviewed and synthesized to provide comparative insight into the clinical profiles of sertraline and fluoxetine.

3. ADVERSE EFFECTS

3.1. Hepatic Effects

Sertraline and fluoxetine primarily undergo hepatic metabolism, predominantly by cytochrome P450 enzymes, particularly CYP2D6, CYP3A4, and CYP2C19 [9], which can influence their risk of hepatic adverse effects.

Fluoxetine has a long half-life (2-4 days), and the active metabolite norfluoxetine has an even longer half-life (7-15 days). It is mainly metabolized by CYP2D6 and is a potent inhibitor of this pathway, which means it may interact more with other drugs and accumulate at higher concentrations, especially in poor metabolizers and patients with liver enzyme abnormalities. Sertraline, by comparison, has a shorter half-life of about 1 day and is mainly metabolized to desmethylsertraline by CYP3A4.

Sertraline is a weak inhibitor of CYP2D6 compared to fluoxetine and therefore has a lower risk of clinically important drug interactions [10]. Fluoxetine is more likely to interact with other drugs due to its potent CYP2D6 inhibitory properties and long half-life, whereas sertraline is somewhat more likely to be hepatotoxic, particularly with long-term treatment and/or in susceptible patients [11]. Rarely, Sertraline can cause liver damage (drug-induced liver injury or DILI), leading to serious health problems. Liver damage from medications can manifest in various ways, and some individuals may have no signs or symptoms [12]. While fluoxetine is generally safe, it has fewer stomach or digestive side effects in people who are taking it for depression than other antidepressant drugs in the same class [13]. Rare but serious hepatotoxicity causing withdrawal was reported by the US Food and Drug Administration post-marketing surveillance [14]. Mechanistically, sertraline hepatotoxicity may be associated with down-regulation of drug-metabolizing enzymes and mitochondrial dysfunction, thereby decreasing the liver's ability to metabolize other drugs [15].

Fluoxetine is generally considered to be low risk for liver toxicity, although rare reports of drug-induced liver injury have been reported. Furthermore, it can affect oxidative stress markers in the liver, suggesting potential effects on liver function [16]. Severe drug-induced liver injury is rare, and clinically significant hepatotoxicity (increased liver enzyme levels) is uncommon for either type of SSRI. Experimental data indicate that fluoxetine-induced liver injury can be mediated by inflammatory and oxidative pathways, while sertraline-induced liver injury is associated with mitochondrial dysfunction and oxidative stress.

3.2. Cardiac Effects

SSRIs are generally considered cardio-safe. The SSRIs are generally considered to be cardio-vascularly safe, particularly compared with tricyclic antidepressants. However, the rare risk of QT interval prolongation is known, especially with high doses or when combined with other drugs [17]. Fluoxetine-induced QT prolongation in some patients with strong CYP2D6 inhibitory results in supratherapeutic serum levels of concomitant drugs also metabolized by CYP2D6 [18]. This would potentially be more harmful to the elderly or individuals with a congenital long QT syndrome [19].

Sertraline is more cardiovascular safe and is often preferred as an SSRI in patients with coronary artery disease and/or arrhythmia risk [20]. This has been shown in a randomized cardiac study, in which there was no significant prolongation of the QTc interval, even at higher sertraline doses [21]. It has been shown to be well tolerated, safe, and effective in elderly patients with vascular comorbidities, even when co-administered with other medications, and has not been associated with an increased risk of adverse cardiac events [22]. Other large cohort studies do not detect any differences in the risk of sudden cardiac death or total mortality between sertraline and fluoxetine, indicating that both are relatively safe; however, sertraline may be the preferred option in individuals with a higher cardiovascular risk [23]. The 2021 guidelines from the American Heart Association for patients who already had a MI indicate that sertraline is the safest of the SSRIs to use in these patients [24].

3.3. Neurological / CNS Effects

Fluoxetine and sertraline are centrally acting drugs that both increase serotonin levels in the synapse [25]. But they have dissimilar CNS side effects related to onset [26]. The risk for early activation symptoms such as anxiety, agitation, insomnia, and restlessness is higher with fluoxetine than with other drugs [27]. This particularly manifests in young adults and adolescents, so that suicidal ideation is among the drug's black box warning in individuals 24 years or younger [28]. The side effects of Sertraline are somnolence, tremor, and dizziness [29], and it is more sedating. Its sedative effect is at present small, but this will, at first, be beneficial for patients with comorbid insomnia [30]. Intriguingly, sertraline was neuroprotective in some preclinical models, and neuroinflammation was a potential application for sertraline in the treatment of post-stroke depression. Interestingly, sertraline was neuroprotective in some, but not all, preclinical models, and sertraline was promising in relation to the treatment of post-stroke depression and neuroinflammation [31].

3.4. Sexual Dysfunction

Two selective serotonin reuptake inhibitors (SSRIs) commonly used, sertraline and fluoxetine, have been

consistently linked to a high risk of sexual dysfunction, although there are some differences in the profiles of these medications [8]. According to the study-level meta-analysis by Serretti & Chiesa (2009), 31 studies reported that: Sexual dysfunction: a high incidence of sexual dysfunction in both men and women was produced by fluoxetine: 57 % of men and 73 % of women treated reported sexual dysfunction [32]. Sertraline was still more likely to be reported with delayed ejaculation and decreased libido, but reported sexual satisfaction was slightly better [33]. The physiologic mechanism involves an increase of synaptic serotonin due to SSRIs, which inhibits the dopamine/nitric oxide pathway, known to be involved in sexual arousal and orgasm [34]. Both drugs can lead to a decrease in libido and orgasm in men; however, the decrease in progressive sperm motility is more evident at clinically relevant doses of fluoxetine [35], and the decrease in sperm motility is more evident at higher, supratherapeutic doses of sertraline.

Treatment strategies for SSRIs-induced SD are:

- Decrease dose (where appropriate)
- Drug holidays (less preferred for fluoxetine owing to long half-life)
- Switching to or initiating bupropion, mirtazapine, or PDE5 inhibitors [36].

Table 1. Summary of comparative adverse effects of sertraline and fluoxetine

Parameter	Sertraline	Fluoxetine	Clinical Significance
Hepatic Effects	Rare hepatotoxicity; possible mitochondrial dysfunction and oxidative stress-related liver injury	Rare hepatotoxicity; increased interaction risk due to CYP2D6 inhibition and long half-life	Use cautiously in patients with hepatic disorders
Cardiac Effects	Lower risk of QT prolongation; often preferred in coronary artery disease and post-MI patients	QT prolongation is reported particularly at high doses or with CYP2D6 interactions	Sertraline is generally preferred in patients with higher cardiovascular risk
CNS Effects	More associated with somnolence, dizziness, and tremor	More activating: insomnia, agitation, anxiety, restlessness	Drug selection should consider the patient's sleep and anxiety profile
Sexual Dysfunction	Delayed ejaculation, decreased libido, and orgasm difficulties	High rates of libido reduction and orgasm dysfunction	The major cause of treatment non-adherence

4. CLINICAL PHARMACOKINETICS (ADME)

SSRIs are subject to a complex set of drug-disposition processes that play a leading role in the time course of their effects, clinical effectiveness, tolerability, and clinical application across different patient populations [37]. The ADME properties (Absorption, Distribution, Metabolism, Excretion) of sertraline and fluoxetine contribute to understanding their pharmacological effects and dosing regimens. Norfluoxetine remains active in the body for a long time, which helps to maintain constant therapeutic effects and minimizes withdrawal effects. However, the potential of metabolite accumulation can lead to longer effects and make it more difficult to switch antidepressants. Sertraline, however, has a shorter half-life, offering greater flexibility in dose adjustment and safer washout strategies [38], [39].

4.1. Absorption

Fluoxetine is well absorbed by oral administration, with ~72% bioavailability. The peak plasma levels are reached at 6–8 hours after dosing. Food intake has no clinically significant effects on fluoxetine absorption [40]. The absolute bioavailability of sertraline is ~44%, although food significantly increases its absorption by up to 40%, and the time to reach peak plasma concentration (Tmax) ranges from 4.5 to 8.4 hours [41]. In 2020, researchers conducted a study on the pharmacokinetics of sertraline and found that its effects are quite heterogeneous among individuals. The drug's absorption and blood levels, however, are more stable and predictable at doses ≥50. The study also confirms that administering sertraline with food increases its efficacy [42]. One study conducted in 2023 included 41 healthy men who took fluoxetine (20 mg) with or without food; there was no significant difference in the drug's effects in the body between the two treatments. The key measures, such as the amount absorbed, the duration of time in the system, and the manner of processing, were virtually identical in both scenarios. The only difference was that food slightly delayed reaching peak levels, but this did not affect effectiveness [43].

4.2. Distribution

Both fluoxetine and sertraline have high plasma protein binding and large volume of distribution (Vd), that is, a large amount of drug is distributed into tissues rather than staying in the bloodstream [44], [45]. Pharmacokinetic studies have revealed that sertraline has an apparent volume of distribution of about 20 L/kg [46] and fluoxetine has a reported volume of distribution of 20-42 L/kg [47]. Fluoxetine and its active metabolite, norfluoxetine, are also highly distributed and 98.5% protein bound. Both drugs have large Vd values, suggesting they penetrate tissues and have a long duration of action; this is especially true for fluoxetine due to the persistence of its active metabolite.

4.3. Metabolism

Fluoxetine is predominantly metabolized through CYP2D6, but also by CYP2C9 and CYP3A4 to its active metabolite, norfluoxetine. Norfluoxetine is as pharmacologically active as fluoxetine and has a longer half-life [48]. Sertraline is metabolized by CYP2B6, CYP2C19, and CYP2D6 to produce the weakly active desmethylsertraline metabolite [49].

CYP inhibition: Fluoxetine is a significant CYP2D6 inhibitor, which may affect drug-drug interactions, particularly when multiple drugs are co-administered [18]. Sertraline weakly to moderately inhibits CYP2D6 with less severe interactions [50].

Table 2. CYP450 Interaction Profile of Sertraline and Fluoxetine [18, 48-50].

CYP450 Parameter	Sertraline	Fluoxetine	Clinical Relevance
CYP2D6 Inhibition	Weak to moderate inhibitor	Potent inhibitor	Fluoxetine has greater drug–drug interaction potential
CYP3A4 Interaction	Mild interaction potential	Moderate interaction potential	Important in polypharmacy patients
CYP2C19 Metabolism	Significant metabolic pathway	Minor metabolic role	Genetic polymorphisms may affect sertraline exposure
Drug Interaction Risk	Lower l interaction risk(overall)	Higher interaction risk	Important with antipsychotics, beta-blockers, tamoxifen

4.4. Excretion

Fluoxetine and its metabolite are mainly excreted by the kidneys (approximately 65%), with 5–10% excreted unchanged. A smaller portion, around 15%, is eliminated via feces [51]. On the other hand, Sertraline is also eliminated via both renal and fecal routes. But less than 1% is excreted unchanged through urine [52].

4.5. Half-Life

Pharmacokinetic parameters showed that the elimination half-lives of the parent drugs and their pharmacologically active metabolites were extended. The half-life (t½) of fluoxetine following chronic use was 1–4 days, and its major active metabolite, norfluoxetine, had an even longer half-life of 7–15 days [53]. Similarly, the half-life of sertraline has been reported to be related to gender, age, and dose, with some studies suggesting that it is shorter in young males (approximately 22 hours) and longer in elderly individuals and females (up to 36 hours) [54]. It does not seem to inhibit serotonin reuptake; its major active metabolite, desmethylsertraline [55], does. Clinical implications: The delayed onset of adverse effects and extended washout periods are the other drawbacks of fluoxetine's long half-life, which allows for once-weekly dosing [56]. A physician swiftly switching to other antidepressant medications is possible due to sertraline's short half-life [57].

5. PHARMACOKINETIC CONSIDERATIONS

The significant pharmacokinetic parameters used to evaluate the onset, intensity, and duration of antidepressant effects include the area under the plasma concentration time curve (AUC), maximum plasma concentration (Cmax), time to reach maximum plasma concentration (Tmax), and elimination half-life (t1/2). Multiple doses of sertraline at 200 mg/day result in an AUC of approximately 2000-3000 ng·h/mL [42], and multiple doses of fluoxetine at 20 mg/day (with both parent drug and active metabolite norfluoxetine included) also result in an AUC of approximately 2000-3000 ng·h/mL [58].

The pharmacological activity of fluoxetine is longer than that of paroxetine; however, because norfluoxetine has a long circulation time, leading to an

increased cumulative exposure and prolonged effect [59]. Sertraline's Cmax is 20–166 ng/mL and dose-dependent [42], and if fluoxetine and norfluoxetine are included, then fluoxetine's Cmax is 66–627 ng/mL [60]. Tmax is not significantly different between the two drugs, as sertraline's peak plasma level is reached in 4.5–8 hours [42] and fluoxetine's in 4–8 hours after administration [61]. Their elimination half-lives also differ significantly: sertraline has a half-life of about 32 hours [62], whereas during chronic use, fluoxetine has a half-life of 2–6 days, and its active metabolite, norfluoxetine, may have a half-life of up to 16 days [53]. Thus, the typical time to reach steady state is 7 days for sertraline [52] and 4–5 weeks for fluoxetine due to the slow accumulation of norfluoxetine [63]. The clinical implications of these pharmacokinetic differences include dosing regimens, discontinuation of drugs, and switching antidepressant drugs.

Table 3. Comparative Pharmacokinetic Parameters of Sertraline and Fluoxetine [40-41], [44-56]

Pharmacokinetic Parameter	Sertraline	Fluoxetine
Bioavailability	Approximately 44%	Approximately 72%
Tmax (Time to Peak Concentration)	4.5–8 hours	6–8 hours
Cmax (Peak Plasma Concentration)	20–166 ng/mL	66–627 ng/mL
AUC (Area Under the Curve)	~2000–3000 ng·h/mL (nanogram-hours per milliliter)	~2000–3000 ng·h/mL including norfluoxetine
Half-life (t1/2)	Approximately 32 hours	Approximately 1-4 days
Active Metabolite Half-life	Desmethylsertraline weakly active	Norfluoxetine: 7–15 days
Steady-State Achievement	Approximately 7 days	Approximately 4–5 weeks
Protein Binding	Approximately 98%	Approximately 98.5%
Volume of Distribution (Vd)	Approximately 20 L/kg	Approximately 20–42 L/kg
Primary Metabolic Enzymes	CYP2B6, CYP2C19, CYP2D6	CYP2D6, CYP2C9, CYP3A4
Primary Excretion Route	Renal and fecal	Mainly urinary
Food Effect on Absorption	Food increases absorption up to 40%	Minimal food effect

6. DOSING AND CLINICAL USE

Understanding the dosing regimens of sertraline and fluoxetine is important for optimizing treatment in patients with major depressive disorder and anxiety disorders. For sertraline, treatment typically begins at 50 mg/day, continues within a 50-200 mg/day maintenance range, and tops out at 200 mg/day [64]. Fluoxetine starts at 20 mg/day, is maintained between 20 and 60 mg/day, and may be increased to 80 mg/day [65]. Physicians may also raise sertraline in weekly doses of 25-50 mg. The dose titration would have been more quickly reflected in the plasma concentration [66] since it has a shorter half-life. The titration of fluoxetine is slower because of its long half-life and metabolite accumulation. Also available for maintenance therapy is 90mg/week dosing [67].

Special Populations, such as elderly patients: Sertraline is the typical antidepressant used as it has a shorter half-life and there is less accumulation or drug-drug interactions. For Pregnancy/lactating women: Fluoxetine is category C; although neonatal adaptation syndrome and possible septal defects have been reported [68]. Sertraline is category C as well, though with more reassuring data for use in pregnancy and breastfeeding [69]. Switching Antidepressants: Fluoxetine is a long-acting drug that requires a 5-week washout period to prevent serotonin syndrome, as it inhibits monoamine oxidase inhibitors (MAOIs) [70], [71]. Furthermore, sertraline is cleared from the body in only 2 weeks, which provides greater flexibility for cross-tapering or switching [72].

7. DISCUSSION

This review demonstrates that, while sertraline and fluoxetine belong to the same therapeutic class and primarily inhibit serotonin reuptake, there are clinically significant differences in pharmacokinetic characteristics, adverse-effect profiles, drug-drug interaction potential, and patient-specific applications. These

differences may impact antidepressant selection in specific therapeutic contexts.

Fluoxetine is metabolized to the active metabolite norfluoxetine, which helps to maintain therapeutic activity and minimize withdrawal symptoms in patients with intermittent adherence [58]. However, extended exposure to the parent medication and metabolite may delay the resolution of undesirable effects and complicate transitioning to other antidepressants. Moreover, fluoxetine is a potent CYP2D6 inhibitor, which may increase exposure to co-administered medicines, including antipsychotics, β-blockers, and tamoxifen, thereby increasing the likelihood of clinically significant drug-drug interactions [73].

Table 4. Clinical dosing comparison of sertraline and fluoxetine [64-72]

Clinical Parameter	Sertraline	Fluoxetine
Initial Dose	50 mg/day	20 mg/day
Maintenance Dose	50–200 mg/day	20–60 mg/day
Maximum Dose	200 mg/day	80 mg/day
Dose Titration	Faster titration possible	Slower titration due to long half-life
Once-Weekly Formulation	Not available	Available (90 mg/week)
Elderly Adjustment	Often preferred because of fewer interactions and shorter half-life	Requires caution because of accumulation
Pregnancy Considerations	Commonly preferred during breastfeeding	More fetal exposure concerns reported
Cardiovascular Patients	Preferred SSRI	Use cautiously in QT-risk patients
Switching Antidepressants	Easier switching, cross-tapering, and washout quicker. (2 weeks)	Longer washout period required (5- week)

Sertraline, on the other hand, inhibits CYP450 less strongly, has a shorter elimination profile, and allows for better dosing flexibility. These properties make it especially useful for individuals who take many drugs or have concomitant illnesses that necessitate cautious pharmacological treatment. Sertraline has also shown good cardiovascular tolerance and is often chosen in individuals with coronary artery disease due to its modest effects on cardiac conduction [74]. However, recent data indicate that both sertraline and fluoxetine are linked with a low risk of clinically significant QT prolongation, with no consistent differences observed between the two drugs [75,76].

Although both drugs are typically well tolerated, variations in adverse-effect patterns may impact treatment adherence. Sertraline appears to cause greater gastrointestinal side effects, including nausea and diarrhea, but fluoxetine is typically tolerated better. The two drugs have different central nervous system symptoms. Fluoxetine is known to cause activating effects such as anxiety and sleeplessness, whereas sertraline is more typically associated with light sedation [30]. Sexual dysfunction remained one of the leading causes of treatment dropout for both drugs, despite some studies indicating somewhat higher tolerability with sertraline in male patients [8].

Pharmacokinetic variations could potentially affect the duration and durability of adverse effects. The increased systemic exposure associated with fluoxetine contributes to sustained pharmacological activity, whereas sertraline's faster elimination profile allows for more rapid dose adjustment and may be beneficial in patients who are particularly sensitive to serotonergic side effects [77].

In terms of hepatic safety, either SSRI is unlikely to cause clinically significant liver impairment, and severe hepatotoxicity is quite rare. The majority of existing evidence comes from individual case reports and pharmacovigilance investigations, whereas higher-level clinical studies and post-marketing data consistently indicate that both drugs have favorable liver safety profiles. As a result, hepatic side effects should be considered rare and interpreted with caution in ordinary clinical practice. Reproductive concerns have a major impact on antidepressant choice. Current research generally supports sertraline as one of the preferred SSRIs during pregnancy and nursing because of lesser infant exposure and better neonatal outcomes [78].

Overall, both SSRIs show equivalent efficacy in the treatment of major depressive illness; however, differences in metabolism, interaction potential, and adverse-effect profiles provide unique advantages in some patient populations. Fluoxetine may be especially good for those who are concerned about their adherence, but sertraline looks to be beneficial for people who have cardiovascular illness, polypharmacy, or are more susceptible to drug-drug interactions. As a result, antidepressant selection should be tailored to the patient's specific comorbidities, concurrent drugs, tolerability, reproductive concerns, and preferences**.**

8. CONCLUSIONS

The decision to choose between sertraline and fluoxetine should consider individual patient characteristics to ensure a safe, effective, and well-tolerated medication. One of the major variations is how the drugs work in the body. Fluoxetine has a very long half-life and an active metabolite, which may be beneficial for those who may forget to take doses. Conversely, the same property makes rapid dose adjustments more challenging, increases the risk of drug–drug interactions (particularly by CYP2D6 inhibition), and increases the risk of prolonged side effects if the drug needs to be discontinued.

In contrast, sertraline has a shorter half-life, has fewer troublesome drug interactions, and is more readily dosed. This can be a suitable choice for people who need to take more than one medicine, elderly people, or those who require a change to their treatment or a dose adjustment without a long delay. For safety, patients with heart disease, particularly coronary artery disease, or a concern for QTc prolongation, may prefer to use sertraline.

Fluoxetine is also relatively safe but may cause activation (such as anxiety or insomnia) during early treatment and may have a greater risk of sexual side effects. Both drugs, though extremely rarely, influence the liver, so some caution and monitoring are always necessary. Other health conditions (particularly heart or liver problems), other medicines, sensitivity to certain side effects, pregnancy or breast-feeding, and a patient's ability to take a medicine regularly are all important. These considerations can help clinicians move beyond a 'one-size-fits-all' approach to treatment and select the most appropriate antidepressant for each patient, thereby optimizing therapeutic outcomes in the management of major depressive disorder.

9. LIMITATIONS AND FUTURE RECOMMENDATIONS

Future studies should examine pharmacogenetic variability, CYP450 polymorphisms, and real-world comparative effectiveness to further optimize antidepressant treatment on an individual basis.

Supplementary Materials

Not applicable.

Author's ORCID iDs

Md.Toufiqul Islam1: https://orcid.org/0009-0007-1144-7245
Fatema Akhter1: https://orcid.org/0009-0007-0114-4240
Fahamida Binta: https://orcid.org/0009-0005-1068-5271

Author Contributions

Author Contributions: Conceptualization, M.T.; Methodology, M.T.; Software, M.T., F.A., and F.B.; Validation, M.T., F.A. and F.B.; Formal Analysis, M.T.; Investigation, M.T., F.A., and F.B.; Resources, F.A., F.B.; Data Curation, F.A. and F.B.; Writing—Original Draft Preparation, M.T., F.A., and F.B.; Writing—Review and Editing, M.T., F.A., and F.B.; Visualization, M.T.; Supervision, M.T.; All authors have read and approved the published version of the manuscript.

Funding Information

This research received no external funding.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

Data Availability Statement

No new data were generated or analyzed in this study.

Acknowledgments

The authors sincerely acknowledge the valuable suggestions and support provided by faculty members during the preparation and revision of this manuscript.

Artificial Intelligence (AI) Declaration

During the preparation of this manuscript, the authors used Grammarly Premium for language editing and grammatical refinement. The authors reviewed, verified, and edited the generated content as necessary and take full responsibility for the final content of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Szoke-Kovacs Z, More CS, Szoke-Kovacs RI, Mathe EN, Frecska E. Selective inhibition of the serotonin transporter in the treatment of depression: sertraline, fluoxetine and citalopram. Neuropsychopharmacol Hung. 2020;22(1):4-15.
2. Namiot ED, Smirnovová D, Sokolov AV, Chubarev VN, Tarasov VV, Schiöth HB. Depression clinical trials worldwide: a systematic analysis of the ICTRP and comparison with ClinicalTrials. gov. Transl Psychiatry. 2024;14(1):315. doi:10.1038/s41398-024-03031-6
3. Huang J, Wang Y, Chen J, Zhang Y, Yuan Z, Yue L, Haro JM, Moneta MV, Novick D, Fang Y. Clinical outcomes of patients with major depressive disorder treated with either duloxetine, escitalopram, fluoxetine, paroxetine, or sertraline. Neuropsychiatr Dis Treat. 2018;26:2473-84. doi:10.2147/NDT.S159800
4. Edinoff AN, Akuly HA, Hanna TA, Ochoa CO, Patti SJ, Ghaffar YA, Kaye AD, Viswanath O, Urits I, Boyer AG, Cornett EM. Selective serotonin reuptake inhibitors and adverse effects: a narrative review. Neurol Int. 2021;13(3):387-401.
5. Hidalgo RB, Davidson JR. Selective serotonin reuptake inhibitors in post-traumatic stress disorder. J Psychopharmacol. 2000;14(1):70-6. doi:10.1177/026988110001400110
6. Hemeryck A, Belpaire FM. Selective serotonin reuptake inhibitors and cytochrome P-450 mediated drug-drug interactions: an update. Current drug metabolism. 2002;3(1):13-37. doi:10.2174/1389200023338017
7. Seifouri K, Kahdemi R, Hajikolaei FA, Rasekh F, Azadikhah F, Mehraban I, Alikhani R, Mirjalili A, Alipour M, Sadat-Madani SF, Chichagi F. Sertraline in depressed patients with or at risk for coronary heart disese: a systemic review. Am J Cardiovasc Dis. 2024;14(6):318.
8. Khazaie H, Rezaie L, Payam NR, Najafi F. Antidepressant-induced sexual dysfunction during treatment with fluoxetine, sertraline and trazodone; a randomized controlled trial. Gen Hosp Psychiatry. 2015;37(1):40-5. doi:10.1016/j.genhosppsych.2014.10.010
9. Lloret-Linares C, Bosilkovska M, Daali Y, Gex-Fabry M, Heron K, Bancila V, Michalopoulos G, Perroud N, Richard-Lepouriel H, Aubry JM, Desmeules J. Phenotypic assessment of drug metabolic pathways and P-glycoprotein in patients treated with antidepressants in an ambulatory setting. The J Clin Psychiatry. 2018;79(2):16m11387. doi:10.4088/jcp.16m11387
10. Spina E, Santoro V, D'Arrigo C. Clinically relevant pharmacokinetic drug interactions with second-generation antidepressants: an update. Clin Ther. 2008;30(7):1206-27. doi:10.1016/S0149-2918(08)80047-1
11. Dekelbab B, Brito E, Osman M. SUN-282 Sertraline-Induced Dyslipidemia and Liver Toxicity in a 17-Year-Old Adolescent. J Endocr Soc. 2019;3(Suppl 1):SUN-282. doi:10.1210/js.2019-SUN-282
12. Renemane L, Rancans E. Sertraline induced acute hepatocellular liver injury in patient with major depressive disorder: a case report. Front Psychiatry. 2024;15:1456455. doi:10.3389/fpsyt.2024.1456455
13. Wang Z, Li H, Kang Y, Liu Y, Shan L, Wang F. Risks of digestive system side-effects of selective serotonin reuptake inhibitors in patients with depression: a network meta-analysis. Ther Clin Risk Manag. 2022;18:799-812.doi:10.2147/TCRM.S363404
14. Babai S, Auclert L, Le-Louët H. Safety data and withdrawal of hepatotoxic drugs. Therapies. 2021;76(6):715-23. doi:10.1016/j.therap.2018.02.004
15. Almansour MI, Jarrar YB, Jarrar BM. In vivo investigation on the chronic hepatotoxicity induced by sertraline. Environ Toxicol Pharmacol. 2018;61:107-15. doi:10.1016/j.etap.2018.05.021
16. Ganguly R, Kumar R, Pandey AK. Baicalin provides protection against fluoxetine-induced hepatotoxicity by modulation of oxidative stress and inflammation. World J Hepatol. 2022;14(4):729. doi:10.4254/wjh.v14.i4.729
17. Beach SR, Kostis WJ, Celano CM, Januzzi JL, Ruskin JN, Noseworthy PA, Huffman JC. Meta-analysis of selective serotonin reuptake inhibitor-associated QTc prolongation. The J Clin Psychiatry. 2014;75(5):e441-9. doi:10.4088/jcp.13r08672
18. Deodhar M, Rihani SB, Darakjian L, Turgeon J, Michaud V. Assessing the mechanism of fluoxetine-mediated CYP2D6 inhibition. Pharmaceutics. 2021;13(2):148. doi:10.3390/pharmaceutics13020148
19. Borges JV, Ferraz MJ, Ja-nuzzi WA, Leila SA, Souto JG, Ejima GW. Long QT syndrome in-duced by elevated dose of Fluoxetine Cloridrate: case report. Brazilian Journal of Case Reports. 2024;4(3):66-70. doi:10.52600/2763-583X.bjcr.2024.4.3.66-70
20. Gutlapalli SD, Prakash K, Swarnakari KM, Bai M, Manoharan MP, Raja R, Jamil A, Csendes D, Desai A, Desai DM, Alfonso M. The risk of fatal arrhythmias associated with sertraline in patients with post-myocardial infarction depression. Cureus. 2022;14(9):e28946. doi:10.7759/cureus.28946
21. Abbas R, Riley S, LaBadie RR, Bachinsky M, Chappell PB, Crownover PH, Damle B. A thorough QT study to evaluate the effects of a supratherapeutic dose of sertraline on cardiac repolarization in healthy subjects. Clin Pharmacol Drug Dev. 2020;9(3):307-20. doi:10.1002/CPDD.749
22. Krishnan KR, Doraiswamy PM, Clary CM. Clinical and treatment response characteristics of late-life associated with vascular disease: a pooled analysis of two multicenter trials with sertraline. Prog Neuropsychopharmacol Biol Psychiatry. 2001;25(2):347-61. doi:10.1016/S0278-5846(00)00168-8
23. Wayne A, Chung CP, Murray KT, Hall K, Stein CM. High-dose citalopram and escitalopram and the risk of out-of-hospital death. J Clin Psychiatry. 2017;78(2):190-195. doi: 10.4088/JCP.15m10324
24. Wilkowska A, Bohdan M, Jerzy Cubała W. Commentary concerning treatment of depression in patients with heart failure according to 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur J Prev Cardiol. 2022;29(16):2140-1. doi:10.1093/eurjpc/zwac077
25. Frizzo ME. Can a selective serotonin reuptake inhibitor act as a glutamatergic modulator?. Curr Ther Res. 2017;87:9-12. doi:10.1016/j.curtheres.2017.07.001
26. Anagha K, Shihabudheen P, Uvais NA. Side effect profiles of selective serotonin reuptake inhibitors: a cross-sectional study in a naturalistic setting. The Prim Care Companion CNS Disord. 2021;23(4):20m02747. doi:10.4088/PCC.20m02747
27. Brambilla P, Cipriani A, Hotopf M, Barbui C. Side-effect profile of fluoxetine in comparison with other SSRIs, tricyclic and newer antidepressants: a meta-analysis of clinical trial data. Pharmacopsychiatry. 2005;38(02):69-77. doi:10.1055/S-2005-837806
28. Dubrall D, Fekete S, Leitzen S, Paschke LM, Romanos M, Schmid M, Gerlach M, Sachs B. Selective serotonin reuptake inhibitors and suicidality in children and young adults: analyses of pharmacovigilance databases. BMC Pharmacol Toxicol. 2023;24(1):22. doi:10.1186/S40360-023-00664-Z
29. Doruk N, Nihat Dogrul B. Sertraline induced oromandibular dystonia and galactorrhea: a case report. Psychiatr Danub. 2021;33(2):191-2. doi:10.24869/psyd.2021.191
30. Gandotra K, Jaskiw G, Fuller M, Vaidya P, Chiang A, Konicki E, Strohl KP. Sertraline as an adjunctive treatment for insomnia comorbid with other mental health disorders. J Affect Disord Rep. 2022;10:100389. doi:10.1016/j.jadr.2022.100389
31. Stuckart I, Siepmann T, Hartmann C, Pallesen LP, Sedghi A, Barlinn J, Reichmann H, Puetz V, Barlinn K. Sertraline for functional recovery after acute ischemic stroke: a prospective observational study. Front neurol. 2021;12:734170. doi:10.3389/fneur.2021.734170
32. Serretti A, Chiesa A. Treatment-emergent sexual dysfunction related to antidepressants: a meta-analysis. J Clin Psychopharmacol. 2009;29(3):259-66. doi:10.1097/JCP.0b013e3181a5233f
33. Yi ZM, Chen SD, Tang QY, Tang HL, Zhai SD. Efficacy and safety of sertraline for the treatment of premature ejaculation: systematic review and meta-analysis. Medicine. 2019;98(23):e15989. doi:10.1097/MD.0000000000015989

34. Atmaca M. Selective serotonin reuptake inhibitor-induced sexual dysfunction: current management perspectives. Neuropsychiatr Dis Treat. 2020:1043-50. doi:10.2147/NDT.S185757
35. Santos RA, Sousa AP, Almeida-Santos T, Ramalho-Santos J, Tavares RS. In vitro effects of antidepressants on human sperm function. Asian J Androl. 2025;27(1):30-6. doi:10.4103/aja202459
36. Rothmore J. Antidepressant-induced sexual dysfunction. Med J Aust. 2020;212(7):329-334. doi: 10.5694/mja2.50522
37. Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. Clin Pharmacol Ther. 2023;114(1):51-68. doi:10.1002/cpt.2903
38. Stahl SM, Grady, MM, Muntner, N. Stahl's Essential Psychopharmacology: Neuroscien-Tific Basis and Practical Applications. 5th Ed. United Kingdom: Cambridge University Press; 2021.
39. Brunton LL, Knollmann BC, Hilal-Dandan R, editors. Good-Man & Gilman's the Pharmacological Basis of Therapeutics. New York: McGraw-Hill Education; 2018. doi:10.25259/SNI_184_2023
40. El Orche A, Cheikh A, El Khabbaz C, Bouchafra H, Faouzi ME, Cherrah Y, Ansari SA, Alkahtani HM, Ansari SA, Bouatia M. Advancing bioanalytical method validation: a comprehensive ICH M10 approach for validating LC–MS/MS to quantify fluoxetine in human plasma and its application in pharmacokinetic studies. Molecules. 2024;29(19):4588. doi:10.3390/molecules29194588
41. Nair AB, Singh B, Shah J, Jacob S, Aldhubiab B, Sreeharsha N, Morsy MA, Venugopala KN, Attimarad M, Shinu P. Formulation and evaluation of self-nanoemulsifying drug delivery system derived tablet containing sertraline. Pharmaceutics. 2022;14(2):336. doi:10.3390/pharmaceutics14020336
42. Alhadab AA, Brundage RC. Population pharmacokinetics of sertraline in healthy subjects: a model-based meta-analysis. The AAPS J. 2020;22(4):73. doi:10.1208/s12248-020-00455-y
43. Al-Tamimi D, Al-Kinani K, Taher S, Hussein A. Effect of Food on the Pharmacokinetics of Fluoxetine in Healthy Male Adult Volunteers. Iraqi J Pharm Sci. 2022;31(Suppl.):153-61. doi:10.31351/vol31issSuppl.pp153-161
44. Grimsley SR, Jann MW. Paroxetine, sertraline, and fluvoxamine: new selective serotonin reuptake inhibitors. Clin Pharm. 1992;11(11):930-57.
45. Aronoff GR, Bergstrom RF, Pottratz ST, Sloan RS, Wolen RL, Lemberger L. Fluoxetine kinetics and protein binding in normal and impaired renal function. Clin Pharmacol Ther. 1984;36(1):138-44. doi:10.1038/clpt.1984.152
46. Castillo CE, Garibay SE, Segovia RD, Guzmán SZ, Cook HJ, Contreras MO, Moreno SR. Population pharmacokinetics of sertraline in psychiatric and substance use disorders. The J Clin Pharmacol. 2024;64(10):1267-77. doi:10.1002/jcph.2457
47. Zakaraya Z, Abu Assab M, Tamimi LN, Karameh N, Hailat M, Al-Omari L, Abu Dayyih W, Alasasfeh O, Awad M, Awad R. Pharmacokinetics and pharmacodynamics: a comprehen-sive analysis of the absorption, distribution, metabolism, and excretion of psychiatric drugs. Pharmaceuticals. 2024;17(3):280. doi:10.3390/ph17030280
48. Jeong HC, Chae YJ, Lee S, Kang W, Yun HY, Shin KH. Prediction of fluoxetine and norfluoxetine pharmacokinetic profiles using physiologically based pharmacokinetic modeling. The J Clin Pharmacol. 2021;61(11):1505-13. doi:10.1002/jcph.1927
49. Obach RS, Cox LM, Tremaine LM. Sertraline is metabolized by multiple cytochrome P450 enzymes, monoamine oxidases, and glucuronyl transferases in human: an in vitro study. Drug Metab Dispos. 2005;33(2):262-70. doi:10.1124/dmd.104.002428
50. Brouwer JM, Nijenhuis M, Soree B, Guchelaar HJ, Swen JJ, van Schaik RH, et al. Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction be-tween CYP2C19 and CYP2D6 and SSRIs. Eur J Hum Genet. 2022;30(10):1114-20. doi:10.1038/s41431-021-01004-7
51. Lemberger L, Bergstrom RF, Wolen RL, Farid NA, Enas GG, Aronoff GR. Fluoxetine: clinical pharmacology and physiologic disposition. The J Clin Psychiatry. 1985;46(3 Pt 2):14-9.
52. De Vane CL, Liston HL, Markowitz JS. Clinical pharmacokinetics of sertraline. Clin Pharmacokinet. 2002;41(15):1247-66. doi:10.2165/00003088-200241150-00002
53. Altamura AC, Moro AR, Percudani M. Clinical pharmacokinetics of fluoxetine. Clinical pharmacokinetics. 1994;26(3):201-14. doi:10.2165/00003088-199426030-00004
54. Ronfeld RA, Tremaine LM, Wilner KD. Pharmacokinetics of sertraline and its N-demethyl metabolite in elderly and young male and female volunteers. Clin Pharmacokinet. 1997;32(Suppl 1):22-30. doi:10.2165/00003088-199700321-00004
55. MacQueen G, Born L, Steiner M. The selective serotonin reuptake inhibitor sertraline: its profile and use in psychiatric disorders. CNS Drug Rev. 2001;7(1):1-24. doi:10.1111/j.1527-3458.2001.tb00188
56. Andrade C. Psychotropic Drugs With Long Half-Lives: Implications for Drug Discontinuation, Occasional Missed Doses, Dosing Interval, and Pregnancy Planning. The J Clin Psychiatry. 2022;83(4):22f14593. doi:10.4088/jcp.22f14593
57. Gury C, Cousin F. Pharmacokinetics of SSRI antidepressants: half-life and clinical applicability. L'encephale. 1999;25(5):470-6.
58. Moraes MO, Lerner FE, Corso G, Bezerra FF, Moraes ME, De Nucci G. Fluoxetine bioequivalence study: quantification of fluoxetine and norfluoxetine by liquid chromatography coupled to mass spectrometry. The J Clin Pharmacol. 1999;39(10):1053-61. doi:10.1177/00912709922011827
59. Hiemke C, Härtter S. Pharmacokinetics of selective serotonin reuptake inhibitors. Pharmacol Ther. 2000;85(1):11-28. doi:10.1016/S0163-7258(99)00048-0
60. Wong SH, Dellafera SS, Fernandes R, Kranzler H. Determination of fluoxetine and norfluoxetine by high-performance liquid chromatography. J Chromatogr A. 1990;499:601-8. doi:10.1016/S0021-9673(00)97004-3
61. Sommi RW, Crismon ML, Bowden CL. Fluoxetine: a serotonin-specific, second-generation antidepressant. Pharmacotherapy. 1987;7(1):1-4. doi:10.1002/j.1875-9114.1987.tb03496
62. Warrington SJ. Clinical implications of the pharmacology of sertraline. Int Clin Psychopharmacol. 1991;6:11-22. doi:10.1097/00004850-199112002-00004
63. Wilens TE, Cohen L, Biederman J, Abrams A, Neft D, Faird N, Sinha V. Fluoxetine pharmacokinetics in pediatric patients. J Clin Pharmacol. 2002;22(6):568-75. doi:10.1097/00004714-200212000-00006
64. [64] Luo X, Zhu D, Li J, Ren M, Liu Y, Si T, Chen Y. Selection of the optimal dose of sertraline for depression: A dose-response meta-analysis of randomized controlled trials. Psychiatry Res. 2023;327:115391. doi:10.1016/j.psychres.2023.115391
65. Mohebbi N, Motamed M, Panahishokouh M. The Efficacy and Safety of Fluoxetine Delayed-Release 90 mg/Weekly in Psychiatry: An Evidence-Based Mini-Review. Iran J Psychiatry Behav Sci. 2024;18(18). doi:10.5812/ijpbs-146023s
66. Zhang Z, Guo Z, Tan Y, Li L, Wang Z, Wen Y, Huang S, Shang D. Population pharmacokinetic approach to guide per-sonalized sertraline treatment in Chinese patients. Heliyon. 2024;10(3):e25231. doi:10.1016/j.heliyon.2024.e25231
67. Wagstaff AJ, Goa KL. Once-weekly fluoxetine. Drugs. 2001;61(15):2221-8. doi:10.2165/00003495-200161150-00006
68. Ramsteijn AS, Jašarević E, Houwing DJ, Bale TL, Olivier JD. Antidepressant treatment with fluoxetine during pregnancy and lactation modulates the gut microbiome and metabolome in a rat model relevant to depression. Gut Microbes. 2020;11(4):735-53. doi:10.1080/19490976.2019.1705728
69. Muijsers RB, Plosker GL, Noble S. Sertraline: a review of its use in the management of major depressive disorder in elderly

patients. Drugs Aging. 2002;19(5):377-92. doi:10.2165/00002512-200219050-00006
70. Stika CS, Wisner KL, George Jr AL, Avram MJ, Zumpf K, Rasmussen-Torvik LJ, et al. Changes in sertraline plasma concentrations across pregnancy and postpartum. Clin Pharmacol Ther. 2022;112(6):1280-90. doi:10.1002/CPT.2746
71. Feighner JP, Boyer WF, Tyler DL, Neborsky RJ. Adverse consequences of fluoxetine-MAOI combination therapy. The J Clin Psychiatry. 1990;51(6):222-5.
72. Keks N, Hope J, Keogh S. Switching and stopping antidepressants. Aust Prescr. 2016;39(3):76. doi: 10.18773/austprescr.2016.039
73. Bahar MA, Kamp J, Borgsteede SD, Hak E, Wilffert B. The impact of CYP2D6 mediated drug–drug interaction: a systematic review on a combination of metoprolol and paroxetine/fluoxetine. Br J Clin Pharmacol. 2018;84(12):2704-15. doi:10.1111/BCP.13741
74. Saiz-Rodríguez M, Belmonte C, Román M, Ochoa D, Koller D, Talegón M, et al. Effect of polymorphisms on the pharmacokinetics, pharmacodynamics and safety of sertraline in healthy volunteers. Basic Clin Pharmacol Toxicol. 2018;122(5):501-11. doi:10.1111/BCPT.12938
75. Oliva V, Lippi M, Paci R, Del Fabro L, Delvecchio G, Brambilla P, et al. Gastrointestinal side effects associated with antidepressant treatments in pa-tients with major depressive disorder: a systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2021;109:110266. doi:10.1016/j.pnpbp.2021.110266
76. Funk KA, Bostwick JR. A comparison of the risk of QT prolongation among SSRIs. Ann Pharmacother. 2013;47(10):1330-41. doi:10.1177/1060028013501994
77. Preskorn SH, Alderman J, Chung M, Harrison W, Messig M, Harris S. Pharmacokinetics of desipramine coadministered with sertraline or fluoxetine. J Clin Psychopharmacol. 1994;14(2):90-8.
78. Desaunay P, Eude LG, Dreyfus M, Alexandre C, Fedrizzi S, Alexandre J, et al. Benefits and Risks of Anti-depressant Drugs During Pregnancy: A Systematic Review of Meta-analyses. Pediatr Drugs. 2023;25(3):247-65. doi:10.1007/S40272-023-00561-2